Winfried V. Kern
ECCMID Programme Director
says Goodbye

ECCMID 2014
Deputy Programme Director

ECCMID 2015 – 2020
Programme Director
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**Disclaimer:** The abstracts are presented here as they were submitted for inclusion in the proceedings of the 30th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID). Outside of page layout and formatting, only the abstract titles have been proofed and edited by ESCMID. All other content entirely represents the work of the submitting author[s], and does not reflect the views of ESCMID, its staff, or its executive. ESCMID does not take responsibility for misspellings or misrepresentation of registered names, copyrights or trademarks.
Introduction

Welcome Address

Dear colleagues and friends,

It is our pleasure to present in this volume the scientific abstracts which were selected to appear at the 30th European Congress on Clinical Microbiology and Infectious Diseases (ECCMID).

While the on-site congress in Paris did not occur in April of 2020 as a consequence of COVID-19 pandemic, we would like to acknowledge the hard work that went into the planning of ECCMID, and the messages of support that have been received since the announcement of the on-site cancellation.

It was again another record-breaking year for the submission of ECCMID abstracts, with 6,980 pieces of scientific work being submitted in late 2019 for inclusion, as well as 181 abstracts that were received in February 2020 as latebreaker submissions. A big thank you to all submitters for being part of this record-breaking year!

The scientific abstracts are subject to a stringent review process, with each submission being viewed and rated by at least three ECCMID abstract reviewers. These reviewers represent the pre-eminent experts in various specialties from the fields of Clinical Microbiology and Infectious Diseases. As with every year, we thank them all for their outstanding and essential work in the abstract rating process.

Once the ratings were finalised, the ECCMID Programme Committee decided on the accepted abstracts by specific topic, and allocated them into abstract sessions, as presented herein.

The ECCMID Abstract Programme represents the latest studies and findings from the last year of Clinical Microbiology and Infectious Diseases, and we congratulate all of the authors who had their work included. We hope that the works included herein spark conversations and collaborations between scientists across disciplines and across the world.

We are also looking forward to receiving abstract submissions later this year for inclusion in the ECCMID 2021 abstract programme.

We hope that you enjoy reading the ECCMID 2020 abstracts, and we are looking forward to seeing you in person in Vienna for ECCMID 2021!
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Acknowledgements

The ECCMID Programme Committee is proud to acknowledge the scientific input from the following organizations in setting up the scientific programme and/or organizing joint workshops and symposia:

ASM – American Society for Microbiology
EACS – European AIDS Clinical Society
EANM – European Association of Nuclear Medicine
ECDC – European Centre for Disease Prevention and Control
EF-CLIF – European Foundation For the Study of Chronic Liver Failure
EITaF – ESCMID Emerging Infections Task Force
ERS – European Respiratory Society
ESDPPP – European Society for Developmental, Paediatric and Perinatal Pharmacology
ESPID – European Society for Paediatric Infectious Diseases
EU Commission’s Directorate-General for Research and Innovation
EUCAST – European Committee on Antimicrobial Susceptibility Testing
EUCIC – European Committee on Infection Control
EU-JAV – European Joint Action on Vaccination
FEMS – Federation of European Microbiological Societies
GARDP – Global Antibiotic Research and Development Partnership
ISF – International Sepsis Forum
ISIRV – International Society for Influenza and other Respiratory Virus Diseases
MSF – Médecins Sans Frontières
WHO – World Health Organization
Future Congresses

31st ECCMID
VIENNA, AUSTRIA
10 – 13 April 2021
Reed Messe Vienna

32nd ECCMID
LISBON, PORTUGAL
23 – 26 April 2022
Altice Arena Lisbon / FIL Lisbon
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Visit ECDC and find out about the organization!

A group of 15 observers (ESCMID members) will participate in a five-day programme at the European Centre for Disease Prevention and Control (ECDC) in Solna, Sweden.

The application period for this five-day visit will be announced via the ESCMID website as well as the ESCMID social media channels.

www.escmid.org/ECDC.Observer
www.ecdc.europa.eu
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Abstract Programme

1. Viral infection & disease

- HIV/AIDS (incl diagnostics & epidemiology, anti-retroviral drugs, treatment & susceptibility/resistance)

- Viral hepatitis (incl diagnostics & epidemiology, antiviral drugs, treatment & susceptibility/resistance)

- Influenza and respiratory viruses (incl diagnostics & epidemiology, antiviral drugs, treatment, excl vaccination)

- Herpesviruses (incl diagnostics & epidemiology, antiviral drugs, treatment & susceptibility/resistance, excl clinical studies in immunocompromised hosts)

- Emerging/re-emerging, vector-borne and zoonotic viral diseases (all aspects)

- Diagnostic virology (other than respiratory viruses, herpesviruses, hepatitis & HIV)

- Viral epidemiology – general, prevalence studies, molecular and genomic epidemiology (other than respiratory viruses, herpesviruses, hepatitis & HIV)

- Antiviral drugs, treatment, susceptibility/resistance (other than respiratory viruses, herpesviruses, hepatitis & HIV)

- Other
Abstract Categories 2020

Session accepted as Paper Poster Session

Clinical aspects of non-flu respiratory viruses

2414 Comparison of the clinical features of human metapneumovirus infections in children between paediatric patients with severe mental and physical disabilities and those without undergoing diseases at a children's hospital in Japan.

A. Shimizu* (Gunma, Japan)

2664 Baloxavir drug exposure after single-dose baloxavir marboxil is similar between children aged 1 to <12 years and adults: analysis of the miniSTONE-2 trial.

J. Baker, S. De Buck* (Brussels, Belgium), V. Duval, L. Macutkiewicz, S. Dimonaco, S. Wildum, N. Collinson, B. Clinch, B. Matharu

2775 Measles outbreak in Catania: a retrospective study and clinical revision.

A. Pampaloni* (Catania, Italy), L. Todaro, F. Cosentino, M. Locatelli, A. Marino, V. Moscati, D. Scuderi, V. Boscia, M. Gussio, G. Lupo, A. Donorante, A. Zagami, B. Celesia, B. Capocarro

8495 Human metapneumovirus infections among patients with haematological malignancies including haematopoietic stem cell transplant: analysis of a 6-year period.

L. Labate, E. Balletto, L. Magnasco* (Genoa, Italy), A. Raiola, F. Guolo, E. Angelucci, L. Roberto Massimo, C. Viscoli, M. Bassetti, M. Mikulska

Session accepted as Mini-oral ePoster Session

Constant threat of emerging infections

359 Resolving within-host, full length, dengue virus variants without haplotype reconstruction using Oxford Nanopore Technology.


3640 Antimicrobial stewardship intervention in FLU/ respiratory syncytial virus adult hospitalisations: major impact on antimicrobial management of a systematic epidemiological surveillance process including training and feed-back.

M. Bourgeois, N. Ausselet, E. Dupont, L. De Cannière, N. Scius, I. Michaux, T. Huang, P. Bogaerts, O. Denis* (Brussels, Belgium), B. Bihin, B. Delaere

5042 Respiratory syncytial virus and influenza virus infection in adult primary care patients: association of age with prevalence, diagnostic features and illness course.

R. Bruyndonckx, S. Coenen, C. Butler, T. Verheij, P. Little, N. Hens, P. Beutels, M. Ieven* (Edegem, Belgium), H. Goossens

5571 The variability of the lymphocyte populations in the cerebrospinal fluid of patients with tick-borne encephalitis.

S. Grygorczyk* (Bialystok, Poland), J. Osada, A. Moniuszko, J. Dunaj, S. Panczewicz

5715 Efficacy of ribavirin in post-exposure prophylaxis in Crimean-Congo haemorrhagic fever.


7219 Positive respiratory viral panel results moderately shorten antibiotic duration in patients with presumed respiratory tract infections.

J. Van Bulow* (Wall, United States), L. Rodriguez, S. Lee, K. Oto Sullivan, J. Gallagher

7730 In-hospital and midterm out-hospital complications of hospitalised respiratory syncytial virus-positive adults in France.

A. Descamps* (Paris, France), P. Loubet, N. Lenzi, F. Goitier, L. Fabrice, Z. Lesieur, P. Vonhems, X. Duval, F. Carrat, D. Launay

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Meningitis due to Toscana virus: analysis of clinical and laboratory features of the cases observed in the period 2008-2018 at the Careggi University Hospital, Florence, Italy
M. Spinicci* [Firenze, Italy], P. Sponga, G. Corti, M. Pozzi, B. Sponga, L. Zammarchi, A. Bartoloni

Dealing with the current dengue viral fever outbreak: an experience from a tertiary care hospital in Karachi
S. Sarfaraz* [Karachi, Pakistan], F. Herekar, S. Iftikhar

Dengue virus infects HBMEC cell model and regulates proteins related to the blood-brain barrier function
J. Yu* [Guangzhou, China], X. He, X. Liu, W. Zhao

Dengue awareness in patients with acute febrile illness in Sindh province of Pakistan
J. Farooqi* [Karachi, Pakistan], M. Long, K. Barr, K. Imtiaz, E. Khan

Post-viral fatigue in dengue infection
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Vimentin may inhibit dengue virus invasion of HBMEC cells
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The first report of concurrent infections by two dengue serotypes among tribal population in central India
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Molecular differentiation of dengue serotypes in the public health system in Santo André, Brazil
K. Gois* [Santo André, Brazil], S. Dos Chagas Mendes, B. Alves, F. Luis Affonso Fonseca, F. Gehrke

Safety of temporary interruption of anti-platelets in dengue fever with thrombocytopenia
P. Chia* [Singapore, Singapore], L. Htet, Y. Leo, D. Lye

Diagnosis of acute dengue infection in Navarra
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Detection of dengue virus antibodies in febrile patients suspected of malaria attending a health centre in Jos, Nigeria
N. Miri* [Jos, Nigeria], J. Mawak, N. Chuwang, T. Ezekiel, S. Acheng, C. Chukwu

Evaluation of the impact of dengue infection in gestation and conception: an ecological study using time series analysis
O. Lupi* [Rio de Janeiro, Brazil], F. Meque, D. Villela, P. Brasil

High-resolution mapping reveals emergence and autochthonous transmission of dengue fever outbreak in a previously low-epidemic region in south-east China, 2019
Y. Zhang* [Shanghai, China], J. Ai, W. Zhang

Evaluation of the diagnostic accuracy of a rapid dengue NS1 antigen lateral flow immunochromatography test in UK returned travellers
B. Patterson, K. Macgregor* [Porton, United Kingdom], S. Wilmore, T. Brooks, R. Davidson, A. Mcgregor

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Dealing with the current dengue viral fever outbreak: an experience from a tertiary care hospital in Karachi
S. Sarfaraz* [Karachi, Pakistan], F. Herekar, S. Iftikhar

Dengue virus infects HBMEC cell model and regulates proteins related to the blood-brain barrier function
J. Yu* [Guangzhou, China], X. He, X. Liu, W. Zhao

Dengue awareness in patients with acute febrile illness in Sindh province of Pakistan
J. Farooqi* [Karachi, Pakistan], M. Long, K. Barr, K. Imtiaz, E. Khan
8960 Multiplex respiratory pathogen PCR and parental work absenteeism
S. Mattila, N. Paalanne* [Oulu, Finland], M. Honkila, T. Pokka, T. Tapiainen

9511 Adenovirus types associated with severe respiratory diseases in intensive care unit-admitted patients during the 2017-2019 period
A. Piralla* [Pavia, Italy], F. Novazzi, F. Giardina, A. Fratini, G. Salve, S. Pregnolato, F. Baldanti, F. Mojoli

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1143 Phylogenetic analysis of complete genomes reveals the circulation of multiple lineages of rabies lyssavirus in India
H. Pulleri Kandi Anuraj* [Bengaluru, India], C. Pattabiraman, G. Yale, A. Mahadevan, R. Mani

1817 Epidemiological investigation of newly detected highly lethal Borna disease virus 1 cases reinforcing indirect shrew contact as possible source of infection: results from in-depth interviews, Germany, 2019
P. Kirsten* [Berlin, Germany], C. Frank, H. Wilking, D. Rubenstruth, M. Böhmer

2155 Viral and immunologic factors associated with fatal outcome of patients with severe fever with thrombocytopenia syndrome in Korea
J. Kwon* [Seoul, South Korea], J. Kim, S. Ra, T. Kim, S. Park, M. Kim, S. Park, D. Kim, H. Cha, H. Lee, N. Jeon, M. Kim, Y. Chang, S. Lee, S. Choi, Y. Kim, J. Woo, K. Lee, S. Kim, S. Kee

2525 Disease course, management and predictors of fatality in hospitalised patients with real-time PCR confirmed Lassa fever in Nigeria: a prospective cohort study

2675 Predictors of worse outcome in patients with West Nile virus infection: a multi-centre study

2747 Rift Valley fever in pregnancy: a systematic review and meta-analysis of foetal outcomes
N. Kayem* [Oxford, United Kingdom], C. Benson, C. Aye, S. Baker, M. Tome, S. Kennedy, P. Ariana, P. Horby

5194 Neurodevelopment outcomes at 24 months of age in ZIKV-exposed and ZIKV-unexposed infants in French territories in the Americas: preliminary results from the ZIKA-DFA-BB cohort study
R. Grant* [Paris, France], O. Flechelles, B. Tressières, M. Dia, N. Elenga, N. Mediamolle, A. Mallard, J. Hebert, N. Lachoume, E. Couchy, B. Hoen, A. Fontanet

6399 Post-exposure prophylaxis for high risk contacts of Ebola virus using immunotherapies with monoclonal antibodies in the eastern DRC: a compassionate use program

6929 Toscana virus: clinical and biological studies based on 864 cases
N. Ayhan* [Marseille, France], R. Charrel

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A. Fall* [Dakar, Senegal], N. Ndiaye, N. Ndiaye, O. Kebe, M. Jollow, D. Kiori, S. Sy, D. Goudiaby, M. Dia, M. Niang, N. Dia

1115 Incidence of hospitalisation for respiratory syncytial virus in children aged 0-5 years in Ontario, Canada

1437 Multi-centre study of common pathogen epidemiology in hospitalised children with acute respiratory tract infection in winter from 2017 to 2018, China
L. Meng* [Shanghai, China], H. Zhang, X. Shao, J. Zhou

1710 Replication of MERS and SARS Coronaviruses in bat cells offers insights to their ancestral origins
J. Fung* [Hong Kong, Hong Kong], S. Lau, H. Luk, U. Wernery, P. Woo

2333 Proposing the spike gene of Coronavirus OC43 as a target for nosocomial outbreak investigation in long-term care facilities
H. Mistry* [Toronto, Canada], L. Yip, K. Bozek, H. Mbareche, A. Linkenheld-Sturk, R. Kozak, V. Williams, D. Pajak, J. Leis, S. Mubareka

2451 Impact of Point-of-Care testing on the surveillance of respiratory viral infections in West Midlands, England
D. Ironmonger* [Birmingham, United Kingdom], A. Bains, T. Hong, D. Todkill, J. Hawker, D. Edgehere

3369 Morbidity burden of different viral and bacterial pathogens in acutely ill children
H. Päyry* [Oulu, Finland], M. Kiviöneni, A. Raapanna, N. Paalanen, T. Pokka, P. Valmari, T. Tapiainen
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3985 Assessing Pharyngeal Respiratory virus Carriage in healthcare workers Over Time (APRICOT): a feasibility study
A. Melhuish, J. Mintan* [Leeds, United Kingdom]

3986 Comparative virulence of respiratory viruses on the winter seasons from 2017 to 2019: a southern European multi-centre cohort study
A. Almeida* [Lisbon, Portugal], M. Boattini, E. Christaki, T. Marques, I. Moreira, L. Cruz, V. Tosatto, D. Antao, G. Bianco, M. Iannaccone, C. Costa, G. Tsilolakis, E. Khattab, D. Kasapi, R. Cavallo, R. Corte Real

4046 Burden of viral pneumonia among patients with lung infiltrates undergoing bronchoalveolar lavage: a retrospective one-year study
C. Mouret* [Trieste, Italy], E. Gibbin, L. Segat, R. Luzzatti

4278 Respiratory syncytial virus bronchiolitis and recurrent wheezing: a 1-year follow-up study
P. Venkat Ramanan* [Chennai, India], K. Subbiah

4691 Respiratory pathogens detected in children with community-acquired sepsis-like syndrome in 6 European countries
V. Matheussen* [Edegem, Belgium], K. Loens, K. Jacobs, P. Horby, H. Goossens, M. Kohns Vasconcelos, M. Sharland, M. De Jong, M. Koopmans, P. Fraaij, M. leven

5169 Building a predictive score for local risk of respiratory syncytial virus hospitalisation: Normative Outcome Hospitalisation Assessment for Newborns (NOHAN)
C. Jean-Sebastien* [Lyon, France], M. Jourdain, R. Kramer, S. Couray-Targe, A. Myard-Dury, D. Plain, Y. Gillet, E. Javouhey, B. Lina, M. Benchaiba

5391 Comprehensive analysis of evolutionary dynamics of circulating strains and immunopathogenesis of respiratory syncytial virus-associated acute lower respiratory tract infections in children
S. Sarkar* [Chandigarh, India], R. Ratho, M. Singh, A. Singh, M. Singh

6025 Aetiology and outcome of children hospitalised for acute respiratory tract infections in Europe: findings from a multi-country combined case-control and cohort study
M. Kohns Vasconcelos* [London, United Kingdom]

6120 Comprehensive analysis of evolutionary dynamics of circulating strains and immunopathogenesis and co-infections of human metapneumovirus associated acute lower respiratory tract infections in children
R. Ratho* [Chandigarh, India], S. Sarkar, M. Singh, A. Singh, M. Singh

5649 Nanopore metagenomic sequencing to investigate nosocomial transmission of human metapneumovirus from a unique genetic group among haematology patients in the United Kingdom

6779 Clinical characteristics and outcomes of respiratory syncytial virus infection among hospitalised adult patients: risk factors of intensive care unit hospitalisation and 30-day mortality
C. Youngeun* [Seoul, South Korea], J. Kim, S. Kim, Y. Yoon, J. Sohn, M. Kim

6910 Viral respiratory tract infections in children: epidemiology and impact of the implementation of a multiplex PCR
A. Armine Khodja, B. Boufedi, B. Mespes, L. Landraud, M. Cotillon, R. Basmaci, F. Joannes* [Colombes, France]

7191 Epidemiology and outcomes of respiratory syncytial virus infection in haematopoietic cell transplant recipients: findings from a multinational respiratory viral infection consortium (RVIC)

7289 Comparison of humoral response against both haemagglutinin and neuraminidase after seasonal influenza vaccination
J. Mendez Legaza, I. Sanz, R. Ortiz De Lejarazu, L. Sanchez De Prada* [Valladolid, Spain]

7926 Nosocomial respiratory syncytial virus infections: a two-season European multi-centre cohort study
T. Moreira Marques* [Lisbon, Portugal], A. Almeida, M. Boattini, E. Christaki, R. Corte Real, M. Moreira, V. Tosatto, D. Antao, L. Cruz, G. Bianco, C. Costa, R. Cavallo, M. Iannaccone, G. Tsilolakis, D. Kasapi, E. Khattab

7932 Severe viral respiratory infections in paediatric intensive care unit: a 4-year experience in an Italian paediatric hospital

8010 A retrospective study of rhinoviruses molecular diversity in three Paris hospitals: differential behaviours of HRV groups?
G. Haddad, M. Bertein, N. Fidouh, D. Bouzid, X. Duval, V. Bunel, R. Borie, J. Lucet, D. Descamps, B. Visseaux* [Paris, France]

8295 A majority of adult hospitalised patients with community-acquired lower respiratory tract infections had viral infections
N. Sundell, L. Gustavsson, M. Lindh, L. Andersson, J. Westin* [Gothenburg, Sweden]

8919 Different expression of CD26 and CD66 receptors on PBMCs from MERS Coronavirus infected patients
A. Alheetheli* [Riyadh, Saudi Arabia], A. Albarraq, Z. Shakoor, A. Samiyl, M. Barry, M. Bakhrabah, M. Nassar, Z. Memish, A. Asiri
Abstract Categories 2020

9028 Medical software approach for French IL1 sentinel surveillance
L. Vaillant* [Paris, France], R. Pans, T. Lounay, D. Simon, C. Goupillon, C. Hervé, V. Roussel, C. Turbelin, T. Blanchon

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9595 Evolution of awareness and knowledge of congenital cytomegalovirus infection among healthcare providers in France between 2011 and 2018

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Herpesviruses: old foes, new problems

1063 Diagnostics value of Epstein-Barr virus DNA load in whole blood and plasma from paediatric transplant recipients
B. Kasztelewicz* [Warsaw, Poland], J. Teisseyre, K. Janiszewska, J. Jankowska, P. Kaliczński, K. Dzierzanowska-Fangrat

1919 Anti-apoptotic role of human cytomegalovirus miRNAs, miR UL-70-3p and UL-148D on hydrogen peroxide-induced apoptosis in HEK 293T cells
S. Gosipatela* [Lucknow, India], A. Pandeya, S. Saxena

2660 Metagenomics next-generation sequencing for the identification of undiagnosed DNA and RNA viruses in adult allogeneic haematopoietic cell transplant recipients with steroid refractory graft-versus-host disease

Clinical validation of an ELISPOT-based in vitro diagnostic assay to monitor cytomegalovirus-specific cellular immunity in immunocompromised transplant recipients

Neonatal screening for congenital cytomegalovirus infection: identification of a viral DNA diagnostic cut-off value in saliva samples

Herpes simplex virus resistance testing: an automated interpretation platform linking genotype to phenotype
E. Gallagher* [London, United Kingdom], D. Bibby, D. Williams, J. Mbisa
Central nervous system infections caused by herpes simplex virus and varicella zoster virus in France, 2014-2018: a nationwide retrospective study

D. Boutolleau* [Paris, France], S. Burrel

Novel mutations found in UL56 terminase subunit and UL54 DNA polymerase after human cytomegalovirus infection treatment with letermovir M. Santos Bravo* [Barcelona, Spain], S. Sanchez-Palomino, M. Mosquera Gutiérrez, C. Martin Gandul, M. Rodríguez Hernandez, N. Piault, V. Gonzalo, E. Cordera Matias, S. Alain, M. Marcos

Detection of high rates of HIV-seropositivity in urban university hospital emergency department L. May* [Sacramento, United States], T. Chechi, S. Voang, N. Tran

Squamous cell carcinoma of the anus screening in people living with HIV: HPV genotyping is as important as cytology in anal cancer early diagnosis M. Digaetana, C. Rogati, M. Menozzi* [Modena, Italy], A. Bonazza, F. Spatapofora, A. Farinetti, R. Gelmini, M. Pecorari, S. Tagliazucchi, L. Reggiani Bonetti, R. Iachetta, R. Villani, C. Mussini

Sexual behaviour and incidence of sexually-transmitted infections in high-risk men who have sex with men following pre-exposure prophylaxis commencement Sophocles-P4G demonstration study M. Psychogiou* [Athens, Greece], M. Papadopoulou, V. Sypsa, S. Roussos, S. Chanos, N. Dedes, G. Daikos, J. Schneider, A. Hatzakis

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1234 Factors associated with low uptake of HIV testing among middle aged 15-17 adolescent girls in Uganda
M. Rwetabi* [Kampala, Uganda], A. Lutaya

2532 Cascade of HIV care in three different settings in Mozambique
P. Magro, C. Cerini, A. Da Gioia, S. Tembe, F. Castelli* [Brescia, Italy], L. Tomasoni

3900 Would HIV infections and AIDS cases decrease in Japan? Time series analysis using Bayesian inference
K. Iwata* [Kobe, Japan], C. Miyakoshi

4216 Checkpoint Plus Freiburg: performance of an on-site integrated, low-threshold sexual transmitted diseases/HIV counselling and treatment service in Germany
M. Müller* [Freiburg, Germany], S. Usadel, S. Zimmermann, U. Hoffmeister, A. Fahrhöfer, W. Kern, S. Rieg

4813 Characteristics and trends of recently HIV infected individuals in Estonia in 2013-2017
E. Jõgeda* [Tartu, Estonia], R. Avi, P. Merit, P. Soolda, T. Põll, E. Kallas, H. Rajasaar, K. Rüütel, I. Lutsar, K. Huik

5305 Performance of the new random access molecular diagnostics analyser Alinity m
R. Ehret* [Berlin, Germany], J. Dhein, S. Breuer, M. Obermeier

5486 End-to-end Workflow for HIV-1 drug resistance genotyping of protease and reverse transcriptase in major group-M subtypes

5791 Implementation of a smartphone application intervention to increase linkage to and engagement with HIV care among people with tuberculosis and substance use in Irkutsk, Siberia

7381 Performance evaluation of a new screening and viral load monitoring HIV-1 assay on the NeuMoDx molecular system
A. Norwold, C. Couture* [Ann Arbor, United States], H. Lee, J. Bezenah, C. Nguyen, C. Butcher, M. Mastronardi, B. Wu, S. Brahmasandra

7721 Non-B subtypes are a major driver of clustered HIV-1 transmission in north Italy in recent years
L. Colagrossi* [Milan, Italy], M. Moioli, A. Nava, S. Carta, S. Chiappetta, V. Costabile, D. Motta, L. Chianura, R. Rossotti, D. Fanti, P. Carlo Federico, M. Puoti, C. Alteri

8037 Potential use of data from a national HIV testing surveillance system to improve community-based testing strategies, Ireland

8151 Prevalence of non-B HIV-1 subtypes in north Italy and analysis of transmission clusters based on sequence data analysis
G. Lorenzin* [Brescia, Italy], F. Gargiulo, A. Carusa, F. Caccuri, E. Focà, A. Celotti, M. Quires Roland, I. Izzo, F. Castelli, S. Corbellini, F. Gurnieri, G. Piccinelli, M. De Francesca

8667 Performances of a new random access system for human immunodeficiency virus RNA quantification
A. Maillard, C. Pronier* [Rennes, France], G. Lagathu, P. Comacile, C. Grañier, V. Thibault

8773 Implementation of a full-length HIV-1 NGS assay into clinical diagnostics

8804 Epidemiological profile, mortality and causes of death in the first year of newly HIV-diagnosed patients of a national referral centre in Costa Rica from January 2015 to December 2017
M. Brenes Madrigal* [San José, Costa Rica], M. Villalobos Zúñiga

8857 Evaluation of HIV-1 and hepatitis B and C viruses quantification by a new molecular system in comparison to established routine methods
L. Martinez Garcia* [Madrid, Spain], B. Romero, A. Sanchez Diaz, M. Rodriguez, R. Canton Moreno, J. Galán

Session accepted as 1-Hour Oral Session

HIV in 2020

4521 Evaluation of a dual therapy and a simplified, patient-centred monitoring strategy for the long-term management of HIV infection: a non-inferiority, randomised, controlled, open-label clinical trial (SIMPL’HIV)

5290 Risk of failure in dual vs. triple therapy in naive HIV patients: a meta-analysis
A. Russo* [Naples, Italy], M. Pisaturo, L. Onorato, S. Martini, S. Signoriello, P. Maggi, N. Coppola

6541 Unravelling HIV proviral latency by comparing HIV-1 and HIV-2 expression and reactivation with single round, double reporter constructs
A. Bruggemans* [Leuven, Belgium], G. Vansant, Z. Debyser

8004 Exposure to maternal antiretroviral therapy in utero frequently differs between twins
M. Louchet, H. Didelot, G. Peytavín, M. Le, A. Bourgeois-Moine, L. Carbillon, D. Luton, I. Matheron, L. Rigonnett, L. Mandelbrot* [Bagnolet, France]
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| 901 | The progress towards achieving the UNAIDS ambitious 95% viral suppression target among adults living with HIV in South-Western Nigeria  
S. Usman* (Abuja, Nigeria) |
| 1945 | Alterations in the gut microbiome of HIV-infected patients under antiretroviral therapy  
S. Ray* [Stockholm, Sweden], A. Narayanan, C. Giske,  
U. Neogi, A. Sönnerborg, P. Nowak |
| 2041 | Real-world experience of bictegravir/emtricitabine/tenofovir alafenamide in a diverse Dublin cohort  
M. Moriarty* (Dublin, Ireland), G. Melanophy, E. Devitt |
| 2492 | Effectiveness and safety of a dual therapy with boosted darunavir and dolutegravir in patients with an advanced HIV infection  
J. Pasquaau* [Granada, Spain], C. García-Valleccillos,  
S. Seguera, L. Muñoz-Medina, M. Galido, T. Brieva,  
J. Santos, G. Verdejo, S. Ferra Murcia, F. Téllez Pérez,  
J. Garcia, D. Rial, J. Iribarren Loyarte, C. Hidalgo Tenorio |
| 2879 | Rapid antiretroviral therapy initiation in the era before universal treatment, Croatia, 2005 to 2014  
N. Bogdanic* (Zagreb, Croatia), L. Bendig, L. Davorka,  
Š. Zekan, J. Begovac |
| 3095 | Darunavir/cobicistat monotherapy as simplification strategy for HIV patients: a retrospective Multi-centre Spanish Study [DRV-simply]  
A. Inciarte Portillo* [Barcelona, Spain], J. Bernardino,  
Á. Mena De Cea, R. Mican Rivera, D. Carlos, C. García-Valleccillos,  
P. Callau, M. Castro Iglesias, J. Pasquaau,  
E. Martinez, J. Blanco |
| 4175 | Lipid profile change in HIV naïve patients treated with therapy tenofovir alafenamide-based  
L. Alessio* [Caserta, Italy], S. Martini, P. Maggi,  
L. Onorato, S. Ferrara, V. Esposito, G. Di Filippo,  
A. Masiello, R. Santoro, V. Rizzo, C. Bellacosa, A. Iodice,  
N. Coppola |
| 4771 | HIV-1 transmitted drug resistance is slowly rising in Estonia in 2017  
A. Säblinskaja* [Tartu, Estonia], P. Merit, E. Jägeda,  
H. Rajasaar, P. Soodla, E. Kallas, T. Päät, K. Rüütel, I. Lutsar,  
K. Huik, R. Avi |
| 4815 | Analysis of the evolution of the rate and the associated factors of antiretroviral treatment switch due to intolerance symptom on children in France  
L. Cohen* [Paris 19, France], J. Warszawski,  
J. Le Chenadec, P. Frange, V. Avetand-Fenoel, J. Sibiude,  
C. Dolfus, M. Caseris, A. Faye |
| 5282 | Evaluation of integrase strand transfer inhibitors on weight gain and body mass index  
M. Badowski* [Chicago, United States], R. Goldberg,  
A. Kania, T. Chiampas, M. Patel, S. Michienzi |
| 6006 | Adherence to routine monitoring guidelines for people living with HIV is poorer in higher-volume outpatient settings: when more is not better!  
D. Ng* [Singapore, Singapore], I. Wee, E. Sng, S. Lee,  
Z. Ling, L. Wijaya, Y. Teh |
| 6241 | Application of logistic regression model in the identification of potential HIV-1 drug resistance-associated mutations  
T. Wang* [Taipei, Taiwan], J. Chang, P. Lin, C. Hung,  
S. Chang |
| 6531 | Improvements in HIV-1 transmitted drug resistance surveillance in Ireland  
M. Neary* [Dublin, Ireland], M. Brady, J. Moran,  
J. Connell, S. Coughlan, S. Doyle, D. Ennis, F. Cooney,  
N. Eichler, S. Keating, C. Hurley, E. Nugent, S. O’Dea,  
L. Preston, H. Tuite, F. Lyons, K. O’Donnell, D. Igoe,  
C. Degascun |
| 6552 | Bone density, microarchitecture and tissue quality after 1 year of treatment with dolutegravir-abacavir-lamivudine  
J. Soldado, E. Lerma-Chipirraz, I. Arrieta, A. Gonzalez-Mena, I. Domingo, H. Knobel, R. Güieri Fernandez*  
[Barcelona, Spain] |
| 6820 | A review of the resistance to integrase inhibitors in HIV-1 patients in a third level hospital: a four-year experience  
L. Haces Pinto, D. Ampuero, A. Candela* [Madrid, Spain],  
P. García Morales, M. Jadad Checa, R. Alonso, P. Muñoz |
| 6955 | Immunootherapy in patients with relapsed/refractory HIV-related lymphomas  
M. Popova, Y. Rogacheva* [Saint Petersburg, Russian Federation], I. Tsygankov, K. Lepik, A. Nekrasova,  
L. Stelmah, I. Maiseev, S. Bondarenko, N. Mikhaylova,  
V. Baykov, A. Afanasiev |
| 7520 | Cabotegravir and bictegravir placental transfers in ex vivo human cotyledon perfusion  
L. Pencolé* [Colombes, France], M. Le, F. Bouchet Crivat,  
D. Duro, G. Peytavin, L. Mandelbrot |

**Session accepted as Paper Poster Session**

**Influenza epidemiology and clinical aspects**

| 244 | Hospital-acquired influenza characteristics and its correlation with the population-based surveillance in a tertiary care centre in Istanbul  
H. Bilgin* [Istanbul, Turkey], E. Avci, G. Culha, N. Pazar,  
S. Guneytepe, I. Sagir, R. Can Sarmağlu, E. Baran, U. Sili,  
V. Kerten |
607 Flu isolation wards: does medical specialty matter? Comparison of three specialties on outcome and antibiotic usage in hospitalised influenza A infected patients in Vienna during the season 2018/19
M. Karolji* [Vienna, Austria], E. Pawelka, H. Kelani, G. Funk, B. Lindner, C. Porpaczy, S. Publig, T. Seitz, M. Traugott, A. Zaufal, C. Wenisch

2114 Incidence of medially-attended influenza and influenza-related hospitalisations by co-morbidities among a commercially insured population in the United States
A. Near, J. Tae, Y. Yound-Xu, L. Connolly, C. Reyes* [San Francisco, United States]

2610 The difference in mortality between adult patients with laboratory-confirmed influenza A and B, a single centre observational study
D. Mabayoje* [London, United Kingdom], T. Cutinamoguel, J. Haigh, M. Wilks, C. Welch, M. Melzer

3666 Estimating the burden of influenza on hospitals using severe acute respiratory infections in metropolitan France, 2012-2018
A. Bernadou* [Bordeaux, France], N. Fortin, B. Hubert

4416 Triaging influenza in patients attending fever clinical scoring system for a modified influenza case definition
W. Liguang* [Beijing, China], J. Zhao, Q. Zhou, X. Lu

4427 Prevalence and clinical outcomes associated with viral and atypical bacterial co-infections in a large global study of adults hospitalised with influenza [INSIGHT FLU003 Plus]
D. Dwyer* [Westmead, Australia], D. Wentworth, N. Gerry, M. Hoover, J. Neaton, R. Davey, M. Polizzotto, T. Clark, A. Poez, J. Paño Pardo, J. Lundgren, A. Babiker, S. Pett

4461 Hospital-based surveillance of influenza in Switzerland: a pilot study, season 2018/19
A. Iten, A. Thiabaud* [Geneva, Switzerland], N. Troillet, L. Senn, D. Flury, S. Kuster, C. Balmelli, C. Gardiol, A. Goncalves Cabecinhas, L. Kaiser, D. Keiser

4466 Epidemiology of influenza in Thailand: findings from near real-time laboratory-based influenza system, a network of 40 hospitals in Thailand, 2010-2019
T. Eamchotchawalit* [Bangkok, Thailand], P. Piyaraj, P. Narangdej, S. Charoensakulchai

4643 Laboratory-confirmed influenza infection and acute myocardial infarction
Y. Young-Xu, J. Smith* [White River Junction, United States], S. Mahmud, E. Russo, R. Van Aalst, E. Thommes, J. Lee, A. Chit

4651 Different age distribution of influenza B virus infection by lineage
Y. Kim, S. Han* [Seoul, South Korea], K. Lee

5894 Delayed diagnosis and increased length of stay in patients requiring hospitalisation with influenza who present without fever
B. Smith, M. Putland, B. Garbutt, D. Johnson, L. Irving, S. Tong* [Melbourne, Australia]

7769 Bacterial and fungal infections associated with influenza virus in hospitalised patients
F. Arnáiz De Las Revillas* [Santander, Spain], L. Gibert Hernandez, J. Garcia Polacios, P. Gonzalez Garcia, N. Puente Ruiz, M. Gozalo Margüello, C. Armiñanzas Castillo, M. Gutiérrez-Cuadra, M. Faninias

8102 Analysis of patients with severe complicated influenza in a hospital, 2015-2019
Y. Huang* [Taiichung, Taiwan]

8516 Multidisciplinary interventions to reduce nosocomial transmission of influenza
B. Warne* [Cambridge, United Kingdom], M. Reacher, M. Zambon, H. Jalal

8702 Aspergillosis complicating severe influenza in intensive care unit patients: a retrospective case-control study
C. Visek* [Chicago, United States], H. Nam, M. Ison

9125 Nosocomial influenza
E. Rothman* [Lund, Sweden], B. Bottiger, U. Karlsson

9288 Descriptive analysis of patients with influenza virus admitted to intensive care unit from 2010 to 2019
M. Valverdú, S. Carvalho Brugger* [Lleida, Spain], M. Miralbés, S. Iglesios, B. Balsera, J. Caballero

9399 Burden of influenza C in a paediatric population with severe respiratory disease
A. Wong, A. Presbitero, K. Pabbaraju, K. Fonseca, N. Zelyas, B. Berenger* [Calgary, Canada]
2403 Examining factors impacting influenza vaccination amongst healthcare workers in Asia and the Pacific
H. Seale* [Sydney, Australia], A. Thomson, R. Kaur

2748 Can adjuvanted influenza vaccine given as standard of care reduce the risk for influenza outbreaks in nursing homes: evidence from a cluster-randomized trial of 823 nursing homes
K. Mcconehgy* [Providence, United States], H. Davidson, L. Han, E. Saade, D. Canaday, V. Mor, S. Gravenstein

2751 EUCIC survey on influenza vaccination among infection control team: Action speaks louder than words
Ş. Keske, N. Mutters* [Heidelberg, Germany], C. Tsiooutis, Ö. Ergönül

3493 A quality improvement project to increase influenza vaccination uptake amongst inpatients in a tertiary care centre supported by Electronic Healthcare Records [EHR]

4092 Influenza vaccine in chronic obstructive pulmonary disease

4498 Effectiveness of influenza vaccine in preventing medically attended influenza virus infection among healthcare personnel: a test-negative case-control study in Bangkok, Thailand, 2018/19 season
T. Eamchatwalo† [Bangkok, Thailand], P. Piyaraj, P. Narongdej, S. Charoensakulchai

4832 A multi-centre analysis of the value of systematic screening of influenza virus and vaccination on emergent admissions to a cardiac intensive care unit

6039 Coverage of influenza vaccination in patients over 64 years hospitalised for severe acute respiratory infection according to their chronic diseases
L. Miriam* [Zaragoza, Spain], A. Larrauri, A. Gherasim, C. Mazagatos, N. Martínez Cameo, M. Hernández, Y. Gracia, V. Guerrero, A. Rezusta, A. Milagro Beamonte

6157 Chronic pluripathological patients in over 64 years old with flu or serious acute respiratory infection, according to flu vaccination status
L. Miriam* [Zaragoza, Spain], A. Larrauri, A. Gherasim, C. Mazagatos, N. Martínez Cameo, M. Hernández, Y. Gracia, V. Guerrero, A. Martínez-Sapiña, A. Rezusta, A. Milagro Beamonte

6193 Severity of chronic diseases in patients over 64 years old with flu or serious acute respiratory infection, according to flu vaccination status
L. Miriam* [Zaragoza, Spain], A. Larrauri, A. Gherasim, C. Mazagatos, N. Martínez Cameo, M. Hernández, Y. Gracia, V. Guerrero, A. Martínez-Sapiña, A. Rezusta, A. Milagro Beamonte

6492 Study of the humoral response against adjuvanted and non-adjuvanted influenza vaccine in the elderly by age groups
L. Sanchez De Prada* [Valladolid, Spain], I. Sanz, S. Tamames, A. Lopez, J. Méndez-Legaza, S. Rojo, R. Ortiz De Lejarazu, J. Eiros

6586 Study of the serological efficacy of influenza vaccine along 28 consecutive seasons
L. Sanchez De Prada* [Valladolid, Spain], I. Sanz, S. Tamames, A. Lopez, J. Méndez-Legaza, S. Rojo, R. Ortiz De Lejarazu, J. Eiros

7072 Public health impact of the introduction of a high dose quadrivalent inactivated influenza vaccine in France
M. Costa, F. Bianic, N. Larseran, F. Alvarez, M. Levant, M. Uhart* [Lyon, France]

7189 Neuraminidase antibody response in a population vaccinated with split and adjuvant influenza vaccines
J. Mendez Legaza, I. Sanz, R. Ortiz De Lejarazu, L. Sanchez De Prada* [Valladolid, Spain]

8352 Immunodominance Hierarchy after seasonal Influenza vaccination
L. Sanchez De Prada* [Valladolid, Spain], I. Sanz, R. Ortiz De Lejarazu, J. Eiros, A. Garcia-Sastre, T. Aydillo

J. Kubes, J. Jacob* [Atlanta, United States]

**Session accepted as Paper Poster Session**

**Influenza: diagnostics**

603 Nasopharyngeal viral load determinants among influenza-infected patients receiving primary care in France: 2010-2018
R. Gueneau* [La Tranche, France], S. Behilili, E. Vincent, M. Yoann, S. Van Der Werf

666 Cost-benefit analysis of rapid influenza testing in German emergency rooms
R. Diel, A. Nienhaus, J. Becker* [Kornwestheim, Germany]
Impact of a routine molecular Point-of-Care test-and-treat strategy for influenza in adults hospitalised with acute respiratory illness: a pragmatic, multi-centre, randomised controlled trial (FluPOC) T. Clark* [Southampton, United Kingdom], K. Beard, N. Brendish, A. Malachira, S. Mills, C. Chan, S. Poole, S. Ewings, N. Cortes

Evaluation of the FebriDx host response Point-of-Care test to differentiate viral from bacterial aetiology in adults hospitalised with acute respiratory illness during influenza season K. Beard* [Southampton, United Kingdom], N. Brendish, S. Poole, C. Chan, S. Mills, T. Clark

Performance of two rapid influenza diagnostic testing compared to real-time PCR Y. Oh* [Yongin, South Korea], S. Jin, S. Yoon, S. Park, H. Bae

Can a combination of several biological markers help to diagnose influenza co-infections? N. Delettre* [Rouen, France], A. Schrapp, A. Baron, L. Joly, V. Brunel

Serum IFI27 mRNA as a novel host response biomarker of monitoring the influenza A virus infection W. Dong* [Shanghai, China], D. Yu, D. Zhang, G. Shi, X. Zhang

Performance evaluation of the STANDARD F Influenza A/B FIA for detection of influenza A/B virus infection K. Choi* [Daejeon, South Korea], H. Kim, M. Koo, J. Kim, S. Koo


Assessment of the performances of the second generation of the ID NOW influenza A&B and comparison with the GeneXpert E. Farfour* [Suresnes, France], A. Roux, M. Ballester, M. Vasse

Influenza and respiratory syncytial virus antigen diagnostic tests: do they still have a place in a routine diagnostic laboratory? B. Vanmassenhove* [Östend, Belgium], A. Hervent, L. Persijn, L. Vynckier, G. Alliet

Suspected reverse zoonosis of influenza A[H1N1] pdm09 virus infection found in Allouroopoda melanoleuca in Hong Kong Oceanarium C. Chang* [Hong Kong, Hong Kong], Y. Fong, J. Teng, S. Lau, P. Woo

Laboratory-confirmed seasonal influenza virus infection in Qatar: 2016-2018 national surveillance data J. Daghfal Nader* [Doha, Qatar], A. Omrani, M. Al-Maslamani, P. Coyle, M. Shebash, A. Hashim

Rapid diagnosis of seasonal influenza virus and cohorting of hospitalized patients on a ‘flu ward’: a prospective analysis of outcomes B. O’Kelly* [Dublin, Ireland], A. Kelly, A. Conway, S. Mcconkey, C. McNally, E. De Barra

Evaluation of Genomera CDX system for influenza and respiratory syncytial virus infections E. Choquet, C. Chessa, M. Prat, A. Lanivière, A. Beby Defaux, N. Lévêque, M. Pichon* [Poitiers, France]

Clinical benefits of Point-of-Care rapid molecular influenza test at a hospital emergency service J. Nordh* [Växjö, Sweden], H. Janson

Comparison of Illumina and nanopore sequencing methodologies for whole genome sequencing of influenza A virus from clinical isolates J. Heaney* [London, United Kingdom], D. Frampton, H. Gliddon, M. Byott, P. Grant, R. Mckendry, E. Nastouli

Next generation sequencing of influenza A virus from environmental samples at the human-animal interface N. Bell* [Toronto, Canada], B. Kwok, L. Yip, C. Bekking, Y. Berhane, K. Prost, M. Oaidir, S. Mubareka

Cost analysis of a Point-of-Care diagnostic test for detecting influenza A/B and respiratory syncytial virus in the ER setting in Norway J. Mewes, A. Voermans, T. Østfold* [Oslo, Norway], T. Halvorsen, K. Eresk, L. Steuten

Laboratory diagnosis and circulation of respiratory syncytial virus (A and B subgroups) and influenza virus A [H1 and H3 subtypes] and B in a three-winter season (2016-17 to 2018-19) hospital-based survey in northern Italy M. Arcangeloletti, C. Maccari* [Parma, Italy], F. De Conito, F. Ferraglia, F. Pinardi, P. Montagna, C. Chezzi, A. Calderaro

Impact of influenza Point-of-Care testing in the emergency department on clinical care of adult patients at three hospitals in Lanarkshire, Scotland: an observational study A. Hao, P. Anstey, H. Black, E. Kerr, J. Mcllister, C. Mullen, M. Tate* [Glasgow, United Kingdom], D. Cramie, I. Mccormick, S. Whitehead

Influenza: therapeutics

Treatment of influenza and influenza-like illnesses with antiviral having anti-inflammatory efficacy N. Pshenichnaia* [Moscow, Russian Federation], V. Bulgakovskaya, E. Volchkova, E. Kareva, V. Gorodin, A. Grekova

Five-day versus ten-day oseltamivir chemoprophylaxis to prevent hospital influenza transmission: a non-inferiority randomised open-label study L. Lepen, M. Velušček, R. Blagus, A. Hadžič, M. Mavrič, R. Saletinger, D. Stupica* [Ljubljana, Slovenia]

Nucleoside analogue for the treatment of influenza N. Lvov* [St. Petersburg, Russian Federation]
Abstract Categories 2020

4000 Template RNA loops determine aberrant RNA synthesis and innate immune activation during influenza virus infection
H. French* [Cambridge, United Kingdom], A. King, A. Te Velthuis

4819 Protection against H9N2 Influenza A(H9N2) virus induced by recombinant M2e-HA2 fusion protein
M. Moghadaszaadeh* [Tabriz, Iran], M. Zeinalabedin, M. Golchin, R. Ghanbarpour, H. Tavakkoli

5126 Preclinical efficacy, pharmacokinetics and safety of CD377, a novel antiviral Fc-conjugate against influenza

5707 CD377, a novel antiviral Fc-conjugate, demonstrates a lower resistance potential than baloxavir and oseltamivir against pandemic influenza A(H1N1)
A. Almaguer* [San Diego, United States], A. Borchardt, W. Jiang, Z. Chen, T. Brady, J. Locke, L. Tari

5788 Antiviral treatment in severe influenza pneumonitis
Y. Pai, Y. Huang* [Taipei City, Taiwan], C. Su, K. Tsao, C. Hung, Y. Hsieh, K. Kao, C. Huang, A. Dutta, C. Huang

5793 Efficacy of CD377, a novel antiviral Fc-conjugate against seasonal influenza in lethal mouse models
J. Levin* [San Diego, United States], K. Amundson, K. Shathia, A. Borchardt, T. Lam, W. Jiang, Z. Chen, T. Brady, S. Döhrmann, V. Ong, L. Tari

6009 Efficacy of CD377, a novel antiviral Fc-conjugate, against influenza A(H1N1) in a lethal mouse model of Severe Combined Immunodeficiency (SCID)
J. Levin, K. Amundson, K. Shathia, A. Borchardt, T. Lam, W. Jiang, Z. Chen, T. Brady, S. Döhrmann, V. Ong, L. Tari* [San Diego, United States]

7868 Adjuvants that contain saponin may be an important component of influenza peptide vaccines to induce broadly reactive functional antibodies
C. Sei* [Gaithersburg, United States], N. Rikhi, R. Schuman, K. Muema, L. Daum, G. Fischer

8820 Fc-mediated Fcγ receptor engagement of CD377, a novel antiviral Fc-conjugate, translates into potent antibody-dependent cellular phagocytosis and antibody-dependent cellular cytotoxicity activity
S. Döhrmann* [San Diego, United States], R. Grewal, E. Abelovski, T. Brady, W. Jiang, Z. Chen, A. Borchardt, J. Cole, L. Tari

8832 CD377, a novel antiviral Fc-conjugate, demonstrates potent broad-spectrum activity in multiple in vitro assays against influenza A and B
S. Döhrmann* [San Diego, United States], A. Almaguer, N. Dedec, T. Brady, W. Jiang, Z. Chen, A. Borchardt, J. Cole, J. Locke, L. Tari

Session accepted as 1-Hour Oral Session
Innovative therapeutic approaches against influenza

2693 Baloxavir treatment of ferrets infected with influenza A virus reduces transmission

7514 Comparative effectiveness of combined favipiravir and oseltamivir therapy versus oseltamivir monotherapy in critically-ill patients with influenza virus infection
Y. Wang* [Beijing, China]

8045 Influenza immunoglobulin in hospitalised patients with serious influenza A
A. Dahl* [Winnipeg, Canada], M. Ison, T. Babinchat, C. Hall, D. Anderson

8839 CD377, a novel antiviral Fc-conjugate, demonstrates superior reduction of viral burden and cytokine levels compared to oseltamivir in a lethal mouse model of influenza A(H1N1) infection

Session accepted as Paper Poster Session
Neurotropic flaviviruses

856 Treatment of flaviviruses in solid organ transplant recipients with intravenous immunoglobulin and interferon alpha-2b: a Mayo Clinic Arizona experience
S. Kasule* [Phoenix, United States], R. Patron, M. Grill

2380 An imported case of West Nile virus neuroinvasive disease in the UK
N. Khan* [London, United Kingdom], R. Lewis, P. Papineni, W. Lynn, G. Sandhu

3953 In vitro modeling of patient-specific susceptibility to neurotropic flavivirus infection by using induced pluripotent stem cells
S. Riccetti* [Padova, Italy], A. Sinigaglia, G. Desole, M. Pacenti, T. Smura, R. Kaint, O. Vapalahi, M. Trevisan, L. Barzon

5019 West Nile virus 2018 season in Italy: rapid spreading of West Nile neuroinvasive disease in northwest Italy
E. Burdino* [Turin, Italy], T. Allice, M. Milia, G. Gregori, G. Marleo, R. Cipriani, C. Pasqualini, P. Ferrero, V. Ghisetti
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7233 Characteristics of the initial phase of tick-borne encephalitis
P. Bogovic* [Ljubljana, Slovenia], S. Lotric-Furlan, K. Ogrinc, T. Avsic, F. Strle

7342 10 years surveillance of West Nile virus neuroinvasive disease

9540 Monitoring mosquito populations and detection of West Nile virus and Usutu virus in mosquito pools collected in Attica regional units, Greece, 2017-2018
E. Patsoula* [Athens, Greece], S. Beleri, G. Balatsos, V. Karras, N. Tegos, F. Sereti, D. Papachristos, A. Michaelakis

Session accepted as Paper Poster Session

Paediatric and perinatal infections

861 Comparison of immune function between T, B lymphocytes, Th17, Th22 and Treg cells in children with hand, foot and mouth disease caused by EV71 and other enterovirus infections
W. Song* [Hangzhou, China], S. Zhao, Y. Wei

3291 Mother-to-child transmission of curable sexually-transmitted infections in HIV-infected women in South Africa

3729 Congenital toxoplasmosis: outcomes of newborns from mothers with documented seroconversion out of a multi-centre cohort in two tertiary referral hospitals
V. Meron* [Pavia, Italy], A. Bonetti, A. Comelli, L. Tomasoni, F. Genca, A. Chiesa, F. Prefumo, V. Spinoni, S. Colagaris, C. Bonfanti

3754 Challenges in setting-up and conducting a global multi-centre prospective observational cohort of sepsis in hospitalised neonates: the NeoOBS study
A. Riddell* [London, United Kingdom]

4500 Uncovering the role of airborne transmission and asymptomatic contact shedding in outbreaks of scarlet fever
R. Cordery* [London, United Kingdom], A. Purba, L. Begum, E. Mills, M. Mosavie, E. Jauneikaité, P. Hoffman, T. Lamagni, S. Sriskandan

4576 A comparison of GenomEra GBS PCR and GeneXpert GBS PCR assays with culture of group B Streptococcus with and without broth enrichment
S. Nielsen* [Aarhus, Denmark], J. Kjølseth Møller, M. Khalil

5196 Vaccination uptake in sickle cell disease: results from a London teaching hospital
K. Isitt* [London, United Kingdom], A. Calvert, M. Haq, P. Heath, C. Cosgrove

5275 Modulation of the immune status in pyelonephritis caused by Pseudomonas aeruginosa in children with hydronephrosis
M. Svitlana* [Kharkiv, Ukraine], M. Maryna, I. Marchenko, V. Davydenko, Y. Mozgova

6306 Global multi-centre prospective observational cohort of sepsis in hospitalised neonates highlights complex case mix: the NeoOBS Study
A. Cook* [London, United Kingdom]

6481 Phylogenetic groups and virulence factors of uropathogenic Escherichia coli in pregnant and non-pregnant women in St. Petersburg, Russia
M. Razinkova* [St. Petersburg, Russian Federation], T. Khusnutdinova, E. Shipitsyna, D. Budilovskaya, A. Krysanova, K. Shalepo, A. Savitcheva

6497 Innovative diagnosis strategy for pneumococcal infections in children using an immunochromatographic test in respiratory specimens
C. Haddar* [Saint-Priest-En-Jarez, France], J. Joly, A. Carricajo, P. Verhoeven, G. Florence, O. Mary, E. Begaud, Y. Germani, A. Cantais, P. Bruno

6497 Global assessment of neonatal sepsis incidence and case fatality
C. Fleischmann-Struzek* [Jena, Germany], F. Reichert, A. Cossini, T. Harder, N. Kissoon, K. Reinhart, B. Allegranzi, T. Eckmanns

7115 Invasive pneumococcal disease in children: the risk of a moving target
M. Corcoran* [Dublin, Ireland], J. Mereckiene, S. Murchan, S. Cotter, R. Cunney, H. Humphreys

7145 Investigation of hypervirulent Group B Streptococcus ST17 clone by MALDI-TOF MS
M. De Fazio, A. Surace, D. Talarico, P. Minchella* [Catanzaro, Italy]

7145 Fast and reliable detection of group B Streptococcus during antepartum screening: evaluation of the PCR-based Simplexa GBS Direct assay in comparison to routine culture after Lim Broth enrichment and from ESwabs without enrichment
T. Alcaro, S. Nisticò, M. Colosimo, G. Panduri, G. Caruso, M. De Fazio, A. Surace, D. Talarico, P. Minchella* [Catanzaro, Italy]

8767 Outcome of a screening programme for the prevention of neonatal invasive early-onset Group B Streptococcus infection in a maternity unit of the University Hospital “Dr Dragisa Misovic” [Belgrade, Serbia]
M. Lacković, M. Gostimirović* [Belgrade, Serbia], S. Mihajlović
Vaginal carriage of *Enterobacter cloacae* and *Klebsiella pneumoniae* among pregnant women in Bukavu, Democratic Republic of Congo: prevalence, risk factors and adverse pregnancy outcomes


Re-evaluating and refining predictors of bacterial infection in children with cancer and febrile neutropenia

G. Haeusler* (Melbourne, Australia), K. Thursky, M. Slavin, F. Babi, R. De Abreu Lourenco, F. Mechinaud, B. Philips

Role of epitopes of four immunogenic Group B streptococci [GBS] proteins and their derivatives indistinguishability between pregnant GBS carriers and non-carriers

A. Dobrut, A. Malska-Wazniak, E. Brzozowska, S. Gorska, A. Gamian, M. Brzychczy-Wloch* [Krakow, Poland]

Diagnosing neonatal sepsis: question under discussion


Characterisation of the human cytomegalovirus genome diversity in longitudinally collected breast milk samples


Clinical diagnostic evaluation of a real-time PCR assay for the quantitative detection of cytomegalovirus from EDTA-plasma and urine samples

U. Egner* [Heidelberg, Germany], N. Hefner, M. Kolb, U. Betz

Validation of Simplexa HSV 1 & 2 Direct and Simplexa VZV Direct kits for herpes simplex virus and varicella zoster virus detection from low-volume cerebrospinal fluid samples

S. Burrel, O. Bomme, D. Roger, J. Pirot, B. Le Labousse, N. Henn, E. Chaicaud, D. Boutolleau* [Paris, France]

Transforming a multiplex laboratory developed real-time PCR for herpes simplex virus type 1 and 2 & varicella zoster virus into a sample-to-answer, cassette-based format

M. Dierckx, R. Cartuyvels, M. Raymaekers* [Hasselt, Belgium]

Design of a varicella zoster virus PCR combined with a herpes simplex virus PCR in a multiplex assay: a diagnostic evaluation study

B. Schmid* [Zurich, Switzerland], M. Affolter, A. Buttafuoco, M. Glatz, P. Bosshard

Quantitative detection of human cytomegalovirus and Epstein-Barr virus using the real-time PCR STAT-NAT CMV and STAT-NAT EBV assays

D. Rigamonti, A. Mancon, G. Ferri, A. Di Cosima, L. Spinelli, G. Torini, L. Bavagnoli, I. Merli, M. Incandela, M. Gismondo, M. Gramenga* [Milan, Italy], V. Micheli

Molecular detection of cytomegalovirus in intestinal tissue

N. Bastón Paz* [Las Palmas de Gran Canaria, Spain], M. Hernández-Betancor, M. peñate balaños, P. Hernandez Cabrera, T. Tosco-Núñez

A new approach for the quantification of clinical samples viral load based on virtual qPCR standard curves

A. Gani* [Padova, Italy], N. Paccognella, D. Corradini, C. Savio, A. Palacchini, D. Paladin, R. Costacurta

Characterisation of the human cytomegalovirus genome diversity in longitudinally collected breast milk samples


Clinical diagnostic evaluation of a real-time PCR assay for the quantitative detection of cytomegalovirus from EDTA-plasma and urine samples

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Transforming a multiplex laboratory developed real-time PCR for herpes simplex virus type 1 and 2 & varicella zoster virus into a sample-to-answer, cassette-based format

M. Dierckx, R. Cartuyvels, M. Raymaekers* [Hasselt, Belgium]
### 3774 Automation in full genotyping of human papilloma viruses: evaluation of the analytical performance of Anyplex HPV28 assay
B. Vanmassenhove* (Ostend, Belgium), A. Hervent, L. Persijn, L. Vynckier, G. Alliet

### 4013 Prevalence of high-risk human papilloma virus genotypes responsible for cervical cancer in Blida, Algeria
S. Oukid* (Blida, Algeria), M. Dakhya, M. Boudjella, N. Sadouki, R. Beloumi

### 5295 Evaluation of the NeuMoDx HPV assay
B. Hesselink* [Amsterdam, Netherlands], S. Doorn, C. Meijer, D. Heideman, E. Craig, J. Zhu, S. Brahmasandra

### 6810 Diagnosis and sampling of human papilloma virus in men
J. Muehlberger* (Vienna, Austria), A. Stary, K. Schwarz

### 7268 Novel taxonomic and functional cervical microbiome biomarkers of persistency and histological progression to CIN2+ in women infected with high risk human papilloma virus
T. Iftner, F. Stubenrauch, A. Iftner, M. Willmann* (Tübingen, Germany)

### 7746 Human papilloma virus 16 viral load quantification using droplet digital PCR and correlation with cervical lesion
M. Martineili* [Mozza, Italy], C. Giubbi, R. Musumeci, F. Perdoni, F. Sina, R. Fiscico, F. Landoni, C. Cocuza

### 8198 Cost-effectiveness analysis for human papilloma virus mitigation strategies implemented since 2019 in the Republic of Moldova based on infectious disease modelling
A. Jarynowski* [Kishinev, Moldova]

### 8657 Identification of a clinically relevant anal HPV infection in HIV-positive men having sex with men: data from Czech anal cancer screening programme
J. Nemcova* [Plzen, Czech Republic], K. Cerna

### 9054 Prevalence of human papilloma virus 16, 18 and other high-risk genotypes in Baku, Azerbaijan
A. Gumral* [Baku, Azerbaijan], A. Agayev, L. Veliyeva, A. Mammadova, V. Narimanov, R. Bayramli, V. Huseynov

### 3774 Quantitative detection and impact of 5’ terminally deleted Group B enterovirus populations on type I IFN response in peripheral blood or heart tissue samples from acute myocarditis paediatric patients
M. Glenet, Y. N’Guyen, A. Mirand, C. Henguell, A. Lebreil, F. Berri, F. Bani Sadr, B. Lina, I. Schuffenecker, L. Andreoletti* [Reims, France]

### 5284 Perspective of the phase mini-antibodies for virus detection by using electro-acoustic sensor
D. Karavaeva* [Saratov, Russian Federation], O. Guliy, B. Zaitsev, I. Boradina

### 6373 Performance evaluation of a novel BKV Quant Assay in plasma and urine specimens
M. Gramegna* [Milan, Italy], G. Ferri, A. Di Cosimo, G. Torini, L. Gong, D. Krause, C. Butcher, M. Mastronardi, B. Wu, S. Brahmasandra

### 6509 Clinical application of polyomavirus detection by metagenomic next-generation sequencing in urinary tract infection
N. Li* [Shanghai, China], B. Hu

### 7050 Effect of brincidofovir on adenovirus and cellular transcriptome profile
M. Salomona* [Paris, France], L. Feghouli, S. Mercier-Delarue, E. Díaz, A. Armero, J. Dutrieux, J. Le Goff

### 7562 Study on the diagnostic value of serum amyloid A(SAA) in pathogen classification and clinical stage identification of hand, foot and mouth disease
W. Yidong* [Hangzhou, China], W. Yi

### 7795 Identification of DNA virus in conventional culture by MALDI-TOF MS
G. Martin* [Oviedo, Spain], S. Rojo, R. Campo Ramos, I. Costales, Z. Pérez, X. García, M. Alavarez-Arguéelles, S. Melón-García

### 8308 Diagnostic value of IgG avidity and/or Western blot test for the diagnosis of Rubella virus infection during pregnancy
G. Ofa, A. Chtaourou, S. Gargouri, H. Triki, B. Feiza, L. Fekri-Berarajah, A. Hammami* [Sfax, Tunisia], H. Karray-Hakim

### 9440 Comparison of different nucleic acid extraction methods for viral metagenomic analysis
M. Sabatier* [Lyon, France], A. Bal, G. Destrus, F. Morfin, B. Lina, V. Navratil, L. Josset

### 9497 Characterisation of the host lipidome in Enterovirus-infected cells: implications on pathogenesis and potential antiviral strategies
J. Chan* [Hong Kong, Hong Kong], B. Yan, Z. Zou, H. Chu, J. Tsang, S. Yuan, C. Yip, R. Kao, K. Sze, S. Lau, K. Yuen

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**Spreadsheet of abstracts:**

- **Abstract Categories 2020**
- **Session accepted as Paper Poster Session**
- **Recent findings in diagnosis of viral infections**
- **Viral epidemiology**
Abstract Categories 2020

Molecular epidemiology and clinical features of human adenovirus: a 20-year retrospective observational study in Bern, Switzerland
J. Akello* (Bern, Switzerland), R. Kamgang, M. Barbani, F. Suter-Rinkler, S. Leib, A. Ramette

Human parechoviruses infections in northern of Spain, 2016-2019
A. Navascués Ortega, A. Aguinaga Perez, M. Cabreroza, M. Portillo* (Pamplona, Spain), C. Ezepeleta Baquedano

Seroprevalence of Coxsackievirus B1-6: retrospective study in an Italian population

Seroprevalences of ten ToRCH infectious pathogens in women residing in Europe, Latin America and China

National outbreak of norovirus genogroup II in a sushi restaurant chain associated with an internationally distributed seaweed product

Subtyping of adenovirus strains isolated from pre-diagnosed patients with keratoconjunctivitis
A. Güner* (Pendik, Turkey), A. Karahasan, R. Can Sannoğlu, F. Aydin, E. Toker, S. Akkaya Turhan

Molecular epidemiology of varicella zoster virus in Pitié-Salpêtrière University Hospital, Paris, France
M. Cheminet, S. Burrel, D. Boutolleau* (Paris, France)

Viral aetiology and epidemiology of acute paediatric gastroenteritis in southern region of Saudi Arabia with Yemen borders
A. Babiker* (Abha, Saudi Arabia), M. Hassan, A. Al-Hakami, A. Alghantani

Enterovirus surveillance in an Italian paediatric hospital
L. Piccioni, S. Ranno, L. Coltella, C. Auriti, G. Pizzichemi, S. Chiavelli, L. Lancella, L. Cursi, C. Concato* (Rome, Italy)

Genetic diversity and possible recombination of Rs-BatCoV HKU32 related viruses in southern China
C. Wong* (Hong Kong, Hong Kong), S. Lou, H. Luk, S. Ahmed, J. Cai, P. Zhao, J. Teng, K. Yuen, P. Woo

Enterovirus-C99 associated with cases of acute flaccid paralysis in the south-eastern region of Brazil
R. Carmona* (São Paulo, Brazil), B. Machado, J. Dias, A. Chirelli, L. Louzado, A. Luchs, C. Sousa, M. Timenetsky, M. Eduardo

Metagenomics analysis of novel viruses in dromedaries from the Middle East
H. Lee* (Hong Kong, Hong Kong), J. Teng, J. Fung, K. Yeong, K. Chan, S. Lau, P. Woo

Phylogenetic and geographical analyses of bat coronaviruses
T. Chan* (Hong Kong, Hong Kong), C. Wong, H. Luk, S. Lou, P. Woo

Impact of enteric viral co-infections on gastroenteritis among hospitalised children in Palermo, Italy, during a 10-year surveillance
S. De Grazia* (Palermo, Italy), F. Banura, L. Mangiaracina, C. Filizzolo, C. Bonura, V. Martella, G. Giannanco

Varicella zoster virus seroepidemiology in Caribbean Netherlands: implications for vaccine policy

Prevalence and quantity of parvovirus B19 DNA among blood donors
A. Uskudar Guclu* (Ankara, Turkey), S. Yilmaz, M. Baysal, I. Avci

Epidemiological and molecular characteristics of human parechovirus infection in children <6 months hospitalised with symptoms of sepsis-like illness: Milan 2015-2018
L. Pellegrinelli, S. Udèda Renteria* (Milan, Italy), C. Galli, A. Orlandi, S. Bindo, E. Pariani

Introduction and spread of the novel GII.P16 pandemic recombinant norovirus in Italy detected by a newly designed PCR primer pair
G. Giannanco* (Palermo, Italy), N. Urone, F. Bonura, C. Filizzolo, L. Mangiaracina, C. Bonura, V. Martella, S. De Grazia

Molecular investigation of a 4-year outbreak of human adenovirus A31 (HAdV-A31) infection on a paediatric haematopoietic stem cell transplantation ward

Changing seroprevalence of viral diseases among young adults in a tertiary care educational university hospital? Experience with 1993 cases
M. Isikgöz Tasbakan, D. Akyol* (Izmir, Turkey), A. Yezitinoğlu, H. Pullukcu

Session accepted as Paper Poster Session

Viral hepatitis A and E

New freeze-dried multiplex one-step real-time qPCR assay with room temperature storage for hepatitis A virus and and norovirus detection in clinical and food/environmental samples
C. Pilotti* (Lodi, Italy), C. Casali, M. Savoldi Boles
Abstract Categories 2020

3138 Presence and persistantce of hepatitis E virus PCR in patients with specific IgM positivity
C. Mendoza Lopez* (Zaragoza, Spain), J. Gil, A. Rivero-Juarez, A. Legva, R. Benito

4664 An outbreak of hepatitis A among young adult men in Cyprus
P. Dimitriou, C. Flourou, G. Nikolopoulos, M. Koliou, E. Constantinoú, C. Azino, M. Papagiotou, E. Christaki*
(Thessaloniki, Greece)

4741 Hepatitis E virus infection is a risk for liver transplant recipients in Sweden
M. Karlsson* (Göteborg, Sweden), C. Skoglund, M. Karlsson, M. Logging, M. Castedal, H. Norder

5642 Seroprevalence of hepatitis E virus among blood donors in the Qassim Region, Saudi Arabia
B. Alhatlani* (Unayzah, Saudi Arabia), W. Aljabr, M. Almarzuqi, S. Alhatlani, A. Almusallam

8642 Development of a methodology for reverse transcription and amplification of small RNA amounts in serum for whole genome sequencing of hepatitis A virus
P. Bardon, S. Tapia, L. Mara, E. Martínez, E. Clavijo*
(Malga, Spain)

6145 Hepatitis B and hepatitis D virus infection in immigrants living in south Italy: epidemiological and virological characteristics
M. Pisaturu* (Naples, Italy), L. Onorato, L. Alessio, C. Monari, L. Gualtieri, C. Minichini, G. Di Caprio,
M. Starace, M. Caraprese, L. Occhiello, G. Scotto, M. Mocera, E. Sagnelli, N. Coppola

6153 Effects of mutations in the hepatitis B virus genome on viral loads testing
(Be'er Sheva, Israel)

7262 Evaluation of the whole blood spot on plasma separation card as a sample type for serological screening for hepatitis B and hepatitis D infection
F. Velasquez* (Barcelona, Spain), A. Rando Segura, P. Salmerón, U. Aldama, A. Najarro, A. Esteban, G. Ruiz,
M. Rivero-Barciela, M. Buti, E. Marins, F. Rodriguez Frias
Evaluation of the whole blood spot on plasma separation card as a sample type for hepatitis B virus viral load quantification on the COBAS 6800 system
F. Velasquez* (Barcelona, Spain), A. Rando Segura, P. Salmerón, U. Aldama, A. Esteban, A. Najarro, G. Ruiz,
M. Rivero-Barciela, M. Buti, E. Marins, F. Rodriguez Frias
MALDI-TOF MS as new tool for the identification of serological biomarkers for diagnosis of hepatitis B and C viruses infections
A. Calderaro, M. Buttrini* (Parma, Italy), S. Montecchini, F. Ferraglia, F. Pinardi, M. Arcangeletti, F. De Conto,
C. Chezzi

7760 Construction and investigation of IncRNA-associated ceRNA network in chronic hepatitis B infection
S. Wang* (Chengdu, China), Y. Wei, J. Chen
Performances of a new random access system for hepatitis B and C viral load quantification
J. Besombes, C. Pronier* (Rennes, France), A. Maillard, G. Lagathu, P. Camacle, C. Grolhier, V. Thibault
Detection of hepatitis B virus reactivation and near complete sequencing of the viral genome by high-throughput sequencing in a kidney transplant
M. Etoundi, S. Aherfi, A. Motte, V. Moal, P. Calson*
(Marseille, France)

Longitudinal assessment of liver fibrosis rates using non-invasive APRI and Fib-4 scores in HIV, HBV and HIV-HBV co-infected patients
D. Iacob* (Bucharest, Romania), M. Luminos, B. Otilia, A. Tudor, S. Iacob, C. Olariu, A. Tudor, I. Arin, S. Ruta

Session accepted as Paper Poster Session

Viral hepatitis B

1070 Performance evaluation of the Xpert HBV Viral Load assay for the quantification of hepatitis B virus DNA in plasma samples
H. Lam* (Hong Kong, Hong Kong), B. Tang

1071 Performance evaluation of the Alinity m HBV assay for the quantification of hepatitis B virus DNA in plasma samples
H. Lam* (Hong Kong, Hong Kong), M. Ng, B. Tang

1629 Cardiovascular Disease risk in liver transplant recipients for hepatitis B, C and delta virus-associated cirrhosis
P. Cirilo* (Caserta, Italy), F. Calò, G. Stornaiuolo, G. Gaeta, P. Maggi

3721 HBV RNA and HBcAg: two new biomarkers for monitoring chronic hepatitis B virus infection
G. Roncarati* (Bologna, Italy), S. Galli, A. Moroni, G. Furlini

4047 Use of chemiluminescence and electrophochemistry in the diagnosis and monitoring of hepatitis B viral infection
D. Velcheva, A. Gotseva* (Soﬁa, Bulgaria), Y. Slaveyкова

5897 Hepatitis B virus epidemiology among chronic kidney disease patients under haemodialysis
L. Villar* (Rio de Janeiro, Brazil), K. Frajo, J. Miguel, E. Da Silva, B. Marques, A. Da Fonseca Mendonça,
L. Lewis-Ximenez
Abstract Categories 2020

Session accepted as Paper Poster Session

Viral hepatitis C

503  Dried blood spots tested with the Abbott m2000 sp/rt system perform well to identify patients with active HCV infection in Vietnam
T. Tran, B. Nguyen, T. Nguyen, T. Pham, T. Nguyen, T. Mai, B. Pham, T. Nguyen, H. Phan, N. Do, M. Ait Ahmed, F. Taiseb, M. Yoan* [Paris, France]

5288  Serore prevalence of anti-HCV antibodies in the Bulgarian population
D. Velcheva, A. Gotsева* [Sofia, Bulgaria], G. Popov

2789  Detection and quantification of hepatitis C Virus in cadaveric tissue donors’ blood using different molecular kits
V. Stadler Tasca Ribeiro, S. Raboni, P. Suss, J. Cieslinski, L. Kraft, J. Santos, L. Pereira, J. Telles, L. Arent* [Curitiba, Brazil], F. Tuon

3087  Treatment of hepatitis C with direct-acting antiviral (DAA) agents: sustained virological response rate in a real care setting in the state of Ceará, north-eastern Brazil
R. Pires Neto* [Fortaleza, Brazil], E. Bomfim Hypolito, J. Milton De Castro Lima, E. Antonio Gomes De Arruda, F. Sérgio Rangel De Paula Pessoa

3227  Applicability of dried blood spot for molecular epidemiology of HCV in coagulopathy patients
L. Villar* [Rio de Janeiro, Brazil], A. Da Fonseca Mendonça, B. Marques, J. Barbosa, J. Colares, D. Lima

3852  Extreme short course therapy for chronic hepatitis C infection
G. Stroffolini* [Turin, Italy], L. Baglione, T. Lupia, G. Cariti, G. Di Perri

3992  The Caserta Model: an hepatitis C virus way out in persons who use drugs in Italy
G. Di Caprio* [Caserta, Italy], V. Messina, A. Russo, E. Parente, G. Russo, T. Raimondo, A. Salzillo, F. Simeone, M. Pisaturo, N. Coppola

4244  Direct-acting antiviral failure in hepatitis C virus genotype 3: virological features and efficacy of re-treatment

4509  Effect of antiviral therapy against hepatitis C virus on gut microbiota
B. Pinchera* [Naples, Italy], R. Scotto, E. Zappulla, A. Buonomo, A. Maranola, N. Schiano Mariello, F. Gison, F. De Filipps, D. Ercolini, I. Gentile

4763  The future of hepatitis C virus nucleic acid amplification techniques standardization?
J. Fryer* [Potters Bar, United Kingdom], P. Rigsby, J. Hockley, C. Morris

503  Direct-acting antivirals failure in HCV genotype 3: virological features and efficacy of re-treatment

503  Using dried blood spots in drug dependency treatment centres to diagnose active hepatitis C infection
M. Lara, D. García Martínez De Artola* [Santa Cruz de Tenerife, Spain], J. Alcaba Flores

503  Reliable HCV genotyping and resistance associated substitutions identification by a new next-generation sequencing approach

503  Real-world drug resistance profile of hepatitis C patients who failed direct-acting antivirals: SHARED

503  Detection of antibodies to hepatitis C virus using the Ortho VITROS: evaluation of the signal-to-cutoff ratio
G. Colomba, N. Urone, C. Mascarella, D. Ferrara* [Palermo, Italy]

503  Patients related barriers for delay in seeking confirmatory test and treatment of hepatitis C in treatment naïve patients visiting a tertiary care hospital in Karachi, Pakistan
H. Ashraf* [Karachi, Pakistan], N. Mahmood, U. Shujat, N. Baig-Ansari, S. Iftkhur, R. Ansari

503  Goal achieved! Elimination of hepatitis C in three penitentiary centres
S. García Martín* [Puerto Real, Spain], C. Freyre, F. Téllez Pérez, I. Virto, M. Martinez Rubio

503  Hepatitis C reflex testing in Spain in 2019: a story of success
F. García García* [Granada, Spain], A. Aguilara, J. Calleja Panero, J. Eiros, A. Blasco Bravo, P. Lazaro, F. Garcia-Samaniego Rey, J. Crespo

503  An optimised strategy for linkage to care of patients newly diagnosed of active hepatitis C infection
A. Fuentes* [Granada, Spain], F. García García, E. Ruiz, F. Sousa, F. Garcia Garcia
Abstract Categories 2020

Session accepted as Mini-oral Flash Session

Viral hepatitis in the real world

2897 Changes in the characteristic of the population with chronic hepatitis C receiving treatment with direct acting antivirals in a referral centre during the post-interferon era

4403 Virological patterns of HCV-patients with failure to second-generation direct-acting antivirals

Identification of mutations in hepatitis B virus reverse transcriptase associated with a tenofovir-resistant phenotype in South African adults

Whole genome sequencing to investigate genetic diversity in HBeAg-positive and HBeAg-negative hepatitis B virus infection

Progress towards the targets for the elimination of viral hepatitis in the European Union
E. Duffell* [Stockholm, Sweden], A. Mozalevskis, T. Noori

Direct-acting antiviral based treatment for HCV-infected persons who inject drugs: a multi-centre real-life study
L. Onorato* [Naples, Italy], G. Di Caprio, A. Russo, C. Caruso, V. Rosato, E. Claar, V. Iovinella, V. Messina, N. Coppola

Direct-acting antivirals-based treatment for HIV/hepatitis C virus co-infected patients: analysis of factors of virological sustained response in a real-life study

HEV infection as an emergent public health issue: is it a concern for Italian blood donors?
L. Colagrossi* [Milan, Italy], M. Mercuri, A. Nava, E. Matarazzo, D. Campisi, P. Carlo Federico, D. Fant

Prevalence of Hepatitis E Virus in allogeneic-haematopoietic stem cell transplant recipients from Portugal
S. Cruz* [Rebordosa, Portugal], N. Santos-Ferreira, M. Nascimento, C. Pinho Vaz, F. Campilho, L. Leite, R. Branca, A. Campos Jr, R. Medeiros, H. Sousa

Micro-elimination of hepatitis C in HIV co-infected persons in Slovenia: analysis of HCV infection in a national HIV cohort
J. Ceronsa* [Smarje pri Jelsah, Slovenia], J. Tomášič, T. Vovko, B. Pecavar, G. Turel, M. Kordiš, M. Pleško, B. Ulan, J. Meglič, M. Poljak, J. Lazarus, M. Maticic

High-resolution influenza mapping of a city reveals socioeconomic determinants of transmission within and between urban quarters

Too much of a good thing? Evaluation of respiratory viral panel usage in paediatric bone marrow transplant patients
M. Precit* [Los Angeles, United States], M. Glucoft, K. Mongkolrattanothai, J. Dien Bard

Predictors of mortality of influenza virus infections in a Swiss hospital during four influenza seasons: role of quick sequential organ failure assessment
M. Papadimitriou Olivergis* [Lausanne, Switzerland], N. Gkikopoulos, M. Wust, A. Balif, V. Simonin, M. Maulini, C. Nusbaumer, L. Bertaiola Monnerat, J. Tschapp, E. Kampouri, P. Wilson, E. Huplain

EnteroVirus D68: biennial circulation and molecular epidemiology in New York, USA, 2014-2018
G. Wang* [Valhalla, United States], V. Gilrane, J. Zhuge, W. Huang, C. Yin, C. Salib, S. Nolan, A. Dhand, J. Fallon

Effect of rapid influenza detection tests on antibiotic prescriptions
A. Berwa* [Meylan, France], M. Gallouche, S. Larrat, J. Fauconnier, J. Bossard, C. Landelle

Measurement of influenza antibodies in a cohort of vaccinated patients admitted to a cardiac intensive care unit: are they clinically relevant?

Nanopore metagenomic sequencing of influenza virus directly from respiratory samples: diagnosis, drug resistance and nosocomial transmission
F. Fouad, M. Lemaître, A. Bessou, F. Carrat, P. Crépey, J. Gaillot* [Fringy, France], G. Gavazzi, D. Launay, A. Masnier, M. Levant, M. Uhart

8890 Evaluating the performance of a host-protein signature for distinguishing between bacterial and viral disease in adults with Lower Respiratory Tract Infection (LRTI): results from the OBSERVER clinical study

Session accepted as Paper Poster Session
Viruses and transplantation

615 Survival outcome in allogeneic haematopoietic stem cell transplant recipients with multiple, sequential cytomegalovirus, Epstein-Barr virus, BK virus and respiratory viral infections
S. Tia* [Parkville, Australia], M. Slavin, D. Ritchie, L. Chee, A. Bajel, J. Sosadeusz, C. Malpas, M. Yong

824 International survey on diagnosis and management of human herpes virus-8 infection in solid organ transplant recipients
A. Mularoni* [Palermo, Italy], L. Adamioli, M. Mikulska, M. Giannella, P. Grossi

1006 In vitro evaluation of the influence of immunosuppressive agents on human polyomavirus BK replication
S. Lucia* [Milan, Italy], E. Favi, M. Ferrareso, M. Dolci, R. Ticozzi, F. Ferrante, S. Delbue

1522 Do cytomegalovirus infection and valganciclovir exposure increase the risk of BK viremia and associated nephropathy after kidney transplantation?

1990 Optimisation of a series of salicylamide derivatives of niclosamide as potent antiviral agents against human adenovirus

2382 Cidofovir-associated nephrotoxicity in adult allogeneic haematopoietic cell transplant recipients

5029 Impact of letermovir (LTV) on utilisation of pre-emptive therapy for cytomegalovirus after allogeneic haematopoietic cell transplantation: a single-centre experience
J. Fang* [New York, United States], P. Zavras, Y. Su, A. Stern, T. Nawar, M. Perales, G. Papanicolaou

5402 Retrospective study of cytomegalovirus infection in orthotopic liver transplantation recipients receiving low dose valganciclovir prophylaxis
M. Lucey* [Dublin, Ireland], S. Fitzgerald, S. Mcdermott

5685 Kaposi sarcoma herpes virus infection in solid organ transplant recipients
L. Adamoli, F. Todaro, E. Conoscenti, D. Di Carlo, M. Miele, M. Di Bella, A. Gallo, P. Grossi, P. Conaldi, A. Mularoni* [Palermo, Italy]

5830 Cytomegalovirus in intensive care unit immunocompetent patients: mortality and clinical aspects
A. Lazo, C. Ramírez* [San Jose, Costa Rica], J. Castro, M. Somagyi, J. Villalobos, L. Montero, R. Arguedas

7069 Impact of letermovir and associations of antivirals in vitro and in ex vivo first-trimester placenta model
D. Andouard* [Limoges, France], B. Gastineau, C. El Harel Bellili, S. Hantz, S. Alain

7776 Letermovir reduces rehospitalisations among cytomegalovirus-seropositive allogeneic haematogenous stem-cell transplant recipients
Y. Golan* [Boston, United States], Y. Tang, S. Mt-Isa, H. Wan, V. Teal, C. Basdshah, S. Dadwal

7948 Evaluation of association between immune modulation and incidence of cytomegalovirus reactivation in sepsis-induced immunosuppression
G. Lambe* [Maharashtra, India], F. Kapadia, C. Rodrigues, A. Shetty, S. Khodaiji, D. Mansukhani

8039 Cytomegalovirus reactivation as a diagnostic and prognostic indicator of increased risk of cardiovascular diseases
V. Centa, L. Colagrossi* [Milan, Italy], A. Nova, E. Matarazzo, M. Mercuri, F. Pansera, E. Piccinelli, I. Bossi, D. Armenia, P. Paba, F. Marcuccilli, D. Campisi, D. Fantì, F. Oliva, F. Cecherini Silberstein, C. Giannattasio, P. Carlo Federico

8079 Letermovir pre-existent mutations in human cytomegalovirus UL56 terminase in solid organ and haematopoietic stem cell transplant recipients
M. Santos Bravo* [Barcelona, Spain], S. Sanchez-Palomino, N. Plaut, M. Masquera Gutiérrez, V. Gonzalo, F. Fernández, M. Sudrez-Lledó, M. Rovira, F. Cofan, M. Moreno Camacho, L. Linares, M. Bodro Marimont, S. Alain, M. Marcos

8320 Evaluation of clinical safety and efficacy of letermovir for cytomegalovirus infection prevention in allogeneic hematoopoietic cell transplant recipients
M. Korostelev* [Paris, France], D. Michanneau, I. Madelaine, T. Sophie
Relevance of EBV load monitoring in renal transplant recipients: a retrospective cohort study

Session accepted as Paper Poster Session
Viruses causing hemorrhagic syndromes

Crimean-Congo hemorrhagic fever in an emergency department in Spain

Seroprevalence of anti-CCHF IgG in population in different districts of endemic region and Crimean-Congo hemorrhagic fever morbidity
N. Pshenichnaia* [Moscow, Russian Federation], N. Golovchenka, L. Ermakova, E. Volchkova, A. Zhuravlev, A. Grekova

Forecasting of Crimean-Congo hemorrhagic fever outcome
N. Pshenichnaia* [Moscow, Russian Federation], G. Abuava, F. Berdalieva, B. Khodzhabekov, L. Ermakova, A. Zhuravlev

Lassa fever infection and prevention control availability and use at healthcare facilities in South-Western Nigeria
I. Usman* [Osogbo, Nigeria], S. Usman

The ultrastructural visualisation of Severe Fever with Thrombocytopenia Syndrome (SFTS) virus in human PBMC sample
Y. Lee, H. Lee, E. Park, H. Kim, S. Kim, C. Lee, S. Jun* [Daejeon, South Korea]

Geographical clustering of hantavirus isolates from Apodemus agrarius identified in the Republic of Korea indicates the emergence of a new hantavirus genotype
D. Kim* [Gwangju, South Korea], J. Sehrish, C. Kim, S. Jun-Won

Hantavirus registry (HantaReg): a novel worldwide platform for epidemiological and clinical studies of hantavirus diseases
F. Köhler* [Cologne, Germany], M. Späth, J. Hoyer-Allo, M. WanKen, O. Corneli, V. Di Cristanziano, F. Schaefer, R. Müller, V. Burst

Crimean–Congo haemorrhagic fever in pregnancy: a systematic review and meta-analysis of clinical presentation and maternal and foetal outcomes
N. Kayem* [Oxford, United Kingdom], C. Aye, C. Benson, S. Baker, M. Tame, S. Kennedy, P. Ariana, P. Horby

Safe and high-throughput screening of natural compounds using pseudo-virus expressing SFTSV glycoprotein
H. Cha* [Seoul, South Korea], J. Kim, S. Park, I. Kim, S. Kim
Abstract Categories 2020

2730 A marked decrease in HIV-1 acquired drug resistance in Italy over the last decade

4724 Evaluation of analytical and clinical performances of four commercial HIV-1 viral load assays on a wide panel of HIV-1/M and HIV-1/O
M. Gueudin* (Rouen, France), P. Cappy, E. Alessandri-Gradl, F. Diamond, J. Moriceau, D. Descamps, A. Vabret, S. Laperche, J. Plantier

7150 Early, potent and sustained virus-specific antibody-dependent complement-mediated inactivation activity in HIV-2 infection

8101 The N-terminus of APOBEC3C regulates the antiviral activity against HIV-1
K. Balakrishnan* (Düsseldorf, Germany), A. Jaguva Vasudevan, A. Sangwimon, S. Banerjee, C. Münk

9109 Conservation in p24 capsid protein regions in HIV-1 groups M, O, P and H
P. Tragana Hernandez* (Alcalá de Henares, Spain), R. Reina, A. Holguin

Session accepted as 2-Hour Oral Session
What’s new in viral hepatitis?

1032 Prospective evaluation of serological and virological response in chronic hepatitis B genotype E treated with tenofovir or entecavir
I. De Benedetto* (Turin, Italy), L. Boglione, T. Lupia, G. Cariti, G. Di Perri

4164 Eliminating mother-to-child transmission of hepatitis B virus in Namibia: a cost-effectiveness analysis
C. Tamanjou Tchuem* (Cape Town, South Africa), M. Andersson, J. Mufenda, C. Wiysonge, D. Diergaardt, C. Tamandjou Tchuem* (Cape Town, South Africa), W. Preiser, S. Cleary

4340 Virological features and efficacy of re-treatment in hepatitis C virus patients: a real-world experience in southern Italy

4884 Chronic hepatitis C care cascade in France: substantial impact of direct-acting antivirals but the path to elimination is still long

4922 Characteristics of Resistance Associated Substitutions (RASs) in “unusual” HCV subtypes: a worldwide network of HCV resistance database

5068 HCV resistance patterns in a large international cohort of DAA-naïve and -experienced patients with GT3a infection

5141 Hepatitis E virus genotype 3 subtype-dependent clinical outcomes in Belgium 2010-2018

5592 Innovative procedures for micro-elimination of hepatitis C virus infection in a high-risk population of undocumented migrants and low-income refugees

Session accepted as Paper Poster Session
Yellow fever, Zika, and Chikungunya

672 Clinical manifestations of hospitalised chikungunya fever cases during epidemic in the state of Ceará, Brazil, from 2017 to 2019
R. Pires Neto* (Fortaleza, Brazil), F. Liliyyn Christyan Nunes Beserra, J. D’Arc Rocha Damasceno, D. Mendes De Melo, E. Girão

2950 Clinical outcomes of 3-day course of adjunctive oral ivermectin for the patients with chikungunya virus infection: a preliminary study
S. Chusri* (Songkhla, Thailand), T. Hortivakul, P. Surasombatpatana, K. Silpopajakul

3210 Clinical evaluation of the mosquito-borne virus panels of Genematrix based on multiplex real-time PCR
J. Ju, S. Cho, S. Yang, K. Lee* (Gyeonggi-Do, South Korea), S. Hong, S. Kim
Malaria outbreak investigations reveal high seroprevalence of arbovirus infections among febrile cases in Baringo County, Kenya
T. Nzama* (Nairobi, Kenya), R. Abdi

Chikungunya positive reference material based on lentiviral vector system for RT-qPCR assays
C. Escolar* (Zaragoza, Spain), S. Valledor, E. De Tomas Mateo

Epidemiology of dengue, chikungunya, Zika and West Nile diseases from 2012 to 2019: data from an Italian regional reference centre
N. Zanchetta, A. Rizzo, C. Bassi, C. Pontariero, R. Grande* (Milan, Italy), G. Venturi, M. Gismondo

Epidemiology and differential diagnosis of chikungunya and O’nyong-nyong virus: many gaps of knowledge to be filled
L. Pezzi* (Marseille, France), I. Diarra

Results of a Zika virus screening programme in asymptomatic pregnant women in Spain
C. Castelló-Abietar, I. Costales* (Oviedo, Spain), S. Rojo, M. Alavarez-Argüelles, S. Melán-García, M. Rodríguez-Perez

Zika virus: a global health threat and current situation in Pakistan
K. Imtiaz, J. Farooqi, D. Prakoso, K. Barr, M. Long, E. Khan* (Karachi, Pakistan)

First vector-borne cases of Zika virus diseases in Europe: a seroprevalence survey
H. Noël* (Saint-Maurice Cedex, France), F. Franke, G. Durand, J. Paireau, S. Giron, G. Grard, P. Chaud, A. Decoppet, S. Cauchemez, M. Paty, H. De Valk

Characterisation of ZIKV NS1 protein and development of ZIKV-specific monoclonal antibodies for rapid diagnosis
H. Kim* (Cheongju-Si, South Korea), S. Jun, E. Park, S. Kim

Detection of Zika and Chikungunya viruses circulation in Pointe Noire district (Republic of Congo) during the 2019 Chikungunya outbreak

Chikungunya virus: neuromotor evaluation of infants born to infected mothers
R. Freire, C. Gaspari* (Rio de Janeiro, Brazil), L. Albuquerque

A new menace emerges in South America: yellow fever outbreak looms in Venezuela

Can HLA type I and II alleles presence be associated with the clinical spectrum of chikungunya virus infection

The impact of Zika virus epidemic on maternal mental health in Brazil

Zika, dengue and chikungunya viruses seroprevalence among adolescents in Brazil

Accuracy of chikungunya case definition in patients with arbovirus illness seeking care in an urban emergency department in Rio de Janeiro, Brazil
H. De Paula, C. Lamas* (Rio de Janeiro, Brazil), J. Moreira, R. Santana De Aguiar, S. Carodozo

Who should we test for arboviral infection? Rational diagnostic testing in an era of increased global prevalence
R. Ryan* (London, United Kingdom), I. Milligan, S. Logan, E. Nastouli, A. Checkley, T. Ramping

What does the space-time dynamics of arboviral diseases epidemic in Curaçao tell us? Unravelling potential factors of disease persistence and spread
M. Vincenti-Gonzalez* (Groningen, Netherlands), Y. Halabi, I. Gerstenbluth, A. Duits, A. Friedrich, M. Grillet, A. Tami

“Tell me and I forget, involve me and I learn”: citizen science for mosquito management in a Dutch Caribbean island
M. Vincenti-Gonzalez* (Groningen, Netherlands), D. De Kort, D. Haarsma, R. Haan, D. Van Der Leest, B. Sagel, A. Duits, E. Schoop, M. Kelie, Y. Halabi, M. Braks, L. Tromp, A. Friedrich, M. Grillet, A. Tami

Clinical evolution of yellow fever patients in the 2017-2018 outbreaks in Minas Gerais, Brazil: preliminary analysis of risk factors for death
C. Rodrigues* (Belo Horizonte, Brazil), W. Clemente, C. Bonis, P. Mourão
Abstract Programme

2. Bacterial infection & disease

- Tuberculosis and other mycobacterial infections (incl antimycobacterial drugs, treatment & susceptibility/resistance, diagnostics & epidemiology)

- Severe sepsis, bacteraemia & endocarditis (incl host bio-markers)

- Community-acquired respiratory infections

- Community-acquired abdominal/gastrointestinal, urinary tract & genital infections

- Skin, soft tissue, bone & joint (excl prostheses) & central nervous system infections

- Zoonotic bacterial diseases (incl foodborne and waterborne pathogens and One Health aspects)

- Other intracellular or rare bacteria

- Other
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<td>9321 Exploring barriers to penicillin allergy de-labelling in a UK teaching hospital</td>
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Mortality in patients with Staphylococcus aureus bacteraemia and the implications of Staphylococcus aureus bacteriuria for in-hospital: results of a monocentric retrospective cohort study
T. Kramer* [Berlin, Germany], B. Schlosser, F. Schwab, D. Gruhl, M. Behnke, P. Gastmeier, R. Leistner

Evaluation of quality indicators in Staphylococcus aureus bacteraemia in a university hospital
S. De La Villa Martinez* [Madrid, Spain], P. Muñoz, A. Arias, A. Rojas, C. Sanchez Carrillo, M. Valeria Minero, A. Galar Recalde, A. Alvarez-Uria, E. Bouza Santiago

Immunochemical detection of quorum-sensing autoinducers, an innovative strategy to diagnose infections by identifying Staphylococcus aureus strains
E. Montagut Cañete* [Barcelona, Spain], G. Godoy, J. Salvador, A. Lacoma, C. Prat, M. Marco

Distribution of meca in Staphylococcus aureus isolates in a multi-centre clinical study
A. Thornberg* [Carlsbad, United States], N. Whitfield, D. Traizer, J. Reid

Clinical characteristics and prognosis of Staphylococcus aureus Bloodstream Infections in a French General Hospital
S. Nguyen* [Béthune, France], P. Wallard, O. Oddoux, M. Anastay, D. Descamps

Distinguishing clinical characteristics and outcomes in patients with polymicrobial Staphylococcus aureus bacteraemia
C. Kelsom* [Pasadena, United States], E. Minejima, K. Tan, P. Nieberg, A. Wong-Berenger

Healthcare-associated Staphylococcus aureus bloodstream infection (HA-SABSI): clinical practice variation in its management
M. Garcia-Gasalla* [Palma de Mallorca, Spain], C. Collado Giner, A. Villoslada Gelabert, L. Ventajol-Aguiló, M. Perez-Seco, M. Arrizabalaga Asenjo, M. Gallegas Alvarez

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L. Campos, C. Rizek, M. Farrel Cortés, S. Santos, A. Marchi, G. Gonçalves, S. Figueiredo Costa* [São Paulo, Brazil]

Characterising the incidence and outcomes of endogenous endophthalmitis in hospitalised patients with Staphylococcus aureus bacteraemia
L. Wardlow* [Columbus, United States], M. Sobhanie

Secular trends in the epidemiology and clinical characteristics of Enterococcus faecalis infective endocarditis in a referral centre [2007-2018]
L. Escolà-Vergé, N. Fernandez-Hidalgo* [Barcelona, Spain], N. Larrosa, B. Almirante

Development of a predictive score for Enterococcus spp. in biliary tract-related bloodstream infections: Results from the PROBAC study

Impact of infectious diseases consultation and appropriate empirical antibiotic therapy on mortality in patients with Staphylococcus aureus bloodstream infection: a two-year retrospective analysis
A. Cona* [Milan, Italy], L. Gazzola, O. Viganò, R. Castoldi, A. Renzelli, T. Bini, G. Marchetti, A. D’Arminia Monforte

Recurrent bacteraemia with Enterococcus faecalis is predominantly caused by the same clone
C. Tellapragada* [Stockholm, Sweden], H. Östlund, P. Naucler, M. Rasmussen, C. Giske, A. Berge

Bloodstream infections caused by Enterococcus spp.: incidence, clinical features, and outcomes
T. Lupia, L. Scaglione, A. Curtoni, R. Cavallo, F. De Rasa, S. Corcione* [Turin, Italy]

Delayed diagnosis and increase mortality in native vs prosthetic/device-related coagulase-negative staphylococci infective endocarditis

Clinical practice variation in the management of Staphylococcus aureus bacteraemia among infectious disease specialists in Latin America: an international study
Usefulness of the 16S rRNA gene PCR and sequencing in the diagnosis of prosthetic joint infections

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Total knee and hip arthroplasty after septic arthritis: retrospective analysis of 53 cases managed in a reference centre for bone and joint infections
E. Portier, V. Zeller* (Paris, France), S. Godat, Y. Kerroumi, B. Heym, V. Meyssonnier, S. Marmor, P. Chazerain

Particularities of brucellar spondylodiscitis
F. Hammami, M. Makram, A. Zayni, K. Rekik, F. Smoufi, E. Elleuch, C. Marrakchi, M. Ben Jemaa* (Sfax, Tunisia)

Should serum D-dimer be added as a first-line screening test for prosthetic joint infection?
M. Fernandez Sampeda* (Santander, Spain), I. Sanliés González, C. García Ibarbia, N. Fariñas Rodríguez, D. Pablo-Marcos, G. Menendez Solana, C. Fariñas

Oral versus intravenous antibiotics in the treatment of osteomyelitis in adults: a systematic review and meta-analysis
R. Larrazabal, H. Chiu, M. Arcegono* (Manila, Philippines), C. Abad

Metagenomic antimicrobial resistance prediction from nanopore sequencing of orthopaedic implant-related infections: can we do more than detect species from sonication fluids?
T. Street* (Oxford, United Kingdom), C. Kolenda, N. Sanderson, C. Taunt, S. Oakley, B. Atkins, M. McNally, J. O’Grady, D. Crook, D. Eyre

Vertebral osteomyelitis in patients with Staphylococcus aureus bloodstream infection: evaluation of risk factors for failure

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8001 Efficacy and safety of intravenous fosfomycin in patients with periprosthetic joint infection: preliminary results from the PROOF study: a prospective multi-centre study
S. Karbysheva* (Berlin, Germany), P. Morovic, D. Margaryan, L. Johannsen, A. Trampuz

8053 Comparison between Bedside Blind Bone Biopsy (B4) and Basic Bone Biopsy (B3) in the management of diabetic foot osteomyelitis

8154 Retrospective analysis of spinal infections over a 10-year period (2008-2018) in tertiary care hospital
A. Kan, E. Vyronis* [Coventry, United Kingdom], V. Cajic

8261 Comparison of the molecular-based test system hyborg Dx and culture for the diagnosis of prosthetic joint infections
A. Boesl* (Feldkirch, Austria), H. Dirschmid, C. Ohmayer, A. Neugebauer, A. Brachner, B. Ronacher, F. Offner

8281 Intra-osteoblastic activity of dalbavancin during treatment of Staphylococcus aureus bone and joint infection
C. Pierre, L. Abad, A. Souche, C. Dupieux, J. Josse, T. Ferry, F. Laurent, F. Valour* (Lyon, France)

8285 Extended-spectrum ß-lactamase-producing/carbapenemase-producing Enterobacterales prosthetic joint infection in patients with positive rectal screening

8379 Risk factors for mortality in diabetic foot infections
P. Sen, T. Demirdal* (Izmir, Turkey)

8487 Granulicatella sp. and Abiotrophia sp. as a rare cause of osteoarticular infections

8545 Epidemiology, complications, and outcomes of vertebral diskitis/osteomyelitis among patients with Staphylococcus aureus bacteremia
H. Ishaq, R. Ramesh* (Hyderabad, India), J. H. Kralove, Czech Republic, L. Baddour, M. Sauh, V. Baratharaj Palraj

8686 Osteomyelitis in sickle cell adults: descriptive study in a high-income country
C. Pierre-Louis* (Saint-Mandé, France), O. Steichen, A. Santin, C. Bachmeyer, P. M. Bappe, F. Lionnet, S. Mattioni

8694 Performance of EUCAST’s rapid antibiotic susceptibility testing on sterile body fluids in blood culture bottles
S. Zimmermann* (Heidelberg, Germany), J. Jasuja, I. Burckhardt

8715 Perioperative administration of cefepime-daptomycin combination during prosthetic joint replacement is associated with high bone and synovial concentrations

8893 Risk factors for amputation in diabetic foot infections
T. Demirdal* (Izmir, Turkey), P. Sen

9021 Acinetobacter baumannii-complex related osteomyelitis
P. Oliveira* (Sao Paulo, Brazil), E. Saconi, V. Carvalho, J. Silva, A. Munhoz

9119 Cotrimoxazole in bone and joint infections is the “old” antibiotic still relevant
M. Baroud, P. Seng* (Marseille, France), A. Stein

9429 Diabetic foot osteomyelitis: an epidemiological retrospective analysis in a Portuguese university hospital
A. Cipriano* (Loulé, Portugal), D. Guerra, M. Abreu, A. Carvalho, M. Matos Dias Reis

Session accepted as Paper Poster Session
BSI: new spectrum, new data

Misuse of tampons and menstrual toxic shock syndrome in France: a community-based case-control study
A. Billon, M. Gustin, A. Tristan, C. Gustave, P. Vanhems, G. Lina* (Lyon, France)

Daptomycin decreased mortality in methicillin-resistant Staphylococcus aureus bacteremia compared to vancomycin: a monocentric retrospective study of 96 cases
A. Froment, R. Guiheneuf, C. Mobille, J. Lanoix* (Amiens, France)

Focus on nuclear imaging and other complementary exams for bacteremia in early post-operative cardiac surgery
M. Thy* (Paris, France)

Efficacy and safety of cefazidime-avibactam in adults with Gram-negative bacteremia from five phase III randomised clinical trials

Can we use sepsis scores to predict bacteremia in the elderly?
S. Subbarao* (London, United Kingdom), S. Subba Rao, M. Andrews, Y. Milner, C. Nicitiogortaigh

Rising incidence and mortality of bloodstream infections in Finland: a nation-wide population-based study during 2004–2018
K. Kantula* (Helsinki, Finland), K. Skogberg, J. Ollgren, O. Lyytikainen, A. Järvinen
Impact of positive blood culture occurring in early post-operative cardiac surgery: a retrospective study  

Ceftaroline fosamil for the treatment of methicillin-resistant Staphylococcus aureus bacteraemia: a real-world comparative clinical outcomes study  
J. Hammond, M. Benigno, R. Chambers, N. Patino, W. Ansari* [New York, United States], J. Nguyen

Escherichia coli bloodstream infections: a multinational population-based perspective  
M. Mackinnon* [Guelph, Canada], S. McEwen, O. Lytikainen, G. Jacobsson, P. Callignon, D. Gregson, K. Laupland

Clinical features and outcomes of patients with Staphylococcus aureus bacteraemia of unknown origin  
E. Minejima, E. Chan* [Los Angeles, United States], K. Tan, C. Kelsom, P. Nieberg, A. Wong-Beringer

Early-onset of bloodstream infections in a burn unit  
S. Scabini* [Turin, Italy], A. Pensa, S. Mornese Pinna, C. Filippini, A. Curtoni, M. Stella, F. De Rosa, S. Corcione

Comparative effectiveness of empiric antistaphylococcal penicillins versus cefazolin in methicillin-susceptible Staphylococcus aureus bacteraemia  
J. Cusumano* [Warwick, United States], H. Appaneal, V. Lopes, K. Laplante, A. Caffrey

Outcomes of bacteraemic and non-bacteraemic patients presenting to the emergency department  
R. Sparks* [Neutral Bay, Australia], R. Chavada, C. Trehewy, A. Harada

Antibiotic combination versus monotherapy for the treatment of Pseudomonas aeruginosa bacteraemia: a multi-centre retrospective study  

The relationship between clinical outcomes and empirical antibiotic therapy in patients with community-onset Gram-negative bloodstream infection: a cohort study from a large teaching hospital  
A. Aryee* [London, United Kingdom], P. Rockenschaub, M. Gill, A. Hayward, L. Shallcross

Predictors of 30-day mortality rate in patients with Pseudomonas aeruginosa bacteraemia  
W. Rose* [Madison, United States], L. Bagnell, L. Pazniak, L. Schulz

Short-term and long-term mortality rates among patients with bloodstream infections receiving appropriate antibiotic therapy: a multi-centre, prospective cohort study  

Enterococcal bacteraemia: epidemiology, clinical characteristics and causes of inappropriate treatment  

Sepsis-3: a prospective clinical study of the clinical diagnosis and blood culture performance  

Risk factors for mortality, intensive care unit admission, and bacteraemia of patients admitted with suspected infection in the emergency department  
V. D’Onofrio* [Genk, Belgium], A. Meersman, S. Vijgen, P. Messiaen, R. Cartuyvels, I. Gysens

Community-Acquired Bacteraemia (CAB) in senior adults: risk factors, outcomes and correlation with frailty  
S. Ahmed* [Leeds, United Kingdom], D. Kehlenbeck, S. Yaseen, G. Saigad, J. Minton

Central nervous system infections

Determination of pentraxin 3 levels in cerebrospinal fluid during central nervous system infections  
M. Zatta* [Trieste, Italy], S. Di Bella, B. Bottazzi, F. Rossi, L. Segat, P. D’Agoara, M. Fabbiani, A. Montovani, R. Luzzati

Multiplex detection of meningitis and encephalitis pathogens: a study from laboratory to the clinical  
Y. Zhou* [Chengdu, China], W. Min Jin, T. Wu, S. Guo, Z. Meng, T. Wu, B. Ying

Clinical utility of syndromic meningitis/encephalitis testing in children  
R. Yee* [Los Angeles, United States], U. Pandey, C. Holifield, J. Flores, M. Fahit, S. Naccache, J. Dien Bard

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1884 Viral meningitis in adults: what are we missing? The use of viral capture sequencing to detect pathogens in the cerebrospinal fluid of adults with meningitis

2484 Encephalitis in elderly patients in France, 2016-2019
A. Mailles* [Saint-Maurice, France], M. Martinot, E. Piet, C. Biron, G. Amandin, G. Isabelle, X. Argemi, S. Patrat-Delon, J. Stahl

2642 Unexpectedly high false positive Haemophilus influenzae rates using a meningoencephalitis syndromic PCR panel in two tertiary centres

2842 Cerebrospinal fluid metabolomics profile in herpes virus type 1 encephalitis
A. Mastrangelo* [Campobasso, Italy], D. Franciotta, C. Preziosi, [Rome, Italy], M. Zingaropoli, M. Iannetta

3282 Monitoring enterovirus human infections in Italy: molecular analysis of two recent outbreaks due to Echovirus 30
S. Fontana* [Rome, Italy], D. Franciotta, C. Preziosi, [Rome, Italy], M. Zingaropoli, M. Iannetta

3550 Monitoring enterovirus human infections in Italy: molecular analysis of two recent outbreaks due to Echo virus 30
S. Fontana* [Rome, Italy], D. Franciotta, C. Preziosi, [Rome, Italy], M. Zingaropoli, M. Iannetta, D. Rodio, M. Altieri, A. Conte, V. Vullo, M. Ciardi, A. Polamarà, V. Pietrapaola

3813 Comparison of three commercial sample-to-result platforms to an established real-time PCR assay for the detection of herpesviruses in cerebrospinal fluid
R. Schuurman, E. Fries* [Utrecht, Netherlands], S. Safak, N. Plantinga

5015 Human parechovirus 3 “outbreak” at a tertiary hospital
M. Urrutikoetxea-Gutierrez* [Bilbao, Spain], M. Imaz Perez, B. Elgoibar Alvarez, J. Remerentiera Radigales, M. Cabreroz, J. Diaz De Tuesta

5527 Do we really have to worry about acyclovir-induced nephrotoxicity?
I. Hasanoglu* [Ankara, Turkey], A. Kaya Kalem, B. Kayaaslan, Z. Atlay Alttinkaynak, R. Guner

5742 Profile of neurological manifestations related to varicella zoster virus reactivation

5786 The frequency and clinical implications of Epstein-Barr virus DNA in the cerebrospinal fluid of immunocompetent and immunodeficient patients diagnosed with meningoencephalitis
N. Papic* [Zagreb, Croatia], J. Begovac, A. Vince, S. Zidovec Lepej

6243 Characteristics and outcome of acute viral encephalitis in an infectious disease unit
S. Hela* [Kalaat Sghira, Tunisia], M. Wafa, I. Kooli, A. Toumi, A. Aouam, M. Chakroun

6612 Rapid syndromic panel for the diagnosis of infectious meningitis and encephalitis: a systematic review and meta-analysis of accuracy
G. Menchinelli* [Rome, Italy], B. Posteraro, M. Sanguevetti, T. Spanu, G. De Angelis

68 61 Two-year experience of meningitis/encephalitis multiplex PCR assay on cerebrospinal fluids in comparison with conventional methods: advantages and disadvantages
A. Calderaro, M. Butrini, M. Martinelli* [Parma, Italy], S. Montecchini, S. Covari, A. Ruggieri, M. Antonaci, F. Casula, M. Dell'Anna, S. Larini, F. Ferraglia, F. Pinardi, M. Montagna, M. Arcangeletti, F. De Cona, C. Chezzi

7032 Rapid syndromic panel for the diagnosis of infectious meningitis and encephalitis: a systematic review and meta-analysis of accuracy
G. Menchinelli* [Rome, Italy], B. Posteraro, M. Sanguevetti, T. Spanu, G. De Angelis

7283 Two-year experience of meningitis/encephalitis multiplex PCR assay on cerebrospinal fluids in comparison with conventional methods: advantages and disadvantages
A. Calderaro, M. Butrini, M. Martinelli* [Parma, Italy], S. Montecchini, S. Covari, A. Ruggieri, M. Antonaci, F. Casula, M. Dell’Anna, S. Larini, F. Ferraglia, F. Pinardi, M. Montagna, M. Arcangeletti, F. De Cona, C. Chezzi

7576 Performance of the rapid molecular assay BioFire FilmArray Meningitis/Encephalitis for the diagnosis of CNS infections: a one-year evaluation in a tertiary care hospital
G. Opota* [Lausanne, Switzerland], Z. Naseri, R. Brouillet, L. Senn, G. Prad’Hom, G. Greub, K. Jatan

7822 Does tigecycline have a place in therapy for rickettsial infections of the central nervous system?
A. Mastroianni* [Cosenza, Italy], G. Guadagnino, S. Greco, V. Vangeli, S. De Santis, G. Apuzzo

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F. Hamilton* [Bristol, United Kingdom], D. Arnold, W. Henley, R. Payne

9463 Evaluation of on-site polymerase chain reaction technology for cerebrospinal fluid samples at Cork University Hospital versus referral to reference laboratories in suspected cases of meningitis or encephalitis
W. Henley, R. Payne

9544 Using a syndromic meningitis/encephalitis panel in children without cerebrospinal fluid pleocytosis
W. Henley, R. Payne

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W. Henley, R. Payne

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V. Baskaran* [Nottingham, United Kingdom], W. Lim, T. Mckeever

193 Antimicrobial susceptibility of Streptococcus pneumoniae strains, isolated from children carriers after PCV10 in Bulgaria
M. Malcheva* [Sofia, Bulgaria], I. Simeonovski, K. Vladeva, T. Kostadiev

235 Effects of previous antibiotic exposure on the clinical course of pneumonia in the elderly: a single-centre prospective observational study
S. Surme, I. Balkan, O. Bayramlar, R. Kara Ali, R. Mete, G. Can, F. Tabak, N. Saltoglu* [Istanbul, Turkey]

652 Correlation between serum C-reactive protein levels and CURB-65 in elderly patients with community-acquired pneumonia
W. Nseir* [Poriya, Israel], A. Amara, R. Farah, T. Saidahmad

The optimal strategy of empirical antibiotic therapies for non-severe community-acquired pneumonia: a bayesian network meta-analysis of randomised controlled trials
J. Lee, S. Moon* [Jeju, South Korea]

1578 Aspirin reduces cardiovascular events in patients with pneumonia: a prior events rate ratio analysis in a large primary care database
F. Hamilton* [Bristol, United Kingdom], D. Arnold, W. Henley, R. Payne

1591 Impact of a multiplex PCR in the management of viral meningitis
G. Pean De Poncelet* [Paris, France], A. Chauvin, H. Benmansour, E. Lecoreche, F. Mougari, A. Munier, S. Temim, J. Le Goff, E. Cambou, H. Jacquier

937 The optimal strategy of empirical antibiotic therapies for non-severe community-acquired pneumonia: a bayesian network meta-analysis of randomised controlled trials
J. Lee, S. Moon* [Jeju, South Korea]

925 Challenges in the management of community-acquired pneumonia

1936 Borderetella holmesii in suspected cough: a frequent pathogen?
S. Trombert Paolantonio* [Saint Ouen L’auomme, France], S. Guillot, S. Briese, J. Toublanc

9135 Centre experience. Pneumonia: a prior events rate ratio analysis in a large primary care database
F. Hamilton* [Bristol, United Kingdom], D. Arnold, W. Henley, R. Payne
2005 Single-shot azithromycin in treatment of *Legionella pneumophila*: 18-year experience at the Vienna General Hospital, Austria

M. Karer* [Vienna, Austria], M. Kussmann, M. Obermüller, H. Burgmann, H. Lagler

2253 Prevalence and clinical characteristics of *Mycoplasma pneumoniae* in Navarra [Spain], 2014-2018

Á. Ana Isabel, A. Navascués Ortég, A. Aguinaga Perez, J. Castilla Catalan, C. Ezpeleta Baquedano* (Pamplona, Spain)

2342 Comparative effectiveness of macrolides, fluoroquinolones or combination therapy for the treatment of Legionnaires’ disease in the US Department of Veterans Affairs health system

V. Stevens* [Salt Lake City, United States], S. Gamage, A. Jasper, G. Roselle, N. Safdar

2364 In vitro activities of ceftaroline and comparator agents against bacterial pathogens frequently causing community-acquired respiratory tract infections in patients from Latin America: ATLAS surveillance programme 2016-2018

J. Karlowsky, M. Hackell* [Schaumburg, United States], S. Bouchillon, G. Stone, D. Sahm

2390 High burden and undetected clusters of pneumococcal disease in long term care in Ontario, Canada

A. Mcgee* [Toronto, Canada], W. Rudnick, W. Demczuk, W. Gold, I. Kitai, S. Kjærden, R. Lovinsky, I. Martin, M. Muller, J. Powis, N. Rau, G. Tyrell, A. Simor, I. Tibdin

2395 Shorter duration of antibiotic therapy in super-infection pneumopathy occurring in viral infection

S. Bessis* [Paris, France], M. Trichet, A. Beresteau, A. Matt, B. Davido, A. Dinh

2517 Surveillance for epidemic of *Mycoplasma pneumoniae* and macrolide resistance [A2063G and A2064G] using consecutive multiplex real-time PCR in Korea

K. Roh* [Goyang, South Korea], J. Park, Y. Yang, Y. Kim, H. Lee, S. Hong

2551 Ceftaroline for severe community-acquired pneumonia: a real-world two-centre experience in Italy and Spain

M. Bassetti, A. Russo* [Pisa, Italy], C. Cilloniz Campos, D. Giacobbe, A. Vena, R. Amaro, E. Graziano, A. Sorião, A. Torres

2600 Concordance of early and late endpoints for community-acquired bacterial pneumonia (CAP) trials

S. Bart* [Silver Spring, United States], S. Nambiar, R. Gopinath, D. Rubin, J. Farley

2753 Methicillin-susceptible *Staphylococcus aureus* in community-acquired pneumonia: risk factors and outcomes

C. Cilloniz Campos* [Barcelona, Spain], E. Moreno, C. Domíneñ, D. García Vidal, C. Vargas, A. Gabarrus, J. Becerrí, C. Cardozo, D. Tovar, A. Torres

2806 Incidence and risk of hospitalised pneumococcal pneumonia among Catalonian adults with distinct underlying medical conditions

O. Ochoa-Gondar* [Tarragona, Spain], A. Vila-Córrcoles, I. Hospital-Guardiola, A. Vila-Rovira, C. De Diega, E. Satue

Antibiotic treatment for paediatric outpatients with community-acquired pneumonia: findings from 10 years of prescribing habits in Italy

P. Costenaro* [Marostica, Italy], A. Cantarutti, E. Barbieri, A. Scamarcio, A. Diletto, P. Sacerdotti, R. Lundin, L. Cantarutti, C. Giaquinto, D. Dana

Pneumococcal serotypes distribution in older adults hospitalised with CAP using the UAD Test (The CAPA study)


Evolution of pneumococcal serotypes causing CAP in adults by co-morbidities in Spain using the UAD test (the CAPA study)

P. España, R. Menendez, A. Torres* [Barcelona, Spain], J. Fernández Villar, J. Marimon, A. Martínez De La Fuente, J. López-Hontangas, F. Marco Reverte, F. Vassalo Vidal, M. Ercibengoa, I. Cifuentes, C. Méndez

Effectiveness of the 23-valent pneumococcal polysaccharide vaccine against vaccine serotype pneumococcal pneumonia in adults


Serotype, antimicrobial resistance and virulence profile of invasive *Streptococcus pneumoniae* isolates in a nation-wide surveillance study in Lebanon

L. Reslon* [Beirut, Lebanon], S. Khafaja, M. Moumneh, M. Finianos, M. Darwish, C. Boutros, A. Araij, G. Matar, G. Dbaibo

Accuracy of emergency department diagnosis of community-acquired pneumonia

A. Bloch* [Brunswick, Australia], V. Sundarajan, G. Wawryzk, A. Siddiqui, A. Attreya, K. Visvanathan

If breaking a hip feels like a concern for the elderly, then getting pneumonia should be twice as concerning!

L. Grammatico-Guillón* [Tours, France], H. Coralie, C. Gaborit, J. Mizgerd, A. Guillon

The effect of live attenuated influenza vaccine on pneumococcal colonisation densities among children aged 24-59 months in Gambia

Abstract Categories 2020

3995 Legionella pneumophila sqPCR in serum and respiratory samples as a marker of Legionnaires’ disease severity
C. Allam* [Lyon, France], N. Fessy, C. Ginevra, L. Beraud, J. Chastang, F. Ader, G. Descours, S. Jarraud

4257 Burkholderia spp. and Gram-negative non-fermenters in cystic fibrosis patients in Belgium: 2012-2018
F. Echahidi, C. Peetters, E. De Canck, I. Wybo, D. Pierard* [Brussels, Belgium], P. Vandamme

4441 Resistance trends among the common bacterial causes of community-acquired lower respiratory tract infection in the UK and Ireland, 2008-2018
C. Horner* [Birmingham, United Kingdom], S. Mushtaq, D. Livermore

4505 Invasive pneumococcal disease in the Comunidad Valenciana, Spain, 2011-2019
M. Garrido Jareño* [Valencia, Spain], A. Gil Brusala, N. Lozano Rodríguez, O. Sabalza, J. Frasquet, J. López-Hontangas

4684 Population-based incidence and mortality of community-acquired pneumonia in Germany

5355 Nocardia infection over 10 years (2008-2019) in a Greek tertiary university hospital
E. Kalogeropoulou, F. Kontas* [Athens, Greece], S. Damianidou, P. Tsilikis, K. Orlandou, B. Basilopoulou, P. Vorda, M. Kostoula, S. Pournaras

5702 An audit of community-acquired pneumonia antimicrobial compliance using a mobile audience response system (ARS) care bundle in an Irish hospital
B. O’Kelly* [Dublin, Ireland], M. Regan, A. Rueda Benito, K. Finan

5836 Evaluation of the clinical economic efficacy of the antibiotic therapy of inpatients with community-acquired pneumonia
A. Demchuk* [Vinnytsia, Ukraine], Y. Mostovoy

5869 Does herd immunity from conjugate vaccines alter the epidemiology of invasive pneumococcal disease in adults?

6444 Persistence of serotype 19F and the importance of non-vaccine serotypes in paediatric non-invasive pneumococcal pneumonia in Portugal: 2015-2018
C. Silva-Costa, J. Gomes-Silva, M. Ramírez* [Lisbon, Portugal], J. Melo-Cristino

6450 Impact of recent vaccine schedule changes on pertussis epidemiology in France

6480 Improving antibiotic prescribing for community-acquired pneumonia in resource-limited settings: pilot implementation of quality standards in a provincial hospital in northern Vietnam
N. Do* [Hanoi, Vietnam], R. Li, H. Dinh, H. Nguyen, M. Dao, T. Nghiem, B. Nadjin, N. Luong, T. Cao, D. Le, F. Cluzeau, C. Ngo Ouy, H. Chu, Q. Vu, C. Roberts, H. Rogier Van Doorn

6577 Epidemiology of serotypes of Streptococcus pneumoniae in patients older than 18 years in Russia
R. Kozlov* [Smolensk, Russian Federation], A. Muraviy, A. Chagaryan, A. Kurkova, N. Ivanichik

7041 Trends in invasive pneumococcal disease in Italy, 2010-2018

7644 An extreme chain reaction-based multiplex assay for detection of group A/C/G streptococci directly from throat swab specimens
L. Gong* [Ann Arbor, United States], B. Keusch, M. Olson, M. Carey, A. Ripley, B. Green, D. Kolk, M. Mastronardi, B. Wu, S. Brahmasandra

7655 Aging influences effector functions of neutrophil granulocytes in Pseudomonas aeruginosa lung infection
S. Charline, N. Cramer, L. Müller, D. Danov* [Hannover, Germany], B. Tümmers, A. Braun, K. Sewald, C. Brandenberger, S. Dehmel, S. Wranski
8012 Prevalence of *Mycoplasma pneumoniae* infections during six years (2014-2019) in two hospitals of Saint Petersburg
O. Kameneva, S. Morazova, N. Kameneva, V. Zhukova, K. Kasyakova* (Saint Petersburg, Russian Federation)

8030 The role of procalcitonin as a predictor of severity, prognosis and appropriate empirical antibiotic therapy in community-acquired pneumonia of bacterial aetiology
A. Milia* (Florence, Italy), L. Suardi, C. Nazzoli, F. Pieralli

8393 Impact of the use of C-reactive protein in micro-methods on the prescription of antibiotics in case of suspected respiratory infection in children and adults in ambulatory care in France
R. Touitou, C. Levy, S. Béchet, E. Pinto, A. Laplante, J. Lion-Altmayer, B. Trincard, C. Jung, R. Cohen* (Créteil, France)

8506 Excessive antibiotic use and costs in hospitalised adults with chronic heart failure
O. Zorya, S. Rachina* (Moscow, Russian Federation), A. Babylev, G. Hewathanthirige

8697 Treatment outcome and clinical characteristics of patients with community-acquired pneumonia treated in an infectious disease intensive care unit
M. Popovic* (Zagreb, Croatia), R. Novak, M. Kutlesa, M. Santini, B. Barșić, V. Krajinovic

8875 New trends in microbial aetiology of severe community-acquired pneumonia in intensive care unit
A. Chillek* [Nîmes, France], C. Paris, R. Stephan, C. Roger, S. Barber, J. Lefrant, H. Marchandin, J. Lavigne, L. Muller

8990 Severe community-acquired pneumonia in the Czech Republic
H. Bartos* [Usti nad Labem, Czech Republic], O. Drupova

9104 Secretion of TNFα by human macrophages is dependent of the sequence type of clinical *Legionella pneumophila* isolates
J. Guillomet* [Villeurbanne, France], C. Ginevro, P. Doubet, A. Chapalain, S. Jarraud

9681 Levels of evidence supporting European and American community-acquired pneumonia guidelines
J. Ferreira Freitas Caímbraga* [Porto, Portugal], S. Tejada Magraner, L. Campogiani, J. Rello

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**Session accepted as Paper Poster Session**

### Diagnosis of tuberculosis and drug resistance

**1699**
One day detection of live *Mycobacterium tuberculosis* from sputum by measuring heat-induced MT64 secretion with ultra-sensitive ELISA
R. Takeuchi* [Izunokuni-shi, Japan], W. Wang, S. Jain, Y. Jiang, S. Watanuki, Y. Ohtaki, K. Nakaiishi, S. Watabe, P. Lu, E. To

**1725**
Interim analysis: a large-scale clinical evaluation of QMAC-DST for rapid drug susceptibility testing of *Mycobacterium tuberculosis*
K. Seok, S. Kim* [Seoul, South Korea], J. Na, S. Lee, E. Jo, H. Kim, D. Kim, S. Kwon

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**1902** Application of matrix-assisted laser desorption ionisation: time of flight mass spectrometry for *Mycobacterium tuberculosis* Beijing and Non-Beijing genotyping
F. Yi* (Chengdu, China)

**2125**
Evaluation of the cobas MTB and MTB RIF/INH assays on samples from Sierra Leone and Germany at a supranational reference laboratory for tuberculosis serving both low-incidence and high-burden settings
D. Nadarajan* [Sülfeld, Germany], D. Sievert, M. Kernbach, R. Kamara, L. Faray, M. Merker, A. Kuchta, J. Lau, M. Njoga, S. Krishnamurthy, A. Witt, K. Kranzer, F. Maurer

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**2347**
Evaluating the effectiveness of current microbiological tools on time to diagnosis of pulmonary tuberculosis
D. Umerah* [Leicester, United Kingdom], H. Patel, R. Verma, N. Perera, M. Barer, G. Woltmann, P. Haldar

*New research, novel approaches and new diagnostic tools: methods for rapid and accurate detection of antibiotic resistance in *Mycobacterium tuberculosis***

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**2588**
A novel standardised artificial sputum for external quality control of the whole TB-diagnostic workflow
M. Beutler* [Gauting, Germany], U. Antonenko, F. Gerbl, M. Mihalic, S. Plesnik, E. Ramancenco, S. Hofmann-Thiel, H. Hoffmann

**2612**
Multiplex detection of SNPs conferring rifampicin resistance in *Mycobacterium tuberculosis*
F. Nazé* [Gembloux, Belgium], B. Gicquel, P. Mertens, L. Avrain

**3111**
Head-to-head comparison of analytical sensitivities of BD MAX MDR-TB, Xpert MTB/Rif Ultra and FluoroType MTB using human and artificial sputum
M. Beutler* [Gauting, Germany], S. Plesnik, M. Mihalic, L. Olbrich, N. Heinrich, S. Schumacher, M. Lindner, I. Koch, W. Grasse, C. Metzger-Boddien, S. Hofmann-Thiel, H. Hoffmann

**3335**
Contaminating microflora during examination for tuberculosis: saprophytes or potential pathogens?
A. Lyamin* [Samara, Russian Federation], D. Ismatullin, A. Zhestkov, A. Kovalyov, T. Persiyantseva, D. Davydova, A. Kozlov

**3381**
Clinical evaluation of a cartridge-based DNA extraction method for the whole molecular TB-diagnostic workflow
M. Beutler* [Gauting, Germany], M. Mihalic, S. Plesnik, A. Homann, N. Paust, M. Eckart, V. Allerheiligen, D. Czurratis, B. Maharjan, B. Shrestha, S. Hofmann-Thiel, H. Hoffmann

**3630**
DNA thermo-protection facilitates whole genome sequencing of mycobacteria direct from clinical samples by ONT MinION

Analyzing of analytical performances of the new MDR/MTB ELItē MGB kit for the detection of *Mycobacterium tuberculosis* complex and rifampicin- and isoniazid-associated mutations in comparison with the MTB ELItē MGB kit
S. Svraka-Latifovic* [Hilversum, Netherlands], L. Bakker, C. Timmerman, J. Dorgo-Zetsma
CRISPR-based rapid and ultra-sensitive diagnostic test for smear-negative or sputum-scarce tuberculosis using bronchoalveolar lavage fluid: a prospective, multi-centre study in China

N. Mvelase, K. Swe Swe Han

Evaluation of BD MAX multidrug-resistant tuberculosis assay for detection of Mycobacterium tuberculosis complex in clinical specimens and identification of genetic resistance markers

S. Hofmann-Thiel, S. Plesnik, M. Mihalic, M. Beutler, H. Hoffmann

Improved detection of acid-fast bacteria using an automated slide scanner with integrated deep learning analysis

L. Harvath, S. Haenselmann, H. Mannsperger, S. Degenhardt, K. Last, S. Zimmermann, B. Burchhardt

Evaluation of the performance of CSF pyrosequencing in the diagnosis of TB meningitis- a single-centre retrospective diagnostic accuracy study

K. Aljan, M. Kazi, U. Agrawal (Mumbai, India), R. Soman, A. Shetty, A. Sunavala, C. Rodrigues

MYCO-TB kit: rapid and efficient digestion and decontamination method for the detection of mycobacteria in extrapulmonary specimens

F. Bisognin, S. Felici, G. Lombardi, C. Vocale, G. Biundo, M. Re, P. Dal Monte

Identification and discrimination of Mycobacterium tuberculosis and Mycobacteroides abscessus complex species directly from Mycobacteria Growth Indicator Tube (MGIT) culture media by Orbitrap ultra high-resolution mass spectrometry

A. Bajaj, J. Freeke (Vantaa, Finland), M. Hutchins, B. Stiell, A. Barker

From DNA to diagnosis: a rapid, next-generation sequencing pipeline for detecting multidrug-resistant Mycobacterium tuberculosis mutations

L. Daum* (San Antonio, United States), M. Agonafir, J. Eicher, I. Wright, N. Wood, S. Travers, J. Rodriguez, B. Fourie, G. Fischer

Time to positivity for mycobacterial culture as a measurement of bacillary load in clinical practice

M. Jonsson Nordvall, A. Bornefall, V. Khald, B. Andersson, K. Niward, T. Schön

Routine use of genotype Genotype MTBDRsl assay on clinical samples in a high TB burden setting in South Africa: a descriptive analysis

K. Lutchminarain* (Durban, South Africa), A. Kajee, N. Mvelase, K. Swe Swe Han

Rapid simultaneous detection of TB and first line drugs gene mutations onto direct paediatric samples

C. Russo* (Rome, Italy), L. Gentile

Xpert MTB/RIF Ultra: multi-centre evaluation of result “TRACE” in tuberculosis diagnosis

S. Torri* (Milan, Italy), C. Farina, P. Cicera, A. Lombardi, F. Marini, E. Spata, F. Guerrieri, V. Ragnoni, C. Perna, E. Mazzola

Evaluation of Myco-TB kit for decontamination of urine and stool specimens to detect mycobacteria

R. Grossi* (Rome, Italy), A. Careddu, R. Nicotra, M. Sanguinetti, M. Sali

One-year evaluation of Genelead VIII combined to Deepex-MycTB to detect rapidly the genotype and the resistance profile of Mycobacterium tuberculosis complex directly from clinical samples


Performance assessment of MDR/MTB ELITE MGB Kit for tuberculosis diagnosis


Performance of XpertMTB/RIF Ultra assay on respiratory and extra-respiratory specimens in a high-resource setting with a low TB prevalence

C. Martín Higuera* (Madrid, Spain), M. Ruiz Serrano, C. Toro-Diez, M. Toto, M. Simon, D. Domingo, P. Lopez-Roa

The concordances of genotypic and phenotypic drug susceptibility testing of Mycobacterium tuberculosis isolates from MDR TB patients

C. Nelly* (Chisinau, Moldova), S. Alexandru, A. Codreanu, N. Turcan, E. Nistor, V. Vilc, A. Donica, E. Chesov, D. Chesov, V. Crudu

Direct detection of Mycobacterium tuberculosis complex in clinical specimens from patients in Norway by two different polymerase chain reaction tests

I. Szpinda* (Oslo, Norway), J. Kaur, M. Hagbø, S. Hamsund, D. Wold, T. Tanum
1517 Five versus seven days nitrofurantoin for urinary tract infections in women with diabetes: a non-inferiority study
K. Hendriks-Spoor* {Hilversum, Netherlands}, T. Ten Doesschate, F. Wille, T. Verheij, M. Bonten, C. Van Werkhaven

1717 The effectiveness of nitrofurantoin, fosfomycin and trimethoprim for cystitis in relation to renal function
T. Ten Doesschate* {Utrecht, Netherlands}, E. Van Haren, R. Wijma, B. Koch, M. Bonten, C. Van Werkhaven

2049 Antimicrobial treatment and treatment duration for urinary tract infections in adult males

4678 Clinical and bacteriological outcome in urinary tract infections caused by ESBL-producing Enterobacterales and characterisation of isolated pathogens: a prospective, multi-centre study
H. Montelin* {Uppsala, Sweden}, A. Camporeale, A. Hallgren, M. Voding, G. Giske, T. Tängdén

3255 The urinary pharmacokinetics of nitrofurantoin in patients with uncomplicated urinary tract infections: interim analysis
R. Wijma, B. Koch, T. Van Gelder, E. Van Haren, H. Karim, S. Croes, A. Muller* {The Hague, Netherlands}

7980 Examining the urinary tract infection patient journey to identify opportunities to enhance the role of community pharmacists
N. Peiffer-Smadja* {Paris, France}, R. Allison, L. Jones, D. Lecky, C. McNulty, R. Ahmad

Session accepted as Paper Poster Session
Emerging Gram-negative infections: from A to S

3132 Piperacillin-tazobactam versus carbapenem for the treatment of bloodstream infection caused by CTX-M-type ESBL-producing Enterobacteriaceae

3255 Comparison of pneumonia and bacteremia caused by Stenotrophomonas maltophilia: analysis of risk factors, clinical outcomes and impact on antibiotic resistance
W. Lee* {Taipei, Taiwan}, F. Chen

3516 Non-carbapenem beta-lactams for the treatment of Acinetobacter baumannii bacteremia: a multi-centre retrospective analysis
G. La Martire* {Paris, France}, V. Fihman, A. Galy, D. Le Puu, L. Nourissair, A. Lecapitaine, E. Canou, A. Munier, C. Richaud, R. Lepeule

5232 Use of N-acetylcysteine in critically ill patients with septic shock caused by carbapenem-resistant Klebsiella pneumoniae and Acinetobacter baumannii: a case-control study
A. Oliva* {Rome, Italy}, A. Bianchi, A. Russo, G. Cecarelli, F. Aloj, D. Alunni Fegatelli, C. Mastroianni, M. Venditti

7214 First case of osteomyelitis caused by hypervirulent Klebsiella pneumoniae spread within a family in Korea
J. Chae* {Seoul, South Korea}, C. Lee, W. Choe, H. Lee, Y. Sohn

7501 Surveillance culture-guided empirical therapy for febrile neutropenia: low prevalence of inappropriately treated Gram-negative bloodstream infections
J. De La Court* {Amsterdam, Netherlands}, J. Heijmans, J. Janssen, K. Sigaloff, R. Schade

8089 Ceftazidime-avibactam monotherapy for 7 days as treatment of KPC carbapenemase-producing Enterobacteriaceae bacteremia in severely immunosuppressed patients

8729 Differences in clinical characteristics and prognosis of patients with AmpC-producing Enterobacteriaceae versus Escherichia coli bloodstream infection

Session accepted as 2-Hour Oral Session
Endocarditis: what’s new?

2898 One-stage extraction and replacement of infected cardiac implantable electronic devices

3049 Does early de-escalation to anti-staphylococcal beta-lactams impact the duration of bacteremia in patients with methicillin-susceptible Staphylococcus aureus endocarditis?
M. Wungwattana* {Portland, Maine, United States}, M. Mangino, G. Ben, P. Stogsdill, A. Casapao

3150 Clinical and epidemiological characteristics of infective endocarditis with negative blood cultures: a multi-centre case-series in the south of Spain
L. Suardi* {Florence, Italy}, L. Lopez-Cortes, L. Rafael, J. Ruiz Morales, A. Plata Ciezar, J. De La Court* {Amsterdam, Netherlands}, J. Heijmans, A. Mugimura, A. Casapao

3678 First case of osteomyelitis caused by hypervirulent Klebsiella pneumoniae spread within a family in Korea
J. Chae* {Seoul, South Korea}, C. Lee, W. Choe, H. Lee, Y. Sohn

5232 Use of N-acetylcysteine in critically ill patients with septic shock caused by carbapenem-resistant Klebsiella pneumoniae and Acinetobacter baumannii: a case-control study
A. Oliva* {Rome, Italy}, A. Bianchi, A. Russo, G. Cecarelli, F. Aloj, D. Alunni Fegatelli, C. Mastroianni, M. Venditti

5728 Surveillance culture-guided empirical therapy for febrile neutropenia: low prevalence of inappropriately treated Gram-negative bloodstream infections
J. De La Court* {Amsterdam, Netherlands}, J. Heijmans, J. Janssen, K. Sigaloff, R. Schade

6442 Ceftazidime-avibactam monotherapy for 7 days as treatment of KPC carbapenemase-producing Enterobacteriaceae bacteremia in severely immunosuppressed patients

7192 Differences in clinical characteristics and prognosis of patients with AmpC-producing Enterobacteriaceae versus Escherichia coli bloodstream infection

8089 First case of osteomyelitis caused by hypervirulent Klebsiella pneumoniae spread within a family in Korea
J. Chae* {Seoul, South Korea}, C. Lee, W. Choe, H. Lee, Y. Sohn

8220 Surveillance culture-guided empirical therapy for febrile neutropenia: low prevalence of inappropriately treated Gram-negative bloodstream infections
J. De La Court* {Amsterdam, Netherlands}, J. Heijmans, J. Janssen, K. Sigaloff, R. Schade

8729 Ceftazidime-avibactam monotherapy for 7 days as treatment of KPC carbapenemase-producing Enterobacteriaceae bacteremia in severely immunosuppressed patients

9445 Differences in clinical characteristics and prognosis of patients with AmpC-producing Enterobacteriaceae versus Escherichia coli bloodstream infection
Comparative outcomes of cefazolin versus anti-staphylococcal penicillins for treatment of methicillin-susceptible Staphylococcus aureus endocarditis: a prospective multi-centre cohort study
R. Lecomte* [Nantes, France], A. Bourreau, D. Colin, N. Issa, P. Le Tourneur, B. Gabarit, M. Chauveau, T. Le Tourneur, N. Asseray Madani, F. Raffi, F. Camou, D. Boutaille

Anaemia is associated with mortality in patients with left-sided endocarditis: a POET sub-study
M. Pries-Heje* [Copenhagen, Denmark], N. Ihlemann, N. Bruun, E. Fosbøl, N. Tønder, C. Moser, K. Iversen, H. Bundgaard

Mural endocarditis from a prospective national registry: the GAMES series

Analysis of the practices of the multidisciplinary consultation meeting on infectious endocarditis
L. Sauvat* [Clermont-Ferrand, France], M. Rosburger, A. Mulliez, F. Rabin, M. Farhat, G. Clerfond, M. Vidal

Contrast-enhanced ultrasound for the detection of abdominal complications in infective endocarditis

Early experience with percutaneous vegetation suction (Penumbra) versus valve replacement surgery for right-sided infective endocarditis in people who inject drugs
M. Veve* [Knoxville, United States], Y. Akhtar, P. McKeown, M. Morelli, R. Shorman

Impact of referral bias on prognostic assessment in infective endocarditis: insights from a population-based cohort
M. Collannaz* [Vandoeuvre Les Nancy, France], M. Erpelding, F. Alla, F. Goethring, F. Delahaye, B. Jung, V. Le Moing, B. Hoen, C. Selton-Suty, N. Agrinier

Kingella endocarditis in children: a distinct entity or not?

External validation of the NOVA and DENOVA scores for clinical prediction of endocarditis in patients with Enterococcus faecalis bacteremia
P. Danneels* [Angers, France], F. Chabrun, A. Beaudron, C. Riher, C. Vannier, M. Kempf, V. Dubee

Clinical and microbiologic factors associated with infective endocarditis among patients with Staphylococcus aureus bacteremia
M. Papadimitriou Olivergeris* [Lausanne, Switzerland], P. Monney, C. Ting, C. Soldini, N. Ciocca, S. Giulieri, B. Guery

Clinical and echocardiographic predictors of embolism in infective endocarditis
M. Papadimitriou Olivergeris* [Lausanne, Switzerland], C. Ting, C. Soldini, N. Ciocca, M. Kirsch, S. Giulieri, B. Guery, P. Monney

Delayed diagnosis of infective endocarditis: retrospective analysis conducted at an university hospital in the south of Italy
A. Spera* [Salerno, Italy], R. Benveniga, G. Galasso

Clinical experience of dalbavancin in infectious endocarditis: stratifying its impact on treatment

 Infective endocarditis in older adults: distinguishing features

Haemodialysis-associated infective endocarditis

Challenges in infective endocarditis: valvular infective endocarditis in patients with cardiac implantable electronic devices: clinical characteristics and outcome: analysis on a national cohort

Clinical features of late prosthetic valve endocarditis in a cardiac referral centre [2006-2019]
L. Ribeiro-Da-Silva, L. Lemos, M. Correa, D. Menezes, J. De Andrade, R. Garrido, B. Zappa, G. Barbosa, C. Weksler, W. Golebiowski, C. Lamas* [Rio de Janeiro, Brazil]

A multi-national study for the treatment of enterococcal endocarditis with ampicillin-daptomycin combination therapy
M. Sierra Hoffmann, R. Deliz, A. Sekhon* [Tamball, United States], A. Gollapalli, K. Saddler, M. Stevens, M. Castro-Lainez, J. Pericas

Risk factors for in-hospital mortality in a prospective contemporary cohort of adult patients with infective endocarditis in a cardiac surgery hospital
Cardiac 18F-fluorodeoxyglucose Positron Emission Tomography (18-F-FDG-PET/CT) use in infective endocarditis: a 10-year multi-centre cohort study

Abstract Categories 2020

5491  Definite prolonged antibiotic treatment in complicated prosthetic valve endocarditis with absolute contraindication to surgery: a single-centre retrospective analysis
N. Cesta* [Grottaglierata, Italy], T. Mulas, V. Malagnino, M. Iannetta, M. De Masi, G. Ruvolo, M. Andreoni, L. Sarmati

5613  Short- and long-term outcomes of infective endocarditis admission in adults: a population-based registry study in Finland
E. Ahtela* [Turku, Finland], J. Oksi, T. Vahlberg, P. Routava, J. Sipilä, V. Kyto

5652  Predictive value of sepsis scores for in-hospital mortality in patients with left-sided infective endocarditis
B. Leal De Almeida* [Sao Paulo, Brazil], T. Strabelli, M. Sammer Bittencourt, A. Mansur, M. Ribeiro Fuxiao, L. Zoboli Posebon, D. M. Gualandra, F. Goldeberg, R. Focaccia Siciliano

5673  Examining the modified Duke criteria in infective endocarditis: a comparison of outcomes for ‘typical’ and ‘atypical’ bacteria
R. Mehta* [London, United Kingdom], P. Pabari, A. Hartley, Y. Razvi, B. Rana, A. Ghazy, M. Shehata, A. Abbara

7251  Epidemiology, characteristics and outcomes of bacteraemia and endocarditis caused by Staphylococcus aureus in cancer patients

7511  Impact of the anti-coagulant therapy before hospitalisation on cerebrovascular complications and mortality in infectious endocarditis
J. Solera Rallo* [Madrid, Spain], F. Galván Román, L. Domínguez Pérez, S. De Cossio Tejida, F. Lopez-Medrano

8072  Daptomycin or vancomycin for methicillin-resistant Staphylococcus aureus infective endocarditis complicated by septic pulmonary emboli
L. Vuong, T. Trinh* [San Francisco, United States]
Abstract Categories 2020

2166 Risk factors of severe dehydration among children under five
A. Mkhaygan* [Yerevan, Armenia], A. Demirchyan

2513 Role of enteropathogenic Escherichia coli in people with diarrhoea in Gipuzkoa
M. Gómez Ruiz De Arbulu* [Salvatierra, Spain], P. Vallejo Recuna, M. Arrasti Erviti, D. Grandioso Vas, T. Martín Peñaranda, M. Alkorta Gurutxaga

3126 Heat wave-associated Vibrio infections in Germany 2018 and 2019
T. Brehm* [Hamburg, Germany], L. Berneking, H. Rohde, M. Christner, S. Schmiedel

3276 Characterisation of prevalence and resistance of Aeromonas isolated from patients with acute diarrhoea in Zhejiang province from 2010 to 2017
X. Chen* [Hangzhou, China], W. Ruoran, Z. Diaoqun

3473 Prevalence and genetic characterisation of Shiga toxin-producing Escherichia coli isolates from cattle in Portugal
H. Oliveira* [Braga, Portugal], A. Balem, S. Gonçalves, I. García-Meniño, S. Flament-Simon, J. Blanco Alvarez, C. Pinto, J. Blanco, G. Almeida, C. Almeida

3474 A case of recurrent Campylobacter cured by faecal microbiota transplant in an immunosuppressed patient with common variable immune-deficiency

4173 The frequency of diarrhoeagenic Escherichia coli isolates in children with acute diarrhoea under five years
A. Koc, H. Turk Dagi* [Konya, Turkey]

4368 Rapid increase of CTX-M-producing ST152 Shigella sonnei isolates in Switzerland
E. Campos-Maduena, O. Bernascini, C. Casanova, M. Elzi, C. Maffioli, T. Bodmer, A. Kronenberg, A. Endimiani* [Bern, Switzerland]

4512 Evaluation of commercial multiplex real-time PCR panels to detect bacterial, parasitic and viral gastrointestinal pathogens in clinical specimens
P. Bird* [Leicester, United Kingdom], C. Holmes

4610 Emergence of CTX-M-producing Salmonella enterica serotype Typhimurium in Greece
E. Protonotariou, G. Meletis, G. Kagkalou, D. Papadopoulou, A. Tychala* [Thessaloniki, Greece], F. Netsika, O. Vasilaki, P. Mantzana, M. Kachrimanidou, L. Skouras

4969 Treatment responses to azithromycin and ciprofloxacin in uncomplicated Salmonella Typhi infection: a comparison of clinical and microbiological data from a controlled human infection model
M. Gibani* [London, United Kingdom], C. Jin, S. Pennington, X. Liu, A. Ardrey, G. Aljayyoussi, M. Moore, B. Angus, C. Parry, G. Biagini, N. Feasey, A. Pollard

5032 Escherichia coli serotype O55:H9 as a new multidrug resistant hybrid pathotype producing Shiga toxin and carrying extra-intestinal virulence plasmid
A. Cointe* [Paris, France], P. Mariani, B. Philippe, A. Birgy, S. Lefèvre, S. Delannoy, P. Fich, F. Weill, S. Bonacorsi

5080 Whole genome sequencing of Salmonella enterica from Spanish hospitals with resistance to third generation cephalosporins
X. Vázquez* [Oviedo, Spain], V. García Menéndez, M. De Toro, N. Rodríguez, M. Bances, M. Alkorta, J. Rodríguez-Lozano, J. Calvo-Montes, J. Fernández, M. Rodicio

5211 Epidemiology and comparative genomics of clinical isolates of Salmonella enterica serotype Typhimurium carrying the virulence-resistance plasmid pSU-StVR2
N. Rodríguez, I. Montera, X. Vázquez, M. Bances, M. De Toro, J. Fernández, M. Rodicio, M. Rodicio* [Oviedo, Spain]

5364 Antimicrobial drug resistance, molecular typing and whole genome sequencing of Salmonella enterica serovar Derby from human clinical samples and pork products
V. García Menéndez* [Lugo, Spain], X. Vázquez, R. Garcia-Fierro, P. Quiroso, R. Granda, C. Cuervo, M. Bances, M. Rodicio, M. Rodicio

5730 Epidemiological study of main enteropathogens causing infectious gastroenteritis in a Madrid tertiary hospital
A. Yarci Carrión, L. Fontan, S. Gómez De Frutos, E. Navarro Lara, A. García, T. Alarcon Caverò* [Madrid, Spain]

6069 Comparison of clinical spectrum and outcomes of patients with extremely drug-resistant Salmonella enterica with multidrug-resistant strains
F. Herekar* [Karachi, Pakistan], S. Sarfaraz, S. Shahid, M. Mahesar, N. Ghouri

6664 Detection rates of the bacterial causes of gastroenteritis using a multiplex molecular assay in the South-African private sector
C. Kingsburgh* [Pretoria, South Africa], K. Strydom

6669 Yersinia enterocolitica-associated diarrhoea: descriptive epidemiology in a low-prevalence setting
L. Goterris Bonet* [Barcelona, Spain] from January 2016 to October 2019

7653 Entericaggregative Escherichia coli in mid-Norway
I. Haugan* [Trondheim, Norway], M. Husby, D. Aamnes Mostue, A. Brun, H. Lange, R. White, L. Vold, J. Afset
Abstract Categories 2020

7689 The burden of enteric fever from three urban centres: a multi-centre, multi-component prospective epidemiological study with 626,219 person years of observation

8214 Slovenian national outbreak of Salmonella Paratyphi B variant Java between 2014 and 2016
Š. Klemen, M. Trkov, A. Storman, Z. Petrovic, A. Jurcetic Dadic, I. Berce, M. Ravnik, M. Pirš*[Ljubljana, Slovenia]

8548 Epidemiology of bloody diarrhoea in Georgia and haemolytic-uraemic syndrome associated with it
M. Atskverel*[Tbilisi, Georgia], K. Gvantsa, N. Shulaia

8588 Diagnostic impact of molecular detection of enteropathogenic bacteria compared to stool culture
S. Rodríguez-Pollare*[Cádiz, Spain], A. Ruiz-Castillo, P. Pánes-Ortega, F. Arroyo Navarro, F. Galan-Sanchez, M. Rodríguez-Iglesias

8608 Rise in Campylobacter jejuni antimicrobial resistance in Split-Dalmatia County, Croatia: 2013 - 2018
S. Oureshi*[Karachi, Pakistan], F. Noz, A. Naveed, T. Yousafzai

8775 Should we change our diagnostic strategy for the detection of verotoxigenic Escherichia coli infection?
S. Illescas*[Ciudad Real, Spain], S. Sanchez, V. Carmona, J. Martinez-Alarcon, M. Vidal

9114 Therapeutic response of meropenem and azithromycin in the treatment of extensively drug-resistant (XDR) typhoid fever in a lower-middle income country
S. Oureshi*[Karachi, Pakistan], F. Noz, A. Naveed, T. Yousafzai

9185 Etiology of viral and bacterial gastroenteritis in a third-level hospital in Spain in relation to age
E. Léon, M. Gasca Santiago, B. Palop*[Málaga, Spain]

9589 Listeriosis in Avila, Spain: a real warn amongst immunocompromised hosts
M. Pedramingo Kus*[Madrid, Spain], T. Meiras Arriaga, A. San Pedro Garrido, O. Fraile Santos, N. Iglesias Nuñez, R. Sanchez Arroyo, J. Barragan Casas, A. Antoli Royo

Session accepted as 1-Hour Oral Session

Hot topics in central nervous system infection

2766 Treatment of community-acquired bacterial brain abscess: an international multi-centre survey
J. Bodilsen*[Aalborg, Denmark], P. Tattievin, S. Tang, M. Brouwer, D. Van De Beek, P. Nacler, H. Nielsen

3274 Normocellular bacterial meningoitis in adults: a prospective nationwide cohort study
H. Vestergaard*[Aalborg, Denmark], J. Bodilsen, H. Nielsen

6754 Recurrent community-acquired bacterial meningitis in adults
L. Ter Horst*[Amsterdam, Netherlands], M. Brouwer, A. Van Der Ende, D. Van De Beek

6769 Clinical features and prognostic factors in adults with community-acquired pneumococcal meningitis
D. Koelman*[Amsterdam, Netherlands], M. Brouwer, L. Ter Horst, M. Bijlsma, A. Van Der Ende, D. Van De Beek

Session accepted as Paper Poster Session

Implications of Gram-negative infections

634 The potential benefit of a second C-reactive protein measurement in patients with Gram-negative bacteraemia presenting to the emergency medicine department

715 Excluded versus included patients in a randomised controlled trial of infections caused by carbapenem-resistant Gram-negative bacteria: relevance to external validity

2057 Comparative efficacy of piperacillin-tazobactam versus third-generation cephalosporins or carbapenems against susceptible ampc-bearing Enterobacteriaceae

2210 Relation of risk factors and mortality in carbapenem-resistant Klebsiella pneumoniae ST11 bloodstream infections
T. Xiao*[Zhejiang, China], X. Yonghong

2628 Risk factors for functional decline among survivors of Gram-negative bloodstream infection

2827 No negative conversion at follow-up blood culture (FUBC) is significant predictors of early (1-week) mortality in carbapenem-resistant Enterobacteriaceae or vancomycin-resistant enterococci bacteraemia patient: univariate and multivariate analysis
S. Hygejin*[Seoul, South Korea], H. Choi, Y. Cho, J. Eom
Accuracy of predicting early mortality of severity indicators among carbapenem-resistant Enterobacteriaceae or vancomycin-resistant enterococci bacteremia patient: univariate and multivariate analysis
S. Hyejin* [Seoul, South Korea], H. Choi, Y. Cho, J. Eom

Combination empiric treatment is equivalent to monotherapy in 317 sepsis episodes due to carbapenemase-producing Klebsiella pneumoniae in critically ill patients
M. Papadimitriou Olivieris* [Lausanne, Switzerland], C. Bartzaval, A. Lambropoulou, V. Karamouzos, A. Georgakopoulou, F. Kolonitsiou, F. Filgou, M. Christofidou, M. Marangos

Carbapenem-resistant Escherichia coli causing neonatal sepsis: NDM-5 gains prominence
A. Bhattacharya, S. Mitra, S. Naha, B. Saha, S. Dutta, S. Basu* [Kolkata, India]

Escherichia coli bloodstream infections in a university hospital of northern Italy: resistance pattern and prognostic factors
G. Volpata* [Milan, Italy], D. Pocaterra, G. De Nadai, F. Tardato, B. Varisso, L. Canziani, F. De Fazio, M. Casana, M. Morelli

Risk factors and mortality for patients with bloodstream infections of Klebsiella pneumoniae during 2014-2018: clinical impact of carbapenem resistance in a large tertiary hospital of China
J. Wei, C. Haiyan, Y. Chen, C. Wu* [Nanjing, China]

Clinical profile of patients with bacteremia caused by Enterobacter cloacae and Klebsiella aerogenes: more similarities than differences

Meliodosis in an Indian intensive care unit: the enigma of a “Silent Killer”
T. Shaw* [Manipal, India], V. Kalwaje Eshwara, C. Mukhopadhyay

Outcome of community-onset extended-spectrum β-lactamase-producing Escherichia coli bacteremia and urinary tract infection: a historical population-based cohort study
R. Richelsen* [Aalborg, Denmark], P. Mariadas, J. Smit, H. Schønheyder, J. Rodriguez-Baño, H. Nielsen

C-reactive protein patterns by age, sex and pathogen in patients with Gram-negative bacteremia

Evaluation of carbapenem-resistant Enterobacteriaceae treatment outcomes in a quaternary hospital in the United Arab Emirates
A. Ali* [Abu Dhabi, United Arab Emirates], R. El Lababidi, M. Balkis, R. Ismail, F. Kablaoui

Ceftolozane-tazobactam for the treatment of bloodstream infection due to Pseudomonas aeruginosa in neutropenic cancer patients: a real-life experience (ZENITH study)

Clinical characteristics, aetiology and risk factors for mortality of neutropenic patients with bloodstream infection presenting with septic shock

Clinical management of serious infections attributable to carbapenem-resistant Gram-negative pathogens in Spanish hospitals

Amikacin or colistin monotherapy for complicated urinary tract infections by extensively drug-resistant Pseudomonas aeruginosa
I. López Montesinos* [Barcelona, Spain], S. Gómez-Zorrilla, N. Prim, D. Echeverría-Esna, M. Gracia-Amilllas, M. Montero, L. Sorlí, E. Padilla, S. Grau, J. Harcajada

Are carbapenems a choice in OXA-163 carbapenemase-producing Enterobacteriaceae infections? Clinical outcomes of 29 OXA-163 infections in a general hospital in Argentina
M. Jaume, M. Flor Mantero, M. Amaya, A. Sisto, L. Abusomra, L. Errecalde, F. Fuster* [Buenos Aires, Argentina], L. Guelfand, M. Rolón

Delayed treatment response in healthcare-associated infections by OXA-48 carbapenemase-producing Enterobacteriaceae
M. Amer, D. Helmy* [Cairo, Egypt], H. El-Mahallowy, M. Amin

Session accepted as Paper Poster Session
Increasing knowledge on NTMs
L. Fallico, L. Salvador, S. Mondino, R. Cazzaro
A novel celecoxib-derivative kinase inhibitor, AR-12 (OSU-03012), is active against Mycobacterium abscessus complex in vitro
B. Li* [Shanghai, China], Y. Zou, S. Zhang, H. Chu

Contact effect of a Myceliobacterium sp. extract on biofilm of a Mycobacterium chimaera strain isolated from a 3T heater-cooler system
I. Pradal, J. Esteban-Moreno* [Madrid, Spain], J. Aguilera-Corra

Prevalence of non-tuberculous mycobacteria in a tertiary hospital in Beijing, China, January 2013 to December 2018
J. Huang* [Beijing, China], M. Xiao, T. Kudinha

Pattern of osteoarticular infections caused by non-tuberculous mycobacteria: 9 years’ experience
A. Bleibtreu* [Paris, France], I. Bonnet, S. Jauréquiberry, B. Fautrel, E. Caumes, J. Robert, E. Fourniols, A. Aubry

Performances comparison between rapidly growing mycobacteria medium for direct-isolation of non-tuberculous mycobacteria, and its industrial version
M. Vignaud* [La Balme les Grottes, France], E. Déleâge, S. Orenga, D. Stephenson, J. Perry

Differential drug susceptibility patterns of Mycobacterium avium complex isolates recovered in Greek university hospitals
F. Kontos* [Athens, Greece], G. Movromanolakis, S. Pouranaras

In vitro antimicrobial susceptibility testing of rapidly growing mycobacteria isolated in a university hospital, Athens, Greece
F. Kontos* [Athens, Greece], S. Pouranaras

Decontamination strategies used for AFB culture significantly reduce the viability of Mycobacterium abscessus in sputum samples from patients with cystic fibrosis
D. Stephenson, A. Perry, A. Nelson, A. Robb, M. Thomas, S. Bourke, J. Perry* [Newcastle upon Tyne, United Kingdom], A. Jones

Genomic analysis of cardiac surgery-associated Mycobacterium chimaera infections in Italy
A. Ghoudosti* [Pessano con Bornago, Italy], M. Peracchi, E. Borroni, G. Fallico, V. Quaresima, V. Manfrin, M. Rassu, V. Monzella, R. Manganeli, E. Tortoli, D. Cirillo

Antimicrobial susceptibility of non-pigmented rapidly growing mycobacteria
S. Girod, V. Dejardin, A. Raveau, K. Deledalle, E. Caumes, J. Robert, L. Felten

Compatibility of the new NTM Elite agar with MALDI-TOF for direct isolation and identification of non-tuberculous mycobacteria
M. Vignaud* [La Balme les Grottes, France], E. Déleâge, L. Devigne

Identification and clinical significance of Mycobacterium avium complex isolates in a university hospital in a 13-year period
F. Kontos* [Athens, Greece], G. Skyllas, I. Kouva, I. Korbila, E. Manali, A. Antoniadou, S. Papiris, S. Pouranaras

Efflux pumps contribute to intrinsic clarithromycin resistance in clinical Mycobacterium abscessus isolates
Q. Gao* [Shanghai, China], B. Li, H. Chu

New lean preparation method for identification of mycobacteria by MALDI Biotype
M. Timke, A. Pranada* [Dortmund, Germany], M. Kostrzewa

A novel deep sequencing platform for genotyping and drug resistance detection of Mycobacterium leprae
S. Braet* [Antwerp, Belgium], P. Suffys, S. Ezidio Gonçalves Vasconcellos, G. Bisch, A. Ferre, E. Hasker, Y. Assoumani, A. Mzembaba, P. Supply, B. De Jong

A new high-resolution melting PCR assay for a rapid detection of linezolid-resistance-associated mutations in Mycobacterium avium complex
R. Musumeci* [Monza, Italy], L. Molteni, E. Mazzola, S. Torri, D. Fanti, A. Nova, M. Martinelli, F. Perdoni, C. Villa, P. Carlo Federico, C. Cocuzza

Optimization of Mycobacterium avium complex therapy with synergistic and bactericidal drug combinations
V. Sonawane* [Nijmegen, Netherlands], M. Ruth, L. Pennings, J. Van Ingen

Next-generation microscopically-observed drug susceptibility assay (NG-MODS) allows more rapid and precise phenotypic drug-susceptibility testing: preliminary results for Mycobacteroides abscessus
W. Chiu* [Leuven, Belgium], C. Foo, P. Leysens, E. Andre

Genomic identification of clinically relevant Mycobacterium species by target sequencing
V. Collin* [La Balme les Grottes, France], F. Allard, M. Rumigny, F. Joverialat

A radiologic score for pulmonary non-tuberculous mycobacterial infection: preliminary results
M. Colaneri* [Pavia, Italy], A. Lombardi, A. Di Matteo, M. Fabbiani, S. Vancheri, A. Valentini, V. Monzillo, R. Bruno

Intact bacteria species-specific lipid profiling using the MALDI Biotype Sirius can identify mycobacteria in one step
B. Agnieszka, X. Gonzalo, M. Kostrzewa, F. Drabniewski, G. Larrouy-Maumus* [London, United Kingdom]

Cluster of invasive Mycobacterium chimaera infection in a single cardiac surgery unit: clinical features and management
N. Riva* [Reggio Emilia, Italy], L. Cavazzuti, L. Pescarolo, G. Marini, G. Magnani, M. Massari

Detection of antimicrobial resistance in Mycobacterium abscessus complex by MALDI-TOF MS
A. Godmer* [Paris, France], N. Veziris, C. Eckert, S. Gallah, A. Aubry, L. Benzerara

Routine use of MALDI-TOF MS for identification of non-tuberculous mycobacteria species in the clinical laboratory
D. Rodriguez-Temporari* [Barcelona, Spain], N. Vila, E. Garcia, M. Mas, F. Alcaide
Abstract Categories 2020

Is Mycobacterium lentiflavum “the new” Mycobacterium avium?
S. Gómez De Frutos* [Madrid, Spain], A. Fraile Torres, A. Yarci Carrió, T. Soler Maniega, L. Cardeñosa, R. Girán, D. Domingo

Identification of Mycobacterium species with MALDI-TOF mass spectrometry
Z. Saribas, O. Koksalan, H. Gur* [Ankara, Turkey], S. Demirici, A. Alp

Mycobacterium mucogenicum in hospital water: a potential source for human infection
J. Ory* [Nîmes, France], C. Aumeran, O. Traore, E. Lecorche, C. Enault, E. Cambau, J. Lavigne, A. Pantel

Identification by proteomic (MALDI-TOF MS) of non-tuberculous mycobacteria from liquid medium in clinical practice
R. Sainz Rodriguez, M. Mediavilla Gradelph, F. Ana Maria, B. Palop* [Málaga, Spain], A. Correa, M. Bermúdez Ruiz

Long lasting outbreak of severe Mycobacterium chimaera infection among cardiac surgery patients operated with contaminated heater-cooler devices: Italy, 2010 to 2019

Monitoring and control of the heater-cooler unit colonisation by Mycobacterium chimaera and other NTMs used during open-heart surgery
B. Casini* [Pisa, Italy], B. Tuvo, G. Privitera

Evaluation of the MGIT 960/EpiCenter TB eXiST system for drug susceptibility testing for Mycobacterium abscessus group
N. Carvalho, S. Bombara, S. Leão, R. ArbeIt, E. Chimara* [Sao Paulo, Brazil]

Epidemiology of non-tuberculous mycobacteria in bronchiectasis and non-bronchiectasis patients in a university teaching hospital in Madrid
S. Gómez De Frutos* [Madrid, Spain], L. Fontan, E. Navarro Lara, N. Zurita Cruz, L. Cardeñosa, J. Garcia Pérez, D. Domingo

Prevalence of non-tuberculous mycobacteria in patients with cystic fibrosis in a tertiary hospital
D. OrtégA Larrea* [Zaragoza, Spain], E. López, M. Moreno Hijazo, S. Mormeneo Bayo, S. Nabal Díaz, E. Valverde, M. Arias, B. Fortuño, M. Elu, J. Viñuelas

Evaluation of the FluoroType mycobacteria assay for the detection and differentiation of clinically relevant mycobacteria
C. Niccolae* [Florence, Italy], A. Bartolesi, F. Marcelli, A. Andreini, R. Mannino, A. Antonelli, E. Tortoli, G. Rossolini

Non-tuberculous lymphadenitis in children: epidemiology and management strategy in France during the last decade

Characterisation of the unique contributions of bedaquiline and rifabutin against actively-growing and nutrient-starved populations of Mycobacterium abscessus
J. Lee, N. Ammerman* [Baltimore, United States], E. Nuernberger

Rapid detection of Mycobacterium abscessus complex and associated antibiotic resistance directly in cystic fibrosis samples
A. Bordin* [Brisbane, Australia], C. Coulter, J. Clark, S. Pandey, S. Bell, C. Wainwright, G. Nimmo, A. Jennison, M. Syrnis, C. Pardo, H. Hackett, D. Whiley

Using whole genome sequencing to assess M. leprae transmission in French overseas Territories
E. Lecorche* [Paris, France], B. Violaine, M. Dahiia, A. Charlotte, K. Elise, F. Mougari, H. Benmansour, V. Jarlier, E. Cambau

Surveillance of Mycobacterium leprae in Analamanga region of Madagascar
D. Randriariimanana* [Antananarivo, Madagascar], M. Andrinarison, T. Rasamoelina, F. Rakotomalala, A. Charlotte, L. Ramarazatovo, B. Cauchoux, J. Berland, F. Rapolana Rabenja

Complete genome sequencing and identification of Mycobacterium chimaera by MALDI-TOF MS: a modified approach to discriminate Mycobacterium chimaera and Mycobacterium intracellulare
J. Bagnarino, V. Monzillo, D. Barbarini, A. Pirallo* [Pavia, Italy], A. Ghoudaoui, E. Tortoli, P. Marone

Infections in the prism of One Health

Comparison of multidrug-resistant Salmonella enterica serovar I 4,[5],12:i:- and Salmonella enterica serovar Typhimurium isolated from swine in the USA
S. Gonzalez* [College Station, United States], K. Norman, R. Harvey, H. Scott, S. Lawhon, J. Vinasco

Comprehensive proteomics and active immunisation reveals that extracellular vesicles derived from Streptococcus equi subspecies equi as an effective candidate for vaccine platform
H. Lee* [Cheongju, South Korea], S. Kim, L. Sang-Yeop, S. Yun, S. Jun, H. Ro

Healthy people in Zanzibar are frequently colonised at intestinal level with MDR Enterobacteriaceae identical to those detected in poultry and retailed chicken meat
T. Büdel, E. Kuenzli, O. Bernasconi, E. Campos-Madueno, J. Zinsstag, C. Hatz, A. Endimiani* [Bern, Switzerland]

Genetic diversity evident from comparative genome analysis of ESBL-producing Escherichia coli isolated from swine microbiomes in Cameroon and South Africa
L. Njoungang Yontchoung Epse Founou* [Yaounde, Cameroon], R. Founou Zangue, S. Essack

Session accepted as Paper Poster Session
2424 Molecular evidence of bacteria with medical relevance in fleas parasitising cats and dogs
G. Doupas* [Athens, Greece], A. Tsaikris, A. Mageropoulou, A. Priftis, T. Lytras, S. Beleri, E. Patsoula, M. Linou, C. Billinis, J. Papaparaskevas

2556 Antibiotic and biocide resistance among staphylococci causing skin and soft tissue infections in companion animals in Portugal
S. Santos Costa* [Lisbon, Portugal], R. Ribeiro, V. Oliveira, M. Serrano, C. Ferreira, C. Morais, M. Pomba, I. Couto

2991 Detection and antibiogram of Escherichia coli O157 from Oreochromis niloticus [Tilapia] sold in Ibadan, Nigeria
S. Ogunleye* [Ibadan, Nigeria], O. Adedeji, O. Ishola, O. Okunlade

4048 First report of CCS-methicillin-resistant Staphylococcus aureus IV-SCCFus “Maitese clone” in bat guano
M. Assia, A. Touati, A. Pantel, A. Sotto, C. Dunyach-Remy, J. Lavigne* [Nimes, France]

4128 Analysis of resistance transmission among humans and livestock using microbiome profiling
H. Pai* [Seoul, South Korea], M. Rho, J. Kim, S. Lim, M. Seo, B. Kim

4273 Incidence rates of multidrug-resistant indicator pathogens increase in hospitalised horses during stay
A. Kauter* [Berlin, Germany], A. Lübbe-Becker, D. Kopp, S. Stäckle, L. Epping, K. Semmler, H. Gehlen, B. Walther

4374 Recreational waters: a reservoir for Shiga toxin-producing Escherichia coli?
L. O’Connor, C. Brehony, B. Hooban, K. Fitzhenry, N. Cahill, L. Burke* [Galway, Ireland], P. Hickey, S. Keane, A. Mcnamara, M. Cormican, D. Morris

4524 Fast Point-of-Care biomimetic receptor-based biosensor for detection and quantification of zoonotic Campylobacter
M. Heyndrickx* [Melle, Belgium], S. Givanoudi, A. J. Robbens, P. Cornelis, G. Wackers, K. Hertogs, D. Yongabi, M. Heyndrickx* [Melle, Belgium]

5334 Piglets as a potential reservoir of atypical enteropathogenic Escherichia coli (aEPEC) with serotypes of human enterohemorrhagic Escherichia coli (EHEC), including the O80:H2-A-ST301 (CH27-54) eae-ξ clone

5555 Atelerix algirus as host of Salmonella species in Tenerife, Spain
E. Izquierdo Rodríguez, N. Martín Carrillo* [San Cristobal de La Laguna, Spain], E. Baz-Gonzalez, P. Faranda Rodriguez

6314 Genomic investigation of Klebsiella pneumoniae complex isolates recovered from pigs and humans in Thailand
T. Leangapichart* [Oslo, Norway], K. Lunha, J. Jiwakanan, S. Angkititrakul, J. Järhult, U. Magnusson, M. Sunde

First report of colistin resistance in Salmonella spp. isolated from fresh minced meats and poultry faeces from primary production phase in Bosnia and Herzegovina
M. Ibrahimagic* [Zenica, Bosnia and Herzegovina], A. Fetaha-agic, J. Dizdarević, E. Idrizović, S. Uzunovic, A. Kapidžić, A. Šanjta-Reis, M. Gladan

Cefotaxime-resistance in Escherichia coli strains isolated from fleas parasites in primary production phase
M. Fetaha-agic* [Zenica, Bosnia and Herzegovina], A. Ibrahimagic, J. Dizdarević, S. Uzunovic, A. Šanjta-Reis, A. Kapidžić, M. Gladan

Antibiotic resistance in Staphylococcus pseudintermedius associated with skin and soft tissue infections in dogs and cats
M. Morais* [Lisbon, Portugal], S. Santos Costa, P. Abrantes, M. Pomba, I. Couto

Development of a ery-C recombinant protein-based ELISA approach for differentiating brucellosis infected cattle from vaccinated ones
W. Abdelwahhab* [Cairo, Egypt], M. Salah El-Din Diab, A. Amin Samy, J. Abd Elhalm Eljaky

One Health investigation of Chlamydia psittaci in Denmark in 2019
R. Petersen* [Copenhagen, Denmark], S. Uldum, Ø. Angen

Genomic insights into the dynamic of OXA-48-producing Enterobacteriaceae in a veterinary hospital
M. Haenni* [Lyon, France], H. Boulouis, C. Pierre, E. Hirchaud, J. M. Macé

Microbiome ecology drives the epidemiology of antibiotic resistance and the efficacy of antibiotic stewardship interventions: a mathematical modelling study
D. Smith* [Paris, France], L. Temime, L. Opatowski

Public health impact of similar ESBLs/pAmp-producing Escherichia coli causing urinary tract infections in non-related companion animals and humans
A. Belas* [Lisbon, Portugal], J. Menezes, L. Tejo Da Gama, J. Carriço, M. Pomba

Development of bovine herpesvirus 4-based vaccines as an antibiotic-free strategy to control bacterial infection in livestock
H. Nichols* [Plymouth, United Kingdom], M. Jarvis, A. Murphy, T. Mauch, S. Henderson, Y. Wezel

Resistance and virulence determinants of faecal Salmonella spp. isolated from slaughter animals in Benin
V. Dougnou* [Abomey-Calavi, Benin], E. Deguenon, L. Baba-Moussa

Development of attenuated bovine herpesvirus 4 as a safe, inexpensive, single-dose vaccine to control Streptococcus suis infection in domestic pigs
K. Sealey* [Plymouth, United Kingdom]
Abstract Categories 2020

9395 Global spread of poultry-associated Campylobacter jejuni genotypes to the Peruvian Amazon
B. Pascoe* [Both, United Kingdom], M. Kasek, S. Sheppard
9529 Identification of meticillin resistance in Staphylococcus spp. of dogs with pyoderma
L. Guimarães, I. Silva, M. Antunes, C. Fonseca, C. Pesset, I. Teixeira, A. Santos, B. Penna* [Rio de Janeiro, Brazil]

Session accepted as Paper Poster Session

Intra-abdominal infections

267 Acute cholangitis secondary to choledocholithiasis in older population: subtle presentation and severe illness
A. Hamdi* [Rochester, United States], S. Khalil, M. Fida, E. Beam
507 Evaluation of efficacy of antibiotic prophylaxis in case of paraprostitis
S. Zyrjanov, G. Rodoman, M. Ivzhits* [Moscow, Russian Federation], D. Ramashov, M. Chenkurov, G. Putsman
1377 Pyogenic liver abscess: predictive factors of unfavorable course
1458 A retrospective cohort study investigating the clinical features, outcomes and risk factors leading to a poor unfavorable course
J. Widdrington, B. Tomlinson, J. Williams, I. Kubelka, M. Kalra, J. Cheaveau* [Middlesbrough, United Kingdom], O. Romashov, M. Chenkurov, G. Putsman
1684 A retrospective study of pyogenic liver abscess caused by Klebsiella pneumoniae as a primary pathogen: computed tomography and clinical differentiation as a primary pathogen:
S. Hong, Y. Jang* [Incheon, South Korea], J. Eom, Y. Cho
2309 Microbiology and molecular characterisation of Enterobacterales from children enrolled in global, prospective, controlled paediatric clinical trials for complicated intra-abdominal and urinary tract infections for ceftazidime-avibactam
R. Mendes* [North Liberty, United States], T. Doyle, G. Stone, A. Gardner, M. Castanheira, J. Bradley
2940 What is the optimal timing and technique for the source control in the subgroup of septic shock patients with intra-abdominal infections?
3352 Optimal antimicrobial therapy duration for patients with acute cholangitis after successful drainage by Endoscopic retrograde cholangiopancreatography (ERCP)

6406 Outbreak of Arcobacter butzleri? An emerging enteropathogen
C. Ruiz De Alegria Puig* [Santander, Spain], M. Fernández-Martínez, O. Pablo-Marcos, J. Aguero, J. Calvo-Montes

Session accepted as 2-Hour Oral Session

JARMILA JELÍNKOVÁ MEMORIAL SESSION - Early life infections: what, when and how?

1044 No benefit with empiric aminoglycosides in paediatric febrile neutropenia: analysis of a nationwide cohort study
B. Mcmullan* [Randwick, Australia], G. Haeusler, L. Hall, C. Blyth, C. Jones, P. Konecny, K. Thursky
5352 Feasible approach to reduce antibiotic overuse in preterm neonates
J. Arnmann* [Dresden, Germany], L. Mense, B. Seippol, M. Rüdiger, R. Berner

Impact of the FILMARRAY gastrointestinal polymerase chain reaction panel on the clinical management of children with suspected acute bacterial-diarrhoea
J. Truong* [Paris, France], E. Leroux, M. Michel, J. Boize, P. Mariani, A. Cointe, M. Desmarest, L. Titomanlio, A. Faye, S. Bonacorsi

Preliminary data on initial antimicrobial regimen from a prospective cohort study of sepsis in hospitalised neonates: the NeoOBS study
W. Stöhr* [London, United Kingdom]

Initial clinical features from preliminary analyses of a global multi-centre prospective observational cohort of sepsis in hospitalised neonates: the NeoOBS study
N. Russell* [London, United Kingdom]

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R. Sparks* [Neutral Bay, Australia], R. Chavada, C. Tretewy, A. Harada

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A systematic literature review of the efficacy and tolerability of polymyxins in resistant Gram-negative infections
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**Mycobacterial pathogenesis and population studies**

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2088 Evaluating the usefulness of whole genome sequencing in tuberculosis treatment decisions in a low-incidence clinical setting
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3524 Costs and impact of whole genome sequencing on tuberculosis diagnostics in a high prevalence and high MDR-TB burden country
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6525 Genomic and structural protein characterisation of mutations conferring bedaquiline resistance in *Mycobacterium tuberculosis* clinical strains
A. Spitaleri, S. Battaglia, J. Carter, A. Ghodousi* [Pessano con Barnago, Italy], A. Cabibbe, P. Fowler, S. Hoosdally, D. Cirillo

6811 Efficient long-term storage of mycobacteria using conventional laboratory reagents
F. Schramm* [Strasbourg, France], E. Talagrand-Reboul, P. Boyer, A. Chabaud, B. Jaulhac, C. Koebel

7271 Genetic mutations in drug-resistant paediatric tuberculosis: experience from a paediatric tertiary care centre in north India
P. Khurana* [Delhi, India], K. Saigal, A. Ghosh

7480 Genomic analysis of multi-resistant *Mycobacterium tuberculosis* strains in France: evolution from 2006 to 2018

8103 Assessment of the performances of the novel BioNumerics-7.6 MTBC plugin for phylogenomic analysis and drug resistance prediction from *Mycobacterium tuberculosis* whole genomes
W. Sougakoff* [Paris, France], F. Morel, G. Millot, A. Aubry, J. Robert

8350 *Mycobacterium tuberculosis* genotypes’ landscape in HIV-negative and HIV-positive tuberculosis patients in Russia
A. Panova* [Moscow, Russian Federation], G. Kaminski, A. Vinokurov, A. Shemetova, M. Shulgina, I. Vasilyeva

9066 Evaluation of PrimeStore molecular transport medium for long-term preservation of mycobacterial RNA at ambient temperature and subsequent detection of *Mycobacterium tuberculosis* Ag85B
S. Matsukane, B. Fourie* [Pretoria, South Africa]

9626 Structural study of new KatG mutations selected on isoniazid-resistant strains of *Mycobacterium tuberculosis* in vivo
A. Bastanaru* [Iasi, Romania], M. Mares

Session accepted as Mini-oral Flash Session

**New interventions for NTMs: from diagnosis to treatment**

1395 Pathogen Box screening identifies novel antimicrobials that target *Mycobacterium chimaera*
D. Cantillon* [Brighton, United Kingdom], A. Goff, S. Taylor, S. Stoneham, S. Waddell

2453 Benzimidazole SPR719/720 is a potent new candidate for treatment of non-tuberculous mycobacterial infections
L. Pennings* [Nijmegen, Netherlands], T. Lister, D. Melnick, N. Cotroneo, I. Critchley, M. Pucci, T. Parr, S. Stokes, J. Van Ingen

4307 Performance of RealAccurate Quadruplex *Mycobacteria* PCR for detection of non-tuberculous mycobacteria in clinical samples
J. Cappens* [Edegem, Belgium], S. Van Goethem, K. Bergs, M. Michiels, L. Rigouts, H. Goossens, H. Jansens, V. Mattheussen
ECOFFs for non-tuberculous mycobacteria: towards a EUCAST reference method and clinical breakpoints for antimicrobial susceptibility testing


Transglutaminase 2 inhibitors as a future intervention against non-tuberculous mycobacteria

I. Palucci* (Rome, Italy), A. Salustri, M. Sali, F. De Maio, L. Petrone, G. Fimia, M. Sanguinetti, D. Goletti, M. Piacentini, G. Delogu

Synergistic activity of a three-drug combination against clinical isolates of Mycobacterium abscessus complex

M. Fernandez* (Barcelona, Spain), M. Monte, A. Raman, E. Portell Buj, A. Lópezc, G. Tudó, J. Gonzalez

Preclinical evaluation of liposomes carrying bioactive lipids as an immune therapeutic tool in vitro and in vivo infection with Mycobacterium abscessus

C. Riva* (Sorèina, Italy), N. Poerio, M. Rossi, F. De Santis, E. Tortoli, M. Fraziano, D. Cirillo

Amikacin resistance mechanisms in Mycobacterium abscessus

M. Sandermelle* (Paris, France), G. Sbaa, E. Lecorche, H. Benmansour, F. Mougari, E. Cambau

Blocking mycobacterial efflux pumps might potentiate efficacy of antimycobacterial drugs in vitro

M. Ruth* (Nijmegen, Netherlands), L. Pennings, J. Schildkraut, V. Koeken, H. Wertheim, J. Van Ingen

Investigation of the prevalence of Verocytotoxigenic Escherichia coli [VTEC] contamination of private groundwater wells in Ireland


Characterisation of methicillin-resistant Staphylococcus aureus strains isolated from porcine subcutaneous lesions of food-producing rabbits


Emergence of multiple ESBL-producing Salmonella enterica serovars in hospitalised horses due to an epidemic spread of a CTX-M-3 plasmid pSIEL-3

Z. Doo, A. Shnaiderman-Torban, K. Konratjyeva, M. Dovdovich, A. Rokney, A. Steinman, S. Novon-Venezia* [Ariel, Israel]

Genomic evidence that the recurrence of Salmonella enterica serovar Weltevreden in human salmonelloses in Asia is triggered by the aquatic environment

Y. Hounmanou* [fredenskibsg, Denmark], A. Dalsgaard, T. Sapacua, G. Uddin, P. Leekitcharoenphon, R. Hendriksen, M. Larsen

The transmission risk of multidrug-resistant organisms between pets and humans: n exploratory case control study protocol

C. Hackmann* [Berlin, Germany], P. Gornaer, D. Gruhl, B. Laos De Henner, A. Lübbe-Becker, S. Schwarz, R. Leistner

Presence and zoonotic potential of Escherichia coli ST131 recovered from wildlife and food-producing animals, with high prevalence of mcr-1 within porcine isolates


One Health in practice: longitudinal screening of antibiotic residues, antibiotic resistance genes and zoonotic bacteria in soils fertilised with pig manure

M. Heyndrickx* [Melle, Belgium], T. Van Der Meersche, E. Daelesteire, E. Van Collie, G. Rasschaert

Antimicrobial resistant and enteropathogenic bacteria in ‘filth flies’: a cross-sectional study from Nigeria

M. Onwugbula* [Münster, Germany], A. Mellmann, N. Oluahegbual, F. Schauburg

Detection of pathogenic Vibrio species in estuary water samples in southwest Spain

T. Trujillo-Soto* [Cádiz, Spain], J. Ruiz-Cayusa, I. Guerero Lozano, F. Galan-Sanchez, S. Papaspyrou, M. Rodriguez-Iglesias

Investigation of the prevalence of Verocytotoxigenic Escherichia coli [VTEC] contamination of private groundwater wells in Ireland


An ultrasensitive rapid single molecule counting method detects Bacillus anthracis lethal factor directly in blood samples

D.Straus* [Chelmsford, United States], A. Tempesta, S. Gite, S. Schulz, B. Walsh, L. Bowers

A rocky road: lessons learned from a case of disseminated Rhodococcus haagi infection

R. Hoffmann* [Bellville, South Africa], C. Van Der Westhuizen, M. Newton-Foot

Streptococcus pneumoniae: the chameleon of ocular diseases

C. Andre* [Chatou, France], J. Rouhana, M. Gilmore, P. Bispo

Lawsonella clevelandensis: an emerging cause of vascular graft infection

R. Ramesh* [Hradec Kralove, Czech Republic], Z. Esquer Garrigos, K. Rodina, B. Pritt, M. Sohail

Chlamydia psittaci / C. abortus detection in respiratory samples [England and Wales, 2012-2018]

S. Mayet* [London, United Kingdom], J. Day, L. Vaghji, A. Peace, D. Ready, V. Chalker, M. Chand, B. Afshar

A study of Bartonella bacilliformis bacteriemia in asymptomatic individuals during an inter-outbreak period in an endemic region

H. Biasizzo* [Postojna, Slovenia], P. Ventosilla, C. Augusto Ugarte Gil, D. Moore
3079 *Bacillus subtilis* as a causative of true bacteraemia in patients with peritonitis
C. Sassa* (Tokyo, Japan), K. Sonobe, N. Ichimura, Y. Hadana, S. Tohda

3930 Failure to perform a repeat ascitic tap at 48 hours is associated with poor outcome in patients with spontaneous bacterial peritonitis
J. Tan* (London, United Kingdom), J. King, J. Ryan, M. Morgan, R. Westbrook, E. Wey

5753 An eight years-long experience of *Nocardi*a spp. infection in Italy: does immunosuppression matter?
M. Colaneri* (Pavia, Italy), V. Monzilla, B. Mariani, A. Lombardi, E. Brunetti, M. Sambro, E. Seminari

6649 *Toxigenic Corynebacterium ulcerans* isolated from an Italian hunter
G. Zambolin* (Brescia, Italy), B. Saccani, G. Tomasoni, A. Lombardi, E. Brunetti, M. Sambo, E. Seminari

6796 *Moraxella keratitis*: investigating emerging pathogenicity through clinical and microbiological findings and whole genome sequencing for virulence determinants

7302 *Streptococcus suis* infection: a series of 37 cases from a community-based hospital, Thailand
S. Pinsai* (Bangkok, Thailand)

7390 Clinical features and outcomes of patients with *Elizabethkingia meningoseptica* infection: an emerging pathogen
N. Nasir* (Karachi, Pakistan), A. Umair

7472 *Corynebacterium ulcerans* spp.
A. Ang* (Singapore, Singapore), K. Chew

7648 *Meliodosis* in patients suspected with recurrent tuberculosis: a disease in disguise
R. Garg* (Manipal, India), T. Shaw, C. Mukhopadhyay

7884 Impact of early infectious diseases intervention and microbiologically led antimicrobial therapy in patients with idiopathic granulomatous mastitis

8056 Low incidence of Gram-negative infections in people who inject drugs in Tennessee
M. Veve* (Knoxville, United States), G. Cooksey, B. Nabors, Z. Smith, M. Sherman

8356 Comparison of clinical characteristics and mortality between patients with pulmonary nocardioses and patients with pneumonia
I. Margalit* (Petah Tikva, Israel), E. Goldberg, K. Muhisen

9565 *Corynebacterium ulcerans*: lessons learned from a rare emerging infection
R. Huq* (Manchester, United Kingdom), R. Shortern, A. Jha, A. Cardozo, I. Chaudry, L. White, A. Muir, G. Amirthalingam, M. Chand, P. Jumaa

9662 Outbreak of mixed cases of gastrointestinal and cutaneous anthrax in the rural village of northern Luzon, Philippines, March 2017
K. Lonogan* (Baguio City, Philippines), A. De Guzman, V. De Los Reyes, N. Sucaldito, F. Avellana

Session accepted as Paper Poster Session
Sepsis: an ever evolving story

1314 Community and nosocomial sepsis in older adults with bacteremia: a retrospective study in a geriatric ward
M. Saotetti, G. Orlando* (Modena, Italy), O. Moioli, C. Mussi, M. Menozzi, M. Meschiari, E. Franceschini, C. Pizzolante, A. Bedini, M. Digaetano, C. Mussini, M. Bertolotti

1362 Bloodstream infections caused by strong biofilm-producing bacteria increase the risk of end-organ disease and mortality in patients with haematologic malignancies

Clinical and microbiological characteristics and outcomes for community-onset sepsis patients in a teaching hospital in Latvia: a retrospective, single-centre, cohort study
L. Puceta* (Riga, Latvia), A. Grāmatniece

Clinical characteristics and outcome of bloodstream infections in HIV-infected patients with febrile neutropenia: A case-control study

Characteristics of bloodstream infections in patients with liver cirrhosis in a general hospital
S. Nguyen* (Béthune, France), P. Wallard, O. Oddoux, M. Anastay, D. Descamps

Assessing the contribution of sepsis to mortality in Oxfordshire
E. Pritchard* (Oxford, United Kingdom), A. Walker, T. Petoe, D. Crook, L. Petto, N. Fawcett, A. Brent

Analysis of causes of death and mortality risk factors in extreme elderly patients with sepsis
J. Delgado Correal* (Rio de Janeiro, Brazil), R. Rufino, M. Fornasario, C. Albuquerque, M. Martins, P. Damasco

Analysis of *Escherichia coli* phenotypes and known sepsis-causing sequence types in UK sewage reveals a direct link between sepsis rates and carriage of pathogenic sequence types in the community
M. Toleman* (Cardiff, United Kingdom), J. Mathias, A. Almusallam, D. Babenko
Prospective evaluation of septic shock patients in a tertiary care educational university hospital: a series of 739 cases

Epidemiological changes in bloodstream infection in southern Spain during the last ten years: results from the PROBAC study

Epidemiology, risk factors and treatment of anaerobic bloodstream infections: a 7-year study
R. Figueroa-Cerón, M. Macha, A. Gonzalez Sarria* [Bilbao, Spain], C. Aspichueta, M. Urrutia-Koethea-Gutierrez, F. Calvo Muro, J. Díaz De Tuesta

Hospital admission for sepsis and mortality in Brazil from 2009 to 2018: analyzing 10 years of government database (Datasus) information
R. Fleury, W. Freitas* [Rio de Janeiro, Brazil]

Epidemiology and risk factors for mortality in patients with Pseudomonas aeruginosa bacteraemia
I. Perez-Camacho* [Malaga, Spain], J. Ruiz-Mesa, I. Márquez Gómez, L. Caballero Martinez, B. Sobrino, L. Valiente De Santis, A. Plata Ciézar, J. Reguera Iglesias

Clinical characteristics and treatment outcome of patients with sepsis treated in an infectious disease intensive care unit
R. Novak* [Zagreb, Croatia], M. Popović, B. Baršić, M. Santini, M. Kutlesa, V. Krajnović

Dynamics and distribution of attributable and non-attributable mortality in Staphylococcus aureus bacteraemia

The effect of mesenchymal stem cells on the mortality of severe sepsis and septic shock: a promising therapy
E. Alp Mese, Z. Gonen, K. Gundogan, A. Esmaeili, L. Kaynar, A. Cetin, M. Korakucku, M. Cetin, G. Kalin Ünüvar* [Kayseri, Turkey], M. Doganay

A randomised prospective clinical trial to assess the role of procalcitonin-guided antimicrobial therapy to reduce long-term infections’ sequelae [PROGRESS]

Impact of rapid molecular detection of sepsis on time to optimal antimicrobial therapy in paediatric cancer patients at the National Cancer Institute, Egypt
H. El-Mahallawy, E. Ebeid, S. Hassan, F. Naguib, R. Khedr* [Cairo, Egypt]

The global burden of sepsis in adults: updated systematic review and meta-analysis
C. Fleischmann-Struzek* [Jena, Germany], L. Mellhammer, N. Rose, A. Cassini, K. Rudd, P. Schlattmann, B. Allegranzi, K. Reinhart

Genetic characterisation of co-circulating community Staphylococcus aureus and Streptococcus pyogenes causing skin and soft tissue infections in Gambia

Effectiveness of implementing a locally developed antibiotic use guideline for community-acquired cellulitis at a large tertiary care university hospital in Thailand
R. Sirijatuphat* [Bangkok, Thailand], P. Nookeu, V. Thamilkitkul

Characterisation of Staphylococcus aureus in soft tissue infections: relevance of PVL producers
N. Leal, G. Vieira, N. Osório, C. Antunes Chaves, F. Rodrigues, A. Rodrigues* [Coimbra, Portugal]

Impact of underlying comorbidities on outcomes of patients treated with ceftaroline fosamil for complicated skin and soft tissue infections: pooled results from three phase III clinical trials
M. Wilcox* [West Yorkshire, United Kingdom], M. Kantecki, J. Yan, M. Dryden

Actinotignum schaali in breast abscesses, an emerging pathology? Report on five cases
L. Deroche* [Poitiers, France], C. Nadeau, V. Huguier, M. Pichon, L. Brouin, P. Chioè, C. Burucoa, A. Michaud

Comparison of genetic diversity in Streptococcus pyogenes isolates from Gambia and United Kingdom causing skin and soft tissue infections
S. Bah* [Sheffield, United Kingdom], A. Keeley, E. Armitage, E. Senghore, J. Manneh, L. Tilley, S. Darboe, A. Sesay, T. De Silva, C. Turner

Exclusive oral post-surgical antibiotic therapy is effective for infectious flexor hand tenosynovitis: a study of 127 patients
C. Dujeux, A. Fournier, M. Malherbe, F. Guérin, G. Rochcongar, A. Baldelli, R. Verdon, J. Michon* [Caen, France]
2481 Self-reported health status in ambulatory acute bacterial skin and skin structure infection patients who inject drugs, who received oral therapy with omadacycline or linezolid
K. Lapensee* [King of Prussia, United States], S. Chitra

5500 Acute rheumatic fever in children in Morocco: a prospective study
S. Himri* [Fes, Morocco], B. Oumakhtar, S. El Fakir, S. Atmani

6260 An epidemiological description of Panton-Valentine leukocidin-positive Staphylococcus aureus (PVL-SA) at ambulatory health units of the Rhine-Ruhr metropolitan region in North Rhine-Westphalia, Germany
C. Tellez-Castillo* [Bochum, Germany], M. Griego, P. Göcke, R. Rujbr, U. Scharmann, C. Scharmann

6327 Cutaneous lesions due to Staphylococcus aureus in inflammatory bowel disease patients undergoing anti-TNFα treatment: molecular characteristics and strains comparison in different niches
H. Hač, C. Dunyach-Remy* [Nîmes, France], E. Schowb, O. Dereure, R. Altwegg, A. Du-Thanh, J. Lavigne

5650 MRSA from skin and soft tissue infections in Poland
M. Orczykawska-Kotyna* [Warsaw, Poland], D. Żura, M. Orczykowska-Kotyna* (Warsaw, Poland), D. Żura, M. Orczykowska-Kotyna* (Warsaw, Poland), D. Żura, M. Orczykowska-Kotyna* (Warsaw, Poland)

6994 Dalbavancin use in the United Kingdom: a multi-centre, retrospective evaluation of real-world use of an extended dosing interval lipoglycopeptide

8111 Biomarker profiles in streptococcal skin and soft-tissue infections with or without necrosis or shock: a prospective multi-centre study

8645 Characteristics and management of skin and soft tissue infections caused by Panton-Valentine leukocidin-producing Staphylococcus aureus (PVL-SA): a retrospective study of 99 cases
A. Assaf* [Lille, France], C. Loiez, M. Chapin, S. Panaget, A. Dozier, E. Faure, K. Faure, F. Vuotto

9238 Clinical characteristics and treatment of 255 patients hospitalised with bacterial cellulitis
L. Lucić* [Zagreb, Croatia], M. Mudrovčić, M. Puljiz, I. Puljiz

9419 Factors contributing to the duration of hospitalisation of patients with bacterial cellulitis
M. Mudrovčić* [Zagreb, Croatia], L. Lucić, M. Puljiz, I. Puljiz

Session accepted as Paper Poster Session
STIs: epidemiology, diagnosis, treatment

146 Sexually-transmitted infections in soldiers: a cross-sectional assessment and a review of literature
C. Gottwald, N. Schwarz, H. Frickmann* [Hamburg, Germany]

1066 Triple site versus urine only N. gonorrhoea/C. trachomatis testing among Israeli MSM in the condom fatigue era: a prospective study
D. Zoker, D. Turner, R. Ben-Ami, A. Adler, I. Singer, Y. Dizitzer, T. Halperin* [Tel Aviv, Israel]

1267 Mycoplasma genitalium infections in men who have sex with men: prevalence and macrolide resistance in north-east Italy
L. Clemente* [Monfalcone, Italy], M. Drabeni, G. Moise, F. Fontana

2001 Streptococcus pneumoniae: an uncommon possible cause of male urethritis?
F. Menotti, S. Cornini, C. Croccoli, R. Sparti, G. Amaru, C. Solimine, A. Cuffini, V. Allizond, G. Banche* [Turin, Italy]

2332 Detection and genotyping Lymphogranuloma venereum in Tenerife, Spain
B. Pino-Calm, D. García Martínez De Artola* [Santa Cruz de Tenerife, Spain], J. Alcoba-Florez, O. Diez Gil

2339 Prevalence of Mycoplasma genitalium and frequency of resistance to macrolides and fluoroquinolones in Tenerife, Spain
B. Pino-Calm, D. García Martínez De Artola* [Santa Cruz de Tenerife, Spain], J. Alcoba-Florez, O. Diez Gil

2345 Opportunistic screening for sexually-transmitted infections in young men with leukocyturia and negative urine culture in primary care
I. Angulo López, A. Gonzalez Sarria* [Bilbao, Spain], J. Aragón-Diez, M. Imaz Perez, L. Hernandez Raga, J. Alava Menica, J. Díaz De Tuesta

2632 Rapid detection of ciprofloxacin susceptible strains of Neisseria gonorrhoeae: an important guide for treatment
C. Cox* [Belfast, United Kingdom], J. Mckenna

2993 Genetic relatedness of ceftriaxone-resistant multidrug-resistant Neisseria gonorrhoeae isolates in Singapore
N. Abdul Rahman* [Singapore, Singapore], M. Chio, S. Goh, A. Tan, T. Koh, K. Ko

3039 The rapid method for detecting Neisseria gonorrhoeae and antimicrobial susceptibility
J. Sakai* [Moroyama-cho, Japan], N. Tarumoto, K. Imai, T. Maeda, S. Maekawa

3089 Inflammatory changes on routinely-performed Papancilou smear are more frequently associated with bacterial vaginosis
S. Baka* [Athens, Greece], A. Chasiakou, S. Demeridou, G. Kaparos, E. Kouskouni, V. Gennimata, A. Tsakris

3110 Trichomonas vaginalis trends for women and men in a national reference laboratory database
E. Marlowe* [San Juan Capistrano, United States], R. Kagan
Abstract Categories 2020

3916 Prevalence of Mycoplasma genitalium and macrolide resistance in Israel
O. Treigerman* {Tel-Aviv, Israel}, G. Prajgrod, D. Shasha

4229 High prevalence of sexually-transmitted infections among at-risk HIV-positive patients

4262 Reduced clinical improvement after treatment for urethritis in men with azithromycin resistant Mycoplasma genitalium
J. Braam* {Amsterdam, Netherlands}, A. Van Dam, S. Bruisten, M. Van Der Loeff, M. Van Rooijen, H. De Vries, C. Vergunst

4314 Experimental evolution of high-level azithromycin resistance in Neisseria gonorrhoeae during morbidostat culture

4597 Active search through multiplex PCR method for sexually-transmitted infections in patients with sterile pyuria
H. Gil Campesino, L. Sante* {San Cristobal De La Laguna, Spain}, M. Callejón Fernández, E. Callejas Castro, M. Lecuona

4962 Mycoplasma genitalium resistance against antibiotics in a Berlin MSM cohort tested with the Allplex MG & AziR Assay and Allplex MG & MixIR Assay
M. Obermeier* {Berlin, Germany}, S. Breuer, R. Ehret

4992 Prevalence of Chlamydia trachomatis and Neisseria gonorrhoeae at extragenital sites in the north metropolitan area in Catalonia
C. Casan, G. Fernández Rivas, A. Hernández Rodríguez, M. Carrasco, G. Linares, B. Rivaya Sanchez* {Badalona, Spain}, N. Romani Radés, A. Fernández Navarro, L. Matas Andreu

5100 Haemophilus influenzae as the causing pathogen of epididymo-orchitis: a case report
T. Demuyser* {Brussels, Belgium}, K. Vandoorslaer, S. Jacobs, L. Van Dijck, D. Pierard

5138 Incidence and predictors of Chlamydia trachomatis, Ureaplasma urealyticum, Mycoplasma hominis and Mycoplasma genitalium in patients with sterile pyuria
A. Aggarwal* {New Delhi, India}, B. Dhawan, N. Wig, N. Vikram, M. Soneja, R. Chaudhry, A. Kapil

5341 Microbiological features of vulvovaginitis in prepubescent girls
M. Damala, A. Nikolakopoulou, C. Anthoulaki* {Athens, Greece}, I. Koumpi, E. Prifti, L. Michala, N. Loukapoulou

5441 Neisseria gonorrhoeae transcriptome analysis: profiling molecular determinants of resistance
H. Machado, G. Toledo-Silva, J. Martins, M. Schörner, L. Goijetta, R. Mazzan, M. Pozzo* {Florianópolis, Brazil}

5482 Mycoplasma genitalium infections can comprise mixtures of both quinolone-susceptible and quinolone-resistant strains
E. Sweeney* {Herston, Australia}, K. Lowry, C. Bletchly, G. Nimmo, D. Whiley

5518 Association between the detection of human papilloma virus and pathogens causing sexually-transmitted infections in woman in reproductive period
I. Hadji Petrusheva Meloska* {Skopje, Macedonia}, K. Icse, A. Hadji-Petrusheva Jankijevik

5616 Epidemiology of Neisseria gonorrhoeae antimicrobial resistance and evaluation of alternative antibiotics
J. Yan* {Hangzhou, China}, S. Van Der Veen

5664 Bacterial STI-testing in the private sector in France, 2006-2018

5696 Detection rates of bacterial vaginosis and sexually-transmitted pathogens associated with genital discharge syndrome in the South-African private sector
C. Kingsburgh* {Pretoria, South Africa}, K. Strydam, M. Kock

5727 The natural history of gonorrhoea infection: an illustrative review
J. Whelan* {Amsterdam, Netherlands}, E. Beck

5764 Epidemiology and treatment outcome of Neisseria gonorrhoeae infections
J. Parke-Smith, C. Palmer, A. Jennison, V. Hicks, L. Ariotti, S. Bell, D. Whiley, A. Walker, G. Playford, A. Henderson* {Brisbane, Australia}

5793 Does trichomonas hurt? A five-year comprehensive full-region study
M. Berends* {Groningen, Netherlands}, D. Scoop, J. Weel, T. Schuurs

5820 Lactobacillus crispatus as a marker of cytolytic vaginosis in women under 45-years old?
L. Fontan, A. Yarci Carrión, S. Gómez De Frutos, A. Fraile Torres, L. Cardenal* {Madrid, Spain}, A. García

5851 High prevalence of Lymphogranuloma venereum in men who have sex with men in Alicante, south-east Spain
V. Ortiz-De La Tabla* {Alicante, Spain}, G. Gázquez, A. Infante

6902 Determination of prevalence of Chlamydia trachomatis in pregnant women between 15 to 25 years old at Hospital Universitario La Paz, Madrid, Spain B. Gómez Arroyo* [Madrid, Spain], P. González Danapetery, C. Fabra Garrido, M. Darado Criado, C. González Arboleya, E. Merino San Martín, C. Calvo Rey, M. De La Calle Fernández-Miranda, I. Quiles, J. García Rodríguez

7009 The role of using the UBU (Urethritis Basic Unit) and the FVU (First-Void Urine) in the quick diagnosis and adjustment of treatment in urethritis T. Martín Peñaranda* [Donostia/San Sebastian, Spain], I. De La Caba, D. Grandioso Vas, M. Gómez Ruiz De Arbulo, P. Idigoras


7075 Haemophilus influenzae parainfluenzae as triggers of urethritis in men: risk factors and characteristics of this emerging problem L. Fontan, A. Yarci Carrión, E. Navarro Lara, N. Zurita Cruz, L. Cardénoso* [Madrid, Spain], A. García

7425 Evaluation of ResistancePlus GC assay for the detection of Neisseria gonorrhoeae and markers associated with ciprofloxacin-susceptibility and resistance P. Salmerón* [Barcelona, Spain], P. García, M. Viñado, B. Romero, J. Colomina Rodríguez, O. Martínez, G. Martín-Saco, N. Sanchez Oliver, E. Alcoceba, L. Villa, A. Torreblanca, T. Pumarola-Suñé, Y. Hoyos-Mallecot, J. Serra Pladevall

7450 Resistance to azithromycin in Mycoplasma genitalium from patients of a tertiary hospital from Madrid, Spain P. García Clemente, V. Guédez López, S. Román Soto* [Madrid, Spain], J. Bernardino, E. Sendagorta, I. Quiles

7506 Antimicrobial susceptibility of Neisseria gonorrhoeae in southern Spain and co-infection with other sexually-transmitted pathogens L. Rojas, C. Gómez-Camara, A. De Salazar* [Granada, Spain], F. Ferrer, E. Serrano-Conde

7786 Fluoroquinolones and Macrolide resistance-associated mutations in Mycoplasma genitalium M. Oggioli* [Milan, Italy], S. Uceda Renteria, L. Tartaglione, C. Melchianno, M. Maddea, A. Orlandi, M. Cusini, G. Lunghi

7849 Genomic epidemiology and antimicrobial resistance surveillance of gonococci in Spain C. Francés-Cuesta* [Valencia, Spain], J. Serra, A. Fabregat-Boluyfer, B. Romero, T. Pumarola-Suñé, J. Colomina Rodriguez, J. Golán, F. Gonzalez-Candelas

7904 Mycoplasma genitalium: evaluation of macrolide resistance in a very large setting of sexually-transmitted infections A. Nava, E. Matarazzo, L. Colagrossi* [Milan, Italy], P. Carlo Federico, D. Fantino

7958 Distribution of minimum inhibitory concentration of ceftriaxone to gonococcal strains in a reference sexually-transmitted disease clinic in Madrid, Spain C. Lejarraza* [Madrid, Spain], B. Menendez, E. Tello, F. Geriz, O. Ayerdi, T. Puerta, M. Garcia, J. Ballesteros, P. Clavo, G. d’Elia, C. Rodríguez, J. Del Romero

8003 Characterisation of multidrug resistant Shigella sonnei isolated from men who have sex with men in Zagreb, Croatia J. Vranes* [Zagreb, Croatia], N. Prazic, B. Bedenic, B. Matica, G. Zarfel, I. Mareković


8081 Prevalence of resistance-associated mutations for ciprofloxacin in Neisseria gonorrhoeae and azithromycin and moxifloxacin in Mycoplasma genitalium R. Nijhuis* [Amersfoort, Netherlands], R. Duinsbergen, F. Godskałk

8114 Clonality and molecular resistance to tetracyclines of Neisseria gonorrhoeae among men who have sex with men using post-exposure prophylaxis with doxycycline B. Bercot* [Paris, France], A. Braille, D. Carrette, I. Charreau, N. Schnepf, C. Delaugerre, L. Cotte, C. Bébéar, P. Gilles, C. Capitant, R. Nijhuis, B. Roca


8271 Prevalence of resistance-associated mutations for ciprofloxacin in Neisseria gonorrhoeae and azithromycin and moxifloxacin in Mycoplasma genitalium R. Nijhuis* [Amersfoort, Netherlands], R. Duinsbergen, F. Godskałk

8300 Prevalence of resistance-associated mutations for ciprofloxacin in Neisseria gonorrhoeae and azithromycin and moxifloxacin in Mycoplasma genitalium R. Nijhuis* [Amersfoort, Netherlands], R. Duinsbergen, F. Godskałk


8505 Prevalence of resistance-associated mutations for ciprofloxacin in Neisseria gonorrhoeae and azithromycin and moxifloxacin in Mycoplasma genitalium R. Nijhuis* [Amersfoort, Netherlands], R. Duinsbergen, F. Godskałk

8523 Clonality and molecular resistance to tetracyclines of Neisseria gonorrhoeae among men who have sex with men using post-exposure prophylaxis with doxycycline B. Bercot* [Paris, France], A. Braille, D. Carrette, I. Charreau, N. Schnepf, C. Delaugerre, L. Cotte, C. Bébéar, P. Gilles, C. Capitant, R. Roffa, J. Molina

8557 Drug-resistant Neisseria gonorrhoeae and Mycoplasma genitalium identified in the private healthcare sector in South Africa L. Maduna, R. Peters, C. Kingsburgh, K. Strydom, M. Kock* [Pretoria, South Africa]
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443 Prevalence and antimicrobial susceptibility of *Ureaplasma* species and *Mycoplasma hominis* in female patients in Korea: increasing trend of pristinamycin-resistant isolates
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2858 Global prevalence estimates of syphilis among men who have sex with men: a systematic review and meta-analysis
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6853 Microbiology of tubo-ovarian abscess in a tertiary hospital in Spain
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7458 Alarming high occurrence of multidrug resistance of *Mycoplasma genitalium* in a cohort of men who have sex with men using pre-exposure prophylaxis in Belgium (Be-PreEP-ared study)
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The multiresistance strikes back

430 Multidrug resistant Gram-negative infections among critically ill patients: analysis of baseline characteristics and factors associated with mortality
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1074 Mortality outcome in critically ill CRO infection patients treated with polymyxin-B and its prediction based on morbidity and mortality scores
S. Patil* [Mumbai, India], B. Jibkhate, K. Shah, K. Parikh, A. Bhattacharya, N. Shinde, S. Bhagat, H. Barkate

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M. Hovan* [Piscataway, United States], N. Narayanan, V. Cedarbaum, T. Bhowmick, T. Kim

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J. Wang* [Geneva, Switzerland], M. Zhou, J. Sauser, W. Zingg

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Y. Yang* [Guangzhou, China], G. Chen, Y. Yang, M. El-Sayed Ahmed, M. Lin, X. Wen, G. Tian

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7555 Improved prediction of mortality in sepsis using peripheral capillary oxygen saturation to estimate the respiratory dysfunction score: a cohort study
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9323 Impact of out-of-hours results and infection specialist intervention on the time to the first appropriate antimicrobial therapy in patients with Gram-negative bacteraemia: the South London CLAHRC cohort experience
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1831 Detection of rifampin and isoniazid resistance using molecular testing to initiate an ethambutol-free 3-drug regimen in pulmonary tuberculosis: a French non-inferiority multi-centre randomised clinical trial

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**Tuberculosis management and treatment**

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**Monitoring of difficult-to-treat tuberculosis patients in Ghana identifies additional pre-XDR and XDR cases**


**Clinical impact of ceasing isolation procedure using a single molecular test for suspected pulmonary tuberculosis in The Royal Melbourne Hospital**

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**Targeting membrane transporters and energy metabolism in *Mycobacterium tuberculosis* through *in silico* drug repurposing**

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**A prospective randomised controlled trial comparing the effectiveness of smartphone video directly-observed therapy (VDOT) versus in-person DOT in newly-diagnosed pulmonary tuberculosis patients**

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Are large cities at higher risk for tuberculosis drug resistance? A French appraisal
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Telehealth use in tuberculosis: results from a systematic review and focus group interviews in six countries worldwide
M. Ioana* [Groningen, Netherlands], D. Akkerman, C. Louka, Y. Stienstra, J. Alffenaar

Therapy directly observed by video for the supervision of tuberculosis treatment: experience in a series of patients from Cali, Colombia, 2019
M. Tello-Cajiao, J. Garcia-Goez, N. Romero-Rosas, S. Ardila-Giraldo* [Cali, Colombia], J. Mosquera-Hernández, L. Parra-Lara

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A. Azizi* [Kabul, Afghanistan], K. Hashemi

Drugs repurposing: in vitro testing of licensed drugs to assess role against MDR/XDR-TB
X. Gonzalo* [London, United Kingdom], F. Drabniowski

A model-based analysis identifies differences in phenotypic resistance between in vitro and in vivo: implications for translational medicine within tuberculosis
D. Clewe, A. Faraj* [Uppsala, Sweden], Y. Hu, A. Coates, U. Simonsson

Graphene oxide-linezolid combination as potential new anti-TB treatment
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Evaluation of efflux pump inhibitor combination with fluoroquinolones and aminoglycosides in resistant clinical isolates of Mycobacterium tuberculosis
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Development and validation of a questionnaire to explore tuberculosis knowledge, attitudes and practices in foreign-born subjects from high tuberculosis-incidence countries
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The real-life impact of the Xpert MTB/RIF Ultra assay on the diagnosis of tuberculosis in a hospital in central Israel
O. Schwartz, O. Yosseppowitch, Y. Maor* [Holon, Israel]

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S. Israïls* [London, United Kingdom], J. Millard, K. Bailesy, E. Ngam, J. Der, A. Grant

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Y. Lambert* [Cayenne, French Guiana], V. Sainte-Rose, C. Leborgne, B. Moreau, M. Demar

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S. Tan* [Singapore, Singapore], I. Wee, Y. Coo, N. Abdul Rohman, A. Tan, K. Ko

First report of blaNDM-1 and blaOXA-181 harbouring P. vermicola from Nepal
K. Haque* [Narita, Japan], T. Matsumoto, T. Sekizuka, M. Kuroda, R. Sah

Genomic characterisation of Kersteria gyiorum, an isolate from a patient with acute otitis media
A. Kruglov, V. Gostev* [Saint Petersburg, Russian Federation], D. Likhaletova, O. Generalova, S. Sidorenko

Understanding the molecular history of an ancient Pseudomonas species isolated from a pharaonic Egyptian mummy: a genomic tale from the 11th dynasty of the middle kingdom
M. El-Sayed Ahmed* [Guangzhou, China], Y. Yang, C. Shen, X. Wen, Y. Yang, G. Tan

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3187 Efficiency of antibiotic prophylaxis in recurrence of UTI among kidney transplant recipients
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4474 Phenotypic and genotypic comparison between *Escherichia coli* isolates causing recurrent and sporadic cystitis
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[Vandoeuvre lès Nancy, France]

Prevalence of ST131 in community-acquired Escherichia coli urinary tract infections in Gauteng, South Africa
K. Hoog, J. Pitout, E. Hoosien, M. Ehlers, M. Kock*
[ Pretoria, South Africa]

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F. Carrasco* [Madrid, Spain], J. Cuadros, D. Roca, M. Górgolas, R. Perez Tanoira

Identification, genotyping and antimicrobial susceptibility testing of Brucella spp. isolated from livestock in Egypt
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Neurological manifestations of rickettsiosis
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A. Aubin, C. Eldin* [Marseille, France], E. Braunberger, J. Jaubert, Y. Kouram, M. Moïton, P. Poubée, N. Zemali, P. Gerardin, A. Bertolotti

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M. Tetens* [Copenhagen, Denmark], R. Haahr, R. Dessau, K. Kragfelt, J. Badilsen, N. Skaarup Andersen, J. Kjelseth Møller, C. Roed, C. Christiansen, S. Ellermann-Eriksen, J. Bangsborg, K. Hansen, T. Benfield, C. Østergaard, N. Obel, L. Omland, and A. Lebech

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Cat scratch disease in children and adults: what a difference?
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Rickettsiosis: a series of 80 cases
F. Larbi, M. Ben Azaiez* [Monastir, Tunisia], J. Chelli, S. Arfa, O. Berriche, M. Sfar

Study on Bartonella related to small mammals in the Canary Islands, Spain

Clinical profile and associated comorbidities to predict outcomes in patients with scrub typhus with acute kidney injury: a study from Central India
D. Jeswani* [Nagpur, India], B. Jeswani
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3. Bacterial susceptibility & resistance

- Resistance surveillance & epidemiology: MRSA, VRE & other Gram-positives
- Resistance surveillance & epidemiology: Gram-negatives
- Susceptibility testing methods (incl assay validation and comparative studies, excl TB)
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- Resistance detection / prediction approaches (rapid and/or molecular assays, resistome analysis, inference methods)
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K. Bansal* [Chandigarh, India], P. Patil, T. Saroha, A. Kaur, S. Kumar, S. Kaur, V. Gautam, P. Patil

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K. Xanthopoulou* [Cologne, Germany], J. Wille, J. Zweigner, K. Lucassen, H. Seifert, P. Higgins

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C. Meyer* [Cologne, Germany], K. Lucassen, K. Xanthopoulou, T. Wille, H. Seifert, P. Higgins

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Multidrug-resistant A. baumannii beyond colistin era: in vitro synergy of ceftazidime/avibactam in combination with antibiotics
H. Moraitou* [Athens, Greece], V. Perdios, M. Makarana, A. Mavrommatis, K. Pontikis, S. Triantafyllou, M. Voutou, T. Kioussi, S. Karabela

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M. Gimenez* [Badalona, Spain], M. Monsonis, N. Larrosa, P. Perez, A. Rivera, F. Gomez, A. Bernet, G. Trujillo, E. Clapes, J. Llaberia, M. Perez, C. Martí, R. Rubio Casino, V. Pineda

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R. Benko, M. Gajdacs* [Szeged, Hungary], M. Metuz, G. Soós, L. Andrea, E. Hujdú, P. Hanner, Z. Peto

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E. Fagan* [London, United Kingdom], S. Seaton, P. Shah, N. Bunkock, S. Bi, P. Chadwick

In vitro activity of commonly used antimicrobial agents against clinical Gram-negative bacterial isolates from ATLAS Indian centres in 2018
P. Hsueh* [Taipei, Taiwan]

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A. Tuohy, N. Delapole, E. Mcgrath, W. Brennan, M. Maguire, M. Cormican* [Dranmore, Ireland]

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M. Gonzalez Sanz* [London, United Kingdom], N. Marshall, A. Claxton, K. Woods

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M. Lekalakala* [Bendor, Polokwane, South Africa]

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Y. Yu* [Guangzhou, China], C. Cui, X. Kuang, C. Chen, X. Liao, J. Sun, Y. Liu

Epidemiology and antimicrobial resistance of methicillin-resistant Staphylococcus aureus isolates colonising pigs with different exposure to antibiotics
E. Lopes, T. Conceição, L. Poirel, H. De Lencastre, M. Aires de Sousa* [Lisbon, Portugal]

Comparison of the distribution of quinolone resistance markers in Escherichia coli in a human-animal health interface model
J. Silva-Sanchez* [Morelos, Mexico], G. Sanchez, C. Alpuce-Aranda, E. Tamayo, V. Gonzalez, U. Garza-Ramos, H. Barrios, D. Arellano

Triangulating the molecular epidemiology of carbapenem-resistant Enterobacteriales in humans,
food-producing animals and the environment in a One Health context
Y. Ramsamy* [Durban, South Africa], K. Misana, D. Gyanfi Amoako, M. Alham, A. Ismail, A. Luther King, R. Singh, S. Essack

Carriage of ESBL-producing Gram-negative bacteria by households captured in hospital and suburban surroundings in Ethiopia differs greatly

Global increase in antibiotic-resistant Escherichia coli in food-animal: a genomic public data approach
J. Pires* [Zurich, Switzerland], J. Huisman, S. Bonhoeffer, T. Van Boeckel

Nasal carriage of livestock-associated Staphylococcus aureus in Poland
A. Mrczkowska* [Warsaw, Poland], N. Marszałek, M. Orczykowska-Katyna, T. Tomczak, M. Brzozowska, J. Zmudzki, A. Skoczyńska, J. Empel

High-level AmpC beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae in Dutch hospitals and livestock farms: results from the i-4-1-1-Health project
E. Den Drijver* [Breda, Netherlands], M. Kluytmans - Van Den Bergh, B. Diederen, S. Pas, J. Stohr, F. Velkers, J. Verhulst, J. Verweij, A. Stegeman, J. Kluytmans

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Metagenomic insights into the dynamics and transmission of resistance genes in poultry and human beings
Q. Luo* [Hangzhou, China], H. Fu, Y. Xiao

Global dissemination of multidrug-resistant E. coli co-expressing ESBL/pAmpC and mcr-1 genes in chicken farms in Lebanon
M. Mikhael* [Beirut, Lebanon], S. Leclercq, B. Doublet, D. Karam Sarkis

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Q. Zhao, Y. Zhang, Y. Lu, R. Cai, H. Jiang* [Guangzhou, China]

Limited genetic diversity of blaCMY-2-containing Incl1-ST12 plasmids from Enterobacteriaceae of diverse human and bovine origin in the Netherlands
E. Den Drijver* [Breda, Netherlands], J. Stohr, J. Verweij, C. Verhulst, F. Velkers, A. Stegeman, M. Kluytmans - Van Den Bergh, J. Kluytmans

Rural and urban dogs as a source of ESBL-producing Enterobacteriaceae in northwest Spain
Lamb meat as a source of dissemination of cephalexin-resistant \textit{Escherichia coli}

K. Gazi, L. Deus Aude, L. Kalir Pradela* (Sao Jose do Rio Preto, Brazil), M. Barrosa, C. Silva, M. Nogueira, T. Casella

Emergence of \textit{mcr}-1 among diverse multidrug-resistant \textit{Escherichia coli} in gulls from a coastal city uncoverts potentially underestimated transmission routes


\textbf{ESBL- and p\textsuperscript{AmpC}-producing \textit{Escherichia coli}} in imported broiler breeding birds for the Swedish broiler production

S. Börjesson* (Uppsala, Sweden), O. Nilsson, A. Landén, C. Greko, B. Bengtsson

\textbf{CREATE:Carbapenem-Resistant Enterobacteriaceae: Animal Testing and Epidemiology. A plan for veterinary medicine}

S. Cole, D. Oakley, S. Rankin* (Philadelphia, United States)

Complete genome sequencing of extended-spectrum \textit{beta-lactamase-} (ESBL) producing \textit{Escherichia coli} isolated from dairy cattle in Japan

H. Kudo* (Saitama, Japan), M. Usui, K. Oka, M. Takahashi, Y. Tamura

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\textbf{Investigating the prevalence of ESBL-producing \textit{Escherichia coli} in rooks (\textit{Corvus frugilegus}) wintering in an urban area and comparing these isolates to contemporary human faecal and clinical isolates}

J. Nagy* (Debrecen, Hungary), B. Balázs, I. Damjanova, A. Toth, P. Gyüre, L. Kövér, G. Kardos

\textbf{Characterisation of a cfr gene variant in multidrug-resistant (MDR) livestock-associated methicillin-resistant \textit{Staphylococcus aureus} (LA-MRSA), isolated from Italian pig herds}

E. Diaconu* (Rome, Italy), P. Alba, M. Iurescia, V. Carfora, A. Caprioli, A. Franca, A. Battisti

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M. Camoez* (Oeiras, Portugal), A. Botelho, O. Bouchami, H. Fernandes, N. Faria, D. Lawal, M. Fraqueza, M. Miragaia

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L. Schuele* (Boeblingen, Germany), G. Fleres, K. Strutzberg-Minder, C. Erdmann, C. Lambrecht, J. Hanlizius, S. Schütze, S. Löbert, N. Couta, J. Rossen

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R. Garcia Sierra* (Lyon, France), A. Drapeau, M. Dazas, E. Saras, E. Hirchoud, C. Parada Rodrigues, S. Brisse, J. Madec, M. Haenni

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M. Qamar* (Faisalabad, Pakistan), M. Rizwan, I. Bashiri, M. Rasool, S. Kariuki, G. Palmer

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W. Mansour, Y. Mani, R. Grami, E. Saras, O. Bouallègue, M. Haenni* (Lyon, France), J. Madec

\textbf{Genetic relatedness, antimicrobial resistance, virulence and biofilm-forming abilities of \textit{Klebsiella pneumoniae} from healthy broilers and turkeys}

F. Franklin* (Oslo, Norway), M. Hetland, R. Bakksjø, L. Nesse, I. Lühr, A. Telke, M. Sunde

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C. Silva, M. Barroso, K. Gozi, J. Froes, L. Kalir Pradela, J. Peiró, L. Nogueira Mendes, M. Nogueira, T. Casella* (Sao Jose do Rio Preto, Brazil)

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Genetic antimicrobial resistance determinants found in Escherichia coli and other environmental microorganisms isolated from raw vegetables expended in Ibarra, Ecuador
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D. Rodriguez-Lozaro, L. Casado, J. Santamaría, E. Pontille, R. Rodríguez-Pollan, M. Hernandez, I. Fernández-Natal* [León, Spain]

Screening and characterisation of multidrug-resistant Enterobacteriaceae in healthy companion animals in close contact with humans
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Interspecific transfer of a blaVIM-2-containing plasmid between Pseudomonas spp. during a nosocomial outbreak
J. Pirzadian* [Rotterdam, Netherlands], N. Streps, A. Heikema, W. Zandijk, H. Koene, W. Goessens, M. Vos, C. Kloassen, J. Severin

CrrP-like fluoroquinolone-modifying enzymes among Pseudomonas aeruginosa clinical isolates in Europe
J. Ortiz De La Rosa* [Fribourg, Switzerland], P. Nordmann, L. Poirel

Co-production of KPC and SPM carbapenemases by Pseudomonas aeruginosa in same hospital in northern Brazil
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<td>9339 VIM-producing <em>Pseudomonas aeruginosa</em> isolated in Southern Tunisia, 2012-2018 Y. Jellouli, N. Ben Ayed, B. Mnif, A. Hammami* [Sfax, Tunisia]</td>
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<td>9469 Integrons &amp; antibiotic resistance: do integrons provide ‘adaptation on demand’? C. Souque* [Oxford, United Kingdom], J. Escudero, C. Macleod</td>
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<td>9588 Carbapenemase-producing <em>Pseudomonas aeruginosa</em> in south Brazil C. Sanches Ito, L. Bail* [Ponta Grossa, Brazil], L. Arend, M. Pilonetto, G. Becker, K. Nagueira, F. Tuon</td>
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**Session accepted as Mini-oral Flash Session**

### Antimicrobial resistance in the community

| 3196 Bacteriophage control the prevalence of *Escherichia coli* ST131 in different countries J. Mathias* [Cardiff, Wales, United Kingdom], D. Babenko, A. Almusallam, R. Farzana, M. Toleman |
| 4075 Fluoroquinolone resistance in *Escherichia coli* isolates after exposure to non-fluoroquinolone antibiotics: a retrospective case-control study L. Chaname Pinedo, R. Bruyndonckx, B. Catry* [Brussels, Belgium], K. Lator, S. Abrams, H. Goossens, S. Coenen |
| 4146 Optimised positioning of carbapenem-sparing options for treatment of UTIs by molecular antibiotic susceptibility testing N. Adamakoh, N. Mahfouz, P. Harris, F. Franceschi, A. Henderson, S. Beisken, E. Littinringer, A. Posch* [Wien, Austria] |
| 4185 Clonal spread of *mcr*-3-carrying multidrug-resistant *ST34 Salmonella Typhimurium* and its monophasic from human globally L. Fang* [Guangzhou, China], R. Sun, W. Guo, J. Sun, X. Liao, Y. Liu |
5341  Population structure dynamics of *Escherichia coli* ST131 over time
G. Peirano* [Calgary, Canada], T. Lynch, R. Devinney, T. Finn, Y. Matsumura, J. Pitout

6705  Restriction modification systems affect the ability of *Escherichia coli* ST73 to acquire plasmids
J. Alves Gama* [Tromsø, Norway], J. Klaas, P. Johnsen, D. Samuelson

8075  SNP-based phylogeny revealing establishment of ciprofloxacin-resistant *Shigella sonnei* lineage in India
D. M. S.* [Vellore, Tamil Nadu, India], A. Pragasam, K. Vasudevan, D. Murugan, S. Anandan, V. Balaji

9632  Measuring and mapping the burden of antimicrobial resistance in enteric infections

**Session accepted as Paper Poster Session**

**Antimicrobial resistance in urinary tract infections**

911  High prevalence of antimicrobial resistance in community-acquired urinary tract infections in Harare, Zimbabwe
I. Olara* [London, United Kingdom], M. Chisenga, R. Ferrand, S. Yeung, H. Hopkins, R. Stabler, P. Chonzi, J. Bradley, K. Kranzer

1278  Antimicrobial resistance and genotypic markers of trimethoprim resistance in *Escherichia coli* and *Klebsiella* spp. isolated from patients with urinary tract infections
Y. Somorin* [Belfast, United Kingdom], N. Wei, M. Higgins, C. Hughes, D. Gilpin, M. Crockard, M. Tunney

1548  Comparison of antibiotic susceptibility of *Escherichia coli* between community-acquired and post-prostate biopsy acute bacterial prostatitis
G. Song* [Chuncheon, South Korea], J. Lee, M. Park, S. Kwon, H. Choi, K. Kim, S. Bae

3173  Prevalence of antibiotic resistance among *Enterobacteriaceae* isolates recovered from urinary samples in France

3319  Antimicrobial resistance in urinary tract infection cases submitted to a computerised decision support system for antibiotic prescribing in primary care in France
T. Delory* [Paris, France], P. Jeanmougin, S. Lariven, F. Tubach, P. Boëlle, E. Bouvet, X. Lescure, J. Le Bel

4061  Urinary tract infections in children: antibiotic resistance of major pathogens in Western Attika, Greece [October 2014 to October 2019]

4823  Resistance among urinary tract infection pathogens collected in Europe during 2018
I. Critchley* [Cambridge, United States], N. Coteonne, M. Pucci, A. Jain, R. Mendes

5684  Increase of *Escherichia coli* with reduced susceptibility to cepheime and OXA-1 compatible phenotype in urinary tract infections along the years
S. Nabil Diaz, J. Bueno, P. Pilar, S. Morneno Bayo, B. Sanz, C. Guererra, J. Garcia-Lechuz Moya, A. Rezusta, A. López-Calleja* [Zaragoza, Spain]

5854  Antimicrobial resistance among urinary *Enterobacteriaceae* from patient living in nursing homes
S. Thibaut* [Nantes, France], T. Coeffic, D. Boutoille, G. Birgand, J. Caillon, P. Network

6871  In vitro susceptibility of carbapenem-resistant *Enterobacteriaceae* urinary isolates to nitroxoline and other oral urinary antibiotics
A. Sonnevend* [Pécs, Hungary], A. Ghazawi, T. Pal

7433  Antimicrobial resistance among bacteria causing asymptomatic bacteriuria in pregnant women, rural Burkina Faso

9434  Retrospective analysis of antibacterial resistance among uropathogen *Escherichia coli* in a veterinary teaching hospital [Italy, 2014-2019]
P. Nebbia* [Turin, Italy], A. Bellata, A. Attili, M. Stella, F. Canavesi, P. Robino

**Session accepted as Paper Poster Session**

**Antimicrobials against Gram-positive bacteria**

1019  Activity of omadacycline and comparator agents against bacterial pathogens from the United States by infection type [2019]
M. Huband* [North Liberty, United States], M. Pfaller, J. Streit, L. Duncan, R. Flamm

1043  In vitro surveillance of eravacycline against Gram-positive pathogens, including resistant isolates, collected from European hospitals in 2018
S. Hwang, S. Hawser, I. Morrissley* [Monthey, Switzerland], F. Monti, E. Efimova, M. Olesky

1322  Resistance mechanisms associated with pleuromutilins among Gram-positive clinical isolates from the worldwide surveillance programme for lefamulin in 2018
R. Mendes* [North Liberty, United States], T. Doyle, M. Castanheira, R. Flamm, S. Gelone, S. Paukner, H. Sader
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1650 Distinct effectiveness of oritavancin against
tolerance-induced *Staphylococcus aureus*
L. Harven, V. Bingley, P. Kulkarni, S. Khaira, S. dey,
P. Smolenski, A. Bertii* (Detroit, United States)

1886 Longitudinal [2011-2018] activity of oritavancin
against Gram-positive isolates causing bacteremia
and endocarditis in Europe, including enterococcal
infections requiring adjusted daptomycin dosing
C. Goday Carvalhoes* (North Liberty, United States),
H. Sader, J. Streit, R. Flamm, R. Mendes

1887 Delafloxacin activity against drug-resistant
*Streptococcus pneumoniae*, *Haemophilus influenzae*,
*Haemophilus parainfluenzae*, and *Moraxella
catarrhalis* from European medical centres
(2014-2018)
D. Shortridge* (North Liberty, United States), J. Streit,
M. Huband, R. Flamm

2338 Evaluation of tedizolid and comparators activity
against Gram-positive bacterial isolates causing skin
and skin structure infections from paediatric patients
in Europe and surrounding countries [2015-2019]
C. Goday Carvalhoes* (North Liberty, United States),
H. Sader, J. Streit, R. Flamm, R. Mendes

2359 Tedizolid activity against a global collection of Gram-
positive bacterial isolates causing bone and joint
infections [2017-2019]
C. Goday Carvalhoes* (North Liberty, United States),
H. Sader, J. Streit, R. Flamm, R. Mendes

2367 European regional analysis of the *in vitro* activities of
delafloxacin and comparator agents against bacterial
pathogens frequently isolated from patients with
community-acquired respiratory tract infections:
ATLAS surveillance programme 2015-2018
J. Karlowsky, M. Hackel* (Schaumburg, United States),
S. Bouchillon, G. Stone, D. Sahn

2371 *In vitro* activity of ceftaroline and comparator agents
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with skin and soft tissue infections in Europe: a
regional analysis of results from the ATLAS
surveillance programme 2015-2018
J. Karlowsky, M. Hackel* (Schaumburg, United States),
S. Bouchillon, G. Stone, D. Sahn

2735 5-year surveillance of iferumig against Gram-positive
cocci collected from Adult Bacterial Skin and Skin-
Structure Infections (ABSSSI) and Bloodstream
S. Pauknner* (Vienna, Austria), S. Gelone, S. Arends,
H. Sader

2774 Ozenoxacin, a topical fluoroquinolone, demonstrates
activity versus methicillin-susceptible and methicillin-
resistant *Staphylococcus aureus*, and *Streptococcus
gyogenes* wound isolates including fluoroquinolone-, fucidic acid- and mupirocin-resistant strains
P. Lagacé-Wiens* (Winnipeg, Canada), H. Adam,
M. Baxter, J. Karlowsky, G. Zhanel

3010 *In vitro* activity of omadacycline against pathogens
isolated from mainland China during 2017-2018
Y. Guo, D. Dong, Q. Chen, Y. Zheng, Y. Yang, S. Wu, D. Zhu,
J. Deng* (Shanghai, China), P. Bradford, H. Reinhart, F. Hu

3561 Delafloxacin *in vitro* activity in skin and soft tissue
infections by methicillin-resistant and levofloxacin-
resistant *Staphylococcus aureus*
M. Liras Hernández* (Madrid, Spain), J. García
Rodríguez, R. Gmez

3606 Antimicrobial activity of XF-73 against clinically
relevant Gram-positive bacteria
I. Romeo-Melody* (Birmingham, United Kingdom),
D. Hynes, W. Rhys-Williams, B. Love, P. Lamb, T. Worthington

3840 Reporting antimicrobial susceptibilities and resistance
phenotypes in *Staphylococcus* spp.: a nation-wide
proficiency study
F. Fernández-Cuenca* (Seville, Spain), I. López-
Hernández, M. Canedo, N. Tormo, C. Gimeno Cordona,
E. Cercenado, A. Pascual Hernández

4060 Cefotiboprole susceptibility of European Gram-positive
and *Enterobacteriaceae* clinical isolates from different
infection sources collected in 2018
S. Hawser* (Monthey, Switzerland), I. Morrissey,
N. Kothari, N. Jenney

4292 Comparison of susceptibility of rifabutin and
rifampicin on *Staphylococcus* spp. isolated in bone and
joint infections
P. Thill, O. Bobineau, E. Senneville* (Tourcoing, France),
B. Nicolas

4704 In *vitro* activity of ceftaroline and comparators against
*Staphylococcus aureus* clinical isolates from a tertiary
hospital in Greece
A. Tychali* (Thessaloniki, Greece), M. Arhanti, F. Netsika,
G. Meletis, P. Mantzana, O. Vasilaki, G. Kagkalou,
E. Protonotariou, L. Skoura

4715 Increased fusidic acid resistance among
*Staphylococcus aureus* skin and soft tissue infections
in Portugal
T. Conceição* (Oeiras, Portugal), C. Ferreira, R. Luzio,
H. De Lencastre

4740 Antimicrobial activity of ceftobiprole against clinical
*Staphylococcus aureus* isolates from Germany
F. Layer* (Wannigerode, Germany), B. Strommenger,
I. Klare, G. Werner

5472 Therapeutic innovation in bone and joint infections:
evaluation of the activity of exebacase [CF-301 lysis]
on clinical strains belonging to *Staphylococcus
erdimeris* species
A. Souche* (Lyon, France), C. Kolenda, C. Dupieux,
R. Schuch, T. Ferry, F. Laurent, J. Josse

5738 Prevalence of antibiotic resistance in skin infections
among migrants compared to Danish-born patients
G. Köse* (Norrebro, Denmark), L. Sloth, R. Nielsen,
C. Østergaard, M. Nørredam

6951 *In vitro* activity of ceftaroline and ceftobiprole against
*Enterococcus faecalis* recovered from infective
endocarditis and/or bloodstream infections
R. Rodríguez García, I. Costales, A. Rodríguez-Esteban,
M. Telenti, E. Garcia, J. Fernández* (Oviedo, Spain)
6997 Distinct augmenting contribution of hyperbaric oxygen therapy to neutrophil function and antibiotic efficacy against Staphylococcus aureus
F. Schwartz* [Copenhagen, Denmark], L. Christophersen, P. Jensen, C. Johann Lerche, C. Moser

7007 Pleuromutilin resistance in methicillin-resistant Staphylococcus aureus at the human-animal interface, Denmark
J. Larsen* [Copenhagen, Denmark], A. Petersen, R. Sieber, A. Larsen, U. Sönksen

7217 In vitro activity of delafloxacin against high-level levofloxacin-resistant invasive isolates of Streptococcus pneumoniae
E. Cercenado* [Madrid, Spain], C. Laras, A. Cobos, J. Sanz

7328 Mupirocin exposure in the preceding year is associated with mupirocin resistance among methicillin-resistant Staphylococcus aureus in a tertiary care hospital in the United States of America
E. Drehs* [Tampa, United States], L. Holt, S. Lakshmi, J. Kalter, A. Abraham, K. Atrubin, P. Thompson, S. Silbert, A. Kumar

7377 Evolution of teicoplanin susceptibility pattern of Staphylococcus aureus and coagulase-negative Staphylococcus spp. related to orthopaedic infections
P. Oliveira, V. Carvalho, A. Anjos, J. Araujo* [Sao Paulo, Brazil], C. Panico, T. Vitoriano, L. Silva Neto, I. Marinho, V. Amorim, F. Rossi, A. Munhoz

8343 Prevalence of blaZ gene types and the inoculum effect with ceftazolin among bloodstream isolates of methicillin-susceptible Staphylococcus aureus
I. Guerrero Lozano, F. Galan-Sanchez* [Cádiz, Spain], J. Peñate, V. Andrade-Brazo, M. De La Rubia, M. Rodriguez-Iglesias

8944 Antibiotic resistance patterns of Staphylococcus aureus isolated in blood cultures in primary care patients with renal diseases
U. Ghoshal* [Lucknow, India], A. Pathak, S. Singh, C. Sahu, N. Prasad

1116 Costs and benefits of OXA-48 variants selected under sub-lethal concentrations of ceftazidime
C. Fröhlich* [Tromsø, Norway], J. Alves Gama, K. Harms, P. Johnsen, O. Samuelsen, H. Leiras

Emergence of blaNDM and mcr-1 positive pan-and extremely-drug resistant bacterial infections in patients with renal diseases
U. Ghoshal* [Lucknow, India], A. Pathak, S. Singh, C. Sahu, N. Prasad

Prevalence of carbapenemase-producing Gram-negative bacilli in a health area of southern Spain

Qualitative detection of OXA-23-like, OXA-24-like and OXA-58-like carbapenemases from Acinetobacter species by real-time PCR
M. Mentasti, K. Prime, K. Sands, S. Khan, M. Wootton* [Cardiff, United Kingdom]

Whole genome sequence analysis of Klebsiella pneumoniae isolates belonging to sequence type 231 harbouring rapidly disseminating blaOXA-232 located on ColKP3 plasmid in Kuwait
A. Al Fadhli* [Kuwait, Kuwait], W. Jamal, V. Rotimi

Prevalence and impact of meropenem-resistant among nonresistant OXA-48-producing Klebsiella pneumoniae
N. Bustos De Godoy, L. Lopez-Cerera* [Seville, Spain], M. Sánchez, E. Recacho, M. Conejo, A. Pascual Hernandez

Effect of biocides on the mobilisation of plasmid-encoded OXA-48 carbapenemases from Klebsiella pneumoniae growing in biofilms
P. Pérez-Palacios, A. Gual-De-Torrella* [Seville, Spain], M. Delgado-Valverde, J. Oteo, A. Pascual Hernandez, F. Fernández-Cuenca

Identification of genetic factors increasing carbapenem resistance in Klebsiella pneumoniae with blaOXA-48
M. Cremanns* [Bochum, Germany], S. Gattermann, N. Pfennigwerth

Diversity of ESBL- and carbapenemase-producing Enterobacteriaceae with emergence of mcr-1 and carbapenem transferable resistance in a cancer clinical setting in Egypt
M. Mersa* [Porto, Portugal], J. Palmeira, H. Ferreira

The application of CRISPR/Cas9-based genome editing in knockout out the blaNDM-1 gene to study the mechanisms of pandrug resistance in clinical isolates
X. Yu* [Hangzhou, China], Y. Xiao

IS26-mediated transfer of blaNDM-1 as the main route of resistance transmission during a polyclonal, multispecies outbreak in a German hospital
R. Weber* [Wernigerode, Germany], M. Pietsch, A. Frühlauf, Y. Pfeifer, M. Martin, D. Luft, S. Gatermann, N. Pfennigwerth, M. Kaase, G. Werner, S. Fuchs

Rapid detection of OXA-23-, OXA-40- and OXA-58-mediated carbapenem resistance in Acinetobacter baumannii
S. Mertins* [Cologne, Germany], P. Higgins, C. Thunissen, Q. Gillemann, P. Martens, H. Seifert, M. Kroenke, A. Klimka
4994 A retrospective study to evaluate the epidemiology, standard of care, outcomes and resource utilisation in patients with confirmed or suspected infection by a carbapenem-resistant Gram-negative organism in the UK: the CARBAR study part 2
S. Goldenberg* [London, United Kingdom], A. Dodgson, G. Barlow, B. Parcell, L. Jones, M. Albur, P. Wilson, D. Enoch, A. Marek, D. Manissero, C. Longshaw, K. Tone, S. Lopes

5021 The resistance ratchet tightens: widespread penicillin-binding protein-3 insensitivity in carbapenem-producing Escherichia coli
S. Mushtaq* [London, United Kingdom], M. Ellington, N. Woodford, D. Livermore

5075 Characterisation of resistance-increasing determinants of OXA-48-bearing clinical isolates of Klebsiella pneumoniae
L. Höfken* [Bochum, Germany], M. Cremanns, S. Gatermann, N. Pfennigwerth

5569 Characterisation of carbapenemase-producing Enterobacteriales isolates with phenotypic and genotypic methods in southern Hungary
M. Gajdics* [Szeged, Hungary], M. Ábrók, L. Andrea, L. Jámvári, A. Tóth, K. Burian, G. Terhes

5729 Investigation of antibiotic susceptibilities, clonal relationships and carbapenem resistance mechanisms of Serratia marcescens obtained between 2011 and 2019 in a university hospital
G. Hazralan* [Ankara, Turkey], S. Nigiz, A. Gundogdu, G. Altinkan-Gelmez, M. Hasdemir, F. Bayrakdar, D. Gür

6385 A mobilisable plasmid spreads the blaGES-6 carbapenemase gene among multidrug-resistant Enterobacter cloacae complex isolates
J. Rodríguez Lozano* [Santander, Spain], M. Garcillán, M. Lucas, L. Martinez-Martinez, J. Aguero, J. Calvo-Montes

6648 Mitigating the fitness costs of carbapenemase-encoding clinical plasmids in Escherichia coli: Piggy-backing on environmental adaptation
J. Klaas, J. Alves Gama* [Trondheim, Norway], J. Hegstad, O. Samuelsen, D. Johnsen

7080 Detection of the novel variant of NDM-type metallo-β-lactamase: significance of D130N amino acid substitution
P. Stárnová* [St Petersburg, Russian Federation], D. Sultan, D. Likoš, V. Ageevets, I. Lazareva, J. Sopova, S. Sidorenko

7167 Co-production of two types of carbapenemases in Enterobacteriales from Poland
E. Literacka* [Warsaw, Poland], R. Izbicki, A. Baraniak, P. Urbanowicz, M. Herda, K. Molinowska, D. Żabićka, W. Hryniewicz, M. Gniadkowski

7182 The impact of H-NS-like protein on InX3 plasmid dissemination and stability
L. Baomo* [Guangzhou, China], C. Zhuo, L. Shui, Y. Guo

7382 Carapbenem hetero-resistance in blood isolates of OXA-48-producing Klebsiella pneumoniae and Escherichia coli
A. Biçakçığil, B. Sancak* [Ankara, Turkey]

7438 Hospital outbreak of Klebsiella pneumoniae producing GES-1 or GES-5 β-lactamases in Poland
E. Literacka* [Warsaw, Poland], R. Izbicki, D. Żabićka, A. Baraniak, P. Urbanowicz, I. Zák, I. Sowa-Sierant, M. Herda, K. Molinowska, W. Hryniewicz, M. Gniadkowski

7551 Emergence of “high risk clone” Klebsiella pneumoniae ST307 producing KPC-3 and NDM-1 in Argentina
D. Cejas, M. Ferrara, F. Magaritioú, C. Alfonsu, A. Elena, G. Gutkind* [Buenos Aires, Argentina], M. Radice

7878 Evaluation of carbapenem resistance in Enterobacteriaceae isolated from intensive care unit using phenotypic and genotypic methods
N. Shaikh* [Mumbai, India], L. Drego, A. Shetty, C. Rodrigues

8158 Impact of porin deficiency and expression levels of environmental CRH-1 and CRP-1 class A β-lactamases on carbapenem and ceftazidime resistance

8401 Local prevalence of molecular resistance mechanisms in carbapenem-resistant Enterobacteriaceae at a tertiary healthcare centre in Lebanon
G. Zmerli* [Beirut, Lebanon], S. Saliba, A. Chami, C. Afji, E. Azar

8687 X-ray induced changes in substrate specificity of OXA-48
M. Dabos* [Le Kremlin-Bicêtre, France], M. Mondini, E. Deutsch, T. Naas

9346 Evolutionary insights of multidrug-resistant hypervirulent ST23 Klebsiella pneumoniae predominantly driven by ICEKp
C. Shankar* [Vellore, India], J. Jacob, K. Vasudevan, M. Venkatesan, S. Anandan, V. Balaji

Session accepted as Mini-oral ePoster Session
Carbapenemases learn geography: they are everywhere!

1524 Epidemiology of carbapenemase-producing Enterobacteriales in the Netherlands in 2018
C. Wielers* [Bilthoven, Netherlands], L. Schouls, D. Notermans, A. Hendrickx, E. Kuijper, A. Schaffelen, S. De Greeff

1786 Temporal and regional prevalence of carbapenemase-producing Enterobacteriales in Switzerland from 2013 to 2018
M. Gasser* [Bern, Switzerland], A. Ramette, R. Zbinden, J. Schrenzel, P. Nordmann, D. Perisa, A. Kronenberg

2198 National pathogen surveillance for carbapenem-resistant Enterobacteriaceae in Japan, 2017-2018
M. Matsui* [Tokyo, Japan], S. Suzuki, M. Sugai

2918 Prevalence of different resistance mechanisms in carbapenemase-producing organisms in Kenya: a phenotypic study
A. Amulele* [Kilifi, Kenya], J. Waichungo, A. Mwanza, E. Machanja, D. Wareham, J. Berkley, N. Gordon
3121 National survey of carbapenemase-producing Klebsiella pneumoniae and Escherichia coli in Belgium in 2019
T. Huang* [Yvoir, Belgium], P. Bogaerts, C. Berhin, M. Hoebeke, Y. Glupczynski, D. Denis

3748 High levels of carbapenem resistance in paediatric bloodstream infection across WHO regions influenced by variation in relative pathogen prevalence
A. Cook* [London, United Kingdom], Y. Yau, J. Bielicki, M. Sharland


9400 KpnBR: Brazilian genomic database for monitoring resistance and virulence of Klebsiella pneumoniae

M. Polemis* (Athens, Greece), K. Tryfinopoulou, A. Vatopoulos

Session accepted as Paper Poster Session
Carriage of resistant enterobacteria: a gut feeling!

1315 Resistance to extended-spectrum β-lactams, aminoglycosides and quinolones in multidrug-resistance Enterobacteriales isolated in patients receiving an allogeneic haematopoietic stem cell transplantation: the ENHERE-SCT Study.
M. Fernández-Martínez* [Santander, Spain], C. González Rico, M. Bermúdez-Rodríguez, I. García-García, L. Vázquez, J. Aguado García, C. Martín Calvo, L. Martinez-Martínez, J. Calvo-Montes, M. Fariñas

2469 Prevalence of carriage and characterisation of extended-spectrum beta-lactamase-producing Escherichia coli in healthy pregnant women living in Madagascar
M. Milenkov* [Lyon, France], E. Westeel, S. Rasoanandrasana, L. Rahajamanana, R. Rakotomalala, O. Clermont, L. Rasoanandrasana, A. Koutoucheva, S. Fenlon, D. Bertrand, D. Lye, B. Ang, E. Perencevich, O. Ng, B. Cooper, N. Nagarajan, S. Chen, T. Barkham

4062 Household transmission of carbapenemase-producing Enterobacteriales: a prospective case-ascertained cohort study
K. Marimuthu* [Singapore, Singapore], Y. Mo, M. Ling, A. Koutoucheva, S. Fenlon, D. Bertrand, D. Lye, B. Ang, E. Perencevich, O. Ng, B. Cooper, N. Nagarajan, S. Chen, T. Barkham

4276 Increased carriage of ESBL-producing Enterobacteriaceae among men who have sex with men
E. Van Dulm* [Amsterdam, Netherlands], W. Van Bilsen, A. Matser, I. Linde, Y. Van Duijn, Prins, M. Prins, A. Boyd, A. Van Dam

4510 Epidemiology of ESBL-producing Enterobacteriaceae among healthcare students, Portuguese Red Cross Health School of Lisbon, Portugal
C. Fournier* [Fribourg, Switzerland], M. Aires De Sousa, B. Fuster, P. Nordmann, L. Poirel

4657 Prevalence of and risk factors for extended-spectrum beta-lactamase genes carriage in a middle-aged and elderly population-based cohort
M. Mulder, P. Arp, D. Radjabzadeh, J. Kiefte-De Jong, A. Uitterlinden, C. Klaassen, R. Kraaij, W. Goessens, B. Stricker, A. Verbon* [Rotterdam, Netherlands]

6457 Faecal carriage of extended-spectrum beta-lactamase-producing members of order Enterobacteriales among patients in Bulgarian hospitals

6720 Longitudinal large-scale survey on blaCTX-M faecal carriage in children from Bolivian Guaraní indigenous communities
S. Boncompagni* [Siena, Italy], T. Di Maggio, A. Mantella, M. Micieli, A. Villagrán, M. Spinicci, M. Strahmeyer, M. Cecchetti, H. Gamboa Barahona, V. Poma, A. Bartoloni, G. Rossolini, L. Pallecchi

6919 Healthy carriage of colistin-, ESC- and carbapenem-resistant Enterobacteriales in workers in Lebanese pastries
A. Hiba* [Lyon, France], M. Osman, J. Madec, M. Hamze, M. Haenni

7875 Community faecal carriage of extended-spectrum beta-lactamase-producing Escherichia coli in Niger

6092 Household transmission of carbapenemase-producing Enterobacteriaceae: a prospective case-ascertained cohort study
K. Marimuthu* [Singapore, Singapore], Y. Mo, M. Ling, A. Koutoucheva, S. Fenlon, D. Bertrand, D. Lye, B. Ang, E. Perencevich, O. Ng, B. Cooper, N. Nagarajan, S. Chen, T. Barkham

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E. Van Dulm* [Amsterdam, Netherlands], W. Van Bilsen, A. Matser, I. Linde, Y. Van Duijn, Prins, M. Prins, A. Boyd, A. Van Dam

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Prevalence of and risk factors for extended-spectrum beta-lactamase genes carriage in a middle-aged and elderly population-based cohort
M. Mulder, P. Arp, D. Radjabzadeh, J. Kiefte-De Jong, A. Uitterlinden, C. Klaassen, R. Kraaij, W. Goessens, B. Stricker, A. Verbon* [Rotterdam, Netherlands]

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Longitudinal large-scale survey on blaCTX-M faecal carriage in children from Bolivian Guaraní indigenous communities
S. Boncompagni* [Siena, Italy], T. Di Maggio, A. Mantella, M. Micieli, A. Villagrán, M. Spinicci, M. Strahmeyer, M. Cecchetti, H. Gamboa Barahona, V. Poma, A. Bartoloni, G. Rossolini, L. Pallecchi

Healthy carriage of colistin-, ESC- and carbapenem-resistant Enterobacteriales in workers in Lebanese pastries
A. Hiba* [Lyon, France], M. Osman, J. Madec, M. Hamze, M. Haenni

Community faecal carriage of extended-spectrum beta-lactamase-producing Escherichia coli in Niger
Abstract Categories 2020

Session accepted as 2-Hour Oral Session
Clinical and molecular epidemiology of key antimicrobial-resistant enterobacteria: the devil lies in the details
721 Genomic analysis of carbapenemase-encoding plasmids from Klebsiella pneumoniae across Europe highlights three major patterns of dissemination S. David* [Cambridge, United Kingdom], V. Cohen, S. Reuter, T. Gian, G. Rossolini, E. Feil, H. Grundmann, D. Aannensen


1908 Burden and impact of carbapenem resistance caused by Enterobacteriales in a Bangladeshi hospital: an epidemiological, clinical and molecular study R. Farzana* [Cardiff, United Kingdom], L. Janes, A. Rahman, K. Sands, E. Portal, I. Boosten, M. Pervin, B. Hassan, A. Barratt ?, T. Walsh

2488 Community outbreak of OXA-48-producing Escherichia coli linked to a food premises: New Zealand, 2018-19 C. Thornley* [Lower Hutt, New Zealand], M. Kelly, M. Bloomfield, A. Nesdale, X. Ren

2942 Carbapenemase-producing and colistin-resistant Enterobacteriaceae in intensive care unit patients from Mediterranean countries, 2019 S. Borges Dos Santos, S. Diene, B. Amina, K. Zerouali, D. Ghath, R. El-Mahdy, S. El Tayeb, A. Hammami, I. Boutiba, R. Husni, Z. Daoud, L. Mereghetti, P. François, N. Van Der Mee-Marquet* [Tours, France]

Evidence of high prevalence, transmission rate and persistence of Escherichia coli ST131-Rx among residents of nursing homes in south Spain (JPI-ST131TS project) E. Salamanca* [Seville, Spain], L. Lopez-Cerero, M. Delgado-Valverde, J. Rodriguez-Baño, A. Pascual Hernandez

6240 A multi-year decline of multidrug-resistant Escherichia coli in French nursing homes and primary care: are we on the good track? S. Thibaut* [Nantes, France], T. Coeffe, D. Boutaille, G. Birgand, J. Caillon, P. Network


6673 Identifying the drivers of multidrug-resistant Klebsiella pneumoniae at a European level V. Kachalov* [Zurich, Switzerland], H. Nguyen, S. Balakrishna, L. Salazar Vizcaya, R. Sommerstein, S. Kuster, A. Houser, P. Abel Zur Wiesch, E. Klein, R. Kouyos

Session accepted as Mini-oral Flash Session
Colistin resistance and other resistance mechanisms in the horizon

1894 Identification of novel mobile colistin resistance gene mcr-10 C. Wang, Y. Feng, Z. Zong* [Chengdu, China]

3486 Widespread distribution of the acquired colistin resistance gene, mcr-9, amongst Enterobacteriales in England and Wales M. Ellington* [London, United Kingdom], T. Dallman, D. Meunier, K. Hopkins, N. Woodford

5117 Colistin resistance in human Salmonella spp. isolates collected from Italian Enter-Net surveillance during the period 2016-2018 D. Perlino, S. Owczarek, A. Dioni, I. Benedetti, L. Busani, C. Lucarelli, L. Villa* [Rome, Italy], A. Garcia-Fernandez


5240 Sequential time-kill experiments to characterize lyopolysaccharide-modifying genes involved in polymyxin resistance in Escherichia coli and Klebsiella pneumoniae carrying mcr-1 H. Ih* [Poitiers, France], N. Gregoire, W. Couet, S. Marchand, J. Buycck

An OXA-48 variant hydrolysing carbapenems, expanded-spectrum cephalosporins and aztreonam: welcome OXA-793 M. Dabas* [Le Kremlin-Bicêtre, France], R. Bonnin, L. Dortet, T. Naas

A novel plasmid-mediated RND family efflux pump confers tigecycline resistance in Klebsiella pneumoniae S. Sun* [Beijing, China], H. Gao, L. Yu, L. Jin, R. Wang, X. Wang, D. Wang, H. Wang

Within-patient evolution of a clinical isolate of Escherichia coli uncovers an IS26-linked amplification of blaTEM-1 leading to piperacillin-tazobactam resistance T. Edwards* [Liverpool, United Kingdom], J. Mason, P. Roberts, C. Parry, J. Van Aartsen, A. Howard, A. Roberts, E. Adams, A. Hubbard

Inter- and intraspecies spread of mcr-1 between twenty-nine distinct Enterobacteriaceae isolates from one patient H. Xu* [Hangzhou, China], B. Zheng, Y. Xiao
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9444 Investigation of colistin resistance mechanisms in Klebsiella pneumoniae strains
B. Borsa* [Linköping, Sweden], G. Karabiyik, I. Karalti, B. Guvenc-Tuna, I. Acuner

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Commercial AST methods: what’s new?

1079 ETEST Eravacycline for antimicrobial susceptibility testing of Enterobacteriaceae and Enterococcus spp.: performance results from a multi-centre study
L. Blanchard* [Marcy-l’Étoile, France], T. Armstrong, D. Gerald, Y. Ying, M. Kresken, J. Carpenter, V. Sauvonnnet, G. Zambardi

1138 Evaluation of the accuracy of the panel for antimicrobial susceptibility testing of Enterobacteriaceae and carbapenemase detection
H. Cho* [Seoul, South Korea], Y. Park, J. Kim, J. Choi, S. Ha, Y. Cha

1813 Does automated susceptibility testing overcall temocillin resistance?
M. Campbell* [Oxford, United Kingdom]

2300 Multi-centre evaluation of cephalxin MIC results for Enterobacteriaces using EUCAST breakpoints on MicroScan dried Gram-negative MIC panels
[West Sacramento, United States]

2304 Luminogenic phosphatase substrate for rapid susceptibility testing of Gram-positive strains
V. Chalansonnet* [La Balme-les-Grottes, France], F. Macé, S. Brenga

2366 Using T2Dx and rapid AST with blood culture presampling for combined ID and AST before blood culture positivity
C. Malmberg* [Uppsala, Sweden], L. Flintheldt, P. Yuen, J. Fernberg, H. Öhrn, C. Johansson, T. Tängdén, J. Kreuger

2724 Phenotypic testing of ceftriaxone susceptibility on the Pheno system in characterised Enterobacteriaces
A. Bhalodi* [Tucson, United States], N. Magnano, R. Humphries

3715 Comparative study of two susceptibility testing methods for carbapenem-resistant Klebsiella pneumoniae clinical isolates

3779 An evaluation of an automated broth microdilution platform versus the EUCAST disk diffusion methodology
P. D’Arcy-Grover* [Southampton, United Kingdom], I. Taylor

3822 A low-cost nanoliter droplet handling system for pathogen identification and antimicrobial susceptibility testing on microtitre plates
Q. Yi* [Beijing, China], W. Du, Y. Xu

4069 Rapid generation of a standard inoculum direct from positive blood cultures using electrical biosensor technology
E. Deak* [Menlo Park, United States], S. Putney, Y. Nga, W. Yip, K. Vo, T. Abbey, M. Herget

4673 Evaluation of a new commercial fosfomycin agar dilution-kit against reference agar dilution
L. Davies, L. Jones, F. Demetro, S. Pompomio, F. Brocco, M. Wootton* [Cardiff, United Kingdom]

4887 A multi-site study comparing a commercially-prepared dried MIC susceptibility system to the CLSI/ISO broth microdilution method for ceftazidime-aztreonam (formerly ceftazidime/VNRX-5133) using Gram-negative non-fastidious organisms

5636 Evaluation of Bacillus anthracis agar-based susceptibility testing by Etest for ciprofloxacin, levofloxacin, doxycycline and tetracycline
B. Cherney* [Atlanta, United States], P. Michel, J. Bugrysheva, A. Gargin, T. Kangphet-Tran, C. Lascols, H. Mclaughlin, D. Sue

5834 Evaluation of antimicrobial susceptibility testing assays for ceftazidime-avibactam and ceftolozane-tazobactam with Gram-negative bacteria directly from positive blood culture on the Pheno system
N. Oppermann, A. Ndobegang, A. Sikorski, A. Taku, D. Gamage, C. Chantell, R. Humphries* [Los Angeles, United States]

6316 Clinical evaluation of FASTinov kits for ultra-rapid antimicrobial susceptibility testing directly from positive blood cultures
A. Silva-Dias, B. Pérez-Visa, R. Gomes, I. Martins-Oliveira, A. Rodrigues, R. Canton Moreno, C. Pina-Vaz* [Porto, Portugal]

6516 Detection of colistin resistance in Pseudomonas and Acinetobacter by the ATB PSE EU strips
S. Petre, E. Pillon* [La Balme Les Grottes, France], M. Roland

6486 Comparative study of two susceptibility testing methods for carbapenem-resistant Klebsiella pneumoniae clinical isolates

6516 Evaluation of different commercial methods for fosfomycin susceptibility testing of Staphylococcus aureus
F. Campanile, A. Aprile* [Catania, Italy], C. Bonomo, C. Imbrasciano, A. Mirabile, D. Bangiorno, S. Stefani, M. Mezzatesta

6925 ETEST Imipenem-rellebactam for antimicrobial susceptibility testing of Enterobacteriaceae and Pseudomonas aeruginosa: performance results from a multi-centre study
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<td>6998</td>
<td>Performance of the Accelerate Pheno system in a tertiary care hospital in Germany</td>
<td>B. Berinson* [Hamburg, Germany], F. Olearo, A. Bath, M. Aepfelbacher, H. Rohde</td>
<td>2016</td>
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<td>7195</td>
<td>Validation of three MicroScan antibiotic susceptibility testing microplates designed for low-resource settings</td>
<td>J. Ronat* [Paris, France], S. Oueslati, A. Natale, O. Vandenben, J. Jacobs, T. Naas</td>
<td>2021</td>
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<td>8081</td>
<td>Evaluation of the PROMPT inoculation system with the MicroScan antibiotic susceptibility testing microplate designed for low-resource settings</td>
<td>J. Ronat* [Paris, France], S. Oueslati, A. Natale, O. Vandenben, J. Jacobs, T. Naas</td>
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<td>8813</td>
<td>Antimicrobial susceptibility testing directly from positive blood culture with the Reveal Rapid AST System: clinical results for Gram-negative pathogens</td>
<td>R. Tietbets, S. George, P. Rhodes, P. Singh, L. Samuel* [Detroit, United States]</td>
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<td>8814</td>
<td>Evaluation of a urinalysis predictive model and the performance of direct-from-urine susceptibility testing</td>
<td>C. Doern* [Richmond, United States], S. Hedrick, L. Matthews, A. Bryson, K. Bradbrook, C. Jay, N. Taylor, A. Sima, M. Jomerson</td>
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<td>8971</td>
<td>Multi-centre study performance results of ETEST delafloxacin for antimicrobial susceptibility testing against Gram-positive organisms and Pseudomonas aeruginosa</td>
<td>C. Anglade* [Marcy-l'Étoile, France], T. Armstrong, C. Burnham, H. Dwight, M. Wootton, G. Zambardi, V. Sauvanet</td>
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**Session accepted as Paper Poster Session**

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**Dissecting resistance trends in polymyxins**

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<td>456</td>
<td>Insights of colistin resistance and flexible transmission of mcr-1</td>
<td>Y. Yu, X. Li, X. Liao* [Guangzhou, China], J. Sun, Y. Liu</td>
<td>2018</td>
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<td>459</td>
<td>Clinical and molecular perspectives of colistin-resistant Klebsiella from an oncology centre in a lower-middle income country</td>
<td>K. Abdul Ghafur* [Chennai, India], C. Shankar, S. Rajendran, T. Ma, V. Balaji</td>
<td>2018</td>
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<td>490</td>
<td>Rough-type and loss of the LPS due to lpx genes deletions are associated with colistin resistance among multidrug-resistant Escherichia coli clinical isolates not harbouring mcr genes</td>
<td>M. Savari* [Ahvaz, Iran], N. Emam, M. Moosavian</td>
<td>2018</td>
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<td>1675</td>
<td>Low horizontal transfer rate of mcr-8 may constrain the spread of mcr-8 genes</td>
<td>Q. Yang* [Cardiff, United Kingdom], T. Walsh</td>
<td>2018</td>
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Serotype is associated with high rate of colistin resistance among clinical isolates of Salmonella from China
Q. Luo* (Hangzhou, China), H. Fu, X. Yu, Y. Wang, Y. Xiao

First epidemiological report on colistin- and carbapenem-resistant Enterobacteriaceae isolates obtained from selected tertiary hospitals in south-eastern Nigeria
U. Ugah** (Abakaliki, Nigeria), T. Udeani

Emergence of mobile mcr-8 colistin resistance in Klebsiella pneumoniae from clinical infections of hospitalised patients in Bangladesh
R. Farzana* (Cardiff, United Kingdom), L. Jones, A. Barratt?, A. Rahman, K. Sands, E. Portal, Q. Yang, T. Walsh

Role of AcrAB-ToIC multidrug efflux pump in mcr-1-mediated colistin resistance
W. Liang* (Guangzhou, China), Z. Zhao, D. Lin, S. Feng, L. Liang, J. Li, W. Wen, C. Shen, G. Tian

The intestinal carriage of colistin-resistant Enterobacteriaceae in a tertiary care hospital setting and whole genome sequence data analysis of mcr-1 positive Escherichia coli isolates
J. Tkadlec* (Prague, Czech Republic), E. Smelikova, A. Bárková, M. Cabnnochova, G. Tereza, R. Karpiskova, O. Nycz, P. Drevinek, M. Krutova

Molecular detection of the mcr-1 mobile colistin resistance gene in healthy humans and a dog with skin infection from Portugal
J. Menezes* (Lisbon, Portugal), A. Belas, I. Cunha E Silva, M. Pamba

Coproduction of mcr-9 and KPC-2 by archived clinical Enterobacter spp. strains from Colombia
L. Rojas Cay* (Cleveland, United States), W. Shropshire, S. Marshall, S. Rudin, E. De La Cadena, A. Dinh, M. Villegas, B. Hanson, C. Arias, R. Bonam

Persistor response of Klebsiella pneumoniae to colistin exposure
C. Vatansever* (Istanbul, Turkey), N. Atac, B. Özer, B. Kılıçoğlu, M. Berkkan, U. Guler, D. Baskurt, E. Sever, O. Dogan, F. Can

Stable mutants and persisters variants are involved in heteroresistance to colistin in wild-type Klebsiella pneumoniae of clinical origin
I. Sánchez León* (Córdoba, Spain), C. Elias-Lopez, L. Martínez-Martinez

Comparison of colistin-resistant Klebsiella pneumoniae strains in five Greek hospitals
M. Maisi* (Heraklion, Greece), G. Tsioulas, E. Maisi, I. Choudalaki, P. Giakkoupi

mcr-8-mediated colistin resistance in a carbapenem-resistant Klebsiella pneumoniae isolate
R. Bonnin, S. Bernabeu, F. Jauregui, T. Naas, L. Dortet* (Paris, France)

Genetic characterisation of multidrug-resistant Klebsiella pneumoniae harbouring colistin resistance gene mcr-1 from North India
A. Pathak* (Lucknow, India), S. Singh, K. Prasad

Rapid detection of colistin-resistant Klebsiella pneumoniae using colistin drop test
V. Rocha* (Salvador, Brazil), D. Nascimento, M. Sales, A. Martins, J. Azevedo, A. Malheiro, L. Ataide, M. Reis, J. Reis

Colistin hetero-resistant Klebsiella pneumoniae and Escherichia coli blood isolates
Ü. Liste, E. Kirbaş* (Ankara, Turkey), A. Biçakçgil, B. Sancak

Hetero-resistance to colistin in Stenotrophomonas maltophilia isolates: challenges in colistin susceptibility testing
Ü. Liste, A. Biçakçgil, C. Özkyuymcu, B. Sancak* (Ankara, Turkey)

Acquired resistance to colistin in Enterobacteriaceae isolated at university hospital of Algiers
B. Mohamed Azzedine* (Algiers, Algeria), D. Fazio, L. Farah, M. Tazir, W. Amhis

First national survey on colistin resistance among Escherichia coli in Belgium
O. Denis* (Brussels, Belgium), P. Bogaerts, C. Berhin, M. Hoebeke, W. Bouchahrouf, Y. Glupczynski, T. Huang

Diversity of colistin resistance mechanisms in carbapenemase-producing Klebsiella pneumoniae isolated in Bulgaria from 2013 to 2018
K. Ivanova* (Sofia, Bulgaria), I. Ivanov, S. Sabtcheva, V. Dobrinov, M. Nedjalkov, E. Dobreva, R. Hristova, T. Kantardjiev

Molecular surveillance of mcr gene in gut microbiome of healthy individuals, acute diarrhoea and inflammatory bowel diseases patients from India
S. Banerjee* (New Delhi, India), T. Senapati, J. Verma, A. Mani, A. Kapil, B. Das

Clonality and genetic determinants of resistance in paired isolates of Klebsiella pneumoniae with divergent polymyxin B phenotypes
S. Sampaio, R. Carvalho, M. Mimica, C. Da Silva, A. Lima, K. Lima, D. Rocha, J. Mello-Sampaio* (São Paulo, Brazil)

Characterisation of KPC-50, a novel transferable KPC-3 variant conferring resistance to ceftazidime-avibactam in a colistin-resistant Klebsiella pneumoniae from Switzerland
L. Poirel* (Fribourg, Switzerland), X. Vuillemin, A. Masseron, M. Juhas, S. Mancini, R. Zbinden, S. Tiziani, U. Bechtel-Grosch, P. Nordmann

Genomic characterisation of meropenem/vaborbactam resistant KPC-producing Klebsiella pneumoniae strains isolated from bacteremic patients
P. Gaibani* (Bologna, Italy), M. Re, S. Ambretti

A silent mcr-9 and a novel class A beta-lactamase in Citrobacter telavivum sp. nov. colonising hospital patients
T. Gancalves Ribeira* (Porto, Portugal), R. Izdebski, P. Urbanowicz, Y. Carmeli, M. Gniadkowski, L. Peixe
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4051 Chemical genomics to reverse the colistin resistance of MDR Klebsiella pneumoniae
B. Jana* (Brighton, United States), K. Baker, A. Cain, W. Doerrler, L. Guardabassi

5028 Acquired resistance to fosfomycin through acquisition of an ISecp1-blaCTX-M-14 tandem in a Klebsiella pneumoniae clinical isolate
N. Kieffer, L. Poiré* (Fribourg, Switzerland), L. Mueller, P. Nordmann

5510 Mechanisms of resistance in Pseudomonas aeruginosa against ceftazidime-avibactam and ceftolozane-tazobactam from Qatar
M. Sid Ahmed* (Doha, Qatar), F. Ahmad Khan, H. Abdel Hadi, A. Sultan, M. Al-Maslamani, A. Al-Khal, B. Söderquist, E. Ibrahim, A. Omrani, J. Jass

7656 Multiple mutational possibilities allow ceftazidime-avibactam resistance in KPC-type carbapenemase

9106 Characterisation of mcr-5 action suggests a unified mechanism for polymyxin resistance
Y. Feng* (Hangzhou, China)

EUCAST rapid disk diffusion: the story so far

3616 Evaluation of EUCAST rapid antimicrobial susceptibility testing (RAST) on blood cultures in a clinical laboratory
P. Rydström* (Växjö, Sweden), E. Jonasson

4028 Evaluation of rapid AST in blood cultures using CHROMagar Mueller-Hinton orientation agar
B. Mnif* (Sfax, Tunisia), F. Zouari, S. Gouiaa, N. Sallem, A. Hammami

4543 Usefulness of RAST-EUCAST directly from blood culture bottles combined with rapidly interpreted antibiogram reading to detect ESBL/carbapenemase-producing Enterobacteriales
V. Cerrudo Lopez* (Madrid, Spain), J. Cortes Cuevas, S. Garcia-Fernández, R. Canton Moreno, M. Morosini, A. Sanchez Diaz

4978 The EUCAST Rapid AST directly from positive blood culture bottles: breakpoints for additional antimicrobial agents for Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa
E. Jonasson, E. Matuschek, G. Kahlmeter* (Växjö, Sweden)

5113 Direct-from-blood-culture disk diffusion to determine antimicrobial susceptibility of Escherichia coli and Klebsiella pneumoniae

5127 Automated rapid antimicrobial susceptibility testing from positive blood cultures using Copan WASPlab
C. Verduin, S. Derksen, J. Stalpers* (Veldhoven, Netherlands), T. Liebregts, M. Nijs, A. Jansz

6278 Evaluation of the rapid antimicrobial susceptibility testing (RAST) from positively-flagged blood cultures
T. Ka* (Taipei, Taiwan), P. Chuang, C. Hsu, T. Lee, P. Hsieh

6845 EUCAST rapid AST directly from positive blood culture bottles: breakpoints for Acinetobacter baumannii
E. Jonasson, E. Matuschek* (Växjö, Sweden), G. Kahlmeter

6934 Evaluation of the EUCAST rapid antimicrobial susceptibility testing directly from positive blood cultures for Escherichia coli and Staphylococcus aureus in a routine laboratory
E. Jonasson* (Växjö, Sweden), P. Rydström
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Molecular detection of mutations involved in *Helicobacter pylori* antimicrobial resistance in Ecuador

Evaluation of *Stenotrophomonas maltophilia* non-susceptibility and associated risk factors: a multi-centre analysis
C. Bland, N. White, J. Lin, J. Wagner, K. Stover, B. Bookstaver, D. Chastain* (Albany, United States), H. Matson, M. Motes, B. Jones

Limited multidrug-resistant efflux pump overexpression among multidrug-resistant *Escherichia coli* of ST131
J. Camp* (Freiburg, Germany), S. Schuster, M. Yavra, T. Schweigger, J. Rossen, W. Kern

The rational of antibiotic failure in *Helicobacter pylori*
S. Ghofourian, E. Aboualigalehdari* (Ilam, Iran), B. Bodakhsh

Session accepted as Paper Poster Session

**In vitro activity of ceftolozane/tazobactam**

Emergence of non-susceptibility among Gram-negative respiratory pathogens from a phase III clinical trial for treatment of nosocomial pneumonia [ASPECT-NP]
M. Motyl* (Kenilworth, United States), M. Castanheira, M. Johnson, B. Yu, J. Huntington, P. Carmelitana, C. Bruno, C. De Anda, E. Rhee

In vitro activity of ceftolozane/tazobactam against clinical isolates of carbapenem-resistant *Pseudomonas aeruginosa* from Japan hospitals
T. Nakamura* (Kyoto, Japan), M. Fujiwara

Ceftolozane/tazobactam-resistant *Pseudomonas aeruginosa* isolates in a teaching hospital in central Italy
M. Gianluca* (Ancona, Italy), L. Breccini, A. Brenchiani, A. Antonelli, V. Di Pilato, S. Castelletti, S. Fioriti, T. Giani, G. Rossolini, A. Giacometti, O. Cirioni

In vitro activity of ceftolozane/tazobactam and comparators against *Pseudomonas aeruginosa* isolates collected in the United States: SMART 2018
K. Kazmierczak* (Schaumberg, IL, United States), J. Raddatz, K. Young, M. Motyl, D. Sahm

Characterisation of ceftolozane/tazobactam resistance among *Enterobacteriales* and *Pseudomonas aeruginosa* isolates recovered during the SUPERIOR study using whole genome sequencing

Confronting ceftolozane/tazobactam susceptibility in multidrug-resistant *Enterobacteriales* isolates and whole genome sequencing results [STEP study]

Activity of ceftolozane/tazobactam against prevalent Gram-negative pathogens across Asia: PACTS 2016-2018
M. Tulloch* (Sydney, Australia), D. Shortridge, M. Motyl, P. Moise, W. Chen

Important resistance issues in enterococci

K. Loens* (Antwerp, Belgium), S. Van Koeveringe, H. Goossens, V. Matheeussen

Prevalence and outcome of ampicillin-susceptible but penicillin-resistant *Enterococcus faecalis* bacteraemia: a multi-centre retrospective study
E. Rosselli Del Turco* (Bologna, Italy), M. Bartoletti, S. Carvalho Brugger, S. Ambretti, M. Garcia, M. Giannella, R. Pascale, L. Raumer, P. Viale, J. Pericàs Pulido

Risk factors and outcomes associated with the carriage of tigecycline-non-susceptible vancomycin-resistant *Enterococcus faecium*
J. Kessel* (Freiburg, Germany), J. Bender, G. Werner, M. Griskaitis, E. Herrmann, A. Leh, H. Serve, K. Zacharowski, S. Zeuzem, M. Vehreschild, T. Wichelhaus, V. Kemptf, M. Hogardt

Molecular epidemiology of vancomycin-resistant enterococci: changing paradigms at the crossroads of Europe
C. Correa-Martinez* (Münster, Germany), A. Jurke, J. Schmitz, S. Kempfmeier, A. Mollmann

First vancomycin-variable enterococci from France: molecular mechanisms of phenotypic susceptibility
Z. Mamou* (saint gregoire, France), A. Zouari, S. Potrel, A. Collet, G. Auger, V. Cattoir

Session accepted as 1-Hour Oral Session

Important resistance issues in enterococci

Molecular detection of mutations involved in *Helicobacter pylori* antimicrobial resistance in Ecuador

Evaluation of *Stenotrophomonas maltophilia* non-susceptibility and associated risk factors: a multi-centre analysis
C. Bland, N. White, J. Lin, J. Wagner, K. Stover, B. Bookstaver, D. Chastain* (Albany, United States), H. Matson, M. Motes, B. Jones

Limited multidrug-resistant efflux pump overexpression among multidrug-resistant *Escherichia coli* of ST131
J. Camp* (Freiburg, Germany), S. Schuster, M. Yavra, T. Schweigger, J. Rossen, W. Kern

The rational of antibiotic failure in *Helicobacter pylori*
S. Ghofourian, E. Aboualigalehdari* (Ilam, Iran), B. Bodakhsh

In vitro activity of ceftolozane/tazobactam against prevalent *Pseudomonas aeruginosa* isolates from Japan hospitals
T. Nakamura* (Kyoto, Japan), M. Fujiwara

Ceftolozane/tazobactam-resistant *Pseudomonas aeruginosa* isolates in a teaching hospital in central Italy
M. Gianluca* (Ancona, Italy), L. Breccini, A. Brenchiani, A. Antonelli, V. Di Pilato, S. Castelletti, S. Fioriti, T. Giani, G. Rossolini, A. Giacometti, O. Cirioni

In vitro activity of ceftolozane/tazobactam and comparators against *Pseudomonas aeruginosa* isolates collected in the United States: SMART 2018
K. Kazmierczak* (Schaumberg, IL, United States), J. Raddatz, K. Young, M. Motyl, D. Sahm

Characterisation of ceftolozane/tazobactam resistance among *Enterobacteriales* and *Pseudomonas aeruginosa* isolates recovered during the SUPERIOR study using whole genome sequencing

Confronting ceftolozane/tazobactam susceptibility in multidrug-resistant *Enterobacteriales* isolates and whole genome sequencing results [STEP study]

Activity of ceftolozane/tazobactam against prevalent Gram-negative pathogens across Asia: PACTS 2016-2018
M. Tulloch* (Sydney, Australia), D. Shortridge, M. Motyl, P. Moise, W. Chen
4302 In vitro activity of ceftolozane-tazobactam and comparators against beta-lactam-resistant pathogens isolates collected from patients with urinary tract, intra-abdominal and lower respiratory infections in Lebanon and Jordan (SMART Study Data 2016-2017) [Beirut, Lebanon], W. Hayajneh, A. Adame, N. Hakime, M. Malik Hamdan, J. Maalouf, R. Alsamarneh, M. Motyl, D. Sahim, I. Alekseeva, D. Karam Sarkis

8680 Activity of ceftolozane-tazobactam and combinatorial regimens against a contemporary collection of carbapenem-resistant Pseudomonas aeruginosa C. Black* (San Antonio, United States), J. Shurko, C. Chen, D. Burgess, G. Gowrys, G. Lee

5626 The effect of intestinal alkaline phosphatase and physical activity on the course of experimental colitis in obese mice D. Wójcik* (Kraków, Poland), M. Surmiak, M. Hubalewska-Mazgaj, Z. Śliwowski, S. Kwiecień, T. Brzozowski

6955 Molecular analysis of metronidazole-resistant Bacteroides strains from Kuwait Z. Baity* (Szeged, Hungary), W. Jamal, K. Burian, V. Rotimi, J. Soki

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KPC-producing enterobacteria


3282 Plasmid diversity among genetically related Klebsiella pneumoniae blakPC-2 and blakPC-3 isolates collected in the Dutch national surveillance A. Hendrickx* (Bilthoven, Netherlands), F. Landman, A. De Haan, D. Borst, S. Witteveen, M. Van Santen, H. Van Der Heide, L. Schouls


4671 Absence of the Type I-E CRISPR-Cas system in Klebsiella pneumoniae clonal complex 258 is associated with dissemination of blakKPC plasmid in this clonal complex Z. Ying* (Shanghai, China), T. Yu, X. Jiang


4889 Antimicrobial susceptibility in Clostridioides difficile varies according to European region and isolate source J. Freeman* (Leeds, United Kingdom), V. Viprey, V. Tkalec, D. Ewin, W. Spittal, E. Clark, J. Vernon, W. Fawley, A. Benson, G. Davis, M. Rupnik, M. Wilcox, K. Davies

Session accepted as Paper Poster Session
It’s a gas: anaerobes and AMR

2315 Descriptive epidemiological analysis of antimicrobial resistance in strict anaerobes in Scotland, 2013-2018 J. Wilson, A. Zalewska, M. Lockhart* (Glasgow, United Kingdom), E. Mcardle, W. Malcolm

2410 Evaluation of the antimicrobial activity of dinilbazole and six comparators against Chinese, Japanese and South Korean isolates of Clostridioides difficile D. Collins* (West Leederville, Australia), Y. Wu, K. Tateda, H. Kim, R. Vickers, T. Kierski


3386 The antimicrobial susceptibility profile and prevalence of known anaerobic resistance genes in less common anaerobic Gram-negative bacteria, isolated in the Netherlands K. Boiten* (Groningen, Netherlands), W. Baas, P. Buijs, J. Rossen, A. Veelø

3511 Descriptive epidemiology of antimicrobial resistance in strict anaerobes in Scotland, 2013-2018 J. Wilson, A. Zalewska, M. Lockhart* (Glasgow, United Kingdom), E. Mcardle, W. Malcolm

3928 Aetiology and antimicrobial susceptibility of anaerobic bacteria causing serious infections in a tertiary hospital of Madrid J. López-Pintar* (Madrid, Spain), A. Sánchez-Diaz, P. Ruiz-Garbajosa, R. Canton Moreno, M. Morosini Reilly, S. García-Fernández

4489 Antimicrobial susceptibility in Clostridioides difficile varies according to European region and isolate source J. Freeman* (Leeds, United Kingdom), V. Viprey, V. Tkalec, D. Ewin, W. Spittal, E. Clark, J. Vernon, W. Fawley, A. Benson, G. Davis, M. Rupnik, M. Wilcox, K. Davies

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6819 Epidemic of carbapenem-resistant Klebsiella pneumoniae in a tertiary referral hospital for an annual surveillance in China Y. Jiang* (Hangzhou, China), Q. Shi, D. Zhao, P. Zhang, Y. Wang, J. Quan, X. Han, R. Yan, H. Liu, X. Wu, X. Hua, Y. Yu
Abstract Categories 2020

8303 Genomic features of Argentinean KPC-2 producing Klebsiella pneumoniae ST25 and comparative genomics with carbapenem susceptible ST25 isolates
D. Cejas, V. Di Pilato, L. Henrici De Angelis, S. Di Gregorio, L. Pallecchi, F. Arena, G. Rossolini, G. Gutkind* [Buenos Aires, Argentina], M. Radice

8602 Vertical transmission of the gene blaKPC-3 in clinical isolates of carbapenemase resistant Klebsiella pneumoniae
C. Ferreira* [Porto, Portugal], J. Rocha, S. Bikkarolla, K. Frykholm, S. Pohjanen, M. Brito, C. Lameiras, O. Nunes, F. Westerlund, C. Manaia

9415 Prevalence of genes encoding 16S RNA methyltransferase in carbapenemase-producing Serratia spp. in south Brazil
L. Bari* [Ponta Grossa, Brazil], C. Sanches Ito, L. Arend, K. Nogueira, F. Tuan

Session accepted as Paper Poster Session

Metallo-beta-lactamases and OXAs on the spot

425 Persistence of high-risk clones of carbapenem-resistant Klebsiella pneumoniae in a tertiary hospital in Valencia, Spain
B. Foster Escriva* [Oliva, Spain], N. Torno, C. Salvador Garcia, M. Beldu, C. Gimeno Cardona

597 Occurrence of NDM-1-producing Morganella morganii and Proteus mirabilis in a single patient, Portugal: probable in vivo transfer by conjugation
M. Aires De Sousa, J. Ortiz De La Rosa, M. Goncalves, F. Mattner, A. Wendel* [Cologne, Germany]

1269 Characterisation of NDM-producing Klebsiella pneumoniae isolates from different Roman hospitals

3818 Complex polyclonal outbreak of blaVIM-1-harboursing and mcr-9-cohabouring Enterobacter cloacae complex linked to drains in a German hospital
M. Malecki, P. Higgins, K. Xanthopoulou, H. Seifert, F. Mattner, A. Wendel* [Cologne, Germany]

4054 Carbapenemase-producing Klebsiella pneumoniae in a Tunisian university hospital: emergence of hypervirulent strains
B. Mnif* [Sfax, Tunisia], N. Sallem, F. Zouari, A. Hammami

4188 Oxacillinase-48-like [OXA-48] carbapenemases along with New Delhi metallo-β-lactamase in a neonatal unit
S. Naha, S. Mukherjee, K. Sands, P. Chattopadhyay, S. Mukherjee, S. Basu* [Kolkata, India]

4434 Dissemination of carbapenem-non-susceptible Klebsiella pneumoniae from Oman
M. Coorens, H. Al Farsi* [Stockholm, Sweden], J. Sylvin, Z. Al-Muharrmi, S. Al-Azri, A. Al Jardani, C. Giske

4508 Detection and successful containment of a NDM-1-producing Proteus mirabilis clone spread in an Italian sub-acute care unit
A. Mercato* [Grotte, Italy], I. Bitar, V. Mattioni Marchetti, F. Marchesini, M. Mancinelli, S. Bracco, V. Ragnani, A. Anesi, E. Nuclea, R. Migliavacca

4602 Whole genome sequencing investigation into a single-site outbreak of NDM-mediated carbapenem resistance disseminated across multiple species predominantly via IncI/M plasmids

5311 Molecular epidemiology and genetic characteristics of New Delhi metallo-β-lactamase among Gram-negative bacteria in a tertiary care hospital of north India
S. Singh* {Lucknow, India}, A. Singh, A. Pathak, C. Sahu, K. Prasad

Extensively drug-resistant Klebsiella pneumoniae ST383 co-harbouring OXA-48 and NDM-5 outbreak at a tertiary care centre in Lebanon
O. Zmerli* [Beirut, Lebanon], A. Chamieh, S. Saliba, Z. Daoud, C. Afif, E. Azar

Phenotypic and molecular investigation of ST11 NDM-1-producing Klebsiella pneumoniae isolates persisting between 2015 and 2018 in a Bulgarian hospital
T. Kostyanov* [Witrjik, Belgium], R. Yatcheva-Dobrevska, B. Xavier, V. Dicheva, P. Stefanowa, C. Lammens, H. Goossens, S. Malhotra-Kumar

Integrated molecular surveillance of carbapenem-resistant Enterobacteriaceae in Germany

Investigation of increased prevalence of IMP carbapenemases by next-generation sequencing in Wales
M. Woottton* [Cardiff, United Kingdom], M. Mentasti, K. Prime, S. Khan, K. Sands, J. Watkins, S. Corden, T. Connor, L. Jones

Investigation of a hospital outbreak of multi-drug resistant Klebsiella pneumoniae ST307, including isolates producing OXA-244 carbapenemase
L. Jones* [Cardiff, United Kingdom], M. Mentasti, K. Sands, J. Watkins, M. Morgan, S. Lingard, K. Prime, S. Khan, M. Bull, E. Davies, S. Corden, B. Healy, T. Connor, M. Woottton

Regional outbreaks of Enterobacter cloacae complex NDm-1 in Poland, 2015-19
R. Izdebski* [Warsaw, Poland], P. Urbanowicz, M. Biedrzycka, D. Żabicka, E. Literacka, W. Hryniewicz, M. Gniadkowski

Dissemination of OXA-244-producing Escherichia coli in Germany
J. Hars* [Bachum, Germany], B. Neumann, R. Kramer, K. Kremer, S. Haller, N. Pfennigwerth, A. Reuss, Y. Pfeifer, G. Werner, T. Eckmanns, S. Gatterman

Emergence of Klebsiella quasipneumoniae carrying New Delhi metallo-β-lactamase (blaNDM-1) gene in a Brazilian hospital
B. Boettger* [Sao Paulo, Brazil], A. Pignatari
7341 Regional dissemination of Klebsiella pneumoniae ST147 NDM-1 in Poland
M. Biedrzycka, R. Izedbski* (Warsaw, Poland), A. Baraniak, M. Machuliska, P. Urbanowicz, D. Żabińska, E. Literacka, W. Hytniewicz, M. Gniadkowski

7351 OXA-48 producing Klebsiella pneumoniae in non-hospitalised elderly patients in Zagreb, Croatia
J. Vranes* (Zagreb, Croatia), S. Šuto, B. Bedenic, A. Milinar-Dzepeina, S. Likić, S. Kibel, J. Knezevic, M. Anusic, V. Ticic, A. Grisold

7454 Epidemic clonal lineages of Enterobacteriales producing VIM-type carbapenemasases in Poland, 2013-18
R. Izedbski* (Warsaw, Poland), D. Żabińska, E. Literacka, P. Urbanowicz, A. Baraniak, W. Hytniewicz, M. Gniadkowski

8992 Unexpected detection of clinical isolates of Proteus mirabilis producing OXA-48 but susceptible to carbapenems and piperacillin-tazobactam
M. Artacho* (Málaga, Spain), R. Pedraza Merino, M. Cousse, M. Muñoz De La Rosa, E. Perez-Nadales, C. Pitart, M. Hernández García, J. Vila Estape, R. Canton Moreno, M. Egea, L. Martínez-Martínez

9072 Emergence of biaVIM-2 and detection of biaVIM-24 in Pseudomonas sp. from clinical samples in Brazil

9209 The emergence of new STs of blaNDM-positive hypervirulent Klebsiella pneumoniae isolates in an oncology hospital, Russia
P. Starkova* [Saint Petersburg, Russian Federation], I. Lazareva, V. Ageyevts, J. Sopova, V. Gostev, I. Tsvetkova, M. Lebedeva, S. Sidorenko

9373 Multidrug-resistant Klebsiella pneumoniae ST231: the new endemic super bug of India?
C. Shankar* (Vellore, India), J. Jacob, K. Vasudevan, B. Abirami, S. Anandan, V. Balaji

9593 Genomic epidemiology of NDM-producing Enterobacteriaceae in Portuguese hospitals
V. Manageiro* (Lisbon, Portugal), E. Ferreira, M. Caniça

Session accepted as Paper Poster Session
MIC: are all methods equal?

150 Assessment of trimethoprim-sulfamethoxazole susceptibility testing methods for fastidious Haemophilus spp.
Y. Sierra Urueña* [Barcelona, Spain], A. González Díaz, F. Tubau, A. Carrera-Salinas, J. Moleres, P. Bajanca-Lavado, J. Garmendia, M. Domínguez Luzon, A. Ardanuy Istaíre, S. Martí

1108 Reduced in vitro killing of methicillin-resistant Staphylococcus aureus blood culture isolates by vancomycin as the bacterial inocula increases
A. Alsaede, J. Rubin, S. Sanche, H. Deneer, J. Blondeau* [Saskatoon, Canada]

3564 Benzylpenicillin gradient tests underestimate MICs for penicillin non-susceptible Strephtococcus pneumoniae
F. Nilsson, E. Matuschek* [Växjö, Sweden], G. Kahlmeier

3658 Area of technical uncertainty for ciprofloxacin in Enterobacteriales: evaluation of MIC values using the E-test method
V. Viaggi, E. Meroni, O. Spezia, S. Tanolo, B. Pini, F. Luzzaro* [Lecco, Italy]

4613 Evaluation of commercial media for susceptibility testing of Neisseria gonorrhoeae
L. Davies, M. Cole, C. Horner, F. Ismail, Z. Ivanov, H. Fijer, L. Jones, R. Howe, M. Wootten* [Cardiff, United Kingdom]

4746 Stability studies with tigecycline in bacterial growth medium and impact of stabilising agents: a pre-requisite for in vitro susceptibility testing
L. Amann* [Hamburg, Germany], E. Ruda Vicente, M. Rathke, A. Broeker, S. Wicha

5137 Comparison of methods to evaluate the activity of ceftolozane/tazobactam against clinical isolates of carbapenem-resistant Pseudomonas aeruginosa from Chile

5433 Performance of VITEK 2 AST-GN meropenem/ vaborbactam for antimicrobial susceptibility testing of Enterobacteriaceae and Pseudomonas aeruginosa: a multi-centre study
S. Franklin* [St. Louis, United States], H. Dwivedi, G. Procop, M. Tračzewski, O. Garner, P. Deol

6184 The Insertion Sequence (IS) disruption of mgrB gene is critical for colistin susceptibility testing efficiency of Sensititre in carbapenem-resistant Klebsiella pneumoniae
B. Ozer* [Istanbul, Turkey], C. Vatansever, B. Gundogdu, O. Dogan, F. Can

6413 Molecular and phenotypic investigation of resistance in Neisseria gonorrhoeae
F. Luzzaro* (Lecco, Italy)

7351 Area of technical uncertainty for ciprofloxacin in Enterobacteriales: evaluation of MIC values using the E-test method
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V. Manageiro* (Lisbon, Portugal), E. Ferreira, M. Caniça

Session accepted as Paper Poster Session
Molecular and phenotypic investigation of resistance in staphylococci

369 Molecular characterisation of Staphylococcus aureus clinical strains from endotracheal tubes of patients with intensive care unit-acquired pneumonia
R. Cabrera* [Barcelona, Spain], L. Fernandez Barat, A. Motos, R. López, N. Vázquez Burgos, M. Panigada, F. Alvarez-Lerma, Y. Lopez, M. Acuña, D. Ramírez, F. García, J. Munita* [Santiago, Chile]

4746 Stability studies with tigecycline in bacterial growth medium and impact of stabilising agents: a pre-requisite for in vitro susceptibility testing
L. Amann* [Hamburg, Germany], E. Ruda Vicente, M. Rathke, A. Broeker, S. Wicha

5137 Comparison of methods to evaluate the activity of ceftolozane/tazobactam against clinical isolates of carbapenem-resistant Pseudomonas aeruginosa from Chile
1194 Mutant prevention concentration values of linezolid, moxifloxacin and vancomycin against Staphylococcus pseudintermedius strains recovered from humans
L. Blondeau* [Saskatoon, Canada], J. Rubin, R. Kanthan, S. Sanche, H. Denee, J. Blondeau

1298 Effect of short-term antimicrobial therapy on the tolerance and antibiotic resistance of multidrug-resistant Staphylococcus capitis
X. Yu* [Hangzhou, China]

1479 Risk factors associated with daptomycin non-susceptible Staphylococcus aureus bloodstream infections
S. Gudipati, A. Vahia* [Detroit, United States], M. Perri, R. Tibbetts, M. Zervos, G. Suleyman

1933 Nasal methicillin-resistant Staphylococcus aureus colonisation among adults and children in Russia: predominance ST22-subclone “Gaza Strip”

1942 Involvement of walK gene mutations in antibiotic resistance increase in daptomycin-unsusceptible methicillin-resistant Staphylococcus aureus
A. Hugo Campano, N. Gómez Casanova, J. Munoz-Bellido* [Salamanca, Spain]

2274 Molecular characterisation of methicillin-resistant Staphylococcus aureus isolates from the United Arab Emirates: emergence of novel strains and variants

3388 Minimum Inhibitory Concentration distributions and putative new resistance mechanisms for methicillin and trimethoprim in Staphylococcus saprophyticus

3626 Genomic analysis of Pantone-Valentine leukocidin-positive methicillin-resistant Staphylococcus aureus in hospitalised patients in Germany by whole genome sequencing: 2015-2018
S. Klein* [Heidelberg, Germany], J. Hannesen, P. Zanger, K. Heeg, S. Boutin, D. Nurjadi

3980 Direct detection of PBP2a using the high-resolution Orbitrap mass spectrometer and rapid discrimination of antibiotic resistance in Staphylococcus aureus using the Acron system
J. Neil* [Cambridge, United States], A. Verma, M. Viirtola, W. Mcgee, S. Kronewitter, J. Stephenson

4245 Investigation of linezolid resistance mechanisms of Staphylococcus epidermidis isolates collected in Gauteng, South Africa
K. Addison, K. Strydom, E. Hoosien, Y. Bolukaoto, M. Kock, M. Ehlers* [Pretoria, South Africa]

4271 Bloodstream infections caused by Staphylococcus aureus non-susceptible to daptomycin: clonal and clinical aspects
D. Fernandes, R. Władyka, A. Ferreira, S. Nouer* [Rio de Janeiro, Brazil], K. Dos Santos

4533 Rapid nuc and mecA gene testing by polymerase chain reaction is useful to choose appropriate antibiotics in Staphylococcus aureus bacteraemia
M. Ikemachi* [Kobe, Japan], Y. Go, H. Takekawa, K. Miyagawa

4550 The temporal dynamics of Staphylococcus aureus carriage among healthcare workers in a tertiary referral hospital with a history of endemic methicillin-resistant Staphylococcus aureus, investigated by whole genome sequencing
A. Kearney* [Dublin, Ireland], P. Kinnevey, M. Earls, T. Poovelikunnel, G. Brennan, A. Shore, H. Humphreys, D. Coleman

Linezolid resistance mechanisms in Staphylococcus capitis and Staphylococcus haemolyticus isolates collected in Gauteng, South Africa
K. Addison, K. Strydam, E. Hoosien, Y. Bolukaoto, M. Kock, M. Ehlers* [Pretoria, South Africa]

Methicillin-resistant Staphylococcus aureus bacteraemia: clinical-epidemiological characteristics and evolution of oxacillin resistance in 17 years
L. Vinuela, G. Santillana, R. Martinez, P. Bardon, C. Garcia, E. Clavijo, M. Garcia López* [Málaga, Spain]

Worldwide dissemination of linezolid-resistant Staphylococcus epidermidis clones
N. Faria, N. Bogas, C. Torres, A. Robinson, E. Petinati, J. Empel, N. Ishiwada, B. Kahl, F. Campanile, H. De Lencastre, F. Laurent, M. Miragaia* [Leiria, Portugal]

Penicillin-binding protein 2a temperature-sensitive folding defect: a new path to tackle methicillin resistance in Staphylococcus aureus
M. Roach* [Geneva, Switzerland], E. Lelong, R. Sierra, O. Panasenko, A. Renzon, W. Kelley

Evaluation of a culture surveillance application for the detection of methicillin-resistant Staphylococcus aureus in the clinical setting
M. Bois, E. Mcelvania, M. Gosnell, C. Orny, V. Jean-Marc, J. Lemstra, M. Van Der Lei* [Drachten, Netherlands], R. Marcelpoil

A study of virulence factors and antimicrobial resistance in Staphylococcus epidermidis isolates from ocular infections
N. Hussain Ahmed* [Delhi, India], A. Basu, G. Satpathy, B. Tezpur, N. Sharma, R. Chawla

Stepwise in vitro daptomycin resistance selection of Staphylococcus aureus: accumulation mutations and heteromutations
V. Gostev* [Saint Petersburg, Russian Federation], O. Kalinogorskaya, J. Sapova, I. Tsvetkova, M. Velizhanina, S. Sidorenko
Prevalence and molecular characteristics of Staphylococcus aureus carrying Panton-Valentine leukocidin genes isolated from patients accessing at emergency department in 2016-2018 period

A. Lai* [Milan, Italy], A. Bergna, S. Rimoldi, A. Ridelfo, M. Gismondo, C. Bolotta, M. Galli, G. Zehender

qPCR to detect mecA in faecal samples: a tool for assessing resistance burden amongst pets and their owners in the microbiological ‘fast age’?

S. Frosini* [Hatfield, United Kingdom], G. Gallow, J. Menezes, A. Belas, C. Saraiva Marques, C. Aborim, M. Pombo, A. Loeffler

Penicillin-binding protein 2 (PBP2), PBP2a and PBP4 clone-specific polymorphisms are not associated to cefotaroline- (CPT) susceptibility in Chilean clinical isolates of methicillin-resistant Staphylococcus aureus [MRSA]

M. Spencer, R. Martinez, L. Rivas, M. Rojas, R. Ríos, A. Dinh, L. Díaz, J. Reyes, B. Hanson, P. García, C. Arias, J. Munita* [Santiago, Chile]

Decline of the Brazilian endemic clone and dominance of internationally disseminated lineages among MRSA from bacteraemic patients in Porto Alegre, Brazil


Study of penicillin-susceptible Staphylococcus aureus in patients with bacteraemia. a multi-centre study in Spanish hospitals


Performance of the PBP2a (Alere-Abbott) immunochromatographic test on early primary cultures from positive MRSA/MR-CoNS blood cultures

C. Munier* [Lyon, France], C. Dupieux, C. Kolenda, M. Bes, O. Dauwalder, F. Vandenesch, A. Triston, F. Laurent

Evaluation of an immunochromatographic assay for rapid identification of PBP2a-positive Staphylococcus aureus

R. Sainz Rodriguez* [Málaga, Spain], M. Valverde Traya, M. Gasco Sanjuán

Linezolid resistance in coagulase-negative Staphylococcus spp. in six private hospitals in Sao Paulo, Brazil


An emerging methicillin resistance mechanism due to loss-of-function of the GdpP protein in mec gene-negative staphylococci undetected by reference methods


Genomic analysis reveals persistence and microevolution of methicillin-resistant Staphylococcus aureus in recurrent carriers


Increase of daptomycin-resistant Staphylococcus aureus with a possible link to antiseptic wound treatment in three medical centres in Cologne, Germany

A. Wendel* [Cologne, Germany], R. Otchwemah, F. Mattner, H. Oberländer, T. Tellez-Castillo, R. Skov, G. Werner, F. Bayer, B. Strommenger

The dissemination and molecular characterisation of clonal complex 361 methicillin-resistant Staphylococcus aureus in Kuwait hospitals, 2016-2018

E. Udo, E. Sarkhoo* [Jabriya, Kuwait], S. Boswini, E. Müller, S. Monecke, R. Ehrich

Accessory gene regulator (agr) functionality differences among closely related methicillin-resistant mecC-Staphylococcus aureus


Nasopharyngeal carriage of methicillin-resistant Staphylococcus aureus in newly HIV-diagnosed, antiretroviral therapy naïve adults, Dar es Salaam, Tanzania

J. Manyahi* [Bergen, Norway], S. Moyo, S. Aboud, N. Langeland, B. Blomberg

Lineage CC398 among methicillin-susceptible and methicillin-resistant Staphylococcus aureus isolates of blood cultures. A multi-centre study in Spanish hospitals


Zooming into the CoNS group on a species level exposes high heterogenicity in prevalence and antibiotic resistance: an in-depth data analysis in the MALDI-TOF era

M. Berends* [Groningen, Netherlands], C. Luz, Y. Roelofs, J. Arends, G. Andriesse, C. Clasen, A. Friedrich

Changing profile of invasive disease-causing Staphylococcus aureus in Australia

S. Baines* [Melbourne, Australia], S. Giuliani, A. Gançalves Da Silva, N. Holmes, G. Coombs, S. Pang, T. Stinear, B. Howden

Session accepted as 2-Hour Oral Session

Molecular epidemiology and detection of resistant staphylococci

Epidemiology of the Staphylococcus aureus CA-MRSA USA300 in Belgium

M. Argüin* [Brussels, Belgium], D. Marting, N. Yin, A. Deplano, C. Nonhoff, A. Meghraoui, C. Michel, M. Hallin
Development and preliminary evaluation of Multidrug Resistance Direct Flow Chip kit, a molecular method for a rapid detection of multiple antibiotic resistance markers
J. Carrero* (Granada, Spain), A. Galiana, D. Gomez, A. Olmo, M. Ruiz, N. Gonzalo-Jiménez

Molecular and cultural tests in a multi-centre point prevalence surveillance study on carbapenem-resistant Enterobacteriaceae in long-term care facilities’ residents in northern Italy area
G. Lo Cascio* (Verona, Italy), A. Azzini, A. Bazaj, G. Be, L. Lambertenghi, N. Salerno, I. Coledan, F. Mazzaferrì, L. Maccacaro, E. Concia, E. Tacconelli, G. Cornaglia

Evaluation of the EasyScreen ESBL/CPO kit for the detection of β-lactam resistance genes
C. Gonzalez* [Le Kremlin-Bicêtre, France], S. Dueslati, D. Girlich, L. Dortet, T. Naas

Molecular methods for carbapenemase detection

343 Expediting antibiotic therapy management of critically ill patients with pneumonia by the detection of the main carbapenemase and ESBL-encoding genes directly from bronchoalveolar lavage
M. Boattini* [Turin, Italy], G. Bianco, M. Iannaccone, C. Costa, R. Cavollo

593 Evaluation of a new commercial assay for detection and characterisation of carbapenemase genes
G. Eltringham* [Newcastle upon Tyne, United Kingdom], M. Suwara, M. Bakheit, S. Stack, E. Gillies, J. Perry

1054 Establishment and clinical application of a multiple touchdown PCR for detection of carbapenemase genes
X. Li* [Nanjing, China], N. Sun, L. Zhang, B. Yu, W. Wang, X. Yao, J. Yu

1800 Application of a new molecular biology method for carbapenem-resistant Enterobacteriaceae detection in rectal swabs
G. Parisi* [Rome, Italy], A. Denara, S. D’Inzeo, R. D’Arrigo, D. Gallone, B. Mariani, R. Oliverio

2126 Evaluation of a novel high-definition PCR multiplex assay to identify nine genetic targets associated with multidrug-resistant organisms
D. Gerstbrein, B. Mesich, N. Ledeboer, M. Faran, B. Buchan* [Milwaukee, United States]

4657 Performance of the Xpert Carba-R assay versus the ChromID CARBA SMART for the detection of carbapenemase-producing Gram-negative bacteria from rectal swabs

5630 Surveillance of circulating carbapenemase genes with automated molecular system (BD Max) at a healthcare centre in Buenos Aires, Argentina
M. Zárate* [Buenos Aires, Argentina], G. Weltman, G. Serruto, P. Mainetti, B. Wisner, J. Zaracho

6146 Novodiag Carba-R+ assay for the detection of carbapenemase-producing bacteria
S. Bernabeu* [Le Kremlin-Bicêtre, France], D. Girlich, W. Bouchahraf, S. Dueslati, I. Langlois, N. Arangia, C. Begasse, T. Huang, P. Bogaerts, Y. Glupczynski, T. Naas

6472 Development of LAMP-based multiplex real-time assay for rapid detection of genes of NDM, VIM, KPC and OXA-48 carbapenemase groups
A. Nosova* [Moscow, Russian Federation], Y. Savochkina, A. Ibragimova, G. Shipulin

7215 Evaluation of the Revogene Carba C assay for detection and differentiation of carbapenemase-producing bacteria
D. Girlich, M. Laguide, L. Dortet, T. Naas* [Le Kremlin Bicêtre, France]

7386 Utility of Xpert Carba-R in identifying carbapenem resistance in blood culture isolates in critically ill patients
V. Krishna* [Chennai, India], R. Vimal Kumar, S. Uma

7945 Rapid, direct antimicrobial susceptibility testing of positive blood cultures within 4 hours using ATP bioluminescence detection and machine learning method
S. Kawabe* [Kokubunji-shi, Tokyo, Japan], Y. Uchiha, H. Noda, A. Matsui, H. Niimi, I. Kitajima

5695 Implementing rapid susceptibility testing directly from positive blood cultures in the routine laboratory workflow for sepsis
P. Mantzana, E. Kandiliotou, M. Kyriakopoulou, F. Nitskina, M. Arhonti, A. Tychala* [Thessaloniki, Greece], G. Meletis, G. Vasilaki, G. Kagkalou, E. Protonotariou, L. Skoura

5630 Molecular and cultural tests in a multi-centre point prevalence surveillance study on carbapenem-resistant Enterobacteriaceae in long-term care facilities’ residents in northern Italy area
G. Lo Cascio* (Verona, Italy), A. Azzini, A. Bazaj, G. Be, L. Lambertenghi, N. Salerno, I. Coledan, F. Mazzaferrì, L. Maccacaro, E. Concia, E. Tacconelli, G. Cornaglia

3257 Rapid phenotypic susceptibility testing of Neisseria gonorrhoeae using Graver-Wade medium, broth microdilution, and the flow cytometry-assisted susceptibility test (FAST)
C. Gonzalez* [Le Kremlin-Bicêtre, France], S. Dueslati, D. Girlich, L. Dortet, T. Naas

6690 Impaired membrane integrity as a marker for colistin susceptibility: a flow cytometry method for rapid AST in Pseudomonas aeruginosa and Acinetobacter spp.
G. Ekelund, E. Sturegård, T. Schön, S. Samajo* [Karlskrona, Sweden]

6194 The flow cytometry-assisted susceptibility test [FAST] accurately predicts colistin MICs for Gram-negative bacilli directly from positive blood culture in less than four hours
T. Paton* [Perth, Australia], K. Mulroney, M. Kapczyk, C. Inglis

6194 The development of rapid multidrug resistance surveillance methods in acute care facilities
K. Mulroney, M. Kapczyk, C. Inglis

6194 Evaluation of the EasyScreen ESBL/CPO kit for the detection of β-lactam resistance genes
C. Gonzalez* [Le Kremlin-Bicêtre, France], S. Dueslati, D. Girlich, L. Dortet, T. Naas

6194 Development and preliminary evaluation of Multidrug Resistance Direct Flow Chip kit, a molecular method for a rapid detection of multiple antibiotic resistance markers
J. Carrero* (Granada, Spain), A. Galiana, D. Gomez, A. Olmo, M. Ruiz, N. Gonzalo-Jiménez

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Abstract Categories 2020

Evaluation of FAST-Prep Liquid Colony for early antimicrobial sensitivity testing of positive blood culture by disk diffusion method
A. Khine* [Richmond Hill, Canada], N. Fernandez, L. Pandey, A. Telepbour, S. Novak, T. Alavie

Session accepted as Paper Poster Session
Phenotypic AST: still important!

Adjunction of daptomycin for the treatment of bacterial meningitis: in vitro study
T. Maldiney, D. Bonnat, N. Anzala, S. Albac, D. Labrousse, E. Varon, C. Neuwirth, D. Croisier, P. Chavanet*
[Dijon, France]

Can Rapid Antimicrobial Susceptibility Testing (RAST) improve the time to the optimal therapy for bloodstream infections?
F. Oleara* [Hamburg, Germany], B. Berinson, M. Christner, H. Rohde

Evaluation of EUCAST disk diffusion criteria to screening mecA gene in species of Staphylococcus epidermidis-like group
V. Pietta Perez* [João Pessoa, Brazil], M. Da Silva, A. Rossato, P. Alves D’Azevedo

Effective antimicrobial combination testing: linking rapid microcalorimetry screening to in vivo efficacy
K. Kragh* [Copenhagen, Denmark], D. Gijon, A. Maruri, A. Antonelli, M. Copp, M. Kolpen, S. Crane, C. Tellapragada, B. Hasan, C. De Vogel, W. Van Wamel, A. Verbon, C. Giske, G. Rossolini, R. Canton Moreno, N. Frimodt-Moller

In vitro evaluation of ceftolozane-tazobactam-aztreonam and ceftolozane-tazobactam-fosfomycin combinations by time-kill assays according to SPM-1-producing Pseudomonas aeruginosa clinical strains
G. Santos, G. Cuba* [São Paulo, Brazil], C. Silva Nodari, A. Streling, R. Caoy Da Silva, A. Gales, A. Pignatari, D. Nicolau, C. Kiffer

The predictive value of disc diffusion assay results for resistance in Gram-negative bacteraemia: a UK district general hospital experience
T. Swaine* [London, United Kingdom], C. Dominic, R. Buchanan

EUCAST improved screening algorithm for beta-lactam resistance in Haemophilus influenzae
E. Matuschek* [Växjö, Sweden], J. Ahman, J. Thegerström, F. Resman, S. Bengtsson, G. Kahlmeter

EUCAST temocillin breakpoints and antimicrobial susceptibility testing guidelines
C. Giske* [Stockholm, Sweden], E. Matuschek, R. Canton Moreno, J. Turnidge, G. Kahlmeter

Variations in categorical agreement between fosfomycin agar dilution and disk diffusion using standard and high inoculum protocols for Klebsiella pneumoniae testing

A rapid adenosine triphosphate bioluminescence-based assay for predicting antibiotic combinations against dividing and non-dividing live carbapenem-resistant Enterobacteriaceae
Y. Cai* [Singapore, Singapore], N. Begam, N. Fauzi, H. Wong, T. Lim, J. Tea, T. Tan, J. Sim, A. Kwa

Evaluation of ceftolozane-tazobactam disk diffusion testing of Pseudomonas aeruginosa in a multi-centre UK study
J. Diggle, I. Monahan, A. Alvarez Buylla, E. Manu, M. Allen, T. Planche, M. Wootton* [Cardiff, United Kingdom]

A study comparing the performance of an eravacycline oxoid antimicrobial susceptibility testing disc against an FDA-cleared predicate device
K. Church* [Basingstoke, United Kingdom], D. Carpenter, M. Olesky

SynAST, a reliable in vitro synergy test as support for New Delhi metallo-beta-lactamase Klebsiella pneumoniae infection therapy
A. Leonardi* [Pisa, Italy], C. Girodara, E. Tagliaprente, M. Falcone, G. Tisea, S. Barnini, F. Menichetti

Ceftazidime-avibactam/aztreonam synergism assay against carbapenem-resistant Enterobacteriaceae and Pseudomonas aeruginosa carrying metallo-beta-lactamases
J. Barbosa, K. Moraes* [São Paulo, Brazil], E. Sanchez Espinazo, L. Perdigao Neto, S. Santos, A. Marchi, R. Ruedas Martins, T. Guimaraes, F. Rossi, S. Figueiredo Costa

In vivo and in vitro synergistic activity of colistin combining with meropenem and sulbactam against multidrug-resistant and pandrug-resistant Acinetobacter baumannii clinical isolates
C. Kulah* [Zonguldak, Turkey], E. Subasi, A. Atalar

AST for fastidious bacteria: a reliable automation to standardise the EUCAST disk diffusion test
M. Paolucci* [Brescia, Italy], C. Lacchini, N. Schepis, L. Navarrina

Impact of lung transplantation on the phylogenetic diversity of Pseudomonas aeruginosa isolates from end-stage cystic fibrosis patients
R. Datar* [La Balme Les Grottes, France], A. Coello Pelegrin, S. Urengi, A. Perry, J. Samuel, A. Van Belkum, H. Goossens, V. Chalansonnet

Predicting Pseudomonas aeruginosa susceptibility phenotypes from whole genome sequence resistance analysis
S. Cortes-Lara* [Palma, Spain], C. Lopez Causpe, E. Del Barrio-Tofiño, A. Oliver

Whole genome sequencing to detect antimicrobial resistance-associated determinants in Staphylococcus epidermidis
K. Cole* [Brighton, United Kingdom], B. Young, D. Wilson, B. Atkins, J. Paul, M. Llewellyn
Abstract Categories 2020

1644 Prediction of antibiotic resistance in Helicobacter pylori by whole genome sequencing and open-source bioinformatics tools
A. Miqueleiz, A. Blanco Suárez, C. Alba Rubia, P. Urruzune, K. Thorell, T. Labarca Caveró* [Madrid, Spain]

1658 TOF MS-typing: employment of bioinformatics by MALDI-TOF MS

4828 Understanding discordance between observed and WGS-predicted resistance: a study of amoxicillin-clavulanate in Escherichia coli
T. Davies* [Oxford, United Kingdom], A. Sheppard, J. Swann, N. Stoesser, M. Ellington, N. Woodford, T. Peto, D. Crook, M. Anjum, A. Walker

4940 Bioinformatic fake news: the important but under-appreciated caveats of identifying resistance genes from whole genome sequencing data
T. Davies* [Oxford, United Kingdom], A. Sheppard, J. Swann, N. Stoesser, M. Ellington, N. Woodford, T. Peto, D. Crook, M. Anjum, A. Walker

5117 Optimisation of the MALDixin test for the rapid identification of colistin resistance in Klebsiella pneumoniae using MALDI-TOF MS
W. Xu* [Singapore, Singapore], S. Prakki, N. Thevasagayam, L. Wang, K. Marimuthu, I. Venkotchalam, J. Teo, O. Ng

5896 Quantitative detection of bacterial resistance by meropenem hydrolysis using MALDI-TOF MS
C. Wilhelm* [Porto Alegre, Brazil], M. Carneiro, P. Wink, A. Barth

5960 Evaluation of a liquid chromatography and tandem mass spectrometry-based Carba detection method using the Acron system for clinical isolates expressing multiple carbapenemases

6130 Metagenomic analyses of antibiotic resistance genes in gut microbiome of healthy people in Korea: high carriage rate of blaCTX-M, blaCMY-2 and plasmid-mediated quinolone resistance genes
J. Kim* [Guri, South Korea], M. Sea, K. Park, H. Park, H. Hwang, B. Kim, R. Rho, H. Pai

6679 Evaluation and differentiation of carbapenemase-encoding plasmids by short-read sequencing data: validation by ONT long-read hybrid assembly of a large Singaporean carbapenem-resistant Enterobacteriaceae collection
W. Xu* [Singapore, Singapore], S. Prakki, N. Thevasagayam, L. Wang, K. Marimuthu, I. Venkotchalam, J. Teo, O. Ng

6917 Big data analysis of all bacterial genomes establishes a triple whammy of carbapenemases, ICEs and mediated quinolone resistance genes
T. Tomaz Santos Batelha* [Porto, Portugal], J. Cordeiro

7035 Rapid MALDI-TOF MS-based method for vancomycin-resistant Enterococcus faecium detection
A. Candela* [Madrid, Spain], L. Quiraga, M. Arroyo, A. Ruiz, E. Cercenado, G. Méndez, M. Marín, P. Muñoz, L. Mancera Pascual, B. Rodríguez-Sanchez

7646 Accurate differentiation of carbapenemases by MALDI-TOF MS-typing: employment of bioinformatics
E. Goto, J. Arca Suárez, B. Rodrí, G. Méndez, M. Arroyo, L. Mancera Pascual, G. Bou Arevalo, M. Oviño García* [A Coruña, Spain]

8627 Rapid non-molecular methods for detection of beta-lactam and polymyxin resistance
M. Sorensen, E. Nilsson, F. Gardner, S. Ramadan, D. Goodlett, R. Ernst* [Baltimore, United States]

9635 Characterisation of extended-spectrum beta-lactamases by mass spectrometric analysis
S. Lee* [Seoul, South Korea], W. Yang, H. Suh, H. Jang, Y. Park, S. Hwang, J. Baek

Session accepted as Paper Poster Session
Proteomics beyond bacterial identification

256 Evaluation of a novel method for detection of carbapenem hydrolysis with an automated software (Clover BioSoft) by MALDI-TOF MS
E. Goto, G. Méndez, L. Mancera Pascual, G. Bou Arevalo, M. Oviño García* [A Coruña, Spain]

1658 Accurate differentiation of carbapenemases by MALDI-TOF MS-typing: employment of bioinformatics
E. Goto, J. Arca Suárez, B. Rodrí, G. Méndez, M. Arroyo, L. Mancera Pascual, G. Bou Arevalo, M. Oviño García* [A Coruña, Spain]

3385 MBT STAR-Carba assay: going beyond the routine protocol
M. Zlach* [Toruń, Poland], M. Peer, K. Sparbier, M. Kastrzewa, B. Buszewski

4757 Extended antibiotic panel to analyse the susceptibility of Enterobacteriaceae by the MALDI-TOF MS-based MBT FAST Assay
K. Sparbier, D. Drews, M. Peer, I. Nix, E. Idelevich, K. Becker, M. Kastrzewa* [Bremen, Germany]

5896 Quantitative detection of bacterial resistance by meropenem hydrolysis using MALDI-TOF MS
C. Wilhelm* [Porto Alegre, Brazil], M. Carneiro, P. Wink, A. Barth

6476 Optimization of the MALDixin test for the rapid identification of colistin resistance in Klebsiella pneumoniae using MALDI-TOF MS
L. Dortet* [Paris, France], S. Bernabeu, P. Bogaerts, R. Bonnin, T. Naas, A. Filloux, G. Larrouy-Maumus

8718 Antimicrobial susceptibility testing by MALDI-TOF MS of lipids determines true MICs in six hours
M. Sorensen, E. Nilsson, F. Gardner, S. Ramadan, D. Goodlett, R. Ernst* [Baltimore, United States]

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E. Goto, J. Arca Suárez, B. Rodrí, G. Méndez, M. Arroyo, L. Mancera Pascual, G. Bou Arevalo, M. Oviño García* [A Coruña, Spain]
Detection of carbapenemases in *Pseudomonas* and *Acinetobacter* by the Mast Carba PâcE kit
O. Fournier, K. Jeannot* [Besançon, France], L. Gabriel, P. Tripolley, J. Rousselot, A. Potran, P. Plé siat

Rapid detection of piperacillin/tazobactam resistance and extended spectrum β-lactamases in clinical isolates of *Escherichia coli*
A. Rodríguez Villodres* [Seville, Spain], A. Gutiérrez-Linares, J. Pachon-Díaz, J. Lepe, Y. Smani

Direct detection of extended-spectrum β-lactamases in bacteria isolated in blood culture bottles using a lateral flow assay
G. Cuesta Chasco* [Barcelona, Spain], J. Bosch, Y. Zboromyrska, C. Pitart, A. Vergara, F. Morales, E. Rubio García, B. Fidalgo, M. Fernández, C. Casals-Pascual, J. Vila Estape

Evaluation of the rapid ResaPolymyxin Acinetobacter/*Pseudomonas* NP test for rapid screening of colistin resistance in non-lactose fermenters
H. Jung* [Pretoria, South Africa], J. Pitout, B. Mitton, K. Strydom, C. Kingsburgh, N. Mbelle, M. Ehlers, M. Kock

Polymerase chain reaction (PCR) uses as a screening tool to detect polymyxin B susceptibility in *Enterobacterales*

Investigation of carbapenemases by RESIST-4 O.K.N.V Immunochromatographic lateral flow assay in *Enterobacteriaceae* isolates
M. Yasar* [Izmir, Turkey], F. Cilli, Y. Tekintas, F. Polat, M. Holubar, S. Deresinski, N. Banaei

Evaluation of the RESIST-4 O.K.N.V K-SeT test for the detection of carbapenemase production in *Enterobacteriaceae*
A. Both, L. Jávnári, A. Hanczvikkel, A. Tóth* [Budapest, Hungary]

Improved NG-test Carba5 assay for the detection of previously undetected IMP-variants

Comparison of four ESBL detection tests directly from blood cultures and urine samples
F. Camétena* [Paris, France], H. Kafando, A. Ly, P. Thiebot, M. Rouveau, T. Sophie, M. Lafaurie, B. Ber cot

Evaluation of the new BL-RED electrochemical test for the detection of 3GC-resistant *Enterobacteriaceae* directly from positive blood cultures
C. Durand, A. Boudet* [Nîmes, France], J. Lavigne, A. Pantel

High-throughput bacterial phenotyping to characterise antimicrobial resistance mechanisms
B. Warne* [Cambridge, United Kingdom], J. Bartholdson Scott, S. Forrest, M. Maes, S. Sridhar, M. Török, G. Dougan

Clinical impact of rapid susceptibility testing in Gram-negative bloodstream infections
V. Antón Vázquez* [London, United Kingdom], C. Suarez, S. Adjepong, T. Planche

Improving Outcomes and Antibiotic Stewardship for patients with bloodstream Infections (IOAS): a quasi-experimental multi-centre analysis of time to optimal therapy
A. Bhaladi* [Tucson, United States], S. Mavane, M. Morgan, M. Ben-Aderet, M. Madhusudhan, J. Kolev, R. Daré, E. Rosenbaum, K. Wolfe, B. Ford, D. Ince, P. Kinn, K. Percival, R. Humphries

Implementation of EUCAST rapid antimicrobial susceptibility testing combined with routine infectious disease bedside consultation
T. Valentín* [Graz, Austria], T. Loizenbaur, E. König, J. Prattes, S. Wunsch, C. Zurl, R. Krause, I. Zollner-Schwetz

Impact of rapid antimicrobial susceptibility testing on antimicrobial stewardship and clinical outcomes of patients with Gram-negative rod bloodstream infection

Very good results for the use of the RAST methodology and for identification of agents of sepsis directly from the blood cultures by MALDI-TOF to optimise antibiotic therapy
J. Maman Pariona, F. Oliveira, P. Scatoni, T. Zaccariotto, N. Lincopan, C. Levy* [Campinas, Brazil]
2670 Potentiation of quinolones activity against *Escherichia coli* by suppression of SOS response and oxidative detoxification systems

3101 Identified beta-lactamase genes in *Aeromonas* species: an experience from Qatar
A. Hussain* (Doha, Qatar), S. Skariah, M. Sid Ahmed, M. Badawi, H. Ahmedullah, M. Al-Maslamani, A. Al-Khal, H. Al Souh, A. Sultan, E. Ibrahim, H. Ziglam

3418 Enhancing fosfomycin activity via glycerol-3-phosphate transporter activation
M. Ortiz Padilla* (Seville, Spain), I. Portilla Calderón, B. De Gregorio Laria, J. Rodríguez-Baró, A. Pascual Hernandez, J. Rodríguez Martínez, F. Docobo Perez

3790 Unveiling the role of nisin on resistance development by diabetic foot staphylococci: mutant selection window and horizontal gene transfer
M. Costa, E. Cunha, L. Tavares, M. Oliveira* (Lisbon, Portugal)

4124 Characterising a novel mechanism of inducible carbapenem resistance in toxigenic *Corynebacterium diphtheriae*
B. Forde* (Brisbane, Australia), A. Henderson, G. Playford, D. Paterson, S. Beatson

4264 Prevalence of macrolide resistance mutations in *Mycoplasma pneumoniae* from patients with respiratory tract infections in Europe
I. Edelstein* (Smolensk, Russian Federation), A. Romanov, A. Kuzmenkov, N. Alyabyeva, T. Pleskachevskaia, E. Groshenkova, R. Kozlov

4380 Spontaneous and clinically relevant tet(A)-dependent tigecycline resistance development
J. Jagdmann* (Uppsala, Sweden), D. Andersson, H. Nicoloff

4699 Carbapenem-resistant *Pseudomonas aeruginosa* in cystic fibrosis children
E. Samoylova, E. Ibrahim, H. Ziglam

5546 A novel variant of CTX-M β-lactamase in a clinical strain of *Serratia marcescens*
P. Celejewski-Marciniak, R. Wolinowska, M. Wroblewska* (Warsaw, Poland)

5835 Two antibiotics are better than one: using functional genomics to elucidate mechanisms of action in combination therapy
G. Sullivan* (North Ryde, Australia), R. Maharjan, N. Delgado, A. Cain

5948 Induction of erythromycin resistance in *Bordetella* sp. confirmed by whole genome sequencing
W. Fong* (Westmead, Australia), V. Timms, E. Sim, T. Nguyen, V. Sintchenko

6164 The rates of antimicrobial resistance in leprosy are higher among cases diagnosed in France than in those diagnosed in African countries [WHO sentinel surveillance network]

6229 Antimicrobial susceptibility of medically important *Nocardia* species in Korea
K. Hur* (Seoul, South Korea), K. Park, M. Kim, H. Sung

6312 Do bacterial growth conditions affect antibiotic resistance evolution?
J. Littler* (Coventry, United Kingdom), F. Harrison

7866 Piperacillin-tazobactam resistance developed during febrile neutropenia
C. Gomes* (São Paulo, Brazil), E. Sanchez Espinaza, M. Farrel Cortes, A. Marchi, T. Guimaraes, F. Rossi, L. Perdigao Neto, V. Rocha, S. Figueiredo Costa

9132 Aminoglycoside resistance mechanisms in invasive *Klebsiella pneumoniae* and *Escherichia coli*: a threat of rmtC-mediated resistance
I. Uzun* (Istanbul, Turkey), T. Celik, B. Aksu, N. Ulger Toprak, M. Hasdemir

Session accepted as Paper Poster Session

**Resistance issues in streptococci**

1280 Multiple mutations in dihydrofolate reductase gene in cotrimoxazole-resistant *Streptococcus pneumoniae* isolated from HIV adults in a community setting, Tanzania
J. Manyahi* (Bergen, Norway), S. Mayo, S. Aboud, N. Langeland, B. Blomberg

1237 Whole genome analysis of non-PCV13 emergent serotypes 8, 12F, 9N and 22F causing invasive pneumococcal disease in Spain
A. González Díaz* (Barcelona, Spain), J. Cámara, M. Ercibengoa Arana, E. Cercenado, N. Larrosa, M. Quesada, D. Fontals, M. Cubero, J. Marimon Ortiz De Zorate, J. Yuste, C. Ardany Tisaire

2277 Colonisation dynamics of *Achromobacter xylosoxidans* in the airways of cystic fibrosis patients: a longitudinal study
S. Kampmeier* [Münster, Germany], A. Mellmann, B. Kuhl

2299 Enhanced fosfomycin activity via glycerol-3-phosphate transporter activation
M. Ortiz Padilla* (Seville, Spain), I. Portilla Calderón, B. De Gregorio Laria, J. Rodríguez-Baró, A. Pascual Hernandez, J. Rodríguez Martínez, F. Docobo Perez

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G. Sullivan* (North Ryde, Australia), R. Maharjan, N. Delgado, A. Cain

5948 Induction of erythromycin resistance in *Bordetella* sp. confirmed by whole genome sequencing
W. Fong* (Westmead, Australia), V. Timms, E. Sim, T. Nguyen, V. Sintchenko
Emergence of the uncommon multiple drug-resistant non-PCV13 serotype 13/ST2754-clone among paediatric nasopharyngeal pneumococci isolated in Russia: 2010-2018
E. Brzhazovskaya* [Moscow, Russian Federation], N. Alyabyeva, T. Savinova, O. Panomarekova, A. Mirzaeva, T. Kalichenko, V. Mikhailova, D. Shagin, N. Mayanskiy

In the absence of pressure, physical interaction within nasopharyngeal pneumococcal biofilms leads to acquisition of cephalosporin resistance but not to capsule switch events
X. Wu* [Hangzhou, China], L. Santiago, Y. Tzeng, D. Stephens, J. Vidal

Resistance patterns and serotype distribution of Streptococcus pneumoniae isolates responsible for respiratory tract infections in Poland, 2006-2018
A. Gołębiowska* [Warsaw, Poland], I. Waśko, P. Rankiewicz, M. Kiedrowska, I. Wróbel, A. Bojarska, D. Stephens, J. Vidal, X. Wu* [Hangzhou, China], L. Santiago, Y. Tzeng, D. Stephens, J. Vidal

Identification of a multidrug-resistance cluster in clinical isolates of Streptococcus pyogenes that confers resistance to macrolides, lincosamides, tetracyclines, chloramphenicol and co-trimoxazole
D. Berbel Palau, G. López De Egea, J. Câmara* [Barcelona, Spain], A. González Díaz, M. Cubera, F. Tubau, M. Dominguez Lucon, C. Ardanyu Tisoire

Clonal spread of multidrug-resistant penicillin-nonsusceptible Streptococcus agalactiae
J. Chang* [Goyang-si, South Korea], H. Sung, M. Kim

A multi-centre evaluation of the US prevalence and regional variation in macrolide-resistant Streptococcus pneumoniae from blood or respiratory cultures among adult patients
V. Gupta* [Naperville, United States], K. Yu, J. Schranz, H. Jakinen-Guzon, S. Gelone

Collateral responses to fluorquinolone resistance in Streptococcus pneumoniae
A. Liakopoulos* [Leiden, Netherlands], M. Buffoni, D. Rozen

Emergence of penicillin non-susceptible Group B streptococci within the hypervirulent CC17 clone colonising pregnant women in Portugal: a genomic analysis
R. Mamede, J. Melo-Cristino, M. Ramirez* [Lisbon, Portugal], E. Ferreira Martins

Genetic diversity of invasive, non-invasive and colonising Group B Streptococcus isolates in Southern Brazil
O. May-Fuerschutter, E. Alves, A. Vilela, F. Barazetti, J. Palmeiro, M. Scheffler* [Florianopolis, Brazil], M. Bazzo

Antimicrobial susceptibility of Streptococcus dysgalactiae subspecies equisimilis isolates recovered from invasive infections in Portugal
A. Castro, J. Melo-Cristino, M. Ramirez, M. Pinho* [Lisbon, Portugal]

Non-lethal concentrations of ceftazidime and ceftazidime-avibactam select for multiple-resistant genotypes
C. Fröhlich* [Tromsø, Norway], J. Alves Gama, P. Johnsen, H. Leiros, O. Samuelsen

Dual therapy with aztreonam & ceftazidime/avibactam against multi-drug resistant Stenotrophomonas maltophilia on tricuspide valve endocarditis
J. Alexander* [Orlando, United States], A. Carr, S. Minor, D. Navas

Baseline resistance to ceftazidime-avibactam and aztreonam-avibactam in carbapenemase-producing Enterobacteriales from Argentina mediated by the co-expression of PER ESBL: role of imipenem-relebactam and aztreonam-relebactam as therapeutic alternatives
F. Pasteran* [Buenos Aires, Argentina], J. De Mendieta, M. Rappaport, S. Ramirez, D. Faccone, C. Lucera, P. Ceriana, A. Corso

Genomic and transcriptomic approach to unravel the resistance mechanisms to ceftazidime-avibactam in Pseudomonas aeruginosa and Enterobacter cloacae
A. Bösch* [St. Gallen, Switzerland], S. Schmitt, M. Held, J. Findlay, A. Egli, H. Seth-Smith, V. Hinic, V. Gisler, H. Fankhauser, M. Oberle, P. Kohler, S. Seiffert, N. Oliver, B. Babouee Flury

A novel KPC-3 variant associated with CAZ/AVI resistance in an Klebsiella pneumoniae ST512 causing bacteremia
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L. Papa, A. Negu?, I. Czabor* [Bucharest, Romania], I. Gheorghe, S. Mohsin, M. Mitache, M. Papa, L. Marutescu, M. Chifiriuc

8993 Carbapenem resistance mechanisms uncovered by nanopore sequencing in wastewater canalisations from Ghana

J. Delgado Blas* [Madrid, Spain], E. Marin Rodriguez, C. Valenzuela, C. Serna Bernaldo, N. Montera, C. Saba, B. Gonzalez-Zorn

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Water and surfaces as reservoir for resistance

532 Are residual waters vehicles of transmission of resistance mechanisms? DARWIN JPI AMR-2016 study

E. Torres Sangiao* [Santiago de Compostela, Spain], A. Diequez, E. Rabuñal-Rey, S. Balboa, M. Quintela-Bujan, R. De La Cruz Moreno, M. Paul, S. Sørensen, J. Kreft, D. Graham, A. Dechesne, B. Smets, J. Romalde, C. García-Riestra

5469 Pathogenic, antimicrobial-resistant Escherichia coli in low-income settings household soils: origins and genetic diversity

M. Montealegre* [Dübendorf, Switzerland], A. Talavera Rodriguez, S. Roy, M. Hossain, V. Fernandez Lanza, M. Islam, T. Julian

9034 Association of carbapenemase-producers in hospital effluents with carbapenemase-producer’s infection incidence and sewages heavy metals concentrations: results from the Canalis project

L. Romero-Orad* [Seville, Spain], J. Borrego-Jiménez, F. Galan-Sanchez, R. Tejera-García, M. Rojo Martín, M. Rodríguez-Mateos, A. Pérez-Pérez, V. Merino Bohórquez, L. Lopez-Cerero

9330 Clinical class 1 integrin patterns and relative antibiotic resistance gene carriage in urban compartments

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9452  KPC-producing and colistin-resistant Klebsiella pneumoniae ST258 persistence during wastewater treatment plant processes  
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690  Dissemination of a blaNDM-1-carrying IncA/C2 plasmid in a broiler flock: a possible real-life scenario
S. Hadziabic* [Berlin, Germany], J. Fischer, B. Malorny, I. Szabo

1541  One Health surveillance of extended-spectrum beta-lactamase-producing Enterobacteriales in urban and rural Malawi  
D. Cocker* [London, United Kingdom], A. Singer, T. Marse, C. Jewell, A. Roberts, N. Feasey

3202  Bacteriophage-controlling dominant sequence types of carbapenem-resistant Escherichia coli in Bangladesh  
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3623  Seawater: a risk for transmission of antimicrobial resistance?

4227  Colistin-resistant Enterobacteriaceae in Belgian broiler and pig farms  
S. De Koster* [Antwerp, Belgium], M. Ringenier, C. Lammens, M. Kluytmans - Van Den Bergh, J. Kluytmans, J. Dewulf, H. Goossens

4318  Quantification and characterisation of antibiotic resistance in greywater discharged to the environment  
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4319  Tracing of ESBL-producing and ciprofloxacin-resistant Escherichia coli in Belgian broiler and pig farms: a longitudinal study  
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5271  A One Health approach identifies the environment surrounding food animals as a potential reservoir of blaCTX-M genes in the community in Vietnam  
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8162  Persistence of antimicrobial resistance genes in treated sewage water intended for reuse  
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4551  Ongoing dissemination of OXA-244 carbapenemase-producing Escherichia coli in Switzerland  
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5299  Molecular diversity of carbapenem-resistant Enterobacteriaceae [CRE] in Singapore  
J. Teo* [Singapore, Singapore], C. Tang, S. Ong, S. Lee, S. Tan, Y. Cai, T. Lim, T. Tan, J. Sim, R. Ong, A. Kwa

7832  Unexpected genetic diversity among KPC-producing Klebsiella pneumoniae in France  
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7839  Ongoing dissemination of OXA-244 carbapenemase-producing Enterobacteriaceae over 5 years reveals transmission clusters of clones and plasmids and extensive diversity of bacterial species encoding carbapenemases  
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8137  Complex sharing of KPC-producing Klebsiella pneumoniae carbapenemase [KPC] plasmids in patients harbouring multiple KPC-positive organisms  
A. Mathers* [Charlottesville, United States], H. Parikh, D. Eyre, K. Barry, N. Stoesser, A. Sheppard, D. Crook, A. Walker

8137  Evolutionary dynamics of carbapenem resistance genes among different international clones of Acinetobacter baumannii: resistance and dissemination implications  
S. Vijayakumar* [Tamil Nadu, India], J. Jacob, K. Vasudevan, V. Balaji

8137  Colistin heteroresistance in carbapenemase-producing Acinetobacter baumannii  
D. Machado* [Lisbon, Portugal], S. Gothe, M. Martins, T. Pacheco, J. Batista, C. Toscano, M. Viveiros
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4. Diagnostic bacteriology & general microbiology

- Diagnostic bacteriology – culture based and general microbiology
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- Molecular diagnostics (incl POCT and syndromic testing)
- Molecular and genomic typing and surveillance
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- Clinical metagenomics
- Bioinformatics tools & pipelines
- Other
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<td>5852 Evaluation of an investigation-use-only prototype of the BIOFIRE FILMARRAY Blood Culture Identification 2 (BCID2) panel for detection of bacteria, yeast, and antimicrobial resistance markers from positive blood cultures A. Vasilakopoulou, A. Tarpatzi, S. Vourli, P. Tsilikis, Y. Lu, K. Holmberg, U. Spaulding, K. Koch, A. Alvanidi, N. Kourmasti, S. Pournaras* [Athens, Greece]</td>
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<td>6019 The effectiveness of two rapid identification technologies in Gram-negative bacteraemia without antimicrobial stewardship interventions L. Nguyen* [Loma Linda, United States], D. Chong, J. Vo, J. Lee, T. Ho</td>
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<td>6694 Prospective, non-interventional, multi-centre clinical study of the T2Resistance system for detection resistance genes in bacterial bloodstream infections: an interim analysis T. Walsh* [New York, United States], A. Mencacci, R. Paggi, E. Douka, C. Vrettou, D. Guzman, R. Smith, T. Lowery</td>
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<td>7031 Impact of the FilmArray Blood Culture Identification Panel (BCID) compared to VITEK-MS and the VITEK-2 ID/AST instrument in the diagnosis and management of bloodstream infections in a 24-hour laboratory setting R. Davidson* [Halifax, Canada], D. Holdane, J. Leblanc, I. Davis, Z. Hussain, G. Patrignin, H. Alsidiari, T. Hatches</td>
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<td>1544 Clinical factors associated with empirical antibiotics resistance in febrile patients with urinary tract calculus J. Lee, M. Park, S. Kwon, H. Choi, K. Kim* [Incheon, South Korea], S. Bae, G. Song</td>
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<td>1653 High diagnostic yield of splenic core biopsy in patients with pyrexia or inflammation of unknown origin: a descriptive analysis of imaging (including FDG-PET) and pathological findings at a major tertiary centre Y. Yim* [London, United Kingdom], G. Wallis, J. Saeed, S. Voo, I. Proctor, C. Mccamara, M. Brown</td>
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<td>1942 A selective culture medium for screening ceftriaxone/avibactam resistant Gram-negative isolates P. Nordmann* [Fribourg, Switzerland], M. Sadek, C. Tinguely, L. Pairel</td>
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<td>5277 Performance of the NTM Elite agar for the detection of non-tuberculous mycobacteria in sputum samples of patients with cystic fibrosis E. Andre* [Leuven, Belgium], L. Raymaekers, S. Dewick, J. Gafsi, P. Van Bleyenbergh, L. Dupont, B. Kahl, N. Lorent</td>
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7586 Efficient inactivation of clinically relevant antimicrobial drug concentrations by two resin-containing media in simulated paediatric blood cultures

7686 Fever of unknown origin: a prospective observational study from a tertiary university hospital
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8577 Chorioamnionitis: time for changes in management?
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9445 Culture-dependent analysis of the bacterial profile of breast milk samples from women with diagnosis of subacute lactational mastitis
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3106 Artificial intelligence and automation of microbiology: the urinalysis 3.0

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8769 The impact of rapid identification of blood culture pathogens by MALDI-TOF MS and their direct antibiotic susceptibilities on antimicrobial stewardship at a large district general hospital, United Kingdom
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7756 What clinicians and researchers should know about machine learning for infection management: review of methods, targeted outcomes and reporting of future technologies
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7801 Impact of unique blood culture sampling in the emergency departments of Strasbourg University Hospital, France
P. Boyer* (Strasbourg, France), A. Chabaud, P. Bilbault, D. Menahem, E. Fonti, V. De Peyrecave, T. Lavigne, B. Jaulhac

7926 Dipstick urinalysis: an alternative screening test for urine cultures to rule out negatives?
F. Daganci, M. Karaoglan, B. Erdir, S. Aslan, O. Ozel, A. Ilki* (Istanbul, Turkey)

8976 Time to positivity of blood cultures and its role in the diagnosis of bacteraemia
A. Aguirre Quinonera* (Vitoria, Spain), M. Marroyo-Salazar, E. Saez De Adana Arroz, A. Canut

9276 Impact of artificial intelligence on time to result in culture-based MRSA screening
A. Nowag, N. Jozmati, S. Giglia, S. Wirth, B. Pohl, X. Quante, H. Wisplinghoff* (Cologne, Germany)

9329 Accuracy of sepsityper methodology for identifying microorganisms directly from positive blood culture bottles using MALDI-TOF MS
R. Gorton* (London, United Kingdom), R. White, C. Baker, R. Smith

9342 Sepsis diagnosis: have we solved the riddle yet?
A. Rohit* (Chennai, India), A. Danangi, M. Prasad, A. Jenifer, S. Dorairajan, C. Boahen, V. Kumar

Session accepted as Mini-oral ePoster Session

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Abstract Categories 2020

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Gastrointestinal infections and molecular diagnosis

866 Application of a multiplex polymerase chain reaction test for diagnosing bacterial enteritis in children in a real-life clinical setting
E. Lee* [Seoul, South Korea], H. Lee, S. Han

947 Should a molecular bacterial syndromic approach totally replace culture for the diagnosis of gastrointestinal tract infections?
A. Boudet* [Nimes, France], R. Stephan, A. Pantel, M. Carles, C. Enault, S. Charachon, J. Lavigne, H. Marchand

1519 Evaluation of the Oiastat-Dx Gastro-intestinal Panel at the University Hospital of Liege (Belgium)
J. Schmitt, C. Diop* [Liege, Belgium], L. Schoneveld, C. Meex, P. Melin, M. Hayette

1583 Evaluation of the filmarray GI panel in the microbiological diagnosis and management of the patient with infectious gastroenteritis
J. Parra Martínez, R. Carranza González* [Albacete, Spain], M. Castano Aroco, V. Salves Ferriz, F. Ferrer Amate, C. Sáinz De Baranda Camino

1801 Impact of ribotype on Clostridioides difficile diagnostics
K. Rizzardi* [Solna, Sweden], T. Åkerlund, T. Norén, A. Matussek

2685 Evaluation of the Novodiag Bacterial GE+ kit for the diagnosis of intestinal bacterial infections
C. Roy, D. Robert, D. Baraud, A. Buissounniere, L. Benejat, A. Ducournau, F. Megraud, E. Bessède, P. Lehours* [Bordeaux, France]

2736 Diagnostic utility of stool polymerase chain reaction in enteric fever: experience from a high-incidence London hospital
D. Hsu* [London, United Kingdom], S. Tiberi, R. Buchanan, C. Rosmarin

3084 Development of a biosensor for the detection of Campylobacter jejuni
S. Shams* [Qom, Iran], B. Bakhshi, T. Tahidi Moghodam

4406 Improved diagnostic of acute gastrointestinal disease by a multiplex real-time PCR semi-automated method for the detection of enteropathogens

6094 Evaluation of a Point-of-Care molecular system for rapid detection of toxigenic Clostridioides difficile in paediatric patients: impact on diagnostic yield and time to result

7755 Prospective evaluation of three rapid multiplex PCR assays for the detection of gastrointestinal pathogens from stool samples

7793 Evaluation of Novodiag C. difficile and GenePOC CDiff test for quick and accurate detection of Clostridioides difficile infection
A. Petersson* [Lund, Sweden], L. Rebihic, S. Karlsson Sobirk

7991 Performances of BD MAX Cdiff assay for detection of toxigenic Clostridioides difficile in 1321 clinical stool specimens using FecalSwab
A. Ranc* [Lyon, France], D. Dauwalder, S. Celia, A. Tristant, B. Coralie, K. Santos, F. Sonia, P. Duraffourg, F. Vandenekens, F. Laurent

8443 Laboratory evaluation of a cartridge-based multiplex PCR assay for the detection of gastrointestinal pathogens
C. Holmes, P. Bird* [Leicester, United Kingdom]

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Genomic epidemiology: from local to global

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4406 Improved diagnostic of acute gastrointestinal disease by a multiplex real-time PCR semi-automated method for the detection of enteropathogens

5096 Improved diagnostic of acute gastrointestinal disease by a multiplex real-time PCR semi-automated method for the detection of enteropathogens

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6585 The distribution, transmission and adaptation of Klebsiella species in multiple clinical and non-clinical settings

7168 Bordetella pertussis in the Netherlands, 2015-2019: a sharp increase in prn-deficient isolates
R. Mariman* [Leiderdorp, Netherlands], C. Schot, J. Groot, F. Reubsaet, R. Noomen, T. Bosch

7168 Bordetella pertussis in the Netherlands, 2015-2019: a sharp increase in prn-deficient isolates
R. Mariman* [Leiderdorp, Netherlands], C. Schot, J. Groot, F. Reubsaet, R. Noomen, T. Bosch

7168 Genomic analysis of Group B streptococci colonising pregnant women in Portugal reveals the emergence of novel genetic lineages resulting from capsular switching
E. Ferreira Martins, R. Pedrosa, J. Melo-Cristino, M. Ramirez* [Lisbon, Portugal]
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7623  The role of mobile genetic elements and virulence factors in the typing of vancomycin-resistant *Enterococcus faecium* outbreak isolates of a successful MLST ST117 cluster type 24


7865  Understanding the *Corynebacterium diphtheriae* population through whole genome sequencing

N. Groves* [London, United Kingdom], M. Chand, D. Litt, S. Rose, C. Gower, A. Enefer, G. Amirthalingam, N. Fry

8122  Phylogenetic and taxonomic approaches to elucidate the *Citrobacter* genus

T. Goncalves Ribeiro* [Porta, Portugal], C. Rodrigues, L. Peixe

8981  A genomic snapshot of antimicrobial resistance in *Campylobacter fetus*

B. Duim* [Utrecht, Netherlands], A. Zomer, T. Looft, A. Timmerman, J. Wagenaar, L. Van Der Graaf-Van Bloois

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Improvements in diagnosis

1184  Does *C. Diff Quik Chek* display the same sensitivity than *C Diff Quik Chek Complete* for GDH detection?

C. Gateau* [Paris, France], R. Syed-Zaidi, A. Youssouf, V. Lalande, J. Couturier, F. Barbut

1459  Two novel fastidious anaerobes from the genus *Bacteroides* isolated from chicken gastrointestinal tracts

S. Králova* [Brno, Czech Republic], L. Davidova Gerzova, M. Medvecky, I. Rychlik, M. Cigánek, A. Cizek

1798  Serodiagnosis of Lyme borreliosis: is IgM in serum more harmful than helpful?

H. Hillerdal, A. Henningsson* [Jönköping, Sweden]

1952  A comparative prospective study for the qualitative detection of *Helicobacter pylori* specific antigens in stool samples at Sheffield Teaching Hospitals Foundation Trust, England

S. Coleman* [Sheffield, United Kingdom], S. Davies, H. Carr

Discordant *Clostridioides difficile* diagnostic assay and treatment practice: a retrospective observational study

L. Lenggenhager* [Geneva, Switzerland], M. Zanella, A. Ponce, L. Kaiser, J. Schrenzel

Staphylococcus lugdunensis: coloniser or pathogen: outlining the clinical importance: a study of 295 clinical samples from hospital patients received for culture at the department of Medical Microbiology, SI Lillehammer, Norway, from November 2016 to November 2019

S. Hartzen* [Lillehammer, Norway], C. Dahlseide, A. Hartzen

Campylobacter concisus prevalence in microscopic colitis: a cultivation study

M. Agaard* [Aalborg, Denmark], K. Kirk, H. Nielsen, I. Targgaard, J. Hansen, H. Nielsen

The importance of CXCL13 cytokine as a biomarker in the molecular diagnosis of Lyme neuroborreliosis versus multiple sclerosis

T. Carreira* [Lisboa, Portugal], F. Geraldo Dias, A. Armada, M. Vieira

Early syphilis infection: a clinical case

M. Bozhilova, D. Velcheva* [Sofia, Bulgaria]

Diagnosing disseminated histoplasmosis in an AIDS patient: the role of bone marrow evaluation

N. Mussá* [Lisbon, Portugal], D. Carvalho, S. Ismail, A. Jääskeläinen* [Helsinki, Finland], S. Salmenlinna, J. Antikainen, A. Pätäri-Sampo

Stool multiplex PCR for *Shiga* toxin-producing *Escherichia coli* sufficiently equals with culture for clinical diagnosis and follow-up

A. Jääskeläinen* [Helsinki, Finland], S. Salmenlinna, J. Antikainen, A. Pätäri-Sampo

Faster and more sensitive diagnostics of *Shigella* by *Shigella* specific PCR and improved culture

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7605  Group B Streptococcus vaginal colonisation from antenatal screening to 2 months after delivery: results from a prospective cohort study in France

8660  Antibiotic resistance in anaerobic infections in a hospital in Tenerife
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9614  Prevalence and susceptibility profile of Corynebacterium glucuronolyticum in semen cultures
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1678  Decreasing reporting time of blood cultures by workflow optimisation with the WASPLab system

5002  How to accelerate bacteria identification from positive blood culture in a routine microbiology laboratory with the aid of MALDI-TOF MS: a simple and rapid in-house protocol
P. Barth* [Porto Alegre, Brazil], Á. Celestino De Souza, L. Lutz, E. Wurdig Roesch, V. Aquino, D. Castro Pereira

5204  Time-to-result quantification for different blood culturing workflows in an external microbiology laboratory setting
J. Fonville* [Veldhoven, Netherlands], M. Van Den Broek, A. Jansz, T. Liebregts

6854  Identification of microorganisms direct from signal positive blood culture using Acrion system
J. Sako* [Vantaa, Finland], S. Gurung, O. Niiranen, N. Chant, M. Wilks

7161  Light scatter AST for positive blood cultures, how impactful on antimicrobial therapy management of septic patient?
A. Curtoni* [Torino, Italy], D. Ghiauda, L. Imperatore, C. Veglia, G. Bianco, S. Corcione, S. Scabini, C. Costa, L. Scaglione, F. De Rosa, R. Cavalla

7261  Prospective evaluation of BinaxNOW for rapid identification of Streptococcus pneumoniae from positive blood culture bottles
K. Žnidar* [Ljubljana, Slovenia], D. Tratnik, M. Pirs, M. Mueller-Premru

7357  Speeding up identification and antimicrobial susceptibility testing of bacteria from positive blood cultures by the use of Alifax HBBL system
Y. Wang* [Beijing, China], Y. Dai, D. Li, H. Sun, Y. Zhao, Y. Xu

9244  Easy technique for ultra-fast identification of positive blood cultures with MALDI-TOF MS
F. Bressant, M. Messy, H. Rodriguez-Villalobos, A. Verraken* [Brussels, Belgium]

9520  Rapid identification of bacteria directly from positive blood cultures by a modified method using a Serum Separator Tube (SST) and MALDI-TOF MS
G. Carretero, G. Rivas, C. Loras, M. Orellana Miguel* [Madrid, Spain]

Session accepted as Mini-oral ePoster Session
Innovative approaches for faster ID/AST from positive blood cultures

179  A rapid direct from specimen MALDI-TOF MS diagnostic for bacterial and fungal pathogens
D. Goodlett* [Baltimore, United States], M. Sorensen, F. Gardner, L. Leung, C. Chandler, E. Nilsson, R. Ernst

929  Pilot evaluation of machine learning for the classification of Streptococcus pneumoniae PCV-13 serotypes from non-PCV13 serotypes based on MALDI-TOF MS analysis
J. Zintgraff* [Caba, Argentina], M. Rocca, D. Napoli, M. Moscoloni, G. Ayala, C. Lara

1891  Typing of emm1 Group A streptococci using MALDI-TOF MS
M. Sakuma, K. Shima* [Kyoto, Japan], S. Funatsu, K. Ogata, M. Morozumi, S. Iwata

1980  Rapid identification of uropathogens by combining Alfred 60 system with matrix-assisted laser desorption ionisation-time of flight mass spectrometry technology
K. Athamna* [Hadera, Israel], A. Zbriger, M. Shapira, Y. Tal, S. Freimann

2459  Comparison of two commercial platforms for identification of bacteria and Candida isolates at species-level by MALDI-TOF MS in Shenzhen, China
W. Lau* [Shenzhen, China], J. Chan, S. Lo, L. Yan, Y. Ting, L. Caijuan, L. Huijuan, K. Yuen

2746  A Peptoniphilus species nova closest to P. harei from human clinical materials but which was misidentified by Bruker Biotyper as P. indolificus
K. Bernard, D. Wiebe, A. Velboa* [Groningen, Netherlands], A. Ebbing

3117  Identification of clinical isolates of Tannerella forsythia by MALDI-TOF mass spectrometry
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3477  Differentiation of the members of the Staphylococcus aureus complex by MALDI-TOF using the VITEK MS platform
B. Celliere* [La Balme les Grottes, France], V. Collin, C. Meunier, D. Giraud, V. Monnin, V. Girard, F. Javerliat

4880  Achromobacter identification using nr4A gene phylogeny and MALDI-TOF MS
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<td>M. Santarossa* [Maywood, United States], R. Ukani, K. Wolding, A. Harrington, N. Clark, G. Reid</td>
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<td>L. Castain* [Nantes, France], G. Gricourt, D. Vanessa, A. Rodallec, C. Bressollette-Bodin, B. Imbert-Marcille, C. Rodriguez</td>
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**Abstract Categories 2020**

**6682** Pan-pathogen microbiological diagnosis by accredited routine clinical metagenomics: one-year experience

P. Woerther* [Créteil, France], R. Lepeule, D. Vanessa, G. Gricourt, C. Lamoureux, V. Fihman, S. Faurati, F. Botterel, C. Angebault, J. Pawlotsky, C. Rodriguez

**6850** Rescue diagnosis of a cerebral nocardiosis by accredited clinical metagenomics: a case report

V. Courbin, D. Riller, G. Gricourt, D. Vanessa, R. Lepeule, J. Pawlotsky, C. Rodriguez, P. Woerther* [Créteil, France]

**7238** Comparative analysis of kitleme identification methods in viral metagenomic data


**7886** Clinical metagenomics next-generation sequencing for diagnosis of suspected clinical infections, a prospective multi-centre cohort study

J. Ai* [Shanghai, China], H. Zhang, Y. Zhang, J. Ma, W. Zhang

**8055** Next-generation sequencing for kinetics of the respiratory microbiota of intensive care unit intubated patients

S. Meyer* [Limoges, France], T. Daix, B. Francois, D. Chaine, A. Gay, M. Ploy, P. Vignon, D. Barnaud

**8070** The rapid clinical diagnosis of lower respiratory infection by an unbiased real-time metagenomics methods in validated intensive care unit patients

H. Zhang* [Shanghai, China], J. Ai, O. Zhang, W. Zhang

**8863** Rapid, non-invasive detection of Legionella and resolution of species diversity in clinical infections using the Karius test, a microbial cell-free DNA sequencing test for pathogen detection

A. Ahmed* [Redwood City, United States], S. Dalai, D. Hong, L. Blair, M. Lindner, D. Hollemon, S. Bercovici, T. Blauwkamp, M. Kertesz, A. Macintyre

**9069** Direct sequencing from clinical samples in the diagnostic microbiology laboratory without capital expenditure or specialised bioinformatic training is possible using nanopore technology

A. Alcolea Medina* [London, United Kingdom], C. Niehaghartaigh, J. Lambourne, R. Sorajna-Wani, M. Wilks

**9251** Long-read sequencing for the diagnosis and characterisation of pathogens in severe pneumonia: the role of simulation and standards in clinical metagenomics pipeline development

M. Chand* [London, United Kingdom], N. Groves, G. Amos, V. Chalker

**9458** Application of a user-friendly, end-to-end metagenomics platform for rapid pathogen identification in children with osteoarticular infections

R. Stinnett, N. Ramchandar, H. Xie, S. Flygare, T. Schwarz, K. Broadbent, A. Davis, L. Farnaes, R. Schlaberg* [Salt Lake City, United States]

**9503** Application of a comprehensive, user-friendly metagenomic sequencing platform for rapid pathogen identification in a paediatric population with meningitis and encephalitis

R. Stinnett, N. Ramchandar, K. Broadbent, T. Schwarz, S. Flygare, H. Xie, J. Foley, A. Davis, L. Farnaes, R. Schlaberg* [Salt Lake City, United States]

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**Microbiome and human disease: from top to bottom**

**595** Longitudinal analysis of lung microbiota in intensive care unit patients undergoing mechanical ventilation


**1744** Characterisation of the microbial community in patients with pharyngeal gonorrhoea infection

C. Foschi* [Bologna, Italy], C. Ceccarani, T. Camboni, C. Consolandi, M. Salvo, V. Gaspari, A. D’Antuono, M. Belletti, M. Re, M. Severgnini, A. Marangoni

**3552** The role of the eye microbiome in health and disease states of the lacrimal system

Y. Yagel* [Beer Sheva, Israel], Y. Matro, T. Kornhauser, S. Kardulak, S. Green, J. Morán-Gilad, E. Tsumi

**3553** Intestinal microbiome in critical care patients: association with patient status and outcome


**4102** Diversity of the gut microbiome before haematopoietic cell transplantation is an independent predictor of respiratory failure and sepsis requiring intensive care in the post-transplant period

F. Adhi* [Cleveland Heights, United States], E. Littmann, E. Pamer, J. Peled

**6133** Diagnosis of invasive pneumococcal disease in children by using a classification method based on nasopharyngeal microbiota signatures


**6309** Role of the gut microbiota in the anastomotic leakage after colorectal surgery

P. Herráez-Pérez* [Madrid, Spain], M. Ponce-Alonso, J. Barquin, A. Camino-Lizarraide, E. Conde, B. Romero, J. Garcia-Pérez, R. Del Campo

**6359** Evolution of cutaneous bacterial microbiota of pressure ulcers in patients with spinal cord injury

C. Dungyach-Remy* [Nimes, France], A. Géli, S. Bastide, A. Yahiaoui-Martinez, J. Lavigne, A. Sotto

**6590** Individuals at risk of developing rheumatoid arthritis possess a unique microbiome

C. Rooney* [Leeds, United Kingdom], S. Mitra, K. Mankia, I. Moura, P. Emery, M. Wilcox
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**Session accepted as Paper Poster Session**

**Microbiome impact in health and disease**

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**32** Metatranscriptomic analysis reveals active bacterial communities in diabetic foot infections

F. Sadeghpour Heravi* [Sydney, Australia], M. Zakrzewski, K. Vickery, H. Hu

**4479** Determining the lung microbiome of chronic obstructive pulmonary disease patients from hospitals in Pretoria, South Africa using IS-Pro method and 16S rDNA sequencing

I. Goolam Mahomed* [Pretoria, South Africa], R. Peters, G. Pretorius, A. Goolam Mahomed, V. Ueckermann, A. Stoltz, M. Kock, M. Ehlers

**228** Gut microbiome interferes with host tryptophan metabolism pathway and regulates basal anxiety-like behaviour

J. Shaﬁq* [Karachi, Pakistan], B. Khan, G. Abbas, A. Ahmed

**4629** Surface ocular microbiome in dry eye syndrome: a preliminary study

C. Foschi, P. Versura, C. Consolandi, M. Sevrignini, M. Re, A. Marangoni* [Bologna, Italy]

**810** A new perspective: microbiota, the role of Streptococcus galactilyticus in childhood colorectal cancer

A. Büyükcam* [Ankara, Turkey], C. Akyüz, N. Gursoy, D. Orhan, B. Otu, B. Sancak, A. Kara

**5440** Differences in the lower respiratory tract microbiota in patients with severe pneumonia of viral or bacterial origin

J. Marimon Ortiz De Zarate* [Donostia-San Sebastian, Spain], A. Perez-Gavilán, M. Ercibengoa, N. Azcue, M. Alonso, L. Vidaur

**1471** Relationship between intestinal microbiota and infantile colic

C. Haddad, T. Itani* [Beirut, Lebanon], A. Moukarzel, D. Karam Sarkis

**5575** A multi-omics approach to understanding the aetiology of Q fever fatigue syndrome

R. Ruijmakers* [Nijmegen, Netherlands], M. Roerink, A. Jansen, S. Keijmel, R. Gacesa, Y. Li, L. Joosten, J. Van Der Meer, M. Netea, C. Bleeker-Rovers, C. Xu

**2371** Assessment of quantitative composition of Bacteroides fragilis in children with coeliac disease at the time of diagnosis and after a six-month period of diet

A. Krawczyk* [Krakow, Poland], D. Salamon, K. Kowalska-Duplaga, Z. Grzenda-Adamek, A. Kozioł-Kozakowska, K. Fyderek, T. Gosiewski

**6236** Characterisation of vaginal microbiota in pregnant women with preterm prelabor rupture of the foetal membranes

A. Vergara* [Barcelona, Spain], T. Cobo, E. Rubio Garcia, J. Bosch, J. Vila Estape, C. Casals-Pascual

**2221** Microbiome analysis of samples from patients with idiopathic pulmonary fibrosis in the A Coruña University Hospital, Spain: a pilot study

K. Conde* [A Coruña, Spain], J. Vallejo, L. Alvarez-Fraga, S. Rumbo-Feal, B. Rodiño-Janeiro, G. Bou Arevalo, C. Montero Martínez, I. Vidal Garcia, M. Poza Dominguez

**6544** Differences in nasopharyngeal microbiota composition according to the severity of human rhinovirus infection in the first 1000 days of life


**6790** Long-term effect of dietary preferences and nutritional regimes on intestinal microbiota diversity and composition

M. Hora, A. Gundagdu* [Kayseri, Turkey]

**3498** The female reproductive tract microbiome and its relationship with infertility and hydrosalphinx

Y. Yagel* [Beer Sheva, Israel], A. Weintraub, E. Pardo, S. Green, Y. Motro, J. Moran-Gilad

**6794** Chemotherapies for acute lymphoblastic leukaemia may have a long-term impact on bacterial gut microbiota

M. Payen* [Paris, France], A. Cointe, A. Pascault, G. Mahemed, M. Fadh, S. Delannoy, P. Fach, A. Baruchel, A. Monjault, S. Bonacorsi, A. Birgy

**4187** Vaginal microbiota in Japanese women undergoing infertility treatment

A. Matsumoto* [Saitama, Japan], Y. Yamagishi, S. Takahashi, Y. Kuroki, A. Minemura, K. Oka, M. Takahashi, H. Mikamo

**6839** Akkermansia muciniphila in multiple sclerosis


**4451** Microbiota as a marker of mucoid Pseudomonas aeruginosa and Haemophilus influenzae in non-cystic fibrosis bronchiectasis

R. López, L. Fernandez Barat* [Madrid, Spain], N. Vazquez, V. Alcaraz, L. Bueno, R. Cabrera, G. Sciascia, P. Oscañoa, R. Amara, A. Torres

**7021** Interplay between genetic disorders and gut microbial community: Rubinstein-Taybi syndrome as a model

G. Bassanini, E. Di Fede, E. Colombo, C. Ceccarini, E. Ottaviano, V. Masso, C. Gervasini, E. Borghi* [Milan, Italy]
7370 Gut microbiota of full-term and late preterm newborns in Moscow
P. Totiana, E. Isaeva, V. Muravev, A. Gardeev* (Moscow, Russian Federation), A. Melkumyan, L. Lyubasovskaya, M. Mesyan, L. Timofeeva, V. Zubkov, E. Sukhikh

7582 Faecal microbiota in Romanian ankylosing spondylitis patients
M. Oprea* (Bucharest, Romania), D. Cristea, D. Predateanu, V. Bojinca, M. Trandafir, S. Dinu, S. Ciontea, C. Usein

7893 Studying the association of the human vaginal microbiome with HPV infection using enriched metagenomic sequencing
A. Latszuzbioa* (Dudelange, Luxembourg), A. Wienecke-Baldacchino, M. Herald, I. Karabegovic, J. Topp, M. Fischer, F. Mühlischlegel, J. Massong

8400 Dynamic study of microbial interactions in the skin microbiota of patients with epidermal necrolysis (DynaMiCut)

8758 Dystbiosis in a triplet with an autism spectrum disorder: a case study
S. Hazan* (Ventura, United States), J. Daniels, A. Popoutsis

8760 Correlation between vaginal microbiota diversity and human papilloma virus induced cervical carcinogenesis in population of Santander, Colombia
L. Torrado Garcia* (Bucaramanga, Colombia), B. Rincon-Martínez, A. Vergara, J. Martínez

8830 Preliminary analysis of a pilot study using a new oral encapsulated formulation of faecal microbiota
V. Rico Caballero* (Barcelona, Spain), A. Aire, E. Rubio Garcia, C. Casals-Pascual, A. Vergara, J. Martínez Martínez, A. Soriano

999 Modulation of the microbiota by oral intake of a synbiotic mixture in healthy volunteers: a single-centre one-armed pilot study
I. Rubin* (Frederiksborg, Denmark), S. Mollerup, M. Pinholt, M. Pedersen, T. Kollemose, H. Westh, A. Petersen

1730 Effects of penicillin V on the intestinal microbiota in patients with pharyngo-tonsilitis
P. Edquist* (Stockholm, Sweden), K. Rystedt, C. Giske, K. Hedin, S. Mölstad, M. Ringman, G. Skaag Ståhlgren, P. Sundvall, C. Edlund

3435 Using metagenomics to study the impact of hospital stay on the human gut resistome
M. Yokoyama* (Brighton, United Kingdom), L. Peto, A. Walker, M. Llewelyn

3809 Long-term exposure to ceftriaxone sodium induces alteration of gut microbiota accompanied by anxiety-like and depression-like behaviours in mice
Z. Zhao* (Chengdu, China), L. Zhou, C. Tao

4298 Effects of spectrum of antibiotics on microbiome compositions and resistome levels
K. Nielsen* (Copenhagen, Denmark), M. Olsen, A. Palleja, S. Ebdurp, N. Sørensen, O. Lukjancenko, R. Marvig, K. Møller, N. Frimodt-Moller, F. B. Hertz

4942 Bacterial consortium: the evolution of the Faecal Microbiota Transplantation (FMT)
G. Quaranta* (Rome, Italy), G. Fancelli, R. Graffea, G. Ianiri, G. Cammarota, M. Sanguinetti, L. Masucci

4998 Donor selection in the Belgian Ghent Stool Bank: a relief to help
H. Hamerlinck* (Ghent, Belgium), J. Vandevoije, E. Naessens, S. Vandenbossche, L. Coevert, J. Boelens, B. Verhasselt

5420 Early microbiome changes associated with the novel, targeted-spectrum antibiotic ACX-362E compared to oral vancomycin

5805 Disease prevention not decolonisation: a cohort study for faecal microbiota transplantation for patients colonised with multidrug-resistant organisms

5833 Impact of different antimicrobial exposures on the gut microbiome and resistome characterised by metagenomic sequencing
L. Peto* (Oxford, United Kingdom), N. Fawcett, T. Peto, D. Crook, M. Llewelyn, A. Walker

6174 Change of gut microbiome and resistome of the patients with Clostridioides difficile infection and those with chronic obstructive pulmonary diseases compared with healthy population
J. Kim* (Guri, South Korea), M. Sea, M. Bae, B. Kim, M. Rho, H. Pai

6210 Gut microbiota of healthy volunteers with or without stool carriage of Klebsiella pneumoniae in an area with invasive Klebsiella pneumoniae syndrome
Y. Huang* (New Taipei, Taiwan), C. Liao

6230 Characterisation of the human gut microbiome in a high antibiotic use and resistance setting in Vietnam
Gut microbiome characterisation in irritable bowel syndrome patients following faecal microbiota transplant: a case report study
M. Surleac, S. Paraschiv* (Bucharest, Romania), C. Apostolescu, D. Otelea

Recruiting donors for faecal microbiota transfer: a one year experience
A. Airo* (Barcelona, Spain), V. Rico Caballero, E. Rubia Garcia, C. Cosals-Pascual, A. Soriano

Ceftriaxone and cefotaxime have similar impact in emergence of resistance in gut microbiota from hospitalised patients
P. Benoit* (Paris, France), O. Jiang, A. Mizrahi, J. Zahar, A. Le Monnier

Bacteroides as a next-generation of probiotics in neonatology
L. Lyubasovskaya, P. Tatiana, V. Muravieva, E. Isaeva, D. Serdyukova, A. Gordeev, N. Shabanova* (Moscow, Russian Federation), G. Sukhikh

Is periodic screening of donor faeces with temporary quarantine storage effective in preventing transmission of multidrug-resistant organism during faecal microbiota transplantation?

What constitutes a healthy faecal microbiome?
S. Mitra, A. Buckley, I. Moura, D. Ewin, W. Spittal, E. Clark, K. Bentley, J. Freeman* [Leeds, United Kingdom], M. Wilcox

Impact of selective digestive and oropharyngeal decontamination on the gut microbiome and resistome in intensive care patients
B. Xavier* [Antwerp, Belgium], S. Patz, N. Plantinga, B. Wittekamp, C. Lammens, D. Huson, M. Bonten, K. Singkhamanan, A. Chukamnerd, K. Silpapojakul

Continuous infusion versus intermittent antipseudomonal β-lactam antibiotics for acute pulmonary exacerbations of cystic fibrosis: effect on the respiratory microbiome
K. Langan* [Kensington, Australia], J. Choa, G. Rogers, D. Keating, R. Stirling, J. Wilson, A. Cheng, C. Chang, T. Kotsimbos, A. Peleg

Longitudinal microbiome analysis defines expected and aberrant antibiotic effects on the human respiratory microbiome
E. Clarke, E. Lautenbach, E. Reesey, M. Wernovsky, P. Tolameo, B. Kelly* [Philadelphia, United States]
5025 Epidemiological typing of Neisseria gonorrhoeae with whole genome sequencing: a vital supplement in transmission surveillance
K. Hajj Bhattarai* [Stockholm, Sweden], E. Ericsson, F. Dyrkell, D. Arnellois, G. Bratt, M. Ullberg, N. Bjärkström, H. Fang

5082 Evaluation of meningococcal B vaccine antigen variants in Neisseria meningitidis: Italy 2012-2018
P’Vacca* [Rome, Italy], L. Ambrosio, C. Fazio, A. Neri, A. Palmieri, A. Coranante, P’Stefanelli

5303 European Centre for Disease Prevention and Control system for cluster detection and interactive exploration of WGS data
E. Alm* [Stockholm, Sweden]

6000 Metagenomic sequencing to identify environmental reservoirs of carbapenem-resistant Acinetobacter baumannii associated with clinical outbreaks
B. Forde* [Brisbane, Australia], L. Roberts, P’Harris, A. Jennison, K. Hajkowicz, T. Hurst, M. Doidge, S. Beatson, D. Paterson

6250 Molecular epidemiology of leptospirosis in Tahiti, French Polynesia, during the 13-year-time spanning from 2007 to 2019
H. Angermeier* [Paris, France], L. Grillová, S. Lastere, M. Levy, M. Picardeau

6834 Phylogenetic and resistome analysis of human and animal Acinetobacter baumannii ST25 isolates
A. Lupo* [Lyon, France], B. Valiot, E. Saros, M. Bour, E. Hirchaud, M. Haenni, P’Plésiat, J. Madec, A. Potron

7177 Genomic surveillance of Bordetella pertussis in Austria
A. Cabol Rosel* [Vienna, Austria], D. Schmid, O. Soetens, S. Denayer, D. Pierard* [Brussels, Belgium]

7799 Prevalence, antimicrobial susceptibility and molecular typing of Legionella pneumophila in hot water systems in Morocco
A. Assaïdi* [Beni Mellal, Morocco], M. Elouadi, H. Latrache, H. Zohir, C. Ginevra, S. Jarraud, M. Mliji

7838 Multi locus sequence typing of Treponema pallidum subspecies pallidum in Barcelona
C. Fernández Naval* [Barcelona, Spain], M. Aranda, M. Espasa, A. Anton, M. Fernández-Huerta, J. González-López, J. Serra Pladevall, T. Pumarola-Suñé, M. Vall, J. Espejarla

7858 Macrolide-resistant Mycoplasma pneumoniae detection
S. Leung* [Hong Kong, Hong Kong]

9062 National survey of Neisseria gonorrhoeae isolates by whole genome sequencing in France in 2018

Session accepted as Paper Poster Session

Molecular and genomic typing of Gram-negatives

1598 Routine use of whole genome sequencing for Salmonella Enteritidis surveillance in the Netherlands in 2019
M. Van Den Beld* [Bilthoven, Netherlands], R. Pijnacker, A. Verbruggen, K. Van Der Zwaluw, S. Kuiling, E. Franz

3377 Distribution of capsular types among multi-resistant Klebsiella pneumoana isolates in the south of Spain by using a whole genome sequence-based solution

3781 Escherichia coli ST457: an emerging pathogen with wildlife and food-producing animals’ reservoirs
K. Nesperova* [Brno, Czech Republic], E. Wyrsch, I. Jamborova, A. Valček, I. Literak, S. Djordjevic, M. Dalejska

3952 Developing a pragmatic framework for genomics-informed surveillance of endemic Salmonella Typhimurium in Australia
P Andersson, W. Pritchers, D. Hennessy, M. Valcanis, J. Gregory, Z. Cutcher, M. Easton, B. Howden* [Parkville, Australia], D. Williamson

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6414 Continuous genomic surveillance of the third generation cephalosporin-resistant *Enterobacteriaceae* circulating in intensive care units of a 1600 bed university hospital, France F. Gravey* [Caen, France], M. Fines-Guyon, C. Isnard, F. Ethuin, D. Samba, D. Du Cheyron, C. Daubin, A. Mouet, C. Lesteven, O. Jain-Lambert, M. Auzou, F. Guérin, S. Le Hello

7314 Molecular characterisation of 15 strains of OXA-181-producing *Klebsiella pneumoniae* in Spain N. Romani Radés* [Badalona, Spain], A. Moreno-Mingorance, M. Ouesada, N. Larrosa, M. Gimenez, J. González-López

7423 Unexpected genomic variability among *Enterobacteriaces* causing bloodstream infections in European neonates and infants less than 90 days L. Folgori* [Milan, Italy], A. Piazza, F. Comandatore, A. Witney, Y. Hsia, N. Russell, K. Loing, I. Monahan, M. Perini, G. Zuccotti, T. Planche, P. Heath, M. Sharland


8701 Molecular epidemiology of carbapenem-resistant *Klebsiella pneumoniae* isolates in France 2018 M. Budia* [Le Kremlin-Bicêtre, France], R. Bannin, L. Dortet, T. Noas

517 Prevalence and serotype distribution of *Streptococcus agalactiae* colonisation among pregnant women in Taiwan C. Yu-Fen* [Changhua, Taiwan], F. Yu-Ping, C. Lee

723 Typing of MRSA isolates from bloodstream infections in the Dutch-German border region and Berlin N. Couto* [Groningen, Netherlands], E. Raangs, J. Rossen, J. Hellkamp, J. Elias, R. Köck, A. Friedrich


1336 Emergence of a mupirocin-resistant, methicillin-susceptible *Staphylococcus aureus* clone associated with skin and soft tissue infections in Greece N. Giormezis* [Patras, Greece], A. Doudouloakakis, K. Tsilipoudiakidou, M. Mitsipoulou, G. Kalogeras, V. Stamoulis, F. Klonitsiou, E. Petinaki, E. Lebessi, I. Spiliopoulou

1363 Genetic structure and treatment for *Listeria monocytogenes* infections W. Yu* [Hangzhou, China], Y. Huang, L. Guo, J. Zhang, Y. Zhan, L. Zhang, Y. Qiu


Molecular epidemiological survey of *Staphylococcus lugdunensis* isolates with different copies of the repeat region in the gene encoding the von Willebrand factor-binding protein J. Lu* [Taoyuan, Taiwan], L. Lin


Prospective surveillance of invasive group A *Streptococcus* disease in the Netherlands L. Rumke* [Utrecht, Netherlands], S. Vestjens, A. Van Der Ende, B. De Gier, N. Van Sorge, B. Vlaminckx

The unexpected stability of Group B *Streptococcus* clones/serotypes colonising the genitourinary tract of healthy young women M. Ksiezarek, A. Guimarães, V. Martins, J. Rocha, S. Ugarcina Perovic, F. Grosso* [Porto, Portugal], L. Vieira Peixe

Prevalence and molecular characterisation of methicillin-susceptible *Staphylococcus aureus* carrying Panton-Valentine leucocidin gene isolated from patients with invasive infections and nasal carriers D. Tapia, C. Sanhueza, C. Campusano, I. Gallardo, L. Porte* [Santiago, Chile], C. Varela, M. Ulloa

Paediatric invasive pneumococcal disease in Portugal: dominance of serotype 3 and increase in serotype 8 four years after PCV13 inclusion in the national immunization plan C. Silva-Costa, J. Gomes-Silva, L. Prados, M. Ramirez* [Lisbon, Portugal], J. Melo-Cristino

Clinical and bacterial characteristics of paediatric invasive infections caused by *Streptococcus pyogenes* C. Gouveia, L. Varandas, M. Ramirez* [Lisbon, Portugal], J. Melo-Cristino, A. Fábres
6485
The PCV13 serotypes still account for a large fraction of invasive pneumococcal disease in adults three-years after PCV13 introduction in the paediatric vaccination schedule [Portugal: 2015-2018]
C. Silva-Costa, J. Gomes-Silva, I. Teodoro, M. Ramirez* (Lisbon, Portugal), J. Melo-Cristino

6986
Genomic analysis of invasive Streptococcus pyogenes isolated in 2013 and 2018 from Hungary
K. Kristof, P. Forkas, M. Iván, E. Ungvári, T. Erdős, A. Toth* (Budapest, Hungary)

7196
Characterisation of Group B streptococci (GBS) colonising pregnant women in Belgium, 2018: antimicrobial susceptibility profile and distributions of capsular-types, pili-types and sequence-types
C. Mee* (Liège, Belgium), S. Douillez, A. Kinet, R. Sacheli, P. Melin

8772
Genomic epidemiology of paediatric invasive Group A Streptococcus infections in British Columbia, Canada
I. Sekirav* (Vancouver, Canada), W. Demczuk, I. Martin, S. David, M. Naus, J. Sigley, L. Hoang

9094
Streptococcus agalactiae in adults in England and Wales 2014-2015, large scale recombination and capsular shifting
U. Khan* (Cardiff, United Kingdom), E. Jauneikaite, R. Andrews, V. Chalker, B. Spiller

9231
Sharing of MLVA clusters of Listeria monocytogenes among bovine and human invasive clinical isolates
I. Dirigo* (Fontane di Villorba, Italy), E. Mozollini, C. Bacchin, A. Barberis, L. Barco, M. Cocchi, L. D’este, M. Favretti, T. Gallo, A. Gattuso, A. Lettini, E. Schiavon, A. Tavella, F. Agnoletti

Session accepted as Paper Poster Session
Molecular diagnosis of genital infections

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Screening of Chlamydia trachomatis and Neisseria gonorrhoeae in female sex workers: pooled versus single site testing
N. Verougstraete, V. Verbeke, A. De Cannière, E. Padalka, L. Coorevits* (Ghent, Belgium)

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Sexually-transmitted infections detection using real-time PCR Allplex in the east coast of Spain
B. Foster Escriva* (Oliva, Spain), M. Belda, M. Ocete, C. Gimeno Cardona

1075
Evaluation of simultaneous detection of pathogens associated with sexual transmitted infection and vaginal disorders on a real-time qPCR microfluidics platform in an asymptomatic female college student’s cohort
M. Montesinos Hernández* (Bs-Hertogenbosch, Netherlands), S. Lutgens-Dumont, M. Herrmans

1319
MYCOPLASMA IST3, a new in vitro medical device to aid the diagnosis of urogenital mycoplasma infection: performance results from an international multi-centre trial
Y. Bala* (Marcy l’Etoile, France), I. Boostram, J. Minic Vasic, A. Barratt ?, E. Chanard, J. Gluvakov, B. Spiller, L. Devigne

1677
ESwab collection device allows both detection of human papilloma virus with molecular assays and culture with WASP automation
R.Gatej, M. Giuca, S. Constanda* (Bucharest, Romania), R. Musat, M. Dinescu

1728
Evaluation of the Aptima BV assay for detection of bacterial vaginosis by comparison with the BD MAX vaginal panel assay
S. Vaagd, B. Ridwan, D. Willemse-Erix* (’s-Hertogenbosch, Netherlands), S. Lutgens-Dumont, M. Herrmans

4351
Evaluation of a multiplex PCR in genital ulceration diagnosis

4805
Molecular detection of Mycoplasma ammoniforme and Ureaplasma species from patient samples previously investigated for Mycoplasma pneumoniae infection in England and Wales between 2016 – 2017
S. Rehman, S. Maddocks, B. Afshar, J. Day, V. Chalker, M. Beeton* (Cardiff, United Kingdom)

4827
Rapid molecular Chlamydia trachomatis/Neisseria gonorrhoeae testing is now a reality
B. Van Der Pol* (Birmingham, United States), L. Crane, S. Taylor, J. Lebed, A. Ermel, L. Mena, C. Mcneil, A. Sukhija-Cohen

4839
Comparison of analytical performances of the new QiaGen NeuMoDx CT/NG assay with the Abbott RealTime CT/NG assay for detecting Chlamydia trachomatis and Neisseria gonorrhoeae
S. Svraka-Latjovic* (Hilversum, Netherlands), T. Dzebisasjvili, R. Doorn, C. Timmerman, L. Bakker, R. Nijhuis, J. Dorigo-Zetsma

4911
Clinical validation of the BD CT/GC/TV2 for BD MAX system in vaginal, endocervical and female urine specimens
B. Van Der Pol* (Birmingham, United States), E. Torres-Chavolla, S. Kodsí, C. Cooper, T. Davis, K. Fife, S. Taylor, M. Augenbraun, L. Bachmann, C. Gaydos

4946
Clinical validation of the BD CTGCTV2 for BD MAX system assay in male urine specimens
B. Van Der Pol* (Birmingham, United States), E. Torres-Chavolla, S. Kodsí, C. Cooper, T. Davis, K. Fife, S. Taylor, M. Augenbraun, L. Bachmann, C. Gaydos

5059
Method comparison: Abbott Alinity m STI (CT, NG, MG, TV) vs Hologic Aptima CT/NG & Aptima MG
R. Gatej, M. Giuca, S. Constanda* [Bucharest, Romania], R. Musat, M. Dinescu

5528
Epidemiology of sexually-transmitted infections in women with suspected pelvic inflammatory disease admitted to gynaecology emergency unit of an Italian hospital
S. Fiorentini* (Brescia, Italy), A. Pirazzi, A. Matteelli, V. Marchese, R. Stellini, M. Traversi, F. Caccili, S. Rubessa, M. Gulletta
Abstract Categories 2020


6640 Assessment of the performance of the Vaginosis kit Aptima BV on Panther system from vaginal samples during a 3-month period at Nantes university hospital L. Ruffier D’Epenoux, A. Guillouzouic, P’Bemer, S. Corvec* [Nantes, France]

6822 Molecular cpn60-targeted PCR sequencing to assess the diagnostic characteristics of the Nugent Score diagnosis of bacterial vaginosis in reproductive age Kenyan women T. Fear* [Toronto, Canada], E. Shwartsman, J. Russell, M. Richmond, C. Perciani, S. Vancuren, J. Hill, P.Sandstrom, K. Macdonald

7110 Performance of two commercial multiplex PCR assays on the detection the aetiologies of sexually-transmitted infections in men who have sex with men T. Lee* [Taipei, Taiwan], K. Lin, S. Chang, C. Hung, P.Hsueh

7394 Performance evaluation of a novel Trichomonas vaginalis and Mycoplasma genitalium assay in urine and swab specimens C. Lounds, L. Gong* [Ann Arbor, United States], E. Craig, C. Couture, M. Mastronardi, B. Wu, S. Brahmasandra

7502 Use ESwab in sexually-transmitted disease diagnosis by STD Direct Flow Chip Kit T. Soler Maniega* [Madrid, Spain], N. Zurita Cruz, A. Fraile Torres, S. Gómez De Frutos, A. García, L. Cardero

7700 Evaluation of a multiplex real-time PCR assay for detection of the aetiologic agents of vaginitis P. Salmerón* [Barcelona, Spain], P. García, M. Fernández-Huerta, C. Fernández Naval, T. Pumarola-Suñé, Y. Hoyos-Mallecatt, J. Serra Piadevall

8491 A study to investigate the utility of confirmatory testing of oropharyngeal samples positive for Neisseria gonorrhoeae by Cobas 4800 CT/NG test S. Jones* [Cardiff, United Kingdom], R. Drayton, C. Knapper, M. Perry

8592 Performance and comparison of the rapid VivalyticSTI multiplex assay for the detection of sexually-transmitted infections (STI) in specimens from male patients attending an STI dermatologist practice G. Lang* [Vienna, Austria]

Session accepted as Paper Poster Session

Molecular diagnosis: additional aspects

2022 The impact of transport media, shipping time and DNA extraction kits on the absolute abundance of key vaginal bacterial species T. Haahr, J. Jensen* [Copenhagen, Denmark]

3297 A highly sensitive, non-amplification detection method of nucleic acids in bacilli and viruses E. Ito* [Tokyo, Japan], N. Kawada, Y. Kyosei, M. Okamatsu, Y. Sakoda, T. Yoshimura, R. Takeuchi, T. Ohta, K. Nakaishi, S. Watabe

3965 Evaluation of multiplex PCR for rapid detection of bacteria and antibiotic resistance in spontaneous bacterial peritonitis: a pilot study J. Tan* [London, United Kingdom], N. Burke, N. Roth, D. Owen, J. Ryan, M. Morgan, R. Westbrook, E. Wey

4016 Highly sensitive and specific detection and serotyping of five prevalent Salmonella serovars by multiple cross displacement amplification X. Zhang* [Sutherland, Australia], M. Payne, Q. Wang, V. Sintchenko, R. Lan

4255 Evaluation of the Allplex H. pylori and ClariR Assay PCR kit on gastric biopsies Q. Jehanne, L. Benejet, F. Megraud, E. Bessède, P. Lehours* [Bordeaux, France]

4458 qPCR inhibitors/enhancers: the interference in the reaction by drugs used for patient treatment or ingested by the patients E. Machetti-Mareca, R. Morales Hernández, C. Escolar* [Zaragoza, Spain], M. Gil-Rodríguez


6601 Viral versus bacterial infection diagnosis: Affimer proteins as alternative molecular recognition reagents M. Ajayi* [Leeds, United Kingdom], D. Tomlinson, M. Mcpherson

6640 Automation of laboratory developed tests using CSF, transport medium, and whole-blood specimens on the NeuMoDx molecular system C. Lounds, B. Zgheib, P. Mateas, C. Couture* [Ann Arbor, United States], M. Mastronardi, B. Wu, S. Brahmasandra

6752 Molecular testing of the bone marrow in post-mortem samples for the detection of fatal disseminated infections M. Navarro* [Barcelona, Spain], J. Hurtado, P. Castilla, N. Rakislova, A. Martinez-Palhares, I. Casas, M. Freire, L. Ferreira, M. Lacerda, W. Monteiro, L. Marimon, J. Vila Estape, O. Bassat, C. Menéndez, J. Ordí, M. Martinez

6947 Development of an in-house cell-SELEX methodology for Acinetobacter baumannii aptamers selection M. Farrel Côrtes* [Sao Paulo, Brazil], T. Marli Bes, B. Déo, E. Cerdeira Sabino, S. Figueiredo Costa, C. Santos
Abstract Categories 2020

Session accepted as 1-Hour Oral Session

Molecular testing and multiplex panel approaches for diagnosis

3983 Assessing impact of Multiplex PCR Point-of-Care testing in patients with respiratory tract infection: a French national study

4090 Discriminating bacterial and viral infection using a rapid host gene expression test

7249 The effects of introduction of a syndromic PCR sputum testing in intensive care unit pneumonia patients in a tertiary trauma centre
D. Kluczna* [Hull, United Kingdom], P. Burns, D. Wearmouth, P. Lillie

Session accepted as Mini-oral Flash Session

Molecular tools for bacterial diagnosis: how, when and why to use them?

5469 Syndromic tests for meningitis: patient screening before testing allows a high efficient medical value
O. Dauwalder* [Lyon, France], C. Jean-Sebastien, L. Chelghoum, B. Viseux, C. Gustave, D. Dupont, P. Girard, H. Saikia, F. Mzou, T. Solomon, M. Griffiths* [Sydney, Australia], W. Huston, N. Lima

5944 Do DNA based NAAT tests lead to over diagnosis of Chlamydia trachomatis infections?
J. Todd* [Sydney, Australia], W. Huston, N. Lima

6135 Molecular pathogen identification and resistance gene detection from positive blood cultures
A. Brachner, L. Marki, H. Enroth* [Skåne, Sweden], B. Ronacher

6926 Towards an enhanced diagnosis of relapsing fevers by the use of dried blood spots
E. Talagrand-Reboul* [Strasbourg, France], P. Boyer, A. Grillon, C. Bartel, L. Baldinger, M. Engel, L. Zilliox, B. Jaulhac, N. Boulanger

6941 Diagnostic evaluation of the new FluoroType MRSAfast assay for the detection of MRSA from clinical swab specimens
S. Dargel, B. Herberth, M. Eckart* [Nehren, Germany], V. Allerheiligen, T. Bradegeger

7018 Clinical evaluation of ChromaCode’s HDPCR tick-borne pathogen panel
L. Petersen* [Lebanon, United States], J. Jefferts, G. Tsangalis

7094 Rapid distinction of capsules Acinetobacter baumannii using a density gradient method

7098 Rapid diagnostics of bloodstream infections using sybodies and nanobodies as capturing agents
L. Huber, M. Sorgenfrei* [Zurich, Switzerland], R. Melissa, H. Keserue, P. Keller, M. Seeger

7267 Loop-primer endonuclease cleavage loop-mediated isothermal amplification technology for singleplex or multiplex target detection and single-nucleotide polymorphism identification
O. Higgins* [Galway, Ireland], T. Smith

7385 Fighting antimicrobial resistance with breath analysis
E. Adams* [Liverpool, United Kingdom], E. Brodrick, J. Covington, N. Feasey, J. Skinner, M. Radice, D. Sanders
Abstract Categories 2020

Direct detection of Escherichia coli in clinical samples by an ultrasensitive fluorescent copper nanoparticles-aptasensor
Y. Xiao* [Chengdu, China], P. Zhang, L. Wang, Z. Wang, J. Geng

Evaluation of EUCAST rapid antimicrobial susceptibility testing (RAST) directly from blood culture bottles
S. Waled, Y. Soo, S. Ng, Y. Peh, K. Chew* [Singapore, Singapore]

Evaluation of diagnostic method with sonication and culturing of orthopaedic implant-associated infection at Karolinska University Hospital, Sweden
B. Saeedi, D. Kartou Boukdr* [Stockholm, Sweden]

Neural networks for prediction of minimum inhibitory concentration
E. Carlsson, F. Dyrkell* [Gothenburg, Sweden], T. Lundh

Performance of the urine flow cytometer Sysmex UF-5000 in rapid diagnosis of urinary tract infections
K. Haugum* [Trondheim, Norway], M. Haugan, J. Skage, M. Tetik, A. Jakovljev, H. Schjelderup Nilsen

Light scattering technology in the diagnosis of infections in children on dialysis
L. Boronina* [Ekaterinburg, Russian Federation], E. Samatova

Comparison of the Accelerate Pheno rapid diagnostic system with standard of care for diagnosing Gram-negative bloodstream infections: bacterial identification, antimicrobial sensitivity and turnaround time

A clinical predictive model of multidrug resistance in neutropenic cancer patients with bloodstream infection due to Pseudomonas aeruginosa [IRONIC study]

Predicting phenotypic polymyxin resistance in Klebsiella pneumoniae through machine learning analysis of genomic data
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D. Goldenberger* [Basel, Switzerland], A. Egli, V. Hinic, A. Blaich, T. Roloff, H. Seth-Smith

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L. Van Heirstraeten, I. Wouters, S. Desmet, C. Lammens, J. Verhaegen, H. Goossens, P. Van Damme, P. Beulens, H. Theten* [Antwerp, Belgium], S. Malhotra-Kumar

Molecular biomarker to monitor NDM-producing *Klebsiella pneumoniae* outbreak in two Belgian hospitals: a whole genome sequencing-based infection control application
A. Heinrichs* [Brussels, Belgium], M. Argudín, L. Nienhaus, C. Nonhoff, L. Filippin, F. Bogaerts, T. Huang, Y. Glupczynski, D. Denis

Investigating the feasibility and clinical impact of a prospective genomics workflow for hospital infection control
**Development of a high-throughput single nucleotide polymorphism (SNP) typing assay for Klebsiella pneumoniae**

E. Shaidualina* [Smolensk, Russian Federation], E. Sheck, A. Mikotina, A. Mardanova, M. Edelstein

**Typing of carbapenemase-producing Klebsiella pneumoniae: IR Biotyper meets NGS**

M. Cordavano* [Bologna, Italy], H. Seth-Smith, A. Deni, V. Hinic, A. Egli, S. Ambretti

**It takes two to tango: antimicrobial resistance and virulence contribute to the success of particular Acinetobacter baumannii clones**

F. Grossa* [Porto, Portugal], L. Silva, C. Rodrigues, M. Ksiezek, H. Ramos, L. Vieira Peixe

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**Multi-centre whole genome sequencing bioinformatic outbreak analysis proficiency test conducted in The Netherlands**

J. Coolen* [Nijmegen, Netherlands], C. Jamin, P. Savelkoul, H. Wertheim, J. Rossen, S. Matamoras, L. Van Alphen

**Whole genome sequences analyses by a new easy-to-use software solution confirm a neonatal ward outbreak of MRSA CC22 being related to strains in the neighbouring region**

M. Slott Jensen, M. Chen, M. Skov, M. Kemp* [Odense, Denmark]

**Biochemical description of seven putative novel species of the genus Yersinia identified by core-genome multilocus sequence typing (cgMLST)**

H. Angermieier* [Paris, France], A. Le Guern, S. Bremont, C. Savin, J. Pizarro-Cerdá

**What's new in bacterial typing?**

**A k-mer-based approach for MLST and cgMLST analysis of nanopore sequenced Staphylococcus aureus**

O. Aspelin* [Gothenburg, Sweden], F. Dyrkell, D. Arnellos

**Using machine learning for improving MLST analysis of nanopore sequenced bacteria**

O. Aspelin* [Gothenburg, Sweden], E. Carlsson

**Subtyping Escherichia coli in spontaneous bacterial peritonitis with use of IR biotyper and whole genome sequencing**

J. Tan* [London, United Kingdom], C. Leboereia, P. Solanki, R. Westbrook, E. Wey

**K-mer based prediction of Clostridioides difficile ribotypes and relatedness**

M. Moore* [Oxford, United Kingdom], D. Eyre

**Systematic review: transmission inference using single nucleotide polymorphism (SNP) differences between isolates of ESBL and CR-Enterobacteriaceae. Can a SNP cutoff be defined?**

A. Jamali* [Toronto, Canada], A. Carbeil, L. Farooqi, Z. Zhong, E. Uleryk, A. Mcgeer

**Standardisation and validation of the PCR technique for detection of ST16-KL51 serotype among Klebsiella pneumoniae isolates**

J. Paulino, D. Andrey, W. Martins, N. Lincopan, A. Gales* [São Paulo, Brazil]
Whole genome sequencing in outbreak analysis

301 Whole genome analysis of vancomycin-resistant Enterococcus faecium causing nosocomial outbreaks suggests the occurrence of few endemic clonal lineages in Bavaria, Germany
D. Eisenberger* [Erlangen, Germany], C. Tuschk, S. Nickel, V. Lehner-Reindl, C. Höller, B. Liebl, G. Valenza

2082 Drain water as a potential source of in-hospital room-to-room transmission of carbapenemase-producing Klebsiella pneumoniae
L. Heireman* [Ghent, Belgium], H. Hamerlinck, J. Boeles, S. Vandendriessche, L. Coorevits, I. Leroux-Roels, M. Chlebowicz, J. Rossen, B. Verhasselt

2116 Whole genome sequencing investigation of iGAS outbreak in elderly care
J. Coelho, N. Groves, D. Ready* [London, United Kingdom], C. Brown, O. Olufon, R. Manuel, K. Paranthaman, I. Braithwaite, M. Cummins, C. Allam* (Lyon, France), C. Ginevra, C. Campese, C. Ebberson, D. Lawrence, T. Lamagni, E. Wynne-Evans

3981 Legionnaires’ disease and sleep apnea devices: retrospective analysis of a 9-year-investigation and contribution of whole genome sequencing
C. Allam* [Lyon, France], C. Ginevra, C. Campese, A. Prugne, D. Morel, L. Beraud, G. Descours, S. Jarraud

4973 Retropective WGS of Acinetobacter baumannii over 6.5-year-period reveals former unknown structure of clusters and uncovers resistance profile
A. Grafit* [Freiburg, Germany], J. Rauch, W. Ebner, H. Grundmann, S. Reuter

5665 Whole genome sequencing clarifies potential outbreak with extended-spectrum beta-lactamase-producing Escherichia coli
S. Mernelius* [Jönköping, Sweden], L. Berglind

7848 An unusual cluster of community-acquired skin infections by a multidrug-resistant MRSA harbouring genes that encode for exfoliative toxins
D. Notermans* [Bilthoven, Netherlands], E. Denie, W. Silvis, B. Postma, S. Bantjes, A. Schoffelen, M. Dimmendaal, H. Ruijs, F. Coenen-Bennett, M. Petrignani, K. Vandrik, L. Schouls, E. Kuiper

8157 Use of whole genome sequencing for rapid detection of a national nosocomial outbreak of Listeria monocytogenes associated with contaminated prepacked sandwiches in England, 2019
G. Godbole* [London, United Kingdom], G. Sabitowska, T. Dallman, L. Byrne, A. Simbo, J. Mclauchlin, S. Lai, N. Phin

9126 A home humidifier responsible for Legionnaires’ disease: input of WGS for genomic investigation in a ST1 case

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Whole genome sequencing: from molecular characterization to typing

677 Pan-genome analysis supports the differentiation of Bacteroides fragilis in division I and the potentially carbapenem-resistant cf+ division II into two species
T. Vognbjerg Sydénham* [Vejle, Denmark], U. Justesen

1976 In silico identification of host-associated genomic determinants in Escherichia coli using bacterial genome-wide association study

New polysaccharide capsule identification in urogenital Haemophilus parainfluenzae related to capsular locus present in Haemophilus spp.
A. Ganzález Díaz* [Barcelona, Spain], Y. Sierra Uruéña, F. Tubau, J. Ayats, M. Cubero, A. Ardanuy Tisaire, S. Marti

2203 Stx2K-producing Escherichia coli in China
X. Xiang* [Beijing, China], X. Bai, X. Yang

2284 Temporal acquisition of IS1548 in Streptococcus agalactiae clonal complexes
S. Khazaal* [Tours, France], R. Al Safadi, D. Osman, A. Hiran, P. Gilat

2568 Genomic characterisation of multidrug-resistant Klebsiella michiganensis strains
P. Shibu, F. McCuigh, M. Kujawski, L. Hall, A. McCartney, L. Hayes* [Nottingham, United Kingdom]

2609 Implementing pathogen genomics effectively: a seamless service

2626 NDM-1 emerging on distinct plasmid backbones from the IncL/M family
M. Lopez* [A Coruna, Spain], N. Ellaby, N. Woodford, M. Tomas, M. Ellington

3568 Genetic diversity of blaKPC gene containing IncF plasmids from epidemiologically related and unrelated Enterobacteriaceae
J. Stohr* [Breda, Netherlands], M. Klyuytman - Van Den Bergh, V. Weterings, J. Rossen, J. Klyuytman

3817 Recurrence of multidrug-resistant Klebsiella pneumoniae ST48 at Charité, Universitätsmedizin Berlin
F. Maechler, A. Weber* [Berlin, Germany], P. Gastmeier, A. Kola
4522 High-throughput genome sequencing highlights Pseudomonas aeruginosa adaptative evolution in the urinary tract
A. Cottalorda, S. Dahyot* (Rouen, France), M. Leoz, F. Gravey, F. Aujoulat, K. Alexandre, S. Le Hello, E. Jumas-Bilak, M. Pestel-Coran

5264 Whole genome sequencing of heterochronous isolates of Burkholderia cenocepacia and B. contaminans from two patients with cystic fibrosis using Nanopore and Illumina platforms
A. Bernier* (Winnipeg, Canada), S. Tyson, T. Burdz, D. Wiebe, K. Bernard

5479 Genetic characterisation of virulence factors of non-O1 non-O139 Vibrio cholerae strains from clinical and environmental origin isolated in Chile between 1992 and 2018

6522 Whole genome sequencing reveals differences between previously indistinguishable isolates of tobramycin resistant Staphylococcus aureus
S. Mernelius* (Jönköping, Sweden), A. Jogenfors, L. Berglind, A. Matussek

6623 Relatedness of European Clostridioides difficile strains from humans, food and animals by whole genome sequencing, ribotyping and toxinotyping; results from COMBACTE-CDI

7669 First insight into the genome sequence of Clostridioides difficile strains isolated from Romanian patients
I. Czobor* (Bucharest, Romania), V. Cristea, I. Gheorghe, C. Chifiriuc, Y. Feng, X. Wang, L. Papa, M. Popa, L. Marutescu, V. Lazar, M. Popa, Z. Zong

7698 Optimisation of bacterial whole genome sequencing workflow for implementation in routine clinical and epidemiological applications
C. Heismoortel* (Leuven, Belgium), L. Laenen, E. Souche, L. Dehaspe, N. Dedoncker, W. Bossuyt, S. Desmet, E. Andre

7970 Virulence profile and comparative genomics analysis of the emerging Klebsiella pneumoniae genotypes ST45, ST101 and ST629
E. Esposito* (Naples, Italy), M. Cervoni, C. Roe, L. Peixe, S. Pournaras, S. Brisse, J. Sahl, F. Imperi, R. Zarrilli
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• New or repurposed antibacterial agents: clinical trials

• Pharmacoepidemiology (incl economics and cost-effectiveness), improved prescribing and antibiotic stewardship (incl decision-support / prediction tools, behavioural aspects)

• Other
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Adverse effects of antibiotics: data from clinical trials

2197 Impact of combining vancomycin with piperacillin/tazobactam or with meropenem on vancomycin-induced nephrotoxicity
R. Tokhi, N. Kabli, M. Hantool, A. Thabit* [Jeddah, Saudi Arabia]

2538 A retrospective matched cohort study evaluating the rate of acute kidney injury in patients with severe Gram-negative infections treated with colistin or new β-lactam + β-lactamase inhibitor antibiotics
C. Doremus* [New Jersey, United States], S. Marcella, B. Cai, R. Echols

2889 Antimicrobial therapy with aminoglycoside or meropenem in the intensive care unit for hospital-associated infections and risk factors for acute kidney injury
R. Pitta, J. Gasparetto, T. De Moraes, J. Telles* [Sao Paulo, Brazil], F. Tuan

4180 Nephrotoxicity during teicoplanin therapy in combination with piperacillin/tazobactam or other anti-pseudomonal β-lactams
C. Tai* [Taipei City, Taiwan], C. Shao, C. Wang, F. Lin, C. Palacios

4310 Effect of a serum lactate monitoring recommendation policy on patients treated with linezolid
J. Baek* [Incheon, South Korea], J. Im, J. Lee, H. Kwon

5518 Daptomycin and pulmonary eosinophilia: An unrecognised opportunity
K. West* [Portland, United States], A. Sheeti, G. Forrest

5678 Occurrence and predictors of nephrotoxicity in adult patients treated with intravenous colistin: a cohort study
L. Graça, J. Torres, A. Silva-Pinto, F. Almeida, N. Rocha Pereira* [Porto, Portugal], P. Andrade, R. Duro, C. Alves

5874 Impact of safety alerts and warnings on fluoroquinolone and alternative antibiotic use in Colombian outpatient care
M. Silva-Medina Weil* [Cali, Colombia], P. Ricardo, M. Palacios

6435 Phase II clinical data showed that lower recurrence of Clostridioides difficile infection with ridinilazole is associated with minimal impact on the gut microbiota and bile acid composition
E. Duperchy* [Abingdon, United Kingdom], X. Dian, K. Yanagi, A. Kane, N. Alden, M. Lei, D. Snydman, R. Vickers, D. Rabin, K. Lee, C. Thorpe

8138 Real-world experience with prolonged courses of tedizolid at a large academic medical centre
W. Alegria* [Stanford, CA, United States], D. Ho, M. Holubar, L. Meng, E. Mui, S. Deresinski

8337 Vancomycin plus piperacillin-tazobactam and the risk for acute kidney injury: what is the effect size?
S. Avedissian* [Nebraska, United States], J. Liu, G. Pais, M. Scheetz, N. Rhodes

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Antibiotic hospital consumption measurements around the world

1381 Antibiotic use in French hospitals 2012-2018: improvements to be confirmed!

2907 The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS): roll-out of a successful antimicrobial stewardship programme in Nigeria using the global-PPS tool
O. Oduyebo, A. Roberts, O. Ola-Bello, A. Versporten* [Antwerp, Belgium], I. Pauwels, C. Osuagwu, I. Fojolu, P. Oshun, H. Goossens, P. Akintan, E. Temiye

3384 A novel methodical approach to quantifying the value of an antibiotic: enablement-, insurance- and productivity-value
J. Kowalik* [London, United Kingdom], A. Blake, R. Russell, D. Mircea, D. Leonard, N. Meadows

5360 The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS): the results of antimicrobial prescribing in 33 hospitals in Guinea
M. Sow* [Conakry, Guinea], A. Versporten, I. Pauwels, D. Djiro, H. Goossens

5680 Antimicrobial stewardship in Cambodia: the importance of antimicrobial point prevalence survey and lessons learned from the field
G. Khim* [Phnom-Pen, Cambodia], F. Dailly, P. Pen, R. Kong, S. Sok, S. Yim, S. Oung, J. Hesse, J. Letchford, J. Ferguson

6638 Trends in antimicrobial use in Brazilian hospitals: 2017 and 2018 point prevalence surveys
Trends of antibiotic consumption in German hospitals from 2015-2018
B. Schweickert* [Berlin, Germany], M. Feig, M. Schneider, K. Groeschner, M. Behnke, L. Pena Díaz, P. Gastmeier, M. Abu Sin, D. Richter, H. Blank, H. Wehrmeyer, A. Hoffmann, T. Eckmanns

Comparing the financial burden of hospitalised patients within the same Diagnosis Related Groups (DRGs) with and without an infection: a multi-centre evaluation in the USA
L. Puzniak, K. Yu* [New Jersey, United States], V. Gupta

Using point prevalence methodology to evaluate antimicrobial prescribing in the UK’s largest renal dialysis centre
A. Chavda* [London, United Kingdom], A. Ghazy, L. Whitney, M. Gilchrist, A. Holmes

Nation-wide audit with feedback of antibiotic stewardship in Norwegian hospitals: a low cost initiative with many opportunities
P. Akselsen* [Bergen, Norway], M. Neteland, J. Høgli, B. Skodvin, S. Harthug

The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS): results of antimicrobial prescribing at Ghana’s National Referral Centre
M. Mirfenderesky* [London, United Kingdom], J. Mahungu, A. Aggar, A. Versporten, I. Pauwels, H. Goossens, D. Ankrah

The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS): an opportunity to lead global stewardship actions in Belgian hospitals?
X. Holemans* [Charleroi, Belgium], C. Van Wetter, A. Versporten, O. Tassin, I. Pauwels, H. Goossens, M. Ventura

Improving country-level antimicrobial prescribing with the implementation of a uniform and standardised surveillance method: the Global-PPS Chilean experience, year 2015 and 2017
C. Carvajal* [Santiago, Chile], A. Versporten, A. Rojas, M. Cifuentes, F. Silva, H. Goossens, J. Labarca

Consumption of antibiotics effective against multi-resistant Gram-positive pathogens: data of German hospitals from 2015-2018
B. Schweickert* [Berlin, Germany], M. Feig, M. Schneider, K. Groeschner, W. Niklas, M. Behnke, L. Pena Díaz, P. Gastmeier, D. Richter, H. Blank, H. Wehrmeyer, T. Eckmanns, M. Abu Sin

14-year evolution of antimicrobial consumption in a Belgian tertiary hospital based on the BeH-SAC surveillance
F. Bugle* [Ghent, Belgium], S. Callens, A. Somers, S. Commeyne, D. Vogelaers

A global point prevalence study of antimicrobial use in the neonatal intensive care unit: the NO-More-Antibiotics and Resistance study (NO-MAS-R)
P. Prusakov* [Columbus, United States], D. Goff, P. Wozniak, A. Medoro, P. Sanchez

A nation-wide parent survey of antibiotic use in Australian children

Antibiotic consumption in very low birth weight neonates on neonatal intensive care units in Germany: a longitudinal study 3 years of national surveillance
F. Salm, T. Kramer* [Berlin, Germany], F. Schwab, M. Behnke, P. Gastmeier, C. Geffers, B. Pieing

Impact of antibiotic stewardship programme on the most utilised antibiotics’ utilisation and financial expenditure in 57,357 Children Cancer Hospital Egypt inpatient setting
E. Khaled Mohamed Abu Alaanain, A. Elteiny, M. Nagy, A. Koshef, A. Badie* [Cairo, Egypt], A. Sameh, L. Shalaby

Prescribing in paediatric inpatients in England, 2016: factors associated with prescribing “watch” and “reserve” antibiotics
A. Demirjian* [London, United Kingdom], R. Freeman, B. Muller-Pebady, D. Ashish-Uredope, S. Hopkins

Community antibiotic prescribing for children in France from 2015 to 2017: a prospective national study

Heterogeneity of antimicrobial prescribing in large paediatric tertiary centres: implications for future interventions and benchmarking of antimicrobial stewardship activities
M. Gilchrist* [London, United Kingdom], A. Chavda, F. Chappell, C. Dalton, A. Demirjian, R. Freeman, A. Kashef, A. Badie* [Cairo, Egypt], A. Sameh, L. Shalaby, E. Khaled Mohamed Abualanain, A. Elzeiny, M. Nagy

Infectious disease specialist intervention in the neonatal intensive care unit: a safe approach to reduce antibiotic exposure in neonates
J. Armann* [Dresden, Germany], B. Seipolt, M. Rüdiger, R. Berner

Introducing end-of-life considerations into a computerised decision support system for antibiotic treatment: effects on the system’s recommendations and comparison to physicians’ behaviour
Y. Dishon-Benattar* [Haifa, Israel], I. Pfeffer, M. Magensen, L. Ward, L. Leibovici, E. Dagan, M. Paul
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2170 How an inflammatory marker Point-of-Care test can reduce inappropriate antibiotic use in urinary tract infections: perceptions of physicians and nurses in Dutch nursing homes
S. Kui* (Amsterdam, Netherlands), C. Schneeberger, M. De Jong, F. Van Leeh, J. Harting

3035 Impact of an antimicrobial stewardship programme on antibiotic resistance profile of urinary Enterobacteriaceae isolated from nursing home residents: a retrospective cohort study

3602 Antibiotic use at the end-of-life in patients with advanced cancer: a systematic literature review
A. Marra, M. Puig-Asensio* (Iowa City, United States), E. Perencevich

5774 Antibiotic consumption in 417 nursing homes: results from a pilot survey

6057 Development of an antimicrobial stewardship programme for post-acute and long-term care centre by the use of teledicine
S. Gómez-Zorrilla* (Barcelona, Spain), M. Marin, P. García, D. Echeverría-Esnal, N. Prim, M. Gracia-Arnillas, E. Padilla, O. Vázquez, J. Horcajada, S. Grau

7099 Spectrum overly broad and duration too long: an assessment of appropriateness of antimicrobial prescriptions in older patients admitted to an Australian tertiary teaching hospital
L. Gebremichael, R. Visvanathan, M. Warner* (Adelaide, Australia)

8884 A new approach of antibiotic stewardship in geriatric facilities
R. Collarina* (Le Kremlin-Bicêtre, France), C. De Villelong, X. Lescure, V. Fossey-Diaz, L. Deconinck, L. Vaillant

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Assessment of community and outpatient antibiotic prescribing worldwide

996 Antibacterial prescribing in the outpatient setting: results from a longitudinal surveillance programme and a sentinel network of physicians: Switzerland, 2018
C. Pluess-Suward* (Bern, Switzerland), D. Perisa, O. Friedli, M. Mäusezahl-Feuz, A. Kronenberg

1129 National ambulatory care programme of oral antibiotics and prevalence of inappropriate prescribing in the United States, 2009 to 2016
E. Young* (San Antonio, United States), A. Yap, R. Panchal, K. Reveles

1225 Overuse of antibiotics in primary care: a secondary analysis of standardised patient studies across four low- and middle-income countries
G. Sulis* (Montreal, Canada), B. Daniels, A. Kwan, J. Das, M. Pai

2258 Community-acquired and hospital-acquired Clostridioides difficile infections in the context of a trans-sectoral antibiotic stewardship intervention in Berlin, Brandenburg and Thuringia
S. Schneider, C. Schröder, F. Salm, I. Petruschke, A. Mooser, S. Hagel, M. Pletz, P. Gastmeier* (Berlin, Germany)

2698 Impact of a national antimicrobial stewardship programme to switch from trimethoprim to nitrofurantoin for treatment of urinary tract infections on the incidence of Escherichia coli bloodstream infection in England, 2015–2019
A. Au-Yeung* (London, United Kingdom), A. Soei, A. Charlet, O. Nsonwu, R. Hope, B. Muller-Pebady, S. Hopkins, R. Freeman

2716 Antibiotic prescription practices in primary care in low- and middle-income countries: a systematic review and meta-analysis
G. Sulis* (Montreal, Canada), P. Adam, V. Nafade, G. Gore, B. Daniels, A. Daftary, J. Das, S. Gandra, M. Pai

A computerised decision support system (CDSS) for antibiotic prescribing in primary care: Antibiotic: implementation, adoption and sustainable use in the era of extended antimicrobial resistance
T. Delory* (Paris, France), P. Jeannougin, S. Lariven, J. Aubert, N. Peiffer-Smadja, P. Boëlle, E. Bouvet, X. Lescure, J. Le Bel

3186 Optimising the treatment of upper respiratory tract infections and tackling antibiotic resistance: effect of online education on physician knowledge and confidence
J. Duffey* (Matlock, United Kingdom), V. Lund, D. Hoban, B. Rubin, S. Voorn

Ten-year trends in Estonian ambulatory antibiotics use and comparison of ESAC quality indicators with Nordic countries
J. Lass, O. Laius, E. Linask, E. Sepp, I. Lutsar* (Tartu, Estonia)

3389 Community antimicrobial stewardship programme in pregnant women with urinary tract infections in primary care service
J. Asimbaya, P. Zambrano Sánchez* (Quito, Ecuador)

4043 Antibiotics prescribing in the outpatient setting: results from a longitudinal surveillance programme and a sentinel network of physicians: Switzerland, 2018
C. Pluess-Suward* (Bern, Switzerland), D. Perisa, O. Friedli, M. Mäusezahl-Feuz, A. Kronenberg

4398 Variations in antibiotic prescribing among village doctors in rural Shandong province, China
O. Dyar* (Stockholm, Sweden), Y. Ding, Y. Jia, S. Qiang, C. Stälsby Lundborg

4402 Acceptability of selective reporting of antibiotic susceptibility testing results in primary care
M. Simon* (Chaligny, France), G. Le Dref, S. Fougnout, P. De Monchy, J. Kivits, C. Pulcini, N. Thilly
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4705 Acceptability of a public commitment charter associated with patient information leaflets on antibiotics by general practitioners
A. Essilini* [Nancy, France], G. Le Dref, J. Kivits, A. Welter, C. Pulcini, N. Thilly

4825 Antibiotic use prior to seeking medical care in patients with persistent fever in four low- and middle-income countries
B. Ingelbeeen* [Antwerp, Belgium], K. Koiraia, K. Verdonck, B. Barbé, D. Mukendi Mulumba, T. Phe, S. El Safi, E. Bottieau, M. Van Der Sande, M. Boelaert, F. Chappuis, J. Jacobs

5125 Association between susceptibility to quinolones in Escherichia coli and tetracycline use in the community: analysis with community-specific ARIMA models
M. Viñet, O. Le Bastard, M. Low, B. Gottesman, J. López-Lazano, E. Montassier, E. Batard* [Nantes, France]

5799 Evaluation of large urban-rural outpatient antibiotic stewardship programme
L. Mag* [Sacroanto, United States], T. Chechi, H. Bettencourt, M. Wang

5946 Perceptions of general practitioners on antimicrobial stewardship: a nation-wide survey in Australia
S. Saha* [Melbourne, Australia], D. Kong, K. Thursky, D. Maaza

6263 Geodes Antibiotiques: restituting French antimicrobial consumption in the ambulatory sector using two indicators and an interactive website
P. Cavalié* [Saint Maurice, France], M. Boussac, S. Moufet, E. Lucas, A. Berger-Carbonne, L. Watier, B. Coignard

6962 Monitoring outpatient antibiotic utilisation using sales and reimbursement data: a population-based comparison in France, 2012-2017

7556 Bridging the gap between human and animal antimicrobial resistance and consumption surveillance data, antibiotic policy and stewardship: the EPI-Net and ARCH projects
M. Pezzani* [Verona, Italy], F. Arieti, E. Carrara, R. Cuada, M. Campri, S. Goepel, F. Mazzaferrì, E. Mazzolini, M. Mendelson, N. Mûters, N. Babu Rajendran, R. Schrijver, M. Sibani, A. Voss, E. Tacconelli

8186 Impact of a French regional centre infection hotline on antibiotic prescriptions in general medical practice
M. Bachelet, P. Thibon, A. Lessourd, S. Dargèrè, F. Caron, R. Verdon, E. Fiaux* [Rouen, France]

8325 An automated data extraction from primary-care-paediatricians’ computers: a French paediatric ambulatory research in infectious diseases
S. Béchet, A. Werner, F. Vie Le Sage, G. Thiebault, N. Gelbert, F. Cahn-Sellem, F. Kochert, C. Levy, R. Cohen* [Créteil, France]

9250 Population-level antimicrobial consumption is associated with cultural factors in 37 high-income countries: a global ecological analysis
C. Kenyon* [Berchem, Belgium]

9291 Antibiotic stewardship: assessment of education and awareness tools for improving citizen involvement
F. Grimaud* [Créteil, France], X. Lescure, J. Le Bel, Y. Yazdanpanah

9504 Epidemiology of previous antibiotic treatment in a community setting infectious diseases consultation office
J. Choucair* [Beirut, Lebanon]

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Bacteriophage therapy goes viral

865 Bacteriophage therapy against multidrug-resistant Acinetobacter baumannii infections
R. Rothore* [Tbilisi, Georgia], N. Karumidze

1268 Quality control of therapeutic bacteriophages: the Belgian experience
A. Leray, L. Cuignet, C. Vanhee, E. Deconinck, P. Ceyssens* [Brussels, Belgium]

1329 Efficacy of bacteriophage-antibiotic combinations on two different phenotypes of methicillin-resistant Staphylococcus aureus
R. Kebriaei, K. Lev, T. Morrissette, P. Maassen, J. Abdul-Mutakabbir, S. Morales, M. Rybak* [Detroit, United States]

1532 Personalised production and administration of bacteriophages: lesson learned from a unique European academic collaboration to treat a patient with pandrug-resistant Pseudomonas aeruginosa spinal infection
T. Ferry* [Lyon, France], J. Pirnay, C. Gustave, C. Kolenda, M. Merabishvili, L. Gilles, A. Marchet, C. Barrey, T. Perpoint, F. Laurent, G. Resch

Diversity and therapeutic potential of Klebsiella pneumoniae bacteriophages and their depolymerases: genomics and enzymatic activity
R. Ragupathy* [Manchester, United Kingdom], J. Redfern, M. Enright

Intravenous administration of personalised cocktail of bacteriophages as salvage therapy in combination with ceftazidime/avibactam in patients with relapsing Pseudomonas aeruginosa bacteremia associated with intravascular implants: lesson to be learned from two cases
**Abstract Categories 2020**

**4070 In vitro activity of four lytic bacteriophages specific for OXA-72-producing Acinetobacter baumannii**
W. Martins* (São Paulo, Brazil), J. Ciro, E. Medeiros, M. Toleman, A. Gales

**4556 Phage-MR003 prevents infection caused by clinical isolated meccillin-resistant Staphylococcus aureus in mouse wound model**
T. Suda* [Katka, Japan], T. Hanawa, Y. Tanji, K. Miyagawa, H. Ohnishi, T. Matsuda

**5553 Effectiveness of bacteriophage-antibiotic combinations for daptomycin-resistant Enterococcus faecium harbouring LiaS and LiaR substitutions**
T. Morrisette* [Detroit, United States], K. Lev, R. Kebriaei, J. Abdul-Mutakabbir, P. Maassen, S. Morales, C. Arias, M. Rybak

**6054 Characterisation of phage obtained from meccillin-resistant Staphylococcus aureus**
D. Ulusan* [Izmir, Turkey], F. Sahin, M. Kiyar

**7992 Bacteriophage therapy in the treatment of burn wounds**
M. Alexander, I. Grigoryan* [Moscow, Russian Federation], A. Melikumyan, O. Safronova, Y. Turnikov

**9964 Late spot evaluation reveals enhanced phage lytic activity**
D. Rezevska* [Riga, Latvia], K. Racenis, J. Kraica

**9007 Anti-biofilm activity of bacteriophage φWL-3 conjuncted with ciprofloxacin, fosfomycin, gentamicin, meropenem or ceftriaxone against a ciprofloxacin-ceftiraxone-resistant Escherichia coli clinical isolate**
L. Wang* [Hefei, China], T. Tkhiashvili, B. Bernal Andrés, A. Trampuz, M. Gonzalez Moreno

**9015 Biofilm killing activity of bacteriophage φWL-3 against antibiotic-resistant Escherichia coli clinical isolate**
L. Wang* [Hefei, China], T. Tkhiashvili, B. Bernal Andrés, A. Trampuz, M. Gonzalez Moreno

**9063 In vitro evaluation of single or combined bacteriophages targeting different Staphylococcus aureus clinical isolates**
J. Orcastegui Delso* [Berlin, Germany], F. Kunisch, A. Trampuz, M. Gonzalez Moreno

**9153 Bacteriophage therapy in orthopaedic and cardiovascular surgery: first clinical experience with difficult-to-treat infections**
P. Marovic* (Berlin, Germany), T. Tkhiashvili, D. Margaryan, S. Karbysheva, A. Trampuz

Session accepted as **Paper Poster Session**

**Clinical experience with recently approved antibiotics**

**1152 Efficacy of ceftazidime-avibactam for multidrug-resistant Gram-negative bacteria infections: a retrospective evaluation in a Belgian teaching hospital**
V. Gancette, N. Layias, F. Frippiat* [Liège, Belgium]

**1214 Exposure-efficacy analyses support optimal dosing regimens of ceftolozane/tazobactam in patients with hospital-acquired pneumonia /ventilator-associated pneumonia in ASPECT-NP**

**2946 Optimal PK/PD target and high efficacy rates of ceftolozane-tazobactam in patients with infections caused by extensively drug-resistant Pseudomonas aeruginosa**
E. Navarete-Rouco, S. Luque, L. Sorli, A. Arancon, N. Campillo, M. Montero, N. Prim, A. Bentitez-Cano, E. Samso, J. Horcajada* [Barcelona, Spain], S. Grau

**SUSANA project: real-world data coming from the use of new antimicrobial drugs**

**Ceftolozane-tazobactam for treatment of severe ESBL-producing Enterobacteriaceae infections: a multi-centre nationwide clinical experience [Ceftabuse II Study]**

**Delafloxacin (DLX) in the treatment of community-acquired bacterial pneumonia [CABP]: patients with PORT Risk Class III-V**
R. Alvarez-Salo, M. Popescu, L. Lawrence, S. Cammarata, D. Zinzi* [Pomezia, Italy]

**Resistance to ceftolozane-tazobactam and ceftazidime-avibactam in extensively drug-resistant [XDR] and multidrug-resistant [MDR] Pseudomonas aeruginosa: comparing antimicrobial activity, associated risk factors and clinical outcomes**
M. Meschiari* [Modena, Italy], K. Shaniok, V. Bianco, M. Sarti, G. Orlando, A. Bedini, C. Mussini
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Clinical experience with ceftazidime-avibactam (CAZ-AVI) in the treatment of infections caused by XDR Klebsiella pneumoniae producing OXA-48 carbapenemase
A. Bykav, M. Savorova, I. Sychev, E. Burrmistrova, A. Ismagilov, D. Protosenko, S. Yakovlev* [Moscow, Russian Federation]

5234 Experience after analysing a ceftazidime/avibactam national registry of infections caused by KPC-producing Klebsiella pneumoniae

Comparative effectiveness of ceftolozane/tazobactam versus aminoglycosides or polymyxins in multidrug-resistant Pseudomonas aeruginosa infections
A. Coffrey, E. Piehl* [Providence, United States], V. Lopes, L. Puzniak, K. Laplante

Real-world multi-centre experience with eravacycline at academic hospital systems
S. Alosaimy, K. Molina, K. Claegs, J. Andrade, J. Truong, M. King, B. Pullinger, G. Huang, T. Morrisette* [Detroit, United States], A. Lagrjf, M. Rybak

Real-life experience with ceftazidime-avibactam in South Spain

Radiologic features of Pneumocystis pneumonia differ between patients with and without HIV Infection
H. Wu* [Kaohsiung, Taiwan], K. Wu, S. Lee, D. Chang, S. Dai, S. Kua, C. Chou, Y. Weng, Y. Tseng, J. Chen, C. Sy, H. Tsai, Y. Chen

Successful use of the novel antifungal oroflom in the treatment of disseminated coccidiodymycosis
E. Harvey, L. Fitton, J. Rex* [Wellesley, United States], G. Thompson

Outcomes of candidaemia caused by biofilm-forming isolates in haematological patients
G. Klyasova* [Moscow, Russian Federation], A. Malchikova, K. Tandilova, S. Kravchenko, P. Elena, V. Savchenko

Clinical evaluation of an investigational use only Aspergillus galactomannan lateral flow assay at a tertiary cancer care centre
K. Jani, T. Mcmillen, E. Babady* [New York, United States]

Performances evaluation of the first sample-to-result system for detection and quantification of Pneumocystis jirovecii in respiratory tract samples
S. Patanè* [Torino, Italy], G. Bovolenta, A. Camporese, R. Tedeschi, P. Stano, S. Costa, C. Bittoto, G. Stefanuto

Effectiveness and safety of isavuconazole treatment for invasive fungal infections in solid organ transplant recipients

Antimicrobial stewardship teams in candidaemia management: advise or take care of the patient?
A. Alemán Alemán, N. Gómez-Manero, M. Fernández Regueras, M. Mantecón, L. Buzón Martín, M. Morán-Rodriguez, C. Navarro San Francisco* [Burgos, Spain]

Evaluation of the antifungal stewardship programme at St George’s Hospital, London 2018-19
A. Rusdiah* [London, United Kingdom], T. Yau, C. Logan, T. Bicanic

Population pharmacokinetic/pharmacodynamic assessment of a clinical imipenem/cilastatin and relebacbam in patients with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia
M. Patel* [Kenilworth, United States], P. Patel, N. Daryani, W. Copalu, P. Kulkarni, D. Hilbert, K. Young, M. Rizk

Pharmacokinetic/Pharmacodynamic benefit of prolonged ceftazidime/avibactam infusion
S. Baklouti, C. Massip, C. Mane, H. Guet-Revillet, M. Murris, D. Concordet, P. Gandia* [Toulouse, France]

Evaluating the predictive performance of ID-ODS software in critically ill patients for piperacillin: a comparison using IV bolus and continuous infusion data
A. Alsultan* [Riyadh, Saudi Arabia], S. Wallis, J. Lipman, J. Roberts

Development of a simultaneous population pharmacokinetic model for aztreonam-avibactam
R. Xie* [Singapore, Singapore], P. Chan, M. Mcfadyen, S. Rober

Ceftolozane/tazobactam probability of target attainment in patients with hospital-acquired pneumonia/ventilator-associated pneumonia
Z. Zhang, Y. Patel, H. Feng* [Kenilworth, United States], M. Johnson, J. Fiedler-Kelly, C. Bruno, E. Rhee, C. De Anda, W. Gao

Utilising the full potential of model-based dosing tables: an interprofessional collaboration to develop and integrate meropenem dosing tables into clinical routine
Abstract Categories 2020

1812 Once-daily dose ceftriaxone plus ampicillin: an alternative for Enterococcus faecalis infective endocarditis OPAT treatment


2657 Use of therapeutic drug monitoring to optimise cephazolin dosing in the treatment of methicillin-susceptible Staphylococcus aureus bacteraemia V. Venugopalan, S. Hernandez, K. Desean, C. Peloquin, K. Cherabuddi, A. Casapao* (Jacksonville, United States)

3028 Capillary micro-sampling versus conventional sampling to conduct a clinical pharmacokinetic study for meropenem in critically ill patients Y. Guerra Valero* (Queensland, Australia), J. Roberts, J. Lipman, C. Fourie, T. Storr, S. Wallis, S. Parker

3531 New evidence-based recommendations for cefazolin prophylaxis in patients undergoing cardiac surgery with cardiopulmonary bypass S. Zelenitsky* (Winnipeg, Canada), D. Calic, R. Ariano, R. Arora, H. Gracott

4024 Pharmacokinetic/pharmacodynamic simulation of cost-effective dosage regimens of ceftazidime/avibactam in patients with renal impairment L. Dhegiat, L. Bourguignon, M. Leray, T. Ferry, S. Goutelle* (Lyon, France)

4150 Impact of hypoalbuminemia and augmented renal clearance on fluoroquinolone plasma concentrations: a real-life retrospective study D. Marriott* (Sydney, Australia), A. Duckworth, G. Jones, C. Lau, D. Cottoneo

4362 Population pharmacokinetics of ceftriaxone administered as continuous or intermittent infusion in critically ill patients E. Leegwater* (The Hague, Netherlands), B. Kraajenbrink, D. Moes, I. Purmer, E. Wilms

4908 Plasma population pharmacokinetic modelling of ceffepime and enmetazobactam in patients with complicated urinary tract infections M. Machacke, F. Bernhard, M. Mameli, A. Kelley, P. Knechtle* (St. Louis, France)

5078 Large variability of unbound active fraction of ceftriaxone in contrast to ciprofloxacin in plasma of critically ill patients T. Ewoldt, A. Abdulla* (Rotterdam, Netherlands), D. Gommers, A. Muller, H. Endeman, B. Koch

5228 Variability in ceftazidime exposure and probability of target attainment of different dosing regimens of ceftazidime in critically ill patients with a proven or assumed Pseudomonas aeruginosa infection A. Werumeus Buning* (Amsterdam, Netherlands), C. Hadiamont, N. Lechner, P. Eibers, N. Juffermans, R. Mathot, R. Van Hest


8785 A Monte Carlo simulation modelling meropenem bolus to prolonged infusion dosing and expected suppression of resistance in Pseudomonas aeruginosa S. Moore* (Louisville (KY), United States), M. Kays, C. Cheatham

Session accepted as Paper Poster Session
Clinical trials: PK and dosing

Can gentamicin concentrations be used to estimate glomerular filtration rate in intensive care unit patients? A. Smekal* (Stockholm, Sweden), M. Swartling, M. Furebring, E. Nielsen, A. Larsson, M. Liptcsey

Retrospective evaluation of appropriate dosing of cefmetazole for invasive urinary tract infection due to ESBL-producing Escherichia coli K. Hayakawa, Y. Matsumura, Y. Hamada, S. Saito, M. Nagashima, K. Uemura, N. Ohmagari, Y. Dai* (Pittsburgh, United States)

Clinical and economic outcome evaluation of cefepime 4 grams/day extended infusion in pneumonia and sepsis E. Dionne, A. Khole, M. Campion* (Worcester, United States)

A phase I study in healthy volunteers to assess the absolute bioavailability of the bilayer tablet of sulopenem etzadroxil with probencid M. Dunne* (Old Saybrook, United States), M. Dai, R. Zhou, S. Aronin, J. Wald
Abstract Categories 2020

4426 Human mass balance study of enmetazobactam using 14C analysed by AMS
P. Matta* [Saint-Louis, France], S. English, P. Barth

5246 Factors associated with inadequate intravenous colistin dosages: results from a multi-centre, cross-sectional study
M. Mirabella* [Genoa, Italy], D. Giacobbe, A. Vena, C. Saffioti, M. Rinaldi, A. Losito, F. Raffaelli, M. Mikulska, M. Giannella, P. Viale, M. Tumbarello, M. Bassetti

5581 The trouble with gentamicin: a realistic evaluation exploring two distinct protocols for prescribing gentamicin in hospital settings
N. Dyar* [Barrack Road, United Kingdom], K. Mattick, R. Bethune

Session accepted as Mini-oral ePoster Session

119 Dynamic in vitro pharmacodynamics evaluation of piperacillin/tazobactam-tobramycin combination therapy against Escherichia coli and Klebsiella pneumoniae clinical isolates
C. Sumi* [Brisbane, Australia], A. Heffernan, S. Naicker, K. Cottrell, P. Harris, F. Sime, J. Roberts

1187 Effect of antiretroviral therapy on resistant Escherichia coli
R. Hammond* [St Andrews, United Kingdom], A. Coates, S. Gillespie

1224 Exebacase resensitises methicillin-resistant Staphylococcus aureus to oxacillin in a rabbit model of infective endocarditis
J. Oh, D. Lehoux, C. Cassino, W. Abdelhady, Y. Xiong, A. Bayer, R. Schuch* [Yonkers, United States]

1885 Optimising the combination of ceftazidime/avibactam and gentamicin against KPC-producing Klebsiella pneumoniae (KPC-Kp) with aminoglycoside-modifying enzymes
Y. Huang, K. Sokolowski, A. Rana, N. Kadiyala, Z. Bulman* [Chicago, United States], K. Krupp, E. Ozer, A. Hauser

4916 In vivo bactericidal activity of minocycline and rifampicin combination in a lung infection model in neutropenic mice

7002 Evaluation of the interactions of polymyxin B in combination with aztreonam, minocycline, meropenem and rifampicin against NDM- and OXA-48-like producing Escherichia coli
A. Olsson* [Uppsala, Sweden], M. Hong, H. Al Farsi, C. Giske, P. Lagerbäck, T. Tängdén

7570 Dose-dependent in vitro interactions of colistin with meropenem against carbapenem-resistant Gram-negative bacteria

Session accepted as Paper Poster Session

Drug combinations: 1+1 does not equal 2

2270 Colistin, turns active an otherwise ineffective rifampicin-linezolid combination in Gram-negatives
E. Armengol Rivero* [Barcelona, Spain], I. Perez-Guillen, M. Jorba, R. Herraez Moral, J. Sierra

2644 Pharmacodynamic analysis of meropenem in combination with a novel B-lactamase inhibitor ANT2681 against New Dehli metallo B-lactamase-producing Escherichia coli
A. Johnson* [Liverpool, United Kingdom], L. Mcintee, N. Farrington, A. Kirby, R. Kolamunnage-Dona, M. Everett, M. Zalacain, C. Sable, L. Ailboud, N. Harper, S. Das, W. Hope

Evaluation of omadacycline alone and in combination with rifampin against biofilm-producing Staphylococcus aureus and Staphylococcus epidermidis
T. Morissette* [Detroit, United States], K. Lev, R. Kebriaei, J. Abdul-Mutakabbib, M. Rybak

Predicting antistaphylococcal effects of daptomycin and gentamicin in an in vitro dynamic model using MICs determined at pharmacokinetically-derived concentration ratios
M. Golikova, E. Strukova, Y. Portnoy, S. Zinner* [Cambridge, United States], A. Firsov

MPC-based prediction of anti-mutant effects of linezolid/daptomycin combinations against Staphylococcus aureus: a study in an in vitro dynamic model
K. Alieva* [Moscow, Russian Federation], M. Golikova, E. Strukova, Y. Portnoy, S. Zinner, A. Firsov

Combined effect of fosfomycin and amikacin against fosfomycin-heteroresistant Escherichia coli isolates
I. Portilla Calderón* [Seville, Spain], M. Ortiz Padilla, B. De Gregorio-Iaria, V. Merino Bohórquez, J. Blazquez, J. Rodríguez-Baño, J. Rodríguez Martínez, A. Pascual Hernandez, F. Docabo Perez

Imipenem/sulbactam, a repurposed drug combination for the treatment of MDR Acinetobacter baumannii infections
M. Meiqi Tan, L. Phee, J. Standing, D. Wareham* [London, United Kingdom]

Activity of enmetazobactam in combination with cepafine in a murine urinary tract infection model challenged with an ESBL-producing isolate of Escherichia coli
C. Vingsbo Lundberg, A. Belley, P. Knechtle* [St. Louis, France]

Antibacterial activity of aztreonam-epigallocatechin gallate combinations versus multidrug-resistant strains of Acinetobacter baumannii
J. Betts, K. Lucassen, J. Salgueiro-Bades, M. Hornsey, H. Seifert, R. La Ragione, P. Higgins* [Cologne, Germany]
Cannabidiol synergic antimicrobial activity combined with polymixin B (PB) against PB susceptible and resistant Gram-Negative bacilli
N. De Lima Martins Abichabki* [Ribeirao Preta, Brazil], L. Zacharias, T. Ogasawara, F. Campioni, A. Seribelli, J. Falcão, A. Zuardi, J. Hallak, J. Crippa, A. Darini, L. Andrade

Efficacy of ceftolozane-tazobactam in combination with colistin against extensively drug-resistant Pseudomonas aeruginosa including high risk clones, in an in vitro pharmacodynamic model

Antimicrobial combination activity of vancomycin and antimalarial quinacrine against methicillin-resistant Staphylococcus aureus isolated from infected diabetic foot ulcers
A. Oliveira Da Silva* [Vila Real, Portugal], D. Correia, V. Silva, J. Carvalhal, A. Castro, G. Igrejas, R. Rego, P. Poeta

In vitro activity of imipenem/relebactam among Gram-negative clinical isolates in two Spanish tertiary hospitals
M. Perhuelas Martínez, C. García Salguero, M. Ihiaga, F. Candel* [Madrid, Spain], J. Del Pozo, E. Culebras

Combinations activity of azithromycin and colistin against colistin-resistant Klebsiella pneumoniae in a murine model of urinary tract infection
R. Odreda, D. Corbett, A. Coates, D. Molnar, Y. Hu, P. Warn, P. Thommes*[Cheshire, United Kingdom]

Glutoxin, a new candidate against methicillin-resistant Staphylococcus aureus showing synergistic effect with classical antimicrobial drugs in Caenorhabditis elegans infection model
P. Estebon*[Zaragoza, Spain], S. Redrado, L. Comas, C. Seral, J. Pardo Jimeno, M. Arias, E. Gálvez

Evidence from in vitro pharmacokinetic/pharmacodynamic studies on polymyxin-based combination therapies to treat infections due to carbapenem-resistant Gram-negative bacteria
M. Chiamenti* [Mantova, Italy], D. Bragantini, L. Scudeller, L. Paddock, F. Franceschi, S. Ellis, M. Sanguinetti, G. Menchinelli, A. Savoldi, E. Righi, E. Tacconelli

Pharmacodynamic properties of amoxicillin-clavulanic acid in a neutropenic mouse thigh infection model
A. Muller*[The Hague, Netherlands], W. Kloezen, B. De Winter, A. Van Der Meijden, H. Van Der Spek, M. Ten Kate, S. Van Den Berg, J. Meletiadis

Tackling resistance to carbapenem and colistin in clinical isolates of Acinetobacter baumannii
R. Ravichandran, D. Machado* [Lisbon, Portugal], M. Viveiros, C. Kroeger, M. Martins

Impact of an antimicrobial stewardship team on the de-escalation of carbapenem use in a tertiary hospital
M. Maeda*[Tokyo, Japan], Y. Nagatomo, Y. Naita, E. Akima, K. Nakane, K. Ugojin, M. Yoshikawa, T. Takuma, I. Tokimatsu, Y. Niki

Essential human resources for antimicrobial stewardship teams in Japan: estimates from a nationwide survey

Design and implementation of a Real-Time Carbapenem List (RTCL) using Electronic Patient Record (EPR) to enable Post Prescription Review and Feedback (PPRF) as a carbapenem stewardship strategy for resource-constrained antimicrobial stewardship team
C. Hickey*[Dublin, Ireland], M. Kelly, G. Courtney, K. Flannery, B. Boyle

Mandatory computerised decision support system is necessary for sustained control of carbapenems and piperacillin-tazobactam usage in a multi-faceted hospital antimicrobial stewardship programme: interrupted time series with segmented regression analysis
B. Chua*[Singapore, Singapore], S. Heng, L. Ang, S. Tan, H. Tay, M. Yap, J. Ouek, C. Teng, B. Young, R. Lin, B. Ang, T. Lee, D. Ly, T. Ng

Multidisciplinary treatment model led by infectious physician reduce the unreasonable use of antibiotics and improve the efficacy in the treatment of patients with diabetic foot infection
L. Xianguan*[Beijing, China], X. Qi, S. Tian, S. Jiang, R. He

Outcomes of the antibiotic stewardship programme in a teaching hospital of southern Italy: an interrupted time-series analysis
M. Macera*[Naples, Italy], F. Calò, L. Onorato, N. Coppola

Impact of antibiotic stewardship programme in an intensive care unit in Brazil
W. Freitas*[Rio de Janeiro, Brazil], M. Silvana Alves, S. Souer

Epidemiology and management of pneumonia based on data entry in a computerised decision support system for antimicrobial prescriptions: a retrospective study
G. Catho*[Geneva, Switzerland], A. Ranzani, J. Strinemann, V. Prendki, B. Huttner

Adherence to antibiotic guidelines at a Danish university hospital, a quantitative and qualitative prospective study
P. Rasmussen*[Aalborg, Denmark], S. Sørensen, L. Mygind
3160 Implementing antibiotic stewardship in humanitarian contexts: MSF’s experience
A. Filali* [Paris, France], R. Kanapathipillai, L. Noonan, B. Molla, J. Michel, N. Hurtado, M. Nada, C. Mills

3423 Setting up antimicrobial stewardship programme in tertiary area hospitals in India
K. Walia* [New Delhi, India], V. Ramasubramanian, V. Ohri

3499 Improving the adequacy of empirical antimicrobial therapy at regional level in bacteriaemia due to Escherichia coli of urinary source: an intervention of the VINCat programme (infection control and antimicrobial stewardship Catalan programme)

3661 Review of the hospital empiric antibiotic guideline in treating community-onset bloodstream infection in a Singapore tertiary hospital
G. Foo* [Singapore, Singapore], J. Samani, C. Teng, T. Tan, K. Chew

4018 Patient level predictors of vancomycin never events

4025 The antimicrobial stewardship in surgery (ASCHI) project: long-term follow-up
A. Chiesa* [Brescia, Italy], A. Zoncada, N. Brianse, E. Van Hauwermeiren, A. Ferrarese, S. Lorenzetti, C. Fornabaio, P. Lanza, A. Patrani, C. Tinelli, N. Pasquali, M. Rovatti, M. Martinotti, A. Pan

4085 Increase of parenteral antibiotic use in Japan could be explained by the society aging
R. Koizumi* [Tokyo, Japan], Y. Kusama, Y. Gu, M. Ishihane, Y. Muraki, D. Yamasaki, M. Tanabe, N. Ohmagari

4371 Persuading the prescriber: the impact of prospective audit with feedback on hospital antibiograms
M. Chatzopouloou* [Larissa, Greece], A. Kyriakaki, L. Reynolds

4914 Transforming care through data transparency: impact on cellulitis therapy standardisation
S. Minor* [Maitland, United States], N. Sankar, J. Burns, K. Calise, V. Herrera

5056 Infectious disease consultation reduces time to appropriate antimicrobial treatment in Gram-negative bacteriaemia: data from an area of high prevalence of antibiotic resistance
V. Da Prat* [Milan, Italy], L. Galli, M. Maro, P. Cichero, B. Castiglioni, C. Ottolini, C. Tassan Din, A. Poli, C. Ossi, A. Andolina, A. Ambrosio, A. Lazzarin, A. Castagna, P. Scarpellini, M. Ripa

5246 Prospective observational study of antimicrobial stewardship programmes in Brazil: preliminary results
R. Menezes, M. Gonçalves, M. Costa, E. Krummenauer, C. Reuter, J. Renner, M. Carneiro* [Santa Cruz do Sul, Brazil]

5779 Antibiotic use indicators: which and how? Pilot study of 3 indicators in French hospitals

6116 The appropriateness of prescribing antimicrobials in an infectious emergency outpatient department
M. Logar* [Ljubljana, Slovenia], I. Korpar, M. Uršič

6442 Personal experience and availability of surveillance data, diagnostics and therapeutics are the main drivers for treating carbapenem-resistant Gram-negative bacteria infections
A. Savoldi* [Verona, Italy], E. Carrara, L. Piddock, F. Franceschi, S. Ellis, E. Tacconelli

6712 Quality of documentation on antibiotic treatment in medical records: evaluation of the long-term impact of an antimicrobial stewardship intervention
C. Vercheval* [Lieu, Belgium], P. Damas, F. Frippiat

7022 Impact of the inpatient infectious disease consultations at a tertiary care university hospital
J. Choucair* [Beirut, Lebanon], D. Jaafar, M. Chedid, E. Haddad, G. Saliba, R. Waked

7176 Implementing an antibiotic stewardship programme without increasing the surgical site infection rate in a highly antibiotic-resistant setting
W. Harb, F. Mansour, J. Mourad, M. Trelles, A. Williams* [Luxembourg, Luxembourg]

7554 Persuasive antimicrobial stewardship intervention in the context of a KPC outbreak: a controlled interrupted time-series analysis
N. Roche Pereira* [Porto, Portugal], P. Figueiredo, S. Correa, S. Shahriari, J. Neves, J. Teixeira, J. Paiva, C. Alves, A. Azevedo

7559 Monitoring of interactions with clarithromycin: evaluation of routinely performed drug interaction checks
A. Weber* [Munich, Germany], J. Jung, R. Draenert

7639 SAVE: Stewardship Antibiotica Verona: a new model of stewardship to reduce antimicrobial overuse in a setting with high levels of antimicrobial resistance rates

7640 Antimicrobial stewardship in oral and maxillofacial surgery: melting the iceberg
I. Jaost* [Düsseldorf, Germany], M. Kempe, L. Schorn, C. Mackenzie

7697 Implementation of a homegrown electronic antimicrobial prescribing authorisation process at King Abdulaziz Medical City (KAMC) in Saudi Arabia
N. Shamas* [Riyadh, Saudi Arabia], M. Al Ahmadi, A. Alsaedi, D. Naeem, D. Alijefri, M. Aseeri, M. Alshamrani

7701 Digital antimicrobial dashboard facilitates antimicrobial stewardship in a large London teaching hospital
L. Whitney, M. Gilchrist* [London, United Kingdom], A. Chavda, A. Kinderterer, S. Mookerjee, A. Holmes
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8203 The role of co-morbidities in the prescription of carbapenemes
A. Makina* (Athens, Greece), G. Poulakou, E. Liakapoulou, A. Makina, A. Papadopoulos, L. Sybardi

8358 The case for infectious disease-centered antimicrobial stewardship: a 10-year experience at Saint George Hospital
S. Saliba* (Beirut, Lebanon), D. Zmerli, A. Chamieh, C. Afff, E. Azar

8426 Antimicrobial stewardship practices in Brazil: where are we?
R. Menezes, M. Gonçalves, M. Costa, E. Krummennauer, J. Renner, C. Reuter, M. Carneiro* (Santa Cruz do Sul, Brazil)

9412 A critical appraisal of the new antibiotic prescription chart using HAPPI (Hospital Antibiotic Prudent Prescribing Indicators) in a large UK district hospital
A. Liu* (Cheltenham, United Kingdom)

9575 Clinical and financial impact of an empiric antibiotic prescribing policy: single department experience
L. Melo, M. Barosa, R. Marques* (Amadora, Portugal), J. Delgado Alves

9596 eHealth-based antimicrobial stewardship programme focused on individual prescriptions assessment: sustainability at 4 years
C. Palos* (Loures, Portugal), L. França, P. Rodrigues, R. Tavares, A. Silva

Session accepted as 2-Hour Oral Session
Hospital antimicrobial stewardship interventions: models, tools, experience, impact!

8426 Antimicrobial stewardship practices in Brazil: where are we?
R. Menezes, M. Gonçalves, M. Costa, E. Krummennauer, J. Renner, C. Reuter, M. Carneiro* (Santa Cruz do Sul, Brazil)

9596 eHealth-based antimicrobial stewardship programme focused on individual prescriptions assessment: sustainability at 4 years
C. Palos* (Loures, Portugal), L. França, P. Rodrigues, R. Tavares, A. Silva

Session accepted as Mini-oral ePoster Session
From new TDM technology to optimised dosing

318 Renal function and albumin are drivers for exposure of fluoroquinoloxin in critically ill patients
N. Jager* (Amsterdam, Netherlands), R. Van Hest, R. Brüggemann, J. Lipman, J. Roberts

1153 Continuous infusion and outpatient parenteral antimicrobial therapy with ceftazidime-avibactam: evaluation of efficacy based on therapeutic drug monitoring
V. Gancette, N. Layios, F. Frippiat* (Liège, Belgium)

1334 Administration of ceftazidime to patients undergoing haemodialysis: are trough levels consistently above the EUCAST breakpoints for Enterobacteriales and Pseudomonas?

1419 Dose optimisation of cefotaxime in critically ill patients: a population pharmacokinetic study
E. Roelofs* (Zuid Holland, Netherlands), B. De Winter, A. Abdulla, H. Endeman, A. Dijkstra, A. Muller, B. Koch

1904 The positive impact of infectious diseases consultation on antimicrobial appropriateness in hospitalised patients with antimicrobial stewardship oversight: a propensity-score matched study
J. Bark* (Baltimore, United States), K. Claesys, E. Heil, M. Banoub, S. Leekha, J. Sarkin, M. Kleinberg

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<td>James Hegarty* [Cork, Ireland], M. O’Donnell, B. Healy, C. Hill, P. Ross, M. Rea, R. Farquhar, L. Chesnel</td>
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<td>2726</td>
<td>In vitro activity of lefamulin against isolates commonly causing community-acquired pneumonia collected during the SENTRY surveillance programme 2015–2019 in Europe</td>
<td>S. Paukner* [Vienna, Austria], S. Gelone, S. Arends, H. Sader</td>
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<td>Dihydropyridine-class antihypertensive drugs exhibit strong bactericidal activities against Helicobacter pylori and significantly reduce gastric colonisation in mice</td>
<td>A. González Rodríguez* [Zaragoza, Spain], J. Casado, E. Chueca, S. Saillias, A. Velázquez-Campaq, V. Espinosa Angarica, L. Benezet, J. Guignard, A. Giese, J. Sancho, P. Lehours, A. Janas</td>
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<td>In vitro activity of eravacycline and comparators against 931 non-fastidious and 323 fastidious clinical isolates from China</td>
<td>Y. Yang* [Shanghai, China], Q. Shi, Y. Sun, Y. Zheng, D. Dong, Y. Guo, D. Zhu, F. Hu</td>
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<td>3489</td>
<td>Assessment of ceragenin CSA-131-poloxamer for treatment of Stenotrophomonas maltophilia infections as a potential antimicrobial agent</td>
<td>D. Ogarder* [Istanbul, Turkey], C. Bozkurt Guzel, P. Savage, E. Demir, Z. Erturan</td>
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<td>In vitro activity of carbapenemase-producing Enterobacteriales to mecillinam</td>
<td>F. Fuchs* [Cologne, Germany], A. Hamprecht</td>
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<td>Impact of suppression of envelope stress responses on bacterial sensitisation to antimicrobial agents</td>
<td>E. Recacha* [Seville, Spain], S. Díaz Díaz, J. Machuca Bárdena, A. García-Duque, F. Docobo Perez, A. Pascual Hernandez, J. Rodríguez Martínez</td>
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<td>Analysis of the microbiological data from the delafloxacin (DLX) phase III community-acquired bacterial pneumonia (CABP) trial using European analysis sets</td>
<td>S. Mccurdy, L. Lawrence, S. Cammarata, A. Nuti, D. Zinzi* [Pomezia, Italy]</td>
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<td>4125</td>
<td>Assessment of antimicrobial molecules and bacteriocins isolated from Pseudomonas species for activity against multidrug-resistant bacteria</td>
<td>S. Adufa-Appaegue* [London, United Kingdom], PWilson, S. Ali, S. Yui</td>
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4720 Antimicrobial activity of enacyloxin Ila and gladiolin against the urogenital pathogens Neisseria gonorrhoeae and Ureaplasma species
N. Heath, R. Rowlands, G. Webster, E. Mahenthiralingam, M. Beeton* [Cardiff, United Kingdom]

4843 Novel small-molecule inhibitors of bacterial lipoprotein transport against Enterobacteriaceae

4937 Rifaximin leads to eradication of KPC Klebsiella pneumoniae gut colonisation in a rice model
E. Xenofontos, G. Reniers, D. Draggit, K. Synadinou, L. Sabokos, E. Giamarellos-Bourboulis* [Chaidari, Greece]

5167 Omadacycline in a comparative analysis of in vitro activity on Clostridioideae difficile isolates from Stockholm, Sweden
A. Comporale* [Stockholm, Sweden], C. Tellapragada, C. Nord, C. Giske

5483 Molecular characterisation of Fusarium oxysporum species complex isolates from the United States and susceptibility profile of the investigational antifungal olorofim
H. Badali* [San Antonio, United States], C. Gibas, H. Patterson, C. Sanders, J. Mele, H. Fan, N. Wiederhold

5509 Comparison in vitro activity of ceragenins for treatment of Burkholderia cepacia complex infections
E. Demir* [Istanbul, Turkey], D. Ogardi, D. Attay, P. Savage, C. Baskurt Guzel

5572 Effectiveness of ceftazidime-avibactam in a tertiary hospital of Spain
M. Aguirregabiria, M. Antona Urieta, L. Lopez Soria, J. Goikoetxea, M. Castaño Lopez, J. Barrios Andrés*

5599 Evaluation of in vitro activity of new polymyxin B analog SPR206 against clinical multidrug-, colistin- and tigecycline-resistant Gram-negative bacilli
Y. Zhang* [Beijing, China], C. Zhao, Q. Wang, X. Wang, H. Chen, H. Li, F. Zhang, H. Wang

6231 Screening research of antibacterial potential of selected released-active forms of antibiotics
N. Petrova* [Moscow, Russian Federation], E. Demir, A. Emelyanova, E. Kardash, S. Tarasov

6897 Synthesis and antibacterial evaluation of 9-substituted palmitate analogues as a new class of anti-H. pylori agents targeting urease
W. Yanxiang* [Beijing, China], J. Pang, T. Fan

7264 A broad-spectrum bacterial gyrase inhibitor with a novel scaffold
A. Vassort* [Marcy l’Étoile, France], D. Knafl*, C. Roma-Rodrigues, M. Castanheira* [North Liberty, United States], M. Martínez Guitián, J. Arca Suárez, C. Gonzalez-Bello, M. Ferreira, C. Aguiar, C. Carneiro, M. Oliveira, L. Tavares, F. Aires Da Silva, S. Aguair

7461 The antimicrobial role of a commonly used mucolytic agent in Chlamydia pneumoniae infection
D. Kárai, D. Paróczai, D. Vírők, V. Endresz, K. Burian* [Szeged, Hungary]

7942 Drug repurposing as an effective strategy to treat multidrug-resistant infections: teaching old drugs new tricks
D. Alves Ferreira* [Dublin, Ireland], C. Roma-Rodrigues, P. Baptista, A. Fernandes, M. Martins

8046 SOS response to a novel inhibitor of DNA replication
S. Renard* [Lyon, France], V. Bazin, F. Davy

8078 Next-generation sequencing for the research and development of novel antibiotics
C. Monlong, A. Delherme, M. Deuez, C. Tailliez, T. Vermon, M. Mourez, S. Coyne, E. Lessoud* [Marcy l’Étoile, France] In vitro antimicrobial activity of liposomal cetriaxone and liposomal amoxicillin and clavulanic acid against clinical strains isolated from companion animals with urinary tract infections
M. Ogren* [Caravelos, Portugal], M. Gaspar, S. Gil, M. Ferreira, C. Carneiro, M. Oliveira, L. Tavares, F. Aires Da Silva, S. Aguair

8424 Dananase: discovery of a novel Pseudomonas aeruginosa active polypeptide type-1 synthetase
D. Krafft* [Vienna, Austria], G. Mitulovic, P. Pichler, T. Reiter, L. Wagner, W. Winnicki

8429 Development of novel inhibitors of metallo-β-lactamases in carbapenem-resistant Gram-negative pathogens
V. Savage* [Macclesfield, United Kingdom], N. Ooi, A. Wilkinson, R. Newman, V. Lee, K. Maskew, N. Chalam-Judge, D. Orr, A. Bunt, S. Lee, D. Lindsay, I. Cooper

News in beta-lactamase inhibitors

1853 Activity of the β-lactamase inhibitor LN-1-255 against plasmid-mediated Class C cephalosporinases enzymes from Enterobacteriaceae
J. Vazquez-Ucha* [A Coruña, Spain], C. Lasarte, M. Martinez Guiltián, J. Arco Suárez, C. Gonzalez-Bello, G. Bou Arevalo, A. Beceiro

2113 Activity of novel β-lactamase inhibitor QPX7728 combined with various β-lactams against Enterobacterales collected from urinary tract infections, including β-lactamase-producing isolates
M. Castonheira* [North Liberty, United States], J. Lindley, H. Becker, R. Mendes, O. Lomovskaya

2206 Development of novel inhibitors of metallo-β-lactamases in carbapenem-resistant Gram-negative pathogens
V. Savage* [Macclesfield, United Kingdom], N. Ooi, A. Wilkinson, R. Newman, V. Lee, K. Maskew, N. Chalam-Judge, D. Orr, A. Bunt, S. Lee, D. Lindsay, I. Cooper

2397 Complementary inhibition of penicillin binding proteins by cephepine and zidebactam in presence of VIM-1 results in potent in vitro and in vivo bactericidal action against metallo-β-lactamase producing Pseudomonas aeruginosa
B. Moya, S. Bhagwat, G. Cabot* [Palma, Spain], G. Bou Arevalo, M. Patel, A. Oliver

2420 Meso-2,3-dimercaptosuccinic acid in combination with a carbapenem against metallo-β-lactamase producing Escherichia coli in murine peritonitis: a proof-of-concept
G. Cheminet* [Paris, France], V. De Lastours, N. Kieffer, F. Chau, K. Peoc’H, L. Massias, B. Fantin, P. Nordmann
Antimicrobial use for asymptomatic bacteriuria: first, do no harm
Y. Shpunt, I. Estrin, H. Saadon, G. Ben-Youssef, L. Goldstein,
D. Klafter, Y. Levi, S. Zilberman-Itskovich, D. Katz,
T. Lazarovitch, R. Zaidenstein, D. Marchaim*
(Beer Yaacov, Israel)

An opportunity for antimicrobial stewardship in urinary tract infections using rapid tests directly on urine samples
A. Alvarez-Uria* [Madrid, Spain], A. Burillo, L. Jiménez-
Navarro, N. Perez, C. Sánchez-Sánchez, M. Palomo,
M. Olmedo Samarpero, P. Muñoz, E. Bouza

Understanding antibiotic prescribing behaviours among hospital physicians and exploring strategies currently used by infectious diseases physicians to influence change: a qualitative interview study
V. Zanichelli* [Ottawa, Canada], C. Nott, J. Grimshaw,
J. Squires, J. Presseau, K. Suh

Characterising the patients with negative blood cultures as a potential target for stewardship [NOBACT project]: predictors for mortality in patients with obtained blood cultures
J. Girón Ortega* [Seville, Spain], R. Fernández Guerrero,
C. Sánchez Tembleque, M. Montes De Oca, E. Morte
Ramea, P. Luque Gómez, M. De Cueto-López, L. Suárdi,
F. Guerrero-Sanchez, Z. Palacios Baena, S. Jiménez-
Jorge, J. Rodriguez-Baño, P. Retamar Gentil

Antimicrobial stewardship opportunities at discharge: current prescribing at Boston Medical Centre
N. Rebold* [Boston, United States], K. Brade

Adequacy of antibiotic treatment in patients with negative blood cultures: identifying a novel target for antimicrobial stewardship [NOBACT study]
R. Fernández Guerrero* [Seville, Spain], J. Girón Ortega,
E. Morte Ramea, P. Luque Gómez, C. Sánchez Tembleque,
M. Montes De Oca, F. Guerrero-Sanchez, M. De Cueto-
López, L. Suárdi, Z. Palacios Baena, S. Jiménez-Jorge,
J. Rodriguez-Baño, P. Retamar Gentil

Why don’t hospital prescribers stop antibiotics when it would be safe to do so? Results of a discrete choice experiment
L. Roope, J. Buchanan, E. Morrell, K. Pouwels, K. Sivyer,
F. Mowbray, L. Abel, E. L.A. Cross, L. Yardley, T. Peto,
A. Walker, M. Llewelyn* [Brighton, United Kingdom],
S. Wordsworth

Hospital physicians’ perspective on antibiotic prescribing and antimicrobial resistance: a qualitative study
I. Christensen* [Sarpsborg, Norway], J. Haug,
J. Vildershøj Bjørnholt, D. Berild, B. Skodvin,
L. Jelsness-Jergensen
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9160 Assessment of de-escalation of empirical antimicrobial therapy in medical wards with high rates of multidrug-resistant bacteria: a multi-centre prospective cohort study

9494 Knowing local cumulative antibiogram: does it matter?
S. Carvalho, J. Caldas, R. Duro, C. Alves, N. Rocha Pereira* [Porto, Portugal]

9642 Systematic blood culture testing identifies a large proportion of patients in whom antibiotics could be safely discontinued: hospital-associated infections in a tertiary care hospital in Ethiopia

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Optimised prescribing through diagnostics

1822 TZ magnetic resonance technology in the diagnosis of sepsis and clinical impact in patient management
R. Paggi* [Perugia, Italy], G. De Socio, A. Belati, F. Allegrucci, A. Repetto, E. Cenci, A. Mencacci

2189 Is it safe to use rapid molecular tests for the detection of microorganisms in blood to optimise antimicrobial therapy in septic patients?
C. Rodrigues* [Sao Paulo, Brazil], T. Varejao Strabelli, R. Focaccia Siciliano, R. Zeigler, L. Højjar, A. Matos Porto

2925 Decrease in antibiotic days of therapy after notification of Clostridioides difficile carriage status: an interventional study
M. Gibboa* [Ramat-Gan, Israel], E. Meltzer, L. Maizels, S. Raibman-Spector, A. Segev, G. Rahav, G. Smollan, A. Leibowitz, G. Regev-Yochay

3461 Impact of restricting procalcitonin measurements on antibiotic use, clinical outcomes and costs in a Swiss tertiary care hospital: an interrupted time-series analysis
M. Abbas* [Geneva, Switzerland], N. Vennaz, E. Von Dach, N. Vuilleumier, S. Harbarth, B. Huttner

3778 High clinical impact on antimicrobial stewardship using multiplex PCR syndromic panels for severe community-acquired infections: a real-life experience
A. Alvarez-Uria* [Madrid, Spain], M. Valerio Minero, M. Kestler Hernandez, C. Sanchez-Sanchez, S. De La Villa Martinez, M. Veintimilla Yanez, M. Machado, P. Muñoz, E. Bouzo

4712 Impact of diagnostic and antimicrobial stewardship on time-to-appropriate therapy and clinical outcomes in infections caused by carbapenem-resistant Gram-negative organisms

4967 Communication of rapid identification results from positive blood cultures decreases time to effective therapy
R. Haj, L. Taggart, J. Forbes, E. Leung, J. Wu, R. Fattouh, L. Matukas* [Toronto, Canada]

7484 Evaluation of a new tool in diagnostic process of sepsis: reporting results to a smartphone
N. Zurita Cruz* [Madrid, Spain], A. Fraile Torres, T. Saler Manieiga, L. Fontan, S. Gómez De Frutos, A. Yarci Carrión, E. Navarro Lara, M. De Las Cuevas, L. Cardeño

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PK/PD studies and applications

24 High-dose ceftaroline fosamil recommendations for paediatric patients with Staphylococcus aureus complicated skin and soft-tissue infections using an extrapolation approach
P. Chan* [Sandwich, United Kingdom], M. Mcfadyen, A. Quaye, H. Leister-Tebbe, V. Hendrick, J. Hammond, S. Rober

Interim pharmacokinetic analysis of a multi-centre randomised open label phase IIb study in neonates to validate the meta-analysis population pharmacokinetic model used to simulate an optimised dosing regimen in neonates and infants aged < 90 days: the NeoVanc trial

Globally intravenous dosing of antibiotics in infants and children clusters around a small number of strategies but is not completely uniform

Probability of target attainment analyses inform ceftolozane/tazobactam dosing regimens in hospital-acquired pneumonia/ventilator-associated pneumonia patients with end-stage renal disease on intermittent haemodialysis
H. Feng* [Kenilworth, United States], Y. Patel, Z. Zhang, J. Fiedler-Kelly, C. Brunó, E. Rhee, C. De Anda, W. Gao

Cost-benefit analysis comparing trough, two-Level AUC, and Bayesian AUC dosing for vancomycin
B. Lee* [Los Angeles, United States], G. Fong, M. Bolaris, M. Neely, E. Minejima, A. Kang, G. Lee, C. Gong

Population pharmacokinetic modelling and simulations to support ceftazidime-avibactam dosing regimen for paediatric patients with nosocomial pneumonia
M. Mcfadyen* [Kent, United Kingdom], M. Vourvahis, M. Lovern, R. Franzese, T. Riccobene, T. Carrothers, M. Tawadrous

Development of intravascular microdialysis as a tool for therapeutic drug monitoring and intensive PK studies in children
V. Al Jalali* [Vienna, Austria], B. Wulkersdorfer, P. Matzneller, E. Lackner, S. Poschner, W. Jaeger, M. Zeitlinger
1587 The pharmacodynamics of omadacycline against *Escherichia coli* and *Acinetobacter baumannii* studied in an *in vitro* pharmacokinetic model of infection
A. Noel, M. Attwood, K. Bowker, A. Macgowan*
[Bristol, United Kingdom]

1693 *Imipenem/relebactam pharmacokinetic/pharmacodynamic analyses from an in vivo neutropenic murine thigh infection model*
M. Patel* [Kenilworth, United States], N. Daryani, H. Feng, D. Hilbert, M. Melchers, E. Movridou, K. Young, M. Rizk

1716 *Ceftobiprole and daptomycin concentrations in valve tissue in a patient with aortic native valve endocarditis*

1834 *Vancomycin pharmacokinetics in patients undergoing extracorporeal membrane oxygenation after 48 hours of treatment*
L. Herrera-Hidalgo, M. Munoz-Burgos, J. Laimerao, M. Mejias-Trueba, A. Garcia-Avello, J. Martinez, L. Lopez-Cortes* [Sevilla, Spain], M. Gil-Navarro

2086 *Pharmacokinetic model for intravenous vancomycin in pregnant rats and pups*
M. Pham* [Omaha, United States], S. Avedissian, G. Pais, M. Joshi, B. Griffin, J. Chang, K. Hlukhenka, W. Prozialeck, M. Scheetz

2050 *Prolonged versus intermittent infusion of beta-lactam antibiotics: a systematic review and meta-regression of bacterial killing in preclinical infection models*
S. Dhaese* [Ghent, Belgium], A. Heffernan, D. Liu, M. Abdul Aziz, V. Stove, V. Tam, J. Lipman, J. Roberts, J. De Waele

2368 *Comparison of intermittent versus continuous infusion vancomycin therapy for severe patients in intensive care unit*
C. Yamada, J. Telles* [Sao Paulo, Brazil], D. Santos, J. Cieslinski, V. Stadler Tasca Ribeiro, J. Gasparetto, F. Tuon

2727 *Exploring minocycline pharmacodynamics against *Acinetobacter baumannii* and *Staphylococcus aureus* in a lung model in neutropenic mice: clinical implications on optimal dosing regimens*

2782 *Amikacin probability of target attainment in critically ill oncological patients: results from a prospective observational cohort*
O. Borges, K. Migotto, J. Souza Framil, M. Campos, P. Carusa, J. Telles* [Sao Paulo, Brazil], I. Leonardo Franca Jr

2927 *Effect of augmented renal clearance on the extended-interval dosing of aminoglycosides in critically ill paediatric patients*
N. Rhodes* [Downers Grove, United States], S. Avedissian, A. Hadid, J. Bradley, J. Le

3146 *Extracorporeal membrane oxygenation does not impact the pharmacokinetics of liposomal amphotericin B*
C. Mane* [Toulouse, France], S. Ruiz, C. Monchaud, D. Concordet, G. Bernard, P. Gandia

3342 *Amikacin initial dosing in emergency surgery: pharmacokinetics and determinants of optimal dose S. Goutelle* [Lyon, France], G. Fritsch, M. Leray, C. Piron, C. Salvez, A. Frigeri

3588 *Pharmacodynamics of amikacin and fosfomycin combination therapy in neonatal sepsis modelled in a hollow fibre infection model*
C. Darlow* [Stockport, United Kingdom], F. Dacobo Perez, N. Farrington, A. Johnson, L. Mcentee, A. Jimenez-Valverde, J. Unsworth, R. Da Costa, S. Ellis, F. Franceschi, M. Sharland, L. Piddock, S. Das, W. Hope

4428 Does cefepime require dose adjustments in critically ill patients on extracorporeal membrane oxygenation? A pharmacokinetic study

4499 Treatment of urinary tract infections in haemodialysis patients: the controversy about antimicrobial urine concentration
W. El Nekidy* [Abu Dhabi, United Arab Emirates], A. Eshbair, M. Mooty, N. Attallah, A. Cherfan, F. Hijazi, I. Ghazi

4520 Investigating dynamic protein binding of clindamycin in vivo by means of intravasal microdialysis in healthy volunteers
B. Wulkers dorfer* [Vienna, Austria], S. Wicha, E. Kur dina, P. Matzneller, V. Al Jalali, M. Vossen, S. Riesenhuber, E. Lackner, C. Dorn, F. Kees, M. Zeitlinger

4658 *PK/PD of intravenous and oral fosfomycin in neonates with presumed serious bacterial Infection Z. Kane* [London, United Kingdom], S. Gastine, P. Williams, J. Berkley, S. Ellis, E. Correia, C. Darlow, W. Hope, M. Sharland, J. Standing

5008 Exploring minocycline pharmacodynamics against *Acinetobacter baumannii* and *Staphylococcus aureus* in a lung model in neutropenic mice: clinical implications on optimal dosing regimens
Simulated exposures of oritavancin in in vitro PK/PD models select for MRSA with reduced susceptibility to oritavancin but minimal cross-resistance or seesaw effect with other antimicrobials
B. Werth* [Seattle, United States], N. Ashford, J. Barreras Beltran, K. Penewit, E. Holmes, A. Waalke, S. Salipante

Population pharmacokinetics of cefazolin in paediatric patients undergoing cardiac surgery
S. Parker* [Brisbane, Australia], G. Moloney, B. Bierbach, J. Ungerer, J. Suna, A. Alphonso, J. Roberts

Beyond the minimal inhibitory concentration: novel pharmacokinetic/pharmacodynamic metrics quantify the exposure-effect relationship of levofloxacin- against fluoroquinolone-resistant Escherichia coli based on in vitro infection models
J. Seeger* [Berlin, Germany], R. Michelet, S. Guenther, C. Kloft

Obesity affects interstitial space fluid of subcutaneous adipose tissue concentrations of meropenem after single application: a controlled clinical trial

Cefepime 2g plus enmetazobactam 0.5g administered IV q8h achieves high probability of target attainment in patients with complicated urinary tract infections
J. Vollmer, M. Machacek, A. Kelley, P. Knechtle* [St. Louis, France]

Influence of extracorporeal membrane oxygenation on the pharmacokinetics of ceftolozane/tazobactam

Impact of pharmacist-driven antimicrobial stewardship interventions on multicomponent patient outcomes
E. Beasley, C. Georgescu, G. Suleyman, K. Cole* [Sylvania, United States]

Survey of attitudes, beliefs, and knowledge of community pharmacists in the United States on antimicrobial stewardship
D. Bowers* [Yakima, United States], C. Bran Morales, C. Daly, D. Jacobs

Organisation of an ID consultation: are medical reports more important than patients?
J. Tschapp* [Lausanne, Switzerland], B. Guery

Aims and challenges of founding a national network of young clinical microbiologists: a French experience

Outcomes of a pharmacist-led antimicrobial stewardship programme within a family medicine resident clinic
L. Dumkow* [Belmont, United States], L. Westerhof, T. Hanrahan, S. McPharlin, N. Egwuatu

Mapping the implementation of a clinical pharmacist-driven antimicrobial stewardship programme at a tertiary care centre in India
V. Nampaathi* [Kochi, India], S. Sudhir, M. Varsha, Z. Mohamed, V. Menon, E. Charani, S. Singh
Two in three final-year veterinary students demand improved education in rational antimicrobial use

Half of prescribed antibiotics are not needed: a pharmacist-led antimicrobial stewardship intervention and clinical outcomes in a referral hospital in Ethiopia

Real-world experience of dalbavancin use for the treatment of Gram-positive infections
N. Spernovasilis* (Heraklion, Greece), A. Mathioudaki, P. Ioannou, A. Gikas, G. Samonis, D. Kofteridis

De-escalation of carbapenems to ciprofloxacin in the treatment of bacteraemia caused by extended spectrum beta-lactamase-producing Enterobacteriaceae
J. Lim, W. Tong, J. Sheah, H. Shafi* (Singapore, Singapore), C. Teng

Efficacy of temocillin versus carbapenems for the treatment of extended spectrum beta-lactamase-producing Enterobacteriaceae urinary tract infections: a case control study
S. Gravier* (Colmar, France), T. Delory, D. Le Puart, G. Gaube, S. Siméon, B. Davido, S. Lejeune, E. Piet, R. Lepeule, P. Lesprit, M. Lafaurie

Treatment of bacteraemia caused by Enterobacter spp.: should the potential for AmpC induction dictate therapy?
G. Drozdinsky* (Petah-Tikva, Israel), A. Neuberger, M. Paul, D. Yahav

Efficacy of temocillin against multidrug-resistant Enterobacteriales: a retrospective cohort study
F. Leysour De Rohella, M. Etienne, S. Dabyat, I. Tret, M. Pestel-Caron, C. Caron, K. Alexandre* (Rouen, France)

Real-life dalbavancin use in acute bacterial skin and skin-structure infections and bone and joint infections: clinical experience at Florence university hospital (Italy)
N. Di Lauria* (Florence, Italy), F. Bartalesi, D. Bartolozzi, M. Cecchi, P. Corsi, A. Ipponi, F. Lagi, E. Mantengoli, A. Bartoloni

Retrospective analysis of intravenous fosfomycin use at Florence University Hospital, Italy: clinical and microbiological analysis
N. Di Lauria* (Florence, Italy), E. Mantengoli, N. Aiezza, A. Antonelli, S. Bresci, T. Giani, F. Lagi, K. Kaye, P. Patel, G. Rossolini, A. Bartoloni

A multi-centre study of dalbavancin use in Italy [DALBITA Study]: which could be the appropriate place for this easy-to-manage antibiotic to treat Gram-positive infections?
C. Aldieri* (Milan, Italy), F. Bai, F. Raumer, E. Di Meco, A. Cattelan, M. Moiali, P. Morelli, M. Rizzi, F. Castelli, M. Guglielmo, B. Menzaghi, G. Rizzardini, A. Saracino, A. Coscio, M. Puoti, A. D’Arminio Monforte, G. Marchetti

The 2020 Dutch working party on antibiotic policy guideline for empirical antibacterial therapy of sepsis in adults

Trimethoprim-sulfamethoxazole as de-escalation agent in bloodstream infections due to Enterobacter spp, Serratia marcescens and Citrobacter freundii

Optimising antimicrobial stewardship: an evaluation of temocillin in the treatment of Gram-negative bacteraemia
L. Cottom* (Glasgow, United Kingdom), L. Bagrade, R. Dhillon, J. Gillies, B. Jones
6. Fungal infection & disease

- Fungal disease epidemiology
- Diagnostic mycology (incl molecular)
- Antifungal drugs & treatment (incl clinical trials)
- Antifungal resistance & susceptibility testing (incl surveillance)
- Other
Session accepted as Paper Poster Session

**Antifungal stewardship, therapeutic drug monitoring and pharmacokinetics**

931 A multi-site evaluation of antifungal prescribing and the use of fungal diagnostics in critical care
C. Logan* [London, United Kingdom], C. Hemsley, A. Fife, J. Edgeworth, D. Wynnoil, P. Hopkins, F. Bicanic

986 Development of an antifungal stewardship programme at a London teaching hospital
L. Whitney, R. Wilson* [London, United Kingdom], F. Davies, M. Coleman, J. Woo, R. Polanicawarand, M. Gilchrist

1702 Evaluation of voriconazole therapeutic drug monitoring practice: experience of a tertiary referral centre
Y. Kwang, A. Nettuch, T. Lai, S. Chen, H. Kim* [Sydney, Australia], I. Sandaradura, J. Alffenaar

1765 Clinical feasibility of simultaneous microdialysis of voriconazole and its N-oxide metabolite at target site demonstrated by in vitro investigations
J. Schulz* [Berlin, Germany], R. Michelet, F. Kluwe, C. Klaft

1929 Antifungal cost in the patients with febrile neutropaenia episodes due to haematological malignancies
H. Gedik* [Istanbul, Turkey]

2533 The cost-effectiveness of isavuconazole compared to voriconazole, the standard of care in the treatment of patients with invasive fungal infection prior to differential pathogen diagnosis in Spain
J. Azanza, S. Grau Cerrato, L. Vázquez, P. Rebollo, C. Peral, L. Alejandra, V. Lopez Gomez* [Alcobendas, Spain]

3709 Posaconazole versus voriconazole as antifungal prophylaxis for invasive fungal diseases in patients with haematological malignancies

4311 Isavuconazole for the treatment of invasive fungal infection in solid organ transplant recipients: experience from a referral centre

5009 Pharmacokinetic variability and target attainment of fluconazole in critically ill patients
R. Van Daele* [Leuven, Belgium], J. Wauters, R. Brüggemann, R. Denoaz, M. Hayette, Y. Debaveye, I. Sriet

5180 A new Lichtheimia corymbifera mouse model close to human pathophysiology to test antifungal drugs
K. Brunet* [Poitiers, France], J. Martellosio, F. Arrivé, T. Brunet, I. Lamarche, S. Marchand, B. Rammaert

5566 Serum concentrations of intravenously administered posaconazole in critically ill patients
W. Heinzi* [Weiden, Germany], D. Wichmann, H. Klinker, S. Kluge

Session accepted as Paper Poster Session

**Aspergillus infections: not always the same!**

5831 Safety and efficacy of triazole use for prophylaxis and treatment of invasive fungal diseases in patients receiving gilteritinib, a novel tyrosine kinase inhibitor for the treatment of acute leukemia
M. Aleissa* [Boston United States], M. Luskin, B. Alshehri, H. Leblebijn, A. Mcdonnell, F. Marty

6803 Frequency and severity of potential drug-drug interactions before, during and after an antifungal stewardship pilot project
S. Lachenmayr* [Munich, Germany], A. Gretler, D. Strabach, H. Mannell, K. Berger, H. Ostermann

6969 Experience of 319 post-surgical abscesses: focus on empiric antifungal therapy
E. Taddei* [Roma, Italy], F. Giovanneness, E. Birocchi, R. Murri, L. Carelini, F. Taccari, R. Cauda, M. Fontoni

7211 Plasma exposures following posaconazole injection and delayed-release tablet
Y. Wang, S. Tsai, Y. Fu, P. Chen, S. Lin, Y. Chen, Y. Chen, S. Lin* [Taipei, Taiwan]

9280 Chitosan-coated magnetite nanoparticles as a biocompatible nystatin carrier: physicochemical characterisation and in vitro fungicidal determination
S. Yazdanpanah* [Shiraz, Iran], K. Zomorodian, H. Veisi, H. Veisi

9375 Invasive pulmonary aspergillosis after heart transplantation
K. Monosova* [Saint Petersburg, Russian Federation], M. Simonenko, Y. Sazonova, K. Zagarodnikova, L. Vasiljeva, R. Vadim, M. Bortsova, P. Fedotov

980 The Danish nationwide surveillance of azole-resistance in Aspergillus fumigatus: data from the first nine months
M. Risum* [Copenhagen, Denmark], R. Krøger Hare, J. Gertsen, L. Kristensen, F. Rosenvinge, S. Sulim, E. Marmolin, B. Røder, J. Bangsborg, E. Dzajic, M. Pedersen, K. Astvad, S. Andersen, M. Arendrup

3256 Relevance of EORTC-MSG criteria in invasive fungal infections in lung transplant recipients

3382 Invasive aspergillosis by cryptic Aspergillus species in a 700-bed third level hospital

4002 Aspergillosis complicating severe respiratory syncytial virus in intensive care unit patients: a retrospective cohort study
H. Nam* [Chicago, United States], M. Isom
Abstract Categories 2020

4246 Epidemiology of respiratory colonisations and infections caused by Aspergillus and non-Aspergillus moulds in lung transplant patients

4385 Emergence of cryptic Aspergillus species infection and importance of antifungal susceptibility testing
J. Tang* (Hong Kong, Hong Kong), C. Tsang, H. Ye, F. Xing, S. Lo, C. Xiao, A. Wu, A. Ngn, K. Law, Y. To, D. Sze, T. Hui, T. Zhu, C. Yao, B. Tse, S. Lau, P. Woo

4866 Invasive aspergillosis and influenza virus infection: an accidental relationship?

4939 Clinical, microbiological and molecular studies of invasive pulmonary aspergillosis caused by Aspergillus lentulus in China
S. Yu* (Beijing, China), M. Zhou, Y. Xu

5220 Prevalence of azole resistance in clinical Aspergillus fumigatus isolates in Greece

5557 Antifungal susceptibility of Aspergillus section Flavi clinical isolates in France
E. Bjenerontin* (Créteil, France), J. Costa, A. Benmostefa, B. Mousavi, N. Lin, C. Guillot, N. Ait-Ammar, J. Guillot, L. Delhaes, F. Botterel, E. Dannaoui

6944 Invasive CNS aspergillosis in non-neutropenic patients: a review of nine cases from North India
N. Gupta* (Manipal, India), A. Mittal, P. Kodan, N. Mundadan, R. Kumar, T. Kumar, G. Singh, D. Xess, P. Ramteke, M. Soneja

8473 Limitations of the diagnostic criteria for invasive aspergillosis in solid organ transplantation: a national cohort (DIASPERTOS study)

Keep the attention high on Putative Invasive Pulmonary Aspergillosis (PIPA) in medical wards and intensive care units: a four-year retrospective analysis
T. Lupia, S. Raviolo, A. Trentalange, A. Curtoni, R. Cavallo, F. De Rosa, S. Corcione* (Turin, Italy)

The emerging non-conventional invasive aspergillosis: 5-year experience

9599 The burden of chronic pulmonary aspergillosis on the respiratory service at a district general hospital
F. Maghrabi* (Manchester, United Kingdom), R. Cade, C. Kosmidis, R. Sundar, D. Denning

Session accepted as Paper Poster Session

Candida and Cryptococcus: treatment options and novel agents

988 Clinical experience of oral ibrexafungerp for treatment of four patients with invasive candidiasis from the FURI study
J. Prattes* (Graz, Austria), C. Zurl, N. Azie, D. Angulo Gonzalez, R. Krause

Candida spp. in the respiratory tract secretions of critically ill patients and the impact of antifungal treatment
N. Spernovasilis* (Heraklion, Greece), A. Voudaski, C. Alexeopoulos, A. Papazachariou, E. Paraschou, A. Achyropoulou, S. Maraki, D. Ieradiakonou, G. Samonis, D. Kofeidis

Treatment status and prognosis of 203 cryptococcosis in non-human immunodeficiency virus-infected and nontransplant patients
S. Yi* (Shanghai, China), B. Hu

Empiric treatment with fluconazole, as compared to echinocandins or amphotericin B, was associated with lower mortality among intensive care unit patients with sepsis due to candidaemia
M. Papadimitriou Olgiviers* (Lausanne, Switzerland), A. Spiliopoulos, F. Kolontsiou, A. Lambropoulou, V. Karamouzos, A. Georgakopoulou, I. Spiliopoulos, F. Filgo, M. Marangos, M. Christofidou

Synthesis of nano-capcsulated caprylic acid: evaluation of antifungal activity and its effect on EFG1 gene expression in Candida albicans
M. Roudbar* (Tehran, Iran), S. Roudbar Mohammadi, R. Zarimeidi, S. Mardani
Severe cryptococcal meningoencephalitis with large vessel vasculopathy and multi-territory cerebral infarcts
C. Sun* [Adelaide, Australia], M. Kernich, N. Chia, R. Nelson

Progressive disseminated histoplasmosis in a population with HIV/AIDS in the Colombian coffee triangle
J. Hogas Pulgarin* [Medellin, Colombia], A. Alzate, G. Moreno, J. Sierra, A. Jaramillo Torres

Chronic mucocutaneous candidiasis in children in Saint Petersburg, Russia
O. Kozlava, E. Frolova, T. Bogomolova, E. Suspsitin, T. Gabrusskaya, E. Dosavskay, N. Klimka*
[Saint Petersburg, Russian Federation]

Personalised prediction with machine learning approach to predict candidaemia in medical wards
A. Ripoli, E. Sazio, S. Sbrana, G. Bertolino, C. Pallotto, S. Meini, B. Viaggi, G. Cardinali, C. Tascini* [Naples, Italy]

In vitro activity of novel biofilm-disrupting agents against Candida auris and other Candida species
J. Vazquez* [Augusta, United States], S. Wokade, E. Manavathu, M. Bogacz, M. Myntti, S. Thompson

S. Emerj, M. Vannini, V. Mondain, N. Retur, R. Collomp, L. Hassine, F. Lieutier-Colas* [Strasbourg, France]

Analysis of outcomes by geographic region of enrolment in STRIVE, the phase II of rezafungin for the treatment of candidaemia and invasive candidiasis
J. Fortun Abete* [Madrid, Spain], A. Skoutelis, R. Viani, T. Sandison

Early empirical anidulafungin therapy reduces the prevalence of invasive candidiasis in critically ill sepsis patients: a retrospective study
M. Hason* [Dhaka, Bangladesh], S. Neelotpol, R. Rabbani

Clinical outcome of early central venous catheter removal in children with candidaemia: a retrospective multi-centre study
N. Poey* [Paris, France], M. Caseris, A. Faye, S. Bonacorsi, M. Lorrat, J. Toubiana, P. Mariani

In vitro activity of novel propionohydrazide derivatives BG-354 and KTU-341 against multidrug-resistant Candida auris
P. Kavaliauskas* [New York, United States], B. Grybaite, K. Anusevicius, V. Mickevicius, R. Planienien
R. Grigaleviciute, T. Walsh, R. Petraitiene, V. Petraitis
K. Anusevicius, V. Mickevicius, R. Planienien
P. Kavaliauskas* [New York, United States], B. Grybaite

Screening the antifungal activities of monoterpenes and their isomers against Candida species
K. Zomorodian* [Shiraz, Iran], A. Ir. S. Yazdanpanah
Comparison between visual reading, smartphone image and digital scanner interpretation of lateral flow device result for detecting Aspergillus-specific IgG
B. Wilopo* [Manchester, United Kingdom], E. Hunter, P. Goodwin, E. Phillips, G. Platt, M. Richardson, D. Denning

Evaluation of two lateral-flow assays with galactomannan in BAL fluids for the detection of invasive pulmonary aspergillosis: a retrospective two-centre study

Interest of immunoblotting with Aspergillus fumigatus western blot IgE assay for the differential diagnosis of IgE sensitisation and allergic broncho pulmonary aspergillosis
R. Piarroux* [Lyon, France], S. Ranque, J. Vitte

Aspergillosis IgE sensitisation and allergic broncho pulmonary western blot IgE assay for the differential diagnosis of invasive pulmonary aspergillosis: a retrospective two-centre study

Evaluation of a new lateral-flow test for detection of galactomannan in blood for the diagnosis of pulmonary invasive aspergillosis in patients with hematological neoplasms

Baseline activity test use for identification of fungal sensitisation in severe asthma patients
Y. Kazzola, E. Frolova, A. Uchevatkina, L. Filippova, O. Aak, G. Soloveva, V. Kuznetsov, N. Vasilyeva, N. Klimko* [Saint Petersburg, Russian Federation]

Diagnostic value of the IMMY Aspergillus LFA on bronchoalveolar lavage fluid of intensive care patients
A. Dunbar, T. Mercier* [Leuven, Belgium], V. Veldhuizen, B. Rijnders

Bismethylgliotoxin is detected in serum from oncohaematological neutropaenic paediatric patients: presentation of two cases of probable IPA with negative galactomannan and positive bmGT

Comparison of diagnostic performance of two Aspergillus antigen ELISAs

Clinical evaluation of the ID-fungi plates for direct identification of dermatophytes on nail, hair and skin samples by MALDI-TOF MS
R. Sacheli* [Liege, Belgium], S. Winandy, A. Adjetey, R. Darouf, O. Legras, C. Meex, L. Marechol, J. Arrese, M. Hayette

Direct identification of Candida species from positive blood culture by MALDI-TOF MS using a commercial pre-treatment kit
Y. Yamagishi* [Aichi, Japan], T. Mouri, H. Suematsu, A. Masuya, K. Ashizawa, Y. Shimpo, H. Mikamo

Species delimitation of clinically challenging fungi by Orbitrap ultra high-resolution mass spectrometry: a case study in Mucor, Rhizopus and Lichtheimia
I. Moser, A. Jamaliam* [Landsmeer, Netherlands], B. Stielow, J. Knuuttila, A. Giraldo Lopez, S. De Hoog, J. Freeke

Comparative evaluation of the Bruker Biotyper and Vitek MS MALDI-TOF MS systems for identification of non-albicans Candida and uncommon yeast isolates
L. Teke* [Istanbul, Turkey], B. Bayraktar, A. Boris

Rapid diagnostic test: identification of Candida spp. directly from the blood culture bottle using short-term subculture incubation and MALDI-TOF MS in a routine microbiology laboratory
A. Celestino De Souza P.Barth* [Porto Alegre, Brazil], P. De Souza Sampaio, L. Lutz, V. Aquino, E. Wurdig Roesch, D. Castro Pereira

Optimisation of culture protocol for the recovery of fungal pathogens from expectorated sputum of cystic fibrosis patients
W. Memon* [Baltimore, United States], R. Abellera, S. Zhang, R. Marayan

Evaluation of the performance of Vitek MS and Bruker MS on the identification of Candida haemulonii species complex
X. Hou* [Beijing, China]

Candida auris species and lineage identification from plate and blood cultures applying Orbitrap ultra high-resolution mass spectrometry
A. Jamaliam* [Landsmeer, Netherlands], J. Freeke, B. Stielow, I. Moser, A. Giraldo Lopez, H. Friedricht, J. Meis, S. De Hoog

Ultra high-resolution mass spectrometry database improves identification of clinical yeasts from blood cultures by the Action system
A. Jamaliam* [Landsmeer, Netherlands], J. Freeke, I. Moser, H. Friedricht, J. Knuuttila, A. Rantakari, J. Salo, K. Haapasalo-Tuomainen, B. Stielow, S. De Hoog

High-resolution mass spectrometry database (Acron) improves identification of clinical yeasts
J. Freeke* [Vantaa, Finland], A. Jamaliam, I. Moser, A. Giraldo Lopez, J. Knuuttila, O. Niiranen, B. Stielow, S. De Hoog
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<td>329</td>
<td>Rapid semi-quantitative format PCR for the detection of <em>Pneumocystis jirovecii</em> replacing the direct examination</td>
<td>A. Coste, R. Brauillet, J. Diserens, M. Moraz, F. Lamothe, P. Hauser, G. Greub, K. Jaton* (Lausanne, Switzerland)</td>
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<td>505</td>
<td>Potential value of qPCR for the early detection of <em>Mucorales</em> in high-risk patients</td>
<td>D. Schmidt* (Essen, Germany), U. Scharrmann, J. Buer, P. Roth</td>
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<td>873</td>
<td>Development of a routine laboratory test enabling the detection of dermatophytes as well as the identification of <em>Trichophyton rubrum</em> by means of duplex real-time PCR from mycological samples and cultures</td>
<td>T. Pablo, F. Decruyenaere, M. Meo, A. Mzabi* (Dudelange, Luxembourg), M. Perrin</td>
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<td>1779</td>
<td>Cross-platform comparison of one qPCR assay with four leading technologies and six master mixes for the detection of <em>Pneumocystis jirovecii</em></td>
<td>S. Dellière* (Paris, France), M. Gits-Muselli, S. Bretagne, A. Alainia</td>
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<td>2399</td>
<td>Examining discordance in blood culture and T2 positivity in the detection of candidaemia: modelling the odds of blood culture and T2 discordance as a function of candidaemia risk factors</td>
<td>A. Vahia* (Detroit, United States), G. Alangaden, G. Suleyman</td>
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<td>3518</td>
<td>Evaluation of two <em>Aspergillus</em> PCR assays testing of bronchoalveolar lavage fluid and serum for diagnosis of chronic pulmonary aspergillosis</td>
<td>Z. Li* (Guangzhou, China), P. Zeng, S. Li, Z. Wang, F. Ye</td>
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<td>3620</td>
<td>Commercial real-time PCR implementation for rapid diagnosis of onychomycosis: a new workflow in a clinical laboratory</td>
<td>A. Blanco Suárez* (Viladecavalls, Spain), E. Cuchi Burgos, R. Rubio Casino, M. Ballesteros Tellez, P. Perez</td>
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<td>3864</td>
<td>Development and validation of a specific real-time PCR assay for the rapid detection of <em>Candida auris</em></td>
<td>A. Ibrahim, S. Baron, H. Youssfi, R. Lalaoui, L. Hadjadji, S. Morand, J. Rolain* (Marseille, France), F. Bittar</td>
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<td>4424</td>
<td>Comparison of two commercially available qPCR kits for the detection of <em>Candida auris</em></td>
<td>A. Brunke* (Cologne, Germany), J. Sattler, G. Plum, P. Wiegelt, O. Kurzai, J. Meis, A. Hamprecht</td>
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<td>4460</td>
<td>Primary evaluation of three <em>Aspergillus</em> PCRs compared to galactomannan assay</td>
<td>L. Verdurme* (Saint-Ouen-l’Aumône, France), M. Gama, E. Hedbaut</td>
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<td>4719</td>
<td>Rapid diagnostics of <em>Pneumocystis jirovecii</em>: so far not good enough</td>
<td>A. Sand* (Oslo, Norway), A. Ingebretsen, J. Vildershøj Bjørnholt</td>
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<td>5530</td>
<td>Cycle of quantification (Cq) does not differentiate colonisation from <em>Pneumocystis jirovecii</em> pneumonia, using real-time PCR</td>
<td>P. Basazemajja, T. Schuurs, A. Stellingwerff, A. Al Moujahid* (Leeuwarden, Netherlands)</td>
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<td>6065</td>
<td>Presence and distribution of fungal species and dermatophytes in nail and skin samples</td>
<td>L. Marki, A. Brachner, B. Ronacher, H. Enroth* (Skövde, Sweden)</td>
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<td>6106</td>
<td>Diagnosis of deep cutaneous mycoses in kidney transplant recipients by clinical metagenomics approach</td>
<td>E. Sitterlé, G. Gricourt, D. Vanessa, A. Scemla, J. Pawlotsky, M. Bougnoux, C. Rodriguez* (Creteil, France)</td>
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<td>6272</td>
<td>Evaluation of the combined use of galactomannan antigen and <em>Aspergillus</em> DNA real-time PCR detection in laboratory diagnosis of invasive aspergillosis among haematological patients</td>
<td>G. Vrioni* (Athens, Greece), C. Tsiamis, M. Mavrouli, K. Theodoridou, V. Kapsimali, A. Tsakris</td>
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<td>7227</td>
<td>Development of two new techniques based on real-time PCR for the detection of <em>Candida auris</em> in clinical settings</td>
<td>L. Bernal Martinez* (Madrid, Spain), A. Mesa, L. De Francisco, A. Gomez Lopez, M. Buitrago</td>
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<td>7227</td>
<td>Comparison of <em>Candida</em> PCR and blood culture results in high-risk patients with candidaemia in the intensive care unit</td>
<td>T. Simsek Baoz, F. Gucu, T. Baoz, S. Komur, A. Ulu, A. Inal, B. Kurbaren, F. Kirby, Y. Tosova* (Adana, Turkey)</td>
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<td>7284</td>
<td>An evaluation to assess the performance of the Fungiplex Aspergillus real-time PCR and the Fungiplex Aspergillus Azole-R IVD real-time PCR Kits following the implementation of an extraction control</td>
<td>J. Green* (Glasgow, United Kingdom)</td>
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<td>7550</td>
<td>Evaluating the extraction and molecular detection of <em>Candida auris</em> strains using commercial kits</td>
<td>J. Green* (Glasgow, United Kingdom)</td>
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<td>7692</td>
<td>Development of an extraction control in Fungiplex Candida IVD real-time PCR Kit</td>
<td>J. Green* (Glasgow, United Kingdom), C. Dalton</td>
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<td>7719</td>
<td>A real-time PCR for the detection of <em>Mucor</em> spp.</td>
<td>J. Green* (Glasgow, United Kingdom), K. Dempsey</td>
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<td>7817</td>
<td>Diagnostic approach for <em>Aspergillus</em> infection: performance evaluation of a new molecular assay for detection and quantification of <em>Aspergillus</em> spp. in clinical samples</td>
<td>R. Tedeschi* (Pordenone, Italy), P. Stano, L. Pagani, G. Suleyman</td>
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<td>8179</td>
<td>Rapid semi-quantitative format PCR for the detection of <em>Pneumocystis jirovecii</em> replacing the direct examination</td>
<td>A. Coste, R. Brauillet, J. Diserens, M. Moraz, F. Lamothe, P. Hauser, G. Greub, K. Jaton* (Lausanne, Switzerland)</td>
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<td>8321</td>
<td>Detection of <em>Aspergillus</em> spp. in bronchoalveolar lavage fluid of haematological and non-haematological patients with invasive aspergillosis by real-time PCR</td>
<td>S. Ignatyeva* (Saint Petersburg, Russian Federation), T. Bogomolova, V. Spiridonova, O. Shadrivova, N. Vasilyeva, E. Desyatik, Y. Borzova, N. Klímková</td>
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8616  Comparison of six simple methods for ribosomal DNA extraction directly from nail sample suspected to onychomycosis for PCR-based assay
M. Motamedi* [ Shiraz, Iran], M. Mahmoudi, S. Yazdanpanah

8654  Comparison of the performances of three commercial real-time PCR kits with an in-house real-time PCR assay for the diagnosis of invasive aspergillosis
C. Dulac, A. Bourguignon, L. Mollier-Pierret, D. Dupont, M. Wallon, M. Rabodonirina, F. Persat, J. Menotti* [ Lyon, France]

Session accepted as 2-Hour Oral Session
Different diagnostic tools for different fungal infections

1036  Accuracy and clinical impact of fungal cell-free DNA PCR panel on plasma for diagnosis of invasive fungal infection
F. Senchyna* [ Palo Alto, United States], C. Hogan, D. Ho, A. Subramanian, I. Budvytiene, S. Gombar, H. Costa, M. Budvytis, N. Banaei

1103  Improved molecular diagnosis of dermatomycosis
L. Berlinger* [ Lucerne 6, Switzerland], R. Lombriser, A. Gisler, S. Steiner, S. Pranghofer, M. Altwegg

2416  Clinical evaluation of a novel rapid test for Aspergillus galactomannan
H. Wang* [ Beijing, China], J. Peng, Y. Zhang, K. Sun, J. Wen, Y. Su, Z. Zhou

2929  Serum [1-3]-ß-D-glucan has suboptimal performance for the diagnosis of Pneumocystis jirovecii pneumonia and correlates poorly with respiratory burden measured by quantitative PCR in patients with cancer
A. Szvalbo* [ Houston, United States], A. Malek, Y. Jiang, D. Kontoyiannis

3014  Quantitative PCR detection of circulating DNA for the diagnosis of mucormycosis: prospective evaluation in the ModiMucor study

3573  Serum lateral flow tests for invasive aspergillosis: a prospective cohort study
T. Mercier* [ Leuven, Belgium], E. Guldentops, K. Lagrou, J. Moertens

3574  Evaluation of the performance of the Dynamiker Fungus [1-3]-ß-D-glucan assay for the diagnosis of invasive aspergillosis in high-risk patients with haematological malignancies
M. Siopi* [ Athens, Greece], M. Krmelj, S. Karakatsanis, C. Roumpakis, E. Eldeik, K. Karantasis, H. Sambatakou, P. Tsirigotis, M. Pagoni, N. Sypsas, S. Pouraras, J. Meletiadis

5965  The diagnostic accuracy of cryptococcal antigen detection in serum and cerebrospinal fluid in HIV patients with suspected cryptococcal meningitis: systematic review and meta-analysis

7133  Diagnostic performance of two novel semi-quantitative cryptococcal antigen assays
C. Skipper* [ Minneapolis, United States], K. Tadeo, E. Martyn, D. Meya, B. Kafufu, J. Rhein, D. Boulware

7142  Usefulness of serum as a non-invasive sample for the detection of Histoplasma capsulatum: comparative analysis of different diagnostic techniques
L. Bernal Martinez, P. De La Cruz, S. Gago, L. Alcazar-Fuoli, M. Buitrago* [ Madrid, Spain]

Session accepted as Paper Poster Session
Fungi and antifungal drugs: a complex relationship

45  In vitro activity of manogepix (APX001A) and comparators against 1294 fungal isolates collected worldwide during the SENTRY surveillance programme (2018)
M. Huband* [ North Liberty, United States], M. Pfaffer, R. Flamm, P. Bien, M. Castanheira

708  Detection of echinocandin resistance in Candida glabrata in the microbiology laboratory using commercial methods: interpret with caution!
P. Escribano* [ Madrid, Spain], L. Alguacil, J. Diaz-Garcia, C. Sanchez Carrillo, P. Munoz, J. Guineo Ortega

1358  Antifungal susceptibility profiles of orofom [formerly F901318], and currently available systemic antifungals against mould and yeast phases of Talaromyces marneffei
J. Zhang, H. Liu, L. Xi, Y. Chang, K. Kwan-Chung, S. Seyedmousavi* [ Bethesda, United States ]

1926  Spectrophotometric MICs reading of azoles and amphotericin B shows high agreement with visual reading MIC interpretation using EUCAST 9.3.1 methodology

2096  Occurrence, susceptibility profiles, evaluation of synergistic activity of isavuconazole or voriconazole plus anidulafungin and genetic characterisation of Candida auris detected in a surveillance programme
M. Castanheira* [ North Liberty, United States], L. Deshpande, P. Rhomberg, E. Utt, S. Messer, M. Pfaffer

2106  Application of whole genome sequencing analysis to detect the azole-resistance mechanisms in Aspergillus fumigatus in a global surveillance programme
M. Castanheira* [ North Liberty, United States], A. Davis, L. Deshpande, P. Rhomberg, M. Pfaffer
2614 \textit{In vitro} synergy of isavuconazole in combination with colistin against \textit{Candida auris}

P. Schwarz* (Marburg, Germany), A. Bidau, E. Dannaoui

3218 \textit{In vitro} activity of ibrexafungerp in pH 7.0 and pH 4.5 testing environments against 187 fluconazole-susceptible and -resistant \textit{Candida} species from vulvovaginal candidiasis patients

J. Sobel* (Detroit, United States), S. Barat, K. Borroto-Escocha, N. Azie, D. Angulo Gonzalez

3659 Antifungal susceptibility description in \textit{Candida parapsilosis} bloodstream infection: is there a change in the last years?

A. Ferre Beltran* (Palma de Mallorca, Spain), A. Olmos Torres, H. Vilchez Rueda, F. Fanjul Losa, E. Alcaceba, A. Oliver, J. Murillas Angotti, M. Riera

4266 Impact of proposed revised EUCAST breakpoints on susceptibility classification of contemporary Danish mould isolates

K. Jørgensen* (Copenhagen, Denmark), R. Datcu, R. Krøger Hare, M. Arendrup

4369 Antifungal susceptibility testing practices in mycology laboratories in France, 2018

A. Bellanger, F. Persat, F. Foulet, C. Bonnal, F. Botterel, E. Dannaoui* (Paris, France)

5558 Antifungal susceptibility patterns among clinical isolates of \textit{Aspergillus fumigatus} from paediatric cystic fibrosis patients in Greece: a laboratory-based study with focus on azole resistance

M. Siopi* (Athens, Greece), A. Stathi, H. Krikou, L. Zachariadou, S. Pournaras, J. Meletiadis

6173 Novel qPCR demonstrates azole-resistant TR34/L98H and TR46/Y121F/T289A \textit{Aspergillus fumigatus}, in air spore-samplings around Danish agricultural fields

R. Krøger Hare* (Copenhagen, Denmark), T. Heick, L. Jørgensen, M. Arendrup

6505 Comparison of antifungal activity against clinical isolates of \textit{Candida albicans} and \textit{Candida glabrata} of originator and generics of voriconazole and anidulafungin

A. Nussbaumer-Pröll* (Vienna, Austria), S. Eberl, B. Seiftsch, C. Dorn, F. Kees, T. Gasperetti, J. Marx, R. Welte, R. Bellmann, M. Zeitlinger

6610 Spectrophotometric detection of azole-resistant \textit{Aspergillus fumigatus} clinical isolates with EUCAST broth microdilution method. Is it time for automating EUCAST antifungal susceptibility testing of \textit{Aspergillus} spp.?

I. Efstatithiou, H. Van Der Lee, M. Arendrup, P. Verweij, J. Meletiadis* (Athens, Greece)

6658 Role of TAC1 orthologs in \textit{Candida auris} azole resistance

J. Li* (Lausanne, Switzerland), A. Coste, D. Bachmann, D. Sanglard, F. Lamoth

7376 Impact of calmodulin inhibition by flufenazine on susceptibility, biofilm formation and pathogenicity of caspofungin-resistant \textit{Candida glabrata}

A. Ceballos, D. Amada, E. Robert, C. Parra Giraldo, P. Lepape* (Nantes, France)

7647 Whole genome sequencing (WGS) and antifungal susceptibility testing of \textit{Candida glabrata} (\textit{C. glabrata}) reveals new associations of antifungal resistance (AFR) with gene variants

I. Stefanini, E. Stoakes, H. Wu, L. Mcrae, A. Hussain* (Birmingham, United Kingdom), J. Moat1, C. Dowson, M. David, C. Constantinidou

7902 Exploring posaconazole pharmacodynamics against \textit{Candida krusei} isolates: determination of EUCAST PK/PD susceptibility breakpoints

M. Beredaki* (Athens, Greece), M. Arendrup, S. Pournaras, J. Meletiadis

7975 Early (within 72h) phenotypic detection of fluconazole-resistant \textit{Candida glabrata} isolates

P. Georgiou* (Athens, Greece), M. Arendrup, S. Pournaras, J. Meletiadis

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Session accepted as \textit{Mini-oral ePoster Session}

**Improving diagnostics in the fungal field**

216 Evaluation of newly formatted \textit{Aspergillus} lateral flow assay for IgG antibody detection in chronic pulmonary aspergillosis

Anna Yang* (Tianjin, China), Y. Wang, B. Lu

2745 The accuracy of \(\beta\)-D-glucan and \textit{Aspergillus} DNA detection by PCR in serum and bronchoalveolar lavage fluid for the diagnosis of pulmonary aspergillosis in critically ill patients with suspected ventilator associated pneumonia

L. Loughlin* (Belfast, United Kingdom), T. Hellyer, P. White, D. Mcauley, R. Posso, M. Richardson, D. Denning, J. Simpson, R. Mckmullan

3083 Usefulness of anaerobic blood culture vials for the microbiological diagnosis of candidaemia

E. Farfour* (Suresnes, France), C. Le Brun, A. Mizrahi, T. Guillard

3479 Differentiation at species level of the members of the PSC complex (\textit{Pseudallescheria boydii} / \textit{Scedosporium apiospermum}) involved in cystic fibrosis by MALDI-TOF MS

V. Monnin* (La Balme Les Grottes, France), L. Picoulet, D. Giraud, S. Arend, B. Celliere, P. Courault, B. Pincus, G. Durand, V. Girard

3805 \(18F\)-fluorodeoxyglucose positron emission tomography: computed tomography is a better tool for chronic disseminated candidiasis follow-up than conventional imaging


4367 Orbitrap ultra high-resolution mass spectrometry proteomics data mirrors clinically relevant functional associations of black dematiaceous hyphomycetes (black yeast-like fungi)

S. de Hoog* (Utrecht, Netherlands), A. Giraldo Lopez, I. Moser, J. Knuyt, J. Freeke, A. Jamalai, B. Stielow
Conserved host transcriptomic responses to acute infection are observed in the presence of multiple fungal pathogens
J. Steinbrink* [Durham, United States], A. Zaas, M. Johnson, E. Tsalik, B. Alexander, C. Woods, M. McClain

Multi-centre validation of a EUCAST method for the antifungal susceptibility testing of microconidia-forming dermatophytes
M. Arendrup* [Copenhagen, Denmark], K. Jørgensen, J. Guinea Ortega, K. Lagrou, E. Chryssanthou, M. Hayette, F. Barchiesi, C. Lass-Fliör, P. Hamal, E. Dannyaoui, A. Chowdhary, J. Meletiadis

Olorofim for a case of severe disseminated Lomentospora prolificans infection
S. Tia* [Parkville, Australia], K. Thursky, G. Ng, J. Rex, D. Carney, M. Slavin

Risk factors for mortality in patients with pulmonary mucormycosis
H. Son* [Seoul, South Korea], J. Song, S. Choi, J. Jung, A. Kim, Y. Chang, S. Lee, S. Choi, Y. Kim, J. Woo

Matched-paired analysis of patients treated for invasive mucormycosis with isavuconazole versus standard treatment

The guideline compatibility of mucormycosis management: a retrospective review of the case reports from European quality (EQUAL) score perspective
H. Koc, G. Metan* [Ankara, Turkey]

A case of Lomentospora prolificans (LoPro) treated with the novel antifungal olorofim
S. Chen, N. Joshi Rai, S. Cunneen, J. Rex, C. Heath, E. Harvey* [Manchester, United Kingdom]

The trend of changes in paraanasal computed tomography of patients with haematologic malignancies and febrile neutropaenia
S. Shafeeq* [Stockholm, Sweden], S. Pannanusorn, K. Pakshir, S. Rezaie, Z. Zare Shahrabadi, K. Zomorodian* [Shiraz, Iran], Pediococcus acidilactici

Successful salvage therapy for mucormycosis with isavuconazole: a murine model
A. Chowdhary, J. Meletiadis

A comparative phenotypic study of aggregate versus non-aggregate Candida isolates
K. Chan* [Hong Kong, Hong Kong], C. Tsang, J. Chan, A. Ngan, W. Chan, S. Lau, P. Woo

The role of complement and diabetes in invasive candidiasis
V. Harpf, R. Würzner* [Innsbruck, Austria]

Evaluation of potential implication of the wastewater microbiome in fungal pathogens spreading using next-generation sequencing technology
H. Yousfi* [Yerres, France], I. Rodriguez, E. Robert, I. Ourliac Garnier, M. Albassier, P. Bonnet, A. Ceballos, H. Koc, G. Metan* [Ankara, Turkey], C. Parra Giraldo, C. Alvarez, H. Son* [Seoul, South Korea], J. Song, S. Choi, J. Jung, A. Kim, Y. Chang, S. Lee, S. Choi, Y. Kim, J. Woo

Morphogenesis and pathogenesis regulation of Candida parapsilosis isolates from nosocomial bloodstream infections
S. Shafeeq* [Stockholm, Sweden], S. Pannanusorn, J. Morschhäuser, U. Römling
Abstract Categories 2020

Session accepted as 2-Hour Oral Session

Optimising antifungal treatment in different clinical settings

331 Systemic antifungal therapy (AFT) with isavuconazonium sulfate (ISAVUSULF) or other AFT in adults with invasive mucormycosis (IM) or invasive aspergillosis (IA) caused by a non-\emph{fumigatus} species (IA-nf): A multi-centre, non-interventional registry study

G. Thompson, J. Garcia-Diaz, M. Miceli, M. Nguyen, L. Ostrosky-Zeichner, J. Young, C. Fisher, N. Clark, R. Greenberg, A. Spec, L. Kovanda, R. Croas-Dabrera, D. Kontoyiannis* [Houston, United States]

1191 An open-label, phase I, multi-centre study to evaluate the pharmacokinetic, safety and tolerability profile of oral isavuconazol sulfate in paediatric patients


1580 Optimising the use of triazole therapeutic drug monitoring using quality improvement methodology

R. Wilson* [London, United Kingdom], F. Davies, R. Palanicwandar, K. Mcdaouagh, M. Coleman, J. Woo, C. Parkinson, L. Whitney, M. Gilchrist

2611 Evaluation of targeted antifungal prophylaxis after liver transplantation: are echinocandins the optimal choice?

M. Rinaldi* [Bologna, Italy], M. Bartoletti, A. Ferrarese, E. Franceschini, C. Campoli, S. Coladonato, S. Ambretti, A. Siniscalchi, M. Morelli, M. Cescon, P. Burra, C. Mussini, R. Lewis, P. Viale, M. Giannella

Session accepted as 1-Hour Oral Session

Pharmacokinetic considerations in fungal infections

2953 Posaconazole dosing and association with therapeutic drug levels in allogeneic cell transplant recipients

M. Kraljevic* [Basel, Switzerland], N. Khanna, M. Medinger, J. Passweg, Y. Chalandon, S. Masouridi, Levrat, N. Mueller, U. Schanz, C. Van Delden, D. Neofytos

3221 Using saliva for precision dosing of antifungal drugs: saliva population pharmacokinetic model

H. Kim* [Sydney, Australia], A. Martson, E. Dreessen, I. Spriet, S. Wicha, A. Melachlan, J. Alfenaar

4800 Pharmacokinetic evaluation of micafungin prophylaxis for invasive mould disease in childhood acute lymphoblastic leukaemia: part of the OPTIMA study

D. Bury* [Utrecht, Netherlands], R. Ter Heine, W. Tissing, E. Mulijwijk, T. Wolfs, R. Brüggemann

7419 Therapeutic drug monitoring of isavuconazole in patients undergoing antifungal therapy in Denmark

R. Jergensen* [Copenhagen, Denmark], M. Risum, M. Arendrup

Session accepted as Mini-oral ePoster Session

Population and pathogenesis in fungi

1775 \emph{NDT}80 transcription factor acts as a repressor of \emph{Candida parapsilosis} virulence attributes

J. Branco* [Porto, Portugal], C. Cruz, L. Rodrigues, T. Goncalves, I. Miranda, A. Rodrigues

1979 Prevention of pneumocystis pneumonia by Ibrexafungerp in a murine prophylaxis model

S. Barat, K. Borrato-Esada, A. Ashbaugh, D. Gonzalez* [Jersey City, NJ, United States], M. Cushion

2065 Differential innate immune responses of human macrophages and bronchial epithelial cells against \emph{Talaromyces marneffei}

C. Tsang* [Pokfulam, Hong Kong], Y. Tan, K. Kok, S. Lau, P. Wou

5459 Candidaemia management: can we do better?


5206 Mycobacterium \emph{microbiome} cross-talk analysis during acute pulmonary exacerbation: focus on \emph{cystic} \emph{fibrosis}


5014 Mycobacterium sequencing reveals a high fungal diversity in patients with severe atopic dermatitis

B. Schmid* [Zurich, Switzerland], E. Bersuch, A. Künstner, A. Fähnrich, H. Busch, M. Glatz, P. Bosshard

6617 Understanding the pathogenicity of \emph{Scedosporium} species, the emerging cystic fibrosis pathogens

M. Homa* [Szeged, Hungary], C. Szebenyi, O. Jager, C. Vágvölgyi, T. Papp
**Abstract Categories 2020**

**8567** Polyclonal antibody anti-CR3-RP Ab inhibits biofilm of *Candida albicans* and decreases an expression of the genes related to biofilm-formation and cell surface hydrophobicity. J. Dekkerova* [Bratislava, Slovakia], H. Bujdáková, S. Kendra

**4093** Identification, antifungal susceptibility profile, and biofilm formation of *Rhodotorula mucilaginosa* in China (August 2010 to July 2015): a multi-centre study. J. Huang* [Beijing, China], M. Xiao


**Session accepted as Paper Poster Session**

**Rare fungi: are they really so rare?**

**295** Characterisation of airborne fungi present in two hospitals in Kabale District, Uganda. A. Odebode* [Akoka, Nigeria], G. Niwamanya


**1217** Genotyping, phylogenetic analysis, and in vitro antifungal susceptibility profile of clinical isolates of *Neoscytalidium* species. M. Hedayati* [Sari, Iran], S. Heidari, M. Gheisari, M. Abastabar, M. Poorabdollah, M. Mirenagat, N. Basharzad, S. Ansari, V. Mortezaei, S. Seyedmousavi, A. Alastruey-Izquierdo


**2429** The clinical and economic burden of mucormycosis in Japan. R. Ueno* [Tokyo, Japan], S. Nishimura, G. Fujimoto, D. Ainiwaer, S. Kim


**2608** An updated analysis of the burden of fungal diseases in Uganda. F. Bangomin, B. Kirenga, R. Kwizera, D. Meya, D. Denning* [Manchester, United Kingdom]

**2656** Species distribution and antifungal susceptibility profile of the emerging yeast pathogen *Blastobasidium Badali*, C. Gibas, H. Patterson, D. McCarthy, J. Mele, H. Fan, N. Wiederhold* [San Antonio, United States]

**Sacccharomyces cerevisiae* fungaemia: a 10-year review in the CHU of Liege [Belgium]. C. Diop* [Liege, Belgium], J. Descy, C. Meex, R. Sacheli, M. Hayette

**3183** Neutrophoroccidioidiomycosis: analysis of 10 cases observed in an endemic area in Argentina. P. Villalba, G. Mendez, C. Niveyro* [Posadas, Argentina], V. Sosa

**4003** Prevalence and risk factors for *Histoplasma Capsulatum* infection amongst HIV patients attending the Buea Regional Hospital using the *Histoplasma* urine antigen detection enzyme immunoassay. K. Marius Paulin* [Buéa, Cameroon], D. Denning, C. Mondengue, N. Raymand

**3132** Twelve years of chromoblastomycosis in Martinique. Y. Le Govic* [Fort-de-France, Martinique], N. Berrette, E. Baubion, E. Amazan, G. Ferrari-Fidelin, C. Miossec, S. De Hoog, N. Desbois-Nogard


**5356** The epidemiology and antifungal susceptibility of *Rhodotorula* spp. in a tertiary care hospital. I. Costales* [Oviedo, Spain], C. Castelló-Abiater, H. Lorenzo Juanes, A. Templado-Barroso, A. Ramirez, M. Sandoval, T. Pelaez Garcia

**5712** Twenty-seven years of chromoblastomycosis in Martinique. Y. Le Govic* [Fort-de-France, Martinique], N. Berrette, E. Baubion, E. Amazan, G. Ferrari-Fidelin, C. Miossec, S. De Hoog, N. Desbois-Nogard

**6028** Epidemiological and clinical characteristics among HIV adults with invasive fungal infections in north-eastern Mexico. G. Aguirre Garcia* [monterrey, Mexico], J. Cázares González, M. Martínez-Reséndez, R. Lara-Medrano, C. Alfaro-Rivera, N. Gaona Chavez, J. Rodríguez, H. Villanueva-Lozano

**6304** The epidemiology, genotypes, antifungal susceptibility of *Trichosporon* species, and impact of voriconazole therapy on outcome of *Trichosporon* fungaemia. K. Shin-Huei* [Kaohsiung, Taiwan], P. Lu, Y. Chen, M. Ho, C. Lee, S. Lin

**6320** An updated analysis of the burden of fungal diseases in Uganda. F. Bangomin, B. Kirenga, R. Kwizera, D. Meya, D. Denning* [Manchester, United Kingdom]

**6556** *Saccharomyces cerevisiae* fungaemia: a 10-year review in the CHU of Liege [Belgium]. C. Diop* [Liege, Belgium], J. Descy, C. Meex, R. Sacheli, M. Hayette

**6624** Species distribution and antifungal susceptibility profile of the emerging yeast pathogen *Blastobasidium Badali*, C. Gibas, H. Patterson, D. McCarthy, J. Mele, H. Fan, N. Wiederhold* [San Antonio, United States]
Fungal disease burden: an underestimated health challenge in Cote d'Ivoire
D. Koffi* (Abidjan, Côte d'Ivoire), B. Ira, O. Toure, R. Jambou, D. Denning

Evaluation of fungi isolates from cystic fibrosis adult patients in a tertiary hospital of Madrid, Spain
A. Fraile Torres* (Madrid, Spain), L. Fontan, S. Gómez De Frutas, T. Soler Maniega, T. Alarcon Cavero, R. Girón, L. Cardehilo, B. Buendia

Clinical and laboratory study on invasive infections due to Fusarium species in critically ill adult and paediatric patients in Serbia: ten years’ experience of National Laboratory for Medical Mycology
V. Arsic Arsenijevic* (Belgrade, Serbia), S. Otasevic, A. Tortorana, D. Ivanovic, J. Kolarovic, L. Paripovic

Serum galactomannan antigenemia of HIV-positive patients in an endemic area for Tolypomyces marneffei
Y. Huang* (New Taipei, Taiwan), C. Liao, C. Yang

Pulmonary mucormycosis: a large French survey

Lichtheimia corymbifera cutaneous infection

Trichomonadine association with Pneumocystis jirovecii: a retrospective study
S. Mille, D. Toubas, F. Foudrinier, D. Jerôme, A. Huguenin* (Reims, France)

Prevalence and clonal distribution of azole-resistant Candida parapsilosis isolates causing human bloodstream infections in a tertiary Italian hospital

Nationwide azole resistance survey in clinical Aspergillus fumigatus isolates: a snapshot of the situation at 30 Spanish hospitals

Histoplasmosis epidemiology in Costa Rica
J. Villalobos, J. Castro, C. Ramírez*

Needles in a haystack: ultra-orphan invasive fungal infections reported in FungiScope: global registry for emerging fungal infections
J. Salmanton-Garcia* (Cologne, Germany), P. Köhler, S. Mellinghoff, H. Wisplinghoff, D. Cornelj, D. Seidel

Comparative variant analysis of Aspergillus fumigatus hmg1 genes for identification of novel mutations in candidate genes possibly be involved in mediation of azole resistance

Whole genome sequencing and comparative analysis of echinocandin susceptible and resistant sequential Candida glabrata clinical isolates
A. Albarraza* (Riyadh, Saudi Arabia), K. Alzahrani

Mechanisms of resistance and virulence of azole-resistant Aspergillus flavus clinical isolates
E. Dannaoui* (Créteil, France), B. Mousavi, N. Lin, L. Lachaud, M. Cornet, J. Guillot, L. Delhaes, F. Botterel, E. Dannaoui

Mutations in Aspergillus fumigatus hmg1 confer increased expression of ergosterol biosynthesis and efflux pump encoding genes
J. Rybak* (Memphis, United States), W. Ge, N. Wiederhold, V. Bruno, P. Rogers, J. Fortwendel

Genotyping and antifungal susceptibility of Candida albicans isolates from vaginal samples: are the genotypes different from blood?
A. Mesquida* (Madrid, Spain), J. Diaz-Garcia, T. Vicente, E. Reigadas Ramirez, M. Palomo, P. Muñoz, J. Guinea Ortega, P. Escribano

Outcome and characteristics of invasive fungal infections in critically ill burn patients: a multi-centre retrospective study
Candidaemia in South Africa
S. Chen, F. Kong, Y. Xu

Prevalence of haematogenous seeding at distant sites in patients with Candida bloodstream infections
S. Ahmad* [Safat, Kuwait], Z. Khan, N. Al-Sweih, W. Afjouzan, L. Joseph, M. Asadzadeh

Severe candidaemia in a tertiary care hospital
M. Vaquero-Herrera* [Salamanca, Spain], S. Ragozzino, M. Siller Ruiz, M. Marcos, H. Ternavasio De La Vega

Species distribution and antifungal susceptibility of Candida spp. causing candidaemia in China: an update from the CHIF-NET study
M. Xiao* [Beijing, China], S. Chen, F. Kong, Y. Xu

Species identification and antifungal resistance of yeasts causing fungaemia at a tertiary care hospital in Madrid, Spain: the coast is clear
J. Diaz-Garcia* [Madrid, Spain], C. Sanchez Carrillo, E. Reigadas Ramirez, P. Muñoz, P. Escribano, J. Guinea Ortega

The changing scenario of Candida infections
Session accepted as Paper Poster Session

Species distribution and antifungal susceptibility of yeast bloodstream isolates in adult patients at three teaching hospitals in central China
S. Yu* [Beijing, China], M. Zhou, Y. Xu

Epidemiology and antifungal susceptibility patterns of invasive fungal infections from 2012 to 2014 in a teaching hospital in central China
S. Yu* [Beijing, China], M. Zhou, Y. Xu

Epidemiology of nosocomial candidaemia in paediatrics: a multi-centre study in Iran
A. Jimenez* [Miami, United States], K. Sposato, G. Rosello, D. De Pascale, A. Flanagan Giroud, L. Abbo

Not all candidaemias are the same: utility of a rapid identification
C. Leli, L. Di Matteo, S. Bussu, V. Cavollo, A. Rocchetti* [Alessandria (AL), Italy]

Investigation of Candida parapsilosis outbreaks by microsatellite genotyping and emergence of clonal antifungal drug-resistant strains in a multi-centre surveillance in China
Z. Li* [Beijing, China], S. Yu, S. Chen, M. Xiao, F. Kong, Y. Xu

Evolution of candidaemia epidemiology and outcomes over the last 10 years: a single-centre study
J. Battistolo* [Lausanne, Switzerland], E. Glampedakis, L. Damonti, J. Poissy, T. Calandra, J. Pagani, P. Eggimann, P. Bochud, D. Marchetti, F. Lamoth

Changes in epidemiology, treatment and outcomes of candidaemia at a tertiary care children's hospital
A. Arrieta* [Orange, United States], N. Ashouri, D. Nieves, R. Adhikary* [Bangalore, India], B. Mv, S. Joshi, B. Hb, A. A

Candidaemia: a decade-long experience from India
R. Adhikary* [Bangalore, India], B. Mv, S. Joshi, B. Hb, A. A

Pathogens and efficacy of caspofungin therapy C. Cohen
N. Govender* (Johannesburg, South Africa), J. Todd, G. Rosello, D. De Pascale, A. Flanagan Giroud, L. Abbo

Species distribution and antifungal resistance of Candida spp. causing candidaemia: a multi-centre case-control-control study

Risk factors for candidaemia in hospitalised patients with liver cirrhosis: a multi-centre case-control-control study

The impact of candidaemia management on mortality: a 4-year retrospective study from a tertiary care hospital
A. Martins* [Porto, Portugal], C. Silva, J. Caldas, E. Alves Branco, S. Almeida Lacerda Pereira, B. Prista Leão, R. Filipe, S. Magalhães, M. Pinheiro, A. Silva-Pinto, A. Sarmento, L. Santos
8235 Characterisation of a Portuguese population with candidemia in a tertiary care hospital
C. Silva* [Santa Maria da Feira, Portugal], J. Coldes, A. Martins, S. Almeida Lacerda Pereira, E. Alves Branco, R. Filipe, B. Prista Leão, S. Magalhães, M. Pinheiro, A. Silva-Pinto, A. Sarmento, L. Santos

9159 Surveillance for control of antifungal resistance in Candida bloodstream infections fails to inform antifungal stewardship in European countries
L. Gala, A. Collegeri* [Spresiano, Italy], E. Carrara, N. Babu Rajendran, M. Compri, E. Tacconelli

9390 Update on Candida auris in Russia
N. Barantsevich* [Saint-Petersburg, Russian Federation], O. Orlova, L. Ivanova, I. Churkina, Y. Belsky, S. Andrey, A. Vetokhina, E. Barantsevich

Session accepted as Paper Poster Session
Treatment options in aspergillosis
624 Clinical experience with isavuconazole in Chinese healthy volunteers and Chinese patients with invasive aspergillosis
J. Zhang* [Shanghai, China], Y. Zhang, D. Wu, G. Cao, K. Hamed, A. Desai, J. Aram, X. Guo, R. Fayyad, O. Cornely

1720 Current use of baseline chest CT in haematology patients at high risk for invasive fungal infection
J. Stemler* [Cologne, Germany], C. Bruns, S. Mellinghoff, P. Köhler, O. Cornely

1844 Clinical and laboratory features of mixed invasive mycoses in adult haematologic patients with invasive aspergillosis

2919 Salvage treatment of invasive pulmonary aspergillosis with isavuconazole and caspofungin combination in a lung transplant recipient
P. Pavone* [Rome, Italy], C. Carillo, Y. Pecoraro, F. Venuta, C. Mastroianelli, G. Russo

3887 A surgical take on broncho-pulmonary Aspergillosis: 20 years of experience
L. Bertrand* [Munich, Germany]

4722 Proposition of a uniform methodological approach to attribution of invasive aspergillosis as a cause of death
R. Van Grootveld* [Leiden, Netherlands], R. Van De Peppel, H. Jolink, P. Van Der Borne, A. Bernards, M. Van Der Beek, M. De Boer

4818 Pharmacogenetic approach to the antifungal drug administration: clinical case
A. Taraskina, Y. Borzova, E. Desyatik, D. Vera, N. Regina, N. Vasilyeva* [Saint Petersburg, Russian Federation]

8013 Evaluation of the efficacy of combination of antifungals against invasive aspergillosis in an invertebrate animal model
S. Jemel* [Créteil, France], V. Jullien, E. Billaud, J. Guillot, F. Botterel, E. D'ettaorre

8676 Allergic bronchopulmonary aspergillosis (ABPA) complicating chronic obstructive pulmonary disease (COPD) without asthma: responses to antifungal therapy
S. Aggarwal* [Manchester, United Kingdom], C. Kosmidis

9427 Diagnostics and treatment of invasive aspergillosis in B-cell lymphoma patients after cytostatic chemotherapy and autologous stem cell transplantation

9449 Incidence, risk factors and clinical impact of invasive pulmonary aspergillosis in patients hospitalised with influenza infection
V. Bellelli* [Rome, Italy], G. Siccardi, L. Celoni, P. Vassalini, E. Congeduti, C. Borrazzo, M. Venditti, G. D'ettaorre

Session accepted as Mini-oral Flash Session
Yeast wars: the rise of auris
246 Delineation of the direct impact of Candida auris ERG11 mutations on clinical triazole resistance
J. Rybak* [Memphis, United States], C. Sharma, L. Doorley, G. Palmer, P. Rogers

3356 Differential resistance of Candida auris biofilms against surface disinfectants commonly used in the hospital
B. Zatorska, M. Diab-Elschahawi* [Vienna, Austria], D. Moser, E. Presterl

3646 Ibrexafungerp demonstrates potent and consistent in vitro activity against >400 global Candida auris isolates, including isolates with elevated MIC’s to echinocandins
S. Barat, K. Borroto-Esoda, D. Angulo Gonzalez* [Jersey City, NJ, United States]

3958 In vitro evolution reveals mutations in Candida auris EFG6 to confer high level amphotericin B resistance
J. Rybak* [Memphis, United States], K. Barker, J. Parker, Y. Li, J. Múnoz, G. Palmer, C. Cuomo, S. Kelly, P. Rogers

4126 Candida auris in a large healthcare system in South Florida: importance of active surveillance testing to prevent spread
A. Jimenez* [Miami, United States], K. Sposato, G. Rosello, D. De Pascale, J. Cardozo, O. Orazco, B. De Pascale, O. Martinez, V. Salazar, K. Deronde, A. Vega, L. Abbo
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7239 Candida auris compared to other Candida spp. candidaemia: a two-year experience in a Spanish tertiary hospital

9313 Echinocandin resistance in emerging multidrug-resistant yeast Candida auris and investigation into the mechanism of resistance
D. Sharma* (Chandigarh, India), R. Paul, S. Rudramurthy, S. Paul, H. Prakash, S. Bhattacharya, A. Chakrabarti

9353 Rapid identification of Candida auris from direct blood culture positive samples by MALDI-TOF MS from patients with candidaemia in a tertiary care hospital
R. Marak* (Lucknow, India), S. Yadav, A. Dixit

9422 Molecular and epidemiological characterisation of an outbreak of Candida auris in a Spanish hospital
E. Cortes-Acosta, I. Sigona-Giangreco, A. Ruiz* (Valencia, Spain), A. Martínez-Martínez, E. Valentín, J. Peman
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- Antiparasitic susceptibility & resistance
- Antiparasitic drugs & treatment
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- International & public health
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Falciparum infections in asymptomatic adults in forest a low transmission area in Amazonia, French Guiana

Epidemiological and laboratory features last 10 years: a systematic review

Plasmodium ovale curtisi and wallikeri infections in imported malaria: a 2013-2018 retrospective study from the French National Malaria Reference Centre

Neurologic complications in Chagas disease: results from a systematic review of published literature

Evaluation of salivary protein rTiSP14.6 as a marker of exposure to the bite of the insect Triatoma infestans, vector of Trypanosoma cruzi

Prevalence of positive serology for Trypanosoma cruzi in a sample population of migrants from El Salvador and Honduras living in the Metropolitan Area of Milan (MAM)

Screening and management of Chagas disease in at-risk blood donors in a non-endemic country: experience of a north-western tertiary care centre in Italy

Toxocariasis in children in south Russia: epidemiological and laboratory features

Deaths of emerging and re-emerging infectious diseases outbreaks, epidemics and pandemic in the last 10 years: a systematic review

High prevalence of Plasmodium falciparum and non-falciparum infections in asymptomatic adults in forest Ghana

Evaluation of cystic echinococcosis prevalence in an endemic region of Kazakhstan

Leptospirosis in hospitalised patients in Ambatondrazaka, Madagascar: incident cases and exposure factors
Difficult-to-treat mucocutaneous leishmaniasis in an elderly Italian traveller returning from Argentina resolved with combination treatment


Genetic polymorphism of metabolic enzymes of Leishmania spp. parasites isolated from different clinical types of cutaneous leishmaniasis patients

M. Nateghi Rostami* [Tehran, Iran], M. Hosseini, F. Darzi

Visceral leishmaniasis burden in Bologna province, Italy

G. Fornaro* [Bologna, Italy], G. Bonati, E. Vanino, I. Zaghi, F. Hatami, I. Alavidarazam* (Tehran, Iran), S. Shokouhi, N. Sethuraman, P. Kumar S, P. Selvakumaar, S. Nagusah, K. Abdul Ghafur* [Chennai, India], G. Palani, T. Ma, M. Nateghi Rostami* [Tehran, Iran], M. Hosseini, F. Darzi

Comparative inflammatory cytokines gene expression in culture of human macrophages infected with Leishmania tropica and Leishmania major parasites

D. Darzi* [Tehran, Iran], M. Nateghi Rostami, R. Davoodian

Leishmaniasis in immunocompromised individuals without HIV: not so different. A comparative analysis of 60 patients

C. Tortajada* [Valencia, Spain], L. Castellana, E. Calabuig, C. Corralata, A. Farga, M. Fernandez, J. Flores

Hunt for Leishmania RNA Virus (LRV) in transcriptome database of Leishmania species: which is best for bioinformatic analysis?

D. Kaya* [Istanbul, Turkey], D. Ozcan, D. Kurt, U. Sezerman

Genotypic investigation of Leishmania spp. in dog population of northern Greece

A. Papoutsis* [Thessaloniki, Greece], G. Chatzisimeonidis, N. Vastarouchas, A. Karamitros, N. Zoumpoulidis, U. Giannakou, E. Andreadou, T. Lialiaris

The impact of war on cutaneous leishmaniasis disease transmission and its control in Syria

R. Allan* [Haywards Heath, United Kingdom], G. Muhjazig

Resistant bacteria in retail meat

S. Malig* [Odense, Denmark], E. Knudsen, S. Hoegh, U. Justesen

Colistin-resistant bacteria in Indian raw food samples

K. Abdul Ghofur* [Chennai, India], G. Palani, T. Ma, N. Sethuraman, P. Kumar S, P. Selvakumaar, S. Nagusah, R. Antony

Botulism early recovery: one-decade experience in a referral centre

F. Hatami, I. Alavidarazam* [Tehran, Iran], S. Shakouhi, M. Mardani Dashti

Investigation of waterborne outbreaks due to drinking water consumption in Greece, 2004-2019 (1st semester): time to learn our lessons


Mass visitation of show caves as a threat to human health

R. Tomazin* [Ljubljana, Slovenia], T. Matos, J. Mulec

Detection of Legionella spp. and Legionella pneumophila in environmental samples using culture and live/dead-qPCR

M. Zamfir* [Munich, Germany], S. Walser-Reichenbach, S. Heinez, C. Herr

Evaluation of rapid extraction methods coupled with recombinase polymerase amplification assay for point-of-need diagnosis of post-kala-azar dermal leishmaniasis


Effective control strategies for cutaneous leishmaniasis after Syrian influx in Turkey

G. Unuvor* [Kayseri, Turkey], S. Topluoglu, T. Kayman, H. Ilter, F. Kara, E. Alp Mese

Leishmania species diagnosed in European specialised treatment centres in the period 2014-2019


Leishmanial Localised Lymphadenopathy (LLL) by Leishmania infantum: a benign disease different from visceral leishmaniasis

J. San Martin* [Fuenlabrada, Spain], J. Ruiz-Giardini, L. Horrillo, A. Castro, I. Garcia Arata, J. Garcia-Martinez, J. Jaqueti, L. Molina, B. Matia

Visceral leishmaniasis by Leishmania infantum in immunocompetent adults: update of the leishmaniasis outbreak in Madrid (Spain)

J. San Martin* [Fuenlabrada, Spain], J. Ruiz-Giardini, L. Horrillo, A. Castro, I. Garcia Arata, J. Garcia-Martinez, J. Jaqueti, L. Molina, B. Matia

Biomarkers help to stop secondary prophylaxis on Leishmania-HIV co-infected patients


Diagnosis of cutaneous leishmaniasis through shotgun metagenomics

C. Angebault* [Creteil, France], C. Bernincaud, F. Foulet, T. Duong, D. Vanessa, L. Chauvet, C. Rodriguez, F. Benetoul

Session accepted as Mini-oral ePoster Session

Leishmania in the spotlight

Evaluation of rapid extraction methods coupled with recombinase polymerase amplification assay for point-of-need diagnosis of post-kala-azar dermal leishmaniasis


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Malaria News

643 A systematic analysis of the direct antiglobulin test in post-artsunate delayed haemolysis during severe imported Plasmodium falciparum malaria: a multi-centre retrospective study
O. Paccoud* [Paris, France], X. Chamillard, K. Ndiaye, I. Vinatier, M. Khalloufi, C. Boulat, L. Surgers, B. Wyplosz, O. Bouchaud, S. Matheron, E. Caumes, S. Jauréguiberry

1461 Utility of multiplex PCR in the screening, diagnosis and follow-up of malaria in patients attended in a tropical medicine referral centre


2132 Specific antibody responses to recombinant UB05 and MSP3 proteins displayed through the surface of Coliphage Qβ in mother-neonate couples
A. Lissom* [Yaounde, Cameroon], R. Megnekou, C. Sanders, J. Djountu, L. Ngú, A. Waffo, G. Nchinda

2527 Imported malaria: the innovative approach of machine learning on clinical management and severity prediction
A. D’Abramo* [Rome, Italy], F. Rinaldi, L. Lepore, A. Corpolongo, L. Scorzolini, N. Bevilacqua, A. Mariano, A. D'Abramo* [Rome, Italy], F. Rinaldi, L. Lepore

3213 Genomic analysis and exploration of putative drug resistance loci in malaria parasites
J. Han* [Melbourne, Australia], J. Munro, M. Bahlo

5784 Short-term prognosis and factors associated with acute kidney injury in imported severe malaria: results of a multi-centre retrospective study
C. Pierre-Louis* [Saint-Mandé, France], E. Gaudray, T. Martinez, M. Boutonnet, S. De Rudnicki, P. Pasquier, C. Ficka, E. Peytel, L. Lachaud, M. Bailey, A. Bart, C. Ravel, E. Caumes, G. Van Der Auwera, J. Blum, D. Lockwood, P. Buffet*

7459 Ugandan increase in malaria cases is reflected in imported cases to Norway of which surprisingly many have mixed infections identified by PCR
H. Brekke* [Oslo, Norway], C. Fladeby, G. Løvgården, F. Pettersen, L. Dedi, F. Müller

9230 Do we re-admit after outpatient artemether-lumefantrine? Evaluating the safety and efficacy of an ambulatory guideline for the treatment of uncomplicated Plasmodium falciparum malaria in a busy district general hospital in east London, UK
W. Niven, J. Quinn, N. Studd, J. Healy, J. Abukar, A. Boyd

9564 Malaria outbreak response in a nomadic pastoralist setting, Kenya 2019
R. Rono* [Kabarnet, Kenya]

Epidemiology and genetic diversity of Plasmodium falciparum in Kobeni, south-eastern Mauritania
S. Diallo* [Dakar, Senegal], L. Basco

Patients presenting with malaria: are we missing opportunities to screen for other travel-associated infectious diseases?
E. Mcguire* [London, United Kingdom], J. Klein, A. Goodman

A glance at the endothelial activation in complicated and uncomplicated malaria
N. Makkar* [Chandigarh, India], P. Malhotra, J. Ahluwalia, R. Singh, R. Sehgal

Knowledge, attitude, and practice of Visiting Friends or Relatives (VFR) travellers towards prevention of malaria
F. Heinrich* [Hamburg, Germany], T. Brehm, M. Addo, I. Rolling

Ugandan malaria cases to Norway of which surprisingly many have mixed infections identified by PCR
H. Brekke* [Oslo, Norway], C. Fladeby, G. Løvgården, F. Pettersen, L. Dedi, F. Müller

Artesunate-containing therapies and abnormal haemoglobin: do we need to adapt the treatment?

Do we re-admit after outpatient artemether-lumefantrine? Evaluating the safety and efficacy of an ambulatory guideline for the treatment of uncomplicated Plasmodium falciparum malaria in a busy district general hospital in east London, UK
W. Niven, J. Quinn, N. Studd, J. Healy, J. Abukar, A. Boyd, K. Woods* [London, United Kingdom]

Economic evaluations of malaria interventions: a systematic review
A. Klicpera* [Vienna, Austria], A. Bank-Thompson

Session accepted as 2-Hour Oral Session

Malaria: still here?

306 Genomic analysis and exploration of putative drug resistance loci in malaria parasites
J. Han* [Melbourne, Australia], J. Munro, M. Bahlo

1465 Plasmodium vivax diversity, population structuration and history of origin in Sudan
M. Ali Albsheer* [Khartoum, Sudan], E. Iyasu, D. Keppe, E. Lo, M. Ibrahim, M. Hamid
Impact of chemoprophylaxis on the outcomes of 
Plasmodium vivax and Plasmodium ovale imported 
malaria cases among civilian travellers 
M. Le Goff* [Brest, France], E. Kendja, M. Thellier, 
R. Piarroux, P.Boelle, S. Joureugiberry

Failure of artemether-lumefantrine treatment for 
Plasmodium falciparum malaria imported from sub-
Saharan Africa to the UK 
H. Adler* [Liverpool, United Kingdom], J. Cruise, J. Jones, 
I. Slack, A. Neary, J. Van Aartsen, E. Carter, P. Hine, 
E. Okenyi, R. Taggart, D. Nolder, L. Stewart, C. Sutherland, 
S. Astan, T. Blanchard, T. O’Dempsey, M. Beadsworth, 
N. Beeching

Post-artesunate delayed haemolysis presenting with 
persistent direct antiglobulin test: are steroids a 
therapeutic option? 
T. Ascoli Bartoli* [Rome, Italy], L. Lepore, A. D’Abramo, 
A. Corpolongo, A. Mariano, N. Bevilacqua, M. Giancola, 
C. Palazzo, L. Scorzolini, P. Buffet, E. Ricastru

The first blood-stage controlled human malaria 
infected model in Europe for Plasmodium vivax 
vaccine efficacy testing 
A. Minassian* [Oxford, United Kingdom], 
Y. Themistocleous, S. Silk, J. Barrett, C. Nielsen, 
D. Quinkert, I. Poulton, F. Ramos Lopez, C. Mitton, 
R. Piarroux, M. Le Goff*, S. Jauréguiberry, 
E. Kendjo, M. Thellier, S. Jauréguiberry, F. Gay, 
J. Siriez, M. Danis, F. Bruneel, O. Bouchaud, 
S. Larréché, A. Taieb, C. Bernigaud, J. Guillot* (Créteil, France)

Medications to fight parasites: what’s new?

Mitofosine as a promising agent for chronic cutaneous 
leishmaniasis: an in vivo model 
V. Tunali* [Mugla, Turkey], I. Cavus, A. Yildrim, 
D. Zorbozan, M. Harman, C. Gündüz, A. Özbilgin, N. Turgay

Safety and efficacy of fumagillin for the treatment of 
testinal microsporidiosis: a French prospective 
cohort study 
A. Mailard* [Paris, France], A. Scemla, B. Laffy, 
M. Mohlau, J. Molina

Quinacrine is effective for treatment of resistant 
giardiasis 
K. Andersson Ydsten* [Stockholm, Sweden], U. Hellgren, 
H. Åsgeirsson

Leishmaniasis in Turkey: assessment of the efficacy of 
antimicrobial peptides against Leishmania tropica in 
vitro 
N. Unubol, I. Cavus, Ö. Kurt* [Istanbul, Turkey], 
A. Özbilgin, T. Kocogaz

In vitro activity of beauvericin against Sarcoptes scabiei: may a mycotoxin help for the control of 
sabies? 
C. Al Khoury, N. Nemer, G. Nemer, M. Kurban, 
C. Bernigaud, K. Fischer, J. Guillot* [Créteil, France]

Lemongrass oil: a promising acaridical and ovidicial 
agent against scabies? 
L. Melin, L. Buming, C. Bernigaud, J. Guillot* 
[Créteil, France], F. Fang

Implementation of intravenous artesunate for severe 
malaria in France: analysis of outcome in 1391 
patients 
C. Roussel, P. N’dour, E. Kendjo, S. Larréché, A. Taieb, 
B. Henry, B. Lebrun-Vignes, C. Chambrière, N. Argy, 
S. Houze, O. Mour, D. Courtin, A. Angoulvant, H. Delacour, 
F. Gay, J. Siriez, M. Danis, F. Bruneel, O. Bouchaud, 
V. Ok, M. Bouba, S. Escoda, F. Sorge, A. Mandelcwaig, 
A. Fay, P. Mariani, L. De Pontual

A systematic evaluation of the anti-plasmodial activity 
of low molecular weight heparin against human 
malaria parasite Plasmodium falciparum 
M. Hmoud* [Baghdad, Iraq], N. Harrocks

Imported schistosomiasis in children: a French 
prospective multi-centre study of prevalence, clinical 
features and diagnostic methods 
C. Leblanc* [Bondy, France], S. Brun, O. Bouchaud, A. Izri, 
M. Caseris, M. Husain, A. Bergevin, L. Pham, A. Paugam, 
S. Jauréguiberry, V. Levy, C. Bloch Queyrat, 
S. Jauréguiberry, F. Gay, J. Siriez, M. Danis, F. Bruneel, O. Bouchaud, 
S. Larréché, A. Taieb, C. Bernigaud, J. Guillot* (Créteil, France)

Is strongyloidiasis currently endemic in Croatia? 
N. Pshenichnaia* [Moscow, Russian Federation]

Frequency of Toxoplasma gondii infection in 
schizophrenic patients: a pilot study 
A. Pietrzyk, P. Smyk, P. Kochan, V. Lunde* [Oslo, Norway], 
H. Renneberg, K. Fus, B. Papir, A. Depukat, M. Bulanda

Antichonous human and canine Strongyloides 
stercoralis infection in Europe: a systematic review 
L. M. Ottino* [Florence, Italy], D. Buonfrate, P. Paradies, 
Z. Bisoffi, A. Antonelli, G. Rossolini, S. Gabrielli, 
A. Bartoloni, L. Zommarchi

Occurrence of sporadic human ascariasis in non-
endemic regions: the importance of zoonotic 
transmission from swine 
T. Fritsche* [Marshfield, United States], J. Meece, 
S. Meyer, K. Ortega, N. Wolff, M. Hall
4258 An outbreak of scabies in the north-east region of Ghana

4733 First study on Giardia intestinalis assemblages in Algerian individuals
S. Belkessa, D. Vincent Thomas López, H. Nielsen, K. Houali, F. Ghalmi, C. Stienstra

4948 Strongyloidiasis in patients with Chagas disease in Barcelona
E. Dopico* [Barcelona, Spain], L. Solsana, M. Aguilar, Y. Rando-Matos, L. Guerrero, G. López De Egea, J. Mascort, E. Sulleira

5322 Usefulness of qPCR for the assessment of vectorial competence of wild caught sand flies species: preliminary results
L. Remadi* [Monastir, Tunisia], N. Chargui, M. Jiménez, J. Mascort, E. Sulleira

5942 A rare case of paragonimiasis infected by Paragonimus ohirai
Y. Zhang* [Shanghai, China], W. Jin, O. Miao, J. Pan, B. Hu

6095 Prevalence and genetic diversity of Blastocystis in asymptomatic and symptomatic individuals from Puducherry, India
S. Padukone* [Puducherry, India], A. Selvarathinam, M. Kumar, J. Mandal, N. Rajkumari, B. Vishnu Bhat, R. Swaminathan, S. Paria

7416 Preliminary evidence of absence of cystic echinococcosis in the Dibrugarh district of Assam state, North-East India
R. Taye Gam, I. Phukan, S. Deb, A. Saikia, P. Sharma, N. Nirmoliya, B. Rupali, T. Manciulli* [Pavia, Italy]

7638 Estimation of cystic echinococcosis prevalence in an endemic region in Uzbekistan
A. Colpani* [Pavia, Italy], O. Achilova, G. D’Alessandro, M. Dell’Anna, M. Arcangeletti, C. Chezzi, F. De Conto

7707 Distribution during 10 years of the genotypes A and B of Giardia intestinalis among the infected subjects attending to an Italian tertiary care hospital
A. Calderara, S. Montecchini* [Parma, Italy], M. Buttrini, S. Rossi, F. Motta, G. Piccolo, M. Antonaci, M. Dell’Anna, M. Arcangeletti, C. Chezzi, F. De Conta

7963 Delayed diagnosis of neuroschistosomiasis in a non-endemic country: a tertiary referral centre experience
A. De Wilton* [London, United Kingdom], D. Aggarwal, P. Chiodini

8744 A case of cystic hydatid disease acquired in Ireland
C. Grant* [Dublin, Ireland], C. Conlon, C. Fleming, H. Tuite, E. Slattery

9133 Risk factors for epilepsy and cystercerosis in Abidjan, Ivory Coast: a case-control study
M. Soumahoro* [Abidjan, Côte d’Ivoire], J. Melki, Y. Kangah, A. Tanoh, N. Iano, M. Diandé, M. Camara, M. Ngouan, T. Sonan, B. Assi, R. Jambou

9362 Study of brain-derived neurotrophic factor gene expression in brain tissue of rat infected to acute and chronic toxoplasmosis: a study in animal model
M. Fallah* [Hamadan, Iran], M. Matini, A. Maghsoud, M. Arabestani, M. Shahbazi

9538 Genetic diversity of the Plasmodium vivax circumsporozoite protein in isolates from Brazilian Amazon rainforest and Rio de Janeiro Atlantic Forest

Session accepted as Paper Poster Session

Parasitic Diseases: diagnosis and treatment

784 Launch of a new faecal molecular external quality assessment scheme by UK NEQAS Parasitology
J. Shrivastava* [London, United Kingdom], A. Saez, P. Chiodini

983 New raw materials for serology immunoassay quality controls
P. Monsbrat* [Limoges, France], G. Champier, C. Dollack, T. Schumacher, M. Dardé, S. Hantz

1925 Preliminary results of microRNA expression profile in patients with cystic echinococcosis and identification of possible cellular pathways

2163 Chagas disease in Japan, 2012-2019: clinical presentation and diagnostic delay
K. Imai* [Saitama, Japan], N. Tarumoto, J. Sakai, T. Murakami, S. Maesaki, S. Miura, T. Maeda

2482 Molecular diagnosis of toxoplasmosis: impact of sample storage duration for five types of biological samples

2683 Clinical efficiency of anti-Blastocystis therapy in ulcerative colitis patients
A. Tsyglev* [Tashkent, Uzbekistan], S. Osipova

2687 Evaluation of endoperoxides and tetrahydropyrans as potential anti-leishmanial drugs
M. Ortizali, S. Varani* [Bologna, Italy], G. Cimato, R. Veronesi, M. Lombardo, C. Trombini, M. Monari, A. Quintavalla
Diagnostic value of the molecular detection of *Sarcopes scabiei* from a skin scraping in patients with suspected scabies

M. Bae* [Seoul, South Korea], J. Kim, J. Park, S. Bae, J. Jung, H. Cha, N. Jeon, H. Lee, M. Kim, S. Chang, S. Kim

Development of new bicyclic nitroimidazoles as antitubercular and antiparasitic agents

C. Wei Ang, A. Jarrad, A. Debnath, L. Tan, M. Sykes, Y. Wang, M. Butler, P. Bernhardt, N. West, V. Avery, A. Popat, S. Franzblau, M. Cooper, M. Blaskovich*

[Brisbane, Australia]

Pulmonary sparganosis: a case report with 20 months follow-up

Z. Lei, J. Liu* [Guangzhou, China], S. Zhu, Y. Pang, H. Ma, J. Zhu, L. Xu, B. Lin, Z. Gao

A new rapid test on whole blood and on serum for the toxoplasmosis screening in pregnancy

V. Meroni* [Pavia, Italy], G. Ferrari, F. Genco, E. Dore, B. Mariani, M. Furione, M. Zavattoni, L. Scudeller, F. Peyron

Diagnostic accuracy of toxoplasma Western blot test in suspected seroconversion in pregnancy: a multi-centre study

V. Meroni* [Pavia, Italy], A. Corcione, F. Genco, L. Scudeller, H. Pelloux, F. Hélène, M. Brenier-Pinchart, C. L'Ollivier, L. Paris

Chagas disease diagnosis: comparison between two different native antigen assays

J. Wang Wang* [Barcelona, Spain], B. Rivaja Sanchez, G. Fernández Rivas, M. Navarro Albareda, S. Roure, L. Matas Andreu

Diagnosis of amoebic liver abscess by detection of *Entamoeba histolytica* DNA in serum using quantitative PCR

G. Theo* [Paris, France], M. Gits-Muselli, N. Guigue, M. Picat, S. Hamane, S. Bretagne

Association between the *Blastocystis* spp. load and patient's socio-demographic and clinical profile in the north-eastern area of Spain

C. Motavelle Ochoa* [Zaragoza, Spain], E. Rubio, P. Chueca, P. Goñi, A. Betran Rosel

Diagnostic performance and validation of two ready-to-use real-time PCR assays for the detection of *Plasmodium* spp. and the principal species capable to infect human

C. Escolar* [Zaragoza, Spain], N. Martínez Camea, M. Hernández, P. Egido, A. Milagra, A. Rezusta

Comparison of the performance of hydralid fluid and the recombinant antigen recDipol in the diagnosis of cystic echinococcosis patients

E. Akdur Öztürk* [Izmir, Turkey], M. Akil, F. Bilgic, C. Sánchez Ovejero, R. Román, A. Casulli, M. Siles-Lucas, N. Altıntaş, A. Unver

Changes occurred in immunological and molecular determinations of toxoplasmosis in pregnancy and newborn children

C. Istrate* [Bucharest, Romania], C. Cretu, P. Mihaiescu

Toxoplasmosis screening in pregnant women: results of the recombinant antigen recDipol in the diagnosis of cystic echinococcosis patients

G. Hartmeyer* [Odense, Denmark], S. Hoegh, M. Kemp

MoCA-T as first option in the cystic echinococcosis treatment: what we have obtained

C. Popa* [Bucharest, Romania], C. Cretu, M. Petru Escu, L. Papa, C. Botezatu, P. Mihaiescu, B. Mastalier

Value of soluble programmed death-1 (sPD-1) and sPD-ligand-1 (sPD-L1) as early biomarkers for the post-surgical monitoring of cystic echinococcosis in Tunisian paediatric patients

E. Ben Salah* [Monastir, Tunisia], W. Sakly, C. Barrera, S. Mosbah, R. Farhani, A. Bellanger, A. Ksia, B. Gottstein, A. Nouri, H. Babba, L. Millon

Differentiation of *Blastocystis* subtypes by PCR and Sanger sequencing versus NGS-based total ribosomal DNA analysis

K. Ascuña Durand, R. Salazar Sanchez, L. Andersen, J. Ballon Echegaray, C. Stensvold*

[Copenhagen, Denmark]

Performance of a commercially available LAMP assay and RDT for diagnosing *Plasmodium falciparum* malaria at very low parasitemias in a controlled human malaria infection trial

R. Payne* [Sheffield, United Kingdom], N. Edwards, K. Ellis, Y. Thermistocleous, S. Silva, J. Barrett, A. Flaxman, D. Bellamy, R. Morter, T. Rawlinson, S. Draper, A. Minassian

Delayed haemolytic anaemia following artesunate treatment in a returning African traveller

R. Oconnor, F. Carroll* [Dublin, Ireland], C. Doyle, C. Merry, C. Bannan

Comparison of native and a new recombinant fusion protein (AgB8/1+AgB8/2+Ag5) for serological diagnosis of cystic echinococcosis

F. Bilgic* [Izmir, Turkey], D. Dirim Erdogan, C. Gundüz, E. Akdur Öztürk, M. Korkmaz

Laboratory capacity for the diagnosis of leishmaniasis in Greece, 2018: a national surveillance study


[Athens, Greece]

Application of MALDI-TOF MS for identification of helminths in clinical samples

I. Sy* [Homburg/Saar, Germany], T. Wendel, M. Feucheroles, A. Nimmesgern, A. Suermann, Y. Endriss, J. Utzinger, S. Poppert, S. Becker

An unusual case of recurrent lymphocytic meningitis

M. Raza* [Milton Keynes, United Kingdom], P. Kapila, K. Omar, R. Randhawa

Role of PRAS40/mTOR/Akt in the intracellular development of *Toxoplasma gondii* tachyzoites

M. González-Del Carmen, V. Cartés Mollinedo*

[Cordoba, Mexico], G. Rojas García
7282 Genetic variability of Trypanosoma cruzi, in clinical samples from Latin American immigrant patients, living in Barcelona, Spain
M. Tavares De Oliveira* (Barcelona, Spain), E. Sulleira Igual, A. Silgado Gimenez, M. De Lana, B. Zingales, J. Santana Da Silva, J. Marín-Neto, I. Molina

7363 Application of molecular techniques in the diagnosis and follow-up of patients with imported malaria in a non-endemic country

7422 Comparison of PCR assays for detection of Echinococcus multilocularis from human formalin-fixed paraffin-embedded tissue preparations
J. Knapp, F. Mannien, S. Felix, D. Florent, B. Heyd, C. Richau, C. Bresson Hadni, L. Millon* (Besançon, France)

7567 Evaluation of a multiplex real-time PCR for the diagnosis of intestinal protozoa
E. Oliva, A. Raglio* (Bergamo, Italy), S. Varani, N. Menegotto, R. Gargiulo, A. Bruno, S. Cavallari, M. Cappola, C. Farina

7645 Performance of the Allplex Assay in comparison to microscopy and in-house real-time PCR for the detection of helmiths in Tanzanian stool samples
R. Wampfley, B. Barda, M. Ruf* (Basel, Switzerland), J. Keiser

7993 Amphotericin B as rescue therapy for alveolar echinococcosis in patients with benzimidazole treatment failure or toxicity

8019 Genome sequencing of Leishmania infantum causing cutaneous leishmaniosis from a Turkish isolate: metagenomic study for evaluation of proteins with polymorphism
D. Goldemir* (Ankara, Turkey), S. Naibantaglu

8170 Neglected tropical diseases contribute to the number of years with civil war
K. Last* (Hamburg, Germany), C. Papan, C. Becker, N. Mutters

8239 Role of glucose transporters in the intracellular proliferation of Toxoplasma gondii
T. Fernández Rebolledo* (Veracruz, Mexico), W. Diaz Beltrán, M. González-Del Carmen

8607 Weekly surveillance of bacterial, viral and parasitic infections involving private and public medical analysis laboratories through 317833 diagnostic tests in the Provence-Alpes-Côtes-d’Azur region, 2014-2019

8625 Evaluation of the performance of a commercial rapid diagnostic test for cystic echinococcosis in a clinical setting
A. Vola* (Pavia, Italy), A. De Silvestri, M. Mariconti, R. Lissandrin, M. Maestri, A. D’Addiego, E. Brunetti, T. Manciulli

8670 Impact of hand hygiene intervention on hand washing ability of school-aged children
S. Khan* (Karachi, Pakistan), H. Ashraf, S. Ifikhar, N. Baig-Ansari

1335 Human dirofilariasis in a changing world, evolving zoonosis just under the skin
G. Straffolini, A. Calcagnà, S. Scabini, T. Lupia, G. Di Perri, R. Angilletta* (Turin, Italy), P. Caramella

1671 Imported malaria: overview of the diagnosed and suspected cases of malaria in a Spanish city (15 years of experience)

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9166 The bacterial gut microbiota during controlled human infection with Nectator americanus larvae
Q. Ducarmon, M. Haagerveef, J. Janse, A. Geelen, J. Koopman, R. Zwittink* [Leiden, Netherlands], J. Goeman, E. Kuiper, M. Roestenberg

Session accepted as 2-Hour Oral Session

2289 Increasingly limited options for the treatment of enteric fever in travelers returning to England, 2014-2017
M. Herdman* [London, United Kingdom], B. Karo, J. Dave, P. Katwa, J. Freedman, G. Godbole, S. Balosegaram

3351 Incidence of Doxycycline Responding Illnesses (DRI) in returning travellers with fever

5487 The role of genomics in typhoid control: sentinel traveller surveillance, in-host evolution and transmission dynamics
Z. Dyson* [Cambridge, United Kingdom], V. Balaji, F. Dadri, T. Dollman, A. Pollard, G. Dougan, K. Holt

6281 First European outbreak of eosinophilic meningitis in travellers returning from Cuba
S. Roure, G. Fernández Rivas* [Badalona, Spain], B. Rivaya Sanchez, G. Lladoís, L. Grau, L. Guarro, S. Poppert, M. Ruf, L. Valerio, B. Nickel, L. Matas Andreu

9548 Non-human primate injuries in returning travellers: implications for pre- and post-travel management
T. Rampling* [London, United Kingdom], S. Balijekar, M. Brodermann, M. Brown, N. Longley

Session accepted as 2-Hour Oral Session

64 Tuberculosis among migrant people in Sicily: a real-life report
G. Pipitone* [Palermo, Italy], T. Prestileo, A. Sanfilippo, F. Di Lorenzo, A. Ficalora, S. Corrao

957 Results of a schistosomiasis screening programme in an immigrant population

1789 Results of a screening programme for Strongyloidiasis in HIV-positive immigrants

2400 Improving adherence to treatment of malaria among immigrants
M. Rodriguez-Perez, A. Rodriguez-Guardado* [Oviedo, Spain]

2866 A machine learning model for evaluating Chagas disease screening in immigrant populations

3104 Should Chlamydia trachomatis be part of migrant screening?
M. Bonneton* [Paris, France], L. Surgers, V. Lalande, N. Valin, K. Lacombe

3506 Clinical and economic impact of three different strategies for the management of schistosomiasis in Sub-Saharan immigrants to Italy
A. Botta* [Florence, Italy], M. Tilli, A. Bartoloni, L. Zammarchi, S. Boccalini

4811 Chronic schistosomiasis and strongyloidiasis amongst Ethiopian immigrants in Netanya
T. Finn* [Netanya, Israel], F. Babushkin, K. Geller, T. Grossman, R. Cohen

7122 Country-specific approaches to latent tuberculosis screening and its current effectiveness in migrants to Europe

9548 Non-human primate injuries in returning travellers: implications for pre- and post-travel management
T. Rampling* [London, United Kingdom], S. Balijekar, M. Brodermann, M. Brown, N. Longley

Session accepted as Paper Poster Session

64 Travel medicine and migrant health

728 Ignatzschineria bacteraemia following maggot wound infestation
K. Nadrah* [Ljubljana, Slovenia], U. Glinšek Biškup, B. Šoba, V. Čvitković Špič, M. Mueller-Premru

1474 Knowledge and awareness of inadvertent use of yellow fever vaccine among renal transplant recipients
L. Cabral Miranda* [São Paulo, Brazil], F. Agena, A. Sartori, L. Azevedo, E. David-Neto, L. Pierrotti

1612 Review of enquiries to the UK national travel advice line by healthcare professionals regarding immunocompromised travellers
B. Merrick* [London, United Kingdom], S. Kanagarajah, D. Patel

1789 Results of a screening programme for Strongyloidiasis in HIV-positive immigrants

2301 Results of a screening programme for Strongyloidiasis in HIV-positive immigrants

2398 Outpatient clinic for tuberculosis screening: an opportunity to promote healthcare access among applicants for international protection
J. Testa* [Busto Arsizio, Italy], M. Pizzi, M. Farinazza, B. Menzaghi, F. Franzetti
2460  Encephalitis in French travellers, 2016-2019
A. Mailles* [Saint-Maurice, France], M. Martinot, X. Argemi, F. Bourdain, P. Jaquet, J. Krause, E. Canoui, J. Stahl

3162  An unusual case of a Spanish traveller patient with chyliuria and molecular diagnosis of schistosomiasis
M. Sempere Alcocer* [Nueva Andalucía, Spain], F. Jose M., C. Beatriz, H. Luis, J. Saugor, P. Fernández-Soto

3628  Imported leishmaniasis in a Parisian hospital, France: a 6-year experience
N. Aissioui* [Paris, France], S. Hamane, M. Gits-Muselli, N. Guigue, A. Petit, S. Delliere, A. Alanio, S. Brettegne

3982  Cognitive impairment following severe malaria in travellers
A. Duvignaud* [Bordeaux, France], B. Glize, H. Lemistre, P. Berreau, D. Nguyen, L. Martin, T. Pistone, A. Desclaux, D. Malvy

5563  Intestinal colonisation with extended-spectrum beta-lactamase-producing Escherichia coli after international trips in travellers attending a travel clinic in Rio de Janeiro
S. Tufic, L. De Araujo Longa, G. Caramano De Oliveira, L. Cecilio Vilar, V. Brígida De Carvalho, B. Meurer Mareira, K. Rodrigues* [Río de Janeiro, Brazil]

6368  Yellow fever enquiries to a national telephone advice line regarding travellers who are pre-conception, pregnant or breastfeeding
C. Patterson* [London, United Kingdom], S. Kanagarajah, D. Patel

7612  Screening for latent tuberculosis infection among asylum seekers in Brescia, Italy: results from the E-DETECT Project
V. Marchese* [Brescia, Italy], P. Zanotti, B. Formenti, B. Rossi, E. Girardi, L. Barcellini, G. Stancanelli, D. Cirillo, I. El Hamad, A. Matteelli

7947  Acquisition of antimicrobial resistance organisms by US international travellers

8069  Travel health advice: do travellers follow the recommendations?

8484  Evaluating the healthcare utilisation of undocumented migrants in the Helsinki and Uusimaa hospital district, Finland: a protocol for a register-based cross-sectional study
K. Rautila* [Helsinki, Finland], O. Helve, P. Tiittala

8160  Travel-related meningitis: results from a thirteen-year retrospective study
C. Pierre-Louis* [Saint-Mandé, France], F. Charton, L. Labarbe, M. Cabon, M. Gominet, D. Andriamanantena, C. Ficko

9201  Travel patterns and knowledge of risk of infections during international travels in solid organ transplantation

9232  Imported dengue fever in French travellers: a multicentre retrospective study
C. Pierre-Louis* [Saint-Mandé, France], C. Ficko, A. Perignon, C. Rapp, E. Caumes

9360  Sepsis caused by Salmonella Paratyphi B variant producing a blaOXA-48 in a traveller patient
A. Balandraud, L. Hadjadj, G. Dubourg, J. Rolain, S. Baron* [Marseille, France]

9451  Dengue fever in returning travellers: a retrospective study in London, UK
A. Duret* [London, United Kingdom], I. Suchett-Kaye, S. Adnan Aali, P. Papineni

9527  Microbiota modifications in travellers to tropical and subtropical areas

Session accepted as 1-Hour Oral Session
Travellers as vehicles of AMR

2118  ESBL-producing Enterobacteriaceae in patients with travellers’ diarrhoea: a prospective cohort study
D. Ljungquist* [Skäret, Sweden], S. Nematzadeh, C. Giske, F. Resman, K. Riesbeck, J. Tham

3675  Does our microbiome travel well? Microbiome resilience and acquisition of multidrug-resistant bacteria in travellers
M. Davies* [Birmingham, United Kingdom], J. Van Hattem, C. Schultsz, M. De Jong, D. Melles, A. McNally, W. Van Schaik, P. Wolffs, J. Penders

3769  Real-time sampling of travellers to Laos: epidemiology of mobile genetic elements
S. Dunn* [Birmingham, United Kingdom], A. Snaith, A. Kantele, E. Kuenzli, J. Corander, A. McNally

3966  The colonisation of Czech travellers and expatriates living in the Czech Republic by colistin-resistant Enterobacteriaceae including Escherichia coli harbouring mcr-1 genes on a plasmid or chromosome
M. Krutova* [Prague, Czech Republic], A. Baráková, E. Nyčova, G. Tereza, R. Karpiskova, O. Nýc, P. Drevinek, J. Tkadlec

8160  The rise and fall of a resistome: travel returners shed light on the dynamics of ESBL-producing Escherichia coli
A. Mari* [Basel, Switzerland], F. Bonfiglio, E. Kuenzli, D. Lang, D. Nagarth, H. Seth-Smith, A. Egli
Abstract Programme


- Intravascular catheter-related infections
- Other foreign-body and implant infections
- Surgical site infections
- Healthcare-associated pneumonia
- Nosocomial infection surveillance & screening methods
- Epidemiology and transmission (incl. observational studies)
- Infection control interventional trials (incl. microbiota transplantation)
- Disinfection & biocides
- Other
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Session accepted as Paper Poster Session

Advances in implant infection management

1295 Transjugular intrahepatic portosystemic shunt and infections: a single-centre retrospective study
A. Lombardi* (Pavia, Italy), M. Sambo, M. Colaneri, A. Cambianica, P. Sacchi, V. Zuccaro, A. Di Matteo, P. Quaretti, L. Maramarco, N. Cionfoli, M. Mandelli, R. Bruno

1430 Outcome impact of a highly bactericidal scheme as initial treatment of acute staphylococcal PJI

1545 Does iodine-impregnated incision drape prevent periprothetic joint infection? One-year follow-up of 1187 patients in a randomised controlled trial
A. Brun Hesselvig* (Dyssegaard, Denmark), M. Arpi, T. Bjarnsholt, A. Odgaard

2058 Arthroscopic debridement, antibiotic and implant retention (DAIR) with local administration of Exebacase (Lysin CF-301) (LysinDAIR) followed by suppressive tedizolid as salvage therapy in elderly patients for relapsing multidrug-resistant Staphylococcus epidermidis prosthetic knee infection
T. Ferry* (Lyon, France), B. Cecile, C. Kolenda, C. Cassino, C. Chidiac, T. Perpoint, C. Le Corvaisier, J. Josse, A. Souche, S. Lustig, F. Laurent

2268 Prosthetic joint infections treated with two-stage revision procedure: a case series

2400 Appropriacy of empirical antibiotic therapy in percutaneous endoscopic gastrostomy site infection among head and neck cancer patients: a 15-year retrospective study
S. Park* (Seoul, South Korea), J. Oh, J. Kim, E. Joo, J. Lee

2981 Ultrasound-guided local administration of personalised cocktail of bacteriophages followed by suppressive antibiotic therapy as salvage therapy in patients with relapsing total femur prosthetic joint infection (PJI)
T. Ferry* (Lyon, France), C. Kolenda, F. Craighero, S. Park*, S. Etienne, C. Chidiac, L. Gilles, F. Laurent

3224 Risk factors for treatment failure of prosthetic joint infections: a multi-centre prospective cohort study
L. Cardoso, J. Matos, L. Jorge, M. Carneiro, K. Morejon, B. Bassetti, M. Graf, C. Pilati, J. Rocha, R. Leme, M. Salles* (Sao Paulo, Brazil)

3312 Exploration of the added value of rifampicin to antibiotic regimens for the management of Cutibacterium periprosthetic joint infection

3405 Pseudomonas aeruginosa prosthetic joint infection: results from a prospective cohort
H. Prié* (Paris, France), V. Meyssonnier, Y. Kerroumi, B. Heym, O. Lidave, S. Marron, V. Zeller

Impact of multidisciplinary management on the outcome of aortic prosthetic vascular graft infections: a retrospective, single-centre experience
M. Puges* (Bordeaux, France), A. Cluzeaud, C. Cazanave, V. Brizzi, C. Caradu, E. Ducassee, X. Bérand

Risk factors for treatment failure in patients with deep spinal SSI with foreign bodies treated with debridement, antibiotic and implant retention (DAIR): an international multi-centre retrospective cohort study

Successful treatment of osteoarticular infections caused by quinolone-resistant Gram-negative bacilli with colistin plus ß-lactams: preliminary results of a prospective multi-centre clinical study

Features and outcomes of biliary tract-related bloodstream infections in patients with biliary prosthesis: results from the PROBAC study

Risk factors for prosthetic joint infections caused by Gram-negative bacteria: experience at an infectious disease referral centre
S. Tedeschi* (Bologna, Italy), L. Pancaldi, N. Rossi, E. Zamparini, M. Neri, M. De Paolis, A. Di Martino, P. Viale
Abstract Categories 2020

7507 Fungal prosthetic vascular graft infections: beware of aorto-enteric fistulas!
M. Pugès* [Bordeaux, France], X. Bérard, T. Caulier, L. Stecken, D. Leray, E. Senneville, I. Accoceberry, F. Gabriel, O. Robineau, C. Cazanave

8405 Enterococcus species involvement in vascular graft infections
J. Bauer* [Touroping, France], D. Leray, P.d’Elia, J. Sobocinski, O. Robineau, E. Senneville

8833 Optimising the microbiological diagnosis of prosthetic joint infection: a 5-year evaluation
L. Cottom* [Glasgow, United Kingdom], P. Wright

9509 Characteristics of vascular graft infection: a prospective single-centre cohort study
D. Margaryan* [Berlin, Germany], T. Khilaishvili, N. Cesta, M. De Mosi, A. Trampuz

57 Combined antibiotic stewardship and infection control measures to contain an outbreak of linezolid-resistant Staphylococcus epidermidis in an interdisciplinary intensive care unit
C. Papan* [Hamburg, Germany], F. Berger, K. Last, M. Hoffmann, H. Knall, M. Schrädter, T. Volk, U. Schlotthauer, B. Gärtnert, S. Becker

Infection control, antimicrobial consumptions and incidence of hospital-acquired Clostridioides difficile infection in acute care hospitals in Catalonia

Impact of antimicrobial stewardship and infection control programmes on the incidence of carbapenem-resistant Klebsiella pneumoniae: a nonlinear time-series analysis
M. Meschiari* [Modena, Italy], C. Nebot, A. Cea, M. Sarti, A. Bedini, G. Orlando, J. Lopez Lozano, C. Mussini, M. Luchter

Impact of antimicrobial stewardship and infection prevention interventions on a cluster of VIM-producing Pseudomonas aeruginosa in a large, academic health system in Miami, Florida
G. Rosello* [Miami, United States], A. Jimenez, K. Deronde, A. Bedini, G. Orlando, J. Lopez Lozano, C. Mussini
Impact of early carbapenemase notification on infection control management and antimicrobial stewardship
L. Perez* (Porto Alegre, Brazil), C. Magagnin, C. Dias, G. Narvaez

Exploring social links and networks of communication in relation to infection prevention and control and antibiotic stewardship across surgical specialties in South Africa
C. Bonaconsa, O. Mbabalu* [Cape Town, South Africa], A. Boutall, M. Hampton, A. Holmes, M. Mendelson, T. Pennel, E. Charani

Mapping the roles and responsibilities for infection prevention and antibiotic prescribing along the surgical pathway in India and South Africa: case studies
S. Singh, M. Mendelson, S. SURENDRAN, C. Bonaconsa, O. Mbabalu* [Cape Town, South Africa], V. Nampoothiri, A. Boutall, M. Hampton, P. Dhar, T. Pennel, C. Tarrant, A. Holmes, E. Charani

Modulating the microbiota of the hospital environment by microbial cleaning: impact on infections and antimicrobial resistance
M. D’Accolti, I. Soffritti, L. Lanzoni, M. Bisi, A. Volta, S. Mozzacane, E. Caselli* [Ferrara, Italy]

A combined strategy of antimicrobial stewardship and hospital-acquired infection control reduced the incidence of bacterial infection in a kidney transplantation programme [Hippomenes-PACTA-PROA study]

Is there any risk factor in terms of mortality in patients with nosocomial colistin-resistant Klebsiella pneumoniae infection?
Ç. Ataman Hatipoğlu, F. Erding, G. Ertem, S. Ceresa, E. Kaya Kilic, S. Altun Demircan, K. Arslan, A. Büyükdemirci, N. Tulek* [Ankara, Turkey], S. Kinikli

Clinical impact of infections caused by carbapenemase-producing Enterobacteriaceae

A retrospective study to evaluate the epidemiology, standard of care, outcomes and resource utilisation in patients with confirmed or suspected infection by a carbapenem-resistant Gram-negative organism in Spain: the CarBAR study part 1, epidemiology of Gram-negative organisms
J. Harcojeda* [Barcelona, Spain], M. Salavert, J. De La Torre Cisneros, J. Gracia-Ahufiger, J. Paño Pardo, H. Vilchez Rueda, N. Benito, A. Rivera, D. Sousa Regueiro, V. Estrada Perez, M. Ibarjurein Pinilla, D. Manissera, C. Langshaw, K. Tone, S. Lopes

The economic burden of carbapenem-resistant non-fermenting Gram-negative bacteria healthcare-associated infections
Y. Cai* [Singapore, Singapore], C. Wong, W. Lee, J. Teo, T. Lim, B. Tan, A. Kwa

Healthcare-associated bacteraemic urinary tract infections: results of the prospective multi-centre ITUBRAS-2 project

Flat lining of nine-year deaths rate throughout various carbapenem-resistant Gram-negative outbreaks at Saint George Hospital, Lebanon
A. Chamieh* [Marseille, France], O. Zmerli, S. Saliba, C. Ajif, G. Juvelekian, J. Rolain, E. Azar

Epidemiology, risk factors and outcomes of infections caused by carbapenem-resistant Gram-negative bacteria in paediatric intensive care unit
L. Celani, M. Ridoif, C. Borrazzo, M. Trancassini, G. Antonelli, P. Popoff, C. Mastroianni, G. D’etorre, P. Pavone* [Rome, Italy]

Seasonal patterns in the burden of common bacterial pathogens in south-east Michigan post-acute care facilities
M. Cassone* [Ann Arbor, United States], J. Mantey, K. Gontjes, B. Lansing, K. Gibson, L. Mody

Carbapenem-resistant Enterobacteriaceae infections: more could be worst?
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**Session accepted as Mini-oral ePoster Session**

**Clostridioides difficile: prevalence, diagnosis and outcomes**

3194  *Clostridioides difficile* NAAT-positive with toxin-negative test results: impact of antibiotic treatment on clinical outcomes  
J. Haque* [Milwaukee, United States], A. Dawson, K. Osinski, M. Thakkar, A. Yarur, L. Munoz-Price

A phase II open-label clinical trial of investigational microbiota-based drug RBX2660 for prevention of recurrent *Clostridioides difficile* infection: two-years evaluation of efficacy, durability, microbiome changes and participant demographics  
C. Reimer* [Copenhagen, Denmark], R. Grenstein, L. Bancke, C. Gonzalez, K. Blount

Microbiome analysis of faecal microbiota transplantation via lyophilised capsules for recurrent *Clostridioides difficile* infection  

**Session accepted as Paper Poster Session**

**Environmental contamination and infection prevention**

76  Architecture fundamentally influences opportunity costs during an outbreak in a neonatology unit: real-life data and simulation of room designs  
S. Scheithauer* [Göttingen, Germany], M. Kaase, D. Fenz, H. Küster, S. Horn, B. SiIwa

Risk factors of environmental dissemination of different multidrug-resistant organisms  
R. Saliba* [Bobigny, France], D. Seytre, G. Theo, T. Delerue, F. Joureguy, E. Carbonnelle, D. Karam Sarkis, T. Billard-Pomares, J. Zohar

Inhibitory effect of whole blood on the antiseptic action of E-101 solution, a myeloperoxidase-mediated formulation, compared to conventional wound cleansers  
G. Denys* [Indianapolis, United States], J. Carpenter, R. Allen, J. Stephens, Jr.

**Session accepted as 1-Hour Oral Session**

**Do you really want to know what is in your hospital room?**

2441  Short-term environmental contamination with MRSA explained by in-room activity of MRSA-colonised patients  
A. Wolfensberger* [Zürich, Switzerland], N. Mang, K. Gibson, M. Cassone, K. Gontjes, H. Sax, L. Mody

Variable number tandem repeat analysis on patient *Pseudomonas aeruginosa* (PsA) bacteraemia isolates and hospital shower water PsA strains to determine their links  
Ö. Yetiści [London, United Kingdom], P. Wilson, J. Turton, Z. Payne, S. Ali

When cold water is too warm: healthcare-associated Legionnaires’ disease associated with hot season  
F. Waldeck* [St. Gallen, Switzerland], P. Kohler, M. Frischknecht, R. Kuhn, M. Von Kietzell, W. Albrich, M. Schlegel

A simple cleaning intervention to prevent transmission of carbapenemase-producing *Enterobacteriales* from hospital sinks  
J. Kwong* [Melbourne, Australia], M. Leroi, T. Bannam, D. Edmonds, E. Grabsch, S. Narayanasamy, J. Greenough, C. Lane, M. Easton, B. Howden, P. Johnson, M. Grayson

Environmental contamination and infection: two-years *Clostridioides difficile* infection in adult patients admitted in Spanish hospitals: multi-centre, retrospective, observational study  

Microbiome characterisation of patients with *Clostridioides difficile* infection and colonised patients  
S. Vazquez Cuesta* [Madrid, Spain], N. Lozano, L. Villar Gamara, L. Alcalá, M. Marín, P. Muñoz, E. Bouza, E. Reigadas Ramirez

**Community-acquired *Clostridioides difficile* infection: a prospective study in an unselected population**  
L. Villar Gamara* [Madrid, Spain], S. Vazquez Cuesta, L. Alcalá, M. Marín, P. Muñoz, E. Bouza, E. Reigadas Ramirez

**Clinical and gut microbiome characterisation of *Clostridioides difficile* infection in immunosuppressed patients**  
S. Vazquez Cuesta* [Madrid, Spain], L. Villar Gamara, N. Lozano, L. Alcalá, M. Marín, P. Muñoz, E. Bouza, E. Reigadas Ramirez

**The sink as source of transmission of VIM metallo-
β-lactamase-producing *Pseudomonas aeruginosa* in the intensive care unit**  
V. Robin* [Brussel, Belgium], D. De Geyter, I. Wybo, F. Crombe, D. Pierard
Abstract Categories 2020

2326 Increases in environmental cleaning and reduction in in-hospital mortality in multi-patient rooms with single-use disinfection wipes hung at the patient bed: a prospective, crossover trial


2438 Genomic and environmental investigation of hospital room occupied by an imported case of meningitis due to extensively drug-resistant (XDR) *Pseudomonas aeruginosa*


2326 Influence of the Built Environment (BE) microbiota on the epidemiology of antimicrobial resistance at intensive care unit of a tertiary hospital


2438 Control of hospital-wide outbreak of OXA-48-producing *Enterobacteriaceae* outbreak


3398 Achieving sustained decolonisation of CPE in sinks


4136 Dynamics of *Staphylococcus aureus* in the hospital environment and in patients: is the environment identified as a reservoir?

A. Van Der Schoor (*Rotterdam, Netherlands), A. Voor In, T. Holt, C. Klaassen, J. Severin, D. Gommers, M. Bruna, J. Hendriks, M. Vos

3398 Activity of peracetic acid against MDR *Enterococcus faecium* and non-typhoidal Salmonella from diverse epidemiological and genetic backgrounds

A. Rebulo (*Porto, Portugal), B. Duarte, A. Freitas, A. Callejón, L. Vieira Peixe, C. Novais, P. Antunes

3403 Take care of the cents and the euros look after themselves? Antimicrobial activity of European money

J. Knoblich (*Hamburg, Germany), C. Belmar Campos, E. Klupp, G. Franke

3403 Systematic review of *Legionella* amelioration systems in healthcare facilities

J. Mcdanel, A. Marra, D. Diekema, E. Kiscaden, H. Healy, L. Herwald (*Iowa City, United States)

3403 Environmental epidemiological survey of carbapenem-resistant *Klebsiella pneumoniae* in 5 intensive care unit

Q. Shi (*Shanghai, China), Y. Huang, W. Sun, Y. Cui, B. Hu, X. Gao

3403 Elevated tolerance to disinfectants in a carbapenemase-producing *Klebsiella pneumoniae* isolate obtained from a duodenoscopy-associated outbreak

K. Konrat, M. Brunke (*Berlin, Germany), Y. Pfeifer, L. Becker, C. Schaudinn, B. Pieening, I. Schwebke, M. Arvand

3403 Dynamic interactions between methicillin-resistant *Staphylococcus aureus* and methicillin-sensibler *Staphylococcus aureus* contamination of the near patient and extended environment and patient colonisation revealed by whole genome sequencing in a tertiary referral hospital

P. Kinnevey (*Dublin, Ireland), A. Kearney, M. Earls, T. Poovelikunnel, G. Brennan, A. Share, H. Humphreys, D. Coleman
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**Session accepted as Paper Poster Session**

**Epidemiology and surveillance of hospital-acquired infections**

| 81     | A regional survey on the level of implementation of key infection prevention and control structures in acute-care hospitals in Crete, Greece  |
|        | E. Astrinaki, E. Kritsotakis, E. Bolikas, E. Panagiotaki, D. Christofaki, A. Chalkiadaki, A. Salvaraki, E. Ioannidou, E. Stamati, G. Pavlidaki, E. Lagoudaki, M. Moustaki, V. Kataxaki, D. Stamati, M. Katsidioutati, S. Karakonstantis* [Heraklion, Greece], A. Gikas  |
| 460    | Prevalence of device use and transmission-based precautions in nineteen large Australian acute care public hospitals: secondary outcomes from a national healthcare-associated infection point prevalence survey  |
|        | P. Russo* [Melbourne, Australia], A. Stewardson, A. Cheng, T. Bucknall, B. Mitchell  |
| 669    | Incidence rate of health care associated infection in tertiary care children's hospital in Ukraine  |
|        | A. Odiannyk* [Kiev, Ukraine], K. Soiak, A. Aleksandrin  |
| 994    | Prospective surveillance of health-care associated infections in residents in long term care facilities in Graz, Austria  |
|        | E. König* [Graz, Austria], M. Haubenwallner, C. Pux, K. Prisching, W. Schippinger, E. Staisser, R. Krause, I. Zollner-Schweitz  |

**Beyond the contact precaution: what does the surveillance culture tell us about multidrug-resistant microorganisms in critically ill patients? Data of the Public Hospital of São Paulo City, Brazil**

|       | C. Abboud* [Sao Paulo, Brazil], E. Evangelista De Souza, D. Feriani, L. Gardiho Mutti Corvalha, A. Santos Ibanes, E. Vasconcelos, V. Barros Barbosa, F. Inoue, J. Monteiro  |

**Prospective genomic surveillance of multidrug-resistant organisms in Vietnamese intensive care units**


**Adherence to an admission screening for multidrug-resistant organisms in a tertiary care hospital in Switzerland**

|       | F. Waldecker* [St. Gallen, Switzerland], P. Kohler, M. Schlegel, E. Lemmenmeier  |

**Multidrug-resistant organisms (MDRO) colonisation pattern, prevalence and acquisition in a neonatal intensive care unit, evidence for guiding active surveillance cultures: a 2-year experience active surveillance process at Saint Joseph Hospital, Jerusalem**

|       | A. Sabateen* [East Jerusalem, Palestine]  |

**Multilevel analysis of the regional variation in healthcare-associated infections and antimicrobial use prevalence in acute-care hospitals in Greece**

|       | E. Kritsotakis, E. Astrinaki, T. Machaira, S. Karakonstantias* [Heraklion, Greece], A. Gikas  |

**Healthcare associated infections and outcomes: changes between 2013 and 2018 in Turkey**


**Hospital onset bloodstream infection (HOBSI) as a marker of the burden of hospital associated infection (HAI) at a tertiary care hospital in South India**

|       | R. Iyer* [Hyderabad, India], R. Jongam  |

**Active follow-up of patients colonised with highly-resistant microorganisms to discontinue isolation measures**

|       | C. Haanappel* [Rotterdam, Netherlands], A. Voor In, T. Holt, L. Bode, I. De Goeij, M. Vos  |

**Nosocomial bloodstream infection rates: exploration of a quality indicator for infection prevention**

|       | B. Laan* [Amsterdam, Netherlands], S. Geerlings, T. Holt, L. Bode, I. De Goeij, M. Vos, C. Haanappel* [Rotterdam, Netherlands], A. Voor In, T. Holt, L. Bode, I. De Goeij, M. Vos  |
Healthcare-associated infections, antibiotic use and resistance in Swiss long-term care facilities: a multi-centre point prevalence study

Automated detection of antimicrobial-resistant bacteria based on real-time microbiological data
V. Schechner* [Tel-Aviv, Israel], T. Grossman

Impact of applying mucosal barrier injury laboratory-confirmed bloodstream infection criteria in patients with solid tumours and haematologic malignancies

Mucosal barrier injury laboratory-confirmed bloodstream infection in oncology patients: descriptive analysis of epidemiological and laboratorial data

Increasing trends of emerging extensively drug-resistant bacteria cases at Lyon University Hospital, 2015-2019
E. Christelle* [Lyon, France], D. Hilliquin, E. Munier-Marion, E. Kuczewski, C. Dananché, C. Barreto, S. Gardes, B. Grisi, S. Gerbier Colomban, G. Jacqueline, C. Dupieux-Chabert, P. Vanhems

Polymerase chain reaction-based active surveillance of multidrug resistant pathogens in a paediatric intensive care unit: to screen or not to screen?
Ó. Martínez Expósito, E. Morteruel Arizkuren, J. Barrios Andrés, F. Pilar Orive, M. Aranzamendi Zaldumbide* [Barakaldo, Spain]

Effectiveness of monitoring colonisation by multidrug-resistant bacteria in polytrauma patients: 7 years of experience
S. Torri* [Milan, Italy], A. Bielli, V. Cento, G. Colombo, O. Chiara, F. Sammartano, C. Vismara, C. Perna, E. Mazzola

Evolution of multidrug-resistant organisms active surveillance strategy in a Portuguese acute care hospital, from 2015 to 2018
D. Peres* [Matosinhos, Portugal], A. Cipriano, V. Alves, F. Vieira, I. Devesa, I. Neves

Computerised registry as a potential tool for surveillance and management of complex bone and joint infections in France
Abstract Categories 2020

849 Baseline microbiology, susceptibility, molecular characterisation, and emergence of non-susceptibility in a recent randomised, controlled trial (RESTORE-IMI 2) comparing imipenem/cilastatin (IMI)/relebactam (REL) versus piperacillin/tazobactam (PIP/TAZ) for hospital-acquired or ventilator-associated bacterial pneumonia (HABP/VABP)


1345 Increased serum hydrogen sulfide as determinant of resolution of ventilator associated pneumonia caused by P. aeruginosa

G. Renieris* [Athens, Greece], K. Katrini, E. Karakike, N. Antonakos, A. Karageorgos, L. Sabrakos, E. Giamarellos-Bourboulis

1865 Risk score for non-ventilator-associated hospital-acquired pneumonia (nvHAP)

A. Wolfensberger* [Zürich, Switzerland], V. Kashalov, W. Jakob, S. Kuster, S. Balakrishna, R. Kouyos

2909 Impact of early appropriate antimicrobial therapy on new hierarchical endpoint for ventilator-associated bacterial pneumonia

E. Weiss, S. Rucklig, C. Dupuis, J. Zahar, J. Timsit* [Paris, France]

3006 Antimicrobial susceptibility and clinical characteristics of severe pneumonia due to Haemophilus influenzae: an observational study

P. Donnelly, M. Postorina, A. Stazzulla* [Melun, France], A. Pitsch, S. Jochmans, M. Monchi, V. Dubee, S. Diamantis

3027 Effectiveness of trimetoprim-sulfametoxazole for treatment of ventilator-associated pneumonia: a cohort study


3867 Health economics of nosocomial pneumonia in UK intensive care units: an exploratory study

A. Wagner, D. Turner, V. Enne* [London, United Kingdom], R. Baldan, C. Russell, D. Livermore

4306 Revision of clinical guidelines for hospital-acquired pneumonia led to a reduction in carabapenem prescriptions at a Swiss cantonal hospital

F. Schefer, T. Fehr, F. Fleisch, A. Cusini* [Chur, Switzerland]

4431 Clinical efficacy of ceftolozane-tazobactam versus other active agents for the treatment of bacteremia and nosocomial pneumonia due to drug-resistant Pseudomonas aeruginosa

M. Bassetti, D. Giacobbe, E. Rizzo, N. Castaldo* [Udine, Italy], C. Mussini, A. Cattelan, A. Russo, C. Mastroianni, A. Capone, M. Tumbarello, A. Vena

A prediction model for identification of patients at high risk for Staphylococcus aureus intensive care unit pneumonia and implications for trial design


Comparison of Hospital Resource Utilisation (HRU) among patients who received either ceftolozane-tazobactam (C/T) or meropenem in ASPECT-NP: a randomised, controlled, double-blind study of adult patients with Ventilated Nosocomial Pneumonia (V-NP)

L. Puzniak* [Kenilworth, United States], T. Lodise, J. Yang, R. Dillon, M. Kolle

Role of multidrug-resistant bacteria on nosocomial pneumonia mortality


Preliminary results for the evaluation of the impact of syndromic lower respiratory tract panel on antimicrobial management and infection control

R. Can Sarınoğlu* [İstanbul, Turkey], E. Tukenmez-Tigen, H. Bilgin, B. Aksu, V. Korten, G. Soyletir

Diagnostic test characteristics of radiographic keywords in the diagnosis of bacterial pneumonia

D. Albin* [Ann Arbor, United States], J. Pogue, L. Petty, J. Mills, K. Kaye

Incidence of ventilator-associated pneumonia in children intubated in paediatric intensive care unit


Double carbapenem therapy for isolated pneumonia in carbapenem-resistant Klebsiella spp. and Acinetobacter spp.

D. Akyol* [İzmir, Turkey], S. Chousein Memetali, M. Demir, G. Gülüyeva, U. Onal, H. Sipahi, S. Ulusoy, D. Sipahi

Impact of the Spanish Neumonia Zero project on ventilator-associated pneumonia rates

S. Carvalho Brugger* [Lleida, Spain], M. MiraLbés, B. Balsera, S. Rodriguez, M. Vallverdú, J. Caballero

The burden of nosocomial pneumonia caused by Pseudomonas aeruginosa and Staphylococcus aureus for ventilated patients in European intensive care units: a weighted multi-state analysis

M. Von Cube* [Freiburg, Germany], T. Bluhmki, K. Kaier, F. Sijfakis, O. Ali, J. Hasen, F. Paling, J. Kuytjman, S. Malhotra-Kumar, J. Beyersmann, M. Wolkevitz
Nontoxicigen Clostridioides difficile strains against C. difficile colonisation: an experimental study
J. Couturier* [Paris, France], L. Franconeri, C. Janoir, L. Ferraris, S. Hoyas, J. Aires, F. Barbut

The effects of antibiotic cycling and mixing on acquisition of antibiotic-resistant bacteria in the intensive care unit: a post-hoc analysis of a prospective cluster-randomised crossover study

Changing the hospital microbiome: a cluster-randomised controlled trial to analyse the influence of environmental cleaning on hospital-acquired infections using disinfectant, soap or probiotic agents
R. Leistner* [Berlin, Germany], B. Köhlmorgen, J. Golembus, D. Gruhl, E. Lemke, B. Raguse, G. Zakansky, P. Gastmeier

Impact of selective decolonisation of critically ill extreme elderly patients using invasive devices with chlorhexidine 2% daily bath on healthcare-associated infection rates
J. Delgado Correal* [Rio de Janeiro, Brazil], R. Rufino, M. Fornasari, C. Alburquerque, M. Martins, D. Santos, P. Damasco

Participatient: Patient Engagement Counter Catheter-associated urinary tract infections with an App (PECCA)
R. Bentvelsen* [Leiden, Netherlands], B. Loan, S. Geerlings, N. Chavannes, K. Veldkamp

Is it cost effective to use a 2% chlorhexidine gluconate wipes bath to reduce primary bloodstream infection? A quasi-experimental study experience
C. Abboud* [São Paulo, Brazil], D. Feriani, L. Gordillo Mutti Carvalho, A. Santos Ibanes, E. Vasconcelos, V. Barros Barbosa, E. Evangelista De Souza

Effectiveness of chlorhexidine-impregnated dressing and a bundle of interventions for prevention of central line-associated bloodstream infections
B. Madran* [Istanbul, Turkey], Ş. Keske, V. Bakır, O. Ergünül

Risk for antibiotic resistance in patients hospitalised with urinary tract infection: a matched case-control study using the French health insurance database

Prevalence and risk factors of inappropriate use of intravenous and urinary catheters in surgical and medical patients
B. Loan* [Amsterdam, Netherlands], M. Vos, J. Maaskant, M. Van Berge Henegouwen, S. Geerlings

Impact of a continuous improvement programme on central venous catheter care in reducing the incidence of primary bloodstream infection in neonatal intensive care unit
R. Cantarim Inacio* [São Paulo, Brazil], E. Medeiros

Short-term peripheral venous catheter-related bloodstream infections
T. Vu, J. Goritsas, H. Torres Diaz, K. Reveles, C. Dickerson, J. Cadena-Zuluaga* [San Antonio, United States]

Utilility of central venous catheter cultures in predicting blood culture susceptibilities in catheter-related bloodstream infections due to Staphylococcus spp.
H. Nomoto* [Tokyo, Japan], M. Ishikane, K. Mezaki, N. Ohmagari

Ultrasound guidance and risk for intravascular catheter-related infections among peripheral arterial catheters. A post hoc analysis of two large randomised controlled trials
N. Buetti* [Paris, France], S. Ruckly, J. Lucet, L. Bouadma, C. Schwobel, O. Mimoz, J. Timsit

Peripheral venous catheter-related bloodstream infection in hospitalised children: the role of Gram-negative bacteria
I. Berger* [Herzliya, Israel], T. Cohen, E. Rahmani, I. Levy, A. Lowenthal, L. Goldberg, Y. Levinsky, H. Ben Zvi, G. Scheuerman

Effectiveness of chlorhexidine dressings to prevent catheter-related infections: Does one size fit all? A systematic literature review and meta-analysis
M. Puig-Asensio* [Iowa City, United States], A. Marra, C. Childs, E. Perencevich, M. Schweizer

Differences in clinical characteristics and causative pathogens between central line-associated bloodstream infections and catheter-related bloodstream infections using modified definition in medical intensive care unit
J. Hyun, J. Yeom, J. Choi, N. Ku, S. Jeong, J. Ahn* [Seoul, South Korea]

Urinary catheter use in university hospital: a prospective intervention study
I. Vorta, M. Bojáre, U. Dumps, A. Vilde* [Riga, Latvia]

Catheter-associated bloodstream infections: Empirical antibiotic recommendations based on microbiological data
C. Collado Giner* [Palma De Mallorca, Spain], M. García-Gasolita, M. Arrizabalaga Asenjo, L. Ventayol-Aguiló, M. Perez-Seqo, M. Gallegos Alvarez, A. Payeras

The risk of microbial contamination associated with nine different needle-free connectors
Q. Shi* [Shanghai, China], Y. Cui, W. Sun, Y. Shen, X. Chen, J. Lin, B. Hu, X. Gao

An outbreak of Ralstonia picketti bloodstream infection among paediatric leukaemia patients
T. Bedir Demirdag, A. Parlakay, F. Bayrakdar, B. Gulhan, S. Kanik, S. Sütüük, I. Mumcuoglu* [Ankara, Turkey], B. Dinc, N. Yarali
Catheter-associated urinary tract infections in patients hospitalised in intensive care unit
M. Hamidi* [Algiers, Algeria], H. Belekhel, S. Yahia, D. Bougdal, S. Sadat, K. Guenane, M. Denia

Serum Galectin-3 status in hospitalised patients with catheter-associated asymptomatic bacteriuria
S. Ifitimi, A. Hernández-Aguilera, L. Ana Felisa, I. Pujal, F. Ballester, A. Castra, J. Camps* [Reus, Spain]

Successful reduction of urinary catheter days and inadequate catheterisation after introduction of a prevention bundle
M. Ciprian* [St. Gallen, Switzerland], M. Schlegel, M. Schwark-Bähler, P. Kohler, W. Albrich

Correlation of central line-associated bloodstream infections with employee turnover: continuity in nursing staff matters!
S. Kuster, M. Dunic, C. Falk, H. Sax, P. Schreiber* [Zurich, Switzerland]

Nation-wide survey of catheter-related bloodstream infections in medical, surgical and intensive care settings, 2019
M. Decalonne, F. Goube, R. Gimenes, A. Petiteau, A. Berger-Carbonne, S. Le Vu, N. Van Der Meer-Martquet* [Tours, France]

Short-term peripheral venous catheter-related bloodstream infections in French healthcare settings, 2019
M. Decalonne, R. Gimenes, F. Goube, A. Petiteau, A. Berger-Carbonne, S. Le Vu, N. Van Der Meer-Martquet* [Tours, France]

Local signs at insertion site and prediction of catheter-related infections in short-term central venous and arterial catheters in the intensive care unit: individual findings from four multi-centre randomised controlled trials
N. Buetti* [Paris, France], S. Ruckly, J. Lucet, L. Boudina, M. Garrouste-Orgeas, C. Schwebel, O. Mimos, B. Sauweine, J. Timsit

Surveillance of central venous catheter bloodstream infections in critical care units in England: April 2017-March 2019
S. Gerver* [London, United Kingdom], A. Zaidi, P. Wilson, R. Hope

Impact of the Spanish Bacteraemia Zero project on central line-associated bloodstream infection rates
S. Carvalho Brugger* [Leida, Spain], M. Vallverdú, M. Miralbés, B. Balsera, S. Rodriguez, S. Iglesias, J. Caballero

Indwelling time of peripherally inserted central line-associated bloodstream infections rates
L. Bouadma, M. Garrouste-Orgeas, C. Schwebel, O. Mimoz, N. Buetti* [Tours, France], M. Vidal, N. Mrozek, D. Martineau, B. Pereira, O. Lesens

Clinical implementation of routine whole genome sequencing for hospital infection control of multidrug-resistant pathogens
P. Harris* [Herston, Australia], B. Forde, A. Jennison, K. Hodge, G. Playford, J. Clark, S. Beatson, D. Paterson

Population structure of extended spectrum beta-lactamase-producing Klebsiella pneumoniae ST48 in a hospital setting and genomic plasticity driven by transposable elements
M. Nguyen Ngoc* [Antwerp, Belgium], F. Maechler, J. Rodriguez Ruiz, B. Xavier, C. Lammens, H. Goossens, P. Gastmeier, S. Malhotra-Kumar

Whole genome sequencing of bloodstream isolates of Staphylococcus aureus reveals prolonged transmission chains within neonatal intensive care units
C. Goswami, S. Fox, M. Holden, A. Leanord, T. Evans* [Glasgow, United Kingdom]

Impact of different components of a national intervention on CLABSI rates
D. Ben-David* [Tel Aviv, Israel], A. Vaturi, E. Soiter, E. Temkin, Y. Carmeli, M. Schwaber

Comparing ethanol lock therapy versus vancomycin lock on a salvation strategy for totally implantable vascular access device infections due to coagulase-negative staphylococci (the ETHALOCK study): a prospective randomised clinical trial
C. Theis* [Clermont-Ferrand, France], M. Vidal, N. Mrozek, D. Martineau, B. Pereira, O. Lesens

Impact of unrestricted movement of carbapenemase-producing Enterobacteriaceae [CPE] carriers on transmission of CPE in nursing homes: a prospective cohort study
K. Linn* [Singapore, Singapore], P. Hon, H. Xiaowei, S. Syed Husen, L. Chan, J. Ng, O. Ng, S. Vasoo, M. Ling, D. Fisher, K. Marinimuthu

Endemic extended-spectrum beta-lactamase-producing Klebsiella pneumoniae in a neonatal intensive care unit in Greece
G. Kalageras, M. Miliotopoulou, E. Bouzavatoglou, A. Doudoulakakis, N. Girmizis* [Patras, Greece], A. Nika, A. Papaiaiannou, M. Tsolia, I. Spiliopoulou, E. Lebessi

Impact of unrestricted movement of carbapenemase-producing Enterobacteriaceae [CPE] carriers on transmission of CPE in nursing homes: a prospective cohort study
K. Linn* [Singapore, Singapore], P. Hon, H. Xiaowei, S. Syed Husen, L. Chan, J. Ng, O. Ng, S. Vasoo, M. Ling, D. Fisher, K. Marinimuthu

Linking advanced molecular diagnosis with infection control: is that effective?
K. Linn* [Singapore, Singapore], P. Hon, H. Xiaowei, S. Syed Husen, L. Chan, J. Ng, O. Ng, S. Vasoo, M. Ling, D. Fisher, K. Marinimuthu

Session accepted as 2-Hour Oral Session
Household transmission of ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* after hospital discharge of an ESBL carrier

Variation in strain types of extended spectrum beta-lactamase-producing *Enterobacteriaceae* in long-term care facilities: a multi-centre, prospective cohort study

Modelling pathogen transmission in intensive care units by integrating screening and antibiogram data
T. Pham* (Utrecht, Netherlands), M. Kretzschmar, X. Bertrand, M. Bootsma

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### Session accepted as 2-Hour Oral Session

**Meeting the challenges of implant infections’ diagnosis and management**

1160 **Streptococcal and *Staphylococcus aureus* prosthetic joint infections: are they really different?**

3004 **A second surgical debridement for acute periprosthetic joint infections should not be discarded**

3176 **Retrospective study of nosocomial infections in patients with extracorporeal membrane oxygenation therapy in a coronary unit**


5556 **Analysis of treatment failures of haematogenous prosthetic joint infections: new infections occur more often than infection persists or relapses**
N. Renz* (Berlin, Germany), A. Rakow, C. Perka, A. Trampuz

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Nasal colonisation with *Staphylococcus aureus* is a risk factor for ventricular assist device infection in the first year after implantation: a single-centre cohort study

Tolerance of prolonged oral tedizolid (TDZ) antibiotic therapy for peri-prosthetic joint infections (PJIs): results of a pilot multi-centre French study
E. Senneville* (Tourcoing, France), A. Dinh, T. Ferry, D. Robineau

Diagnostic accuracy of synovial cell count at reimplantation in periprosthetic knee infection undergoing two stage procedure
T. Ascione* (Naples, Italy), P. Pagliano, M. Mariconda, A. Baldini, G. Balato

Spinal implant-associated infections: results from a four-year prospective cohort study
D. Margaryan* (Berlin, Germany), N. Renz, P. Vajkoczy, A. Trampuz

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Nasal colonisation by *Staphylococcus aureus* in nursing home residents in Crete, Greece
K. Moschou, P. Ioannou* (Heraklion, Greece), E. Moraitaki, D. Stafylaki, E. Boutakoglou, V. Koutsouroumpsi, S. Maraki, G. Samonis, D. Kerferidis

Hospital organisation, management and implementation of culture of excellence in infection control and prevention of hospital-acquired infections at Ziv medical centre, Israel
J. Tarabeia* (Zefat, Israel), S. Edelstein, M. Sudri, H. Ben-Amram, S. Zarka

Rethinking the involvement of patients in infection prevention and control and antimicrobial stewardship
H. Seale* (Sydney, Australia)

Effective utilisation of limited isolation rooms to provide safe patient care and staff safety in lower-middle-income country
R. Roshan* (Karachi, Pakistan), Z. Rafique

An agent-based model to simulate the transmission of glycopeptide-resistant enterococci in hospital according to several control strategies
S. Debosscher, T. Lavigne* (Strasbourg, France), F. Severac, C. Méard, N. Meyer, J. Gaudart

Evaluation in general practice of the patient’s feelings about a recent hospitalisation and isolation for a multidrug-resistant infection
D. Hereng, A. Dinh, S. Bessis, S. Siméon, M. Mott, B. Davido* (Garches, France)

Presence of multidrug-resistant bacteria on uniforms of healthcare professionals in healthcare settings in Cyprus: implications for targeted infection control interventions
P. Lena, S. Karageorgos, D. Larnisios, P. Papageorgis, C. Tsiloutis* (Nicosia, Cyprus)
Abstract Categories 2020

5007 Nurse density matters in antimicrobial resistance: A 30-country observational modeling study
H. Kaba, E. Kuhlmann, S. Scheithauer* [Göttingen, Germany]

5223 Interest of a systematic surgical mask wearing policy to decrease nosocomial flu burden at hospital
V. Forget, S. Gros, E. Barneoud-Roussel, M. Demange, M. Ravry, A. Fourneret-Vivier, M. Paggio, L. Combrin, J. Gosjean, A. Pellicier, C. Dumillard, A. Wielandts, I. Guinot, E. Forestier* [Chambéry, France], F. Mallaual

6507 Omitting the nightly dose of selective digestive tract decontamination provides equally effective decontamination of potential pathogenic bacteria: a cost reducing and sleep-promoting intervention
J. De La Court* [Amsterdam, Netherlands], T. Groot, K. Sigaloff, H. Van Der Spoel, R. Schade

8016 Predict to prevent: system dynamic modeling for healthcare-associated influenza
M. Sansone* [Gotenborg, Sweden], L. Andersson, J. Westin, R. Norden

9205 Relevance of intra-hospital patient movements for the spread of healthcare-associated infections: a mathematical modelling study

9260 The dissemination and reservoirs of ESBL-producing Escherichia coli in intensive care unit
L. Baomo* [Guangzhou, China], C. Zhuo, Y. Guo

9364 Patient perceptions of antimicrobial resistance: are we getting the right messages across?
J. Doukrou Calsina, T. Planche, C. Suarez* [London, United Kingdom]

Session accepted as Paper Poster Session

Outbreaks’ epidemiology and management

508 Investigation of an Enterobacter cloacae OXA-436 carbapenemase outbreak: when everything goes down the drain
A. Holm* [Odense, Denmark], A. Toft, M. Nordestgaard, A. Hammerum, H. Hasman, M. Kemp, U. Justesen

2616 Challenges in investigation and control of invasive group A Streptococcus outbreaks associated with community health services delivered at home

3336 Outbreak of an uncommon rifampicin-resistant blaNDM-1 Citrobacter amalonaticus strain in a digestive rehabilitation centre: the putative role of rifaximin
G. Royer* [Crétel, France], F. Fourreau, C. Gomart, A. Maurand, B. Hacquin, D. Ducellier, F. Cizeau, S. Lo, C. Cordonnier Jourdin, M. Darty, J. Decousser

4233 Adenovirus-associated epidemic keratoconjunctivitis outbreak in a tertiary hospital
E. Miró* [Barcelona, Spain], M. Del Cuerpo, C. Berengua, P. Marin, J. Vela, V. Pomar, N. Rabella

4472 Epidemiology of nosocomial highly resistant microorganism outbreaks in the Netherlands
A. Reuland* [Utrecht, Netherlands], A. Schoffelen, F. Bijkerk, P. Bergervoet, S. De Greeff, C. Vandenbroucke-Grauls

5154 Investigating a cluster of community-acquired methicillin-resistant Staphylococcus aureus infections in a school in Eastern Switzerland
F. Waldeck* [St. Gallen, Switzerland], N. Oliver, S. Monse, D. Reinholz, A. Walt, M. Schlegel, S. Seiffert, C. Kahler

5603 A leak in compliance with ventilation system maintenance instructions resulted in an aspergillosis outbreak

7208 Partnering with bedside nurses: questionnaire-based approach during an outbreak of carbapenem-resistant Acinetobacter baumannii in two separate intensive care units
S. Kim, H. Seo, S. Oh, S. Seo, B. Lee, E. Bum, J. Eun, J. Chae, K. Lee, T. Kim* [Ulsan, South Korea]

7451 Outbreaks of multidrug-resistant Klebsiella pneumoniae in neonatal intensive care units in Ghana: a case for improved surveillance and infection control

8472 Identifying nosocomial transmission of influenza and associated deaths: a prospective, observational study
L. Snell* [London, United Kingdom], J. Vink, H. Mitchell, C. Beviz, M. Kabia, J. Edgeworth, G. Nebbia

8566 Long-lasting outbreak of Serratia marcescens in a veterinary hospital due to contaminated chlorhexidine

8741 Prospective surveillance of multidrug-resistant Gram-negative bacteria in a UK intensive care unit using whole genome sequencing

9773 Hospital outbreak of carbapenem-resistant Enterobacteriaceae associated with an OXA-48 plasmid hosted mainly by Escherichia coli ST399
1096  Antimicrobial prophylaxis administration after umbilical cord clamping in caesarean section does not increase risk for surgical site infection: a prospective analytic study with 55,301 patients
R. Sommerstein* [Bern, Switzerland], J. Marschall, A. Atkinson, D. Surbek, M. Dominguez, N. Troillet, A. Widmer

1251  Implementation of appropriate antibiotic prophylaxis in surgery: high benefit with no risk
B. Madran* [Istanbul, Turkey], Z. Akbulut, S. Tanju, Ş. Keske, S. Ersu, M. Kapadaglı, S. Pala, Ş. Dilege, Ö. Ergönü

1773  Multiple evaluation of surgical antimicrobial prophylaxis in Japanese university hospitals

2068  Effects of a strict postoperative glycemic control on surgical site infection's incidence following liver transplantation: a randomised clinical trial
R. Oliveira* [São Paulo, Brazil], J. Mancero, J. Tanner, V. Brito Poveda

2564  Single dose cefazolin is feasible in orthopaedics: behavioural change success with collaborative working
F. Erdinç, N. Tüek* [Ankara, Turkey], B. Alemdaroğlu, S. İltar, G. Ertem, S. Kinikli, C. Ataman Hatipoğlu

2768  Efficacy of fosfomycin-trometamol versus fluoroquinolone single-dose as prophylaxis for transrectal ultrasound-guided prostate biopsy

2841  Bacterial contamination of collagen membranes in dental surgery
A. Rachkov* [Minsk, Belarus], T. Shevelo

2850  Improvement of infection rates and hand hygiene adherence in pre-post comparison after introduction of an infection-prevention-meaasures-bundle implemented by an infection prevention link physician
M. Neuwirth* [Cologne, Germany], F. Mattner, R. Galante, I. Dombrowski, R. Otchwemah

3168  Impact of beta-lactam allergy label on preoperative antibiotic prophylaxis
C. Nguyen* [Chicago, United States], K. Petrucci, E. Daily, A. Brown, J. Pisano, N. Petit

3714  Current practices and evaluation of barriers and facilitators to surgical site infection prevention measures in Jimma, Ethiopia
A. Lang* [Rochester, United States], L. Berman, B. Gelano, D. Yilma, D. Siraj, D. Shirley

4029  Social and physical opportunities to improve surgical antimicrobial prophylaxis prescribing: utilisation of the behaviour change wheel
C. Jerana, A. Rajkhowa, K. Thursky* [Melbourne, Australia], C. Marshall, T. Peel, D. Ayton

4444  Epidemiology of cardiac surgical site infection in England, 2018/19
T. Lamagni* [London, United Kingdom], K. Cooper, C. Wloch, P. Harrington

4549  Assessing the impact of interventions designed to reduce the rate of postoperative sternal wound infection at a tertiary cardiothoracic centre
T. Locke* [Sheffield, United Kingdom], H. Parsons, N. Briffa, T. De Silva, T. Darton

5166  Prophylactic antibiotics administration in low- and middle-income countries: what are the consequences on antibiotic resistance? A systematic review

5350  Successful introduction of a bundle of measures to reduce surgical site infection by Staphylococcus aureus in patients undergoing coronary artery bypass grafting
E. Evangelista De Souza, L. Gordinho Mutti Carvalho, D. Feriani, A. Santos Ibañes, V. Barros Barbosa, E. Vasconcelos, C. Abboud* [São Paulo, Brazil]

6244  Effects of a carbapenem-sparing regimen for treating post-surgical intra-abdominal infections: a case-control study
F. Giovannenzen* [Rome, Italy], E. Taddet, R. Murri, L. Ceralini, E. Biracchi, F. Taccari, R. Caudea, M. Fantoni

6418  Mediastinitis: an incidence study and case series in an elderly adult centre

7661  Bacterial contamination of collagen membranes in dental surgery
A. Rachkov* [Minsk, Belarus], T. Shevelo

7765  Risk factor for nosocomial and surgical site infection after cardiac surgery
M. Pérez-Rodríguez* [Vigo, Spain], B. Vilas, A. Sousa, J. Lugo, M. Pereira, D. Lima, A. Nodar, R. Longueira, V. Del Campo, J. Legarra, M. Crespo

F. Nacinovich* [Buenos Aires, Argentina], P. Fernandez Oses, N. Spinelli, M. Viruel, F. Piccinini, M. Camporrotondo

9594  Airborne antibiotic-resistant Staphylococcus epidermidis in inpatient wards linked to deep surgical site infections
A. Johansson* [Umeå, Sweden], M. Widerström, T. Monsen, A. Larsen, M. Stegger
Validation of a semi-automated surveillance of surgical site infections: improving exhaustiveness, representativeness and efficiency
R. Molheira* [Porto, Portugal], N. Rocha Pereira, R. Dura, C. Pereira, C. Alves, S. Correia

Surgical site infections in orthopaedic surgery: a retrospective analysis of the risks associated with multi-drug resistant bacteria isolation

Antimicrobial stewardship and perioperative antimicrobial prophylaxis: results of an educational intervention
F. Segala* [Rome, Italy], R. Murri, E. Teddei, F. Giovannenze, P. Del Vecchio, E. Briocchi, F. Taccari, R. Cauda, M. Fantoni

Built environment microbiological surveillance in a large intensive care unit revealed abiotic reservoirs of highly persistent clones of Klebsiella species [K. pneumoniae, K. oxytoca, K. variicola]

Automated surveillance of urinary tract infections in a tertiary care hospital in Stockholm
S. Van Der Werff* [Stockholm, Sweden], E. Thiman, H. Tanushi, J. Karlsson Valik, A. Henriksson, M. Alam, H. Dalianis, A. Ternhag, P. Naucler

Intestinal colonisation by carbapenemase-producing Enterobacteriaceae detected by polymerase chain reaction in patients with negative cultures: do they really have an increased risk of infection?

Minimizing pseudo-cluster suggestions in infection control surveillance using pathogen DNA sequencing and artificial intelligence
D. Chen, Md, R. Sussens, Bsn, Rn, Cíc, M. Quinn, Bsn, Rn, Cíc, G. Wang, M. Chanza, Bo, W. Huang, C. Scurlock, Md, Mba, C. Becker, Md, Phd, J. Fallon, Md, Phd, K. Hansen, Phd, Ms, D. Heller, Bs, Emr, J. Ashworth, Mscs, Mt [Ascp], M. Fortunato-Habib, Dnp, Ms, Bs, Rn, J. Carmona, B. Gross* [Cambridge, United States]

Shared hospital epidemiology of respiratory viruses: a 3-year analysis using multiplex PCR in a university hospital
A. Valdes, B. Visseaux* [Paris, France], D. Bouzid, N. Fidouh, B. Descamps, D. Van-Gysel, F. Lenne, V. Goldstein, J. Lucet

The epidome: a species-specific approach to quantify population dynamics and heterogeneity of Staphylococcus epidermidis colonisation and infection in primary samples
A. Robinson, T. Johannesen, E. Mamsen, S. Iversen, S. Baig, J. Jensen, B. Söderquist, P. Andersen, M. Stegger* [Copenhagen, Denmark]

Active surveillance mitigates the risk of donor-derived infections in solid organ transplant recipient: the role of infection control
M. Campanella* [Palermo, Italy], A. Medaglia, E. Conoscenti, S. Caruso, G. Panarello, V. Lamonaca, F. Barbera, F. Monaco, A. Pasquariello, F. Cardinale, D. Di Carlo, P. Conaldi, P. Grossi, M. Mularoni

Performance of a computerised decision support system for the semi-automated detection of healthcare associated infections: an explorative pilot study
A. Ranzi* [Milano, Italy], G. Catho, A. Metsini, W. Zingg, B. Hurtner

Stay in the emergency department increases the risk of colonisation by carbapenem-resistant Enterobacteriaceae in the intensive care unit
M. Solomão, M. Freire* [Sao Paulo, Brazil], I. Bosczowski, S. Raymundo, A. Guedes, A. Shafferman, Levin

Risk factors for healthcare-associated infections caused by cefepime resistant Pseudomonas aeruginosa in a tertiary care hospital in Serbia
I. Petrovic* [Kragujevac, Serbia], Z. Djordjevic, M. Folic, S. Jankovic

Predictors of vancomycin-resistant enterococci gut microbiome colonisation among patients with Clostridioides difficile infection 6.4.1
E. Zasowski* [Vallejo, United States], M. Ali, A. Anugo, K. Dotson, B. Endres, K. Garey

Risk factors for colonisation with carbapenemase-resistant Acinetobacter baumannii in hospital
M. Meschieri* [Modena, Italy], K. Shanik, S. Selmi, M. Sarti, G. Orlando, M. Menozzi, C. Mussini

Risk factors associated with carbapenemase-producing Enterobacteriaceae infection

Epidemiology and dissemination of multidrug-resistant Pseudomonas aeruginosa colonisation in an intensive care unit
M. Portillo* [Pamplona, Spain], J. Lobo, A. Bacaicoa, J. Otero, A. Navascués Ortega, C. Ezpeleta Baquedano
Stigma in MDRO carriers exposed to isolation precautions: an exploratory quantitative questionnaire study
R. Wijnakker* [Leiden, Netherlands], M. Lambregts, B. Rump, K. Veldkamp, R. Reis, L. Visser, M. De Boer

Gastrointestinal colonisation by vancomycin-resistant enterococci and carbapenem-resistant Gram-negative bacteria in an endemic setting: prevalence, risk factors, and outcomes
A. Vasilakopoulou, P. Karakosta, S. Vourli, A. Tarpazti, A. Papadomanolaki, P. Varda, M. Kostoula, A. Antoniadou, S. Pournaras* [Athens, Greece]

Hospital related factors associated with multidrug-resistant organism acquisition: a multilevel case control study
N. Nasir* [Karachi, Pakistan], S. Khan, S. Rozi, N. Baig-Ansari, N. Khan, N. Rehmani, R. Roshan, B. Jamil, F. Mahmood

The impact of medical drugs on the acquisition of ESBL-producing Enterobacteriales: a matched case-control study
P. Klauke* [Berlin, Germany], F. Schwab, P. Gastmeier, F. Maechler

Gut colonisation with carbapenemase-producing Enterobacteriales: predicting factors for prolonged colonisation among adults
L. Dortet, L. Escaut, G. Cuzon, I. Bukreyeva, N. Fortineau, T. Naas* [Le Kremlin Bicêtre, France]

Invasive Acinetobacter baumannii infections in paediatric infectious disease intensive care unit
L. Stemberger Marić* [Zagreb, Croatia], N. Krajcar, N. Papic, I. Butić, G. Tesovic

Identifying drivers of acquisition of extended-spectrum beta-lactamase producing Enterobacteriales in Malawi using whole genome sequencing and mathematical modelling
J. Lewis* [Liverpool, United Kingdom], M. Mphasa, R. Banda, E. Smith, C. Jewell, B. Faragher, N. Thomson, N. Feasey

Risk factors for mortality in bloodstream infections in cancer patients
A. Ulu, S. Kamur, F. Kuscu, A. İnal* [Adana, Turkey], B. Kurtaran, Y. Tasova

What is the role of colonisation by carbapenem-resistant Enterobacteriaceae in older people who live in nursing homes? A multi-centre study
P. Favier* [Buenos Aires, Argentina], N. Carrión, R. Martins, E. Serio, M. Gallino, D. Torres, C. Raffo

Colonisation and infection with ESBL-producing and carbapenem-resistant Enterobacteriaceae in kidney transplant recipients: risk factors, impact on renal graft function and use of hospital resources
E. Solis, A. Palmiso, O. Simonetti* [Parma, Italy], M. Cotrufo, P. Fenaroli, U. Maggiore, E. Fiaccadori, C. Ferrari, A. Degli Antoni

Antibiotic exposure and the risk of CRE acquisition
N. Hassoun Kheir* [Haifa, Israel], K. Hussein, M. Saffuri, S. Badaan, S. Peleg, Y. Geffen, M. Paul

Relationship between local-area socioeconomic status and rates of bloodstream infection and Clostridioides difficile infection
S. Thelwall* [London, United Kingdom], R. Hope, S. Hopkins

Gram-negative screening the neonatal unit: can we predict bloodstream infections?
V. Price* [Birmingham, United Kingdom], J. Swindells

Risk factors for colonisation with multiple species of extended-spectrum beta-lactamase producing Enterobacteriales: a case-case-control study
I. Vock* [Basel, Switzerland], L. Aguilar Bultet, A. Egli, P. Tamma, S. Tschudin-Sutter

Infections in patients colonised with extended-spectrum beta-lactamase-producing Enterobacteriales: a retrospective cohort study
I. Vock* [Basel, Switzerland], L. Aguilar Bultet, A. Egli, P. Tamma, S. Tschudin-Sutter

Patient transfers as a risk factor for Clostridioides difficile infection: a case-control study
J. Edman-Waller* [Gothenburg, Sweden], S. Suominen, M. Werner

Faecal microbiota transplantation in the treatment of Clostridioides difficile infection
R. Stebel* [Brno, Czech Republic], L. Vožitálová, R. Vysák, P. Hůsa

Efficacy of pulsed xenon ultraviolet disinfection of multidrug-resistant bacteria and Clostridioides difficile spores
H. Kitagawa* [Hiroshima, Japan], K. Tadera, T. Hara, S. Kashiyama, H. Ohge

Approaches to identify new onset diarrhoea among hospitalised patients and the frequency of stool sample collection for Clostridioides difficile infection: a pilot for the CLOUD Louisville study
S. Furmanek, S. Pena-Oliva, R. Carrico, E. Gonzalez, K. Ford* [Collegeville, United States], S. Gray, J. Ramirez

Session accepted as Paper Poster Session
Update on Clostridioides difficile infection

Session accepted as Mini-oral ePoster Session
Understanding risk factors for HAI to tailor infection control

Identification of individual risk factors for acquisition of vancomycin-resistant Enterococcus faecium (VRE) during an outbreak in an university hospital and implication in prevention strategies
T. Abrassart* [Mons, Belgium], H. Strale, D. Martiny, B. Byl

Is there an increased risk for Clostridium difficile infection months after hospitalisation in a room occupied previously by a patient with C. difficile?
H. Zayyad* [Yafia, Israel], A. Peretz, S. Cohn, K. Labay
1851  An ultrasensitive test for the detection of Clostridiodes difficile toxins in stool samples using a single-molecule counting method
D. Straus* [Chelmsford, United States], A. Zuniga, A. Garces, A. Tempesta, A. Williams, B. Lauzier, J. Hickey, S. Gite, S. Clancy, Y. Rosario, J. Bowers

4059  Incidence and economic burden of Clostridioides difficile infections in inpatient settings of the German health care system: preliminary results of the ISIB study
Y. Khodamoradi* [Frankfurt, Germany], R. Cruz Aguilar, T. Schmidt-Wilcke, E. Schalk, S. Schmediek, I. Wieters, C. Lübbert, A. Stallmach, W. Holtmeier, S. Graefe, A. Ullah, M. Vehreschild

2279  Evaluation of an ultrasensitive test for the detection of Clostridium difficile and other enteric pathogens
M. Bonten, O. Cornely, J. Vehreschild

2624  Clostridioides difficile burden of disease in adults: early experiences of a prospective population-based surveillance study of hospitalised CDI cases in the inpatient module of the City of Louisville diarrhoea (CLOUD) study
S. Penna-Oliva, S. Furmanek, R. Carrico, J. Zampano, E. Gonzalez* [Collegeville, United States], J. Ramirez

2829  Factors associated with the recurrence of Clostridioides difficile infection in a university hospital

3942  Clostridioides difficile ribotypes 001 and 176 with reduced susceptibility to moxifloxacin are the main cause of healthcare-associated C. difficile infections in Slovakia
A. Plankaova, A. Soltésová, J. Škalová, P. Drevinek, V. Čapek, M. Krutova* [Prague, Czech Republic]

4280  Characterisation and comparison of farm animal and human Clostridioides difficile isolates in Italy
V. Spagglia* [Rome, Italy], F. Barbanti, M. Vescovi, R. Cerutti, C. Gaspano, S. Faccini, M. Merenda, C. Rossignoli

4281  Real-life experience with bezlotoxumab for the prevention of recurrent Clostridioides difficile infection

4453  An outbreak of Clostridioides difficile infections due to a 027-like PCR ribotype 181 in Slovakia
M. Kachrimanidou* [Thessaloniki, Greece], A. Baktash, D. Dimagliou, F. Netsika, O. Tsachouridou, D. Papadopoulou, E. Pratantariou, L. Skoura, M. Symeon, E. Kuijper

4859  Factors associated with the recurrence of Clostridioides difficile infection in a hospital university

4861  Impact of a dedicated Clostridioides difficile infection isolation ward on clinical outcomes
M. Varadarajan* [Orpington, United Kingdom], G. Barlow

5182  Heterogeneity of Clostridioides difficile infection testing and the impact on missed diagnoses: results from COMBACTE-CDI
V. Viprey, D. Ewin, W. Spittal, J. Vernon, A. Benson, G. Davis, M. Wilcox

5313  Predicted risk and observed occurrence of Clostridioides difficile infection in patients with community-acquired bacterial pneumonia treated with omadacycline or moxifloxacin
M. Rodriguez* [San Antonio, United States], K. Wright, B. Noble

5416  Impact of immunosuppression on Clostridioides difficile infection
E. Kuijper* [Lausanne, Switzerland], M. Papadimitriou

5461  Healthcare resource utilisation for treatment of Clostridioides difficile infection across 12 European countries: health economic results of COMBACTE-CDI
S. Wingen-Heimann* [Cologne, Germany], L. Lurienne, K. Davies, A. Benson, G. Davis, V. Viprey, M. Wilcox, M. Bonten, O. Martín Segarra, L. Alcalá, M. Marín, P. Muñoz, E. Reigadas Ramirez

3115  Key differences between community and in-patient Clostridium difficile infection: results from COMBACTE-CDI case-control study
K. Davies* [Leeds, United Kingdom], V. Viprey, D. Ewin, W. Spittal, J. Vernon, A. Benson, G. Davis, M. Wilcox

3529  An outbreak of Clostridioides difficile infections in a university hospital

3676  Effectiveness and safety of levulinic acid as prophylaxis for Clostridioides difficile infections in high-risk patients
A. Casapao* [Jacksonville, United States], L. Nilles, C. Sothoron, C. Tucker, A. Pirasteh

3744  Predicted risk and observed occurrence of Clostridioides difficile infection in patients with community-acquired bacterial pneumonia treated with omadacycline or moxifloxacin
M. Rodriguez* [San Antonio, United States], K. Wright, B. Noble

5182  Current diagnosis, management and control strategies for Clostridioides difficile infection in Europe
M. Cataldo* [Rome, Italy], G. Granata, N. Petrosillo, K. Davies

5461  Epidemiology and outcomes of Clostridioides difficile infections among allogeneic haematopoietic cell transplant recipients in Switzerland: 2009-2019
Abstract Categories 2020

5567  Outcome of Clostridioides difficile infection in patients that are PCR positive: comparison of toxin positive with toxin negative cases  
C. Johnston* [Swansea, United Kingdom], B. Carter, S. Weinberg, A. Holborow, A. Bone, J. Blyth, J. Walters, M. Perry, T. Morris, H. Hughes, J. Hargreaves, C. Richards, J. Harris, B. Healy

5615  European and national Clostridioides difficile infection surveillance  
K. Vendrik* [Leiden, Netherlands], T. Van Der Kooi, V. Viprey, K. Davies, E. Kuijper

5689  Possibilities of implementation of lactobacilli’s antagonistic properties for Clostridioides difficile growth suppression  
M. Sukhina, A. Sofin* [Moscow, Russian Federation], A. Zagaynova

5886  Risk factors for Clostridioides difficile infection among hospitalised patients in Brazilian centres: a multi-centre prospective study  

6354  Faecal microbiota transfer in real-life is more effective for recidivant Clostridioides difficile infection than for highly resistant bacteria decolonisation  

6626  Association between first episode Clostridioides difficile infection management and recurrence in a tertiary hospital  

6680  Changing epidemiology of Clostridioides difficile infection in a French university hospital  
N. Khanafær* [Lyon, France], L. Ottra, V. Pergay, O. Dauwalder, F. Vandenesch, P. Vanhems

6695  Oral vancomycin prophylaxis for primary and secondary prevention of Clostridioides difficile infection in patients treated with systemic antibiotic therapy: a systematic review and meta-analysis  
A. Maraoło* [Naples, Italy], E. Zappulo, R. Scatto, G. Granata, R. Andini, E. Durante Mangoni, N. Petrasillo, I. Gentile

6713  A comparative study to assess the prevalence and risk factors for Clostridioides difficile infection in patients with and without inflammatory bowel disease in a tertiary care hospital in northern India  
U. Ghoshal* [Lucknow, India], N. Tejan, R. Singh, A. Pandey, U. Ghoshal

7095  Is there any association between microbiological variables and toxigenic Clostridioides difficile infection (CDI) in a tertiary hospital?  

7112  Bezlotoxumab in real-life treatment of Clostridioides difficile infections in a tertiary centre in Spain  
M. Olmedo Sampería, M. Kestler Hernandez* [Madrid, Spain], M. Valerio Minero, M. Machado, A. Alvarez-Uria, B. Padilla, P. Muñoz, E. Bouza

7116  Clinical outcomes in oncological patients with Clostridioides difficile infection in Catalonia: a cohort study  

7495  Predictors of asymptomatic Clostridioides difficile colonisation on admission: prospective cohort study in a French university hospital  
N. Khanafær* [Lyon, France], S. Bennia, G. Martin-Gaujard, L. Juillard, T. Rimmelé, L. Argaud, D. Martin, P. Cassier, F. Vandenesch, P. Vanhems

7509  Local and national diagnostic and typing capacity for Clostridioides difficile infection, Europe, 2018  
S. Roda, E. Kanitz* [Vienna, Austria], D. Schmidt, E. Kuijper, C. Suetsens, P. Kinross

7510  Delafloxacin activity against moxifloxacin-resistant Clostridioides difficile clinical isolates  
S. Rodriguez-Pallarés* [Cádiz, Spain], F. Galan-Sanchez, J. Arca Sudrez, F. Cano, M. Rodriguez-Iglesias

7667  Does the new recommendations of treatment for non-severe Clostridioides difficile-associated diarrhoea ensure a better outcome?  
M. Lupsé* [Cluj-Napoca, Romania], I. Darau, C. Diaconu, K. Kamladi, K. Mamani, M. Planta, N. Todar

7840  The association of antibiotics and Clostridioides difficile infections in allogeneic stem cell recipients  
C. Jakab* [Cologne, Germany], M. Vehreschild, U. Holtick, C. Scheid, A. Walker, N. Jazmati, C. Carnely, J. Vehreschild

8468  Faecal lactoferrin is associated with severity at presentation but not relapse risk in Clostridioides difficile infection  

8591  An intervention bundle to improve compliance with clinical guidelines for Clostridioides difficile infection: a quasi-experimental study  

8726  Clostridioides difficile infection in haematological patients: a 14-year experience  
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8730 Epidemic *Clostridioides difficile* isolates are significantly more lethal and persist at higher rates than non-epidemic isolates in hamsters following vancomycin treatment
M. Pulse* [Fort Worth, United States], J. Vitucci, W. Weiss, J. Simecka

8754 Epidemiology and risk factors for *Clostridioides difficile* at a referral cancer centre in Mexico: a case-control study
F. Rivera* [Tlajpan, Mexico], D. De-La-Rosa-Martinez, E. Rivas-Pichon, B. Garcia-Pineda, P. Cornejo, D. Vilar

8794 Prevalence and outcome of *Clostridioides difficile* infection in a multi-centre study in Southern Brazil
A. Maestri, S. Rabani, H. Paz Morales, L. Ferrari, F. Tuan, A. Lasso, C. Marcon, K. Nogueira* [Curitiba, Brazil]

8947 National reporting of severe *Clostridioides difficile* infections in Germany between 2014 and 2018
N. Schmidt* [Berlin, Germany], A. Reuss, D. Altmann, M. Diercke, T. Eckmanns

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Session accepted as Paper Poster Session

843 Impact of coagulate-negative staphylococci positive blood culture occurring in early postoperative cardiac surgery
M. Thyg* [Paris, France]

1078 Rapid detection of methicillin-resistant *Staphylococcus aureus* in patients with late hospital-acquired/ventilator-associated pneumonia
L. Bussini* [Bologna, Italy], C. Monari, R. Pascale, M. Rinaldi, S. Ianniruberto, E. Rosselli Del Turco, S. Ambretti, M. Giannella, P. Viale

1285 Epidemiology typing and molecular analysis of vancomycin-resistant *Enterococcus faecium* in haemat-oncological patients
M. Bezdiček* [Brno, Czech Republic], M. Nykrynova, K. Dufkova, K. Plevová, M. Lengerova

2291 Rapid molecular screening for vancomycin-resistant *Enterococcus faecium* [VRE] allows to expedite evaluation of VRE-exposed patients and is cost saving
A. Büchler* [Basel, Switzerland], S. Raggiozina, D. Goldenberger, M. Wicki, A. Egli, A. Widmer

2324 Modelling the impact of antibiotic use and infection control agents on the incidence of methicillin-resistant *Staphylococcus aureus* incidence rates in hospital, informed by identifying antibiotic usage thresholds utilising non-linear time series analysis
S. Gardner* [Northern Ireland, United Kingdom], P. McCarron, G. Conlon-Bingham, D. Farren, M. Scott, K. Burnett

2547 *Staphylococcus aureus* intestinal colonisation in patients undergoing bowel preparation for colonoscopy
J. Gagnaire* [Saint-Etienne, France], L. Rinaldi, F. Grattard, A. Carriçao, E. Del Tedesco, N. Williet, J. Rigail, E. Botelho-Nevers, X. Roblin, P. Verhoeven, P. Berthelot

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Session accepted as Paper Poster Session

8535 Adaptation and validation of a quantitative *vanA/vanB* PCR on a high-throughput PCR system
A. Both* [Hamburg, Germany], L. Berneking, B. Berinson, H. Rohde, M. Lutgehetmann

9355 Comparison of the Panther Fusion MRSA assay with conventional culture for patient swabs in Ames transport medium with charcoal
N. Otten, R. Jansen, D. W. Van De Laar* [Amsterdam, Netherlands]

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951 Computerised Tomography (CT) as a risk factor for the acquisition of carbapenem-resistant *Acinetobacter baumannii*
Z. Dadon, E. Ben-Chetrit* [Jerusalem, Israel], M. Dahan, O. Benjaminov, P. Levin
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Abstract Programme

9. Experimental Microbiology, Microbial Pathogenesis & Biofilm

• Microbial pathogenesis & virulence
• Host-pathogen interaction
• Preclinical biofilm studies
• Experimental and cellular microbiology
• Other
Antibiofilm strategies

Session accepted as Paper Poster Session

218 Binding interference between Bartonella adhesin A and fibronectin as a novel therapeutic concept to treat bacterial infections
D. Vaca, A. Thibau, J. Malmström, L. Happonen, V. Kempf* (Frankfurt, Germany)

1571 Effect of hybrid organo-inorganic sol-gel coating loaded with antifungals on Candida strains
D. Romero, J. Aguilera-Correa, A. Garcia-Casas, B. Toirac, A. Jimenez-Morales, J. Esteban-Moreno* (Madrid, Spain)

1795 Anidulafungin-loaded hybrid organo-inorganic sol-gel coating can prevent the prosthetic joint infections provoked by Candida albicans
H. Garlito-Diaz, B. Toirac, A. Garcia-Casas, A. Jimenez-Morales, J. Esteban-Moreno* (Madrid, Spain), J. Aguilera-Correa

2193 Proof of concept: efficacy of surgical titanium implants coated with linear gentamicin against osteomyelitis in pigs

2256 Polyarginine nanocapsules carry and deliver genetic material inside bacteria
L. Alvarez-Fraga, J. Recente-Campo, K. Conde* (Coruña, Spain), A. Cés-Martinez, J. Vazquez-Ucha, A. Becerra, G. Bou Arevalo, M. Alonso, M. Poza Dominguez

2286 Destruction of Staphylococcus aureus biofilm matrix by innovative combination therapies between antibiotic and non-antibiotic substances
J. Liu* (Toulouse, France), A. Bousquet-Melou, J. Madec, M. Hoenni, A. Ferran

2790 Evaluation of biofilm formation and removal efficacy of three medical-device detergents by bacterial and yeast species
K. Park* (Songpa-Gu, South Korea), K. Hur, H. Sung, M. Kim

2880 Nonsteroidal anti-inflammatory drugs as a promising alternative to antibiotics to combat methicillin-resistant Staphylococcus aureus biofilms
V. Silva* (Vila Real, Portugal), J. Pereira, L. Matez, J. Capelo, G. Igrejas, P. Poeta

3009 Activities of eight antifungal agents against Candida auris biofilms
A. Chatzimoschou, J. Meis* (Nijmegen, Netherlands), E. Rolides

3341 Micafurazole/dominiphen bromide: a fungicial combination treatment against biofilms of variousazole-sensitive and azole-resistant Candida spp.
J. Tits* (Heverlee, Belgium), F. Cools, P. Cos, K. Verbruggen, J. Berman, B. Cammue, K. Thewisren

3526 Unravelling the anti-biofilm mechanism of action of an antimicrobial peptide: an atomic force microscopy study
A. Silva Herdade* (Lisbon, Portugal), S. Dias, S. Pinto, A. Coutinho, M. Cestanho, A. Veiga

Microbial biosurfactants: a new approach for the control of polymicrobial biofilm development on biomedical materials
C. Ceresa* (Novara, Italy), E. Fedeli, F. Tessarola, D. Maniglia, E. Tambone, M. Rinaldi, I. Banat, M. Diaz De Rienzo, L. Fracchia

Rhamnolipid coating reduces formation of Candida albicans-Staphylococcus aureus mixed biofilm on titanium implants: an in vitro study

Vaccinium macrocarpon urine metabolites inhibit Candida albicans adhesion and biofilm formation
E. Ottaviano* (Milan, Italy), G. Baron, L. Fumagalli, P. Allegretti, A. Riva, G. Morace, G. Aldini, E. Borghi

Polyphasic validation of a nisin-biogel aiming at the control of canine periodontal disease
E. Cunha* (Lisbon, Portugal), F. Bernardino De Freitas, B. Sào Braz, J. Moreira, L. Tavares, A. Veiga, M. Oliveira

Local anti-Pseudomonas IgY therapy prevents pyelonephritis in a novel murine experimental model
M. Pays Bendixen* (Copenhagen, Denmark), F. Schwartz, S. Baekdahl, L. Christophersen, I. Bull Rasmussen, M. Joergensen, C. Johann Lerche, K. Thomsen, N. Høiby, C. Moser

Cationic antimicrobial polymers as new anti-biofilm agents
R. Garcia Maset* (Coventry, United Kingdom), F. Harrison, S. Perrier

Prevented ciprofloxacin resistance development in Pseudomonas aeruginosa urinary tract infection model
A. Laulund* (Sæborg, Denmark), F. Schwartz, L. Christophersen, K. Thomsen, D. Ciofu, H. Tøstrup Pedersen, N. Høiby, C. Moser

Human milk oligosaccharides exhibit biofilm inhibition and eradication activity against biofilms formed by yeast isolated from cystic fibrosis patients
S. Jarzynka* (Warsaw, Poland), A. Bialkowska, B. Garcewksa, E. Augustynowicz Kopeć, G. Olędzka

Adequate exposure time of cold atmospheric pressure plasma on Staphylococcus aureus biofilms
F. Fahmide* (Tehran, Iran), P. Ehsani, S. Atyabi

Ability of antibiotic-loaded bone cement to prevent bacterial adhesion, biofilm formation and selection of resistance
A. Bidossi* (Milan, Italy), M. Bottagisio, E. De Vecchi

Session accepted as 1-Hour Oral Session

Bacteria dwelling in cystic fibrosis lungs

Trophic cooperation promotes Pseudomonas aeruginosa and Staphylococcus aureus survival in cystic fibrosis patients
L. Camus* (Lyon, France), B. Paul, S. Bastien, A. Doleans, S. Elsen, V. Vandenesch, K. Moreau
Abstract Categories 2020

**Session accepted as Paper Poster Session**

**Biofilm mechanisms and effects**

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<td>3453</td>
<td><em>Staphylococcus aureus</em> pathogenicity in cystic fibrosis patients: virulence genes, phylogeny and horizontal gene transfer</td>
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<td>3582</td>
<td>Sputum iron metabolism in patients with cystic fibrosis as a marker of infectious complications</td>
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<td>A. Kozlov* (Samara, Russian Federation), A. Lyamin, D. Gusyakova, O. Kandratenko, D. Ismatullin, A. Khaliulin</td>
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<td>6692</td>
<td>An ex vivo pig lung model demonstrates potential to distinguish key aspects of chronic and acute infection in the cystic fibrosis lung</td>
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<td>E. Sweeney* (Coventry, United Kingdom), N. Harrington, B. Crealock-Ashurst, F. Allen, F. Harrison</td>
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**Session accepted as Mini-oral Flash Session**

**Biofilm-associated infections**

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<td>3811</td>
<td>Anti-biofilm activity of ozenoxacin against methicillin-resistant <em>Staphylococcus aureus</em> strains</td>
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<td>Y. López Cubillos* (Barcelona, Spain), I. Zsolt, J. Vila Estape</td>
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<td>4209</td>
<td>Validation of new anti-staphylococcal compounds within a group of potential sortase A inhibitors</td>
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<td>G. Moshynets* (Kiev, Ukraine), G. Volynets, T. Baranovskiy, G. Nitulesscu, M. Denisa, A. Ungurianu, V. Băzhol, G. Nitulesscu, S. Yarmaluk</td>
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<td>4754</td>
<td>Characterisation of relationships between <em>Staphylococcus aureus</em> and <em>Escherichia coli</em>, <em>Acinetobacter baumannii</em> and <em>Candida auris</em> and their implications for survival and persistence in the dry environment</td>
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<td>N. Amaeze* (Abuja, Nigeria), G. Ramage, W. Mackay, C. Williams, R. Keen</td>
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<td>5317</td>
<td>Antibiotic penetration and bioavailability of vancomycin alone and in combination with rifampin in <em>Staphylococcus epidermidis</em> biofilms</td>
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<td>E. O'Neill* (Cranston, United States), E. Piehl, K. Daffinee, G. Williams, K. Laplante</td>
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<td>7247</td>
<td>Delivering antibiotics locally to biofilms by targeted drug delivery and prodrug therapy</td>
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<td>R. Meyer* (Aarhus, Denmark), R. Wolther, S. Nielsen, P. Andersen, L. Hansen, R. Christiansen, H. Quang, J. Kjems, A. Zelinka</td>
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<td>8987</td>
<td>Plant-based biomolecules against antibiotic-resistant microbes in skin infections and diseases</td>
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<td>9091</td>
<td>Metabolomic comparison of biofilm matrix of six species of <em>Candida</em></td>
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<td>9235</td>
<td>Graphene oxide sheets affect expression of biofilm formation key genes in <em>Escherichia coli</em></td>
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<td>C. Vuotto* (Rome, Italy), L. Pappalardo, G. Donelli, I. Francolini</td>
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<td>9285</td>
<td>Multi-omics approaches to understand the regulation of biofilm formation in high biofilm-forming clinical isolate of <em>Candida parapsilosis</em></td>
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<td>S. Shafeeq* (Stockholm, Sweden), B. Sennblad, M. Grabher, U. Römling</td>
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3456 Interleukin 1-α and vascular endothelial growth factor support the growth and persistence of biofilm-growing Cutibacterium acnes in individuals with acne

4494 Biofilms and catheter-related bloodstream infections: a tale of two kingdoms
V. Borges, S. Wenner, I. Nogueira, I. Faria, M. Pessanha, C. Verissimo, R. Sabino, J. Rodrigues, R. Matias, F. Martins, P. Carvalho, J. Gomes, L. Jordao*
[Lisboa, Portugal]

5412 Microbial aetiology of prosthetic joint infections: what’s growing in the cultures?
E. Piehl* (Providence, United States), V. Lopes, A. Caffrey, K. Laplante

6142 Intracellular persistence of uropathogenic Escherichia coli is undetectable in urinary bladders from mecillinam-treated pigs
K. Stærk* (Odense, Denmark), R. Grønnemose, Y. Palarasah, H. Kolmos, L. Lund, T. Andersen

7585 Development of in vitro and ex vivo wound biofilm models for the assessment of wound dressings
K. Tiirik* (Tartu, Estonia), L. Preem, K. Sagar, M. Putrins, T. Tenson, K. Kogermann

8242 Within-host genetic diversity of Staphylococcus epidermidis in prosthetic joint infections: consequences for microbiological diagnosis
M. Widerstrom* (Umeå, Sweden), M. Stegger, I. Yu, B. Mcdonald, A. Mcnally

9556 Adaptation to host of a Staphylococcus schleiferii responsible of an elbow prosthetic infection
A. Bidossi, M. Bottagisio, E. De Vecchi* [Milan, Italy]

Microbiological factors of Escherichia coli from adult patients with bacteraemia and sepsis/septic shock from 21 hospitals in Spain: PROBAC-EC study

Insights into reservoir and pathogenicity of Escherichia coli ST183: role of haemolysin A operon duplication in severity of uropathogenic infections
M. Ksiezarek* [Porto, Portugal], Á. Novais, H. Felga, F. Mendes, M. Escobar, L. Vieira Peixe

Novel putative AHL-lactonases widely distributed across diverse carbapenemase-producing Enterobacteriaceae
M. Lopez* (A Coruña, Spain), N. Ellaby, N. Woodford, M. Ellington, M. Tomas

Mouse colonisation by multidrug-resistant Escherichia coli in the absence of antibiotic selection
C. Connor* [Birmingham, United Kingdom], A. Zucolota, I. Yu, B. Mcdonald, A. McNally

Contribution of microbial virulence factors on mortality in adult patients with bacteraemia due to Escherichia coli presenting with sepsis/septic shock: exploratory analysis of the PROBAC-EC cohort

Proton pump inhibitors increase the digestive carrying of OXA-48-producing Enterobacteriaceae in a mouse model
F. Javaudin* [Nantes, France], O. Le Bastard, M. Dion, Y. Bezabih, E. Montassier, E. Batard

ESBL-producing Escherichia coli causing community-onset bloodstream infection and the association of bacterial clones and virulence genes with septic shock
I. Fröding* [Stockholm, Sweden], B. Hasan, I. Sylvin, P. Naucier, C. Giske

Comparison of β-lactamase-producing Escherichia coli ST131 C1-M27 and ST131 non-C1-M27 by whole genome analysis using next-generation sequencing in Japan
N. Noguchi* [Tenri, Japan], A. Nakamura, M. Kamatsu

Association of the prophage BTP-1 with anti-virulence of Salmonella typhimurium sequence type 313
A. Herrero* [Copenhagen, Denmark], M. Spiegelhauer, P. Guerra, J. Olsen

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Escherichia coli and Salmonella pathogenicity and virulence

571 Proton pump inhibitors increase the digestive carrying of OXA-48-producing Enterobacteriaceae in a mouse model
F. Javaudin* [Nantes, France], O. Le Bastard, M. Dion, Y. Bezabih, E. Montassier, E. Batard

6456 Genetic architecture of interspecies hybrids
K. Bartke* [Uppsala, Sweden], L. Garoff, D. Huseby, G. Brandis, D. Hughes

2007 Association of the prophage BTP-1 with anti-virulence of Salmonella typhimurium sequence type 313
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7006 Genome wide mutations in a clinical Escherichia coli isolate with a DNA mismatch repair gene defect after exposure to remnants of a phagemid-containing Escherichia coli
J. Stohr* [Breda, Netherlands], M. Kluytmans - Van Den Bergh, C. Verhulst, J. Rossen, J. Kluytmans

Within host genetic comparison of Escherichia coli strains isolated from patients with urosepsis
A. Cuénod* [Basel, Switzerland], J. Agnetti, H. Seth-Smith, O. Grüniger, J. Reist, S. Tschudin-Sutter, S. Bassetti, N. Thomson, A. Egli
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Microbial predictive virulence factors for pyelonephritis caused by extended-spectrum beta-lactamase-producing Escherichia coli in children harbouring such strains in their gut microbiota

B. Philippe* [Paris, France], A. Birgy, C. Levy, F. Madhi, E. Sobral, R. Cohen, S. Bonacorsi

Depicting the pathogenicity and genomic traits of hypermucoviscous Enterobacteriaceae clinical isolates N. Rodriguez Medina* [Cuernavaca, Mexico], U. Garza-Ramos, H. Valdivinos-Torres

Ocbinidine: new insights in the detailed killing mechanism on Gram-negative bacteria at a cellular and molecular level

N. Molanovic* [Graz, Austria], A. Oen, G. Pabst, K. Lohner

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Gram-Positives: Pathogenicity, identification and treatment

Characterisation and virulence of fibronectin-binding protein of Streptococcus intermedius

M. Sasaki* [Shiawagun, Japan], Y. Kadama, T. Ishikawa, Y. Shimoyama

Reduced production of bacterial membrane vesicles predicts mortality in ST145/USA600 methicillin-resistant Streptococcus aureus bacteriaemia

S. dey* [detroit(Michigan), United States], S. Gudipati, C. Giuliani, M. Zervos, J. Monk, R. Szubin, S. Jorgensen, G. Sakoulas, A. Berti

Characterisation of a fibronectin binding protein in the virulence of Streptococcus parasanguinis FW213

Y. Chen* [Taoyuan, Taiwan]

esp17 and its importance in dry stress resistance

N. Kordzakhia* [Tbilisi, Georgia]

Combined inhibition of CD14 and C5 in Enterobacteriaceae and its importance in dry stress resistance

C. Giuliano, M. Zervos, J. Monk, R. Szubin, S. Jorgensen, G. Sakoulas, A. Berti

Inter- and intra-clonal diversity in Streptococcus haemolyticus prosthetic joint infection

A. Both* [Hamburg, Germany], J. Huang, M. Oi, S. Weisselberg, H. Buettner, C. Lausmann, M. Alawi, P. Hoffke, H. Rohde

Platelet trends early during Staphylococcus aureus bacteraemia are predictive of persistence and mortality

B. Lee* [Los Angeles, United States], C. Kelsam, K. Tan, A. Wong-Beringer

The type I histidine triad protein HtspA contributes to the capsule development and virulence of Streptococcus suis serotype 2

X. Pan* [Nanjing, China], Z. Shao, M. Li, H. Ni

Characterisation of biofilm formation by Staphylococcus pseudointermedius on a variety of medical devices

C. Pesset, M. Antunes, C. Fonseca, M. Ferreira, I. Teixeira, E. De Oliveira Ferreira, B. Penna* [Rio de Janeiro, Brazil]
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4570 Genome-wide transcriptional responses of *Escherichia coli* with different levels of zinc tolerance to zinc chloride exposure

V. Johanns, S. Wolf, L. Epping, A. Lübke-Becker, T. Semmler, B. Walther* [Berlin, Germany], L. Wieler

5035 *Klebsiella pneumoniae* type VI secretion system allows the implantation and survival of the pathogen within the intestinal microbiota

T. Mercieca, L. Nakusi, S. Bornes, C. Besnard, E. Rifa, S. Thell, C. Forestier, S. Miquel* [Clermont-Ferrand, France]

584 Acylated homoserine lactone- (AHL) mediated quorum sensing in dental plaque: an opportunity for novel antimicrobial treatment of oral diseases

A. Muras, P. Otero-Casal, A. Otero* [Santander de Compostela, Spain]

5257 A widespread toxin-antitoxin system exploiting growth control via alarmone signalling


6300 A high-throughput real-time liquid-based *Caenorhabditis elegans* model for assessing the virulence of clinical encapsulated multidrug-resistant *Klebsiella pneumoniae* isolates

A. Gancz* [Ariel, Israel], D. Cohen-Eli, S. Navon-Venezia

7061 Meningococcal disease-associated prophage-like elements are present in *Neisseria gonorrhoeae* and some commensal *Neisseria* sp.

B. Al Suwayyid, D. Speers, M. Wise, G. Coombs, C. Kahler* [Perth, Australia]


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<td><strong>Klebsiella genomes and phenotypes</strong></td>
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2696 Genome-based analyses of *Klebsiella pneumoniae* to detect possible host-associations, host-adaptation and effects on virulence

K. Klaper* [Wernigerode, Germany], L. Heinrich, R. Gerlach, S. Fuchs, Y. Pfeifer, G. Werner

3657 A novel chaperone-usher pill system associated to the worldwide-disseminated high-risk clone *Klebsiella pneumoniae* ST-15

E. Gato* [A Coruña, Spain], B. Rodiño-Janero, M. Pérez-Vázquez, A. Romero, G. Bou Arevalo, A. Pérez

4950 Food and clinical human isolates of *Klebsiella pneumoniae*: is there correlation between multidrug resistance and biofilm formation capacity?


5930 Influence of biofilm formation on clinical outcome and their associated genetic virulence factors in *Klebsiella pneumoniae* bloodstream infections in India

D. Naveen Kumar* [Sheffield, United Kingdom], K. Asokan, K. Vasudevan, D. Murugan, E. Karunakaran, P. Monk, V. Balaji

6013 Effect of the capsule exchange between serotype K1 and K20 *Klebsiella pneumoniae* on serum killing, neutrophil phagocytosis and mice lethality

E. Liu, J. Chang, J. Lin, F. Chang* [Taipei, Taiwan]

6228 Prevalence of virulence factors in colonising and infecting *Klebsiella pneumoniae* isolates obtained from a German multi-centre surveillance study

K. Lucassen* [Calâgna, Germany], J. Kahn, J. P. Antoniou, J. Wille, A. Walker, Y. Steizer, V. Persy, H. Seifert, P. Higgins

6978 Characterisation of virulence in KPC-2-producing *Klebsiella pneumoniae* CG258 from an outbreak in high complexity hospital in Brazil

T. Rezende* [São Paulo, Brazil], C. Morais, J. Monteiro, C. Abbboud, J. Setubal, A. Pignatari, C. Kiffer

8050 Diversity of capsular switch among carbapenemase-producing *Klebsiella pneumoniae*

A. Chiarelli* [Paris, France], N. Cabanel, R. Bonnin, P. Glaser

8449 Contrastng molecular epidemiology of *Klebsiella* spp. and *Escherichia coli* bloodstream infections in Oxfordshire (UK) 2009-2017

S. Lipworth* [Oxford, United Kingdom], K. Vhta, J. Kavanagh, L. Barker, K. Chau, S. George, A. Vaughan, D. Griffiths, M. Morgan, M. Andersen, K. Jeffery, T. Peto, D. Crook, N. Stoesser, A. Walker

8764 Genomic characterisation and pathogenicity determination of the classical, hypermucoviscous and hypervirulent *Klebsiella pneumoniae* isolates in Mexico

U. Garza-Ramos* [Morelos, Mexico], J. Rodríguez-Santiago, A. Sagal-Prado, J. Silva-Sanchez

9052 In vivo virulence of different clones of OXA-48-producing *Klebsiella pneumoniae* in Galleria mellonella infection model

A. Leal, L. Forcellleda Espino, A. Rodríguez-Guardado, F. Vazquez, M. Rodicio, J. Fernández* [Oviedo, Spain]

Do we need to screen the colibactin genomic island (CGI) for diagnosis of colorectal cancer? Paradigm of *Klebsiella pneumoniae*

M. Ben Khedher, S. Khabthani, R. Ruimy, J. Rolain, M. Ben Khedher, S. Khabthani, R. Ruimy, J. Rolain, S. Diene* [Marseille, France]

Co-aggregation of uropathogenic *Klebsiella oxytoca* with *Klebsiella pneumoniae* and probiotic *Escherichia coli* on the cell line

A. Giliazeva* [Senftenberg, Germany], J. Noack, A. Mardanova

9477 Novel biofilm models and methods

454 Combined effects of low incubation temperature, minimal growth medium and low hydrodynamics optimise *Acinetobacter baumannii* biofilm formation

E. Eze* [KwaZulu-Natal, South Africa]

2048 Formation of enterobacterial aggregates in presence of bovine synovial fluid

A. Macias-Valcayo* [Madrid, Spain], J. Aguiler-Corra, A. Staarts, T. Gupta, D. Dusane, P. Stoodley, J. Esteban-Moreno
Detection of microorganisms in sonicated titanium screw model after in vitro biofilm production using culture, MALDI-TOF MS and qPCR
J. Cieslinski, V. Stadler Tasca Ribeira, L. Kraft, P. Suss, E. Rosa, L. Morella, M. Pilionetto, J. Teilles*
[Sao Paulo, Brazil], F. Tuon

It’s a trap! The development of a versatile drain biofilm model
K. Ledwoch* [Cardiff, United Kingdom], J. Maillard, P. Norville

Galleria mellonella as a novel in vivo drug discovery platform using bioluminescent KAPE pathogens
V. Francis* [Exeter, United Kingdom], A. Smith, C. Kemmer, V. Trebosc, B. Schellhorn, R. Tittball, O. Champion

The efficiency of antimicrobial coatings in whole blood: development of a realistic in vitro model
J. Valtin* [Dresden, Germany], C. Werner

A five-species biofilm model for confirming the potential of a nisin-biogel aiming at canine periodontal disease control
E. Cunha* [Lisbon, Portugal], S. Rebelo, L. Tavares, M. Carreira, M. Oliveira

Effect of Bdellovibrio bacteriovorus on clinical pathogens and biofilms
S. Kahraman, Y. Tekintas* [Izmir, Turkey], F. Cilli, M. Hosgar-Limoncu

A new ultra-fast specimen preparation method for SEM visualization of bacterial biofilms
I. Chebotar* [Moscow, Russian Federation], A. Subbot, Y. Bocharova, N. Fedorova, I. Novikov

Investigation of electric signaling in bacterial biofilms with the Specialised Thin Agar Method (STAM)
J. Assmann* [Berlin, Germany], S. Bürge, C. Schaudinn, B. Wolther

Study of microbial adhesion to nanostructured and nanostructured orthoprosthetic material through dynamic models
S. Leonetti* [Pisa, Italy], B. Tuvo, B. Campanella, M. Onor, S. Legnaiali, E. Bramanti, A. Baggiani, M. Totaro, P. Parchi, B. Casini

In vitro model of Pseudomonas aeruginosa pulmonary biofilm to evaluate the efficacy of cationic antibiotics
R. Awad* [Poitiers, France], F. Tewes, S. Marchand, W. Couet, M. Nasser

Acinetobacter baumannii and Klebsiella pneumoniae: intelligent design of phage cocktails against multidrug-resistant pathogens
M. Jalasvuori* [Jyvaskyla, Finland], K. Kaskinen, M. Yläne, R. Penttinen

Exploiting CRISPR-Cas9 to eradicate ESBL genes and tracing conjugative plasmids within complex microbial communities at single-cell resolution
R. Penttinen* [Turku, Finland], L. Ambrosio Leal Dutra, P. Ruotsalainen, O. Franz, C. Given, K. Nurminen, P. Salmi, M. Tiirala, M. Jalasvuori

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Overcoming infections caused by non-fermenters

Filamentous bacteriophage [PF-8] in Pseudomonas aeruginosa isolates belonging to the international cystic fibrosis clone [CC274]

The in vitro effect of azithromycin on P. aeruginosa biofilms
A. Jimenez San Mauro, N. Heiby, O. Ciofu* [Copenhagen, Denmark]

Ceftolozane/tazobactam for multidrug-resistant Pseudomonas aeruginosa in a swine model of severe pneumonia

First evidence of systemic efficacy of a pathogen-targeted, engineered lisyn [GN-370] against carbapenem-resistant Pseudomonas aeruginosa in a rabbit pneumonia model
D. Lehoux* [Yonkers, United States], W. Abdelhady, Y. Xiong, K. Sauve, J. Oh, A. Watson, S. Swift, C. Cassino, A. Beyer, R. Schuch

Efflux pump inhibitors based on novel cyclic peptides as an approach against ESKEPAE pathogens
J. Moreno Morales* [Barcelona, Spain], C. Cosgaya Castro, C. Ballesté, E. Giralt, J. Vila Estape

Co-evolutionary adaptations of Acinetobacter baumannii and an OXA-23-encoding plasmid under carbapenem pressure
L. Zhang* [Hangzhou, China], X. Hua, Y. Yu

Effects of ceramergins to intracellular Pseudomonas aeruginosa infections formed in human airway epithelial cells
Ö. Oyardı* [Istanbul, Turkey], C. Bozkurt Guzel, P. Savage

Modulation of antibiotic-associated virulence of Pseudomonas aeruginosa in cystic fibrosis bacterial biofilms
M. Hassan, N. Harrington* [Coventry, United Kingdom], F. Harrison
In silico and in vitro investigation of a novel putative toxin-antitoxin system in Acinetobacter baumannii
S. El-Banna* [Cairo, Egypt], R. Samir, R. Aziz, N. Maneib

The solitary parE-type toxin gene in Pseudomonas aeruginosa sequence type 111 clinical isolates collected in a paediatric intensive care unit in Moscow
Y. Bocharova* [Moscow, Russian Federation], T. Savinova, D. Shagin, I. Chebator

Estimation of the prevalence of the plasmid-encoded septocin gene in carbapenem-resistant Acinetobacter baumannii
N. Rakovitsky* [Tel Aviv, Israel], S. Frenk, P. Elmalih, R. Roy, E. Temkin, D. Schwartz, Y. Carmeli, J. Lelouche

Comparative in vitro activities of eravacycline and various antibiotics against multidrug-resistant clinical strains of Acinetobacter baumannii isolated from intensive care units
M. Ataman* [Istanbul, Turkey], E. Mataraci-Kara, B. Ozbek Çelik

Comparative metabolomics of Pseudomonas aeruginosa in response to polymyxin B
M. Hussin* [Melbourne, Australia], M. Han, B. Tsuji, R. Hancock, T. Veikov, J. Li

Carbapenem-resistant Acinetobacter baumannii fitness in murine model is associated with 14-day mortality in humans
A. Nutman* [Tel-Aviv, Israel], J. Lelouche, E. Temkin, G. Daikos, A. Skiada, J. Wain, G. Langridge

Plasticity in a bacterial global regulator drives the switch to antibiotic resistance and virulence

The profile of virulence gene exoS, exoT, exoU and exoY from gene encoding effector protein type III secretion system of Pseudomonas aeruginosa in clinical isolates in Sanglah Hospital Bali
I. Saputra* [Bali, Indonesia], N. Mertiawati, N. Fatmawati

Host adaptive changes of Staphylococcus aureus through respiratory colonisation and bloodstream infection
A. Carrera-Salinas* [L’Hôpital de Llobregat, Spain], A. González Díaz, D. Vázquez-Sánchez, J. Sañudo, M. Mrakovcic, M. Domínguez Luzon, S. Niemann, S. Martí

Lower respiratory tract infection by Staphylococcus aureus in mechanically-ventilated patients: genotypical and phenotypical characterisation
A. Lacoma* [Badalona, Spain], M. Loabei, G. Godoy, B. Muriel-Moreno, J. Moreno, F. Arméstcar, C. Prat

In-host evolution of methicillin-resistant Staphylococcus aureus within individual carriers using core genome multi-locus sequence typing and single-nucleotide polymorphism analysis
A. Compillay Lagos* [Örebro, Sweden], M. Sundqvist, F. Dyrkell, M. Stegger, B. Säderquist, P. Mölling

Unravelling the mechanism of virulence of M1 protein of Streptococcus pyogenes
E. Torres Sangiao* [Santiago de Compostela, Spain], L. Happonen, F. Palm, P. Pyl, O. Shannon, C. García-Riestra, J. Malmström

Bronchial abundance of Streptococcus as a potential biomarker for lung cancer

Transcriptome analysis of pneumococci isolated from meningitis patient’s cerebrospinal fluid identifies multiple genes important for pathogenesis, including a novel operon of unknown function
E. Wall* [London, United Kingdom], J. Guerra-Assunção, M. Yang, S. Panagiotou, T. Audshasai, R. Aprianto, E. Ramos Sevillano, V. Terra, D. Van De Beek, J. Veening, M. Mrakovcic, M. Domínguez Luzon, S. Niemann, S. Martí

Enterococcus faecalis inhibits Klebsiella pneumoniae growth in polymicrobial biofilms
V. Ballén Torres* [Barcelona, Spain], S. Soto

Microdiversity of Enterococcus faecalis isolates from infective endocarditis
G. Royer* [Crêteil, France], L. Raisin, S. Lo, D. Vanessa, H. Jacquier, R. Lepeule, V. Fihman, P. Lim, C. Rodriguez, P. Woerther
Identification of new small-RNAs involved in growth and virulence of Enterococcus faecium

Development of a new murine model for Enterococcus faecium intestinal colonisation
S. Reissier* (Rennes, France), V. Bordeaux, F. Brice, V. Cattoir, M. Revest

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Understanding and treating biofilms

Staphylococcus aureus inhibits opsonophagocytosis and modulates neutrophils extracellular traps formation efficiently during the early stages of biofilm formation
A. Sultan* (Rotterdam, Netherlands), N. Lemmens-Den Toom, A. Verbon, W. Van Wamel

Co-infection with Staphylococcus aureus after primary influenza virus infection results in endothelial damage
S. Deinhardt-Emmer* (Jena, Germany), A. Van Krüchten, E. Schicke, K. Rennert, S. Ludwig, Z. Cseresnyes, M. Figge, A. Mosig, R. Heller, B. Löffler, C. Ehrhardt

Methicillin-resistant Staphylococcus aureus USA300 persister cells show chaperone upregulation in contrast to planktonic cells and the biofilm phenotype

Sub-inhibitory concentrations of mupirocin stimulate Staphylococcus aureus biofilm formation by up-regulating cdiA
Y. Jin* (Hangzhou, Zhejiang Province, China)

Genomic adaptation of Staphylococcus aureus in a diabetic foot environment
C. Pouget* (Nimes, France), M. Hosny, A. Pantel, B. La Scola, F. Laurent, A. Sotta, C. Dunyach-Remy, J. Lavigne

The mouse ear skin model reveals specific innate immune signatures into study of the dynamics of innate immune responses against to Staphylococcus aureus biofilms
A. Abdul Hamid* (Clermont-Ferrand, France), A. Cara, A. Diot, J. Josse, E. Billard, F. Laurent, P. Guérard

Candida albicans adhesion to central venous catheters: impact of yeast and hyphae morphotypes
J. Jung* [Hamburg, Germany], C. Mischo, G. Gunaratnam, C. Spengler, S. Becker, K. Jacobs, M. Bischoff

Three-dimensional in vitro Staphylococcus aureus abscess communities are not affected by antibiotics or neutrophils
M. Hofstee* [Davos Platz, Switzerland], M. Riol, K. Thompson, M. Stoddart, S. Zaai, F. Mariarty

An innovative model to analyze anti-biofilm immune response in vivo
L. Sauvat* (Clermont-Ferrand, France), A. Abdul Hamid, C. Blavignac, F. Laurent, O. Lesens, P. Guérard

Non-steroidal anti-inflammatory drug administration impairs antibiotic treatment of orthopaedic device-related infection in a rat model
F. Mariarty* (Davos, Switzerland), G. Richards, K. Thompson

What happens when the host and pathogen meet

A pathogen and a non-pathogen spotted fever group Rickettsia trigger differential proteome signatures in macrophages
P. Cardoso Curto* [Cantanhede, Portugal], C. Santa, P. Allen, B. Mananas, I. Simoes, J. Martinez

Impact of corticosteroids on alveolar macrophage interaction with mucorales
F. Arrivé* (Poitiers, France), K. Brunet, J. Martellosia, I. Lamarche, S. Marchand, B. Rammaert

Insight into Chlamydia trachomatis persistence
C. Faschi, M. Bortolotti, C. Zalamboni, R. Fato, L. Polito, A. Bolognesi, A. Marangoni* [Bologna, Italy]

Evaluation of neuro-filament light chain as a biomarker for neuronal damage in experimental pneumococcal meningitis
N. Le* (Bern, Switzerland), D. Grandgirard, J. Kuhle, D. Leppert, S. Leib

Estrogen enhances host-pathogen interactions in ex vivo and in vitro models of the inflammatory phase of age-related impaired healing
M. El Mohtadi* (Manchester, United Kingdom), K. Whitehead, N. Dempsey-Hibbert, J. Ashworth

Perinatal hormones favor CC17 Group B Streptococcus intestinal translocation through M cells and hypervirulence in neonates
C. Hays, G. Touak, A. Bouaboud, A. Fouet, J. Guignot, C. Payart, A. Tazi* [Paris, France]

Markers of inflammation, neural injury and regeneration in a neonatal mouse model of Listeria monocytogenes meningococcal sepsis

Impact of interferon gamma on Staphylococcus aureus internalisation within human osteoblasts
C. Pierre, A. Souché, L. Abad, P. Verhoeven, J. Josse, T.erry, F. Laurent, F. Valour* (Lyon, France), A. Diet
Abstract Programme

10. Immunology & Vaccinology

- Host genetics: infection susceptibility & immunodeficiency
- Clinical epidemiology of infections in immunocompromised hosts
- General vaccinology (incl. policy, social aspects)
- Antiviral vaccines
- Antibacterial vaccines
- Immune response to infection (excl sepsis biomarkers)
- Other
966 Ceftazidime-avibactam for the treatment of carbapenemase-producing Enterobacteriaceae bacteraemia in oncohaematological patients: calm after the storm

1521 Predictors of mortality in solid-organ transplant recipients with bloodstream infections due to carbapenemase-producing Enterobacteriales: the impact of cytomegalovirus disease and lymphopenia

1816 Burden of surgical site infections after solid organ transplantation in the Swiss transplant cohort study

2108 Pre-emptive therapy utilisation after haematopoietic cell transplantation
G. Papanicolaou* (New York, United States)

2121 Bloodstream infection survey in high-risk oncology patients (BISHOP) with fever and neutropenia (FN) in the United States: Gram-negative susceptibility and treatment patterns

3161 Infectious complications in kidney transplant recipients: a prospective cohort study

6606 Burden of viral infections among autologous stem cell transplant patients: a prospective longitudinal study

7744 Short versus extended antibiotic treatment with a carbapenem for high-risk febrile neutropenia in haematology patients (SHORT trial): results from a randomised multi-centre non-inferiority trial

8752 Infectious complications after chimeric antigen receptor modified T cells in adolescent and young adult relapse/refractory B cell precursor acute lymphoblastic leukaemia: report of the French experience

8938 Home-based care of low-risk febrile neutropenia in children: an implementation study in a tertiary paediatric hospital

1664 Validation of a machine learning model for prediction of mortality among patients with community-acquired pneumonia
L. Ward* (Aalborg, Denmark), M. Mogensen, R. Méndez, P. Gonzalez-Jimenez, C. Collizón Campos, A. Ceccato, A. Torres, R. Menendez

3545 Can machine learning predict a positive blood culture?
B. Mcfadden* (Perth, Australia), M. Reynolds, T. Inglis

7478 A machine learning-based model to predict bloodstream infections
R. Murri* (Rome, Italy), G. De Angelis, C. Masciocchi, B. Posteraro, N. Capacchiano, A. Marchetti, A. Damiani, P. Sergi, G. Scambia, R. Cuda, V. Valentini, M. Fantoni, M. Sanguinetti

7615 Artificial intelligence to support antibiotic decision-making processes in haematological patients with febrile neutropenia

8115 Supervised machine learning algorithms to predict the patient outcome during febrile neutropenia
C. Jakob* (Cologne, Germany), M. Schons, M. Stecher, F. Fuchs, A. Walker, O. Carnely, J. Vehreschild
**Abstract Categories 2020**

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**Session accepted as** Paper Poster Session

**Epidemiology and prevention of infection in immunocompromised hosts**

52  *Clostridioides difficile* infection in immunocompromised hospitalised patients is associated with a high recurrence rate

A. Atamna* [Petah Tikva, Israel], T. Avni, J. Bishara

5686 Interplay between inflammation and infection in a single-centre cohort of patients with X-linked agammaglobulinemia


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2093 Epidemiology of *Pseudomonas jiroveci* pneumonia in HIV-negative patients from 2005-2014 in the United States

B. Hollenbeck* [Boston, United States], K. Counterman, G. Miley

2779 Infectious complications of patients with breast cancer treated with palbociclib: unexpected serious and opportunistic infections


3808 TB screening and treatment in an Italian cohort of haematopoietic stem cell transplant recipients

A. Della Vecchia* [Genoa, Italy], C. Di Grazia, A. Dominiello, A. Raiola, E. Angelucci, M. Bassetti, V. Claudia, M. Mikulska

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4076 Strategy for cytomegalovirus reactivation prevention with ganciclovir and high dose of valacyclovir in allogeneic stem cell transplantation

M. Lopez* [Bogota, Colombia], E. Pedraza, J. Figueroa, E. Mora, M. Gomez, S. Ardila, A. Guarin, O. Peña, C. La Madrid, G. Lopez, L. Villamizar, D. Diaz

5413 Antifungal prophylaxis in acute myeloid leukaemia patients receiving chemotherapy is cost-effective in a resource-limited country

T. Pungprasert* [Lampang, Thailand], P. Phikulsod, V. Srinanprasert, D. Dhirachaikulpanich, N.untai, S. Maneean

5632 Treating nocardiosis with cotrimoxazole monotherapy in solid organ transplant recipients: real-life data from a multi-centre retrospective study


5686 The effectiveness of antibiotic prophylaxis in the prevention of respiratory tract infections in antibody-deficient patients: a single-centre cohort study

M. Albur* [Bristol, United Kingdom], A. Grammatikos, S. Johnston

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**Session accepted as** Paper Poster Session

**Evaluating host responses to diagnose infection**

437 Dynamic monitoring of sTREM-1 and other biomarkers in biliary tract infection

J. Jiang* [hangzhou, China], D. Yu

1528 Comparison of host immune responses in *vivo* versus *ex vivo* lipopolysaccharide stimulation in humans using an immune transcriptomic profiling panel

D. Tawfik* [Lyon, France], J. Lankelma, L. Ganee, E. Cerrato, A. Pachot, W. Wiersinga, J. Textoris

1655 Comparison of prognostic capacity of presepsin and procalcitonin in adult septic patients: results from a prospective observational study in two university clinical centres

A. Aliu Bejta* [Pristhine, Kosovo], S. Namani, B. Halili, D. Plana-Hajdari, B. Baršić, A. Atež

1726 Reactive hyperaemia measured by peripheral arterial tonometry correlates with glycocalyx degradation and the presence of sepsis in the critically ill patient

L. Malheiro* [Porto, Portugal], R. Garcia, M. Vaz-Da-Silva, S. Martins, A. Sarmenta, L. Santos

4008 Comparison of a cartridge-based host gene expression test to a manual method for use in the diagnosis of sepsis

W. Sinclair* [Salt Lake City, United States], J. Mccleave, P. Sillekens, I. Keuleers, T. Vanhoey, S. Cermelli, B. Lopansri
Host biomarkers to differentiate bacteraemias from microbiologically proven viral infection in adults with acute fever episodes attending outpatient clinics in Tanzania

Predictive value of CD4+T helper lymphocytes, associated biomarkers and procalcitonin in the prognostication of polytrauma patients with sepsis
S. Khurana* [Delhi, India], P. Mathur, N. Bhardwaj, S. Kumar, S. Sagar, R. Aggarwal, K. Soni, R. Malhotra

The REAnimation Low Immune Status Markers study: phenotypic and functional alterations of innate immune response in critically ill patients

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is elevated in bloodstream infections and correlates with C-reactive protein
C. Pollotto* [Perugia, Italy], V. Scaglione, S. Bastianelli, C. Bisti, D. Francisci

Proinflammatory biomarkers are not useful as sepsis outcome predictors in patients older than 75
S. Mitic* [Novi Sad, Serbia], S. Adamovic, A. Vukelic, B. D. Bjelic, L. Chetkovich

Regulation of intestinal bacterial translocation by intestinal lamina propria dendritic cells expressing TLR5 after trauma/haemorrhagic shock
Z. Yun* [Hangzhou, China], J. Zhang, C. Zhang

Generation of protective antibodies against heterologous Acinetobacter baumannii isolates
G. Kamuyu* [London, United Kingdom], S. Willcocks, F. Agostini* [Oullins Cedex, France], M. Delles

The role of liposome positive charge on immune responses generated in BALB/c mice immunized with Leishmania homologue of receptors for Activated C Kinase (LACK) of Leishmania major
M. Soosaraei* [Sari, Iran]

Serum active Granzyme A: a new biomarker that contributes to the pathogenesis of peritoneal sepsis

Bacterial DNA promotes tau and beta-amyloid aggregation and is suggested as a novel therapeutic target for Alzheimer’s disease
G. Tetz* [New York, United States], S. Pritzkow, M. Pinha, N. Mendez, C. Sota, V. Tetz

Efficacy of memory B lymphocytes in experimental model of pneumonia caused by Pseudomonas aeruginosa
T. Cebrero Cangueiro* [Seville, Spain], G. Labrador Herrera, M. Carretero Ledesma, Y. Smani, J. Pachon-Diaz, M. Pachon-Ibáñez

Efficacy of immunoglobulin enriched in IgM, alone and in combination, in experimental model of pneumonia caused by Pseudomonas aeruginosa
T. Cebrero Cangueiro* [Seville, Spain], G. Labrador Herrera, M. Carretero Ledesma, Y. Smani, J. Pachon-Diaz, M. Pachon-Ibáñez

Host responses to infection evaluated in vitro and in vivo

Regulation of intestinal bacterial translocation by intestinal lamina propria dendritic cells expressing TLR5 after trauma/haemorrhagic shock
Z. Yun* [Hangzhou, China], J. Zhang, C. Zhang

 invocation of innate immunity pulmonary mechanism after influenza virus infection of mice model
F. Riviere* [Bretigny sur Orge, France], C. Vigne, J. Burger, A. Garnier, J. Tournier, E. Billon-Denis

Investigation of the pro-autophagic effect of IL-36α and lipopolysaccharide in THP-1 cell line
Z. Al-Luhaibi* [Szeged, Hungary], K. Megyeri, G. Seprényi

Monocyte progenitors are effector cells in mycobacterial infections
A. Hanrath* [Newcastle upon Tyne, United Kingdom], C. Hatton, C. Browne, J. Vowles, S. Cowley, W. James, S. Hambleton, D. Duncan

Investigation of the pro-autophagic effect of IL-36α and lipopolysaccharide in THP-1 cell line
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A. Hanrath* [Newcastle upon Tyne, United Kingdom], C. Hatton, C. Browne, J. Vowles, S. Cowley, W. James, S. Hambleton, D. Duncan

Pharmaceuticals of radiolabeled anti-mousePD-L1 in immune-challenged tumour-bearing mice
G. Sandker, P. Wierstra, J. Molkenboer-Kuenen, M. Gotthardt, G. Adema, J. Bussink, S. Heskamp, E. Aarnsten* [Nijmegen, Netherlands]

Cell immunity in maxillofacial actinomycescises disease
N. Agayeva* [Baku, Azerbaijan], V. Marimanov, E. Agayeva, H. Aliyeva, R. Bayramova

Inflammatory response of murine macrophages and alveolar epithelial cells following exposure to Aspergillus fumigatus spores
F. Agostini* [Gullins Cedex, France], M. Delles, T. Déméauté, G. Devouassoux, A. Bentaher, J. Menotti

NK cell deficiency and cryptococcosis
M. Martinot* [Colmar, France], C. Fornier, S. Li, C. Pipероглу, C. Démerle, M. Mohseni-Zadeh, C. Mody, F. Vely

Characterisation of immune response of patients with rheumatic disorders and latent tuberculosis infection
E. Petruccioli, V. Vanini, G. Ippolito, D. Goletti* (Rome, Italy)

Tuberculosis impacts immune-metabolic pathways resulting in perturbed cytokine responses
2669 Streptococcus pneumoniae intracellular survival in THP-1 macrophages activated with different doses of lipopolysaccharide
P. Conde, N. Vázquez Burgos* (Malins de Rei, Spain), R. López, L. Fernandez Barat, A. Torres

2688 Toll like receptors, IFN-lambdas and IFN-stimulated genes expression in cystic fibrosis patients with rhinovirus infection

2921 Bacteremia with ESBL-producing Enterobacteriaceae is associated with increased levels of IgG antibodies specific to CTX-M-15 and/or CTX-M-27
T. Sahlinström, D. Ljungquist* (Skäret, Sweden), Y. Su, F. Resman, E. Mattsson, J. Thom, K. Riesbeck

445 Immunisation: new challenges and new solutions
Session accepted as Paper Poster Session

4608 Live probiotic vaccine against influenza virus infection
T. Gupalova, Y. Desheva, G. Leontieva, E. Kuleshevich, T. Kramskaya, E. Bormotova, A. Tsapieva, A. Suvorov*

600 Impact of a catch-up strategy of Tdap vaccination during hospitalisation on vaccination coverage among people over 65 years of age in Sarthe: the HOSPIVAC study
S. Bianchi* (Le Mans, France), N. Crochette, L. Hery, S. Laforest, J. Toque, J. Vaux

5764 Th2 response may be deleterious to protect against Staphylococcus aureus bacteremia
A. Le Bot* (Rennes, France), V. Bordeau, S. Reissier, S. Dian, C. Gonzalez, M. Greogio, M. Lesouhaitier, Chabeskaia, F. Bricé, M. Revest

6943 Utility of early kinetics of TTVDNA in stool for the prediction of intestinal graft versus host disease in the allogeneic haematopoietic stem cell transplantation setting

Session accepted as Paper Poster Session

668 Analysis of the vaccination coverage in a dispensary in Mayotte, an overseas department and region of France
C. Pascol* (Blavaoy, France), O. Lesens

7383 Association of IL-27 and STAT3 genetic polymorphism on the susceptibility of tuberculosis in western Chinese Han population
M. Li* (Chengdu, China), L. Jiao, W. Min Jin, H. Bai, Q. Wu

7525 Innate immunity measured by leukocyte deformability predicts outcomes in undifferentiated emergency department patients with urinary symptoms
C. Thomas, M. Musso, D. Hamer, R. Sheybani, T. Caffery, H. Tse, A. Shah, H. O’Neal Jr*

8221 Controlled human infection with Neisseria lactamica induces B cell responses that are cross-reactive with Neisseria meningitidis
A. Dale* (Southampton, United Kingdom), A. Theodosiou, J. Laver, E. Roche, A. Hill, A. Gorringe, M. Polak, A. Vaughan, R. Read

5514 Pentameric IgM does not improve clinical outcome in adults with sepsis after major abdominal surgery

4044 Is associated with increased levels of IgG antibodies specific to CTX-M-15 and/or CTX-M-27

G. Cimino, P. Palange, A. Pierangeli, C. Scagnolari, M. Mazzone, P. Pafundi, M. Montanaro, P. Saturnino

S. Chabelskaia, F. Brice, M. Revest

Session accepted as Paper Poster Session

7525 Physicochemical characterisation of aluminium hydroxide and aluminium phosphate and their potential adjuvant function in combination with squalene emulsion for EV71 vaccine development
M. Huang* (Zhunan, Taiwan)

2640 Utility of early kinetics of TTVDNA in stool for the prediction of intestinal graft versus host disease in the allogeneic haematopoietic stem cell transplantation setting

J. Michon* (Caen, France), A. Fournier, X. Lecoutour, R. Verdon, J. Michon

Factors influencing vaccination coverage among children aged 2–3 months in Afghanistan
M. Mohammad Yousuf* (Kabul, Afghanistan), A. Aalemi, K. Shahpar

395 The economic burden of Clostridioides difficile infection in patients with haematological malignancies: a case-control study
L. Duhalde, L. Lurienne* (Paris, France), S. Wingen-Heimann, L. Guillou, R. Buffet, P. Bandinelli
936 Risk factors and clinical characteristics of virus infection after haematopoietic stem cell transplantation
G. Koğar Ünivar* (Kayseri, Turkey), Z. Tun Yuce, A. Ulu Kilic

1895 Dalbavancin as definitive therapy for Gram-positive infections in patients with haematologic malignancies and haematopoietic cell transplant recipients
C. Howard* [Morgantown, United States], A. Cumpston, D. Stain

4889 Infections in haematological patients receiving CD19 CAR-T cell immunotherapy: real-life data
C. Cardoso* [Barcelona, Spain], J. Delgado, V. Ortiz-Maldonado, P. Puerta, E. Moreno, M. Chumbita, N. Garcia-Pouton, A. Urbano-Ispizua, J. Esteve, M. Juan, A. Sariano, C. Garcia Vidal

5088 Trends in Gram-negative bacteraemia in adult febrile neutropaenic cancer patients in a high-resistance setting during the last decade
C. Ayaz, E. Bilgin, G. Hazırolan, B. Sancak, M. Akova* [Ankara, Turkey]

5470 Catheter-related and non-catheter-related bloodstream infections in oncological patients

5474 Infectious complications during anti-CD19 targeted chimeric antigen T cell receptors [CAR-T] immunotherapy in relapsed/refractory aggressive B cell non-Hodgkin lymphomas [NHL]: observational retrospective study in one centre

6970 Predictive value of a positive Pneumocystis jirovecii DNA result in the diagnosis of Pneumocystis jirovecii pneumonia in haematological patients

7421 Infections associated with kinase and antiapoptotic Bcl-2 inhibitors in a cohort of real-life haematological patients

7604 Incidence and utility of follow-up blood cultures in haematology/oncology patients with Gram-negative bacteraemia
A. Clemmons* [Augusta, United States], D. Chastain, H. Young, M. Hayashi, E. Kennedy, C. Bland

7710 Clinical characteristics and mortality-related factors of bloodstream infections in patients with acute leukaemia: a single-centre experience with 152 patients
G. Mendez, C. Niveyro* [Posadas, Argentina], P. Villaiba, K. Salvatierra, C. Villaiba, H. Bernard

7863 The management of Enterococcus bloodstream infections in cancer patients: impact of central venous catheters
H. Awadh, M. Khalil, A. Chaftari* [Houston, United States], J. Fares, Y. Jiang, R. Wilson Dib, S. Ali, R. Hachem, I. Raad

7994 Potential role of procalcitonin in antimicrobial stewardship programme in febrile neutropenic cancer patients
P. Chaftari* [Houston, United States], A. Chaftari, R. Hachem, S. Yeung, Y. Jiang, A. Malek, V. Mulanovich, I. Raad

8178 Application of WISCA [Weighted Incidence Syndromic Combination Antibiotic] to guide empiric therapy in oncological paediatric patients with febrile neutropenia
E. Barbieri* [Padova, Italy], D. Bottiglengia, P. Costenaro, A. Marzolla, M. Petris, M. Pierobon, G. Biddeci, C. Giaquinto, A. Biffi, D. Donà

8465 Infectious complications in patients with relapsed/refractory Hodgkin’s lymphoma during new agents’ therapy

9053 Trends in antimicrobial resistance in Gram-negative pathogens among haematological patients: results of multi-centre study
G. Klyasova* [Moscow, Russian Federation], A. Korobova, S. Khrulnova, A. Fedorova Mironova, I. Frolova, K. Tandilova, A. Vetokhina, I. Molchanova, O. Kutsevalova

9131 Carbapenemase-producing Klebsiella pneumoniae belonging to sequence type 23 is a predictor of poor outcome in haematological patients
K. Tandilova* [Moscow, Russian Federation], G. Klyasova, S. Khrulnova, P. Elena, S. Kravchenko, E. Gribanova, E. Zvankov, G. Galstyan, V. Savchenko

9377 Discontinuation of antimicrobial therapy during fever of unknown origin in adult neutropenic patients according to ECIL-4 criteria: RELAPS, a descriptive cohort study

9542 Outcome of infections caused by carbapenemase-producing Enterobacteriales in patients with haematological disorders
K. Tandilova* [Moscow, Russian Federation], G. Klyasova, S. Khrulnova, P. Elena, S. Kravchenko, E. Gribanova, E. Zvankov, G. Galstyan, V. Savchenko
Abstract Categories 2020

9566 Cytomegalovirus reactivation in allogeneic stem cell transplant recipients: frequency, time to reactivation and dynamic of viremia in different types of donors and in repeated episodes
M. Garnica* [Rio de Janeiro, Brazil], S. Dalcolmo, B. Gaio, I. Alves, M. Valetim, A. Moialino

1577 Efficacy of beta-lactam/beta-lactamase inhibitors to treat extended-spectrum beta-lactamase-producing Enterobacteriaceae bacteraemia secondary to urinary tract infection in kidney transplant recipients

1883 Post-transplant lymphoproliferative disorders and association of antiviral prophylaxis in a nationwide cohort study

2187 Risk factors for developing BK virus associated nephroptathy: a single-centre retrospective cohort study of kidney transplant recipients
C. Larant* [Uppsala, Sweden], G. Westman, A. Bergqvist, B. Von Zur-Mühlen, B. Eriksson

2509 Hospital-acquired pneumonia in liver transplant recipients
V. Khillan* [New Delhi, India], G. Pindi, V. Pamecha, P. Kale

3373 High-dimensional single cell analysis identifies unexpected distribution of T cell populations in liver transplanted HIV-positive patients

3581 Epidemiology and outcomes of microbiologically documented bacterial foodborne infections in solid organ transplant recipients: a 10-year nationwide cohort
L. Van Den Bogaart* [Lausanne, Switzerland], A. Egli, L. Walti, D. Neofytos, C. Garzoni, K. Boggian, C. Berger, N. Mueller, D. Manuel, M. Mombelli

Session accepted as Paper Poster Session

Infections after solid organ transplant

429 Late-onset Pneumocystis jirovecii pneumonia in renal transplant recipients
A. Cruz* [Sterling Heights, United States], C. Jarrin Tejada

1577 Efficacy of beta-lactam/beta-lactamase inhibitors to treat extended-spectrum beta-lactamase-producing Enterobacteriaceae bacteraemia secondary to urinary tract infection in kidney transplant recipients

5968 Measles seropositivity in renal transplant recipients in the presence of ongoing outbreaks: a single centre analysis
F. Wagner, D. Sidler, M. Barbani, F. Suter-Riniker, P. Jent, C. Hirsle, L. Walti* [Bern, Switzerland]

5297 Impact of pretransplant norfloxacin prophylaxis on multidrug-resistant post–liver transplant infections

5409 Investigating the microbiological growth of donor organ preservation fluid in liver and kidney transplantation
J. Helliwell, N. Cutmore* [Leeds, United Kingdom], N. Young

5638 Risk factors for carbapenem-resistant Enterobacteriaceae acquisition among kidney transplant recipients
M. Freire* [Sao Paulo, Brazil], L. Carvalho, F. Spadao, F. De Paula, W. Nahas, E. David Neto, L. Pietrrotti

5361 Usefulness of human cytomegalovirus (HCMV)-specific immunological monitoring in the management of HCMV infection in lung transplant recipients

5409 Protective role for cytomegalovirus-specific neutralising antibodies in kidney transplant recipients treated with T-cell-depleting agents

6841 Infections due to multidrug-resistant bacteria among Swiss solid organ transplant recipients between 2012 and 2017

7210 Brucellosis in different types of transplantation
M. Rabiei, F. Imanzade, I. Alavidarazam* [Tehran, Iran], S. Shokouhi
Early cytomegaloovirus reactivation and bacterial infections affect the mortality of patients after kidney transplant
I. Spalliera* (Rome, Italy), M. Iannetta, N. Cesta, M. De Masi, V. Malagnina, C. Cerva, L. Ferraris, L. Tati, G. Tison, M. Andreoni, L. Sarmati

Session accepted as Mini-oral Flash Session
Moving targets: vaccines and the changing epidemiology of measles and pneumococcal disease

Increase in potentially measles-susceptible young healthcare workers in South Korea
Y. Kim* (Wonju, South Korea), B. Ha, H. Jeong, G. Hwang, Y. Uh, I. Jung, H. Kim

Comparison of early effects of Streptococcus pneumoniae vaccination policies on nasopharyngeal carriage in a Palestinian population
M. Ramlawi* (Jerusalem, Palestine), K. Azmi, Z. Abdeen

Vaccination perception and factors influencing MMR vaccination decisions during a university measles outbreak in a country with a high vaccine hesitancy
J. Michon* (Caen, France), A. Fournier, F. Appia, S. Villedieu, A. Leprieur, C. Porterie, R. Verdon, A. Baldolli

Vitamin D3 supplementation with a daily dose of 400 or 1200 IU results in similar antibody concentrations to measles, mumps and rubella in vaccinated 2-year-old Finnish children

The proportion of invasive pneumococcal disease and pneumococcal pneumonia in UK adults potentially covered by the 13-valent and the next-generation of pneumococcal conjugate vaccines under development

Invasive pneumococcal disease among adults in Germany, nine years after PCV13 introduction
M. Van Der Linden* (Aachen, Germany), A. Itzek, S. Perniciaro, M. Imöhl

Streptococcus pneumoniae: serotype distribution in adults with invasive disease after 8 years of systematic vaccination of children with PCV13

Potential coverage of invasive pneumococcal disease by current and next generation of anti-pneumococcal vaccines in children and adults in Spain
S. De Miguel, M. Domenech, J. Sempere, I. Del Rio, B. López Ruiz, F. González Camacho, J. Yuste* (Madrid, Spain)

Mapping a nosocomial outbreak of measles, coinciding with a period of sustained transmission in south London in 2018

A prolonged measles outbreak in a vaccine refusing community, Austria, 2019
L. Henszel* (Vienna, Austria), D. Schmid, A. Grisold, H. Holzmann

Stenotrophomonas maltophilia bloodstream infections in umbilical cord blood transplant recipients

Shortened antibiotic treatments for Gram-negative bacteriaemia in cancer patients: less is possible

Incidence of bloodstream infection from multidrug-resistant bacteria in haematological patients with rectal colonisation
M. Peradotto* (Turin, Italy), G. Bianco, M. Boattini, A. Bondi, M. Iannacccone, Z. Teresa, R. Cavallo, C. Costa

Breakthrough blood culture isolates whilst on broad spectrum antimicrobial therapy for high-risk neutropenic fever: more common and resistant that previously thought
A. Douglas* (Parkville, Australia), S. Tio, K. Thursky, L. Worth, A. Bajel, M. Slavin

Optimal treatment duration of Pseudomonas aeruginosa infections in allogeneic haematopoietic cell transplant recipients

Intestinal colonisation by multidrug-resistant Enterobacteriaceae and infections in patients receiving an allogeneic haematopoietic stem cell transplantation: the ENTHERE-SCT Study (PI16/01415)

Haematology/oncology patients might have different risks for MDR according to different types of chemotherapy
J. Barbosa* (São Paulo, Brazil), K. Yaqub Ibrahim, P. Banazzi, D. Peixoto, R. Ito, E. Abdala, M. Freire
Impact of non-use of levofloxacin prophylaxis during neutropenia on reduction of resistance among Gram-negatives causing bloodstream infection in haematopoietic stem cell transplantation patients: very successful preliminary data

T. Guimaraes* [São Paulo, Brazil], F. Spadao, L. Caroline, M. Nascimento, V. Rocha, S. Figueiredo Costa

The probability of infection caused by carbapenemase-producing Enterobacteriales (CPE) in haematological patients with rectal carriage of CPE

K. Tandilova* [Moscow, Russian Federation], G. Klyasova, S. Khrulnova, P. Elena, S. Kravchenko, E. Gribanova, E. Zvankov, G. Galstyan, V. Savchenko

Identification of anti-TPI H8 antibody-epitope analogues as putative active vaccine against Staphylococcus aureus

L. Rummler* [Cologne, Germany], S. Mertins, M. Kroenke, A. Klimka

Novel lipid A mimetics [BECC438 and BECC470] act as potent adjuvants in bacterial and viral subunit vaccines

E. Harberts, D. Varisco, A. Jain, R. Ernst* [Baltimore, United States]

Novel lipid A mimetics act as potent adjuvants in bacterial and viral subunit vaccines

E. Harberts, D. Varisco, A. Jain, R. Ernst* [Baltimore, United States]

Susceptibility to Group A Streptococcus invasive infections in children: preliminary results of a multicentre prospective study in France: the STREPTOPEDIA study


High-frequency of Specific Polysaccharide Antibody Deficiency [SPAD] in adults with unexplained recurrent and/or severe bacterial infections: the SPIDAC French Study


Integrating genome-wide association study with bulk and single-cell RNA sequencing reveals a role for LY8 in the anti-Candida host response

V. Kumar* [Groningen, Netherlands], D. De Vries, V. Matzarakis, O. Bakker, H. Brugge, H. Westra, M. Netea, L. Franke, M. Van Der Wijst

The difficulties of differentiating central nervous system infection from disease relapse in a cohort of adult patients with haematological malignancy: 10 years’ experience from a central London hospital

E. Lim, R. Gnanadurai, M. Escobedo-Cousin, L. Bell* [London, United Kingdom], N. Mccann, J. Ellis, D. Ming, K. Cwynarski, R. Miller, E. Wall, R. Heyderman, H. Hyare

Epidemiology, clinical characteristics and outcomes of central nervous system infections in solid organ transplant recipients: a nationwide cohort study

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Deputy Programme Director
Jacob Moran-Gilad
Abstract 1

The impact of microbiome DNA enrichment methods on host DNA depletion efficiency and bacterial community structure of infected tissue samples

Fatemah Sadeghpour Heravi1, Martha Zakrzewski2, Karen Vickery1, Honghua Hu1

1Macquarie university, Sydney, Australia, 2QIMR Berghofer Medical Research Institute, Brisbane, Australia

Background: Shotgun metagenomic sequencing is a genome-wide sequencing approach to explore bacterial communities directly from their habitat or infected sites. However, extracting high-quality bacterial DNA with minimum host DNA contamination from infected tissue samples suitable for metagenomics studies is very challenging. Although metagenomics has shown great promise in environmental samples, it is particularly difficult in infected tissue samples with a great amount of host DNA contamination. The co-extraction of host DNA with bacterial DNA can mask the microbial signals in the sequencing process.

Materials/methods: In this study, we evaluated the impact of different microbiome DNA enrichment methods (NEBNext Microbiome DNA Enrichment kit, Molzym Ultra-Deep Microbiome Prep, QIAamp DNA Microbiome kit, and HostZERO microbial DNA kit) on host DNA depletion efficiency and bacterial composition of infected tissue samples (diabetic foot infection) using quantitative real-time PCR and 16S ribosomal RNA sequencing methods. The host DNA depletion ratio and the microbial profile of diabetic foot infections were compared before and after applying the selected microbiome enrichment kits.

Results: Molzym extracted the lowest amount of bacterial load with a high level of host DNA contamination. In contrast, HostZERO and QIAamp methods recovered the highest amount of bacterial genomes with a minimum amount of host DNA contamination, attesting to the efficacy of these two methods in shotgun metagenomic sequencing studies. Microbial composition was also highly similar between the original and enriched samples processed by NEBNext, resembling most of the predicted taxa in the control sample. Also, ten of the sixteen genera predicted in the control sample were recovered by all the enrichment methods of which the NEBNext method recovered all of the genera and Molzym recovered the lowest number of bacterial genera.

Conclusions: Our findings can provide a useful guideline for scientists in selecting DNA enrichment methods, particularly those who wish to deplete a high amount of host DNA contamination and preserve a high amount of bacterial DNA load from infected tissue samples for shotgun metagenomic sequencing.

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**Abstract 7**

**Bacteraemia with anaerobic bacteria and association with colorectal cancer**

Ulrik S. Justesen*1; Stig Lønberg Nielsen2; Thøger Gorm Jensen3; Ram B. Dessau1,4; Jens Kjelseth Møller5; John E. Coia6; Steen Lomborg Andersen7; Court Pedersen2; Kim Oren Gradel8

1Odense University Hospital, Department of Clinical Microbiology, Odense, Denmark, 2Odense University Hospital, Department of Infectious Diseases, Odense, Denmark, 3Slagelse Hospital, Department of Clinical Microbiology, Slagelse, Denmark, 4University of Southern Denmark, Department of Regional Health Research, Odense, Denmark, 5Lillebælt Hospital, Department of Clinical Microbiology, Vejle, Denmark, 6Sydvestjysk Sygehus, Department of Clinical Microbiology, Esbjerg, Denmark, 7Sygehus Sønderjylland, Department of Clinical Microbiology, Sønderborg, Denmark, 8Odense University Hospital, Center for Clinical Epidemiology, Odense, Denmark

**Background:** Studies have reported an association between Bovis group streptococci, *Clostridium septicum* and colorectal cancer (CRC). Recently associations between different *Bacteroides* spp., *Fusobacterium nucleatum* and CRC have also been reported. We wanted to investigate this further in a large scale study.

**Materials/methods:** We performed a population-based cohort study including data on blood cultures from 2007 to 2016 covering a population of more than 2 million people. We combined blood culture data with the national register for colorectal cancer (Danish Colorectal Cancer Group Database) and identified incident CRC after bacteraemia. The risk of incident CRC until 2018 was investigated for *Bacteroides* spp., *Clostridium* spp. and *Fusobacterium* spp. and compared with Bovis group streptococci, *Escherichia coli*, *Staphylococcus aureus* and negative blood culture controls matched 1:5 by age and sex.

**Results:** We included 45,760 bacteraemia episodes, of which 492 (1.1%) were diagnosed with CRC after the bacteraemia; 241 (0.5%) within 1 year. The risk of CRC for selected bacteria is shown in Table 1 (results for *E. coli* and *S. aureus* are not shown but were similar to negative blood cultures). Most anaerobic species were associated with a considerable increased risk of CRC (up to 40 times) compared with negative blood cultures.

**Conclusions:** In this large scale cohort study, it was found that in patients with bacteraemia caused by selected anaerobic bacteria the risk of incident CRC was increased up to 40 times compared with patients with bacteraemia caused by non-anaerobic bacteria or negative blood cultures. Bacteraemia with certain anaerobic bacteria could potentially result in a recommendation of further evaluation for CRC in selected patients.

**Table 1.** No. bacteraemia episodes followed by CRC/total no. episodes [%]

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Without a time limitation</th>
<th>Within 1 year</th>
</tr>
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<tbody>
<tr>
<td>Clostridium spp.</td>
<td>22/457 [4.8]</td>
<td>20/457 [4.4]</td>
</tr>
<tr>
<td>Fusobacterium spp. (excluding <em>F. necrophorum</em>)</td>
<td>6/100 [6.0]</td>
<td>3/100 [3.0]</td>
</tr>
<tr>
<td>Bovis group streptococci</td>
<td>6/117 [5.1]</td>
<td>5/117 [4.3]</td>
</tr>
<tr>
<td>Negative blood cultures</td>
<td>2475/231629 [1.1]</td>
<td>1035/231629 [0.5]</td>
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</table>

**Presenter email address:** ulrik.stenz.justesen@rsyd.dk
Crimean-Congo haemorrhagic fever in an emergency department in Spain

Lia Monsalve-Arteaga1, Moncef Belhassen García1,2, Juan-Luis Munoz-Bellido1,2, Montserrat Alonso Sardón2, Anabel Negredo3, María Paz Sanchez Seco1, Fernando De Oru Manchón1, Nuria Leralta1, Isabel Bas García1, Jesús Sánchez Serrano2, Jorge García Criado2, Antonio Muro Alvarez2, Amparo López Bernús2

1Universidad de Salamanca, Salamanca, Spain; 2Complejo Asistencial Universitario de Salamanca, Salamanca, Spain; 3Instituto de Salud Carlos III, Majadahonda (Madrid), Spain

Background: Crimean-Congo haemorrhagic fever (CCHF) is a widespread tick-borne viral disease caused by the homonymous virus (CCHFV), a Nairovirus of the Nairoviridae family. It has been implicated in severe viral haemorrhagic fever outbreaks. During the summer of 2016, the first two cases of this disease were reported in Spain. Nowadays, this disease is difficult to get eradicated because of its enzootic life cycle. The aim of this study was to determine the presence of CCHF among patients coming for a febrile illness to Complejo Asistencial Universitario de Salamanca (CAUSA), Salamanca, western Spain, during the spring-summer periods in 2017 and 2018.

Materials/methods: We evaluated prospectively patients older than 18 years, who came to the Emergency Department of CAUSA presenting fever as the only or main symptom. We determined specific IgM and IgG antibodies against CCHFV by the VertoCrimea ELISA kit-test (Vector-Best, Russia), an in-house ELISA and two immunofluorescence assays (Euroimmun, Germany) against two different glycoproteins [nucleoprotein and glycoprotein], and an in-house nested RT-PCR. Details were collected from the medical records.

Results: 133 patients were selected for the study. Mean age (±SD) was 67.63 years (±18.8). 81 patients (60.9 %) were male. Most patients were diagnosed as genitourinary or respiratory syndromes. The 3rd most frequent diagnosis was acute undifferentiated febrile illness. Three patients had anti-CCHFV IgG antibodies, suggesting a past infection. Two patients were found to have anti-CCHFV IgM antibodies, and one of them was also positive by RT-PCR. Both patients lived in the province of Salamanca (western Spain). One patient was involved in animal husbandry. None of these two cases were associated to a nosocomial outbreak.

Conclusions: This study suggests that CCHF is an identifiable cause of febrile illness in Spain, and therefore should be suspected when a patient comes to the emergency department with fever and hepatic impairment, and/or haemorrhagic phenomena, especially in spring and summer seasons, and if they have risk activities. All of this, in order to establish support treatment and isolation measures as soon as possible, thus reducing the risk of mortality and nosocomial outbreaks.

Figure 1: Acute and past infections by CCHFV identified in Spain

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Abstract 19

**Genetic characterisation of co-circulating community *Staphylococcus aureus* and *Streptococcus pyogenes* causing skin and soft tissue infections in Gambia**

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**Background:** *Staphylococcus aureus* and *Streptococcus pyogenes* are major global pathogens. Infection ranges from asymptomatic carriage to fatal invasive infection. Understanding the transmission dynamics and genetic diversity within low- and middle-income countries (LMIC) with a high burden of disease is required for effective vaccine development and public health interventions. We aimed to characterize the genetic diversity of *S. aureus* and *S. pyogenes* causing skin and soft tissue infection (SSTI) in children in The Gambia using whole genome sequencing.

**Materials/methods:** A point prevalence study of pyoderma was conducted over 4 months in randomly-selected census-derived geographical clusters of Sukuta, a peri-urban area in The Gambia. Swabs from pyoderma lesions were cultured for *S. aureus* and *S. pyogenes*. A single colony of each bacteria was sub-cultured, DNA extracted and sequenced using an Illumina MiSeq platform. Multi-locus sequence typing (MLST, MOST), de novo assembly (SPAdes), gene annotation (prokka), emm typing (CDC-typing-tool), core genome determination (roary) and maximum likelihood phylogenetic tree construction (RAxML) were used to analyse sequence data.

**Results:** Of 1441 children from nine geographical clusters, 251 (17.4%) had pyoderma. Of these, *S. aureus* was isolated from 202 children (80.5%) and *S. pyogenes* from 129 (51.4%). Co-infection was seen in 104 children (41.4%), which is comparable to the limited data from LMICs. Thus far sequence data from 93 *S. aureus* isolates and 105 *S. pyogenes* isolates were suitable for analysis. The predominant *S. aureus* MLST clonal complexes (CC) were CC15 (29%), CC152 (20.4%), CC1 (14%) and CC5 (12.9%), collectively representing 76.3% of all sequenced isolates. *S. pyogenes* showed no emm-type predominance, with no single emm-type representing more than 5.7% of sequenced isolates and 44 distinct emm types. Within the three geographical clusters with the largest number of pyoderma cases, a single CC type was responsible for 25.5 – 35.7% of *S. aureus* infections, compared to 8.7 – 12.0% caused by any single *S. pyogenes* emm-type.

**Conclusions:** Our study provides the first whole genome sequence analysis of co-circulating community *S. aureus* and *S. pyogenes* causing SSTI from The Gambia. Further detailed interrogation of the larger dataset is ongoing, including evidence for transmission using combined epidemiological and genetic data.

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**Abstract 24**

**High-dose ceftaroline fosamil recommendations for paediatric patients with *Staphylococcus aureus* complicated skin and soft-tissue infections using an extrapolation approach**

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1Pfizer, Sandwich, United Kingdom, 2Pfizer, Tadworth, United Kingdom, 3Pfizer, Collegeville, United Kingdom, 4Pfizer Inc, Collegeville, United States, 5Pfizer, La Jolla, United States

Abstract third-party references: Study sponsored by Pfizer.

**Background:** For adults and adolescents (aged 12 to <18 years with body weight ≥33 kg), the standard ceftaroline fosamil dose is 600 mg by 5–60 min intravenous (IV) infusion every 12 h (q12h) for complicated skin and soft-tissue infections (cSSTIs) caused by *Staphylococcus aureus* with ceftaroline minimum inhibitory concentration (MIC) ≤1 mg/L, whereas a “high dose” of 600 mg by 2-h IV infusion q8h is approved in Europe for MICs of 2 or 4 mg/L, based on population pharmacokinetic (PopPK) analyses and Phase III clinical trial data (NCT01499277). We conducted further PopPK analyses to support high-dose recommendations for paediatric patients (aged 2 months to <18 years) with cSSTI caused by *S. aureus* with suspected high MIC (2 or 4 mg/L).

**Materials/methods:** A PopPK model for ceftaroline fosamil and ceftaroline based on adult (n=944) and paediatric (n=304) data was used to simulate steady-state ceftaroline exposures and perform probability of target attainment (PTA) simulations for various paediatric high-dose regimens and renal function categories. PTA was calculated as the percentage of simulated patients achieving free ceftaroline plasma concentrations above the MIC per dosing interval (%fT>MIC) of 27%, 31% and 35% (*S. aureus* PK/pharmacodynamic targets for stasis, 1-log10 and 2-log10 kill, respectively). Exposures and PTA were matched to adults with normal renal function (body surface area-normalised creatinine clearance ≥80 mL/min/1.73 m²) receiving ceftaroline fosamil 600 mg by 2-h IV infusion q8h. Safety/tolerability data were extrapolated from paediatric trials of higher ceftaroline fosamil doses.

**Results:** For the proposed ceftaroline fosamil high-dose regimens [Table], across paediatric age groups and renal function categories, simulated ceftaroline exposures were similar to adults with normal renal function, with PTA >99% for MIC of 2 mg/L, and PTA similar to or higher than that in adults with normal renal function (>80%) for MIC of 4 mg/L.

**Conclusions:** These analyses support the extrapolation of efficacy based on PTA from adult to paediatric patients (aged 2 months to <18 years) with cSSTI caused by *S. aureus* with ceftaroline MICs of 2 or 4 mg/L at the proposed ceftaroline fosamil high-dose regimens for paediatric patients.
Table. Steady-state exposures and PTA based on simulations for paediatric patients (aged 2 months to <18 years) with normal renal function or renal impairment, at the proposed high-dose regimens of ceftaroline fosamil for treatment of cSSTI with MIC >1 mg/L

<table>
<thead>
<tr>
<th>Age group</th>
<th>Recommended high-dose (2-h IV infusion)</th>
<th>C_{max,ss} (mg/L)</th>
<th>AUC_{0-24h} (mg/L*h)</th>
<th>C_{max,ss} Ratio to adults</th>
<th>AUC_{0-24h} Ratio to adults</th>
<th>35% &gt;MIC of 2 mg/L</th>
<th>35% &gt;MIC of 4 mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reference: Normal renal function (nCrCl ≥80 mL/min/1.73 m²)</td>
<td>600 mg q8h</td>
<td>18.4 (10.4, 32.2)</td>
<td>155 (85.7, 285)</td>
<td>N/A</td>
<td>N/A</td>
<td>99.7</td>
<td>82.7</td>
</tr>
<tr>
<td>Normal renal function (nCrCl 260 to &lt;80 mL/min/1.73 m²)</td>
<td>12 to &lt;18 years</td>
<td>12 mg/kg (max 600 mg) q8h</td>
<td>21.7 (12.6, 35.9)</td>
<td>173 (99.1, 206)</td>
<td>1.18</td>
<td>1.12</td>
<td>99.8</td>
</tr>
<tr>
<td></td>
<td>6 to &lt;12 years</td>
<td>23.5 (14.5, 37.5)</td>
<td>178 (106, 302)</td>
<td>1.26</td>
<td>1.15</td>
<td>99.8</td>
<td>91.8</td>
</tr>
<tr>
<td></td>
<td>2 to &lt;6 years</td>
<td>21.4 (13.2, 33.9)</td>
<td>153 (90.9, 258)</td>
<td>1.16</td>
<td>0.987</td>
<td>99.5</td>
<td>81.8</td>
</tr>
<tr>
<td></td>
<td>12 to &lt;24 months</td>
<td>10 mg/kg q8h</td>
<td>19.2 (11.9, 30.4)</td>
<td>146 (86.9, 247)</td>
<td>1.04</td>
<td>0.940</td>
<td>99.7</td>
</tr>
<tr>
<td></td>
<td>2 to &lt;12 months</td>
<td>20.3 (12.6, 32.0)</td>
<td>168 (98.9, 284)</td>
<td>1.11</td>
<td>1.08</td>
<td>99.9</td>
<td>90.6</td>
</tr>
<tr>
<td>Mild renal impairment (nCrCl ≥50 to &lt;60 mL/min/1.73 m²)</td>
<td>12 to &lt;18 years</td>
<td>12 mg/kg (max 600 mg) q8h</td>
<td>23.2 (13.5, 38.6)</td>
<td>193 (111, 334)</td>
<td>1.23</td>
<td>1.22</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>6 to &lt;12 years</td>
<td>24.9 (15.3, 39.7)</td>
<td>197 (116, 333)</td>
<td>1.33</td>
<td>1.25</td>
<td>100</td>
<td>95.3</td>
</tr>
<tr>
<td></td>
<td>2 to &lt;6 years</td>
<td>22.7 (14.1, 36.1)</td>
<td>170 (101, 286)</td>
<td>1.22</td>
<td>1.08</td>
<td>99.8</td>
<td>89.7</td>
</tr>
<tr>
<td></td>
<td>12 to &lt;24 months</td>
<td>10 mg/kg q8h</td>
<td>21.8 (13.3, 35.2)</td>
<td>183 (104, 322)</td>
<td>1.16</td>
<td>1.16</td>
<td>99.9</td>
</tr>
<tr>
<td></td>
<td>2 to &lt;12 months</td>
<td>23.2 (14.1, 37.3)</td>
<td>210 (119, 370)</td>
<td>1.23</td>
<td>1.32</td>
<td>100</td>
<td>97.0</td>
</tr>
<tr>
<td>Moderate renal impairment (nCrCl ≥30 to &lt;50 mL/min/1.73 m²)</td>
<td>12 to &lt;18 years</td>
<td>10 mg/kg (max 400 mg) q8h</td>
<td>18.2 (10.4, 31.6)</td>
<td>168 (94.2, 296)</td>
<td>0.974</td>
<td>1.06</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>6 to &lt;12 years</td>
<td>25.1 (14.1, 37.0)</td>
<td>201 (119, 338)</td>
<td>1.23</td>
<td>1.28</td>
<td>100</td>
<td>96.8</td>
</tr>
<tr>
<td></td>
<td>2 to &lt;6 years</td>
<td>21.7 (13.4, 34.4)</td>
<td>178 (108, 301)</td>
<td>1.16</td>
<td>1.13</td>
<td>100</td>
<td>93.2</td>
</tr>
<tr>
<td>Severe renal impairment (nCrCl ≥15 to &lt;30 mL/min/1.73 m²)</td>
<td>12 to &lt;18 years</td>
<td>8 mg/kg (max 300 mg) q8h</td>
<td>17.0 (9.58, 30.0)</td>
<td>178 (98.7, 326)</td>
<td>0.907</td>
<td>1.13</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>6 to &lt;12 years</td>
<td>22.3 (13.5, 36.1)</td>
<td>222 (130, 370)</td>
<td>1.19</td>
<td>1.41</td>
<td>100</td>
<td>98.7</td>
</tr>
<tr>
<td></td>
<td>2 to &lt;6 years</td>
<td>21.2 (13.1, 33.9)</td>
<td>200 (119, 343)</td>
<td>1.13</td>
<td>1.27</td>
<td>100</td>
<td>97.2</td>
</tr>
</tbody>
</table>

1Median (5th, 95th) based on summary of 100 trials and corresponds to median (90% prediction interval). AUC_{0-24h}, area under the plasma concentration–time curve over 24 h at steady state; C_{max,ss}, maximum concentration at steady state; cSSTI, complicated skin and soft-tissue infection; %T>MIC, percent of time that free plasma concentrations are above minimum inhibitory concentration; MIC, minimum inhibitory concentration; nCrCL, body surface area-normalised creatinine clearance; PTA, probability of target attainment; q8h, every 8 h.

Study sponsored by Pfizer.

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Metatranscriptomic analysis reveals active bacterial communities in diabetic foot infections

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Background: DNA sequencing approaches have identified the complexity of bacterial communities present in diabetic foot infections. Despite the extended view of diabetic foot ulcers (DFUs) and diabetic foot infections (DFIs) microbiota, little is known about which active bacteria, bacterial pathways, and resistance genes are pertinent to infection, and if any differences in function are associated with increased infection severity.

Materials/methods: In this study, we applied RNA sequencing (metatranscriptomics) of DFI tissue samples to analyze the bacterial taxonomic composition, function, and antibiotic resistance of the active DFI microbiota at mild, moderate and severe stages of infection. Total RNA was extracted from infected tissue samples and rRNA was depleted. Putative bacterial mRNA was sequenced using the Illumina TruSeq protocol. Human RNA was filtered and quality control and trimming were performed on the sequencing reads. Bacterial mRNAs were mapped to bacterial genomes using Kraken, KEGG and CARD databases to identify the taxonomic composition, functional pathways, and antibiotic resistance profile of active DFI microbiota.

Results: Taxonomic profiling of bacterial transcript indicated that the main features in DFI consisted of fourteen bacterial phyla. Bacterial transcripts assigned to genera Spiroplasma, Vibrio, and Mycoplasma were significantly different between different infection severity (Anova, p<0.05). Mild and severe stages were dominated by the species Staphylococcus aureus and Porphyromonas asaccharolytica, respectively. The functional activity profile of the DFI microbiota was comprised of 132 metabolic pathways of which ribosome and thiamin being among the most highly expressed pathways. Moreover, a total of 131 antibiotic resistance genes, primarily involved in the expression of multidrug efflux pumps/exporters, and resistance to beta-lactam, macrolide, and tetracycline antibiotics were identified in the active DFI microbiota.

Conclusions: Taxonomic profiling, functional characterization and antibiotic resistance identification of the transcriptionally active microbial community analyzed in this study may help to provide an understanding of the role of key microorganisms in DFI and their association with disease severity. Such information may be clinically useful allowing replacement of DFI empirical therapy with targeted treatment.

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Abstract 35

Evaluation of EUCAST rapid antimicrobial susceptibility testing (RAST) directly from blood culture bottles

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Background: Rapid antimicrobial susceptibility testing (RAST) method for direct disk diffusion from positive blood cultures (BCs) with shortened incubation time was released by EUCAST in late 2018. An evaluation was performed for Gram-negative BC isolates at a 24-hour laboratory in a tertiary hospital.

Materials/methods: BCs positive with Gram-negative bacilli between 23/4/2019 and 21/6/2019, and forty-one spiked isolates were included. RAST was performed using six disks (ceftazidime, piperacillin-tazobactam, meropenem, ciprofloxacin, gentamicin, and amikacin) and compared against the routine method, Vitek 2 (bioMérieux). An audit of Vitek turnaround-time was also performed.

Results: Sixty-eight Escherichia coli (EC), forty-seven Klebsiella pneumoniae (KP), and thirty-three Pseudomonas aeruginosa were included. Categorical agreement (CA), very major errors (VME), and major errors (ME) were determined among interpretable results. The highest error rates were MEs in piperacillin-tazobactam for EC at 4 hours (7/11, 63.6%), and PA at 6 hours (1/1, 100%). Combined results of all isolates are presented in the table. Median turnaround-time to availability of Vitek results was 19.58 hours for EC (IQR: 17.38 – 21.38 hours), 19.43 hours for KP (IQR: 17.72 – 20.67 hours), and 23.3 hours for PA (IQR: 21.32 – 24.35 hours).

Conclusions: Introduction of RAST could significantly shorten turnaround-time of susceptibility testing. With the exception of piperacillin-tazobactam, the absolute number of errors for the majority of drug-bug combinations was low. A larger-scale evaluation is required to confirm these findings.

<table>
<thead>
<tr>
<th>Drug</th>
<th>4-hour-reading</th>
<th>6-hour-reading</th>
<th>8-hour-reading</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CA</td>
<td>VME</td>
<td>ME</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>71/73 (92.3%)</td>
<td>0/30 (0%)</td>
<td>2/43 (4.7%)</td>
</tr>
<tr>
<td>Piperacillin-tazo-</td>
<td>37/45 (83.2%)</td>
<td>0/21 (0%)</td>
<td>8/24 (33.3%)</td>
</tr>
<tr>
<td>Bacactam</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meropenem</td>
<td>92/99 (92.9%)</td>
<td>0/9 (0%)</td>
<td>1/84 (1.2%)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>84/85 (98.8%)</td>
<td>1/49 (2.0%)</td>
<td>0/36 (0%)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>85/86 (98.8%)</td>
<td>0/17 (0%)</td>
<td>1/69 (1.4%)</td>
</tr>
<tr>
<td>Amikacin</td>
<td>56/60 (93.3%)</td>
<td>0/5 (0%)</td>
<td>0/51 (0%)</td>
</tr>
</tbody>
</table>

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Mass-Up: free software for the analysis of mass spectra biomarkers

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Background: In Clinical Microbiology, MALDI-TOF analysis of proteins is mainly used to obtain mass spectra for bacterial identification. Furthermore, discriminatory mass peaks [biomarkers] have been searched to identify different strain-specific traits such as antimicrobial resistance or virulence determinants. “Mass-up” is an open-source software that can be used in the analysis of MALDI-TOF-obtained spectra that allows the quick and easy identification of specific mass-peaks.

Materials/methods: This study was performed in the Microbiology Department of Donostia University Hospital (Basque Country, Spain). Mass-up software was used to find biomarkers to differentiate between Shigella spp. and Escherichia coli studying the MALDI-TOF mass spectra of 40 clinical isolates (4 S. boydii, 1 S. dysenteriae, 10 S. flexneri, 11 S. sonnei, 14 E. coli) and 6 reference strains (S. boydii CECT583, S. dysenteriae CECT584, S. flexneri CECT4804, S. sonnei CECT457, S. sonnei CECT4887 and E. coli ATCC25922). Mass-up software was also used to try to discriminate between S. aureus and MRSA (methicillin-resistant S. aureus) by analysing the mass spectra of 32 MRSA and 9 S. aureus clinical isolates based on described biomarkers [reviewed in Østergaard C. et al. Int J Med Microbiol. 2015;305:838.] To identify specific biomarkers, bacterial mass spectra were analysed using the Mass-up software [http://www.sing-group.org/mass-up/] developed by the University of Vigo (Galicia, Spain). This software allows in ten easy steps to perform different analysis such as quality control, discriminatory peaks discovery [biomarkers], principal component analysis, hierarchical clustering, biclustering and classification analysis on the aligned peak list.

Results: No species-specific peaks were observed in the mass spectra of E. coli and Shigella isolates: their differentiation was not possible. In addition, probably due to variation in the methodologies, previously reported biomarkers to differentiate between S. aureus and MRSA only partially matched with our findings. Some of the 44 MRSA biomarkers analyzed were found in both S. aureus and MRSA isolates, enabling the differentiation of 28/41 (68.3%) of the strains.

Conclusions: Mass-up is an easy-to-use, quick, free and reliable tool for the analysis of MALDI-TOF-obtained mass spectra. Using Mass-up no biomarkers could be found to differentiate between E. coli and Shigella species or between S. aureus and MRSA.

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Abstract third-party references: This study was performed by JMI Laboratories and supported by Amplyx Pharmaceuticals, which included funding for services related to preparing this abstract.

Background: Existing antifungal agents are active against many common opportunistic fungal pathogens; however, breakthrough fungal infections occur and often involve less frequently encountered yeast and mould isolates. These rarer isolates tend to exhibit diminished susceptibility to current agents. Manogepix (APX001A) is a novel inhibitor of the fungal Gwt1 enzyme [required for acylation of inositol during glycosylphosphatidylinositol anchor biosynthesis. The prodruk fosmanogepix, is being evaluated in Phase 2 clinical trials for invasive candidiasis/candidemia, Candida auris infections, invasive aspergillosis, and Cryptococcus meningitis. Manogepix is active against Candida [except C. krusei], Aspergillus, and difficult-to-treat moulds including Fusarium and Scedosporium species. In this study, we evaluated the in vitro activity of manogepix (MGX), anidulafungin (ANF), micafungin (MCF), fluconazole (FLU), and others against 1,294 clinical fungal isolates collected worldwide during 2018.

Materials/methods: Fungal isolates were collected from 69 medical centers in 24 countries in North America (46.3%), Europe (36.5%), Asia-Pacific (11.3%), and Latin America (5.9%). Among the isolates tested, 75.0% were Candida, 4.2% were non-Candida yeasts, including 33 Cryptococcus neoformans var. grubii (2.6%), 19.0% were Aspergillus, and 1.9% were other moulds. All isolates were tested by CLSI reference broth microdilution.

Results: MGX (MIC50/90, 0.008/0.03 mg/L) was the most potent antifungal agent tested against Candida isolates [Table]; ANF, MCF, and FLU MIC90 values were 64-, 32-, and 128-fold higher, respectively. MGX (MIC50/90, 0.25/0.5 mg/L) was 2-8-fold more active than ANF, MCF, and FLU against C. neoformans var. grubii. Similarly, MGX (MIC50/90, 0.06/1 mg/L) was 24-fold more active than ANF, MCF, and FLU against other yeast. Against Aspergillus, MGX (MIC50/90, 0.008/0.015 mg/L) was comparable in activity to ANF and MCF. MGX (MICvar, 0.03 mg/L) was ≥128-fold more active than ANF and MCF against Scedosporium isolates.

Conclusions: MGX demonstrated potent antifungal activity against Candida, Aspergillus, C. neoformans, and less common non-Aspergillus moulds including Scedosporium. Notable activity was seen against C. auris, echinocandin-resistant Candida, azole-resistant Aspergillus, and Scedosporium isolates. Further clinical development of fosmanogepix in difficult-to-treat resistant fungal infections is warranted.

<table>
<thead>
<tr>
<th>Organism (no. tested)</th>
<th>Manogepix (mg/L)</th>
<th>ANF</th>
<th>MCF</th>
<th>FLU</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Candida spp. (870)</strong></td>
<td>0.008/0.03</td>
<td>0.02/2</td>
<td>0.03/1</td>
<td>0.5/4</td>
</tr>
<tr>
<td>C. albicans (238)</td>
<td>0.004/0.009</td>
<td>0.016/0.03</td>
<td>0.015/0.03</td>
<td>0.12/0.25</td>
</tr>
<tr>
<td>C. glabrata (42)</td>
<td>0.004/0.004</td>
<td>0.03/0.06</td>
<td>0.03/0.03</td>
<td>0.12/0.25</td>
</tr>
<tr>
<td>C. parapsilosis (174)</td>
<td>0.008/0.015</td>
<td>0.03/0.06</td>
<td>0.04/0.12</td>
<td>0.1/0.25</td>
</tr>
<tr>
<td>C. tropicalis (127)</td>
<td>0.008/0.015</td>
<td>0.016/0.06</td>
<td>0.03/0.06</td>
<td>0.25/1</td>
</tr>
<tr>
<td>Cryptococcus neoformans var. grubii (33)</td>
<td>0.25/0.5</td>
<td>≥4/4</td>
<td>≥4/4</td>
<td>2/8</td>
</tr>
<tr>
<td>Other yeast*</td>
<td>0.06/1</td>
<td>4/4</td>
<td>2/4</td>
<td>6/32</td>
</tr>
<tr>
<td>Aspergillus spp. (248)*</td>
<td>0.008/0.015</td>
<td>0.008/0.015</td>
<td>0.008/0.015</td>
<td>-/-</td>
</tr>
<tr>
<td>Scedosporium spp. (11)*</td>
<td>0.03/0.03</td>
<td>4/4</td>
<td>0.5/4</td>
<td>-/-</td>
</tr>
</tbody>
</table>

* Aureobasidium pullulans (1), Cryptococcus gattii (2), C. laurentii (1), C. neoformans var. neoformans (3), Geotrichum candidum (3), Pichia norvegica (4), Rhodotorula minuta (1), R. mucilaginosa (2), Saccharomyces cerevisiae (1), Trichosporon asahii (1), T. inlaii (1), unspeciated Pichia (1)

† Aspergillus flavus species complex (34), A. fumigatus (168), A. lentulus (1), A. niger (21), A. niger species complex (7), A. nomius (1), A. parasiticus (1), A. tamari (1), A. terreus (8), A. terreus species complex (8), A. versicolor (2)

‡ Scedosporium apiospermum/S. boydii (8), S. aurantiacum (2), S. boydii (1)

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Abstracts 2020

Abstract 46

**Post-viral fatigue in dengue infection**
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**Background:** Dengue is the most significant mosquito borne viral infection in the world in terms of morbidity. Post-viral fatigue (PVF) is observed after a dengue infection in both adults and children, but not studied extensively in the adult population.

**Materials/methods:** A prospective study was carried out to assess the incidence of fatigue in hospitalized dengue patients after 2 months of their hospital discharge. Non-pediatric (>12 years of age) and non-pregnant patients with an acute febrile illness (≤ 3 days) admitted to National Hospital of Sri Lanka from January 2018 to April 2019 were included this study. Dengue fever was confirmed with NS1 antigen testing or RT-qPCR. PVF was measured by contacting the patients, using the fatigue questionnaire developed by Dittner et al in 2004. The score of 4 or above consider as the cut off for fatigue. Demographic characteristics and clinical data of the patients were also collected.

**Results:** A total of 104 patients were recruited to the study (mean age – 34 years, SD ± 14.9, males – 61%): 69 dengue patients and 35 non-dengue patients. Out of 69 dengue patients, 27 (26%) were diagnosed with dengue hemorrhagic fever and 15 (14%) with severe dengue. PVF was present in 16 patients (13 dengue patients and 3 without dengue). There was no difference of development of fatigue between dengue and non-dengue patients (p<0.05).

Among dengue patients, symptoms of vomiting and bleeding, decreased hemoglobin level and decreased hematocrit within the first three days of fever showed a significant association with PVF (p<0.05). But after correction for multiple comparisons by Bonferroni correction, none of the variables showed a significant association with PVF. Severity of dengue and presence and absence of plasma leakage (p<0.05) had no association with PVF. Among non-dengue patients, only increased aspartate aminotransferase level showed a significant association with PVF (p<0.05) but it was not significant when corrected for multiple comparisons.

**Conclusions:** Severely symptomatic disease in early dengue fever may be associated with PVF but none of the predictors were significantly associated with PVF in this study after corrections for multiple comparisons. Financial assistance from, University of Colombo is gratefully acknowledged.

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Abstract 48

The phylogenetic landscape and nosocomial spread of the multidrug-resistant opportunistic Stenotrophomonas maltophilia

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Background: Recent studies portend a rising global spread and adaptation of human- or healthcare-associated pathogens, thereby challenging the prevailing concepts of disease acquisition and transmission of these pathogens in the hospital setting. Global genome-based collections are missing for the emerging pathogen Stenotrophomonas maltophilia, listed by the World Health Organization as one of the leading drug-resistant nosocomial pathogens worldwide.

Materials/methods: Here, using a novel whole genome multilocus sequence typing scheme, we analyzed an international collection of 1,305 isolates of the emerging, multidrug-resistant, opportunistic pathogen Stenotrophomonas maltophilia from 22 countries to infer population structure, clonality, and transmission dynamics at a global level.

Results: We show that the S. maltophilia complex is divided into 23 monophyletic lineages, most of which harboured strains of all degrees of human virulence. Lineage Sm6 comprised the highest rate of human-associated strains, linked to key virulence and resistance genes. Transmission analysis identified a number of potential outbreak events of genetically closely related strains isolated within days or weeks in the same hospitals.

Conclusions: This first, large scale sequencing study at global scale for S. maltophilia provides evidence for the global prevalence of particular circulating lineages with hospital-linked clusters collected within short time interval suggesting transmission. This emphasizes the need to instate or re-enforce hygiene and infection control practices to minimize in hospital spread of these pathogens.
Figure: Spatiotemporal cluster analysis of 1,205 S. melliloti complex strains.  

a. The coloured ranges across the outer nicks and branches indicate the 23 lineages. The black dots indicate the location of the genome datasets used for whole genome Multilocus sequencing typing scheme generation. The rings, from inside to outside: 1) the isolation source of the strains classified as either environmental, anthropogenic, human, or unknown; 2) the detailed isolation source of strains similar to the first ring with the human strains subclassified into human-invasive, human-non-invasive, and human-respiratory; 3) the city of isolation; 4) the year of isolation (where available), with light colours representing earlier years and darker brown colours more recent isolation dates. The outer rings in black to grey indicate the single linkage-derived clusters based on the number of allelic differences between any two strains for 100 (d100 clusters) and 10 (d10 clusters) allelic mismatches. Red dots on the nodes indicate support values of 100%. 

b. Distribution of the number of wgMLST allelic differences between pairs of strains among the 1,205 S. melliloti complex strains.

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**Abstract 52**

**Clostridioides difficile infection in immunocompromised hospitalised patients is associated with a high recurrence rate**

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Abstract third-party references: Rabin medical center, Beilinson hospital

**Background:** Clostridioides difficile infection (CDI) may pose a serious threat to immunocompromised patients (IMC). Herein, we evaluated the clinical outcomes of IMC patients with CDI.

**Materials/methods:** All consecutive hospitalized patients between January 1, 2013 and December 31, 2018 with laboratory confirmed CDI, were included in the study. Subjects were divided into two groups: IMC patients and controls. Primary outcome was the recurrence rate of CDI (rCDI) at 30/90 days after the first CDI episode. Secondary outcomes included 30/90 day all-cause mortality, length of hospital stay (LOS) and readmission rates. A multivariate analysis adjusted other risk factors for recurrence. An analysis of IMC patient subgroups (based on type of IMC conditions) was also performed. Results are reported as odds ratios (OR) with a 95% confidence interval (95% CI).

**Results:** A total of 573 patients were included, amongst them 149 IMC patients (36 solid organ transplants, 38 undergoing chemotherapy, 62 haematological conditions, 13 receiving high dose prednisone) and 424 controls. IMC patients were younger, independent and exhibited less significant comorbidities. On multivariable analysis, the rate of rCDI was significantly higher in IMC patients (OR 2.7, 95% CI 1.6-5). rCDI was also associated with vancomycin therapy, haemodialysis and previous hospitalizations. Mortality, LOS, CDI complications and rehospitalization rates were similar in both.

**Conclusions:** IMC patients with CDI have an increased risk of 90 days rCDI. Vancomycin treatment for CDI endangers recurrence in IMC patients. Further research should explore other therapies for IMC patients with CDI with alternative agents such as Fidaxomicin and Bezlotoxumab.

**Table. Univariate and Multivariate Model for Risk Factors of rCDI at 90 Days**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate OR (95% CI)</th>
<th>Multivariate OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immunocompromising condition</td>
<td>2.7 (1.6-4.7)</td>
<td>2.19 (1.2-4.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>Younger age</td>
<td>0.9 (0.57-1.0)</td>
<td>1.001 (0.982-1.02)</td>
<td>0.9</td>
</tr>
<tr>
<td>Past abdominal surgery</td>
<td>1.5 (1.1-3.5)</td>
<td>1.3 (0.7-2.4)</td>
<td>0.5</td>
</tr>
<tr>
<td>Antibiotic exposure during the last 3 months</td>
<td>3.6 (1.9-6.5)</td>
<td>1.9 (0.9-3.9)</td>
<td>0.06</td>
</tr>
<tr>
<td>Previous hospitalization during 3 months</td>
<td>4.5 (2.2-9.4)</td>
<td>2.51 (1.1-5.9)</td>
<td>0.04</td>
</tr>
<tr>
<td>Vancomycin treatment for CDI</td>
<td>2.2 (1.3-3.9)</td>
<td>1.9 (1.03-3.4)</td>
<td>0.04</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>3.8 (1.4-10.1)</td>
<td>3.2 (1.1-9.4)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

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Abstract 57

Combined antibiotic stewardship and infection control measures to contain an outbreak of linezolid-resistant *Staphylococcus epidermidis* in an interdisciplinary intensive care unit

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**Background:** *Staphylococcus epidermidis* constitutes a major part of the human skin flora, but can cause healthcare-associated infections, especially in immunocompromised patients. The imprudent use of linezolid has been linked to the emergence of linezolid-resistant *S. epidermidis* (LRSE). We report an outbreak in an interdisciplinary intensive care unit (ICU) and the effects of combined antibiotic stewardship and infection control measures.

**Materials/methods:** Microbiological and infection surveillance data were reviewed to identify all LRSE between November 2018 and October 2019 detected in clinical or screening samples. Quantitative data on the use of antibiotics with Gram-positive coverage were obtained in defined daily doses (DDD) per 100 patient-days (PD). An antibiotic stewardship intervention was started in May 2019, focusing on linezolid restriction and promoting vancomycin, wherever needed. In addition, a catheter-care bundle as an infection control measure was initiated. We compared data from the pre-intervention period (November 2018 through April 2019) to the post-intervention period (June 2019 through October 2019).

**Results:** Infection control measures were implemented immediately upon outbreak recognition. In the pre-intervention period, LRSE were isolated from 16 patients, 6 of which were blood culture isolates. The average consumption of linezolid and daptomycin decreased from 7.6 DDD/100 PD and 16.5 DDD/100 PD per month in the pre-intervention period to 2.5 DDD/100 PD and 2.4 DDD/100 PD per month in the post-intervention period, respectively. Conversely, vancomycin consumption increased from 0.6 DDD/100 PD per month to 3.9 DDD/100 PD per month. In the post-intervention period, three LRSE isolates were detected in clinical or screening samples, while the total number of all *S. epidermidis* isolates from blood cultures dropped from 74 (of 840 ordered blood cultures; 8.8%) in the pre-intervention period to 27 (of 617 ordered blood cultures; 4.4%) in the post-intervention period.

**Conclusions:** Complementing infection control measures by targeted antibiotic stewardship proved to be beneficial in the efforts to contain this LRSE outbreak in an interdisciplinary ICU. Next-generation sequencing results will help to clarify the genetic relatedness of the isolates (results pending). Follow-up measures and a high level of alertness are critical in order to sustain this favorable outcome.

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Abstract 64

Tuberculosis among migrant people in Sicily: a real-life report

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Abstract third-party references: on behalf of I.T a.C.A. (Immigrant Take Care Advocacy) team, Palermo

Background: From 2014 to 2017, the number of migrants who came to Italy via the Mediterranean route has reached an unprecedented level. The majority of refugees and migrants were rescued in the Central Mediterranean and disembarked in the Sicily region. Tuberculosis represent a social disease and migration, as a social determinant of health, increases tuberculosis-related morbidity and mortality. In May 2014 the World Health Assembly passes a resolution in which calls on governments to adapt and implement the “end tuberculosis strategy”. Early diagnosis, particularly in high-risk group, such as migrants, is the first step to achieve the aim. This study aims to estimate the frequency of both tuberculosis and latent tuberculosis infection among migrant population, from 2011 to 2017, afferent to the permanence centers of different Sicilians cities.

Materials/methods: Migratory phenomenon shown different scenario and socio-political context among years. Consequently, methodology used for taking charge, diagnostic procedure and the data collection have not always been homogeneous, highlighting possible sample bias, often justified by the critical nature of the migratory phenomenon and the need to ensure early correct diagnosis and treatment. In the most cases observed, the screening was done by Mantoux or quantiferon test and was carried out 4-6 weeks after arrival and, in any case, within 2 months of landing. In all migrant with the screening test positive it was performed x-ray chest and smear examination.

Case definition: Latent tuberculosis infection case: defined by positivity of Mantoux or quantiferon test with x-ray chest and smear examination negative.

Active tuberculosis case: radiological and/or clinical and/or sputum positivity in a patient with a Mantoux/quantiferon positivity.

Results: From 2011 to 2017 we evaluate a total of 6,020 migrants, all African. 4,711 males, 1,309 females with an age range from 16 to 29 years. tuberculosis infection was diagnosed in 1,304 people (21,6%); active tuberculosis disease was diagnosed in 185 (3,1%) people, 50 of these (0,8%) were bk-positive on the smear.

Conclusions: Despite the particular vulnerability of this cohort, the frequency of a smear positive tuberculosis infection was less than 1%, data already seen in other Italian experiences.

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Impact of referral bias on prognostic assessment in infective endocarditis: insights from a population-based cohort

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Background: Most prognostic studies on infective endocarditis (IE) are derived from samples of patients managed in tertiary hospitals, mixing patients admitted directly and referred secondarily to tertiary hospitals, which may introduce referral bias. We aimed to assess this bias.

Materials/methods: We analysed data from a population-based cohort study conducted in France in 2008. A total of 497 patients with Duke-Li definite IE were included. Patients had been admitted directly to a tertiary hospital (group T), or admitted to a non-tertiary hospital and referred secondarily to a tertiary hospital (group NTT) or not (group NT). We compared patients’ characteristics, 1-month, 3-month and 1-year survival rates between groups. Using Cox models, we identified prognostic factors first in the whole sample, and then in the pooled (NTT+T) group.

Results: Compared to group T patients (N=291), group NTT patients (N=144) were more often males (81.3% vs 72.5%, p=0.046), injection drug users (9.7% vs 4.5%, p=0.033), had higher proportions of echocardiographic abnormalities (97.2% vs 91.1%, p=0.017) and of indications for valve surgery (78.5% vs 64.3%, p=0.003). Compared to group NT patients (N=62), group NTT patients were more often males (81.3% vs 67.7%, p=0.034) and presented more often with indications for valve surgery (78.5% vs 19.4%, p<0.001). One-year survival was higher in (NTT+T) patients than in NT patients (73.0% vs 56.1%, p=0.01). The same prognostic factors were identified across groups, although the magnitude of their effect (HR estimates) differed.

Conclusions: When derived from samples mixing IE patients admitted directly and secondarily referred to tertiary hospitals, validity of patients’ characteristics description and survival estimates is threatened by referral bias. Studies based on these heterogeneous samples also result in biased estimation of HRs.

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Abstract 76

**Architecture fundamentally influences opportunity costs during an outbreak in a neonatology unit: real-life data and simulation of room designs**

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**Background:** Limiting the spread of nosocomial pathogens and stopping outbreaks at an early stage are fundamentally relevant aims of infection control especially in neonates. Timely isolation of infected from exposed and non-infected babies is a cornerstone in termination of outbreaks. However, rising costs challenge hospitals without the opportunity to reimburse lost revenues. The aim of this investigation was to define the best room design during an outbreak from the cost perspective.

**Materials/methods:** An outbreak of *Serratia marcescens* in a neonatal ICU and a neonatology ward including six patients and 34 contacts was assessed. Opportunity costs based on the G-DRG system were calculated for real-life scenario (ICU: two 2-bed, one 3-bed, two 4-bed, one 5-bed room; neonatology: two 3-bed, two 4-bed, one 7-bed room) and compared to simulation A (ICU: two 1-bed, four 2-bed, two 3-bed, one 4-bed room; neonatology: two 1-bed, four 2-bed, one 3-bed, two 4-bed rooms) and simulation B (four 1-bed, others 2-bed rooms; neonatology: five 1-bed, others 2-bed rooms), respectively.

**Results:** Patients were enrolled during 05-07/2018. In the real-life setting a total of 128 (N1(ICU)=29 and N2(neonatology ward)= 99) bed-days could not be served, thereof 97 due to isolation of colonized or infected patients and 31 due to isolation of contacts. This resulted in opportunity costs of 130.379€.

In simulation A the number of contacts was reduced by 41% to 20, the number of bed-days not served due to isolation was reduced by 23% to 99, and finally the costs were reduced by 23% to 100.839€, respectively.

In simulation B the number of contact patients was reduced by 76% to 8, the number of bed-days not occupied for isolation was reduced by 42% to 74, and finally the costs were reduced by 42% to 75.375€, respectively.

**Conclusions:** Room design has a relevant impact on patients at risk for infection. Moreover, room design with rooms caring for less patients saves costs during an outbreak. These findings should be a) verified for transferability and generalizability, b) assessed for potential shortcomings and c) taken into account for planning and constructing new wards or hospitals.

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A regional survey on the level of implementation of key infection prevention and control structures in acute-care hospitals in Crete, Greece

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**Background:** Data on assessment of Infection Prevention and Control (IPC) programmes in Greek hospitals are scarce. We conducted a situational survey on the level of implementation of the WHO guidelines on core components of IPC programmes aiming to identify local strengths and gaps that can inform planning and promote the use of standardized IPC assessment tools.

**Materials/methods:** The survey took place on August 2019 including all of 7 hospitals in one health region in Greece. The WHO IPC Assessment Framework (IPCAF) was completed through discussions between an external assessor and Infection Control Committee members. ICPAF is a facility-level diagnostic tool to identify areas for improvement based on 81 IPC indicators grouped into 8 sections reflecting the WHO IPC core components. An associated scoring system (maximum score, 800), classifies the level of IPC promotion and practice as inadequate (score, 0-200), basic (201-400), intermediate (401-600), or advanced (601-800).

**Results:** Surveyed hospitals had 2,166 beds and admitted 183,129 patients in 2018 (6.6% and 7.3% of the country’s total, respectively). The overall mean IPCAF score for all hospitals was 465 out of 800 (range 340-618), corresponding to an intermediate level of IPC. Only 1 (14%) hospital achieved an advanced IPC level, whereas 3 (43%) hospitals attained an intermediate level and 3 (43%) hospitals had a basic level. More profound variability was found between the respective core components of IPC. A high mean score of 90 out of 100 (range, 85-95) was obtained in relation to built environment, materials and equipment for IPC. Basic or intermediate scores were obtained regarding the implementation of IPC programmes (mean, 72; range, 58-95), guidelines (mean, 63; range, 43-88) and surveillance activities (mean, 47; range 25-83). Particularly low scores were revealed for education and training (mean, 47; range, 25-85), multimodal strategies (mean, 39; range, 10-85), monitoring/audit and feedback (mean, 47; range, 15-68), and workload and staffing (mean, 46; range, 35-55).

**Conclusions:** Surveyed hospitals in Greece are, on average, at an intermediate level of IPC implementation. This IPCAF-based survey helped us recognise areas for improvement in IPC and motivated regional hospitals to develop long-term improvement plans.

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Abstract 97

**Vimentin may inhibit dengue virus invasion of HBMEC cells**

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**Background:** Dengue virus (DENV), belongs to the genus flavivirus, caused dengue fever prevalent in tropical and subtropical regions whose epidemic has intensified in recent years. Vimentin, one of the cytoskeletal components involved in the infection of DENV, was observed to reorder significantly during infection. However, the mechanism of infection is still poorly understood.

**Materials/methods:** A vimentin knockout human brain microvascular endothelial cells (HBMEC) cell model was first exploited to clarify the role of vimentin when DENV2 invasion the cells, and we further built a knockout SV129 suckling mouse model for DENV2 infection. Finally, the dynamic changes of vimentin in vitro and the changes of disease course in vivo were combined to demonstrate the relationship between vimentin and dengue infection.

**Results:** Phosphorylation and soluble percentage of vimentin were observed to change dynamically during DENV2 infection of HBMEC, suggesting that DENV2 infection regulates these dynamic changes. During this process, the phosphorylation reaction of vimentin has a certain consistency with the dynamic change of the percentage of soluble, and the two may be related. Compared with the control group, the DENV2 viral load detected in vimentin knockout HBMEC cells was significantly increased. Interestingly, 4-5 days after the suckling mice injected DENV2, SV129 (vim-knockout) had higher viral loads in serum and brain tissue, and this result is consistent with the cell experiments. Compared with SV129, SV129 (vim-knockout) suckling mice not only have disordered cerebral cortical nerve cells, but also disappeared in the molecular layer, outer cone layer, outer granular layer, inner cone layer, inner granular layer, and a large number of necrotic apoptosis, which confirmed that vim-knockout mice were more susceptible to DENV2 infection and caused severe brain damage based on animal models.

**Conclusions:** DENV2 infection can cause cell vimentin to rearrange, and both dynamic changes are highly correlated during the infection process. Presence of vimentin may inhibit viral infection to reduce disease or affect disease course. This helps to identify a possible host-targeted antiviral strategy to combat DENV infection, or avoids potential resistance of direct-acting antivirals.

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Abstract 101

A new nano-sized formulation of amphotericin B-loaded chitosan with remarkable improved antileishmanial effects for the treatment of *Leishmania major*

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**Background:** This study aims to improve the *leishmania major*’s pathological effects through increasing the dose of loaded amphotericin B (Amp) into nanochitosan.

**Materials/methods:** Nanochitosan was synthesized and loaded with Amp using phase separation method. To perform this, a novel solvent was designed. The therapeutic effects of the synthesized nanodrug were evaluated in vitro and in vivo environments using pathological studies.

**Results:** A nanodrug was synthesized with the high drug loading efficiency (90%) and cellular uptake (98.6%) which released Amp in a slow drug release manner. To evaluate the toxicity effects of the nanodrug, MTT assay and balb/c mice peritoneal macrophages were used. The results showed that Amp-chitosan (AK) caused a significant decrease in the toxicity effects of Amp by 100%. Also, the efficacy of the nanodrug to inhibit the promastigotes and amastigotes of the parasite (*leishmania major*) was evaluated and the results showed that the nanodrug inhibited the parasite by 85%.

To evaluate the potency of the nanodrug in vivo environment, a novel solvent was prepared which could dissolve Amp-nanochitosan10 mg/kg (AK10 mg/kg). Then, the toxicity effects of the formulation (AK10 mg/kg) were evaluated using measurement the kidney and liver related enzymes and pathological studies. The results showed that the nanodrug had no toxicity effects. Next, the potency of AK in the treatment of *leishmania major*-infected balb/c mice was evaluated. For this purpose, the lesion size was measured using a caliper and the results showed that the nanodrug was completely effective to reduce the lesion size and improve the wound healing. These results were confirmed by pathological studies. The potency of the nanodrug to inhibit the parasite burden was also evaluated using limited dilution assay (LDA) and popliteal lymph node and the results showed that AK10 mg/kg was effective to inhibit the parasite by 83% (p<0.001).

**Conclusions:** Increasing the therapeutic dose of AK to 10 mg/kg was found critical in the treatment process and caused *l. major*’s pathological effects to be successfully treated in vitro and in vivo environments.

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**Abstract 105**

**Comparison of molecular rapid diagnostic testing panels for Gram-negative bacteraemia using Desirability Of Outcome Ranking Management of Antimicrobial Therapy (DOOR-MAT)**

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**Background:** Rapid diagnostic tests (RDTs) are becoming increasingly employed to assist in the management of gram-negative bacteraemia. Given the diversity of pathogenic organisms and resistance mechanisms, clinical data regarding optimal management using RDT is lacking. Moreover the choice of optimal RDT platform remains elusive, as comparisons are limited to sensitivity and specificity in small samples. This study compared a key clinical outcome, potential antimicrobial decisions, based on results of different commonly used RDT platforms, using a novel methodology termed Desirability of Outcome Ranking Management of Antimicrobial Therapy (DOOR-MAT).

**Materials/methods:** Retrospective observational study at University of Maryland Medical Center from 08/2018 – 11/2019 of adult patients with gram-negative bacteremia comparing Verigene® Blood Culture (VBC) to BioFire® FilmArray® Blood Culture Identification (BCID) and BCID 2 research use only (RUO) panels for clinical blood cultures. Verigene was part of standard of care, BCID and BCID 2 were run on discarded frozen samples. The RDT results and local susceptibility data were applied by an Infectious Diseases-trained pharmacists to make decisions regarding potential antimicrobial selection. DOOR-MAT, a partial credit scoring system, was used to compare antimicrobial decisions as a function of final phenotypic susceptibility patterns as determined by VITEK® 2 automated susceptibility testing. DOOR-MAT scores were compared between panels using Kruskal-Wallis with p < 0.05 statistically significant.

**Results:** A total of 103 patients with positive clinical cultures for gram-negative bacteria were included. The average DOOR-MAT score for VBC was 85.8 (SD 25.7) and median score was 100 (IQR 62.5, 100). BCID resulted in an average score of 60.8 (SD 33.4) and median 50 (IQR 50, 100). BCID 2 (RUO) demonstrated an average score of 89.7 (SD 24.7) and median score 100 (IQR 100, 100). Overall, BioFire® FilmArray® BCID 2 (RUO) produced the highest scores for optimal therapy. There was a significant difference in DOOR-MAT scores (p < 0.0001) between tested panels.

**Conclusions:** The BioFire® FilmArray® BCID 2 (RUO) performed best among the three panels tested. Use of a partial credit scoring system such as the DOOR-MAT allows for comparisons between RDT systems beyond sensitivity and specificity allowing for enhanced clinical interpretation.

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Abstract 107

Risk factors for non-ventilator-associated hospital-acquired pneumonia in patients outside the intensive care unit
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Background: Hospital-acquired pneumonia in non-ventilated patients (nvHAP) belong to the most common healthcare-associated infections. As understanding of risk factors for nvHAP is key for targeting prevention measures to patients at highest risk, this study aimed to investigate risk factors for nvHAP in patients outside the intensive care unit (ICU).

Materials/methods: We included patients ≥18 years of age who were discharged during the years 2017 and 2018 from the University Hospital Zurich, Switzerland. A total of 29 potential risk factors - both constant and time-varying - were extracted from electronic medical records, including demographic data, signs and symptoms (many assessed by daily nursing assessments), procedures, medication, and devices. Hazard ratios for nvHAP were derived from univariable and multivariable Cox proportional hazards models. Patient days on ICUs were excluded from analyses.

Results: We included 69'559 patients of whom 396 (0.57%) had nvHAP. Median age was 57 years (Interquartile range [IQR]: 39-72) and 34'558 (49.7%) patients were male. Independent risk factors for nvHAP were: age ≥60 years (hazard ratio [HR]: 1.54, 95% confidence interval [CI]: 1.22-1.96), male sex (HR: 1.66, CI: 1.34-2.07), affiliation to high risk clinic (HR: 1.35, CI: 1.07-1.71), impaired activity and mobility (HR: 2.38, CI: 1.72-3.31), acute problems with breathing (HR: 1.60, CI: 1.21-2.13), being “at risk for delirium” (HR: 1.55, CI: 1.08-2.23), impaired consciousness (HR: 1.69, CI: 1.16-2.47), drugs for acid related disorders (HR: 1.37, CI: 1.05-1.78), antineoplastic agents (HR: 1.71, CI: 1.18-2.47), antibiotics (HR: 1.41, CI: 1.10-1.81), antimycotics (HR: 2.00, CI: 1.42-2.81), opioids (HR: 1.37, CI: 1.05-1.78), swallowing difficulty without tube feeding (HR: 1.89, CI: 1.32-2.71), and tube feeding (HR: 2.06, CI: 1.49-2.86).

Conclusions: We identified several modifiable and non-modifiable risk factors for nvHAP. The modifiable risk factors like impaired activity and mobility, might be conditions potentially targetable by specific prevention measures. Non-modifiable risk factors like male gender, older age or swallowing difficulties will allow to identify high-risk patients and focus nvHAP prevention efforts on these patients.
Figure 1 – Forest plot of hazard ratios for potential risk factors for nvHAP

### Risk factors

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>HR [95%CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &gt;= 25</td>
<td>0.96 (0.70, 1.35)</td>
</tr>
<tr>
<td>Age &gt;= 60</td>
<td>2.03 (1.64, 2.50)</td>
</tr>
<tr>
<td>Sex (Male)</td>
<td>1.56 (1.07, 2.28)</td>
</tr>
<tr>
<td>Abdominal or thoracic injuries or surgeries</td>
<td>0.98 (0.95, 1.18)</td>
</tr>
<tr>
<td>Severely impaired activity and mobility</td>
<td>1.04 (0.87, 1.26)</td>
</tr>
<tr>
<td>Acute problems with breathing</td>
<td>1.19 (0.94, 1.51)</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>1.51 (1.20, 1.93)</td>
</tr>
<tr>
<td>Impaired orientation</td>
<td>1.40 (1.02, 1.86)</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>1.33 (1.00, 1.78)</td>
</tr>
<tr>
<td>Anxiolytics and Hypnotics/Sedatives</td>
<td>1.26 (1.04, 1.54)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1.25 (0.97, 1.60)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1.87 (1.46, 2.39)</td>
</tr>
<tr>
<td>Gastroscopy or ERCP</td>
<td>1.19 (0.94, 1.51)</td>
</tr>
<tr>
<td>Patient at risk for delirium (DOS &gt;2)</td>
<td>2.14 (1.56, 2.93)</td>
</tr>
<tr>
<td>Impaired consciousness</td>
<td>2.03 (1.48, 2.78)</td>
</tr>
<tr>
<td>Status post intubation or tracheotomy</td>
<td>0.76 (0.54, 1.08)</td>
</tr>
<tr>
<td>Analgesia</td>
<td>0.30 (0.10, 0.90)</td>
</tr>
<tr>
<td>General anesthesia</td>
<td>1.04 (0.80, 1.33)</td>
</tr>
<tr>
<td>Drugs for Acid related disorders (ATC A02)</td>
<td>2.47 (1.58, 3.86)</td>
</tr>
<tr>
<td>Antineoplastic agents (ATC L01)</td>
<td>1.54 (1.12, 2.13)</td>
</tr>
<tr>
<td>Immunomupreproterostats (ATC L04)</td>
<td>1.29 (0.91, 1.82)</td>
</tr>
<tr>
<td>Antibiotics (ATC J01)</td>
<td>0.59 (0.26, 1.37)</td>
</tr>
<tr>
<td>Antimycotics (ATC J02)</td>
<td>2.94 (2.15, 4.03)</td>
</tr>
<tr>
<td>High risk clinics *</td>
<td>1.73 (1.41, 2.13)</td>
</tr>
<tr>
<td>Swallowing difficulty but no tube feeding</td>
<td>3.77 (2.67, 5.32)</td>
</tr>
<tr>
<td>Tube feeding</td>
<td>4.36 (3.38, 5.63)</td>
</tr>
<tr>
<td>Non-Opioid analgetics but no moderate/severe pain and no opioids</td>
<td>1.38 (0.93, 2.05)</td>
</tr>
<tr>
<td>Moderate/severe pain but no opioids</td>
<td>1.72 (1.13, 2.64)</td>
</tr>
<tr>
<td>Opioids</td>
<td>2.76 (1.93, 3.96)</td>
</tr>
</tbody>
</table>

**Abbreviations**: ATC, anatomical therapeutic chemical classification; BMI, body mass index; CI, confidence interval; DOS, delirium observation scale; ERCP, endoscopic retrograde cholangiopancreatography; HR, hazard ratio; ICU, intensive care unit; nvHAP

* High risk clinics: Internal medicine and all subspecialties, clinics performing major surgical procedures on chest, abdomen, or extremities.

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Abstract 118

Olorofim for a case of severe disseminated Lomentospora prolificans infection
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Abstract third-party references: F2G, Ltd.

Background: Though rare, invasive Lomentospora prolificans infection causes significant morbidity and mortality particularly in immunocompromised patients. Mortality rate is least 65%, and near 100% if infection becomes disseminated. We describe a case of disseminated Lomentospora prolificans infection in an immunosuppressed patient who failed to respond to conventional therapy, and was commenced on Olorofim under clinical trial [NCT03583164].

Case report: A 56-year-old lady developed disseminated Lomentospora prolificans infection following HyperCVAD cycle-1b for T-cell acute lymphoblastic leukemia (T-ALL), including fungaemia, endophthalmitis, lumbar spine (L4/5 vertebrae) and presumed pulmonary involvement [avid pulmonary nodule on Positron Emission Tomography (PET)]. Voriconazole and terbinafine were immediately started. She was unable to achieve therapeutic voriconazole levels despite measures to augment levels, and had worsening PET uptake in the lumbar spine. Lomentospora prolificans was again isolated from lumbar vertebral biopsy after 3 months of combination regime. Failure of medical therapy prompted surgical debulking and spine stabilisation surgery. Patient then developed new PET uptake at aortic root and aortic valve five months after spinal surgery. Serial echocardiography showed progressive moderate to severe aortic regurgitation. Eleven months into management of the infection, Olorofim was started at loading dose 180mg followed by 60mg twice daily (BD), and later increased to 90mg BD as guided by drug levels. Serial PET scan over six months demonstrated improvement in uptake at aortic root and lumbar spine, despite needing radiotherapy and Pralatrexate to control relapsed T-ALL (Figure 1). As of November 2019 patient has been on Olorofim for a year without adverse effects. Regular therapeutic drug monitoring confirmed stable drug levels. She is well, active and has gained weight since on Olorofim. Her vision is stable and reports of no further back pain.

Conclusions: Lomentospora prolificans is routinely intrinsically resistant to all antifungals, hence poses a therapeutic challenge. An open-label single-arm phase Ib study of F901318 is currently underway. Olorofim monotherapy has successfully controlled a case of osteomyelitis due to this pathogen, demonstrating its potential use in treatment of resistant invasive mould infections in patients lacking suitable alternative treatment options.

Figure 1. Serial PET showing improvement in metabolic uptake at aortic root and lumbar spine.

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Abstract 119

Dynamic in vitro pharmacodynamics evaluation of piperacillin/tazobactam-tobramycin combination therapy against Escherichia coli and Klebsiella pneumoniae clinical isolates

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Background: Piperacillin/tazobactam monotherapy has been associated with increased mortality for treating patients with ceftriaxone-resistant Escherichia coli or Klebsiella pneumoniae bloodstream infection; however this leads to a reliance on carbapenem therapy. Consequently, rationally optimized antibiotic combination therapy could be a promising carbapenem-sparing approach to maximize bacterial killing and suppress the emergence of resistance. A piperacillin/tazobactam-tobramycin combination was tested against less-susceptible extended-spectrum beta-lactamase (ESBL) producing E. coli and K. pneumoniae clinical isolates using the dynamic hollow-fiber infection model (HFIM).

Materials/methods: Piperacillin/tazobactam and tobramycin pharmacokinetics observed in critically-ill patients were simulated in the HFIM over 168h (initial inoculum ~10^7 CFU/ml). We evaluated piperacillin/tazobactam (4/0.5g every 6h, given as 0.5h and 3h infusions, and 16/2g continuous infusion) alone and in combination with tobramycin (7mg/kg daily) regimens against CTX-M-55 producing E. coli 50 (EC50) and SHV-106 producing K. pneumoniae 68 (KP68) clinical isolates (MIC 8mg/L).

The total and less-susceptible bacterial populations were quantified using cation-adjusted Mueller-Hinton agar with and without antibiotic at a concentration fourfold the baseline MIC respectively.

Results: For all dosing regimens of piperacillin/tazobactam monotherapy against EC50 and KP68, there was an initial 4 log_{10} bacterial kill over 8h [Figure 1]. However, regrowth of a less-susceptible subpopulation exceeded the initial inoculum within 24h for all dosing regimens tested. The MIC of resistant subpopulations exceeded 256mg/L after 72h. Tobramycin monotherapies, displayed rapid initial killing (≥6 log_{10} at 8h) followed by extensive regrowth within 24h. A combination of piperacillin/tazobactam and tobramycin against EC50 and KP68 achieved synergistic killing (≥6 log_{10} at 8h) and prevented regrowth throughout the 7-day HFIM course.

Conclusions: This study shows that piperacillin/tazobactam monotherapy (C_{min}/MIC >5) was insufficient to achieve sustained bacterial killing and suppress resistant subpopulation against EC50 and KP68. Piperacillin/tazobactam-tobramycin combination therapy provided rapid bacterial killing and suppressed the emergence of resistance over 7-days. These results support the re-evaluation of the potential clinical utility of combination therapy against less-susceptible ESBL producing isolates as a carbapenem-sparing approach.
Figure 1: Effect of each dosing regimen on the total bacterial population using simulated human exposures of piperacillin and tobramycin against ESB-producing EC50 and KP68 (q6h, every 6 h; q24h, every 24 h)

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Microscopic agglutination test in determining leptospirosis seroprevalence in Western Province, Sri Lanka

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Background: Leptospirosis is a globally distributed zoonosis common in tropical regions, including Sri Lanka. Microscopic agglutination test (MAT) is considered to be the gold standard in leptospirosis diagnosis, which uses panels of live leptospires representing the circulating serovars from the area. MAT provides epidemiological data on infecting serovars. In this study, we analyzed MAT results of confirmed cases of leptospirosis in Western province, Sri Lanka to determine commonly infecting serovars.

Materials/methods: This was a prospective hospital based study carried out during 2017 in 2 selected hospitals in Western province of Sri Lanka. Clinically suspected leptospirosis patients were recruited according to Communicable Disease Epidemiology Profile Sri Lanka, WHO. Leptospirosis was confirmed by either single MAT titre ≥1:320 or by positive polymerase chain reaction (PCR). MAT was carried out at the Medical Research Institute, Sri Lanka which is the national reference laboratory for leptospirosis and consists of a panel of 15 Leptospira serovars.

Results: Out of 172 clinically suspected patients, 42.44% were confirmed leptospirosis patients by either MAT (50.68%) or PCR (67.12%). Of the 37 MAT positive patients, 29 (78.37%) were positive for L. interrogans serovar bakeri, strain L79 in Tarassovi. Two patients were positive for L. interrogans serovar poi, Strain Poi in Javanica, while one patient each was positive for L. interrogans serovar cynopteri, strain 3522C in Cynopteri and L. interrogans serovar bangkinang, strain Bangkinang 1 in autumnalis respectively. Four patient sera was found to be positive for two serovars (L. interrogans serovar bakeri, strain L79 in Tarassovi with one of the following serovars: serovar rathnapura, strain wimalasena in Grippotyphosa, serovar bangkinang, strain Bankinang 1 in autumnalis, serovar pyrogenes, strain Salinem in pyrogenes and serovar australis, strain Ballico in Autumnalis) each having similar MAT titres, while 9 were positive for two serovars with a MAT titre ≥1:320 including serovars namely serovar australis, serovar bataviae, serovar bakeri, serovar icterohaemorrhagiae, serovar canicola, serovar bangkinang, serovar hebdomadis, serovar poi and serovar pyrogenes.

Conclusions: L. interrogans serovar bakeri, strain L79 in Tarassovi was the predominant serovar identified in this study among patients of leptospirosis in the Western province, Sri Lanka.

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Sexually-transmitted infections in soldiers: a cross-sectional assessment and a review of literature

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Background: Sexually transmitted infections (STI) show a wide prevalence range in military forces, ranging up-to more than 40 per cent in cross-sectional studies. Scarce information is available on STI in soldiers from Europe. Therefore, we have performed a retrospective assessment on prevalence and determinants of occurrence of STI in German paratroopers and navy soldiers by anonymously analyzing medical records from the medical departments of two German barracks.

Materials/methods: Medical records from 80 paratroopers and 80 navy soldiers were screened for records of STI as well as documented medical history associated with the likely mode of transmission next to information on risk factors as well as diagnostic and therapeutic management.

Results: Proportions of suspected STI were 17.5% and 20%, proportions of diagnosed STI 13.9% and 11.3% for predominantly male paratroopers and navy soldiers, respectively. On average, acquisition of STI occurred in the second half of the third decade of the patients’ life. The proportion of infected officers was higher in the population of the navy soldiers, while more infected privates were among the paratroopers. Living as singles or unmarried but with a primary partnership was the most frequently observed lifestyle. Only one case of STI acquisition on deployment was documented for the navy soldiers and no such incident for the paratroopers, although nearly half of the assessed patients in both groups had deployment experience. In a relevant minority of about 20%, partner therapy was neglected and especially for the navy soldiers, considerable delay between onset of clinical symptoms and medical assessments was registered. While pharmacological therapy was always performed and adherence with national guidelines was acceptable with more than 80%, adherence with diagnostic therapy control was poor with proportions round about 50%, while clinically apparent recurrences were occasionally observed.

Conclusions: Although clinical hints for STI were frequently observed, clinical management was usually restricted to syndrome-based antibiotic treatment without detailed diagnostic workup. Altogether, occurrence of STI was comparable with reports from other armed forces, stressing an ongoing need for preventive medical approaches.

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Assessment of trimethoprim-sulfamethoxazole susceptibility testing methods for fastidious Haemophilus spp.

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Background: Several discrepancies were found in clinical routine regarding trimethoprim-sulfamethoxazole (SXT) susceptibility determination depending on antimicrobial susceptibility (AST) method used and growth media. We aimed to compare the determinants of SXT resistance with established susceptibility values for fastidious Haemophilus spp., in order to provide recommendations for optimal SXT measurement.

Materials/methods: We collected 50 strains each of Haemophilus influenzae and Haemophilus parainfluenzae at Bellvitge University Hospital. SXT susceptibility was tested by microdilution, E-test, and disc diffusion using both Mueller-Hinton Fastidious (MH-F) and Haemophilus Test Medium (HTM) following EUCAST and CLSI criteria respectively. Mutations in folA, folP and additional determinants of resistance were identified in whole-genome sequenced isolates.

Results: Strains presented generally higher rates of SXT resistance when grown on HTM than on MH-F, independent of the methodology used [average MIC 2.6-fold higher in H. influenzae and 1.2-fold higher in H. parainfluenzae]. The main resistance-related mechanisms were as follows: I95L and F154S/V in FolA; 3 and 15 base pair insertions and substitutions in folP; acquisition of sul genes; and FolA overproduction potentially linked to mutations in -35 and -10 promoter motifs. Of note, 2 of 19 H. influenzae strains (10.5%) and 9 of 33 H. parainfluenzae strains (27.3%) with mutations and assigned as resistant by microdilution were inaccurately considered susceptible by disc diffusion. This misinterpretation was resolved by raising the clinical resistance breakpoint of the EUCAST guidelines to ≤30 mm.

Conclusions: Given the routine use of disc diffusion, a significant number of strains could potentially be miscategorised as susceptible to SXT despite having resistance-related mechanisms. A simple modification to the current clinical resistance breakpoint given by the EUCAST guideline for MH-F ensures correct interpretation and correlation with the gold-standard method of microdilution.

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Abstract 151

**A meta-analysis of the burden of non-typhoidal Salmonella in humans in the Middle East and North Africa**

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**Background:** To enhance efforts related to controlling foodborne pathogens in the Middle East and North Africa (MENA), we quantified the overall regional and country-specific NTS prevalence in different human populations and identified the most common serotypes.

**Materials/methods:** Published literature of NTS prevalence was systematically reviewed and reported following PRISMA guidelines. Pooled NTS prevalence measures were estimated using a random-effects model.

**Results:** We identified 46 research reports that reported 84 NTS prevalence measures in 15 countries in MENA. The pooled NTS prevalence in MENA was estimated at 6.6% (95% confidence interval (CI): 5.4–7.9%). The highest pooled prevalence measures were in Morocco (17.9%, 95% CI: 5.7–34.8%), Tunisia (10.2%, 95% CI: 4.3–18.0%), and Sudan (9.2%, 95% CI: 6.5–12.2%) while the lowest were in Jordan (1.1%, 95% CI: 0.1–3.0%), Oman (1.2%, 95% CI: 1.2–1.3%), and Palestine (1.2%, 95% CI: 0.4–2.1%). NTS pooled prevalence in gastrointestinal asymptomatic and food handlers population groups was 11.4%, and 3.8%, respectively. *S. Enteritidis* (29.8%) and *Typhimurium* (23.6%) were the most common.

**Conclusions:** NYT is a common foodborne pathogen in MENA countries, particularly in North African countries. Findings inform the scientific community, the public, and the decision makers with NTS prevalence and gaps in evidence in MENA to support control and prevention strategies.

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Abstract 152

Whole genome sequencing of *Pseudomonas aeruginosa* isolates from across the United Kingdom: population structure and molecular predictors of resistance

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**Background:** *Pseudomonas aeruginosa* (PSA) infections are difficult to treat due to virulence and antibiotic resistance. We present a large whole genome sequencing (WGS) study of PSA from non-cystic fibrosis (CF) patients to examine the epidemiology, virulence and resistance to anti-pseudomonal antibiotics, including ceftolozane/tazobactam (C/T).

**Materials/methods:** 1,123 consecutive, clinically relevant, non-CF PSA isolates from 14 participating centres from Jan/15-Apr/2018 were studied. In vitro activity of C/T and nine other antibiotics were evaluated using EUCAST disc diffusion testing, a subset of 159 isolates (C/T diameter ≤26mm) tested by broth microdilution (BMD) with 7 antibiotics. Data were collected on the infection site, specimen and ward type.

304 isolates were chosen for WGS on Illumina HiSeq platform. Isolates were chosen based on C/T BMD (MIC ≥4 µg/mL) plus control isolates based on site and resistance pattern (1:8 ratio). Assembled sequences were annotated then the contigs screened using abricate: on CARD for resistance, VFDB for virulence factors. Reference alignment was performed to identify known resistance mutations. In addition, Multi-Locus Sequence Types (MLST) were generated from assemblies.

**Results:** 26/1,123 (2.3%) isolates were resistant to C/T and 10 had an MIC ≥ 4 µg/mL. MLST were identified in 281/304 (92%) isolates with 106 distinct MLSTs. 14 MLST comprised 50% of isolates. Dendrogram and analysis of virulence genes showed two PSA populations, one containing the exoS type III secretion systems, and the other exoU.

BMD of 159 isolates found sensitivity to colistin (93%), C/T (84%), ceftazidime (66%), piperacillin/tazobactam (61%) and imipenem (71%). Beta-lactamase sequences were found in 10/26 (38%) C/T resistant isolates, however no resistance mechanism was found for 16/26 (62%). Similarly, beta-lactamases were found in 10/46 (22%) of carbapenem resistant isolates. Carbapenemases detected were IMP, VIM, NDM, but also unusual carbapenemases including OXA-119, OXA386 DIM1 and L1 (only reported in Stenotrophomonas).

**Conclusions:** Clinically significant PSA in non-CF patients has a diverse population across the UK with a division into 2 groups based on type III secretion systems. The majority of resistance in PSA to beta-lactams is not due to carbapenemases. Several unusual or unique carbapenemases to PSA were identified. C/T was the most effective beta-lactam against PSA.

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Abstract 154


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Abstract third-party references: This work was supported by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, New Jersey, USA (MSD)

Background: Imipenem/cilastatin and relebactam (IMI/REL)—a fixed-dose combination of imipenem, a carbapenem antibacterial agent, cilastatin, a renal dehydropeptidase, and relebactam, a β-lactamase inhibitor—was compared with piperacillin/tazobactam for the treatment of patients with HABP/VABP in a phase 3 clinical trial. We developed population pharmacokinetic models, integrating data from this trial with prior phase 1–3 data, to evaluate the effects of covariates on imipenem and relebactam exposure and analyze the probability of target attainment (PTA) among patients with HABP/VABP.

Materials/methods: A previous population pharmacokinetic model was updated with data from the phase 3 trial (NCT02493764) to include patients who were exposed to a ≥1.25-g IMI/REL dose (500 mg imipenem, 500 mg cilastatin, and 250 mg relebactam) and had ≥1 measurable postdose concentration. The updated population pharmacokinetic model, comprising data from 1 197 participants among 12 completed phase 1–3 trials, was used to assess the effect of clinical covariates on imipenem and relebactam pharmacokinetic parameters. Joint PTA analyses were performed to assess achievement of pharmacokinetic/pharmacodynamic targets.

Results: A 2-compartmental model with first-order elimination best described both the imipenem and relebactam plasma concentration–time profiles. Significant covariates for both imipenem and relebactam included body weight on clearance (CL) and central volume of distribution (V1), creatinine clearance (CrCL) on CL and V1, and ventilation status on V1 (but not on CL). Among patients with normal renal function (90 mL/min ≤ CrCL < 150 mL/min), area under the concentration–time curve (AUC) and maximum plasma concentration (Cmax) were higher in patients with HABP/VABP compared with healthy participants, while AUC, Cmax, and CL were comparable across ventilated and nonventilated patients with pneumonia (Table). Among patients with HABP/VABP, joint PTA was >98% regardless of renal clearance or ventilation status.

Conclusions: Inclusion of data from patients with HABP/VABP into the imipenem and relebactam population pharmacokinetic models demonstrated that pharmacokinetic exposures are higher in patients with HABP/VABP compared with healthy participants. The joint PTA was sufficient to justify the 1.25-g IMI/REL dose administered every 6 hours in this patient population. No dose adjustments are required for patients with HABP/VABP based on ventilation status.

Table. Summary of steady-state pharmacokinetic exposures in healthy participants and patients with pneumonia with normal renal function (90 mL/min ≤ CrCL < 150 mL/min)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Population</th>
<th>Pharmacokinetic Parameters*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AUC0–24h (µM h)</td>
<td>Cmax (µM)</td>
</tr>
<tr>
<td>Imipenem</td>
<td>Healthy participants</td>
<td>483.3 (60.4)</td>
</tr>
<tr>
<td></td>
<td>Patients with pneumonia</td>
<td>812.2 (59.4)</td>
</tr>
<tr>
<td></td>
<td>Ventilated patients with pneumonia</td>
<td>808.0 (58.8)</td>
</tr>
<tr>
<td></td>
<td>Nonventilated patients with pneumonia</td>
<td>816.3 (59.9)</td>
</tr>
<tr>
<td>Relebactam</td>
<td>Healthy participants</td>
<td>348.4 (49.6)</td>
</tr>
<tr>
<td></td>
<td>Patients with pneumonia</td>
<td>655.2 (47.9)</td>
</tr>
<tr>
<td></td>
<td>Ventilated patients with pneumonia</td>
<td>663.4 (47.0)</td>
</tr>
<tr>
<td></td>
<td>Nonventilated patients with pneumonia</td>
<td>647.2 (48.8)</td>
</tr>
</tbody>
</table>

AUC0–24h, area under the concentration–time curve from 0 to 24 hours; CL, clearance; Cmax, maximum plasma concentration; CrCL, creatinine clearance.

*Shown as geometric mean parameter estimates with percent geometric coefficient of variation values in parentheses.

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Abstract 159

**Plasma levels of hepcidin, a potential biomarker during septic shock**
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**Background:** Septic shock is a severe infectious condition with high mortality despite intensive care treatment. In conditions of acute systemic inflammation e.g. sepsis, iron metabolism, in which hepcidin plays a key role, is disturbed. The objective for this observational prospective study was to explore whether hepcidin has a potential as a biomarker for septic shock complementary to conventional biomarkers, i.e. procalcitonin (PCT), C-reactive protein (CRP) and white blood count (WBC).

**Materials/methods:** Patients with septic shock (n=81) or non-infectious conditions (n=44) who fulfilled the pre-set clinical and ethical inclusion criteria were included within an hour of admittance to the Intensive Care Unit (ICU) at Helsingborg hospital, Sweden. Patients were included at random, blood samples taken every day for 7 consecutive days. Adequate microbiological tests and cultures were obtained before or at inclusion. Sequential Organ Failure Assessment (SOFA)-score as well as plasma levels of hepcidin, WBC, CRP, PCT, and lactate, were determined directly after inclusion and then every morning for seven consecutive days. Alterations of hepcidin and conventional biomarkers in the group with septic shock are presented descriptively.

**Results:** Hepcidin was significantly elevated in patients with septic shock (median 41 nmol/L; reference interval 1-12 nmol/L, p-value<0.001), compared to non-septic patients (median 14.5 nmol/L, p-value<0.001). Maximal plasma levels of hepcidin were seen on Day 1 in the group with septic shock, whereafter levels declined steadily with a time course similar to lactate. PCT, CRP, lactate, and WBC demonstrated a dynamic pattern as expected from previously published results, whereas WBC and lactate were not significantly elevated. The linear graph presented shows the dynamics of the biomarkers in the group with septic shock (n=81). The median inclusion value of each biomarker was indexed to 100% and the daily change from the arrival value was calculated.

**Conclusions:** Hepcidin was shown to be a rapidly changing biomarker in septic shock, the initial high values were significantly higher in patients with septic shock compared to non-septic patients. Hepcidin decreased rapidly within the first 48 hours upon recovery of the patients, superior to PCT, CRP, lactate and WBC.
Abstract 174

Primary care re-consultation after hospitalisation for community-acquired pneumonia in England: a large population-based cohort study

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Abstract third-party references: This study was supported by the National Institute for Health Research (NIHR) Nottingham Biomedical Research Centre (BRC).

Background: There is paucity of information on the burden of disease during recovery from community acquired pneumonia (CAP). This study aims to describe primary care re-consultations within 30 days after hospitalisation for CAP.

Materials/methods: Adults aged ≥18 with the first ICD-10 code for CAP (J12- J18) recorded in Hospital Episode Statistics (HES) between July 2002 and June 2017 were included. Patients were followed-up for 30 days from hospital discharge. Re-consultation was defined as recording of any medical Read codes (excluding admin-related codes) in a primary care database of anonymised medical records from general practitioners (Clinical Practice Research Datalink) after the discharge date. Re-consultation was counted as a single episode if there were multiple Read codes recorded in a day per patient.

Results: There were 93,687 patients with CAP. Excluding patients who died (n=5,456; 5.8%) or were readmitted within 30 days of hospital discharge (n=13,729; 15.1%), 38.7% (n=29,037) re-consulted primary care at 30 days for any reason. The highest rate of re-consultation was within 7 days (26 per 100 person-days).

Multivariate analysis found the strongest predictor for re-consultation was higher number of primary care consultations in the previous 2 years. Patients were less likely to re-consult if they were females, aged ≥65 years, from more deprived areas (Carstairs index=3) and if they had a Charlson comorbidity index score of between one and four.

Of those who re-consulted, 43.2% (n=12,546) re-consulted primary care twice or more. A large proportion of patients re-consulted for a respiratory disorder (37.5%, n=10,880) whilst a lower proportion re-consulted for a cardiac disorder (7.1%, n=2066). At re-consultation, 30.8% (n=8,951) received a further course of antibiotics; most (76.9%, n=6,884) received a single course of antibiotic. Penicillins (41.9%, n=5290) and macrolides (21.9%, n=2762) were the commonest antibiotics prescribed.

Conclusions: A high burden of re-consultation is placed on primary care following hospital admission for CAP. Approximately 40% re-consult primary care more than once following CAP. Of those who re-consult, 30% are prescribed a further course of antibiotics.

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Abstract 179

**A rapid direct from specimen MALDI-TOF MS diagnostic for bacterial and fungal pathogens**

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**Background:** Pathogen identification from single colonies by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) analysis of high abundance proteins is now well established in large hospitals in the EU and US. We present updates to BACLIB, a MALDI-TOF MS method previously shown to utilize mass spectra of readily extracted bacterial lipids as chemical barcodes for identification and speciation (Leung et al. Sci Repo 2017). Unlike protein-based methods, direct from specimen identification is possible and we now show that the same extraction protocol allows fungi to be identified.

**Materials/methods:** Microbial lipids were extracted directly on a MALDI plate. Mass spectra were acquired in negative ion mode on a Bruker Microflex using the matrix norharmane. A mass spectral library was developed with over 2000 primary clinical and laboratory isolates, including Gram-negative and -positive bacteria, acid-fast bacteria including Mycobacterium tuberculosis, filamentous fungi, and over 15 Candida species. For unknown identification, mass spectra were submitted to a secure web service machine-learning software platform called Postal Service [unpublished] that reported speciation and resistance profiles by comparison to the library.

**Results:** Time required for a single analysis (from colony selection to identification) by BACLIB is approximately 60 minutes. Postal Service independently identified over 150 bacterial and fungal species (and where appropriate subspecies) with confidence scores similar to protein-based results reported for the Bruker Biotyper and bioMérieux VITEK MS platforms. BACLIB was also able to identify pathogens directly from blood bottles, but also urine, BALs and wound effluent, without culture on solid medium and determine antimicrobial peptide resistance (i.e. colistin) as well as identification from polymicrobial mixtures (Fondrie et al. Sci Repo 2018).

**Conclusions:** Previously, BACLIB has been shown to be a novel diagnostic approach for identifying Gram-negative and -positive bacteria from single colonies and mixtures, but here we report its use for identification of budding yeast and filamentous fungi. BACLIB can stand alone or strengthen the overall diagnostic power of microbial speciation using current protein-based diagnostics in clinical microbiology laboratories. Postal Service allows BACLIB to work via an internet-based approach that is capable of independently reporting speciation and where appropriate, antimicrobial peptide resistance patterns.

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**Abstract 193**

### Antimicrobial susceptibility of *Streptococcus pneumoniae* strains, isolated from children carriers after PCV10 in Bulgaria

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**Background:** Bulgaria introduced PCV10 in 2010 in the National Immunization Calendar. Prior the vaccine invasive *S. pneumoniae* isolates were analyzed and the dominant resistant serotypes were 19F, 6B, and 19A. In the current study we aim to detect the serotype distribution and patterns of resistance in vaccinated healthy children.

**Materials/methods:** Vaccinated healthy children n=834, aged 1 to 6 years were sampled in the period 2017-2019 by a nasopharyngeal swab. Specimens were cultured on Columbia CNA Agar with 5% Sheep Blood and optochin disk, 37°C for 24 hours, in an aerobic atmosphere enriched with CO2. Identification of *S. pneumoniae* was done by the presence of alpha-hemolysis and inhibition by optochin. Typing of cultures was made by DNA based methods - conventional PCR and the Operon S.PneumoStrip kit. Antibiotic susceptibility testing was done with the disc-diffusion method for oxacillin (MIC Benzylpenicillin and Ampicillin), tetracycline, erythromycin, clindamycin, vancomycin, teicoplanin, linezolid, norfloxacin, trimethoprim-sulfamethoxazole (TMP-SMX). Interpreted by the EUCAST Clinical Breakpoint Tables v. 9.0.

**Results:** The total number of isolated strains was 174 (21% culture positive samples). Each sample was typed and predominantly there were the non-vaccine serotypes – 6C (27%), 24 B/F (12.5%), 3 (11%), 11A/D (10%) and 23A (7.5%) from all cultures respectively. The antimicrobial susceptibility of *S. pneumoniae* cultures to different agents during the study period was: 100% to vancomycin, teicoplanin and linezolid, 96.5% to norfloxacin, 93% to sulfamethoxazole / trimethoprim, 85.6% to oxacillin (at screening), 58% to tetracycline, 50% to clindamycin and 48.9% to erythromycin. Multidrug resistant (MDR) strains that were not sensitive to at least three antimicrobial classes were 44% of the isolated strains. Erythromycin-resistant pneumococci in the study were 51.2% of all cultures, most of them co-resistant to clindamycin.

**Conclusions:** The high macrolide resistance detected in carriage corresponds to the data from invasive *S. pneumoniae* isolates in the ECDC report and can serve as a tool for measuring resistance patterns in the country. There were less serotypes expressing β-lactam non susceptibility in low levels mainly serotypes 19A, 24 B/F, 35B that are non-vaccine clones.

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Abstracts 2020

Abstract 195

Implementation and one-year results of antimicrobial stewardship programme in a tertiary reference hospital in San Jose, Costa Rica

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Background: Antimicrobial Stewardship Programs (ASP) are relatively new in Latin America when compared to other regions, in most cases as individual projects, in response to rising rates of resistance and adverse effects associated with inappropriate antimicrobial utilization, and not in answer to official national policies. This study evaluated the impact of a multidisciplinary, rounding-based APS strategy on antimicrobial utilization (AU), prescribing practices and health-care associated infection (HAI) rates.

Materials/methods: This is a one-year review of implementation of ASP in early 2018 in a tertiary-reference hospital in San Jose, Costa Rica. Multidisciplinary ASP committee was established with representation from infectious diseases, clinical pharmacy, infection control, nursing, microbiology and epidemiology. The hospital implemented targeted stewardship efforts in Orthopaedics and Traumatology, with initial focus on advanced education, daily audit and feedback for targeted antibiotics. We created a checklist of CDC Core Elements for committee review. The primary objective of this initiative was to evaluate changes in AU and to determine HAI rates within the program over time. Subgroup analysis evaluated annual antimicrobial cost. Descriptive statistics were performed on all continuous and categorical data as appropriate.

Results: Baseline overall AU analysis was based on 2017 and the intervention period included 2018. Baseline overall AU in 2017 was 425 DDD/100PD. We observed a decline in overall AU in 2018 (257 DDD/100PD). Targeted analysis revealed decline from 2017 to 2018 in carbapenems (32 vs 15 DDD/100PD), colistin (9 vs 3 DDD/100PD) and cefotaxime (26 vs 15 DDD/100PD), as well in ampicillin and cephalotin (66 vs 9 DDD/100PD, and 25 vs 8 DDD/100PD, respectively). Overall decline was also noted in rates of HAI and Clostridium difficile infections (CDI). Decline in overall antimicrobial cost was noted from 2017-2018 ($166,340.6 vs $128,418.3).

Conclusions: We present implementation of an effective health system wide multidisciplinary ASP. With ASP efforts over one year, we were able to show decline and positive correlation in overall as well as targeted AU and HAI rates. We also noticed a decline in antimicrobial cost in this timeframe.

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Abstract 203

Diffusion of KPC-carbapenemases among urinary tract isolates of Klebsiella pneumoniae in Croatia

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**Background:** Recently, emergence of carbapenem-resistance was observed among Klebsiella pneumoniae causing urinary tract infections in Croatia. Isolates confirmed to harbour KPC carbapenemases were further characterized on molecular level.

**Materials/methods:** The antimicrobial susceptibility to a wide range of antibiotics was determined by broth microdilution method. The transferability of meropenem resistance was determined by conjugation (broth mating method) employing E. coli A15R strain resistant to sodium azide. Genes encoding broad and extended-spectrum β-lactamases, plasmid-mediated AmpC β-lactamases, group A and B carbapenemases, and carbapenem hydrolyzing oxacillinases (blaOXA-48), respectively, were determined by PCR. Plasmids were characterized by PCR based replicon typing (PBRT).

**Results:** In total 23 KPC positive urinary isolates were analysed. Twenty isolates were collected in the University Hospital Centre Split and three in the nursing homes located in Zagreb County. The isolates were uniformly resistant to all tested antibiotics (including ceftaroline and ceftolozane/tazobactam) with the exception of variable susceptibility to gentamicin and uniform susceptibility to sulphamethoxazole/trimethoprim and ceftazidim/avibactam. Only one strain was resistant to colistin with MIC value of 4 mg/L. Sixteen isolates transferred meropenem resistance to E. coli recipient strain by conjugation with the frequency ranging from 7.8x10⁻⁸ to 4.2x10⁻⁵. Other resistance markers to gentamicin, ciprofloxacin, chloramphenicol and tetracycline were not cotransferred alongside with meropenem resistance. PCR was positive for blaKPC and blashv genes in all isolates whereas eleven isolates tested positive also for blaTEM genes. Sequencing revealed blaSHV-1 and blaTEM-1 genes. PBRT revealed the presence of FII plasmid in the three ESBL positive isolates from the nursing homes.

**Conclusions:** The study showed dissemination of KPC producing K. pneumoniae in urinary tract isolates in Croatia. Sulphamethoxazole/trimethoprim, ceftazidime/avibactam and colistin remain so far as the only therapeutic options although the colistin resistance already arose. Two different clones of KPC positive K. pneumoniae were observed: one with additional ESBL detected in the nursing homes and the other without ESBL identified in the University Hospital. At the national level the spread of carbapenemase-producing isolates began with OXA-48 producing strains, but KPC isolates recently emerged in southeast geographic region of Croatia posing a new epidemiological and therapeutical challenge.

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Abstract 208

**Antileishmanial effects of amphotericin B-chitosan, amphotericin B-dendrimer, betulinic acid-chitosan and betulinic acid-dendrimer in the treatment of Leishmania major: real-time PCR assay plus**

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**Abstract third-party references:** Part of PhD student thesis in Pasteur institute of Iran

**Background:** Amphotericin B (A) and Betulinic acid (B) are antileishmanial agents with low water solubility and high toxicity.

**Materials/methods:** To increase the solubility and reduce the toxicity, they were loaded into chitosan nanoparticles (K) with the size of 102 nm and Anionic Linear Globular Dendrimer (D) with the size of 90 nm for the first time and used as the nanoformulations for the treatment of *Leishmania major*.

**Results:** The drug loading efficiency of 90% for Amphotericin B-chitosan (AK), 93% for Betulinic acid-chitosan (BK), 84% for Amphotericin B-dendrimer (AD) and 96% for Betulinic acid-Dendrimer (BD) was obtained. The characterization results confirmed that A and B were loaded into nanoparticles physically. The drug solubility rate was increased by 478 folds in AD and 790 folds in BD and by using a novel solvent, these values were increased by 80 folds for AK and 300 folds for BK. Also, the results of drug release studies showed that the all nanodrugs showed the slow drug release pattern with cellular uptake of 98.6% for AK10 µg/ml, 98% for BK20 µg/ml, 64% for AD50 µg/ml and 94.6% for BD40 µg/ml. Moreover, the nanocarriers reduced the toxicity effects of A and B by 100% in vivo and in vitro environments. AK10 mg/kg and BK20 mg/kg caused a reduction in the parasite burden by 83% [P<0.001], while AD50 mg/kg and BD40 mg/kg reduced toxicity effects to a lesser extent. Overall, all of the synthesized nanodrugs were found to be completely effective in the improvement of the pathological effects caused by *leishmania major* by 100% in infected footpad.

**Conclusions:** The results of this study showed that AK and BK were effective to a large extent in the treatment of *leishmania major* infectious [P<0.001], suggesting that AK and BK can be considered as suitable alternatives of choices drugs.

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Abstract 216

**Evaluation of newly formatted *Aspergillus* lateral flow assay for IgG antibody detection in chronic pulmonary aspergillosis**

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**Background:** Detecting *Aspergillus*-specific IgG is critical to diagnosing chronic pulmonary aspergillosis (CPA). Existing assays are often costly and require sophisticated equipment, making them unsuitable for use in low- and middle-income countries where tuberculosis prevalence is high. It is necessary to diagnosis CPA in early stage to distinguish it from tuberculosis with similar presenting conditions. Genbio Pharmaceutical Co., Ltd. has recently commercialized a lateral flow assay based on immunochromatographic technology that detects *Aspergillus* IgG antibody in 10 minutes without any instruments.

**Materials/methods:** 137 CPA patient serum and control patient serum collected from the China-Japan Friendship Hospital (Beijing, China) were evaluated. Samples were applied to the FungiXpert® Aspergillus IgG Detection K-Set (Lateral Flow Assay) for IgG antibody detection and results were read qualitatively. Outcomes were compared with *Aspergillus* IgG titers in CPA patients, measured by Platelia™ Aspergillus IgG. Gradient dilutions were performed on samples that both assays were positive, then detect the samples repeatedly by FungiXpert® kit and results were semi-quantitatively.

**Results:** For proven CPA patients versus controls, sensitivity and specificity for the FungiXpert® Aspergillus IgG were 97.87% and 99.0%, respectively. And, the routinely-used Platelia™ Aspergillus IgG exhibited 95.74% sensitivity for the same cohort (cut off of 10 AU/mL). For the 45 samples that both assays were positive, the semi-quantitative results of FungiXpert® were similar to the titers of Platelia™ for each sample.

**Conclusions:** The FungiXpert® Aspergillus IgG lateral flow assay exhibits excellent sensitivity and specificity for serological diagnosis of CPA. Due to the short run time, simplicity, and limited resources needed, the Aspergillus IgG lateral flow assay is a suitable diagnostic tool for CPA in resource-constrained settings.

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Abstract 218

**Binding interference between Bartonella adhesin A and fibronectin as a novel therapeutic concept to treat bacterial infections**

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**Background:** Bartonella henselae is a facultative intracellular bacterium, responsible for various human diseases like cat scratch disease and vascular proliferations [bacillary angiomatosis]. Bartonella adhesin A (BadA), a trimeric autotransporter adhesin, is a major pathogenicity factor of *B. henselae* mediating bacterial adherence to endothelial cells and extracellular matrix (ECM) proteins. The identification of specific binding sites between BadA and ECM proteins might give insights about the use of BadA-specific antibodies or peptides interfering with fibronectin binding ["anti-ligands"] to treat bacterial infections by a new class of antibiotics. The project aims the detailed analysis of fibronectin and BadA binding as the basis of the interaction between BadA and ECM proteins in host-cell adhesion processes, and the design of adhesion-inhibiting peptides for later anti-ligand application.

**Materials/methods:** *B. henselae* strains (wildtype and BadA deficient) were exposed to fibronectin and human endothelial cells to study binding interactions using *in vitro* infection models. A broad screening of fibronectin binding sites was performed using standardized *in vitro* binding assays. The relation between fibronectin and BadA was analyzed using mass spectrometry. As further steps, fibronectin will be genetically modified [e.g. deletion/modification of the identified binding domains]. Finally, after definition of the BadA-fibronectin binding sites, synthetic molecules will be generated for the inhibition of bacterial adhesion.

**Results:** We expect the definition of the fibronectin domains involved in the bacterial adhesion process to use this information in the generation of artificial peptides for bacterial adherence inhibition to host cells [anti-ligands]. To this purpose binding experiments using fibronectin fragments were performed showing binding with a 70 kDa fragment located at the N-terminal of the fibronectin molecule. To further analyze this interaction, crosslinking and mass spectrometry analysis using the complete fibronectin molecule and proteolytic fragments were performed to describe the sequence of amino acids involved in this interaction.

**Conclusions:** The project aims the detailed analysis of fibronectin and BadA binding as the basis of the interaction between BadA and ECM proteins in host-cell adhesion processes, and the design of adhesion-inhibiting peptides for later anti-ligand application.

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Identification of novel pathogenicity factors in Bartonella bacilliformis

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Background: Carrion’s disease is a vector-borne biphasic illness restricted to the South American Andes. The causative agent of this neglected disease is Bartonella bacilliformis. The pathogen infects human erythrocytes causing a serious, acute hemolytic anemia called “Oroya fever” with mortality rates as high as 80% in untreated patients. In a second chronic phase the infection of endothelial cells results in the formation of blood-filled nodular hemangiomas in the skin (“verruga peruana”). Underlying molecular mechanisms of host infection are still widely unknown. Trimeric autotransporter adhesins (TAAs) play an essential role in bacterial pathogenicity, and are encoded in all Bartonella spp. Bartonella bacilliformis adhesin A (BbadA), has been identified in the genome of B. bacilliformis.

Materials/methods: Molecular genetic strategies using bacterial mutants (e.g., transposon mutagenesis library, promoter library) and recombinant protein expression strategies (e.g., heterologous expression library) are used to identify immunodominant proteins and pathogenicity factors of B. bacilliformis. The genomes of B. bacilliformis (strains KC583 and KC584) are sequenced using PacBio technology. Deletion mutants of BbadA and flagellin are generated using homologue recombination techniques. We want to predict possible immunodominant outer membrane proteins by using reverse vaccinology. A genomic deletion of bbadA and subsequent infection experiments with erythrocytes and endothelia cells will be performed to characterize the role of BbadA in the infection process.

Results: A genomic DNA expression library containing random genomic B. bacilliformis DNA inserts was established in E. coli BL21 (DE3). The development of a high throughput screening for immunodominant proteins is still ongoing. Electron microscopy clearly reveals the presence of BbadA on the surface of B. bacilliformis. Furthermore, the deletion of bbadA leads to a reduction in cell adhesion to endothelial cells. Western blot analysis with recombinant BbadA or flagellin reveals immunodominance using rabbit-anti B. bacilliformis serum.

Conclusions: The object of this work is the identification and characterization of immunodominant proteins of B. bacilliformis and the genetic and functional characterization of BbadA and flagellin. Furthermore, potential target proteins will be analyzed for diagnostic and therapeutic usability and to establish a basis for the development of a vaccine.

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Abstract 223

Evaluation of diagnostic method with sonication and culturing of orthopaedic implant-associated infection at Karolinska University Hospital, Sweden

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Background: Despite known low sensitivity, culture of prosthesis tissue specimens in Fastidious Anaerobe Broth (FAB) is a routine procedure in many laboratories. For increasing the chance to detect more positive specimens in order to improve the diagnosis of prosthesis infections caused by the bacteria that are apt to form biofilms, our laboratory in Stockholm since November 2018 has introduced a new method with sonication fluid inoculated into blood culture from prosthesis material in combination with culturing of periprosthetic tissue specimens in FAB. The aim of this retrospective study is to compare the results obtained after sonication and culturing of the prosthesis/implant with tissue-culture.

Materials/methods: The materials used in this study is the prosthesis/implant and infected tissues taken from the patients with suspected orthopedic implant-associated infection during November 2018 until October 2019. Data are obtained from the results recorded in the laboratory analysis system. In this study we considered include only patients with delivery of material both from prosthesis/ implant and infected tissues. The prosthesis has been sonicated and the fluid of sonication were inoculated into a blood culture bottle. All tissues have also been cultured into a FAB according to routine procedures.

Results: A total of 88 patients’ sample were analyzed with both sonication and FAB Culture at Karolinska laboratory/Huddinge during study period. Of these samples 47 showed growth and 41 samples showed no growth with sonication method which showed a total of 83% agreement with FAB culture method. The disagreement was found in 15 samples. Of these samples 12 were positive with just sonication and 3 samples were just positive in FAB with growing of Cutibacterium acnes.

Conclusions: Overall this study shows that after introduction of sonication in routine diagnostic method, we have increased the possibility to detect 25% more bacteria, but sonication is still not optimal method for detection of low growth bacteria. At this moment it is necessary to combined both methods for detection of low growth bacteria such as Cutibacterium Acnes.

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Abstract 227

Genome-wide analysis of resistance-related transposable elements in multidrug-resistant Haemophilus parainfluenzae clinical isolates

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Background: Haemophilus parainfluenzae is emerging as an opportunistic multidrug-resistant (MDR) pathogen. Since data about the acquisition of resistance are scarce, we aimed to determine the contribution of mobile transposable elements (Tn) to enhance antimicrobial resistance in clinical H. parainfluenzae isolates.

Materials/methods: All the available MDR H. parainfluenzae strains (n=57) collected at Hospital Universitari de Bellvitge between 2013 and 2017 were characterized by Next-Generation Sequencing (Illumina MiSeq). In-silico screening of mutations targeting genes was performed with Geneious R9, using the closed genomes of H. parainfluenzae T3T1 and H. influenzae Rd KW20 as references. The acquired resistance mechanisms were screened using Abricate v0.8.0 for ResFinder databases. The antimicrobial susceptibility was tested by microdilution following EUCAST guides.

Results: Tn-family elements were identified in 47 of the 57 MDR H. parainfluenzae strains. Overall, 38.6% (22/57) of the strains carried two or more Tn-elements conferring them resistance to at least three antimicrobial families; eleven of them (19%) had the three transposable elements detected. Tn-elements distribution was as follows: Tn10 which harboured efflux-related genes associated with tetracycline resistance (tetBCDR) was carried by 66.7% (38/57) of the strains, of which 15 also contained a catA2 related to chloramphenicol resistance. Additionally, a Tn3 that included a blaTEM-1 involved in ampicillin resistance was found in 54.4% (31/57) of the strains. Finally, 21.1% (12/57) of the strains presented a Tn6026-like, similar to that identified in Enterobacteriaceae and linked to aminoglycoside and co-trimoxazole resistance. Among this group, 8 strains harboured the strB-strA-sul2 cluster and aph(3’)-Ia; 2 strains lacked the sul2 gene; 1 strain had an additional ant(2’)-Ia; and 1 strain harboured aac(3’)-Ia instead of aph(3’)-Ia, also conferring aminoglycoside resistance. These Tn structures were identified forming part of an integrative conjugative element (ICE) derived from H. influenzae (ICEHin1056) and H. parainfluenzae (ICEHpaT3T1), that also included genes involved in replication, secretion (type IV system), and integration. Concomitantly, 31.6% (18/57) of the strains acquired the MEGA-element linked to tetracycline (tetM) and azithromycin (mefA and msrD) resistance.

Conclusions: The acquisition of transferable elements is common among H. parainfluenzae and responsible for the multidrug resistance, becoming a reservoir and contributing to the spread of antimicrobial resistance.

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Abstract 228

**Gut microbiome interferes with host tryptophan metabolism pathway and regulates basal anxiety-like behaviour**

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**Background:** Host-microbiome interactions has emerged as promising research field to understand complexity of this symbiotic relationship. Microbiome–gut–brain axis is bidirectional communication system involved in regulation of host brain development and functions. Gut microbiome communicates with brain via neural, endocrine and immune pathways. Germ free mice have decrease basal anxiety levels due to alterations in their brain ultrastructure. The aim of this study was to explore the microbiome related changes in host basal anxiety levels with mechanistic insights in conventional laboratory mice.

**Materials/methods:** Gut dysbiosis mice model was developed using combination of non-absorbable antibiotics and anxiety level was evaluated using EPM. Neurochemical changes in brain were analyzed with HPLC. 16S rRNA sequencing of fecal content was performed to study gut microbial profiles, data was processed using standard bioinformatics tools, taxonomic and statistical analysis was performed on MEGAN and STAMP. Transcription levels of specific genes were analyzed using RT-qPCR.

**Results:** Behavioral analysis showed anxiolytic – like behavior in dysbiosis group. The hippocampus of antibiotic treated mice showed significant decrease in levels of tryptophan, serotonin and 5-HIAA. Beta diversity analysis showed taxonomic shift of microbial communities among groups. At genus level control group microbiome was dominated by *Muribaculum*, *Clostridium* and *Bacteroides*, while dysbiosis group showed dominance of *Klebsiella*, *Escherichia* and *Enterobacter*. Gene expression studies showed down regulation of serotonin transporter in mice hippocampus.

**Conclusions:** Our data suggest that taxonomic shift in gut microbiome can modulate host anxiety levels via interfering with its tryptophan metabolism pathway, as low levels of tryptophan in brain attributes to the reduce synthesis of serotonin which regulate basal anxiety – like behavior. This study highlights gut microbiome as drug and drug target due to inter-individual differences in gut microbial profiles and will further lead to advancement in personalized medicine by inclusion of individual’s microbiome profile.

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Misuse of tampons and menstrual toxic shock syndrome in France: a community-based case-control study

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Background: Menstrual tampons are widely used in western countries. Here we assessed whether tampon misuse was associated with increased risk of menstrual toxic shock syndrome (MTSS).

Materials/methods: We conducted a community-based, nationwide, case-control study in France, including women with MTSS diagnoses reported to the French National Staphylococcal Center of Lyon between 2011–2017. Controls were women with no MTSS history. Using a standardized questionnaire, we collected information regarding tampon use during a 6-month period. Associations between tampon misuse and MTSS were assessed using logistic regression models stratified by residential area.

Results: We analyzed data from 181 subjects (age≤30 years; 55 cases and 126 controls). Compared to controls, cases more frequently reported maximum tampon wear of >6 hours (62% vs. 41%, P<0.05), overnight tampon use (77% vs. 54%, P<0.05), and not having read and followed tampon instructions (65% vs. 42%, P<0.05). In univariate analysis, MTSS risk was two-fold higher with tampon use for >6 consecutive hours [odds ratio (OR)=2.3, 95% CI: 1.2–4.6, P<0.05], and three-fold higher with tampon use during sleep for >8 hours (OR=3.2, 95% CI: 1.4–7.7). In multivariate logistic regression analysis, maximum tampon use for >6 hours (OR=2.3; 95% CI: 1.04–4.6), and not reading and following the tampon instructions (OR=2.25; 95% CI: 1.15–4.39) were independent MTSS predictors.

Conclusions: MTSS risk can be reduced by using sanitary napkins overnight, using tampons for <6 consecutive hours, and receiving education about tampon use and its relation with MTSS. These findings have major public health implications for women’s health.

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Abstract 235

Effects of previous antibiotic exposure on the clinical course of pneumonia in the elderly: a single-centre prospective observational study

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Background: The aim of this study was to investigate the effects of previous antibiotic exposure on the outcomes of pneumonia in the elderly population.

Materials/methods: In this prospective observational study, the patients with pneumonia were stratified into two groups as younger (18 to 64 years) and older (≥65 years). A "poor prognosis" was assessed as the development of septic shock associated with infection and/or the need for intensive care and/or death within 30 days. Poor prognostic indicators for each group were determined and compared.

Results: There were 184 pneumonia episodes in 155 patients. The median age of the cases was 72 (range, 18-104) of whom 127 (69%) were ≥65 years old and 110 (59.8%) were male. Mental status changes were significantly more frequent in the elderly group (p=0.04). Pseudomonas species (n=11, 29.7%) was the most common agent, followed by Streptococcus pneumoniae (n=6, 16.2%), Haemophilus influenzae (n=5, 13.5%), Acinetobacter species (n=4, 10.8%) and Staphylococcus aureus (n=4, 10.8%). The rates of carbapenem resistance were high; 45.4% in Pseudomonas spp. and 50% in Acinetobacter spp. And 25% of Staphylococcus aureus strains were methicillin resistant. Multivariate regression analysis determined three variables that could be potential independent risk factors for poor prognosis in the elderly: dyspnea at the onset (OR:5.85, CI:5.18-6.52, p=0.01), previous antibiotic use within the last 3 months (OR:2.97, CI:2.51-3.43, p=0.02), and acute renal failure (OR:2.51, CI:2.06-2.96, p=0.04). A receiver operating characteristic analysis showed that the area under the curves of procalcitonin and C-reactive protein (CRP) as indicators of poor prognosis in the elderly were 0.846 (p<0.001) and 0.650 (p=0.008) respectively (Figure 1). In addition, mental status changes (p<0.001), the CURB-65 score (p<0.001), and the pneumonia severity index (PSI) (p<0.001) were associated with poor prognosis.

Conclusions: Previous antibiotic exposure, serum procalcitonin and CRP levels along with the PSI and the CURB-65 scores should minutely be evaluated in terms of need for hospitalization and intensive care. Furthermore, local epidemiology and resistance profiles should be taken into consideration for appropriate antimicrobial therapy.

Figure 1. Receiver operating characteristic curves of serum parameters for prediction of poor prognosis of elderly with pneumonia

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Abstract 244

Hospital-acquired influenza characteristics and its correlation with the population-based surveillance in a tertiary care center in Istanbul

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Background: Influenza virus related respiratory infections causes major mortality and morbidity. Hospital acquired seasonal influenza (HA-SI) is reported up to 55% of inpatient influenza cases in Geneva University Hospital. Also, the proportion of HA-SI is correlated with the population-based influenza surveillance in some studies. We investigated the incidence of HA-SI and correlation with national influenza surveillance (NIS) data in a tertiary care center in Istanbul, Turkey.

Materials/methods: This is a retrospective study which includes seasonal influenza cases between October 2018 and March 2019. (The Sofia Influenza A+B Fluorescent Immunoassay, Quidel, USA) and/or Influenza A/B RT-PCR test (The Film Array Respiratory Panel, Biomerieux, France or Xpert Flu, Cepheid, USA). Cases were defined as HA-SI when symptoms onset and/or positive influenza PCR ≥ 72 hours after hospital admission, without previous respiratory symptoms or with negative influenza screening. The correlation between HA-SI and NIS data was analyzed using interclass-correlation test.

Results: During the study period 4423 patients tested for influenza and 786 (17.8%) of them were found positive. Out of 786 patients 119 were inpatients (15.1%) Of these 119 patients 29 (24.6%) were defined as HA-SI. Influenza-A represents the 88.2% of all inpatients with influenza and 89.7% of HA-SI. Majority of HA-SI cases occurred in medical wards (65.5%) and intensive care units (17.2%). The incidence density of HA-SI was 16.1 per 10,000 patient-admissions for the given period. Weekly rate of HA-SI cases and weekly NIS data for of sentinel inpatient influenza rate were significantly correlated. Whereas the NIS data for outpatients showed no correlation with HA-SI rates (Figure-1). The influenza vaccination coverage of health-care-workers was 10% for 2018-2019.

Conclusions: This study shows that during the 2018-2019 influenza season nearly 25% of the inpatient influenza cases acquired from the hospital. The data show the potential room for improvement in our medical center. Education about infection-prevention and control measures for influenza and achieving high vaccination coverage for health-care-workers and patients must be a priority. Also, the population-based surveillance can estimate the burden of HA-SI in our medical center which can be used to guide the institutional policies for influenza management in our medical center.

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Abstract 245

Carbapenem antimicrobial stewardship programme

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Background: The prevalence of carbapenem resistance throughout the world is increasing and carbapenems are considered critically important antimicrobials by the WHO. The aim of study is to evaluate clinical and antibiotic resistance impact of carbapenems Antibiotic Stewardship Programs (ASP).

Materials/methods: Descriptive study between January-2012/December-2018, pre-post-intervention. A carbapenems ASP was initiated in January 2015, in patients who started treatment with carbapenems (meropenem/ertapenem). An infectious diseases physician performed treatment recommendations to prescribers. Prospective information was collected to evaluate adequacy of carbapenems prescription to local guidelines and to compare results between cases with accepted or rejected intervention. Cases with carbapenems prescription during the last 4 months of 2014 were retrospectively reviewed, this sample of the pre-intervention period was used to compare with patients who started treatment with carbapenems during the intervention period. Appropriate treatment with carbapenems was considered when it was prescribed in patients with: 1. Severe sepsis; 2. history of ESBLs colonization; or 3. hospital-acquired infection in which a broad-spectrum antibiotic treatment was considered necessary. Analysis was performed to verify variables associated with any significant change in clinical evolution, carbapenems consumption, hospital-acquired multidrug-resistant (MDR) bloodstream infections (BSIs) and 30-day all-cause crude death in MDR-BSIs.

Results: Adequacy of carbapenems prescription improved progressively over time, after ASP implementation (p <0.001). Interventions on prescription were performed in 416 (34.5%) patients without carbapenems justified treatment (meropenem 389/ertapenem 27), in 339 (81.5%) intervention was accepted and in 77 was not. Intervention acceptance was associated with shorter duration of treatment (11.3±10.2 vs 13.4±8.6) and inpatient days (18.4±16.8 vs 27.3±23.6, p=0.002), without differences in clinical evolution. During the 2015-2018 period meropenem consumption in DDD/100 patients-day decreased compared with 2012-2014 [Rate ratio 0.61; 95%CI: 0.58-0.64, p<0.001], and ertapenem consumption increased somewhat [Rate ratio 1.07; 95%CI: 0.94-1.22]. Hospital-acquired MDR-BSIs rate and 30-day all-cause crude death in MDR-BSIs deceased [0.66; 95%CI: 0.44-1.00, p=006] and [RR 0.60; 95%CI: 0.28-1.34, p=0.29], respectively, coinciding in time with ASP start-up.

Conclusions: The decrease and better use of carbapenems achieved was associated with shorter duration of treatment and of inpatient days, without differences in clinical evolution, and with a decrease of hospital-acquired multidrug-resistant bloodstream infections rate.

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Delineation of the direct impact of Candida auris ERG11 mutations on clinical triazole resistance

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Background: Candida auris has emerged as a healthcare-associated multi-drug resistant pathogen of great clinical concern. When isolated, approximately 90% of all clinical C. auris isolates are highly resistant to fluconazole, the most widely utilized antifungal, with modal MIC ≥256mg/L. While the majority of fluconazole-resistant clinical isolates are found to possess one of three different mutations in ERG11, the gene encoding the target of the triazoles, it remains unknown whether these mutations alone explain the high level of fluconazole resistance present among clinical C. auris isolates.

Materials/methods: To assess the direct contribution of all three clinically relevant C. auris ERG11 mutations, ERG11 alleles encoding the amino acid substitutions VF125AL, Y132F, and K143R, as well as a wildtype control were introduced into the fluconazole susceptible clinical isolate AR0387 using CRISPR-Cas9 mediated transformation system. Introduction of ERG11 mutations were confirmed using Sanger sequencing. Additionally, the K143R encoding mutation present in the highly fluconazole-resistant clinical isolate AR0390, was corrected to the ERG11 wildtype sequence. In vitro antifungal susceptibility testing was then performed using CLSI broth microdilution methodology.

Results: Introduction of each of the three mutant ERG11 alleles into the AR0387 fluconazole-susceptible background was observed to increase fluconazole MIC by 8 to 16-fold, while fluconazole MIC were unchanged upon introduction of the wildtype control allele. The MIC for the other clinically available triazoles were more minimally impacted by any of the three ERG11 mutations, with the most prominent change observed in voriconazole MIC (2 to 4-fold change). In the AR0390 fluconazole-resistant clinical isolate background, correction of the K143R encoding mutation to the wildtype sequence led to a corresponding 8-fold decrease in fluconazole MIC, and 4-fold decrease in voriconazole MIC, while the MIC of other triazole antifungals was unchanged.

Conclusions: Taken together, the findings of this study demonstrate mutations in C. auris ERG11 significantly contribute to the fluconazole resistance, but alone cannot explain the substantially elevated MIC observed among clinical isolates of C. auris. Further research is needed to identify additional mechanisms contributing to fluconazole resistance in clinical isolates of C. auris.

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Abstract 248

Stay in the emergency department increases the risk of colonisation by carbapenem-resistant Enterobacteriaceae in the intensive care unit

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Background: Carbapenem-resistant Enterobacteriaceae [CRE] colonization on admission to the intensive care unit (ICU) is common and the impact that hospitalization in the emergency department (ED) has on colonization is unknown. CRE-colonization on admission to ED was described in approximately 7% of patients of our hospital and one third of patients arrive in the ICU from ED. This study aimed to evaluate the impact of previous hospitalization in the ED on CRE-colonization at ICU admission.

Materials/methods: Hospital das Clinicas (HC) is a 2,200-bed public tertiary-care hospital in São Paulo, the largest hospital complex in Latin America. The ED is a very busy unit, with more than 69 thousand emergency consultations performed per year. In order to monitor and control colonization by CRE, all patients admitted to ICUs are routinely submitted to CRE surveillance cultures on admission to the unit. This is a retrospective case-control study that covered the period from September 2015 to July 2017, with 103 cases and 201 controls, analyzing ED hospitalization and other risk factors for colonization by CRE on ICU admission. Cases were patients colonized by CRE on admission to ICU and controls were patients admitted to ICU not colonized by CRE on admission.

Results: We found ED stay longer than 2 days (OR: 2.60; 95%CI: 1.35-4.99; p: 0.004), transfer from another institution (OR: 2.61; 95%CI: 1.43-4.74; p: 0.002), use of carbapenem on ICU admission (OR: 4.56; 95%CI: 1.92-10.83; p: 0.001), dialysis (OR: 2.94; 95%CI: 1.05-8.24; p: 0.04), and upper digestive endoscopy (OR: 4.15; 95%CI: 1.14-15.07; p: 0.031) as risk factors for CRE colonization on ICU admission.

Conclusions: This is the first study to demonstrate that prolonged ED stay (> 2 days) is a risk factor for CRE colonization on admission to the ICU. Other risk factors were transfer from another hospital, use of carbapenem, dialysis, and upper digestive endoscopy. The implications of these findings should lead to interventions in the ED if we are to control CRE in other hospital units.

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Abstract 256

Evaluation of a novel method for detection of carbapenem hydrolysis with an automated software (Clover BioSoft) by MALDI-TOF MS

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Background: Rapid detection of Carbapenemase-producing Enterobacterales (CPE) is one of the main goals of microbiology laboratories. One of the recommended methodologies by the EUCAST guidelines is using MALDI-TOF MS for measuring the hydrolysis of carbapenems. However, all assays evaluated are single center studies and no multicenter evaluation has ever been made to standardize the methodology as recommended. Here, we expose our first objectives of a further multicenter study, that is the development of a universal and in-house protocol for measuring carbapenem hydrolysis by MALDI-TOF MS and the development of an automated software (Clover BioSoft) for spectra interpretation.

Materials/methods: A total of 81 Enterobacterales fully characterized, 50 CPE and 31 isolates with different resistance mechanisms (not carbapenemases) or no resistance mechanisms at all, were submitted to a standard operating procedure, using imipenem as carbapenem and 30 min of incubation. The developed software (Clover BioSoft) allows the semi-quantification of the hydrolysis of imipenem. For the calculation of the ratio of hydrolysis (RH), two different analyses were applied. The first one (a) took into account the intensity and the second one (b) the area of imipenem mass peaks (Image 1). The procedure was performed in parallel with the only commercially available method, the MBT STAR®-Carba IVD Kit in the MBT STAR®-BL IVD Module (Bruker Daltonik) following manufacturer’s instructions (c).

Results: According to the sensitivity analysis (ROC curve) the AUC was 0.994 (a), 0.990 (b) and 0.977 (c), proving our in-house method with the developed software (a) as best method. The optimum cut-off for the RH was ≥ 0.5 for positivity with a 94% sensitivity and 100% specificity. The negative cut-off is established for a RH ≤ 0.2 with 100% sensitivity and 90% specificity.

Conclusions: The optimized methodology proved useful for detection of CPE in less than 1 hour with a novel and online software (Clover BioSoft). The next phases of the study will include an international and multicenter validation of the technology for CPE detection in both MALDI biotyper (Bruker Daltonik) and VITEK MS (BioMérieux) systems.

Image 1. Boxplot diagram for imipenem hydrolysis with the main carbapenemases included in the study.

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Abstract 260

The role of food and environment in the transmission of Clostridioides difficile
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Background: Clostridium difficile is the most common cause of healthcare-related diarrhea in high-income countries. However, with increased reports of (i) community-associated C. difficile infection (CA-CDI), (ii) the findings of clinically-important C. difficile in animals, food and the environment, and (iii) whole-genome sequencing (WGS) showing that the majority of hospital-associated CDI cases are genetically distinct from one another, the traditional notion that CDI is primarily a hospital infection transmitted between symptomatic patients is currently being challenged. Yet, little is known about the possible role of community reservoirs in the transmission of CDI.

Materials/methods: Food and environmental samples were collected in Western Australia (WA). Enrichment culture, toxin profiling, PCR ribotyping and antimicrobial resistance (AMR) susceptibility testing were performed. WGS and core genome single nucleotide variant (cgSNV) analysis were carried out on a selection of C. difficile ribotypes (RTs) that frequently cause CDI in humans and animals.

Results: A high prevalence of C. difficile was found in retail vegetables (30.0%), compost (27.2%) and public lawn (58.5%) in WA. A diversity of strains was isolated including RTs associated with CDI in humans and animals [RTs 014/020 (28.3%) and 056 (3.0%)]. Food and environmental C. difficile displayed AMR patterns comparable to already published data of human and animal isolates with multidrug resistance only detected in compost isolates. Two clusters of human and food/compost RT 056 strains with ≤2 SNV suggest a very recent shared ancestry, consistent with recent transmission.

Conclusions: Currently, there are ample published genomic data that demonstrate CDI has a zoonotic and/or anthropogenic transmission, with little to no evidence of an epidemiological link between humans and animals. Food and the environment are likely acting as a conduit between the two hosts, in part due to the practice of recycling human and animal waste for agricultural use and decades of antimicrobial use/misuse in production animals that has amplified C. difficile in animals and promoted AMR. Community acquisition of C. difficile from reservoirs is undoubtedly contributing to CA-CDI and asymptomatic colonization. To address this CDI issue, a One Health approach is needed.

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Epidemiological and clinical characteristics of patients with *Campylobacter* bloodstream infection: a retrospective case-control study

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**Background:** *Campylobacter* is a frequent cause of sporadic enterocolitis, but is considered a rare cause of bloodstream infection.

**Materials/methods:** We performed a single center retrospective case-control study comparing patients with *Campylobacter* bloodstream infection (C-BSI) (cases) to nonbacteremic patients with positive *Campylobacter* stool culture (controls) from 2007 through 2016. Case and control patients were matched by age and sex at a ratio of 1:2. Demographic characteristics, clinical features and microbiology data were extracted from patient medical records. Death within 30 days of culture, hospital stay duration, need for intensive care and recurrent hospitalization were compared between groups.

**Results:** We identified 42 patients with C-BSI and matched them with 83 nonbacteremic patients with positive *Campylobacter* stool culture. The rate of C-BSI increased sharply in 2014, with 38 cases (90%) identified from 2014 to 2016. Case patients were more likely than controls to be infected with *C. jejuni* (85% vs. 59%, *P*=0.008). Cases and controls did not differ in age, sex and comorbidities (median Charlson score 5 in both groups). Cases were more likely to present with fever (78% vs 53%, *P*=0.006) and functional deterioration (19% vs 4%, *P*=0.008), whereas control patients were more likely to have abdominal pain (54% vs 28%, *P*=0.008) and diarrhea (94% vs 57%, *P*<0.001). More patients with C-BSI were treated with PPI at baseline (55% vs 34%, *P*=0.056) and had a report of recent antibiotic exposure (33% vs 11%, *P*=0.002).

C-BSI was associated with higher 30-day mortality (19% vs. 2.4%, *P*=0.002), more frequent need for intensive care (11.9% vs. 1.2%, *P*=0.008) and doubling of the median hospital duration (6 days vs. 3 days, *P*<0.001). Rates of recurrent hospitalization were similar. Neutropenia and hematological malignancy were associated with higher mortality rate.

**Conclusions:** C-BSI is identified more frequently in recent years, possibly as a result of improved sensitivity of blood culture systems. Compared with nonbacteremic patients with positive stool culture, patients with C-BSI had significantly higher rates of death and other adverse outcomes. Previous antibiotic exposure, PPI use and infection with *C. jejuni* were identified as risk factors for C-BSI.

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Abstract 267

Acute cholangitis secondary to choledocholithiasis in older population: subtle presentation and severe illness
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Background: Acute cholangitis continues to be a serious and possibly life-threatening diagnosis despite the advances and widespread availability of abdominal imaging and endoscopic intervention.

The classic Charcot’s triad lacks sensitivity and is reported to be positive in only 30% of acute cholangitis cases. Older population, defined in different studies by age >65 to >80 years old, are higher risk group with sparse literature regarding differences in clinical presentation and outcome.

Materials/methods: Retrospective chart review of 383 cases with acute cholangitis secondary to biliary stones managed between January 2012 and December 2017.

We reviewed clinical presentation, diagnostic criteria, disease severity, microbiology and 30 day outcome of acute cholangitis in patients aged >75 years.

Results: Our sample included 183 patients aged >75 years, 107 (58%) males, median age was 85 years (IQR 80-89) and 11/183 (6%) were immuno-suppressed.

The clinical presentation was with abdominal pain in 160 (87.4%), subjective fever in only 102 (55.7%), jaundice in 62 (33.8%) and altered mentation in 39 (21.3%). At time of presentation, LFTs of >1.5 upper normal limit was found in 171 (94%), abnormal WBC count (>10 or <4) was found in 150 (82.8%), total bilirubin of >= 2 mg/dL was in 145 (80%) and abnormal abdominal imaging was found in 167 (92%).

Severity of cholangitis following 2018 Tokyo guidelines was grade III in 46%, grade II in 45% and grade I in 9%.

Blood cultures were positive in 79/155 (51%). This was with gram-negative organisms in 63/79 (80%), gram-positive organisms in 7/79 (9%) and polymicrobial in 9 (11%).

Biliary drainage was pursued in 178 (97.2%). This was with ERCP in 170 (95%) cases. Overall mortality was 11/183 (6%).

Conclusions: Compared to younger population, acute cholangitis in patients >75 years is characterized by high-grade disease but with a more subtle clinical presentation. This group was found to have higher incidence of altered mentation but absence of fever in almost half of the cases. Laboratory blood testing and radiological imaging were abnormal in more than 80% of the cases.

Our findings suggest need for a high index of suspicion to pursue appropriate treatment and timely source control.

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Adjunction of daptomycin for the treatment of bacterial meningitis: in vitro study

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Background: Due to intrinsic virulence factors, Streptococcus pneumoniae is responsible for the highest morbimortality associated with bacterial meningitis worldwide. Despite a global reliance on the use of beta-lactam antibiotics, several studies suggest a significant risk of worsening cerebral lesions owing to the release of pro-inflammatory toxins during bacterial cell lysis. As non-bacteriolytic antibiotic may help containing an excessive inflammatory host response, the adjunction of daptomycin is currently under clinical evaluation in a multicenter phase II study to improve the prognosis and survival of pneumococcal meningitis (AddaMAP, NCT03480191). However, its impact on the activity of standard treatment for other bacterial meningitis remains unknown. The present project aims at evaluating in vitro the antimicrobial activity of daptomycin-based associations against the most frequent species associated with bacterial meningitis.

Materials/methods: National Reference Centers were contacted for an epidemiological selection of the most relevant strains regarding five bacterial species: Streptococcus pneumoniae, Neisseria meningitidis, Listeria monocytogenes, Haemophilus influenzae and Streptococcus pyogenes. The antimicrobial activity of amoxicillin, cefotaxime, and rifampicin - either alone or in association with daptomycin - was explored through the determination of minimal inhibitory concentration (MIC), fractional inhibitory concentration index (FICI) and Time-Kill Kinetics Assay (TKA) using broth microdilution method.

Results: All species taken together, the adjunction of daptomycin had no deleterious impact on the antimicrobial activity of amoxicillin, cefotaxime and rifampicin in vitro. Regarding Gram-positive bacteria, FICI values confirmed a significant improvement of growth inhibition due to the adjunction of daptomycin, up to a synergistic effect with FICI largely below 0.5 for Streptococcus pyogenes. In addition, TKA analysis showed increased bactericidal activity with daptomycin, as demonstrated by the reduction of integrated AUC/24h by a factor varying from 1.5 to 3, depending on the species and antibiotic (Figure). Finally, lipopeptide-based associations did not modify the activity of beta-lactam antibiotics or rifampicin against Gram-negative bacteria, notably Neisseria meningitidis.

Conclusions: These results bring comforting evidence towards the potential of daptomycin adjunction in the treatment of bacterial meningitis. Such additional in vitro data constitute critical supplementary information supporting the ongoing AddaMAP clinical trial.

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Assessment of the quality of data supporting the efficacy of new antibiotics for multidrug-resistant bacteria

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Background: Infections caused by multidrug resistant (MDR) bacteria are major public health threat. We aimed to assess the data supporting US Food and Drug (FDA) approval of new agents aimed to treat MDR bacterial infections, and the data provided by post-marketing studies.

Materials/methods: We identified all drugs with in-vitro activity against MDR bacteria initially approved by the FDA between January 2010 and December 2018. Characteristics of trials supporting approval and regulatory pathways were collected from Drugs@FDA. Characteristics of post-marketing studies were extracted from drug labels and ClinicalTrials.gov entries effective on June 1, 2019.

Results: Initial approval of 11 newly approved antibiotics with anti-MDR activity was supported by 20 trials, all with non-inferiority design. All initially approved indications were for common infections, mostly acute bacterial skin and skin-structure infections, regardless of causative microorganism. The proportion of MDR bacteria in most trials was low (<10% for Gram-negative infections, <1% for Gram-positive pneumonia). Most trials (90%) excluded immunocompromised and critically ill patients. Of 16 additional post-marketing phase III trials identified through ClinicalTrials.gov, only 2 exclusively included infections caused by MDR bacteria, comprising 116 patients. No drug was granted accelerated approval, which would mandate post-marketing efficacy studies.

Conclusions: The approval of new drugs presumed to have clinical activity versus MDR bacteria is supported by trials evaluating infections caused by non-MDR organisms, using non-inferiority design and excluding the patients most likely to require these agents. Subsequent post-marketing efficacy data against these organisms are scarce. Healthcare professionals and regulators should demand more robust data to support clinical decision making.

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Screening of Chlamydia trachomatis and Neisseria gonorrhoeae in female sex workers: pooled versus single site testing

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Background: As the majority of women infected with Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) are asymptomatic, targeted screening of patients in specified risk groups is indicated in order to reduce transmission and (long-term) complications. Testing of extra-genital is warranted for optimal detection and treatment of those infected. As this comes with a substantial cost, analysis of a pooled sample from vaginal and extra-genital sites could be beneficial. In this study, we evaluated the feasibility of CT/NG testing in pooled versus single site samples in a large cohort of female sex workers.

Materials/methods: We sampled 501 women with the Abbott multi-ColleCTSpecimen Collection Kit in the pharynx (taken by the physician), vagina and rectum (either self-collected or by the physician). For each woman, all three samples were vortexed and 400 µL of transport medium was pooled into an empty tube. The pooled sample was tested for CTand NG alongside each single-site sample using the Abbott RealTime CT/NG assay on the m2000sp/rt system.

Results: Overall, 5.1% of sex workers were positive for CT; 2.0% were positive for NG and 1.4% were co-infected, resulting in an overall prevalence of 6.5% for CT and 3.5% for NG. From the 42 women positive on at least one single-site sample, only 5 had a negative result on the pooled sample resulting in a sensitivity of 94% for CT and 82% for NG. The false negative pooled samples were from women with a single-site NG (n=3) or CT (n=2) infection with low bacterial load. Inadequate self-sampling was ruled out as a possible cause of false negativity, as the number of samples from infected women collected by the physician was comparable to the number of self-collected samples. Testing extra-genital samples led to a significantly higher detection rate, as 40% of the CT and 60% of the NG infections would have been missed if only vaginal samples were tested.

Conclusions: Pooling samples is a cost-effective strategy for the detection of CT and NG in females, with minimal decrease in sensitivity. By reducing costs, more extra-genital samples can be tested, resulting in higher detection rates.

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Abstract 288

**Patient transfers as a risk factor for Clostridioides difficile infection: a case-control study**

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**Background:** Clostridioides difficile (previously Clostridium difficile) is a spore-forming bacterium; the spores are highly resilient and can survive for long periods in the hospital environment despite cleaning and disinfection efforts. Most Clostridioides difficile infections (CDI) are hospital-acquired. Colonization of spores or vegetative bacteria in the large intestine is necessary for infection to occur, and the risk of infection is modulated by the state of the intestinal microbiome and the host’s immune status. Patient transfers within and between wards are commonplace in modern healthcare, exposing patients to more areas of the hospital environment where spores may exist. We hypothesised that frequent transfers between wards and/or rooms within a ward is a risk factor for developing CDI.

**Materials/methods:** A case-control study of all hospital-acquired CDI cases at Södra Älvsborg Hospital, Borås, Sweden, during two years: 2012 and 2015 (n=65). A random selection of patients tested negative for CDI served as control group (n=101). Odds ratios were calculated by univariate logistic regression followed by multivariate logistic regression for variables where there was a statistically significant difference in the univariate analysis. These covariates were room transfers, transfers or ward, use of proton pump inhibitors, and use of antibiotics.

**Results:** The number of patient transfers both between and within wards was significantly higher in the case group in univariate analysis, however, there was no significant difference between groups when data were adjusted for other known risk factors. In the multivariate analysis, time of care was the only statistically significant variable (OR per additional day of care: 1.07, 95% confidence interval: 1.02-1.07).

**Conclusions:** The study could not demonstrate patient transfers as an independent risk factor for CDI, but underlines the importance of time of care as a risk factor for CDI.

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Abstract 292

**Risk of invasive pneumococcal infection in patients with asplenia/hyposplenism: a nationwide population-based study compared to the general population**

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**Abstract third-party references:** This study was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education [2019032869]

**Background:** Asplenia is a well-known risk factor of invasive pneumococcal infection (IPI), but nationwide cohort studies have not been conducted on how the risk increases in patients with asplenia compared to the general population.

**Materials/methods:** All cases of newly-diagnosed asplenia that were claimed to the National Health Insurance Service in South Korea from January 2009 to December 2018 were included. Information were extracted from Health Insurance Review and Assessment Service database. Asplenia patients were defined as those who were diagnosed with congenital asplenia/hyposplenism or underwent splenectomy. To compare the incidence of IPI between these patients and the general population, we used the case definition and the 2017 data of National Infectious Disease Surveillance System at Korean Center for Disease Control.

**Results:** Over a period of 10 years, a total of 2,1376 cases were identified; 20,524 cases (96.0%) underwent splenectomy and 852 cases (4.0%) had diagnosis of congenital asplenia/hyposplenism. Fifty-seven patients had an IPI, and one was accompanied by *H. influenza* infection. Six deaths (10.5%) were reported within 2 weeks of antimicrobial treatment. The incidence of IPI was 36.4 per 100,000 person-year, and the cumulative incidence of IPI was 0.1%, 0.4%, and 0.6% at 1-year, 5-year, and 8-year, respectively. The 8-year cumulative incidence rate of infection in the group aged under 5 years old was 14.2%, which was significantly higher than that in other age groups (0.5%, p<0.0001 by log-rank test). The relative risk of IPI in asplenia group was 37.6 times higher than that in the general population. In particular, the standardized incidence ratios (SIRs) in the age groups of 5 to 19, 20-39, and under 5 were 349.0, 342.2, and 225.8, respectively.

**Conclusions:** To our knowledge, this is the largest population-based study to show a significant increase of IPI in asplenia patients compared to the general population. Our findings reinforce that asplenia patients, especially those aged under 5 years, are at a very high risk for IPI.

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Sexually-transmitted infections detection using real-time PCR Allplex in the east coast of Spain

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**Background:** Worldwide sexually transmitted infections (STIs) stand as a major global health concern, and more than a million of STIs are acquired per day. Common bacterial agents causing STIs are: *Chlamydia trachomatis*, *Neisseria gonorrhoeae*, *Mycoplasma genitalium*, and *Trichomonas vaginalis*. The aim of this study has been to establish the prevalence of STIs in the area of Consorcio Hospital General de Valencia, Spain during a two-year period of time.

**Materials/methods:** A total of 4541 clinical specimens from different anatomical sites (urine and endocervical, pharyngeal and anal swabs) according to the reported type of sexual practices (vaginal, oral and/or anal intercourse) of 3894 participants were included in the study. Testing was performed using the multiplex RT-PCR Allplex® STI Essential Assay (Seegene, Seoul, Korea). This assay can simultaneously detect 7 STI pathogens (*C. trachomatis*, *N. gonorrhoeae*, *T. vaginalis*, *M. genitalium*, *M. hominis*, *U. urealyticum* and *U. parvum*).

**Results:** Global sexually-transmitted infection rates in our area are around 40%. In the table below there is the distribution of the different infections and the number of cases for each infection. *Chlamydia trachomatis* and *Neisseria gonorrhoeae* co-infections were detected in four cases, whereas co-infections of different species of Mycoplasma and Ureaplasma were found in more than 20% of the cases.

<table>
<thead>
<tr>
<th>Sexually-transmitted microorganism</th>
<th>Number of cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Chlamydia trachomatis</em></td>
<td>326 (8%)</td>
</tr>
<tr>
<td><em>Mycoplasma genitalium</em></td>
<td>104 (3%)</td>
</tr>
<tr>
<td><em>Mycoplasma hominis</em></td>
<td>494 (14%)</td>
</tr>
<tr>
<td><em>Ureaplasma parvum</em></td>
<td>1013 (29%)</td>
</tr>
<tr>
<td><em>Ureaplasma urealyticum</em></td>
<td>498 (14%)</td>
</tr>
<tr>
<td><em>Neisseria gonorrhoeae</em></td>
<td>188 (5%)</td>
</tr>
</tbody>
</table>

**Conclusions:** Untreated STIs can lead to serious long-term health consequences, especially for adolescent girls and young women. Testing STI with multiplex PCR allows a more accurate diagnosis and covers the main agents causing these type of infections that could not be diagnosed otherwise. This is of major importance, as nowadays we are attending to a notorious increase in the rate of sexual infections that need to be detected and treated.

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**Abstract 295**

**Characterisation of airborne fungi present in two hospitals in Kabale District, Uganda**

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**Background:** Fungi are an increasing public health problem worldwide because they have a great impact on human health and on different areas of our activities. Fungi infection are a serious threat to quality of human life. Hospital environments contain different types of microorganisms such as airborne fungi which causes fungal diseases. In the present study, the total count and diversity of airborne filamentous and yeasts fungi were investigated in indoor air of selected wards of two major hospitals in Uganda. The study also examined the proportion in fungal infection cases most commonly reported in the two hospitals.

**Materials/methods:** Samples of indoor air from Outpatient ward, Maternity, Pediatrics and Emergency wards were collected by open plate technique on Potato dextrose agar media once a week. Samples were collected in triplicates. The cultures were then examined and evaluated according to macroscopic and microscopic examination criteria for genotypic identifications. The obtained results were analyzed by SAS and Plotly software.

**Results:** A total of 22 different fungi species were isolated from the two hospitals with *Aspergillus flavus* (17.9%) followed by *Aspergillus fumigatus* (12.3%), yeast (9.6%), *Penicillium citrinum* (8.5%), as the most abundant and frequently surveyed fungal species in the two hospital while *Trichoderma*, *Nigrospora* and *P. marneffei* had the least values of spore count in all locations. All the wards showed high rates of contamination by various fungi. However, the analysis of the data showed that indoor air of OPD department (28.4%) had the highest number of fungi colonies in Kabale hospital while maternity ward (31.1%) had the highest for Rugarama hospital with the highest fungal pollution. Females also had more asthma cases for Kabale hospital with patient’s ages 6-59 years visiting the hospital for either asthma or fungi infection cases while for Rugarama hospital, fungi infection cases was more prevalent. Rainfall and relative humidity were positively correlated with high fungi load in the atmosphere of the two hospitals.

**Conclusions:** Data on the abundance/prevalence of fungi spores in hospital environment of sub-Saharan Africa is limited. Therefore, it is important to evaluate and strengthen the infection prevention practice of the hospital.

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Abstract 301

Whole genome analysis of vancomycin-resistant Enterococcus faecium causing nosocomial outbreaks suggests the occurrence of few endemic clonal lineages in Bavaria, Germany

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Background: Among clinical isolates of vancomycin-resistant Enterococcus faecium (VREfm), sequence type (ST) 117 and ST80 are highly prevalent in German hospitals and represent a frequent cause of nosocomial outbreaks. In this study, we investigated the genetic diversity of clinical isolates of VREfm recovered from different nosocomial outbreaks in Bavaria, Germany, by whole-genome sequencing (WGS).

Materials/methods: Between January 2018 and April 2019, 100 non-replicate clinical isolates of VREfm originating from nosocomial outbreaks at eight different hospitals in Bavaria were investigated for genetic diversity by WGS using the Illumina MiSeq platform (Illumina Inc., San Diego, USA) and laboratory procedures according to the manufacturer’s instructions. Afterwards, complex types (CTs) were identified by a gene-by-gene approach based on 1423 genes (core genome multilocus sequence typing, cgMLST) using SeqSphere+ software version 6.0.2 (Ridom GmbH, Muenster, Germany). Furthermore, a single-nucleotide polymorphisms (SNP)-analysis was conducted for all VREfm strains using BioNumerics 7.6 software (Applied Maths, Sint-Martens-Latem, Belgium).

Results: Most of the isolates of this study (84%) belonged to three major clonal groups: ST80/CT1065like vanB (n = 45; 6 hospitals), ST117/CT71like vanB (n = 20; 5 hospitals) and ST78/CT894like vanA (n = 19; 3 hospitals) (Figure 1). Isolates of the predominant lineage ST80/CT1065like vanB occurred in 6 different Bavarian hospitals and showed by SNP analysis a maximum difference of 34 SNPs.

Conclusions: Whole-genome analysis of VREfm causing nosocomial outbreaks suggests the occurrence of few endemic clonal lineages (ST80/CT1065like vanB, ST117/CT71like vanB and ST78/CT894like vanA) in Bavarian hospital settings.

Figure 1: Minimum-spanning-tree of all vancomycin-resistant Enterococcus faecium (VREfm) isolates of this study based on core genome multilocus sequence typing (cgMLST).

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Abstract 303

Management of tuberculosis: are the practices homogeneous in Europe?

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Background: Tuberculosis remains a global burden. This study aims to evaluate and to compare practices regarding the diagnosis, isolation and treatment of tuberculosis (TB) in Europe.

Materials/methods: A survey was conducted from November 2018 to April 2019 within the ESCMID study group for mycobacterial infections (ESGMYC). The practices observed were compared to the main international guidelines.

Results: Among 136 ESGMYC members, 58 responded to the questionnaire representing 14 countries. The participants are working in an infectious diseases (67%, n=43) or clinical microbiology (30%, n=19) department. In their practice, two (20.7%) or three sputum samples (79.3%) were collected for the diagnosis of pulmonary TB. If a patient was unable to provide a sputum sample, the alternatives were induced sputum (n = 37 / 67.2%), bronchoscopy (34 / 58.6%), and gastric aspiration (15 / 25.9%). Nucleic acid amplification tests were performed by 41 (64%) respondents whatever the smear result and by 47 (73%) in case of smear-positive specimens, to detect mutations conferring resistance to rifampicin by 84% (n= 52), to isoniazid by 29% (n=18), and to other drugs by 7% (n=4) of 62 respondents. NAAT and adenosine deaminase measurement were used for extrapulmonary TB diagnosis in 83.6% and 40.4% of cases, respectively. For isolation duration, 21 respondents (42.9%) are keeping isolation until smear negativity. An initial treatment without ethambutol was offered by 14% (n=9) of respondents. Corticosteroid therapy, cerebrospinal fluid opening pressure testing, and repeated lumbar puncture were carried out for central nervous system TB by 79.6%, 51.9% and 46.3% of the respondents, respectively. For patients with HIV-TB coinfection, the preferred antiretroviral therapy included dolutegravir 50mg BID (56.8%). For HIV-positive patients with latent TB, all respondents offered preventive treatment.

Comparing with the recommendations of the main guidelines, the practices are not totally consistent.

Conclusions: This study shows heterogeneous practices within Europe, particularly for diagnosis and isolation, although the role of rapid molecular testing seems to be important in most centers. Recent international recommendations are not followed. Better dissemination of these recommendations in collaboration with ESCMID and the promotion of studies validating good TB management practices in the European context are necessary.

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Abstract 306

Genomic analysis and exploration of putative drug resistance loci in malaria parasites

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Background: Plasmodium falciparum (Pf), the major parasite causing malaria, accounts for over 90% of malaria deaths, and demonstrates considerable resistance to current antimalarial drugs. Whole-genome sequencing can be employed to identify regions that are under high drug selective pressure, notably by looking at the single nucleotide polymorphism (SNPs), copy number variants (CNVs), and short tandem repeats (STRs). Here, we re-analysed data from a published study in which Cowell et al. set out to identify drug resistance inducing variants, which were either SNPs, CNVs or STRs.

Materials/methods: The druggable-genome dataset was downloaded from the NCBI Sequence Read Archive which contains 237 P.falciparum strains, resistant to 31 diverse compounds derived from 3 background strains: 3D7 (168), 7G8 (5) and Dd2 (64). As there is a considerable difference between the genome of 3 background strains, reads were aligned to corresponding reference genome, compared to only single reference genome (3D7) in Cowell et al. We used our in-house pipelines to re-analyse the SNPs and CNVs, and HipSTR to analyse STRs, which were not analysed in Cowell et al. Variants were then compared between isogenic parent and offspring compound-resistant clones to explore mutations possibly associated with drug resistance.

Results: Our results showed that alignment to the appropriate reference genome greatly reduces the number of variants, allowing causative variants to be better identified. We identified 305 putative drug resistance genes from 307 samples, 146 genes from Dd2 samples, and 7 genes from 7G8 samples. Among them, 68 genes were observed in multiple, independent clones, 4 of which were known drug resistance loci (pfcm, pfcr, pfmdr and pfmrp). Additionally, 17 genes were identified as associated with multi-drug resistance. Compared with Cowell et al., we have 20 putative drug resistance genes that are identical between their and our analysis, 6 genes identified only by them, and 45 genes unique to our analysis.

Conclusions: This study presents a comprehensive analysis of the different types of genomic variations to identify mutations possibly associated with drug resistance. This information can be used for the investigation of drug resistance mechanisms and help in designing combination drug therapies to overcome emerging drug-resistance.

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Abstract 314

**Fully automatic (1-3)-β-D-glucan test for the invasive fungal detection**

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**Background:** Invasive fungal disease threatens millions of human’s life every year, people are exploring the diagnosis solutions currently. Fungus (1-3)-β-D-Glucan (BG) test is a widely recommended and used technology for the detection of pan-fungal infections. However, BG test has high requirements for the personnel operation and requires very careful operation because (1-3)-β-D-Glucan is a substance that also exists in the environment. Era Biology’s FungiXpert Fully Automatic Kinetic Tube Reader (IGL-200) was introduced to make BG test automated. This technique would allow elimination of contamination origin from human operation and reduce the operational error.

**Materials/methods:** The aim of this study was to evaluate the performance of fully automatic BG test. The evaluation test was performed at Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, a total 140 serum samples were involved and collected on site. Samples were tested by both manually (performed on kinetic tube reader MB-80X) and automatically (performed on Fully Automatic kinetic tube reader IGL-200) immediately after collection. The reagent used in this program is Goldstream® Fungus (1-3)-β-D-Glucan Test (Chromogenic Method). The final detection results were compared with clinical evidences and diagnostic from hospital.

**Results:** Compared with results performed on MB-80X and fully automatic IGL-200, the total coincidence rate of IGL-200 results was 97.85% (137/140). Among the 3 inconsistent samples, one is the special hemolysis sample; one sample showed weak positive on IGL-200 and in indeterminate with manual operation. Another inconsistent sample was clinically proved to be negative but show positive on MB-80X with unknown cause, which was suspected to be the result of man-made contamination. For the experiment on IGL-200, there is no complicated procedures but only need place the reagents and samples on the rack, much easier for laboratory.

**Conclusions:** The BG test on Fully Automatic Kinetic Tube Reader IGL-200 has a high agreement rate and low contamination rate compared with manual operation. IGL-200 permits a quick result and convenient operation, benefits clinical laboratory with its high efficient and intelligent. BG test automated with IGL-200 is a significant diagnostic method.

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Abstract 318

Renal function and albumin are drivers for exposure of flucloxacillin in critically ill patients
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Background: Our objective was to describe population pharmacokinetics (PPK) of flucloxacillin in critically ill patients and to identify covariates that can explain variability in PK behavior, in order to optimize flucloxacillin dosing regimens.

Materials/methods: First, we developed a PPK model and estimated between patient variability (BPV) through non-linear mixed effect analysis, using total and unbound concentrations obtained from adult critically ill patients treated with intermittent flucloxacillin for (suspected) infections. Second, we identified covariates that could explain BPV. Third, the impact of the identified covariates on flucloxacillin exposure and probability of PK/PD target attainment (PTA, 100% ft>MIC, ECOFF S. aureus cloxacillin 0.50mg/L) was evaluated by Monte Carlo simulations and externally validated in two critically ill patient cohorts.

Results: Thirty-five patients yielded 79 total and 104 unbound flucloxacillin plasma concentrations. In a two-compartment model with non-linear protein binding, BPV of the maximum binding capacity decreased from 42.2% to 30.4% upon inclusion of serum albumin concentrations (ALB). BPV of unbound clearance decreased from 88.1% to 71.6% upon inclusion of estimated glomerular filtration rate (eGFR, CKD-EPI). The model with ALB and eGFR performed statistically significantly better than the model without covariates in the external patient cohorts: median absolute percentage error (MAPE) of population predicted concentrations decreased from 55.3 to 39.6% (p=0.004) for total and from 59.2 to 51.7% (p=0.01) for unbound flucloxacillin in the Nijmegen dataset, and from 70.3 to 33.4% (p=0.0005) for unbound flucloxacillin in the Brisbane dataset. The PTA was 91% for patients with eGFR 33ml/min and 1g q6h, 87% for patients with eGFR 96ml/min and 2g q4h and 71% for patients with eGFR 153ml/min and 2g q4h.

Conclusions: For patients with high creatinine clearance infected with moderately susceptible pathogens, therapeutic drug monitoring is advised as a risk for underexposure exists even with the currently used highest dosing regimens. When total flucloxacillin concentrations are measured and converted using protein binding values from the literature, there is a risk of underestimating unbound concentrations, especially in patients with hypoalbuminemia.

Figure 1. Simulated flucloxacillin concentration-time profiles: (A) total and (B) unbound concentrations after 1g q6h; (C) total and (D) unbound concentrations after 2g q4h.

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Rapid semi-quantitative format PCR for the detection of *Pneumocystis jirovecii* replacing the direct examination

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**Background:** *Pneumocystis jirovecii* (PCJ) is an opportunistic pathogen causing infection in immunocompromised patients. Conventional diagnostic is done on respiratory samples by microscopy. However PCR exhibits a higher sensitivity and allows accurate quantification. At the CHUV we developed a quantitative RT-PCR on our molecular platform and the PCJ DNA copy number was correlated with clinical significance ([P#2194, ECCMID 13-16 April 2019 Amsterdam, Netherlands]). However our platform has a TAT of 4 hours and is opened 5/7 days a week. We, thus decided to transfer this home-brew PCR on the rapid BD MAX™ system (BD Diagnostics) providing results in 90 minutes, 7/7 days a week. We now aimed to extrapolate PCJ quantity from the obtained BD MAX™ system Ct in order to give to clinicians a clinical significant result.

**Materials/methods:** A prospective study on 247 patient respiratory samples was performed to compare both PCR systems: quantification (Ct=copy number/ml) home-brew PCR on the platform and semi-quantification (Ct) on the BD MAX™ system.

**Results:** On 247 samples, 8 were not taken into account in our analysis due to technical problems on one or another platform. On the 239 remaining samples, 18 were not concordant due to very low quantities (high Ct value) of DNA, not corresponding to clinical significant amount of PCJ. On the 49 positive on both platforms, a good correlation (R² = 0.93) of the Ct values between the two systems was observed with an average of 0.68 +/- 1.3 Ct difference (BD MAX™ system Ct - molecular platform Ct).

**Conclusions:** These results allow us to extrapolate PCJ DNA copy number for a given Ct value obtained with the rapid BD MAX™ system allowing the clinicians to interpret a positive result according to the clinical situation. Due to these results, direct examination was stopped for PCJ and replaced by the rapid PCR system 7/7 days a week.

1- Perret et al., Ability of *Pneumocystis jirovecii* quantitative PCR to discriminate pneumocystosis from colonisation. 29th ECCMID 13-16 April 2019 Amsterdam, Netherlands, Poster #2194.

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Systemic antifungal therapy (AFT) with isavuconazonium sulfate (ISAVUSULF) or other AFT in adults with invasive mucormycosis (IM) or invasive aspergillosis (IA) caused by a non-fumigatus species (IA-nf): A multi-centre, non-interventional registry study

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Abstract third-party references: This abstract was submitted by Cello Health MedErgy, on behalf of the authors. Editorial assistance was provided by Cello Health MedErgy, funded by Astellas Pharma Global Development, Inc., Northbrook, IL, USA.

Background: ISAVUSULF is the prodrug of isavuconazole, a broad-spectrum mould-active triazole antifungal used for the treatment of IM and IA in adults. This real-life registry examined all-cause mortality (ACM) in adults treated with ISAVUSULF or other systemic AFT for IM or IA-nf.

Materials/methods: Multicentre, noninterventional registry of adult patients with proven/probable IM or IA-nf according to European Organisation for Research and Treatment of Cancer/Mycoses Study Group criteria who received systemic AFT. There were no exclusions based on liver/renal dysfunction. Cumulative data from 33 US centres for participants treated from January 2016 through November 2018 were analysed. Patients were stratified into primary ISAVUSULF, salvage ISAVUSULF for refractory infection/intolerance to another AFT or as oral step-down/maintenance, or other AFT groups (see table for group definitions). ACM was assessed at days 42 and 84 post-AFT initiation. Investigators assessed adverse drug reactions (ADRs) suspected to be related to ISAVUSULF. ADRs for other AFT were only reported during use of ISAVUSULF for non-treatment reasons (prophylaxis or empirical therapy for <4 days) (n=7).

Results: 204 patients were enrolled (104 ISAVUSULF and 100 other AFTs). Seventy-four (71.2%) received ISAVUSULF as primary AFT (24 ISAVUSULF-monotherapy and 50 ISAVUSULF-combination therapy) and 30 (28.8%) as ISAVUSULF-salvage treatment (11 monotherapy and 19 combination therapy). Baseline characteristics were similar in both ISAVUSULF and other AFT groups (Table). Most IA-nf infections affected the lungs±other organs while most IM infections were extrapulmonary (Table). Primary ISAVUSULF, salvage ISAVUSULF and other AFT day 42 ACM rates were 14.8%, 0% and 17.8%, respectively, for IA-nf and 33.3%, 20.0% and 41.3% for IM, respectively (Table). Fourteen ISAVUSULF-treated patients experienced ADRs [primary ISAVUSULF: 7/74 (9.5%); salvage ISAVUSULF: 7/30 [23.3%]; and other AFT 0/7 [0%]]. ADRs leading to ISAVUSULF discontinuation were experienced by 4/74 (5.4%) patients in the primary ISAVUSULF and 3/30 (10%) in the salvage ISAVUSULF groups. Only 3 patients developed serious ADRs: 1/74 (1.4%) and 2/30 (6.7%) in the primary and salvage-ISAVUSULF groups, respectively. No fatal ADRs were reported.

Conclusions: ISAVUSULF, either as monotherapy or combination therapy, is well tolerated, and ACM results are consistent with previous reported results in adult patients with IA-nf or IM.
### Table. Baseline characteristics, type of IA-nf or IM (single or mixed), site of infection and ACM

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Primary ISAVUSUL† (N=74)</th>
<th>Salvage ISAVUSUL† (N=30)</th>
<th>Other AFT‡ (N=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD) age, years</td>
<td>55.2 (4.7)</td>
<td>57.2 (4.6)</td>
<td>56.5 (15.6)</td>
</tr>
<tr>
<td>Male, n/N (%)</td>
<td>44/74 (59.5)</td>
<td>19/30 (63.3)</td>
<td>53/100 (53.0)</td>
</tr>
<tr>
<td>eGFR &lt;60 mL/min/1.73 m², n/N (%)</td>
<td>31/74 (41.9)</td>
<td>10/30 (33.3)</td>
<td>32/100 (32.0)</td>
</tr>
<tr>
<td>Allogeneic BMT recipient, n/N (%)</td>
<td>14/74 (18.9)</td>
<td>4/30 (13.3)</td>
<td>14/100 (14.0)</td>
</tr>
<tr>
<td>Other malignancy, n/N (%)</td>
<td>13/74 (17.8)</td>
<td>4/30 (13.3)</td>
<td>15/100 (15.0)</td>
</tr>
<tr>
<td>Neutropenia, n/N (%)</td>
<td>31/74 (41.9)</td>
<td>8/30 (26.7)</td>
<td>34/100 (34.0)</td>
</tr>
<tr>
<td>Hematologic malignancy, n/N (%)</td>
<td>35/74 (47.3)</td>
<td>11/30 (36.7)</td>
<td>39/100 (39.0)</td>
</tr>
<tr>
<td>Use of corticosteroids, n/N (%)</td>
<td>48/74 (64.9)</td>
<td>18/30 (60.0)</td>
<td>60/100 (60.0)</td>
</tr>
<tr>
<td>T-cell immunosuppression, n/N (%)</td>
<td>37/74 (50.0)</td>
<td>10/30 (33.3)</td>
<td>44/100 (44.0)</td>
</tr>
<tr>
<td><strong>Pathogen causing IFD, n/N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single IA-nf</td>
<td>27/74 (36.5)</td>
<td>8/30 (26.7)</td>
<td>45/100 (45.0)</td>
</tr>
<tr>
<td>Single IM</td>
<td>26/74 (48.6)</td>
<td>18/30 (60.0)</td>
<td>34/100 (34.0)</td>
</tr>
<tr>
<td>Mixed IA-nf</td>
<td>0</td>
<td>2/30 (6.7)</td>
<td>5/100 (5.0)</td>
</tr>
<tr>
<td>Mixed IM</td>
<td>6/74 (8.1)</td>
<td>2/30 (6.7)</td>
<td>12/100 (12.0)</td>
</tr>
<tr>
<td><strong>Site of single IA-nf infection, n/N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>14/74 (18.9)</td>
<td>3/30 (10.0)</td>
<td>22/100 (22.0)</td>
</tr>
<tr>
<td>Disseminated</td>
<td>7/74 (9.6)</td>
<td>2/30 (6.7)</td>
<td>8/100 (8.0)</td>
</tr>
<tr>
<td>Extrapulmonary</td>
<td>6/74 (8.1)</td>
<td>3/30 (10.0)</td>
<td>15/100 (15.0)</td>
</tr>
<tr>
<td><strong>Site of single IM infection, n/N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>9/74 (12.2)</td>
<td>3/30 (10.0)</td>
<td>3/100 (3.0)</td>
</tr>
<tr>
<td>Disseminated</td>
<td>5/74 (6.6)</td>
<td>1/30 (3.3)</td>
<td>10/100 (10.0)</td>
</tr>
<tr>
<td>Extrapulmonary</td>
<td>21/74 (28.4)</td>
<td>12/30 (40.0)</td>
<td>21/100 (21.0)</td>
</tr>
<tr>
<td>Unknown</td>
<td>1/74 (1.4)</td>
<td>2/30 (6.7)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Serious ADR, no. per patient/group total (%)</strong></td>
<td>1/74 (1.4)</td>
<td>2/30 (6.7)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Day 42th ACM, no. deaths/group total (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA-nf</td>
<td>4/27 (14.8)</td>
<td>0/8 (0)</td>
<td>8/45 (17.8)</td>
</tr>
<tr>
<td>IM</td>
<td>14/42 (33.3)</td>
<td>4/20 (20.0)</td>
<td>19/46 (41.3)</td>
</tr>
<tr>
<td><strong>Day 84th ACM, no. deaths/group total (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IA-nf</td>
<td>8/27 (29.8)</td>
<td>1/8 (12.5)</td>
<td>13/45 (28.9)</td>
</tr>
<tr>
<td>IM</td>
<td>17/42 (40.5)</td>
<td>5/20 (25.0)</td>
<td>23/46 (50.0)</td>
</tr>
<tr>
<td><strong>ACM with unknown pathogen, n/N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 42th</td>
<td>0</td>
<td>0</td>
<td>1/1 (100)</td>
</tr>
<tr>
<td>Day 84th</td>
<td>0</td>
<td>0</td>
<td>1/1 (100)</td>
</tr>
</tbody>
</table>

ACM, all-cause mortality; ADR, adverse drug reactions; AFT, antifungal therapy; BMT, bone marrow transplant; eGFR, estimated glomerular filtration rate; IA, invasive aspergillosis; IA-nf, invasive aspergillosis caused by a non-*fumigatus* species; IFD, invasive fungal disease; IM, invasive mucormycosis; ISAVUSUL†, isavuconazonium sulfate. Data are number with characteristic or event/total number (%) unless otherwise stated. †Non- ISAVUSUL† systemic AFT as primary therapy and received at least one dose of ISAVUSUL† against IM or IA-nf after primary AFT due to intolerance, refractory or oral step-down/maintenance. ‡ISAVUSUL† as primary therapy against IM or IA-nf. §Patients received non- ISAVUSUL† systemic AFT as primary therapy and received no ISAVUSUL† against IM or IA-nf after primary AFT due to intolerance, refractory or oral step-down/maintenance. Patients who received ISAVUSUL† as prophylaxis or empirical therapy for <4 days were included in this group. ¶Noncardiac chest pain and liver-enzyme elevation with primary ISAVUSUL†; leucopenia and hypoesthesia/paresthesia with salvage ISAVUSUL†. ‡For the ISAVUSUL† and other AFT groups, days are relative to the first dosing day of ISAVUSUL† or the primary AFT. Day 84 mortality rates are cumulative. *Patients who died or whose survival status was unknown were classified as dead.

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Abstract 334

Prevalence of the suggestion of the influenza vaccine to pregnant women among gynaecologists and obstetricians

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Background: Influenza is a systemic infectious disease and pregnancy is a factor that increases the mortality of the disease. Therefore, it is recommended that all pregnant women receive an influenza vaccine. However, rates of influenza vaccination in pregnant women are low. The aim of this study is to estimate the prevalence of Gynecologists and Obstetricians (GOs) recommending the influenza vaccine to their pregnant patients.

Materials/methods: This study was designed as a cross-sectional survey. The population of the study was calculated to be 364 people based on a 95% confidence interval and a 5% margin of error. The data were collected through a questionnaire consisting of 17 questions, distributed through a Facebook group.

Results: Of the physicians participating in the study, 43.5% reported that they recommended the influenza vaccine to pregnant women and 62.8% reported that 50% or more of the pregnant women to whom they recommended the vaccine, rejected the vaccine. According to a Multivariate Logistic Regression analysis, three factors increased the rate of physicians not recommending vaccination: their age, not having had an influenza vaccination themselves, and not knowing that the cost of the vaccine would be reimbursed. The mean age of the 384 GOs participating in the study was 39.7 ± 10.2 years.

Conclusions: Vaccinating pregnant women is necessary because of increased influenza mortality during pregnancy. Even though GOs are not vaccination practitioners in routine pregnancy follow-up, they can contribute to vaccination rates by recommending vaccination. Physicians’ application of scientific knowledge and transfer of this knowledge to their patients will contribute to increased adult immunization rates.

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Abstract 335

Risk factors for mortality in patients with pulmonary mucormycosis

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Background: Pulmonary mucormycosis (PM) results in serious burden in terms of morbidity and mortality in immunocompromised patients. However, there are limited studies with small number of patients on prognostic factors in patients with PM.

Materials/methods: Adult patients who were diagnosed with proven and probable PM according to the modified definitions of the EORTC/MSG criteria were enrolled at a tertiary hospital, Seoul, South Korea, between 1992 and 2014 (retrospectively) and 2015 and 2019 (prospectively). Proven PM was defined as positive fungal culture results for mucormycosis from lung biopsy specimens and/or histologic evidence of tissue invasion of hyphae with positive mucormycosis immunohistochemistry test result. Probable PM was defined as the presence of host and clinical factors together with mycological evidence of mucormycosis agents in non-sterile culture. Risk factors for 90-day mortality of PM were analyzed.

Results: A total of 52 patients including 34 (65%) patients with proven PM and 18 (35%) with probable PM were enrolled. The 90-day mortality rate was 46% (24/52). Neutropenia, thrombocytopenia, use of voriconazole at clinical suspicion, positivity of non-sterile culture, use of corticosteroids, and treatment without surgery were more common in fatal patients than non-fatal patients. Voriconazole use at clinical suspicion for invasive mold pneumonia (adjusted OR 7.78, \( P = 0.004 \)) and prolonged neutropenia (adjusted OR 5.45, \( P = 0.02 \)) were independent risk factors for mortality. Voriconazole use at clinical suspicion was related with positive galactomannan [GM] assay (adjusted OR 6.48, \( P = 0.01 \)) and history of invasive pulmonary aspergillosis (adjusted OR, 7.35, \( P = 0.04 \)).

Conclusions: About half of patients with PM died within 90-day of diagnosis, and these fatal outcomes were common in patients with prolonged neutropenia and empirical voriconazole use. Cautious use of voriconazole is needed even in patients with positive GM results and prior history of invasive pulmonary aspergillosis in whom PM cannot be ruled out in differential diagnosis.

TABLE. Risk factors for mortality in patients with pulmonary mucormycosis.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>( P ) value</td>
</tr>
<tr>
<td>Age</td>
<td>1.02 (0.98 – 1.07)</td>
<td>0.41</td>
</tr>
<tr>
<td>Neutropenia more than 10 days</td>
<td>6.00 (1.59 – 22.62)</td>
<td>0.01</td>
</tr>
<tr>
<td>Steroid use (any dose)</td>
<td>3.24 (1.02 – 10.28)</td>
<td>0.046</td>
</tr>
<tr>
<td>Voriconazole use at clinical</td>
<td>8.40 (2.21 – 31.88)</td>
<td>0.002</td>
</tr>
<tr>
<td>Surgery with antifungal therapy</td>
<td>0.16 (0.32 – 0.84)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

OR, odds ratio; aOR, adjusted odds ratio

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Abstract 343

Expediting antibiotic therapy management of critically ill patients with pneumonia by the detection of the main carbapenemase and ESBL-encoding genes directly from bronchoalveolar lavage

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Background: Among critically ill patients with pneumonia, the growing treat of antimicrobial resistance hampers the empirical treatment choice and relies heavily on rapid microbiological results. The detection of carbapenemase and extended-spectrum β-lactamase (ESBL) producers Enterobacterales (EB) has become a major issue among ICU patients, due to their clinical impact. Our aim was to determine whether molecular assays would expedite the detection of genes encoding carbapenemases and ESBL directly from bronchoalveolar lavage (BAL) and antibiotic therapy management in critically ill patients with pneumonia.

Materials/methods: The CRE and ESBL ELITe MGB® kits are two real-time PCR assays for the detection in less than 3h of the most prevalent carbapenemase and ESBL encoding genes in EB, respectively. From December 2018 to June 2019 all BALs of critically ill patients submitted for standard of care bacterial culture were prospectively collected. The CRE and ESBL ELITe MGB® assays were performed directly on 197 BALs sampled from 120 critically ill patients. Molecular results were compared to routine culture-based microbiological diagnostics results. A retrospective analysis of the therapeutic antimicrobial management was performed to evaluate the potential contribution of molecular assays to early optimization of empirical antibiotic therapy.

Results: Carbapenemase and ESBL encoding genes were detected in 20 (10.2%) and 12 (6.1%) BALs sampled from 15 and 11 patients, respectively. Positive (PPV) and negative (NPV) predictive values of the CRE ELITe MGB® kit were 85% [IC 95%: 64.9-94.6] and 100%, respectively. PPV and NPV of the ESBL ELITe MGB® kit were 75% [IC 95%: 49.4-90.2] and 100%, respectively. Retrospective analysis of medical records revealed that more than 50% of critically ill patients with pneumonia caused by carbapenemase- and/or ESBL-producing EB were initially treated with inadequate therapy. Overall, approximately 50% of patients could have been treated with appropriate therapy at least 24 h earlier if molecular data had been used.

Conclusions: Validity assessment of molecular assays detecting the main antibiotic resistance genes directly from BAL showed a high accuracy when compared to culture-based results. Molecular assays detecting the main carbapenemase and ESBL encoding genes provide an interesting tool for expediting appropriate antibiotic therapy in critically ill patients with pneumonia.

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Significance of candidaemia causing neonatal sepsis and efficacy of caspofungin therapy
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Background: Invasive candidiasis in extremely premature infants is the second most common cause of infectious disease-related death. The incidence of hematogenous infections due to Candida specially non-albicans species among immunocompromised neonates has increased significantly in recent decade. The emerging fungal pathogens comprising the Candida haemulonii complex are notable for their antifungal resistance with higher mortality and morbidity. Caspofungin is effective, safe and well-tolerated as an alternative therapy for persistent and progressive candidiasis in those neonates who are resistant, unresponsive to or intolerant of conventional antifungals.

Materials/methods: We here report our experience of caspofungin therapy in four cases of neonatal fungemia caused by C haemulonii. All these neonates were pre term, low birth weight with multiple invasive devices and had history of bacterial sepsis for which were on broad spectrum antibiotics. All the isolates were recovered in BACTEC Peds plus/F culture vials. Species identification was done in VITEK 2 yeast ID system. Confirmation of the species was done by PCR based molecular methods and MALDI-ToF mass spectrometry-based assay. Caspofungin therapy started with serial blood culture. Caspofungin therapy was continued two weeks after last negative culture.

Results: In all the 4 cases clinical and microbiological cure were possible. The dosage of caspofungin was 2 mg/kg/day, and the mean treatment duration was 14 days and the mean duration of antifungal therapy was 21 days. 2 out of the 4 patients had multifocal multidrug resistant (MDR) colonization and had history of azole exposure. 2 of the patients had adverse events are fever and rash. Increase of hepatic transaminases and hypokalemia was found in 1 patient.

Conclusions: The resistance of C. haemulonii represents a therapeutic challenge in the treatment of invasive candidiasis in immunocompromised neonatal patients. Caspofungin therapy is well tolerated, safe and effective in these resistant fungal infections. Caspofungin is FDA-approved for adults and children >3 months of age. These promising results suggest a potential role for caspofungin as an additional first-line treatment of systemic resistant candidiasis in immunocompromised neonates. This drug should be further investigated in this special patient population group.

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Abstract 358

**Pneumococcal vaccination introduced between the chemotherapy cycles decreases the incidence of pneumonias in patients with multiple myeloma**

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1Belarusian state medical university, Minsk, Belarus, 2Minsk scientific-practical center for surgery, transplantation and hematology, Minsk, Belarus

**Background:** Invasive pneumococcal infections (IPI) are life-threatening, but vaccine preventable complications in a range of immunosuppressed patients. Among the high-risk groups susceptible to IPI are patients with hematological malignancies receiving target treatment, novel agents and monoclonal antibodies. Novel agents to treat multiple myeloma (bortezomib, lenalidomide, ixazomib) are reported to be associated with high risk of pneumonias. The aim of the study was to assess the clinical efficacy of a 3-dose regimen of vaccination by 13-valent conjugate pneumococcal vaccine introduced in between the chemotherapy cycles with novel agents.

**Materials/methods:** Adult patients with multiple myeloma were included in this study, based at tertiary hematology and transplantation center in 2017-2019. Vaccination of adult multiple myeloma patients by 13-valent pneumococcal conjugate vaccine (PCV13) was performed during the intervals between the chemotherapy cycles with novel agents [bortezomib, lenalidomide, ixazomib]. A vaccination regimen was based on 3 doses of pneumococcal vaccine with a minimum of 1 month interval. There were totally 18 adult patients who were vaccinated by PCV13 along with 18 patients of a control group matched by age, sex, main diagnosis and treatment regimens. Incidence of clinically and radiologically confirmed pneumonias during one-year observation period was taken as a primary outcome. The study has been registered with ClinicalTrials.gov Identifier: NCT03619252. Logistic regression was performed to assess the independent effect of PCV13 vaccination on the risk of pneumonias.

**Results:** No adverse effects of vaccination were registered, while a statistically significant independent effect of 3-dose regimen of PCV13 vaccination on the incidence of clinically-radiologically confirmed pneumonias was observed (OR 0.14; 95% CI 0.02-0.93; p=0.041). Number needed to treat (NNT) for PCV13 vaccination in multiple myeloma patients receiving novel agents was 3.0 (95% CI 1.61-22.10; p = 0.0571).

**Conclusions:** Despite the expected decrease in response to vaccination during the chemotherapy with novel agents, we have shown the clinical effectiveness of PCV13 vaccination schedule based on 3 doses given with a minimum 1 month interval between the chemotherapy cycles. Further implication of pneumococcal conjugate vaccines in adult immunocompromised patients may serve as a basis for decrease in frequency of pneumonias.

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Resolving within-host, full length, dengue virus variants without haplotype reconstruction using Oxford Nanopore Technology

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Background: Despite the advances in sequencing technologies and the small size of RNA viral genomes, identifying full-length within-host viral variants has been a challenge. Previously we developed a protocol for full-length dengue virus sequencing (single molecule) using Oxford nanopore technology (ONT). Now, we introduce a new bioinformatic pipeline to resolve full-length within host dengue variants from ONT sequences.

Materials/methods: This pipeline takes an alignment of ONT reads as the input, selects reads with a user-defined length and a starting codon, cleans them of indels and mismatches using a reference sequence and the quality scores at each base position. A hierarchical clustering algorithm is used to identify phylogenetically close read clusters to create a consensus per cluster (a within host variant). The final output of the pipeline is a list of within host variants and their relative abundance as a percentage. The accuracy of the pipeline was tested using in silico clonal mixtures of the hepatitis C virus.

Results: Forty clinical dengue samples were sequenced with ONT after multiplexing with either PCR based barcodes or ligated barcodes. Of these, only 19 samples had more than 100 reads (range 105 – 17,672) greater than 10kb after the initial cleaning steps of the algorithm (arbitrary lower limit to proceed to full pipeline). The number of within host variants detected ranged from 2-27 per sample with 2-3 dominant variants and the rest being minor variants. The number of minor variants identified depends on the total read count used (figure 1). More variants can be detected with increasing the input DNA, avoiding multiplexing or multiplexing with ligation barcoding.

Conclusions: This pipeline, combined with our method for pan-serotypic dengue full length genome amplification, offers the capacity to resolve within host viral variants without haplotype reconstruction for the first time for dengue virus (and for any RNA virus with a single open reading frame). This creates a new front in understanding within host viral evolution, closely related human to human transmission events and virological determinants of virulence in dengue.

Figure 1. Detected minor variants (<5% abundance) increases linearly with the input number of reads.

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Molecular characterisation of Staphylococcus aureus clinical strains from endotracheal tubes of patients with intensive care unit-acquired pneumonia

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Abstract

Background: Staphylococcus aureus is among the most frequently isolated microorganism responsible for intensive care unit (ICU)-acquired pneumonia of which 29% are resistant to methicillin (MRSA). Our aim was to determine the antimicrobial susceptibility, the associated molecular mechanisms of resistance and the epidemiology relatedness of S. aureus strains from the endotracheal tubes (ETT) of intubated critically ill patients with S.aureus ICU-acquired pneumonia.

Materials/methods: Clinical S. aureus (17 MRSA and 3 methicillin susceptible S. aureus) were collected from ETTs after extubation during a prospective observational study carried out in four European tertiary hospitals. Antimicrobial susceptibility test, using the Kirby-Bauer method was performed to vancomycin, linezolid, ciprofloxacin, clindamycin, erythromycin, chloramphenicol, fusidic acid, gentamicin, quinupristin-dalfopristin, rifampicin, Sulfamethoxazole/trimethoprim, and tetracycline. Interpretation of results was carried out according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Molecular characterization of each resistance mechanism was screened by PCR, electrophoresis and sequencing. Molecular epidemiology was analyzed by Multi locus sequence typing. Phylogenetic analysis was carried out using comparative eBURST V3 software [http://www.phyloviz.net/goeburst]

Results: S. aureus isolates were resistant to ciprofloxacin (85%), erythromycin (65%), gentamicin (35%), tetracycline (30%), clindamycin (20%), and fusidic acid (5%). Three strains showed hetero-resistant subpopulations to linezolid. The most frequent mutations in ciprofloxacin resistant S. aureus strains were S84L in the gyrA gene, V511A in the gyrB gene, S144P in the grlA gene, and K401R/E in the grlB gene. Strains resistant to erythromycin carried the ermC, ermA, and msrA genes; the same ermC and ermA genes were detected in strains resistant to clindamycin. The aac(6')-aph(2") gene was related to gentamicin resistance, whereas resistance to tetracycline was related to tetK (efflux pump). The fusB gene was detected in the strain resistant to fusidic acid. The most frequent sequence types were ST22, ST8, and ST23. These were distributed in four clonal complexes (CC5, CC22, CC45, and CC59).

Conclusions: High levels of resistance to second-line antimicrobials threatens the treatment of ICU-acquired pneumonia due to methicillin-resistant S. aureus, with decreased susceptibility to linezolid and vancomycin. The wide genotypic diversity found, even within the same ICU, reinforces the crucial role of ICU prevention bundles in cross-transmission.

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Impact of biocide residues on *Escherichia coli* antimicrobial susceptibility
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**Background:** There is no standardised approach to predict the residues of biocides remaining on surfaces as a result of the use of disinfectants, nor is there a standardised way to predict the potential risk that these levels might pose to antimicrobial resistance. Although of practical relevance, bacterial selection and adaption to biocide surface residues has not been fully investigated to date. This study explores links between exposure effects of chlorhexidine at concentrations found on surfaces post-application and changes in phenotypes and the metabolome in *E. coli*.

**Materials/methods:** Chlorhexidine (CHX) surface concentration post-treatment was determined by High-Performance Liquid Chromatography. A modified standard efficacy carrier test was used against five genotypically distinct *E. coli* exposed to in-situ concentrations of CHX. Minimal inhibitory concentrations (MIC), antibiotic susceptibility profiles, efflux activity, and conjugal plasmid transfer were assessed and compared before and after exposure to CHX. Changes in susceptibility after CHX exposure were investigated for stability. The effect of CHX exposure on the broader phenotype was assessed using the OmniLog microarray (BioLog, US).

**Results:** CHX surface concentration post-application was on average 0.006 mg/mL after 0-7 days. CHX susceptible bacteria survived exposure to this residual concentration and were shown to adapt through metabolic alterations, such as those responsible for cell wall biosynthesis, along with transient insusceptibility to CHX, imipenem and cefoxitin, and stable resistance to amoxicillin/clavulanic acid, ampicillin, cefpodoxime and cefotaxime. Results show that a transiently adapted population may be selected amongst less tolerant sub-populations. CHX however did not increase transfer of ampicillin resistance at a residual concentration and prevented conjugal transfer at a concentration of 0.002 mg/mL.

**Conclusions:** CHX has the potential to promote the emergence of resistance and cross-resistance at concentrations found on surfaces after disinfection. Findings in this study warrant further investigation into residual concentrations of biocides found in the environment, their effects on common pathogens and potential markers for the risk of resistance development as a result of exposure.

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Abstract 379

**Staphylococcus aureus bloodstream infection: can the practice of the VIRSTA score replace the infectious disease consultation in case management?**

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**Background:** *Staphylococcus aureus* bacteremia (SAB) causes life-threatening complications such as infective endocarditis (IE). Although de SAB management is well codified, its mortality remains high. The VIRSTA score was developed to guide physicians in the management of SAB, improve outcomes and risk stratification of IE. In this framework, the role of the infectious disease specialist has yet to be specified. Our primary objective was to assess whether an early infectious disease specialist consultation (IDC) could improve the management and outcomes of SAB. Our secondary objectives were to evaluate the adequacy of clinical practices to the VIRSTA score by ID and non-ID management.

**Materials/methods:** We performed a retrospective cohort study, in a 800-bed teaching hospital, in Reunion Island, over a one-year period in adult patients with SAB (≥1 positive blood culture with SA). Clinical practice was deemed adequate to VIRSTA score when no transesophageal echography (TEE) but only one transthoracic echography (TTE) was performed for scores ≤2 and when either one TEE or two TTE were performed for scores ≥3.

**Results:** Fifty-two SAB were included of which 73.1% were of nosocomial origin, and 90.4% were methicillin sensitive. ID specialists were solicited for 28 (53.9%) patients, in an average time of 3.3±6.6 days. ID specialists tended to be more often solicited when blood cultures remained positive beyond 48 hours (**P**=0.054). A TTE (OR 91.00, 95%CI: 1.389-595.97) and a control TTE (**P**=0.005) were more likely when an ID specialist managed the infection.

Antibiotic treatment was more appropriate when the patients benefited from an IDC (OR 25.00, 95%CI: 5.50-113.46). Clearance of bacteremia was more likely achieved after ID management (OR 4.28, 95%CI: 1.13-16.27).

Patients who benefited an IDC had a decision more likely conform to VIRSTA score (OR 4.60, 95%CI: 1.31-16.14). An IDC was associated with protection against the risk of death within three months (OR 0.26, 95%CI: 0.06-0.98).

**Conclusions:** Our study supports a central role of the ID specialist in the management of patients with SAB, this being associated with better outcomes and respectful of up-to-date guidelines. The VIRSTA score, when applied early could help the diagnostic strategy of SAB before the IDC.

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Neural networks for prediction of minimum inhibitory concentration
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Background: Antibiotic resistance is listed by the World Health Organization as one of the biggest threats to global health and causes about 33 000 deaths, in the EU/ESS region only, each year. Lately, several machine learning methods have been purposed for autonomous resistant profiling of bacteria and this work aims to use neural networks for prediction of minimum inhibitory concentration (MIC).

Materials/methods: We have developed a neural network based machine learning model for prediction of minimum inhibitory concentration (MIC) from k-mers extracted from whole-genome sequencing. To handle the curse of dimensionality associated with k-mers we perform dimensionality reduction through principal component analysis. The dataset used consists of 4964 Salmonella samples with MICs measured, for up to 15 antibiotics, for each sample. All MICs were measured on a 2-fold dilution. The evaluation of the model was done using a 5-fold cross validation.

Results: For prediction of exact MIC the accuracy of our model varied from 0.61 for streptomycin to 0.93 for tetracycline with an average for all antibiotics of 0.78. When translating the MICs to labels, S/I/R, our model had an average accuracy of 0.97. Further, the model was compared to already existing machine learning model trained on the same dataset. Our model outperformed the already existing machine learning model when it comes to predicting exact MIC for 13 of the 15 antibiotics considered. Greatest improvement were for the antibiotics ampicillin, amoxicillin-clavulanic acid and tetracycline.

Conclusions: We conclude that our neural network outperforms the other machine learning model and yields a great improvement when it comes to accuracy. This is somewhat expected since neural networks tends to be the superior model in other areas such as image processing and natural language processing. The results also illustrates the complexity of predicting exact MIC. Comparing the exact accuracy to the accuracy for S/I/R of the model, which on average was 0. 97, we observe a vast improvement which shows that prediction of S/I/R is a more feasible and simpler problem compared to prediction of exact MICs.

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Abstract 387

A k-mer-based approach for MLST and cgMLST analysis of nanopore sequenced Staphylococcus aureus
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Abstract third-party references: 1928 Diagnostics

Background: Genotypic typing, such as MLST or cgMLST, is an important tool for infection control and is typically used today in combination with NGS data. However, one disadvantage of using NGS is the slow sample-to-result turnaround time, which can amount to several days. With the advent of Nanopore sequencing, it is possible to rapidly generate sequencing data at the expense of higher error rates, which could speed up the analysis and potentially revolutionize the field of clinical infection control.

Materials/methods: Eight double-sequenced bacterial samples (Illumina + Nanopore, Staphylococcus aureus, EMBL-EBI project PRJDB8599) were analyzed with MLST and cgMLST. The goal was to evaluate the ability to predict sequence types [STs] and cluster samples based on cgMLST profiles using only Nanopore data. Here, the Illumina data was used as a reference to verify the results. The raw Nanopore reads were analyzed in a custom, kmer-based bioinformatic pipeline and the Illumina reads were analyzed in the 1928D platform (https://1928diagnostics.com/). One of the samples was discarded due to a contamination and the remaining seven samples were included in the full analysis.

Results: The results from the MLST analysis showed that five samples had the same ST prediction between the two platforms. The remaining two samples were classified as novel STs by the 1928D platform, which was consistent with the Nanopore analysis, as these samples did not have any ST hit with full kmer-coverage. As for the cgMLST analysis, different kmer-sizes were used and the similarity to the Illumina result was calculated. A smaller kmer size decreased the allele prediction accuracy and the opposite was true for larger kmer sizes. The distances between samples were, however, different when comparing Illumina to Nanopore regardless of the kmer-size. This was mainly due to novel cgMLST alleles, which could be accurately detected in Illumina data only.

Conclusions: These results show a proof of concept that a kmer-based approach for MLST and cgMLST analysis of Nanopore sequenced Staphylococcus aureus is possible. However, a lot of effort needs to be directed towards improving the data quality in order to generate results accurate enough for the clinical setting.

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Abstract 395

The economic burden of *Clostridioides difficile* infection in patients with haematological malignancies: a case-control study

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**Background:** The burden of *Clostridioides (Clostridium) difficile* infection (CDI) is profound and patients with haematological malignancies are at high risk for developing the infection. Very few studies have assessed the economic burden of CDI in this specific population, whereby primarily hospital costs were analyzed. This study aims at describing all direct healthcare costs attributable to CDI (in-hospital and out-of-hospital) in patients suffering from haematological malignancies.

**Materials/methods:** A retrospective analysis was conducted based on databases of Truven Health Analytics®, part of the IBM Watson HealthTM business. Comprehensive data of hospital stays and services, out-of-hospital services and drug prescriptions of patients newly diagnosed with haematological cancer (acute myeloid leukemia [AML], acute lymphoblastic leukemia, Hodgkin’s lymphoma and non-Hodgkin lymphoma [NHL]) between 01/2014 – 12/2017 were analyzed. Patients with CDI after cancer diagnosis (CDI+ or cases) were matched to patients without CDI (CDI- or controls). Matched cases and controls were compared to identify the CDI-attributable costs and changes in care in the 90 days following the CDI onset (study period).

**Results:** 622 CDI+ patients were matched with 11,111 controls. NHL and AML were the predominant underlying diseases in the CDI+ group accounting for 41.7% and 30.9% of cases, respectively. Overall, CDI increased costs of care by an average of US$57,159 per patient, an increase of 41.9%, mainly driven by in-hospital costs. Costs data are presented in Table 1.

**Conclusions:** Findings confirm that CDI treatment results in substantial costs in patients with haematological malignancies, highlighting the need for better treatment and prevention options for this specific patient population.

Table 1: Healthcare costs per patient

<table>
<thead>
<tr>
<th>Healthcare costs, (over study period, 2017 US$)</th>
<th>CDI+</th>
<th>CDI-</th>
<th>Difference</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In-hospital</strong></td>
<td>Mean (95% CI)</td>
<td>151,208 (136,679 - 165,738)</td>
<td>98,552 (95,696 - 101,207)</td>
<td>52,657 (37,887 - 67,427)</td>
</tr>
<tr>
<td><strong>Out-of-hospital services</strong></td>
<td>Mean (95% CI)</td>
<td>37,612 (34,083 - 41,141)</td>
<td>34,850 (33,691 - 36,010)</td>
<td>2,762 (-952 - 6,476)</td>
</tr>
<tr>
<td><strong>Out-of-hospital drugs</strong></td>
<td>Mean (95% CI)</td>
<td>4,704 (4,003 - 5,404)</td>
<td>2,963 (2,802 - 3,125)</td>
<td>1,740 (1,021 - 2,460)</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>Mean (95% CI)</td>
<td>193,524 (178,527 - 208,521)</td>
<td>136,365 (133,390 - 139,340)</td>
<td>57,159 (41,870 - 72,448)</td>
</tr>
</tbody>
</table>

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Abstract 411

The first report of concurrent infections by two dengue serotypes among tribal population in central India
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Background: Dengue is spreading to newer areas in the world, including India. Concurrent infection by multiple serotypes are documented in certain areas in India, but not in tribal areas. We investigated an outbreak occurred in a tribal area in central India, during months of August to September 2015. We report markedly high percentage of concurrent infections by 2 dengue serotypes first time among tribal population in India.

Materials/methods: Acute phase sera samples were collected from 746 patients and tested for NS1 ELISA and MAC-ELISA. NS1 positive samples were subjected to serotyping by real time RT-PCR.

Results: of 746 samples tested, 167 (49.4%) were positive for NS1 ELISA while 171 (50.6%) were for MAC-ELISA. Positive NS1 samples were tested for serotyping, all 4 serotypes were found to be circulating in the outbreak, with predomination of DEN-3 serotype. Moreover, concurrent infections by 2 serotypes were observed in 26.2% of cases.

Conclusions: Dengue outbreak in tribal villages of Sukma district in central India experienced all 4 serotypes and concurrent infections, where health authorities never perceived dengue as a major health concern. Thus this outbreak emphasizes on continuous active surveillance to monitor spread of dengue virus, especially in hard to reach areas, so that effective vector control programme could be implemented at the earliest to prevent outbreaks.

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Abstract 414

A descriptive study of tuberculosis hospital admissions in Ireland
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Background: Ireland is a low incidence tuberculosis country with 6.6 cases per 100,000 population in 2018. The last reform of TB services in Ireland was in 2003. It was recommended that most TB management should be delivered on an outpatient basis in general hospitals with a small number of beds allocated in 3 hospitals for inpatient management. This resulted in 3 hospitals (Cork University Hospital, University College Hospital Galway, St. James’s Hospital, Dublin) being designated as TB centres. Evaluating resource utilisation by patients admitted to hospital with TB may provide insight into how TB service organization could be improved.

Materials/methods: The Hospital In-Patient Enquiry (HIPE) system is a computerized health information system designed to capture hospital activity data. It is the principal source of demographic and clinical data on inpatient discharges from public hospitals in Ireland. The National Quality Assurance and Improvement System (NQAIS) Clinical is an online interactive application that analyses hospitals’ own HIPE data. The NQAIS Clinical was searched for all TB discharges between 01/01/2015-31/12/18. An estimate of the projected cost of respiratory TB admissions was calculated using the Healthcare Pricing Office Admitted Patient Price List 2019.

Results: 1185 discharges with TB as the principal diagnosis were identified. 802/1185 (68%) of admissions were emergencies and 383/1185 (32%) were elective. Most emergency admissions, 735/802 (92%), were discharged after an overnight stay of at least one night while the remainder 67/802 (8%) were same day discharges. In total, 16,005 bed-days were used by patients with a principal diagnosis of TB, an average of 4,001 bed-days per annum. This equates to an average of 12.8 bed-days per notified case of TB. The ten longest emergency admissions made up only 10/802 (1.2%) of admissions but 1,935/14,072.5 (13.8%) of emergency bed-days used. We estimate that between 67% (834/1248) and 74% (928/1248) of TB cases notified were admitted to hospital. We estimate that between 78% (653/839) and 87% (729/839) of respiratory TB cases notified were admitted to hospital. The projected cost of respiratory TB admissions for 2019 is €1,813,346-2,413,137.

Conclusions: There is a significant burden on the acute hospital inpatient service due to TB.

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Abstract 418

The INHALE trial: designing a prescribing algorithm to aid antibiotic choices for the FilmArray Pneumonia Panel Plus

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Background: The NIHR-funded INHALE Programme aims to improve antimicrobial stewardship through molecular diagnostics for HAP/VAP in ICUs. Its first phase selected the BioFire FilmArray Pneumonia Panel as the best-performing relevant test, and this is now deployed at point of care (POC) in 12 UK ICUs, with patients randomized to FilmArray-guided or Standard antimicrobials. The test seeks 34 organism and gene targets, providing results in 1.5h. The results’ complexity, combined with rapid round-the-clock availability, prompted us to design an antimicrobial prescribing algorithm to support clinicians at the point of decision. To our knowledge, this is the first instance of prescribing advice being directly linked to a rapid PCR test.

Materials/methods: We designed the algorithm based on (i) organism and resistance gene targets detected alone or in combination, (ii) national resistance surveillance data and (iii) patient’s allergy status. Narrow spectrum agents were preferred, and good antimicrobial stewardship encouraged. Site microbiologists, ICU pharmacists, and ICU clinicians were consulted and local adaptation allowed.

Results: Where single organisms are found the algorithm favours, e.g. temocillin vs. Enterobacterales, flucloxacillin vs. MSSA and co-amoxiclav vs. Haemophilus influenzae; discontinuation is advised if no organism is found and the patient lacks convincing evidence of infection; broader spectrum agents are favoured for combinations of organisms. Among 10 adult sites, 4 adopted the algorithm essentially unaltered and 2 with minor variation only. Common concerns were: unwillingness to adopt: (i) temocillin for Enterobacterales; (ii) ceftazidime vs. Pseudomonas; or (iii) cephalosporins for patients with mild β-lactam allergy. There was considerable debate apropos infection control implications of ICU-based (rather than laboratory-based) detection of carbapenemase producers. Substantial variation was needed at 2 paediatric ICUs, principally because temocillin lacks a paediatric licence.

Conclusions: Prescribing algorithms such as this will ensure that potential benefits of rapid syndromic tests are realised at POC. Whilst it was not possible to impose a single algorithm at all hospitals, core elements and principles were retained. An early audit of RCT results indicates that most test-arm treatments are being guided by the algorithm, as sought. The sites’ willingness to adopt this approach illustrates the potential for a major shift to molecular-guided chemotherapy.

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Abstract 419

Is it cost effective to use a 2% chlorhexidine gluconate wipes bath to reduce primary bloodstream infection? A quasi-experimental study experience

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Background: Bathing with 2% chlorhexidine (CHG) wipes is an important measure regarding infection prevention in critically ill patients. At our ICU, central line-associated bloodstream infections rates (CLABSI) was higher than expected (9.05/1,000 central line-days) and as an additional measure were introduced a daily bathing with 2% CHG wipes. The aim of the study were to evaluate the impact of introducing the CHG wipes bath in CLABSI prevention and determine if such measure is cost-effective.

Materials/methods: Quasi-experimental study with pre-intervention period from July 2017 to May 2018, and intervention, June 2018 to April 2019. Were evaluated the CLABSI rate, the costs with guided antimicrobials for proven CLABSI, and CHG wipes. Antimicrobials (ATM) given empirically at the suspicion of the CLABSI were not evaluated.

Results: Were observed a reduction in CLABSI rates in the intervention period (9.05 to 1.35/1,000 central line-days; P= 0.01), mainly due to Kp-KPC BSI (P= 0.05) decrease and a substantial cost reduction with guided antimicrobials (US$ 45,278.93 to US$ 1,799.82 in intervention period). The average monthly consumption of CHG wipes in the ICU were 190 towels/month, with unit value of US$ 14.20, generating a monthly cost of US$ 2,698.00. The total costs (guided ATM plus CHG wipes) are shown on TABLE 1.

Conclusions: The introduction of daily bath with 2% CHG wipes at our ICU was effective in CLABSI reduction, being a good cost-effective measure, saving 30% of total costs.

TABLE 1 - Pre-intervention & Intervention period, Costs (US$) x CLABSI rates

*total costs = CHG wipes plus guided ATM

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Abstract 425

**Persistence of high-risk clones of carbapenem-resistant Klebsiella pneumoniae in a tertiary hospital in Valencia, Spain**

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**Background:** High-risk clones of Klebsiella pneumoniae have contributed to the spread of mobile genetic elements among Enterobacteriaceae. The aim of this study is to characterize carbapenem-resistant K.pneumoniae strains and to determine clonal relationship among them.

**Materials/methods:** Bacterial identification was performed by mass spectrometry, whereas antimicrobial susceptibility testing was obtained using the MicroScan Walkaway system [Beckman Coulter]. Carbapenem-resistant strains were selected. Phenotypic methods for the detection of carbapenemase production included beta-carbatest [Biorad] and disk-synergy test [Rosco Diagnostica]. Isothermal amplification with Eazyplex Superbug system [Amplex] was performed to genotypically determine carbapenemase genes. Clonal studies with pulse-field gel electrophoresis included all the strains that shared similar features. Strains belonging to predominant clones were sequenced using next-generation sequencing (NGS). Data from NGS provided information regarding sequence-type, plasmid-typing and resistance genes.

**Results:** 130 strains were submitted to NGS. Data regarding clones, resistance genes, STs and plasmid replicons is shown in the table below:

<table>
<thead>
<tr>
<th>Nº of Strains</th>
<th>Years</th>
<th>CLones</th>
<th>MLST</th>
<th>Carbapenemase</th>
<th>CTX-M</th>
<th>DHA-1</th>
<th>SHV</th>
<th>Others</th>
<th>Replicons</th>
</tr>
</thead>
</table>

**Conclusions:** During four years, five different clones of K.pneumoniae, belonging to three different sequence-types have been circulating in the same hospital. Interestingly, there are differences between the carbapenemase genes detected in 2015 and those detected in 2018, even in the same sequence-type, suggesting that the same clone acts as a recipient and as a donor for resistance determinants, depending on the environmental situation they are found in each time. Non beta-lactam antibiotics are also enormously affected by resistance to carbapenems, as resistance genes to different antimicrobials are usually found in the same plasmid.

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Abstracts 2020

Abstract 428

**Doramapimod treatment inhibits granuloma formation and improves antibiotic activity in *Mycobacterium tuberculosis*-infected mice**

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**Background:** *Mycobacterium tuberculosis* (*Mtb*), the causative agent of tuberculosis (TB), is the major killer among infectious agents which led to 1.5 million deaths in 2018. Treatment of TB requires combinations of antibiotics for several months, a strategy which becomes increasingly complicated in times of rising numbers of multi-drug resistant *Mtb*-isolates. Adjunctive host directed therapy (HDT) might improve and accelerate treatment by modifying host pathways targeted by *Mtb*. We have recently shown that genetic or chemical inhibition of p38 mitogen-activated protein kinase (MAPK) results in abrogation of *Mtb*-induced host cell death and decreased release of inflammatory alarmins such as High-Mobility-Group-Protein B1 (HMGB1) ex vivo.

**Materials/methods:** To evaluate the potential of p38 MAPK inhibition as an adjuvant treatment for TB and to determine the risk for exacerbation of the disease during monotherapy, we analyzed the outcome of experimental TB under p38 MAPK inhibition and antibiotic treatment during acute and chronic infection of C57BL/6 mice.

**Results:** We show that treatment of *Mtb*-infected C57BL/6 mice with doramapimod, a p38 MAP-kinase inhibitor, results in reduced inflammation, granuloma formation and lung pathology. Moreover, doramapimod, together with a standard antibiotic treatment significantly reduced lung and spleen mycobacterial loads compared to antibiotic treatment alone.

**Conclusions:** Our data suggest the opportunity to repurpose p38 MAPK inhibitors for adjunct host directed therapies. We also provide first data on safety of p38 MAPK inhibition which is of relevance for future application of these substances in inflammatory diseases and concomitant TB.

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Abstract 429

**Late-onset *Pneumocystis jirovecii* pneumonia in renal transplant recipients**

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**Background:** The risk of *Pneumocystis jirovecii* pneumonia (PJP) in solid organ transplant patients is 5-15%, with highest risk at 6-12 months post-transplantation. There has been an increase in the number of cases seen much later post-transplant. We describe 7 patients presenting with PJP over 6 months post renal transplant during the period March 2018 thru April 2019. All these patients had their renal transplant and follow-up care at our institution.

**Materials/methods:** Renal transplant recipients (RTR) presenting with PJP in 2018 and 2019 were retrospectively studied. Definitive diagnosis of PJP was defined as positive PJP stain from BAL. Patients with positive PJP PCR, elevated serum \(1 \rightarrow 3\) \(\beta\)-D-glucan (BDG), elevated serum LDH were also included as possible diagnosis of PJP. Period from renal transplant to development of PJP, clinical presentation and severity of disease, immunosuppression and level of immunosuppressant, presence of rejection, treatment and clinical outcomes were included.

**Results:** All but 1 patient developed PJP at least two years after their kidney transplant. None of the patients was receiving PJP prophylaxis at the time of diagnosis. Mean period between transplant and infection was 4024 days. Five patients presented with atypical pneumonia and 2 had hypoxic respiratory failure. Four patients had definitive diagnosis of PJP and 3 had possible diagnosis of PJP. Five patients were cured and 2 patients died despite treatment and modification of immunosuppression; these patients also had the highest levels of LDH.

**Conclusions:** *P. jirovecii* should be considered as a cause of atypical pneumonia and/or hypoxic respiratory failure, in RTR receiving immunosuppression who are no longer on PJP prophylaxis. Nosocomial outbreaks of PJP infection should be considered in RTR who present with PJP late into their transplant.

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Multidrug resistant Gram-negative infections among critically ill patients: analysis of baseline characteristics and factors associated with mortality

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Background: Bacterial infections are a frequent cause of hospitalization and a leading cause of death particularly with the emergence of antibiotics resistance. The emergence of Carbapenem resistance among gram negative bacteria (GNB) is one of the evolving alerts as its use is considered the last resort of treatment. Therefore, this urged studying the risk factors for development of multi-drug resistant (MDR) GNB, identify the clinical outcomes and factors associated with mortality especially among critically ill patients who are expected to have the worst outcomes.

Materials/methods: This is a retrospective observational study of critically ill patients who had an infection with Carbapenem-resistant Enterobacteriaceae (CRE), or MDR Pseudomonas aeruginosa, or MDR Acinetobacter spp. between May 2016-Nov 2018. Baseline demographics, co-morbidities and clinical outcomes were collected, and were evaluated for association with 28 days mortality. Approval of the research was obtained from the Institutional Review Board (IRB) before commencement of the study.

Results: A total of 255 patients with MDR Gram-negative cultures were screened, 77 patients met the inclusion criteria. Pseudomonas aeruginosa was the most common index organism (53% of patients), followed by Acinetobacter spp. and CRE, respectively. 28 days mortality was (59.7%). Non survivors were significantly older (mean age 64 vs 44 years, P= 0.0001), had significantly worse disease severity scores on ICU admission, higher incidence of chronic kidney disease (CKD) (43% vs 16%, P= 0.010), and required more continuous renal replacement therapy (CRRT) (54% vs 13% P= 0.0001), longer hospital length of stay prior to infection (median 34 vs 13 days, P= 0.018), required longer inotropic and vasopressors support (median 19 vs 8 days, P = 0.0001). In multivariate logistic regression the following factors were significantly associated with mortality; requirement of inotropic support post infection [OR 10.01 (95% CI 1.55-64.77); P= 0.015], age [OR 1.05 (95% CI 1.0- 1.1); P=0.01], and APACHE IV score on ICU admission [OR 1.03 (95% CI 1.0- 1.06); P = 0.04].

Conclusions: MDR Gram-negative infection is associated with significant in-hospital mortality among critically ill patients. Old age, high APACHE IV score, and higher hemodynamic support are associated with higher mortality.

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**Background:** Substantial scientific evidence has accumulated that contamination of environmental surfaces in hospitals plays an important role in the transmission of Multi-Drug-Resistant-Organisms (MDRO). In this work, we propose to assess the overall risk of environmental dissemination of different MDRO, by evaluating the contamination of the environment, taking into consideration the individual risk factors together with the microbiological aspect of resistance.

**Materials/methods:** We conducted a prospective cohort study from May 2018 to May 2019. We included 91 patients admitted to Avicenne Hospital, older than 18, carriers of MDRO (BLSE-PE, CPE, VRE); known at admission or detected in the first 48 hours. Rectal and environmental sampling were realized. For each patient, we did a quantification of MDRO in stool, a qualitative evaluation of presence of MDRO in 4 different environmental sites and collected data including demographic characteristics, ward and duration of hospitalization, antibiotic administration, Charlson’s score of comorbidities, Katz’s score of dependence, nursing procedures, urinary/fecal incontinency, MDRO species and mechanisms of resistance.

**Results:** Fifty-three (58%) patients were admitted in a medical ward, 11 (12%) in surgery and 27 (30%) in ICU. MDRO were *Escherichia coli* (52%), *Klebsiella pneumoniae* (36%), *Enterobacter cloacae* (4%) and *Enterococcus faecium* (8%). Resistance mechanisms of detected MDRO were ESBL (41%), OXA48 (51%) and VanA (8%). Contamination of at least one environmental site was observed for only 14 (15%) patients: 36% (n=5) ESBL-PE, 36% (n=5) CPE and 28% (n=4) VRE. We didn’t find any statistically significant difference in age, sex, wards of admission, duration of hospitalization, Charlson’s score, Katz’s score, antibiotic consumption, recent stay abroad and interestingly relative abundance of MDRO in stool, between the group of patients having contaminated their environment (15%) and those who have not (85%). However, only VRE, among the other MDRO, appeared to colonize significantly more the patients who contaminated their environment (15%) and those who have not (85%). However, only VRE, among the other MDRO, appeared to colonize significantly more the patients who contaminated their environment (p=0.009).

**Conclusions:** Our preliminary study shows that only VRE colonized/infected patients seemed to be associated with a higher risk of spreading in the environment. Although this result needs to be confirmed on a larger scale, it raises questions about our national policies for contact isolation.

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Abstract 437

Dynamic monitoring of sTREM-1 and other biomarkers in biliary tract infection
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Background: Sepsis is a common complication of biliary tract infection (BTI), which is associated with high mortality. We explored the significance of white blood cell (WBC), C-reactive protein (CRP), procalcitonin (PCT), soluble triggering receptor expressed on myeloid cells 1 (sTREM-1) and temperature (T) alone or combined together in early identification of BTI with or without sepsis and the monitor of treatment effect.

Materials/methods: 65 cases with BTI and 76 control cases were divided into three groups: Group A (BTI patients with sepsis), Group B (BTI patients without sepsis) and Group C (individuals without BTI or other infection). We dynamically measured the levels of WBC, CRP, PCT, sTREM-1 and temperature of all study subjects. Comparisons between groups were made using Non-parametric test. Receiver operating characteristic (ROC) curves were established to evaluate the diagnostic value for discriminating among three groups above. The cutoff values, area under curves (AUC) with corresponding 95% confidence intervals (CI), and sensitivity/specificity at optimal cut-off were calculated. Spearman rank correlation analysis was used to explore correlations between sTREM-1 and WBC in three groups.

Results: CRP had the highest AUC to identify BTI and sepsis from healthy controls (AUC = 1; sensitivity 100%; specificity 100%). Among various single indexes, PCT performed best (AUC = 0.785; sensitivity 75.8%; specificity 72.2%) to distinguish sepsis in patients with BTI. While combined multi-biomarkers didn’t perform better. From day 1 to day 5 of hospitalization, the levels of sTREM-1 in Group A were highest (P<0.05); on day 8, sTREM-1 levels in Group A and B declined back to normal. Both in Group A and B, sTREM-1 levels declined fast between day 1 and day 2 (P<0.05). The results of dynamic monitoring of WBC, CRP, PCR, T and sTREM-1 in three groups were shown in Figure 1.

Conclusions: CRP is the best biomarker to suggest infection. PCT alone is well used for diagnosing BTI with sepsis, meanwhile sTREM-1 and temperature should be taken into account. sTREM-1 has great value to monitor patients’ response to antimicrobial therapy and biliary drainage. The correlation between WBC and sTREM-1 was not very strong when diagnosing sepsis and observing curative effect.

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**Abstract 442**

**Antimicrobial resistance and pathogenicity of Corynebacterium striatum clinical isolates collected from three tertiary hospitals in China**

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**Background:** In recent years, more and more reports regarding multi-drug resistance and potential pathogenicity of Corynebacterium striatum were published, which may pose a knotty issue for clinicians. The pathogenicity potential of C. striatum strains isolated from different origins need to be further investigated.

**Materials/methods:** C. striatum clinical strains were isolated and identified with VITEK-2 ANC card, MALDI-TOF microTyper and 16S rRNA sequencing technique. Broth microdilution method was used to detect the antibiotic susceptibility profiles of 420 C. striatum clinical isolates, and PFGE method was used to discriminate different clones. Furthermore, in vitro adherence assay and mouse toxicity assay were performed to assess the pathogenicity of the strains with different genotypes.

**Results:** 420 C. striatum isolates were all sensitive to vancomycin, linezolid and daptomycin. Based on antibiotic resistance results, 420 strains were classified into 19 resistance patterns, when R1, R2 and R3 patterns accounted for 45.2% (190/420), 20.2% (85/420) and 22.4% (94/420), which were all multi-drug resistant patterns. PFGE typing results showed that 107 C. striatum strains were classified into 52 types (T01-T52), when 4 epidemic clones (T36, T28, T32, T14) accounted for 14.02% (15/107), 11.21% (12/107), 5.61% (6/107) and 3.73% (4/107), respectively. All of these 4 clones belonged to resistance patterns R1, R2 and R3. Among 27 C. striatum strains, 92.6% (25/27) strains showed moderate to strong in vitro adherence abilities, while only 7.4% (2/27) strains showed weak adherence ability on polystyrene surfaces. Furthermore, mouse lethality of different strains differed greatly, when non-dominant clone (Strain NMGYC339, T24) showed the strongest mouse lethality (90.0%).

**Conclusions:** The majority of the C. striatum clinical isolates tested in this study were multi-drug resistant, except vancomycin, linezolid and daptomycin. Most of the C. striatum strains showed moderate to strong adherence abilities and varied greatly among different hospitals. The C. striatum strains belonging to specific genotypes showed significant lethality in vivo, and the potential pathogenicity of C. striatum should be paid more attention to.

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Abstract 443

Prevalence and antimicrobial susceptibility of Ureaplasma species and Mycoplasma hominis in female patients in Korea: increasing trend of pristinamycin-resistant isolates

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Background: Ureaplasma species and Mycoplasma hominis, commonly found in the lower urogenital tract, have been associated with various urogenital infections. Tetracycline and macrolide antibiotics are available for the treatment of urogenital tract infections caused by genital mycoplasmas. However, an increase in the prevalence of antibiotic-resistant mycoplasmas has been reported worldwide. Therefore, this study aimed to estimate the prevalence and antimicrobial susceptibility trend of genital mycoplasmas in female patients and to evaluate risk factors for acquisition of pristinamycin-resistant mycoplasma.

Materials/methods: Endocervical swabs from 4,035 specimens obtained from March 2016 to December 2018 were analyzed using Mycoplasma IST2 Kits. Since pristinamycin and josamycin are not available in Korea, we performed an age- and date-matched case-control study to evaluate the risk factors for acquisition of pristinamycin-resistant isolates.

Results: A total of 1,589 (37.4%) cases of genital mycoplasmas were identified, which included 1,243 (78.2%), 49 (3.1%), and 279 (18.7%) cases of Ureaplasma species, Mycoplasma hominis, and both respectively. The antibiotics susceptibility rate decreased over the years for pristinamycin (99.8%, 99.3% and 96.7% for 2016, 2017, and 2018, respectively, p<0.001), josamycin (97.4%, 97.6% and 94.8%, p=0.001), tetracycline (89.5%, 85.8%, and 82.7%, p=0.008) and doxycycline (96.0%, 93.1%, and 92.3%, p=0.061). In the multivariate analysis, coinfection with Candida species was an independent risk factor for the acquisition of pristinamycin-resistant isolates (odds ratio 6.35, 95% confidence interval, 1.36 to 29.76, p=0.019).

Conclusions: The antibiotic-resistant genital mycoplasmas have been gradually increasing every year. Nationwide surveillance, proper antibiotics stewardship, and culture-based treatment strategy are needed to control this upcoming threat.

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Abstracts 2020

Abstract 445

Immunisation and multiple sclerosis: recommendations from the French Multiple Sclerosis Society

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Abstract third-party references: on behalf SFSEP and France4MS

Background: Vaccines have been suspected in the past to trigger Multiple Sclerosis (MS) or MS exacerbations. Other concerns arose more recently, with the extension of the immunomodulatory treatment arsenal, about an increased risk of infections or a decreased effectiveness of immunization in immunosuppressed patients. The objective of this work is to establish recommendations on immunization and multiple sclerosis.

Materials/methods: The French Group for Recommendations in Multiple Sclerosis (France4MS) did a systematic review of articles from PubMed and universities databases (January 1975 through June 2018). The RAND/UCLA appropriateness method, which has been developed to synthesize the scientific literature and expert opinions on health care topics, was used for reaching a formal agreement. Twenty-four MS experts worked on the full-text review and a group of 110 multidisciplinary health care specialists validated the final evaluation of summarized evidences.

Results: Neurologists should double check vaccination status as soon as possible after MS diagnosis and before the disease-modifying treatment (DMT) introduction. The French vaccines calendar should be applied to MS patients and they should be advised to receive seasonal influenza vaccine. If possible, serological status, including A, B, C hepatitis, measles, mumps, pertussis, rubella, small pox, varicella-zoster should be checked before starting a DMT. In case of treatment-induced immunosuppression, MS patients should be informed about infections risks and vaccine standards from the French High council of Health should be applied. Live attenuated vaccines are contra-indicated in MS patients currently or recently treated with immunosuppressive drugs, including corticosteroids; other vaccines can be proposed whatever the treatment, but their effectiveness may be partly reduced with some drugs.

Conclusions: Physicians and patients should be aware of the updated recommendations for immunizations and MS. Practice guidelines will be delivered by the French MS Society (SFSEP) for the medical and patients communities.

On behalf the SFSEP and the FRANCE4MS group

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**Abstract 446**

**Haemophagocytic lymphohistiocytosis in human immunodeficiency virus: a systematic review of literature**

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**Background:** Hemophagocytic lymphohistiocytosis (HLH) is a hyper-immune condition secondary to malignancy, infection or auto-immune conditions. HLH in patients with human immunodeficiency virus infection (HIV) can be either be due to a co-existent malignancy/infection or due to uncontrolled replication of HIV itself. The aim of this systematic review (SR) was to delineate the number of reported cases of HLH in HIV, their possible triggering factors, treatment and outcome.

**Materials/methods:** Search strategy: We conducted a comprehensive search of English medical literature via the Medline / PubMed database using different synonyms of „HIV” AND „HLH”. The review was registered under PROSPERO CRD42018099987. Study selection: The titles and abstracts of 185 articles between January 1986 and April 2018 were screened for inclusion. The reasons for exclusion were- articles not in English [19], absence of either HIV or HLH [48], non-case studies [17], non-availability of full articles [10] and unfulfillment of HLH 2004 diagnostic criteria [50]. A total of 41 articles with 52 patients were included in the analysis.

**Results:** Of the 52 patients, 42 (80.8%) were male. The mean age was 38.2 +/- 14.2 years. The median CD4 count at the time of diagnosis of HIV with HLH was 41/ml (IQR: 8-94/ml). HLH was associated with malignancy in 17 patients [Lymphoma [n=11], Kaposi sarcoma [n=6]] while associated infection was found in 25 patients [Fungal [Histoplasmosis-15, penicilliosis-1, invasive candidiasis-1, invasive aspergillosis-1], Parasitic [leishmaniasis-1, toxoplasmosis-2], Bacterial [bartonellosis-1], Viral [cytomegalovirus-2, Epstein-barr virus-1] and tuberculosis [n=1]]. Presence of either malignancy (p=0.051) or opportunistic infection (p=0.69) was not associated with increased chances of death by uni-variate analysis. A total of 26 patients were treated with steroids while etoposide was used in only four patients. Death was reported in 21 patients. Intake of steroids as a treatment of HLH was associated with more chances of death (p=0.048).

**Conclusions:** Malignancy and opportunistic infections are important triggers for HLH in HIV. Acute HIV and IRIS by itself can act as a trigger for HLH. Evidence on the use of steroids as a treatment of HLH is not convincing.

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Abstract 453

**Value of the CXCL13 ELISA and a CXCL13 lateral flow immunoassay in the diagnosis of Lyme neuroborreliosis**

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**Background:** Diagnosis of Lyme neuroborreliosis (LNB) can be challenging in an early disease stage especially if *Borrelia*-specific intrathecal antibodies are still negative. This study aimed to assess the performance of CXCL13 ELISA and the ReaScan® CXCL13 lateral flow immunoassay (LFA) in the diagnosis of Lyme neuroborreliosis.

**Materials/methods:** In this dual-center case-control study 90 CSF samples were retrospectively analysed by the Euroimmun CXCL13 ELISA and the ReaScan® CXCL13 LFA. Overall, 34 CSF samples from patients with definite LNB, 10 samples from patients with possible LNB and 46 samples from patients with other predominantly inflammatory CNS diseases (non-LNB control group) were included. Patients with definite or possible LNB were classified according to the EFNS guidelines.

**Results:** CXCL13 ELISA was significantly elevated in all 34 patients with definite LNB (median 1409 pg/mL) compared to 46 control patients (median 20.7 pg/mL, \( p < 0.0001 \)). In the control group patients with possible LNB were not included. For a cut-off of 78.6 pg/mL a sensitivity of 100% and a specificity of 84.8% (AUC 0.93) was calculated. The ReaScan® CXCL13 LFA was significantly elevated in 31 patients with definite LNB (median 223.5 arbitrary values) compared to 46 control patients (median 0 arbitrary units, \( p < 0.0001 \)). A cut-off of 22.5 arbitrary values (AV) had a sensitivity of 91.2% and a specificity of 93.5% (AUC 0.94). Overall, the agreement of the LFA with the ELISA was 90%; 98% for ELISA values < 250 pg/mL; 22% for ELISA values from 250-500 pg/mL and 96% for ELISA values > 500 pg/mL, respectively. The correlation between the CXCL13 ELISA and the LFA was \( r = 0.89 \) and \( p < 0.0001 \).

**Conclusions:** CXCL13 ELISA and the ReaScan® CXCL13 LFA in CSF are reliable diagnostic tools for the identification of patients with definite LNB.

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Abstract 454

Combined effects of low incubation temperature, minimal growth medium and low hydrodynamics optimise Acinetobacter baumannii biofilm formation

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Background: Biofilm formation is an important virulence factor expressed by microorganisms. It shields and protects microbial cells from host immune responses, antibiotics and other anti-infectives. It is hypothesized that microbial cells demonstrate enhanced biofilm formation in nutrient limiting environment. The aim of this study was to investigate if limiting environmental conditions act synergistically to promote biofilm formation in multidrug resistance Acinetobacter baumannii.

Materials/methods: Biofilm was cultivated using quantitative microtiter plate method. The combined effects of temperature, medium and shear force were determined by measuring adherence (OD570 nm) following incubation at 26°C, 30°C and 37°C for 24 hr. when biofilm was cultured with minimal nutrient medium (EAOB) and nutrient-rich medium (TSB) without or with agitation at 50 rpm. Antibiotic susceptibility test of selected antimicrobials were tested with Kirby-Bauer disc method. P < 0.05 was considered statistically significant for all the tests.

Results: A noticeable variation in adherence was observed among the isolates cultured with both media. Biofilm forming capacity of the isolates range from 0.09 to 0.33. Majority of the isolates had their relative biofilm-forming capacity significantly higher than the positive control, Acinetobacter baumannii ATCC 19606. The biofilm biomass during growth in nutrient-rich medium (TSB) without shaking was significantly different (p < 0.05) among the three temperatures tested compared with when cultured in EAOB without shaking. A positive correlation was observed between biofilm formation and resistance to imipenem (r = 0.2889; p = 0.05). There is a statistically significant difference among the median of the three source groups (p < 0.05) compared with the median between the source groups.

Conclusions: This observation extended further the view that A. baumannii biofilm formation is enhanced when nutrient-poor medium was used at room temperature (26°C) with or without agitation compared to growth at 37°C.

Table:

<table>
<thead>
<tr>
<th></th>
<th>Non-Adherent</th>
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<th>Moderate Adherent</th>
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<td>Average</td>
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<tr>
<td>OD ± SD</td>
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<td>0.09 ± 0.01</td>
<td>8 (11.3)</td>
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Biofilm formation assay data is the mean of three independent experiments carried out in triplicate ± SD after growth in minimal (EAOB) and rich (TSB) media at 26°C, 30°C, and 37°C under dynamic conditions.

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Insights of colistin resistance and flexible transmission of mcr-1
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Background: Colistin, a cationic antimicrobial peptide, is regarded as one of the last-resorts to treat clinical infections caused by MDR Gram-negatives bacteria. However, colistin resistance has been increasingly emerged recently, primarily mediated by plasmid-mediated colistin resistance gene mcr-1, which has drawn attention to mcr-like genes and the needs to systemically and accurately monitor colistin resistance.

Materials/methods: Feces were collected from swine, chicken and waterfowl and detected for the mcr-positive bacteria. Antimicrobial susceptibility testing and PCR screen were performed to investigate the phenotype and genotype of tigecycline resistance. Conjugation, S1-PFGE, and WGS were used to determine the transferability, location of mcr gene, and the further study the bacterial genomic profiles.

Results: We collected 2747, 1217 and 1104 fecal samples from swine, chicken and waterfowl during 2016 to 2018. The results show that 40%, 57.1% and 41.8% of the samples are mcr-1 positive. A four-year monitoring of colistin resistance in a specific pig farm in Jiangxi, the resistance rate and mcr-1 positive detection rate displays a downward trend, but the prevalence of mcr-1 is still high in 2017 (33.78%) and 2018 (23.08%). The mcr-1-positive E. coli isolates show distinct genetic relatedness, and the mcr-1 gene can be located on the chromosome and the IncX4, IncI2, IncHI2, IncFII and IncFIB type plasmids. In addition, we observed substantial within-host diversity of mcr-1-positive Enterobacteriaceae isolates from different aspects [e.g. species, clone relatedness, plasmid types and genetic context of mcr-1]. To further clarify the transmission mechanism[s] of rapid and wide spread of mcr-1 gene, we engineered E. coli strains that carry an intact Tn6330 transposon or its deletion derivatives, providing direct evidence that mcr-1 transposition relies on the presence of an intact Tn6330.

Conclusions: Extensive heterogeneity and flexibility of mcr-1 transmission exist in both intra-host and with-in host level. mcr-1 transposition mediated relies on the presence of an intact Tn6330. Considering that gut is a melting pot for active horizontal gene transfer, it will take long for regulations to control colistin resistance, and continuous supervision of colistin usage and colistin resistance genes is necessary.

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Dissemination of tet(X4)-positive Escherichia coli on duck farms in south-east China
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Background: Carbapenems, colistin and tigecycline are critically important antibiotics in clinics and tigecycline is considered the last-resort drug against severe human infections caused by multi-drug resistant bacteria. This is especially true after the global appearance of blaNDM and mcr mediating the resistance to carbapenems and colistin respectively. Recently, a mobile tigecycline resistance gene tet(X4) has been identified in Escherichia coli, Klebsiella pneumoniae and Acinetobacter baumannii that causes high resistance to tigecycline and other tetracyclines. In this study, the prevalence of tet(X4) in E. coli isolates from duck farms in Southeast China was identified and characterized.

Materials/methods: Feces, soil, sewage and dust samples were collected from duck and goose farms along with the southeast coast provinces of China. Antimicrobial susceptibility testing and PCR screen were performed to investigate the phenotype and genotype of tigecycline resistance. Conjugation, S1-PFGE, and WGS were used to determine the transferability, location of tet(X4) gene, and further study the bacterial genomic profiles.

Results: We collected 1716 samples and 16 isolates (0.9%) were identified carrying the tet(X4) gene with tigecycline MICs ≥ 8 mg/L. Sequencing analysis demonstrated these isolates belonged to diverse sequence types, mostly ST3997 from Jiangsu province. Conjugation assay to E. coli C600 was succeeded for 11 isolates, and correspondingly IncHI1- and IncX1-plasmids bearing tet(X4) were detected by sequence analysis. tet(X4) was found adjacent to an insertion sequence ISCR2 downstream and a catD gene upstream for all isolates. In addition, multiple-drug resistance to meropenem, ceftazidime, ampicillin, ciprofloxacin, trimethoprim/sulfamethoxazole and fosfomycin was profiled in all the tet(X4)-positive isolates.

Conclusions: The identification of tet(X4) harboring E. coli strains in duck farms and their surroundings enlarges our knowledge of the variety and prevalence of tigecycline resistance. Additionally, the prevalence of tet(X4) raises concern for the use of tetracyclines in animal farming and the tet(X4) gene should be listed as primary gene for resistance surveillance.

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Clinical and molecular perspectives of colistin-resistant Klebsiella from an oncology centre in a lower-middle income country

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Background: There is limited available data on the clinical and molecular perspectives of colistin resistant Klebsiella from Lower Middle Income countries.

Materials/methods: We did a retrospective observational study of a cluster of 20 patients with CoRKp infections in our tertiary care oncology centre, from June to November 2017. Clinical details were collected from the case records. Broth micro dilution was performed to derive colistin MIC. The bacteremic isolates (14) were subjected to Whole Genome Sequencing (WGS) to determine mechanism of colistin resistance.

Results: The study included 20 patients with a median age of 60 years, majority were females (70%) and with a median APACHE score of 18. Most patients (19/20) were immunocompromised, receiving treatment for malignancy. Prior exposure to a polymyxin (B/E) was 50%(10/20), an additional 15% (3/20) patients developing bacteremia while on the drug. Fourteen patients had CoRKp bacteremic and 6 non bacteremic infections (4 pneumonia, one UTI and one intrabdominal). All patients received a polymyxin (B/E) in combination with one or more of the following drugs - tigecycline, fosfomycin, chloramphenicol, minocycline or a carbapenem based on the susceptibility and MIC. The time taken for the development of CoRKp infection was a median of 22 days since hospitalisation. Mortality was 75% (15/20), with a median time of death 7 days since the onset of sepsis. Colistin MIC for the isolates ranged from 32-64µg/ml. Of the 14 bacteremic isolates, 12 belonged to ST231, the other two being ST395 and ST147. The carbapenemases identified were OXA-232 in 11, NDM-1 in one isolate and two isolates did not carry any carbapenemase. Mutations in chromosomal genes such as eptA (n=12), arnB (n=1) and arnT (n=1) contributed to colistin resistance. mgrB was disrupted in one of the isolates by insertion of IS903B. Plasmid mediated colistin resistance due to mcr and its variants were absent.

Conclusions: Patients with CoRKp infections have a high mortality rate, despite receiving combination therapy. The commonest carbapenem resistance gene identified was OXA 232. ST231 is the predominant clone among colistin resistant K. pneumoniae. mcr and its variants were absent in all isolates. Mutations in chromosomal genes contributed to colistin resistance.

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Abstract 460

Prevalence of device use and transmission-based precautions in nineteen large Australian acute care public hospitals: secondary outcomes from a national healthcare associated infection point prevalence survey

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Background: The use of invasive devices increases the risk of healthcare associated infections (HAI). The recent national Australian HAI point prevalence survey secondary objectives aimed to estimate the prevalence of patients with an indwelling urinary catheter device and vascular access devices; and also identify prevalence of those managed under transmission based precautions (TBP); and those colonised or infected with a multi drug resistant organism (MDRO). Data was also collected on the ratio of infection control professional (ICP) per 100 beds and the proportion of single rooms at each hospital.

Materials/methods: A point prevalence study (PPS) was conducted in large acute care Australian public hospitals. All data were collected by two trained Research Assistants. Surveillance methodology was based on the European Centre for Disease Prevention and Control (ECDC) PPS Protocol. Data was also collected on prevalence of TBPs and MDROs.

Results: A total of 2767 acute adult inpatients were sampled across 19 hospitals. The prevalence of peripheral vascular, central vascular and urinary catheters devices was 55.2% (95%CI: 53.3%-57.1%), 14.8% (95% CI: 13.5%-16.1%) and 20.7% (95%CI: 19.2%-22.3%) respectively. Of the 2767 patients sampled 285 (10.3%, 95%CI: 9.2%-11.5%) were documented as either being infected or colonised with a MDRO, and 781 (11.8%) patients were being managed under the hospital TBP policy. Overall proportion of single rooms was 46% (range 16%-100%) and the mean ICP ratio per 100 beds was 0.9 (range 0.3-1.7).

Conclusions: This is the first national study to describe the prevalence of devices, TBPs and MDROs in Australian healthcare settings. Furthermore, it has identified broad variation in ICP resources (staff and single rooms) across a homogenous sample of 19 Australian hospitals. In an era where device use should be constantly reviewed to minimise risk of HAI, combined with the increasing challenges of managing patients with MDROs, it would appear that some hospitals are clearly better able meet these challenges. This data will serve as a benchmark for future studies.

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Prevalence of ESBL Klebsiella pneumoniae infections in Nigeria: a systematic review
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Background: Surveillance is an important strategy used in the control of antimicrobial resistance. It guides selection of empirical antimicrobial therapy and identifies priority areas for infection prevention and control as well as antimicrobial stewardship interventions. Nigeria has no antimicrobial resistance surveillance system at the moment. This review evaluates the prevalence of Extended Spectrum Beta-Lactamase (ESBL) among clinical K. pneumoniae isolates in Nigeria (2007 – 2017).

Materials/methods: This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statements. PubMed, Scopus and Google scholar electronic databases were searched to identify eligible studies. Search terms used include: Extended Spectrum Beta-Lactamse, ESBL, Klebsiella pneumoniae, enterobacteriaceae, and Nigeria. Studies that reported prevalence of ESBL K. pneumoniae in at least 30 non-duplicate clinical specimens were selected. Studies involving animals and healthy human population were excluded. Study characteristics and prevalence of ESBL K. pneumoniae isolates were extracted using a data collection form.

Results: Of the 283 articles screened, only seven met the inclusion criteria including three and four studies conducted in Southern and Northern Nigeria, respectively. All the selected studies used prospective study design. Overall, the selected studies involved a total of 244 K. pneumoniae isolates and 237 ESBL phenotypes. Available data indicated that there was an increase in the prevalence of ESBL K. pneumoniae in both regions: from 12.7% (2005 – 2007) to 37.5% (2011) in the South-West zone and from 14.8% (2010 – 2011) to 62.9% (2012 – 2014) in the North-West. The prevalence of ESBL K. pneumoniae in the South-South, North-East and North-Central was 43.8%, 33.1% and 26.7% respectively. ESBL K. pneumoniae was more common in urine and surgical wound specimens.

Conclusions: Prevalence of ESBL K. pneumoniae infection in Nigeria was high and has increased during the period under review. Active surveillance of ESBL K. pneumoniae infections is recommended. In addition, Infection control and antimicrobial stewardship interventions should be strengthened to reduce the burden of antibiotic resistance.

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Abstract 467

Investigation of positive blood culture bottles with the hemoFISH test: a beacon-based fluorescence in situ hybridisation technique

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Background: Pathogenic isolates that responsible for bacteraemia are need to identified rapidly and accurately. Blood culture is the gold-standard method for detection pathogens in blood, but culture-based methods are time-consuming. Beacon-based fluorescence in situ hybridization (bb-FISH) technique is thought to be one of the methods that may fill this gap. Therefore, a bb-FISH test (HemoFISH, Miacom diagnostics, Germany) was evaluated.

Materials/methods: A total of 72 BACTEC Plus Aerobic/F blood culture bottles which were gave positive signal were collected. The isolates growth on subcultures were identified by conventional/automated (Vitek-2, BioMérieux, France) reference methods. Also, appropriate hemoFISH assay (Gram-positive or Gram-negative) was performed from signal-positive blood culture bottles after Gram staining.

Results: From the 72 signal-positive blood culture bottle, 75 different isolate were isolated. A total of 69 (95.8%) specimen had monomicrobial, 3 (4.2%) specimen had polymicrobial growth with two species. Twenty-four (32%) Gram-negative and 51 (68%) Gram-positive strain identified with the reference methods. All of the positive control wells were positive for 72 signal-positive blood culture bottles with the hemoFISH assay. From the 75 of the isolates, 67 (89.3%) were classified within the level of species, genus or family by the specific probes of the assay. From the 8 undetected isolates, 2 (Alcaligenes faecalis and Achromobacter xylosoxidans) were not identified by the assay due to absence of specific probes to these pathogens. Also, 6 of these isolates (2 Acinetobacter spp., 1 Klebsiella pneumoniae, 1 Pseudomonas aeruginosa, 1 Enterococcus spp. and 1 Staphylococcus hominis subspecies hominis) could not classified within the levels despite the presence of probes. Total processing time for one signal-positive blood culture bottle was approximately 45 minutes with the hemoFISH assay. When the classical subculture is applied, minimum time for identification is about 36 hours.

Conclusions: Rapid technologies for the determination of the bacteraemia is important to start appropriate empirical treatment. The hemoFISH assay has shortened the evaluation time of bacteraemia but the ability to identify at species level is limited to some pathogens. Thus, it is recommended to use bb-FISH assays in parallel with reference-methods to ensure appropriate empirical therapy.

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Abstract 470

Molecular differentiation of dengue serotypes in the public health system in Santo André, Brazil

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Abstract third-party references: Supported by Fapesp 2016/14457-0

Background: Dengue virus has four serotypes (DENV1-4). It is an arbovirus belong to the family Flaviviridae, whose main vector is the mosquito Aedes aegypti. Dengue infection has nonspecific symptoms (high fever, retro-orbital pain, myalgia and rash) and similar to other arbovirus infections, laboratory diagnosis becomes essential. In 2018, 163,236 dengue cases were confirmed in Brazil, and of these 301 cases of severe dengue and 3,386 dengue cases with alarm signals. Until April 2019, 15,953 cases of Dengue were confirmed. Early diagnosis can positively influence the clinical management of these patients and consequently reduce mortality.

Materials/methods: From June 2018 to June 2019, 645 patients were admitted to the public health service of the municipality of Santo André in the state of São Paulo with clinical suspicion of Arboviroses. From each patient 5 mL of peripheral blood were collected. The immunochromatographic test was performed for research of protein NS1, IgG and IgM. Viral RNA was isolated from the patient’s serum using the QIAamp Viral RNA kit. Complementary DNA synthesis was performed from 1 μg of viral RNA using the QuantiNova Reverse Transcription kit. RT-qPCR was performed with the aid of specific oligonucleotides for the 4 Dengue serotypes and the endogenous gene RPL13a. Amplification reactions were performed on an ABI 7500 thermocycler.

Results: Of the samples evaluated, 48.9% were female and 51.1% male. In immunochromatographic test 601 (93,1%) were negative, 9 (1,4%) NS1 positive, 3 (0,5%) positive IgM and 32 (5%) positive IgG. In RT-qPCR 22/645 (3,41%) dengue 2 was detected and in 1 2/645 (1,86%) genetic material from the dengue 1 has been detected.

Conclusions: The serological method was able to detect 12 (1,86%) patients in the acute phase while molecular biology testing was able to detect viral RNA in 34 (5,27%) of the samples and even differentiate into dengue 1 and dengue. 2. Therefore, the implementation of molecular diagnosis of the virus in the acute phase of infection in the public health service has shown to be a promising tool in the clinical management of these patients.

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Antimicrobial activity of ceftazidime-avibactam, ceftolozane-tazobactam and comparators tested against *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* isolates collected from US medical centres in 2016-2018

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**Abstract third-party references:** This study was performed by JMI Laboratories and supported by Allergan, which included funding for services related to preparing this abstract.

**Background:** Very few agents remain active against *Pseudomonas aeruginosa* (PSA) and *Klebsiella pneumoniae* (KPN) in some geographic regions. We evaluated the *in vitro* activity of ceftazidime-avibactam (CAZ-AVI), ceftolozane-tazobactam (C-T) and many comparator agents against a large collection of contemporary PSA and KPN isolates from United States (US) medical centers.

**Materials/methods:** A total of 6,210 PSA and 6,041 KPN isolates were consecutively collected from 85 US medical centers (37 states) in 2016-2018. MICs were determined by reference broth microdilution method and susceptibility rates were calculated using EUCAST breakpoints. KPN with elevated MIC for broad-spectrum cephalosporins were submitted to whole genome sequencing analysis to detect resistance genes.

**Results:** CAZ-AVI (97.1% susceptible [S]) and C-T (97.0%) were the most active compounds against PSA [Table], and retained activity against meropenem-nonsusceptible [MEM-NS; 88.5-89.0%] and piperacillin-tazobactam-NS [PIP-TAZ-NS; 86.6-87.0%] isolates; 40.7% of C-T-NS PSA were CAZ-AVI-S and 44.2% of CAZ-AVI-NS PSA were C-T-S. PSA S rates for MEM, PIP-TAZ and tobramycin were 78.2%, 79.1%, and 93.3%, respectively. The most active agents against KPN were CAZ-AVI (>99.9%), colistin (98.3%), amikacin (97.6%), and MEM (97.5%). C-T was active against 92.3% of KPN and showed limited activity against ESBL- and carbapenemase (CPE)-producers (67.2% and 0.0%, respectively). Among KPN, 10.2% were ESBL-producers (excluding CPE co-producers) and 2.7% were CPE-producers. The most common ESBLs were CTX-M-15 (75.9%) and OXA-1/OXA-30 (52.4%), 54.4% produced >1 ESBL, mainly CTX-M-15+OXA-1/OXA-30 (50.2% of ESBL-producers). The most common CPE among KPN were KPC-3 (57.8% of CPE-producers) and KPC-2 (39.8%), and only 1 metallo-beta-lactamase-producing isolate was observed (NDM-1). The most active agents against ESBL-producing KPN were CAZ-AVI (100.0%), MEM (98.7%), and colistin (96.2%), and only CAZ-AVI (99.4%) and colistin (82.4%) were active against >45% of CPE-producers.

**Conclusions:** CAZ-AVI and C-T showed similar coverage (%) against PSA (97.0-97.1%), including against isolates resistant to other antipseudomonal agents. In contrast, C-T was less active than CAZ-AVI against KPN in general and exhibited limited activity against ESBL and/or CPE producers.

<table>
<thead>
<tr>
<th>Organism (no. tested)</th>
<th>MIC50/MIC90 (%)</th>
<th>CAZ-AVI</th>
<th>C-T</th>
<th>PIP-TAZ</th>
<th>MEM</th>
<th>AMK</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>P. aeruginosa</em> (6,210)</td>
<td>2/4 (97.1)</td>
<td>0.5/2 (97.0)</td>
<td>4/64 (79.1)</td>
<td>0.5/6 (76.2)</td>
<td>4/16 (69.8)</td>
<td></td>
</tr>
<tr>
<td>MEM-NS (1,352)</td>
<td>4/15 (88.5)</td>
<td>1/8 (93.0)</td>
<td>32/&gt;64 (42.3)</td>
<td>8/32 (0.0)</td>
<td>8/32 (75.0)</td>
<td></td>
</tr>
<tr>
<td>PIP-TAZ-NS (1,298)</td>
<td>4/15 (88.5)</td>
<td>2/8 (97.0)</td>
<td>&gt;64/64 (0.0)</td>
<td>8/32 (39.5)</td>
<td>8/32 (75.8)</td>
<td></td>
</tr>
<tr>
<td>CAZ-NS (1,025)</td>
<td>4/18 (82.2)</td>
<td>2/15 (33.2)</td>
<td>&gt;64/64 (6.1)</td>
<td>8/32 (40.0)</td>
<td>8/32 (73.6)</td>
<td></td>
</tr>
<tr>
<td><em>K. pneumoniae</em> (6,041)</td>
<td>0.12/0.26 (&gt;99.9)</td>
<td>0.25/1 (92.5)</td>
<td>4/16 (95.5)</td>
<td>0.03/0.03 (97.5)</td>
<td>1/2 (57.6)</td>
<td></td>
</tr>
<tr>
<td>ESBL-producers (614)</td>
<td>0.25/0.6 (100.0)</td>
<td>1/8 (97.2)</td>
<td>8/64 (53.7)</td>
<td>0.03/0.03 (88.7)</td>
<td>2/8 (53.3)</td>
<td></td>
</tr>
<tr>
<td>CPE-producers (161)</td>
<td>1/2 (98.4)</td>
<td>&gt;16/16 (0.0)</td>
<td>&gt;64/64 (0.5)</td>
<td>1/32 (10.0)</td>
<td>1/32 (42.5)</td>
<td></td>
</tr>
</tbody>
</table>

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Abstract 481

Reducing paediatric blood culture contamination rates: a benefit to arterial catheter-drawn cultures
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Background: Contamination of blood cultures occurs universally, often impeding medical care. Catheter-drawn cultures are considered less reliable compared to cultures obtained by venipuncture in adults. We aimed to reduce pediatric blood culture contamination rates using educational and technical interventions. We also assessed the positive predictive value (PPV) of catheter-drawn cultures in pediatric patients.

Materials/methods: The study was conducted at the Ruth Rappaport Pediatric Hospital, a tertiary medical center in Israel. All blood cultures drawn from patients aged 0-18 years were included. Cultures were drawn by nurses and physicians. For 6 months, we performed specialized training, personal feedbacks, and departmental reports of contamination rates. Blood culture contamination rates during the 6 month intervention period were compared to rates in the preceding year. We analyzed contamination rates according to age, department and drawing method.

Results: Pediatric blood culture contamination rates were reduced from 2.18% in the year prior to intervention to 1.93% during the intervention period (1.93% and 2.18% respectively OR 0.89 [95% CI 0.67 – 1.16]). Across all pediatric departments, neonates aged 0-30 days had significantly lower blood culture contamination rates compared to patients aged 1-2 months or older. Cultures drawn from arterial catheters had lower contamination rates than those drawn from a central venous catheter (2.2% versus 3.7% respectively OR 1.72 95% CI 1.14-2.6, see table).

Conclusions: Reducing pediatric blood culture contamination rates below 2% is challenging. Technical difficulties likely play an important role in contamination, therefore arguing for use of a dedicated phlebotomy team, especially in patients aged >1 month. While drawing from vascular catheters, arterial blood cultures are less likely to be contaminated, suggesting a benefit to blood draw from arterial catheters for cultures obtained in intensive care settings.

Contamination rates according to drawing method

<table>
<thead>
<tr>
<th>Drawing method (blood source)</th>
<th>Contamination rate %</th>
<th>OR (95% CI)</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial catheter</td>
<td>2.2%</td>
<td>1</td>
<td>84%</td>
</tr>
<tr>
<td>Peripheral venous</td>
<td>1.9%</td>
<td>0.86 (0.61 - 1.22)</td>
<td>66%</td>
</tr>
<tr>
<td>CVC</td>
<td>3.7%</td>
<td>1.72 (1.14 – 2.6)</td>
<td>38%</td>
</tr>
<tr>
<td>PICC</td>
<td>2.3%</td>
<td>1.07 (0.33 – 3.51)</td>
<td>40%</td>
</tr>
</tbody>
</table>

CVC – Central venous catheter, PICC – peripherally inserted central catheter

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Abstract 490

Rough-type and loss of the LPS due to lpx genes deletions are associated with colistin resistance among multidrug-resistant *Escherichia coli* clinical isolates not harbouring mcr genes

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**Background:** The emergence of multi drug resistant *Escherichia coli* (*E. coli*), is a great challenge in treating nosocomial infections. Colistin is the last line of therapy for such strains, but resistance to colistin is increasingly emerge in the public health systems.

**Materials/methods:** In this study, we examined 38 clinical isolates of *E. coli*, with decreased susceptibility to colistin. After confirmation of the isolates, antimicrobial susceptibility tests were done to characterized the resistance pattern of these isolates to the different classes of antibiotics, using the disk diffusion test, and then, MIC of colistin was determined by broth microdilution methods according to CLSI recommendations. The isolates were examined for the presence of mobile colistin resistance (*mcr-1* and *mcr-2*) genes, using the PCR methods. Cloning of *mcr-1* gene was done to prove its role in colistin resistance. LPS was extracted from the isolates to determine the presence or the absence of this bacterial target for colistin. *lpx* genes were analyzed by PCR and sequencing for detecting any mutation.

**Results:** Among 38 clinical isolates of *E. coli*, with decreased susceptibility to colistin, 52.6% (n=20) were resistant to colistin. The MICs of colistin ranged between 0.5 µg/ml and >256 µg/ml. among the colistin resistant isolates, 6 isolates were harboring the *mcr-1* gene but not the *mcr-2*. The transformed *E. coli* DHα, showed a 8-fold increase in colistin MIC. The other 14 isolates, were negative for *mcr* genes. Among these, 6 isolates were negative for LPS production in SDS-PAGE analysis and five showed the rough type LPS phenotype, and all were significantly associate with resistance to colistin.

**Conclusions:** this study, presented evidences that loss of LPS or lipid A-deficiency can lead to colistin resistance among clinical isolates of *E. coli*, according to the loss of the drug target or a less affinity of LPS for colistin.

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Abstract 492

**Treatment of influenza and influenza-like illnesses with antiviral having anti-inflammatory efficacy**

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**Background:** Enisamium iodide (EI) (Nobazit) is a Russian drug whose molecule was developed in the Institute of Pharmacology and Toxicology of Ukraine as an anti-inflammatory and antipyretic agent. Later, other properties of EI were found: inhibition of the influenza virus hemagglutinin, increasing the production of interferon-γ, level of Th1, blood antioxidant activity, inhibition TNF-α and other pro-inflammatory cytokines, activation of macrophages and lysozyme activity.

The aim of study was to evaluate the efficacy of antiviral therapy with EI in out-patient patients with influenza and influenza-like illnesses (ILI) without risk factors for severe course of disease.

**Materials/methods:** 124 patients aged 18-55 years with influenza and ILI within 6-48 hours of symptoms onset were randomized into 2 groups. 1th group (n=66) was treated with EI 500 mg tid 5 days, 2nd group (n=63) received placebo according to the same scheme. In the 1th group the proportion between influenza and other respiratory viruses was 32.2%-67.8%, in the 2th group 31.7%-68.3%, accordingly. Duration of disease and main clinical symptoms, frequency of complications and speed of the virus elimination from the nasopharynx were estimated.

**Results:** The number of cases with complete recovery within 96 hours was 56 (84.8±4.2%) in 1st group and 44 (69.8±5.8%) in 2nd group (p=0.047). The duration of fever was 68.0±2.8 hours in 1th group and 77.1±2.9 hours in 2nd group (p=0.044), muscle pain - 52.3±2.3 and 60.6±2.6 hours (p=0.041), headache-52.1±2.6 and 65.1±2.5 hours (p=0.032), weakness – 75.5±2.3 and 90.4±2.5 hours (p=0.001), accordingly. On the 4th day of treatment the viruses were isolated in 37.8±5.9% of cases in the 1st group and 57.1±6.2% in 2nd group; p=0.048. Bacterial complications were observed in 3.0±2.1% and 12.6±4.2% accordingly, p=0.048.

**Conclusions:** The study is demonstrated the effectiveness of EI in the treatment of influenza and ILI in adult outpatient patients. The antiviral and anti-inflammatory effects of the drug, which was administered within 48 hours of the symptoms onset were demonstrated by a more rapid reduction of clinical symptoms, frequency of bacterial complications and reduction in the time of virus elimination. Continuation of EI clinical trials are necessary for more full evaluation of its effectiveness.

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**Abstract 494**

**Tuberculous lymphadenitis: are Asians at greater risk?**

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**Background:** Lymphadenitis are the main localization of extra-pulmonary tuberculosis. Despite the existence of treatment recommendations, clinicians are sometimes faced with diagnostic and treatment difficulties. The objective of this study was to describe characteristics and follow-up of patients with Tuberculous Lymphadenitis (TL).

**Materials/methods:** Analysis of TL cases diagnosed by PCR (Cepheid MTB/RIF test) and/or by culture in Avicenne Hospital from January 1, 2015 to January 31, 2019. Clinical presentation and evolution were compared by continent of birth.

**Results:** Seventy-two patients [19%] of the 382 tuberculosis cases diagnosed during the period, were TL. Majority were male [n=58, 81%], median age was 32 years [IQR 26-44]. Fifteen percent [n=11] of patients were born in India, 11% [n=8] in Pakistan, 10% [n=7] in Bangladesh and 8% [n=6] in Sri-Lanka. Asians peoples accounted for 44% of TL compared to 22% (68/310) of pulmonary tuberculosis cases (p<0.01). Sub-Saharan African people accounted for 38% of patients. Localization was mainly cervical (54%, n=39), and supra-clavicular (36%, n=26). Lung damage was associated in 31% (n=22) of patients, 7% (n=5) of patients were HIV-infected and none were diabetic. Smears were positive in only 14% (n=10) of cases, while PCR, when performed, was positive in 89% (n=25/28) of cases. Only 8% (n=6) of patients had an isoniazid-resistant strain, all were rifampicin-sensitive. Median duration of treatment was 6 months and 22% (n=16) were treated for 9 months or more. Corticosteroid treatment was associated in 18% of cases (n=13) for a duration of 1 to 3 months. Adenopathy was noted to be persistent on clinical examination at 12 months in 13% [n=6] of the 47 patients reported. Due to poor progress, surgical excision was performed in 3 patients. Clinical presentation and evolution were similar between the different birth continents, except for people born in Asia who had more exclusive lymphadenitis (82% versus 58%, p=0.03).

**Conclusions:** In our study, TL accounts for nearly 1/5th of tuberculosis cases and affects patients born in Asia in particular. Risk factors or genetic factors that may explain the greater susceptibility of this population have to been studied. The use of corticosteroids and surgery should be better specified.

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Investigation of hetero-VISA among MRSA isolates in Gaziantep, Turkey

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Abstract

Background: Heteroresistant vancomycin intermediate Staphylococcus aureus (hVISA) is defined as isolates which are susceptible to vancomycin, but with minority populations having MIC>2 µg/ml for vancomycin. hVISA testing is recommended when therapeutic failure is suspected. Since population analysis profile is difficult to perform, Satola et al. proposed a practical method for screening of hVISA using brain heart infusion (BHI) agar containing vancomycin and casein and stated that this test had 90% sensitivity and 95% specificity. This test was also cited by EUCAST guidelines for detection of resistance mechanisms V2.01. Here, we aimed to investigate the prevalence of hVISA among MRSA isolates and compared Satola’s test with two other agar screening methods for detection of hVISA.

Materials/methods: One hundred MRSA isolates were collected in our university hospital laboratory between 01.04.2018 and 30.09.2019. For screening of hVISA, we prepared two screening agar plates and one commercial media; BHI agar plates containing 4 µg/ml vancomycin and 16 g/liter casein (Satola’s test), BHI agar plates containing 4 µg/ml vancomycin (BHIAV), and commercially obtained vancomycin resistant enterococci (VRE) agar. A standard of 0.5 McFarland from an overnight culture in tripticase soy broth was prepared for each isolate. All three screening plates were inoculated with these bacterial suspensions. Colonies which could grow on plates were counted manually at 24th and 48th hours. MICs of the growing colonies in Satola’s test were determined using gradient test for vancomycin to see whether the MICs of VISA colonies would decrease or not.

Results: Among 100 MRSA isolates, 43 (43%) were found as hVISA using Satola’s test. BHIAV and VRE agar screening test results were found 70% and 4%, respectively. Finally, at the step of gradient test, MIC values of 20 (47%) hVISA isolates reduced to 2 µg/ml after subculturing for the test.

Conclusions: At the step of gradient test, nearly half of the clones of hVISA isolates remained as VISA (MIC>2) after subculturing. When we compared VRE agar and BHIAV screening test with Satola’s method, we concluded that both two tests failed to detect hVISA properly. Finally, we found higher rates of hVISA comparing other studies in Turkey.

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Dried blood spots tested with the Abbott m2000 sp/rt system perform well to identify patients with active HCV infection in Vietnam

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Background: In recent years, the treatment advances of direct acting antivirals (DAA) have radically changed the management of HCV patients. However, in resource-limited countries, identification of patients with active HCV infection continues to present a challenge in remote settings due to the limited access to laboratories able to measure HCV viral load. Dried blood spots (DBS) transferred to a central laboratory may be able to overcome this challenge.

Materials/methods: A total of 315 HCV-infected patients, who never received anti-HCV treatment, provided each three type of samples: plasma, DBS with calibrated quantities of venous blood and DBS with uncalibrated quantities of capillary blood. Qualitative comparison was conducted in terms if detection of HCV viral load on DBS as opposed to plasma to estimate sensitivity and specificity. Quantitative comparisons were conducted by means of correlation estimation and Bland-Altman analysis.

Results: Of the 250 patients with detected plasma HCV viral load, 245 also had detectable DBS HCV viral load (capillary or venous) leading to a sensitivity of 98.0% (95% confidence interval [CI]: 95.4%-99.3%); importantly, all measurements with an HCV viral load >118 IU/mL on plasma were also detected on DBS. When HCV was not detected with plasma, it was also not detected with DBS resulting in 100% specificity (95% CI: 94.5%-100%). Quantitative HCV viral load results were very similar when utilizing plasma or DBS sample types as illustrated by correlations >0.99 and by the Bland-Altman analyses.

Conclusions: DBS sample types performed well to distinguish patients with active HCV infection, and who therefore need treatment, from the other patients. DBS with either uncalibrated capillary blood or calibrated venous blood provided similar results.

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Abstract 505

Potential value of qPCR for the early detection of Mucorales in high-risk patients

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**Background:** Mucormycosis is a rare but often fatal infection in immunocompromised patients. Early and appropriate treatment is paramount for the outcome of the patients. Diagnosis based on clinical symptoms, histopathology, computerized tomography (ct) can be unreliable. Additionally, culture is often negative despite an infection. In order to evaluate the benefit of qPCR as an early and specific diagnostic marker for Mucorales infections we have tested respiratory samples from hematotoxicological and oncological patients of the University Hospital Essen.

**Materials/methods:** Overall we have analyzed 120 respiratory samples from 92 patients (64 % male, age 11-78 years, median = 61 years) for the presence of Mucorales using an inhouse qPCR (Bialek 2005, Löffler 2016) and culture. The qPCR assay simultaneously detected a 175bp fragment of the 18s rRNA gene and a 107bp fragment of the 28s rRNA gene. Limit of detection (LOD) was established by serial dilutions of Mucorales DNA and by serial dilutions of fungal material in a respiratory sample. Aliquots of diluted fungal material were inoculated onto an agar plate for fungal count (fungus forming unit, ffu).

**Results:** LOD of the qPCR assay was 0.1pg/ µl (18s) and 1pg/ µl (28s) when using diluted DNA, and 2ffu/ ml for both targets when using diluted fungal material. A clinical sample was defined as positive only when both targets were amplified (cycle threshold value below 40). Nine samples (7.5%) of six patients were tested positive for the presence of Mucorales DNA by qPCR. Culture was only positive in two samples from two patients (1.7%). Ct scans revealed characteristic signs for mold infections in all six patients. The outcome of all patients was fatal.

**Conclusions:** Culture based microbiology is of limited value for the early detection of Mucorales. Our results generally indicate a good agreement between the qPCR assay and the results of ct scans. The qPCR assay we performed was sensitive and specific enough to detect infected patients. We therefore consider qPCR a potential tool for the early detection for Mucorales. Additionally, we recommend regular screening of high-risk patients by qPCR.

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**Evaluation of efficacy of antibacterial prophylaxis in case of paraproctitis**

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**Background:** The treatment of acute paraproctitis is a topical problem in coloproctology. There is little reliable data on the effectiveness of Ceftriaxone / Sulbactam in preventing postoperative complications. The purpose of this study is to evaluate the effectiveness of Ceftriaxone / Sulbactam in the prevention of postoperative complications, using various schemes of pre- and perioperative prevention.

**Materials/methods:** In a prospective study conducted in the period from December 2018 to March 2019 were analyzed cases of acute paraproctitis in patients of different age groups. Patients were stratified into 2 groups: patients of the 1st group - with a mild course of paraproctitis, requiring only antibiotic prophylaxis, and the 2nd group - patients with moderate and severe course, who received additional therapy with Ceftriaxone / Sulbactam.

**Results:** The study involved 95 people. In 25 patients (26.3%) of 95, prolongation of perioperative antibiotic therapy was required. In 88 cases out of 95 (92.6%) bacterial cultures were taken. In 43 bacterial inoculations out of 82 (52.4%) was found monoculture and in 39 cases - association of microorganisms (47.6%). In bacterial inoculations was determined sensitivity to Ceftriaxone. In most cases, seeded pathogens were sensitive to this drug. The causative agents of acute paraproctitis were, as elsewhere in world practice, in most cases typical pathogens:

Were received monocultures of microorganisms:

- *Escherichia coli* 24 out of 43 (55.8%)
- *Staphylococcus spp.* 9 out of 43 (20.9%)
- *Streptococcus spp.* 4 out of 43 (9.3%)

And association of microorganisms. *Escherichia coli* with:

- *Bacteroides spp.* 6 out of 39 (15.4%)
- *Klebsiella spp.* 6 out of 39 (15.4%)
- *Staphylococcus spp.* 3 out of 39 (7.7%)
- *Streptococcus spp.* 3 out of 39 (7.7%)
- *Enterococcus spp.* 3 out of 39 (7.7%)

**Conclusions:** Ceftriaxone/sulbactam shows high clinical efficacy when used as a preparation for pre- and perioperative prophylaxis in patients with acute paraproctitis. The effectiveness of the drug in monotherapy [40% of patients] in the absence of postoperative complications is more than satisfactory with mild to moderate paraproctitis. It is possible to recommend the use of the pre- and perioperative prophylaxis with Ceftriaxone / Sulbactam.

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Abstract 508

Investigation of an Enterobacter cloacae OXA-436 carbapenemase outbreak: when everything goes down the drain
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Background: In August 2017, a patient (index) at the Department of Cardiology, Odense University Hospital, Denmark, was diagnosed with Enterobacter cloacae ST90 from a wound swab harbouring an OXA-436 (OXA-48 like) carbapenemase gene, located on a conjugative plasmid. This specific combination of sequence type and gene had not been observed in Denmark before (OXA-436 was initially observed in Denmark in September 2013 in E. asburiae at a hospital in the Copenhagen area). There was no history of recent travel outside of Denmark. In the following 1½ year, six patients from the same department as the index patient were also diagnosed with the same E. cloacae OXA-436 (Figure 1). However, there was no direct epidemiological link between several of the patients apart from the department. Screening (rectal swab) of all patients at the department was performed several times during the outbreak. Staff and procedures were audited by the infection control team, but no source or route of transmission was revealed. Finally, an investigation focusing on the department facilities, including sinks and drains, was performed.

Materials/methods: In February 2019, all drains, sinks and bedpan boilers/instrument washers from the affected department were sampled with eSwab (Copan, Italy) and cultured on selective agars for carbapenemase detection (Chrom ID Carba Smart, bioMerieux, France). Cultured isolates of Enterobacterales were submitted for whole genome sequencing and compared to the index patient E. cloacae isolate.

Results: Seven drains, 25 sinks and three bedpan boilers/instrument washers were sampled. E. cloacae ST90 with the OXA-436 gene were detected from two shower drains in the patient bathrooms.

Conclusions: The shower drains were the most likely source of this outbreak. Staff reported that the shower drains had been partly clogged resulting in regular overflow of water returning from the drains. Drains were unclogged and cleaned, and extra cleaning of the bathrooms was initiated. No further cases have been seen for eight months. Patients and staff should be aware of the potential of transmission of resistant bacteria from shower drains.

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Trophic cooperation promotes *Pseudomonas aeruginosa* and *Staphylococcus aureus* survival in cystic fibrosis patients

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**Background:** Lungs of cystic fibrosis (CF) patients are colonized by numerous microorganisms including *Pseudomonas aeruginosa* (PA) and *Staphylococcus aureus* (SA). These bacteria are can co-infect up to 40% of patients according to the age class. Different interaction patterns between PA and SA can be observed throughout infection: PA strains can either inhibit SA growth through well-described mechanisms or coexist with SA. We aim to better understand the coexistence interaction state with SA by characterizing its impacts on PA physiology.

**Materials/methods:** Twenty-two PA/SA strain pairs in coexistence were isolated from CF patient sputa and cultivated in monocultures or co-culture. PA genomic expression was assessed in these conditions by RNAseq (2 strains pairs) and confirmed by RT-qPCR (22 pairs). Deletion mutants of the aco system were produced in a clinical PA isolate and cultivated in regular or long-term co-culture with SA, during which acetoin concentration and bacterial survival were monitored. Acetoin dosages were also performed on CF patient sputa.

**Results:** Transcriptomic analyses show that co-culture with SA significantly affects the expression of numerous genes involved in nutrient metabolism in PA. In presence of SA, 70% of PA strains presented an important overexpression of the aco system, involved in acetoin catabolism. Acetoin, produced by clinical SA strains and detected in CF patient sputa, was shown to be responsible for aco system induction in PA. Clinical PA strains actually catabolized acetoin produced by SA, especially during coexistence interaction. This catabolism promoted the survival of both pathogens in nutrient-depleted conditions, as acetoin constituted a carbon source for PA and presented a dose-dependence toxicity towards SA.

**Conclusions:** Our results indicate that coexistence with SA induces the up-regulation of the aco system and acetoin catabolism in PA. Due to its beneficial effects on both bacteria, acetoin catabolism could testify to the establishment of trophic cooperation between SA and PA in the CF lung environment, promoting their persistence.

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Evaluation of prevalence and risk factors of *Helicobacter pylori* infection in an urban population

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Background: High prevalence rates of *Helicobacter pylori* infection have been reported in developing countries like Nigeria. This infection is known to significantly contribute to the development of gastric cancer and other non-communicable diseases. It is imperative that risk factors associated with this infection are explored to develop evidence-based prevention strategies and improve the health of developing communities.

Materials/methods: A hospital-based cross-sectional study was conducted between May and July 2017 among dyspeptic adults in the GOPD of Garki Hospital Abuja. Two hundred and eighty participants were tested for *Helicobacter pylori* using serum *H. pylori* Immunoglobulin G antibody test kits. Data was collected using pre-tested interviewer-administered questionnaires to assess the risk factors, presenting symptoms and signs and prevalence of *H. pylori*. Epi-info 7.2 was used for data entry and SPSS version 25 for analysis. Logistic regression and odds ratios with 95% confidence intervals were computed to identify risk factors and clinical features associated with *H. pylori* infection.

Results: Out of 280 study participants, 150 (53.6%) tested positive for *H. pylori* infection. Age group 26 – 35 years (OR = 8.40: 95% CI = 1.777 to 39.722), age group 56 – 65 years (OR = 6.78: 95% CI = 1.133 to 40.524), monthly income group $150 to $200 (OR = 11.81: 95% CI = 1.868 to 74.731) and monthly income group of $300 and above (OR = 7.53; 95% CI = 1.565 to 36.195) were positively associated with *H. pylori* infection. Family history of dyspepsia or peptic ulcer disease (OR = 0.32: 95% CI = 0.128 to 0.784), regular consumption of fruits and vegetables (OR = 0.11: 95% CI = 0.046 – 0.281) and regular hand-washing with soap and water (OR = 0.02: 95% CI = 0.006 – 0.040) were negatively associated with *H. pylori* infection.

Conclusions: The prevalence of *H. pylori* amongst dyspepsia patients in Garki Hospital Abuja was found to be high. Interventions to increase awareness of *H. pylori* infection and prevent infection and transmission of *H. pylori* through good dietary and hygiene practices are vital.

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Abstract 514

Seroprevalence of anti-CCHF IgG in population in different districts of endemic region and Crimean-Congo haemorrhagic fever morbidity

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Background: 710 cases of Crimean-Congo hemorrhagic fever (CCHF) were recorded in the Rostov region of Russia from 2000 to 2019. This region is endemic for CCHF since the sixties of the last century.

Aim of study: to detect the level of seroprevalence in the 12 endemic for CCHF districts of the Rostov region and compare it with CCHF morbidity in the same areas.

Materials/methods: 522 serum samples of conditionally healthy individuals from 12 districts of Rostov region were checked on anti-CCHF-IgG by ELISA. Analysis of CCHF morbidity from 2015 to 2019 in the same districts was implemented

Results: Within 4 years (2015-2018) the decrease of CCHF morbidity was observed. 77 CCHF cases were recoded in this area in 2015, 51 in 2016, 37 in 2017, 24 in 2018. In 2019 CCHF morbidity raised up to 48 cases. The largest number of cases (72%) were registered in 8 endemic districts. anti-CCHF-IgG were found in individuals from 6 districts. On average, the proportion of seropositive individuals for CCHF was 1.2%. 10 years ago, this level was 0.4%. This indicator ranged from 0% (in Dubovsky, Martynovskiy, Kamensky, Peschanokopsky and Tselinsky, Proletarsky districts) to 1.4-1.7% (in Zavetinsky, Remontensky Orlovsky, Bagavevsky districts) and 2.2% - 2.3% in Salsky and Zimovnikovsky districts. In areas with a high incidence of CCHF we have observed positive correlation with a level of seroprevalence (r = 0.8, p=0.04). But in districts with the high prevalence of anti-CCHF-IgG, the level of morbidity (5-9 cases of CCHF annually) was more than 10 years ago (13-14 cases). From other side, In the 1/3 of districts with 0% seroprevalence (Dubovsky and Martynovsky districts) the incidence of CCHF was higher than 10 years ago (4-5 versus 0-1). Increasing the level of seropositive individuals in the region as a whole is inversely related to the incidence rate (r = -0.8, p=0.04).

Conclusions: These data allow to predict a further increase the incidence of CCHF in the districts with low level of seroprevalence and annual registration of cases of CCHF and should be used in the CCHF epidemiological forecast.

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**Abstract 517**

**Prevalence and serotype distribution of *Streptococcus agalactiae* colonisation among pregnant women in Taiwan**

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**Background:** Group B streptococcus (GBS), also known as *Streptococcus agalactiae*, is a prevailing pathogen that leads to neonatal bacteremia, sepsis, meningitis, and even mortality. The study was aimed to investigate the antennal GBS colonization in pregnant women at the gestational age of 35-37 weeks in Taiwan, including prevalence, serotype distribution, antimicrobial resistance profiles, and molecular characters.

**Materials/methods:** A total of 977 vaginal swabs were collected throughout the 2016 calendar year at single hospital in Taiwan. All GBS isolates were tested for capsule serotypes by using multiplex polymerase chain reaction (PCR) assay. Multilocus sequence typing (MLST) was carried out on selective representative isolates. Antimicrobial susceptibility profile to penicillin, ampicillin, erythromycin, clindamycin, levofloxacin, and ceftriaxone was determined in accordance with CLSI guideline. PCR targeting the major virulence gene, *HvgA*, was performed in isolates of clonal complex (CC) 17.

**Results:** Of the 977 swab cultures, 219 were positive for GBS (22%). In total, seven serotypes were identified, and serotype III was the leading capsular type (25.1%) followed by VI (22.4%), V (14.6%), Ia (13.7%), II (11.9%). Serotype IV was not detected in the present study. MLST analysis was carried out in 105 isolates and depicted 14 sequence types (ST). The leading three sequence types in order were ST1 (50, 47.6%), ST12 (10, 9.5%), ST17 (8, 7.6%). Of 105 MLST tested isolates, 21 were serotype VI and fully were ST1 (100%). For ST12, serotype II was the dominant type (9/10, 90%). In addition, a total of 8 isolates were identified as CC17 strain and all were serotype III. All these 8 ST17-III isolates harbored *HvgA* gene. Four clonal complexes were found in this study and the predominant clonal complexes were CC1 (51, 48.6%), followed by CC23 (19, 18.1%). Regarding of antimicrobial resistance, all the isolates were susceptible to penicillin (100%). Resistance rates of erythromycin and clindamycin were 41.1% and 39.3%, respectively.

**Conclusions:** In this present study, GBS colonization rate of pregnant women in Taiwan is 22%. Serotype III and VI are the two leading capsule types and the CC1 is the predominant clonal complex. Penicillin was still the first choice for treating GBS infection.

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Interim pharmacokinetic analysis of a multi-centre randomised open label phase IIb study in neonates to validate the meta-analysis population pharmacokinetic model used to simulate an optimised dosing regimen in neonates and infants aged < 90 days: the NeoVanc trial

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Background: Vancomycin remains one of the most widely prescribed antibiotics for Gram-positive neonatal late onset sepsis (LOS), however, a consensus on optimal vancomycin dosing and duration is lacking. Robust neonatal clinical pharmacokinetic (PK) data comparing different vancomycin dosing regimens remain sparse. NeoVanc (NCT02790996) is a European, randomised controlled, non-inferiority trial comparing an optimised and standard vancomycin regimen in infants aged ≤ 90 days with suspected/proven Gram-positive LOS. The optimised regimen was determined through pre-clinical studies including a population PK meta-analysis of individual data from >1600 babies.

Materials/methods: Babies with clinical sepsis (≥3 clinical/laboratory criteria) or confirmed sepsis (Gram-positive blood culture and ≥1 clinical/laboratory criterion) were recruited. Participants were randomised 1:1 to the optimised regimen [vancomycin loading dose (25 mg/kg) followed by 5±1 day course] or a standard regimen [no loading dose; 10±2 day vancomycin course]. An interim PK analysis was performed; the validation dataset was collected from 8 centres in 5 European countries. Data collected included demographic variables (gestational and postnatal age, birth and current weight), vancomycin administration (dose, time of start and end of infusion, exact sampling time), creatinine concentrations (Jaffe, enzymatic), vancomycin concentrations (ultraperformance liquid chromatography-tandem mass spectrometry).

Results: 68 babies recruited between March 2017 and April 2018 were included in the interim analysis. Gestational age was <29 (n=16), 29–36 (n=22), >35 (n=30) weeks. Median (IQR) birthweight was 1258 (455–4040) g with median weight at randomisation being 1525 (590–4156) g. Median post-menstrual age at randomisation was 33.8 (25.1–47) weeks. Median serum creatinine was 41.5 (8.84–96.36) µmol/L. 240/255 PK and scavenged PK samples were evaluable. Vancomycin concentrations were used to confirm the reliability of the meta-analysis model where clearance (CL) was dependent on current weight, method used to quantify creatininaemia, renal maturation (RM) and renal function (RF) according to CL = 86 × [CW/1350]^0.68 × RM × RF × F_{Jaffé-Enzymatic} × F_{race}

Conclusions: External validation with NeoVanc trial PK data confirmed the predictive performance of the model developed from the PK meta-analysis.

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Abstract 523

Unravelling the mechanism of virulence of M1 protein of Streptococcus pyogenes

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Background: Most pathogenic bacteria form complex extracellular protein-protein interaction networks (PPINs) with host proteins on the bacterial surface. The dynamic PPIN and the way they are formed and regulated, can deepen our understanding of bacterial infection and host immune response. However, it still remains a challenge to quantitatively determine the dynamics, structure and function of such host-pathogen interactions in a systems-wide manner.

Materials/methods: To enable quantitative analysis of PPINs we have established a generic affinity-purification mass spectrometry-based proteomics strategy (AP-MS)1 to investigate bacterial pathogen-host PPINs at a grand scale. We have applied the AP-MS strategy to determine how human host and mouse (BALB/c) plasma proteins competitively interact with main virulence factor - the M1-protein – of the human pathogen Streptococcus pyogenes.

The experimental workflow includes isolation of interacting proteins using affinity-enrichment followed by highly quantitative MS techniques including sequential window acquisition of all theoretical fragment ion spectra analysis MS (SWATH-MS)2.


Results: The dynamic regulation of the PPINs was assessed using a mixture of human and BALB/c mouse (50/50 vol/vol dilution) plasma to measure any inherent competition between both mammalians’ protein interactions. Eleven different clusters of proteins with different binding patterns were identified, being human and mouse albumin, fibrinogen, C3 protein of complement system or mouse IgM and human IgGs, enrichment proteins [clusters V, VI and VI, Figure 1A]. A full peptide-level analysis unraveled several common peptides among human and mouse proteins [Figure 1B], of which fibrinogen was the most conserved protein among mammalians, showing a high homology human to mouse. (Figure 1C).

Conclusions: These results demonstrate how M1 protein assembles a complex PPIN in plasma which could modulate the host immune response. Excitingly, the M1-protein is shown to be a ligand for human and mouse fibrinogen, but also for human IgGs or heavy chain variable domains of mouse Igs.
Characterisation of internalin genes in Listeria monocytogenes food strains, and their association with invasiveness in vitro

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Background: Listeria monocytogenes (Lm) is a facultative intracellular pathogen and the causative agent of a food-borne disease listeriosis. The bacterium colonizes niches in food processing environments due to ability to survive in a variety of stress conditions. Internalization enables Lm to invade non-phagocytic cells like intestinal epithelium. The process is mediated mainly through a group of proteins called internalins (Inl), of which InlA and InlB have been shown to play a critical role. In this study, 16 strains of L. monocytogenes collected from food samples in Poland were tested for the hemolytic activity and invasiveness in cultured cells. Data from phenotypic analysis were integrated with genomic approach to assess the biodiversity of the pathogen and reveal genetic variants of internalin genes.

Materials/methods: Invasiveness was tested in gentamycin protection assays using epithelial (HeLa), placental (JEG-3), and neuronal (Neuro-2a) cell lines. Simultaneously, the isolates were subjected to Illumina MiSeq whole genome sequencing (WGS). In silico multi-locus sequence typing (MLST) and core genome MLST were performed using Institute Pasteur Lm MLST database. Sequence search for the presence of virulence genes, manual annotation etc. were performed with UGENE program. Sequences of LIPI-1 pathogenicity island and internalin clusters were aligned using MAUVE software.

Results: The isolates were differentiated into 2 phylogenetic lines (I, n=9; II, n=7), and 8 sequence types (ST), with ST580 (5/16) being the most common. Five internalin profiles were distinguished: I (CC9), II (ST1 41 3), III (CC2, CC3, CC5), IV (ST51 7) and V (CC1). Premature stop codon mutation (AA 685) in inlA were identified in all line II isolates, of which only one exhibited unimpaired invasion to placental epithelial cells.

Conclusions: Comparative analysis revealed the presence of globally distributed sequence types along with differences among the isolates at a genomic level. Two strains exhibit unique features. LM-UW02, classified as the second known representative of ST1413, uniquely does not encode Vip protein and carries the A112T mutation in LRR region of inlB gene. LM-UW11 from phylogenetic line I, encodes InlG previously attributed to line II strains only and harbors LIPI-4 pathogenicity island characteristic mainly for clinical strains with increased CNS and placenta invasion capacity.

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**Regulation of intestinal bacterial translocation by intestinal lamina propria dendritic cells expressing TLR5 after trauma/haemorrhagic shock**

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**Background:** Enterogenous infection is a major cause of death induced by traumatic/hemorrhagic shock (T/HS). Specific toll-like receptors (TLR5⁺) lamina propria dendritic cells (LPDCs) are critical antigen presenting cells (APCs) for modulating the intestinal mucosa-related immunological state to defend against bacterial translocation. We aimed to investigate LPDCs’ responses after T/HS, which would deeply affect the subsequent local immunity of the intestinal mucosa as well as bacterial translocation.

**Materials/methods:** Wild-type (WT) and Tlr5⁻/⁻ mice were divided into T/HS and sham groups. After T/HS, TLR5⁺ LPDCs were sorted. Hemodynamic parameters and intestinal mechanical barriers were determined. Th1 differentiation was analyzed in mouse intestinal lamina propria (LP) or in a co-culture system of LPDCs and naïve T cells. Moreover, intestinal bacterial translocation and mouse survival were also monitored.

**Results:** CD11c⁺ MHCII⁺ LPDCs specifically expressed TLR5. No differences were observed between WT and Tlr5⁻/⁻ mice regarding hemodynamic parameters and intestinal mechanical barriers after T/HS. LPDCs sourced from T/HS WT mice induced decreased Th1 polarization and more bacterial translocation, however, Tlr5 knockout conferred LPDCs with abilities to induce increased Th1 polarization and remain stable under T/HS hit. Moreover, retinoic acid (RA) released by TLR5⁺ LPDCs might play a key role in modulating Th1 polarization. Finally, RA treatment clearly increased the quantity of Th1 cells in LP and attenuated bacterial translocation after T/HS in WT mice but not Tlr5⁻/⁻ mice (Figure 1), though mouse survival after T/HS was not prolonged by RA enteral supplementation.

**Conclusions:** Disordered LPDC TLR5-RA downregulation-induced Th1 differentiation might be an immunological mechanism of intestinal bacterial translocation and enterogenous infection after T/HS, and a TLR5-RA-independent mechanism that is relatively stable and rarely affected by T/HS may exist for LPDCs to polarize Th1 cells. In summary, both TLR5-RA-dependent and TLR5-RA-independent pathways within LPDCs may be therapeutic targets for interfering with Th1 differentiation and intestinal bacterial translocation.

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Are residual waters vehicles of transmission of resistance mechanisms? DARWIN JPI AMR-2016 study

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Abstract 532

Background: One of the biggest health problems is antimicrobial resistance (AMR) complicating the treatment of infections and community health. In 2016, DARWIN project (Dynamics of Antimicrobial Resistance Project in the Urban Water Cycle in Europe) emerges with the objective of developing a dynamic predictive model to assist in wastewater management, analyzing and quantifying resistant microorganisms and their genetic determinants, from their excretion in hospital and urban sources, to the water receiving surface (http://www.amr-darwin.eu/)

Materials/methods: Sampling has been carried out in 3 cities simultaneously, Copenhagen, New Castle and Santiago de Compostela, by 8 different points of the wastewater treatment system: hospital and urban effluent, wastewater treatment plant, relevant plant compartments, and in the Sar River up- and down-stream of the WWTP (purification plant), in Santiago de Compostela (ES). CHROMID®ESBL and CHROMID®CARBA (BioMerieux) were the chromogenic medias used for detection of ESBLs and carbapenemases respectively, plus a non-commercial MBO medium supplemented with antibiotics. Isolates were identified by MALDI Biotyper Bruker and sequencing of the 16S rRNA gene.

Results: A total of 504 resistant strains were isolated from the different sampling points in Santiago de Compostela city. MALDI Biotyper showed a correlation index with respect to 16S sequencing up 0.9 at genus level, because of the identification of environmental isolates non-associated with infection. The isolates with greater clinical relevance and resistance were isolated in the hospital effluent, highlighting the isolate of Klebsiella pneumoniae producing BLEEs and carbapenemases, and being Escherichia spp the most ubiquitous Enterobacteria. The greatest confluence of Aeromonas spp came from the residential effluent, although they were isolated at all points. After the treatments carried out in the wastewater, the resistant bacteria decreased by 80%. Downstream of the Sar River the largest isolates producing BLEEs were Aeromonas caviae complex, and resistant to carbapenemases were Pseudomonas spp

Conclusions: The isolates with greater clinical relevance and resistance, especially to carbapenemases, were isolated at hospital effluent. WWTPs could act as a vehicle for transmission of resistance mechanisms to environmental strains. Therefore, current wastewater treatments could be insufficient to eliminate resistant strains, especially those resistant to carbapenemases.
### DISTRIBUTION OF ISOLATES COLLECTED FROM DIFFERENT SAMPLING POINTS IN SANTIAGO COMPOSTELA CITY

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### DISTRIBUTION OF ISOLATES BY PHYLOGENETIC GROUP FAMILY

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Abstract 538

Hepatosplenic bartonellosis in immunocompetent adults: a case series and literature review

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Background: Bartonella henselae, agent of cat-scratch disease (CSD) is rarely responsible from visceral granulomatosis, reported by few case series with low numbers. The objective was to better characterize hepatosplenic bartonellosis (HSB) in immunocompetent adults, a rare complication of B. henselae infection.

Materials/methods: Retrospective study of all HSB diagnosed in 4 French tertiary care university hospitals in 2001-2018. Inclusion criteria were i) radiological lesions in liver and/or spleen; ii) B. henselae infection documented by PCR, or serology. We excluded patients <15-year-old or immunocompromised. A literature review was performed using Medline, Embase, and Scopus database, with no language or time restriction.

Results: Of 414 cases of bartonellosis documented during the study period in the 4 centres, 24 (5.8%) were HSB in immunocompetent adults [estimated incidence, 0.19/million inhabitants-year]. Literature review identified 72 additional cases. Overall, there were 53 men and 43 women, median age was 41 years [IQR 27-52], 79 (82.3%) reported contact with cats. Main symptoms were fever [n=80, 83.3%], weight loss [n=56, 58.3%], abdominal pain [n=45, 46.9%], and peripheral lymphadenopathy [n=45, 46.9%]. Median duration of symptoms before diagnosis was 30 days [15-60]. Abdominal imaging found round-shaped lesion[s] in liver [n=16, 16.7%], spleen [n=28, 29.2%], or both [n=52, 54.2%], multiple in 82 patients [85.4%]. B. henselae infection was documented by serology [n=80], and/or PCR [n=38]. Antibacterial treatment was prescribed for 81 patients [84.4%], mostly macrolides [n=38], cyclines [n=36], and quinolones [n=21], for a median duration of 30 days [14-60]. Surgery was performed in 12 patients [12.5%]. Of the 89 patients with follow-up data, 85 were cured [95.5%].

Conclusions: HSB is a rare disease in immunocompetent adults, with favourable outcome in most cases, whatever the management.

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Prophages, plasmid integration and lack of CRISPR-Cas elements underlie genome adaptation in European human-associated Staphylococcus aureus ST398


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Abstract third-party references: on behalf of COMBACTE-NET 6A & 6B working groups

Background: Staphylococcus aureus (SA) sequence type (ST) 398 causes both moderate livestock-associated and severe-to-fatal human-associated (HA) infections. HA-ST398 infections are common in Asia (AS) and are also gaining epidemiological importance in European (EU) hospitals. Due to geographic separation, we hypothesized divergent evolutionary trajectories among AS-HA-ST398 and EU-HA-ST398 and investigated these in ST398 isolated from hospitalized patients in both continents.

Materials/methods: EU-SA (n=868) obtained from mechanically-ventilated ICU or from surgical ward patients enrolled in ongoing clinical trials in COMBACTE-NET [NCT02413242, NCT02935244, NCT02296320] during 2014-2018 in 9 countries were whole-genome sequenced (short-read, Illumina-MiSeq; and long-read, n=2, Pacbio Sequel). Raw read processing and assembly, MLST-typing, resistance/virulence gene identification and genome annotation were performed with BacPipe (v1.2.6; https://github.com/wholeGenomeSequencingAnalysisPipeline/BacPipe) and SMRTLink v7.0.1. EU-HA-ST398 (n=44) were identified and genomic relatedness of 1 isolate/patient (n=26), together with AS-HA-ST398 sequences (n=8, hospitalized patients in China, 2010) obtained from NCBI, was studied using allelic-loci-comparison (cg/wgMLST) with a study-specific ST398-scheme (chewBBACA), comparative genome analysis (Mauve v2.4.0) and SNP calling (CLC v9.5.1).

Results: Analysed strains (n=34) formed three clades based on core-genome and whole-genome MLST (Figure A & B). EU-HA-ST398 segregated in 2 clades (average 341 allelic-loci-differences) differentiated by the presence and absence of the highly-conserved φST398_5 prophage that inserts in smpB which encodes a SsrA-binding protein. In both core and accessory genome analysis, EU-HA-ST398 Clade 2, containing primarily ST398 isolated from South-Eastern Europe, clustered closer to AS-HA-ST398 (n=6, Clade 1) than to Clade 3 that consisted of strains from Western Europe. All ST398 lacked CRISPR-Cas elements and EU-HA-ST398 genomes harbour integated plasmids and resistance-gene clusters (Figure C). On average, the accessory genome ratio determined for the 5 long-read-sequenced HA-ST398 (2 EU & 3 AS) was 6.5% which is higher than USA300-FPR3757 (ST8; 4.807%) but lower than TW20 (ST239; 11.088%).

Conclusions: Our data shows that HA-ST398 genomes are labile, easily acquire and integrate mobile elements that might underlie the emergence and success of the clone. The remarkable genome relatedness of the Chinese and the South-Eastern European clade indicates that an intercontinental spread of this clade might have been a recent occurrence.
Allelic loci comparison of HA-ST398 isolates

Three clades formed in the cgMLST (A) and wgMLST (B) trees. AS-HA-ST398 mainly clustered separately from EU-HA-ST398 (Clade 1) (left). Two clades formed in EU-HA-ST398 based on the presence of ampi-disrupting φST398_5 (right). EU-HA-ST398 Clade 2, containing East European strains, linked closer to Clade 1 than Clade 3. C) Schematic view of EU-HA-ST398, AS-HA-ST398 and their similarity to existing plasmids. pUR3912 was completely integrated in the EU-HA-ST398 chromosome of Clade 2 (100%) and almost completely in EU-HA-ST398 Clade 3 (93%) but was missing in the AS-HA-ST398 chromosome. Green lines indicate shared genes. (blue: insertion elements – orange: resistance genes – yellow: replication genes).

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Abstract 567

Can Rapid Antimicrobial Susceptibility Testing (RAST) improve the time to the optimal therapy for bloodstream infections?

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Background: Gram-negative bloodstream infections (BSI) remain an important cause of morbidity and mortality. Fast and reliable antimicrobial susceptibility assays ensure early adequate therapy and may reduce the prolonged use of empiric broad-spectrum antibiotics. EUCAST has validated new breakpoints for short incubation disk diffusion testing directly from positive blood culture bottles, interpretable after 4, 6 and 8 hours (RAST). We aimed to evaluate the effect of RAST on BSI management in our hospital.

Materials/methods: RAST was implemented at the University Medical Center Hamburg-Eppendorf (Germany) in addition to standard of care [SOC; Vitek2], i.e. availability of AST results a day after blood culture positivity. For all interpretable results (zone diameter outside the area of technical uncertainty, ATU) categorical agreement (CA, concordant interpretation by SOC and RAST), very major error (VME, resistant by SOC, susceptible by RAST), major error (ME, susceptible by SOC, resistant by RAST) and minor error (mE, susceptible, increased exposure by SOC, resistant or susceptible by RAST) rates were calculated. The proportion of patients receiving optimal antimicrobial therapy after communication of RAST results was determined.

Results: For 97 blood cultures growing species for which RAST breakpoints are available, overall categorical agreement between RAST and SOC was 97.1%; mE rate was 1.5%, ME rate was 1.4% and no VME were observed (Table 1). A significant number of results within the ATU [15B/879] was found. Clinical impact of RAST was evaluated for 51 patients from 1st May to 31th July 2019. In 90.2% [46/51] of the cases RAST was available after 4h, in 7.8% [4/51] after 6h and in 2% [1/51] after 8h. Optimal treatment was achieved in 21/51 (41.2%) patients according to the RAST results and among these, RAST allowed for early escalation to a broad-spectrum antibiotic in 6 cases related to multi-resistant isolates. An unnecessary escalation based on RAST occurred in 9/51 (17.6%) patients.

Conclusions: Our findings suggest that the implementation of RAST may be especially helpful for early treatment escalation in BSI caused by multi-resistant bacteria. RAST result communication should be integrated into structured antimicrobial stewardship programs to prevent inadequate or premature treatment adjustments.

Table 1. RAST categorical agreement vs. Vitek2 per species and incubation time from 1st May to 30 September 2019.

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<th>K. pneumonia (10 isolates)</th>
<th>P. aeruginosa (9 isolates)</th>
<th>A. baumannii (1 isolate)</th>
<th>Total (97 isolates)</th>
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<td>4h</td>
<td>6h</td>
<td>8h</td>
</tr>
<tr>
<td>Correct</td>
<td>320 (97.3)</td>
<td>244 (97.2)</td>
<td>51 (96.3)</td>
<td>27 (96.4)</td>
<td>42 (95.5)</td>
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mE: minor error
ME: major error
VME: very major error
ATU: Area of Technical Uncertainty

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Proton pump inhibitors increase the digestive carrying of OXA-48-producing Enterobacteriaceae in a mouse model

François Javaudin*, Quentin Le Bastard¹, Michel Dion¹, Yhiienew Bezabih¹, Emmanuel Montassier¹, Eric Batard¹

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Abstract: Proton pump inhibitors (PPI) are responsible for altering the composition of the gut microbiota but little is known about their impact on the gut resistome. It would appear that PPI consumption is associated with extended-spectrum β-lactamase–producing Enterobacteriaceae rectal carriage at hospital admission. Our objective was to evaluate the effect of PPI on the digestive carriage of OXA-48-producing Enterobacteriaceae in a mouse model.

Materials/methods: C57BL/6J mice were initially treated orally with amoxicillin (0.5 g.l⁻¹ in drinking water) for 7 days before the bacterial challenge (10⁷ CFU of OXA-48-producing Escherichia coli) by gastric gavage. PPI were added to drinking water (0.1 g.l⁻¹ of pantoprazole) for a group of mice (PPI group) throughout the experiment while the control group did not receive them. The stool was collected for 15 days after the bacterial challenge. The bacterial count was performed on selective chromogenic medium for the screening of OXA-48 type Carbapenemase-Producing Enterobacteriaceae. The mice were housed in individual cages to avoid inter-individual contamination.

Results: Height mice were analyzed in the PPI group and 12 in the control group. One day after the bacterial challenge the PPI group had a higher average concentration of E. Coli OXA-48 in the feces (2.1x10⁹ CFU.g⁻¹ versus 2.8x10⁷; P < 0.001). Except for the 3rd day after the bacterial challenge, this concentration was higher in the PPI group than in the control group (P < 0.001 on days 6, 10 and 15). Indeed, there was a clear decrease in E. Coli OXA-48 colonization in the control group from the 6th day post-bacterial challenge [approximately 4 log CFU.g⁻¹], while the PPI group kept a high level of carriage [approximately 8 log CFU.g⁻¹] (Figure).

Conclusions: The use of PPI could be a factor promoting digestive colonization with resistant bacteria. These widely prescribed treatments should be evaluated in humans in order not to ignore a possible factor promoting the spread of this type of bacterium.

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Abstract 572

**Time to positivity of blood cultures and its role in the diagnosis of bacteraemia**

Amaia Aguirre Quinonero, Maitane Marroyo-Salazar, Ester Saez De Adana Arroniz, Andrés Canut

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**Background:** This study aimed to evaluate the time-to-positivity (TTP) of all bacteraemia episodes (true and contaminations) isolated in a tertiary hospital in order to study to what extent the TTP can provide information on the type of microorganism isolated and its involvement in infection.

**Materials/methods:** From January to October 2019 a total of 1121 bacteraemia episodes were recorded. Of them, 742 were considered true (698 monomicrobial, 44 polymicrobial) and 379 contaminations. TTPs of the first positive bottle of all monomicrobial episodes (n=698) and of the ones considered contaminants (n=379) were evaluated. Blood culture samples are routinely incubated at 35ºC until they yield a positive signal or for up to five days in a BD-BactecFX (BD®) automated instrument. Each new episode is daily discussed by the antimicrobial stewardship program team.

**Results:** Table 1. The average TTP for true cases was 17.3h (16.8h excluding yeasts) and 32.5h for contaminations. Bottles of true episodes flagged positive considerably faster (p<0.001) than the ones considered contaminations. Regarding true episodes, 44.3% (309/698) grew in ≤12h, 85.4% (596/698) in ≤24h and 95.7% (668/698) in ≤48h. 98.7% (309/313) of the microorganisms with a TTP<12h were involved in a true episode. Regarding Enterobacterales, in 61.5% (122/343) the TTP<12h. Considering coagulase negative staphylococci (CoNS), the isolates considered contaminants yielded a TTP significantly higher (p<0.001) than the ones involved in infection. No significant differences in TTPs were observed among *Staphylococcus aureus* and significant CoNS, or among Enterobacterales and non-fermenting Gram-negative bacteria.

**Conclusions:** In hospitals with a high contamination rate, TTP can be especially useful in guiding towards the type of microorganism involved and its role in infection.

<table>
<thead>
<tr>
<th>Number of isolates</th>
<th>TPP (hours)</th>
<th>TTP&lt;12h</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>True bacteremia episodes</strong></td>
<td>698</td>
<td>17.3 (2.4-117.6)</td>
</tr>
<tr>
<td>Enterobacterales</td>
<td>343</td>
<td>13.9 (2.4-94)</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>253</td>
<td>13.3 (2.4-94)</td>
</tr>
<tr>
<td>Non-Fermenting Gram negative bacteria</td>
<td>27</td>
<td>21.6 (10.8-59.2)</td>
</tr>
<tr>
<td><strong>Gram-positive bacteria (n=296)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>63</td>
<td>17.6 (6.2-69.4)</td>
</tr>
<tr>
<td>CoNS</td>
<td>95</td>
<td>20.8 (3.2-70.3)</td>
</tr>
<tr>
<td>Yeasts</td>
<td>11</td>
<td>46.7 (13.1-1176)</td>
</tr>
<tr>
<td><strong>Contaminations</strong></td>
<td>379</td>
<td>32.5 (10.6-118.4)</td>
</tr>
<tr>
<td>CoNS</td>
<td>322</td>
<td>27.3 (13.0-103)</td>
</tr>
</tbody>
</table>

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Abstract 583

Treatment of latent tuberculosis infection based on the interferon-gamma releasing assay in allogeneic stem cell transplant recipients

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Background: The tuberculin skin test is being replaced by the interferon-gamma releasing assay (IGRA) for diagnosing latent tuberculosis infection (LTBI) in transplant recipients. However, there is limited evidence that IGRA-based LTBI treatment is effective in preventing TB in hematopoietic stem cell transplant (HCT) recipients. Therefore, we have evaluated its effectiveness.

Materials/methods: We retrospectively enrolled patients who underwent allogeneic HCT from January 2010 to December 2018 in a tertiary hospital in an intermediate TB-burden country, and observed TB development for at least 6 months of follow-up until 24 months after HCT. All patients underwent IGRA using QuantiFERON-TB Gold In-Tube (QFT-TB) to screen for LTBI before HCT. LTBI treatment was defined as taking isoniazid (INH) for at least 6 months. We classified the study population into three groups: the negative or indeterminate QFT-TB group, the positive QFT-TB with full LTBI treatment, and the positive QFT-TB without LTBI treatment [no treatment or early discontinued treatment].

Results: A total of 1,162 patients were followed-up for 1,550.4 person-years. 181 (15.6%) patients gave positive QFT-TB results. There were 981 (84.4%) in the negative (n=911) or indeterminate (n=70) QFT-TB group, 51 (4.4%) in the positive QFT-TB with LTBI treatment, and 130 (11.2%) in the positive QFT-TB without LTBI treatment, of whom 75 had no INH treatment and 55 stopped treatment prematurely. 21 (1.8%) patients developed active TB comprising 15 (1.5%) in the negative group, none in both the indeterminate group and in the positive QFT-TB patients with LTBI treatment, and 6 (4.6%) in the positive QFT-TB without LTBI treatment group. The median time from allogeneic HCT to TB diagnosis was 7.4 months (IQR 3.9-10.8). The incidence of TB in the positive QFT-TB without LTBI treatment group (3.58/100 person-years) was significantly higher than in the negative or indeterminate QFT-TB group (1.15/100 person-years) (p=0.01), and there was a trend towards it being higher than in the positive QFT-TB with LTBI treatment group (0/100 person-years) (p=0.09). The number needed to treat (NNT) was 22 (95% CI 12-99) with positive QFT-TB results.

Conclusions: IGRA-based INH treatment appears to lower the rate of post-transplant TB after HCT, with a reasonable NNT.

Table. Active tuberculosis based on QuantiFERON Gold In-tube assay and treatment of latent tuberculosis in allogeneic hematopoietic stem cell transplant recipients

<table>
<thead>
<tr>
<th>Confirmed or probable TB incidence rates</th>
<th>Number of total patients</th>
<th>Number of TB cases</th>
<th>Number of person-years</th>
<th>TB rate per 100 person-years</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative or indeterminate QFT-TB</td>
<td>981</td>
<td>15</td>
<td>1,393.2</td>
<td>1.15**</td>
<td>0.64-1.90</td>
</tr>
<tr>
<td>Negative QFT-TB</td>
<td>911</td>
<td>15</td>
<td>1,225.5</td>
<td>1.22**</td>
<td>0.69-2.02</td>
</tr>
<tr>
<td>Indeterminate QFT-TB</td>
<td>70</td>
<td>0</td>
<td>77.7</td>
<td>0</td>
<td>0.4-7.5</td>
</tr>
<tr>
<td>Positive QFT-TB with LTBI treatment</td>
<td>51</td>
<td>0</td>
<td>79.8</td>
<td>0</td>
<td>0.4-6.2</td>
</tr>
<tr>
<td>Positive QFT-TB without LTBI treatment</td>
<td>130</td>
<td>6</td>
<td>167.4</td>
<td>3.58**</td>
<td>1.32-7.80</td>
</tr>
</tbody>
</table>

TB: tuberculosis; QFT-TB: QuantiFERON-TB Gold In-tube; LTBI: latent tuberculosis infection. CI: confidence interval.

**P value = 0.34 between the negative or indeterminate group and the positive QFT-TB with LTBI treatment group

*P value = 0.05 between the positive QFT-TB with LTBI treatment group and the positive QFT-TB without LTBI treatment group

**P value = 0.01 between the negative or indeterminate QFT-TB group and the positive QFT-TB without LTBI treatment group

***P value = 0.02 between the negative QFT-TB group and the positive QFT-TB without LTBI treatment group

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Next-generation infection prevention: integrated whole genome sequencing and clinical epidemiology analysis to detect actionable carbapenem-resistant *Acinetobacter baumannii* transmission hotspots

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**Background:** CRAB is a significant hospital-acquired pathogen. In our centre, previous infection prevention and control (IPC) resources were concentrated on other multidrug-resistant organisms other than CRAB as the rate of CRAB was stable with no evidence of outbreaks. We used WGS to uncover horizontal transmission of CRAB and established plausible routes of transmission for targeted IPC actions in an endemic setting.

**Materials/methods:** We prospectively collected epidemiological characteristics of patients with CRAB infection or colonisation, and identified genetic relatedness of CRAB isolates using a pairwise single nucleotide polymorphisms (SNP) threshold of ≤ 11. We investigated patients with genomically-linked CRAB isolates for either spatio-temporal overlap (sharing the same ward at the same time) or spatial only overlap (sharing the same ward at different times). Findings were regularly presented to IPC and intensive care unit (ICU) committees, and follow-up actions were documented.

**Results:** Of 141 CRAB isolates identified between May and November 2016, 70 (48.2%) from 61 patients were available for WGS. Including 22 clinical (from 12 patients) and 11 environmental CRAB isolates from a previous 2015 study, a total of 92 samples (73 patients) were analysed. WGS identified seven distinct CRAB clusters involving a total of 47 patients (cluster size 1 to 28 patients). Genomic transmissions were explained by spatio-temporal overlap in 14 patients (29.8%) and spatial overlap only in 13 patients (27.7%). The focus of transmission was deduced to be the ICUs (Figure 1). Dissemination of CRAB from the ICUs to general wards and onward horizontal transmission were demonstrated in 2 instances. Clusters were also found to be related to the environmental isolates from 2015 suggesting the environment as a possible site or source of the horizontal transmission. Discussion of the above findings at IPC and ICU meetings led to implementation of enhanced control measures, including terminal environmental cleaning supplemented by hydrogen peroxide vapour disinfectant for rooms occupied by CRAB patients.

**Conclusions:** This study showed that WGS could be utilised as a "tool-of-persuasion" for action in IPC by demonstrating presence of ongoing transmission of CRAB in an endemic setting and identifying actionable routes of transmission for directed IPC interventions.

**Figure 1: Phylogenetic tree (left) with concurrent epidemiologic information.**

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Correlation between antibiotic resistance of main Gram-negative pathogens and antibiotic consumption in a general hospital of China

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Background: Our hospital is a newly established hospital in China, which is located in the tropics. Better depicting antibiotic consumption and antibiotic resistance may help better develop and implement an antibiotic stewardship with regional characteristics.

Materials/methods: Total antibiotic prescriptions, patient days and microbiological data from January 2014 to December 2017 were collected. Antibiotic use density (AUD) was expressed as daily defined dose (DDD) and normalized per 100 patient-days. The resistance rates of Gram-negative pathogens against commonly used antibiotics were calculated. The relationship between antibiotic consumption and bacterial resistance rate was described by Pearson's correlation coefficient.

Results: Different from mainland China, Acinetobacter baumannii was the leading Gram-negative pathogen, followed by Klebsiella pneumoniae, Escherichia coli and Pseudomonas aeruginosa. The AUD was gradually increased from 2014 to 2016, while it was slowly decreased in 2017. Ceftazidime/tazobactam, levofloxacin and meropenem were the top three consumed antibiotics. The proportion of multidrug resistant (MDR) Gram-negative bacteria was increased (>40%) before 2016, and it was decreased in 2017. The prevalence of MDR A. baumannii and MDR P. aeruginosa was correlated with the AUD of β-lactam/lactamase inhibitors, fluoroquinolones and carbapenems. The increased AUD of meropenem had positive effects on the incidence of carbapenem-resistant A. baumannii and P. aeruginosa.

Conclusions: Our study showed that there was an association between the resistance density of Gram-negative pathogens and the consumption of β-lactam/lactamase inhibitors, carbapenems and fluoroquinolones. Collectively, a multifaceted antimicrobial stewardship is necessary to decrease resistance density of available antibiotics.

Figure 1. Changing pattern in prevalence of pathogens and AUD of antibiotics from 2014 to 2017. a) MDR Gram-negative bacteria, b) AUD of various antimicrobial agents, c) AUD of mainly used antibiotics. MDR-AB: Multidrug-resistant A. baumannii; MDR-PA: Multidrug-resistant P. aeruginosa; MDR-KP: Multidrug-resistant K. pneumonia. AUD: antibiotic use density; DDD: defined daily dose. pd: patient-day.
**ABSTRACT BOOK – 30th ECCMID 2020**

**Abstracts 2020**

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Identification of individual risk factors for acquisition of vancomycin-resistant Enterococcus faecium (VRE) during an outbreak in an university hospital and implication in prevention strategies

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Background: Erasme hospital is the 864 bed academic hospital of the Université Libre de Bruxelles (Brussels, Belgium). A sustained increase in vancomycin resistant Enterococcus faecium (VRE) acquisition occurred in 2017 and involved several departments {mainly intensive care, haematology, and gastroenterology departments}. We performed a case control study to identify individual risk factors for acquisition of VRE.

Materials/methods: The study involved the 10 concerned hospitalisation wards, where we had implemented a systematic screening for VRE carriage at admission and during hospitalisation, from 1/1/2017 until 30/9/2018. Isolated VRE were genotyped during a limited period to explore the clonality of the outbreak. For each case, a spatio-temporally matched control was selected among screened patients. Case and control files were reviewed retrospectively to collect 36 selected variables (previous hospitalisation, intensive care stay, prior antibiotic therapy, major co-morbidities and procedures). Variables associated with a p-value < 0.1 were integrated into a multivariate model (multiple logistic regression).

Results: 73 patients colonised with vanA (n=72) or vanB (n=1) VRE fulfilled inclusion criteria and were matched with 73 controls. Genotyping demonstrated a high proportion of monoclonality (71% VRE) among the isolated VRE. A recent previous hospitalisation, intensive care stay, solid organ transplantation, and previous exposure to any antibiotics, or to 8 specific antimicrobial agents were associated with acquisition of VRE in univariate analysis. Among 15 variables with univariate p value <0.10, 4 were identified as independent risk factors for VRE colonization using the multivariate model: prior antibiotic therapy (OR 5.5 [1.1-26.5]; p = 0.04), vancomycin (OR 10.2 [1.1-95.8]; p = 0.04) or metronidazole exposure (OR 24 [2.2-267]; p = 0.01) and recent solid organ transplantation (OR 5,8 [1.1-29.3]; p = 0.03).

Conclusions: Our results confirm the role of antibiotic exposure, especially vancomycin but also metronidazole, in the acquisition of VRE. More originally, solid organ transplantation appeared also independently associated with this risk. This last risk factor could have important consequences if confirmed by others, as, in addition to prudent use of antibiotics and infection control measures, it could be recommended to avoid hospitalisation of VRE colonised patients in the same ward than transplanted patients.

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**Evaluation of a new commercial assay for detection and characterisation of carbapenemase genes**
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**Background:** The MAST ISOPLEX® CRE-ART is a loop-mediated isothermal amplification (LAMP) assay for detection of genes encoding carbapenemases in Enterobacterales, *Pseudomonas aeruginosa* and *Acinetobacter* species. We describe here the first evaluation of this assay with bacterial strains.

**Materials/methods:** The assay was evaluated with a diverse collection of 248 Gram-negative bacteria including Enterobacterales (*n* = 203), *Acinetobacter* species (*n* = 37) and *P. aeruginosa* (*n* = 8). A diverse range of carbapenemases were represented as well as a range of controls with other ß-lactamases. Isolates were sampled from Mueller-Hinton agar and DNA was extracted using an extremely simple protocol that involved heating at 95°C for 5 minutes in buffer. An internal process control was added at the point of extraction. The tests were performed on an ABI 7500 real time PCR instrument and the entire procedure (including sample preparation) required approximately 1 hour to generate results.

**Results:** 154 out of 155 (99.4%) carbapenemase-producing Enterobacterales (CPE) with VIM, NDM, IMP, KPC or OXA-48-like carbapenemases were successfully detected as well as 4/4 carbapenemase-producing *P. aeruginosa* (with VIM or NDM carbapenemases). One CPE isolate with NMC-A remained undetected. For *Acinetobacter*, the assay was able to successfully detect all isolates with OXA-23 (*n* = 23), OXA-24 / OXA-40 (*n* = 2) or NDM (*n* = 3). Eighteen other *Acinetobacter* isolates with carbapenemases (with OXA-51, OXA-58 or OXA-69) remained undetected as these genes are not targeted by the assay. The Ct values for isolates with carbapenemases ranged from 5.01 - 10.37 and provided clear distinction from 2/53 isolates without carbapenemases that generated a signal (Ct values > 20). Both of these isolates were negative on repeat testing. Applying a Ct cut-off value of 15 allowed successful detection of all genes that are targeted by the assay with 100% sensitivity and specificity.

**Conclusions:** The MAST ISOPLEX® CRE-ART is a simple and rapid assay that allows highly effective detection and differentiation of the most common carbapenemase genes including the 5 major carbapenemase genes found in Enterobacterales and OXA-23 in *Acinetobacter* species.

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Longitudinal analysis of lung microbiota in intensive care unit patients undergoing mechanical ventilation

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Abstract

Background: A specific and distinct lung microbiota is present in healthy subjects; changes in commensal composition has been associated with various chronic respiratory diseases. Aim of this study was to explore and quantify the potential modification of lung microbiota during mechanical ventilation (MV), paying particular attention to patients developing within 15 days ventilator associated pneumonia (VAP).

Materials/methods: Pilot observational multicenter prospective study involving two neurological and one general Intensive Care Units. All adult patients admitted from 10/2017 to 03/2019 and intubated for extra-pulmonary reasons with expected duration of MV longer than 48 hours were enrolled. All patient were followed until day 15 or at extubation, when earlier. Tracheal aspirate was collected at intubation (T0), day 3 (T3), 5 (T5) and 7 (T7). Pulmonary microbiota analysis through 16S-rRNA gene sequencing was performed in all VAP patients and in a subgroup of non-VAP ones, comparable within center for reason and period of intubation, and antibiotic administration pre-intubation (48h). Microbiota results are presented according to selected indices of α-diversity and β-diversity, as operational taxonomic units (OTUs) number and Principal Coordinates Analysis (PCoA), respectively.

Results: Sixty-nine patients were enrolled and microbiota of 18 VAP and 27 non-VAP was analysed. Groups were comparable for sex, Glasgow Coma Score (mean≈8), intubation days (mean=10) and diagnoses at intubation; although VAP patients were slightly younger (mean=46.8) than non-VAP (mean=57.6 years). When number of OTUs was analyzed over time, despite a wide variability between patients, a significant U-shape was observed, with median values of 139.2, 83.9, 87.2 and 129.8 at T0, T3, T5 and T7, respectively (p-value=0.03 after that age, days of intubation and VAP occurrence were considered into the repeated measures model). When the similarity between patients in terms of microbiota composition (β-diversity) was analyzed at each time point, no major differences emerged between VAP and non-VAP patients, as showed by PCoA figures.

Conclusions: This pilot analysis showed a U-shape time-pattern in the number of OTUs identified in pulmonary microbiota during MV. Considering its wide variability between-patients, larger samples are needed to analyze determinants of this time-pattern and to identify potential differences in microbiota species-composition.

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Occurrence of NDM-1-producing Morganella morganii and Proteus mirabilis in a single patient, Portugal: probable in vivo transfer by conjugation

Marta Aires De Sousa1,2,3; Jose Manuel Ortiz De La Rosa4; Maria Luisa Goncalves5; Augusto Costa5; Patrice Nordmann4; Laurent Poirel*4

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Background: Recent studies showed that KPC is the most common acquired carbapenemase identified among enterobacterial isolates in Portugal, where OXA-181 producers are also identified at low rate. Our study was initiated by the isolation of two carbapenem-resistant, carbapenemase-producing but KPC- and OXA-181 negative enterobacterial isolates from a single patient in Portugal.

Materials/methods: Carbapenemase genes were searched by PCR assays and mating-out assays were performed to further characterize the plasmid support of the carbapenemase genes. Genetic characterization of the plasmid supports was performed by whole plasmid sequencing using the Illumina technology.

Results: The two carbapenemase-producing isolates, namely a Morganella morganii and a Proteus mirabilis, were found to produce the NDM-1 carbapenemase. Surprisingly, both isolates shared the same \( \text{bla}_{\text{NDM-1}} \)-positive plasmid. This 154-kb in-size plasmid belonged to the IncA/C type and co-harbor two AmpC \( \beta \)-lactamase genes, namely \( \text{bla}_{\text{CMY-4}} \) and \( \text{bla}_{\text{DHA-1}} \), in addition to the 16S rRNA methylase gene \( \text{armA} \) encoding high-level resistance to aminoglycosides. Moreover, the \( M. morganii \) isolate produced the CTX-M-33 extended-spectrum \( \beta \)-lactamase possessing weak carbapenemase activity, encoded by another plasmid.

Conclusions: We showed here that, apart from KPC-type and OXA-181 carbapenemases that have been identified as common, another concern is the emergence of NDM-1-producing enterobacterial isolate in Portugal. We demonstrated here the in-vivo plasmid transfer of \( \text{bla}_{\text{NDM-1}} \)-Positive plasmid leading to dissemination of that carbapenemase gene within different enterobacterial species in a given patient.

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Abstract 600

Impact of a catch-up strategy of Tdap vaccination during hospitalisation on vaccination coverage among people over 65 years of age in Sarthe: the HOSPIVAC study

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1Le Mans, France

Background: The Tetanus-Diphtheria-Polio (Tdap) vaccination coverage of the elderly in France is insufficient and decreases with age. The main objective of this study was to evaluate the impact of a catch up strategy of Tdap vaccination during hospitalization among people over 65 years of age in Sarthe. The secondary objectives were to assess the Tdap vaccination coverage of this population and the factors independently associated with the vaccination status being up to date.

Materials/methods: This was a prospective, monocentric, randomized, clustered study. From 28/05/2018 to 27/05/2019, eligible patients over 65 years of age hospitalized in the general medicine ward at Le Mans General Hospital were included. The Tdap vaccination status of patients was collected at inclusion in both groups. In the intervention group, the vaccination update was performed during hospitalization. In case of temporary contraindication or refusal, a prescription was given to the patient upon discharge. The final vaccination status was collected during a call to the patient’s general practitioner two months after discharge from hospital.

Results: 157 patients were included, 73 in the intervention group 84 in the control group. In the intervention and control groups, vaccination coverage increased by 24.6% and 2.4% respectively (p<0.001). The vaccine coverage at inclusion was 46.5%. The factor independently associated with the vaccination being up to date was having been sufficiently informed about vaccination by the general practitioner OR = 5.07 [2.45-10.51]. In terms of knowledge of immunization status, 27.4% of patients who thought they were up to date were not.

Conclusions: The Tdap vaccination coverage of patients over 65 years of age in Sarthe is low. A catch up strategy for Tdap vaccination during hospitalization is effective. The availability of vaccines in hospital should improve immunization coverage. The systematic collection of the vaccination status of patients at entry should be facilitated by new data collection tools. The general practitioner is a source of information on vaccination for the population over 65 years of age.

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**Abstract 602**

**Faecal microbiota transplantation in the treatment of *Clostridioides difficile* infection**

Roman Stebel*1,2, Lenka Vojtilova1,2, Radek Svačinka1,2, Petr Husa1,2

1Masaryk University, Faculty of Medicine, Brno, Czech Republic, 2University Hospital Brno, Department of Infectious Diseases, Brno-Bohunice, Czech Republic

**Abstract third-party references:** Supported by Ministry of Health, Czech Republic – conceptual development of research organization [FNBr, 65269705]

**Background:** Fecal microbiota transplantation represents a unique therapeutic procedure targeted to restore the natural diversity of intestinal microbiota and to prevent recurrence of one of the most significant nosocomial infections – *Clostridioides difficile* colitis. The aim of this prospective study was to assess the success rate and safety of fecal bacteriotherapy in the treatment of *Clostridium* colitis at a clinic that had been the first in the Czech Republic to perform this procedure as early as 2010, and still is the national leader in the number of realized transplantations to-date.

**Materials/methods:** Within the monitored four-year interval [2015–2018], 172 patients were treated by means of intestinal microbiota transplantation. The patients were followed up by means of personal visits or by phone after treatment. If colitis did not recur within eight weeks, the treatment was evaluated as successful.

**Results:** The overall success rate of FMT in the study period was 76%. Advanced patient age was the only separate risk factor for treatment successful identified through subgroup analysis. No statistically significant difference in success rate was demonstrated based on patient sex, the way of fecal transplant application, initial antibiotic therapy or on the application of fresh or frozen donor stool. Two serious adverse events were observed in the study period; both cases were of rectal wall perforation, and occurred during stool suspension application via rectal enema. There was no lethality.

**Conclusions:** Fecal microbiota transplantation is a successful and safe therapeutic alternative for recurrent colitis caused by *Clostridioides difficile*.

**Diagram 1:** Dependence of FMT success rate on the number of previous CDI episodes

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**Nasopharyngeal viral load determinants among influenza-infected patients receiving primary care in France: 2010-2018**

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**Background:** Influenza, a continuing major public health problem due to recurrent seasonal epidemics justifying epidemiological and virologic surveillance. Virus detection by RT-qPCR, widely used for surveillance, is mostly a qualitative diagnosis tool but also allows to estimate the viral load (VL). We analyzed factors associated with VL in nasopharyngeal specimens from patients attending primary care with confirmed influenza virus infection.

**Materials/methods:** Patients recruited by the French primary care surveillance networks in the Northern half of France during the 2010-2011 to 2017-2018 seasons for which a nasopharyngeal swab was found positive for influenza virus type A or B by RT-qPCR were included. For each patient, epidemiological and clinical data were collected. Analyses by RT-qPCR performed at the National Influenza Center also provided influenza A virus subtype and an estimated VL. Determinants of VL were identified using multivariate linear regression and severity (presence of dyspnea or hospitalization) determinants were identified using logistic regression.

**Results:** Overall, specimens from 6297 patients were included, ranging from 365 in 2013-2014 to 1179 in 2015-2016. Of these, 50.7% were men. Median [inter quartile range] age at diagnosis was 20 [6-43] years. Influenza virus was A(H1N1)pdm09 in 1722 [27.4%] patients, A[H3N2] in 2184 [34.7%] patients and B in 2345 [37.2%] patients. Mean [standard deviation] VL was 4.78 [1.43] log copies/µL. In multivariate analysis, patients infected with A[H3N2] and B viruses presented significantly higher VL then those infected with A(H1N1)pdm09 (p<0.001). The 2012-2013 and 2014-2015 seasons were characterized, in multivariate analysis by lower VL than all other seasons (p<0.001). The other factors associated with increased VL were younger and older ages (<2, 2-4, 4-15 and ≥65 years; p<0.001), male gender (p=0.01), presence of rhinitis (p<0.001), and being vaccinated in patients older than 65 years or immunocompromised (p=0.04). In multivariate analysis, higher VL was associated with increased severity, but the type of influenza virus was not associated with severity.

**Conclusions:** After adjusting for confounding factors among which the influenza virus, VL fluctuations remained between seasons, with no appropriate explanations today. However, we noted that the seasons exhibiting the lowest VL levels were always those when the three viruses co-circulated.

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Abstract 607

Flu isolation wards: does medical specialty matter? Comparison of three specialties on outcome and antibiotic usage in hospitalised influenza A infected patients in Vienna during the season 2018/19

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Background: Diagnosis and care of influenza are often provided across several medical specialties. We compared patient outcomes at the infectious diseases (ID), rheumatology (Rheu) and the pulmonology (Pulm) department.

Materials/methods: In this exploratory-prospective-observational multi-centre-study we included all influenza positive patients ≥18 years who were hospitalized for critical medical reasons and treated at flu-isolation-wards in three hospitals in Vienna during the season 2018/19. Diagnosis was made via Cobas® Liat®-POCT.

Results: 490 patients with a median age of 73 years (IQR 61-82) were included. 48.8% were female. No difference regarding age, sex and underlying diseases were present at admission.

The complications were different: pneumonia (ID 27.8%, Rheu 40%, Pulm 39.8%, p=0.031), acute kidney failure (ID 12.7%, Rheu 21.2%, Pulm 37.1%, p<0.001), acute heart failure (ID 4.3%, Rheu 17.1%, Pulm 14.4%, p<0.001), respiratory insufficiency (ID 45.1%, Rheu 41.5%, Pulm 56.3%, p=0.030).

Oseltamivir prescription was lower at the pulmonology flu ward (ID 79.6%, Rheu 90.5%, Pulm 61.7%, p<0.001).

176 patients (35.9%) had pneumonia. Antibiotic treatment differed between specialties (see table 1).

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Infectious diseases</th>
<th>Rheumatology</th>
<th>Pulmonology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=176</td>
<td>[n=45]</td>
<td>(n=80)</td>
<td>(n=51)</td>
</tr>
<tr>
<td>Amoxicillin/Clavulanic-acid</td>
<td>38.1%</td>
<td>28.9%</td>
<td>63.7%</td>
<td>5.9%</td>
</tr>
<tr>
<td>3rd-Generation-Cephalosporin</td>
<td>24.4%</td>
<td>4.4%</td>
<td>5%</td>
<td>72.5%</td>
</tr>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>9.7%</td>
<td>6.7%</td>
<td>15%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>9.1%</td>
<td>4.4%</td>
<td>6.3%</td>
<td>17.6%</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>8.8%</td>
<td>28.9%</td>
<td>1.3%</td>
<td>0%</td>
</tr>
<tr>
<td>Macrolide</td>
<td>8.5%</td>
<td>2.2%</td>
<td>2.5%</td>
<td>23.5%</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>4.5%</td>
<td>17.8%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Other antibiotic</td>
<td>4.0%</td>
<td>6.7%</td>
<td>2.5%</td>
<td>3.9%</td>
</tr>
<tr>
<td>Antibiotic not known</td>
<td>4.5%</td>
<td>4.4%</td>
<td>7.5%</td>
<td>0%</td>
</tr>
<tr>
<td>Combination therapy</td>
<td>9.7%</td>
<td>2.2%</td>
<td>2.5%</td>
<td>27.5%</td>
</tr>
</tbody>
</table>

The median length-of-stay was ID 6 days [IQR 5-8], Rheu 6 days [IQR 5-7] and at Pulm 7 days [IQR 5-9.5], p=0.034. In-hospital-mortality was 4.3%, increased to 9.5% during the 90-day follow-up-period and did not differ between specialties.

Conclusions: We detected differences in oseltamivir usage, length-of-stay and antibiotic choices for pneumonia. Influenza-associated-mortality was not affected by specialty.

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Ursolic acid and its amide derivatives disrupt clinical Acinetobacter baumannii isolates and biofilm formation

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Background: Hospital acquired infections due to antimicrobial resistant ESKAPE pathogens have emerged globally with increased morbidity and mortality. Acinetobacter baumannii is a members of ESKAPE pathogens which acquired multiple drug resistance (MDR) even with the last resort drug colistin at rapid phase which hinder its treatment or management. World Health Organization (WHO) categorized A. baumannii among the list of pathogens for which new pharmacophore required on urgent basis. So, in this study Ursolic acid (UA) and its synthetic amide derivatives were screened against standard (ATCC: 19606) and clinical isolates of A. baumannii strains.

Materials/methods: In the first phase of this study clinical isolates were collected and identified as A. baumannii strains phenotypically as well as genotypically. Then the ursolic acid and its derivatives were screened for antimicrobial, biofilm inhibiting and eradicating potential.

Results: Out of tested compounds amide derivative of UA (KSUA-2,4) was found to possess better antimicrobial concentration at 77.87 μg/ml against colistin resistant A. baumannii strains (Colistin MIC > 100 μg/ml). Compound KSUA-2,4 significantly inhibited or eradicated >60% biofilm formation of tested standard and clinical isolates at MIC. Microscopic analysis further confirms the biofilm inhibition and eradication potential of this compounds. Atomic Force Microscope analysis (AFM) further confirms the antimicrobial properties KSUA-2,4 and suggesting that the antimicrobial action might be due the the membrane leakage. Considering this evidence, microbial membrane potential was determine by using FACS analysis which confirm the loss of membrane potential after compound treatment. Gene expression analysis further explained that this compound inhibit biofilm formation by reducing the gene expression of bap (biofilm gene) and aboR (quorum sensing).

Conclusions: Ursolic acid amide derivative KSUA-2,4 significantly inhibit growth and biofilm formation of colistin resistant A. baumannii strains, so, might be used to tackle Acinetobacter baumannii related nosocomial infections and further evaluated as a drug candidate.

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Survival outcome in allogeneic haematopoietic stem cell transplant recipients with multiple, sequential cytomegalovirus, Epstein-Barr virus, BK virus and respiratory viral infections

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Background: Reactivation of latent double-stranded DNA (dsDNA) viruses [Cytomegalovirus (CMV), Epstein-Barr virus (EBV) and BK polyomavirus (BKV)] as well as community-acquired respiratory viruses can lead to significant morbidity after allogeneic haematopoietic stem cell transplantation [allo-HSCT]. The clinical burden of multiple, sequential viral infections in this population has not been well characterized. We aimed to assess the impact of cumulative viral infections on clinical outcome in recipients of allo-HSCT.

Materials/methods: All patients undergoing allo-HSCT between January 2015 to December 2017 at Royal Melbourne Hospital were included in a retrospective analysis. Episodes of viral infection with time to event were recorded for a minimum follow up period of 12 months or until death. Weekly quantitative CMV and EBV PCR to day 100 was performed and as clinically indicated thereafter. BKV PCR and respiratory virus PCR were tested as clinically indicated. An episode of infection was defined as first detectable CMV, EBV, BKV and/or respiratory virus. Statistical analysis evaluating time to multiple viral events was performed using Andersen-Gill and Cox proportional hazard models.

Results: Two hundred and fifty-five patients [median age=51, male (61%)] were included. Indication for HSCT was AML (41%), ALL (11%), MDS (11%), others (37%). Anti-thymoglobulin (ATG) conditioning regimens were used in n=117 (46%). 401 episodes of viral infection were identified in 206 patients. CMV reactivation = 139 (55%), EBV =131 (51%), BK = 53 (21%) and respiratory viral infections were identified in 78 (31%) patients. 19 patients (7.5%) had reactivation of all 3 dsDNA viruses; 9 patients (3.5%) had all 4 viral events. The 12-month all-cause mortality was 26.7%.

ATG use was associated with increased risk of viral infections overall [HR 1.5, 95% CI 1.2-1.8, p<0.001], and a longer median duration of both CMV viremia (79 vs 72 days, p=0.008) and EBV viremia (36 vs 28 days p=0.03). The risk of twelve-month all cause mortality was increased in patients with multiple, sequential viral infections (HR 1.36 95% CI 1.15-1.62, p<0.001).

Conclusions: Multiple episodes of latent dsDNA or respiratory viral infections occurring within the first 12 months of allogeneic HSCT was associated with an increase in overall mortality.

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Abstract 616

Immunogenicity and safety of a quadrivalent influenza vaccine (GC GLU) versus quadrivalent seasonal influenza vaccine (Fluarix Tetra) in Asian adults aged 20 to 50: a phase III prospective, open labeled, multi-centre study

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Background: The egg based quadrivalent vaccines (IV4) was suggested by WHO for use in the 2019-2020. Due to the high demand of IV4 globally, we conducted a non-inferior phase III clinical trial to evaluate the Immunogenicity and safety of an IV4 (GC GLU), compared with active controlled (AC) (Fluarix Tetra, GSK).

Materials/methods: The randomized, open labelled, active controlled study was conducted in four sites in Taiwan (NCT03718468). Vaccinee aged 20-50 were enrolled. GC flu is an IV4 contained 60ug purified inactivated influenza virus antigen (15ug each), including A [H1N1], A [H3N2], B [Maryland], and B [Phuket]. The primary end point was the non-inferior immunogenicity of GC flu to AC as HAI titers against each virus strain on Day 22 (GMc/GMTgflu<=1.5).

Results: 842 vaccinee were randomized and received one dose of vaccination, and the baseline characteristic was similar in the 2 groups. 840 vaccinee fulfilled PP criteria, with 421 received GC Flu and 419 received AC. For both type A strains, there was no significant difference between GC FLU and the AC. The 95% CI upper bounds of GMTac/GMTgcflu are both 1.00. For both type B strain, the 95% CI upper bounds of GMTac/GMTgcflu are 1.41 (Table 1). Further analyzing GMT using ANCOVA incorporating baseline, study site, and/or age as factors if significant, the upper bounds of the 95% CI of GMTac/GMTgcflu of all 4 strains ≤ 1.5 in PP population. Safety analyses were performed on the 842 ITT population. The local solicited AEs was 80.3% [339/422] in GC flu group and 81.9% [344/420] in AC group. The systemic solicited AEs were 53.6% [238/422] and 45.2% [190/420] and unsolicited AE were 19.2% [81/422] and 16.7% [70/420], respectively.

Conclusions: GC flu exhibit comparable safety profile and immunogenicity non-inferior to Fluarix Tetra.

Table 1 GMTac/GMTgcflu on Day 22 for PP population

<table>
<thead>
<tr>
<th>Strain</th>
<th>GMT (Median, 95% CI)</th>
<th>GMTac/GMTgcflu</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GC FLU</td>
<td>Fluarix Tetra</td>
</tr>
<tr>
<td>A/H1N1</td>
<td>160.77 [159.97, 159.97]</td>
<td>160.77</td>
</tr>
<tr>
<td></td>
<td>[159.97, 159.97]</td>
<td></td>
</tr>
<tr>
<td>A/H3N2</td>
<td>79.84 [80.00, 80.00]</td>
<td>79.84</td>
</tr>
<tr>
<td></td>
<td>[80.00, 80.00]</td>
<td></td>
</tr>
<tr>
<td>B-Yamagata</td>
<td>79.84 [56.54, 80.00]</td>
<td>79.84</td>
</tr>
<tr>
<td></td>
<td>[56.54, 80.00]</td>
<td></td>
</tr>
<tr>
<td>B-Victoria</td>
<td>113.30 [80.00, 159.97]</td>
<td>160.77</td>
</tr>
<tr>
<td></td>
<td>[113.18, 159.97]</td>
<td></td>
</tr>
</tbody>
</table>

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Abstract 624

Clinical experience with isavuconazole in Chinese healthy volunteers and Chinese patients with invasive aspergillosis

Jing Zhang*, Yingyuan Zhang, Depei Wu, Guoying Cao, Kamal Hamed, Amit Desai, Jalal A. Aram, Xuan Guo, Rana Fayyad, Oliver A. Cornely

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Abstract third-party references: Funded by Pfizer Inc. Submitted by Karen Miller from CMC Connect, a division of McCann Health Medical Communications Ltd on behalf of the authors

Background: Invasive aspergillosis (IA) has an increasing incidence in China. We present experience with the antifungal isavuconazole in Chinese subjects from two clinical studies: a Phase I study in healthy volunteers [Study 9766-CL-0038 [NCT01555918]] and the global Phase 3 SECURE study [NCT00412893] in patients with IA.

Materials/methods: Healthy volunteers received an oral or intravenous dose of isavuconazole 200 mg on Day 1 of each 15-day period, followed by a 2-week washout [Part 1], and 200 mg three-times-daily for 2 days followed by once-daily for 10 days [Part 2]. In SECURE, patients were randomised to isavuconazole 200 mg intravenously three-times-daily on Days 1 and 2, then either intravenously or orally once-daily, or voriconazole 6 mg/kg intravenously twice-daily on Day 1, 4 mg/kg intravenously twice-daily on Day 2, then intravenously 4 mg/kg twice-daily or orally 200 mg twice-daily from Day 3 to end of treatment [EOT] (up to 84 days). One patient was randomised to isavuconazole but received voriconazole intravenously for the first 7 days, then switched to oral isavuconazole until EOT and was included in the voriconazole safety population and the isavuconazole intent-to-treat population. Efficacy (SECURE), safety and pharmacokinetic measures were assessed.

Results: Sixty-two Chinese healthy volunteers/patients were included (46 received isavuconazole). Plasma exposure to oral isavuconazole was higher in Chinese than Western healthy volunteers [Studies 9766-CL-0041 [NCT01657890] and 9766-CL-0017 [NCT01565720]] [Table]. In SECURE, trough steady-state isavuconazole concentrations for three Chinese patients were higher [3844–8646 ng/mL] than for the global population [452–8646 ng/mL]. The primary endpoint of all-cause mortality through Day 42 was 10% [1/10] in the isavuconazole group and 25% [4/16] in the voriconazole group. Overall, 88.9% [8/9] of Chinese isavuconazole-treated patients experienced ≥1 treatment-emergent adverse event, as did 94.1% [16/17] of those receiving voriconazole. Efficacy and safety trends were similar to the global population.

Global isavuconazole exposure-response modelling results revealed no statistically significant relationships of exposure with efficacy endpoints. Furthermore, the differences in exposure were not associated with differences in safety outcomes.

Conclusions: Safety/efficacy in Chinese patients was consistent with the global population. Higher exposure did not alter safety/efficacy outcomes in the global analysis.

Table. Comparison of isavuconazole exposure in Chinese healthy volunteers from Study 9766-CL-0038 and Western healthy volunteers after oral administration

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Single-dose</th>
<th>Multiple-dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chinese HVs</td>
<td>Western HVs</td>
</tr>
<tr>
<td>Study</td>
<td>9766-CL-0038</td>
<td>9766-CL-0041</td>
</tr>
<tr>
<td>n</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>C_{max} (μg/mL)</td>
<td>3.4 (0.5)</td>
<td>2.3 (0.5)</td>
</tr>
<tr>
<td>AUC (μg·h/mL)</td>
<td>116.4 (36.3)</td>
<td>98.3 (27.1)</td>
</tr>
</tbody>
</table>

*Note: the pharmacokinetics of isavuconazole are linear and dose-proportional following both oral and intravenous administration.

*AUC is AUC_{int} for single-dose results, AUC_{int} for multiple-dose results.

AUC, area under the time-concentration curve; C_{max}, maximum concentration; HV, healthy volunteer; SD, standard deviation.

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The potential benefit of a second C-reactive protein measurement in patients with Gram-negative bacteraemia presenting to the emergency medicine department

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Background: Low concentrations of C-reactive protein (CRP) in patients presenting with acute bacterial infections to an emergency medicine department could convey the erroneous impression of a relatively mild infection. We focused on a group of patients with gram negative bacteremia, a phenomenon frequently seen in the emergency medicine department.

Materials/methods: Of the 2200 patients with gram negative bacteremia, we reviewed the medical records of 460 patients who presented with CRP <30mg/L and 460 patients with CRP>187mg/L. Following a series of exclusions, we finally investigated 229 and 289 patients with low and high CRP concentrations, respectively. The cut-off values of relatively low and high CRP were obtained by using a large [n=17,206] database of apparently healthy individuals.

Results: We divided our total cohort into low and high CRP groups. Patients were examined following a mean of 1 and 2.7 days (standard deviation of 2.6 and 3.7 days), respectively from symptom onset. Median first CRP was 13.6 and 219.9 mg/L (interquartile range 6.4-21.6 and 195-270.1) for low and high CRP groups, respectively. Compared to patients with first high CRP, patients with first low CRP concentrations had a significant 5-fold higher CRP level with their second test representing a higher CRP velocity.

Conclusions: Patients with gram negative bacteremia can present with CRP concentrations that are within the range of those detected in apparently healthy individuals. A second CRP test obtained in those presenting with low CRP concentrations might prompt the physician to reevaluate the ongoing inflammatory response, thereby avoiding an eventual erroneous decision regarding the severity and prognosis of the infectious condition.

Figure: Frequency of CRP velocity in low and high baseline CRP groups.

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Abstract 638

Daptomycin decreased mortality in methicillin-resistant Staphylococcus aureus bacteraemia compared to vancomycin: a monocentric retrospective study of 96 cases

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Background: MRSA bacteraemia is a severe and frequent infection currently treated with Vancomycin as gold standard. However Vancomycin, has a slow bactericidal effect, a slow diffusion in tissue, and severe adverse effects that may alter prognosis. Daptomycin, a lipoglycopeptide, has less adverse effects and is more bactericidal. Currently data are missing to support the non-inferiority of Daptomycin against Vancomycin in MRSA bacteraemia on clinical outcomes. We aimed to demonstrate the non-inferiority of Daptomycin on mortality in this context.

Materials/methods: In a monocentric retrospective study, we included 96 patients with MRSA bacteraemia treated with Daptomycin or Vancomycin in a university hospital in Amiens, North of France between 2010 and 2019. We excluded patients with pneumonia or with polymicrobial bacteraemia. The primary outcome was survival after 30 days of antibiotic. The secondary outcomes were tolerance (acute renal failure or end of treatment for adverse events), blood culture (BC) negativation, time to BC negativation, time to apyrexia, length of stay and complications (secondary abscess, endocarditis, septic arthritis or spondylodiscitis).

Results: Both groups were similar in terms of age (mean ± SD in vancomycin group vs daptomycine group) [70.5 ± 13 vs 70.2 ± 11.6] and severity (evaluated by SOFA score, median [interquartile range]) [3 [2-4.5] vs 4 [2-5.5]). There was more men treated with Daptomycine (sex ratio H/F=32/7) than with vancomycine (35/22). Mortality was 40% [23/57] and 13% [5/39] in Vancomycin and Daptomycin group respectively (odd ratio (OR) = 0.22, Confidence Interval (CI) 95% = [0.06; 0.69], p<0.005). There were 11 and 4 cases of acute renal failure in Vancomycin and Daptomycin group, respectively (OR = 0.48, IC95% [0.14; 1.65]), 2 and 1 premature end of treatment due to adverse events in Vancomycin and Daptomycin group, respectively. No difference was found regarding length of stay, BC negativation at day 3, time to BC negativation, time to apyrexia or complications.

Conclusions: Daptomycin drastically decreased mortality in MRSA bacteraemia compared to Vancomycin in our cohort but larger study are warranted to confirm these results.

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Abstract 643

A systematic analysis of the direct antiglobulin test in post-artesunate delayed haemolysis during severe imported Plasmodium falciparum malaria: a multi-centre retrospective study

Olivier Paccoud1, Xavier Chamillard2, Ken Ndiaye1, Isabelle Vinatier1, Mohammed Khalloufi1, Claire Boulat1, Laure Surgers1, Benjamin Wyplosz2, Olivier Bouchaud1, Sophie Matheron6, Eric Caumes7, Stéphane Jauréguiberry4,8,9


Background: Post-artesunate delayed haemolysis (PADH) is a frequent adverse effect of artesunate treatment for severe Plasmodium falciparum malaria. Cases of PADH with positive direct antiglobulin tests (DATs) have been reported, but systematic analyses of the DAT and its responsibility in the late haemolytic event during severe imported malaria are lacking.

Materials/methods: In this multicentre retrospective study, we reviewed medical data from all patients with severe imported Plasmodium falciparum malaria in 5 infectious diseases departments over an 8-year period, and included all patients for whom at least one DAT had been performed (DC-Screening I or II, Biorad©). We further analysed parameters of anaemia and haemolysis from day 0 to day +28 of treatment initiation in patients for whom sufficient follow-up data was available. We defined PADH as a 10% drop in haemoglobin levels and a 10% rise in lactate dehydrogenase levels occurring after day 7 of treatment initiation.

Results: Out of 355 patients with severe imported malaria, 46 patients with at least one DAT evaluation were included [including 7 with 2 separate DAT evaluations]. The median age of patients was 44.5 years, and median parasitaemia was 6.4%. Overall, 53 DATs were performed at a median [min-max] of 10 [1-35] days after treatment initiation, which coincided within 7 days of a patient’s haemoglobin nadir in 74% of cases. The DAT was positive in 50.9% [27/53] of cases. Most were positive for IgG [22/27, 81%], among which 63% [17/27] were weakly positive. Among 40 patients with sufficient follow-up data, 17/40 (42.5%) experienced PADH. Compared to patients without PADH, those who experienced PADH had significantly higher median haemoglobin levels [12.4g/dL vs 10.6g/dL, p = 0.021] and parasitaemia [11.4% vs 6%, p = 0.046] at admission. DAT positivity was not significantly associated with the occurrence of PADH [p = 0.36]. No patient received systemic corticosteroids, 41% required one or more erythrocyte transfusions, and outcomes were favourable in all cases.

Conclusions: DAT positivity is frequent during severe imported malaria. Auto-immune haemolysis does not appear to be a significant pathophysiological mechanism in most cases of PADH, although it may be involved in some rare cases.

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Interplay between inflammation and infection in a single-centre cohort of patients with X-linked agammaglobulinemia

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Abstract 645

Background: X-linked agammaglobulinemia (XLA) is a rare primary antibody deficiency associated with increased susceptibility to early-life infections. Various inflammatory manifestations have been reported during XLA but they are less well-characterised than in other primary immune deficiencies (PID), and are sometimes difficult to distinguish from cases of atypical infections.

Materials/methods: We carried out a retrospective cross-sectional analysis of the medical records of all patients with XLA referred to our hospital between 2009 and 2019. We reviewed data on all inflammatory manifestations, including clinical, biological, histological features, and link to a pathogen. In addition, we reviewed data on all infections before XLA diagnosis, at ages 16 to 18, and at last follow-up. Only infections that led to hospitalisation or that were documented were considered. We also retrieved data regarding use of antibiotic prophylaxis, immunosuppressive treatment, and last residual immunoglobulin level.

Results: Sixty patients with definite XLA were included. Median age (range) at last follow-up was 22.5 (4-59) years. Forty-seven inflammatory flares were reported in 14 patients (23.3%). The most frequently affected organ was the gastro-intestinal tract, presenting as inflammatory bowel disease or coeliac-like enteropathy in 8 patients (13%). Eight/14 (57%) patients received systemic corticosteroids and 4 received tumour necrosis factor inhibitors. A total of 188 infections were recorded, including 95 after initiation of immunoglobulin replacement therapy (IgRT). The most common sites of infection were the lungs and the gastro-intestinal tract. Of note, we recorded 13 cases of Giardia intestinalis infections and 12 cases of Campylobacter spp. infections. Overall, 53% of patients experienced either inflammatory or infectious manifestations despite IgRT during a total follow-up of 1470 patient-years. These occurred more frequently during adulthood than before the age of 16. Having a history of at least one inflammatory manifestation was significantly associated with experiencing more infections (0.14 vs 0.04 infections per person-year, p = <0.001) and more hospital admissions (6.29 vs 1.09 admissions, p = <0.001), as well as receiving higher mean monthly IgRT doses (0.74 vs 0.54 g/kg/month, p = 0.014) in adulthood.

Conclusions: Inflammatory manifestations are of increasing importance in XLA patients reaching adulthood and are associated with increased susceptibility to infection

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Abstract 646

**Investigating the sexual protective behaviour among HIV-positive women in Tehran, Iran**

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**Abstract third-party references:** Iranian research center of HIV/AIDS/For validation of data not for fund

**Background:** The third wave of human immunodeficiency virus (HIV) is rising due to high-risk sexual behaviours in Iran. In spite of launching programs to combat HIV in Iran, condom use frequency has not yet reached the optimal level, especially in high-risk groups. The aim of this study was to assess the sexual protection behaviours and awareness among HIV-positive women.

**Materials/methods:** This descriptive study was performed on 100 HIV-positive women who referred to the Voluntary and Counselling Centre (VCT) in Tehran and were recruited using a purposive sampling method. Data collection was carried out using HIV/acquired immunodeficiency syndrome (AIDS) awareness and sexual protection behaviour questionnaires.

**Results:** Condom use was practiced only by 22.2% in all their vaginal and anal sexual intercourse during the three months, and 77.8% of the women never used condoms or failed to use them continuously. Their sexual partners were HIV-positive in 71% of cases. The mean ± SD of awareness score about HIV/AIDS was 7.60 ± 3.31, indicating average awareness of the subjects in the study. A total of 49.1% of the participants stated that their sexual partners’ reluctance was the most important reason for non-use of condoms, while women were not willing to use condoms in 18.2% of cases.

**Conclusions:** The results of the present study indicated poor sexual protection behaviours in HIV-positive women. As a result, gender-based harm reduction programs to promote safe sexual behaviour, awareness level, and negotiation power for condom use in HIV-positive women is more important than ever.

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Abstract 652

Correlation between serum C-reactive protein levels and CURB-65 in elderly patients with community-acquired pneumonia

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Background: CURB-65 is an important clinical score for severity in community-acquired pneumonia (CAP). C-reactive protein (CRP) an acute phase protein marker for bacterial infection or tissue inflammation. Serum CRP levels are well correlated with the severity of CAP. We aimed to investigate whether serum levels of CRP correlates with CURB-65 ranking in hospitalized patients with CAP.

Materials/methods: 858 patients aged 18 - 90 years who were hospitalized with CAP during a period of two years in the departments of Internal Medicine at Ziv Medical Center in Safed, Israel, were collected. Five hundred patients who met the inclusion and exclusion criteria were included. CURB-65 and serum levels of CRP within 24 hours of admission were collected for each participant. The correlation between serum CRP levels and CURB-65 were analyzed by Spearman’s rank correlation test.

Results: The mean age of all study group was 64±19 years, and the means CRP levels and CURB-65 score were 114 ± 100 mg/dl, 1.4±1.1points, respectively. No significant correlation was found between CRP and CURB-65 for all study group (R=-0.014, P=0.768). Nevertheless, we found a significant correlation between CRP and CURB-65 in 320 patients aged ≥ 65 years (R=-0.126, P=0.024).

Conclusions: In this study we found a significant correlation between CRP and CURB-65 among elderly patients aged ≥65 years but not among patients below the age 65 years. We believe that CRP measurements could be used as adjuvant marker to CURB-65 for assessment CAP severity in elderly patients.

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**Abstract 656**

**Genome-based epidemiology and antimicrobial susceptibility of a nation-representative collection of clinical isolates of *Acinetobacter baumannii* obtained from Saudi Arabia**

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**Abstract third-party references:** King Abdullah International Medical Research Center, King Abdulaziz University

**Background:** Multidrug-resistant *Acinetobacter baumannii* has emerged as one of the most troublesome pathogens for health care institutions worldwide. However, limited information is collected on the antimicrobial resistance rates among clinical isolates in Saudi Arabia. Here we characterized a nationally representative collection of isolates.

**Materials/methods:** Isolates (*n*=200) were collected between March-2018 and March-2019 from five National Guard-Health Affairs hospitals covering the east, west and centre of Saudi Arabia. Identification was confirmed by species-specific PCR. Susceptibility testing were obtained with the VITEK II system and broth microdilution. β-Lactamase genes were sought by PCR. Selected (*n*=114) isolates were further characterized by multi-locus sequence typing (*ST*) (*n*=71) using the Oxford scheme or by whole genome sequencing (*n*=43) on the MiSeq instrument. Phylogeny was defined by single nucleotide polymorphism (SNP) analysis.

**Results:** Majority (*122/200, 61%*) of the isolates were resistant to carbapenems among which *118/122 (96.8%)* encoded Oxa-23-like; the remaining *4/122, 3.2%* produced Oxa-24-like. Isolates were variably resistant to gentamicin (*36.5%*) and tobramycin (*42.4%*) but remained mostly susceptible to colistin (*93.7%*) and tigecycline (*78.8%*). MLST and genome sequences identified 26 and 21 different STs among carbapenem-resistant (*n*=90) and -sensitive (*n*=24) isolates, respectively. STs of carbapenem-sensitive isolates were highly diverse whereas most (*88.9%, 80/90*) of those identified in resistant isolates were single or double locus variants of each other and comprised ST557 (*n*=25), ST218 (*n*=23), ST195 (*n*=13), ST1286 (*n*=8), ST451 (*n*=4), ST208 (*n*=2), ST444 (*n*=2), ST214 (*n*=1) and ST1050 (*n*=1), all of which belonged to ST2 (Pasteur scheme). Overall, phylogenetic analysis clustered carbapenem-resistant ST2 isolates according to their Oxford STs, but these were hundreds of SNPs apart. Among most common STs, SNP analysis identified close relatedness between isolates collected from the same or different hospitals suggesting inter- and intra-hospital transmission.

**Conclusions:** Our results showed a high prevalence rate of carbapenem resistance among *A. baumannii* in Saudi Arabia that was mainly associated with the acquisition of Oxa-23-like carbapenemase. Majority of carbapenem-resistant isolates belonged to ST2 (Pasteur scheme) but these were highly diverse at the whole-genome level. Spread of resistance was partially explained by clonal dissemination.

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Abstract 657

Feasibility, reproducibility and first results of a multimodal prevention approach for KPC-Kp in a high prevalence hospital setting

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Background: Targeted actions of infection control on hospital institutions’ local epidemiology and resources are required to contain carbapenemase-producing Klebsiella pneumoniae [KPC-Kp].

Materials/methods: An interchange protocol with the Infectious Diseases Unit of Modena Polyclinic was started to verify the feasibility of “Anti-KPC-Kp bundle” in the setting of S.M. Goretti Hospital of Latina (a tertiary university care centre with a high endemicity of KPC-Kp). A dedicated multidisciplinary working group was set up. Standardized indexes were defined to evaluate setting modifications and proposed targets in 3 high-risk wards (Intensive Care Unit (ICU), Emergency Medicine, Neurosurgery):

- active surveillance of rectal colonization;
- handwashing adherence assessments;
- alcohol solution consumptions, L/1000 patient-days (PD);
- meropenem Defined Daily Dose (DDD)/100 PD;

Statistical analysis: Indexes modifications are shown in percentages or changes in level (average ± SD). A Poisson regression model was applied to analyse the trend of KPC-Kp prevalence in ICU, Emergency Medicine and Neurosurgery. Only for ICU, a Poisson regression model was applied also to analyse the trend of the incidence density rates, considering the total hospitalization days as an offset in the model. Active control by participative focus groups among healthcare workers ensured the continuous implementation of the bundle.

Results: At baseline carbapenem resistance in all Kp hospital’s blood cultures was 71.4% (in ICU 87.5%). KPC-Kp prevalence reported monthly on the first day showed a dramatic reduction (Figure 1).

Figure 1: KPC-Kp colonization prevalence

Results from the Poisson regression models showed a statistically significant negative trend of prevalence in ICU (p<0.001) and Emergency Medicine (p=0.021), but not in Neurosurgery (p=0.259). A statistically significant negative trend was also found for incidence density rates in ICU (p=0.002). At basal, handwashing adherence in ICU was 59.3%. Further assessments are scheduled after starting a structured training program. An increase of alcoholic hand rub consumption was ob-
served from 14,2 (SD±7,56) to 33,59 (SD±13,11). A slight decrease of meropenem DDD was observed from 19,53 (SD±16,98) to 14,09 (SD±9,72).

Conclusions: After 8 months, an improvement of the indexes was observed. The exported model based on a multimodal approach exerted a rapid effect on Kp-KPC diffusion in the intensive area of the hospital, also in a different situation of high basal prevalence. A longer follow-up is necessary to confirm these data together with a more detailed carbapenem resistance rates’ analysis.

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Abstract 663

Matched-paired analysis of patients treated for invasive mucormycosis with isavuconazole versus standard treatment

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Background: Isavuconazole (ISAV) is a novel, broad-spectrum triazole antifungal, available as both an intravenous and oral water-soluble prodrug, for the treatment of adult patients with invasive aspergillosis and mucormycosis. It was first approved for mucormycosis in 2015 based on data from 37 patients enrolled in a single-arm open-label trial (VITAL study) and 33 matched controls from the FungiScope® registry. Additional real-world data documenting the effectiveness of isavuconazole are obtained from an ongoing retrospective study within FungiScope®.

Materials/methods: FungiScope® proven and probable invasive mucormycosis cases treated with ISAV between 2016 and 2018 were matched with amphotericin B-based treatment controls from 1997 to 2018. Case-matching criteria included disease severity (i.e. central nervous system or disseminated disease), hematological malignancy and surgery. Baseline patient characteristics, key outcomes of clinical response according to the European Organization for Research and Treatment of Cancer/Mycoses Study Group (EORTC/MSG) criteria and all-cause mortality (ACM) were compared descriptively.

Results: 17 ISAV cases (16 proven, 1 probable) and 44 controls (41 proven, 3 probable) were identified. In the majority of cases (n=14, 82%), ISAV was administered as treatment for invasive mucormycosis in patients who had received prior lipid formulations of amphotericin B. In the remaining cases, ISAV was administered after prior posaconazole (n=2) or as primary therapy (n=1). In the control group, all patients received an amphotericin B-based therapy at some point, with 70% (n=31) as their initial or primary documented therapy.

Baseline patient characteristics and causative pathogens were similar between ISAV cases and controls. The overall response (complete or partial response) rates at the final assessment were 47% (8/17) for ISAV cases and 45% (20/44) for controls. ACM was 47% (8/17) in ISAV cases as compared to 59% (26/44) in controls.

Conclusions: In this analysis from FungiScope®, ISAV showed similar overall treatment response and improved mortality as compared to amphotericin B-based treatment in patients with invasive mucormycosis.


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Abstract 664

**Anal human papilloma virus infection and disease in HIV-positive and -negative men and women**

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**Background:** Determining the forms of sexual behavior risk factors for various types of HPV infection is the basis for both understanding the natural courses of different HPV types and designing comprehensive strategies. The aim of this study was to evaluate the prevalence of HPV infections in patients with clinical anal lesions and in patients with risky factors of sexual intercourse.

**Materials/methods:** The analysis involved samples from patients who consecutively came to the Virology laboratory of the Department of Sciences for Health Promotion and Mother and Child Care (Policlinico University of Palermo, Italy), between February 2017 and May 2019 with clinicians’ requests for HPV tests. Routine laboratory diagnosis of HPV infection was performed on all samples using routine laboratory procedures as previously reported. HPV genotypes were identified using the INNO-LiPA HPV Genotyping Extra II kit (Fujirebio). All cytology, HPV testing, and histological examination was assessed in enrolled population.

**Results:** We enrolled 113 pts (74 of men and 39 of women), 64 reported anal lesions suggestive of HPV etiology and 49/113 patients showed sexual intercourse as sexual behavior risk factors. 43/113 enrolled pts showed HIV infections (37/74 males and 6/39 females). Among 113 anal sampling investigations we found HPV infection in 74/113 patients. HPV infection was confirmed in 44/64 patients with anal lesion suggestive of HPV etiology. HPV infection was confirmed in 30/49 pts with sexual intercourse. Oncogenic types were found in 48/74 positive samples: 31 were males and 17 were females. Among 74 HPV positive infections we founded multiple HPV genotype positive analysis in 38/74 cases. 36/38 multiple HPV genotype infection showed high risk genotypes. Overall of these were male with sexual intercourse as risk factors. Please copy and paste the corresponding text here.

**Conclusions:** Our study shows that the presence of HPV and multiple HPV infections in the anal district is high especially in subjects with sexual intercourse risk factors and male gender. Anal HPV lesion should be involved in the clinicians to HPV analysis to found multiple and HR HPV infection to prevent cancer evolution and stressed preventive strategies.

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Cost-benefit analysis of rapid influenza testing in German emergency rooms

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Background: Seasonal influenza causes significant morbidity worldwide and has a substantial economic impact on the healthcare system. The objective of this study was to assess the cost-benefit by implementing two influenza tests that provides rapid testing results in emergency rooms (ER) of German hospitals.

Materials/methods: A deterministic decision-analytic model was developed simulating the incremental costs of using the Solana Influenza A+B real time molecular assay or the Sofia Influenza point-of-care A+B antigen assays, as compared to those of using conventional clinical judgement alone to confirm or exclude influenza in adult ILI (influenza-like illness) patients, in German ER, prior to hospitalization. Direct costs were evaluated from the hospital perspective, considering resource use directly related to influenza testing and treatment, as well as indirect costs incurred by nosocomial influenza transmission. Univariate sensitivity analysis was performed to examine the extent to which our calculations were effected by varying the parameters considered in our model between plausible extremes. To capture the interactions between multiple inputs, we also provided a probabilistic sensitivity analysis (PSA) by drawing values at random out of the distributions of the respective parameters in a second order Monte Carlo simulation with 10,000 repetitions.

Results: Through base-case analysis and assuming an influenza prevalence of 42.6%, influenza testing with the Solana and the Sofia assays reduced average costs of hospitalized ILI patients by €132.61 and €52.16 per tested patient, respectively. Moreover, utilizing the Solana assay, but not the Sofia assay saved €6.9 per tested patient in favor of the hospital. In PSA, under all reasonable assumptions, implementing the Solana assay reduced hospital costs on average by €144.13 as compared to the clinical-judgement-only strategy, thus, it was found to be constantly less expensive. In PSA, the Sofia assay also resulted in constantly lower expenditures, but of €119.89 per tested patient compared to the symptom-based approach.

Conclusions: Using highly specific influenza tests that provides a fast testing result in ILI patients at German ER may significantly reduce hospital expenditures.

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Abstract 667

The clinical and molecular epidemiology of non-carbapenemase-producing carbapenem-resistant Enterobacteriaceae: a case-case-control matched analysis

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Background: Risk factors and outcomes associated with CRE acquisitions, are derived primarily of cohorts consisting of carbapenemase-producing (CP) strains, but CRE-non-CP are understudied. Study aims were to analyze the clinical and genomic epidemiology of CRE-non-CP.

Materials/methods: A case-case-control matched analysis was conducted at Shamir (Assaf Harofeh) Medical Center, Israel, 11/2014 to 12/2016. Isolates were Klebsiella spp., Escherichia coli or Enterobacter spp. showing meropenem MIC≥ 2 µg/dL and negative for CP detection by multiplex PCR. CRE-non-CP patients (infected and asymptomatic carriers) were matched to patients with non-CRE Enterobacteriaceae carriage, and to un-infected controls (1:1:1 ratio). Matching criteria (in order of importance) included the 1) bacterial species 2) colonization vs. infection status, 3) age group, 4) calendar year, and 5) time at risk [days from admission to culture]. Matched multivariable regression models were constructed to analyze risk factors for CRE non-CP acquisition, and its independent impact on multiple outcomes. Thirteen representative isolates were whole genome sequenced using Illumina and analyzed for resistome and phylogeny (MLST and cgMLST).

Results: The study included 327 patients: 109 CRE-non-CP carriers (94% asymptomatic) who were perfectly matched to susceptible cases and uninfected controls. Despite multiple associations per univariable analyses, matched logistic regression revealed that the independent predictors of CRE-non-CP acquisition remained: 1) recent [≤ 3 months] exposure to antibiotics [to any class, of at least 2 days’ duration]; 2) ICU admission; and 3) chronic skin ulcers. CRE-non-CP isolation was not independently associated with worse outcomes. Genomic analyses revealed multiple clones (figure), and confirmed the lack of carbapenemases and co-existence of multiple genes contributing to carbapenem-resistance phenotype [multiple beta-lactamases and efflux pumps].

Conclusions: CRE-non-CP acquisitions were almost exclusively associated with asymptomatic carriage. Both the independent predictors [i.e., exposure to antibiotics], and what could be deduced from the genomic analyses [i.e., polyclonality and presence of various resistance mechanisms], imply that the major mode of acquisition is “emergence of resistance”, not “patient-to-patient transmission”, although this needs to be further explored in designated trials. CRE-non-CP remains an epidemiological threat due to the therapeutic challenge it imposes, and directed efforts [i.e., stewardship] should be invested in order to curb its continued spread.

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Abstract 668

Analysis of the vaccination coverage in a dispensary in Mayotte, an oversea department and region of France

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Background: Mayotte has been the 101st French County since April 2011. It has a high-density population explained by a high birth rate and a high immigration population coming from the Comoro islands. The aim of this study was to compare the mandatory vaccine coverage rate in dispensaries for native versus migrants.

Materials/methods: The vaccine status was collected during general practice consultations in the dispensaries of the north of the island of Mayotte from the 12th to the 28th of June 2019. Patients were interrogated by a general practitioner and a translator about their vaccine status written in their health care notebook (carnetiss). We noted the number of injections received of each mandatory vaccine, place of birth, age and gender. We considered that the vaccine status was complete if all the mandatory vaccination for their age was written on their health care notebook.

Results: We included 162 patients [54% (87) children <18-year-old and 57% (93) women. Migrants represented 22% (36/162) of patients and 78% (126/162) were native [French mahorais]. In this population, 23% (37/162) were up to date on their mandatory vaccinations, 45% (73/162) were not and 32% (52/162) of vaccine status were unknown. The health care vaccine notebook of children was better filled in than those of the adults with only 4,60% (4/87) of unknown vaccine status (2 of those were migrant children) against 64% (48/75) of unknown vaccine status for adults. Among children 25.3% (22/87) were up to date on their mandatory vaccinations compared to 20% (15/75) of adults. In total 21% (27/126) of natives versus 21.6% (35/162) of migrants were up to date on their vaccinations (p=0,14).

Conclusions: In this study the vaccination coverage was not affected by the origin of patients whether they are native or migrants. The causes of limitation to health care access for the overall population are multiple: lack of transportation, cost and high waiting time of consultation, lack of social welfare and health insurance, cost of vaccine if they are not realized in a Mother and Children Health care center and for migrants, the fear of being arrested on their way to consultation.

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Abstract 669

**Incidence rate of health care associated infection in tertiary care children’s hospital in Ukraine**

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**Background:** Health care associated infections (HAI) are the most frequent adverse event in health care delivery worldwide. At any given time, the prevalence of HAI in developed countries varies between 3.5% and 12%. In low- and middle-income countries the frequency of HAI in intensive care units (ICU) is at least 2-3 fold higher than in high-income countries and for device-associated infections the frequency is up to 13 times higher.

Previously, health care facilities were not encouraged to use standardized approach for registration and notification of HAI which resulted in lack of data and understanding of the burden of HAI and affect planning on HAI response in Ukraine.

The aim of the study was to calculate the baseline incidence rate (IR) of HAI in ICU and surgical wards of tertiary care children hospital in Ukraine.

**Materials/methods:** Data on HAI was obtained using standardized notification forms that were filled by the doctors from March 1st till October 1st 2019. The case definitions of HAI outlined in EU Commission implementing decision 2018/945 were used.

Data verification and calculations of HAI incidence rates were conducted by department of infection control and risk assessment.

**Results:** The incidence rate of central line-associated bloodstream infections (CLABSIs) was 10.3 per 1000 device-days, the most common causative pathogens were Gram-negatives (60%). The IR of ventilator-associated pneumonia (VAP) was 49.7 per 1000 device-days, the most common causative pathogens were *A. baumannii* (38.8%), *K. pneumoniae* (22.2%). The IR of catheter-associated urinary tract infections (CAUTIs) was 18.3 per 1000 device days. The average length of catheterization was – 6 days for urinary catheters, 18 days for central line catheters and the average length of ventilation was 16 days.

**Conclusions:** The incidence rates of device-associated infections that were obtained are comparable to the HAI rates in low- and middle-income countries. Further surveillance on HAI, reducing the length of device use and implementation of core components for infection control are essential for reducing the burden of HAI.

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Abstract 671

**Trachoma between schoolchildren: epidemiological situation in an endemic region of north-east Brazil**

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**Background:** Trachoma is a chronic relapsing keratoconjunctivitis caused by Chlamydia trachomatis that remains a public health problem and a major cause of morbidity, visual impairment and preventable blindness in Brazil. This study aimed to characterize the epidemiological situation of trachoma in the state of Ceará, northeastern Brazil.

**Materials/methods:** A cross-sectional study was conducted with data from school surveys conducted from 2013 to 2017 in 78 of 184 municipalities in the state of Ceará. The population comprised schoolchildren aged 5 to 14 years old. External ocular examination with 2.5X magnifying binocular loupe and flashlight was performed by reference examiners trained by the Brazilian Ministry of Health for clinical diagnosis of trachoma according to World Health Organization simplified trachoma classification system. Secondary data were obtained from the official Epidemiological Surveillance System of the Health Secretary of the State of Ceará.

**Results:** 936,916 schoolchildren were examined and 32,948 cases of trachoma detected. The proportion of cases decreased in the period with a reduction from 4.49% in 2013 to 2.04% in 2017. Most (72.6%) of the municipalities had a percentage below 5%. However, 42 (13.7%) municipalities still had a case rate above 10%.

**Conclusions:** The epidemiological profile of trachoma in Ceará shows a reduction in the proportion of cases of the disease among schoolchildren. The extension and distribution of trachoma in the state of Ceará is still of great magnitude and demonstrates the need for more effective actions to control the disease among schoolchildren.

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<td>9.183 (4.57)</td>
<td>10.695 (3.56)</td>
<td>3.453 (2.04)</td>
<td>6.317 (3.26)</td>
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</tbody>
</table>

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Clinical manifestations of hospitalised chikungunya fever cases during epidemic in the state of Ceará, Brazil, from 2017 to 2019

Roberto Da Justa Pires Neto*1,2,3, Francisca Lillyan Christyan Nunes Beserra1, Joana D’arc Rocha Damasceno1, David Mendes De Melo1, Evelyne Girão2,4

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Background: Chikungunya fever is a viral illness transmitted by hematophagous arthropods and occurs mainly in tropical and subtropical areas. Chikungunya virus spread to America in late 2013. Autochtonous transmission was confirmed in Brazil in 2014. Chikungunya fever presents typically with fever and joint pain and may also develop severe and atypical manifestations.

Materials/methods: This was a retrospective study which analysed data from patients’ charts in a reference hospital in infectious diseases in Brazil. The study period was from January 2017 to April 2019. São José Hospital of Infectious Disease is located in state of Ceará, in the northeastern region of Brazil. Medical records of patients admitted to this hospital with Chikungunya fever confirmed by serological test were reviewed.

Results: Medical records from 71 patients with confirmed Chikungunya fever were analyzed. The average age was 22 years (±26). Comorbidities were found in 26 patients (36.6%). The most frequent clinical manifestations on admission were fever (68; 95.7%), nausea and vomiting (57; 80.3%), rash (49; 69%), arthralgia (35; 49.3%), and headache (27; 38%). Dermatological manifestations with bullous rash were observed in 13 cases (18.3%), of which 12 (92.3%) were children, and 9 (69.2%) younger than 1-year old. During hospitalization, 25 patients (35.2%) presented complications, especially neurological manifestations (15; 21.1%), of which 7 were meningitis, 5 encephalitis, 1 Guillain-Barré syndrome, 1 myelitis and 1 meningoencephalitis. Other frequent complications were acute kidney injury, hydrolelectrolytic disorders, myocarditis, and sepsis. 64 patients (90.1%) were discharged, 2 (2.8%) died and 5 (7.1%) were transferred to another hospital.

Conclusions: Great variability in the clinical manifestations of patients with Chikungunya fever admitted to a reference hospital in northeastern Brazil was observed. A significant percentage of complications, atypical manifestations, and unfavorable outcomes underscore the importance of early clinical recognition of Chikungunya fever to ensure adequate clinical support and reduce the risk of complications.

<table>
<thead>
<tr>
<th>Clinical manifestations of Chikungunya fever</th>
<th>n(%)</th>
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<tbody>
<tr>
<td>Fever</td>
<td>68(95.7)</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>57(80.3)</td>
</tr>
<tr>
<td>Rash</td>
<td>49(69)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>35(49.3)</td>
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<tr>
<td>Headache</td>
<td>27(38)</td>
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<tr>
<td>Abdominal pain</td>
<td>22(31)</td>
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<tr>
<td>Diarrhea</td>
<td>16(22.5)</td>
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<tr>
<td>Dermatological manifestations with bullous rash</td>
<td>13(18.3)</td>
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<tr>
<td>Hepatomegaly</td>
<td>11(15.5)</td>
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</tbody>
</table>

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**Abstract 677**

Pan-genome analysis supports the differentiation of Bacteroides fragilis in division I and the potentially carbapenem-resistant cfiA+ division II into two species

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**Background:** The commensal, opportunistic pathogen *B. fragilis* comprises at least two DNA homology groups. Division I carry the chromosomal cepA cephalosporinase gene and division II carry the cfiA carbapenemase gene. 5-30% of clinical isolates are cfiA+ and of these 30-50% display phenotypical resistance to carbapenems. The cepA and cfiA carrying isolates can be distinguished using routine MALDI-TOF-MS, but not by 16S rRNA gene sequencing. To investigate the differentiation of core genes between the two divisions we performed preliminary pangenome analysis.

**Materials/methods:** *B. fragilis* genomes were identified and downloaded from NCBI RefSeq using ncbi-genome-download [https://github.com/kblin/ncbi-genome-download](https://github.com/kblin/ncbi-genome-download) and re-annotated using Prokka. Roary with MAFFT was used for pangenome alignment phylogeny analysis. ABRicate [https://github.com/tseemann/abricate](https://github.com/tseemann/abricate) was used for identification of antimicrobial resistance genes.

**Results:** Genome assemblies of 161 *B. fragilis* isolates were available on October 15, 2019. For the 161 isolates a total of 38,247 genes were annotated of which 892 were core genes present in 99-100% of strains (Figure 1). 19 isolates were cfiA+ (division II) isolates. CfiA+ and cepA+ strains respectively, contained a large set of genes not present in the other. Division II isolates shared a core genome of 2602 genes of a total of 14216 genes. For cepA+ (division I) isolates a total of 31415 genes were annotated of which 1627 were core genes.

**Conclusions:** Of the 161 *B. fragilis* genome assemblies 19 are division II strains. The core-genome of the 161 isolates is only 892 genes which is much lower than the core-genome of *E. coli*, which has a comparable genome size to *B. fragilis*. 97% of *E. coli* strains share a core-genome of 2,613 genes (Ambram et al bioRxiv 2019). The core-genome of the 19 division II isolates is 2,602 genes. The current results support further work towards describing *B. fragilis* division II as a separate species.

**Figure 1.** Visualisation of the pan-genome of 161 *B. fragilis* strains from NCBI RefSeq using phandango [https://jameshadfield.github.io/phandango/](https://jameshadfield.github.io/phandango/). The 19 *B. fragilis* division II (cfiA+) are clearly differentiated from the remaining strains. A large set of genes are present in one division but not the other.

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Background: the 13-valent pneumococcal conjugate vaccine (pcv13) was introduced in Navarra in 2010. In 2020 two new pcvs are expected to be manufactured. pcv15 includes pcv13 serotypes plus 22f and 33f. pcv20 includes pcv13 serotypes plus 8, 10a, 11a, 12f, 15b, 22f and 33f. Monitoring of serotype distribution is necessary for surveillance and evaluation of vaccines. We aimed to monitor the circulating serotypes before the possible introduction of pcv15 and/or pcv20 in Navarra.

Materials/methods: we included the cases of invasive pneumococcal disease (ipd) diagnosed in Navarra between 2010-2019. An ipd case was defined as isolation of S. pneumoniae or detection by pcr from a normally sterile body site.

Results: 608 ipd were included: 67 (11%) patients were <5 years old, 239 (39.3%) patients were 5-64 years old and 302 (49.7%) patients were >=65 years old. 55 ipd could not be serotyped. Among the 553 serotyped ipd, the 3 most frequent serotypes were: serotype 3 (17.5%), serotype 8 (9.2%) and serotype 19a (7.4%). Other detected serotypes (between 4-5%) were: 9n, 7f and 22f. The detected serotypes according to the group of age were: in children <5 years old serotypes 19a (14.1%), 24f (14.1%) and 3 (10.7%); in patients between 5-64 years old serotypes 8 (16.4%), 3 (12.6%) and 9n (7.9%); in patients >=65 years old serotypes 3 (22.9%), 19a (6.9%) and 8 and 6b (5.5% each).

The rate of antibiotic resistance and the related serotypes was: 3.5% of penicillin resistance related to serotypes 11a, 14 and 19a; 0.7% of cefotaxime resistance related to serotypes 14 and 19a; 21.2% of erythromycin resistance related to serotypes 24f, 33f and 19a; 0.8% of quinolones resistance related to diverse serotypes.

Conclusions: the most prevalent serotypes causing ipd in Navarra were 3, 8 and 19a. In the last 9 years, in all ages 48.3% and 67.1% of ipd in Navarra were caused by serotypes included in pcv15 and pcv20 respectively. It would be critical to assess the effectiveness of the new vaccines against serotype 3. Serotype 24f caused 3.8% of ipd and is not covered by any of these 2 new products.

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Abstract 681

**Generation of protective antibodies against heterologous Acinetobacter baumannii isolates**

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**Abstract third-party references:** Medical Research Council (MRC), Global Challenges Research Fund (GCRF), Respiratory Department, CITR, University College London

**Background:** Opportunistic nosocomial infections by multi-drug resistant Acinetobacter baumannii (A. baumannii) are associated with high morbidity and mortality rates. The increase in the incidence of infections caused by pan-drug resistant isolates further highlights the urgent need for novel therapeutics. We report on the generation of cross-reactive antibodies that are protective against homologous and heterologous strains in vivo and in vitro.

**Materials/methods:** We immunized CD1 mice with sub-lethal doses of Ab3879 (st215/kl10) and Abapsp-515 (st164/kl47) clinical A. baumannii isolates. We measured in vitro IgG binding to the bacterial surface and lysate by flow cytometry and Western blot analysis. Growth inhibitory/bactericidal activity of antibodies were measured by comparing bacterial growth in the presence anti-sera. Neutrophil phagocytosis of A. baumannii was measured following bacterial opsonisation with either homologous or heterologous sera, followed by incubation with neutrophils isolated from healthy human blood donors. The efficacy of antibodies in vivo was evaluated using a bacteremia mouse model of A. baumannii infection by either passive or active immunization prior to challenge.

**Results:** Flow cytometry and growth impairment assays demonstrated that antibodies in sera recovered from mice previously infected with A. baumannii recognized homologous and heterologous isolates but to different degrees. Anti-Ab3879 antibodies recognized the surface of the homologous isolate to a greater extent when compared to heterologous isolate (Ab3879, 93% versus Abapsp-515, 67%). Similarly, anti-Abapsp-515 bound its homologous isolates to a greater extent than Ab3879. Western blot analysis showed the recognition of both isolate-specific high molecular weight capsule, and multiple proteins. Survival following intraperitoneal challenge with lethal doses of Ab3879 was 100% in both homologous (Ab3879) and heterologous (Abapsp-515) immunized mice compared to 50% in controls, and the bacterial burdens in the lungs, spleen and liver of immunized mice were significantly lower compared to control mice (p-value < 0.05).

**Conclusions:** We demonstrate the generation of cross-reactive antibodies that recognize heterologous isolates both through recognition of structurally-related capsular polysaccharide and/ or conserved proteins. Protective antibodies to specific conserved protein targets could potentially be used for future monoclonal antibody passive immunization therapies.

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Background: Cystic fibrosis patients are prone to bacterial pulmonary infections, mainly with *Burkholderia cepacia* complex. These bacteria are associated with severe complications.

Ceftazidime is currently combined with avibactam (CZA) as a first-line antibiotic. No studies have evaluated the CZA infusion time in patients with cystic fibrosis to date, although this population is known to have its own pharmacokinetic (PK) characteristics. The aim of this study was to evaluate different dosage regimens and to identify those that guarantee microbiological efficacy.

Materials/methods: From the population pharmacokinetic models published by Bulitta *et al.* and Bensman *et al.*, 10,000 PK profiles were simulated. The MIC distribution of *Burkholderia cepacia* complex bacteria was determined at the Burkholderia Observatory (Toulouse University Hospital) from strains isolated from 46 different hospitals. Based on the simulated kinetic profiles and the MIC distribution, the Probability of Target Attainment (PTA) and the Cumulative Fraction Response (CFR) were calculated. The critical values of the pharmacokinetic/pharmacodynamic (PK/PD) criterion were 65% fT>MIC and 50% fT>1mg/L for ceftazidime and avibactam, respectively.

Results: The CFR have shown that a minimum infusion time of 6 h is required to reach the critical value of the PK/PD criterion in more than 99% of patients. The infusion time can then be adapted after determining the MIC of the offending germ. For example, for a germ with a MIC equal to 8 mg/L, an infusion time of 4 h is necessary to guarantee microbiological efficacy in more than 99% of patients.

Conclusions: This work shows that the infusion time of CZA depends on the type of treatment (probabilistic antibiotic therapy or adapted secondarily to the antibiogram) and the sensitivity (MIC) of the causative pathogen.

This simulation-based work must be validated for use in hospital practice. Nevertheless, this approach was adopted for one patient (Toulouse University Hospital). As a result, the critical value of the PK/PD criterion was reached on the one hand and, on the other hand, clinical improvement was quickly obtained.

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Abstract 687

Role of deoxyribonucleic acid content in the composition of microbial biofilm in the pathogenesis of severe respiratory infections

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Background: It has been known about possibility of microorganisms to create specific multi-layered structures called biofilms. Non-cellular deoxyribonucleic acid actively participates in regulation of properties of biofilms. Thus, in biofilms transfer of genetic information including genes responsible for sensitivity to antibacterial drugs occurs much more often than in single-living bacterial cells. However, despite the involvement of extracellular deoxyribonucleic acid in adhesive processes and intercellular interactions, its role has not been fully understood.

Materials/methods: 238 isolates isolated from sputum and pharynx of 175 patients during 2016-2019 were studied. Patients were divided into two groups: the 1st group of 139 people (79.4%) had severe respiratory infections, the 2nd of 36 people (20.6%) - respiratory infections of moderate severity.

Results: A method was developed for determining percentage of deoxyribonucleic acid in microbial community using 4’6-diamidino-2-phenylindole dihydrochloride. Average age of the 1st group was higher than the second (p<0.05). Pseudomonas aeruginosa had the largest mass of biofilm and percentage of deoxyribonucleic acid in group 1, 48.25 [30.5-70.1] mcg/ml and 5.2 [2.1-7.67] %, p = 0.04. A strong relationship was found between percentage of deoxyribonucleic acid in Pseudomonas aeruginosa and severity of disease, r = 0.73, p<0.05. The incidence of adverse outcomes in isolating antibiotic resistant isolates was higher than in antibiotic sensitive (p<0.05). Analysis of results made it possible to propose fatal outcome when mass of microbial biofilm is > 47.5 mcg/well and percentage of deoxyribonucleic acid is >2.33% (p<0.01).

Conclusions: Method for determining percentage of deoxyribonucleic acid in biofilm has been proposed. With age there is a decrease in immune system which contributes to adherence of more pathogenic, antibiotic resistant microflora which has high biofilm weight and deoxyribonucleic acid percentage leading to disease progression and death.

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Abstract 689

**Enterovirus D68 subclade B3 in children with acute flaccid paralysis in west Africa: evidence of spread of outbreaks reported in US and Europe, 2016**


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**Background:** Since 2014, several outbreaks due to Enterovirus D-68 (EV-D68) have been reported, and it was confirmed that the virus can cause upper and lower respiratory tract diseases and be associated with the neurologic syndrome of acute flaccid myelitis (AFM). However, in African countries, the circulation and the molecular epidemiology of EV-D68 is poorly documented particularly on children with AFM. Our study aims to understand the extent of EV-D68 AFP in West Africa but also to know its genetic diversity and molecular epidemiology.

**Materials/methods:** To investigate the circulation of EV-68 in West Africa in AFP during the 2016 outbreak, we retrospectively screened 567 stools sample collected through routine poliomyelitis surveillance activities in seven countries of West Africa including Cape Verde, Gambia, Guinea-Bissau, Guinea Conakry, Mauritania, Niger, and Senegal between June to September 2016. After EV-D68 detection, molecular characterization was performed by amplification of the VP1 regions, followed by nucleotide sequencing.

**Results:** Among the 567 stool specimens tested, EV-D68 was detected in sixteen samples (2.8%) from three countries whose Guinea Conakry (11/391), Niger (1/85) and Senegal (4/59). The majority (62.5%) of the EV-D68 cases were detected in July. Children under 5 years were more vulnerable to EV-D68 infection with a frequency of 87.5%. Phylogenetic analysis of sequences of the VP1 region revealed that all West Africa strains sequenced belongs to the Subclade B3 variant of clade B. Additionally, the Subclade B3 strains of West Africa clustered with several other strains circulating during the same period in Spain and Sweden.

**Conclusions:** This study allowed to understand the extent of EV-D68 AFP in West Africa but also evidence of spread of outbreaks reported in US and Europe in 2016. These findings warrant implementation of enhanced surveillance of EV-D68 in confirmed case of AFM in African countries for a better understanding the disease and it burden.

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**Abstract 690**

**Dissemination of a blaNDM-1-carrying IncA/C2 plasmid in a broiler flock: a possible real-life scenario**

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**Background:** Emergence of carbapenemase-producing Enterobacteriaceae (CPE) in livestock animals poses a worrying concern for public health safety. The sporadic detection of CPE in livestock suggests their low prevalence and a knowledge gap on the spread potential of plasmids carrying carbapenemase-encoding genes. In the frame of an international research project EFFORT, *in vivo* broiler chicken infection experiments were performed, aiming to understand spread and adaptation potential of a *S. Corvallis* native blaNDM-1-carrying broad-host range IncA/C2 plasmid in the absence of antibiotic pressure.

**Materials/methods:** Broiler chicken infection model was selected as an *in vivo* model for the investigation of spread and adaptation of a public health relevant broad MDR-encoding blaNDM-1-carrying IncA/C2 plasmid. Following oral inoculation of NDM-1-producing *S. Corvallis* strain, selection of *S. Corvallis* re-isolates and entero bacterial transconjugants were in-depth analysed by S1-PFGE and by Illumina and Nanopore whole-genome sequencing for a deeper insight into variants of the blaNDM-1-carrying IncA/C2 plasmid at genome level.

**Results:** The conducted *in vivo* study revealed rapid and broad host range dissemination of the blaNDM-1-carrying IncA/C2 plasmid to commensal *E. coli* strains (ST-117, ST-156, ST-2040, ST-2485) and a *K. pneumoniae* strain (ST-1106). Beside plasmid transfer, a transposition event of the blaNDM-1 gene onto another ~30 kb plasmid of an *E. coli* transconjugant strain was detected. Three types of structural deletions of the blaNDM-1-carrying IncA/C2 plasmid were detected (~10 kb deletions, ~70 kb deletions as a co-integrate formation). Despite structural deletions, loss of the blaNDM-1 gene was not observed.

**Conclusions:** Conducted *in vivo* study revealed broad dissemination of the blaNDM-1-carrying IncA/C2 plasmid. This occurrence is worrying as such entrance scenario might lead to broader dissemination of this plasmid in environments with mixed bacterial population. Another concerning observation is the transposition event of blaNDM-1 gene onto another plasmid which might facilitate further dissemination of this gene. Few structural alterations of blaNDM-1-carrying IncA/C2 plasmid indicate adaptation and persistence potential of this plasmid in the absence of antibiotic pressure. With the aim of preventing this scenario, entrance of a NDM-1-producing *S. Corvallis* strain into a broiler flock should be prevented, as broad dissemination of its MDR-encoding blaNDM-1-carrying IncA/C2 plasmid is inevitable.

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Comparing clinical outcomes in Gram-negative bloodstream infections with desirability of outcomes ranking: focus on non-fermenting organisms

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Background: Rapid diagnostic testing (RDT) for the management of bloodstream infections (BSIs) has the potential to decrease time to organism identification and effective antibiotic therapy. These findings are primarily driven by data in gram-positive organisms, with less known regarding the benefits among gram-negatives, especially non-lactose fermenting organisms, where antibiotic resistance is complex and rarely detected by current RDTs.

Materials/methods: Subgroup analysis of retrospective quasi-experimental study of adult patients with gram-negative BSI from 9/2014 to 08/2018, with Verigene intervention in 9/2015. Inverse probability of treatment weighting (IPTW) controlling for Charlson Comorbidity Index and critical illness was used to balance patients. To further analyze risk/benefit IPTW-adjusted desirably of outcomes ranking (DOOR) was derived combining patient disposition and optimal antibiotic therapy. The DOOR designation was as follows; 1 = home, optimal antibiotics; 2 = home, suboptimal antibiotics; 3 = not home, optimal antibiotics, 4 = not home, suboptimal antibiotics, 5 = death.

Results: The original cohort consisted of 832 patients; 700 with Enterobacteriaceae, 99 with P. aeruginosa and 33 Acinetobacter spp. BSI. Among Enterobacteriaceae, median time to optimal therapy significantly decreased with RDT (54.7 vs 25.9 hours, \( P = 0.02 \)); however there was no change among non-lactose fermenters (24.5 vs 25.2 hours, \( P = 0.34 \)). For subgroup analysis, 132 met inclusion; 40 pre-RDT, 92 post-RDT. Among the IPTW subgroup there were no significant differences in time to optimal antibiotics (24.6 vs 25.4 hours, \( P = 0.3 \)) or in-patient all-cause mortality (10.9% vs 16.7%, \( P = 0.54 \)) with the introduction of RDT. Additionally controlling for source of infection there was no difference in in-patient all-cause mortality [adjusted OR = 0.77, 95% CI 0.14, 4.2]. DOOR was similar between groups; the probably of a lower DOOR among the pre-RDT group (Figure 1) was marginally higher (10%, 95% CI 9.6%, 10.5%).

Conclusions: Compared to patients with gram-negative BSI caused by Enterobacteriaceae, among BSI caused by non-lactose fermenting organisms the addition of RDT did not confer significant benefits. This is likely due to the complex, multifactorial mechanisms of resistance rarely detected by available RDT platforms.

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Detection of echinocandin resistance in *Candida glabrata* in the microbiology laboratory using commercial methods: interpret with caution!

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**Background:** Echinocandin resistance in *C. glabrata* can be detected in the clinical microbiology laboratory by using EUCAST and CLSI reference broth microdilution methods. Reference methods are time-consuming and most of microbiology laboratories lie on commercial methods such as Sensititre Yeast One® [SYO] or ETest to perform antifungal susceptibility testing. We assessed the ability of the ETest and SYO to accurately detect echinocandin resistance in *C. glabrata* clinical isolates.

**Materials/methods:** We studied micafungin- or anidulafungin-resistant *C. glabrata* isolates (n=29) according to EUCAST EDef. 7.3.1 methodology and harbouring the following FKS2 gene mutations: Δ658 (n=14), S663P (n=7), W715L (n=3), S663Y (n=1), E655A (n=1), and none (n=3). Echinocandin susceptibility using CLSI M27-ED4, ETest, and SYO (the latter using CLSI breakpoints) was further performed. Agreement between methods and very major errors (false susceptibility) were assessed.

**Results:** Essential agreement (± two-fold dilutions) between EUCAST and CLSI for anidulafungin and micafungin was 86% and 79%, respectively, and all mutants were correctly classified as resistant using both procedures (Figure). SYO yielded 6 isolates with very major errors to only micafungin (n=2, Δ658 and W715L), only anidulafungin (n=2, Δ658), or both (n=2, FKS wild type); the EUCAST MIC ranges against the isolates were 0.06-0.5 mg/L [micafungin] and 0.25-2 mg/L [anidulafungin]. All isolates showed an MIC of micafungin and anidulafungin ≥0.06 mg/L and ≥0.03 mg/L, respectively.

**Conclusions:** Micafungin and anidulafungin MICs against *C. glabrata* obtained by SYO should be interpreted with caution because up to 20% of very major errors (false susceptibility) may come out. In the absence of clinical breakpoints for MICs obtained by ETest, values ≥0.06 mg/L and 0.03 mg/L for micafungin and anidulafungin, respectively, could be used to detect echinocandin resistance. Isolates with suspicion of phenotypic echinocandin resistance using SYO or ETest should be confirmed by CLSI or EUCAST and by further FKS gene sequencing.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Method</th>
<th>Number of isolates at each MIC (in mg/L)</th>
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</table>

Cells in grey indicate phenotypic resistance. CLSI breakpoints were adopted for SYO.

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Abstract 710

Five-day versus ten-day oseltamivir chemoprophylaxis to prevent hospital influenza transmission: a non-inferiority randomised open-label study

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Background: Based on the evidence of a protective effect of antivirals against influenza as well as their generally benign safety profile, some hospital infection control authorities recommend oseltamivir prophylaxis for vulnerable patients who were in close contact with influenza. Given the short incubation period of influenza, the recommended oseltamivir post-exposure prophylaxis for 7 to 10 days after the last known exposure may be too long.

Materials/methods: In an open-label randomized clinical trial, performed in a single-centre university hospital, the effectiveness of a 5-day versus 10-day post-exposure oseltamivir prophylaxis was compared in an intention to treat (ITT) and per protocol (PP) analyses and on a noninferiority premise in adult patients who were exposed as close contacts to influenza. Breakthrough influenza rate was assessed up to 10 days after discontinuation of oseltamivir prophylaxis.

Results: Among 222 randomized contact patients (median age 75 years; male 119 [53.6%]; median Charlson comorbidity index 5), 110 patients [49.6%] were assigned to receive oseltamivir post-exposure prophylaxis for 5 days, and 112 patients for 10 days. Patients in the two prophylaxis groups did not differ regarding basic demographic and clinical characteristics. Because single-patient rooms and cohorting capacities were in short supply, the median duration of exposition to influenza was two days [IQR 1–3 days]. All of 137 identified influenza patients, who served as index cases for 202/222 (91.0%) exposed contact patients, were prescribed oseltamivir treatment for 5 days. Rates of breakthrough influenza were 2/110 [1.8%] with 5-day regimen and 0/112 [0%] with 10-day regimen in the ITT study population (difference, 1.8 percentage points [1-sided 95% CI, –1 to 4.9 percentage points]; P=0.765) and 2/102 [2.0%] and 0/95 [0%), respectively, in the PP study population (difference, 2.0 percentage points [1-sided 95% CI, –1 to 5.3 percentage points]; P=0.745).

Conclusions: In patients, exposed to influenza as close contacts within hospital environment, 5-day post-exposure oseltamivir prophylaxis was noninferior to 10-day regimen with respect to preventing influenza transmission, assuming the predetermined noninferiority margin of 7 percentage points. Both prophylactic regimens were effective even if the exposed contact patients could not have been separated from index patients with influenza.

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Abstract 711

**Association of statin use and microbiological and clinical characteristics of early Lyme borreliosis**

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**Background:** *Borrelia burgdorferi* sensu stricto, the causative agent of Lyme borreliosis (LB) possesses a functional 3-hydroxy-3-methyl-glutaryl-coenzyme A reductase (HMGR), which is a rate limiting enzyme of the mevalonate pathway that contributes to cell wall synthesis. Statins are HMGR inhibitors and have been shown to reduce bacterial burden and alter the immune response to favour clearance of spirochetes in a mouse model of LB.

**Materials/methods:** The association between background statin use and prospectively collected clinical and microbiologic characteristics was investigated in 1220 adult patients with early LB manifesting as erythema migrans (EM) at a single-centre university hospital in Ljubljana, Slovenia. Patients were assessed at enrolment and followed-up for 12 months.

**Results:** Statin treatment was associated with age and prevalence of other comorbidities besides hyperlipidemia, but not with borrelial skin culture positivity rate, serological response to infection, or presence of LB-associated symptoms at enrolment. The proportion of patients taking statins was lower among patients with disseminated disease manifested as multiple EM than among those with solitary EM, but the difference was not significant (10/195, 5.1% vs 84/1025, 8.2%; *P*=0.19). The time to resolution of EM after starting antibiotic treatment was comparable in patients on statins and in those without statins (median 7 days, IQR 4–14). At 12 months, 59/989 (6.0%) patients showed incomplete response. The odds for incomplete response decreased with time from enrolment (odds ratio [OR] 0.49, 0.50, and 0.48 for 2-month vs. 14-days, 6-month vs. 2-month, and 12-month vs. 6-month follow-up visits, respectively), were higher in patients who reported LB-associated constitutional symptoms at enrolment (OR 8.10, 95% CI 5.69–11.55; *P*<0.001), but were not affected by statin use (OR 1.09, 95% CI 0.61–1.98, *P*=0.76).

**Conclusions:** In our study of European patients with EM, most of whom were infected with *B. afzelii*, statin use was not associated with selected clinical and microbiological parameters of infection.

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Abstract 715

Excluded versus included patients in a randomised controlled trial of infections caused by carbapenem-resistant Gram-negative bacteria: relevance to external validity

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**Background:** Population external validity is the extent to which an experimental study results can be generalized from a specific sample to a defined population. In order to apply the results of a study, we should be able to assess its population external validity. We performed an investigator-initiated randomized controlled trial (RCT) (AIDA study), which compared colistin-meropenem combination therapy to colistin monotherapy in the treatment of patients infected with carbapenem-resistant Gram-negative bacteria. In order to examine the study’s population external validity and to substantiate the use of AIDA study results in clinical practice, we performed a concomitant observational trial.

**Materials/methods:** The study was conducted between October 1st, 2013 and January 31st, 2017 [during the RCTs recruitment period] in Greece, Israel and Italy. Patients included in the observational arm of the study have fulfilled clinical and microbiological inclusion criteria but were excluded from the RCT due to receipt of colistin for >96 hours, refusal to participate, or prior inclusion in the RCT. Non-randomized cases were compared to randomized patients. The primary outcome was clinical failure at 14 days of infection onset.

**Results:** Analysis included 701 patients. Patients were infected mainly with Acinetobacter baumannii [78.2% (548/701)]. The most common reason for exclusion was refusal to participate [62% (183/295)]. Non-randomized and randomized patients were similar in most of the demographic and background parameters, though randomized patients showed minor differences towards a more severe infection. Combination therapy was less common in non-randomized patients [31.9% [53/166] vs. 51.2% [208/406], p=0.000]. Randomized patients received longer treatment of colistin [13 days [IQR 10-16] vs. 8.5 days [IQR 0-15], p=0.000]. Univariate analysis showed that non-randomized patients were more inclined to clinical failure on day 14 from infection onset [82% [242/295] vs. 75.5% [307/406], p=0.042]. After adjusting for other variables, non-inclusion was not an independent risk factor for clinical failure at day 14.

**Conclusions:** The similarity between the observational arm and RCT patients has strengthened our confidence in the population external validity of the AIDA trial. Adding an observational arm to intervention studies can help increase the population external validity and improve implementation of study results in clinical practice.

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Investigation of the prevalence of Verocytotoxigenic Escherichia coli (VTEC) contamination of private groundwater wells in Ireland

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Background: Approximately 750,000 people in Ireland obtain their drinking water from a private well. Wells are unregulated and quality testing by users is infrequent. Waterborne transmission of Verocytotoxigenic Escherichia coli (VTEC) through private wells has emerged as an important transmission route. Cattle manure and septic tanks are possible contamination sources, with persistent heavy rainfall contributing to microbial ingress. Ireland has the highest incidence of human VTEC infection, at almost ten times the EU average in 2017. The aim of this study was to investigate the prevalence of VTEC contamination in domestic private wells in Ireland.

Materials/methods: Groundwater wells (n=21) were sampled during October 2019 (Figure 1). Raw and/or treated well water samples (30 L) were collected and analysed using the “CapE” method (Morris, 2016). Filters were enriched overnight in buffered peptone water, DNA was extracted from enrichment broths and tested by multiplex real-time PCR for eae, vtx1 and vtx2 genes. Positive samples were tested for genes associated with serogroups O157, O26, O153, O145, O111 and O104. All samples were assessed for total coliforms and total E. coli using the Colilert-18 system (IDEXX). Data relating to groundwater vulnerability were geospatially linked to each well and assessed for univariate association with VTEC presence/absence.

Results: Verocytotoxin genes were detected in 9/21 wells (43%), 7 of which were also positive for eae. One or more of six serogroup gene targets were identified in all positive samples. Multiple serogroups were detected in 4/9, with O145 (n=6), O157 (n=5) and O103 (n=4) the most prevalent. Presence of live E. coli in well water samples (Colilert-18) was associated with detection of verocytotoxin genes (P=0.0075, Fisher’s Exact test). No significant associations were noted between the groundwater vulnerability variables analysed and presence of VTEC (significance level P<.05).

Conclusions: Private wells in Ireland are at risk of contamination with pathogenic strains of E. coli capable of causing human disease. This research represents preliminary data from the DESIGN (Detection of Environmental Sources of Infectious diseases in Groundwater Networks) study. Data generated from more widespread sampling may lead to policy development to protect private well users in Ireland from waterborne infectious diseases.

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Abstract 721

Genomic analysis of carbapenemase-encoding plasmids from *Klebsiella pneumoniae* across Europe highlights three major patterns of dissemination

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**Background:** The incidence of *Klebsiella pneumoniae* infections that are resistant to carbapenems, a last-line class of antibiotics, has been rapidly increasing. The primary mechanism of carbapenem resistance is production of carbapenemase enzymes, which are most frequently encoded on plasmids by *bla*<sub>OXA-48-like</sub>, *bla*<sub>VIM-like</sub>, *bla*<sub>NDM-like</sub> and *bla*<sub>KPC-like</sub> genes. Using short-read sequence data, we previously analysed genomes of >1700 isolates from the *K. pneumoniae* species complex submitted during the European survey of carbapenemase-producing Enterobacteriaceae (EuSCAPE). Here, we investigated the diversity, prevalence and transmission dynamics of carbapenemase-encoding plasmids in this sample collection.

**Materials/methods:** All carbapenemase-carrying contigs from short-read assemblies (*n*=696) were clustered into gene context (GC) groups, based on the order and nucleotide similarity of coding sequences flanking each carbapenemase gene. We performed long-read sequencing on 79 isolates including one isolate per GC group. These encoded a total of 14 *bla*<sub>OXA-48-like</sub>, 11 *bla*<sub>VIM-like</sub>, 15 *bla*<sub>NDM-like</sub> and 44 *bla*<sub>KPC-like</sub> genes. Long- and short-read sequence data were assembled together using Unicycler. Short-read mapping to the newly-obtained reference plasmids indicated how much of the reference sequence was present amongst all remaining isolates from the collection.

**Results:** We identified three major patterns by which carbapenemase genes have disseminated via plasmids. First, *bla*<sub>OXA-48-like</sub> genes have spread across diverse lineages primarily via the highly conserved, epidemic pOXA-48-like plasmid. Phylogenetic analysis of pOXA-48-like plasmid sequences demonstrated substantial horizontal transmission amongst co-localised chromosomal lineages but also indicated prolonged vertical transmission upon acquisition by high-risk lineages (ST11, ST15, ST101). Second, *bla*<sub>VIM-like</sub> and *bla*<sub>NDM-like</sub> genes have spread via transient associations of diverse plasmids with numerous lineages, albeit with high-risk lineages also playing a primary role in geographic spread. Third, *bla*<sub>KPC-like</sub> genes have transmitted predominantly by stable association with one successful clonal lineage (ST258/512), despite frequent mobilisation between pre-existing yet diverse plasmids within the lineage. These include pKpQIL-like plasmids which have co-evolved with the ST258/512 chromosome.

**Conclusions:** Here, we highlight three predominant modes of plasmid spread that have enabled widespread dissemination of carbapenemase genes. They can be summarised as using one plasmid/multiple lineages, multiple plasmids/multiple lineages, and multiple plasmids/one lineage. Despite these contrasts, all are underpinned by significant propagation along high-risk clonal lineages.

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Abstract 722

**A prospective cohort study of Malawian children presenting with fever**

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**Background:** Of an estimated 4.3 million cases of malaria in Malawi in 2017, the majority of malaria-related deaths occurred in children. Differentiating causes of childhood fever in rural clinics is challenging. Greater understanding of clinical features that differentiate malaria from other causes of fever may improve triage of febrile children in these settings. This study aimed to analyse clinical features associated with malaria and parental perceptions on causation of fever in a rural clinic in Malawi.

**Materials/methods:** This prospective cohort study included 313 children presenting with fever to a charity-funded clinic in rural Malawi between the months of March and June 2019. Children underwent tympanic temperature measurement and malaria rapid diagnostic testing (MRDT). Blood films were not routinely performed. Clinical assessment was performed, and brief interviews conducted with the child’s parent or guardian.

**Results:** 47.3% of children had positive MRDTs and were treated for malaria as per WHO guidelines. Children with a history of vomiting were more likely to have a positive MRDT (Odds ratio 3.4773, Confidence Interval 1.98-6.10, p-value <0.0001). This association increased when combined with a history of headache (OR 11.44, CI 2.6-50.2, p-value 0.0012). Negative MRDTs were predicted by rash (OR 6.6776, CI 1.49-29.90, p-value 0.013) and upper respiratory tract symptoms (OR 9.9716, CI 5.13-19.38, p-value <0.0001). There was no significant difference in time to presentation between MRDT positive and negative children. The likelihood of a positive MRDT was not significantly different where parents predicted a diagnosis of malaria as the cause of symptoms. There was a strong correlation between recorded temperature up to 40°C and likelihood of positive MRDT (r = 0.976, p-value 0.004). Temperature >40°C did not predict positive MRDT.

**Conclusions:** A diagnosis of malaria was predicted by symptoms of vomiting and headache, and by objectively elevated temperatures up to 40°C. Parents did not reliably differentiate the cause of symptoms at time of presentation, and children with malaria did not present earlier. This data should inform triage and malaria testing of febrile children and guide community education regarding malaria symptomatology.

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Abstract 723

Typing of MRSA isolates from bloodstream infections in the Dutch-German border region and Berlin

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Background: Recent surveillance data indicated that in hospitals located in the Northern Dutch part of the Dutch-German border area, the incidence of MRSA bloodstream infections (BSIs) was [although lower than in Germany] higher than expected and exceeded national levels (Jurke et al., 2019). It was speculated that this could be a result of an additive burden of BSIs due to livestock-associated (LA)-MRSA in the border area characterized by a high density of livestock production. In order to evaluate this, we investigated the MRSA isolates from BSIs by using molecular surveillance techniques.

Materials/methods: We retrospectively characterized all available MRSA bacteremia isolates from university hospitals in the Dutch and the German part of the Dutch-German border region, as well as (for comparison) a hospital in Berlin. Typing of the isolates collected between 2016-2018 was performed by using WGS and a gene-by-gene approach (cgMLST, Ridom SeqSphere+ v6.0.2). Antimicrobial resistance genes were detected using CLC Genomics Workbench v12.0.3 and the ResFinder database.

Results: A total of 31 MRSA isolates were characterized (n=6 from Groningen, n=10 from Berlin, n=15 from Oldenburg). Most of the isolates belonged to clonal complex (CC) 22 (n=16), which was the most frequent CC in Groningen and Berlin but not in Oldenburg (Figure 1). Two isolates had new sequence types (STs 5702 and 5703, single locus variants of ST22). Several resistance genes were identified. None of the isolates was PVL-positive. MRSA ST398, indicative for LA-MRSA was not detected. Two possible direct transmission events could have occurred between two patients in Oldenburg and Berlin.

Conclusions: CC22 was the most commonly found clonal complex and none of the isolates belonged to the typical LA-MRSA STs, ruling out the additive burden that could have arisen from a high density of livestock production in this "Euregio".

Figure 1. Most common STs found in the 3 different studied sites.

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Ignatzschineria bacteraemia following maggot wound infestation

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**Background:** Myiasis is an infestation of live humans and other vertebrates by larvae of various flies of the order Diptera which feed on host's dead or living tissue. In humans, it is often associated with precarious living conditions. We describe a case of myiasis with subsequent *Ignatzschineria* bloodstream infection as a complication of maggot wound infestation in a young male migrant.

**Materials/methods:** 18-year-old male patient was admitted to our hospital after being found in the river on the Slovenian border. On admission, he was febrile (39.6°C), normotensive with tachycardia (130/min). Since he was traveling by foot in the rural areas and woodlands of Balkans he had multiple superficial wounds on both legs with surrounding cellulitis and numerous small moving larvae on the skin and in the skin folds. His laboratory results revealed CRP 499, PCT 8.9 and leucocytosis of 25,9 \( \times 10^9 \) with a left shift (8% bands). Debridement of the wounds was performed and the patient was started on flucloxacillin and ciprofloxacin. The wounds were redressed two days later with numerous larvae observed and debrided.

**Results:** According to the shape and pattern of the posterior spiracles the larvae were identified as *Lucilia* sp. Rectal swab yielded *Enterobacter cloacae* ESBL and the skin swabs MRSA, therefore we changed antibiotics to imipenem and vancomycin. Blood cultures yielded *Ignatzschineria* sp., identified from subculture on blood agar only by 16S rRNA gene sequencing and sensitive to piperacillin/tazobactam, ceftazidim, imipenem and ciprofloxacin. After 10 days of antibiotic therapy the CRP levels decreased and clinical condition improved, he was afebrile and discharged. After second debridement there were no more larvae observed and the wounds were healing well.

**Conclusions:** This is the first human case of *Ignatzschineria* bacteraemia in Slovenia. *Ignatzschineria* spp. are emerging bacteria that have known association to myiasis in humans. Bacteraemia caused by these bacteria is rare. Given the increasing number of illegal border-crossers it could become an important migrant health issue. Therefore, it should be suspected by healthcare providers when experiencing maggot wound infestation.

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Abstract 758

**Increasing trend of leptospirosis in an area of northern Spain (1986-2019)**

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**Background:** Leptospirosis is a zoonotic disease more frequent in wet tropical and subtropical regions. Human infection results from indirect exposure to urine of carrier mammals, especially rodents. This work studies the incidence and epidemiological characteristics of leptospirosis in Gipuzkoa (Basque Country, Spain), 712,119 inhabitants.

**Materials/methods:** Retrospective leptospirosis review of clinical and laboratory data, 1986-Sept2019. Laboratory tests: Leptospira agglutination (Diagnostics Pasteur) until 1991, IgM ELISA (Panbio or Novatek) since that year and Leptospira DNA detection using an “in house” PCR (JCM 2014;52:2011) in 2015-2016 and a commercial PCR (Tropical fever, Fast-Track Diagnosis) since 2017. Microscopic Agglutination Test (MAT) (reference laboratories) was used to confirm agglutination or IgM-positive cases. Cases were classified following CDC Leptospirosis 2013 Case Definition.

**Results:** Eighty-two cases were detected in the period of study, being 55 (67.1%) confirmed and 27 (32.9%) probable cases, 72 (88%) in males. PCR only contributed with one more case than serology but allowed to confirm 13 cases that otherwise would have been classified as probable cases. Thirty-one cases (38%) were detected in 1986-2002 and 51 (62%) in 2003-2019 (22 of them in the last three years). Fifty-six cases (73% of the 77 with known age) were 30-69 years-old [group range 13-77 years]. In 2017-2019, the incidence was 1.03 cases/100,000 inhabitants, being in males 30-69 years-old 2/100,000. An epidemiological linkage was known in 60 (73%) cases: job-related [sewer maintenance, agricultural activities, livestock farming] in 67% and recreational activities [immersion in water, hunting, trekking] in 33%. Most cases were autochthonous [93%] and occurred in summer and fall [81%]. Ninety-eight percent of patients needed hospitalization and 50% were admitted in the Intensive Care Unit. There were no deaths. L. icterohaemorrhagiae (71%) and L. canicola (18%) were the most common serogroups.

The increase of cases observed in the last period (2017-2019), could not be attributed to an increase in requests or a common epidemiologically source.

**Conclusions:** In Gipuzkoa, the incidence of leptospirosis increased in recent years without a known cause. The highest rate was detected in 30-69 year-old males. A plausible epidemiological exposure was detected in most cases and PCR allowed confirm many of them.

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Linezolid-resistant strains of Enterococcus faecium in the Czech Republic from 2009 to 2018
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Background: Enterococci has become one of the most important opportunistic pathogens leading to nosocomial infections. Enterococcus faecium is the most clinical relevant. The treatment of infections caused by enterococci is limited since they exhibit intrinsic resistance to a broad spectrum of antibiotics [cephalosporins, sulphonamides, aminoglycosides, macrolides]. However, linezolid was approved and is still used for treatment of vancomycin-resistant enterococci infections, the incidence of linezolid resistant enterococci is worldwide on the rise. Therefore, the aims of this study was to determine mechanism of resistance and to map epidemiology of this pathogen within the Czech Republic since 2009 to 2018.

Materials/methods: The minimum inhibitory concentration (MIC) of 57 strains of E. faecium was examined according to the EUCAST recommendations. Molecular tools, PCR [plasmid carrying genes cfr, optrA], sequencing [23S rRNA, L3, L4 proteins] as well as multilocus sequence typing (MLST) were used to elucidate the mechanisms of resistance of linezolid resistant strains and to determine epidemiological relationship between linezolid resistant enterococci widespread in the Czech Republic within 9 years. Software Bionumerics 7.6.3 was used for sequence and consequently BURP analysis.

Results: All linezolid resistant isolates (n=75, 13%) had MIC for linezolid above 4mg/L. Altogether, 83 % (n=62) of strains were resistant also to vancomycin and/or to aminoglycosides (77%, n=58). Totally, 71 strains were linezolid resistant due to the mutation G2576T in 23S rRNA of 50S ribosomal subunit. The presence of gene cfr was confirmed just once. MLST analysis revealed the presence of only one clonal complex, CC17 [ST18, 78, 80, 117] of linezolid resistant E. faecium in the Czech Republic.

Conclusions: The high risk hospital associated clone CC17 confirmed all around Europe was also observed in the Czech Republic. The main mechanism (95%) of resistance to linezolid among E. faecium was the mutation in 23S rRNA (G2576T).

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RESTORE-IMI 2: randomised, double-blind, phase III trial comparing efficacy and safety of imipenem/cilastatin (IMI)/relbebacam (REL) versus piperacillin/tazobactam (PIP/TAZ) in adult patients with hospital-acquired or ventilator-associated bacterial pneumonia (HABP/VABP)


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Abstract third-party references: Funding for this research was provided by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Background: Due to rising carbapenem resistance, new HABP/VABP treatment options are needed. IMI/REL, a combination of IMI and the class A and class C β-lactamase inhibitor REL, is active against many carbapenem-resistant gram-negative pathogens. We conducted a phase 3 clinical trial evaluating efficacy and safety of IMI/REL in HABP/VABP.

Materials/methods: RESTORE-IMI 2 was a randomized, controlled, double-blind, multinational, phase 3, non-inferiority trial in adult patients with HABP/VABP. Lower respiratory tract specimens were obtained ≤48 hours prior to screening. Patients were randomized 1:1 to IMI/REL 500mg/250mg or PIP/TAZ 4g/500mg, given intravenously every 6h for 7-14d. Patients also received empiric linezolid until baseline cultures confirmed absence of MRSA. The primary endpoint was Day 28 all-cause mortality and the key secondary endpoint was clinical response at early follow-up (7-14d after completing therapy) in the modified intent-to-treat (MITT) population (randomized patients with ≥1 dose of study drug, excluding patients with only gram-positive cocci present on baseline Gram stain). Non-inferiority margins for these endpoints were 10% and -12.5%, respectively. The safety population comprised all patients who received study drug.

Results: The MITT population comprised 531 of 537 randomized patients [264 IMI/REL, 267 PIP/TAZ]; 48.6% had ventilated HABP or VABP, 42.9% were ≥ 65 years old, 66.1% were in the ICU, 47.5% had APACHE-II scores ≥15, and 24.7% had moderate/severe renal impairment. The most common causative pathogens in the microbiologic MITT population (MITT patients with confirmed, eligible causative pathogens) were K. pneumoniae (25.6%), P. aeruginosa (18.9%), A. calcoaceticus-baumannii complex (15.7%), and E. coli (15.5%). IMI/REL was non-inferior [p <0.001] to PIP/TAZ in both primary and key secondary efficacy endpoints [Table]. Rates of adverse events (AEs) in the safety population [IMI/REL 226/266 [85.0%] vs PIP/TAZ 233/269 [86.6%]], and therapy discontinuations due to both overall AEs [IMI/REL 15/266 [5.6%] vs PIP/TAZ 22/269 [8.2%]) or specifically due to drug-related AEs [IMI/REL 6/266 [2.3%] vs PIP/TAZ 4/269 [1.5%]) were similar in both groups. The most frequently reported (>5 patients) drug-related AEs in the IMI/REL arm were diarrhea, increased alanine aminotransferase, and increased aspartate aminotransferase [6/266 [2.3%] each].

Conclusions: IMI/REL is an efficacious and well-tolerated treatment option for HABP/VABP.
Table. Primary and key secondary efficacy outcomes (MITT population)

<table>
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<tr>
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<th>IMI/REL n/N (%)</th>
<th>PIP/TAZ n/N (%)</th>
<th>Adjusted difference&lt;sup&gt;a&lt;/sup&gt; (95% CI)</th>
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<tr>
<td><strong>Primary endpoint</strong></td>
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<tr>
<td>Day 28 all-cause mortality</td>
<td>42/264 (15.9%)</td>
<td>57/267 (21.3%)</td>
<td>-5.3% (-11.9, 1.2)&lt;sup&gt;b&lt;/sup&gt;</td>
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<td><strong>Key secondary endpoint</strong></td>
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<td>Favorable clinical response at EFU</td>
<td>161/264 (61.0%)</td>
<td>149/267 (55.6%)</td>
<td>5.0% (-3.2, 13.2)&lt;sup&gt;c&lt;/sup&gt;</td>
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CI, confidence interval. EFU, early follow-up visit. IMI/REL, imipenem/tobramycin/relebactam. N, total number of MITT patients in treatment arm. n, number of patients who died or had unknown survival status (primary endpoint) or number of patients with favorable clinical response (key secondary endpoint). PIP/TAZ, piperacillin/tazobactam.

<sup>a</sup>Adjusted differences and confidence intervals stratified by pneumonia type (non-ventilated HABP vs. ventilated HABP/VABP) and baseline Acute Physiology and Chronic Health Evaluation II (APACHE II) score (<15 vs. ≥15) using the Miettinen & Nurminen method. <sup>b</sup>The upper bound of the CI is less than the pre-defined non-inferiority margin of 10 percentage points, indicating success for the non-inferiority hypothesis. <sup>c</sup>The lower bound of the CI is greater than the pre-defined non-inferiority margin of -12.5 percentage points, indicating success for the non-inferiority hypothesis.

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Abstract 772

*Mycobacterium tuberculosis* drives expansion of low-density neutrophils equipped with regulatory activities

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**Background:** In human tuberculosis (TB) neutrophils represent the most commonly infected phagocytes, however their role in TB protection and pathology remained contradictory, with some data implicating neutrophils in the TB control and others associating them with TB pathology and progression. Moreover, a subset of low-density neutrophils (LDNs) has been identified in TB, but until now, despite several studies have described the diversity of neutrophil subpopulations, their plasticity in playing different functions is still not fully elucidated.

**Materials/methods:** We have compared the ratio between neutrophils and lymphocytes (N/L) in Active TB patients Cured TB patients and Healthy donors (H.D.). Moreover, in active TB patients, we have analyzed total neutrophils and their low-density (LDNs) and normal-density (NDNs) subsets, in terms of frequency, phenotype, functional features and gene expression signature. Data collection, emocytometer, flowcytometry and confocal microscopy were used in order to evaluate the absolute count of neutrophils and lymphocytes cells, the phenotypical and functional properties of the subsets of neutrophils and their transcriptomic profile for cytokines, chemokines and transcription factors of the innate immunity compartment.

**Results:** Biological properties of the two isolated neutrophil populations suggest their dual role during TB: NDNs provide a mechanism for bacteria killing, through oxidative burst and NETosis, by upregulating transcription factors involved in the release of cytokines and activation of innate and acquired immune cells, LDNs instead exert suppressive activities on T cell response.

**Conclusions:** The balance between these two subsets of neutrophils might influence either the initial steps of innate immune responses or the subsequent development of the adaptive immune response to *M. tuberculosis*, ultimately influencing the outcome of infection.

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Susceptibility of β-lactam-resistant Pseudomonas aeruginosa to last-line antibiotics stratified by carbapenemase production

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Background: Carbapenem-resistant Pseudomonas aeruginosa is a global critical threat. There are various mechanisms of resistance to carbapenems including carbapenemase production. Clonal spread of NDM-producing Pseudomonas aeruginosa has previously been demonstrated in our local population. An investigation was conducted to determine the distribution of carbapenemase production and antimicrobial susceptibility among β-lactam resistant Pseudomonas aeruginosa.

Materials/methods: Polymerase-chain-reaction (PCR) for gene-encoding NDM, KPC, OXA-48, GES, VIM, IMP, and OXA-23 was performed on β-lactam-resistant Pseudomonas aeruginosa isolates from a tertiary hospital in Singapore between 1/1/2019 and 30/6/2019. Only isolates that were non-susceptible to ceftazidime, cefepime, piperacillin-tazobactam, imipenem, and meropenem from routine susceptibility testing (Vitek 2) were included. Extended antimicrobial susceptibility testing to aztreonam, ceftazidime-avibactam, ceftolozane-tazobactam, and colistin was also performed using Sensititre broth-microdilution (ThermoFisher) and interpreted according to EUCAST breakpoints.

Results: Twenty-nine (54.7%) of the 53 Pseudomonas aeruginosa isolates were found to carry carbapenemase genes. Of these, fifteen (28.3%) were NDM-positive, eleven (20.8%) were IMP-positive, and three (5.7%) were GES-positive. The overall susceptibility results are present in Table 1. Metallo-β-lactamase-positive-isolates (NDM and IMP) were all resistant to ceftazidime-avibactam and ceftolozane-tazobactam, while GES-positive-isolates (class A carbapenemase) were susceptible to ceftazidime-avibactam but resistant to ceftolozane-tazobactam. Susceptibility to colistin was variable. All colistin-resistant isolates had a minimum-inhibitory-concentration (MIC) of 4 mg/L.

Table 1: Susceptibility of Pseudomonas aeruginosa isolates stratified by resistance mechanism

<table>
<thead>
<tr>
<th>Drug</th>
<th>NDM (%)</th>
<th>GES (%)</th>
<th>IMP (%)</th>
<th>Carbapenemase negative (%)</th>
<th>Overall (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aztreonam</td>
<td>86.7%</td>
<td>33.3%</td>
<td>45.5%</td>
<td>25% (6/24)</td>
<td>47.2% (25/53)</td>
</tr>
<tr>
<td>Ceftazidime-avibactam</td>
<td>0% (0/15)</td>
<td>100% (3/3)</td>
<td>0% (0/11)</td>
<td>50.0% (14/24)</td>
<td>32.1% (17/53)</td>
</tr>
<tr>
<td>Ceftolozane-tazobactam</td>
<td>0% (0/15)</td>
<td>0% (0/3)</td>
<td>0% (0/11)</td>
<td>62.0% (15/24)</td>
<td>28.3% (13/53)</td>
</tr>
<tr>
<td>Colistin</td>
<td>80% (12/15)</td>
<td>0% (0/3)</td>
<td>72.7% (8/11)</td>
<td>62.0% (15/24)</td>
<td>66.0% (35/53)</td>
</tr>
</tbody>
</table>

Conclusions: High rates of carbapenemase production was demonstrated among our β-lactam-resistant Pseudomonas aeruginosa isolates. High rates of resistance to various last-line antimicrobials were also demonstrated. The antibiogram varied based on carbapenemase-genes. Overall susceptibility was highest for colistin at 66.0%, and less than 50% for other drugs. All colistin resistant isolates had MICs within the area-of-technical-uncertainty (ATU) for colistin, the impact of which is unclear. Further work is needed to control spread of these multi-drug-resistant-organisms and to develop better treatment options.

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Abstract 780

Effectiveness of implementing a locally developed antibiotic use guideline for community-acquired cellulitis at a large tertiary care university hospital in Thailand

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Background: Cellulitis is a common infection among both ambulatory and hospitalized patients. A study conducted in 970 adult patients with cellulitis at Siriraj Hospital revealed that broad-spectrum antibiotic or antibiotic combination was inappropriately prescribed in most of these patients even though only a narrow-spectrum agent and a single agent was needed in most patients. The objective of this study was to determine the effectiveness of implementing a locally-developed clinical practice guideline (CPG) for antibiotic use in adults with community-acquired cellulitis who receive medical care at Siriraj Hospital in Bangkok, Thailand.

Materials/methods: The CPG for antibiotic treatment of community-acquired cellulitis was developed based on data from 970 adult patients treated for cellulitis at Siriraj Hospital during June to December 2016. The CPG is a one-page Thai language document. The CPG was introduced via multiple methods, including posters, brochures, circular letters, social media, conference, classroom training, and interactive education during January to September 2018. Medical records of adult patients with cellulitis were collected and analyzed for demographic and clinical characteristics, antibiotic regimens, clinical outcomes, cost of treatment, and CPG compliance.

Results: Among 360 adult patients with community-acquired cellulitis, 84.4% were ambulatory, and 15.6% were hospitalized. The median age of patients was 62 years, and 59.4% were female. Antibiotic prescription according to CPG (CPG-compliant group) was observed in 251 patients (69.7%), and CPG non-compliance was found in 109 patients (30.3%) (CPG-noncompliant group). The demographics and characteristics of patients were comparable between groups. Patients in the CPG-compliant group had a significantly lower rate of intravenous antibiotics (18.7% vs. 33.9%, p=0.007), lower prescription rate of broad-spectrum antibiotics (14.7% vs. 78.9%, p<0.001) and antibiotic combinations (6.4% vs. 13.8%, p=0.022), shorter median duration of antibiotic treatment (7 vs. 10 days, p<0.001), lower median cost of antibiotic treatment (3 vs. 7 USD, p<0.001), and lower median hospitalization cost (601 vs. 1,587 USD, p=0.008) than those in the CPG-noncompliant group. Treatment outcomes were not significantly different between groups.

Conclusions: Adherence to the CPG could reduce inappropriate prescription of broad-spectrum antibiotics or antibiotic combinations and lower treatment costs in adults with community-acquired cellulitis without differences in favorable outcomes or adverse events.

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Abstract 784

Launch of a new faecal molecular external quality assessment scheme by UK NEQAS Parasitology

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Background: Protozoan infections still cause significant morbidity and are responsible for a large portion of infectious gastroenteritis. They are even believed to be twice as common as bacterial infections. These commonly recognized pathogenic protozoa include Giardia lamblia, Cryptosporidium species and Entamoeba histolytica.

Because of the clinical importance of these protozoa, rapid plus sensitive detection and standardised diagnostic procedures are needed in order to allow for specific and rational treatment. As a result, recent times have seen increased use of molecular methods for detection.

Various molecular methodologies exist each with their own specific and general pitfalls and limitations.

Thus, the need for a fit-for-purpose qualitative External Quality Assessment (EQA) or Proficiency testing scheme for these parasites is very timely.

Materials/methods: We sent out a questionnaire to all participants within our microscopy-based Faecal Parasitology EQA scheme in order to determine level of interest for a molecular EQA scheme.

Freeze dried specimens were prepared using clinical and/or cultured specimens spiked in negative faeces.

The homogeneity and stability of these specimens at various temperatures and time points were analysed.

A pre-pilot survey was performed with 10 labs (UK plus non-UK) and results analysed.

Results: 100% of participants were able to identify faecal parasites in our EQA challenge. No false positive or false negatives were observed in the mini-pilot.

Freeze dried faeces is a suitable matrix due to the following:

- Intended matched participant results.
- Samples travelled well.
- Samples worked well under all DNA extraction and amplification methods used by participants.
- Samples were homogeneous and stable under the tested conditions.

Conclusions: We have produced a fit for purpose EQA scheme for molecular detection of faecal parasites.

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Background: During providing medical care to seriously ill patients with Crimean-Congo hemorrhagic fever (CCHF), the risk of Health care-associated infections (HCAIs) increases in first and second level hospitals. A unified assessment of the severity of the patient’s condition which allow to identify the patients at high risk of death and indications for transfer to a third-level hospital is required.

Aim: to develop a methodology for assessment the risk of death in patients with CCHF based on the clinical and laboratory parameters at the day of hospitalization, which are available in the hospitals of first / second level.

Materials/methods: Based on the analysis of 4 methods of assessment the severity of patients with CCHF [Swanepoel R. et al., 1989; Bakir M. et al., 2012; Dokuzoguz B., 2013; Bakir M. et al., 2015] a mortality risk prediction scale was developed. It based on 12 clinical and laboratory parameters (age, alanine transaminase, aspartate transaminase, leukocyte count, liver size, organ disorders, bleeding, thrombocyte count, prothrombin time, international normalized ratio, fibrinogen) and 2-4 gradations of each parameter, which were reflected in 32 criteria of the scale. The scale was tested on the retrospective analysis of case records of 52 patients with CCHF who were treated in hospitals of the Turkestan region in Kazakhstan in 2000-2018.

Results: Clinical and laboratory parameters of the patients were evaluated in accordance with the developed point scale for assessing the risk of death in patients with CCHF. Each evaluated parameter was assigned a certain number of points and their total amount was determined. With a patient score of ≥11, a high probability of an adverse outcome was predicted. With a score of <11, the probability of an fatal outcome of CCHF was estimated as low. The sensitivity of the proposed method is 100%, specificity - 98%, predicted value - 90%.

Conclusions: The proposed methodology with a high probability allows to predict the development of an unfavorable outcome of CCHF and is suitable for use in hospitals of the first and second levels to optimize the medical care of patients with this pathology and the prevent of HAI's.

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Abstract 787

**A pathogen and a non-pathogen spotted fever group Rickettsia trigger differential proteome signatures in macrophages**

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**Abstract third-party references:** This work was supported in part by Fundos FEDER através do Programa Operacional Factores de Competitividade—COMPETE 2020 and por Fundos Nacionais através da FCT—Fundação para a Ciência e a Tecnologia no âmbito do projeto Estratégico com referência atribuída pelo COMPETE: POCI-01-0145-FEDER-007440; and by POCI-01-0145-FEDER-029592, financiado pelo Programa Operacional Competitividade e Internacionalização na sua componente FEDER e pelo orçamento da Fundação para a Ciência e a Tecnologia na sua componente OE.

**Background:** Spotted fever group Rickettsia are recognized as important agents of human tick-borne diseases worldwide such as Mediterranean spotted fever (*R. conorii*) and Rocky Mountain spotted fever (*R. rickettsii*). Reductive genome evolution in obligate intracellular Rickettsia has resulted in the loss of many metabolic pathways, which culminates with Rickettsia species being strictly dependent on host cells to survive and proliferate. Several efforts have been made to identify host and bacterial determinants that allow bacteria to proliferate inside host cells. We have reported a differential tropism of pathogenic and non-pathogenic Rickettsia species in macrophages, further strengthening the complexity of host–rickettsiae interactions and raising questions on how pathogenic Rickettsia manipulate host pathways to their advantage.

**Materials/methods:** We have herein employed a quantitative high-throughput proteomics approach (SWATH-MS) to profile alterations in THP-1 macrophages upon infection with the highly pathogenic *R. conorii* and the non-pathogenic *R. montanensis*.

**Results:** Our results revealed that *R. conorii* is able to substantially reprogram several host signaling pathways, modulating host cells to a niche apparently more adapted to its needs. Specifically, *R. conorii* induced the accumulation of several enzymes of the tricarboxylic acid cycle, oxidative phosphorylation, fatty acid β-oxidation, and glutaminolysis, as well as of several inner and outer membrane mitochondrial transporters. These results suggest a profound metabolic rewriting of macrophages by *R. conorii* toward a metabolic signature of an M2-like, anti-inflammatory activation program. Moreover, several subunits forming the proteasome and immunoproteasome are found in lower abundance upon infection with both rickettsial species, which may help bacteria to escape immune surveillance. *R. conorii*-infection specifically induced the accumulation of several host proteins implicated in protein processing and quality control in ER, suggesting that this pathogenic Rickettsia may be able to increase the ER protein folding capacity.

**Conclusions:** Our results unfold the intricate pattern of modulation triggered by a pathogenic Rickettsia to control macrophage homeostasis and to maintain a viable intracellular niche. By illuminating the still very poorly studied aspects of macrophage–Rickettsia interactions, our work provides an essential framework for a deeper understanding of the link between rickettsial pathogenicity and host manipulation.

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**Abstract 792**

**Feasible alternatives to dried blood spot in the retrospective diagnosis of congenital cytomegalovirus infection**

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**Background:** Retrospective diagnosis of CMV infection (cCMV) cases plays a crucial role in the management of late-onset symptomatic infants and it is usually achieved by CMV DNA detection in dried blood spot (DBS) cards. However, there is a lack of consensus about the most reliable extraction and PCR protocols to be used. In this study, we describe viral load (VL) results in various clinical samples from confirmed cCMV cases. The objectives were: (1) To compare CMV-VL values in samples obtained at birth from infants with cCMV. (2) To evaluate dried umbilical cord (DUC) samples as an alternative to dried blood samples (DBS).

**Materials/methods:** Saliva and/or urine, peripheral blood, and DBS from 15 infants with confirmed cCMV infection were collected at birth. CMV-VL was determined by real-time polymerase chain reaction (rt-PCR). In two cases, VL was determined from available DUC samples. The Mann–Whitney U test was used to compare VL values.

**Results:** Five (33.3%) of the 15 infants were symptomatic, and 10 (66.6%) were asymptomatic. The CMV-VL found in saliva and in urine were both higher than those found in peripheral blood (p-value: 0.0001). Symptomatic infants presented 100% of detectable VL in peripheral blood and 40% in DBS. Asymptomatic infants showed 75% of detectable VL in peripheral blood and 40% in DBS.

**Conclusions:** When VL was detectable in peripheral blood, the values were lower than in saliva or urine, in both symptomatic and asymptomatic cases of cCMV. The low sensitivity in DBS samples could be due to low blood volume content, making CMV-VL undetectable even when using optimised extraction and PCR protocols. Based on our experience and on published data, DUC could be a reliable alternative to DBS.

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>n</th>
<th>Detectable-VL (%)</th>
<th>Median Log [IQR]</th>
<th>Median IU/ml [IQR]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saliva-VL</td>
<td>10</td>
<td>10 (100%)</td>
<td>Log 6.3 [5.8-6.5]</td>
<td>1,958,525 [597,683-3,483,843]</td>
</tr>
<tr>
<td>Urine-VL</td>
<td>12</td>
<td>12 (100%)</td>
<td>Log 5.8 [5.5-6.5]</td>
<td>691,865 [188,489,5-3,175,696]</td>
</tr>
<tr>
<td>Peripheral blood-VL</td>
<td>12</td>
<td>10 (83.3%)</td>
<td>Log 3.0 [2.6-3.6]</td>
<td>1,019 [364-4,002]</td>
</tr>
<tr>
<td>DBS-VL</td>
<td>15</td>
<td>6 (40%)</td>
<td>Log 2.8 [2.6-2.9]</td>
<td>604,5 [415-858]</td>
</tr>
<tr>
<td>DUC-VL</td>
<td>2</td>
<td>2 (100%)</td>
<td>Log 4.2 [4.0-4.3]</td>
<td>16,05 [9,754-22,341]</td>
</tr>
</tbody>
</table>

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**Kingella endocarditis in children: a distinct entity or not?**

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**Background:** Kingella, a gram-negative coccobacillus, causes various invasive pediatric diseases, including life threatening infective endocarditis (IE). Data on pediatric Kingella endocarditis are scarce. Our aim is to describe the clinical features of pediatric Kingella IE patients and compare them to other causative agents of IE, determining whether they have unique clinical characteristics.

**Materials/methods:** We retrospectively analyzed patients, aged 0-18 years, admitted with IE between the years 1994-2019, in a tertiary pediatric center in Israel.

Inclusion criteria was fulfillment of Duke’s criteria for diagnosis of IE. We compared the epidemiologic, clinical, laboratory, imaging and cardiac features of the patients with Kingella to Streptococcus species and Staphylococcus Aureus IE.

**Results:** 60 patients were included in the study. In 19 the causative pathogen was kingella, 25 had Streptococcus and 16 had Staphylococcus aureus IE. Nine (47%) patients with Kingella endocarditis had no known previous heart defect. The mean age of the patients with Kingella was younger than the Streptococci and Staphylococci groups (16±10 months, 106±70, 68±76 respectively, P< 0.001). A male predominance was noted (69.4% compared with 40.0%, 37.5% respectively). The Kingella IE patients had higher temperature on admission, history of oral aphthae prior to the diagnosis of IE (29.4% compared with 0%, 0% respectively, P<0.002) and higher lymphocye count (4.27K±3.04, compared with 2.09K±1.36, 2.40K±2.38 respectively, P<0.002).

**Conclusions:** Kingella IE pediatric patients have some unique features compared to those with S. aureus and Streptococci IE; Young healthy children (<36 months), especially males, with or without congenital heart defect, with recent history of oral aphthae, that present with prolonged fever should raise the suspicion for Kingella IE.

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Stenotrophomonas maltophilia bloodstream infections in umbilical cord blood transplant recipients

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Background: Limited data are available on Stenotrophomonas maltophilia bloodstream infection (SM-BSI) in umbilical cord blood transplant (uCBT) recipients who exhibit a higher risk of delayed neutrophil engraftment relative to other types of allogeneic hematopoietic stem cell transplant recipients. Additionally, the therapeutic efficacy against SM-BSI and hemato-toxicity of trimethoprim-sulfamethoxazole (SXT) are still unknown in uCBT settings.

Materials/methods: The medical and microbiological records of patients who received uCBTs between December 2008 and December 2015 were reviewed. Identification and drug susceptibility testing were performed using the WalkAway 96 SI system. The current CLSI breakpoints for S. maltophilia were used. Evaluation of SXT was performed only for recipients who received ≥ 7 days of intravenous SXT as treatment for SM-BSI (the evaluation cohort).

Results: Of 561 uCBT recipients, 34 developed SM-BSI. Diabetes mellitus, severe neutropenia for ≥ 21 days, and age ≥ 60 years were significant independent risk factors for SM-BSI. The hazard ratio for all-cause mortality up to 100 days after transplantation was 10.5 (95% CI, 6.79 – 16.1) for patients with SM-BSI, compared to patients without SM-BSI. Of the 34 recipients with SM-BSI, 25 developed SM-BSI during the pre-engraftment phase (neutrophil count < 500/µL) and 24 were treated with an intravenous SXT-based regimen (iSXT-BR). The 7-day- and 30-day-crude-mortality-rates of the recipients with SM-BSI were 64.7% and 73.5%, respectively. Additionally, 7-day-crude-mortality-rate of the recipients with SM-BSI with pneumonia (11/12) was significantly higher than that for recipients without pneumonia (11/22) (P=0.04). The susceptibility rates of the 34 causative strains for SXT and levofloxacin were 97% and 79%, respectively. Nine recipients were included in the evaluation cohort. The doses of iSXT ranged from 2.4 to 6.9 mg/kg/day of the trimethoprim component. Five of the nine recipients developed SM-BSI during the pre-engraftment phase. The 30-day-crude-mortality-rate and the clinical cure rate of the cohort were 22% and 77%, respectively. In addition, only one of the nine recipients experienced significant neutrophil toxicity.

Conclusions: The epidemiology of SM-BSI in uCBT recipients was determined and its negative impact on survival was demonstrated. The iSXT-BR was a tolerable and important therapeutic option for SM-BSI in the uCBT setting, including during the pre-engraftment phase.

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Impact of a routine molecular Point-of-Care test-and-treat strategy for influenza in adults hospitalised with acute respiratory illness: a pragmatic, multi-centre, randomised controlled trial (FluPOC)

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Background: Influenza infections often remain undiagnosed in patients admitted to hospital due to lack of routine testing. When tested for, the diagnosis of influenza is often delayed due to the long turnaround times of laboratory PCR, leading to inappropriate and late antiviral and isolation facility use. Molecular point-of-care tests (mPOCT) for influenza can deliver results in under 1 hour but high quality evidence for impact on clinical management and outcomes is lacking.

Materials/methods: In this pragmatic, multicentre, randomised controlled trial we enrolled adults admitted to hospital with acute respiratory illness (ARI) during influenza season. Patients were randomised (1:1) to receive mPOCT for influenza or routine clinical care. The primary outcome was the proportion of influenza infected patients who received antivirals. Secondary outcomes included; the detection rate of influenza, turnaround time of results, time to antivirals, isolation facility use, antibiotic use, length of stay, time on supplementary oxygen, critical care admission and mortality.

Results: 613 patients were recruited and randomised, 307 to POCT and 306 to routine care. All were analysed in the intention-to-treat (ITT) analysis. 100/307 (33%) patients in the POCT group and 102/306 (33%) patients in the control group were influenza infected. The median [IQR] turnaround time for results was 1.2 [1.1-1.4] hours in the POCT group and 23 [16-29] hours in the control group, p<0.0001. 100/100 (100%) influenza-infected patients were diagnosed in the POCT group but only 55/102 (54%) were diagnosed in the control group, p<0.0001. 99/100 (99%) influenza-infected patients received antiviral treatment in the POCT group versus 63/102 (62%) in the control group, relative risk 1.6 [95%CI 1.4 to 1.9]; p<0.0001. 70/100 (70%) of influenza infected patients in the POCT group were correctly nursed in single room accommodation versus 39/102 (38%) in the control group, p<0.0001. Admission to critical care units or death occurred in 1/100 (1%) patients in the POCT group versus 8/102 (7.8%) in the control group, p=0.035.

Conclusions: A routine mPOCT strategy for influenza in adults hospitalised with ARI improved the detection of influenza and the appropriate and timely use of antivirals and isolation facilities. It was also associated with improvements in clinical outcome.

Figure 1. Kaplan-Meier curve showing time to the administration of antivirals in the point-of-care testing group (red) and the control group (green) in influenza-infected patients. Log rank test, p=0.0001

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Abstract 802

In vitro activity of ceftazidime-avibactam (CAZ-AVI) and comparators against Gram-negative pathogens isolated from patients in Canadian hospitals in 2009-2018: CANWARD surveillance study

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Background: Ceftazidime-avibactam is used for the treatment of infections caused by multi-drug-resistant organisms. We determined the in vitro activity of ceftazidime [CAZ] with and without avibactam and comparators versus Gram-negative pathogens recovered from January 2009 to December 2018 from patients in medical and surgical wards, intensive care units, clinics, and emergency rooms in 15 Canadian hospitals.

Materials/methods: Antimicrobial susceptibility testing was performed using broth microdilution panels following CLSI recommendations (M07, 11th edition). Susceptibility was determined using EUCAST breakpoints [where available] or CLSI breakpoints (M100, 29th edition). Cephalosporin-resistant Escherichia coli and Klebsiella spp. isolates were genetically characterized for ESBL production using PCR and DNA sequencing.

Results:

<table>
<thead>
<tr>
<th>MIC90 (µg/mL)</th>
<th>% susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CAZ-AVI</td>
</tr>
<tr>
<td>Escherichia coli (6902)</td>
<td>0.25/99.9</td>
</tr>
<tr>
<td>E. coli CRO-R (676)</td>
<td>0.5/99.3</td>
</tr>
<tr>
<td>E. coli ESBL (566)</td>
<td>0.5/99.8</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa (3511)</td>
<td>8/93.3</td>
</tr>
<tr>
<td>P. aeruginosa (CAZ-R) (704)</td>
<td>&gt;16/67.1</td>
</tr>
<tr>
<td>P. aeruginosa (TZP-R) (620)</td>
<td>&gt;16/68.1</td>
</tr>
<tr>
<td>P. aeruginosa (MER-R) (279)</td>
<td>&gt;16/54.8</td>
</tr>
<tr>
<td>Klebsiella pneumoniae (2289)</td>
<td>0.5/100</td>
</tr>
<tr>
<td>K. pneumoniae CRO-R (141)</td>
<td>2/99.3</td>
</tr>
<tr>
<td>K. pneumoniae ESBL (127)</td>
<td>2/100</td>
</tr>
<tr>
<td>Enterobacter cloacae (991)</td>
<td>1/99.7</td>
</tr>
<tr>
<td>E. cloacae CRO-R (249)</td>
<td>2/98.8</td>
</tr>
<tr>
<td>E. cloacae ERT-R (97)</td>
<td>2/99.0</td>
</tr>
<tr>
<td>Serratia marcescens (584)</td>
<td>0.5/99.7</td>
</tr>
<tr>
<td>Klebsiella oxytoca (617)</td>
<td>0.5/99.8</td>
</tr>
<tr>
<td>Proteus mirabilis (522)</td>
<td>0.12/100</td>
</tr>
<tr>
<td>Acinetobacter baumannii (181)</td>
<td>&gt;16/55.3</td>
</tr>
</tbody>
</table>

Conclusions: CAZ-AVI demonstrated in vitro activity against clinical Enterobacterales isolates, including those with resistance to oximinocephalosporins by a variety of mechanisms. 93.3% of P. aeruginosa were susceptible to CAZ-AVI while CAZ, MER and TZP-resistant P. aeruginosa were moderately susceptible to CAZ-AVI. Activity against A. baumannii was not improved compared to CAZ alone.

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Abstract 805

Evaluation of the FebriDx host response Point-of-Care test to differentiate viral from bacterial aetiology in adults hospitalised with acute respiratory illness during influenza season

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Background: Diagnostic uncertainly regarding microbial aetiology in patients hospitalised with acute respiratory illness (ARI) contributes to antibiotic overuse. A host response test distinguishing between viral or bacterial infection may reduce unnecessary antibiotic use. The FebriDx is a low cost, rapid, host response point-of-care test that uses fingerpick blood samples to distinguish between viral or bacterial infection by detection of MxA and/or CRP.

Materials/methods: We took fingerpick blood samples from adults with ARI, hospitalised during influenza season, and tested them using the FebriDx. Respiratory samples were tested for viruses on the Biofire FilmArray Respiratory Panel 2 plus. The FebriDx was evaluated for failure rate and accuracy of results (Viral, Bacterial, Negative). FebriDx results were not given to treating clinicians. All patients gave written consent.

Results: We took fingerpick blood samples from adults with ARI, hospitalised during influenza season, and tested them using the FebriDx. Respiratory samples were tested for viruses on the Biofire FilmArray Respiratory Panel 2 plus. The FebriDx was evaluated for failure rate and accuracy of results (Viral, Bacterial, Negative). FebriDx results were not given to treating clinicians. All patients gave written consent.

Conclusions: In this real-world evaluation FebriDx use in adults hospitalised with ARI was associated with a relatively high test failure rate and problems reading test lines. FebriDx had a high specificity (94%) and positive predictive value (94%) for the detection of viruses, especially influenza. Bacterial and negative FebriDx results were often associated with non-influenza virus detection which may represent colonisation, secondary bacterial infection or viral infection confined to the airways.

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Impact of pharmacist-driven antimicrobial stewardship interventions on multicomponent patient outcomes

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Background: Prospective audit and feedback (PAAF) is a core antimicrobial stewardship (AS) strategy recommended to improve antimicrobial use. While studies have demonstrated the benefit of PAAF on clinical outcomes in specific disease states or high-risk groups, few have reviewed the broader impact of this AS initiative. The purpose of this study was to determine the impact of pharmacist-driven AS interventions on multicomponent patient outcomes.

Materials/methods: Retrospective cohort included adult inpatients treated with antimicrobials for ≥ 72 hours from July 2015-December 2015. Patients with an ID consultation, on long-term antibiotics, or made hospice or comfort care during their admission were excluded. Patients were grouped according to the presence or absence of AS intervention performed by a pharmacist. Primary endpoint was a composite of 30-day all-cause mortality, 30-day readmission, 28-day emergence of antimicrobial resistance, and 90-day *Clostridioides difficile* infection (CDI). Secondary endpoints included hospital and intensive care unit (ICU) length of stay (LOS).

Results: 338 patients screened, 200 included: 100 with AS intervention, 100 without. Baseline characteristics were similar between groups except less chronic obstructive pulmonary disease (p=0.01), peptic ulcer disease (p=0.017) and diabetes with organ damage (p = 0.02) in the AS intervention group. Infection types were similar between groups, however more patients were ICU status in the AS intervention group (p = 0.003). Primary and secondary endpoints are listed in Table 1.

Table 1. Study Endpoints

<table>
<thead>
<tr>
<th>Variable</th>
<th>No AS Intervention n = 100</th>
<th>AS Intervention n = 100</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composite</td>
<td>43 (43)</td>
<td>26 (26)</td>
<td>0.011</td>
</tr>
<tr>
<td>30-day Readmission</td>
<td>38 (38)</td>
<td>20 (20)</td>
<td>0.005</td>
</tr>
<tr>
<td>90-day CDI</td>
<td>5 [5]</td>
<td>3 [3]</td>
<td>0.721</td>
</tr>
<tr>
<td>Hospital LOS</td>
<td>6 [5-9]</td>
<td>9 [6-15]</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ICU LOS*</td>
<td>9 [7-12]</td>
<td>12 [8-17]</td>
<td>0.077</td>
</tr>
</tbody>
</table>

Data presented as n (%) or median (IQR)

*n = 25 and 45, respectively

Conclusions: Patients with AS intervention performed by a pharmacist were found to have lower rates of 30-day readmission compared to those without. Overall, these results demonstrate a positive impact of pharmacist-driven AS intervention on long-term patient outcomes; however differences in LOS warrant further investigation.

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Abstract 810

**A new perspective: microbiota, the role of Streptococcus gallolyticus in childhood colorectal cancer**

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**Background:** Colorectal cancer in childhood is rare but usually associated with a higher incidence of unfavorable histotypes (high-grade, poorly differentiated subtypes) and more aggressive tumor behavior. The prognosis is poor due to delayed diagnosis and advanced stage at diagnosis. The tumorigenesis of childhood colorectal cancer, which necessarily occurs over a shorter period, is still unclear and most likely evolves through different steps. There has been limited knowledge about colorectal cancer in childhood. The aim of this study was to investigate the relationship between childhood colorectal cancer and *S. gallolyticus*.

**Materials/methods:** The clinical and pathologic characteristics, and outcomes of colorectal cancer in 21 children and adolescents referred to our Pediatric Oncology Department between 1974 and 2017 were reviewed. The control group (healthy colorectal tissue) consisted of 40 pediatric patients who underwent colon surgery for other reasons. Demographic and clinical findings of the patients were evaluated. *S. gallolyticus* analysis was performed from cancerous and healthy colorectal tissues. DNA was isolated from paraffin tissue for *S. gallolyticus* analysis. The presence of *S. gallolyticus* was screened by the Real-Time PCR method using specific predetermined primers and probes. Positive isolates were confirmed by Sanger sequence analysis.

**Results:** The median age of patients with colorectal cancer was 14 years (range: 10 to 17 years). The male-to-female ratio was 2.5:1. Tumor localization was mostly in the rectum and/or sigmoid region (n=14, 66.7%). The most common stage was stage D (61.9%, n=13). There wasn’t any patient in stage A. The most common histologic subtype was mucinous adenocarcinoma (61.9%, n=13). None of the pediatric patients with colorectal cancer had documented *S. gallolyticus* in blood culture. *S. gallolyticus* was detected in 8 (38.1%) colorectal cancer patients and 2 (5%) children in the control group (p=0.002).

**Conclusions:** Childhood colorectal cancer has distinct features with poor prognosis despite multidisciplinary approaches and new therapies. In our study, *S. gallolyticus* was found to be significantly higher in colorectal cancer tissues in our patients. This is the first study in the literature. Our study provides a new perspective for early diagnosis and understand risk groups for childhood colorectal cancer that may have a different pathophysiology than adults.

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Abstract 812

**Determination of pentraxin 3 levels in cerebrospinal fluid during central nervous system infections**

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**Background:** Pentraxin 3 (PTX3) is an acute phase protein; its plasmatic levels significantly raise during severe infections. Data on PTX3 levels in cerebrospinal fluid (CSF) of patients with central nervous system (CNS) infections are lacking. We aimed: a) to assess the diagnostic potential of measuring CSF PTX3 levels in patients with CNS infections; b) to establish CSF PTX3 cut-offs to distinguish between bacterial and aseptic meningoencephalitis (ROC curve).

**Materials/methods:** In this retrospective observational study, PTX3 levels were measured in CSF from 19 patients admitted to Trieste Hospital, Italy, with CNS infection from January 2016 to September 2018. CSF was collected by lumbar puncture performed within two hours from hospital admission. For each patient four samples of CSF were collected for obtaining these data: 1) leukocyte count, glucose and total protein levels, 2) culture and molecular amplification, 3) real-time PCR for virus (HSV 1-2, CMV, EBV, VZV, WNV, enteroviruses, TBEV and Mumps virus) and 4) PTX3 levels. The latest samples were first stored at -80°C and then analysed in duplicate using a home-made sandwich ELISA. The assay has a lower limit of detection of 100 pg/ml, with 8–10% inter-assay variability.

**Results:** A diagnosis of bacterial infection and aseptic meningoencephalitis was made in 7 (37%) and 12 (63%) patients, respectively. Subjects with bacterial infections showed significantly higher PTX3 levels (13.5 vs 1.27 ng/mL in aseptic meningoencephalitis, p=0.010). We identified two different CSF PTX3 levels cut-offs. 1) The best cut-off to maximize Youden’s J was 9.6 ng/mL with a sensitivity, specificity, positive predictive value and negative predictive value (NPV) of 71.4%, 91.4%, 83.3%, 84.6%, respectively, 2) The cut-off with higher NPV (100%) was 3.6 ng/mL: a diagnosis of bacterial infections was obtained in 0% patients with CSF PTX3 levels < 3.6 ng/mL vs 58% of those with CSF PTX3 levels ≥ 3.6 ng/mL (p=0.017).

**Conclusions:** CSF PTX3 levels are higher in bacterial meningitis than aseptic meningoencephalitis. A cut-off of 3.6 ng/mL of CSF PTX3 has a high NPV and can be used to exclude bacterial CNS infections.

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Physicochemical characterisation of aluminium hydroxide and aluminium phosphate and their potential adjuvant function in combination with squalene emulsion for EV71 vaccine development

Ming-Hsi Huang*1

1National Health Research Institutes, Zhunan, Taiwan

**Abstract**

**Background:** Aluminum phosphate and aluminum hydroxide (generally called Alum) are two conventional adjuvants acceptable for human vaccines. Yet, the physicochemical properties as well as the adjuvanticity associated with the structure of the two forms of gel suspensions are poorly defined.

**Materials/methods:** We designed vaccine formulations based on aluminum phosphate and aluminum hydroxide as adjuvants, and investigated respective mode of action linking the physicochemical properties and the adjuvanticity.

**Results:** The SEM microscopy indicated that aluminum phosphate gel solutions are amorphous, whereas aluminum hydroxide gel solutions have a crystalline structure consistent with boehmite. At very low concentrations, the adsorption of model protein (BSA) onto both aluminum-containing adjuvants followed Langmuir adsorption isotherm, i.e. the antigen adsorption percentage was functional to the antigen/adjuvant ratio. As the protein concentration increases, the adsorbed BSA reduced as less vacant sites were offered on the surface of adjuvants. Notably, 100% of adsorption could be achieved in aluminum hydroxide, whereas a maximal 30% of adsorption was observed in aluminum phosphate, probably due to the presence of the same charge on the adjuvant and antigen. For the investigation of biological interactions, the prepared aluminum salts were tested for their properties to drive the activation/maturation of murine bone marrow-derived dendritic cells (DCs). Flow-cytometry analysis showed that aluminum hydroxide may be an efficient regulator of DC activation, compared with aluminum phosphate. For immunogenicity study of an enterovirus (EV) 71 formalin-inactivated whole virus vaccine, we found that a single-dose intramuscular injection of 0.2 μg inactivated virus could not elicit a forceful EV71 virus neutralized antibody titer. When the same amount of antigen was co-administered with single adjuvant, aluminum phosphate or squalene emulsion, enhances protective EV71-specific serological immunity in mice; moreover, the adjuvant potency of their combination was more potent than individual to induce high levels of antigen-specific antibodies.

**Conclusions:** It was concluded that aluminum hydroxide, rather than aluminum phosphate, is suitable to be adjuvanted in vaccine candidate according to the results from morphology, antigen adsorption efficiency and DCs activation/maturation; in addition, it will be of great interest for co-administrating Alum together with an emulsified vaccine delivery system against the emerging infectious diseases.

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Abstract 821

Introducing end-of-life considerations into a computerised decision support system for antibiotic treatment: effects on the system's recommendations and comparison to physicians' behaviour

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Background: TREAT is a previously developed and validated computerized decision support system for antibiotic treatment, in clinical use. Currently, it does not address end of life (EOL) considerations, when antibiotic treatment does not offer a benefit but inflicts high collateral damage.

Materials/methods: Based on a causal probabilistic network, TREAT advises antibiotic treatment using a cost-benefit calculation. Costs, expressed as life years loss, comprise of drug, adverse events and ecological costs. The latter considering the clinical significance of resistance selection following specific antibiotics in the individual treated and among contacts. We developed an individualized ecological costs model, addressing the higher ecological impact of patients at EOL. The main individualized ecological cost components were patients’ risk for harboring resistant bacteria at baseline, their risk for experiencing a subsequent infection and their potential to transmit resistant bacteria. After implementation into TREAT’s cost-benefit calculation, we compared TREAT’s baseline advice to its individualized ecological costs advice and physicians’ prescribed treatment. Broad-spectrum treatment included piperacillin-tazobactam, carbapenems, vancomycin and colistin.

Results: In a previously collected cohort of 1232 patients with suspected or proven sepsis, a significant difference in ecological costs between 30-day survivors and fatalities was observed. Implementation of individualized ecological costs in TREAT resulted in change of advice for 44.7% [551/1232] patients. Among all patients, the individualized ecological cost TREAT advised significantly less 3rd generation cephalosporins, quinolones and broad-spectrum antibiotics compared to baseline TREAT and significantly more frequently ampicillin, ampicillin-clavulanate and chloramphenicol. Among 30-day fatalities [18.9%, 233/1232], no treatment was advised by individualized TREAT for 11.1% [26/233] patients vs 8.1% [19/233] by baseline TREAT and 16.3% [38/233] by physicians. When prescribing antibiotics, TREAT recommended ampicillin significantly more frequently and ceftriaxone significantly less frequently than physicians. Broad-spectrum treatment and ceftriaxone were advised for 21% [49/233], 44.2% [103/233] and 58.4% [136/233] by individualized TREAT, baseline TREAT and physicians.

Conclusions: Individualization of the ecological costs and EOL considerations are necessary in a decision support system for antibiotic treatment, to approximate physicians’ behavior and to avoid aggressive futile antibiotic treatment. Physicians limited treatment at EOL more frequently than individualized TREAT, but used more broad-spectrum therapy when prescribing antibiotics at EOL.

Figure 1: Top 3 treatments for respiratory and urinary infections

<table>
<thead>
<tr>
<th>Baseline advice</th>
<th>Individualized advice</th>
<th>Prescribed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiratory tract infections (N= 528)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone IV 157 (29.7%)</td>
<td>Doxycycline IV 131 (24.8%)</td>
<td>Ceftriaxone IV 101 (19.1%)</td>
</tr>
<tr>
<td>Doxycycline IV 128 (24.2%)</td>
<td>Ampicillin IV 130 (24.6%)</td>
<td>Ceftriaxone IV + Azithromycin PO 84 (16%)</td>
</tr>
<tr>
<td>Quinolone 50 (9.5%)</td>
<td>No treatment 59 (11.2%)</td>
<td>No treatment 55 (10.4%)</td>
</tr>
<tr>
<td><strong>Urinary tract infections (N= 383)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amikacin IV 198 (51.7%)</td>
<td>Amikacin 165 (43%)</td>
<td>Amikacin 73 (19%)</td>
</tr>
<tr>
<td>Quinolone 45 (11.7%)</td>
<td>Amoxicillin-clavulanate IV 54 (14%)</td>
<td>Ceftriaxone IV 82 (21.4%)</td>
</tr>
<tr>
<td>No treatment 32 (8.3%)</td>
<td>No treatment 40 (10.4%)</td>
<td>No treatment 57 (14.9%)</td>
</tr>
</tbody>
</table>

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Pinpointing the genetic intra-host diversity of *Mycobacterium tuberculosis* and its determinants

Charlotte Genestet*1,2, Elisabeth Hodille1,2, Alexia Barby1,2, Jean-Luc Berland1,3, Laurent Jacob4, Gerard Lina1,2,5, Stéphane Dray4, Samuel Venner4, Oana Dumitrescu1,2

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Abstract third-party references: on behalf of the Lyon TB study group

**Background:** Tuberculosis (TB) caused by *Mycobacterium tuberculosis* (Mtbc) complex results in a variety of disease manifestations and epidemiological success. Recently, studies based on Whole Genome Sequencing (WGS) have revealed micro-diversity in isolates composition. However this diversity and its dynamics have not yet been considered as a source of information to highlight the process leading to adapt and respond to a changing environment. Here we characterized the variability of the composition of pulmonary and extrapulmonary Mtbc isolates and its relations with various host factors.

**Materials/methods:** We explored by WGS Mtbc genomic micro-diversity within hosts, by comparing pairwise isolates obtained from both pulmonary and extra-pulmonary sampling in 37 TB patients. Firstly we determined the frequency of single nucleotide polymorphisms (SNP) called at heterozygous sites, then variants were defined as assemblies harboring SNP with similar frequencies. Diversity was assessed by alpha and beta diversity measures based on the variant assemblies. Clinical data resuming the immune and nutritional status of patients were also recorded.

**Results:** We observed differences between pulmonary and extra-pulmonary isolates from the same patient for 68% of cases, supporting Mtbc micro-diversity within the same host. Differences in variant distribution between the pulmonary and the extra-pulmonary isolates, with overall lower extra-pulmonary diversity, indicates Mtbc compartmentalization in different body sites. Moreover, we observed a variability involving gene functions specifically associated with either pulmonary or extra-pulmonary TB. Our analysis revealed a correlation between Mtbc micro-diversity within pulmonary compartment and low patient body mass indexes. Conversely, Mtbc micro-diversity within extra-pulmonary compartment inversely correlated with patient CD4 T cells count, supporting the selective pressure of the immune response on Mtbc infection spreading.

**Conclusions:** These results confirm that close-related but still different Mtbc variants coexist rather than a clonal population. This micro-diversity is shaped by the interactions between Mtbc and various host factors. Compartmentalization could rely on the higher ability of variants to disseminate and adapt to extra-pulmonary tissues, but more in-depth analysis is required to correlate with some clinical presentations. Taking into account this diversity of Mtbc variants, its intra-host dynamics should lead to a better understanding of the dynamics of this disease.

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Abstract 823

Evaluating the predictive performance of ID-ODS software in critically ill patients for piperacillin: a comparison using IV bolus and continuous infusion data

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Background: Piperacillin displays high interindividual variability in critically ill patients. PKPD Model based dosing software can optimize antibiotic exposure and improve treatment outcome. Our objective is to evaluate and compare the accuracy of the individualized dosing program ID-ODSTM (Individually Designed Optimum Dosing Strategies) in predicting piperacillin concentrations a priori in critically ill patients for both continuous infusion and bolus injections.

Materials/methods: The data used for the validation comes from a prior publication in critically ill patients. Samples were collected on days 1 and 2 in 16 patients, with 8 patients receiving bolus dosing and 8 patients receiving continuous infusion. All patients in the continuous infusion group received a loading dose of 4 g. Patient demographics and dosing information were input into the IDODS software and concentrations were predicted in 0.1 hour increments. To assess the predictability of the software, we compared the observed VS predicted concentrations and estimated the R², bias and precision. Statistical analysis was performed using the R software.

Results: In total we had 116 observations from the 8 patients on continuous infusion and 113 observations from the 8 patients on bolus dosing. For the continuous infusion group, the R² was 0.54, bias was -25 % and precision was 74 %. For the bolus dosing group, the R² was 0.67, bias was -38 % and precision was 72 %. For both groups, we noticed the software is biased and under predicts the early concentrations after dose administration, while bias approaches zero at later time points.

Conclusions: The IDODS software demonstrated reasonable accuracy in predicting piperacillin concentrations. Predictive performance was similar across the two dosing groups indicating it can be applied for either administration method. The software tended to under predict concentrations at early time points after drug administration, given piperacillin has time dependent activity and the focus is on achieving therapeutic trough concentrations, this is not likely to impact dose selection. Overall, IDODS software can be used to optimize initial dosing of piperacillin and decrease the likelihood of suboptimal concentrations compared to standard dosing. Further clinical trials are needed to assess its impact on clinical outcome.

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Abstract 824

**International survey on diagnosis and management of human herpes virus-8 infection in solid organ transplant recipients**

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Abstract third-party references: ESGICH Escmid Study Group of Infections in Immunocompromised Host

**Background:** HHV8/KSHV infection is associated with uncommon but potentially fatal neoplastic and non-neoplastic diseases in Solid Organ Transplant (SOT) recipients. Screening and follow-up protocols are not established.

We aimed to define the current approach of transplant centers worldwide to screening and management of HHV-8 in transplant recipients.

**Materials/methods:** We conducted a survey (June-October 2019) on behalf of Escmid Study Group of Infections in Immunocompromised Host (ESGICH). Study group members received an email containing an introduction and a link to our survey, 12 questions about screening and follow-up for HHV-8 (www.surveymonkey.com/r/ESGICH-HHV8).

**Results:** 51 transplant centers filled out the survey (23 Italy, 8 Spain, 8 other European countries, 4 USA, 1 Canada, 3 Latin America, 1 Israel, 3 anonymous.)

34 centers (67%) do not perform screening for HHV-8; routinely screening is performed in 14 centers (27%) mainly for recipients. Centers where serology is performed use IFA or ELISA in equal proportion. Transplant suitability is not influenced by HHV8 serology in any center.

29 centers (57%) do not monitor HHV8 after transplant, while 10 (20%) perform it only in symptomatic patients, 3 (6%) perform universal follow-up, 9 (17%) use different risk-based approaches. The most used test for monitoring is quantitative commercial PCR (52%). Frequency of monitoring differs widely. Only 2 centers perform HHV8 specific T-cell response.

The most common approach in case of elevated viremia is reducing immunosuppression [n=29, 57%] and/or switching from CNI to m-TOR inhibitor [n=23, 45%] with or without antivirals; [val]ganciclovir is the most used agent.

67% of the centers registered HHV-8-related diseases in SOT in the last five years: cutaneous [n=16] and visceral [n=16] Kapo-si Sarcoma, non-malignant disease [i.e. KICS like syndrome, n=14], MCD [n=8] and PEL [n=4].

**Conclusions:** There is no uniform approach for screening and management of HHV-8 in SOT recipients. 67% of centers do not screen for HHV-8 serology, but the same proportion registered HHV-8 associated diseases: these are probably underestimated in the transplant setting. Considering potentially fatal complications and the possibility to screen and perform prompt diagnosis, collaborative studies to establish the best screening and prevention strategies of HHV8-related diseases in SOT are needed.

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**Abstract 828**

**Performance of a PCR-based syndromic panel compared to routine culture and microscopy in patients suspected of pneumonia**

Vigith Andrews*1, Mette Pinholt1, Uffe Vest Schneider1,2, Lillian Søes1, Kristian Schønning1, Gorm Lisby1

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**Abstract third-party references:** Department of Clinical Microbiology, Hvidovre and Amager Hospital, Denmark

**Background:** Syndromic testing for lower respiratory tract infections with Biofire® Filmarray® Pneumonia Panel (BF) consists of a multiplex PCR with 27 pathogens and a turn-around-time of two hours. Routine diagnostic of bacterial pneumonia in the Capital Region of Denmark consist of culture preceded by microscopy for quality assessment of sputum. Turn-around-time and sensitivity of culture can be a limiting factor for targeted antimicrobial treatment. Hence, we evaluated BF against culture for analytical and clinical performance.

**Materials/methods:** from January to May 2019 298 samples (sputum or endotracheal aspirates) were collected consecutively from hospitalized patients with suspected pneumonia. Samples were referred routinely to the Department of Clinical Microbiology (Copenhagen University Hospital Hvidovre) for culture and additional testing by BF.

Retrospectively, patients were categorized into ‘pneumonia’ according to IDSA definition, ‘probable pneumonia’ for patients without lung infiltrate but otherwise meeting the pneumonia criteria, and “not pneumonia”. Analytical performance was evaluated by bacterial pathogen concordance between the two methods. Clinical performance was determined regarding pneumonia/not pneumonia and detection of a positive/negative bacterial pathogen, and evaluated by sensitivity, positive predictive value (PPV), negative predictive value (NPV) and efficacy.

Patients with probable pneumonia were excluded in clinical performance calculations.

**Results:** 98 patients had pneumonia, 71 had probable pneumonia and 129 had not pneumonia.

Overall positive agreement between culture and BF was 42%. The rate increased to 67% when pathogens in lowest quantity \(10^4\) and \(10^5\) copies/mL) in BF were excluded.

Overall sensitivity of BF was improved from 73% to 89%, and for culture from 50% to 72%, when only high-quality samples as judged by microscopy were included in the analysis. For BF, PPV: 50%, NPV: 69% and efficacy: 57% were comparable to culture (PPV: 49%; NPV: 62%; efficacy: 55%); this increased slightly for both BF (PPV: 55%; NPV: 76%; efficacy: 61) and culture (PPV: 53%; NPV: 62%; efficacy: 56%), when only high-quality samples were included.

**Conclusions:** PPV and NPV of both BF and culture were low. Both tests are therefore best used in patients in whom the pneumonia diagnosis has been established clinically. Indiscriminate use may be diagnostically misleading and a cause of inappropriate use of antibiotics.

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Abstract 831

Correlation of central line-associated bloodstream infections with employee turnover: continuity in nursing staff matters!

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Background: Understaffing has been previously reported as a risk factor for central line-associated bloodstream infections (CLABSI). No previous study addressed the question whether fluctuations in staffing have an impact on CLABSI incidence. We analyzed prospectively collected CLABSI surveillance data and data on employee turnover of health care workers (HCW) to address this research question.

Materials/methods: In January 2016, a semi-automatic surveillance system for CLABSI was implemented at the University Hospital Zurich, a 950 bed tertiary care hospital. Source data including presence of a central venous catheter (CVC), length of hospital stay, and microbial results of blood cultures are prospectively extracted from our patient data management system into Caradigm Intelligence Platform®. In case of positive blood culture results in a patient with a CVC in place at time of sampling, an infection control nurse differentiates between bacteremia of other origin and CLABSI. Monthly incidence rates (IR, CLABSI/1000 catheter days) were calculated and correlated to human resources management-derived monthly data on employee turnover of HCWs (defined as number of HCWs who left the hospital divided by the number of employed HCWs in that month).

Results: Over a period of 24 months, we detected a positive correlation of CLABSI incidence and nursing personnel turnover (Spearman rank correlation, r=0.467, P=0.022) [Figure]. In more detailed analyses on the professional training of nursing personnel, a correlation of CLABSI incidence rates and turnover of nurses with advanced training was confirmed (Spearman rank correlation, r=0.471, P=0.021). Physician turnover did not correlate with CLABSI incidence (Spearman rank correlation, r=-0.058, P=0.787).

Conclusions: Prospectively determined CLABSI incidence correlated positively with the degree of turnover of nurses overall and nurses with advanced training, but not with the turnover of physicians. Efforts to maintain continuity in nursing staff might be helpful for sustained reduction in CLABSI rates.

Figure:

a) Employee turnover of nursing personnel (black line) and nurses with advanced training (blue line)
b) Incidence rates of central line-associated bloodstream infections
c) Correlation of central line-associated bloodstream infection rates and turnover of nursing personnel

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Can gentamicin concentrations be used to estimate glomerular filtration rate in intensive care unit patients?

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Background: Acute kidney injury is common in critical ill intensive care unit (ICU) patients. Accurate assessment of kidney function is vital to correct dosing of important drugs such as antibiotics in sepsis patients. Kidney function can be assessed using plasma creatinine or cystatin C to calculate estimated glomerular filtration rate (eGFR). However, both of these markers are endogenous and require steady-state conditions. As gentamicin is freely filtered in the glomerulus, it is a potential exogenous marker for eGFR when used in ICU patients. The aim of the study was to investigate whether serum gentamicin concentrations correlates to standard estimates of eGFR in an ICU setting.

Materials/methods: All adult patients (>18 years) in the ICU of Uppsala University Hospital treated with gentamicin and with at least one serum gentamicin measurement between January 1, 2009 and December 31, 2013 were included in this retrospective study. Patients on renal replacement therapy, and those with missing gentamicin dose information were excluded. Data on age, sex, weight, gentamicin administration time and dose, serum gentamicin, plasma creatinine and cystatin C were collected. eGFR for creatinine and cystatin C were calculated from the LM-rev and CAPA equations, respectively. Gentamicin clearance was estimated with a population pharmacokinetic model (Hodiamont et al 2017). Correlation, bias and agreement for the two eGFRs compared to gentamicin clearance were calculated.

Results: 254 patients were included. The correlation coefficient for gentamicin clearance vs. eGFR creatinine was 0.69, with a mean difference between the methods 4.6 (1.9-7.3; bias [95% CI]) and limits of agreement -43.7 -52.9 mL/min. The correlation coefficient for gentamicin clearance vs. eGFR cystatin C was 0.67, with a mean difference of -1.9 (-5.1 - 1.3) and limits of agreement -58.3 to 54.5 mL/min.

Conclusions: In the comparison of the two eGFR methods and gentamicin clearance we found low agreement despite low bias. However, cystatin C and creatinine are suboptimal markers of kidney function in the ICU. Gentamicin clearance for estimating GFR in ICU patients cannot be dismissed and should be compared to other exogenous GFR markers.

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Abstract 835

**Epidemiology of carbapenemase-producing *Klebsiella pneumoniae* in Northern Portugal: predominance of KPC-2 and OXA-48**

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**Background:** Carbapenemase-producing *Klebsiella pneumoniae* are increasingly reported in Portugal, but data from the northern region of the country (Trás-os-Montes and Alto Douro) are missing. The aim of the present study was to provide information on the molecular epidemiology of carbapenemase-producing *K. pneumoniae* isolates currently circulating at the tertiary and university hospital of Vila Real, Portugal.

**Materials/methods:** A total of 106 carbapenemase-producing *K. pneumoniae* isolates recovered between January 2018 and March 2019 were included in this study. All isolates were characterized by antimicrobial susceptibility, identification of resistance determinants, pulsed-field gel electrophoresis (PFGE), multilocus sequence typing (MLST), and plasmid analysis.

**Results:** The most common carbapenemase identified was KPC-2 (91%), followed by OXA-48 (9%). The *bla*<sub>KPC-2</sub> gene was mainly carried onto IncN (53%) and IncF (29%) plasmid types, whereas the *bla*<sub>OXA-48</sub> gene was mainly located on the IncL (80%) incompatibility group. Molecular characterization distributed the 106 isolates into 29 PFGE types and 26 STs, but three clones included 50% of the isolates: PFGE A-ST147-KPC-2 (n=31; 29%), B-ST15-KPC-2 (n=16; 15%), and C-ST11-OXA-48 (n=6; 6%). Antimicrobial resistance rates were the following: ciprofloxacin (76%), trimethoprim-sulfamethoxazole (75%), tobramycin (62%), gentamicin (34%), amikacin (25%), tigecycline (21%), fosfomycin (10%), and colistin (7%). None of the colistin-resistant isolates harbored *mcr-1*. All isolates remained susceptible to ceftazidime/avibactam, but 10% presented elevated MICs (3 and 4 mg/L).

**Conclusions:** KPC-2 was found to be the predominant carbapenemase among *K. pneumoniae* isolates currently circulating at this hospital from northern Portugal, followed by OXA-48. These data actually contrast with those obtained from the rest of the country, where KPC-3 predominates. Moreover, this study showed a high diversity of KPC-2-producing *K. pneumoniae* isolates with a predominance of the ST147 and ST15 clones.

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Faecal carriage of extended-spectrum beta-lactamase producing Enterobacteriaceae at hospital admission in Portugal: a prospective survey

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Background: Among Gram-negative bacteria, the wide spread of extended-spectrum β-lactamases (ESBL) producing isolates is considered as a global threat. This study aimed to prospectively evaluate the prevalence of ESBL-producing Enterobacteriaceae fecal carriers at admission in a Portuguese hospital and to determine the epidemiology and antimicrobial resistance pattern of ESBL-producing isolates.

Materials/methods: Between December 1st, 2018 and February 2nd, 2019, rectal swabs were collected within the first 48h from 151 patients admitted to the hospital. In addition, a total of 48 rectal swabs were obtained from weekly screenings of 37 patients hospitalized for more than 48h. All ESBL- and/or carbapenemase-producing enterobacterial isolates were tested for antimicrobial susceptibility, and characterised by PFGE and MLST.

Results: The prevalence of ESBL producers was 17% at hospital admission and 24% among patients hospitalized for >48h, while the prevalence of carbapenemase producers was 3% in both cases. Most of the isolates were Escherichia coli (54%) and Klebsiella pneumoniae (41%). The most common ESBL identified was CTX-M-15 (n=17/34; 50%), followed by CTX-M-14 (n=10; 29%), CTX-M-33 (n=4; 12%), SHV-12 (n=2), and CTX-M-55 (n=1). The 20 E.coli isolates were distributed into 16 pulsotypes and nine sequence types (ST), out of which ST131 included 60% of the isolates. The 15 K. pneumoniae were grouped in 12 PFGE types and nine STs, out of which three (ST17, ST449, and ST147) included 60% of the isolates. A high proportion of isolates showed resistance to ciprofloxacin (86%), SXT (68%), tobramycin (57%), and gentamicin (43%). All isolates remained susceptible to fosfomycin.

Conclusions: A high prevalence of ESBL-producing Enterobacteriaceae was found at hospital admission and more than 50% of the isolates showed resistance to first-line antibiotics for the treatment of uncomplicated lower urinary tract infections. The choice of empiric drugs in the community should be cautious, leaving fosfomycin as a safe alternative.

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Abstract 837

**Focus on nuclear imaging and other complementary exams for bacteraemia in early post-operative cardiac surgery**

Michael Thy*1

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**Background:** In cardiac surgery, the occurrence of bacteremia after cardiac surgery is common (1). European Society of Cardiology introduced nuclear imaging in the diagnostic management of endocarditis but post-operative inflammation could be false positive diagnosis (2–4) the European Association of Nuclear Medicine (EANM). The aim of this study is to describe the impact of imaging complementary exams in the management of early post-operative bacteremia.

**Materials/methods:** Our study is a monocentric retrospective study included any patient over 18-year-old with bacteremia within 30 days of cardiac surgery hospitalized at Bichat Claude Bernard Hospital from January 2013 to December 2016. We included all the patients who had imaging complementary exams during their hospital stay. Every diagnostic and therapeutic decision was decided with a multidisciplinary expert staff. We excluded the blood cultures considered as contamination.

**Results:** Overall, among the 128 patients who had positive blood culture occurring after cardiac surgery, the different complementary exams exploring infectious complications [echocardiography, CT-scan, 18F-FDG-PET CT (PET/CT) and White blood cell scintigraphy (WBC scintigraphy)] are represented in the Table 1. PET/CT was performed in 18.3% (n=19) of the patients in a median time to scan was 53 days (22.8-105). It led to diagnosis while TTE was negative for 6 patients positive on valve and 8 other diagnosis and while TOE was negative for 5 patients positive on valve and 8 other diagnosis. WBC scintigraphy was performed in 11.5% (n=12) of the patients in a median time to WBC was 60 days (17-105). WBC scintigraphy did not give a better sensibility without any patient positive for WBC scintigraphy and negative for PET/CT. WBC scintigraphy seemed more specific as it confirmed prosthesis infection in 2 patients and infirmed it in 1 patient.

**Conclusions:** In our cohort, we found a positive impact of nuclear imaging with better diagnostic performance on positive blood culture occurring after cardiac surgery. Prospective studies could lead to further responses.

<table>
<thead>
<tr>
<th>Table 1: Focus on nuclear imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
</tr>
<tr>
<td>----------------------------------</td>
</tr>
<tr>
<td>Transesophageal echocardiography (TEE)</td>
</tr>
<tr>
<td>Suspicion of endocarditis on TTE (%)</td>
</tr>
<tr>
<td>PET/CT scan done</td>
</tr>
<tr>
<td>WBC scintigraphy done</td>
</tr>
<tr>
<td>Positive</td>
</tr>
<tr>
<td>Transesophageal echocardiography (TOE)</td>
</tr>
<tr>
<td>Suspicion of endocarditis on TOE (%)</td>
</tr>
<tr>
<td>PET/CT scan done</td>
</tr>
<tr>
<td>Positive</td>
</tr>
<tr>
<td>WBC scintigraphy done</td>
</tr>
<tr>
<td>Positive</td>
</tr>
<tr>
<td>Conventional CT scan (%)</td>
</tr>
<tr>
<td>Positive</td>
</tr>
<tr>
<td>Sternal wound infection</td>
</tr>
<tr>
<td>Septic embolism</td>
</tr>
<tr>
<td>Other infection</td>
</tr>
<tr>
<td>Non septic embolism</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>White PET/CT scan negative</td>
</tr>
<tr>
<td>White blood cell scintigraphy negative</td>
</tr>
<tr>
<td>Negative</td>
</tr>
<tr>
<td>PET/CT scan (%)</td>
</tr>
<tr>
<td>Positive</td>
</tr>
<tr>
<td>Positive on valve</td>
</tr>
<tr>
<td>Sternal wound infection</td>
</tr>
<tr>
<td>Other infection</td>
</tr>
<tr>
<td>Cancer</td>
</tr>
<tr>
<td>White conventional CT scan negative</td>
</tr>
<tr>
<td>White blood cell scintigraphy negative</td>
</tr>
<tr>
<td>Negative</td>
</tr>
<tr>
<td>Time to PET/CT scan in days (median [IQR])</td>
</tr>
<tr>
<td>White blood cell scintigraphy (%)</td>
</tr>
<tr>
<td>Positive</td>
</tr>
<tr>
<td>White conventional CT scan negative</td>
</tr>
<tr>
<td>White PET/CT scan negative</td>
</tr>
<tr>
<td>Time to White blood cell scintigraphy in days (median [IQR])</td>
</tr>
</tbody>
</table>

**Presenter email address:** michael245thy@gmail.com
Epidemiology and antimicrobial resistance of methicillin-resistant *Staphylococcus aureus* isolates colonising pigs with different exposure to antibiotics

Elizeth Lopes¹, Teresa Conceição¹, Laurent Poirel², H. De Lencastre¹,³, Marta Aires De Sousa*¹,⁴

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**Background:** In 2016, very high rates of methicillin-resistant *Staphylococcus aureus* (MRSA)-ST398 (99%) were found in different Portuguese pig farms that used colistin, amoxicillin, and zinc oxide as feed additives. Since then, farms A and B banned the use of colistin, and farm C banned the use of both antibiotics. The aim of the present study was to evaluate the impact of the ban of colistin and amoxicillin on pig MRSA carriage rates, clonal types and antimicrobial resistance, and compare data with those obtained in 2016.

**Materials/methods:** In 2018, 103 pigs (52 from farm B using amoxicillin only as a feed additive and 51 from farm C where no antibiotics were included in the feed regimen) were nasally swabbed for MRSA colonization. Isolates were tested for antimicrobial susceptibility, and characterised by *spa* typing, SCCmec typing and MLST. Whole genome sequencing (WGS) was performed for representative isolates.

**Results:** Overall, 96% of the pigs swabbed in 2018 carried MRSA, mostly ST398-SCCmec V-*spa* types t011/t108. MRSA from pigs not receiving antibiotics in the feed regimen showed susceptibility to a higher number of antibiotics, namely erythromycin, ciprofloxacin, gentamicin, and chloramphenicol. Notably, most of these isolates (n=52) presented an unusual erythromycin-susceptibility/clindamycin-resistance phenotype. WGS showed that these isolates lacked the *erm* and the *lnu* genes encoding resistance to macrolides and lincosamides, respectively, but carried the *vga*ALC gene encoding resistance to lincosamides, which is here firstly identified in *S. aureus* ST398.

**Conclusions:** Two years of ban of colistin and amoxicillin as feed additives did not significantly impact the MRSA nasal carriage rates. Nevertheless, the MRSA strains circulating in those farms showed resistance to a lower number of antibiotic classes.

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Impact of coagulase-negative staphylococci positive blood culture occurring in early postoperative cardiac surgery

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Background: The occurrence of bacteremia after cardiac surgery is common [1]. It often involved coagulase-negative Staphylococci bacteremia [CoNS] but with difficulties to distinguish contamination to real infections [2–4]. The objectives of this study are to describe CoNS bacteremia after cardiac surgery.

Materials/methods: This monocentric retrospective study included any patient over 18-year-old with bacteremia within 30 days of cardiac surgery hospitalized at Bichat Claude Bernard Hospital from January 2013 to December 2016. We excluded all the other identified germ in blood cultures. We divided into 2 groups, one with a diagnosis of infection and the others considered as contamination. We defined contaminant as clinical presentation and laboratory criteria [13]. These criteria included a unique positive blood culture, ≥2 days until the first blood culture became positive, the isolated microorganisms [CoNS, Corynebacterium species, Bacillus species other than anthracis and P. acnes] and clinical risk score including negative blood cultures and a favorable evolution without antibiotics. Sepsis was defined by Sepsis 3.0 criteria [14]. Every diagnostic and therapeutic decision was decided with a multidisciplinary expert staff.

Results: Among the 211 patients screened, 41.2% [n=87] had CoNS bacteremia. 80.4% [n=70] were considered as contamination and 19.6% [n=17] were not considered as contamination. The details of the comparison are shown on Table 1. In the group of CoNS infection, the germ the most represented was Staphylococcus epidermidis [n=10 (58.8%)] with same proportion of the others CoNS in the 2 groups. 2 were considered as an endocarditis based on nuclear imaging and treated as so. The patients with infection by CoNS had significantly more surgical treatment related to the wound sternal infection diagnosis. The hospital length of stay and mortality was significantly higher in the group with infection by CoNS.

Conclusions: Positive blood culture by CoNS occurring after cardiac surgery is a common complication but not always as a contaminant with a high rate of mortality with wound sternal infection as a leading cause and some cases of endocarditis. Prospective studies could lead to further responses.

Table 1: CoNS bacteremia: contamination vs infection

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Infection</th>
<th>Contamination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean [SD])</td>
<td>66.4 (10.1)</td>
<td>66.6 (14.9)</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>57 (81.4)</td>
<td>51 (71.2)</td>
</tr>
<tr>
<td>Body mass index (mean [SD])</td>
<td>27.8 (2.8)</td>
<td>26.7 (2.8)</td>
</tr>
<tr>
<td>EuroSCORE (mean [SD])</td>
<td>6.1 (9.2)</td>
<td>5.1 (9.0)</td>
</tr>
<tr>
<td>ISS score (mean [SD])</td>
<td>62.7 (22.9)</td>
<td>52.2 (20.9)</td>
</tr>
<tr>
<td>Odds (%)</td>
<td>8.1 (1.1)</td>
<td>8.2 (1.1)</td>
</tr>
<tr>
<td>Type of surgery (%)</td>
<td>0.825</td>
<td></td>
</tr>
<tr>
<td>Coronary bypass (%)</td>
<td>0.225</td>
<td></td>
</tr>
<tr>
<td>Valve surgery (%)</td>
<td>0.225</td>
<td></td>
</tr>
<tr>
<td>Time to surgery (%)</td>
<td>0.225</td>
<td></td>
</tr>
<tr>
<td>Emergent (n=37)</td>
<td>0.0 (0.0)</td>
<td>11 (11.1)</td>
</tr>
<tr>
<td>Scheduling (%)</td>
<td>12 (25.5)</td>
<td>42 (60.0)</td>
</tr>
<tr>
<td>Urgent surgery within 7 days (%)</td>
<td>4 (20.0)</td>
<td>12 (24.5)</td>
</tr>
<tr>
<td>Relative (%)</td>
<td>2 (7.4)</td>
<td>17 (22.1)</td>
</tr>
<tr>
<td>Duration of CPR, minute (mean [sd])</td>
<td>90.3 (30.1)</td>
<td>85.1 (40.3)</td>
</tr>
<tr>
<td>Duration of C-section (mean [min])</td>
<td>68.2 (26.5)</td>
<td>59.7 (28.1)</td>
</tr>
<tr>
<td>Delay of positive blood culture from surgery in day (mean [SD])</td>
<td>18.2 (17.7)</td>
<td>22.8 (22.2)</td>
</tr>
<tr>
<td>Suppurative wound sternal infection (%)</td>
<td>0.0 (0.0)</td>
<td>0.0 (0.0)</td>
</tr>
<tr>
<td>Deep wound sternal infection (%)</td>
<td>0.0 (0.0)</td>
<td>0.0 (0.0)</td>
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<tr>
<td>Temperature (%)</td>
<td>0.820</td>
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</tr>
<tr>
<td>Hypothermia (&lt;36°C)</td>
<td>0.0 (0.0)</td>
<td>1.3 (1.3)</td>
</tr>
<tr>
<td>Normothermia</td>
<td>0.0 (0.0)</td>
<td>15.8 (16.8)</td>
</tr>
<tr>
<td>Fever (&gt;38.5°C)</td>
<td>4.4 (6.0)</td>
<td>11.8 (12.7)</td>
</tr>
<tr>
<td>Intensive care (%)</td>
<td>0.080</td>
<td></td>
</tr>
<tr>
<td>Catecholamines (%)</td>
<td>16 (09.5)</td>
<td>21 (17.2)</td>
</tr>
<tr>
<td>Inotropic support (mean [SD]) in days</td>
<td>297 (646.6)</td>
<td>233.6 (277.1)</td>
</tr>
<tr>
<td>Transfusion (%)</td>
<td>6 (56.3)</td>
<td>27 (71.6)</td>
</tr>
<tr>
<td>Septic shock (%)</td>
<td>0.088</td>
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<tr>
<td>Complimentary means (%)</td>
<td>0.345</td>
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<tr>
<td>Sepsis of endocarditis on TTE (%)</td>
<td>2 (11.8)</td>
<td>3 (2.1)</td>
</tr>
<tr>
<td>Sepsis of endocarditis on TOE (%)</td>
<td>2 (11.8)</td>
<td>3 (2.1)</td>
</tr>
<tr>
<td>PETGCT scan done (%)</td>
<td>3 (17.6)</td>
<td>3 (17.6)</td>
</tr>
<tr>
<td>Positive on valve (%)</td>
<td>1 (2.0)</td>
<td>4 (2.1)</td>
</tr>
<tr>
<td>WBC staphylococcus done (%)</td>
<td>2 (11.8)</td>
<td>4.5 (7.6)</td>
</tr>
<tr>
<td>Positive on valve (%)</td>
<td>2 (11.8)</td>
<td>4.5 (7.6)</td>
</tr>
<tr>
<td>Final diagnosis and outcomes (%)</td>
<td>4.4 (6.0)</td>
<td>11.8 (12.7)</td>
</tr>
</tbody>
</table>

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Investigation of a nosocomial pulmonary tuberculosis in a French university hospital

Elias Christelle*1,2, Christian Dorado-Cortez2, Oana Dumitrescu3, Florence Ader4, Philippe Ceruse5, Claudine Pasquet-Volkmann6, Béatrice Grisi2, Philippe Vanhems7, Cédric Dananché1;2

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Abstract:

Nosocomial pulmonary tuberculosis (TB) remains nowadays poorly known. Healthcare workers (HCW) are at increased risk for TB infection and disease due to a higher risk of TB exposure in a hospital setting. Pulmonary TB infection control measures are a key component to minimize the risk of transmission and to prevent a further spread of the disease, in particular in healthcare facilities. The aim is to describe two cases of nosocomial TB.

Materials/methods:

Following the diagnosis of a pulmonary TB in a HCW in an Ear Nose Throat ward in a French university hospital, a retrospective descriptive review was performed to understand the route of acquisition.

Results:

In August 2018, 6 patients and 107 HCWs were identified as contact subjects following a delayed pulmonary TB diagnostic and delayed airborne precautions implementation in the index patient, a 74-year-old male with an oropharynx cancer. Subsequent to a TB screening, two secondary cases were identified in HCWs. The first HCW, a 30-year-old man developed a nosocomial pulmonary TB three months after exposure, verified by culture. The ongoing whole genome sequencing (WGS) molecular survey implemented in our center confirmed that the isolate was identical to the one of the index case. Moreover, WGS analysis ruled out any possibility of transmission to an 18-year-old woman admitted to the unit concomitantly with the index case and developing pulmonary TB 4 months later. Further contact-tracing resulted in 79 contacts patients from hospital exposure. The second HCW, a 37-year-old female developed a nosocomial latent tuberculosis infection (LTI) following a positive Quantiferon-TB Gold test. No further investigation was conducted given the low risk of transmission of LTI and that the HCW was treated right after the diagnostic.

Conclusions:

HCWs have to rigorously follow TB infection control measures in order to prevent the occurrence of TB nosocomial cases. They have also to comply with TB screening and testing in case of exposure and should receive TB education regularly.

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**Abstract 845**

**Characterisation of Staphylococcus aureus in soft tissue infections: relevance of PVL producers**

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**Background:** Methicillin-resistant *Staphylococcus aureus* (MRSA) is a group of bacteria able to resist to beta-lactamic antibioti-
cs: This profile is mainly due to the presence of the *mecA* gene present in SScmec cassette. MRSA, due to different characteris-
tics, have been distinguished in community-acquired (CA-MRSA) and hospital-acquired (HA-MRSA) strains. The pathogenicity
of *S. aureus* and the production of virulence factors are responsible for severe infections. PVL is an exotoxin produced by *S.
aureus*, able to lyse the defense cells. The genes that encode this enzyme can integrate the SCCmec, mainly the types IV/V,
common in CA-MRSA, causing infections with more difficult and prolonged treatment.

**Materials/methods:** 139 *S. aureus* isolates responsible to skin and soft tissue infections were identified and characterized
according to its antibiotic susceptibility profile, in Centro Hospitalar e Universitário de Coimbra. DNA extraction was done and
the *mecA* and *lukSF* genes detection were performed by PCR.

**Results:** The 139 isolates of *S. aureus*, according to the phenotype for oxacillin, were classified as MRSA 47 (34%) and as
MSSA 92 (66%). All MRSA presented *mecA* gene and, among the MSSA, 49 (53.3%) were positive and 43 (46.7%) negative. The
vancomycin phenotype was sensitive for all isolates and higher MIC levels were found in superficial infections (80.3%, n = 53),
with more methicillin-sensitive isolates (MSSA). The gene that encodes the PVL was found in 2.2% (3) of the isolates: 2 from
pediatric samples (abscess and non-surgical wound exudate [NSWE]) and 1 from a non-pediatric sample (NSWE).

**Conclusions:** The prevalence of PVL was 2.2%. The 3 isolates carrying-PVL were MRSA/MSSA and probably were acquired in
the community, all had *mecA* gene. 2 isolates were found in pediatric samples, in a total of 13 isolates; the other was found in a
non-pediatric sample, from a total of 126 isolates. PVL shown to have a high prevalence within *S. aureus*, causing skin and soft
tissue infections in children with statistical significance, suggesting that this screening should be done for the better treatment
and avoid prolonged infections.

**Presenter email address:** anamontes81@hotmail.com
Abstract 846

Outcomes in ventilated patients with hospital-acquired/ventilator-associated bacterial pneumonia (HABP/VABP) treated with imipenem/cilastatin (IMI)/relebactam (REL) versus piperacillin/tazobactam (PIP/TAZ): subgroup analysis of the RESTORE-IMI 2 randomised, controlled trial


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Abstract third-party references: Funding for this research was provided by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Background: In the RESTORE-IMI 2 phase 3 trial, IMI/REL was non-inferior to PIP/TAZ for treatment of HABP/VABP in both primary and key secondary endpoints. Since ventilated HABP (vHABP) and VABP are associated with higher mortality than non-ventilated HABP, we specifically evaluated efficacy and safety outcomes in ventilated patients.

Materials/methods: RESTORE-IMI 2 was a randomized, controlled, double-blind, non-inferiority trial in adults with HABP/VABP. Lower respiratory tract (LRT) specimens were obtained ≤48 hours prior to screening. Patients were randomized to 7-14d of IMI/REL 500mg/250mg or PIP/TAZ 4g/500mg. Primary endpoint: Day 28 all-cause mortality (ACM) in the modified intent-to-treat (MITT) population (randomized patients with ≥1 dose of study drug, excluding patients with only gram-positive cocci present on baseline Gram stain). Key secondary endpoint: clinical response at early follow-up (7-14d after end-of-therapy). Another secondary endpoint was Day 28 ACM in the microbiologic MITT population (MITT patients with baseline pathogen species against which IMI/REL is known to have activity). The safety population included all patients who received study drug. Efficacy and safety endpoints were prospectively evaluated in the sub-population of ventilated patients (i.e., primary diagnosis of vHABP or VABP).

Results: In the MITT population, 122/254 (46.2%) IMI/REL and 126/257 (50.9%) PIP/TAZ patients had a primary diagnosis of vHABP or VABP. Of these, 39.3% were ≥65 years old, 66.3% had APACHE-II scores ≥15 (median score: 17.5 IMI/REL, 18.0 PIP/TAZ), and 19.4% had moderate/severe renal impairment. Baseline characteristics in ventilated patients were generally balanced between treatment arms. Most frequent baseline LRT pathogens (assessed in ventilated patients of the microbiologic MITT population) were A. calcoaceticus-baumannii complex (23.0% of patients), K. pneumoniae (21.5%), P. aeruginosa (20.1%), and E. coli (15.8%); baseline pathogens were balanced between arms. IMI/REL was associated with lower ACM than PIP/TAZ and comparable clinical response rates in the ventilated sub-population (Table). In the safety population of ventilated patients, rates of overall adverse events (AEs) [IMI/REL 114/124 [91.9%] vs PIP/TAZ 116/136 [92.6%]] and therapy discontinuations due to any AEs [IMI/REL 10/124 [8.1%] vs PIP/TAZ 14/136 [10.3%]] were similar in both groups.

Conclusions: IMI/REL is an efficacious and well-tolerated treatment option for mechanically ventilated patients with nosocomial pneumonia.

<table>
<thead>
<tr>
<th></th>
<th>IMI/REL (n/N) (%)</th>
<th>PIP/TAZ (n/N) (%)</th>
<th>Difference (96% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary endpoint</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 28 all-cause mortality (MITT)</td>
<td>24/122 (19.7%)</td>
<td>42/136 (30.9%)</td>
<td>-11.2% (-21.6, -0.5)</td>
</tr>
<tr>
<td>Key secondary endpoint</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Favorable clinical response at EFU (MITT)</td>
<td>60/122 (54.1%)</td>
<td>62/136 (45.8%)</td>
<td>8.5% (3.7, 20.5)</td>
</tr>
<tr>
<td>Other secondary endpoints</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 28 all-cause mortality (mMITT)</td>
<td>10/102 (15.6%)</td>
<td>33/107 (30.8%)</td>
<td>-12.2% (-23.7, -0.5)</td>
</tr>
</tbody>
</table>

CI, confidence interval; EFU, early follow-up visit; IMI/REL, imipenem/cilastatin/relebactam; MITT, modified intent-to-treat population; mMITT, microbiologic modified intent-to-treat population. n, number of patients; %, percentage; CI, confidence interval; AEs, adverse events; m, modified; MITT, modified intent-to-treat population; mMITT, microbiologic modified intent-to-treat population. n, number of patients who died or had unknown survival status or number of patients with favorable clinical response (depending on endpoint). PIP/TAZ, piperacillin/tazobactam.

* Differences (i.e., IMI/REL, minus PIP/TAZ) and confidence intervals were calculated using the Miettinen & Nurminen method.

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Abstract 849

Baseline microbiology, susceptibility, molecular characterisation, and emergence of non-susceptibility in a recent randomised, controlled trial (RESTORE-IMI 2) comparing imipenem/cilastatin (IMI)/relebactam (REL) versus piperacillin/tazobactam (PIP/TAZ) for hospital-acquired or ventilator-associated bacterial pneumonia (HABP/VABP)

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Abstract third-party references: Funding for this research was provided by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA.

Background: RESTORE-IMI 2 showed IMI/REL to be non-inferior to PIP/TAZ for treatment of HABP/VABP. Here we present key microbiologic data from that study.

Materials/methods: Randomized, controlled, double-blind, multinational, non-inferiority, phase 3 trial comparing IMI/REL 500mg/250mg versus PIP/TAZ 4g/500mg in HABP/VABP. Baseline lower respiratory tract (LRT) specimens were obtained ≤48h prior to screening, at end-of-therapy (EOT), and early follow-up (7-14d after EOT). Identification and susceptibility of all pathogens were confirmed at a central laboratory. LRT non-Morganellaceae Enterobacterales and Pseudomonas aeruginosa isolates underwent molecular characterization for β-lactamase genes if they were either imipenem-nonsusceptible isolates or imipenem-susceptible baseline isolates from patients with an imipenem-nonsusceptible isolate of the same species collected subsequently during treatment. The microbiologic modified intent-to-treat (mMITT) population included all patients with ≥1 dose of study therapy, without only gram-positive cocci on their baseline LRT specimen, and with baseline pathogen species known to be potentially susceptible to imipenem/REL.

Results: The mMITT population comprised 215 and 218 patients randomized to IMI/REL and PIP/TAZ, respectively. The most frequent baseline LRT pathogens were Enterobacterales, P aeruginosa, and Acinetobacter calcoaceticus-baumannii complex; 84.0% of pathogens in the IMI/REL versus 70.4% in the PIP/TAZ arm were susceptible to randomized study drug according to EUCAST criteria (Table). In both treatment arms, the baseline LRT pathogens’ imipenem/REL minimum inhibitory concentration (MIC) range, MIC50, and MIC90 were similar. Across pathogens, PIP/TAZ had higher MIC values than imipenem/REL. Imipenem/REL MIC distributions in Enterobacterales and P aeruginosa were like those previously reported in global and European 2016-2018 surveillance. Among molecularly characterized study isolates (n=59, 71.2% imipenem/REL, 30.5% imipenem, 33.9% PIP/TAZ susceptible), 8 were KPC-producing Enterobacterales (100% imipenem/REL, 0% imipenem, 0% PIP/TAZ susceptible); 6 OXA-48-like-producing Enterobacterales (66.7% imipenem/REL, 66.7% imipenem, 0% PIP/TAZ susceptible); 4 metallo-β-lactamase-producing Enterobacterales (0% imipenem/REL, imipenem, and PIP/TAZ susceptible); 3 carbapenemase-negative, ESBL-producing Enterobacterales (100% imipenem/REL, 100% imipenem, and 66.7% PIP/TAZ susceptible); and 29 metallo-β-lactamase-negative P aeruginosa (79.3% imipenem/REL, 20.7% imipenem, and 44.8% PIP/TAZ susceptible).

Conclusions: In RESTORE-IMI 2, pathogen and MIC distributions were comparable to recent surveillance data and other recent HAPB/VABP trials. Most pathogens were susceptible to imipenem/REL. REL restored imipenem susceptibility in KPC-producing Enterobacterales and most metallo-β-lactamase-negative P aeruginosa.
<table>
<thead>
<tr>
<th>Pathogen</th>
<th>IMI/REL</th>
<th>PIP/TAZ</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients with pathogen, n (%)</td>
<td>Susceptibility, mM (%)</td>
</tr>
<tr>
<td>All pathogens</td>
<td>215 (100.0)</td>
<td>194/231 (84.0)</td>
</tr>
<tr>
<td><strong>Aerobic Gram-Negative Bacillus</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acinetobacter calcoaceticus-baumannii complex</td>
<td>192 (89.3)</td>
<td>172/207 (83.1)</td>
</tr>
<tr>
<td>Enterobacter cloaceae</td>
<td>32 (14.9)</td>
<td>4/32 (12.5)</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>8 (3.7)</td>
<td>8/8 (100.0)</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>30 (14.0)</td>
<td>30/30 (100.0)</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>58 (27.0)</td>
<td>57/58 (98.3)</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>34 (15.8)</td>
<td>31/35 (88.6)</td>
</tr>
<tr>
<td><strong>Aerobic Gram-Negative Coccobacillus</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenza</td>
<td>13 (6.0)</td>
<td>12/14 (85.7)</td>
</tr>
<tr>
<td></td>
<td>13 (6.0)</td>
<td>12/14 (85.7)</td>
</tr>
<tr>
<td></td>
<td>13 (6.0)</td>
<td>12/14 (85.7)</td>
</tr>
</tbody>
</table>

EUA = European Committee on Antimicrobial Susceptibility Testing. IMI/REL = imipenem/cilastatin/relebactam. LRT = lower respiratory tract. M = number of isolates with susceptibility interpretation (based on EUCAST, Version 9.0) available. m = number of isolates with a susceptibility interpretation of ‘susceptible’. mMIT = microbiologic modified intent-to-treat. ND = not determined. n = number of mMITT patients with the pathogen. PIP/TAZ = piperacillin/tazobactam.

Susceptibility interpretation by broth microdilution testing for PIP/TAZ was based on the European Committee on Antimicrobial Susceptibility Testing breakpoint tables for interpretation of minimum inhibitory concentrations, Version 9.0. Imipenem/relebactam susceptibility was determined using the provisional EUCAST breakpoints. For pathogens without IMI/REL breakpoints, the corresponding imipenem interpretive criteria were applied to determine imipenem/relebactam susceptibility.

*Percentage calculated as number of mMITT patients with the pathogen divided by total number of patients in the mMITT population, within that treatment arm. 4Percentage calculated as number of pathogen isolates with a susceptibility interpretation of ‘susceptible’ divided by total number of pathogen isolates with susceptibility interpretation available, within that treatment arm. 5PIP/TAZ is assumed to not have any activity against this pathogen. 6The lowest PIP/TAZ concentration tested (2 µg/mL) is greater than the EUCAST susceptibility breakpoint (0.25 µg/mL) for H. influenzae, so PIP/TAZ susceptibility according to EUCAST criteria could not be categorized for this pathogen.

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Abstract 856

Treatment of flaviviruses in solid organ transplant recipients with intravenous immunoglobulin and interferon alpha-2b: a Mayo Clinic Arizona experience

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Background: We present a case series of 10 solid organ transplant (SOT) recipients treated for either neuroinvasive West Nile virus (WNV) or St Louis Encephalitis virus (SLEV) at the Mayo Clinic in Arizona between 2011 and 2019.

Materials/methods: Data were queried using the integrating Biology and the Bedside clinical data analytics platform.

Results: All patients were treated with both intravenous immunoglobulin (IVIG) and interferon alpha-2b (IFN alpha-2b). 80% survived with 50% of those recovering completely. On average, recovery occurred on illness day 23, 9 days after treatment initiation. 2 of 4 organ rejections recovered.

Conclusions: Flaviviruses present significant morbidity for SOT patients often requiring ICU admission. IVIG combined with IFN alpha-2b appears to show clinical benefit and is well tolerated in SOT recipients, providing a more standardized role in this population's treatment for neuroinvasive disease. Future prospective studies are needed to confirm these findings.

Table 1. Treatment regimens with outcomes

<table>
<thead>
<tr>
<th>ID</th>
<th>Diagnosis</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Days to response/death after treatment initiation</th>
<th>Organ Rejection</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>WNV</td>
<td>500 mg/kg/d IVIG x 5 3 million units/d IFN α-2b x 4</td>
<td>Deceased</td>
<td>8</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>WNV</td>
<td>500 mg/kg/d IVIG x 4 3 million units/d IFN α-2b x 10</td>
<td>Partial recovery – mild cognitive impairment</td>
<td>5</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>WNV</td>
<td>1000 mg/kg/d IVIG x 1 then 400 mg/kg/d x 6 3 million units/d IFN α-2b x 15</td>
<td>Partial recovery – paralysis persists</td>
<td>6</td>
<td>Yes</td>
</tr>
<tr>
<td>4</td>
<td>WNV</td>
<td>400 mg/kg/d IVIG x 5 3 million units/d IFN α-2b x 4</td>
<td>Partial recovery – weakness persists</td>
<td>14</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>SLEV</td>
<td>400 mg/kg/d IVIG x 5 3 million units/d IFN α-2b x 14</td>
<td>Recovered</td>
<td>8</td>
<td>No</td>
</tr>
<tr>
<td>6</td>
<td>WNV</td>
<td>400 mg/kg/d IVIG x 2 3 million units/d IFN α-2b x 15</td>
<td>Recovered</td>
<td>26</td>
<td>No</td>
</tr>
<tr>
<td>7</td>
<td>SLEV</td>
<td>400 mg/kg/d IVIG x 6 3 million units/d IFN α-2b x 10</td>
<td>Recovered</td>
<td>4</td>
<td>No</td>
</tr>
<tr>
<td>8</td>
<td>WNV</td>
<td>500 mg/kg/d IVIG x 5 3 million units/d IFN α-2b x 9 1 dose WNV enriched product</td>
<td>Recovered</td>
<td>4</td>
<td>No</td>
</tr>
<tr>
<td>9</td>
<td>WNV</td>
<td>400 mg/kg/d IVIG x 5 3 million units/d IFN α-2b x 11</td>
<td>Partial recovery – later died of pneumonia</td>
<td>7</td>
<td>Yes</td>
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<tr>
<td>10</td>
<td>WNV</td>
<td>400 mg/kg/d IVIG x 5 3 million units/d IFN α-2b x 3</td>
<td>Deceased</td>
<td>15</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Presenter email address: sabirah.kasule@gmail.com
Abstract 859

Deaths of emerging and re-emerging infectious diseases outbreaks, epidemics and pandemic in the last 10 years: a systematic review

Tran Thuy Huong Quynh*, Huu Nhat Minh Le2, Ahmad Helmy Zayan3, Gamal Goda Abdel-Samea4, Eman Othman5, Huu-Hoai Le6, Thi Nam Giang Hoang7, Khac Linh Le8, Masahiro Hashizume9, Kenji Hirayama10, Nguyen Tien Huy11

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Background: The emergence and re-emerge of infectious diseases in the last decade has heightened concerns about the possibility of global outbreaks of disease and the ability of national and international health systems to respond and to overcome such infections successfully with the least possible number of victims. This study aimed to determine the death of the recent major emerging and re-emerging infectious disease outbreaks, epidemics, and pandemics.

Materials/methods: We searched 10 electronic databases: PubMed, Scopus, Gh, Vhl, Popline, Isi, Google Scholar, Sigle, Nyam to assess the death of major emerging and re-emerging infectious disease outbreaks from 2006 to 2015. We used Strobe Statement for assessing the risk of bias in our included observational studies. The study protocol was registered on Prospero, number crd42016038138.

Results: Out of the total included 8315 studies, 187 articles were eligible for analysis. Overall case fatality rate (Cfr) was 6.6%. Cfr was the highest with outbreaks (11.3%) followed by pandemics (3.7%) and epidemics (3.2%). South East Asia was the most affected region in outbreaks with Cfr (21.3%). Burkholderia pseudomallei and Nipah virus had the highest outbreak Cfr (80%, and 78.6%). Cfr increased notably in the last two years of our review at 2014 and 2015 with Cfr 25.4%, and 30.1% respectively. Significant risk of bias found with p-values of (0.001) using Egger's regression intercept.

Conclusions: South East Asia Region had the most death cases of infectious disease outbreaks. Burkholderia pseudomallei and Nipah virus were the causative pathogens that caused the highest number of cases of death.

<table>
<thead>
<tr>
<th>Group by species</th>
<th>Study name</th>
<th>Statistics for each study</th>
<th>Event rate and 95% CI</th>
<th>Event rate and 99% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Event rate</td>
<td>Lower limit</td>
<td>Upper limit</td>
</tr>
<tr>
<td>Chikungunya virus</td>
<td></td>
<td>0.154</td>
<td>0.108</td>
<td>0.216</td>
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<tr>
<td>Dengue Virus</td>
<td></td>
<td>0.003</td>
<td>0.002</td>
<td>0.005</td>
</tr>
<tr>
<td>Influenza A Virus</td>
<td></td>
<td>0.007</td>
<td>0.026</td>
<td>0.052</td>
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<tr>
<td>Influenza Pneumonia</td>
<td></td>
<td>0.054</td>
<td>0.028</td>
<td>0.108</td>
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<tr>
<td>Streptococcus pyogenes</td>
<td></td>
<td>0.002</td>
<td>0.001</td>
<td>0.008</td>
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<tr>
<td>Vibrio cholerae</td>
<td></td>
<td>0.036</td>
<td>0.024</td>
<td>0.061</td>
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<tr>
<td>Overall</td>
<td></td>
<td>0.021</td>
<td>0.018</td>
<td>0.025</td>
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</table>

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Abstract 861

Comparison of immune function between T, B lymphocytes, Th17, Th22 and Treg cells in children with hand, foot and mouth disease caused by EV71 and other enterovirus infections

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Background: Hand, foot and mouth disease is a global infectious disease caused by enterovirus, which occurs mostly in children under 5 years of age. There are more than 20 enteroviruses causing hand, foot and mouth disease, mainly Coxsackie A group 16 and enterovirus 71. HFMD caused by EV71 infection progresses rapidly, and it is prone to severe cases and even death. The pathogenesis of severe EV71 infection is still not fully understood. To investigate the difference of cellular immune function between enterovirus 71 (EV71) and other enterovirus infections in children with hand, foot and mouth disease, and to provide clinical diagnosis and treatment for hand, foot and mouth disease.

Materials/methods: The data of 94 children with hand, foot and mouth disease admitted to Hangzhou Children’s Hospital from November 2016 to June 2017 were analyzed. Among them, 45 cases were in EV71 infection group and 49 cases were non-EV71 other enterovirus infection group. Determination of serum total T lymphocytes (%), cytotoxic T cells (%), helper T cells (%), total B lymphocytes (%), CD4+/CD8+ ratio, NK cells (%), Th17 cells, Th22 cells (%), Treg cells (%), Treg/Th17 ratio, and comparison between different groups by cytometry.

Results: The levels of Th17 cells (%), Th22 cells (%) and total B lymphocytes (%) in the EV71 infection group were significantly higher than those in the non-EV71 other enterovirus infection group (t=5.672; t=4.934; t=2.074; P<0.05), and the ratio of Treg cells (%) and Treg/Th17 was lower than that of non-EV71 other enterovirus infection group (t=5.817; t=6.351; P<0.05).

Conclusions: Compared with other enterovirus infections, EV71 is more likely to cause cellular immune function disorder, especially the changes of Th17 cells, Th22 cells, Treg cells and total B lymphocytes.

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Multiplex detection of meningitis and encephalitis pathogens: a study from laboratory to the clinical

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1West China Medical School of Sichuan University, Chengdu, China, 2West China Hospital of Sichuan University, Chengdu, China

**Background:** Infectious Meningitis and Encephalitis as the potentially life-threatening conditions are mostly caused by bacterial, mycobacterium, fungus and viral agents. As the most devastating disease that results in nearly 150,000 deaths per year, early diagnosis and prompt initiation of treatment offer the chance of better prognosis. However, current laboratory testing projects do not meet demand for clinical diagnosis. Therefore, we come up with utilizing Multiplex detection for Meningitis and Encephalitis of 18 pathogens (MME-18) to help physicians achieve rapid and accurate diagnosis in infectious encephalitis and meningitis.

**Materials/methods:** The hospitalized patients with suspected intracranial infection were analyzed retrospectively between May and July in 2019 in West China Hospital of Sichuan University. MME-18 was designed to detect 18 pathogens in cerebrospinal fluid (CSF) of enrolled patients, including *N.meningitidis, M.tuberculosis, L.monocytogenes, S.pneumoniae, Mycoplasma pneumoniae, S.agalactiae, A.baumannii, H.influenzae, E.coli K1, C.neoformans, enterovirus [EV], mumps virus [MuV], herpes simplex virus type 1 [HSV-1], herpes simplex virus type 2 [HSV-2], Epstein-Barr virus [EBV], varicella zoster virus [VZV], cytomegalovirus [CMV], human herpes virus type 6 [HHV-6]. After using the GeneXpert and RT-qPCR to review the consistency of the results of 3 methods, we further informed clinician of the results and collected the feedback information of diagnosis and treatment.

**Results:** Among a total of 581 tested patients, 149 eligible individuals were enrolled in study. 85(57.05%) of the patients were positive for at least one of the 18 target pathogens. *M.tuberculosis, C.neoformans* and virus were the most common causative agents, including separate and multiple infections. According to the feedback of diagnosis and treatment provided by clinicians, 66(77.64%) patients were confirmed by clinical diagnosis and targeted treatment. 9(10.58%) patients results had not been supported by clinicians, but they were still willing to seek further information. At the same time, 10(11.76%) results were rejected or ignored.

**Conclusions:** MME-18 has much wider and accurate range of pathogenic spectrum while it is able to complete detection within 4.5 hours. Moreover, the MME-18 results may help diagnose and provide clinical treatment suggestion about encephalitis/meningitis.

| Table 1 Demographic and clinical Characteristic of the 149 Patients. |
|---------------------------------|---|
| **Characteristic**             | **Value** |
| Age                            | 44.9 |
| Mean — yr                      | 7(4.7) |
| 10 - 19yr                      | 47(31.8) |
| 20 - 39yr                      | 56(37.6) |
| >60yr                          | 39(25.9) |
| Male sex — no. (%)             | 90(59.2) |
| Syndrome — no. (%)             | 58(38.9) |
| Meningitis alone               | 87(58.4) |
| Encephalitis with or without meningitis | 4(2.7) |
| Myelitis with or without meningitis | 29(19.5) |
| Exacerbation of chronic condition — no. (%) | 6(4.0) |
| Immunocompromised — no. (%)    | 4(2.7) |
| HIV-1                          | 2(1.3) |
| Solid-organ transplant         | 6(4.0) |
| ICU admission — no. (%)        | 17(11.4) |
| Death within 30 days — no. (%) | 1(0.8) |
| Median no. of days after hospital admission that CSF was collected for MME-18 assay(range) — days | 2.2(1—8) |
A. Screening, Enrollment, and Follow-up

Clinical diagnosis of TBM agreed with MME-18 results (n=17)

Clinical suspected TBM but MME-18 unsupported (n=17)

MME-18 indicates TBM but Clinical diagnosis unsupported (n=20)

Negative of TBM Control (n=13)

B. Protocol for MME-18 Assay

Figure 1 Results of MME-18 Testing and Clinical Effect
Panel A illustrates the flow of patients through the study. Panel B shows the protocol for multiplex PCR assessment for meningitis and encephalitis assay. Following receiving samples of cerebrospinal fluid (CSF), nucleic acid is isolated. The multiplex PCR is performed while the fragment was analyzed with the use of capillary electrophoresis. Panel C shows the concordance between clinical diagnosis and MME-18 results while the similarity of the red and blue illustrates the consistency of MME-18 and GeneXpert results. The positive results of Mycobacterium tuberculosis were detected in 54 of 149 patients (36.2%), a proportion of 31.4% among 54 patients showed concordant results between clinicians and test results. The diagnostic rate was 68.5%. There were 2 different conditions; one was that clinical suspected tuberculous meningitis (TBM) with negative MME-18 results, the other is that clinical diagnosis of TBM is negative with positive MME-18 results. Panel D shows the pathogens distribution of 149 patients that was enrolled in the study.

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**Abstract 865**

**Bacteriophage therapy against multidrug-resistant *Acinetobacter baumannii* infections**

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**Background:** *Acinetobacter baumannii* is very powerful superbug and ranked 1st among the world deadliest superbugs. These superbugs are killing about 700,000 people per year. All the drug including the last resort drugs is resistant to this type of bacterial strain. The infections which are caused by these superbugs are hard to treat and are too expensive. In the past, we don’t have any proper ways to treat *Acinetobacter* infection but nowadays we found one therapy which can treat such infections and we called it “Phage Therapy”. A virus is used to treat the infections caused by bacteria. A bacteriophage is a virus which infects bacteria only and is harmless to the human cell, they also have high therapeutic ratio and they are better than any of the antibiotics because they can penetrate biofilm easily and are the future for multidrug-resistant bacteria’s.

**Materials/methods:** In our study we used *A. baumannii* G7 strain, isolated from the wound of a soldier injured during the war in 2008. For antibiotic sensitivity were used five different antibiotics – Amikacin (30µg), Norfloxacin (10µg), Imipenem (10µg), Ceftazidime (10µg) and Rifampicin (5µg) by using Kirby-Bauer Disk Diffusion Susceptibility Test for antibiotics sensitivity fig.1 (picture2). Bacteriophage sensitivity was done towards 5 specific *Acinetobacter* monophages and 6 phage lysates by using Spot-test technique fig.1 (picture1).

**Results:** Disk diffusion susceptibility test revealed that *A. baumannii* strain used in our study was sensitive to norfloxacin and amikacin antibiotics, but showed resistance to ceftazidime, rifampicin and also to imipenem. Bacteriophage sensitivity showed that from the 11 phages 2 of fig. 1[1,2] had complete lysis, fig. 1[3,4] bacteriophages had Semi-confluent lysis. Fig. 5 and 6 bacteriophages had opaque lysis; Five of eleven phages showed resistance.

**Conclusions:** Bacteria are becoming immune to all drugs. Alternatives to antibiotics could be considered bacteriophages. They have many characteristics that make phages as potentially attractive therapeutic agents. And in the future, the only solution for all the bacteria is the phage therapy as one day all the bacteria will become resistant to every drug and in this situation phages will work and become our future.

**Fig1.**

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Abstract 866

**Application of a multiplex polymerase chain reaction test for diagnosing bacterial enteritis in children in a real-life clinical setting**

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**Background:** Although a variety of multiplex polymerase chain reaction (mPCR) tests have been used for diagnosing bacterial enteritis as a syndromic approach, few studies determined diagnostic accuracy of mPCR tests based on patients’ symptoms and clinical diagnosis in a real-life clinical setting.

**Materials/methods:** Medical records of 710 inpatient pediatric patients (<19 years of age), in whom an mPCR test for 10 bacterial pathogens was performed, were retrospectively reviewed. Based on the clinical diagnosis on discharge, the enrolled patients were divided into two groups: acute gastroenteritis (AGE) group and non-AGE group. Clinical and laboratory characteristics and the mPCR test result were compared between the two patient groups.

**Results:** Among the enrolled patients, 467 (65.8%) and 243 (34.2%) patients were included in the AGE and non-AGE groups, respectively. Upper (37.9%) and lower (21.8%) respiratory tract infections were most common final diagnoses in the non-AGE group. The mPCR test revealed bacterial pathogens in 199 (28.0%) patients: 163 (34.9%) in the AGE group and 36 (14.8%) in the non-AGE group (P<0.001). *Campylobacter* spp. (n=64, 32.2%), *Clostridium difficile* (n=52, 26.1%), *Salmonella* spp. (n=46, 23.1%), and *Clostridium perfringens* (n=41, 20.6%) were most commonly identified. *Campylobacter* spp. (38.7% vs 2.8%, P<0.001) and *Salmonella* spp. (26.4% vs 8.3%, P=0.020) were more frequently identified in the AGE group; whereas, *C. difficile* (18.4% vs 61.1%, P<0.001) and *C. perfringens* (18.4% vs 30.6%, P=0.103) were more frequently identified in the non-AGE group. Among the 199 patients with positive mPCR test results, patients in the AGE group were older (median 7 years vs 2 years, P=0.002), more likely to have gastrointestinal symptoms (100% vs 86.1%, P<0.001), and less likely to have respiratory symptoms (8.0% vs 44.4%, P<0.001) compared to those in the non-AGE group.

**Conclusions:** More detailed history taking and physical examination can reduce performing unnecessary mPCR tests in patients with gastrointestinal symptoms. In pediatric patients suspected to have AGE, the clinical significance of each bacterial pathogen identified by an mPCR test should be determined individually. *Campylobacter* spp. and *Salmonella* spp. can be considered true pathogens, however, *Clostridium* spp. may be a bystander.

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Abstract 873

Development of a routine laboratory test enabling the detection of dermatophytes as well as the identification of *Trichophyton rubrum* by means of duplex real-time PCR from mycological samples and cultures

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**Background:** Dermatophytes are responsible, in majority, for fungal infections of the skin, hair and nails and *Trichophyton rubrum* is the most frequently isolated dermatophyte. The time of growth in culture and microscopic morphology identification (the "gold standard") requires a total of two to four weeks. Molecular methods were developed to improve time for diagnosis and treatment. We will present and demonstrate here the suitability of an in-house method enabling at the same time the detection, through duplex real-time PCR analysis, of dermatophyte positive samples and the direct identification of *Trichophyton rubrum*.

**Materials/methods:** Prior to real time PCR, nucleic acid extraction and purification steps are crucial. Different sample pre-treatment conditions were tested: with and without agitation and/or heating at 95°C (203°F). The highest yield of nucleic acid was obtained with a complete pre-treatment combining agitation and heating. After the pre-treatment, the samples were processed on the NucliSENS® EasyMag® (bioMérieux) according to the manufacturer’s recommendations. Finally, the extracted nucleic acids were performed on the CFX-96™ (Bio-Rad) with specific probes and primers. All positive samples for dermatophytes were identified by sequencing (ITS1 -5.8S-ITS2).

**Results:** One hundred ninety-nine mycological samples were studied (one hundred forty-four nails and fifty-five skin samples) according to conventional methods and DERTR PCR. The sensitivity, specificity, positive and negative predictive values of each target were calculated and are respectively: 97.9%, 76.8%, 57.3% and 99.1% for dermatophytes; 95.2%, 97.9%, 67.8% and 98.6% for *Trichophyton rubrum*. These results demonstrate that the duplex DERTR PCR is a suitable method for rapid diagnosis of dermatophytosis and identification of *Trichophyton rubrum*.

**Conclusions:** We developed an in-house duplex real-time PCR able to detect dermatophytes and identify at the same time *Trichophyton rubrum* from mycological samples and cultures. This method routinely used as enable a diagnosis within four hours in contrast to the two to four weeks required with the conventional methods. This real time PCR has been submitted for accreditation ISO 15189 in November 2019.

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Abstract 892

The effect of mesenchymal stem cells on the mortality of severe sepsis and septic shock: a promising therapy

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Background: The aim of this study is to assess the effect of mesenchymal stem cells on the mortality of sepsis and septic shock.

Materials/methods: During two years, 10 patients with severe sepsis and septic shock were included into the study from Medical and Anesthesiology and Reanimation Intensive Care Units. Mesenchymal stem cells (MSCs) treatment was added to standard therapy of sepsis. Patients received 1*10^6/kg MSC on the 1st, 3rd, 5th, 7th and 9th days of ICU admission. Peripheral blood samples from patients were obtained before MSCs treatment and on the day of MSCs treatment for the measurement of cytokine (TNF-α, IFN-γ, IL–2, IL–4, IL–6, IL–10) levels. Outcomes of the patients were compared with the previous observational study conducted in the same ICUs.

Results: In the study group, 6 of 10 patients were male, whose ages were ranged from 22 to 68. Their APACHE II scores were ranged between 14-29. In the control group, 8 of 10 patients were male whose ages were ranged from 29 to 80. Their APACHE II scores were between 18-29. Survival rate for the 7th and 14th days of the 10 patients who were administered stem cell is 100%, survival rate for the 28th day is 70%. Except the patients who had advanced malignancy and uncontrolled source, there were improvements at the laboratory findings (CRP, procalcitonin, leukocyte, etc.) during the times when stem cells were administered to the patients. In the stem cell treatment group, decrease in the SOFA score of the analyses, which were adjusted by age and APACHE II, was statistically significant. A statistically significant change was not observed at the cytokine levels, which was compared the basal measurement of cytokine levels to the days of 1, 3, 5 and 7. In the control group, the survival rate of 10 patients was 60%. The deaths were observed at the control group before the 5th and 7th day of the treatment, no deaths were observed at the stem cell treatment group for the first two weeks and the period of mesenchymal stem cell administration.

Conclusions: Mesenchymal stem cell treatment had positive impact on survival rates of sepsis during the early phase.

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Incidence of influenza-like illness among HIV-positive patients: an outpatient clinic survey-based study

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Background: HIV infection has been associated with increased susceptibility to Influenza and Influenza-like illness (ILI), as well as to worse clinical outcomes within this disease spectrum. We aimed to assess the incidence and predictors of ILI in a cohort of HIV-infected outpatients.

Materials/methods: A survey about the occurrence of ILI symptoms during the previous winter season was applied between January and May 2018 on three HIV outpatient clinics in a tertiary care centre. ILI case was defined according to the European Center for Disease Control. The survey was complemented with the clinical and laboratory features retrieved from Hospital electronic data records. An explanatory model for ILI was explored by multivariate regression analysis. The study was approved by the institutional ethics committee.

Results: The study included 232 patients (68% males), aged 47±12 years. Most of the patients were on anti-retroviral therapy (97%) and had suppressed viremia (88%). Median CD4 cell count was 684 cells/μL [interquartile range 455-907]. The cumulative incidence rate was 38.4% (95%CI 30.8-47.2). Influenza vaccination on the concerned season was reported by 45.7% of patients. On multivariate analysis, lower ILI incidence was associated with higher CD4/CD8 ratio (aOR 0.38; 95%CI 0.16-0.94; p=0.04) adjusting for CD4 cell counts. This association was observed only for patients with CD4 counts below 500 cells/μL (aOR 0.10; 95%CI 0.01-0.66; p=0.02). Influenza vaccination and absolute CD4 cell counts were not significantly associated with differing incidence.

Conclusions: A high incidence of seasonal ILI was found. A higher risk of ILI may be associated with lower CD4/CD8 ratio, already described as indicator of an immunosenescent phenotype and increased immune activation. CD4/CD8 ratio may contribute on targeting subsets of patients for vaccination.

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Abstract 894

Safety of temporary interruption of anti-platelets in dengue fever with thrombocytopenia
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Background: Thrombocytopenia commonly occurs in dengue and may be complicated by bleeding. Dengue can occur in adults who may be on long term anti-platelet therapy for comorbidities including myocardial infarction or ischemic stroke. In these cases, clinicians may temporarily discontinue antiplatelet therapy to minimize the risk of bleeding, however this may subject these patients to risk of further ischemic events.

Materials/methods: We conducted a retrospective cohort study of laboratory-confirmed adult dengue patients on antiplatelet therapy and evaluated participants whose anti-platelet therapy was continued versus discontinued. Primary outcome was a composite outcome of major adverse cardiac and cerebrovascular events (MACCE), and all-cause mortality in-hospital and for 1-year post discharge. Secondary outcomes were occurrence of platelet and blood transfusion, and occurrence of dengue hemorrhagic fever (DHF), dengue shock syndrome, dengue with warning signs and severe dengue according to World Health Organization criteria.

Results: In total, 66 patients admitted for dengue fever were on anti-platelet therapy, of which 15 patients were continued on the anti-platelet therapy. We found discontinuation of antiplatelet therapy did not result in higher MACCE and mortality, with 4 (2 non-fatal strokes and 2 mortalities) occurring in the continuation group and 5 (3 non-fatal strokes and 2 mortalities) occurring in the discontinuation group (p=0.192). On the other hand, continuation of antiplatelet therapy did not result in more platelet or blood transfusion (p=0.489 and p=0.567 respectively), DHF (p=0.923) or bleeding manifestations.

Conclusions: Our results suggest that discontinuation or continuation of antiplatelet therapy based on clinical judgement in dengue with thrombocytopenia, is largely safe but further studies are needed.

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Species identification and antifungal resistance of yeasts causing fungaemia at a tertiary care hospital in Madrid, Spain: the coast is clear

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Background: Recent reports alert on an increase of fungaemia episodes caused by either echinocandin resistant C. glabrata isolates or multi-resistant species such as C. auris. We assessed the aetiology and antifungal susceptibility of agents causing fungaemia at a tertiary care hospital in Madrid (Spain) for 12 years.

Materials/methods: Isolates causing fungaemia in patients admitted to Hospital General Universitario Gregorio Marañón from 2007 to 2018 were tested for molecularly identification and in vitro susceptibility to amphotericin B, azoles, anidulafungin, and micafungin according to EUCAST EDef 7.3.1. Fluconazole and echinocandin resistance were assessed using the updated clinical breakpoints v.10.0. Multiple positive blood cultures in a single patient were considered different episodes when separated ≥1 week. Mutations in FKS and ERG11 genes were sought in either echinocandin-resistant isolates or C. albicans fluconazole-resistant isolates, respectively.

Results: We studied 921 episodes from 805 patients (90% of patients developed a single episode). Episodes were caused by C. albicans (45.4%, n=418), C. parapsilosis complex (27%, n=248), C. glabrata complex (12.2%, n=112), C. tropicalis (6.8%, n=63), C. krusei (2.3%, n=21), other Candida spp. (3.1%, n=29), and non-Candida yeasts (3.3%, n=30). Overall, 4.7% (n=42) of Candida isolates were fluconazole-resistant (C. krusei [n=19], C. glabrata [n=11], C. albicans [n=3], C. parapsilosis complex [n=2], and other Candida spp. [n=7]). Echinocandin resistance involved only 0.8% (n=7) of Candida isolates (C. tropicalis [n=3], C. krusei [n=2], C. albicans [n=1], and C. glabrata [n=1]). One out of three fluconazole-resistant C. albicans isolates harboured ERG11 mutations (A114S/G464S). FKS mutations were found in 5/7 echinocandin-resistant isolates (C. tropicalis [R647G FKS1, S645F FKS1]; C. krusei [L701M FKS1, n=2]; and C. glabrata [F659S FKS2]). Non-Candida yeasts showed intrinsic echinocandin resistance and decreased fluconazole susceptibility. Antifungal resistance rate proved steady over the years and was mainly affected by the presence of intrinsically resistant isolates [Figure]. Resistance to amphotericin B was not detected.

Conclusions: Our fungaemia epidemiology did not differ from that previously reported in Spain and C. auris has not been detected in our hospital. Fluconazole and/or echinocandin resistance rates were low and dramatically impacted by species with intrinsic diminished antifungal susceptibility, and did not show signs of increase.

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Abstract 896

Nationwide azole resistance survey in clinical Aspergillus fumigatus isolates: a snapshot of the situation at 30 Spanish hospitals

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Background: Azole-resistant Aspergillus fumigatus isolates, though relatively common in the North of Europe, have been sporadically reported in Spain. We report the largest survey conducted in Spain to assess the burden of azole resistance in A. fumigatus.

Materials/methods: The 30 participating hospitals, covering the majority of Spanish regions, stored all morphologically identified A. fumigatus complex clinical isolates – regardless their clinical significance – from the 15th of February to the 14th of May, 2019. Identification was confirmed by MALDI-TOF and antifungal susceptibility testing performed according to EUCAST 9.3 methodology. Resistant isolates were molecularly identified and cyp51A gene was sequenced in A. fumigatus sensu stricto isolates (itraconazole and/or voriconazole MIC ≥ 2 mg/L).

Results: A total of 848 A. fumigatus complex isolates of 726 patients were collected in 29/30 participating hospitals: A. fumigatus sensu stricto (n=828) and cryptic species [A. lentulus [n=6], A. fumigatiafinis [n=6], Neosartoria tseruiae [n=3], N. udagawae [n=2], A. novafumigatus [n=2], A. thermomutatus [n=1]]. Isolates were mostly (94%) from the lower respiratory tract. The vast majority of patients yielded either A. fumigatus sensu stricto (n=711) or cryptic species (n=10) exclusively, but 5 patients had coexistence of A. fumigatus sensu stricto + cryptic species. Amphotericin B resistance was found exclusively in cryptic species. A total of 64 (7.5%) isolates were resistant to ≥1 azoles. Azole resistance was higher in cryptic species than in A. fumigatus sensu stricto (95%, 19/20 vs. 5.5%, 45/828; Figure), with isavuconazole showing the lowest number of non-wild type isolates. Most of A. fumigatus sensu stricto resistant isolates showed cyp51A gene mutations [TR34-L98H, n=20; other mutations, n=5; WT, n=10]. A. fumigatus sensu stricto harbouring either the TR34-L98H (n=20) or TR46/Y121F/T289A (n=1) mutations were found in patients cared at hospitals located at 7/24 studied cities. We found 50 (7%) patients carrying either cryptic species (n=35) or A. fumigatus sensu stricto (n=15) resistant isolates.

Conclusions: We found 7% of patients carrying azole resistant A. fumigatus complex isolates in Spain. TR34-L98H or TR46/Y121F/T289A were the dominant cyp51A gene mutations in patients (60%) carrying resistant isolates although their presence was not widespread.

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Aetiologies, management and outcome of non-traumatic coma in small children: a prospective study in Benin

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Background: Malaria morbidity and mortality have declined since year 2000 and viral central nervous system infections have been reported as an important cause of hospital admission with coma in malaria-endemic Eastern Africa. Our objectives were to describe the etiologies, management and outcome of non-traumatic comas in small children in Benin.

Materials/methods: This study took place in 2 teaching hospitals. All HIV negative children between 2 and 6 years of age, with a Blantyre Coma Score below or equal to 2 were included. Along with a workup screening for malaria severity signs, a blood culture, a Tropical Fever PCR test (Fast-track diagnostics) and a cerebrospinal fluid (CSF) analysis, including a multiplex PCR (Biofire, Mérieux) were performed. All children with malaria were treated with intravenous artesunate. Patients also had free access to other drugs, including transfusions, prescribed at the study physician’s discretion.

Results: Between March and November 2018, 84 children were included with a M/F sex ratio of 0.68 and a mean age of 43 months. A history of fever was declared in all children, with a mean duration of 4 (1 - 14) days and 90% (76/84) of them had received care provided by a health professional before admission, but only 11 children were given an adequate antimalarial oral therapy. Malaria was the only identified cause of coma in 86% (73/84), 5 had an associated infection (1 aseptic meningitis, 1 Staphylococcus aureus bacteremia, 1 Streptococcus bacteremia, 1 West Nile virus infection, 1 HHV6 CSF infection) and 6 had a non-malarial coma (1 dengue, 1 E. coli bacteremia, 4 unknown). Most (58/84) children received blood transfusions and 23% (20/84) ceftriaxone at admission; the lethality rate was 30 % (26/84).

Conclusions: Cerebral malaria remains by far the most common cause of non-traumatic coma in the study area, with a high lethality rate despite an access to standardized care. For most children, missed opportunities to receive an early and effective antimalarial treatment have been declared. Severe malaria needs to be prevented, but efforts to struggle against malaria should not overlook the capacity building for providing care to life-threatening forms of the disease.

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Abstracts 2020

Abstract 901

The progress towards achieving the UNAIDS ambitious 95% viral suppression target among adults living with HIV in South-Western Nigeria

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Background: In sub-Saharan Africa where genotypic drug resistance testing is rarely performed and poor adherence is blamed for the inability to achieve viral suppression and treatment failure, programmatic approaches to preventing & handling these are thus essential. Hypothesis tested was antiretroviral therapy adherence effect on viral load outcome. This study was aimed at determining and monitoring HIV/AIDS disease progression using viral load to provide prognostic information and evaluate patients for viral suppression.

Materials/methods: This study was an observational study of subjects living with HIV already initiated on antiretroviral therapy for at least six months, enrolled in health facilities across Ondo State, South-Western Nigeria, during a 12-month observation period starting October 2018 till September 2019. Quantitative viral load analysis was done using Polymerase Chain Reaction, Roche Cobas Taqman 96 Analyzer. All data were statistically analyzed, using Statistical Package for the Social Sciences (SPSS), with multiple comparisons done using Post Hoc Bonferonni test.

Results: A total of 8124 adults living with HIV eligible for the study were recruited. Most of them are in the age range of 35 – 39 years, with a mean age of 42.02 ± 10.88 years. 7162 (88.2%) & 1771 (21.8%) of the subjects had viral suppression of <1000 RNA and <20 RNA copies per ml respectively. The unsuppressed subjects went through enhanced adherence counselling (EAC) for three months and viral load test repeated thereafter. 192 patients who had completed the three sessions of EAC and repeated viral load increased the entire suppression numbers to 7339 (90.3%) & 1824 (22.5%) <1000 RNA copies per ml and <20 RNA copies per ml respectively during the period of observation. ART adherence has significant effect on viral load outcome ($\chi^2 = 7.63$, df = 1, P = 0.001).

Conclusions: Current ART regimen & HIV treatment enhanced adherence counseling are key to the achieving viral suppression, thus, routine viral load monitoring will ultimately help in HIV/AIDS disease progression follow up and reduce treatment failure tendencies. This will help more patients stay on first line regimen and prolong their life expectancy, indicating that the UNAIDS last 95 target is achievable.

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Abstract 902

Characterisation and virulence of fibronectin-binding protein of Streptococcus intermedius

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Background: Streptococcus intermedius, a member of the anginosus group of streptococci, is a common commensal organism found in the human oral cavity and gastrointestinal and urogenital tracts. Furthermore, S. intermedius is associated with purulent infections, abscesses and infectious endocarditis. The organism secretes the human-specific cytolysin intermedilysin that is highly homologous to the cholesterol-binding cytolysin streptolysin O from S. pyogenes, pneumolysin from S. pneumoniae, and listeriolysin O from Listeria monocytogenes. In this study, we identified other pathogenic factors and described a fibronectin-binding protein (FBP) homolog of S. intermedius (FbpI) that mediated bacterial adhesion to epithelial cells and virulence in mice.

Materials/methods: S. intermedius GAI 1157 [wild-type (WT)] and isogenic mutant ΔfbpI prepared by homologous recombination were used. The binding activities of S. intermedius strains to fibronectin and epithelial cells were determined using [methyl-3H]-thymidine-labelled bacteria. The fibronectin-binding domain was analysed using recombinant full-length (rFbpI) and N- and C-truncated forms of FbpI. The pathogenicity of FbpI was assessed using a mouse infection model. These mice were subcutaneously injected in the back with suspensions of S. intermedius WT or ΔfbpI. The abscesses were removed and weighed.

Results: The amino acid sequence of FbpI was similar to that of atypical FBPs that do not possess a conventional secretion signal and an anchorage motif. rFbpI was bound to immobilised fibronectin in a dose-dependent manner. The fibronectin-binding activity of the N-terminal construct of rFbpI comprising the translation initiation codon methionine of the open reading frame to Lys265 [rFbpI-N] bound immobilised fibronectin to a much lesser extent than rFbpI. In contrast, a construct comprising the C-terminal domain [Ala266 to Met549; rFbpI-C] bound immobilised fibronectin equivalently to rFbpI. Moreover, the adherence of isogenic mutant ΔfbpI to cultured epithelial cells and immobilised fibronectin was significantly lower than that of the WT strain. Furthermore, the abscess formation of ΔfbpI reduced in the mouse infection model compared with that in the WT strain.

Conclusions: Thus, FbpI may play a role in bacterial adhesion to host cells and represent a critical pathogenic factor of S. intermedius.

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Staphylococcus aureus inhibits opsonophagocytosis and modulates neutrophils extracellular traps formation efficiently during the early stages of biofilm formation

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**Background:** Despite our versatile host immune responses with proven ability to eliminate Staphylococcus aureus invasion, infection with this bacterium is still a serious problem and can be frequently found in clinics, worldwide. Along with acute infection, S. aureus is also associated with biofilm-related chronic infections. In mature biofilms, encapsulated S. aureus cells are well known for their ability to resist the immune system and antibiotic treatment. Contrary, little information is available on immune evasion of S. aureus during the early stages of biofilm formation. Therefore, we studied if S. aureus developed mechanisms to overcome the host innate immune responses during these stages of biofilm development.

**Materials/methods:** S. aureus strains from various genetic background were grown in vitro to form biofilms. The production of immune modulators was studied during the early stage of biofilm formation using mass spectrometry, fluorescence resonance energy transfer (FRET) assay, and Luminex\textsuperscript{\textregistered} based competitive ELISA. The detected immune modulators were studied for their ability to modulate the host innate immune response using several ex vivo setups, like co-incubation of biofilm with complement and study the complement activation. Furthermore, the interactions between biofilm and neutrophils were monitored with confocal microscopy and isothermal microcalorimetry.

**Results:** Contrary to the previous finding, during the early stages of biofilm formation, S. aureus actively releases 87 different proteins which include several immune modulators. Potent immune modulators CHIPS, FLIPr, Map, Sbi, SCIN, thermonuclease (nuc), and Staphylococcal Protein A (SpA) were among the prominent proteins found. We observed that biofilms produce enough SCIN to hinder human complement activation and in this way obstruct C5a release. Furthermore, SpA was found to stimulate NETosis, leading to death of neutrophils. Finally, the thermonuclease produced during the early stages of biofilm formation, broke down these NETs.

**Conclusions:** The main mechanisms of neutrophils to eliminate bacteria, Opsonophagocytosis and NETs formation, can be jeopardized by S. aureus during the early stages of biofilm formation; opsonization and phagocytosis are inhibited by SCIN, while NETs formation and destruction are modulated by SpA and thermonuclease, ensuring the survival of these young S. aureus biofilms.

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Using mechanisms of action to assess new antibiotics against Gram-negative bacteria
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¹KeMyth Biotech Company, Incubation Center, National Health Research Institutes, Miaoli, Taiwan, ²Tri-Service General Hospital, Taipei, Taiwan, ³Taipei Veterans General Hospital, Taipei, Taiwan

Abstract:
In our previous study, a strategic system for testing antibiotics against specific resistance mechanisms has been constructed by using *Klebsiella pneumoniae* (J Antimicrob Chemother 2017; 72: 3302-16), which can facilitate the development of antibiotics that are robustly effective against multidrug-resistant bacteria. Given that the genetic background of several bacterial pathogens with high resistance rates is quite different from that of *K. pneumoniae*, specific resistance genes can be found in these pathogens. In this study, the strategic system has been constructed by using *Acinetobacter baumannii*.

Materials/methods: In-frame deletion, site-directed mutagenesis and plasmid transformation were used to generate genetically engineered strains with various resistance mechanisms from two fully susceptible *A. baumannii* strains. Antimicrobial susceptibility testing was used to test antibiotics against these strains in vitro.

Results: A total of 50 engineered strains with various resistance mechanisms from *A. baumannii* KAB1544 and ATCC 17978 were constructed. These strains included 31 strains with chromosome-mediated resistance and 19 strains with plasmid-mediated resistance, and each of the 50 resistance mechanisms showed similar effects on the MICs for KAB1544 and ATCC 17978. Compared to the parental strains, the engineered strains related to some efflux pumps showed a significant (≥4-fold) difference in the MICs of β-lactams, quinolones, aminoglycosides, tetracyclines, folate pathway inhibitors and/or phenicols, while no significant (≥4-fold) effects on the MICs were found for the engineered strains lacking OmpA, CarO, Omp25, Omp33, OmpW or OprD. Mechanisms due to GyrA/ParC mutations, β-lactamase, aminoglycoside-modifying enzyme, 16S rRNA methylase and tet resistance gene contributed their corresponding resistance as previously published.

Conclusions: Strains constructed in this study have clear resistance mechanisms and can be used to screen and assess compounds against specific resistance mechanisms for treating *Acinetobacter*. In addition to our previously published system for *Enterobacteriaceae* and our under-construction system for *Pseudomonas*, the combination of these three systems could increase the coverage of bacterial types for drug assessment and facilitate the selection process of new candidates in the drug development against superbugs.

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Abstract 908

**Using machine learning for improving MLST analysis of nanopore sequenced bacteria**

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**Background:** Due to the inherently high random and systematic error rates in Oxford Nanopore sequencing data, bacterial typing methods such as MLST are not easily implemented in a long read bioinformatic workflow. To account for the high error rates, different polishing tools have been developed. Here, we investigate if polishing with Racon and Medaka can improve MLST analysis for Nanopore data assembled with the Flye assembler.

**Materials/methods:** We have trained recurrent neural networks for polishing long read assemblies with the Medaka software from Oxford Nanopore Technologies. One of the pre-trained Medaka models was individually fine-tuned on three different data-sets consisting of *Enterococcus faecium*, *Klebsiella pneumoniae* and *Staphylococcus aureus*. We evaluated both Flye assemblies polished by Racon and non-polished Flye assemblies.

Quast and DNAdiff were used to analyze the quality of the polishing and all assemblies were also subjected to a BLAST based MLST analysis where the number of correctly predicted STs and alleles were counted.

**Results:** By training a model on a subset of a specific dataset and evaluating on the remaining samples, we saw a substantial increase in sequence identity for the test samples. The results also show that polishing with Racon prior to polishing with Medaka can actually decrease the performance compared to using Medaka directly on a draft assembly.

Running MLST analysis on the draft assemblies (48 test samples in total) resulted in zero correct STs. However, using the fine-tuned Medaka models, we could correctly predict 42 STs, with an allele prediction rate of 97.6%. The model trained on the *K.pneumoniae* dataset was also evaluated on a larger, unseen *K.pneumoniae* dataset. The MLST analysis for this dataset, consisting of 36 samples, resulted in zero correct STs for the draft assemblies and 26 correct STs after polishing with Medaka. The allele prediction rate increased from 69.4% for the draft assemblies to 96.0% after polishing with Medaka.

**Conclusions:** This study shows that using machine learning for polishing assemblies enables MLST analysis of Nanopore data. However, a more diverse training set is needed in order to build a more robust polishing model.

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Abstract 909

Performance of the urine flow cytometer Sysmex UF-5000 in rapid diagnosis of urinary tract infections

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Background: Urinary tract infection (UTI) is one of the most common bacterial infections worldwide. Urine culture is the gold standard method to diagnose UTI, but is time consuming and tedious. Urine flow cytometry (FCM) can differentiate and quantify particles in urine, and is an alternative method for ruling out UTI. The aim of this study was to evaluate FCM as a rapid screening method to predict urine samples with negative or mixed culture growth.

Materials/methods: We performed standard microbiological analysis and FCM with the Sysmex flow cytometer UF-5000 on 3919 urine samples from both outpatients and hospitalized patients. 2565 (65%) samples were from women and 1354 (35%) were from men. Positive urine culture was defined as growth ≥10⁴ cfu/mL. Results from 17 FCM parameters and culture were evaluated to identify a) positive culture versus no culture and b) mixed culture (>2 organisms) versus pure culture (≤2 organisms) by the use of FCM.

Results: Positive culture (≥10⁴ cfu/mL) was found in 2257/3919 (57%) urine samples; 1351 were pure and 906 were mixed cultures. ROC curve analyses comparing results from culture growth with different FCM parameters identified bacterial count (BACT; area under the curve [AUC] 0.939) and leucocyte count (WBC; AUC 0.809) as possible independent predictors for bacterial growth. Subpopulation analyses [men/women/inpatients/outpatients/immunocompromised/pregnant] revealed little association between FCM results and culture growth in pregnant women, leading to exclusion of this subpopulation (n=452). Investigation of different cut-offs for BACT and WBC, separate and in combinations, indicated that WBC marginally improved the outcome in combination with BACT (sensitivity 96.6%; negative predictive value [NPV] 92.3%), compared to BACT alone (sensitivity 95.2%; NPV 91.2%) using BACT/WBC cut-off 30. There was no difference between urine from in- or outpatients. Analyses comparing FCM parameters squamous epithelial cells (SquaEC) and epithelial cells (EC) with mixed culture indicated that neither were predictors for mixed culture.

Conclusions: FCM cannot predict mixed culture growth [ie, indication of contamination of specimen], but it can predict negative culture growth in both men (NPV 94.7%) and non-pregnant women (NPV 84.7). This reduces time-to-negativity compared to gold standard, which could potentially reduce unnecessary usage of antibiotics.

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Abstract 911

High prevalence of antimicrobial resistance in community-acquired urinary tract infections in Harare, Zimbabwe

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Background: Antimicrobial resistance (AMR) is compromising our ability to successfully treat infections. The Global Action Plan on AMR proposed by the WHO emphasizes the importance of strengthening surveillance in the attempt to limit the effects of AMR. There are few data on gram-negative AMR prevalence in sub-Saharan Africa especially from the outpatient setting. First-line treatment for urinary tract infections [UTIs] as recommended by Zimbabwe National Guidelines is amoxicillin or a fluoroquinolone which may not be optimal in the context of increasing AMR.

The aim of this study is to estimate the prevalence and risk factors for AMR in isolates from outpatients presenting with suspected UTIs to primary care clinics in Harare.

Materials/methods: Adult outpatients presenting with symptoms of UTI to six clinics in southern Harare between July and November 2019 were recruited. A urine sample was collected and inoculated on chromogenic agar. Cultures were considered positive if a growth of >10³ CFU/ml of a known pathogen was obtained. Antimicrobial susceptibility testing [AST] using disc diffusion and EUCAST breakpoints was performed.

Results: Of the 383 adult participants recruited into the study, 256 (66.8%) were female. HIV infection was present in 90/337 (26.7%) patients who knew their status. 125 (32.6%), 222 (58.0%), and 36 (9.4%) cultures yielded an organism at >10³ CFU/ml, no growth, and contamination respectively. The most common pathogen was E. coli, identified in 106/125 (85%) to ampicillin, 94 (82%) to cotrimoxazole, 22 (18%) to ciprofloxacin, and 21 (18%) to third generation cephalosporins. No carbapenem resistance was recorded. HIV infection and a previous UTI were associated with the presence of third-generation cephalosporin resistance (Table).

Conclusions: The prevalence of resistance to first-line antibiotic treatment for uncomplicated UTI in this setting was high, emphasizing the need for AMR surveillance to inform setting specific guidelines. HIV infection may be a driver for AMR in this setting highlighting the need to give special consideration to this group when making empirical treatment decisions.

Table. Risk factors for resistance to third generation cephalosporins in Enterobacteriaceae

<table>
<thead>
<tr>
<th></th>
<th>Total (N=118)</th>
<th>3rd GC resistance (N=118)</th>
<th>No resistance to 3GC (N=97)</th>
<th>OR (95% CI)</th>
<th>aOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>98 (83%)</td>
<td>17 (81%)</td>
<td>81 (84%)</td>
<td>0.83 (0.25-2.84)</td>
<td>-</td>
</tr>
<tr>
<td>Age (years), median (IQR)</td>
<td>29 (22-42)</td>
<td>31 (22-38)</td>
<td>28 (23-46)</td>
<td>0.98 (0.94-1.01)</td>
<td>-</td>
</tr>
<tr>
<td>HIV positive, n (%)</td>
<td>25 (25%)</td>
<td>7 (41%)</td>
<td>18 (21%)</td>
<td>2.61 (0.85-7.98)</td>
<td>2.68 (0.82-8.8)</td>
</tr>
<tr>
<td>Pregnancy, n (%)</td>
<td>12 (13%)</td>
<td>2 (13%)</td>
<td>10 (13%)</td>
<td>1.00 (0.19-5.15)</td>
<td>-</td>
</tr>
<tr>
<td>Prior antimicrobial use, n (%)</td>
<td>44 (37%)</td>
<td>10 (53%)</td>
<td>34 (36%)</td>
<td>1.99 (0.73-5.45)</td>
<td>0.95 (0.28-3.20)</td>
</tr>
<tr>
<td>Prior hospital admission, n (%)</td>
<td>7 (8%)</td>
<td>0 (0)</td>
<td>7 (7%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Prior UTI</td>
<td>23 (20%)</td>
<td>6 (33%)</td>
<td>17 (18%)</td>
<td>2.29 (0.74-7.08)</td>
<td>2.58 (0.69-9.80)</td>
</tr>
</tbody>
</table>

*HIV status was unknown for 16, 8 women did not know their pregnancy status; 3GC third-generation cephalosporin

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Abstract 913

**Lassa fever infection and prevention control availability and use at healthcare facilities in South-Western Nigeria**

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**Background:** Lassa fever is a zoonotic infection caused by arenavirus contracted primarily through contact with the contaminated excreta of Mastomys natalensis rodents. Secondary transmission of the virus between humans occurs through direct contact with infected blood or bodily secretions. The objective of this study was to assess the availability of infection & prevention control measures, consumables & their use in healthcare facilities in Western Nigeria.

**Materials/methods:** This study was a cross sectional study. Data was collected by trained volunteers and supervised by appointed supervisors and investigators, by a face-to-face interview using a pre-tested structured questionnaire on Lassa Fever. Frequency count was generated for all variables and statistical test of significance was performed with Chi-Square test.

**Results:** Eighty five healthcare facilities & workers were surveyed, out of which 80 (94.1%) had wash hand basins but only 48 (56.5%) had running water or any kind of water supply. Most, 55 (64.7%) & 49 (57.6%) of the healthcare workers do not practice hand washing before/after patient contact & had not been trained on infection control while only 48 (56.5%) were regularly using personal protective equipment such as white coat & gloves. There was no association between availability of personal protective equipment & its use ($\chi^2 = 3.02$, df = 1, $P = 0.403$).

**Conclusions:** Healthcare facilities do not meet the minimum standard for infection prevention & control measures. It is therefore recommended that government at all levels should immediately prioritize the infection prevention & control programs its health facilities to curb future spread of infectious diseases even in hospital premises among healthcare workers.

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Abstract 917

Achieving the third 95: Keeping adolescents living with HIV virally suppressed in rural Nigeria in test and treat era using continuous quality improvement model of peer counseling & support group

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**Background:** In 2016, Nigeria transitioned to “Test & Treat”, a policy where all people living with HIV (PLHIV) are treated with lifelong antiretroviral therapy (ART). There are unique challenges achieving viral suppression in ALHIV mainly due to increased stigma, discrimination & lack of social support. Hypothesis tested was antiretroviral therapy adherence effect on viral load outcome. We examined viral suppression among adolescents living with HIV in rural Western Nigeria.

**Materials/methods:** This study was an observational study of adolescents living with HIV (ALHIV) already initiated on antiretroviral therapy for at least six months, enrolled in health facilities in rural parts of Western Nigeria, during a 12-month observation period starting October 2018 till September 2019. Quantitative viral load analysis was done using Polymerase Chain Reaction, Roche Cobas Taqman 96 Analyzer. All data were statistically analyzed, using Statistical Package for the Social Sciences (SPSS).

**Results:** A total of 316 subjects eligible for the study were recruited. Most of them are in the age range of 10 – 19 years, with a mean age of 13.51 ± 2.86 years. 222 (70.3%) & 52 (16.5%) of the subjects had viral suppression of <1000 and <20 RNA copies per ml respectively. The 94 subjects went through peer counseling by trained ALHIV and enhanced adherence counseling (EAC) for three months and viral load test repeated thereafter. 22 patients who had completed the three sessions of EAC and repeated viral load increased the entire suppression numbers to 244 (77.2%) & 60 (19.0%) <1000 and <20 RNA copies per ml respectively during the period of observation. The ALHIVs in the process joined the institutionalized social-media driven support group & adolescent decentralized care model ensuring they achieve the third 95 at undetectable viral load level. ART adherence has significant effect on viral load outcome ($\chi^2 = 20.902$, df = 1, $P = 0.001$).

**Conclusions:** Antiretroviral therapy (ART) treatment adherence counseling is key to the achieving viral suppression and determine infection prognosis, thus, developing robust continuous quality improvement (CQI) plans to address issues across the cascade ultimately helping in the monitoring of HIV/AIDS disease progression and decrease treatment failure tendencies.

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Abstract 922

**Assessment of viral load suppression rates among paediatric patients living with HIV in South-Western Nigeria**

Saheed Usman*

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**Background:** In resource-limited settings, where genotypic drug resistance testing is rarely performed and unsuppressed viral load outcome is a function of poor drug adherence, programmatic approaches in scaling up optimal adherence is essential. The aim of this study was to assess the viral load suppression rates among pediatric patients living with HIV using ART multi-month scripting model in south-western Nigeria.

**Materials/methods:** This study was a longitudinal study conducted on 283 paediatric patients living with HIV (136 males and 147 females) enrolled into antiretroviral therapy from a selected health facilities across Western Nigeria, during a 12-month observation period starting October 2018 till September 2019. Quantitative viral load analysis was done using Polymerase Chain Reaction, Roche Cobas Taqman 96 Analyzer. All data were statistically analyzed, using Statistical Package for the Social Sciences (SPSS), with multiple comparisons done using Post Hoc Bonferroni test.

**Results:** Most of the respondent were within the age range of 6 – 9 years, with a mean age of 6.07 ± 2.08 years. 167 (59.0%) & 37 (13.1%) of the subjects had viral suppression of <1000 RNA copies per ml and <20 RNA copies per ml respectively. The unsuppressed subjects went through enhanced adherence counselling (EAC) for three months and viral load test repeated thereafter. 33 patients who had completed the three sessions of EAC and repeated viral load increased the entire suppression numbers to 200 (70.7%) & 60 (19.0%) <1000 RNA copies per ml and <20 RNA copies per ml respectively during the period of observation. ART adherence has significant effect on viral load outcome from the study hypothesis tested ($\chi^2 = 15.763$, df = 1, $P = 0.001$).

**Conclusions:** Current ART regimen & HIV treatment enhanced adherence counseling are key to the achieving viral suppression, thus, routine viral load monitoring will ultimately help in HIV/AIDS disease progression follow up and reduce treatment failure tendencies. This will help more paediatric patients stay on first line regimen and prolong their life expectancy, indicating that the UNAIDS last 95 target is though achievable but more work is still to be done.

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Abstract 927

Co-infection with *Staphylococcus aureus* after primary influenza virus infection results in endothelial damage

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**Abstract third-party references:** F Jena University Hospital, Center of Sepsis Care and Control, Section of Experimental Virology, Institute of Medical Microbiology

**Background:** The seasonal influenza virus (IV)-associated bronchopneumonia is one of the infectious diseases with the highest population-based mortality. Beyond the virulence of the virus itself, epidemiological data suggest that bacterial co-infections are the major cause of increased mortality. In this context, *Staphylococcus aureus* (*S. aureus*) represents a frequent causative bacterial pathogen in secondary pneumonia. Post-influenza models of *S. aureus* pneumonia demonstrate the severe outcome of a coinfection associated with substantial morbidity and mortality. To date, investigations concerning microbial infections of the lung are usually carried out in animal models. However, lung anatomy and physiology, as well as composition of the immune system differ significantly between rodents and humans.

To investigate the interactions between epithelial, endothelial and immune cells after IV / *S. aureus* co-infection, we established a human alveolus-model that generated a reactive tissue-tissue interface between the vascular endothelium and the airway-facing epithelium.

**Materials/methods:** MOTiF biochips were seeded with human endothelial cells on the vascular site and with epithelial cells and macrophages on the airway site. This organoid was cultured for up to 14 days with a stable and stable air-liquid interphase under dynamic flow conditions.

**Results:** Dynamic conditions that maintain the air-liquid-interface allow a stable barrier with high transepithelial resistance and an intact vasculature. We provide evidence for an increase of barrier integrity after introduction of macrophages, as proven by TEER measurement and permeability tests. Our data indicate a stable surfactant production of alveolar epithelial cells type II. Subsequent infection has been successfully established and pathogenicity factors can be investigated.

**Conclusions:** We established a functional, biochip-based human *in vitro* alveolus model that is suitable for investigation of complex co-infections and immune functions. Separated airway and vascular chambers allow infections with pathogens from the airway site.

Inducing an immune response using this method, it is possible to observe migration of immune cells from the vascular site to the infection to study species-specific mechanism of pathogens. Our results suggest that the endothelium is disrupted earlier than the epithelium, and *S. aureus* is able to inhibit the IV-induced apoptotic cellular response on the level of procaspase 8 inhibition.

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Abstract 929

Pilot evaluation of machine learning for the classification of *Streptococcus pneumoniae* PCV-13 serotypes from non-PCV13 serotypes based on MALDI-TOF MS analysis

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**Background:** *Streptococcus pneumoniae* serotyping is limited to Reference Laboratory. Knowing the serotype is of great significance from an epidemiological and preventive perspective because it makes possible to define the distribution of serotypes causing invasive pneumococcal disease (IPD). The PCV-13 includes 13 serotypes {1,3,4,5,6A,6B,7F,9V,14,18C,19A, and 23F}. The main aim of this work was to assess if the mass spectra obtained by MALDI-TOF MS showed specific discriminatory peaks, using machine learning algorithms, and if those peaks were able to differentiate PCV-13 serotypes from NON-PCV13 serotypes. Therefore using this methodology as screening tool in order to then, use the reference method in a more targeted way.

**Materials/methods:** The study included PCV-13 isolates and the top 10 of the most prevalent NON-PCV13 isolates {12F, 24F, 13, 8, 11A, 15B, 16F, 22F, 7C and 23B}, which were selected according to the Argentina national epidemiology, all isolates were previously serotyped by Quellung reaction. Mass spectrum analysis was performed using a MicroFlex LT mass spectrometer [Bruker Daltonik GmbH] and the procedures were conducted according to the manufacturer’s instructions. Classification models were generated using the machine learning [ML] algorithms in ClinProTools, namely QuickClassifier [QC], Supervised Neural Network [SNN], and Genetic Algorithm [GA]. All the peaks in the spectra were used in model generation.

**Results:** In this first part of the pilot evaluation, we were able to discriminate two groups types, making it possible to differentiate PCV-13 from NON-PCV13 isolates. GA, showed the best cross-validation and recognition capacity values. (Table 1)

**Conclusions:** A combination of MALDI-TOF MS analysis and ML models may be a potentially efficient screening tool for *Streptococcus pneumoniae* serotipification, although an external validation must be done in a second part of the pilot evaluation and more isolates whose serotypes are unknown should be challenged with all the algorithms in order to evaluate the real use of this methodology.

Table 1.

<table>
<thead>
<tr>
<th>CLASSIFICATION ALGORITHMS</th>
<th>RECOGNITION CAPABILITY</th>
<th>CROSS VALIDATION</th>
<th>PEAKS USED IN MODEL</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA</td>
<td>100%</td>
<td>80.0%</td>
<td>15671, 3975, 7054, 2983, 2597</td>
</tr>
<tr>
<td>SNN</td>
<td>100%</td>
<td>81.9%</td>
<td>4303, 7054, 3975, 4795, 4997, 410785</td>
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Factors influencing vaccination coverage among children age 12–23 months in Afghanistan

Mubarak Mohammad Yousuf*1, Ahmad Khalid Aalemi2, Karimullah Shahpar3

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Abstract third-party references: ICF

Background: Childhood vaccination plays a key role in reducing morbidity and mortality from vaccine-preventable diseases. Numerous studies have assessed the influence of demographic and socioeconomic factors on child immunization around the world. There are few such studies in Afghanistan, however. Therefore, this study aimed to identify factors influencing vaccination status among children age 12–23 months in Afghanistan.

Materials/methods: Nationally representative data from the 2015 Afghanistan Demographic and Health Survey were used for this study. A sample of 5,708 children age 12-23 months with a vaccine card and immunization history was analyzed. Multinomial logistic regression was used to identify significant relationships between cofactors and vaccination status.

Results: In the study, half of the subjects were boys (51%), almost half were born at home (48%), and about three-fourths were residents of rural areas (76%). Background characteristics positively associated with vaccination status included delivery in a health facility, maternal age 30-39, attending at least four visits for antenatal care (ANC), health facility visit in the past 12 months, paternal professional occupation, and family in the richer wealth index.

In bivariate analysis, the central region showed the highest prevalence of full vaccination among children age 12-23 months. Controlling for cofactors, however, children in the northeast region were more likely to be vaccinated compared with children in the central region, while children in the southern region were less likely to be fully vaccinated.

Conclusions: This study identified maternal age, ANC visits, place of delivery, health facility visits in past 12 months, paternal occupation, wealth quintile, and geographic region as the factors influencing child’s vaccination status in Afghanistan.

Key words: vaccine; immunization; children age 12-23 months; influencing factors; Afghanistan.

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Abstract 931

A multi-site evaluation of antifungal prescribing and the use of fungal diagnostics in critical care

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Background: Critical care patients are at higher risk of invasive fungal infections (IFI). Understanding the utilisation of antifungal drugs and diagnostics in intensive care units (ICU) is essential for the development of antifungal treatment pathways and stewardship.

Materials/methods: A 6-month evaluation (May-November 2019) of all antifungal prescribing episodes in medical and surgical ICUs across three London Trusts (collectively 168 ICU beds). ‘Antifungal prescribing episode’ was defined as a period of continuous antifungal therapy for a specified indication. Drug; duration; indication; treatment rationale at initiation (prophylaxis, empirical [clinical suspicion alone], pre-emptive [suggestive radiology/positive biomarkers], targeted at IFI, targeted at non-invasive infection [e.g. Oral candidiasis]; fungal diagnostics and final IFI classification were reviewed. Analyses were conducted in Microsoft Excel and GraphPad Prism V7.

Results: There were a total of 353 prescribing episodes in 305 patients (16% patients ≥2 episodes). Prescribing rationale at the start of the episode was 21% prophylaxis (median [IQR] duration of treatment 8 [4-18] days); 48% empirical [7 [3-11] days]; 9% pre-emptive [11 [7-21] days]; 11% targeted for IFI [16 [11-22] days]; 11% targeted for non-invasive infection [4 [2-7] days].

Overall, fluconazole was the most frequently prescribed [fluconazole 42%; echinocandins 38%; triazoles 11%; amphotericin 8%], however echinocandins accounted for the majority (52%) of all empiric/pre-emptive/IFI targeted prescribing.

For empirical therapy, a blood culture was sent in 72% and non-culture based tests in 48%. Serum beta-d-glucan [BDG] turnaround time [TAT] was significantly shorter for the ICU with diagnostics available on-site [median [IQR] TAT of 1 [1-2] day] compared to the two sites processing BDG at external laboratories [14 [12-17] days, 10 [8-12] days] [p =0.001]. There was no significant difference in duration of empirical treatment for those with a negative BDG versus no BDG sent (8 versus 7 days [p=0.37]).

Regarding final IFI classification; 43 (14%) patients had proven IFI [40 invasive candidiasis; 3 invasive mould]. Data on probable/possible/no IFI cases, clinical outcomes and antifungal defined daily dose/occupied bed days will be presented.

Conclusions: In the ICU setting, antifungal prescribing is predominately empirical. Rapid non-culture based diagnostic tests regarded as robust by clinicians, are required to influence antifungal prescribing decision-making in this high-risk patient group.

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Abstract 932

**Antibiotic prescribing decisions in intensive care: a qualitative study**

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**Abstract third-party references:** On behalf of the INHALE WP2 study group

**Background:** Antimicrobial stewardship (AMS) is a key issue in intensive care units (ICUs) where antibiotics are widely prescribed for complex patients. However, there is limited research examining how antibiotic prescribing decisions are made and how antimicrobial resistance (AMR) concerns impact decision-making in this context. INHALE is a comprehensive research programme exploring the influence of molecular diagnostics on prescribing for hospital acquired pneumonia (HAP) in ICU. This study explored how prescriber perceptions and contextual factors influence antibiotic prescribing decisions in ICUs, prior to implementation of molecular tests.

**Materials/methods:** Four focus groups and 34 vignette-based interviews were conducted with clinicians involved in antibiotic prescribing in four UK ICUs. Focus groups explored clinicians’ perceptions of factors influencing their prescribing decisions and semi-structured interviews explored decision-making processes using two clinical vignettes in the context of HAP. Data were analysed using inductive thematic analysis.

**Results:** Prescriber perceptions were key to decision-making. Most clinicians balanced the societal risks of AMR against the needs of the individual patient, with the latter generally given precedence. In situations of doubt, the default was to prescribe antibiotics on the basis that the antibiotics might prevent patient mortality, with clinicians viewing prescribing as more defensible than not prescribing. The side-effects of antibiotics were rarely mentioned. Clinicians were aware of AMR and strove to withhold potentially unnecessary antibiotics where possible. This aim was counter-balanced by their previous experiences of negative consequences, which motivated the prescribing of antibiotics ‘just in case’ of an infection.

Clinicians’ perceptions interacted with the prescribing context. Examples include a lower perceived threshold to prescribe antibiotics out of hours, the influence of input from non-ICU team members, as well as antibiotic prescribing norms and varied adherence to guideline recommendations across ICUs.

**Conclusions:** When making prescribing decisions, clinicians’ understandable fear of undertreating possible infection and worsening outcomes is often in direct conflict with AMS aspirations. Prescribers seem to be driven by perceived negative consequences for patients and themselves over more distal issues of AMR. Evidence-based support from faster and more effective diagnostics may help reconcile these competing priorities by allowing for earlier antibiotic de-escalation and refinement.

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Abstract 933

Resistant bacteria in retail meat
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Background: Surveillance of antimicrobial resistance in foodborne bacteria is part of the WHO "Global Action Plan on Antimicrobial Resistance". Often surveillance focuses on specific bacteria, resistance mechanisms or production animals. We wanted to investigate, with a broad-range culture approach and PCR, if retail meat could be a possible source of resistant bacteria.

Materials/methods: Personnel from the Department of Clinical Microbiology, Odense University Hospital, were asked to swab their non-frozen retail meat in the kitchen just before preparation. Samples of pork, chicken and beef (100 of each) distributed evenly over one year were swabbed (10 cm x 10 cm) with FecalSwab (Copan, Italy) and stored at -80°C. All samples were cultured with selective and non-selective media, including media to detect MRSA, VRE, ESBL, CPO and Clostridioides difficile. MALDI-TOF and disk diffusion were used for identification and susceptibility testing. Also, PCR with the Allplex Entero-DR kit (Seegene, South Korea), detecting NDM, KPC, OXA-48, VIM, IMP, CTX-M, VanA, VanB genes, was performed.

Results: Any growth was seen from 92% of the samples (276/300). Staphylococcus aureus was detected in 23 (8%) samples, mainly chicken (17), of which one was an MRSA from pork. Enterococcus spp. were detected in 46 (15%) samples of which one was a VRE from pork. Twenty-nine different species of Enterobacterales was identified and one or more species were detected in 48% of the samples. No ESBLs were detected with the culture method but several of the identified species harbor chromosomal AmpC. Pseudomonas spp. (non-aeruginosa) were detected in 44% (133) of the samples. In 124 samples Pseudomonas was detected on the CPO selective media. From a random sample of 40 isolates, only three was not fully susceptible to meropenem. C. difficile was not detected in any of the samples. With PCR OXA-48 was detected in four samples, CTX-M in two, and vanA (identical with culture) and vanB in one sample each.

Conclusions: Retail meat could be a possible source of resistant bacteria. However, sequence typing is needed to establish that the same bacteria from this study can be found in humans. Even so, good kitchen hygiene will prevent transmission to humans.

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Abstract 935

Is there an increased risk for Clostridium difficile infection months after hospitalisation in a room occupied previously by a patient with C. difficile?

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Background: Clostridioides difficile (CD) is the most common infectious cause of acquired diarrhoea in healthcare systems with significant morbidity and mortality. Several risk factors for C. difficile infection (CDI) exist; antibiotic use and environmental exposure are probably the most important modifiable risk factors.

Aims: to explore whether hospitalization in room that was previously occupied by a patient with CDI (r-CDI) and cleaned according to standardized protocol is a risk factor for CDI.

Setting: the Baruch-Padeh Medical Center in northern Israel, a 350-bed hospital with a relatively-high rates of acquired CDI (40-45/100,000 cases/patient-days during 2017-2018).

Materials/methods: A retrospective case-control study comparing patients with CDI to a matched control group (age, sex and ward of hospitalization) without CDI during 2017-2018. Clinical and demographic data were collected from electronic medical records, including data on known risk factors, patient-room-placement, and movements during hospitalization. For every participant we determined whether there has been an r-CDI exposure at different timeframes (1, 3, 6 and 12 months previously).

Results: Study population included 75 CDI patients and 75 control patients. The groups had similar performance status and Charlson’s comorbidity index. Length of stay prior to inclusion was similar in both groups, but was on average 2.7 days longer after inclusion in patients with CDI. Thirty-day mortality was higher in patients with CDI (36% versus 16%). In multivariate analysis: the presence of a nasogastric tube, use of 3rd generation cephalosporins and macrolides were independently associated with CDI. Previous exposure to r-CDI was significantly higher in the CDI group through all timeframes examined, the difference was significant if exposure occurred 3, 6 and 12 months previously (p= 0.032, 0.006, and 0.011, respectively); the association was maintained after adjustment for other risk factors (p= 0.014, 0.006, and 0.011, respectively).

Conclusions: Hospitalization in a room previously occupied by a patient with CDI is a significant risk factor for CDI up to 12 months after exposure. This work may assist in planning interventions for reduction of CDI healthcare acquisitions, such as environmental cleaning, antibiotic stewardship and cohorting CDI patients when necessary. Typing of CD isolates is of paramount importance and is currently underway.

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Risk factors and clinical characteristics of virus infection after haematopoietic stem cell transplantation

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Background: BK polyomavirus is an important cause of morbidity and mortality in hematological patients after hematopoietic stem cell transplantation (HSCT). It is acquired in childhood and especially becomes latent in urothelial epithelial cells. Reactivation of virus after HSCT can be seen with asymptomatic viruria or hemorrhagic cystitis (HC). The aim of the study was to assess risk factors, clinical characteristics and treatment options of BK virus infection after HSCT.

Materials/methods: We retrospectively analyzed information about patients with HSCT and BK virus (BKV) disease between January 2017-August 2019. Data included; underlying hematological disease, transplantation type, associated graft versus host disease (GVHD) and recent use of immunosuppressive agent.

Results: In total fifty-eight patients with HSCT were evaluated and BKV disease occurred in 20 (34%). The median age was 40 (range, 20 to 68), 50% were male. The most underlying disease was Acute Myeloid Leukemia (n=11). Five patients had autologous and fifteen patients had allogeneic SCT. The median time to engraftment was 15 days (range, 10 to 20). GVHD was seen eleven patients (40% skin, 15% gastrointestinal GVHD). These patients received systemic glucocorticoid therapy or immunosuppressant agents. The median time elapsed to BK virus disease after HSCT was 60 days (range, 30 to 450). Sixteen patients with BKV disease had high grade (grade 3) HC and four patients had low-grade HC (grade 2). While BK viremia was positive in 17 patients (68%), viruria was positive for all patients. Eight patients (15%) were treated with ciprofloxacin and cidofovir combination, six patients (30%) with cidofovir and three patients (15%) with ciprofloxacin. Three of them (20 patients) was treated by intravesical cidofovir. The complete response to the viruria or viremia was obtained from 11 patients (55%).

Conclusions: HC associated with BKV is an emerging clinical problem after HSCT causing prolonged hospitalization and mortality. It can be severe because the treatment options are often ineffective. The main goal of treatment is to reduce the dose of immunosuppressive agents. Close monitoring of BK virus in high-risk patients can be an important method to improve the complication in the early period.

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Abstract 937

**The optimal strategy of empirical antibiotic therapies for non-severe community-acquired pneumonia: a bayesian network meta-analysis of randomised controlled trials**

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**Background:** The 2019 the American Thoracic Society and Infectious Diseases Society of America guideline described that β-lactam (BL) monotherapy should not be routinely used for inpatients with community-acquired pneumonia (CAP) over fluoroquinolone (FQ) monotherapy or β-lactam/macrolide (BL-ML) combination therapy. However, the controversy about empirical antibiotic therapies is still unresolved. We conducted a systematic review and network meta-analysis to assess comparative efficacy of empirical antibiotic treatment strategies for nonsevere CAP.

**Materials/methods:** A systematic search for randomized controlled trials (RCTs) was performed through MEDLINE, EMBASE, and the Cochrane Central Register. We classified patients into FQ, BL-ML, and BL groups. The clinical success rate at the end to study was the primary outcome of interest. A Bayesian network meta-analysis was conducted and treatments were ranked based on their effectiveness.

**Results:** Twenty-three articles were included in the qualitative and quantitative synthesis using pairwise and network meta-analyses. Forest plots from network meta-analyses showed that the clinical success rates of FQ monotherapy were higher than BL monotherapy (OR 1.23; 95% CI 1.04–1.48). The difference in the clinical success rates for FQ monotherapy versus BL-ML combination therapy was not statistically significant (OR 1.19; 95% CI 0.88–1.68). And there was no difference in treatment success between BL monotherapy and BL-ML combination therapy (OR 1.03; 95% CI 0.73–1.43). On node-splitting analysis, inconsistency between direct and indirect comparison did not exist. In the rank-probability test, FQ monotherapy had the highest rank for the clinical success rate, followed by BL-ML combination therapy.

**Conclusions:** Current evidence showed that FQ monotherapy had better treatment outcomes than BL monotherapy for patients with nonsevere CAP. And the efficacy of FQ monotherapy was similar to BL-ML combination therapy. Our findings provide support for the current guidelines recommendations to propose empirical antibiotic treatment strategies for nonsevere CAP.

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Abstract 942

Accelerated HIV case finding and bridging the gap in antiretroviral therapy enrolment among prison inmates: a break-even in achieving the 95-95-95 UNAIDS targets among key populations in Western Nigeria

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**Background:** The clock is steadily ticking towards 2020 when the UNAIDS 95-95-95 global target in the fight against HIV/AIDS is hoped to be achieved. The hypothesis tested is the significant association between youthful age and HIV test outcome. The aim of the study was to engage in an accelerated HIV case finding and ensure enrolment into care among key populations in Western Nigeria fulfilling the first & second 90 of the UNAIDS targets.

**Materials/methods:** Lay Adhoc Staff/volunteers were purposely selected and trained. Consenting prison inmates had their blood samples taken and tested following the country’s HIV serology National testing algorithm, using the recommended HIV testing kits. Those who tested positive went through a retesting process in the laboratory and confirmed positive. Post-test counselling was then conducted.

**Results:** A total of 771 prison inmates were tested across the four prisons (Male 765, Female 6) with a mean age ± SD is 31.25 ± 9.47 years. Ten of them (Male 9, Female 1) were confirmed new positives with a mean age ± SD is 31.40 ± 6.24 years, yielding a positivity rate of 1.3%. Eight of the ten positives are in their youthful age (<35 years). Odd's ratio shows that youthful age have higher association with HIV test outcome (OR: 2.81, CI: 0.80 – 9.79). The linkage rate for the positives is 100% with good escort service while adherence is ≥ 95%. The patients after six months on tenofovir, lamivudine & dolutegravir achieved viral suppression.

**Conclusions:** This mode of HIV testing service (HTS) has proved to reach a key population yielding more positives in much fewer numbers of people tested and in a short period of time with 100% linkage with better resource/health financing outlook. Community ART Differentiated Service Delivery (DSD) Model is in line for the patients to sustain the gains in the effort to achieve the 95-95-95 fast track UNAIDS targets.

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Abstract 943

HIV-related stigma and discrimination in Western Nigeria: experiences of people living with HIV and rights issues
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Background: HIV-related stigma and discrimination continue to be major social determinants driving the epidemic of HIV globally despite the advances in medical treatment and increases in the awareness. Hypotheses tested was right awareness of people living with HIV/AIDS influencing HIV-related stigma & discrimination. The study aimed at assessing the level of HIV/AIDS related stigma and discrimination, forms, effects, and internal stigma experienced by PLHIVs in South-Western Nigeria.

Materials/methods: This cross sectional study was carried out at eight PEPFAR supported primary, secondary and tertiary level hospitals in South-Western Nigeria. The target population was adult (18 years and above) male and female persons living with HIV (PLHIVs) including key population. Data was collected from 278 consenting respondents by trained volunteers by a face-to-face interview.

Results: The mean age ± SD of the respondents was 38.48 ± 11.48 years, 70.05% females, mostly married in a monogamous setting (48.6%), with a formal education (86.3%), traders (33.5%), live in rural area (88.5%) while people in the key populations accounted for 9.4% of the participants. 78.4% elicited negative feelings such as depression and shame after diagnosis. About one-third (33.1%) PLHIVs have ever experienced HIV-related stigma and discrimination mostly gossip, physical abuse, and verbal insult, of which about two-third (63.2%) occurred in the hospital setting, followed by home/community (25.0%). In addition, 8.6% have been refused a job while 5.0% have lost their job because of their HIV status. Rights awareness by PLHIVs does not rule out HIV-related stigma & discrimination experience (χ² = 5.29, df = 1, P = 0.021).

Conclusions: A remarkable proportion of PLHIV still face stigma/discrimination with possible dramatic impact on their treatment and resultant quality of life. Efforts therefore, should be made to ensure PLHIV are not only aware of their rights, but are empowered to seek redress if these rights are violated.

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Abstract 947

Should a molecular bacterial syndromic approach totally replace culture for the diagnosis of gastrointestinal tract infections?

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Background: Molecular panels are rapid and sensitive tools for the syndromic diagnosis of gastrointestinal (GI) infections. Whether they should totally replace traditional approaches or be combined to non-molecular approaches [enrichment step, culture for species/serotype identification/epidemiological investigations, antimicrobial susceptibility testing (AST)] remains questioned. We retrospectively evaluated the routine use of Seegene Allplex GI panel I [7 bacterial targets] in the Nîmes University Hospital, France, during the first 8 months of implementation.

Materials/methods: At laboratory receipt, diarrhoeal faeces from patients not hospitalized for more than 3 days were inoculated into a Selenite broth [subculture on Hektoën medium] and transferred to a FecalSwab seeded on selective medium upon positive PCR result availability. PCR was performed 3 times a week. We comparatively analyzed PCR and culture results, with a focus on the utility on maintaining a subculture after enrichment and on the rate of strain recovery.

Results: 119 PCR were positive (16%) [5 with >1 pathogen], Campylobacter spp. being the most frequently detected pathogens (47%, one third more than before PCR). Strains have been isolated in 82 cases of positive PCR (66%, 52 to 94% according to the pathogen, cycle threshold (Ct): 21 to 44, time to FecalSwab seeding: 1-3 days). In 5 cases, Salmonella were detected by culture only, discrepant results being reproducible in 3 cases [14% of Salmonella infection diagnoses]. One Plesiomonas shigelloides (out of PCR panel) was cultured. tcdB gene was detected in 22 patients over 3 years, of whom 3 had not been diagnosed for Clostridioides difficile infection.

Conclusions: We confirmed the utility of syndromic approaches in increasing the diagnosis yield of GI infections. Detection of toxin B-encoding gene was also helpful when C. difficile infection was not suspected. The incomplete pathogen recovery from FecalSwab was independent of Ct value and time before seeding in our study, and impaired AST and epidemiological investigations. An adequate load of the FecalSwab, hardly standardizable even in case of inoculation in the lab, is confirmed as an important parameter of pathogen detection. Maintaining a culture medium appears necessary for a larger Salmonella recovery and the detection of pathogens not included in the molecular panel.

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The influence of delivery mode in the oral mycobiome: from childhood to adulthood

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Background: Postnatal acquisition of microorganisms from maternal and environmental sources contributes to the microbiome development of the child, and can potentially influence the future adult microbiome maturation. The mode of delivery may impact oral bacterial colonization as it is observed in several studies; however, the influence of this early life event on oral fungal colonization is still poorly investigated. Therefore, our aims were to perform: 1) a systematic review on the impact of the delivery mode on oral fungi transmission in early age and 2) a cross-sectional study regarding the association between this early life event in oral yeast colonization in young adults.

Materials/methods: A PubMed search was performed from April 25 to June 18, 2019, with inclusion criteria being comparative studies in humans that investigated oral fungi transmission and colonization in relation with the delivery mode. Colonization by yeasts in the oral cavity was evaluated in unstimulated saliva in 185 healthy young adults and correlated with delivery mode. Yeast isolation and identification was performed using Sabouraud Agar medium supplemented with chloramphenicol, followed by ChromAgar Candida and 18S/ITS gene sequencing.

Results: From the 4256 articles retrieved, only 8 articles were included in this review. There was more evidence towards the impact of the delivery mode on the fungal acquisition than against: the majority of the studies (N=6) found a relation between fungal colonization and vaginal delivery and, in 2 of these studies the existence of vertical fungal transmission from mother to child was reported. *Candida albicans* was the most commonly isolated fungal species, followed by *Candida parapsilosis*. Non-cultivable methods of fungal identification were only applied in one of the selected studies. Regarding the cross-sectional study, *Candida* species were isolated from 37.5% of the participants, *Candida albicans* being the most prevalent species. The prevalence of oral yeasts was significantly higher in those who were vaginally delivered compared to those born by caesarean-section.

Conclusions: Together, our results suggest that vaginal delivery appears to promote oral yeast colonization and carriage throughout life, from childhood to adulthood. More longitudinal studies using molecular methods are needed to fulfil the lack of knowledge within this field.

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Abstract 951

**Computerised Tomography (CT) as a risk factor for the acquisition of carbapenem-resistant *Acinetobacter baumannii***

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**Background:** Multiple inanimate objects have been implicated in the transmission of resistant bacteria in the hospital. We examined whether performance of a CT scan increased the risk for colonization.

**Materials/methods:** All patients undergoing CT and all patients colonized or infected with carbapenem-resistant *Acinetobacter baumannii* (CRAB) were identified for 5 years from 2014-2019. Active admission and weekly surveillance was carried out for this bacterium. Each CT visit was classified as either an "Index Case" (presence of resistant bacteria prior to CT visit), an "Acquisition case" (appearance of resistant bacteria within 14 days of CT in a patient without prior colonization/infection), or a "Null case" (uncolonized/uninfected throughout). The risk of colonization/infection was calculated for patients undergoing CT for the first hour, each subsequent 6 hour period, and for days 2 – 7 after an index case. The results were normalized per 1000 CT scans [Number of acquisitions/number of patients undergoing CT during the relevant period normalized to 1000 scans].

**Results:** CT was performed for 115,680 patients during the study period. There were 324 Index cases and 254 Acquisition cases. The normalized risk of CRAB acquisition for the first 7 days is shown in the table. The odds ratio for acquisition during the first hour after a previous CRAB patient compared to 1 to <6 hours thereafter was 2.4 (95%CI 1.3 – 4.3, p=0.003).

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**Conclusions:** Acquisition of CRAB following CT scan is more frequent during the first hour after a previous patient with this bacterium had been examined. This probably reflects inadequate environmental cleaning.

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Abstract 954

**Individualised autovaccination is a promising strategy for managing recurrent urinary tract infections in women**

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**Background:** more than 20% of patients with urinary tract infection are at risk of recurrence. rUTI are a pervasive condition that negatively impacts patients’ Quality of Life (QoL). Causes of recurrence are multifactorial and include non-modifiable risk factors (nmRF). Antibiotic prophylaxis is broadly used to treat rUTI. However, its use is not devoid of adverse effects and can lead to resistance. Efficacy of mono/polyvalent inactivated bacteria has only been demonstrated in selected patient cohorts. Here, we show preliminary results of an ongoing prospective study aimed at evaluating the efficacy of an individualized autovaccine for outpatient management of rUTI in real-life conditions.

**Materials/methods:** women with uncomplicated rUTI were offered participation in a prospective study involving daily administration of a sublingual autovaccine (Uromune®) during 3 months. Individualized vaccines were generated for each patient by isolating inactivated bacteria from their urine culture (UC) samples. Demographic variables and rUTI nmRF were recorded. UC results, number of relapses and QoL using two questionnaires (daily activities: QoLQAct; emotions: QoLQEm) were evaluated as outcomes.

**Results:** the first 18 patients that have finished treatment were evaluated. Age mean±SD was 72.3±7.2 years. Mean±SD nmRF was 5.1±1.6, mainly menopause 18 (100%), urogenital surgery 16 (88.9%), urinary incontinence 13 (72.2%), and diabetes mellitus 9 (50%). Autovaccines were mostly generated from *E. coli* [12 (66.7%)] and *K. pneumoniae* [3 (16.7%)] strains. UC negativity was reached in 61.1% of patients and 82.4% showed a decrease in number of relapses (mean number pre-post 2.9 vs. 1.1, p<0.01). Similarly, QoL parameters improved in 76.5% of patients in QoLQAct (mean score pre-post 2.7 vs 1.5, p=0.02) and 70.5% in QoLQEm (mean score pre-post 11.5 vs 6.5, p=0.01). Improvements were observed regardless of bacteria strain.

**Conclusions:** This is, to our knowledge, the first prospective study evaluating autovaccination for the management of rUTI. We observed promising rates of UC negativization, decrease in rUTI episodes and improvement QoL parameters in non-selected women. Our results suggest that Uromune® autovaccine may be a valid strategy for reducing antibiotic consumption and for improving QoL in women with rUTI.

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Abstract 957

Results of a schistosomiasis screening programme in an immigrant population
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Background: Schistosomiasis is one of the most prevalent tropical diseases in the world. If the infection progresses without treatment, it can produce long-term complications like liver cirrhosis and bladder tumors among others. The results of a schistosomiasis screening program in the sub-Saharan immigrant population are described.

Materials/methods: A prospective screening program of schistosomiasis in all sub-Saharan patients attending in a Tropical Medicine Unit, in Asturias, Spain was performed between January 2009 and December 2017. Three formalin-ether concentrated stool samples and an enzyme-linked immunosorbent assay for serum anti-Schistosoma spp antibodies were used as screening. If urinalysis showed hematuria, we perform three urine analysis for Schistosoma haematobium. We considered infection to be established if the microscopic visualization and/or the ELISA were positive.

Results: We analyzed 481 patients (52% women; average age 34 years; mean age in Spain 1,043 days). The most frequent areas of origin were Central Africa (51.7%), West Africa (45.3%), and East Africa (2.9%). Fifty-nine patients (12.3%) had a positive serology for Schistosomiasis (59.3% were male; mean age of 29 years, mean time in Spain: 641 days). Five patients had a S. intercalatum in stool and three had S. haematobium in urine. Most of them came from Central (45.8%) and West Africa (52.5%), although without significant differences. There is not significantly differences in sex, age or length of stay in Spain, although 62.7% of infections were significantly detected in patients who had been less than one year in Spain (37/22 versus 202/220 p = 0.023 OR 1.832 [1.045-3.2 10]. Twenty-one (35.6%) patients were asymptomatic in the rest the most frequent symptoms were hematuria (10 patients) and abdominal pain (5 patients) and diarrhea (5 patients). One patient with S. intercalatum infection has bloody stools. Twenty-two patients showed eosinophilia in blood.

Conclusions: In our series, schistosomiasis was detected in 12.3% of our patients, most of them diagnosed by serology. It appeared more frequently in male patients from Central and West Africa who had been less than one year of residence in Spain, although without significant differences. A third of them were asymptomatic.

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An ultrasensitive rapid single molecule counting method detects Bacillus anthracis lethal factor directly in blood samples

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Abstract third-party references: This project has been funded in whole or in part with Federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, under Contract No. HHSO100201500022C

Background: Following a bioterrorism attack or infectious disease outbreak, large numbers of people will require a rapid diagnosis to ensure delivery of life-saving therapeutic treatment. We present data for a highly sensitive anthrax test that runs on a benchtop platform that can be deployed in hospitals, clinics, or physician office laboratories. The new anthrax test detects Lethal Factor (LF), the earliest detectable biomarker for Bacillus anthracis infection, from a fingerstick blood sample in 20 minutes. Sensitive detecting LF, which appears in the blood before PCR tests can detect the pathogen, offers the possibility of identifying infected victims early increasing the chances for successful treatment.

Materials/methods: The test uses non-magnified digital imaging to count target-specific magnetic and fluorescent particles that have been tethered together by single LF molecules. A novel dye-cushion eliminates the need for sample preparation. A blood sample (70 µL), either fingerstick or venous, is added directly to the disposable cartridge, minimizing sample handling. Once loaded onto the analyzer, the test proceeds automatically and generates a result in approximately 20 minutes. Contrived clinical samples prepared with blood drawn by venipuncture or fingerstick were used to estimate the limit of detection (LoD), precision, and dynamic range.

Results: The LoD of the Anthrax Toxin Test, determined using whole blood samples spiked with pure LF protein, is 61 pg/mL (Figure 1). The dynamic range of the test covers 5 logs of LF concentration, an important performance metric given the broad range of LF concentrations observed over the course of anthrax infection. In a simulated clinical study, whole blood collected by fingerstick from 40 healthy individuals was tested either spiked with 150 pg/mL purified LF or unspiked. In this study, the test demonstrated 100% sensitivity and 100% specificity.

Conclusions: The performance data demonstrate that the new anthrax test is highly sensitive, rapid, and specific for the detection of B. Anthracis LF in whole blood. Valuable features for crisis surge testing include minimum sample handling, a 20 minute test turnaround, and the benchtop analyzer’s throughput.

Figure 1. Analytical sensitivity of the LF test.

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Multi-centre evaluation of the BIOFIRE FILMARRAY BCID 2 Panel for the detection of microorganisms and resistance markers in positive blood cultures

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Background: The BioFire® FilmArray® Blood Culture Identification 2 (BCID2) Panel is a rapid diagnostic test that provides results for 26 bacterial analytes, seven fungal analytes, and ten antimicrobial resistance (AMR) genes from positive blood culture (PBC) specimens in about an hour. The BCID2 Panel builds upon the existing BCID Panel with several additional assays that include Bacteroides fragilis, Candida auris, and additional AMR genes [CTX-M, IMP, mcr-1, mecA/C and MREJ, NDM, OXA-48-like, and VIM]. Here, we summarize studies conducted to establish clinical performance using an Investigational Use Only version of the BCID2 Panel.

Materials/methods: A total of 1074 residual PBCs were enrolled at 7 US and 2 EU sites between October 2018 and May 2019. BCID2 Panel performance was compared to routine standard of care microbial culture, as well as molecular methods for AMR genes. In addition, BCID2 Panel MRSA results were compared to the FDA-cleared Xpert® MRSA/SA BC test (Cepheid, Inc).

Results: The BCID2 Panel identified at least one organism in 90.9% of enrolled PBCs. Among the 12.8% of positive specimens with multiple organism detections by the BCID2 Panel, combinations of gram-positive (GP) bacteria mixed with gram-negative (GN) bacteria, GP with yeast, GN with yeast, and combinations of all three were observed. The BCID2 Panel demonstrated an overall sensitivity of 99.2% and specificity of 99.6% for the identification of microorganisms compared to culture. Concordance between the BCID2 Panel and the Xpert MRSA/SA BC test for the identification of MRSA was 91.2% positive percent agreement (PPA) and 97.9% negative percent agreement (NPA); however, 100% concordance was observed when compared to phenotypic MRSA characterization by the laboratory. The overall PPA and NPA for the remainder of the BCID2 Panel AMR genes as compared to molecular methods was 98.9% and 99.9%, respectively. The overall success rate of obtaining valid results in initial specimen tests was 99.7%.

Conclusions: The new BCID2 Panel is a sensitive, specific, and robust test for rapid detection of microorganisms [including mixed polymicrobial samples] and a variety of AMR genes in PBCs.

Data presented are from assays that have not been cleared or approved for diagnostic use.

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Abstract 965

**Shortened antibiotic treatments for Gram-negative bacteraemia in cancer patients: less is possible**

Fabian Herrera¹, Diego Torres¹, Alberto Carena¹, María Laura Jorge¹, Elena Temporiti¹, Federico Nicola¹, Andres Nicolas Rearte*¹, Sofia Zerboni¹, Florencia Bues¹, Pablo Bonvehi¹

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**Background:** There are no studies published evaluating 7-day treatment for Gram-negative bacilli (GNB) bacteraemia exclusively in cancer patients and neutropenia.

**Materials/methods:** Prospective observational study performed from May 2014 to August 2019. Adult cancer patients with GNB bacteraemia were included, with the following criteria: having received appropriate empirical antibiotic treatment (EAT), complete clinical response within 7 days with source control and having survived 48 hours after completion of treatment. According to the duration of the antibiotic treatment they were divided into: short, median 7 days (ST) or long, median 14 days (LT). A 30-day follow-up was performed to assess mortality and recurrence of bacteraemia. Categorical variables were analyzed by the Fisher exact test or the Chi-square test and continuous variables were analyzed by the U Mann-Whitney test.

**Results:** 74 patients were included (ST: 36 and LT: 38). No differences were observed in baseline characteristics between ST and LT respectively: age 57 years (47-68) vs 60 years (47-66) (p=0.70); hematologic malignancy 52.8% vs. 44.7% (p=0.48); chemotherapy: 97.2% vs 89.5% (p=0.18); neutropenia 58.3% vs 60.5% (p=0.84); Charlson score 2 (2-4) vs 2 (2-3) (p=0.69); Pitt score 1 (0-2) vs 1 (0-2) (p=0.22). ST patients had a higher APACHE II score: 21 (19-23) vs 17 (14-20) (p<0.0001). There were no differences in clinical presentation and microbiological characteristics between ST and LT respectively: bacteraemia with clinical source 72.2% vs. 76.3% (p=0.68); hypotension 27.8% vs. 34.2% (p=0.55), E. coli 52.9% vs. 31.6% (p=0.065), Klebsiella spp. 27.8% vs. 39.5% (p=0.28); Multidrug-resistant GNB 27.8% vs. 21.1% (p=0.50). Treatment, outcome and recurrence between ST and LT were respectively: combined EAT 38.5% vs 44.7% (p=0.61); prolonged infusion 36.1% vs. 10.5% (p=0.012); ceftazidime-avibactam treatment: 22.2% vs 0 (p=0.002); overall mortality 2.8% vs. 7.9% (p=0.61); recurrence 2.8% vs. 0 (p=0.30). The length of hospitalization in days since bacteraemia and Clostridiodes difficile colitis between ST and LT were respectively: 7 (6-15) vs. 12 (7-19) (p=0.021) and 0 vs 8.9% (p=0.08).

**Conclusions:** In patients with cancer and GNB bacteraemia who receive appropriate EAT, with complete clinical response, 7-day duration may be adequate. They could also benefit from a shorter hospitalization.

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Abstract 966

Ceftazidime-avibactam for the treatment of carbapenemase-producing Enterobacteriaceae bacteraemia in oncohaematological patients: calm after the storm

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Abstract third-party references: On behalf of Argentinean Bacteraemia in Cancer and Hematopoietic Stem Cell Transplant Study Group

Background: There are no studies published demonstrating that treatment with ceftazidime-avibactam (CA) for carbapenemase-producing Enterobacteriaceae bacteraemia (CPEB) improves survival in patients with hematologic malignancies and neutropenia.

Materials/methods: Prospective observational study performed from May 2014 to August 2019. Adult patients with hematologic malignancies or hematopoietic stem cell transplantation and KPC or OXA48-CPEB were included from 12 centers of Argentina. We compared patients who received definitive treatment with CA with patients treated with other antibiotics (OA). The 30-day mortality was examined by the Kaplan-Meier method with the log-rank test, and the Cox regression model was used to test statistical significance.

Results: 110 patients were included (CA: 22 and OA: 88). No differences were observed in baseline characteristics between CA and OA respectively: age 47 years (37-60) vs 50 years (39-64) (p=0.53); acute leukemia 68.2% vs. 59.1% (p=0.43); neutropenia 81.8% vs 84.1% (p=0.79); high risk by MASCC score: 100% vs 94.6% (p=0.31); neutropenia duration > 10 days: 81.8% vs 84.1% (p=0.79); Charlson score 2 [2-2] vs 2 [2-3] (p=0.27); Pitt score 0 [0-1] vs 1 [0-2] (p=0.11); APACHE II score: 13 [11-20] vs 12 [8-17] (p=0.092). There were no differences in clinical presentation and microbiological characteristics between CA and OA respectively: bacteraemia with a clinical source: 68.2% vs. 62.5% (p=0.62); hypotension: 22.7% vs. 36.4% (p=0.31); KPC-CPEB: 95.5% vs 92% (p=0.58); Klebsiella spp.: 90.9% vs. 90.9% (p=1); colistin-resistance: 27.3% vs. 31.8% (p=0.68); Meropenem MIC ≥ 16: 68.2% vs 69.9% (p=0.88). Treatment and outcome between CA and OA were respectively: appropriate empirical treatment: 81.8% [64% received CA] vs 52.3% [p=0.015]; combined definitive treatment: 63.6% vs 92% [p=0.001]; 7-day clinical response: 86.4% vs 52.3% (p=0.004); ICU admission: 18.2% vs 43.3% (p=0.048); 30-day mortality 18.2% vs. 50% (p=0.008). In the multivariate analysis the factors significantly associated with mortality were: Pitt score: OR 1.3, 95% CI, 1.1-1.45 (p=0.0001) and breakthrough CPEB: OR 2.1, 95% CI, 1.2-3.8 (p=0.011), while definitive treatment with CA was a protector factor for survival: OR 0.34, 95% CI, 0.12-0.9 (p=0.049).

Conclusions: Oncohematological patients with CPEB receiving definitive treatment with CA had clinical and survival benefit over OA treatments.

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The dominant model analysis of Sirt3 genetic variants is associated with susceptibility to tuberculosis in a Chinese Han population
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Background: Tuberculosis (TB) is a complex infectious disease caused by the pathogen Mycobacterium tuberculosis (Mtbc) which has coexisted with humanity since the Neolithic. Recent research indicated that SIRT3 plays a pivotal role in promoting the antimycobacterial response of mitochondria and autophagy during Mtbc infection.

Materials/methods: A case-control study comprised 900 TB patients and 1534 healthy controls were retrospectively enrolled to assess the association between Sirt3 gene polymorphisms and TB susceptibility. In total of five single-nucleotide polymorphisms (SNPs) (rs511744, rs3782118, rs7104764, rs536715, and rs28365927) which were selected through database 1000 Genomes Project and offline software Haploview V4.2, and genotyped by a customized 2×48-Plex SNPscanTM Kit.

Results: Our results suggested that the minor allele genotypes (A carriers) of rs3782118 confers the decreased risk of TB susceptibility ($p$ Bonferroni = 0.032), and a similar but more significant effect was observed under the dominant model analysis ($OR = 0.787, 95\% CI = 0.666-0.931, p_{Bonferroni} = 0.026$). Haplotypes analysis showed that haplotype AGAAG (rs511744 / rs3782118 / rs7104764 / rs536715 / rs28365927) was associated with an increased risk of TB ($p = 0.023, OR = 1.159, 95\% CI = 1.019-1.317$). In stratification analysis, we found that rs3782118 was associated with decreased risk of TB in female subgroup under the dominant model analysis ($p_{Bonferroni} = 0.016, OR = 0.678, 95\% CI = 0.523-0.878$). Moreover, functional annotations for three loci (rs7930823, rs3782116, and rs3782115) which are strongly linked to rs3782118 indicated that they may be responsible for the changes in some motifs.

Conclusions: Our study suggested that the SNP rs3782118 was associated with a lower susceptibility to TB, especially under the dominant model analysis, and that the haplotype AGAAG (contains the major allele G of rs3782118) was associated with an increased risk of TB. Further independent cohort studies are necessary to validate the protective effect of Sirt3 genetic variants on the risk of TB.

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Abstract 970

**Measles: clinical manifestations and complications during an outbreak in Bulgaria in 2019**

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¹Specialized hospital for active treatment of Infectious and Parasitic Diseases “Prof. Ivan Kirov”, Sofia, Bulgaria

**Abstract third-party references:** Specialized hospital for Active treatment of Infectious and Parasitic Diseases “Prof. Ivan Kirov”

**Background:** Measles is caused by one of the most pathogenic viruses known to man. Almost every infection is manifested clinically and frequently leads to serious complications. The aim of the present study is to review the clinical presentation of measles during an outbreak in 2019.

**Materials/methods:** Between February and August 2019 in our Institution, a total of 341 cases of measles were hospitalized and verified through IgM antibodies and/or through molecular confirmation for the presence of the virus.

**Results:** 172 are male, 169 are female. In regards to the immunization status, 82 are under the age of immunization - 13 months. From the remaining patients, 106 have unknown status, 119 have not been immunized, 32 have received 1 dose of measles vaccine and 2 have received 2 doses.

In regards to the initial infection, in 77 cases this occurred through contact with a family member and in 49 cases during a prior hospitalization.

**Clinical manifestations and complications:**

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<tbody>
<tr>
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<td>79</td>
<td>66</td>
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<td>335</td>
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<tr>
<td>Conjunctivitis</td>
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<td>58</td>
<td>124</td>
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<tr>
<td>Feverity</td>
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<td>42</td>
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<td>46</td>
<td>95</td>
<td>36</td>
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</tr>
<tr>
<td>Diarrhea</td>
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<td>20</td>
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</tr>
<tr>
<td>Pneumonia</td>
<td>12</td>
<td>5</td>
<td>14</td>
<td>4</td>
<td>35</td>
</tr>
</tbody>
</table>

**Conclusions:** Measles affects primarily individuals who have not been immunized (90.02%), which leads to the necessity for implementation of further practices, aiming at increasing the proportion of immunized individuals in Bulgaria. A significant number of Hospital-acquired infections (14.31%) were noted. This requires further evaluation of the methods for infection control in regards to highly contagious diseases.

Our data shows that generally clinical manifestations during the outbreak in Bulgaria correspond to those described in literature. In regards to complications, bronchitis is more frequently noted in older patients (12-56 y. 44%), while pneumonia is more frequently seen in younger patients (<13 m. 14%).

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**Abstract 971**

**Increasing influenza vaccination rates among healthcare workers and residents of long term care facilities for the elderly in Graz, Austria**

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**Background:** Although annual vaccination against influenza is recommended in Austria for those over 50 years of age, all patients with chronic health conditions and health care workers (HCW) vaccination rates in Austria are as low as 20% according to OECD data. The aims of our study were (1) to evaluate the vaccination rate of residents and HCWs in long-term care facilities (LTCF) in the season 2017/2018, (2) to explore motivations against vaccination, (3) to increase vaccination rates in the season 2018/2019 by a multi-modal intervention bundle.

**Materials/methods:** In January 2018, the rates of influenza vaccination of residents and HCWs of 4 LTCFs (Geriatric Health Centres Graz, Austria) were determined. Residents and HCWs were asked to respond to a survey anonymously asking for their motivation not to get vaccinated. In autumn 2018 an intervention bundle was conducted including: personal letters to all HCWs and residents, posters presenting peers in favour of vaccinations on display, meetings between local experts and residents, training sessions of influenza prevention for HCWs. Vaccination for HCWs was offered free of charge. Vaccination rates were again determined in January 2019.

**Results:** In the season 2017/2018, the vaccination rates were 6% (22/377) in residents and 1% (3/234) in HCWs. Following the interventions, there was a statistically significant increase in vaccination rates to 19% and 20% in residents and HCWs respectively (p < 0.001). 37% (141/377) of residents and 29% (67/234) of HCWs responded to the survey (table 1). 32% of HCWs questioned effectiveness of influenza vaccination.

**Conclusions:** A multi-modal intervention bundle was successful in significantly increasing influenza vaccination rates but vaccination rates were still low. The study revealed strong skepticism about the effectiveness of influenza vaccinations and vaccinations in general among HCWs.

**Table 1: Reasons against influenza vaccination in HCWs and residents of 4 LTCFs in the season 2017/2018**

<table>
<thead>
<tr>
<th>Reason</th>
<th>HCWs</th>
<th>Residents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skeptical if influenza vaccination is effective.</td>
<td>32%</td>
<td>16%</td>
</tr>
<tr>
<td>Skeptical if vaccinations in general are effective.</td>
<td>15%</td>
<td>12%</td>
</tr>
<tr>
<td>Experienced side effects after previous vaccinations.</td>
<td>15%</td>
<td>8%</td>
</tr>
<tr>
<td>I did not get around to get vaccinated</td>
<td>8%</td>
<td>24%</td>
</tr>
<tr>
<td>I am scared of needles.</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Other reasons</td>
<td>11%</td>
<td>38%</td>
</tr>
</tbody>
</table>

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Abstract 972

**Radiologic features of Pneumocystis pneumonia differ between patients with and without HIV Infection**

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**Background:** Pneumocystis pneumonia (PCP) is the leading opportunistic infection in patients with acquired immune deficiency syndrome in Taiwan. However, patients with hematologic diseases and under immunosuppressant use are also at a higher risk for PCP. Radiologic findings on chest computed tomography (CT) scan can be used to aid the diagnosis especially when invasive procedures to obtain tissue for the histopathologic diagnosis is often difficult in critically-ill patients. The aim of the study is to compare the differences in the radiologic features in PCP between patients with and without HIV infection.

**Materials/methods:** We retrospectively reviewed the chest CT findings in 101 patients diagnosed with Pneumocystis pneumonia with or without HIV infection from January 2014 to August 2019. Each image was reviewed by a radiologist and a chest medicine specialist and findings were recorded as diffuse consolidation, ground glass opacity, intralobular/interlobular lines, crazy-paving pattern, pulmonary cysts, pneumothorax, tree-in-bud pattern, pulmonary nodules, pleural effusion, intrathoracic adenopathy, architectural distortion and/or traction bronchiectasis. The distribution were recorded as peripheral or central distribution.

**Results:** The mortality rate was 15.4% (6/39) in HIV-infected patients and 43.5% (27/62) in non-HIV-infected patients in the study. Diffuse consolidation (30.6% vs 12.8%, p=0.04), pleural effusion (43.5% vs 5.1%, p<0.001) and intrathoracic adenopathy (27.4% vs 10.3%, p=0.04) were more often seen in non-HIV-infected patients and HIV-infected patients presented more frequently with ground glass opacity (94.9% vs 67.7%, p<0.001) and peripheral distribution (49.7% vs 29.0%, p=0.05).

**Conclusions:** This study showed that HIV-infected patients and non-HIV-infected patients presented differently on chest CT image; non-HIV-infected patients tend to have atypical presentations such as diffuse consolidation, pleural effusion and intrathoracic adenopathy. HIV-infected patients more often presented with ground glass opacity and peripheral distribution.

**Table 1 Chest CT features in patients with and without HIV infection**

<table>
<thead>
<tr>
<th>Variables, n (%)</th>
<th>All N=101</th>
<th>HIV N=39</th>
<th>Non-HIV N=62</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffuse consolidation</td>
<td>24 (23.8)</td>
<td>5 (12.8)</td>
<td>19 (30.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Ground glass opacity</td>
<td>79 (78.2)</td>
<td>37 (94.9)</td>
<td>42 (67.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Tree-in-bud pattern</td>
<td>10 (9.9)</td>
<td>6 (15.4)</td>
<td>4 (6.5)</td>
<td>0.14</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>29 (28.7)</td>
<td>2 (5.1)</td>
<td>27 (43.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intrathoracic adenopathy</td>
<td>21 (20.8)</td>
<td>4 (10.3)</td>
<td>17 (27.4)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

HIV: human immunodeficiency virus

**Presenter email address:** hywusa@yahoo.com
Invasive pulmonary aspergillosis after heart transplantation

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**Background:** Mold infections are an important cause of morbidity and mortality in the solid organ transplant population. Invasive pulmonary aspergillosis (IPA) are an infrequent but major complication of heart transplantation (HTx). We sought to describe the frequency and determine risk factors of this mold infection at our centre.

**Materials/methods:** From January 2010 to October 2019 it was performed 133 HTx (46±14 year-old; male – 97%). Immunosuppressive therapy was guided by transplant center protocol: methylprednisolone, tacrolimus, mycophenolate mofetil/everolimus plus induction (basiliximab - 80% (n=107), anti-thymocyte globulin - 15% (n=20)). We retrospectively analyzed early and long-term post-heart transplant results.

**Results:** During the whole follow-up 52 episodes of pneumonia were diagnosed, 16 (31%) of them were IPA [54±7 year-old], most cases [91%] were probable. Aspergillus fumigatus was the most common species isolated. All recipients were treated with voriconazole [from 2 to 6 months] with positive clinical outcomes in 81% (n=13) of them. Three patients (n=2 – in 1 month after HTx) died which was associated with sepsis and right ventricular heart failure. Adjunctive therapies included reduction of immunosuppressive therapy and colonystimulating factors for neutropenic patients. Risk factors of IPA were found: prolonged duration in ICU (n=8), neutropenia (n=8) and high doses of immunosuppression, such as triple-drug therapy including steroids (n=14), treatment for 2R/3A rejection (n=3) and 1 month after the conversion to everolimus (n=1).

**Conclusions:** IPA occurred in 31% of all post-HTx pneumonias. The development of IPA was associated with a combination of risk factors. Timely diagnosis of IPA allows initiating antimycotic therapy with positive clinical outcomes.

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Abstract 979

Globally intravenous dosing of antibiotics in infants and children clusters around a small number of strategies but is not completely uniform

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Background: Little is known about consistency of antibiotic prescribing in children.

Materials/methods: We investigated variation in dosing in mg/kg/day in the 16 most common antibiotics [with at least 90 doses recorded] prescribed for intravenous treatment [not prophylaxis or decolonization] across four years of data from the Global Point Prevalence Survey.

Results: Data consisted of 3,572 doses from 2,627 children in 62 hospitals in 23 countries. Almost half (46%) of doses were from the WHO European Region, 31% the Americas, 12% South-East Asia, 6% Western Pacific Region and 5% African Region; none were from Eastern Mediterranean Region. The median age of children was 36 months (IQR: 9–96 months, Range: 1 month–17 years).

The three most common antibiotics were ceftriaxone (14% of doses), meropenem (12%) and vancomycin (11%). Approximately half of antibiotic doses (56%) were for community-acquired infections. The most common diagnoses were bacterial LRTI (24%), sepsis (18%) and Febrile neutropenia/Fever (13%); 16 other diagnoses comprised the remaining 45% of diagnoses but each represented less than 7% doses individually.

Figure 1: Daily dosing in 16 IV antibiotics in children. Vertical lines show minimum and maximum Blue Book recommendations.

The spread of dosing in mg/kg/day for each antibiotic ranged widely: from two-fold (cefazidime) to more than 20-fold (ceftriaxone; figure 1). Dosing in mg/kg/day clustered around a small number of peaks, and all antibiotics had at least one dose used in at least 10% of children. Five antibiotics [amikacin, ampicillin, cefepime, metronidazole, teicoplanin] had a dose used in more than 40% of children, and most antibiotics showed up to three clear peaks in dosing strategy.

Conclusions: Dosing in IV antibiotics appears to cluster around a small number of strategies. Differences could reflect true differences in dosing strategy [e.g. reflecting different recommendations for meningitis] or equipoise towards dosing. Guidance and trials should aim to differentiate between commonly used doses and their relationship to clinical outcomes.

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Abstract 980

The Danish nationwide surveillance of azole-resistance in Aspergillus fumigatus: data from the first nine months
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Background: Azole resistant [azole-R] Aspergillus fumigatus has been increasingly reported worldwide and associated with human and environmental azole use. The environmental resistance mechanisms TR34/L98H or TR46/Y121F/T289A were first found in Denmark in 2007 and 2012, respectively. A nationwide surveillance was established in October 2018. We report results from the first 9-month's surveillance.

Materials/methods: Inclusion criteria were: a) isolates regarded clinically significant and b) isolates detected on a Monday to represent background prevalence. Isolates from same patients were defined as unique if found >30 days apart or with a different susceptibility pattern. The EUCAST E. Def 10.1 method using VIPcheck azole agar plates [Mediaproducts BV, Groningen NL] was used for screening, EUCAST E. Def 9.3.1 for susceptibility testing, and cyp51A sequencing for characterisation of target gene mutations. An isolate was deemed non-susceptible if intermediate or resistant according to EUCAST breakpoints v9.0.

Results: At the time of writing, susceptibility testing was performed for 703 A. fumigatus isolates from 508 patients. Fifty-three (7.5%) isolates were marked “Monday samples.” Thirty-two patients harboured a non-susceptible A. fumigatus isolate (6.3%), incl. 29 resistant (5.7%). A target gene mutation was found in 27 isolates [all resistant], including 20 with tandem repeats from airway samples suggesting environmental origin (3.9% of all patients, 69% of resistant isolates, Table). Among the patients with non-susceptible isolates underlying diseases were: cystic fibrosis (CF, 15/32), other pulmonary disorders (12/32), solid organ transplantation and trauma (one each) and unknown (three patients). Nine out of 20 (45%) with a tandem repeat originated from CF patients. Among the Monday samples TR/L98H was detected in 3/51 (5.9%) at patient level. The TR/L98H isolates originated from all parts of Denmark except the north-Jutland, where it has previously been found. All isolates, except one, with other Cyp51A alterations originated from Zealand.

Conclusions: We report a nationwide azole non-susceptibility and resistance rate of 6.3% and 5.7%, respectively, in A. fumigatus at the patient level. The underlying resistance mechanisms were target gene mutations in all but two resistant cases and notably, the vast majority (69%) were of environmental origin. This implicates that the use of azole fungicides has an impact on human health.

Table. Susceptibility interpretation based on EUCAST breakpoints

<table>
<thead>
<tr>
<th>Cyp51A Profile</th>
<th>n</th>
<th>Patient age range (years)</th>
<th>ITR</th>
<th>PRC</th>
<th>VRC</th>
<th>ISA</th>
<th>non-S</th>
<th>R</th>
<th>Geographic location</th>
</tr>
</thead>
<tbody>
<tr>
<td>TR/L98H</td>
<td>19</td>
<td>0-70</td>
<td>1 R</td>
<td>17 R</td>
<td>19</td>
<td>19</td>
<td>18 R</td>
<td>19</td>
<td>RH, Jutland, Zealand</td>
</tr>
<tr>
<td>TR/Y121F/T289A</td>
<td>1</td>
<td>22</td>
<td>1 R</td>
<td>1 R</td>
<td>1 R</td>
<td>1 R</td>
<td>1 R</td>
<td>1</td>
<td>RH</td>
</tr>
<tr>
<td>GV4R</td>
<td>4</td>
<td>20-55</td>
<td>4 R</td>
<td>4 R</td>
<td>4 R</td>
<td>1 R</td>
<td>1 R</td>
<td>4</td>
<td>RH, Jutland</td>
</tr>
<tr>
<td>M220K</td>
<td>1</td>
<td>58</td>
<td>1 R</td>
<td>1 R</td>
<td>1 R</td>
<td>1 R</td>
<td>1 R</td>
<td>1</td>
<td>RH</td>
</tr>
<tr>
<td>M220K</td>
<td>1</td>
<td>29</td>
<td>1 R</td>
<td>1 R</td>
<td>1 R</td>
<td>1 R</td>
<td>1 R</td>
<td>1</td>
<td>RH</td>
</tr>
<tr>
<td>G425S</td>
<td>1</td>
<td>68</td>
<td>1 R</td>
<td>1 R</td>
<td>1 R</td>
<td>1 R</td>
<td>1 R</td>
<td>1</td>
<td>Zealand</td>
</tr>
<tr>
<td>Wildtype</td>
<td>5</td>
<td>16-53</td>
<td>3 R</td>
<td>3 R</td>
<td>3 R</td>
<td>3 R</td>
<td>2 R</td>
<td>5</td>
<td>RH, Jutland</td>
</tr>
</tbody>
</table>

*One isolate with an M10.7 for itraconazole and voriconazole was contaminated with an isolate harboring a cyp51A wildtype.

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New raw materials for serology immunoassay quality controls
Pauline Monsbrot*, Gaël Champier1, Claudia Dollack2, Thomas Schumacher1, Marie-Laure Dardé3, Sebastien Hantz4
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Background: Reliable antibody-detection in patient samples requires high quality reference materials to determine cut-off values and test assay integrity. Immunoassay quality controls are mainly based on human disease state plasma which is a critical component for the development and manufacturing of diagnostic tests. However, for most indications, plasma sourcing is difficult [availability, expected features, time consuming].

ArkAb and SERION Immunologics collaborated to develop a range of substitutes to disease state plasma for immunoassay quality controls based on human chimeric monoclonal antibodies (mAbs). This study shows performance obtained for anti-Toxoplasma gondii IgM mAbs tested with several diagnostic kits.

Materials/methods: InEps™ transgenic mice expressing human/mouse chimeric IgM were immunized to obtain specific mAbs through classic hybridoma development technique [immunization, B Cells immortalization, IgM specific secreting hybridomas screening and stabilization, pre-industrial IgM mAb production].

First, after production using a standardized and controlled bioprocess, performance of two mAb clones was tested on different diagnostic kits from three various manufacturers. Anti-Toxoplasma gondii IgM were titrated in several dilution rates following manufacturer's instruction and results were compared.

Second, mAb IgM batches reproducibility was tested. In this regard, three independent batches from one clone were produced and tested on a Vidas® Toxo IgM assay from bioMérieux.

Results:

mAb IgM candidate performance: Two clones of human chimeric monoclonal anti-Toxoplasma gondii IgM were titrated with different diagnostic kits. Results showed that the batches reacted in each assay until a pre-dilution of 1/16. Linearity was checked and the coefficient of determination was very good (R²=0.99).

mAb IgM reproducibility: Three independent batches of one clone were produced and tested. The standard deviation was calculated and showed that batches have reproducible reactivity in the Vidas® Toxo IgM assay from bioMérieux.

Conclusions: Human chimeric monoclonal anti-Toxoplasma gondii IgM products were tested and validated in various diagnostic assays. Results showed excellent performance and reproducibility obtained with this synthetic product. Human/mouse chimeric mAb can be easily and efficiently used as an alternative to disease state plasma for immunoassay quality controls.

A full range of products is available for infectious disease diagnostics and show equivalent performances.

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Genomic and proteomic analysis of 42 bacteriophages located in the genomes of 17 clinical strains of Klebsiella pneumoniae resistant to carbapenems

Ines María Bleriot Rial¹, Felipe Fernández-Cuenca¹, Lucia Blasco¹, Rocío Trastoy Pena¹, Antón Ambroa Abalo¹, Laura Fernandez García¹, Elena Perez-Nadales¹, Julián De La Torre Cisneros¹, Jesus Oteo¹, Ferran Navarro¹, Elisenda Miró², Alvaro Pascual Hernandez², Germán Bou Arevalo¹, Luis Martinez-Martínez³, Maria Tomas¹

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Abstract third-party references: Spanish Network for the Research in Infectious Diseases (REIPI), GEMARA-Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC)

Background: Klebsiella pneumoniae is responsible for severe nosocomial infections due to the continuous emergence of multi-drug resistant (MDR) pathogens. The decline in the effectiveness of antimicrobial treatments against MDR bacteria has generated a special interest in the study of bacteriophages. In this study, we identified a total of 42 Caudoviral bacteriophages present in 17 clinical strains of K. pneumoniae that produce carbapenemases belonging to 14 different STs corresponding to a total of 1.66 Mbp of sequence information (genomic/proteomic features). We determined their evolutionary relationship using comparative bioinformatic tools and microscopy techniques.

Materials/methods:
- 17 genomes of clinical strains of K. pneumoniae were sequenced and assembled de novo using the illumina-Miseq system and Velvet V1.2.10, respectively.
- Bioinformatic tools: PHASTER (bacteriophage identification), RAST PSI-BLAST and HHpred (protein annotation), ClustalW (evolutionary relationship), MVP (study interaction between bacteriophage and bacterial host) and GEPARD (dot plot alignment of nucleotide sequence).
- Microscopy studies were carried out by TEM assays.

Results: The study of the genomes resulted in the identification of 42 bacteriophages (Figure 1A), highlighting four of them with 33.3, 36.1, 39.9 and 42.2 kb genome sizes and similar genomic features present in several clinical strains and included in clusters (A, B and D) by phylogenetic analysis. Moreover, these bacteriophages showed high homology with international 4762, 4901,3499 and 4280 clusters of MVP. Bioinformatic analysis revealed the presence of 2363 proteins belonging to viral structure, transcription/replication and regulation. Although the majority of proteins had unknown functions, some of them showed an association with virulence (compounds of secretion systems-T3SS/T4SS or regulators-Mar like), antibiotic resistance (terB protein), and viral defense (Toxin-antitoxin modules, CRISPR-Cas and methyltransferase proteins) in bacteriophage genomes (Figure1B).

Conclusions: The presence of 42 caudoviral bacteriophages in the 17 clinical strains of K. pneumoniae showed relation with international 4762,4901,3499 and 4280 clusters of MVP database. Moreover, these bacteriophages harbored virulence, resistance and defense viral proteins that could determine the bacterial behavior. Future lines of research should focus on obtaining more information about genes of unknown function to achieve a better understanding of viral genomes for possible therapeutic application.
**Figure 1A** Transmission electron microscopy (TEM) images showing the different families of bacteriophages present in the different clusters. (A,B,C,F,G) Myoviridae family obtained from bacteriophages ST11-OXA245phi3.1, ST13-OXA48phi12.1, ST405-OXA48phi12.2, ST101-KPC2phi6.3 and ST846-OXA48phi9.2 of cluster A1, A2, B, D and E, respectively. (D,I) Siphoviridae family obtained from bacteriophages ST13-OXA48PHI12.2 and ST974-OXA48phi18 of cluster C and E, respectively. (E,G) Podoviridae family obtained from bacteriophages ST147-VIM1phi7.2 and ST11-VIM1phi8.2 of cluster D and E, respectively. **Figure 1B** Illustration representative of transmission of virulence, resistance and viral defense genes by bacteriophages in the bacterial chromosome of *Klebsiella pneumoniae* clinical isolates from this study.

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Abstract 985

**Efficacy and safety of ceftazidime-avibactam in adults with Gram-negative bacteraemia from five phase III randomised clinical trials**

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**Background:** An exploratory analysis was conducted in a subset of patients with Gram-negative bacteraemia from five randomised, controlled, multicentre Phase III trials in adults with complicated intra-abdominal infection [cIAI], complicated urinary tract infection [cUTI], hospital-acquired pneumonia [HAP] and ventilator-associated pneumonia [VAP], including infections caused by ceftazidime non-susceptible and multidrug-resistant Gram-negative bacteria.

**Materials/methods:** In each trial, RECLAIM and RECLAIM 3 [cIAI; NCT01499290/NCT01726023], REPRISE [cIAI/cUTI; NCT01644643], RECAPTURE [cUTI; NCT01595438/NCT01599806] and REPROVE [HAP/VAP; NCT01808092], patients were randomised 1:1 to intravenous ceftazidime-avibactam [plus metronidazole for those with cIAI] or comparators (carbapenems in >97% patients) for 5–21 days [treatment durations were defined by protocol for each study]. Efficacy assessments included clinical and microbiological responses at a test-of-cure [TOC] visit [timed according to study protocol] in the Gram-negative extended microbiologically evaluable [GNeME] population bacteraemia subset. Safety outcomes [including adverse events [AEs] and clinical laboratory assessments up to the last visit] were summarised for patients with any positive bacterial blood culture at baseline who received ≥1 dose of study treatment.

**Results:** The overall Phase III pool included 3172 patients [ceftazidime-avibactam treated patients, n=1855; comparator group, n=1857], of whom 101 [ceftazidime-avibactam, n=54; comparator, n=47] comprised the GNeME bacteraemia subset. The most common primary diagnoses among these patients [acute pyelonephritis [47%] and VAP [15%]] and the most frequently isolated pathogens [Escherichia coli [69%], Klebsiella pneumoniae [21%] and Pseudomonas aeruginosa [17%]] were consistent with the overall Phase III pool. Considering the low denominators in the bacteraemia subset, favourable clinical and microbiological response rates at TOC were generally similar for ceftazidime-avibactam and comparators within each indication and combined across indications [Table]. For 30 bacteraemia patients with ceftazidime non-susceptible isolates, overall favourable microbiological response rates were 6/11 [54.5%] for ceftazidime-avibactam ± metronidazole and 9/19 [47.4%] for comparator [difference 7.2%; 95% CI –28.72, 41.08]. The pattern of AEs in patients with bacteraemia was similar between treatment groups and consistent with the known safety profile of ceftazidime-avibactam.

**Conclusions:** This analysis provides supportive evidence of the efficacy and safety of ceftazidime-avibactam in patients with Gram-negative bacteraemia associated with cIAI, cUTI or HAP/VAP.

Study sponsored by Pfizer.

| Table. Clinical cure and favourable microbiological response rates at TOC for patients with Gram-negative bacteraemia associated with cIAI, cUTI or HAP/VAP treated with ceftazidime-avibactam and comparators (GNeME population) |
|---|---|---|---|---|---|---|---|
| Clinical cure | Favourable microbiological response |
| | Clinical cure | Comparator, n (%) | Difference, n (%) | Comparator, n (%) | Difference, n (%) |
| CAZ-av & MTZ, n (%) | Comparator, n (%) | CAZ-av & MTZ, n (%) | Comparator, n (%) |
| 
| UTI | 9/11 (81.8) | 9/10 (90.0) | -0.2 | 9/11 (81.8) | 9/10 (90.0) | -0.2 |
| 
| UTI, including acute pyelonephritis | 29/29 (100) | 29/29 (100) | 0.0 | 29/29 (100) | 29/29 (100) | 0.0 |
| 
| HAP, including VAP | 10/15 (66.7) | 5/6 (83.3) | -1.4 | 10/15 (66.7) | 5/6 (83.3) | -1.4 |
| 
| Overall | 47/54 (86.9) | 38/47 (80.5) | 4.1 | 47/54 (86.9) | 38/47 (80.5) | 4.1 |

Data posted from RECLAIM (NCT01499290), RECLAIM 3 (NCT01726023), REPRISE (NCT01644643), RECAPTURE (NCT01595438/NCT01599806) and REPROVE (NCT01808092). Clinical and microbiological responses at TOC and timing of TOC visits were as defined in each study protocol. All clinical cure definitions included resolution of signs and symptoms of the primary infection such that no additional antibiotics were required. Favourable microbiological response at TOC for patients in the bacteraemia subset required clearance of bacteraemia from post-baseline blood samples with eradication/remission of infection (and no new infection) at the primary infection site; for patients with UTI in RECAPTURE a urinalysis demonstrating <100 CFU/mL of the original uropathogen was also required.

CAZ-av = ceftazidime-avibactam; MTZ = metronidazole; CAZ = ceftazidime; CAZ-av = ceftazidime-avibactam; MTZ = metronidazole; inc = infection; n = number of patients with outcome; R = ratio of patients in group; TOC = test-of-cure; HAP, ventilator-associated pneumonia.

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Abstract 986

**Development of an antifungal stewardship programme at a London teaching hospital**

Laura Whitney1, Richard Wilson*1, Frances Davies1, Meg Coleman1, Jim Woo1, Renuka Palanicawandar1, Mark Gilchrist1

1Imperial College Healthcare NHS Trust, London, United Kingdom

**Background:** The need for antifungal stewardship (AFS) is gaining recognition due to increasing incidence of invasive fungal infection and antifungal resistance. This triggered an AFS quality improvement scheme initially implemented in London hospitals (April 2018), then throughout England (April 2019). Here we describe the first 18-months of an AFS programme in a London teaching hospital.

**Materials/methods:** A series of interventions were implemented (April 2018-November 2019) including; establishing a multidisciplinary (MDT) AFS team, monitoring antifungal consumption and usage through regular audit, monthly fungal MDT reviews of patients on Ambisome®, guideline updates, a quality improvement project to optimise azole therapeutic drug monitoring (TDM) and weekly AFS rounds for in-patients.

**Results:** Antifungal consumption increased from 63,000 DDDs in 2016-17 to predicted 70,000 in 2019-20 (fig.1) with expenditure reducing in year 1 (by £30,000), but predicted to increase in year 2 (due to increasing expenditure on mold-active azoles).

![Figure 1: Total Antifungal Expenditure and Consumption](image)

An audit of 86 patients on antifungal treatment showed high compliance with Trust guidelines on treatment choice (87%) and appropriate imaging (93%). Utilisation of fungal biomarkers for suspected invasive mold infection was relatively low; galactomannan sent in 73% patients in 2018 and 65% in 2019 and beta-D-glucan in 53% and 97%, respectively. Prolonged turn-around-times (median 14d) impact the utility of these tests. MDT reviews of patients on AmBisome® (average 6/month) advise to de-escalate or stop in 39% of patients (28% and 11%, respectively), with additional diagnostics often recommended (44%). Durations of empiric therapy for invasive mold infection where a diagnosis of IFI was not established were shorter after MDT initiation (median 8d in 2019 vs. 16d in 2018).

Appropriate azole TDM increased from 20% of patients to 70-90% following the quality improvement project. Weekly AFS rounds began in November 2019. To date 11 patients have been reviewed with interventions recommended in 82%. These include stopping (n=4) or defining treatment duration (n=1), and recommending diagnostics (n=1) and TDM (n=5).

**Conclusions:** A multi-faceted approach with increased MDT working and central funding has optimised antifungal usage within our organization. Lessons learned from our long-standing antibiotic stewardship programme have facilitated this. Work continues to identify areas for further improvement.

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Clinical experience of oral ibrexafungerp for treatment of four patients with invasive candidiasis from the FURI study

Juergen Prattes*, Christoph Zurl¹, Nkechi Azie², David Angulo Gonzalez², Robert Krause¹

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Abstract third-party references: Synexis

Background: Ibrexafungerp is a novel glucan synthesis inhibitor and the first member of a new class of triterpenoid antifungals. Its mode of action is inhibition of 1,3-β-D-glucan synthesis of the fungal cell wall, similar to echinocandins. However, ibrexafungerp is available orally and retains activity in candida strains resistant to echinocandins. As part of the open-label FURI trial, we report on four invasive candidiasis cases treated with oral ibrexafungerp at the Medical University of Graz.

Methods: FURI is an open-label Phase3 trial to determine the efficacy and safety of oral ibrexafungerp in patients with invasive fungal infections that are refractory to or intolerant of standard antifungal treatments or for whom long-term intravenous (IV) treatment is not feasible.

Results: Twenty-five patients were screened for study inclusion and four patients were ultimately included. The main underlying diseases were malignancy in two patients, psoriatic arthritis and kidney/pancreas transplantation in one patient each. The types of invasive candidiasis were as follows: Femoro-tibial osteomyelitis due to C. glabrata and C. albicans (N=1), candidemia due to C. parapsilosis (N=1), intraabdominal abscess due to C. krusei (N=1) and oropharyngeal candidiasis due to C. krusei and C. albicans (N=1). Two patients received oral ibrexafungerp because long-term IV treatment with an echinocandin was not feasible, one due to azole toxicity and one because of refractory disease despite standard antifungal treatment. The treatment duration with ibrexafungerp ranged from seven to 75 days.

At the end of treatment, two patients (candidemia and abscess) had a complete response, one patient (osteomyelitis) had a partial response and one (oropharyngeal candidiasis) had stable response (persisting thrush).

Most common adverse events possibly or probably related to ibrexafungerp were diarrhoea (n=3), nausea (N=1), rash (N=1) and tooth discoloration (N=1). Gastrointestinal adverse effects resolved in two out of three patients after a couple of days.

Conclusions: Oral ibrexafungerp was well tolerated, besides gastrointestinal side effects in the first days of loading dose. Ibrexafungerp was shown to be an effective treatment for invasive candidiasis infections. In addition, in-hospital stays could be significantly reduced in two patients as long-term IV treatment would be avoided with the use of oral ibrexafungerp.

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The evolving landscape of group A Streptococcus in marginalised populations in England and Wales

Juliana Coelho¹, Natalie Groves¹, Roger Daniel¹, Karen Broughton¹, Colin Brown¹, Lara Utsi², David Leeman³, Katy Sinka⁴, Isabel Oliver⁵, Derren Ready*¹


Background: The PHE streptococcal reference laboratory types all GAS isolates recovered from patients with invasive infections, and from superficial infections for outbreak-related cases. Increasing numbers of GAS isolates from people who inject drugs (PWID), people in prison and/or people who are homeless have been detected, and national investigation established. Surveillance data from the reference laboratory indicates an increase in the number of reported iGAS isolates from an average of 9.5 cases between 2010-2015 to 1 45 cases in 2017; 277 cases in 2018; 190 cases so far in 2019. We report here characterisation of strains received from January 2018 to August 2019 associated within this marginalised population.

Materials/methods: GAS isolates were characterised by emm gene sequence typing. PWID, prison and homeless status were updated from health protection management systems (HPZone) from 2018 onwards, leading to increased case ascertainment. Whole genome sequence data was obtained for a sample of cases to identify risk factors for transmission.

Results: 32 clusters of GAS infections were identified; 17 linked to PWID/homeless shelters and 15 to prisons with a total of 332 and 73 isolates received from these settings, respectively. The dominant emm types were emm 108.1 (29%), emm 66.0 (27%) and emm 94.0 (8%), and do not reflect those commonly found in the general population, being emm 1.0 (20%), emm 89.0 (10%) and emm 3 (8%). SNP analysis of WGS data of emm 108.1 strains suggest recent clonal expansion of single lineage within this population; data from the emm 66.0 strains revealed a number of geographically related clades, suggesting that this strain has been circulating for longer has become established within this population. Infections in PWID, the homeless community and prisoners were predominately found in males, and spread across England and Wales concentrating in some English cities.

Conclusions: These findings indicate increasing burden of severe, invasive GAS infections in PWID, with clusters emerging in prisons in England and Wales, dominated by lineages not commonly found in other communities. Data suggests recent clonal expansion of emm 108.1 strain and increased incidence of previously established emm 66.0 strains. Further investigations are underway to understand transmission networks.

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Abstract 990

Development of a simultaneous population pharmacokinetic model for aztreonam-avibactam

Rujia Xie*, Phylinda Chan, Margaret Lynn Mcfadyen, Susan Raber

1Pfizer, Singapore, Singapore, 2Pfizer, Sandwich, United Kingdom, 3Pfizer, La Jolla, United States

Background: In previously reported population pharmacokinetic (PK) analyses and exposure simulations, aztreonam and avibactam were modelled separately to select the Phase IIa (completed) and Phase III (planned) aztreonam-avibactam dosage regimens [maintenance dose 1500/500 mg 3-h intravenous infusions every 6 h for adult patients with estimated creatinine clearance [CrCl] > 50 mL/min], including loading doses and adjustments for renal impairment.

Materials/methods: The existing aztreonam and avibactam models were updated with additional adult [one Phase IIa trial] and paediatric [avibactam only; one Phase I and two Phase II trials] clinical PK data to develop a simultaneous aztreonam-avibactam population PK model to account for correlation in PK of the two components. Population PK analyses were conducted using nonlinear mixed-effects modelling with first-order conditional estimation method with interaction. Models were evaluated using pre-defined goodness-of-fit criteria and prediction-corrected visual predictive checks (pcVPCs).

Results: In total, 2921 aztreonam plasma concentrations from 141 adults [patients and healthy volunteers], 16,175 avibactam plasma concentrations from 2349 adults, and 510 avibactam plasma concentrations from 154 paediatric subjects [3 months to <18 years] were included in the analysis. The final aztreonam and avibactam population PK models were two-compartment disposition models with first-order elimination, with correlation in interindividual variability (IIV) on clearance [CL] and central volume [Vc]. Body weight [standard allometry] and body surface area-normalised CrCl [nCrCL], or postmenstrual age for subjects <2 years, were key covariates that predicted clearance of both drugs. Estimated base and final model PK parameters for the reference typical healthy subject weighing 70 kg are shown in the Table; final estimates for aztreonam CL, and for the exponent of nCrCL on aztreonam clearance, were similar to previous analyses. In pcVPCs, model predictions of observed data were generally adequate.

Conclusions: Simultaneous modelling of aztreonam and avibactam enables estimation of the correlation of PK IIV on CL and Vc of the two drugs, facilitating efficient parametric simulation. Simulations using these models further support the adult aztreonam-avibactam dosage regimens [including renal dose adjustments] selected for Phase III evaluation and provide initial weight-based doses for evaluation in paediatric studies.

Table. Parameter estimates for the base and final simultaneous aztreonam-avibactam PK models

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<tr>
<th>Parameter</th>
<th>Base model [AST70276]</th>
<th>Final model [AST70687]</th>
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<td>5.96 (0.9)</td>
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<td>Vc (L)</td>
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Presenter email address: rujia.xie@pfizer.com
Abstract 994

Prospective surveillance of health-care associated infections in residents in long term care facilities in Graz, Austria

Elisabeth König*, Mara Haubenwallner¹, Christian Pux², Karin Prisching³, Walter Schippinger⁴, Eric Stoiser⁴, Robert Krause¹, Ines Zollner-Schwetz¹

¹Medical University of Graz, Section of Infectious Diseases, Graz, Austria, ²Geriatric Health Centres Graz, Graz, Austria

Background: Residents in long term care facilities (LTCF) are at increased risk for healthcare-associated infections (HCAI). Incidence rates in the literature range from 1.8 - 13.5 infections per 1,000 resident days. However, data on HCAIs in residents of LTCFs in Austria are scarce. Therefore, the aims of our study were (1) to evaluate the incidence rate of HCAIs per 1,000 resident days in four LTCFs in Graz, Austria (2) to characterise the spectrum of HCAIs and (3) to study the use of antimicrobial substances.

Materials/methods: We conducted a prospective surveillance study from January 1 to December 31, 2018 in four LTCFs of the Geriatric Health Centre of the City of Graz with a total of 388 beds. HCAIs were defined based on ECDC HALT project.

Results: During the 12-month surveillance period, 306 infections of 182 residents (130/182 female) were recorded (136,988 resident days). The mean age of the residents was 85.8 ± 9.2 years (range 51-102 years), 56% (103/182) of residents were older than 85 years. The overall incidence rate of HCAIs was 2.2 per 1,000 resident days. Urinary tract infections occurred most frequently (160/306, 52%, 1.17 per 1,000 resident days), followed by skin, soft tissue and mucosal infections (85/306, 27%, 0.62 per 1,000 resident days), table 1. Only 7/306 (2.2%) HCAIs were acquired outside the LTCFs. 14.3% (23/160) of UTIs were device-associated. 262/306 (85.6%) infections were treated with oral antimicrobial substances. For UTIs (n=160) the most commonly used substances were quinolones (25%), folate antagonists (23%) and pivmecillinam (21%).

Conclusions: The overall incidence rate for HCAI was relatively low at 2.2 per 1,000 resident days. To our knowledge this is the first study on prospective surveillance of HCAIs in LTCFs in Austria.

Table 1:

<table>
<thead>
<tr>
<th>Type of infection</th>
<th>Number of infections</th>
<th>Rate per 1000 resident days</th>
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<tbody>
<tr>
<td>Urinary tract infections</td>
<td>160 (52%)</td>
<td>1.17</td>
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<tr>
<td>Skin, soft tissue &amp; mucosal infections</td>
<td>85 (27%)</td>
<td>0.62</td>
</tr>
<tr>
<td>Lower respiratory tract infections</td>
<td>49 (16%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Influenza</td>
<td>1 (0.3%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>6 (2%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>3 (1%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Unexplained febrile illness</td>
<td>6 (2%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Total</td>
<td>306</td>
<td>2.2</td>
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</table>

Presenter email address: elisabeth.ullrich@medunigraz.at
**Abstract 995**

**Melioidosis in French Guiana? Cases with a clinical isolate of Burkholderia sp., Cayenne, 2012 – 2018**

Yann Lambert¹, Vincent Sainte-Rose², Cyril Leborgne², Brigitte Moreau², Magalie Demar²

¹Centre Hospitalier de Cayenne, Centre d’Investigation Clinique Antilles-Guyane, Cayenne, French Guiana, ²Centre Hospitalier de Cayenne, Laboratoire de biologie polyvalente, Cayenne, French Guiana

**Background:** Melioidosis is an infectious disease caused by *Burkholderia pseudomallei*, a Gram-negative bacterium found in tropical soil and water. It is frequently diagnosed in South-East Asia and Northern Australia. The variety of its clinical presentations complicates the diagnosis of melioidosis, especially in low-incidence areas where it is often little known. For the past few years, cases have been regularly reported in Amazonian countries such as Colombia, Venezuela and Brazil. The disease has never been identified in French Guiana.

**Materials/methods:** Microbial identification of bacterial species at Cayenne Hospital has been relying on VITEK 2 since 2012 and MALDI-TOF since 2014. These two automated techniques have been known to regularly confuse *B. pseudomallei* with other species of the *Burkholderia* genus, in particular that of the *B. cepacia* complex. Cases associated with a *Burkholderia* sp. isolate between 2012 and 2018 were identified from the databases of the bacteriology laboratory of Cayenne Hospital. The clinical history of each case was then documented from their medical record.

**Results:** 63 cases were identified. 51 cases, of which 15 premature neonates, were diagnosed with a nosocomial *B. cepacia* infection or colonization associated with a stay in an intensive care unit. For nine cases the nosocomial origin of the *Burkholderia* isolate cannot be ruled out. Three cases have a clinical history and risk factors compatible with melioidosis; two of them are associated with a clinical isolate of either *B. pseudomallei* or *B. thailandensis*.

**Conclusions:** We hypothesize that melioidosis is encountered in French Guiana sporadically, in consistence with other Amazonian territories. Three observations suggest an endemic potential of melioidosis in French Guiana. Firstly, the possible soil contamination from the regular importation of vegetal species from South-East Asia. Secondly, the high prevalence in French Guiana of known risk factors for melioidosis, diabetes in particular. Thirdly, the population of clandestine gold miners, potentially at risk for transmission through their high mobility in the Region of the Guyana Shield and their repeated exposure to muddy and anthropized soils.

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Abstracts 2020

Abstract 996

Antibacterial prescribing in the outpatient setting: results from a longitudinal surveillance programme and a sentinel network of physicians: Switzerland, 2018

Catherine Pluess-Suard1, Damir Perisa1, Olivier Friedli1, Mirjam Mäusezahl-Feuz2, Andreas Kronenberg1

1University of Bern, Bern, Switzerland, 2Federal Office of Public Health, Bern, Switzerland

Background: Inappropriate or unnecessary use of antibacterials may foster the development of antibiotic resistance. Our goals were to assess the global antibacterial use, the number of antibacterial prescriptions and the proportion of antibacterial classes per clinical indications in the outpatient setting in Switzerland.

Materials/methods: We analyzed two sources of data: (i) IQVIA®, a private provider of manufacturers’ sales, delivered aggregated data which were then converted in the ANRESIS database into defined daily doses (DDD) using the 2019 WHO DDD definition and (ii) all consultations with antibacterial prescriptions reported from 146 practitioners from general and internal medicine during 2018 using the representative Swiss Sentinel Surveillance Network “Sentinella”. The network covers all regions of Switzerland. Extrapolation on population level was done by attributing the estimated covered population to each Sentinella physician. Data from pediatricians were excluded.

Results: In 2018, the total consumption of antibacterials for systemic use in outpatients was 9.0 DDD per 1000 inhabitants per day, corresponding to a reduction of 9% since 2015 (p<0.05). A total of 14092 antibacterial prescriptions were issued by participating physicians in 2018, corresponding to 110.3 antibacterial prescriptions per 1000 inhabitants. Bladder infections (26%), upper respiratory tract infections (26%) and lower respiratory tract infections (20%) were the main clinical indications for prescribing antibacterials. Acute bronchitis and streptococcal pharyngitis accounted resp. for 9% and 7% of total antibacterial prescriptions. Fosfomycin (31%), fluoroquinolones (24%), co-trimoxazol (21%), and nitrofurantoin (15%) were the most prescribed antibacterials for bladder infections. For lower respiratory infections, amoxicillin (33%), macrolides (29%) and penicillins with beta-lactamase inhibitors (9%) were the most prescribed antibacterial classes. Fluoroquinolones accounted for 7% of antibacterials for this indication.

Conclusions: Even if antibiotic consumption in Switzerland is low in comparison with other European countries, the quality of antibacterial prescriptions can be optimized, particularly in reducing (i) the use of antibacterials in acute bronchitis, a viral infection in more than 90% of cases and (ii) the use of fluoroquinolones for bladder infections. Resources for antibiotic stewardship programs in the outpatient setting are also needed in countries with low antibacterial consumption.

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Genomic epidemiology and resistome analysis of Helicobacter pylori

Tal Domanovich-Asor1, Yair Motro1, Boris Khalfin1, Hillary Craddock*1, Avi Peretz2, Jacob Moran-Gilad1

1Ben Gurion University of the Negev, MAGICAL Group, Faculty of Health Sciences, Beer Sheva, Israel, 2Bar-Ilan University, Clinical Microbiology Laboratory, Baruch Padeh Medical Center, Poriyah and Azrieli Faculty of Medicine, Galilee, Israel

Background: Antimicrobial resistance (AMR) in Helicobacter pylori (HP) is increasing globally and can result in treatment failure and inappropriate antibiotic usage. Whole genome sequencing (WGS) allows a comprehensive analysis of the resistome as well as typing and can thus be used to explore the phylogeny of HP in relation to underlying mechanisms of AMR.

Materials/methods: HP isolates (n=48) recovered from routine clinical samples in northern Israel underwent phenotypic antimicrobial susceptibility testing (AST) against five antimicrobials using an E-test as per BSAC guidelines. Literature review identified 114 point mutations reported to correlate with phenotypic resistance against those antibiotics. WGS was performed on an Illumina platform following library preparation using Nextera FLEX. Publicly-available HP genomes (n=992) were assembled (total isolate n=1,040). Analysis was conducted via our in-house bioinformatics pipeline for resistome analysis targeting point mutations in the relevant genes (bpb1A, 23s rRNA, gyrA, rdxA, frxA, and rpoB) and phylogenomic analyses using multilocus sequence typing (MLST) and core genome (cg)MLST methods (chewBBACA and GrapeTree).

Results: Phylogenomic analysis revealed a notable geographical clustering of HP genomes across world regions. The majority of Israeli isolates clustered together, closely with the Asian branch (Figure 1). Resistance to at least one antibiotic was observed in 79% of Israeli isolates. Resistance rates were as follows: 54% for clarithromycin, 31% for metronidazole, 10% for amoxicillin, 4% for rifampicin, and 2% for levofloxacin. Genotype-to-phenotype correlation was inconsistent; for every analysed gene at least one phenotypically susceptible isolate was found to have a mutation previously associated with resistance. This was also observed regarding mutations used in commercial kits to diagnose AMR in HP cases; for example, our study observed that 10/17 isolates with the A2143G/23s rRNA mutation are phenotypically susceptible. Furthermore, 13 novel point mutations were identified which were associated with a resistant phenotype in some but not all studied isolates.

Conclusions: This is the largest study to date featuring the global phylogeny of HP based on >1K genomes in conjunction with a global snapshot of the HP resistome. Analysis of a unique set of Israeli isolates demonstrates that inconsistencies and limitations in inferring a genotype-to-phenotype correlation in HP remains challenging.

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Abstract 998

Carrier prevalence of vancomycin-resistant Enterococcus faecium (VREfm) among patients admitted to emergency departments in Copenhagen (Denmark) compared with VREfm prevalence of the background population

Ingrid Maria Cecilia Rubin1, Mette Pinholt1, Henrik Calum1, Christiane Pahl Kavalris2, Michelle From-Hansen1, Marie Stangerup2, Henrik Westh3, Jenny Knudsen3

1Hvidovre Hospital, Department of Clinical Microbiology, Hvidovre, Denmark, 2Bispebjerg Hospital, Infection Control, København, Denmark, 3Rigshospitalet, Department of Clinical Microbiology, København, Denmark

Background: The aim of our study was to describe the prevalence of VREfm-carriers admitted to two of the hospitals in the Capital Region of Denmark during a 3-week screening period. The main outcome was to examine the prevalence of unknown VREfm-carriers. The secondary outcome was to compare this with the VREfm prevalence in the background population.

Materials/methods: We obtained a rectal swab from all adult patients willing to participate, who were admitted to either the Emergency Department at Bispebjerg Hospital or Frederiksberg Hospital during a 3-week period in June and July 2019. All patients were screened for age, hospital admissions in the last 6 months and antibiotic consumption within the last 6 months. The swabs were analyzed for VREfm by culture and PCR for the vanA gene at the Department of Clinical Microbiology, Hvidovre Hospital. We also obtained 100 fecal samples sent to our department by General Practitioners in the Capital Region of Denmark. The following exclusion criteria were set up: age below 50, VREfm and Clostridium difficile positive within 6 months, hospital admission within 6 months and travel abroad. They were subsequently screened for VREfm as mentioned above.

Results: We included 172 patients who were admitted during the 3-week period. The median age was 72 years. In total, 11 (6.3%) were colonized with VREfm. 6 (3.4%) were known VREfm-carriers and 5 (2.9%) were unknown VRE-carriers. Of these unknown carriers, all had been hospitalized and received antibiotics within the last month.

Of the 100 fecal swabs sent by the General Practitioners, 1 out of 100 (1%) had a positive vanA PCR and none were culture positive.

Conclusions: Hospital admission and antibiotic use within the last month predispose to colonization with VREfm. We found a prevalence of 2.9% of unknown VRE-carriers. In comparison, we found that 1% of the patients without prior hospitalization or antibiotic use, were VREfm positive.

Admission VRE screening could help relieve the burden of VREfm transmission within our hospitals. From this study our recommendation is to screen all patients admitted to the ER who have been hospitalized within the last month.

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**Modulation of the microbiota by oral intake of a synbiotic mixture in healthy volunteers: a single-centre one-armed pilot study**

Ingrid Maria Cecilia Rubin*, Sarah Mollerup*, Mette Pinholt*, Martin Schou Pedersen†, Thomas Kallemose†, Henrik Westh‡, Andreas Munk Petersen§,

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**Background:** A synbiotic product combines one or more probiotic microorganisms with a prebiotic fibre. Synbiotics have been demonstrated to change the microbiota composition in different patient populations.

Prebiotics, which are carbohydrates that are only metabolized by the gut bacteria, have gained much attention in recent years for their health benefits through stimulating growth of specifically the anaerobic bacteria from the *Bacteroides* family that produce short chain fatty acids.

Whether the microbiota in a steady state in healthy individuals will change by the addition of synbiotics is unexplored. Our aims were to monitor the GI-function and explore the modulation of the healthy microbiota by synbiotics in a pilot trial of healthy volunteers.

**Materials/methods:** We recruited 15 healthy volunteers who consumed a synbiotic mixture consisting of *Lactobacillus rhamnosus* [LGG®], *Lactobacillus acidophilus* [LA-5®], *Lactobacillus paracasei* [L. casei 431®], *Bifidobacterium lactis* [BB-12®] and the plant carbohydrate inulin [15g] for four weeks. Faecal samples were collected at visit 1 (baseline) as well as at completion of the intervention. All participants completed a faecal diary based on the Bristol Stool Scale and recorded their gastrointestinal (GI) well-being. We used shotgun metagenomic sequencing for the microbiome studies on an Illumina NextSeq, and performed taxonomic profiling using MetaPhlAn2.

**Results:** 14 out of 15 volunteers successfully completed the four-week synbiotic intervention. One participant was not compliant with the intervention and was therefore excluded from the analyses. At the end of the intervention, 36% experienced a better GI-function in the self-reported diary, 43% reported an unchanged GI-function, while 21% reported a worse GI-function. For our microbiome analyses, the α-diversity was unchanged before and after the intervention. We found a higher relative abundance of *Bifidobacterium* and *Lactobacillus* spp. after the intervention.

**Conclusions:** The intervention with synbiotics leads to higher relative abundance of the potentially beneficial species of *Bifidobacterium* and *Lactobacillus* but it did not affect the α-diversity. Most participants [79%] reported an unchanged or better GI-function at the end of the intervention.

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Rapid, sensitive diagnosis of bloodstream infection using clinical metagenomics

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Background: In the UK, approximately 250,000 cases of sepsis are reported annually, of which ~20% result in death. The estimated economic impact of sepsis is £2 billion/annum. Patients with sepsis need rapid treatment with effective antibiotics, otherwise mortality rates increase dramatically. Rapid and accurate diagnostics are needed to identify the infecting pathogen to determine the appropriate therapy. However, current diagnostic methods rely on blood culture which has low sensitivity and takes 2-5 days before results are available. Here we describe a novel clinical metagenomics-based method for the diagnosis of bloodstream infection in patients suspected of sepsis, combining highly sensitive microbial cell capture with efficient host depletion and nanopore sequencing.

Materials/methods: Whole human blood was diluted (1:1) in liquid transfer medium (Momentum Bioscience Ltd., UK). *Escherichia coli* was incubated at 37°C for 2 hours in the blood-transfer medium, and subsequently tested at 10⁴ to 10² CFU/mL. Samples were subjected to simultaneous blood lysis and magnetic bead-based microbial capture (Momentum Bioscience Ltd.), saponin-based host DNA depletion, whole genome amplification (REPLI-g Single Cell kit, Qiagen) and MinION sequencing (RPB004 kit, Oxford Nanopore Technologies Ltd., UK). Sequence data was analysed using EPI2ME software (Oxford Nanopore Technologies Ltd.). Samples were classified as positive for a pathogen if present at >1% of the total classified reads.

Results: *E. coli* was detected in all samples tested after 1.5 hours sequencing demonstrating a limit of detection <100 CFU/mL (Table 1). Antimicrobial resistance genes were detected in all samples but transferrable resistance prediction was unreliable at low genome coverage (<5x).

<table>
<thead>
<tr>
<th>Sample [CFU/mL blood]</th>
<th>Total reads</th>
<th>Classified</th>
<th>Human</th>
<th>E. coli (genome coverage x)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10⁴ E. coli</td>
<td>93,559</td>
<td>53,827</td>
<td>5,264</td>
<td>35,087 (9.4)</td>
</tr>
<tr>
<td>10³ E. coli</td>
<td>93,060</td>
<td>32,189</td>
<td>4,790</td>
<td>6,909 (2.1)</td>
</tr>
<tr>
<td>10² E. coli</td>
<td>111,638</td>
<td>33,235</td>
<td>7,945</td>
<td>1,779 (0.8)</td>
</tr>
</tbody>
</table>

Conclusions: This proof-of-principle study demonstrates sensitive pathogen and antibiotic resistance profiling directly from blood in <8 hours using nanopore sequencing-based clinical metagenomics. This approach combined with ETGA® [Enzyme Template Generation & Amplification] technology (Momentum Bioscience Ltd.), enables the detection of viable micro-organisms from whole blood for the rapid diagnosis and management of bloodstream infections.

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**Abstract 1004**

**A surface-engineered scaffold implant with direct antibacterial activity against *Staphylococcus aureus***

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Abstract third-party references: Part of this research was supported by Fondazione CRT 2019 (P.I. Prof. Valeria Allizond)

**Background:** Biomedical implants and devices, an essential part of the medical treatments for improving therapeutic efficiency, still suffer from bacterial infections that hamper patients’ recovery and even threaten patients’ lives. Although antibiotics are widely used to treat those infections, it has brought serious problems of antibiotic resistance. Metal ions, such as silver, are believed to be promising additives in developing antibacterial biomaterials, owing to possessing favorable bactericidal effects against antibiotic-resistant bacteria. Furthermore, the incorporation of bioactive, stiff inorganic materials (e.g., hydroxyapatite, HA, and β-tricalcium phosphate, β-TCP) into synthetic biodegradable polymers, such as poly(ε-caprolactone) (PCL) polymer can lead to significant enhancements in mechanical properties, bioactivity, and bone regeneration ability in vivo. The present research purpose is the development of novel PCL-based scaffolds, modified with both silver, to supply antibacterial behavior, and biphasic calcium phosphates (BCP; the mixture of HA and β-TCP) denoted as to impart bioactive/bioresorbable properties.

**Materials/methods:** PCL and BCP/PCL porous pellets, functionalized with silver ions (Ag⁺) were developed by salt-leaching method and both sodium chloride, NaCl, and sodium nitrate, NaNO₃ were used as pore formers. Samples were further characterized from the morphological and chemical point of view. *Staphylococcus aureus* ATCC 29213 adhesion on PCL-based biomaterials was assayed through a sonication protocol to dislodge adherent microorganisms without altering their viability. The planktonic bacteria number was also determined.

**Results:** Field Emission Scanning Electron Microscopy showed that the samples were characterized by square-shaped macropores (Figure 1), whose average dimension was in agreement with that of the starting salt. The presence of PCL and BCP phases and of Ag, in the correct amount, were confirmed by X-Ray Diffraction and Energy Dispersive X-ray Spectroscopy analysis, respectively. The antibacterial tests revealed a significant (p<0.001) decrease either of adherent staphylococci on the Ag-functionalized surfaces (Figure 2) or planktonic bacteria, thus proving the Ag release from the enriched PCL-based samples.

**Conclusions:** Due to the combined antimicrobial and biodegradable properties, the PCL-based scaffolds enriched with silver showed good potential for bone tissue engineering and offer a promising strategy, as an ideal microbial anti-adhesive tool for the reduction in BAls and antimicrobial molecules-targeted delivery.

**Figure 1:** FESEM micrographs of PCL scaffolds obtained by using NaCl (a) and NaNO₃ (b) salts as templates (analysis carried out on the materials sections); (c): higher magnification FESEM micrograph of PLC/BCP sample, showing the fine and homogeneous distribution of the calcium phosphate particles inside the polymer matrix (see the black arrows); Ag-functionalized PCL scaffolds obtained by using NaCl (d) and NaNO₃ (e) salts as templates (analysis carried out on the materials sections); (f): Typical microporous surface of the scaffolds.
Figure 2: Adhered S. aureus ATCC 29213 (log$_{10}$ CFU/ml) on different PCL-based biomaterial pellets: PCL (polycaprolactone), BCP/PLC (polycaprolactone functionalized with biphasic calcium phosphates), PCL+Ag (polycaprolactone enriched with silver ions), BCP/PLC +Ag (polycaprolactone functionalized with biphasic calcium phosphates and enriched with silver ions).

* $p<0.001$

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Abstract 1006

In vitro evaluation of the influence of immunosuppressive agents on human polyomavirus BK replication

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Background: Human Polyomavirus BK (BKPyV) infection is common, ranging from 60% to 100% in the general population. After primary infection, which occurs asymptotically during childhood, BKPyVs establishes a life-long latency in tubular kidney epithelial cells. The immunosuppressive therapy, typical of transplant recipients, is a risk factor for BKPyV reactivation, that causes Polyomavirus Associated Nephropathy (PVAN), and organ rejection in 1 to 10% of patients. Immunosuppression treatment is a complex therapy, constituted by a combination of mTOR and calcineurin inhibitors (FK506, Rapamycin and Everolimus) and antiproliferative agents, such as mycophenolic acid (MPA). In the case of post-transplant BKPyV reactivation, the reduction of the immunosuppressive regimen and the administration of Leflunomide, a nonspecific antiviral treatment, are used as effective actions.

Materials/methods: HEK293T cell line was infected with BKPyV virions. Infected cells were treated with FK506, Rapamycin, Everolimus, and MPA, as single or coupled drug treatments, after the evaluation of the IC50 for each drug. Leflunomide treatment was used as control of viral replication inhibition. The viral replication, in presence or absence of drugs, was tested by means of BKPyV specific quantitative real time PCR (qPCR) on cell medium. BKPyV mean replication level in treated cells was expressed as percentage of replication and normalized using the BKPyV replication level of not treated infected cells.

Results: BKPyV mean replication level were 87.03%, 70.29%, 68.41% and 44.38% after treatment with FK506, MPA, Rapamycin and Everolimus respectively. The treatment composed by FK506 and Everolimus, or MPA or Rapamycin was associated with mean replication level of 69.27%, 79.75% and 90.72% respectively. Additionally, the BKPyV mean replication level was 79.71% and 58.27% after the treatment with MPA and Sirlimus and with MPA and Everolimus, respectively.

Conclusions: Immunosuppressive therapy based on FK506 administration represents an important risk factor for the reactivation of BKPyV and the development of PVAN. However, FK506 post-transplant treatment is fundamental to maintain an adequate level of immunosuppression. For this reason, the administration of FK506 in association with Everolimus, instead of MPA, could represent an alternative therapeutic strategy, able to guarantee a good immunosuppressive regimen and a limited reactivation of BKPyV.

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Abstract 1007

Impact of lung transplantation on the phylogenetic diversity of *Pseudomonas aeruginosa* isolates from end-stage cystic fibrosis patients

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**Background:** Impaired lung function and chronic infections due to colonization and infection by complex microbiota elevates the health risk of patients with cystic fibrosis (CF) which can ultimately lead to full respiratory insufficiency and death. For patients with end-stage CF lung disease, lung transplantation (LTx) is the only remaining therapeutic option. In this context, *Pseudomonas aeruginosa* is a principal cause of chronic lung infections and such strains display different phenotypic and genomic characteristics compared to their wild-type ancestors.

The aim of this study was to analyze the epidemiology and evolution of *P. aeruginosa* strains serially obtained from CF patients, and a non-CF bronchiectasis patient, who underwent LTx (Newcastle upon Tyne, UK).

**Materials/methods:** A panel of 708 *P. aeruginosa* strains from different niches and 4 different strain collections were analyzed for genomic relatedness. These comprised the bioMérieux collection (*n* = 219), Kos collection (*n* = 390), Pirnay collection (*n* = 63) and sequential strains from six LTx patients (*n* = 36). For each LTx patient, samples were collected before, during and after the LTx at different time points. Multi-locus sequence typing (MLST) and construction of a core genome based phylogenetic tree using bioinformatics tools was employed to define the genomic relatedness among the different *P. aeruginosa* strains.

**Results:** The genome wide assessment showed clustering with respect to the origin of the isolates i.e from patients from whom they were isolated implying intra-individual variability. The MLST profiles showed the *P. aeruginosa* strains from the Newcastle CF patients, but not the bronchiectasis one, had previously unidentified sequence types. Strains from Newcastle were scattered among the phylogenetic tree, indicating that the patients were neither cross-colonized nor cross-infected.

**Conclusions:** *P. aeruginosa* isolates from CF patients disclose very specific traits, but they could be phylogenetically distant between patients. On the other hand, LTx and associated treatment had no impact on the phylogenetic type of the *P. aeruginosa* strain harbored by each studied patient. Studying the presence of SNPs may aid our understanding of elevated resistance to the drugs used for treatment.

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Impact of underlying comorbidities on outcomes of patients treated with ceftaroline fosamil for complicated skin and soft-tissue infections: pooled results from three phase III clinical trials

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Background: In three Phase III studies, ceftaroline fosamil was shown to be non-inferior to vancomycin plus aztreonam for the treatment of complicated skin and soft tissue infections (cSSTI). This exploratory analysis evaluated the impact of underlying comorbidities on clinical outcomes in patients with cSSTI pooled from these three studies.

Materials/methods: CANVAS 1 (NCT00424190), CANVAS 2 (NCT00423657) and COVERS (NCT01499277) were Phase III, multi-centre, randomised double-blind studies of ceftaroline fosamil [600 mg every 12 hours [q12h; CANVAS 1 and 2]; 600mg every 8 hours [q8h; COVERS]] vs vancomycin plus aztreonam [1 g q12h each [CANVAS 1 and 2]; vancomycin 15 mg/kg q12h and aztreonam 1 g q8h [COVERS]] in hospitalised adults with cSSTI. The primary efficacy variable in each trial was clinical response at the test-of-cure (TOC) visit in the modified intent-to-treat and clinically evaluable (CE) populations. Subgroup analyses exploring the impact of age and various baseline comorbidities were performed on the pooled CE population.

Results: In total, 1808 patients were included in the CE population (1005 ceftaroline fosamil; 803 vancomycin plus aztreonam). Baseline patient characteristics were generally balanced across treatment groups. Overall clinical cure rate at TOC in the CE population was 89.7% for ceftaroline and 90.8% for vancomycin plus aztreonam (difference [95% confidence interval]: –1.13 [–3.87, 1.67]). Clinical response rates at TOC by comorbidity are shown in the Table; results were generally consistent with those of the overall cSSTI population.

Conclusions: This analysis provides supportive evidence of the efficacy of ceftaroline fosamil in patients with cSSTI with underlying comorbidities.

Study sponsored by Pfizer.

Table. Clinical cure rates at TOC by baseline age and comorbidity subgroups in patients with cSSTI (CE population)

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>Number (%) of patients</th>
<th>Difference, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ceftaroline fosamil</td>
<td>Vancomycin + aztreonam</td>
</tr>
<tr>
<td></td>
<td>(N=1065)</td>
<td>(N=803)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤65</td>
<td>733/817 (89.7)</td>
<td>582/641 (80.8)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>100/186 (59.0)</td>
<td>147/162 (87.8)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>743/832 (89.0)</td>
<td>606/664 (91.3)</td>
</tr>
<tr>
<td>Yes</td>
<td>152/173 (87.9)</td>
<td>123/136 (88.5)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>802/892 (89.9)</td>
<td>645/700 (91.0)</td>
</tr>
<tr>
<td>Yes</td>
<td>99/113 (87.0)</td>
<td>84/94 (96.4)</td>
</tr>
<tr>
<td>Cancer/malignancy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>877/980 (89.7)</td>
<td>714/764 (91.1)</td>
</tr>
<tr>
<td>Yes</td>
<td>24/27 (88.9)</td>
<td>15/19 (78.9)</td>
</tr>
<tr>
<td>Renal status (CrCL: mL/min/1.73m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe impairment (≤26 to ≤39)</td>
<td>3/4 (75.0)</td>
<td>0/1 (0.0)</td>
</tr>
<tr>
<td>Moderate impairment (&gt;30 to ≤59)</td>
<td>30/48 (64.8)</td>
<td>26/57 (78.4)</td>
</tr>
<tr>
<td>Mild impairment or normal (&gt;50)</td>
<td>85/164 (66.0)</td>
<td>69/259 (61.0)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>18/26 (69.2)</td>
<td>10/11 (90.9)</td>
</tr>
<tr>
<td>≥18.5 to &lt;25</td>
<td>310/343 (91.0)</td>
<td>232/258 (89.0)</td>
</tr>
<tr>
<td>≥25 to &lt;30</td>
<td>569/632 (89.9)</td>
<td>486/533 (81.2)</td>
</tr>
</tbody>
</table>

Data not collected for 9 patients in the ceftaroline group and 6 patients in the vancomycin plus aztreonam group.

CE: clinically evaluable; CI: confidence interval; CrCL: creatinine clearance; cSSTI: complicated skin and soft tissue infections; TOC: test of cure.
Abstract 1015

Association of single nucleotide polymorphisms in IL1B and IL28B genes with the outcome of congenital cytomegalovirus infection

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Background: Cytomegalovirus (CMV) is the most common viral cause of congenital infections, which can result in a spectrum of neurodevelopmental disorders. The factors that render developing foetus prone to CMV are not well defined. The aim of this study was to evaluate polymorphisms in genes involved in human viral defence mechanisms in relation to risk and clinical outcome in newborns with congenital CMV infection (cCMV).

Materials/methods: This prospective study comprised 236 newborns, including 92 with cCMV infection confirmed by CMV-DNA detection in urine samples collected during the first 2–3 weeks of life (case group). A healthy control group consisted of 144 CMV-uninfected newborns. All children with cCMV infection underwent complete physical examination, ophthalmologic and hearing evaluation, and cranial ultrasound and/or magnetic resonance imaging. Using hypothesis-driven candidate genes and their function in viral infections, a panel of 8 single-nucleotide polymorphisms (SNPs, including: IL1B rs16944, IL12B rs3212227, IL28B rs12979860, CCL2 rs1024611, DC-SIGN rs735240, TLR2 rs5743708, TLR4 rs4986791, TLR9 rs352140) was genotyped in all newborns by TaqMan SNP Genotyping Assays (Applied Biosystems) and related to the outcome. The association between SNP genotype and cCMV infection or clinical outcome was analysed by co-dominant, dominant, recessive and over-dominant models.

Results: SNP in IL1B gene was associated with increased risk of cCMV under the over-dominant model [OR = 1.74 (95%CI: 1.03 – 2.95); p = 0.039]. On the other hand, analysis in the cCMV subgroup revealed that the same SNP had protective effect by reducing the risk of ventriculomegaly, under the dominant model [OR = 0.40 (95% CI: 0.17 - 0.97); p = 0.039]. In addition, SNP in IL28B gene was associated with ventriculomegaly and thrombocytopenia, under over-dominant model [OR = 2.46 (95%CI 1.03-5.90); p = 0.04 and OR = 2.55 (95%CI 1.03-6.32); p = 0.042, respectively]. Genotype distribution of the remaining SNPs investigated did not show any significant differences.

Conclusions: SNP in IL1B gene may influence both the susceptibility and the clinical course of congenital CMV infection. SNP in IL28B may be associated with increased risk of ventriculomegaly and thrombocytopenia in cCMV newborns. Further, large prospective and genome-wide studies are needed to confirm these finding.

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Abstract 1018

**Analytical performance evaluation of the BIOFIRE Blood Culture Identification 2 (BCID2) panel**

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Abstract third-party references: BioMérieux, BioFire Diagnostics, LLC

**Background:** The BioFire Blood Culture Identification 2 (BCID2) Panel is the next-generation BioFire system for rapid detection of bacteria, yeast and select antimicrobial resistance (AMR) genes in positive blood cultures. Analytical studies evaluated compatibility of the panel with different bottle types and culture systems, established the limit of detection (LoD), reactivity, and specificity of the assays, and assessed the robustness of results from samples containing potentially interfering substances.

**Materials/methods:** Blood culture system compatibility was evaluated by determining organism titers and panel test results from seeded positive blood cultures grown to positivity (and 24 hours post-positivity) in 13 different bottle types incubated in 2 continuously monitoring blood culture systems. Limits of detection were estimated by serial dilution of contrived samples, and LoD was subsequently confirmed by detection in a minimum of 95% of 20 or more replicates. Analytical reactivity and specificity were evaluated by testing over 450 on-panel isolates and 200 off-panel species, and panel robustness was assessed by testing low-level analytes in the presence of over 50 substances. All testing used Investigational Use Only kits.

**Results:** Titers in positive blood cultures from different systems (0-24 hour post-positivity) ranged from f3.0E+05 – 4.5E+07 CFU/mL for yeast and f3.0E+06 – 3.0E+09 CFU/mL for bacteria, which are ≥30-fold higher than the detection capability of the assays (LoD of 5.0E+02 – 1.0E+04 CFU/mL for yeast and 1.0E+03 – 1.0E+06 CFU/mL for bacteria). Testing near LoD demonstrated assay reactivity with a diverse collection of species and AMR genes in isolates from around the globe, and the panel provided reliable results in the presence of potentially interfering substances. Testing at high concentration (>1.0E+08 CFU/mL) demonstrated few instances of cross-reactivity with unrelated off-panel species.

**Conclusions:** The BioFire BCID2 Panel assays are robust, specific, and reactive with expected diversity of bacterial and yeast causes of bloodstream infection. Rapid identification of organisms in blood culture, along with information about antimicrobial resistance gene status for select microorganisms, may aid in timely diagnosis and appropriate treatment decisions for bloodstream infections.

The panel has not been cleared for diagnostic use by the FDA or other regulatory entities.

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Abstract 1019

Activity of omadacycline and comparator agents against bacterial pathogens from the United States by infection type (2019)

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Abstract third-party references: This study was performed by JMI Laboratories and supported by Paratek Pharma, LLC, which included funding for services related to preparing this abstract.

Background: Omadacycline (OMC) is a novel aminomethylcycline approved by the FDA in 2018 to treat acute bacterial skin and skin structure infection (ABSSSI) and community-acquired bacterial pneumonia (CABP) for indicated organisms. OMC phase 2 clinical trials for the treatment of uncomplicated urinary tract infection (UTI; NCT03425396) and acute pyelonephritis (NCT03757234) have completed. OMC has activity against bacterial isolates expressing common tetracycline (TET), penicillin, macrolide and/or fluoroquinolone resistance mechanisms.

Materials/methods: A total of 7,000 clinical isolates were collected from 31 medical centers in the United States in 2019 as part of the SENTRY Surveillance Program. Isolates were collected from bloodstream infection (25.5%), skin and skin structure infection (SSI; 21.5%), pneumonia in hospitalized patients (21.6%), urinary tract infection (UTI; 14.8%), intraabdominal infection (5.4%), community acquired respiratory tract infection (8.9%) and other infection types (2.3%). Only 1 isolate/patient/infection episode was included. Identifications were confirmed by MALDI-TOF. Broth microdilution susceptibility testing of OMC and comparators was conducted according to CLSI M07 (2018) and M100 (2019) guidelines. Results were interpreted using FDA, CLSI (2019) and/or EUCAST (v9.0) breakpoints.

Results: OMC was highly active against Staphylococcus aureus isolates [MIC90, 0.12 mg/L; 99.0% susceptible (S)] from SSSI including 97.8% of MRSA and 97.7% of MSSA from RTI (Table). All (100%) Staphylococcus lugdunensis, Enterococcus faecalis (including vancomycin-resistant [R]) and Streptococcus pyogenes (including macrolide-R) isolates from SSSI were S to OMC. Similarly, 100% of Streptococcus anginosus isolates [MIC90, 0.06 mg/L; multiple infection types] were S to OMC (ABSSSI breakpoints). 99.7% of Streptococcus pneumoniae [CABP] isolates were S to OMC as were 100% of penicillin-R and tetracycline-R S. pneumoniae and all Haemophilus influenzae isolates [MIC90, 1 mg/L; CABP]. OMC was active against Enterobacter cloacae (91.5%) and Klebsiella pneumoniae isolates from SSSI and K. pneumoniae isolates from RTI (91.7%, CABP breakpoints). OMC inhibited 99.5% of Escherichia coli [MIC90, 2 mg/L] and 96.2% of K. pneumoniae [MIC90, 4 mg/L] UTI isolates at ≤4 mg/L.

Conclusions: OMC demonstrated potent in vitro activity against staphylococci, streptococci, E. faecalis, H. influenzae, E. cloacae, K. pneumoniae, and E. coli from ABSSSI, CABP, and UTI including drug-resistant isolates.
### Abstracts 2020

<table>
<thead>
<tr>
<th>Organism (no. of isolates)</th>
<th>Infection Type</th>
<th>MIC (µg/mL)</th>
<th>TET</th>
<th>TGC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus (775)</td>
<td>SSSI</td>
<td>0.12 (56.0)</td>
<td>≤0.5 (84.7 / 92.6)</td>
<td>0.25 (100.0)</td>
</tr>
<tr>
<td>MRSA (314)</td>
<td>SSSI</td>
<td>0.25 (37.3)</td>
<td>≤0.5 (94.1 / 92.7)</td>
<td>0.25 (100.0)</td>
</tr>
<tr>
<td>MSSA (269)</td>
<td>RTI</td>
<td>0.25 (57.3)</td>
<td>≤0.5 (94.2 / 92.3)</td>
<td>0.25 (100.0)</td>
</tr>
<tr>
<td>Staphylococcus lugdunensis (22)</td>
<td>SSSI</td>
<td>0.06 (100.0)</td>
<td>≤0.5 (93.0 / 92.5)</td>
<td>0.06 (100.0)</td>
</tr>
<tr>
<td>Enterococcus faecalis (52)</td>
<td>SSSI</td>
<td>0.12 (100.0)</td>
<td>&gt;16 (22.6 / -)</td>
<td>0.12 (100.0)</td>
</tr>
<tr>
<td>Vancomycin-Resistant E. faecium (54)</td>
<td>All</td>
<td>0.12 (100.0)</td>
<td>&gt;16 (17.2 / -)</td>
<td>0.12 (100.0)</td>
</tr>
<tr>
<td>Streplococcus anginosus group (12)</td>
<td>All</td>
<td>0.06 (100.0)</td>
<td>&gt;4 (66.7 / -)</td>
<td>0.03 (100.0)</td>
</tr>
<tr>
<td>S. pyogenes (55)</td>
<td>SSSI</td>
<td>0.12 (100.0)</td>
<td>&gt;4 (76.6 / 76.4)</td>
<td>0.06 (100.0)</td>
</tr>
<tr>
<td>S. pyogenes (15)</td>
<td>Meningo-R</td>
<td>0.12 (100.0)</td>
<td>&gt;4 (21.7 / 21.1)</td>
<td>0.05 (100.0)</td>
</tr>
<tr>
<td>S. pneumoniae (82)</td>
<td>CASP</td>
<td>0.06 (89.7)</td>
<td>&gt;4 (79.9 / 79.9)</td>
<td>0.05 (86.8)</td>
</tr>
<tr>
<td>S. pneumoniae (28)</td>
<td>Penicillin R (MIC&gt;2)</td>
<td>CASP</td>
<td>0.06 (100.0)</td>
<td>&gt;4 (71.4 / 71.4)</td>
</tr>
<tr>
<td>H influenzae (204)</td>
<td>CASP</td>
<td>0.06 (100.0)</td>
<td>&gt;4 (60.2 / 0.0)</td>
<td>0.06 (100.0)</td>
</tr>
<tr>
<td>E. coli (43)</td>
<td>SSSI</td>
<td>4 (92.7)</td>
<td>&gt;16 (85.3 / -)</td>
<td>1 (95.8)</td>
</tr>
<tr>
<td>Klebsiella pneumoniae (26)</td>
<td>SSSI</td>
<td>8 (86.8)</td>
<td>&gt;16 (84.3 / -)</td>
<td>1 (92.0)</td>
</tr>
<tr>
<td>K. pneumoniae (120)</td>
<td>RTI</td>
<td>4 (91.7)</td>
<td>&gt;16 (74.2 / -)</td>
<td>1 (96.7)</td>
</tr>
<tr>
<td>K. pneumoniae (108)</td>
<td>UTI</td>
<td>4 (96.2)</td>
<td>&gt;15 (86.6 / -)</td>
<td>1 (96.0)</td>
</tr>
<tr>
<td>E. coli (55)</td>
<td>UTI</td>
<td>2.7 (99.5)</td>
<td>&gt;15 (72.6 / -)</td>
<td>0.25 (99.8)</td>
</tr>
</tbody>
</table>

* All, all infection types; CASP, community acquired bacterial pneumonia; SSSI, skin and skin-structure infections; RTI, respiratory tract infection; UTI, urinary tract infection.
* FDA breakpoint interpretive criteria were used for OMC and tigecycline (TGC).
* CLSI/EUCAST breakpoint interpretive criteria applied.
* Using FDA ABSSSI breakpoint criteria for OMC.
* Using FDA CASP breakpoint criteria for CASP.
* Contains 4 E. faecalis and 60 E. faecium isolates.
* ABSSSI breakpoints for E. faecalis applied for comparison purposes.
* ABSSSI breakpoints applied for comparison purposes.
* Percent inhibited at ≤4 µg/mL.

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Gene expression analysis of transport channels in *Enterococcus faecium*

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**Background:** An important aspect of the bacterial response towards stress and environmental stimuli is alteration of gene expression levels¹. A combination of carvacrol, cuminaldehyde, and vancomycin has previously been shown to re-sensitise vancomycin-resistant *E. faecium* (VRE) to vancomycin ². The effect of treatment with the novel antimicrobial combination for 60minutes on gene expression in VRE was analysed by microarray analysis. Microarray data showed that 15 genes were differentially regulated and five genes associated with transport channels were chosen for further analysis; *bcr*, *ecfa_1*, *ecsa_1*, *ylob*, and *nhac_2*. A time course study using qPCR was conducted to further understand the antimicrobial mechanism of action of the novel formula.

**Materials/methods:** qPCR was carried out to validate the microarray data at 60mins. In addition, alterations in the expression levels of the five genes were assessed at 10mins, 30mins, 2hrs and 6hrs, in response to cuminaldehyde and carvacrol alone, in combination, and in combination with the vancomycin.

**Results:** VRE responds to the novel formula in the initial stages of exposure; at 10mins significant changes (*p*≤0.05) were demonstrated in the expression of the five genes, *bcr*, *ecfa_1*, *ecsa_1*, *ylob*, *nhac_2* with fold changes of -1.35, -1.41, -3.95, -5.67, and -6.31 respectively. At 60mins only *nhac_2* showed a significant fold change of -3.09. At 2hrs there were significant fold changes for *bcr* at 15.03, *ecfa-1* at 2.85 and *nhac_2* at 4.7, whereas at 6hrs there were no significant changes for any of the five genes tested.

**Conclusions:** This study has demonstrated that treating VRE with EOs alone and in combination with vancomycin has resulted in fold changes in the expression levels of the transport genes of interest. A new EO-vancomycin formulation to combat VRE could be developed through exploiting transport channels in *Enterococcus* sp.

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Abstract 1032

Prospective evaluation of serological and virological response in chronic hepatitis B genotype E treated with tenofovir or entecavir

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Background: European clinical practice guidelines [EASL] on chronic hepatitis B recently recognized the importance of migration flows in changing the prevalence and incidence of hepatitis B infection in low endemic European countries such as Italy and Germany. Even though differences among genotypes are reported for geographical distribution, virological and serological outcomes and response to IFN therapy, less is known about the role of different genotypes in treatment with nucleos(t)ide analogues. Phylogenetic analyses have shown that genotype E, which is mainly diffused in West Africa, is relatively recent. Decline in qHBsAg during the treatment with entecavir predict longer time to achieve HBsAg loss compared to A and D genotype.

Materials/methods: We prospectively evaluated qHBsAg decline in chronic hepatitis B, HBeAg-negative, E genotype, treated with tenofovir 245 mg [TDF] or entecavir 0.5 mg [ETV] from 2008 to 2014. Inclusion criteria were naïve patients with active chronic hepatitis B with no co-infection HCV, HDV, HIV. qHBsAg test was performed with ARCHITECT HBsAg (Abbott Diagnostics, Ireland)

Results: Sixty-five west-african patients [58; 89.2% males] were enrolled. Median age was 29 years-old [IQR 22-36] and the most prevalent route of transmission was familiar [25; 38.5%]. Median liver stiffness was 7.4 kPa [IQR 4.5-9.3], ALT 65 U/L [IQR 31-122], HBV-DNA 3.4 Log IU/ml [IQR 2.8-4.5], qHBsAg 3.4 Log UI/ml [IQR 2.8-4.5]. According to clinical evaluation, 40 patients (61.5%) started ETV whereas 25 patients (38.5%) TDF. The decline in qHBsAg in ETV-patients showed a statistically significative difference compared to TDF-patients at 2 (p<0.001), 3 (p< 0.001), 4 (p<0.001) and 5 years (p<0.001). At the same time-points higher response rate in HBV-DNA suppression were observed in patients receiving TDF. In the absence of resistance-associated mutations, in 20% of ETV-patients HBV-DNA persisted detectable at 5 years. This might be explained by a lower affinity of ETV to polymerase binding site, resulting in an incomplete saturation and consequently in residual viremia.

Conclusions: In E genotype TDF-treated patients had a significantly higher decline in qHBsAg and HBV-DNA over time achieving higher rates of HBV-DNA suppression with no failure after 5 years. TDF could represent the optimal choice in this setting of patients.

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Abstract 1034

Prevalence and antimicrobial susceptibility of *Campylobacter* species isolated from Greek diarrhoeal patients (2010-2018)

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**Background:** *Campylobacter* species are the leading cause of bacterial foodborne illness throughout the world. In humans, most enteric infections caused by *Campylobacter* spp. are considered self-limited and generally do not require antimicrobial treatment. However, in severe or prolonged disease treatment can shorten illness duration. Aim of the present study was to determine the antimicrobial susceptibility of *Campylobacter* species isolated from stool samples of symptomatic patients in a university hospital in Crete, Greece, through a 9-year period.

**Materials/methods:** A total of 365 *Campylobacter* spp. were isolated from stool samples from 2010 to 2018. Identification of the isolates was performed by conventional methods and antimicrobial susceptibilities to ciprofloxacin, erythromycin, and tetracycline were assessed by the disk diffusion method. The results were interpreted by using EUCAST breakpoints.

**Results:** Considering a single *Campylobacter* isolate per patient, 274 *C. jejuni* subsp. *jejuni* (76.1%) and 91 *C. coli* (24.9%) isolates were identified from stool samples of patients with age ranging from 2 days to 91 years and median age 21 years. Among *C. jejuni* isolates, 74.8% (205/274) were resistant to ciprofloxacin, 1.5% (4/274) to erythromycin, and 50.7% (139/274) were resistant to tetracycline. Among *C. coli* isolates, 74.7% (68/91) were resistant to ciprofloxacin, 5.5% (5/91) to erythromycin, and 52.7% (48/91) were resistant to tetracycline. Among ciprofloxacin resistant *C. jejuni*, 1% (2/205) of isolates were found to be resistant to erythromycin, and 59% (121/205) were also resistant to tetracycline. Furthermore, 0.7% (2/274) of isolates were resistant to all three antibiotics. Similarly, among ciprofloxacin resistant *C. coli*, 7.4% were resistant to erythromycin, and 57.4% were also resistant to tetracycline. Among all *C. coli*, 4.4% (4/91) were resistant to all three antibiotics.

**Conclusions:** In our area, high prevalence rates of resistance to ciprofloxacin and tetracycline were observed among *Campylobacter* spp. Erythromycin remains the preferred treatment option for *Campylobacter* infections.

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Abstract 1036

**Accuracy and clinical impact of fungal cell-free DNA PCR panel on plasma for diagnosis of invasive fungal infection**

Fiona Senchyna*, Catherine Hogan1,2, Dora Ho1, Aruna Subramanian1, Indre Budvytiene3, Saurabh Gombar1, Helio Costa1,2, Martynas Budvytis3, Niaz Banaei1,2

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**Background:** Invasive fungal infection (IFI) is an important cause of morbidity and mortality in oncology and transplant patients. Diagnosis of IFI is often delayed due to need for invasive biopsy and low sensitivity of conventional diagnostics. We evaluated the performance and clinical impact of a fungal cell-free DNA (cfDNA) PCR panel to noninvasively diagnose the 12 most common IFI organisms.

**Materials/methods:** A probe-based PCR panel targeting *Aspergillus* spp., Mucorales agents, *Candida* spp., *Fusarium* spp., *Scedosporium* spp., *Pneumocystis jirovecii* and several pathogenic dimorphic fungi was created using previously published primers and primers designed with a novel bioinformatic pipeline. Plasma cfDNA was extracted on a Promega Maxwell RSC instrument. Assay sensitivity and specificity were assessed using plasma samples from 104 patients with 115 known IFIs consisting of *Aspergillus* spp. (n = 26), Mucorales agents (n = 23), *Candida* spp. (n = 33), *Fusarium* spp. (n = 3), *Scedosporium/Pseudallescheria boydii* complex (n = 6), *Coccidioides immitis/posadasii* (n = 14), *Histoplasma capsulatum* (n = 6), *Blastomyces dermatitidis* (n = 1), and *Pneumocystis jirovecii* (n = 4); and 65 non-IFI patients. Plasma volumes ranging from 1mL to 4mL were tested. Prospective testing was carried out on high-risk patients to determine clinical impact on antifungal therapy and patient management.

**Results:** Sensitivity and specificity of fungal cfDNA PCR on banked plasma samples from patients with proven IFI and non-IFI controls was 56.5% (65/115) overall, and 69.6% (48/69) in cases tested with higher (optimal) plasma volume. In optimal volume samples, sensitivity was 91.7%, 57.9%, and 77.3% for Mucorales, *Aspergillus* spp., and *Candida* spp., respectively. Overall specificity was 99.4%. In a prospective evaluation of 155 patients with suspected IFI, fungal cfDNA testing was positive in 19.4%, leading to positive clinical impact in 40.0% of patients. Clinical impact was highest in patients with a diagnosis of Mucorales infection, with 81.8% (9/11) of results leading to therapeutic optimization or avoidance of surgical biopsy.

**Conclusions:** Fungal cfDNA detection with a PCR panel offers a rapid and accurate non-invasive approach for early diagnosis of IFI, providing actionable results for personalized treatment.

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Abstract 1038

**High prevalence of multi-stress tolerant Campylobacter species causing human infection**

Shaimaa Fekry* 1, Mohamed Elhadidy 2

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**Background:** Campylobacter jejuni and Campylobacter coli are zoonotic pathogens commonly associated with human gastroenteritis. The main cause of human campylobacteriosis is consumption of contaminated poultry meat and other sources as raw milk. Campylobacters encounter variety of stress conditions that potentially affect bacterial survival during food processing, preservation, and cooking; thus, impacting their transmission to humans through the food chain. To survive under harsh conditions, biofilm formation is suggested to be another mechanism for bacterial adaptation in the food environment, thus switching its physiological state to promote survival under stress conditions. The aim of this study is to access the resistance of Campylobacter isolates to adverse stress conditions encountered throughout the food chain and compare the biofilm-forming ability of these strains under both microaerobiosis and aerobiosis.

**Materials/methods:** Phenotypic stress tolerance of (n=111) C. jejuni and C. coli isolates recovered from three different sources including patients suffering from gastroenteritis (n=57), broiler carcass (n=30), and dairy products (n=24) was investigated. To assess the capabilities of hyper-aerotolerant (HAT) and aerotolerant (AT) strains to survive under harsh conditions in foodborne transmission and infection, the survival rate of these isolates under different stress conditions (aerotolerance, temperature variations, freezing and thawing, peracetic acid treatment and osmotic stress) that can be encountered during food processing was investigated. Moreover, the capability of isolates to form biofilm under microaerophilic and aerophilic conditions was examined using crystal violet biofilm assay.

**Results:** HAT strains were highly dominant presenting 63% of the tested isolates, 22% were AT whereas 11% were aero-sensitive (AS). HAT strains exhibited a significant tolerance to stress conditions compared to AS and AT strains (Figure 1). Analyzing the tendency of biofilm formation, it was found that half of HAT strains formed biofilm under microaerophilic/normal conditions while 44% and 85% of HAT and AT strains successfully formed biofilms under aerophilic conditions, respectively.

**Conclusions:** The enhanced ability of HAT strains to cope to numerous stressors (cross protection), and to form biofilm, would potentially impact human infection by increasing the potentials of the foodborne transmission of Campylobacter under aerobic conditions. Thus, HAT strains would potentially be of higher transmission risk than AS ones.

**Figure 1:** HyperAerotolerant, Aerotolerant and Aerosensitive Campylobacter response to different stress conditions

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Abstract 1040

**Trends in resistance of bloodstream infection pathogens in Northwest Russia from 2015 to 2018**

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Abstract third-party references: This abstract was produced and data collected as part of the Nordic Council of Ministers’ Programme “Nordic-Russian Cooperation on Antimicrobial Resistance (AMR) Containment, 2019-2020.

**Background:** The Nordic Council of Ministers launched in 2019 a Nordic-Russian Cooperation Programme on Antimicrobial Resistance, and this study was proposed as part of the baseline mapping in five Russian partner-regions of the cooperation programme.

**Materials/methods:** Results of blood cultures and their antimicrobial susceptibility from 5 laboratories of the Northwest Russia (Karelia Republic, Arkhangelsk Oblast, Murmansk Oblast, Pskov Oblast and St. Petersburg City) between 2015 and 2018 were analysed. Antimicrobial resistance was determined by EUCAST or CLSI criteria.

**Results:** A total of 55,839 blood samples were investigated and 3,026 microorganisms detected (average level at 5.4%). *Staphylococcus aureus* (1055/34.9%) and *Klebsiella pneumoniae* (695/23.0%) were the most frequently identified bacteria followed by *Escherichia coli* (476/15.7%), *Enterococcus faecium* (474/15.7%), *Acinetobacter baumannii* (235/7.8%) and *Pseudomonas aeruginosa* (91/3.0%). A considerable increase in the proportion of positive cultures was observed: 3.7% (2015) – 4.1% (2016) – 5.9% (2017) – 9.4% (2018). An increase in *K. pneumoniae* detection was seen: 14.1% (2015) – 18.4% (2016) – 25.8% (2017) – 28.8% (2018). In contrast, a decrease was noted in the frequency of *S. aureus* (38.0% vs 32.3%) and *E. coli* (18.2% vs 13.7%). The levels of *E. faecium*, *A. baumannii* and *P. aeruginosa* remained stable.

The average proportion of MRSA through the study period was 17.1% (180/1055). The proportion of ESBL-producing *K. pneumoniae* decreased from 70.2% in 2015 to 34.8% in 2018, with average at 49.2%. On average, carbapenem-resistant *K. pneumoniae* was registered in 32.9% cases (229 samples). Over the study period, the proportion of carbapenem-resistant *K. pneumoniae* increased: 16.7% (2015) – 20.3% (2016) – 47.4% (2017) – 46.3% (2018). The level ESBL-producing *E. coli* varied from 30.6% to 51.0%, showing an increasing tendency (average resistance proportion at 40.5%). A total of 10 carbapenem-resistant *E. coli* cultures were identified (average 2.1%). The detection of vancomycin-resistant *E. faecium* remained low (average 1.3%).

**Conclusions:** The increased pathogen detection, mainly due to *K. pneumoniae*, and an enhancement in the level of resistant Enterobacteriaceae shows the importance of further systematic harmonized surveillance and regional cooperation in the Northwest Russia to build adequate response. In the participating regions, microbiology results are stored based on the number of tests, therefore methodology requires standardization.

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Abstract 1041

**Healthcare-associated infections reporting in developing countries: challenges and corrective measures**

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**Background:** Health-care associated infections (HAIs) are the most frequent types of adverse events for providing health care. HAIs surveillance system is a critical part of their prevention and control. The accuracy of HAIs reporting in Iran appears to be questionable. This paper seeks to address challenges of HAIs reporting in national Iranian Nosocomial Infection Surveillance System (INIS) and discusses how to solve them.

**Materials/methods:** The study has been conducted with qualitative approach in two phases. In order to explore effective factors on HAIs case finding and reporting in INIS six related documents and opinions of sixteen experts were analyzed using Walt and Gillson’s policy analysis framework. The experts were selected from hospitals affiliated with Tehran University of Medical Sciences (TUMS) and Ministry of Health (MOH). Consequently an expert panel session was held due to provide the best strategies to deal with each of reported issues.

**Results:** Inappropriate organization structure, poor documentation, lack of participation of stakeholders, inadequate educational programs, health planning without scientific evidences, deficits in executive and evaluation infection prevention and control, individual conflicts of interest lead to poor case finding and reporting of HAIs in INIS. Identifying the lead organization for infection prevention and control programs (IPCs), managerial supports from IPCs, advocacy in order to enhancing health staffs knowledge and participation, developing and implementation a comprehensive HAIs information management system, and provide appropriate job motivation for infection prevention and control team in hospitals are suggested strategies to improve HAIs case finding and reporting in INIS.

**Conclusions:** Our findings indicate that a number of organizational and individual factors lead to inaccurate HAIs reporting in INIS. Accurate case-finding and reporting needs the implementation of some strategies to enhance staffs capabilities and motivation, updating guidelines and software and changing in organizational structure.

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Survey of attitudes, beliefs, and knowledge of community pharmacists in the United States on antimicrobial stewardship

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Background: Approximately 50% of antibiotics are either inappropriate or unnecessary, a problem that antimicrobial stewardship (AMS) programs seek to address. Even though the majority of antibiotic prescribing occurs in the outpatient community setting, most AMS programs are focused on inpatient training and services. In order to address the feasibility of community AMS programs, we performed a cross-sectional survey of community pharmacists investigating their attitudes, beliefs and knowledge towards community-based AMS services.

Materials/methods: The electronic survey was distributed over 6 weeks from June 1, 2019 through July 24, 2019 to pharmacists licensed in the state of Washington, U.S.A. The 40-item survey instrument was developed based on a review of the published literature. We ensured all questions and answer choices were pertinent to community pharmacy respondents. The survey included the following domains: perceptions towards AMS, current pharmacy practices, perceived barriers and facilitators to community AMS services. The questionnaire was pilot tested for readability, length and relevance of specific items. Survey participants were included if they had experience in a community pharmacy setting and completed at least one category of AMS questions.

Results: A total of 204 participants met inclusion criteria. Respondents were mostly female (63.2%), aged 30 – 39 years old (38.7%) and between 1 – 10 years of experience (38.7%). A majority of pharmacists agreed that AMS is important to improve patient care (90.1%), reduce inappropriate antimicrobial use (85.7%) and reduce antimicrobial resistance (89.7%). However, 40.3% of pharmacists disagreed that they have the necessary training to participate in AMS. Most pharmacists actively participate in AMS activities such as contacting the prescriber for appropriateness (73.9%), antimicrobial prescription checking for adverse drug reactions or allergies (92.1%) and effectively counseling on appropriate use of antimicrobials (92.1%). Some potential perceived barriers identified were time (39.0%) and financial compensation (68.7%). Lastly, facilitators for community AMS identified were education to patients (82.4%) and healthcare providers (90.2%) and increased access to patient electronic health record (92.3%).

Conclusions: Our results suggest that AMS is important to patient outcomes in the community setting and could be implemented when identified barriers are addressed.

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**Abstract 1043**

**In vitro surveillance of eravacycline against Gram-positive pathogens, including resistant isolates, collected from European hospitals in 2018**

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**Abstract third-party references:** IHMA, Monthey, Switzerland, Tetraphase Pharmaceuticals

**Background:** Eravacycline (ERV) is a fully-synthetic, fluorocycline antibacterial approved for the treatment of complicated intra-abdominal infections (cIAI) in patients ≥18 years of age in both Europe and the US. Previous surveillance studies of ERV have demonstrated potent *in vitro* activity against specific Gram-positive pathogens. The purpose of this study was to further monitor the *in vitro* activity of ERV against *Staphylococcus aureus* (including methicillin-resistant *S. aureus*, MRSA), *Enterococcus* spp. (including vancomycin-resistant *Enterococcus*, VRE) and *Streptococcus* spp.

**Materials/methods:** Clinical isolates were collected from European hospitals during 2018 from multiple infection sources, including bodily fluids, gastrointestinal, genitourinary and respiratory. Minimum inhibitory concentrations (MICs) were determined by CLSI broth microdilution. Antibiotic susceptibility was determined with EUCAST version 9.0 breakpoints.

**Results:** Summary MIC data for ERV and select comparators are shown in the Table. The MIC₉₀ values of ERV for *S. aureus*, *Enterococcus* spp. and *Streptococcus* spp. were 0.12 mg/L, 0.12 mg/L and 0.03 mg/L, respectively. ERV MICs were 2- to 8-fold lower than tigecycline. ERV susceptibilities ranged from 94.7–100%, including for resistant organisms.

**Conclusions:** ERV demonstrated high susceptibility rates against clinically important Gram-positive pathogens, including resistant isolates. Furthermore, ERV MIC values were up to 8-fold lower than for tigecycline. This activity suggests ERV play a role in empiric treatment choice for cIAI where Gram-positive pathogens are suspected as part of causative infection flora.

<table>
<thead>
<tr>
<th>Organism (N)</th>
<th>Eravacycline MIC₉₀₀₀ %S</th>
<th>Tigecycline MIC₉₀₀₀ %S</th>
<th>Vancomycin MIC₉₀₀₀ %S</th>
<th>Daptomycin MIC₉₀₀₀ %S</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em> (220)</td>
<td>0.05/0.12 98.8%</td>
<td>0.25/0.25 99.6%</td>
<td>1/1</td>
<td>0.25/0.5 100%</td>
</tr>
<tr>
<td>MSSA (163)</td>
<td>0.05/0.12 100%</td>
<td>0.12/0.25 100%</td>
<td>1/1</td>
<td>0.25/0.5 100%</td>
</tr>
<tr>
<td>MRSA (67)</td>
<td>0.05/0.25 94.7%</td>
<td>0.25/0.25 98.3%</td>
<td>1/1</td>
<td>0.25/0.5 100%</td>
</tr>
<tr>
<td><em>Enterococcus</em> spp. (410)</td>
<td>0.06/0.12 99.3%</td>
<td>0.12/0.5 89.0%</td>
<td>1/2</td>
<td>2/4</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em> (197)</td>
<td>0.05/0.12 100%</td>
<td>0.12/0.5 86.3%</td>
<td>1/2</td>
<td>1/2</td>
</tr>
<tr>
<td><em>Enterococcus faecium</em> (213)</td>
<td>0.06/0.06 98.6%</td>
<td>0.06/0.25 91.6%</td>
<td>1/16</td>
<td>2/4</td>
</tr>
<tr>
<td>VRE (37)</td>
<td>0.06/0.06 97.4%</td>
<td>0.06/0.5 89.5%</td>
<td>&gt;10/16</td>
<td>2/4</td>
</tr>
<tr>
<td><em>Streptococcus anginosus</em> group (23)</td>
<td>0.015/0.03 100%</td>
<td>0.03/0.06 100%</td>
<td>0.5/1</td>
<td>0.25/0.5 100%</td>
</tr>
</tbody>
</table>

Units in mg/L; MIC₉₀₀₀₀ - minimum inhibitory concentration required to inhibit growth of 50/90% of isolates; %S - percent susceptible; *S. anginosus, S. constellatus, S. intermedius*

**Presenter email address:** imorrissey@ihma.com
Abstract third-party references: On behalf of the PICNICC investigators

Background: Antibiotics are used to reduce morbidity and mortality in children with febrile neutropenia (FN) undergoing treatment for malignancy, but variation exists among guidelines for prescribing, especially with regard to aminoglycoside therapy.

Materials/methods: We aimed to review antibiotic prescribing and guideline compliance in children with febrile neutropenia. We analyzed data from the prospective PICNICC cohort study, collected from children <18 years admitted to tertiary centers in Australia with FN between November 2016 and January 2018.

Results: Among 858 episodes of febrile neutropenia, children were prescribed up to 4 concurrent antibiotics in the first 12 hours. Piperacillin-tazobactam was the most commonly prescribed antibiotic (n=519, 60.5%) and aminoglycosides were prescribed in 255 episodes (29.7%). Of 1380 antibiotics prescribed in total, 1285 (93.1%) were marked by site research assistant as compliant with local hospital guidelines. Composite unfavorable outcome of death, ICU admission, relapse of infection or late-onset sepsis occurred in 54 episodes (6.3%). In FN episodes with receipt of aminoglycosides in the 1st 12 hours, the adjusted hazard ratio for unfavorable outcome was 3.1 (95% CI 1.7-5.7). On independent assessment of state guideline criteria, 46% (n=184) of guideline-eligible patients did not receive an aminoglycoside but there was no increased risk of unfavorable outcome in this group.

Conclusions: We found substantial variation in antibiotic prescribing for febrile neutropenia in this cohort. We found no evidence for improved outcome with aminoglycosides, even in those who met local guideline criteria for this therapy. Aminoglycosides appear to be associated with unfavorable outcome when given empirically for FN in children and their inclusion in guidelines should be reviewed.

Presenter email address: brendanoch@yahoo.co.uk
In vitro surveillance of eravacycline against Gram-negative pathogens, including multidrug-resistant isolates, collected from European hospitals in 2018

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1Tetraphase Pharmaceuticals, Watertown, MA, United States, 2IHMA, Monthey, Switzerland

Abstract third-party references: Tetraphase Pharmaceuticals, IHMA, Monthey, Switzerland

Background: Eravacycline (ERV) is a fully-synthetic, fluorocycline antibiotic approved for the treatment of complicated intra-abdominal infections (cIAI) in patients ≥18 years of age in Europe and the US. The purpose of this study was to monitor the in vitro activity of ERV against European Gram-negative isolates, including multidrug-resistant (MDR) isolates, collected in 2018.

Materials/methods: Isolates were collected during 2018 from various body sites. Minimum inhibitory concentrations (MICs) were determined by CLSI broth microdilution. Antibiotic susceptibility was determined with EUCAST version 9.0 breakpoints. MDR was defined as resistance to ≥3 antibiotics from aztreonam, a carbapenem (meropenem or ertapenem [ETP]), cefepime/ceftaxime/cefazidime/ceftiraxone (any one), gentamicin, levofloxacin, piperacillin-tazobactam, tetracycline or tigecycline (TIG).

Results: Summary MIC data for ERV and select comparators are shown in the Table. ERV MIC90 values for all-Enterobacteriaceae and MDR-Enterobacteriaceae were 0.5 mg/L and 1 mg/L, respectively. ERV MIC90 for MDR-Enterobacteriaceae was within one dilution as compared for all-Enterobacteriaceae isolates. ERV susceptibilities ranged from 81.6–99.5% for all- and MDR-Enterobacteriaceae. ERV MIC50/90 against carbapenem-resistant Acinetobacter baumannii (CRAB) were 4-fold lower than TIG.

Conclusions: ERV exhibited potent in vitro activity and higher susceptibility rates than TIG against clinically important Gram-negative pathogens, including resistant isolates. This ongoing surveillance further demonstrates the benefit of ERV in the treatment of cIAI, particularly where Enterobacteriaceae are suspected as the causative agent.

<table>
<thead>
<tr>
<th>Organism (N)</th>
<th>ERV MIC90 (%)</th>
<th>TIG MIC90 (%)</th>
<th>ETP MIC90 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacteriaceae (1044)</td>
<td>0.25/0.5</td>
<td>0.5/2</td>
<td>0.015/0.5</td>
</tr>
<tr>
<td>Citrobacter freundii (206)</td>
<td>0.25/0.5</td>
<td>0.5/2</td>
<td>0.015/0.25</td>
</tr>
<tr>
<td>Enterobacter cloacae (205)</td>
<td>0.25/1</td>
<td>0.5/2</td>
<td>0.09/1</td>
</tr>
<tr>
<td>Escherichia coli (210)</td>
<td>0.25/0.25</td>
<td>0.25/1</td>
<td>0.015/0.06</td>
</tr>
<tr>
<td>Klebsiella oxytoca (206)</td>
<td>0.25/0.25</td>
<td>0.25/2</td>
<td>0.015/0.03</td>
</tr>
<tr>
<td>Klebsiella pneumoniae (223)</td>
<td>0.25/1</td>
<td>1/4</td>
<td>0.03/0.8</td>
</tr>
<tr>
<td>MDR-Enterobacteriaceae (248)</td>
<td>0.25/1</td>
<td>0.5/2</td>
<td>0.25/0.8</td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia (40)</td>
<td>0.5/2</td>
<td>1/2</td>
<td>NT</td>
</tr>
<tr>
<td>CRAB (201)</td>
<td>0.5/1</td>
<td>2/4</td>
<td>NT</td>
</tr>
</tbody>
</table>

Units in mg/L; MIC50/90 - minimum inhibitory concentration required to inhibit growth of 50/90% of isolates; %S - percent susceptible; NT - not tested

Presenter email address: imorrissey@ihma.com
Abstract 1054

Establishment and clinical application of a multiple touchdown PCR for detection of carbapenemase genes

Xiaojun Li*, Ning Sun, Liping Zhang, Bai-Zeng Yu, Wei-Ping Wang, Xingyue Yao, Juan Yu

1Department of Clinical Laboratory Science, Jinling Hospital, School of Medicine, Nanjing University, Nanjing, China, 2Lishui People’s Hospital, Zhongda Hospital Lishui Branch, Southeast University, Nanjing, China

Background: Carbapenem-resistant Enterobacteriaceae (CRE) is rising rapidly all over the world. Early detection and identification of carbapenem resistant bacteria are important to control the spread and outbreak of infection. In the present study, we established a multiple touchdown PCR (MT-PCR) assay for detection of five carbapenemase genes.

Materials/methods: CRE resistant genes, including blaOXA-48, blaIMP, blaVIM, blaNDM and blaKPC were selected as target genes. The blaIMP carried P. aeruginosa, blaVIM carried P. putida, blaNDM carried K. pneumoniae, blaKPC carried K. Pneumonia, blaOXA-48 carried E. Coli (DH5α) were applied as positive controls, and the bacteria carried no target genes as negative control. The MT-PCR assay was developed and subsequently analyzed the specificity, sensitivity, and clinical application performance.

Results: The MT-PCR assay was successfully established for the detection of five carbapenemase genes, with limits of detection of 2×10^2 cfu/mL for blaOXA-48, blaVIM and blaKPC, and 2×10^3 cfu/mL for blaIMP and blaNDM. The results obtained from MT-PCR were completely consistent with single PCR in the detection of 42 carbapenem-resistant clinical isolates. Compared to antimicrobial susceptibility testing (AST) as the reference method, there was no significant difference between the results from MT-PCR (genotype) and the results from AST (phenotype) in the detection of 67 clinical sterile body fluid samples, and the clinical sensitivity and specificity was 80% and 100%, respectively.

Conclusions: The MT-PCR assay can be effectively used to detect five carbapenemase genes in clinical isolates and sterile body fluid samples.

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Impact of an antimicrobial stewardship team on the de-escalation of carbapenem use in a tertiary hospital

Masayuki Maeda*, Yasuhiro Nagatomo, Yuika Naito, Etsuko Akima, Kaori Nakane, Kazuhisa Ugajin, Masayuki Yoshikawa, Takahiro Takuma, Issei Tokimatsu, Yoshihito Niki

1 Showa University, Tokyo, Japan, 2 Showa University Hospital, Tokyo, Japan

**Background:** Carbapenems have a broad spectrum of activity and are used for empirical therapy against life-threatening infections. When inappropriate carbapenem use, such as prolonged therapy, is observed, a de-escalation (DE) strategy would change to a narrower spectrum antibiotic when susceptible bacteria were identified. However, the DE strategy has not been considered in clinical settings. We aimed to determine whether an antimicrobial stewardship team (AST) intervention could promote DE of carbapenem therapy.

**Materials/methods:** The AST intervention, launched in July 2017, consisted of a daily post-prescription review and feedback (PPRF) strategy. We evaluated the rate of switching to other antimicrobials or discontinuing carbapenems within 7 days during the pre-intervention (from July 2016 to June 2017) and post-intervention (from July 2017 to June 2018) period. DE was defined as changing to a narrower spectrum beta-lactam antimicrobial or by discontinuation of the carbapenem.

**Results:** A total of 2,685 patients were prescribed carbapenems. Confirming the use with prescribers by face-to-face or telephone contact was the primary intervention by AST (976/1,350), followed by a recommendation for discontinuation or change to another antibiotic (720/1,350). The rate of change to narrower spectrum beta-lactams significantly increased during the post-intervention period (7.0% vs. 13.0%; P < 0.001; Table). In a multivariate analysis, AST intervention was significantly associated with DE therapy (odds ratio: 1.30; 95% confidence interval: 1.10–1.54; P = 0.002).

**Conclusions:** Daily PPRF by AST could enhance the carbapenem antimicrobial stewardship by accelerating DE of carbapenem.

**Table**

<table>
<thead>
<tr>
<th>Category</th>
<th>Pre-intervention (n=1,335)</th>
<th>Post-intervention (n=1,350)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuing ≤ 7 days</td>
<td>29.0%</td>
<td>28.8%</td>
<td>0.921</td>
</tr>
<tr>
<td>Continuing &gt; 7 days</td>
<td>54.1%</td>
<td>51.2%</td>
<td>0.133</td>
</tr>
<tr>
<td>Change to narrower spectrum beta-lactams</td>
<td>7.0%</td>
<td>13.0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Change to other class antibiotics (other than beta-lactams)</td>
<td>4.9%</td>
<td>2.7%</td>
<td>0.004</td>
</tr>
<tr>
<td>Parenteral to oral conversion</td>
<td>5.0%</td>
<td>4.3%</td>
<td>0.374</td>
</tr>
</tbody>
</table>

**Presenter email address:** m-maeda@pharm.showa-u.ac.jp
Abstract 1058

**Essential human resources for antimicrobial stewardship teams in Japan: estimates from a nation-wide survey**

Masayuki Maeda*1, Yuichi Muraki1, Tadashi Kosaka1, Takehiro Yamada1, Yosuke Aoki1, Mitsuo Kaku1, Masafumi Seki1, Yoshinari Tanabe1, Naohisa Fujita1, Yoshihito Niki1, Kunihiko Morita1, Katsunori Yanagihara1, Koichiro Yoshida1, Tatsuya Kawaguchi1

1The Antimicrobial Stewardship Committee of the Japanese Society of Chemotherapy, Tokyo, Japan

**Background:** Antimicrobial stewardship requires structural prerequisites for implementation of antimicrobial stewardship programs (ASPs), such as the presence of a multidisciplinary antimicrobial stewardship team (AST). In 2018, we reported data of a nationwide survey on the implementation of ASPs and staff resources in Japan. The survey revealed a shortage in manpower at most Japanese hospitals. The study aimed to describe the potential staffing structures for ASTs proposed based on a nation-wide survey conducted by the Japanese Society of Chemotherapy (JSC).

**Materials/methods:** Data on implemented ASPs and staff full-time equivalents (FTEs) at 1358 healthcare facilities, which were collected by the nationwide ASP survey of JSC in 2018, were analyzed. Multivariate analysis was performed to evaluate whether physician and pharmacist FTEs were associated with the number of implemented ASPs in each facility, defined as the number of responses in the previous survey.

**Results:** Table 1 presents independent factors related to the number of implemented ASPs. Middle-to-large hospitals, additional reimbursement for infection prevention, presence of an on-site microbiology laboratory, AST organization, physician FTE, and pharmacist FTE were significantly associated with the increased number of implemented ASPs. Additional reimbursement was the strongest contributor for the implementation of ASPs. Among factors regarding staff resources, the contribution of pharmacist FTE to the implementation of ASPs was stronger than that of physician FTE.

**Conclusions:** Our nationwide survey analysis revealed that pharmacist and physician FTEs were significantly associated with the implementation of ASPs after adjustment for several confounders. The current findings reveal the human resources for core members of ASTs that are required for the implementation of functional and sustainable ASPs at Japanese hospitals. This study provides a directive for structural and financial support of ASTs and should aid in planning for the enhancement of AST practices.

<table>
<thead>
<tr>
<th>factors</th>
<th>β (95%CI)</th>
<th>Standardized β</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of beds (≥301)</td>
<td>2.5 [1.8–3.3]</td>
<td>0.16</td>
</tr>
<tr>
<td>Additional reimbursement</td>
<td>6.3 [5.5–7.1]</td>
<td>0.33</td>
</tr>
<tr>
<td>Microbiology laboratory</td>
<td>3.0 [2.2–3.7]</td>
<td>0.19</td>
</tr>
<tr>
<td>AST organization</td>
<td>4.2 [3.4–5.1]</td>
<td>0.22</td>
</tr>
<tr>
<td>Physician FTE, 0.5 increase</td>
<td>1.3 [0.7–1.9]</td>
<td>0.09</td>
</tr>
<tr>
<td>Pharmacist FTE, 0.5 increase</td>
<td>2.1 [1.4–2.7]</td>
<td>0.14</td>
</tr>
</tbody>
</table>

β, partial regression coefficient; CI confidence interval; AST, antimicrobial stewardship team; FTE, full-time equivalent

**Presenter email address:** m-maeda@pharm.showa-u.ac.jp
Abstract 1063

**Diagnostics value of Epstein-Barr virus DNA load in whole blood and plasma from paediatric transplant recipients**

Beata Kasztelewicz*, Joanna Teisseyre, Katarzyna Janiszewska, Irena Jankowska, Piotr Kaliciński, Katarzyna Dzierzanowska-Fangrat

1Children’s Memorial Health Institute, Department of Clinical Microbiology and Immunology, Warsaw, Poland, 2The Children’s Memorial Health Institute, Warsaw, Poland

**Background:** High and/or rising EBV viral loads pose a risk for development of EBV-related post-transplant lymphoproliferative disorder (PTLD), hence quantitative EBV DNA testing was incorporated into routine medical practice to assist in diagnosis and monitoring of transplant recipients. However, there is no consensus regarding the threshold of EBV DNA that warrants preemptive therapy or further diagnostic workup as well as there is no consensus on optimal component of peripheral blood for measuring viral loads. The aim of the study was to assess the utility of EBV DNA monitoring in whole blood (WB) and plasma in paediatric liver transplant recipients (LTx).

**Materials/methods:** This prospective study included 1262 matched WB and plasma samples from 296 LTx patients. To evaluate the diagnostic performance of an EBV DNAemia in whole blood and plasma, a receiver operating characteristics (ROC) curve analysis were conducted. Apart from 2 patients with PTLD confirmed within the study period, data of EBV DNAemia in additional 9 samples (including 5 WB and 4 plasma samples) of 4 patients included in the study but with PTLD diagnosed before [2 patients] and after (2 patients) the study period, were included in the ROC analysis.

**Results:** Higher EBV DNAemia in both whole blood and plasma was detected in patients with PTLD compared to non-PTLD patients [median 4.23 vs 3.48 log_{10} copies/mL; p = 0.044 and median 3.97 vs 1.7 log_{10} copies/mL; p < 0.0001, respectively for WB and plasma samples]. The value of the area under the ROC curve was 0.96 (95% CI 0.94 - 0.99; p = 1.2 x 10^{-24}) and 0.83 (95% CI 0.76 - 0.90; p = 7.0 x 10^{-5}) for EBV DNA load in plasma and WB, respectively (Figure). The optimal cut-off value of EBV DNAemia in plasma was 2.4 log_{10} copies/mL with sensitivity of 100%, specificity of 92.8%, positive predictive value (PPV) of 8.2% and negative predictive value (NPV) of 100%, whereas optimal cut-off value for EBV DNAemia in WB was 3.4 log_{10} copies/mL, with sensitivity of 100%, specificity of 70.3%, PPV of 2.4% and NPV of 100%.

**Conclusions:** Monitoring of EBV DNA in plasma samples had better diagnostics performance compared to WB.

**Figure.** A receiver operating characteristic (ROC) curve of EBV DNAemia in whole blood (WB) and plasma for identification PTLD.

The ROC curve analysis, included samples obtained from 290 non-PTLD patients and 6 PTLD patients. Only samples collected up to one month prior to and at the PTLD diagnosis were considered (samples of PTLD patients collected after treatment was initiated, were excluded). The true positive rate (sensitivity) is plotted in function of the false positive rate (1-specificity) for different cut-off points.

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Abstract 1065

**HLA-DPB1*05:01 is associated with adverse drug reactions to rifampin and isoniazid for treatment of latent tuberculosis infection in South Korea**

Eun-Jeong Joo*, So Yeon Park¹, Jungok Kim², Hae Suk Cheong³, Han-Na Kim⁴, Joon-Sup Yeom⁵

¹Sungkyunkwan University School of Medicine/Kangbuk Samsung Hospital, Seoul, South Korea, ²Hallym Medical University/Kangdong Sacred Heart Hospital, Seoul, South Korea, ³Chungnam National University College of Medicine/Chungnam National University Hospital, Seoul, South Korea, ⁴Sungkyunkwan University School of Medicine/Kangbuk Samsung Hospital, Seoul, South Korea, ⁵Yonsei University College of Medicine/Severance Hospital, Seoul, South Korea

**Background:** Healthcare-workers (HCWs) with latent tuberculosis infection (LTBI) are a potential risk group for tuberculosis leading to its transmission to other HCWs and patients. Therefore, screening and treatment for LTBI are recommended in HCWs. However, adverse drug reactions (ADRs) for rifampicin (RFP) and isoniazid (INH) is often challenging in initiating and completing LTBI treatment. Previous pharmacogenetics studies have reported the association of variants in the human leukocyte antigen (HLA) region with a drug-associated hypersensitivity reaction. The purpose of this study is to evaluate the association between HLA polymorphism and RFP- and INH-associated ADRs.

**Materials/methods:** The present analysis included HCWs who have begun treating LTBI with 3 month-regimen of RFP and INH between February and September 2017 and agreed to perform the HLA genotyping. Participants were questioned about and examined for adverse events during treatment. Association analysis for HLA alleles were conducted with PyHLA for ADRs to RFP and INH.

**Results:** A total of 66 subjects were enrolled; 13 (19.7%) of them met the criteria for hypersensitivity reaction while on RFP and INH treatment. Among 53 treatment tolerant group, 15 participants showed mildly elevated liver enzymes during the follow-up monitoring. In association analyses for HLA alleles with hypersensitivity reaction, we observed the HLA-DPB1*05:01 allele was associated with an increased risk of hypersensitivity reaction (OR, 4.13; 95% CI, 1.47-11.59; \(p = 0.0539\)). In a subgroup-analysis for moderate hypersensitivity reaction, strong associations were identified in DPB1*05:01 (OR, 9.0; 95% CI, 2.37-41.34; \(p = 0.0009\)) and DQA1*01:02 (OR, 7.44; 95% CI, 1.80-30.85; \(p = 0.0354\)). We also found an additional effect of the DPB1*05:01 for mild hepatotoxicity (OR, 5.78; 95% CI, 2.17-15.36; \(p = 0.0026\)).

**Conclusions:** The majority of participants with HLA-DPB1*05:01 allele had higher hypersensitivity reaction on RFP and INH therapy than participants without. The presence of HLA-DPB1*05:01 was also associated with an increased risk for mild hepatotoxicity during RFP and INH treatment. Our results indicated patients carrying the HLA-DPB1*05:01 allele were correlated with a considerable higher risk of ADRs to RFP and INH in the Korean population.

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Abstract 1066

Triple site versus urine only N. gonorrhoea/C. trachomatis testing among Israeli MSM in the condom fatigue era: a prospective study

David Roy Zoker1, Dan Turner1, Ronen Ben-Ami1, Amos Adler1, Ilan Singer1, Yotam Dizitzer1, Tami Halperin*1

1Tel Aviv Sourasky Medical Center / Medical Tourism, Tel Aviv-Yafo, Israel

Background: Chlamydia trachomatis (CT) and Neisseria gonorrhoea (NG) are the most common sexual transmitted infections (STIs) especially among men who have sex with men (MSM). Three site testing is the recommended test for asymptomatic sexually active MSM, especially for those who are using pre exposure prophylaxis or living with HIV, practicing condom less sex. STIs such as C. trachomatis and N. gonorrhoea are site specific and are detectable mostly at the infection site. We prospectively compared triple site and urine only C. trachomatis and N. gonorrhoea testing among asymptomatic Israeli MSM.

Materials/methods: Asymptomatic MSM > 18 years of age were eligible to participate if they had not received any relevant antibiotic treatment in the previous 3 months. Participants provided informed consent, received verbal and written instructions on specimen collection and then self-collected a urine specimen, pharyngeal and rectal swabs. All samples were tested on site using the Xpert CT/NG assay (Cepheid, Sunnyvale, California, USA), according to manufacturer's instructions.

Results: The study cohort included 218 male participants. 34.5% were using PrEP, 24.3% were HIV carriers. 64 participants (29%) were positive to C. trachomatis or N. gonorrhoea in one of the tested sites or more. N. gonorrhoea was detected among 56% (47 samples) of the positive samples while in 44% (37 samples) of them C. trachomatis was detected. Most of detected samples were obtained from rectal swabs (61%), additional 35% were obtained from oral swabs, only 2.2 % were obtained from urine samples.

Conclusions: High infection rates (29%) were detected among asymptomatic Israeli MSM tested for C. trachomatis and N. gonorrhoea, in one or more of the tested sites, mostly rectal. Urine testing had a very low sensitivity raising the question of necessity to screen urine in asymptomatic MSM. The current study underscores the importance of triple site testing for a highly at-risk population.

Presenter email address: tamihal@tlvmc.gov.il
Performance evaluation of the Xpert HBV Viral Load assay for the quantification of hepatitis B virus DNA in plasma samples

Hoyin Lam*1, Bone Tang1

1Hong Kong Sanatorium & Hospital, Hong Kong, Hong Kong

Background: Accurate quantification of Hepatitis B virus (HBV) DNA in the patients with chronic HBV infection is important for providing treatment indication and monitoring treatment efficacy. In this study, we would like to evaluate the performance of the new Cepheid Xpert HBV Viral load assay (Xpert-HBV) in comparison to the QIAGEN artus HBV QA-RQ kit (artus-HBV) for the quantification of HBV DNA in plasma sample. Also, the analytical characteristics of Xpert-HBV were studied.

Materials/methods: A total of 137 archived plasma samples that submitted to our laboratory for HBV DNA quantification between January and October 2016 were used for performance evaluation. All plasma specimens were processed and quantified for HBV DNA using Xpert-HBV and artus-HBV. To access the analytical sensitivity and the precision of Xpert-HBV, a standard panel of HBV containing plasma sample (AcroMetrix HBV Panel 1.2 mL, Thermo Scientific) was serially diluted to 7 HBV concentrations (5, 10, 25, 50, 100, 250 and 500 IU/mL), in which 5 replicates of each HBV DNA concentration were tested.

Results: Of the 137 samples tested, 133 (97.1%) had the qualitative results that agreed on the two platforms. All 4 samples with the discordant qualitative result (detected by artus-HBV but not by Xpert-HBV) had the HBV viral load below the limit of detection of artus-HBV (<10.22 IU/mL). Further analysis of 107 samples quantified by both assays showed an excellent correlation ($R^2=0.9771$) across the dynamic range of quantification. Average bias between two assays, as determined in Bland-Altman analysis, was 0.20 Log$_{10}$ IU/mL (Xpert minus artus-HBV; ±1.96 S.D: -0.29 to 0.70 Log$_{10}$ IU/mL). All the replicates in 7 different HBV DNA concentrations of the standard panel tested positive by Xpert, except a replicate of 5 IU/mL. The precision of Xpert over the 5 HBV DNA concentrations (25, 50, 100, 250 and 500 IU/mL) ranged from 2.3% to 8.5%.

Conclusions: An excellent correlation between Xpert and artus-HBV could be demonstrated in this study. The good clinical and analytical performance, random access capability and rapid turnaround (≤60 minutes per samples) make the assay becomes a valuable tool for HBV DNA quantification in hospital-based laboratories.

Presenter email address: hylam@hksh.com
Abstract 1071

**Performance evaluation of the Alinity m HBV assay for the quantification of hepatitis B virus DNA in plasma samples**

Hoyin Lam*, Man Kin Ng¹, Bone Tang²

¹Hong Kong Sanatorium & Hospital, Hong Kong, Hong Kong

**Background:** Quantification of Hepatitis B virus (HBV) DNA plays an important role in monitoring HBV infection and in assessing the treatment efficacy. In this study, we evaluate the performance of the new Abbott Alinity m HBV assay (Alinity-HBV) in comparison to the QIAGEN artus HBV QA-RQ kit (artus-HBV) for the quantification of HBV DNA in plasma sample. Also, the analytical characteristics of Alinity-HBV were studied.

**Materials/methods:** A total of 195 archived plasma specimens that submitted to our laboratory for HBV DNA quantification between January and December 2017 were used for performance evaluation. Linearity of the Alinity-HBV was evaluated on dilutions series of a clinical sample ranging from 8.60 to 1.60 Log_{10} IU/mL. To assess the assay precision, a standard panel comprising 8 different HBV concentration levels (5, 10, 25, 50, 75, 100, 250 and 500 IU/mL) was prepared, of which 8 replicates of each HBV DNA concentration were tested twice a day for four consecutive days.

**Results:** Of the 195 samples tested, 193 (99.0%) had the qualitative results that agreed on the two platforms. Among the two samples with discordant qualitative result (positive by Alinity-HBV but negative by artus-HBV), both of them had the result below the limit of detection of Alinity-HBV (<10 IU/mL). Further analysis of 138 samples quantified by both assays showed an excellent correlation ($R^2=0.9752$) across the dynamic range of quantification. Average bias between two assays, as determined in Bland-Altman analysis, was -0.08 Log_{10} IU/mL (Alinity minus artus; ±1.96 S.D: -0.64 to 0.47 Log_{10} IU/mL). The slope of the regression line for the linearity analysis was 0.9998. All the replicates in 8 different HBV DNA concentrations of the standard panel tested positive by Alinity-HBV, except 2 replicate of 5 IU/mL. The precision of Alinity-HBV over 6 HBV DNA concentrations (25, 50, 75, 100, 250 and 500 IU/mL) ranged from 2.7% to 8.5%.

**Conclusions:** An excellent correlation between Alinity-HBV and artus-HBV could be demonstrated in this study. The good clinical and analytical performance, random access capability and the extended linear range of quantification make the assay becomes a valuable tool for high-throughput HBV DNA quantification in hospital-based laboratories.

**Presenter email address:** hylam@hksh.com
Predicting *Pseudomonas aeruginosa* susceptibility phenotypes from whole genome sequence resistome analysis

Sara Cortes-Lara*,1 Carla Lopez Causape1, Ester Del Barrio-Toñio1, Antonio Oliver1

1Hospital Universitario Son Espases, Instituto de Investigación Sanitaria de las Islas Baleares, Palma, Spain

**Background:** Frequent *Pseudomonas aeruginosa* antimicrobial resistance is driven by a complex repertoire of resistance phenotypes, resulting from both, mutation-driven and horizontally-acquired mechanisms. The objective of this work was to develop and validate a resistance genotype score, based on the analysis of the whole genome sequence resistome, to predict *P. aeruginosa* antimicrobial susceptibility phenotype.

**Materials/methods:** Published data on clinical strains and in vitro resistance evolution experiments, were used to define the genes potentially involved in mutation-driven and horizontally-acquired resistance for ceftazidime, ceftolozane/tazobactam, meropenem, ciprofloxacin and tobramycin. Resistance genes/mutations were scored from 0 (no effect) to 1 (clinical resistance, EUCAST breakpoints); the negative effect of mutations known to increase susceptibility was also considered. Resfinder was used to detect horizontally-acquired determinants. The first step for the analysis of mutational mechanisms was to determine the natural polymorphisms existing in the genes involved in mutation-driven resistance. For this purpose, 50 wildtype strains obtained from 51 different hospitals during a 2017 multicenter study were fully sequenced and analyzed. Once the resistance genotype score was developed, its capacity to predict the susceptibility phenotype was tested in 204 isolates randomly selected from the 51 hospitals (4 from each hospital). Phenotypic and genetic assays for the characterization of resistance mechanisms were performed as needed.

**Results:** The analysis of the 50 wildtype strains allowed to develop a catalogue of natural polymorphisms in genes involved in mutation-driven resistance. None of the wildtype strains showed horizontally-acquired determinants and the scores were always <1; however a few wildtype isolates showed mutations clearly involved in resistance (for example 2 isolates showed OprD inactivating mutations). The capacity of the score to predict susceptibility (<0.5) or resistance (≥1) in the 204 clinical isolates is shown in the Table.

**Conclusions:** Although a margin for improvement is evidenced, an overall good correlation between the resistance genotype score and the susceptibility profile was documented. Further refining of the score system, automatization and testing of large international cohorts should follow.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>%$I/R$ score &lt;0.5</th>
<th>%$I/R$ score 0.5–&lt;1</th>
<th>%$I/R$ score ≥1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftazidime</td>
<td>99.2/0.8</td>
<td>86/14</td>
<td>35.5/64.5</td>
</tr>
<tr>
<td>Ceftolozane/tazobactam</td>
<td>100/0</td>
<td>100/0</td>
<td>0/100</td>
</tr>
<tr>
<td>Meropenem</td>
<td>90.2/9.8/0.9</td>
<td>59.6/36.5/3.9</td>
<td>13.2/36.8/50</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>96.2/3.8</td>
<td>75/25</td>
<td>5.9/94.1</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>100/0</td>
<td>100/0</td>
<td>18.2/81.8</td>
</tr>
</tbody>
</table>

**Presenter email address:** sara.cortes@ssib.es
Mortality outcome in critically ill CRO infection patients treated with polymyxin-B and its prediction based on morbidity and mortality scores

Saiprasad Patil1, Bipin Jibhkate2, Kalpesh Shah3, Kamal Parikh4, Amal Bhattacharya5, Nitin Shinde6, Sagar Bhagat1, Hanmant Barkate1

1Glenmark Pharmaceuticals Limited, Mumbai, India, 2Wockhardt Hospitals, The Umrao IMSR, Mira Bhayandar, India, 3Dr Jivraj Mehta Smarak Health Foundation, Ahmedabad, India, 4Sterling Hospital, Rajkot, India, 5Parul institute of medical sciences & research, Vadodara, India, 6Kaushalya speciality clinic, Nagpur, India

Abstract third-party references: Glenmark Pharmaceuticals Ltd.

Background: We intent to observe the 28-day mortality in critically ill CRO infected patients treated with polymyxin-B and to analyze the impact of variables along with morbidity and mortality scores on prediction of mortality.

Materials/methods: Retrospective cohort study was planned in all consecutive polymyxin-B treated patients suffering from CRO infections at 5 centers. Patient's demographics, clinical history, and polymyxin-B therapy details were captured. CCI, Pitts score, INCREMENT scores were computed. Along with 28-day mortality, impact of variables was analyzed using Chi-square and Mann-Whitney test amongst survivors and non-survivors.

Results: 51 patients received polymyxin-B during study period, 49 considered suitable for further analysis. Pneumonia (47%) and BSI (18.3%) were the main infections with underlying bacteremia in 85.7% patients. K. pneumoniae (N=23) was the most common pathogen followed by A. baumannii complex. Mean CCI, Pitts and ICS (N=23) scores were 3.16±2.46, 6.32±2.51 and 9.86±5.17 respectively. Mean dose of Polymyxin-B was 11.8 Lakh U/day ±2.73, Range: 10-19.5 L U/d) administered for mean duration of 7.5 days (±4.02, Range: 3-16 days). All-cause 28-day mortality was 30.6%. No significant association between sepsis severity (p = 0.35), neutropenia (p = 1), polymyxin-B dose ≥ 15LU/d (p = 1) and treatment duration > 7d (p = 0.13) with mortality was observed. However, near significant association of 28-mortality was noticed only with CCI ≥ 2. (Table 1)

Conclusions: Polymyxin-B therapy was associated with good (69.4%) overall survival in critically ill patients with CRO infections. We couldn't find significant association of important variables or morbidity or mortality scores with 28-day mortality. Further validation is required in larger cohort to predict the mortality of CRO infection in Indian setting.

Table 1: Mortality association of variables in critically ill patients with CRO infection. (N=49)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Non-survivors (15) Mean±SD</th>
<th>Survivors (34) Mean±SD</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>54.9 (±11.6)</td>
<td>49.9 (±13.3)</td>
<td>0.43</td>
</tr>
<tr>
<td>Sex (M)</td>
<td>10 (66.6%)</td>
<td>25 (73.5%)</td>
<td>0.73</td>
</tr>
<tr>
<td>CCI</td>
<td>4.06 (±2.57)</td>
<td>2.76 (±2.33)</td>
<td>0.094</td>
</tr>
<tr>
<td>Pitts score (Overall)</td>
<td>6.8 (±3.07)</td>
<td>6.11 (±2.24)</td>
<td>0.36</td>
</tr>
<tr>
<td>Pitts score (Bacteremia pts) (N=42)</td>
<td>6.76 (±3.2)</td>
<td>6.37 (±2.2)</td>
<td>0.57</td>
</tr>
<tr>
<td>INCREMENT score (N=23)</td>
<td>11.55 (±4.55)</td>
<td>8.78 (±5.4)</td>
<td>0.15</td>
</tr>
<tr>
<td>CCI ≥ 2</td>
<td>14 (93%)</td>
<td>23 (67%)</td>
<td>0.075</td>
</tr>
<tr>
<td>Pitts ≥ 6</td>
<td>9 (60%)</td>
<td>17 (50%)</td>
<td>0.55</td>
</tr>
<tr>
<td>INCREMENT score ≥ 8 (N=23)</td>
<td>7 (46.6%)</td>
<td>8 (23.5%)</td>
<td>0.39</td>
</tr>
</tbody>
</table>

Presenter email address: saipras300@gmail.com
Abstract 1075

**Evaluation of simultaneous detection of pathogens associated with sexual transmitted infection and vaginal disorders on a real-time qPCR microfluidics platform in an asymptomatic female college student’s cohort**

María Isabel Montesinos Hernández1*, Marie Hallin2, Lotfi Triki3, Busra Tüglü1, Sophie Lorea1, Anne De Vleeschouwer2, Sophie Henrard1, Zoe Kipouros3, Marie-Luce Delforge1, Jean-Christophe Goffard1

1LHUB-ULB Hospital Erasme, Bruxelles, Belgium, 2LHUB-ULB CHU Saint-Pierre, Bruxelles, Belgium, 3Hospital Erasme, Bruxelles, Belgium

**Background:** This study aimed to characterize the performance of a customized microfluidics platform – the Taqman® Array Card (TAC) on vaginal samples in comparison to conventional tests for the diagnosis of sexual transmitted infections (STI), bacterial vaginosis (BV) and vulvovaginal candidiasis (VC).

**Materials/methods:** This study, carried out prospectively from November 2017 to April 2019, included 211 asymptomatic female college students recruited for STI screening. Sera were collected and screened for HIV, HBV, HCV and syphilis on the Liaison XL platform, while vaginal samples were tested by TAC targeting 29 bacteria, 6 yeasts, 3 viruses and 1 parasite involved in STI, BV and VC. *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG) targets were compared with the Abbott Real-time CT/NG assay. *Candida* spp. and *Trichomonas vaginalis* (TV) targets were compared to culture. Targets involved in BV were compared with Nugent’s score (NS) in all samples and to NS and AmpliSens Florocenosis/Bacterial vaginosis-FRT PCR in 132 samples.

**Results:** CT was detected in 9 samples (4%) by TAC and Abbott PCR. No NG or TV was detected by either of the tests. Poor sensitivity (68%) was observed for *C. albicans* by TAC compared to culture. NS identified 99 (75%) students with normal flora, 33 (25%) with intermediate or BV compatible flora. Applying different interpretative algorithms, TAC’s best sensitivity, specificity, PPV and NPV scores to detect disturbed flora were 67%, 94%, 79% and 89%, respectively. Applying the manufacturer’s interpretation algorithm, AmpliSens PCR’s sensitivity, specificity, PPV and NPV were: 85%, 90%, 74% and 95% respectively. All sera were negative for HIV, HCV and syphilis; one was compatible with recovered HBV.

**Conclusions:** TAC is a customized panel-based molecular platform that allows simultaneous detection of STI and vaginal disorders pathogens, simplifying laboratory workflow and reducing turnaround time. CT was the only STI pathogen detected, present in a low percentage in this asymptomatic female cohort. TAC needs to be improved regarding *Candida* spp detection. AmpliSens PCR showed better performances and ease of interpretation than TAC to identify disturbed flora in this asymptomatic cohort. Samples from BV symptomatic patients are needed to optimize an accurate algorithm for BV diagnosis by TAC.

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Rapid detection of methicillin-resistant Staphylococcus aureus in patients with late hospital-acquired/ventilator-associated pneumonia

Linda Bussini*1, Caterina Monari2, Renato Pascale2, Matteo Rinaldi1, Stefano Ianniruberto1, Elena Rosselli Del Turco1, Simone Ambretti1, Maddalena Giannella1, Pierluigi Viale1

1Policlinico Sant’Orsola-Malpighi, University of Bologna, Bologna, Italy, 2University of Campania Luigi Vanvitelli, Caserta, Italy

Background: New syndromic rapid diagnostic tests seem to be promising for antimicrobial stewardship purposes. We have tested one of them, the FilmArray Pneumonia Panel plus [FA-PPP], in patients diagnosed with hospital-acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP) episodes, with the aim to describe its potential impact on the management of anti-methicillin resistant Staphylococcus aureus (MRSA) therapy.

Materials/methods: Single-center observational study of consecutive adult patients diagnosed with HAP, hospitalized from June 2018 to October 2018. We performed FA-PPP on residual samples of endotracheal aspirate (ETA) or bronchoalveolar lavage (BAL) obtained for the etiological diagnosis of pneumonia. The gold standard was culture method. The cut-off of bacterial growth considered as positive was ≥10⁷ cfu/ml for ETA and BAL, respectively. The performance of the test did not interfere in the decision-making process, so that patients were managed according to the standard of care.

Results: 58 patients were diagnosed with late-onset (≥5 days after admission) HAP, 74% was on mechanical ventilation at diagnosis. Collected samples included 43 ETA and 15 BAL. FA-PPP resulted positive for MRSA in 7 cases, but in only one of them standard culture showed the growth of MRSA. On the contrary, none of the 51 samples with a negative FA-PPP result showed bacterial growth on standard culture (Table 1). According to the observed prevalence of MRSA (1.7%), FA-PPP sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for MRSA detection were 100%, 89%, 14% and 100%, respectively. According to the data of our Microbiology laboratory showing a pre-test probability (overall prevalence of MRSA among isolates from lower respiratory tract samples) of 5%, positive and negative likelihood ratio were 9.5 and <0.1 respectively.

Conclusions: Our findings suggest that FA-PPP could be useful in reducing exposure to anti-MRSA drugs in patients with late HAP/VAP. However, further studies assessing the impact of such test on therapeutic management and patient outcome are needed.

Table 1: FilmArray Pneumonia test Operating Characteristics for methicillin-resistant Staphylococcus aureus (MRSA)

<table>
<thead>
<tr>
<th>MRSA Growth in culture</th>
<th>FA Pneumonia positive</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>1</td>
<td>6</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0</td>
<td>51</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1</td>
<td>57</td>
<td>58</td>
<td></td>
</tr>
</tbody>
</table>

Presenter email address: linda.bussini@gmail.com
Abstract 1079

ETEST Eravacycline for antimicrobial susceptibility testing of Enterobacteriaceae and Enterococcus spp.: performance results from a multi-centre study

Laurine Blanchard*1, Thomas Armstrong1, Denys Gerald1, Yun Ying2, Michael Kresken1,6, Jessica Carpenter3, Veronique Sauvonnet1, Gilles Zambardi2

1bioMérieux, bioMérieux, Marcy-l’Étoile, France, 2BioMerieux Inc., Hazelwood, United States, 3Indiana University School of Medicine, Indianapolis, United States, 4med fusion, Lewisville, United States, 5Antimicrobials Intelligence GmbH, Rheinbach, Germany, 6Rheinische Fachhochschule Köln gGmbH, Cologne, Germany, 7bioMérieux, La Balme-les-Grottes, France

**Background:** Eravacycline (XERAVATM), a fluorocycline antibiotic developed by Tetraphase Pharmaceuticals Inc. for the treatment of complicated intra-abdominal infections. This study evaluated the performance of ETEST® Eravacycline (ERV), a new gradient diffusion strip, for determining the minimum inhibitory concentration (MIC) of Enterobacteriaceae, Enterococcus faecalis and Enterococcus faecium as compared to CLSI/ISO-20776-2 broth microdilution reference method (BMD).

**Materials/methods:** A set of 679 isolates including 542 Enterobacteriaceae, 137 Enterococci was tested at 4 clinical trial sites using ETEST® ERV and BMD. Results were analyzed for essential (EA) and category (CA) agreements, major (ME) and very major (VME) error rates using EUCAST breakpoints (E. coli: ≤ 0.5 [S], > 0.5 [R] mg/L, Enterococcus spp.: ≤ 0.125 [S], > 0.125 [R] mg/L) as well as FDA breakpoints (Enterobacteriaceae: ≤ 0.5 mg/L [S], Enterococcus faecium and Enterococcus faecalis: ≤ 0.064 mg/L [S]). Results for Klebsiella pneumoniae were analyzed for EA only for EU claim as EUCAST breakpoints have not been established.

**Results:** Results are summarized in the table below. ETEST® ERV performance for Enterobacteriaceae and Enterococcus spp. met FDA and ISO acceptance criteria for EA (≥ 90%), CA (≥ 90%), ME (≤ 3%) and VME (≤ 2 or ≤ 3% respectively). A trend to over-estimate E. coli, C. freundii and K. aerogenes MICs was observed.

**Conclusions:** Results of this study support the accuracy of ETEST® ERV for determining MICs of Enterobacteriaceae, and Enterococcus spp. As such, the ETEST® ERV is considered as substantially equivalent to BMD.

<table>
<thead>
<tr>
<th>Claim</th>
<th>Pathogens</th>
<th>EA</th>
<th>CA</th>
<th>ME</th>
<th>Adjusted ME*</th>
<th>VME</th>
<th>Adjusted VME*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>US (FDA breakpoints)</strong></td>
<td><strong>Enterobacteriaceae</strong></td>
<td>99.4%</td>
<td>98.0%</td>
<td>1.3%</td>
<td>NA</td>
<td>5.4%</td>
<td>1.1%</td>
</tr>
<tr>
<td></td>
<td><strong>Enterococcus faecium and E. faecalis</strong></td>
<td>100.0%</td>
<td>94.9%</td>
<td>3.1%</td>
<td>0.0%</td>
<td>33.3%</td>
<td>0.0%</td>
</tr>
<tr>
<td><strong>EU (EUCAST breakpoints)</strong></td>
<td><strong>E. coli</strong></td>
<td>99.0%</td>
<td>100.0%</td>
<td>0.0%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td><strong>K. pneumoniae</strong></td>
<td>99.0%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td><strong>Enterococcus spp.</strong></td>
<td>100.0%</td>
<td>100.0%</td>
<td>0.0%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

* In accordance with the FDA response to Susceptibility Testing Manufacturers Association (STMA) letter dated November 3, 2015, for drugs for which there is no intermediate breakpoint, the VME rate and/or the ME rate may be adjusted to exclude the VME results and/or the ME results that were within essential agreement (EA).

**Presenter email address:** laurine.blanchard@biomerieux.com
Abstract 1080

**Metagenomic sequencing of urine to differentiate infected from contaminated samples**

Gail Hayward*1, A. Sarah Walker1, Tim Peto1, Dona Foster1, David Eyre1, Teresa Street1, Nicholas Sanderson1, Leanne Barker2, Gillian Rodger1, Derrick Crook1, Martin Llewelyn3

1University of Oxford, Oxford, United Kingdom, 2University of Warwick, Warwick, United Kingdom, 3Brighton and Sussex Medical School, Brighton, United Kingdom

**Background:** Culture-based diagnostics for urinary tract infection are neither sensitive nor specific. Currently, bacterial growth in urine is semi-quantified and interpreted using thresholds defined over fifty years ago. In reality culture yield depends on patient characteristics and sample handling, and is biased towards easily culturable organisms. Culture is slow, yielding results after treatment decisions. Contamination of urine by perineal flora results in both false-negative and false-positive results. Up to 50% of urines yield ‘mixed growth of uncertain significance’ (MGUS). Metagenomic DNA sequencing could potentially give rapid and unbiased assessment of bacterial DNA in urine.

**Materials/methods:** The CONDUCT trial collected samples from >1000 women with UTI symptoms. We selected 184 urines yielding pure growth (PG) in culture (>10^5 organisms/ml) (n=34), no significant growth (NSG) (n=34) or MGUS (n=116) and compared culture findings with analysis of Illumina HiSeq metagenomic sequencing data and Centrifuge taxonomic classification.

**Results:** The taxonomic profiles of PG and NSG urines were strikingly different (figure). In all 25 PG urines with cultures containing coliforms or Proteus, reads mapping to Enterobacteriaceae or Morganellaceae families respectively predominated, and accounted for >90% of bacterial reads in 20/25. Among nine PG urines yielding Gram-positive organisms, reads mapping to the corresponding family only predominated in four. Among NSG urines, bacterial reads mostly mapped to common perineal commensals; the commonest family usually accounted for a minority of total reads. A single family predominated in 7/34 NSG urines: Enterobacteriaceae [3], Bifidobacteriaceae [3] and Pseudomonadaceae [1]. Bifidobacteriaceae reads represented Gardnerella spp. which is not identified by urine culture. Among MGUS urines, both profiles were apparent. In 33/116, >90% of reads mapped to Enterobacteriaceae, Staphylococcaceae or Enterococcaceae. In 26/116, the commonest family accounted for only 10% of reads; these were typically common perineal commensal families.

**Conclusions:** Our data provide proof-of-principle that the diversity and identity of bacteria present in urine revealed by metagenomic sequencing can differentiate infected from contaminated samples. Our findings highlight how this approach can now be developed through optimizing sample processing and taxonomic classification.

**Figure**

**Abundance and taxonomic classification of the commonest bacterial family present in 184 urines analyzed by Illumina HiSeq metagenomic sequencing.**

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In vitro activity of ceftazidime/avibactam against ceftazidime-resistant Enterobacterales and Pseudomonas aeruginosa from hospitalised patients in Germany: 2016-17

Michael Kresken*1,2; Miriam Korte-Berwanger2,3; Niels Pfennigwerth4; Sören G. Gatermann4

1Antiinfectives Intelligence GmbH, Rheinbach, Germany; 2Rheinische Fachhochschule Köln GmbH, Cologne, Germany; 3Landeszentrum für Gesundheit Nordrhein-Westfalen, Bochum, Germany; 4Ruhr-University Bochum, German National Reference Centre for Multidrug-Resistant Gram-negative Bacteria, Bochum, Germany

Abstract third-party references: On behalf of the Working Party "Antimicrobial Resistance" of the Paul-Ehrlich-Society for Chemotherapy

Background: The combination of ceftazidime plus avibactam (CTV) possesses potent activity against Gram-negative bacteria (GNB) including multi-drug resistant pathogens producing class A (ESBLs, KPCs and others), class C (AmpC), and various class D (including OXA-48) β-lactamas. CTV, however, is not active against Metallo-β-lactamase (MBL)-producing GNB. The purpose of this study was to evaluate the in vitro activity of CTV against ceftazidime (CTZ)-resistant Enterobacteriales (CTZ-R-ENT) and CTZ-resistant Pseudomonas aeruginosa (CTZ-R-PAE), including carbapenem-resistant isolates.

Materials/methods: Susceptibility testing was performed with the broth microdilution method according to the standard ISO 20776-1. EUCAST clinical breakpoints (v.9.0) were applied for interpretation of MICs: S-susceptible, standard dosing regimen; I-susceptible, increased exposure; R-resistant). Phenotypic detection of ESBLs in ENT was performed according to the EUCAST algorithm. Genetic testing on carbapenemases was performed at the German National Reference Centre for Multidrug-Resistant Gram-negative Bacteria.

Results: 1621 ENT and 575 PAE collected at 22 laboratories were tested. There were 232 (14.3%) CTZ-R-ENT (MIC>4 mg/l) and 72 (12.5%) CTZ-R-PAE (MIC>8 mg/l). 119/304 (39.1%) isolates were obtained from intensive care patients. Of the CTZ-R-ENT, 117 group 1 isolates and seven group 2 isolates with an inducible chromosomal AmpC showed an ESBL-phenotype. 23/232 (9.9%) CTZ-R-ENT had meropenem MICs >0.125 mg/l. A carbapenemase was detected in six CTZ-R-ENT, namely in Citrobacter freundii (VIM-1), Enterobacter cloacae (OXA-48), Escherichia coli (NDM-5), Klebsiella oxytoca (VIM-4), and Klebsiella pneumoniae (n=2, VIM-like). Of the 72 CTZ-R-PAE, 24 were carbapenem-susceptible (imipenem MIC≤4 mg/l; meropenem MIC≤8 mg/l), 17 were additionally resistant to one carbapenem, and 31 were additionally resistant to both imipenem and meropenem. Carbapenemases were detected in 12 CTZ-R-PAE: VIM-like (n=6), IMP-like (n=3), GIM-1 (n=2) and NDM-like (n=1). Susceptibility to CTV (MIC≤8 mg/l) was observed in 226/232 (97.4%) CTZ-R-ENT, 226/227 (99.6%) non-MBL-producing CTZ-R-ENT, 55/72 (76.4%) CTZ-R-PAE, and 55/60 (91.7) non-MBL-producing CTZ-R-PAE. Number and percent CTV-susceptible and CTV-resistant isolates for various subgroups of CTZ-R-ENT and CTZ-R-PAE are presented in the Table.

Conclusions: Overall, >99% and about 92% of the non-MBL-producing CTZ-R-ENT and CTZ-R-PAE, respectively, from hospitalized patients in Germany were CTV-susceptible. Based on these findings, CTV represents a valuable option for targeted treatment of infections caused by these pathogens.

Table: Number and percent ceftazidime/avibactam susceptible (CTV-S) and resistant (CTV-R) isolates for various subgroups of ceftazidime-resistant Enterobacterales (CTZ-R-ENT) and P. aeruginos (CTZ-R-PAE)

<table>
<thead>
<tr>
<th>Group / subgroup</th>
<th>N</th>
<th>CTV-S</th>
<th>CTV-R</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n %</td>
<td>n %</td>
</tr>
<tr>
<td>CTZ-R-Enterobacterales*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>232</td>
<td>226 97.4</td>
<td>6 2.6</td>
</tr>
<tr>
<td>Meropenem MIC ≤ 0.125 mg/l</td>
<td>209</td>
<td>209 100</td>
<td>0 0</td>
</tr>
<tr>
<td>Meropenem MIC &gt; 0.125 mg/l</td>
<td>23</td>
<td>17 73.9</td>
<td>6 26.1</td>
</tr>
<tr>
<td>Carbapenemase-producing</td>
<td>6</td>
<td>1 16.7</td>
<td>5 83.3</td>
</tr>
<tr>
<td>Non-MBL-producing</td>
<td>227</td>
<td>226 99.6</td>
<td>1 0.4</td>
</tr>
<tr>
<td>CTZ-R-P. aeruginosa</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>72</td>
<td>55 76.4</td>
<td>17 23.6</td>
</tr>
<tr>
<td>Susceptible to imipenem/meropenem</td>
<td>24</td>
<td>22 91.7</td>
<td>2 8.3</td>
</tr>
<tr>
<td>Resistant to one carbapenem</td>
<td>17</td>
<td>16 94.1</td>
<td>1 5.9</td>
</tr>
<tr>
<td>Resistant to both carbapenem</td>
<td>31</td>
<td>14 54.8</td>
<td>14 45.2</td>
</tr>
<tr>
<td>Carbapenemase-producing</td>
<td>12</td>
<td>0 0</td>
<td>12 100</td>
</tr>
<tr>
<td>Non-MBL-producing</td>
<td>60</td>
<td>55 5</td>
<td>917 8.3</td>
</tr>
</tbody>
</table>

* C. braakii (n=1), C. faeni (n=1), C. freundii (n=10), C. koseri (n=2), C. cloacae complex (n=56), E. coli (n=174), H. alvei (n=9), H. aerogenes (n=19), K. oxytoca (n=1), K. pneumonia (n=43), K. quasaquasuis (n=2), K. variicola (n=1), M. morganii (n=8), P. mirabilis (n=1), P. stuartii (n=1), S. marcescens (n=1)

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Effectiveness of IV fosfomycin in critically ill patients with CRE infection and analysing the impact of variables on mortality in Indian setting

Saiprasad Patil* 1, Prachee Sathe 2, Ajay Bulle 3, Siddharth Shah 4, Sagar Bhagat 1, Hanmant Barkate 1

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Abstract third-party references: Glenmark Pharmaceuticals Ltd.

Background: Though clinical evidence on usage of fosfomycin in CRE infections is promising its limited. We intent to observe the clinical outcome with fosfomycin and also to check the impact of variables amongst survivors and non survivors.

Materials/methods: Multicentric retrospective study conducted among critically ill patients with CRE infection treated with IV fosfomycin. Patient’s medical records analyzed and important variables like mechanical ventilation, mental status, fosfomycin dose and duration, along with CCI, Pitts and INCREMENT score were compared between survivors and non-survivors.

Results: Among 51 critically ill CRE infection patients, successful clinical outcome was observed in 47% patients. Klebsiella was the most common (74.5%) organism and septic shock (41.2%) was the most common clinical diagnosis. Underlying bacteremia was present in 88.2% of the patients. Mean dose of fosfomycin was 13.2 g/d (±3.12, Range: 8-24 g/d) administered for mean duration of 6.7 days (±5.93, Range: 3-39 days). Pitt score was significantly higher among non-survivors (5.44 ± 2.33 vs. 4.36 ± 2.16, p=0.04), however no significant difference was seen in CCI (p=0.22) and INCREMENT score (p=0.1) among survivors and non-survivors. Septic shock was the only factor associated with significant (0.008) impact on the survival. Overall mortality was 35.2%.

Conclusions: IV Fosfomycin therapy was associated with good (64.7%) overall survival in CRE infections in critically ill patients. Presence of septic shock significantly impacted the mortality. Such association was lacking for other variables in our study.

Table 1: Comparison of variables among survivor and non-survivor

<table>
<thead>
<tr>
<th>Variables</th>
<th>Survivor (n=33)</th>
<th>Non-survivor (n=18)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>56.39 ± 18.86</td>
<td>54.55 ± 11.06</td>
<td>0.66</td>
</tr>
<tr>
<td>Male</td>
<td>25 (75.7%)</td>
<td>16 (88.9%)</td>
<td>0.46</td>
</tr>
<tr>
<td>Septic shock</td>
<td>9 (27.3%)</td>
<td>12 (66.7%)</td>
<td>0.008</td>
</tr>
<tr>
<td>Mental status {Other than alert}</td>
<td>26 (78%)</td>
<td>15 (83%)</td>
<td>1</td>
</tr>
<tr>
<td>Mechanical Ventilation</td>
<td>27 (81%)</td>
<td>14 (77%)</td>
<td>1</td>
</tr>
<tr>
<td>CCI ≥ 2</td>
<td>23 (69.7%)</td>
<td>11 (61.1%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Pitts score ≥ 4 {Overall}</td>
<td>25 (75.7%)</td>
<td>15 (83.3%)</td>
<td>0.72</td>
</tr>
<tr>
<td>INCREMENT score ≥ 8 {N=45}</td>
<td>14 (60.9%)</td>
<td>9 (39.1%)</td>
<td>0.75</td>
</tr>
<tr>
<td>Fosfomycin dose ≥ 16 g/d</td>
<td>12 (36.4%)</td>
<td>8 (44.4%)</td>
<td>0.76</td>
</tr>
</tbody>
</table>

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Abstract 1095

**Methicillin-resistant* Staphylococcus aureus* USA300 persister cells show chaperone upregulation in contrast to planktonic cells and the biofilm phenotype**

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**Background:** Bacteria produce biofilms – bacterial communities embedded in an extracellular matrix that protects the organisms from antibiotics and the host immune response – and persisters (PS) – cells that neither grow nor die in the presence of bactericidal agents, thus exhibiting multidrug tolerance. We developed distinct models to isolate PS and biofilms formed by methicillin-resistant* Staphylococcus aureus* USA300 (MRSA-USA300), a highly virulent clone that causes fulminant infections. Here, we compared the transcriptomic profiles of MRSA-USA300 biofilms and PS against planktonic (PL) cells.

**Materials/methods:** MRSA-USA300 biofilm was grown in brain heart infusion (BHI) medium with 0.1% glucose under static conditions for 24h, 48h and 72h. PS were isolated by treating a 16h stationary phase culture with 5 µg/ml ciprofloxacin for 24h. Samples were taken at 0h, 0.5h, 1h, 2h, 4h, 6h, 8h and 24h, washed and plated for viable cell count. As a comparator, PL cultures were generated in parallel in both cases. Total RNA-extraction (MasterPure™ Complete DNA/RNA Purification Kit, Lucigen), rRNA depletion (Ribo-Zero rRNA Removal Kit (Gram-Positive Bacteria), and RNA-seq (NextSeq, Illumina) were performed on all samples. Differential-gene-expression analysis was performed using DESeq2 with log2 fold change (FC) > 1 or < -1 and p≤0.05 considered significant.

**Results:** MRSA-USA300-PS were successfully generated after 24h ciprofloxacin treatment, typified by a biphasic killing curve (Figure A). Components of chaperone-complex dnaK-dnaJ-grpE and complementary genes clpB and tig showed significant upregulation (log, FC: 2.47, 2.08, 3.15, 2.14 and 1.32 respectively) in PS compared to PL (p≤0.001). In contrast, significant downregulation of said genes, except tip (p>0.05), was observed in biofilm (log, FC: -2.72, -1.13, -1.95 and -3.10 respectively) compared to PL (p≤0.024) (Figure B). In addition, chaperone-complex groEL-groES gene showed significant upregulation in PS (log, FC: 1.70 and 2.70 respectively; p≤0.001) and again contrasting significant downregulation in biofilm (log, FC: -2.01 and -1.98 respectively; p≤0.004) compared to PL (Figure C).

**Conclusions:** Our data shows that MRSA-USA300-PS upregulate chaperone-complexes, in contrast to the biofilm phenotype, as was previously suggested for *E. coli* PS. Upregulated chaperone expression aids in preventing protein misfolding and aggregation under stress conditions. Increased activity would also lead to ATP-depletion, a known feature of PS.
Biphasic killing curve of MRSA-USA300 treated with 5 µg/ml ciprofloxacin

A

B Differential expression dnaK-dnaJ-grpE-clpB-tig in biofilm and PS compared to PL

C Differential expression groEL-groES in biofilm and PS compared to PL

Figure: A) When treating MRSA-USA300 with 5µg/ml ciprofloxacin, the killing curve has a biphasic nature. The susceptible cells die faster in the earlier stages of antibiotic treatment whilst the killing plateaus at 6-8h indicating that, at this stage, only PS form a major part of the bacterial population. 0h equals start of antibiotic treatment of a 16h stationary culture. B) Differential expression analysis of dnaK-dnaJ-grpE-clpB-tig shows significant upregulation (log_2 FC > 1; green) in PS compared to PL but contrasting downregulation (log_2 FC < -1; red) in biofilm compared to PL. tig did not show significant differential expression in biofilm (white). (dnaK: Chaperone protein DnaK – dnaJ: Chaperone protein DnaJ – grpE: Nucleotide exchange factor GrpE – clpB: Chaperone protein ClpB – tig: Trigger factor Tig) C) Additionally, differential expression analysis of groEL-groES shows significant upregulation (log_2 FC > 1; green) in PS compared to PL but contrasting downregulation (log_2 FC < -1; red) in biofilm compared to PL.

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Abstract 1096

Antimicrobial prophylaxis administration after umbilical cord clamping in caesarean section does not increase risk for surgical site infection: a prospective analytic study with 55,901 patients

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Background: The World Health Organization (WHO) recommends administration of surgical antimicrobial prophylaxis (SAP) in cesarean section prior to incision to prevent surgical site infections (SSIs), including endometritis. However, SAP may disrupt the developing neonate’s gastrointestinal microbiome if given before umbilical cord clamping.

Materials/methods: Analytic study within the Swiss national SSI surveillance system, from 2009 to 2018. Multicenter study including patients from 178 hospitals. We included all cesarean section patients that were given the SAP agents cefuroxime, cefazolin, amoxicillin/clavulanate or ceftriaxone, either within 60 minutes before incision or after clamping. Data of the 30 day post-discharge follow-up was available in 89%. We assessed the association between SAP administration relative to incision and clamping and the SSI rate, using generalized linear multilevel models, adjusted for patient characteristics, procedural variables, and health-care system factors.

Results: A total of 55,901 patients met the criteria: SAP was administered before incision in 26,405 patients (47.2%) and after clamping in 29,496 patients (52.8%). Overall 846 SSIs were documented, of which 379 (1.6% [95% CI, 1.4-1.8%]) occurred before incision and 449 (1.7% [1.5-1.9%]) after clamping (p=0.759). The adjusted odds ratio (OR) for SAP administration after clamping was not significantly associated with an increased SSI rate (1.14, 95% CI 0.96-1.36; p=0.144) when compared to before incision. Supplementary and subgroup analyses supported these main results.

Conclusions: The results of this large prospective study provide strong evidence that the risk of SSI for the mother in cesarean section is not increased if SAP is given after umbilical cord clamping compared to before incision. Given the latest research on the potentially detrimental effects of early-life antimicrobial exposure, guidance from WHO and other national organisations should reflect this.

Figure: Unadjusted generalized additive model with surgical site infection as the dependent variable and timing relative to incision as the predicting variable

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**Abstract 1098**

**Laser light scattering technology in the diagnosis of infections in children on dialysis**

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**Background:** to assess the possibility of using laser light scattering technology for the diagnosis of infections in children on dialysis.

**Materials/methods:** From January to September 2019, 148 samples, 106 urine and 42 dialysates, were examined from 115 children from the nephrological Department with a chronic renal failure diagnosis.

Dialysate samples were analyzed both by classical culture method on blood-serum agar, thioglycol and two-phase medium and by ALIFAX HB&L LIGHT analyzer (Alifax, Italy) based on laser light scattering technology inoculating 500 µl of the sample into specific enriched broth vials.

Native urine samples, detected positive by ALIFAX HB&L LIGHT analyzer with cutoff of 10E3 CFU/ml, were cultured on blood agar by the Eisenberg method

**Results:** A complete agreement within the 2 methods was found in 42 dialysate samples: 38 negative (90.5%) and 4 positive (9.5%) results.

A pyogenic coccus *Staphylococcus aureus* with a count of 10E4 CFU/ml was detected in two different specimens and in a wound drainage sample cultured along with peritoneal catheter outlet, where *S. aureus* was isolated in moderate growth.

*Corynebacterium sp.* was one of the dialyzates isolated, it belongs to the skin biota and represents a potential contaminant during sample collection.

Polymicrobial culture was detected from one patient, including *E. coli*, *Candida sp.*, *S. haemolyticus*. The latter two are skin and mucous normobiota that could contaminate the sample or colonized the peritoneal catheter.

After three hours’ incubation using alternative technology, a negative result was obtained for 81 urine samples (76.4%), and a positive result for 25 samples (23.5%). Enterobacterales were identified in 39.3% (*E. coli, M. morganii, C. amalonaticus, E. cloacae*), non-fermenting gram-negative bacteria in 14.3% (*P. aeruginosa, R. picketi, Oligella sp.*), Enterococcus sp. in 21.4%, coagulase-negative staphylococci in 10.7% (*S. haemolyticus, S. epidermidis*), *S. viridans* in 7.1%, *C. albicans* and *Corynebacterium sp.* in 3.6%.

**Conclusions:** In our workflow, the data on the absence bacteriuria in urine is received by the physician within 3-4 h allowing a better management of young patients and avoiding unnecessary use of antibiotics in 2/3 cases. Moreover, the system is highly sensitive detecting minimum bacterial concentration in small amount of sample.

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Abstract 1103

Improved molecular diagnosis of dermatomycosis
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Background: PCR is more sensitive than culture and microscopy for the detection of dermatophytes in clinical specimens. However, most assays focus on the detection of the entire group and few important species. We have evaluated the EuroAssay Dermatomycosis, a commercially available test permitting detection and identification of a large number of dermatophyte species and a few other fungi relevant in dermatomycosis.

Materials/methods: A total of 206 clinical specimens (124 nail, 78 skin and 4 hair specimens) from patients with suspected dermatomycosis were included in the study. Specimens were analyzed by microscopy, culture and PCR (EuroAssay Dermatomycosis; Euroimmun). For molecular detection, DNA was extracted with the EZ1Tissue Kit (Qiagen) after overnight incubation in ATL buffer (Qiagen) containing proteinase K. Amplification, hybridization and read-out was according to the instructions of the manufacturer. Fungal species were categorized in three groups A to C based on their clinical significance (true pathogen, possible pathogen, no pathogen). Specimens were grouped accordingly considering the fungal species with the highest significance only.

Results: Group A and group B organisms were found by culture and PCR in 42 and 9, by PCR only in 43 and 22, and by culture only in 4 and 1 specimens, respectively. Thus, PCR detected significantly more group A (85 versus 46) and group B organisms (31 versus 10) than culture. The concordance of species identification by culture and PCR was 100% for the 51 specimens categorized into the same group (A or B) by both methods. Additional organisms of equal or lower significance were found by culture (N=2), PCR (N=6) or both (N=4). Microscopy was positive in 35/42 (83.3%) of specimens with group A organisms detected by culture and PCR and was negative in 82/85 (96.5%) specimens without clinically significant organism (group C).

Conclusions: The Euroimmun assay is significantly more sensitive than culture and microscopy and provides accurate species identification. Microscopy may be especially helpful when PCR detects possibly pathogenic organisms.

<table>
<thead>
<tr>
<th>Number of specimens per group (thereof number with positive microscopy)</th>
<th>Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A</td>
</tr>
<tr>
<td>PCR</td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>42 (35)</td>
</tr>
<tr>
<td>B</td>
<td>0</td>
</tr>
<tr>
<td>C</td>
<td>4 (2)</td>
</tr>
</tbody>
</table>

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Abstract 1106

**Human papilloma virus-testing in extragenital samples: usefulness and importance of complete genotyping**

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**Background:** Human papillomavirus (HPV) infection outcomes range from benign to malignant processes. The correlation between cervical cancer and HPV infection is almost complete, but the impact of HPV infection in the development of tumours in other human anatomical sites (such as anal or head-neck) appears to be slightly lower. There is a growing interest to evaluate the relationship between the presence of HPV in extragenital sites and the development of cancerous processes. However, routine systems for cervical cancer screening are not useful for detection of all HPV-types, especially in extragenital samples.

**Materials/methods:** All extragenital samples tested for HPV from September 2017 to October 2019 in a tertiary hospital in Madrid (Spain) were reviewed. DNA extraction from biopsies was performed using Wizard® SV Genomic DNA Purification System (Promega) and HPV-typing using HPV Direct Flow Chip Kit (Master Diagnóstica). This assay detects 18 high-risk or putative high-risk genotypes (hrHPV) and 17 low-risk genotypes (lrHPV). Demographics and clinical information of the patients were also reviewed.

**Results:** 39 extragenital samples from 35 patients (median age 56.5 years, interquartile range: 37.5-67.5 years; 63.6% males) were analyzed. Most common type of samples were laryngeal biopsy (n=18, 46.2%), pleural biopsy (n=7, 17.9%) and mediastinal adenopathy (n=5, 12.8%). Other 9 samples were recovered from very diverse sites (including 5 oral cavity and 2 skin biopsies). Seventeen samples yielded a positive result (43.6%), but only in 6 of them, hrHPV were detected: HPV-16 in five cases (29.4%) and HPV-58 in one (5.9%). Among them, five cases corresponded to five distant metastases (one pulmonary and four mediastinal adenopathies) from cervical cancer (HPV-16 in four cases and HPV-58 in one). Besides, HPV-16 was detected in a pleural biopsy, being the same HPV-type previously detected in the primary amygdala epidermoid carcinoma. The remaining positive results were lrHPV: 8 HPV-6 (47.1%) and 3 HPV-11 (17.6%), all detected in laryngeal samples.

**Conclusions:** The hrHPV detected in extragenital samples corresponded to distant metastases, suggesting viral dissemination from primary cervical or head-neck carcinoma. The implementation of the nonavalent vaccine could avoid these cases, because all HPV-genotypes detected are included in this vaccine.

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Abstract 1108

Reduced in vitro killing of methicillin-resistant *Staphylococcus aureus* blood culture isolates by vancomycin as the bacterial inocula increases

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**Background:** MRSA blood stream infections (with or without endocarditis) and other serious life threatening infections require prompt and adequate therapy. Vancomycin remains a drug of choice for treating MRSA infections including bacteremia, however, failures necessitating different drugs (i.e. ceftaroline/ceftobiprole, linezolid, daptomycin) are becoming more common. We had previously reported mutant prevention concentration (MPC) values for vancomycin against MRSA strains of ≥32 µg/ml. In an attempt to determine if higher MPC values could impact bacterial activity, we compared killing of MRSA by vancomycin at 4 different drug concentrations and against increasing bacterial densities.

**Materials/methods:** Four unselected MRSA strains were exposed to 4 different vancomycin drug concentrations [minimum inhibitory concentration (MIC), MPC, maximum serum concentration ([Cₘ₃₅; 20 µg/ml]), maximum tissue concentration (Tissue-max; 10 µg/ml)] and the log₁₀ reduction and percent kill of viable cells recorded at 0.5, 1, 2, 4, 6, 12 and 24 hours after drug exposure against bacterial densities ranging from 10⁶-10⁹ colony forming units per milliliter (cfu/ml). Measurements at each time point were in triplicate and results averaged.

**Results:** The MIC/MPC values for the 4 strains were 1/≥32, 0.5/16, 0.5/4 and 1/2. MIC and MPC drug concentrations were poor at killing over all inocula tested. At the 10⁶ cfu/ml density a 1.9 and 3.7 log₁₀ reduction was seen at 12 and 24 hours respectively for the Cₘ₃₅ drug concentration which decreased to a 0.7 and 2.4 log₁₀ reduction at the 10⁷ inocula and growth at the 10⁸ and 10⁹ cfu/ml inocula. For the Tissue-max drug concentration, a 2.1 and 3.3 log₁₀ reduction was seen following 12 and 24 hours of drug exposure at the 10⁶ cfu/ml inocula, a 0.5 and 1.8 log₁₀ reduction at the 10⁷ cfu/ml inocula and growth or a 0.09 log₁₀ reduction at the 10⁸ and 10⁹ cfu/ml.

**Conclusions:** Patients are infected with higher bacterial densities than used in MIC susceptibility testing. Determining antimicrobial activity against higher bacterial densities is essential. As bacterial densities increased, the bacterial activity of vancomycin decreased. Such a finding is a concern for vancomycin therapy where higher bacterial burdens may be present and could explain vancomycin failures.

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**Abstract 1113**

**Added value of throat and perineal *Staphylococcus aureus* screening, in addition to nasal screening, for identifying patients at risk of *S. aureus* surgical site infection**


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Abstract third-party references: This research project receives support from the Innovative Medicines Initiative Joint Undertaking under grant agreement n° 115523, 115620, 115737 resources of which are composed of financial contribution from the European Union Seventh Framework Programme [FP7/2007-2013] and EFPIA companies in kind contribution.

**Background:** Nasal carriage of *Staphylococcus aureus* (SA) increases the risk of surgical site infection (SSI). In centres with pre-operative SA decolonization protocols, it is a common practice to screen the nose only. The aim of this analysis was to estimate the added value of screening the throat and the perineum, in addition to the nose, for identifying patients at risk of SA SSI.

**Materials/methods:** We analysed preliminary data from a prospective observational cohort study conducted at 33 European hospitals (ASPIRE-SSI). Adult patients undergoing surgical procedures were screened pre-operatively in the nose, throat and perineum. All SA colonized (at any of three body sites) and a sample of non-colonized subjects were enrolled into the study cohort in a 2:1 ratio, and followed for 90 days after surgery. Two weighted multivariate mixed-effect logistic regression models, including common risk factors for SSI and a random intercept for hospital, were developed: nasal-only colonization (n-model) or any of the three body sites (ntp-model). The predictive performance of the two models was compared by estimating the area under the receiver operating characteristic curve (AUC), adjusted for the sampling design.

**Results:** We included 3039 SA carriers of whom 72 (2.4%) developed SA-SSI. 2360 SA carriers were positive in the nose (of whom 62 [2.6%] developed SA-SSI) and 679 were negative in the nose and positive in the throat and/or perineum (of whom 10 [1.5%] developed SA-SSI). Out of 6205 non-carriers from the source population, we included 1470 (23.7%) who served as controls (of whom 12 [0.8%] developed SA-SSI). Taking into account the sampling of controls, the sensitivity of the screening increased from 51.7% in the n-model to 60.0% in the ntp-model, while the specificity decreased from 73.9% to 66.3%. The prediction models yielded an AUC of 0.74 (95%CI: 0.67-0.81) in the n-model and 0.74 (95%CI: 0.67-0.81) in the ntp-model.

**Conclusions:** Extending SA pre-operative screening to throat and/or perineum led to identification of 679 additional at-risk subjects (29% increase) and 10 additional SA-SSI episodes in this at-risk group (14% increase), suggesting a potential benefit when implemented in clinical practice.

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Background: In high-income countries, respiratory syncytial virus (RSV) contributes significantly to morbidity in children, placing a substantial burden on the health system. The development of an RSV vaccine has been identified as a public health priority. More data are needed by policy-makers to understand the burden of RSV throughout the lifespan, but particularly among children in order to help identify priority populations as vaccines are developed and licensed.

Materials/methods: We used population-based health administrative data to calculate rates of RSV hospitalizations in children born between May 2009 and June 2015 in Ontario, Canada. Children were followed until their first RSV-hospitalization, death, 5th birthday, or the end of the study period (June 2016). RSV hospitalizations across the province were identified with a validated algorithm using international classification of diseases 10th revision (ICD-10) codes and/or laboratory-confirmed outcomes collected from a subset of hospitals. We calculated hospitalization rates by various characteristics of interest, including finely-stratified age groups, sex, and comorbidities, overall and by gestational age. We also examined RSV hospitalizations by calendar month in order to understand temporal trends, including for individual age groups.

Results: The overall hospitalization rate for children <5 years was 4.2 per 1,000 person-years (PY) with a wide range across age groups [from 0.52 per 1,000PY in children aged 36-59 months to 29.6 per 1,000PY in children aged 1 month]. Rates of RSV hospitalization were higher in males compared to females [4.7 and 3.7 per 1,000PY, respectively] and in children who were born at a younger gestational age [ranging from 3.9 in those born at ≥37 weeks to 23.2 per 1,000PY in those <28 weeks]. For all age groups, rates were highest between December and March; however, there was substantial variation within age groups by calendar month, with the highest risk of RSV-hospitalization in those who were 1 month of age in February (Figure 1).

Conclusions: Our results reiterate the high burden of RSV hospitalization and highlight young infants at increased risk, including with respect to seasonality. These results may help inform current and future prevention efforts.

Figure 1. Rate of RSV hospitalization by age group and calendar month

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Fitness cost of mgrB alterations in carbapenem-resistant *Klebsiella pneumoniae* isolates from Moscow

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**Background:** Several mechanisms of resistance to colistin have been described in *Klebsiella pneumoniae*. One of them includes chromosomally encoded alterations in MgrB, which lead to lipopolysaccharide modification. To assess the impact of this colistin resistance mechanism on the bacterial fitness, we analyzed growth capacity among colistin-susceptible (Col-S) and colistin-resistant (Col-R) *K. pneumoniae* and performed competitive growth experiments.

**Materials/methods:** Colistin susceptibility among carbapenem-resistant (Carba-R) *K. pneumoniae* collected from patients at ICUs in Moscow was determined using the broth microdilution method. In Col-R (MIC >2 mg/L) isolates, the structure of mgrB was detected using the Sanger sequencing. Growth rates were determined by OD600 measuring for 15 hours every 30 minutes. The fitness of Col-R isolates was assessed against a Col-S strain using a competitive growth assay. Exponentially growing cells of Col-R and Col-S strains were mixed in a 1:1 proportion and grown in Luria-Bertani (LB) broth for 18 h. After incubation, the mixture was directly plated onto LB agar plates with or without 10 mg/L of colistin. The competitive index (CI) was calculated as a ratio between the number of Col-R and Col-S colonies.

**Results:** Among 22 Carba-R *K. pneumoniae*, 16 and 6 isolates were Col-R and Col-S, respectively. Colistin MICs of Col-R strains ranged from 16 to 1024 mg/L. In 8 Col-R isolates, the following mgrB alterations were detected: [1] IS*Kpn14*, IS*1A*, and IS*1R* (n=2, n=1 and n=1, respectively; IS1 family); [2] IS*Kpn26* and MITE*Kpn1* (n=1 and n= 2, respectively; IS5 family); [3] mgrB deletion (n=1). Eight Col-R carried a wild-type mgrB. Growth rates of Col-S and Col-R isolates did not differ significantly. Competitive co-culturing experiments demonstrated that 15 of 16 (94%) isolates carrying disrupted or wild-type mgrB displayed similar CIs, which were below 1 ranging from 0.01 to 0.3. One Col-R isolate with wild-type mgrB exhibited the equal fitness with the Col-S isolate (CI=1). Thus, 15 of 16 Col-R *K. pneumoniae* demonstrated a reduced fitness (CI<1) comparing to the Col-S strain.

**Conclusions:** Although colistin resistance did not affect the growth rates, the vast majority of Col-R *K. pneumoniae* demonstrated a reduced fitness (irrespective of the mgrB status) in competitive experiments.

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Abstract 1119

Inhibitory effect of whole blood on the antiseptic action of E-101 solution, a myeloperoxidase-mediated formulation, compared to conventional wound cleansers

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Background: E-101 Solution (E-101) is a myeloperoxidase-mediated antimicrobial wound wash for physical irrigation, cleansing, and moisturizing of open wounds. It is composed of porcine myeloperoxidase (pMPO), glucose oxidase (GO), in an aqueous vehicle and activated by the addition of glucose. Once activated, hydrogen peroxide (H₂O₂) is produced in situ by GO dehydrogenation of glucose and reduction of oxygen. The MPO-catalysed oxidation of chloride ion by H₂O₂ generates hypochlorous acid (HOCl). Once generated, HOCl reacts in a diffusion-controlled reaction with a second H₂O₂ molecule to yield singlet oxygen. We evaluated the effect of blood on the performance of E-101 and three commercially available wound cleansers comprised of stabilized organic derivatives of HOCl.

Materials/methods: Antiseptics were tested against Escherichia coli ATCC 8739, Pseudomonas aeruginosa ATCC 9027, Staphylococcus aureus ATCC 6538, Candida albicans ATCC 10231, and Aspergillus braziliensis ATCC 16404 in accordance with the antimicrobial effectiveness test USP-51. Comparative antiseptics included Vashe (SteadMed), Microcyn (Oculus Innovative Sciences), and NeutroPhase (NovaBay Pharmaceuticals, Inc.). All antiseptics were tested in the absence and presence of 1, 2, and 5% whole human blood. Time kill studies were also performed with E-101 solution against P. aeruginosa ATCC 27853, S. aureus ATCC 43300, E. coli ATCC 25922, and Candida auris CDC B11903 in absence and presence of 2, 5, 10, and 20% blood.

Results: In the USP-51 test, E-101 demonstrated >2-log₁₀ reduction against bacterial and fungal isolates in the presence of 5% blood at day 14 and day 28. With the exception of NeutroPhase vs S. aureus, all comparative antiseptics demonstrated <2-log₁₀ reduction in the presence of 5% blood at days 14 and 28. Time kill results for E-101 against E. coli and P. aeruginosa showed a >5-log₁₀ reduction in the presence of 2, 5, 10 and 20% blood; for S. aureus a >5-log₁₀ reduction in the presence of 2% and 5% blood; for C. auris a >5-log₁₀ reduction in the presence of 2% blood.

Conclusions: E-101 remains active in the presence of blood containing catalase and other competitive substances. In contrast, comparative antiseptics with the active component HOCl were easily inactivated by the presence of blood.

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**Evaluation of the BIOFIRE FILMARRAY Bone and Joint Infection (BJI) panel for the detection of microorganisms and resistance markers in synovial fluid specimens**

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**Background:** Bone and Joint Infections (BJIs) present with non-specific symptoms that may include pain, swelling, and fever and are associated with high morbidity and significant risk of mortality. BJIs can be caused by a variety of bacteria and fungi, including anaerobes and microorganisms that can be challenging to culture or identify by traditional microbiological methods. Clinicians currently rely primarily on culture to identify the pathogen(s) responsible for infection. The BioFire® FilmArray® Bone and Joint Infection (BJI) Panel (BioFire Diagnostics, Salt Lake City, UT) was designed to detect 15 gram-positive (seven anaerobes) and 14 gram-negative bacteria (one anaerobe), two yeast, and eight antimicrobial resistance (AMR) genes from synovial fluid specimens in about an hour. The objective of this study is to evaluate the performance of an Investigational Use Only (IUO) version of the BioFire BJI Panel compared to various reference methods.

**Materials/methods:** Remnant synovial fluid specimens, which had been collected for routine clinical care at 13 study sites in the US and Europe, are undergoing testing using an IUO version of the BioFire BJI Panel. Performance is determined by comparison to Standard of Care (SoC) testing consisting of bacterial culture at each study site (performed according to each site's routine procedures).

**Results:** To date, 336 specimens (out of an anticipated 1,500) have been collected and tested with the panel. The majority are from knee joints (71.7%) and arthrocentesis (86.6%) is the most common collection method. Compared to SoC culture, overall sensitivity is 90% and specificity is 99.8%. Testing is ongoing.

**Conclusions:** The BioFire® BJI Panel is a sensitive, specific, and robust test for rapid detection of a wide range of analytes in synovial fluid specimens. The number of microorganisms and resistance markers included in the BioFire BJI Panel, together with a reduced time-to-result and increased diagnostic yield compared to culture, is expected to aid in the timely diagnosis and appropriate management of BJIs.

*Data presented are from assays that have not been cleared or approved for diagnostic use.*

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Abstract 1129

**National ambulatory care prescribing of oral antibiotics and prevalence of inappropriate prescribing in the United States, 2009 to 2016**

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**Background:** Antibiotic resistance is a global public health issue. A significant proportion of antibiotic use occurs in the outpatient setting for conditions not commonly caused by bacterial pathogens. Despite initiatives to decrease inappropriate antibiotic use, it is unclear how national prescribing rates have changed in recent years. This study aimed to describe outpatient antibiotic prescription trends and evaluate changes in inappropriate prescribing in the United States (U.S.) over an eight-year period.

**Materials/methods:** This was a cross-sectional study using the Centers for Disease Control and Prevention’s National Ambulatory Medical Care Survey (NAMCS) from 2009 to 2016. All patient visits were eligible for inclusion. Antibiotic use was defined by at least one oral antibiotic prescription during the visit as identified by Multum code(s). Patient visits were categorized by health care provider, geographic regions within the U.S., and season. International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes were used for survey years 2009 to 2015 and ICD-10 codes were used for 2016. Appropriate, possibly appropriate, and inappropriate antibiotic use were defined by the patient’s ICD codes during their visit. Lastly, baseline characteristics were compared between visits involving receipt of an antibiotic and those that did not utilizing chi-square or Wilcoxon rank-sum tests where appropriate.

**Results:** A total of 7 million visits were included for analysis, of which 793,415,182 (11.3%) included an antibiotic. Prescribing rates were relatively stable over the study period, ranging from 102.9 to 124.9 prescriptions per 1000 visits; however, 2016 had one of the lowest prescribing rates (107.7 prescriptions per 1000 patient visits). The most commonly prescribed antibiotic class was macrolides (25 prescriptions per 1000 visits). The South region and winter season had the highest antibiotic prescription rates (118.2 and 129.7 prescriptions per 1000 visits, respectively). Of patients that received an antibiotic, 55.9% were classified as inappropriate use, 8.4% had an appropriate indication, and 35.7% had a possibly appropriate indication.

**Conclusions:** There was no significant reduction in outpatient antibiotic prescribing rates among outpatients in the U.S. from 2009 to 2016 and inappropriate antibiotic prescribing was common. Further public health campaigns are warranted to promote outpatient antimicrobial stewardship programs.

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Comparison of multidrug-resistant *Salmonella enterica* serovar I 4,[5],12:i:- and *Salmonella enterica* serovar Typhimurium isolated from swine in the USA

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**Background:** The Centers for Disease Control and Prevention has reported an increase in multi-drug resistant (MDR) *Salmonella enterica* serovar I 4,[5],12:i:-, which has been increasingly isolated from swine and pork products. *Salmonella I 4,[5],12:i:-* is antigenically similar to *Salmonella enterica* serovar Typhimurium yet lacks the phase 2 flagellar antigen; thus, is referred to as monophasic *Salmonella Typhimurium*. The overall objective of this study is to determine and compare phenotypic and genotypic traits of monophasic and biphasic *Salmonella Typhimurium* isolated from swine head trim and cheek meat collected from a pork processing plant in the United States.

**Materials/methods:** Phenotypic antimicrobial susceptibility patterns were identified by broth microdilution on a Sensititre® system. Bacterial growth curves were determined using a BioScreen C under different concentrations of enrofloxacin, tetracycline, ceftiofur, and ciprofloxacin; growth curves were analyzed using a 4-parameter Gompertz-model in Stata® to evaluate bacterial fitness. Motility and biofilm assays were used to assess swimming and swarming and biofilm production capabilities between monophasic and biphasic Typhimurium strains. Whole genome sequencing was performed on an Illumina MiSeq and Oxford Nanopore MinION to detect resistance genes, plasmids, and point mutations. Whole-genome alignment was performed to detect differences in the phase 2 flagellar antigen region using Geneious Software.

**Results:** Phenotypic and genotypic analyses confirmed all 47 *Salmonella I 4,[5],12:i:-* isolates were MDR, 45 displaying the common ASSuT phenotype and 2 the SSuT phenotype, while 44 displayed the ASSuT genotype. Thirty-seven also harbored the plasmid-mediated quinolone resistance gene, qnrB. There was no fitness cost to *Salmonella I 4,[5],12:i:-* harboring the qnrB, *bla*CMY and *tet* genes. There were no significant differences between *Salmonella I 4,[5],12:i:-* and *Salmonella Typhimurium* swarming motility. However, the swimming motility *Salmonella Typhimurium* was greater over a period of 18 hours. Further analyses of bacterial growth curves, motility and biofilm assays, whole-genome alignment, and hybrid assembly between MinION and Illumina reads are ongoing.

**Conclusions:** This study is important to determining the pathogenicity traits of MDR *Salmonella I 4,[5],12:i:-* in order to develop mitigation strategies and prevent this serovar from dissemination into the food chain and ultimately aid in preventing salmonellosis linked to swine and pork products.

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Effectiveness and safety of aminoglycosides for the empirical treatment of patients with upper urinary tract infection

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Background: Aminoglycosides have favorable urinary tract pharmacokinetics and in vitro activity against uropathogens, but their use is limited by concerns over nephrotoxicity. We implemented an institutional program to promote aminoglycosides as initial empirical treatment of patients with upper urinary tract infection (UTI).

Materials/methods: We reviewed the records of patients with upper UTI at the Tel Aviv Medical Center from January 2017 to April 2018. The primary outcome was death within 30 days of index culture. Initial treatment with an aminoglycoside was compared to non-aminoglycoside antibiotics. Propensity score matching was performed to adjust for between-group differences in baseline covariates.

Results: The study cohort included 2,026 patients, 715 treated with aminoglycosides and 1,311 treated with non-aminoglycoside drugs; 589 patients (29%) were bacteremic. Treatment with aminoglycosides was associated with a higher likelihood of in vitro activity against clinical isolates (odds ratio, 2.0; P <0.001). Death at 30 days occurred in 55 (7.6%) versus 145 (11%) of patients treated with aminoglycosides and non-aminoglycoside drugs, respectively (adjusted hazard ratio, 0.78; P =0.013). Aminoglycosides were non-inferior to comparator drugs in all patient subgroups, stratified according to age, glomerular filtration rate, bacteremia, hemodynamic shock and infection with 3rd generation cephalosporin-resistant Enterobacterales. Aminoglycosides were associated with significantly shorter hospital stay, fewer days of antibiotic treatment, and lower rates of readmission within 90 days. The rate of acute kidney injury was similar for aminoglycosides and comparators (2.5% versus 2.9%, respectively; P =0.6).

Conclusions: Within the context of an institutional program, initial empirical treatment of upper UTI with aminoglycosides was associated with higher rates of appropriateness and lower overall mortality compared to non-aminoglycoside drugs, without excess nephrotoxicity.

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Prospective survey of mucormycosis in Israel

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Background:

Mucormycosis is a clinically heterogenous invasive mycosis that can affect a broad population of human hosts. Incidence and associated patient risk factors vary significantly across geographical locations. IsraMOLD is an ongoing prospective multicenter laboratory-based survey of invasive mold disease in Israel. We report on the microbiological and clinical characteristics of mucormycoses identified in IsraMOLD.

Materials/methods:

Clinical filamentous fungal isolates were collected at 10 medical centers throughout Israel [7 tertiary and 3 community hospitals]. Clinical data were collected prospectively by researchers at each center. Isolate identification and drug-susceptibility testing were performed at a central reference laboratory. Mucorales species were identified by sequencing the internal transcribed spacer (ITS) and large subunit (LSU) ribosomal DNA segments.

Results:

363 mold isolates were collected from 1/2015 to 9/2019. Of these, 63 isolates (17%) were Mucorales, second only to Aspergillus species (236 isolates, 65%). 46 isolates (73%) represented invasive infection; neutropenia, stem cell transplantation and high-dose corticosteroid treatment were associated with invasive mucormycosis, whereas structural lung disease was associated with colonization. Median patient age was 49 years [range 1-87 years]; 8 (17%) were aged under 18 years. Predominant risk factors were hematologic malignancy (15 patients, 32%), stem cell transplantation (24%), corticosteroids (24%), diabetes mellitus (21%), and trauma (8.7%). The frequent species were Rhizopus [n=26], Lichtheimia [n=12] and Mucor [n=6]. Pulmonary mucormycosis was associated with hematologic malignancy and corticosteroid treatment, rhino-orbital mucormycosis was associated with hematologic malignancy and Rhizopus species, and soft tissue mucormycosis with trauma, Lichtheimia and Mucor species. Sixteen patients [34%] died within 30 days, similar to other invasive molds [logrank P=0.34]. Death was associated with pulmonary disease, stem cell transplantation, GVH and corticosteroids. Surgery, performed in 28 patients [60%], was not associated with increased survival rate.

Conclusions:

The annual incidence of mucormycosis in Israel was 1.5 per million population, high compared to other surveys. Hematologic malignancy emerged as the predominant risk factor. Mortality rate was similar to that of other invasive mycoses, possibly reflecting improvements in the diagnosis and pharmacotherapy of mucormycosis.

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Evaluation of the accuracy of the panel for antimicrobial susceptibility testing of Enterobacteriaceae and carbapenemase detection

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Background: The recent spread of carbapenemase-producing organisms (CPO) is a global threat. Carbapenem resistance in Enterobacteriaceae can be mediated by extended-spectrum beta-lactamase (ESBL) or AmpC beta-lactamase production in combination with decreased permeability or by carbapenemase production. In 2017, the Phoenix™NMIC-500 panel was launched. In this study, we evaluated the accuracy of antimicrobial susceptibility testing (AST) of Phoenix™NMIC-500 against Enterobacteriaceae.

Materials/methods: A total of 239 isolates were tested. They consisted of 47 CPO, 45 non-carbapenemase-producing carbapenem-resistant Enterobacteriaceae (non-CP-CRE), 47 ESBL-producing Enterobacteriaceae with ciprofloxacin MIC ≤1mg/L, 49 ESBL-producing Enterobacteriaceae with ciprofloxacin MIC ≥2mg/L, and 51 non-ESBL-producing Enterobacteriaceae. Bacterial isolates were subcultured on sheep blood plate and were tested for imipenem, meropenem, ertapenem, amikacin, gentamicin, ciprofloxacin, fosfomycin, ceftazolin, ceftriaxone, nitrofurantoin with Phoenix™NMIC-500. As a reference method, broth microdilution was performed for all antibiotics tested except fosfomycin, for which agar dilution method was performed according to CLSI M07. The rate of category agreement (CA), very major error (VME), major error (ME), minor error (MinE) were calculated. We also evaluated the detection of ESBL and carbapenemase of the panel compared with the PCR results for ESBL and carbapenemase genes.

Results: The CA and error rates are described in the Table. In general, CA was >90% for all antibiotics tested. The ciprofloxacin CA of ESBL-producing Enterobacteriaceae with ciprofloxacin MIC ≤1mg/L and ≥2mg/L are 66.0%, 100%, respectively. The sensitivity and specificity of ESBL detection are 71.1% (69/97), 98.0% (50/51), respectively, and those of carbapenemase detection are 97.9% (46/47), 82.9% (160/193), respectively. Most (30/35) of isolates giving false-positive CPO results were non-CP-CRE. The rate of correct classification of CPO was 85.1% (40/47).

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>CA (%)</th>
<th>VME (%)</th>
<th>ME (%)</th>
<th>MinE (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imipenem</td>
<td>90.4</td>
<td>0</td>
<td>2.5</td>
<td>8.0</td>
</tr>
<tr>
<td>Meropenem</td>
<td>96.8</td>
<td>1.4</td>
<td>0.6</td>
<td>3.3</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>96.2</td>
<td>0</td>
<td>1.5</td>
<td>2.9</td>
</tr>
<tr>
<td>Amikacin/Gentamicin</td>
<td>98.5/97.5</td>
<td>3.6/1.1</td>
<td>0/1.3</td>
<td>1.3/0.8</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>96.4</td>
<td>0.7</td>
<td>2.3</td>
<td>8.4</td>
</tr>
<tr>
<td>Fosfomycin</td>
<td>96.7</td>
<td>3.5</td>
<td>0</td>
<td>2.9</td>
</tr>
<tr>
<td>Ceftazolin</td>
<td>97.9</td>
<td>0</td>
<td>0</td>
<td>2.1</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>98.2</td>
<td>0</td>
<td>3.3</td>
<td>0</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>94.6</td>
<td>0</td>
<td>1.5</td>
<td>4.6</td>
</tr>
</tbody>
</table>

Conclusions: The Phoenix™NMIC-500 panel could provide alternative AST result to the reference method, except ciprofloxacin, especially in Enterobacteriaceae with low MICs. The detection of ESBL showed low sensitivity and CPO showed low specificity.

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Abstract 1142

Comparative variant analysis of *Aspergillus fumigatus* genomes for identification of novel mutations in candidate genes possibly be involved in mediation of azole resistance

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**Background:** Invasive pulmonary aspergillosis (IPA) is a life-threatening infectious disease in immunocompromised patients. In view of characterization of azole resistance whole genome sequencing (WGS) of *Aspergillus fumigatus* specimens was performed with the aim to identify novel genetic alterations leading to resistant phenotypes.

**Materials/methods:** In total, twenty-four *A. fumigatus* isolates from immunocompromised patients were investigated composed of 20 azole resistant and four susceptible samples. WGS was performed using the Illumina next generation sequencing (NGS) system. Results were mapped against the *A. fumigatus* AF293 genome followed by Burrows-Wheeler-Aligner (BWA) based sequence alignment. After variant calling by the use of GATK Haplotype caller, the annotation of variants was performed by implementation of SnpEff and programs based on annotation information provided by the *Aspergillus* genome database.

**Results:** Inspection of the small variant annotation revealed known mutations in the *cyp51A* gene for 11 out of the 20 resistant isolates. The TR46/Y121F/T289A variant was detected in five, the TR34/L98H alteration in two samples. With focus on further members of the ergosterol biosynthetic pathway, mutations in the genes *Hmg1* and *Erg6* were identified. Concerning *Hmg1*, two different mutations located in the sterol sensing domain were detected in two samples. In one sample a mutation in the HMG-CoA reductase domain was found. Three *Erg6* missense variants have been identified in five samples all negative for *cyp51A* mutations. Twenty-seven mutations have been found in the transmembrane transporter *abcA* gene, one missense mutation in the *mdr1* gene was detected in one sample. Missense mutations in the putative ABC multidrug transporter *sitT* have been found in 12 of the resistant strains.

**Conclusions:** Pending further validation in a larger cohort, on protein level and *in vivo*, the WGS of the genomes of azole resistant *A. fumigatus* strains identified several candidate genomic alterations that might pinpoint alternative pathways to acquisition of resistance, independent of the previously described *cyp51A* mutations. The discovery of previously undescribed resistance pathways in fungal strains might aid in identifying suitable biomarkers for effective clinical and epidemiological surveillance. The study was supported by a scientific grant from Gilead Sciences, Germany.

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Phylogenetic analysis of complete genomes reveals the circulation of multiple lineages of rabies lyssavirus in India
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Background: Rabies is fatal zoonotic encephalitis caused by viruses of the Lyssavirus genus, in the family Rhabdoviridae. About 60,000 people die of rabies world-wide every year; India accounts for almost a third of this global burden. Most studies on the phylogenetic analysis/molecular epidemiology of RABV reported from India are based on partial gene sequencing, with only a single report of a complete RABV genome. Further molecular epidemiological and phylogenetic analysis of full-length genomes provide more accurate and precise information compared to partial gene sequences. It is in this context that metagenomic sequencing of rabies infected human and canine brains was carried out by MinION Oxford Nanopore (ONT), Oxford, UK.

Materials/methods: Extracted RNA from post-mortem human brain tissues from confirmed cases of rabies infection (n = 5) and brain tissue from laboratory confirmed canine rabies cases (n = 9) were subjected to metagenomics by protocol supplied by ONT. Fast5 files generated by MinION sequencing were base called, demultiplexed, trimmed, filtered and aligned to human and canine reference genomes. Unaligned reads were analysed further using Geneious Prime software. Mapping based assembly was done with rabies sequences and consensus sequences were submitted to Genbank. Phylogenetic analysis was done with using the maximum likelihood method. Model selection and tree building were carried out using iqtree and visualized in Figtree software.

Results: Full length genome of RABV was obtained in three canine and one human sample. Phylogenetic analysis revealed that RABV sequences from canine samples belonged to the Arctic like lineages and that from human brain sample clustered into the Cosmopolitan lineage.

Conclusions: Phylogenetic analysis of RABV whole genome sequences revealed circulation of two different lineages of RABV in India. Therefore extensive molecular epidemiological survey using full genome sequences of ample number of samples would be useful to study the epidemiology and heterogeneity of circulating Rabies lyssavirus in India.

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Abstract 1152

Efficacy of ceftazidime-avibactam for multidrug-resistant Gram-negative bacteria infections: a retrospective evaluation in a Belgian teaching hospital

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Background: Ceftazidime/avibactam (CAZ/AVI) demonstrates in vitro activity against multidrug-resistant (MDR) Gram-negative bacteria, including KPC-producing Klebsiella pneumoniae (KPC-Kp) and extended-spectrum beta-lactamases (ESBL)-producing Enterobacteriaceae, but clinical data remain limited.

Materials/methods: We aimed to evaluate the CAZ/AVI use in our Belgian tertiary hospital, from December 2016 to October 2019. Patients with confirmed infections and local laboratory in vitro confirmed sensitive strains to CAZ/AVI (≤ 8mg/L) who received CAZ/AVI for ≥ 48h, either as intermittent infusion of 2,5g every 8 hours or as a 24-hour continuous infusion (CI), were included in our retrospective study. Dosage adjustments for renal impairment were taken into account as per manufacturer prescription. Each initiation of treatment was supervised by an infectious disease (ID) specialist.

Results: Thirty-three episodes of infections (EI) occurred in twenty-seven patients and were predominantly caused by KPC-Kp and Pseudomonas aeruginosa (62% and 23,5%, respectively) (Table 1). Complicated intra-abdominal infections (24%), ventilator-associated pneumonia and tracheobronchitis (30%) and complicated urinary tract infections (24%) were the most frequent sites of infection. Bacteremia occurred in 36% of cases. Sepsis and septic shock were present in 36 % and 9 % of cases, respectively. CAZ/AVI was initiated as a first antibiotic therapy in 14 EI (42%). Other antibiotics were prescribed in 58% of the remaining cases with a median duration of 5,5 days before initiation of CAZ/AVI. CAZ/AVI was used as monotherapy in 76 %. Clinical cure or improvement was achieved in 84 % and microbiological cure was observed in 69 % of EI respectively. Median duration of therapy was 11,5 days. Thirty days after the CAZ/AVI treatment onset, eight patients (30%) had died. Except for one patient, no death was directly attributed to infection. Emergence of CAZ/AVI resistance occurred in one patient but was deemed not clinically relevant. Interestingly, 10/33 EI (30%) were treated with CI and reached 70% and 86% of clinical and microbiological cure respectively.

Conclusions: In our cohort of difficult-to-treat infections due to multidrug-resistant Gram-negative bacteria with limited therapeutic options, CAZ/AVI was used predominantly as monotherapy, under ID supervision and allowed good clinical and microbiological outcome with relatively low short-term mortality including when administered as a CI.
### Abstracts 2020

**Table 1. Characteristics of the patients treated with CAZ/AVI**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n (%)</th>
<th>59 (54.5-69.5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean (SD))</td>
<td>61 (40.7)</td>
<td></td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>42 (36.4)</td>
<td></td>
</tr>
<tr>
<td>At the onset of infection (n = 33) (%)</td>
<td>12 (36.4)</td>
<td></td>
</tr>
<tr>
<td>- Sepsis</td>
<td>4 (12.1)</td>
<td></td>
</tr>
<tr>
<td>- Septic shock</td>
<td>3 (9.1)</td>
<td></td>
</tr>
<tr>
<td>- Bacteremia</td>
<td>12 (36.4)</td>
<td></td>
</tr>
<tr>
<td>- Fecal neutropenia</td>
<td>4 (12.1)</td>
<td></td>
</tr>
<tr>
<td>- Kidney</td>
<td>9 (27.3)</td>
<td></td>
</tr>
<tr>
<td>- Medical ICU</td>
<td>23 (69.7)</td>
<td></td>
</tr>
<tr>
<td>- VAP</td>
<td>10 (30.3)</td>
<td></td>
</tr>
<tr>
<td>Type of infection (n = 33)</td>
<td>23 (69.7)</td>
<td></td>
</tr>
<tr>
<td>- cIAI</td>
<td>8 (24.2)</td>
<td></td>
</tr>
<tr>
<td>- UTI</td>
<td>8 (24.2)</td>
<td></td>
</tr>
<tr>
<td>- VAP</td>
<td>8 (24.2)</td>
<td></td>
</tr>
<tr>
<td>- Bone and joint infection</td>
<td>3 (9.1)</td>
<td></td>
</tr>
<tr>
<td>- Bacteremia</td>
<td>2 (6.1)</td>
<td></td>
</tr>
<tr>
<td>- VAT</td>
<td>2 (6.1)</td>
<td></td>
</tr>
<tr>
<td>- Complicated skin and soft tissue infection</td>
<td>1 (3.0)</td>
<td></td>
</tr>
<tr>
<td>- Peritonitis</td>
<td>1 (3.0)</td>
<td></td>
</tr>
<tr>
<td>Type of organisms (n = 34)</td>
<td>8 (24.2)</td>
<td></td>
</tr>
<tr>
<td>- KPC-producing Klebsiella pneumoniae</td>
<td>1 (3.0)</td>
<td></td>
</tr>
<tr>
<td>- Pseudomonas aeruginosa</td>
<td>1 (3.0)</td>
<td></td>
</tr>
<tr>
<td>- ESBL-producing Klebsiella pneumoniae</td>
<td>3 (9.1)</td>
<td></td>
</tr>
<tr>
<td>- Enterobacter aerogenes</td>
<td>2 (6.1)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: CAZ/AVI, ceftazidime-avibactam; cUTI, complicated urinary tract infection; cIAI, complicated intra-abdominal infection; VAT, ventilator-associated pneumonia; VAP, ventilator-associated pneumonia; ICU, intensive care unit.

*Unless otherwise indicated, reference.*

*Including 4 patients with septic shock, 1 patient with distinct episode of infection and one patient with concomitant cIAI and ventilator-associated pneumonia due to the same pathogen.*

*All events defined as a recurrence of infection due to the same pathogen at the same site of infection within a period of time less than or equal to one month except for bone and joint infection when the period of time is less than or equal to 12 months.*

*For one patient, nosocomial pneumonia was due to concomitant ESBL-producing Enterobacter aerogenes and Pseudomonas aeruginosa, with both confirmed sensitive strains to CAZ/AVI.*

*For one patient, duration of therapy with tigecycline was unknown.*

*For one patient, duration of therapy with tigecycline was unknown.*

*No death was directly attributed to MDR infection in 7 patients; one patient died after seven days of therapy for a septicemia pneumonia which was considered severe but not due to other underlying diseases, six patients died of multiple reasons a few days after the end of therapy.*

*Partially under controlled MDR infection cannot be ruled out as a cause of death in a single patient.*

### Table 2. CAZ/AVI treatment results.

<table>
<thead>
<tr>
<th>Antibiotic regimen prior to CAZ/AVI (n = 33)</th>
<th>4 (12.1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Meropenem</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>- Meropenem plus tigecycline</td>
<td>2 (6.1)</td>
</tr>
<tr>
<td>- Piperacillin tazobactam</td>
<td>2 (6.1)</td>
</tr>
<tr>
<td>- Tigecycline</td>
<td>2 (6.1)</td>
</tr>
<tr>
<td>- Amikacin plus meropenem</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>- Ceftriaxone</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>- Ciprofloxacin followed by meropenem</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>- Gentamicin plus ceftazidime</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>- Teicoplanin</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>- Teicoplanin plus tigecycline (plus gentamicin in loco)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>- None</td>
<td>14 (42.4)</td>
</tr>
</tbody>
</table>

**Duration of therapy before CAZ/AVI, days, median (IQR)**

- All infections (n = 32)*
  - 1 (0-5.5)
- Infections with antibiotic regimen prior to CAZ/AVI (n = 18)
  - 5.5 (2.5-12.75)

**Use of CAZ/AVI**

- Empirical therapy
  - 11 (33.3)
- Documented therapy
  - 22 (66.7)
- Microtherapy
  - 25 (75.7)
- Combination therapy
  - 8 (24.2)
- Continuous infusion
  - 10 (30.3)

**Duration of CAZ/AVI, days, median (IQR)**

- All infections (n = 33)
  - 10 (5-14)
- Infections with definite therapy with CAZ/AVI (n = 28)*
  - 11.5 (7.5-15.5)

**Outcomes**

<table>
<thead>
<tr>
<th>Clinical response (n = 32)*</th>
<th>18 (56.3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Cured</td>
<td>9 (28.1)</td>
</tr>
<tr>
<td>- Improved</td>
<td>4 (12.5)</td>
</tr>
<tr>
<td>- Relapsed</td>
<td>1 (3.1)</td>
</tr>
<tr>
<td>- Failed</td>
<td>22 (68.7)</td>
</tr>
<tr>
<td>- 30-day mortality: after the onset of CAZ/AVI treatment (n = 27)</td>
<td>8 (29.6)</td>
</tr>
</tbody>
</table>

Presenter email address: f.frippiat@chuliege.be
Continuous infusion and outpatient parenteral antimicrobial therapy with ceftazidime-avibactam: evaluation of efficacy based on therapeutic drug monitoring

Veronique Goncette, Nathalie Layios, Frederic Frippiat

1University Hospital of Liège, Liège, Belgium

Background: Based on recent PK/PD evidence, continuous infusion (CI) of beta-lactam administration is increasingly recommended for serious infections. Since 2016, the combination of ceftazidime and avibactam (CAZ/AVI) is administered per manufacturer prescription as an intermittent infusion of 2.5g every 8 hours thus CI has not yet been evaluated in clinical trials.

Materials/methods: We aimed to evaluate the use of CI of CAZ/AVI in a retrospective case series, from December 2016 to October 2019. All isolates displayed in vitro susceptibility to CAZ/AVI in agreement with EUCAST breakpoint. Patients were initially given CAZ/AVI as CI of 5g q12h. CAZ/AVI dosages were adjusted according to therapeutic drug monitoring (TDM) of ceftazidime with a therapeutic goal of 4-5xT>MIC in the plasma and/or at the site of infection. The latter was extrapolated from plasma concentrations and literature data.

Results: CAZ/AVI was administered as CI in ten of thirty-three infectious episodes in twenty-seven patients treated with CAZ/AVI in our hospital. These infections were mainly caused by Pseudomonas aeruginosa (54.5%). Bacteremia occurred in 30% of cases and septic shock was only present in one patient. CAZ/AVI was used as monotherapy in 60% of cases. Clinical cure or improvement was achieved in 70% of cases and microbiological cure was achieved in 6/7 (86%) evaluable cases (Table 1). Thirty days after the CAZ/AVI treatment onset, two patients (20%) had died, with death possibly related to uncontrolled infection in one case. Three patients were discharged home with an outpatient parenteral antimicrobial therapy (OPAT). Based on repeated TDM (3.5 samples/patient), therapeutic goals were achieved in 100% of cases in plasma and 88% of cases at the site of infection (8/10 evaluable). CAZ/AVI looked stable for 12-hour infusions and no drug-related adverse events were noted.

Conclusions: Although the sample size was limited, our case series shows promising clinical results for CI of CAZ/AVI, including for OPAT. Based on repeated TDM, therapeutic goals were achieved in 100% of cases in plasma. CAZ/AVI looked stable for 12-hour infusions and no drug-related adverse events were noted.

Table 1 - Ceftazidime-avibactam administered as continuous infusion

<table>
<thead>
<tr>
<th>Patient</th>
<th>Type of infection</th>
<th>Type of organism</th>
<th>CAZ/AVI MIC (mg/L)</th>
<th>Daily dose of CAZ/AVI (g)</th>
<th>Therapeutic goals (4.5xT&gt;MIC (mg/L)</th>
<th>TEM of ceftazidime, mean (mg/L)</th>
<th>Sample of ceftazidime TDM (patient)</th>
<th>Duration of CAZ/AVI as CI (days)</th>
<th>OPAT</th>
<th>Clinical response</th>
<th>Microbiological response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bone and joint infection</td>
<td>KPC-producing Klebsiella pneumoniae</td>
<td>2</td>
<td>10</td>
<td>8 - 10</td>
<td>24 - 30</td>
<td>35,1</td>
<td>5</td>
<td>25</td>
<td>Yes</td>
<td>Cured</td>
</tr>
<tr>
<td>2</td>
<td>cUTI and bacteremia</td>
<td>KPC-producing Klebsiella pneumoniae</td>
<td>8</td>
<td>7.5</td>
<td>18 days</td>
<td>32 - 40</td>
<td>47.6 (7.5g daily)</td>
<td>44.6 (9g daily)</td>
<td>4</td>
<td>23</td>
<td>Yes</td>
</tr>
<tr>
<td>3</td>
<td>VAP</td>
<td>Pseudomonas aeruginosa</td>
<td>8</td>
<td>10</td>
<td>32 - 40</td>
<td>96 - 120</td>
<td>84,3</td>
<td>5</td>
<td>24</td>
<td>No</td>
<td>Improved</td>
</tr>
<tr>
<td>4</td>
<td>VAT</td>
<td>Pseudomonas aeruginosa</td>
<td>8</td>
<td>5</td>
<td>32 - 40</td>
<td>NA</td>
<td>62,0</td>
<td>2</td>
<td>5</td>
<td>No</td>
<td>Cured</td>
</tr>
<tr>
<td>5</td>
<td>VAT</td>
<td>Pseudomonas aeruginosa</td>
<td>0.5</td>
<td>10</td>
<td>2 - 2.5</td>
<td>NA</td>
<td>124,0</td>
<td>1</td>
<td>3</td>
<td>No</td>
<td>Improved</td>
</tr>
<tr>
<td>6</td>
<td>cIAI</td>
<td>Enterobacter aerogenes</td>
<td>6</td>
<td>5</td>
<td>24 - 30</td>
<td>48 - 60</td>
<td>&gt;80</td>
<td>2</td>
<td>7</td>
<td>No</td>
<td>Relapse</td>
</tr>
<tr>
<td>7</td>
<td>VAP</td>
<td>ESBL-producing Klebsiella pneumoniae</td>
<td>10</td>
<td>8 - 10</td>
<td>24 - 30</td>
<td>76,2</td>
<td>2</td>
<td>7</td>
<td>No</td>
<td>Cured</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>cUTI</td>
<td>ESBL-producing Klebsiella pneumoniae</td>
<td>0.25</td>
<td>5</td>
<td>1 - 1.25</td>
<td>7 - 8.75</td>
<td>17,6</td>
<td>7</td>
<td>37</td>
<td>Yes</td>
<td>Cured</td>
</tr>
<tr>
<td>9</td>
<td>prosthesis joint infection and bacteremia</td>
<td>Pseudomonas aeruginosa</td>
<td>4</td>
<td>7.5</td>
<td>16 - 20</td>
<td>48 - 60</td>
<td>56,7</td>
<td>4</td>
<td>12</td>
<td>No</td>
<td>Failure</td>
</tr>
<tr>
<td>10</td>
<td>cIAI</td>
<td>Pseudomonas aeruginosa</td>
<td>2</td>
<td>10</td>
<td>8 - 10</td>
<td>16 - 20</td>
<td>67,4</td>
<td>3</td>
<td>12</td>
<td>No</td>
<td>Relapse</td>
</tr>
</tbody>
</table>

Abbreviations: CAZ/AVI, ceftazidime-avibactam; MIC, minimum inhibitory concentration; TDM, therapeutic drug monitoring; CI, continuous infusion; OPAT, outpatient parenteral antimicrobial therapy; cUTI, complicated urinary tract infection; cIAI, complicated intra-abdominal infection; VAT, ventilator-associated pneumonia; VAT, ventilator-associated tracheobronchitis; ESBL, extended-spectrum beta-lactamase; NA, not applicable; NE, not evaluable.

Presenter email address: f.frippiat@chuliege.be
Transmission dynamics of multidrug-resistant Escherichia coli sequence type 131 in the community

Yin Mo1,2,3,4, Matthew Moore2, Kithalakshmi Vignesvaran3, Wesley Yeung1, Siyu Peng1, Enying Tan1, Melissa Chua4, Lingyue Zhou1, Ivan Seah1, Paul Tambyah1,4

1National University Hospital, Singapore, Singapore, 2University of Oxford, Nuffield Department of Medicine, Oxford, United Kingdom, 3Mahidol Oxford Tropical Medicine Research Unit, Bangkok, Thailand, 4National University of Singapore, Singapore, Singapore

Background: E. coli sequence type (ST) 131 is a predominant cause of community-onset extended-spectrum beta-lactamase-producing Enterobacteriaceae bloodstream infections globally.

Materials/methods: We performed a prospective study from February 2017 to November 2018 to investigate E. coli ST131 transmission dynamics in Singaporean households. We enrolled hospitalized patients with E. coli infections and screened their clinical isolates with qPCR. Families of index participants with E. coli ST131 infections and non-ST131 infections were further consented for a household transmission study. We modelled the transmission dynamics using a multistate model.

Results: One-hundred and thirty participants were enrolled. They contributed 635 stool samples at 2- to 6- week intervals, 200 food and environmental samples. The specimens yielded 6571 isolates (up to 12 E. coli isolates per sample), 7.9% (516/6571) of which were tested positive for E. coli ST131 via qPCR. All but two ST131 positive samples were human stools [one raw chicken and one toilet swab]. During the year of follow-up, 52% (67/130) participants carried E. coli ST131 on at least once occasion and 85% (29/34) of families had at least one family member carrying ST131. The estimated probability for any individual to become colonized with E. coli ST131 in one year was 81% (95% CI 76-85%). The estimated duration of carriage in individuals is 68 days per year. Carriage of E. coli ST131 was strongly associated with the presence of a high-density carrier in the same family [an individual with any stool sample containing ST131 in >20% of all E. coli isolates]. Comorbidities and prior hospital admissions were not associated with carriage. Index patients infected with ST131 had significantly longer mean duration of carriage [137 days vs 21 days] and at higher densities [20% vs 6%] compared to those infected with non-ST131 E. coli. Whole genome sequencing of the ST131 isolates suggest high within-host diversity with multiple lineages of ST131 and repeated acquisition/ decolonization episodes within host across time points and between family members.

Conclusions: There is a high prevalence of E. coli ST131 in the Singapore community where transmission is largely through human-to-human contact particularly in families with high density carriers as ‘reservoirs’.

Presenter email address: moyin@tropmedres.ac
Abstract 1160

**Streptococcal and Staphylococcus aureus prosthetic joint infections: are they really different?**

Yousra Kherabi*, Valérie Zeller¹, Y. Kerroumi¹, Vanina Meyssonnier¹, Beate Heym¹, Olivier Lidove¹, Simon Marmor¹

¹Hopital de la Croix Saint-Simon, Paris, France

**Background:** Streptococci are the second most frequent bacteria isolated in prosthetic joint infections (P JIs) after staphylococci. Only few studies, including a small number of patients, compared streptococcal and staphylococcal P JIs. The objective of our study was to compare characteristics and outcomes of streptococcal and methicillin-susceptible *S. aureus* (MSSA) P JIs.

**Materials/methods:** Monocentric cohort study including all monomicrobial streptococcal and MSSA prosthetic knee (KP JIs) and hip (HP JIs) infections managed in our reference center from 01/2010 to 07/2017. We compared epidemiological data of the population, PJI type and outcome according to the medico-surgical strategy. The following events were noted: reinfection including relapse with the same and new infection with different bacteria, PJI-related and non-related death. Patients were followed for at least 2 years.

**Results:** Two hundred twenty-three P JIs, 91 streptococcal and 132 MSSA, developing on 92 knees and 131 hips, in 209 patients, were included. Comparison between the 2 groups (streptococci vs MSSA) showed that streptococcal PJI patients were older (77 vs 74 years, p=0.031), had more frequently cancer (10% vs 2%, p=0.016) and developed more frequently hematogenous acquired P JIs (88% vs 48%, p=0.0001). Surgical strategies did not differ between groups: debridement and implant retention (DAIR) (17/91 vs 29/132, p=NS), exchange arthroplasty (50/91 vs 84/132, p=NS).

At 2 years, all medico-surgical strategies taken together, reinfection rates were higher in the MSSA group (figure). Reinfection rates after DAIR (n=44) were higher in the MSSA group (2/15 vs 13/29, p=0.032), but not different after exchange arthroplasty (n=129) (5/50 vs 6/79, p=NS). Prolonged suppressive antibiotic therapy (n=33) was more commonly used in the streptococcal group (21/86 vs 12/123, p=0.002). Relapses were higher in the MSSA group (1/21 vs 4/13, p= 0.004).

**Conclusions:** Streptococcal compared to MSSA P JIs showed different characteristics and outcomes. Patients were older, had more frequently cancer, and PJI spread more frequently via the hematogenous way. Outcome after DAIR or suppressive antibiotic therapy was better, but no difference was observed after prosthesis exchange.

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ESBL-producing Escherichia coli causing community-onset bloodstream infection and the association of bacterial clones and virulence genes with septic shock

Inga Fröding*1,2, Badrul Hasan1, Isak Sylvin1, Pontus Naucler4,5, Christian Giske1,2

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Background: Bloodstream infections (BSI) due to extended-spectrum β-lactamase-producing Escherichia coli (ESBL-EC) are an important cause of morbidity and mortality. The relative influence of host immunocompetence versus microbiological virulence factors (VF) in the acquisition and outcome of BSI is poorly understood.

Materials/methods: Whole genome sequencing was used on 278 blood culture isolates of ESBL-EC from 260 patients with community-onset infection collected during 2012-2015 in Stockholm, Sweden. Patient data was collected from medical records. The association of 108 virulence genes (26 operons), sequence types and antimicrobial resistance (ResFinder v2.1) to severity of disease and source of infection was assessed with multivariable logistic regression. SNP-phylograms were obtained with Enterobase.

Results: Results are shown in Figure 1. The fluoroquinolone-resistant high-risk clone ST131 subclade C2 comprised 30% and the emerging clone ST1193, 2%. Risk factors remaining in the final multivariable model for association with septic shock/short-term mortality had the following odds ratios (95% confidence intervals) and p-values: patient history of hematologic cancer/transplantation: 10.8 (95%CI 3.2-36.6), p<0.001, reduced daily living activity: 3.8 (1.4-9.9), p=0.007, infection source urinary tract infection (UTI)/prostate biopsy: 0.3 (0.1-0.9) p=0.026, presence of the E. coli VF iss (increased serum survival) 5.5 (1.3-22.8), p=0.019, multidrug-resistance 0.3 (0.1-0.9), p=0.019 and pap 0.2 (0.1-0.6), p=0.004. Adhesins, particularly pap, were associated with UTI-derived BSI, while isolates from post-prostate biopsy BSI had low overall virulence, low adhesin occurrence and commonly belonged to ST131 subclade C1, ST131 subclade A/B, ST1193 and ST648. ST131 was associated with recurrent episodes and repeated isolates from the same patient were often closely related.

Conclusions: ST131 subclade C2 was the dominating clone in community-onset ESBL-EC BSI in Stockholm. Detection of iss in the E. coli-isolate was associated with septic shock in immunocompetent patients and ISS could be a potential target for anti-virulence treatment.
Figure 1. Maximum likelihood SNP-phylograms with data on patient history, outcome, virulence operons, phenotypic AST and resistance genes. Reference genome EC958 was used for SNP-mapping. The tree scale is number of substitutions per site. Patient isolates and reference genomes shown A) ST131 (n=121) B) Other STs (n=139). SNP: Single nucleotide polymorphism. AST: Antimicrobial susceptibility testing. Cx: Clonal complex.

Presenter email address: inga.froding@sll.se
Abstract 1164

Persistent human papilloma virus type 16 infections in an established cohort of Slovenian women

Tina Triglav*, Lea Hošnjak1, Anja Oštrbenk1, Mario Poljak1

1University of Ljubljana, Faculty of Medicine, Institute of Microbiology and Immunology, Ljubljana, Slovenia

Background: Human papillomavirus (HPV) variants are associated with viral persistence and development of cervical cancer. The objective of our study was to determine and evaluate viral variants in paired HPV16-positive cervical smear samples, obtained at two sampling points (initial and after three years) from women aged 20-64, who were included in the previously described cohort of Slovenian women, attending the routine organized cervical cancer screening program.

Materials/methods: The presence of high-risk HPV infections in baseline and follow-up cervical samples was evaluated using the RealTime High Risk HPV test (Abbott, Wiesbaden, Germany), which allows concurrent partial genotyping for HPV16 and HPV18. In paired samples of women, in whom the presence of HPV16 was found in both samples, the complete long control genomic region (LCR) was amplified using the previously described conventional in-house PCR with g16f-7122/g16r-913 primers, and subsequently Sanger sequenced on the ABI3500 Genetic Analyzer (Thermo Fischer Scientific, Waltham, MA, USA). The obtained nucleotide sequences were edited and compared to HPV16 reference isolates using the Vector NTI Advance v11 software (Invitrogen, Carlsbad, CA) and phylogenetic relationships were inferred from the maximum likelihood tree, obtained based on the MAFFT alignment of eligible nucleotide sequences.

Results: At baseline, 160/4,432 (3.6%) women were HPV16 DNA positive. Of these 160 samples, 104 follow-up samples were available, of which 36 (34.6%) were HPV16-positive. Due to degradation of extracted DNA, further three samples were excluded from subsequent analyses. In available 33 paired cervical samples, identical HPV16 LCR viral variants were identified, suggesting the presence of persistent HPV16 infections. Using phylogenetic analyses, all HPV16 viral variants, obtained from samples of Slovenian women, clustered to the European HPV16 lineage (A).

Conclusions: Identical HPV16 LCR viral variants were found in all 33 paired cervical smears and all identified viral variants clustered to the European HPV16 lineage (A), confirming a significant burden of persistent HPV16 infections in our cohort of Slovenian women.

Presenter email address: tina.triglav@mf.uni-lj.si
**Abstract 1166**

**Comparison of the Accelerate Pheno rapid diagnostic system with standard of care for diagnosing Gram-negative bloodstream infections: bacterial identification, antimicrobial sensitivity and turnaround time**

Luke Blagdon Snell*¹², Jasper Vink¹², Lyndsay Rowley³, Tinuke Awokiyesi⁴, Andrew Taylor⁵, Robert Rusek⁴, Dakshika Jeyaratnam⁴, Simon Goldenberg¹²

¹Dept of Infection, Guy’s and St Thomas’ NHS Foundation Trust, London, United Kingdom, ²Centre for Clinical Infection & Diagnostics Research, King’s College London, London, United Kingdom, ³Viapath, London, United Kingdom, ⁴Department of Microbiology, King’s College Hospital NHS Foundation Trust, London, United Kingdom, ⁵Department of Medical Microbiology, St George’s Hospital, London, United Kingdom

**Abstract third-party references:** Accelerate Diagnostics Inc., AZ, USA

**Background:** The Accelerate Pheno system (AXDX) is a diagnostic assay providing rapid identification (ID) of bacteria and yeast from blood cultures, as well as phenotypic antimicrobial susceptibility testing (AST). This multicentre study evaluated the accuracy and rapidity of AXDX in characterising Gram-negative bloodstream infections (BSI) in comparison with standard of care (SOC).

**Materials/methods:** Positive blood cultures with Gram-negative bacteria from three hospital sites were processed in parallel using AXDX and SOC (MALDI-TOF for identification, VITEK2 for AST). ID discrepancies between AXDX and SOC were classified as either false positive or false negative. Categorical agreement (CA) occurred when AXDX and SOC had the same interpretation of susceptibility of the isolate/antibiotic combination. ‘Very major errors’ (VME) occur when AXDX reported susceptibility but SOC resistance. Multidrug-resistant organisms of interest (MOI) are those resistant to co-amoxiclav and gentamicin. Time difference to AST between AXDX and SOC was calculated for these MOI if patients were on inactive therapy as identified on chart review.

**Results:** 148 blood cultures were included. Of these, 141/148 (95.2%) had valid, reportable results on AXDX. 148 organisms were identified. 133/148 organisms were ‘on-panel’ Gram-negatives. AXDX identified 126/133 organisms correctly (sensitivity 93.3%). 1,128 Gram-negative probes were deployed with 4 false positive results giving a specificity of 1124/1128 (99.6%). From AST, CA was 94.9% (1,270/1,338). There were only 4 VME out of 262 resistant AST results. Turnaround time (TAT) for both ID and AST were calculated for AXDX and SOC. Timing data was available for 111/141 (78%) of blood cultures. Compared with SOC, AXDX gave an average reduction in ID TAT of 16.8 hours ([CI 15.1-18.4 hours, p<0.0001]) and an average reduction in AST TAT of 31.2 hours ([CI 29.9-32.5hrs, p<0.0001]).

There were 15 MOI. 9 of these patients were on inactive therapy, for whom AXDX gave an average time saving to AST results of 12hrs 04min.

**Conclusions:** AXDX provides accurate ID and AST for Gram-negative BSI, and has a significantly improved TAT that may optimise antimicrobial therapy.
Figure: Box plot of TAT for ID and AST from time of blood culture positivity (AXDX vs SOC)

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Abstract 1171

Rapid identification of pathogens, antibiotic resistance genes and plasmids in blood cultures by nanopore sequencing

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Background: Bloodstream infections (BSIs) and sepsis are major causes of morbidity and mortality worldwide. Blood-culture-based diagnostics usually requires 1-2 days for identification of bacterial agent and an additional 2-3 days for phenotypic determination of antibiotic susceptibility pattern. With the escalating burden of antimicrobial resistance (AMR) rapid diagnostics becomes increasingly important to secure adequate antibiotic therapy. Whole genome sequencing approaches offer a way to reduce clinical test turnaround times compared to conventional culture-based methods.

Materials/methods: We spiked eight blood cultures with blaCTX-M positive Escherichia coli and Klebsiella pneumoniae, mecA positive Staphylococcus aureus, or a combination of these, and incubated them until they were flagged as positive. We measured the DNA concentrations and extracted bacterial DNA for sequencing with nanopore. For real-time analyses we used (a) What’s In My Pot, Centrifuge and BLAST against the NCBI Prokaryotic RefSeq for identification of bacterial species; (b) BLAST search against CARD and ResFinder databases for identification of resistance genes; and (c) PlasmidFinder and BLAST searches against plasmid database for identification of plasmids. We verified our results through whole genome sequencing with short-read Illumina sequencing and hybrid assembly using nanopore and Illumina sequences.

Results: Identification of pathogens was possible after 10 minutes of real-time sequencing, and all predefined AMR-encoding genes and plasmids from the different culture experiments were detected within one hour. Furthermore, we demonstrate correct identification of plasmids and blaCTX-M subtypes using de novo assembled nanopore contigs. This proof-of-concept study represents a molecular approach to diagnosis of BSIs which can provide clinicians with detailed information on etiologic agent and AMR within four hours of a blood culture becoming positive. To our knowledge this is the first study applying nanopore sequencing to blood cultures for a rapid and comprehensive analysis of pathogens, plasmids and AMR-encoding genes.

Conclusions: We have shown that with a sequence-based approach to diagnostics it is possible to identify pathogens and specific AMR-encoding genes using raw nanopore sequencing data, obtained within four hours after a blood culture is flagged as positive by the incubation system. Results from this study hold great promise for future applications in clinical microbiology and for healthcare surveillance purposes.

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Influenza vaccine effectiveness against laboratory-confirmed influenza in Europe: results from DRIVE network 2018/19

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Abstract third-party references: Funding: Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 777363. This Joint Undertaking receives support from the European Union’s Horizon 2020 research and innovation programme and EFPIA.

Background: DRIVE (Development of Robust and Innovative Vaccine Effectiveness) aims to establish a public-private platform to annually estimate brand-specific influenza vaccine effectiveness (IVE), in accordance with revised EMA guidance on influenza vaccines. IVE analyses and interpretation are conducted by public partners in the consortium.

Materials/methods: In 2018/19, four test-negative design (TND) studies in primary care (Austria, Italy, England), five TND studies in hospitals (Finland, Italy, Romania, Spain), and one register-based cohort study (Finland) were conducted. Case definitions were ILI, SARI and laboratory-confirmed influenza (LCI), respectively. Site-specific IVE estimates were centrally calculated and pooled through meta-analysis. Data cut-off was the end of influenza circulation at the study site level, or April 30, whichever occurred first.

Results: For the TND studies, 1897 LCI cases and 2570 controls from primary care and 1444 LCI cases and 3440 controls from hospitals were retained for analysis. Confounder-adjusted pooled IVE estimates against LCI for any vaccine were 48% (95%CI 0-78) and 38% (-65-81) in those <17 years (y) in primary care and hospital respectively, 45% (18-63) and 40% (2-63) in those 18-64y, and 18% (-85-71) and 27% (6-44) in those ≥65y. Sample size was still insufficient for reliable brand-specific estimates.

The register-based cohort study included 274,079 vaccinated person-years and 494,337 unvaccinated person-years, obtaining brand-specific IVE. Confounder-adjusted IVE estimates against LCI A, from out- and inpatients combined, were 36% (24-45) for Fluenz Tetra and 54% (47-62) for Vaxigrip Tetra in those <7y and 30% (25-36) for Vaxigrip Tetra in those ≥65y.

Conclusions: DRIVE is a growing new platform, that will expand to thirteen TND sites in 2019/20 and 2 register-based cohort sites. Sample size in future seasons is expected to increase, enabling the calculation of more brand-specific IVE estimates.

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Background: Vancomycin-resistant enterococci (VRE) are a major cause of nosocomial infections for which a only a few treatment options, like linezolid, remain. Linezolid-resistant enterococci (LRE) are still rare but require strict surveillance to identify emerging resistance mechanisms and clones. Linezolid resistance can result from mutational mechanisms [23S rRNA and/or ribosomal protein mutations] or resistance gene acquisition (cfr, cfr(B), optrA and poxT genes). The aim of this study was to investigate the mechanisms of linezolid resistance in Belgian LRE.

Materials/methods: Enterococci (n=2,836), including 2087 VRE, were submitted voluntarily to the Belgian Reference Centre for enterococci between 2013 and 2019. Susceptibility to linezolid was determined by MIC gradient testing according to EUCAST. Conventional PCR was applied for detection of cfr and optrA. WGS was performed on cfr/optrA negative LRE strains using Nextera XT (2 x250bp), MiSeq (Illumina Inc.). Spades v3.10 was used for genome assembly and LRE-finder 1.0 for detection of linezolid resistance mutations or genes. Susceptibility to tigecycline and daptomycin was tested by MIC gradient test for LRE that were also resistant to vancomycin (LVRE).

Results: 38 strains (31 clinical and 7 screening isolates) were identified as LRE (29 E. faecalis and 9 E. faecium) with linezolid MIC levels between 8 and 64 µg/ml (median 16µg/ml). 28/29 E. faecalis LRE were positive for optrA and 5/8 E. faecium LRE carried the G2576T 23S rRNA mutation (Table 1). cfr positive strains were not detected. Of the 8 LVRE (6 vanA and 2 vanB E. faecium strains), 2 were tigecycline resistant (MIC 0.5 µg/ml) and none were daptomycin resistant.

Conclusions: The majority of Belgian LRE are E. faecalis, in contrast to other countries where E. faecium LRE predominate. The linezolid resistance mechanisms in E. faecium LRE consisted of both chromosomal mutations and gene acquisition while E. faecalis LRE contained only transferable resistance determinants, predominantly optrA, which corroborates earlier findings on emerging optrA-mediated resistance.

Table 1. Characteristics Belgian LRE

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<th>E. faecalis (n=29)</th>
<th>E. faecium (n=9)</th>
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<td>optrA</td>
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<td>2</td>
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<tr>
<td>poxtA</td>
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<tr>
<td>G2576T mutation</td>
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<td>cfr(B) and G2576T-mutation</td>
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Abstract 1178

A global point prevalence study of antimicrobial use in the neonatal intensive care unit: the NO-More-AntibioticS and Resistance study (NO-MAS-R)

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Abstract third-party references: On behalf of the NO-MAS-R Study Group, Nationwide Children’s Hospital, The Ohio State University, Merck & Co. Inc

Background: Antimicrobial agents are the most prescribed medications in the NICU. Global assessment of all antimicrobial use provided to infants in the NICU and reasons for their use may inform future antimicrobial stewardship efforts.

Materials/methods: We conducted a prospective one-day (7/1/2019) global NICU point prevalence study of all antimicrobial use and obtained the following: NICU level, census, birth weight, gestational/postnatal age, diagnoses, culture results, antimicrobial therapy (reason for use; duration of therapy), antimicrobial stewardship program (ASP), and 30-day in-hospital mortality.

Results: 528 (27%; range, 0 to 100%) of 1927 infants in 71 NICUs (67, Level 3/4) from 26 countries (1, low; 12, middle; 13, high income; 5 continents) received at least one antimicrobial agent (91%, antibacterial; 19%, antifungal; 4%, antiviral). Of the 483 infants on antibiotics at a median postnatal age of 12 days (IQR, 4-33), their mean gestational age and birth weight were 32.6 ± 6 weeks and 1980 ±1017 grams, respectively. The most common reasons for receiving antibiotic therapy were rule-out sepsis (26%), “culture-negative” sepsis (16%), prophylaxis (15%), culture-positive infection (15%), and pneumonia (13%). The most frequently used antibiotics were ampicillin (40%), gentamicin (35%), amikacin (21%), vancomycin (15%), and meropenem (10%). For definitive treatment of presumed/confirmed infection, vancomycin (15%), amikacin (13%), and meropenem (10%) were the most prescribed agents. Planned duration of therapy was shorter (3 or 7 days) than actual treatment duration (7 to 14 days). Specifically, duration of antibiotic treatment for “culture-negative sepsis” was 7 days (IQR, 5-10 days) and for culture-positive sepsis was 11 days (IQR, 10-14 days; p-value=0.07). Mortality was 4.7%. 63% of the hospitals had an ASP, but among the 55% that had a NICU-specific ASP, antibiotic utilization rate was significantly lower than among those centers without an NICU-ASP (21% vs. 33%; p<0.01).

Conclusions: Ascertainment of overall antimicrobial use among NICU infants showed marked variability by NICU and country, with a single day prevalence of 27%. The majority of antibiotic use was in infants without a culture-confirmed infection. Duration of therapy was prolonged in most instances, and NICU-specific ASPs were associated with lower antibiotic utilization rates, suggesting the need for their implementation worldwide.

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Abstract 1179

Non-lethal concentrations of ceftazidime and ceftazidime-avibactam select for multiple-resistant genotypes

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Background: Drug concentrations below the minimum inhibitory concentration (sub-MIC) resulting from environmental pollution or found in body compartments during therapy can select for antibiotic resistance. OXA-48, unlike other carbapenemases, exhibits negligible hydrolysis towards the cephalosporin ceftazidime (CAZ). Consequently, CAZ and the combination ceftazidime-avibactam (CAZ-AVI) are possible treatment options for infections caused by OXA-48-producers. Here, we show that exposure to sub-MIC concentrations of CAZ and CAZ-AVI selects for clinical resistance and variants of OXA-48.

Materials/methods: E. coli MG1655, harbouring a clinical blaOXA-48-carrying plasmid, was evolved (n=3) for 300 generations in the absence and presence of sub-MIC (0.25xMIC) concentrations of CAZ and CAZ-AVI. At every 50th generation, we determined the proportion of clones exhibiting lower susceptibility towards CAZ/CAZ-AVI and their MICs (broth microdilution). The allele frequencies of blaOXA-48 were identified at 50 and 300 generations using Sanger sequencing.

Results: Sub-MIC evolution using CAZ and CAZ-AVI selected for clones with decreased susceptibility already after 50 generations. No such clones were detectable without selective pressure during the whole evolution experiment, revealing at least a 10,000-fold difference in clones with reduced susceptibility between treatments. We determined the MICs of 50 clones every 50th generation. For CAZ, we found that at all times more than 50% of the tested clones (n=900) exhibited MICs above the clinical breakpoint, but did not show cross-resistance towards CAZ-AVI. For CAZ-AVI, one out of three populations displayed clones (n=18) at 50 generations with an up to 16-fold increase in the CAZ-AVI MICs. Sequencing of blaOXA-48 showed that resistance development towards CAZ-AVI was not due to mutations in blaOXA-48. However, all populations evolved in the presence of CAZ carried clones expressing variants of OXA-48. In total, we identified seven different alleles of blaOXA-48 over the course of the experiment.

Conclusions: Non-lethal concentrations of CAZ and CAZ-AVI select for clinical resistance in E. coli. While the exposure to CAZ-AVI did not select for variants of OXA-48, seven mutants of OXA-48 were identified during the evolution with CAZ. Worryingly, two of the mutants have been described in environmental samples, underlining the importance of antibiotic pollution as a contributor to resistance development.

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Costs and benefits of OXA-48 variants selected under sub-lethal concentrations of ceftazidime

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Background: OXA-48 hydrolyses the 3rd generation cephalosporin ceftazidime (CAZ) inefficiently. Therefore CAZ is a relevant treatment alternative against infections caused by OXA-48-producing Enterobacterales. Antibiotic concentrations below the minimum inhibitory concentration (sub-MIC) can select for high-level resistance. Indeed, we previously found seven different variants of OXA-48 while evolving blaOXA-48-encoding E. coli at sub-MIC levels of CAZ. These displayed single amino acid substitutions within the active site of OXA-48. Here, we characterise these mutants and show that their expression is beneficial, increasing MIC and bacterial fitness due to enhanced hydrolysis activity.

Materials/methods: blaOXA-48 alleles (wild-type and mutants) were sub-cloned into a pCR-blunt II vector, expressed in E. coli TOP10 and subsequently subjected to MIC testing (broth microdilution). All alleles were expressed from a pDest17 vector in E. coli AI for protein isolation and purification using His-trap columns. Purified enzymes were used to determine the catalytic efficiencies (kcat/KM) and thermostabilities. E. coli MG1655 carrying a pACYC184 vector encoding the blaOXA-48 alleles was used in head-to-head competitions against the wild-type allele at sub-MIC concentrations of CAZ to measure fitness.

Results: Expression of mutant blaOXA-48 alleles decreased CAZ susceptibility by 2 to 32-fold, compared to E. coli carrying wild-type blaOXA-48. However, they displayed significantly increased susceptibilities towards carbapenems and penicillins with MICs decreased up to 32-fold. While the catalytic efficiencies of OXA-48 mutants increased by 2 to 44-fold towards CAZ, activity towards imipenem, meropenem and piperacillin decreased significantly. Additionally, all mutants exhibited thermostabilities 4°C to 8°C lower than wild-type OXA-48. While the expression of the OXA-48 variants did not negatively affect fitness in the absence of drug, at sub-MIC concentrations of CAZ (0.25xMIC wild-type OXA-48) all tested mutants displayed an up to 60% increase in relative fitness.

Conclusions: OXA-48 mutants selected under sub-lethal conditions of CAZ exhibited increased MICs and/or catalytic efficiencies towards CAZ. Resistance development imposed functional trade-offs towards other β-lactams, likely due to increased enzyme flexibility. We found these alleles to be beneficial under sub-MIC conditions, and some have been already described in environmental samples, supporting the idea that β-lactam contamination may facilitate the selection of resistance.

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Abstracts 2020

Abstract 1184

Does C Diff Quik Chek display the same sensitivity than C Diff Quik Chek Complete for GDH detection?
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Background: One option for the diagnosis of C. difficile infection is to use an EIA (enzyme immunoassay) for GDH detection (glutamate dehydrogenase) (C Diff Quik Chek (Abbott)) followed, if positive, by an EIA for toxins. Alternatively, a combined test detecting both targets at the same time on the same device (C Diff Quik Chek Complete (Abbott)) can also be used. Based on biologists’ feedback, some discrepancies between GDH detection by a stand-alone test for GDH and the combined test GDH+-toxin have been reported. The objective of this study was to compare the performances of the C Diff Quik Chek and C Diff Quik Chek Complete for detecting GDH compared to culture.

Materials/methods: From November 2018 to March 2019, 88 stool samples positive by culture for C. difficile (58 fresh stools and 30 frozen stools stored at -80°C) and 220 fresh stool samples negative by culture were tested simultaneously by both assays: C Diff Quik Chek and C Diff Quik Chek Complete. Discrepant results were defined as results that do not match with results of culture. In cases of negative-GDH assay and culture-positive, stool samples were tested again by another technician with both assays. In cases of positive-GDH assay from stool samples that were negative by culture, enriched culture was performed. In addition, serial dilution experiments were conducted on 5 culture-positive stool samples. Stool samples were diluted with the diluent from 1/10 to 1/10000 and each dilution was tested by 2 assays.

Results: Among the 88 culture-positive samples, 27 (30.7%) were non toxigenic strains and 61 (69.3%) isolates were toxigenic strains. After resolving discrepant results, both tests displayed a sensitivity and specificity for GDH detection of 97.9% [CI 95% 92.7-99.7] and 97.2% [CI 95% 93.9-99.2], respectively. Using serial dilution experiments, the results of each assays were similar in terms of detection threshold for GDH detection.

Conclusions: The C Diff Quik Chek and C Diff Quik Chek complete display a similar sensitivity and specificity for GDH detection.

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Abstract 1185

Epstein-Barr virus biomarkers in HIV-related non-Hodgkin lymphoma in the modern cART era

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Abstract third-party references: ANRS

Background: The usefulness of Epstein-Barr virus (EBV) biomarkers in HIV-related non-Hodgkin’s lymphomas (NHL) is poorly explored in the context of improvement of the prognosis of these patients in the recent combined antiretroviral therapy (cART) era.

Materials/methods: We evaluated EBV DNA load and a panel of EBV antibodies in HIV-NHL patients prospectively enrolled in the French ANRS-CO16 Lymphovir cohort between 2008 and 2015. Pretreatment whole blood (WB), plasma EBV DNA load and serological profiles were analyzed in 76 HIV-infected patients. Moreover, for the 53 patients with available data, comparisons were performed between values at diagnosis and 6 months after the initiation of chemotherapy.

Results: Pretreatment WB and plasma EBV DNA loads were positive in 80% and 45% of HIV-NHL patients, respectively. Eighteen out of 43 (42%) tested cases for in situ EBV were positive. The detection of the EBV-encoded small RNA (EBER) was associated with plasma EBV DNA positivity (p = 0.002) but not with WB EBV DNA positivity (p = 0.14). Two-year progression-free survival (PFS) estimates did not differ between the patients with pretreatment WB (n = 61) or plasma (n = 34) EBV DNA (+) and the patients with pretreatment WB (n = 15) or plasma (n = 42) EBV DNA (−) [82% vs 67% or 69%, p = 0.15 and 0.52, respectively]. At diagnosis, 62% of patients harbored an EBV reactivation serological profile defined by high anti-EBV IgG antibody levels or high anti-VCA IgG antibody titers combined with high anti-EA IgG antibody titers. Two-year PFS estimates did not differ between the patients with a normal profile or those with a reactivation profile. Following chemotherapy, WB and plasma EBV DNA levels significantly declined from medians of 3970 (interquartile range, 268 – 14400) and 0 (0 – 0) copies/mL to 0 (0 – 0) and 0 (0 – 0) copies/mL, respectively (p < 0.0001 and p < 0.0001, respectively). Anti-EA IgG, anti-EBNA-1 IgG, anti-EBV IgA antibodies significantly dropped at 6 month follow-up (p < 0.0001, p = 0.01 and p < 0.0001, respectively). No significant decrease was observed with the anti-VCA or the anti-EBV IgG antibody titers/levels (p = 0.10 and 0.07, respectively).

Conclusions: WB and plasma EBV DNA loads at NHL diagnosis do not constitute prognostic markers in HIV-NHL patients in the modern cART era.

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Needles in a haystack: ultra-orphan invasive fungal infections reported in FungiScope: global registry for emerging fungal infections

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Abstract third-party references: On behalf of FungiScope® Team

Background: Emerging invasive fungal infections (IFIs) have become a major challenge in patient management, as effective therapies have not been evaluated due to low number of patients affected. Apart from the more frequently described fusariosis, lomentosporiosis, mucormycosis, scedosporiosis, and certain dematiaceous fungi or yeasts, little is known about ultra-orphan IFIs. Our aim is to present an overview of ultra-orphan IFIs collected in the FungiScope® registry

Materials/methods: Ultra-orphan IFIs were collected in FungiScope® registry. Cases were grouped in Rare Ascomycota (sub-groups Rare Dematiaceae, Rare Hypocreales, Rare Saccharomycetales, Rare Eurotiales, and Invasive Dermatomycetes), Rare Basidiomycota, Rare Entomophthorales, and Rare Mucorales.

Results: Between 2003 and June 2019, 187 ultra-orphan IFIs were documented in FungiScope®. Rare Dematiaceae (35.3%), Rare Hypocreales (22.5%), Rare Mucorales (10.7%) or Rare Saccharomycetales (11.8%) caused most IFIs. The majority of the patients had an underlying malignancy (38.0%). Disseminated infection was observed in 48 patients. Complete or partial responses were observed in 67.9% overall, ranging from 50.0% in Rare Entomophthorales to 83.3% in Rare Eurotiales related cases. Overall mortality rate was 28.9%, ranging from 11.1% in Rare Eurotiales to 50.0% in Rare Mucorales.

Conclusions: Physicians are confronted with a complex variety of fungal pathogens, for which treatment recommendations are lacking and successful outcome might be incidental. Only through an international joint effort of physicians and scientists, an adequate number of cases of ultra-orphan IFIs can be collected to further investigate the epidemiology and eventually identify effective therapy regimens.

Figure: Kaplan-Meier survival plots of ultra-orphan invasive infections reported in FungiScope®

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Abstract 1187

**Effect of antiretroviral therapy on resistant *Escherichia coli***

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Dr Robert J H Hammond, University of St Andrews

**Background:** Colistin is one of the last line antibiotics we have in our toolkit against the rising tide of antimicrobial resistance (AMR). When bacteria become resistant to colistin they are classified as untreatable. Zidovudine (AZT) is an antiretroviral that prevents mother-to-child spread of HIV and works by inhibiting DNA reverse transcriptase. Combination therapy is an exciting branch of potential chemotherapy for resistant bacteria. The use of combinations of drugs can overcome resistance mechanism and render untreatable organisms susceptible.

**Materials/methods:** In this work we created a colistin resistant mutant *E. coli* 25922 and subjected it to colistin + zidovudine therapy. We used a Hollow Fiber Bioreactor (HFS) to growth our mutated strain of *E. coli* to $\approx 1 \times 10^5$ cfu/mL in Mueller Hinton cation adjusted broth and then began drug infusion with a syringe driver. We ran four sets of experiments; a drug free trail as a control followed by a colistin only, AZT only and a colistin + AZT run.

**Results:**

Data indicates that the colistin only arm as well as the AZT arm had no effect however when the combination therapy was applied bacterial killing began within 4 hours and continued for 24 hours resulting in a nearly 3-log reduction in viable cells.

**Conclusions:** We hypothesise that AZT is unable to cross the bacterial membrane therefore has no effect on the resistant mutant. However, in the combination therapy the colistin is able to form pores in the bacterial membrane and this facilitates the AZT entry to the cell.

These data imply that combinations of seemingly unrelated antimicrobials could be used as novel treatment options in the cases of extreme drug resistance

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Abstract 1188

UV-C light application after terminal disinfection for vancomycin-resistant enterococci: an additional safety?

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Background: Surfaces may be contaminated by patients colonized or infected with multidrug resistant microorganisms. The environment of patients colonized/infected with Vancomycin-resistant Enterococci (VRE) are commonly contaminated with VRE. Several studies indicate that VRE may survive in these rooms even after terminal disinfection (TD) after discharge of the patient, an established risk factor for the next patient hospitalized in the same room acquiring VRE. Our aim was to see whether UV-C disinfection of rooms occupied by patients colonized or infected with VRE leads to a measurable decrease in VRE compared to standard TD procedures.

Materials/methods: Between 10/2018-10/2019, 29 rooms from 19 different patients colonized with VRE were examined after discharge (5 VanA [26.3%]/14 Van B [73.7%]). Eight samples per site have been checked: Toilet seat, toilet button flush, toilet paper cover, tap, floor, patient bed bell, bedside drawer and folding table. Standard TD was performed by a commercially licensed product – a mix of quaternary ammonium compound with aldehyde (Deconex® 50 FF, 0.5%) by in-house trained cleaning staff. The microbiological samples were taken using RODAC contact plates and eSwab* at three time points: a) before TD, b) after TD and before UV-C disinfection, c) after TD and UV-C disinfection. When growth was detected, isolates were subcultured on Columbia blood agar and CNA plates, and microorganisms were identified by MALDI-TOF massspectrometry, and strains of patients as well as positive environmental samples were typed by whole genome sequencing.

Results: Overall, 688 samples were analyzed. At time point a) 16% (37/232), b) 2% (5/224) and c) 0% (0/232) samples were positive for VRE. In one patient room, 8 samples could not be taken after TD and before UV-C. Significant reductions were achieved before TD as well as after UV-C disinfection (p<0.0001). The addition of UV-C after TD did significantly reduced the environmental burden with VRE, even after TD (p = 0.028).

Conclusions: The applied TD failed to completely eliminate VRE. The additional exposure with UV-C succeeded to eliminate VRE from the analyzed sites, and may be needed to safely provide a clean room to the next patient.

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Abstracts 2020

Abstract 1190

**Systematic evaluation of development pathways of centrally-approved antibiotics in Europe including an innovative graphical illustration method**

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**Background:** Development of new antibacterial agents is necessary as drug-resistant bacteria are a threat to global health. In Europe, the European Medicines Agency (EMA) has been guiding this development process for more than two decades. We investigated preclinical and clinical studies to illuminate the various phases within the authorization process.

**Methods:** All centrally authorized systemic antibacterial and antimycobacterial drugs were included without any time restriction. Additionally, Food & Drug Administration (FDA)-approved antibiotics of the last three years, which were not yet approved by the EMA, were included. We focused on the preclinical pharmacokinetic/pharmacodynamic (PK/PD) studies and phase II and phase III clinical trials. Furthermore, we investigated the recommended dosing regimens and correlation between preclinical studies and finally approved indications. Tree diagrams as a novel way of illustrating the development process of antibiotics were developed.

**Results:** We included 23 (EMA 18, FDA 5) antimicrobials. Tetracyclines, carbapenems and cephalosporins were the leading classes with 13% each. The recommended dosing interval was significantly shorter in time-dependent versus exposure-dependent drugs (median 8 versus 12, Mann-Whitney U test: p = 0.006). The majority of approved indications used non-inferiority trials (i.e. acute bacterial skin and soft tissue infection, community-acquired pneumonia, complicated intra-abdominal infection, complicated urinary tract infection, and complicated skin and soft tissue infection). Phase II and phase III clinical trials investigating community-acquired pneumonia involved the fewest patients (mean 85 and 494 patients, respectively) while complicated urinary tract infections phase III trials included the largest number (mean 688 patients). The Figure depicts the way to approval of ceftazidime-avibactam as one example. The branches of the development process demonstrate the increasing evidence for clinical efficacy.

**Conclusions:** Some promising drugs were marketed in the last years. The individual steps to their authorization were illuminated. We confirmed the relevance of PK/PD studies in dosing optimization and decision making in modern antimicrobial development and identified important differences in pathways according to antimicrobial class and target indication.
Infection: infections due to aerobic gram-negatives

2 Phase III: 1033 patients with complicated urinary tract infection (comparator: doripenem)

Indication: infections due to aerobic gram-negatives

2 Phase III: 1066 + 441 patients with complicated intra-abdominal infection (comparator: meropenem)

Phase III: 879 patients with hospital-acquired pneumonia (comparator: meropenem)

Lung infection mouse model (P. aeruginosa)

Thigh infection mouse model (P. aeruginosa)

Phase III: 137 + 218 patients with complicated urinary tract infection (comparator: imipenem & doripenem)

Phase II: 204 patients with complicated intra-abdominal infection (comparator: meropenem)

Phase II: 204 patients with complicated intra-abdominal infection (comparator: meropenem)

Phase III: 1033 patients with complicated urinary tract infection (comparator: doripenem)

Phase III: 333 patients with ceftazidime-resistant gram-negatives (comparator: best available therapy)

Phase III: 1066 + 441 patients with complicated intra-abdominal infection (comparator: meropenem)

Phase III: 1033 patients with complicated urinary tract infection (comparator: doripenem)

Figure. Pathway towards approved indications of ceftazidime-avibactam.

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Abstract 1191

**An open-label, phase I, multi-centre study to evaluate the pharmacokinetic, safety and tolerability profile of oral isavuconazonium sulfate in paediatric patients**

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**Abstract third-party references:** This abstract was submitted by Cello Health MedErgy, on behalf of the authors. Editorial assistance was provided by Cello Health MedErgy, funded by Astellas Pharma Global Development, Inc., Northbrook, IL, USA.

**Background:** Isavuconazonium sulfate (ISAVUSULF) is the prodrug of isavuconazole (ISAV), a broad-spectrum mould-active triazole with proven efficacy in treating invasive aspergillosis and mucormycosis in adults. The purpose of this study (NCT03241550) was to evaluate the pharmacokinetics (PK), safety and tolerability of multiple-dose oral ISAV in paediatric subjects at risk for invasive mycoses.

**Materials/methods:** Subjects were grouped into two age cohorts [6–<12 years and 12–<18 years]. The ISAVUSULF formulation was a novel 74.5 mg oral capsule equivalent to 40 mg ISAV. Subjects received a target dose of 10 mg/kg [to a maximum of 372 mg], q8h on days 1 and 2, then once daily on days 3–28. Plasma ISAV concentrations were used to update a population PK model previously built using intravenous (IV) data from paediatric subjects [1–<18 years] in this study, plus IV data from a phase I study in adults (NCT01555866). Monte Carlo simulations were performed and area under the concentration–time curve at steady state [AUC_{ss}] was calculated. The target exposure range was based on efficacious ranges from adults in the phase III SECURE (NCT00412893) and VITAL (NCT00534049) studies; an upper safety threshold was derived from an adult study (NCT01565720) that used a supratherapeutic dose [1116 mg] with increased adverse events [AEs].

**Results:** Of 20 enrolled subjects, 19 were evaluable for PK and safety. Using modelling and simulation, paediatric ISAV exposures at the studied oral dosage were similar to paediatric exposures following IV administration and to exposures shown to be efficacious in adults, and were significantly below the safety threshold reported previously following supratherapeutic dosing in adults [Figure]. AEs were reported in 18 subjects, with drug-related AEs in 10. Six drug-related AEs [nausea, vomiting, pyrexia, elevated alanine aminotransferase, elevated aspartate aminotransferase, abdominal pain] led to treatment withdrawal in 3 subjects. No deaths were reported.

**Conclusions:** Oral ISAVUSULF administered to paediatric subjects [10 mg/kg, q8h on days 1 and 2 and once daily thereafter] resulted in steady-state ISAV exposures similar to those observed with IV administration and comparable to the efficacious range observed in adults. The safety profile was similar to that of adults.
**Figure. Paediatric and adult exposures to isavuconazole**

Box-and-whisker plots of simulated drug exposure (AUC_{SS}) for paediatric age cohorts (1–<6 [IV only], 6–<12, 12–<18 years; oral or IV ISAVUSULF 10 mg/kg to a maximum of 372 mg, q8h on days 1 and 2 and once daily thereafter) and predicted drug exposure (AUC_{SS}) for adult populations (data from the SECURE [NCT00412893] and VITAL [NCT00634049] studies; oral or IV ISAVUSULF 372 mg once daily). Boxes represent the medians (thick black lines) and interquartile ranges, whiskers represent the range of maximum and minimum values within 1.5 x the interquartile range, and outliers are shown as circles. The blue line is the AUC_{SS} from the SECURE study (25th percentile; 60 mg/h/L) that represents the lowest targeted value. The green and orange lines are the minimum (233 mg/h/L) and mean (353 mg/h/L) AUC_{SS} values, respectively, in a high-dose adult study (1116 mg; NCT01585720) with increased adverse events.

AUC_{SS}, area under the concentration–time curve at steady state; ISAVUSULF, isavuconazonium sulfate; IV, intravenous; PO, oral; q8h, every 8 hours; Y, years.

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Meropenem-Vaborbactam (VABOREM) in treatment of patients with hospital- and ventilator-acquired pneumonia (HABP/VABP) and bacteraemia due to carbapenem-resistant Enterobacteriaceae

Matteo Bassetti1, Francesco Menichetti2, George L. Daikos3, Sue Cammarata4, Karen Fusaro5, Daniela Zinzi*6

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Abstract third-party references: Menarini, Melinta

Background: Meropenem-vaborbactam (M-V) is a beta-lactamase inhibitor combination active against carbapenemase-producing Klebsiella pneumoniae. We report outcomes in patients with HABP/VABP and bacteremia due to CRE who were treated with M-V monotherapy vs best available therapy (BAT).

Materials/methods: TANGO 2 was a randomized, Phase 3, open-label trial in patients with confirmed or suspected CRE infections, including cUTI, HABP/VABP, bacteremia, or cIAI. Patients were randomized 2:1 to M-V monotherapy or BAT for 7-14 days. BAT could include (alone or in combination): carbapenem, aminoglycoside, polymyxin B, colistin, tigecycline or ceftazidime-avibactam (monotherapy only). Enrollment was stratified by infection type and geographic region. For the patients with HABP/VABP and with primary bacteremia, the primary efficacy endpoint was all-cause mortality at Day 28. The secondary endpoint was the proportion of patients with clinical cure at test of cure (TOC, 7±2 days following end of treatment). This study was not powered for inferential statistical testing; results are presented descriptively.

Results: Of the 75 patients treated in this study, 34 patients had HABP/VABP or bacteremia; 22 (65%) had baseline CRE, comprising the microbiologic CRE modified intent-to-treat primary population (mCRE-MITT). Patients with HABP/VABP or bacteremia were white (61.2%), with mean age 61.2 y (30-84 y). Most patients were from Europe (52.9%) or North America (29.4%) and had a CrCl ≥50 mL/min (76.5%). Charlson comorbidity score of ≥5 was present in 73.5%. Half of patients had SIRS at baseline; 47.1% of patients were immunocompromised.

In HABP/VABP/bacteremia patients with CRE infection, the all-cause mortality at day 28 was 22.2% [4/18] M-V vs 44.4% [4/9] BAT. Clinical Cure at TOC was seen in 66.7% [12/18] M-V vs 22.2% [2/9] BAT. In the study, incidence of AEs was similar between groups (84 % M-V vs 92% BAT). M-V was associated with fewer drug-related AEs [24% vs. 44%], severe AEs [14% vs. 28%], serious AEs [34% vs. 44%] and less nephrotoxicity vs BAT.

Conclusions: In this prospective comparative trial of M-V monotherapy in CRE infections, M-V showed consistent reduction in mortality and improvement in clinical cure and safety/tolerability over BAT. M-V appears to be an effective treatment option for HABP/VABP/bacteremia due to CRE.

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Abstract 1194

Mutant prevention concentration values of linezolid, moxifloxacin and vancomycin against *Staphylococcus pseudintermedius* strains recovered from humans

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**Background:** SP is a commensal and opportunistic pathogen of dogs and cats. SP recovered from human specimens seems to be increasing and multidrug resistant strains from humans are being reported. Two particular cases from our hospital were a 4 month old pediatric oncology patient with SP bacteremia and the second a middle aged female oncology patient with persistent wound infection and catheter tip colonization. SP strains were recovered from family pets of both patients. We tested the SP strains from humans to determine minimum inhibitory concentration (MIC) and MPC values to L, M and V.

**Materials/methods:** A total of 24 isolates from humans were tested. MIC testing was as per the recommended procedure of the Clinical and Laboratory Standards Institute (CLSI) utilizing a \(10^5\) colony forming unit/milliliter (cfu/ml) inoculum and incubation under ambient conditions for 18 to 24 hours. For MPC testing \(\geq10^9\) CFU were applied to the surface of drug containing agar plates. Inoculated plates were incubated under ambient conditions and screened for growth after 24 and 48 hours of incubation. The lowest drug concentration blocking growth was recorded as the MIC or MPC depending on the method.

**Results:** MIC range values for L, M and V were 1-2, \(<0.016-0.63\) and 0.25-0.5 \(\mu\)g/ml respectively. The MIC\(_{50/90}\) values were 1/2, \(<0.016/0.031\) and 0.25/0.5 \(\mu\)g/ml. MPC range values were 1-2, 0.125-0.25 and 4-8 \(\mu\)g/ml with MPC\(_{50/90}\) values of 2/2, 0.125/0.25 and \(\geq8/\geq8\) \(\mu\)g/ml. Considering CLSI breakpoints (BP) and MPC values, all isolates would be susceptible to linezolid (MIC BP \(<4\) \(\mu\)g/ml) and moxifloxacin (MIC BP \(<0.5\) \(\mu\)g/ml). In contrast all strains would be considered non-susceptible to vancomycin (MIC BP \(\geq4\) \(\mu\)g/ml).

**Conclusions:** SP is being recovered more frequently from human infections including invasive disease (i.e. bacteremia). The high vancomycin MPC values reported here are consistent with similar results for *Staphylococcus aureus* and suggest concern with potential therapeutic failure in patients where vancomycin may be used for treat SP infections.

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Abstract 1203

**Real-world experience of dalbavancin use for the treatment of Gram-positive infections**

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**Background:** Dalbavancin is a lipoglycopeptide antibiotic with prolonged half-life approved for the treatment of acute bacterial skin and skin structure infections (ABSSSIs). However, in real life it can be used for several gram-positive infections, when protracted treatment is required. We examined the effectiveness and safety of dalbavancin in the treatment of various gram-positive infections other than ABSSSIs.

**Materials/methods:** This retrospective study was performed in the University Hospital of Heraklion in Greece from September 2017 through August 2019. All adult patients who received at least one dose of dalbavancin with a minimum follow-up of three months post-treatment were included.

**Results:** Twelve patients were identified, 7 (58.3%) were female. Mean age was 65.5 (SD, 13.1) years. Dalbavancin was used for treatment of osteomyelitis, prosthetic joint infection, epidural abscess, and permanent pacemaker lead infection (Table). Nine patients (75%) received dalbavancin as targeted therapy, whereas 3 (25%) were treated empirically. The isolated pathogens were methicillin-resistant *Staphylococcus aureus*, methicillin-resistant *Staphylococcus epidermidis* and *Enterococcus* spp. All patients received dalbavancin as sequential therapy after the administration of vancomycin or daptomycin for a median duration of 14 (range, 10-28) days due to the feasibility for early discharge and treatment on outpatient basis. Dalbavancin was administered as 1000 mg i.v. on Day 1 followed by 500 mg i.v. weekly. The median duration of dalbavancin therapy was 21 (range, 7-42) days. Eleven patients (91.7%) had favourable outcome, while 1 (8.3%) patient with spinal epidural abscess who refused surgical intervention experienced clinical failure. Regarding safety, only the patient with treatment failure experienced a non-clostridial transient diarrhea.

**Conclusions:** The use of dalbavancin for sequential treatment of gram-positive infections other than ABSSSIs seems to be safe and effective. Prospective trials are needed to validate novel indications for this new compound.

<table>
<thead>
<tr>
<th>Infection type</th>
<th>Overall, n</th>
<th>Causative pathogen, n</th>
<th>Culture-negative</th>
<th>Cure, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MRSA</td>
<td>MRSE</td>
<td><em>E. faecium</em></td>
<td><em>E. faecalis</em></td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>7</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Prosthetic joint infection</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Epidural abscess</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Pacemaker lead infection</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

MRSA: *Staphylococcus aureus*, MRSE: methicillin-resistant *Staphylococcus epidermidis*

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Abstract 1204

A multi-modal intervention to improve hand hygiene compliance in peripheral wards of a tertiary care university centre: a cluster randomised controlled trial

Seven Johannes Sam Aghdassi, Petra Gastmeier, Christin Schröder, Michael Behnke, Patricia Manuela Fliß, Janina Wenk, Carolin Plotzki, Tobias Kramer

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Background: Compliance to hand hygiene is a key factor in preventing healthcare-associated infections. It was our objective to assess the effect of a multimodal intervention on hand hygiene compliance at a tertiary care university hospital. As a secondary objective, we investigated the effect of the intervention on the occurrence of device-associated bloodstream infections.

Materials/methods: We performed a single centre cluster randomised controlled trial at a university hospital in Germany. Twenty peripheral wards were invited to participate and randomly assigned to either the intervention (n=10) or control group (n=10). Quarterly, trained observers conducted direct compliance observations on all twenty wards. The intervention entailed dissemination of teaching materials on aseptic procedures, equipment with flexibly mountable alcoholic hand rub dispensers, and quarterly feedback on hand hygiene compliance rates. The duration of the intervention was twelve months in the year 2018. Prospective surveillance was conducted for device-associated infections during the intervention. A multivariable logistic regression analysis was performed to identify factors significantly influencing the likelihood of compliant performance of hand hygiene.

Results: In total, 21424 hand hygiene opportunities were observed. Overall, compliance rates did not change significantly in either group (59% vs. 60% in the control group; 59% vs. 61% in the intervention group). Compliance prior to aseptic procedures improved significantly from 44% to 53% (p=0.03) in the intervention group, while no significant increase was noted in the control group. Multivariable logistic regression analysis revealed that non-nursing, non-physician staff ("others") were significantly less likely to perform compliant hand hygiene than nurses and physicians (p<0.01). In the intervention group, rates of device-associated bloodstream infections were significantly lower than in the control group (p<0.01).

Conclusions: A significant effect of the intervention was observed with regard to hand hygiene compliance prior to aseptic procedures. The lack of a significant overall improvement of hand hygiene compliance shows that comprehensive implementation of hand hygiene interventions and creation of a sense of ownership of the intervention among healthcare workers on multiple wards simultaneously is difficult. Observed differences between professional groups suggest that education of healthcare workers other than nurses and physicians should be a target of future hand hygiene interventions.

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Abstract 1205

**Lyme disease spirochete variants and human endothelial cells determinants for transendothelial migration: development of an in vitro system using primary human microvascular endothelial cells**

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**Background:** Lyme disease is a tick born infection caused mainly by *B. burgdorferi* in North America. Hematogenous dissemination is an important pathogenic strategy for Lyme spirochetes. Since *B. burgdorferi* does not produce any toxins or classical virulence factors, it likely uses a mechanism distinct from what has been observed with other pathogens. In spite of the importance of vascular transmigration in Lyme disease pathogenesis there has been little research into this area and there are only a few conflicting reports on whether *B. burgdorferi* endothelial transmigration is transcellular or paracellular. In addition, cellular features are crucial and no published studies have used primary microvascular endothelial cells, which accurately reflect the site of *B. burgdorferi* transmigration.

**Materials/methods:** We aimed to develop an efficient in vitro system to study *B. burgdorferi* migration through human primary microvascular endothelial cells. We are using two types of primary human microvascular endothelial cells: dermal and synovial. Co-culture conditions were optimized based on spirochete growth, viability and length in the new media. Cell viability was assessed using trypan blue stain, as well as immuno-staining for junction (VE-cadherin) and cytoskeleton (F-actin). Transmigration assays are performed using Transwells chambers. Relative percentages of transmigrated spirochetes were estimated by counting the lower transwell chamber.

**Results:** Using wild type *B. burgdorferi* compared to a non-adherent high passage strain, we showed that our system reflects the in vivo conditions, with a 8 fold higher transmigration of the low passage strain after 4 hours of co-incubation in both synovial and dermal endothelial cells. Studies are now in progress to assess *B. burgdorferi* strains deficient for various adhesins as well as to define the major pathway (paracellular or transcellular) involved in the process and to characterize the required cellular signaling pathways.

**Conclusions:** The potential of our proposed study is the use of resulting information to eventually block hematogenous dissemination of *B. burgdorferi* shortly after tick-bite exposure and cripple the ability of the spirochetes to invade host organ systems.

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Probability of target attainment analyses inform ceftolozane/tazobactam dosing regimens in hospital-acquired pneumonia/ventilator-associated pneumonia patients with end-stage renal disease on intermittent haemodialysis

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Abstract third-party references: This work was supported by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, New Jersey, USA (MSD)

Background: Ceftolozane/tazobactam (C/T) combines a potent anti-pseudomonal cephalosporin with a beta-lactamase inhibitor. The 2g/1g C/T high dose by 1-hour infusion every 8 hours (Q8H) was evaluated in participants with hospital-acquired pneumonia/ventilator-associated pneumonia (HAP/VAP) in the Phase 3 study ASPECT-NP, demonstrating safety and efficacy in this population. Both compounds are eliminated renally, and dose adjustment is necessary based on renal function. HAP/VAP patients with end-stage renal disease (ESRD) on intermittent hemodialysis (HD) were not eligible for ASPECT-NP. This study utilized probability of target attainment (PTA) analyses to inform the C/T recommended dosing regimen in this population.

Materials/methods: Population PK models for C and T in HAP/VAP patients were developed to describe C and T concentration data in plasma collected in 16 clinical studies, including ASPECT-NP and in ESRD subjects without infection, and in pulmonary epithelial lining fluid (ELF) collected in 2 Phase 1 studies. The final population PK models were used to simulate C and T concentration-time profiles in plasma and ELF of ESRD patients at three different dose levels by 1-hour infusion Q8H over a 14-day treatment duration, with HD on every other weekday:

- 1g/0.5g C/T loading+200mg/100mg C/T maintenance (2X cIAI/cUTI)
- 1.5g/0.75g C/T loading+300mg/150mg C/T maintenance (3X cIAI/cUTI)
- 3g/1.5g C/T loading+400mg/200mg C/T maintenance (4X cIAI/cUTI)

Daily C and T exposures and PTA in ELF and plasma were estimated.

Results: For the 14-day treatment duration, daily plasma PTA for all 3 regimens was 100% for C at 30%fT>MIC=4mg/L and >99% for T at 20%fT>Ct=1mg/L. Daily ELF PTA was ≥95% for C at 30%fT>MIC=4mg/L for all 3 regimens and was >90% for T at 20%fT>Ct=1mg/L for the 3X and 4X cIAI/cUTI regimens. ELF PTA for T at the 2X cIAI/cUTI regimen was <80% at 20%fT>Ct=1mg/L on HD days. Plasma AUC distribution for T at the 4X cIAI/cUTI regimen extended above the clinical experience of ASPECT-NP.

Conclusions: Based on the results of the analyses, the 1.5g/0.75g C/T loading+300mg/150mg C/T maintenance by 1-hour IV infusion Q8H is considered to balance efficacy and safety considerations and is recommended for ESRD patients with HAP/VAP.

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Abstract 1211

**Candida spp. in the respiratory tract secretions of critically ill patients and the impact of antifungal treatment**

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**Background:** In critically ill patients *Candida* is often isolated from bronchial secretion (BS) or bronchoalveolar lavage (BAL) samples. The significance of this finding is undetermined. We examined the impact of antifungal treatment in previously immunocompetent patients with intensive care unit (ICU)-acquired respiratory tract infection (RTI) and *Candida* spp. isolation from their BS or BAL.

**Materials/methods:** All adult patients admitted to the ICU of the University Hospital of Heraklion, Greece, from January 2014 through December 2016, with ICU-acquired RTI and *Candida* spp. isolation in their BS were evaluated. Demographics, clinical characteristics, antifungal treatment for any reason ±10 days around *Candida* spp. isolation, and 28-day and in-hospital mortality were recorded. Associations of antifungal treatment and mortality were tested with univariate (chi-square test) and multivariate logistic regression analysis.

**Results:** Seventy-nine patients were evaluated and 58 (73.4%) of them were male. Mean [standard deviation, (SD)] age was 66.1 (16.6) years. Thirty-nine (49.4%) received antifungals and 33 (41.8%) had more than two comorbidities. The mean body mass index (SD) was 28.4 (6.6) and the mean APACHE II score (SD) was 21.6 (7.8). The 28-day and in-hospital mortality rate were 22.8% and 30.4%, respectively. There were no differences in 28-day and in-hospital mortality when patients receiving antifungal treatment were compared to those that did not, even after adjustment for selected confounders [Table].

**Conclusions:** Antifungal treatment in previously immunocompetent patients with ICU-acquired RTI and *Candida* spp. isolation in their secretions did not influence survival. Larger prospective or interventional studies are needed to elucidate the exact importance of *Candida*'s presence in the respiratory tract of ICU-patients.

**Table.** Multivariate logistic regression analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>28-day in-hospital mortality, OR [95% CI]</th>
<th>In-hospital mortality, OR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antifungal administration</td>
<td>1.68 [0.54-5.36]</td>
<td>1.88 [0.66-5.39]</td>
</tr>
<tr>
<td>Age</td>
<td>1.01 [0.97-1.05]</td>
<td>1.01 [0.96-1.04]</td>
</tr>
<tr>
<td>Gender</td>
<td>1.29 [0.36-4.65]</td>
<td>1.47 [0.45-4.81]</td>
</tr>
<tr>
<td>&gt;2 comorbidities</td>
<td>1.08 [0.32-3.65]</td>
<td>1.65 [0.53-5.10]</td>
</tr>
<tr>
<td>APACHE II</td>
<td>1.04 [0.96-1.12]</td>
<td>1.03 [0.96-1.10]</td>
</tr>
<tr>
<td>Body mass index</td>
<td>1.06 [0.97-1.15]</td>
<td>1.04 [0.96-1.13]</td>
</tr>
</tbody>
</table>

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Ceftolozane/tazobactam probability of target attainment in patients with hospital-acquired pneumonia/ventilator-associated pneumonia

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Abstract third-party references: This work was supported by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, New Jersey, USA (MSD)

Background: Ceftolozane/tazobactam (C/T) combines a potent anti-pseudomonal cephalosporin with a beta-lactamase inhibitor. The 2g/1g C/T high dose or equivalent dose adjusted based on renal function administered by 1-hour infusion every 8 hours was evaluated in mechanically ventilated participants with hospital-acquired pneumonia/ventilator-associated pneumonia (HAP/VAP) in the Phase 3 study ASPECT-NP, demonstrating safety and efficacy in this population. Probability of target attainment (PTA) analyses were conducted to support the recommended C/T dosing regimens in HAP/VAP patients.

Materials/methods: Population PK models for C and T in HAP/VAP patients were developed to describe C and T concentration data in plasma from 16 clinical studies, including ASPECT-NP, and in pulmonary epithelial lining fluid (ELF) from 2 Phase 1 studies. The final population PK models were used to simulate C and T concentration time profiles in plasma and ELF in HAP/VAP patients at various dosing regimens over a 14-day treatment duration. PTA in plasma and ELF was calculated using the PK/PD targets of 30% fT>MIC for C and 20% fT>C=1mg/L for T.

Results: Based on projected PTA in plasma and ELF, the C/T dosing regimens in HAP/VAP patients evaluated in ASPECT-NP were:

- 2g/1g C/T (CrCL>50mL/min)
- 1g/0.5g C/T (30mL/min≤CrCL≤50mL/min)
- 500mg /250mg C/T (15mL/min≤CrCL≤29mL/min)

At these C/T dosing regimens, steady-state plasma PTA was 100% for C at 30%fT>MIC=4mg/L and >99% for T at 20%fT>C=1mg/L across renal categories at CrCL up to 150mL/min. Steady-state ELF PTA was >99% for C at 30%fT>MIC=4mg/L and >87% for T at 20%fT>C=1mg/L across renal categories at CrCL up to 150mL/min.

Conclusions: At the dosing regimens evaluated in ASPECT-NP, high plasma and ELF PTA were achieved in HAP/VAP patients across renal function categories. Together with demonstrated safety and efficacy in the study, the PTA results support the appropriateness of these dosing regimens for the treatment of HAP/VAP.

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Abstract 1214

**Exposure-efficacy analyses support optimal dosing regimens of ceftolozane/tazobactam in patients with hospital-acquired pneumonia/ventilator-associated pneumonia in ASPECT-NP**

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**Abstract third-party references:** This work was supported by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, New Jersey, USA (MSD)

**Background:** Ceftolozane/tazobactam (C/T) combines a potent antipseudomonal cephalosporin with a beta-lactamase inhibitor. A C/T dose of 2g/1g, or adjusted based on renal function, was evaluated in patients with HAP/VAP in the phase 3 ASPECT-NP study, demonstrating safety and efficacy in this population. Exposure–response (E–R) analyses were conducted to assess the potential relationship between plasma pharmacokinetics and the clinical efficacy endpoints to support the optimal C/T dose regimens in adult patients with HAP/VAP.

**Materials/methods:** Plasma C/T exposure metrics (%fT>MIC or %fT>C) for each patient at the end of treatment were derived from the population pharmacokinetic models. Actual dosing records and the highest MIC value for relevant baseline lower respiratory tract (LRT) pathogens identified for each patient were used. The primary efficacy endpoints were all-cause mortality (ACM) at day 28 and clinical response at test of cure. The relationship between %fT>MIC for ceftolozane or %fT>C for tazobactam and efficacy endpoints was explored.

**Results:** In the analysis set (N=231), the ACM rate was 16% (36 died on/before day 28) and clinical cure rate 65% (151 achieved cure). No E–R relationship for ceftolozane %fT>MIC was observed for both clinical endpoints.

Additionally, among 177 patients with a baseline LRT pathogen MIC ≤4μg/mL, a low ACM rate (13%) and high clinical cure rate (71%) were observed versus those with MIC >4μg/mL (24% and 48%, respectively). No E–R relationship for ceftolozane was observed in these 177 patients; 173 patients had 99%fT>MIC, with ACM and clinical cure rates of 13% and 70%, respectively, and the remaining 4 patients had ≥73%fT>MIC, with ACM and clinical cure rates of 0% and 100%, respectively. Tazobactam exposure was not considered related to efficacy, as ACM rates increased and clinical cure rates decreased with increasing tazobactam PK measure %fT>C.

**Conclusions:** There was no E–R trend with C/T, and among those with a baseline LRT pathogen MIC below the breakpoint, all patients achieved exposures above the pharmacokinetic/pharmacodynamic targets. These results support the appropriateness of a C/T 2g/1g dose, or adjusted dose for renal function, in adult patients with HAP/VAP.

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Emergence of non-susceptibility among Gram-negative respiratory pathogens from a phase III clinical trial for treatment of nosocomial pneumonia (ASPECT-NP)

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Abstract third-party references: This work was supported by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, New Jersey, USA [MSD]

Background: The phase 3, randomized, double-blind, multicenter ASPECT-NP trial evaluated ceftolozane/tazobactam 3g every 8 hours (q8h) versus meropenem 1g q8h for 8–14 days in adults for treatment of ventilated nosocomial pneumonia. Genetic typing was performed to assess relatedness of baseline and post-baseline Pseudomonas aeruginosa (PsA) and Enterobacteriales (ENT) isolates.

Materials/methods: Pairs of isolates were selected for molecular typing among patients in the microbiological intention-to-treat population when a susceptible baseline organism and a non-susceptible post-baseline organism of the same genus and species were identified. Applied interpretive criteria to determine non-susceptibility were provisional ASPECT-NP breakpoints (susceptible breakpoints: PsA, ≤8 mg/L; ENT, ≤4 mg/L) for ceftolozane/tazobactam and CLSI breakpoints for meropenem. Multilocus sequence typing was performed among baseline and post-baseline pairs; pulsed-field gel electrophoresis was used for Serratia marcescens and Proteus mirabilis isolates. Emergence of non-susceptibility (EoNS) was defined as the isolation of a non-susceptible post-baseline organism with the same sequence type (ST) as the susceptible baseline organism; in contrast, a non-susceptible post-baseline isolate with a different ST was considered to represent the acquisition of a different strain of the same species (ie, new infection, not EoNS). EoNS was compared between ceftolozane/tazobactam and meropenem treatment arms.

Results: Among susceptible PsA isolates at baseline, EoNS was noted in 1 of 61 (1.6%) isolates in the ceftolozane/tazobactam arm versus 13 of 58 (22.4%) in the meropenem arm. Two additional post-baseline PsA isolates in each of the ceftolozane/tazobactam and meropenem arms were non-susceptible but had different STs. In the meropenem arm, the predominant resistance mechanism observed among non-susceptible-PsA isolates was OprD loss/decrease; elevated MexXY-OprM expression was also noted.

Among susceptible ENT isolates at baseline, EoNS was noted in 6 of 189 (3.2%) isolates in the ceftolozane/tazobactam arm (3 S. marcescens, 2 Klebsiella pneumoniae, and 1 Enterobacter cloacae) versus 4 of 192 (2.1%) in the meropenem arm (4 K. pneumoniae). Seven and 5 additional post-baseline ENT isolates in the ceftolozane/tazobactam and meropenem arms, respectively, were non-susceptible but had different STs.

Conclusions: EoNS was more common among PsA isolates in the meropenem arm compared to the ceftolozane/tazobactam arm, but was rare among ENT isolates in both arms.

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Abstract 1216

What is the role of colonisation by carbapenem-resistant Enterobacteriaceae in older people who live in nursing homes? A multi-centre study

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Background: Carbapenem-resistant Enterobacteriaceae (CRE) infections are a worldwide priority. These events are more frequent in elder people. It is known the prevalence of CRE colonization at hospital environment. However, real-life data from other context as nursing homes is still unknown. The aim was to measure the CRE colonization (CREc) rate in institutionalized elders. Secondary objective was to assess linked factors with CREc and new CRE infections during follow-up.

Materials/methods: Prospective observational study which included residents from 6 geriatrics from Buenos Aires City [Argentina], between November 2018 and November 2019. Patients were screened by swab collections (rectal, axillar and inguinal) to evaluate CREc. Chromogenic agar cultures for CRE and molecular techniques for blaKPC, blaNDM and blaOXA were used. We identified possible linked variables with CREc and subsequent infections at the beginning, and after 12-month follow-up. These centers did not apply restrictive policies for admission or contact precautions. Also, these institutions did not assist patients who required mechanical ventilation. p<0.05 was considered significant.

Results: 205 patients were recruited. 77.1% were women, the median age was 87 years (IQR11) and the median length of stay was 26 months (IQR39.8). Median of Katz-Score was 2 (IQR2) and Charlson-Index was 5 (IQR2). At baseline, 17.1% was admitted at hospital wards the previous year and 9.8% had taken antimicrobials the previous month. The initial CREc prevalence was 1.46%. Colonized patients had not shared the same room. During follow-up 11.2% died (n=23); none of them due to CRE infections. It is remarkable that none of colonized patients died. Among survivors, CREc rate was 2.19% (OR 0.66, p=0.60 vs. the initial cohort). No CRE infections were detected. In multivariate analysis, using of antibiotics the previous month was the only linked factor (OR 2.9, CI95% 1.3-737.7, p=0.03). Surprisingly, living with previously colonized residents did not lead to the acquisition of new CREc.

Conclusions: A relatively low CREc rate was observed. Also, prior antibiotic use was associated with this condition. These findings are unprecedented in our continent. Our data suggest that not applying contact precautions for CRE in this scenario could be a safe practice.

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Genotyping, phylogenetic analysis and in vitro antifungal susceptibility profile of clinical isolates of Neoscytalidium species

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Background: The genus Neoscytalidium is mainly distributed in (sub) tropical areas which principally have been described as phytopathogens. However, there are several reports of human infection caused by Neoscytalidium through direct or indirect contact with contaminated plants or soil. The pathogenicity of Neoscytalidium species is not well-known. On the other hand, because of the rarity and emergence of this organism, and no effective treatment approaches, the accurate diagnosis would be critical for therapeutic strategies.

Materials/methods: During two years (from October 2016 to September 2018), all patients with critical underlying conditions referred to the Reference Center for Tuberculosis and Pulmonary Diseases of Iran, Tehran, Iran were included in the study. The isolates of Neoscytalidium species obtained from deep clinical specimens of patients were collected. Partial sequences of five loci (the ITS region, D1/D2 domains of 28S rRNA gene, beta tubulin, elongation factor 1α and chitin synthase genes) of these isolates were analyzed. Phylogenetic analysis of the isolates was also evaluated. In-vitro antifungal susceptibility testing of the isolates against 16 antifungal agents was performed according to the Clinical & Laboratory Standards Institute (CLSI) M38-A2 guideline.

Results: In general, out of 640 clinical samples, 13 (2.0%) were positive for Neoscytalidium species growth, of which 8 isolates were characterized as N. dimidiatum and 5 isolates as N. novaehollandiae according to ITS sequencing. The sequence alignment of 1846 bp in 13 isolates identified nine polymorphic sites (0.49%), representing two sequence types (ST1 and ST2). All of eight N. dimidiatum strains and five N. novaehollandiae species were detected as ST1 and ST2, respectively. The phylogenetic analysis of ITS sequences revealed 2 clades. In addition, we observed the highest in vitro antifungal activity against both Neoscytalidium species by luliconazole, followed by micafungin, amphotericin B and anidulafungin.

Conclusions: This is the first report of N. novaehollandiae isolation from deep clinical samples. One unique genotype could be detected among the studied isolates in each of the species using the mentioned loci. LUL represented the lowest MIC against all isolates which could propose as a good topical antifungal candidate against Neoscytalidium superficial infections.

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The non-tuberculous mycobacteria experience: a single-centre study in Ireland

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Background: Recent studies suggest the increasing prevalence of non-tuberculous mycobacteria (NTM) pulmonary disease (PD). However, NTM is not a reportable disease in Ireland and national data is not available regarding the prevalence of disease. We looked at our NTM isolates from January 2013 to July 2018 and the profile of patients whose care was based in the tertiary care hospital where the study was performed.

Materials/methods: A record of NTM isolates from January 2013 to July 2018 was collected via the laboratory electronic records. Respiratory isolates belonging to patients whose care is based in the tertiary referral hospital was separated for further analysis of patient’s demographics via patient’s electronic record. Patients with at least 1 respiratory isolate were included in the demographic analysis. Identification of Mycobacterium isolates to species level was done by Genotype Mycobacterium CM (Hain-Lifescience). Drug susceptibility testing (DST) was done at a reference laboratory in Scotland.

Results: In the study period, we had 116 isolates in 71 patients. 12 M.chimaera isolates were excluded from this study. Our NTM isolates composed of: Mycobacterium avium complex 45.9%, M.kansasii 8.0%, rapid growing mycobacteria 28.3% and slow growing mycobacteria 13.3%. 49 isolates in 36 patients were included in the analysis of patient’s demographics. 45 of these isolates were from respiratory samples (24 sputum and 21 bronchoalveolar lavage), 1 from a bone marrow biopsy, 1 from tonsillar tissue, 1 from a groin abscess aspirate and 1 from cerebro-spinal fluid. 75% (27/36) of patients had pre-existing pulmonary disease and 30.6% (11/36) were immunosuppressed. The ATS/IDSA diagnostic criteria for NTM lung disease was fulfilled in 27.8% of patients. The microbiologic criteria were fulfilled in 66.7% of patients. 15 patients had radiological changes consistent with nodular-bronchiectatic disease and 5 had changes consistent with fibrocavitary disease. 23.7% (9/38) patients received treatment for NTM disease. 6 had NTM PD and 3 had disseminated disease. The median age of our patients was 61.5 years. 50% of the patients were female.

Conclusions: NTM disease is diverse with regional differences. Our study adds to the available data on NTM isolated from clinical specimens and NTM disease in Ireland.

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Cost-benefit analysis comparing trough, two-Level AUC, and Bayesian AUC dosing for vancomycin

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Background: Trough levels have been demonstrated to be inadequate surrogates for vancomycin exposure, with troughs of 15-20 mg/L associated with increased rates of nephrotoxicity while minimally improving outcomes. Newer dosing methods provide clinical benefit, but with uncertain costs. The objective of this study was to quantify the cost benefits of using two-point or Bayesian AUC vs. trough dosing for patients treated with vancomycin.

Materials/methods: A cost benefit analysis from the institutional perspective was conducted utilizing a decision tree to model the probabilities and costs of acute kidney injury (AKI) associated with vancomycin administered over 48 hours up to 21+ days. Costs included obtaining vancomycin levels, pharmacy time, AKI hospitalization costs, and Bayesian software costs. Probabilities and costs were obtained from primary literature, the Healthcare Cost and Utilization Project National Inpatient Sample, the US Bureau of Labor Statistics, and manufacturer-provided quotes for software costs. Incremental costs were calculated for each strategy in 2019 US Dollars. Robustness of results was assessed via one-way sensitivity analyses varying probabilities and costs in the model.

Results: In the base-case model, two-point AUC vs. trough saved an average $847 per patient encounter. Bayesian AUC vs. trough saved an average $2066 per patient encounter. This translates into annual cost-savings of $846,810 and $2,065,720 for two-point and Bayesian methods vs. trough respectively, assuming 1000 vancomycin-treated patients per year. In one-way sensitivity analyses, “Probability of AKI, 48 Hours to 7 Days” and “Probability of Discharge or Death, 48 Hours to 7 Days” were the most sensitive parameters in the model. Assuming a budget of $100,000 per year for Bayesian software, an institution would need to treat >41 patients with vancomycin for at least 48 hours to break even. At a budget of $20,000 per year, >10 patients would need to be treated with vancomycin to achieve a break-even cost.

Conclusions: There are significant institutional cost-benefits using two-point AUC or Bayesian methods over trough dosing, even after accounting for the annual costs of Bayesian programs. The potential to decrease rates of AKI, improve clinical outcomes, and reduce costs to the institution strongly warrants consideration of newer dosing methods for vancomycin.

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**Abstract 1224**

**Exebacase resensitises methicillin-resistant *Staphylococcus aureus* to oxacillin in a rabbit model of infective endocarditis**

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**Background:** Our recent in vitro data demonstrated that exposure of MRSA to exebacase results in synergy with β-lactam antibiotics and a "resensitization" to these agents, i.e., lowering the MRSA β-lactam MICs into the CLSI "susceptible range". To understand the in vivo impact and relevance of the resensitization, we used a rabbit model of MRSA IE to compare treatment with OXA alone vs treatment with exebacase in addition to OXA.

**Materials/methods:** A indwelling transcarotid artery-to-left ventricle catheter-induced model of aortic valve IE in rabbits utilizing MRSA strain MW2 (USA400) was used. Animals were treated with OXA [50 mg/kg, IM tid x 4 d] alone or with one of two single-dose regimens of exebacase [0.7 or 1.4 mg/kg; IV]. Vehicle controls and exebacase alone were included. At 24 h after the last dose of OXA, cardiac valve vegetations, spleens and kidneys were removed and quantitatively cultured. Vegetations were parallel-plated on media supplemented with exebacase over a range of concentrations, and resulting colonies were subcultured, and tested for exebacase and OXA MICs.

**Results:** Both single-dose regimens of exebacase [0.7 and 1.4 mg/kg] administered in addition to OXA significantly reduced MRSA counts by 5 log₁₀ cfu/g tissue (p<0.0001) compared to OXA treatment alone, exebacase alone, and growth controls. This marked reduction in target tissue MRSA CFUs is consistent with resensitization in vivo (enhanced OXA-mediated killing). Bacteria recovered from vegetations following exebacase + OXA treatments did not exhibit lower OXA MICs, however the majority (>98%) of isolates demonstrated repeatedly reduced exebacase MICs (from 1 to ≤0.5 µg/mL). Bacteria recovered from vegetations exposed to exebacase alone exhibited up to >16-fold reductions in OXA MICs (from 32 µg/mL to <2 µg/mL).

**Conclusions:** In this rigorous model of endovascular infection, the addition of exebacase + OXA, significantly reduced MRSA counts in all target tissues. The observed efficacy may be driven by both the resensitization to OXA and the increased susceptibility to exebacase. The striking ability of exebacase to resensitize MRSA to OXA may have important therapeutic implications and is a potentially promising approach to combat and "reverse" antimicrobial resistance.

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Abstract 1225

**Overuse of antibiotics in primary care: a secondary analysis of standardised patient studies across four low- and middle-income countries**

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**Background:** Antibiotics are largely prescribed in primary care globally. However, an accurate assessment of the extent of inappropriate use is limited by the low quality of available data, especially in low- and middle-income countries (LMICs). Standardized patient (SP) studies offer more insights, since diagnoses are fixed, by design, and inappropriateness of antibiotic use is easier to determine.

**Materials/methods:** We performed a pooled analysis of data from 10 cross-sectional SP studies implemented between 2010 and 2019 to estimate the proportion of patients receiving antibiotics across primary care settings in China, India, Kenya and South Africa. In all studies, SPs portrayed clinical conditions that are commonly encountered in primary care and for which antibiotics should not be given (watery diarrhea, presumptive tuberculosis, angina, asthma, upper respiratory illness). The dataset included information on drug prescription/dispensing for each SP-provider interaction, along with characteristics of providers (qualified or not), facilities (urban/rural, public/private) and cases presented. We analysed overall antibiotic use as the primary outcome and performed stratified analyses to evaluate differences over important variables of interest.

**Results:** Of 6,083 SP-provider interactions in health facilities and 2,722 in pharmacies, 2,928 (48.1%; 95%CI: 46.9-49.4) and 374 (13.7%; 95%CI: 12.5-15.1) respectively resulted in inappropriate use of at least one antibiotic. Access-group antibiotics (mostly penicillins) were predominantly used in Kenya and South Africa (85% and 74% of total antibiotics used) but use of Watch-group antibiotics (especially quinolones and certain cephalosporins) was disproportionately high in China (33%) and India (49%). Across SP conditions in health facilities, 1293/2253 (57.4%; 95%CI: 55.3-59.4) presumptive tuberculosis patients, 490/997 (49.1%; 95%CI: 46.0-52.3) paediatric diarrhea cases, 330/718 (46%; 95%CI: 42.3-49.6) asthmatics, and 169/955 (17.7%; 95%CI: 15.4-20.3) subjects with angina received antibiotics. Factors associated with increased antibiotic use included higher provider qualification (aOR 2.46; 95%CI: 2.16-2.81), urban location (aOR: 1.34; 95%CI: 1.17-1.52) and private sector (aOR: 1.78; 95%CI: 1.38-2.28).

**Conclusions:** Antibiotics, including a substantial proportion of those with a high potential for selecting resistance, are frequently used without indication across primary care settings in 4 countries, and – unexpectedly - providers with higher qualifications were more likely to misuse antibiotics. Why this may be so requires further research.

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Comprehensive proteomics and active immunisation reveals that extracellular vesicles derived from Streptococcus equi subspecies equi as an effective candidate for vaccine platform

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Abstract 1229

Background: Strangles caused by Streptococcus equi subspecies equi (S. equi) is a contagious disease, which can cause economic losses to the equine industry. Therefore, vaccine-based prevention has been recommended. Extracellular vesicles (EVs) are attractive novel vaccine targets because EVs contain many surface proteins, which are antigenic and keep intact form in EV. In this study, we purified EVs from S. equi and performed proteomic analysis to identify antigenic proteins. Then, we confirmed EVs of S. equi as a potential vaccine candidate by vaccine trial.

Materials/methods: For the preparation of purified extracellular vesicles (EVs), we used a QuixStand benchtop system and differential centrifugation method. EVs were quantified using microBCA reagent. Identification and purification purity of the EVs was confirmed by transmission electron microscope (TEM). The vaccination reagents were prepared by mixing the EVs with Freund’s Complete Adjuvant. The 6 weeks female blab/c mouses were divided into two groups [intraperitoneal, intranasal] and were immunized with vaccine reagents for three times on day zero, seven, and fourteen. For active immunization studies, the challenge with LD90 of S. equi occurred day seven after the last immunization (day 21).

Results: We confirmed purity of EVs by TEM and LC-MS/MS analysis. The EVs of S. equi have a circular form with a double layer and the size of EVs is around 50um to 150um. According to LC-MS/MS results, the EVs had a distinct protein profile from whole cell lysates, such as presence of a large number of membrane proteins. The mouse immunization study confirmed the effective vaccination effect in the intraperitoneal group. When challenged with LD90 of S. equi, the control group died in 24 hours, but in the IP group, 60% of mice were survived during the same time, and finally 20% of mice survived for more than 2 weeks. Immuno-proteomic analysis suggest several candidate vaccine proteins, which were originated from EVs

Conclusions: Our results elucidate the overall proteome profiles of S. equi and provide candidates for potential vaccine targets.

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Abstract 1232

Increase in potentially measles-susceptible young healthcare workers in South Korea

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Background: Healthcare workers (HCWs) are known to be at high risk of infection and transmission of measles virus. Although measles had been eliminated in Korea, the resurgence of measles outbreaks related to imported and import-associated case occurred among HCWs. The measles immunity of HCWs was evaluated for vaccination.

Materials/methods: We evaluated the seroprevalence of measles in HCWs in a tertiary university hospital, Wonju, Korea. A total of 2,456 HCWs born from before 1967 to 2000 underwent antibody test using enzyme immunoassay. In Korea, a 2-dose of measles-containing vaccine (MCV) was implemented in the national immunization program (NIP) in 1997. The catch-up program was performed targeted 1985-1993 birth cohort in 2001. According to the policy of NIP, the birth cohort was categorized into A) before 1967, B) 1968-1984, C) 1985-1993, D) after 1994.

Results: The overall seropositivity of measles was 78.3% (95% confidence interval, 76.7 - 79.9). According to birth cohort, the seropositivity as follows; A: 251 of 253 (99.2%), B: 597 of 620 (96.3%), C: 731 of 867 (84.3%), D: 345 of 716 (48.2%). The seropositivity of measles is showed as figure 1.

Conclusions: Young HCWs born after 1994 showed lower seropositivity of measles although 2-dose of MCV. This trend may be related to limitation of vaccine-induced immunity without natural boosting by the wild virus.

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Factors associated with low uptake of HIV testing among middle aged 15-17 adolescent girls in Uganda

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Background: There are significant gaps in the HIV clinical cascade among young people in terms of reaching the 90–90–90 targets set by Joint United Nations Programme on HIV and AIDS. The impact of recent interventions on uptake of HIV testing among women 15-24 years is unknown. To inform efforts in the implementation of 'test-and-treat', we draw on data collected by Uganda Demographic Health Survey 2016 to assess rate of HIV testing uptake and associated factors among young women aged 15–24 years in Uganda.

Materials/methods: UDHS 2016 data was analysed. Univariate analysis was used summarize rate of HIV testing uptake among women 15-25 years. Bivariate analysis to examine associations between socio-demographic factors, HIV knowledge, socio-cultural factors and outcome variable. A complete case analysis was used and missing observations for women were disregarded. All variable with p< 0.2 were included in the multivariate analysis. Using the backward elimination strategy, variables significant at p <0.05 were identified and included in the final model. Statistical analyses were be performed using the Stata version 14

Results: The overall mean age of the study participant’s was 19.3 ± 2.88 years. Uptake of HIV testing was observed to be associated with age group, secondary/higher education, marital status, being employed year-round, media exposure, and age at sexual debut, number of lifetime sexual partners and level of HIV knowledge. Young women with a high level of HIV knowledge were 3.65 (95% CI: 1.68, 7.96) times more likely to uptake HIV testing when compared to those with a low level of HIV knowledge. Compared to those with no lifetime sexual partners, young with one reported lifetime sexual partner were 3.76 (95%CI: 2.88, 4.90) times more likely to uptake HIV testing; those with two partners 3.89(2.86, 5.28) times more likely and 5.53(4.13, 7.39) times more likely to uptake HIV testing among those with 3 or more lifetime sexual partners

Conclusions: There was significant improvement in HIV testing uptake among women 15-24 years, uptake among middle adolescents remained very low. Local and international implementing partners should focus their efforts to promoting HIV testing uptake among middle adolescents

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Emergence of blaNDM and mcr-1 positive pan- and extremely-drug resistant bacterial infections in patients with renal diseases

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**Background:** Infectious diseases are second most common cause of mortality among chronic kidney disease (CKD) patients. With emergence and dissemination of resistance genes like blaNDM and mcr-1, for β-lactam antibiotics and colistin respectively, treatment is becoming difficult. This study aimed to screen the patients with renal diseases for bacterial pathogens and perform their antimicrobial drug resistance profiling.

**Materials/methods:** 100 urine samples from patients with renal diseases (diabetic nephropathy and incompatible renal transplant) admitted in tertiary care hospital, SGPGIMS, India were screened between 2016-2018. The bacterial strains were isolated using standard microbiological techniques. Antibiotic sensitivity testing was done by Kirby-bauer disc diffusion method. The minimum inhibitory concentrations were determined by E-test strips and antibiotic resistance genes were screened by PCR and Sanger sequencing.

**Results:** Twenty of 100 urine samples were positive by culture (20%). Of these, 5/20 (25%) were positive for Gram positive bacteria while 14/20 (70%) were positive for Gram negative bacteria. One sample (5%; 1/20) had both Gram positive and negative bacteria. Among Gram positive, *Enterococcus* sp. and coagulase-negative *Staphylococcus* were dominant while among Gram negative, dominant species were *Enterobacter cloacae*, *Escherichia coli*, *Klebsiella pneumoniae*, *Providencia rettgeri*, *Morganella morganii* and *Pseudomonas aeruginosa*. Antibiotic sensitivity screening revealed that all these were multidrug resistant. Two isolates (*Enterobacter cloacae* and *Klebsiella pneumoniae*) were pan-drug resistant, while one isolate was extremely-drug resistant (*Providencia rettgeri*). Both pan-drug resistant isolates harboured blaNDM-1 gene while in *Klebsiella pneumoniae* isolate Oxa-48 gene was co-harboured. Transmissible colistin resistant gene mcr-1 was present in extremely drug resistant isolate.

**Conclusions:** Extremely-drug resistant isolate was resistant to all antibiotics and harboured the transmissible colistin resistant gene mcr-1. Emergence of pan-drug and extremely drug resistant bacteria in patients suffering from renal diseases is a matter of concern. There are limited or no options available for treatment of such infections.

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Abstract 1239

The clinical application of FILMARRAY respiratory panel in children with acute respiratory tract infections

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Background: The Filmarray respiratory panel (FARP) can reliably and rapidly identify viruses and bacterial pathogens. This study is to evaluate the performance and clinical significance of FARP in children with acute respiratory tract infections (ARTIS).

Materials/methods: A total of 90 nasopharyngeal secretion (NPS) samples from children with ARTIS were enrolled. The FARP assay for 17 pathogens and direct fluorescence assay (DFA) methods for 8 pathogens were performed to analyze these samples. Clinical data of all patients was also collected and evaluated.

Results: Among the 90 samples, 58 samples (64.4%) were positive for 13 pathogens by FARP and 18 positive samples were detected with multiple-virus (31.3%, 18/58). Human rhinovirus/enterovirus (21.0%, 17/58) were predominant pathogen, followed by adenovirus (18.5%). Higher proportions of various pathogens were identified in the infant and toddler (0–2 years) groups with human rhinovirus/enterovirus being mostly virus. Adenovirus were common in the group aged 3–5 years, but only three pathogens including M.pneumoniae, respiratory syncytial virus, and adenovirus were also found in age group (6-14 years). Among 58 FARP positive patients, there were no significant difference in length of hospitalization stay, hospitalization cost, use of anti-virus, rate of secondary infection, and clinical outcome between single organism and multiple organism group (P>0.05), but significant differences were in antibiotic prescription and use of hormone (P<0.05).

Conclusions: This study demonstrated that FARP can provide the rapid detection of respiratory virus and atypical bacteria for children, especially with severe respiratory tract infections.

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Risk factors and clinical manifestations of Group B streptococcal invasive infection in adult population

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Background: The objective of this study is to determine clinical manifestations and risk factors of adult patients who are not pregnant with invasive group B streptococcal (GBS) infection.

Materials/methods: Retrospective study was conducted from January 2014-August 2019. Patients with positive blood culture and/or sterile fluids for GBS were included. Clinical history was consulted to identify underlying diseases, clinical syndrome and focus of infection. Microbiological diagnosis was made by conventional culture of sterile liquids and/or blood culture [BACTEC FX, BD®]. The identification was made by MALDI Biotyper [Bruker®] and the sensitivity following the CLSI criteria.

Results: 72 episodes were diagnosed in 69 patients, which 2 had more than one episode in the study period. 41 (59.42%) were men, with a mean age of 70.07 years (SD ± 16.58 years). 43 (62.32%) were > 70 years old.

63 (91.30%) patients had underlying disease: 43 (68.20%) cardiovascular disease, 24 (38.10%) diabetes mellitus, 19 (30.16%) renal failure, 18 (28.57%) solid organ tumour, 11 (17.46%) respiratory disease, 5 (7.94%) hepatopathy, 5 (7.94%) onco-hematological disease and 1 (1.59%) immunosuppressive treatment.

GBS isolation occurred in: 57 (79.17%) blood, 10 (13.89%) abdominal fluid, 3 (4.17%) joint fluid and 2 (2.78%) pleural fluid. There was no cerebrospinal fluid isolation.

In the case of bacteraemia (57), 17 (29.82%) had origin in skin, 10 (17.54%) pneumonia, 4 (7.02%) abdominal focus, 3 (5.26%) urinary focus and 2 (3.51%) arthritis. In 21 (36.84%) bacteraemia was primary. Three (5.26%) of these patients had complications: 2 (3.51%) endocarditis and 1 (1.75%) spondylodiscitis and meningoencephalitis. In episodes without bacteraemia (15), 10 (13.89%) had abdominal infection, 3 (4.17%) arthritis and 2 (2.78%) respiratory infection.

The 30-day mortality was 17.39%. Nine of the 12 deaths (75%) were >70 years old, and the mortality rate was 20.93% (9/43) in this population.

All GBS isolates were sensitive to penicillin.

Conclusions:
- 79% were bloodstream infection, with the skin being the primary focus of the infection.
- The most common underlying diseases were cardiovascular disease and diabetes mellitus.
- Invasive GBS infection in non-pregnant adults mainly affects patients over 70 years of age, with mortality in this population being 20.93%.

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Abstract 1250

**Comparison of three chromogenic agars for the detection of Candida auris**

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**Background:** Candida auris is a newly emerged pathogen that spreads easily and is highly resistant. To prevent transmission and control outbreaks early and sensitive detection is necessary. According to Dutch guidelines every patient that has been hospitalized abroad recently, is cultured for highly resistant microorganisms upon hospital admission in the Netherlands. To determine which medium should be added to this screening for the detection of *C. auris*, we compared three ready-made chromogenic yeast agar plates.

**Materials/methods:** BD BBL Chromagar Candida Medium (BD Diagnostics), chromID Candida (bioMérieux) and Oxoid Brilliance Candida agar (Thermo Fisher) agar plates were each inoculated with standardized suspensions of *Candida albicans*, *Candida parapsilosis*, *Candida krusei*, *Candida glabrata*, *Candida tropicalis*, *Candida haemulonii*, *Candida lusitaniae*, Trichosporon mucoides and three strains of *C. auris*. Colony colours and sizes were evaluated after 24, 48 and 72 hours of incubation according to the manufacturers’ instructions. We also cultured on each agar a mix of four *Candida* species including *C. auris.

**Results:** On all three media some strains needed 48 hours of incubation to show visible growth. On all three media the colony colours matched the manufacturers’ listing and were stable after 72 hours of incubation. Colonies were smaller on Brilliance Candida agar than on the other media and cream coloured or white colonies were harder to detect on this opaque plate. Different yeast species in a mix were easiest to distinguish on BBL Chromagar Candida Medium due to the different colony colours.

**Conclusions:** *C. auris* grew with uncoloured colonies on all tested chromogenic yeast agars. As long as a specific *C. auris* selective agar is not available, we found that of the three tested agar media BD BBL Chromagar Candida Medium is the best choice to quickly distinguish between possible *C. auris* colonies and other yeasts, especially in a mixed culture. The development of a selective and differential *C. auris* agar is urgently needed.

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Abstract 1251

Implementation of appropriate antibiotic prophylaxis in surgery: high benefit with no risk
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Background: Extended surgical prophylaxis is one of the most common problems in antimicrobial stewardship. Implementation of the shorter duration of prophylaxis is necessary but could be avoided by the fear of surgical site infections (SSIs). Therefore, we aimed to demonstrate the no harm of the shorter duration in surgical antibiotic prophylaxis on the SSIs.

Materials/methods: This study was performed in American Hospital and Koc University Hospital, which are under the umbrella of the Vehbi Koc foundation. We prepared and implemented local surgical prophylaxis guideline for thoracic surgery in January 1, 2015 to decrease inappropriate surgical prophylaxis. Infection control team followed up the process prospectively based on “surgical prophylaxis document” filled in for each case and discussed the data with surgical team, monthly. We compared pre-intervention (January 1, 2011 to December 31, 2014) and post-intervention period (January 1, 2015 to December 31, 2018) in terms of appropriate type, dose and duration of antibiotic use and healthcare associated infections.

Results: In total 1460 patients were evaluated between January 1, 2011 and December 31, 2018 that were operated by thoracic surgery team. Antibiotic prophylaxis was given in 82% of the patients. Inappropriate prophylaxis use decreased from 92% to 14% (p<0.001). The mean duration of antibiotic prophylaxis declined from 60 hours to 23.6 hours, and there was no SSIs in both periods (Table).

Conclusions: We demonstrated that by implementing local surgical prophylaxis guideline, duration of prophylaxis and inappropriate prophylactic antibiotic use decreased without increase in SSIs. Our study results provide evidence for the implementation of appropriate surgical prophylaxis.

Table. The appropriateness of surgical site prophylaxis

<table>
<thead>
<tr>
<th></th>
<th>2011-2014 n=547 (%)</th>
<th>2015-2018 n=913 (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>228 (42)</td>
<td>376 (41)</td>
<td>0.851</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung cancer</td>
<td>149 (27)</td>
<td>332 (36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lung nodule, tumor, cyst</td>
<td>123 (23)</td>
<td>229 (25)</td>
<td>0.286</td>
</tr>
<tr>
<td>Hemothorax and pneumothorax</td>
<td>78 (14)</td>
<td>79 (9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of prophylaxis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean hour [ss]</td>
<td>60 [33]</td>
<td>23.6 [23]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inappropriate prophylaxis</td>
<td>404 [92]</td>
<td>99 [14]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Extended prophylaxis</td>
<td>312/385 [81]</td>
<td>47/31 [6]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inappropriate dose</td>
<td>138 [31]</td>
<td>28 [4]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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**Abstract 1255**

**Filamentous bacteriophage (Pf-8) in Pseudomonas aeruginosa isolates belonging to the international cystic fibrosis clone (CC274)**

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**Abstract third-party references:** GEMARA-Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC)/Spanish Network for the Research in Infectious Diseases (REIP)

**Background:** Cystic fibrosis (CF) chronic respiratory infections are mainly caused by *Pseudomonas aeruginosa*. Bacteriophages of the genus *Inovirus* are filamentous and do not lyse host cells, but they establish a persistent association with the host, producing and releasing phage particles from the growing and dividing host cells and affecting the virulence. In *P. aeruginosa* isolates a group of related filamentous bacteriophages called the “Pf-like” phages have been described (Pf1, Pf4, Pf5, Pf6, Pf7). We analysed the presence of a new “Pf-like”, Pf8 phage, in 25 *P. aeruginosa* genomes belonging to the clonal complex (CC274) from CF-patients.

**Materials/methods:** All isolates had been previously classified within the CC274, 10 from Australian CF-patients and 15 from Spanish patients, all were CF isolates except PAMB148, which was a blood isolate. Isolates were recovered during an 18-year period (1995-2012). Whole-genome sequencing was developed by Illumina MiSeq benchtop sequencer with MiSeq reagent kit v2 (Illumina Inc., USA) and “de novo” assembled using Velvet v1.2.10 (https://www.ebi.ac.uk/~zerbino/velvet/). Bacteriophage genome analysis (PHAST, PHASTER, RAST, HHprep, BLAST-Nucleotide) and protein identification (Protein, CRISPR Finder tools), were performed. The results were confirmed by PCR.

**Results:** We found an intact filamentous bacteriophage (Pf8) in the genome from AUS411.500 isolate. Interestingly, Pf8 showed high protein identity with the Pf4 (*P. aeruginosa* PAO1) and Pf5 (*P. aeruginosa* PA14) filamentous bacteriophages, which have been associated with host virulence via biofilm and dispersal mediated by host cell death (Fig-1). However, new proteins involved in the viral defense were identified in Pf8 bacteriophage such as putative toxin-antitoxin module and methyltransferase. Finally, this Pf8 filamentous bacteriophage was located in all strains belonging to CC274 clone with a query cover and percentage of identities around 51%-76% and 97.75%-99.80%, respectively. Only three strains did not have this Pf8 filamentous bacteriophage (AUS034 and AUS037 strains from CF-patients and PAMB148 blood isolate.

**Conclusions:** We described for the first time the Pf8 filamentous bacteriophage [Pf-likes] in the genome of *Pseudomonas aeruginosa* CC274 from CF-patients. This Pf8 showed high protein identity with Pf4 (*P. aeruginosa* PAO1) and Pf5 (*P. aeruginosa* PA14) filamentous bacteriophages which have been associated with the maintenance of *P. aeruginosa* producing biofilm in long-term chronic CF-infections.

**Fig 1.** Schematic representation and identity of filamentous phage Pf1, Pf4, Pf5 and Pf8. Genes are classified by function into assembly and secretion, structural and replication/integration. Dark gray regions represent >90% of nucleotide sequence identity between Pf genomes.

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Abstract 1257

The role of liposome positive charge on immune response generated in BALB/c mice immunized with Leishmania homologue of receptors for Activated C Kinase (LACK) of Leishmania major

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Background: Leishmaniasis is a complex parasitic disease that represents a major public health problem. Despite numerous attempts over the past decades, yet there is no effective vaccine against human leishmaniasis probably due to the lack of suitable adjuvants. In this study, a first generation liposomal-based Leishmania vaccine was developed using Cloned gene of Leishmania Homologue of receptors for Activated C Kinase (LACK) and IL-12. In this liposome structure, the cationic lipid 1,2-Di-oleoyl-3-Trimethylammonium propane (DOTAP) and 1,2-Dioleoyl-sn-Glycero-3-Phosphoethanolamine (DOPE) provides intrinsic adjuvant activity and cholesterol was added as a membrane stabilizer.

Materials/methods: BALB/c mice were subcutaneously (SC) immunized with different nanoliposomal and non-liposomal samples. Immunization was done three times in a four week interval. The immunized mice were then challenged SC with 1×10^6 stationary phase Leishmania major (L. major) promastigotes (50 µl), at 2 weeks after last booster injection.

Results: Towards this goal, we formulated LACK gene based vaccines that with entrapped within cationic liposomes. The liposomes prepared vesicles showed a diameter of about 200-300 nm, a positive zeta potential. The serum antibody responses increased from 0 to 90 days post infection/challenge. Immunized animals showed greater IgG2a levels in comparison to the infected controls. The splenocytes from immunized mice were cultured, stimulated with LACK and analyzed for cytokine profile. The levels of IFN-γ were greater in immunized mice as compared to control mice.

Conclusions: Immunization with liposomes containing DOTAP and/or DOPE in combination with LACK indicate that liposomes might be used as a suitable immunoadjuvant for development of Leishmania vaccine.

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Abstract 1265

Determined the burden of infectious diseases caused by carbapenem-resistant Gram-negative bacteria in Spain

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Background: According to WHO, approximately 4 million patients are affected by nosocomial infections each year in the EU. Carbapenems are reserved for difficult-to-treat Gram-negative infections, but resistance is increasing. The objective was to estimate the clinical and economic burden of nosocomial infections produced by carbapenem-resistant gram-negative (CRGN) pathogens in Spain for 2017.

Materials/methods: Total CRGN infections were estimated by multiplying the total number of hospital discharges, the incidence of nosocomial infections and the percentage of carbapenem-resistant pathogens (Acinetobacter baumannii, Klebsiella pneumoniae, Pseudomonas aeruginosa). Mortality was calculated by multiplying the percentage of deaths attributed to CRGN pathogens and the total estimated number of patients with CRGN nosocomial infections.

Direct cost was estimated by multiplying the number of patients with CRGN infections by the hospital cost of CRGN infections. Indirect costs included productivity loss (PL) due to temporary disability and premature mortality due to CRGN infections. The PL due to temporary disability was obtained by multiplying the length of stay due to CRGN infections by the average wage and adjusting with the unemployment rate. The cost of premature mortality was estimated by multiplying the total number of years of life lost in working age and the average wage, adjusting by the employment rate. Also, Disability-Adjusted Life Years (DALYs) were obtained.

Results: A total of 12,090 patients were estimated to have a CRGN nosocomial infection in 2017 with P. aeruginosa producing the highest mortality.

In Spain, the direct cost of CRGN nosocomial infections was estimated to be 390M€ with P. aeruginosa accountable for 78% of the total direct cost. Indirect costs were estimated to be 82M€. Life years lost due to premature mortality caused by CRGN nosocomial infections were estimated as 192,833, of which 111,369 were years of productive life lost. Finally, CRGN nosocomial infections produced a total of 13,353 DALYs.

Conclusions: CRGN infections produce a high burden of disease. Total cost was estimated to be more than 472M€ in Spain in 2017. Direct cost accounted for 83% of total economic cost and P. aeruginosa was the pathogen that contributed the most to burden of CRGN infections.

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**Abstract 1267**

*Mycoplasma genitalium* infections in men who have sex with men: prevalence and macrolide resistance in north-east Italy

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**Background:** *Mycoplasma genitalium* (MG), one of the most common bacterial pathogens of sexually transmitted infections (STIs), causes non-gonococcal urethritis in man and has been proposed as a cause of proctitis in Men who have Sex with Men (MSM).

The 2016 European guideline on MG infections recommends treatment with Azithromycin or Josamycin in uncomplicated infections. Given the increasing prevalence of macrolide resistance during the last years, Moxifloxacin is recommended as second line treatment.

We aimed to determine the proportion of MSM who had MG in the rectum and the prevalence of macrolide resistance. We compared these data with the prevalence during the previous 3 years.

**Materials/methods:** From February to September 2019, we retrospectively evaluated the prevalence of MG infections in 358 patients from STIs-AIDS Unit. We also evaluated the prevalence of MG during 3 years before. Anal swabs were tested for MG infection using Allplex™ MG & AziR Assay (Seegene). Test simultaneously detects MG and six 23S rRNA mutations associated with macrolide resistance: A2058C, A2058G, A2058T, A2059C, A2059G, A2059T.

**Results:** Overall, the prevalence of MG was 6.7% [24/358]. All positive-MG patients (median age 41 years) did not present symptoms. During 2014-2016 the prevalence was respectively 12.4% [14/113], 17.0% [27/159], 7.4% [23/313].

23S rRNA mutations were reported in 25.0% [6/24] of strains: A2059G substitution accounted for 66.7% [4/6], A2058C for 33.3% [2/6]. Of six resistant-MG patients, five had been treated with Azithromycin for STIs before.

**Conclusions:** To date, there is no data about prevalence of macrolide-resistant MG in Italy. We report a high presence of MG, decreasing over the years, and resistant strains. Our selected patients may be particularly vulnerable to acquire and transmit MG due to their higher risk of STIs and previous macrolide therapy. Given the 25% of resistance, Azithromycin should not be longer considered a first choice for empirical therapy in our selected population.

Therefore, our findings support the routine use of an assay to detect MG and macrolide resistance-associated mutations, as recommended in the European guideline. This will help to limit inappropriate azithromycin treatment and to control antimicrobial resistance progression.

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Abstract 1268

Quality control of therapeutic bacteriophages: the Belgian experience
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Background: The greatest hurdle to the introduction of phage therapy in Western medicine remains the lack of an appropriate legal and regulatory framework. Since 2018, Belgium is implementing a pragmatic phage therapy framework that centers on the unlicensed ad hoc preparation of tailor-made phage medicines. Central to this approach is a two-step quality control of phage active pharmaceutical ingredients (APIs) effectuated by Sciensano.

Materials/methods: API QC consists of the construction of a genetic passport which contains information of phage's lifestyle, genome size and content, and its capacity for horizontal gene transfer. The host bacterium is checked for the presence of active prophages and phage-inducible chromosomal islands. Secondly, each production lot is checked for microbial contamination, endotoxin levels, pH and presence of the specific active component. The obtained results are condensed in a Certificate of Analysis which is returned to the manufacturer, and then transferred to the hospital pharmacy to enable preparation of the formulation upon a physician's prescription.

Results: To date, Sciensano controlled 7 seed lots and 15 production lots of phage APIs. All 7 phages, infecting either Pseudomonas aeruginosa, Staphylococcus aureus and Mycobacterium abscessus, were found to be strictly lytic and non-transducing. All but one propagation strain were approved; One particular P. aeruginosa strain was found to produce the toxin pyocyanine and contained at least two active prophages which were induced during phage production. All approved production lots were of high quality, with no microbial contamination detected so far, and endotoxin levels frequently below the detection limit of 0.5 IU/ml. However, our experience shows that certain hosts are correlated to much higher endotoxin contaminations.

Conclusions: With the implementation of a national regulatory framework, Belgium is enabling the treatment of desperate patients with phages upon prescription of a physician outside compassionate use. The relative small number of QC requests clearly reflect its current limited implementation and its use as agents of last resort. In addition the already obtained QC data, we will present our broader experience with the various aspects surrounding the implementation of phage therapy, including the political and economic context of the personalized approach pursued in our country.

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Characterisation of NDM-producing Klebsiella pneumoniae isolates from different Roman hospitals

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Background: Multi-drug-resistant (MDR) Klebsiella pneumoniae producing NDM carbapenemase is a serious nosocomial pathogen causing a variety of infections. Treatment options are particularly limited, given their intrinsic and acquired resistance genes. The objective of the study was to investigate the molecular epidemiology of clinical K. pneumoniae isolates from different hospitals of the Latium region.

Materials/methods: Between May and September 2019, 7 K. pneumoniae strains were isolated from clinical samples of patients treated in 4 different hospitals. Identification and antimicrobial susceptibility testing were performed using the Phoenix system (BD). Genome sequences were generated by Next Generation Sequencing (NGS) using the Ion Torrent sequencer (Life Technologies). Antimicrobial resistance genes were extracted from the NGS data identified by in silico analysis using the ResFinder webserver. Molecular typing was performed using the core genome MLST (cgMLST) approach (Ridom), which uses 2358 target genes to characterize allelic profile of K. pneumoniae.

Results: All isolates showed an MDR profile; the blaNDM-1 gene was detected in 6/7 isolates, one isolates harboured blaNDM-5 gene variant. The blaOXA-48 was detected in two isolates, which carried additionally the ampC cephalosporinase blaCMY-6; 5/7 isolates were positive for blACTX-M-15. Five different Sequence Types (STs) were detected among the 7 NDM-producing K. pneumoniae: ST11, ST15, ST147, ST383 and ST307. Two strains belonging to ST15 and ST11. Clonal relationships within the STs using the cgMLST scheme showed the presence of 2 complex type, each composed by two isolates belonging to ST15 and ST11. The strains within each cluster showed a very high level of correlation (up to 8 allele differences) and K. pneumoniae strains ST11 were collected from the same hospital. No genetic correlation was observed for the remaining 3 isolates.

Conclusions: The emergence of NDM-producing K. pneumoniae in Italy is a real threat for the public health. There is a need for increased capacity to support surveillance and investigations with NGS to identify high-risk clones and to implement enhanced control measures in order to avoid further spread; the use of gene-by-gene analysis by cgMLST for epidemiological investigations allows an in-depth analysis, owing to its high discriminatory ability in determining clonal relatedness.

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Abstract 1271

Characterisation of KPC-50, a novel transferable KPC-3 variant conferring resistance to ceftazidime-avibactam in a colistin-resistant Klebsiella pneumoniae from Switzerland

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Background: The widespread of KPC-type carbapenemases in Klebsiella pneumoniae most often possessing additional resistance leading to multidrug resistance represent a very high clinical concern. Avibactam, a non-β-lactam inhibitor, is able to restore the efficacy of ceftazidime against KPC producers. However, resistance to the novel ceftazidime-avibactam (CAZ-AVI) association is increasingly reported among clinical strains producing KPC variants.

We described a novel KPC-3 variant, KPC-50, produced by the K. pneumoniae N859 clinical isolate, recovered in 2019 from an intraabdominal abscess of a patient hospitalized in Zürich, Switzerland. This isolate was resistant to carbapenems but also uncommonly resistant to CAZ-AVI.

Materials/methods: The blaKPC-50 and blaKPC-3 genes were amplified and transformed into E. coli TOP10. Antimicrobial susceptibility was performed by the disc diffusion method. Minimum inhibitory concentrations (MICs) were confirmed by broth microdilution and E-test. Further, KPC-X and KPC-3 enzymes were purified with a cation column and using a lab-scale chromatography system AKTA-prime. Finally, kinetic measurements were performed with a spectrophotometer.

Results: The KPC-50 β-lactamase possessed a 3-amino-acid insertion (E-A-V) located between amino acids 276 and 277 compared to the KPC-3 amino acid sequence. Cloning and expression of this plasmid-borne blaKPC-50 gene in Escherichia coli, followed by determination of MIC values and kinetic parameters, showed that KPC-50, compared to those of KPC-3, has an increased affinity to ceftazidime and a decreased sensitivity to avibactam, leading to resistance to ceftazidime-avibactam once produced in K. pneumoniae. Furthermore, KPC-50 exhibited a decrease of its carbapenemase activity. In addition this strain was resistant to colistin by modification of the pmrB gene that governs the lipopolysaccharide biosynthesis.

Conclusions: This report highlights that (i) insertion/deletion in the KPC sequence may be an important evolution pathway for conferring ceftazidime-avibactam resistance in K. pneumoniae, and (ii) the diversity of KPC variants conferring resistance to ceftazidime-avibactam already circulating in Europe.

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Abstract 1272

The guideline compatibility of mucormycosis management: a retrospective review of the case reports from European quality (EQUAL) score perspective

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Background: Mucormycosis is a rare, but life-threatening disease. European QUALITY (EQUAL) score was recently developed that reflects the strongest recommendations from the international guidelines for the management of mucormycosis. Here, we investigated the compliance of the individual diagnostic and treatment approaches with the guideline recommendations in the published case reports.

Materials/methods: A Pubmed search was performed by using the keyword “mucormycosis” between 01 January 2015 and 31 December 2018. Cases with pulmonary and/or rhinocerebral involvement were included in the analysis. Only the items that were clearly described in the case report were scored.

Results: The search revealed 882 publications. A total of 165 cases were included in the study. The median age of patients was 48.5 years (Minimum 1.5, maximum of 77 years). The 96 were male. The most common underlying disease was diabetes mellitus in 82 patients, followed by hematological malignancy in 37 patients. Rhinocerebral involvement was the most common presentation in 84 patients, 68 patients had pulmonary mucormycosis, and 13 had pulmonary and rhinocerebral mucormycosis. The achievable score from the diagnostic approach was 1.31.4, the achieved score was 631 (48.1%). Direct microscopy was performed in only 18 of 44 patients, culture was performed in 33 out of 44 patients who underwent bronchoscopy, fungal culture from biopsy specimen was performed in only 65 of 135 patients who underwent biopsy, and species identification with antifungal susceptibility test was performed in 14 out of 43 culture-positive patients. The achievable score for treatment was 1024 but achieved to 424 (47.3%). Surgical debridement was performed in 95 patients, amphotericin B deoxycholate was first choice antifungal in 30 patients, the dose was lower than 5 mg/kg/day in 15 of 87 patients who received liposomal amphotericin B, none of the patients who received posaconazole or isavuconazole had therapeutic drug level monitoring, and the control of risk factors such as neutropenia, ketoacidosis, hyperglycemia, and corticosteroids was reported in only 37 patients. The mortality rate was 38.8% (64 out of 165).

Conclusions: The case reports achieved to 50% of the achievable scores, approximately. The management of mucormycosis is an area that needs continuous improvement.

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Population pharmacokinetic modelling and simulations to support ceftazidime-avibactam dose selection for paediatric patients with nosocomial pneumonia

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Background: The ceftazidime-avibactam paediatric investigation programme includes one Phase I and two Phase II completed trials in children with complicated intra-abdominal infection or complicated urinary tract infection. A further single-dose Phase I PK trial in children with NP (NCT04040621) is underway. In this analysis, previously reported population PK models were used to guide ceftazidime-avibactam dosage selection for the paediatric NP trial.

Materials/methods: The ceftazidime and avibactam population PK models included 2130 subjects with 9628 samples and 2403 subjects with 14,223 samples, respectively, including 154 and 153 children with 509 and 488 samples, respectively. Both were two-compartment disposition models in which body weight and renal maturation (subjects ≤2 years) or body surface area-normalised creatinine clearance (nCrCL; subjects >2 years) were key covariates predicting ceftazidime and avibactam clearance. The final PK models using NP population effects were used to simulate steady-state exposures and probability of target attainment (PTA) for various ceftazidime-avibactam dosage regimens (1000 NP patients/simulation), and different age and renal impairment categories. Simulations used plasma-free fractions [85% ceftazidime, 92% avibactam] and a joint PK/pharmacodynamic target (achievement of free plasma ceftazidime ≥8 mg/L and avibactam ≥1 mg/L simultaneously for ≥50% of the dosing interval). Adult NP patients were used as reference for matching exposures and PTA.

Results: In simulated paediatric NP patients (age >3 to ≤6 months) with normal renal function, ceftazidime-avibactam 40-10 mg/kg 2-h infusions q8h achieved similar mean exposures to adult patients with normal renal function receiving 2000-500 mg q8h (Table), joint PTA was 98.0% and 95.4% respectively. In simulated paediatric patients (>6 months to <18 years) with NP and normal renal function, ceftazidime-avibactam 50-12.5 mg/kg (capped at 2000-500 mg) q8h achieved ≥91.8% joint PTA with exposures similar to adults with normal renal function. Dose adjustments for paediatric patients with renal impairment of equivalent magnitude as in adults resulted in similar exposures and PTA.

Conclusions: These analyses support evaluation of ceftazidime-avibactam 40-10 mg/kg (>3 to ≤6 months) and 50-12.5 mg/kg (>6 months to <18 years) q8h in paediatric patients with NP and normal renal function, with dose adjustments for renal impairment (nCrCL <50 mL/min/1.73 m²).

Study sponsored by Pfizer.

Table. Predicted steady-state exposures (geometric mean) and PTA in paediatric patients with NP and normal renal function following administration of ceftazidime-avibactam (40-10 mg/kg or 50-12.5 mg/kg q8h) and adults with NP receiving the standard ceftazidime-avibactam dose

<table>
<thead>
<tr>
<th>Age group</th>
<th>Dose1 (ceftazidime-avibactam)</th>
<th>Cmax,0-3 h (mg/L)</th>
<th>AUC0-3 h (mg h/L)</th>
<th>Cmax,0-24 h (mg/L)</th>
<th>AUC0-24 h (mg h/L)</th>
<th>Cmax,0-3 h Ratio to adults</th>
<th>AUC0-3 h Ratio to adults</th>
<th>Cmax,0-24 h Ratio to adults</th>
<th>AUC0-24 h Ratio to adults</th>
<th>Joint PTA (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;3 months to ≤6 months</td>
<td>40-10 mg/kg q8h</td>
<td>71.4 (19.4)</td>
<td>745 (20.2)</td>
<td>1.10</td>
<td>1.05</td>
<td>12.9 (53.6)</td>
<td>121 (43.5)</td>
<td>1.20</td>
<td>1.15</td>
<td>98.0</td>
</tr>
<tr>
<td>6 months to ≤1 year</td>
<td>50-12.5 mg/kg q8h</td>
<td>80.4 (19.4)</td>
<td>769 (29.9)</td>
<td>1.24</td>
<td>1.08</td>
<td>14.9 (52.1)</td>
<td>132 (43.2)</td>
<td>1.46</td>
<td>1.26</td>
<td>96.8</td>
</tr>
<tr>
<td>&gt;1 year to ≤2 years</td>
<td>50-12.5 mg/kg q8h</td>
<td>78.2 (10.2)</td>
<td>698 (20.8)</td>
<td>1.17</td>
<td>0.98</td>
<td>14.4 (62.8)</td>
<td>125 (42.8)</td>
<td>1.41</td>
<td>1.10</td>
<td>92.3</td>
</tr>
<tr>
<td>&gt;2 years to ≤4 years</td>
<td>50-12.5 mg/kg q8h</td>
<td>70.4 (21.0)</td>
<td>691 (26.9)</td>
<td>1.17</td>
<td>0.97</td>
<td>13.6 (48.9)</td>
<td>116 (41.3)</td>
<td>1.35</td>
<td>1.12</td>
<td>91.8</td>
</tr>
<tr>
<td>&gt;6 years to ≤12 years</td>
<td>50-12.5 mg/kg q8h</td>
<td>80.9 (19.6)</td>
<td>785 (29.8)</td>
<td>1.24</td>
<td>1.10</td>
<td>15.1 (43.2)</td>
<td>138 (38.0)</td>
<td>1.48</td>
<td>1.30</td>
<td>96.8</td>
</tr>
<tr>
<td>≥12 years to &lt;18 years</td>
<td>50-12.5 mg/kg q8h</td>
<td>71.8 (23.1)</td>
<td>747 (30.4)</td>
<td>1.10</td>
<td>1.05</td>
<td>13.0 (67.5)</td>
<td>121 (51.1)</td>
<td>1.27</td>
<td>1.15</td>
<td>96.7</td>
</tr>
<tr>
<td>Adults with NP (normal renal function)</td>
<td>2000-500 mg q8h</td>
<td>65.1 (31.0)</td>
<td>712 (41.8)</td>
<td>NIA</td>
<td>NIA</td>
<td>10.2 (77.6)</td>
<td>105 (71.8)</td>
<td>NIA</td>
<td>NIA</td>
<td>95.4</td>
</tr>
</tbody>
</table>

1Normal renal function defined as body-surface area normalised creatinine clearance (nCrCL) >50 mL/min/1.73 m² or renal maturation based on post-menstrual age for subjects aged <2 years. All doses administered as 2-h IV infusions. Paediatric doses were capped to a maximum dose of 2000 mg ceftazidime and 500 mg avibactam. Exposure values are geometric mean (95% CI). Limit target (50% T >MIC) for ceftazidime and 1 mg/L for avibactam. AUC0-3 h = area under the plasma concentration-time curve over 24 h at steady-state; Cmax, maximum concentration at steady-state; IV, intravenous; NP, nosocomial pneumonia; PTA, probability of target attainment.

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Abstract 1278

**Antimicrobial resistance and genotypic markers of trimethoprim resistance in *Escherichia coli* and *Klebsiella* spp. isolated from patients with urinary tract infections**

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**Background:** Urinary tract infections are among the most common bacterial infections. Isolation of causative uropathogens and their resistance profiles are not routinely performed, hence antibiotic therapy is often empirical. This study aimed to determine antimicrobial susceptibility of urinary *Escherichia coli* and *Klebsiella* spp. isolates from two Health and Social Care Trusts in Northern Ireland and to assess the use of trimethoprim resistance (*dfrA*) and ESBL-encoding (*bla*TEM) genes as biomarkers for rapid detection of trimethoprim resistance.

**Materials/methods:** Antimicrobial susceptibility of *E. coli* and *Klebsiella* spp. (n=124) to trimethoprim, amoxicillin, ceftazidime, ciprofloxacin, co-amoxiclav and nitrofurantoin was determined by ETEST® and interpreted according to EUCAST breakpoints. The *dfrA* and *bla*TEM genes were detected by PCR while ESBL production was measured using the combined disc method.

**Results:** Trimethoprim resistance was found in 37/124 (29.8%) of the isolates with MIC>32 mg/L. Eighty-one of the 124 isolates (65.3%) were resistant to amoxicillin, while 18/124 (14.5%) were resistant to nitrofurantoin. *DfrA* and *bla*TEM genes were detected in 29/37 (78.4%) and 30/37 (81.1%) of the trimethoprim-resistant isolates respectively. The detection of *dfrA* was highly sensitive in predicting phenotypic trimethoprim resistance (93.6%) and resistance to both trimethoprim and amoxicillin (100%). *Bla*TEM was less sensitive in detecting phenotypic trimethoprim resistance (45.8%). ESBL production was observed in 13/124 (10.5%) isolates and there was no significant association (*P*>0.05) between ESBL production and trimethoprim resistance.

**Conclusions:** This study demonstrates that *dfrA* could be used to determine trimethoprim resistance among urinary *E. coli* and *Klebsiella* spp. and guide the timely prescription of appropriate antibiotics for treatment of UTIs.

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Abstract 1280

Multiple mutations in dihydrofolate reductase gene in cotrimoxazole-resistant *Streptococcus pneumoniae* isolated from HIV adults in a community setting, Tanzania

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**Background:** Cotrimoxazole, a combination of trimethoprim and sulfamethoxazole, is widely used in people living with HIV to prevent opportunistic infections, including pneumococcal infections. Resistance to trimethoprim may render pneumococci fully cotrimoxazole-resistant. This study characterizes the molecular mechanisms of trimethoprim resistance in pneumococcal isolates from newly HIV-diagnosed patients in Dar es Salaam, Tanzania.

**Materials/methods:** A total of 1877 nasopharyngeal swabs were collected from 537 individuals newly diagnosed with HIV at four clinic visits during one-year follow-up in 2017 - 2018. Swabs were screened for pneumococcal colonization. Isolates were identified by colonial morphology on sheep blood agar and optochin susceptibility and serotyped by latex agglutination. Antimicrobial resistance was characterized by disk diffusion, E-test, polymerase chain reaction and sequencing.

**Results:** The majority of the pneumococcal isolates (48/76, 63.2%) were penicillin non-susceptible (MIC 0.06 – 2 mg/ml). Isolates were frequently resistant to cotrimoxazole (80.3%), but less so to chloramphenicol (23.7%), tetracycline (21%), erythromycin (22.4%), azithromycin (18.4%) and clindamycin (10.5%). None were resistant to levofloxacin. Twenty-five percent were resistant to three or more antibiotic classes (multi-drug resistant, MDR). The majority (n=40, 59.7%) were conjugate vaccine (PCV 23) serotypes. Vaccine-type pneumococci were more frequently MDR (OR 7.5, 95% CI 1.55 – 36.27, p = 0.01). There was no difference in cotrimoxazole MIC-values between vaccine- and non-vaccine-types [median 4 for both groups, p=0.9]. Cotrimoxazole-resistant isolates carried from 1 to 11 different trimethoprim-resistance mutations, the majority (n=52) having 6-8 mutations. The most common mutations conferring trimethoprim-resistance were Ile100Leu (100%), Glu20Asp (92%), Glu94Asp (61%), Leu135Phe (57%), His26Tyr (53%), Asp92Ala (53%) and His120Gln (53%). There was no difference in numbers of mutations between vaccine-type (median 5.5) and non-vaccine type pneumococci (median 6, p=0.3). There was no significant association between cotrimoxazole MIC-values and type or number of mutations.

**Conclusions:** *Streptococcus pneumoniae* isolated from newly HIV-diagnosed patients are frequently non-susceptible to penicillin and resistant to cotrimoxazole. Most isolates carried multiple mutations in the *dhfr* gene.

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Epidemiology typing and molecular analysis of vancomycin-resistant Enterococcus faecium in haematological patients

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Background: A long-term increased prevalence of vancomycin-resistant Enterococci (VRE) colonization has been observed in the haematological department of the University hospital Brno (CZ). The aim of this study was to describe the genetic diversity of the local VRE population and determine the nosocomial transmission rate. An additional goal was to focus on establishing a rapid VRE typing method suitable for routine practice.

Materials/methods: Between 06/2019-07/2019, all hospitalized patients in one ward were screened for VRE presence. In total, 99 patients were screened on admission, at discharge and once a week during their hospitalization using rectal swabs. All collected VRE isolates were analysed using mini-MLST and whole genome sequencing (WGS).

Results: In total, 331 samples were taken, from which 24 VRE strains and one linezolid-resistant Enterococcus faecium isolate were isolated from 16 patients (16%, n=99). Using mini-MLST, 22/24 (88%) VRE isolates were identified as MelT55 and 3/24 (12%) as MelT420. In silico MLST was performed and allocated the obtained isolates to 6 ST (ST17, ST80, ST117, ST761, ST787 and one new ST). All isolates were VanA positive, 5 isolates were both VanA and VanB positive. The single-nucleotide variant (SNV) number was determined using SeqSphere+ software and was in a range from 1 to 5,687 within the isolates belonging to the same ST.

Conclusions: The whole genome SNV analysis showed high genetic diversity in the VRE population in our haematology ward. Most patients had their unique strain, indicating a lower rate of transmission than expected considering the generally accepted assumption that hospital transmission is the main source of VRE. Thus, other factors such as ATB treatment or patient’s overall health condition are likely to affect higher VRE colonization rates.

The current mini-MLST scheme does not have sufficient resolution power to distinguish VRE strains within our population. Therefore, we developed a new universal algorithm for WGS data to find variable regions that can be used to extend the existing mini-MLST scheme or to replace it with population-specific markers.

This study was supported by MH CZ - DRO (FNBr, 65269705), NV19-09-00430 and MUNI/A/1395/2019

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Abstract 1290

The in vitro effect of azithromycin on *P. aeruginosa* biofilms

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**Background:** Azithromycin (AZM) is efficient for treatment of chronic *P. aeruginosa* biofilm infection in cystic fibrosis (CF) patients although conventional susceptibility testing according to EUCAST shows resistance to AZM. It has, however, been shown that planktonic *P. aeruginosa* are more susceptible to AZM when tested in RPMI 1640 medium due to increased cell-wall permeability and reduced expression of the MexAB-OprM (van Bambecke).

**Materials/methods:** The aim of this study was to investigate the effect of AZM on planktonic and biofilm *P. aeruginosa* in LB vs RPMI 1640 medium in wild-type (WT) *P. aeruginosa* (PAO1) and two different mutants with relevant phenotypes for chronic infections: the hypermutable (ΔmutS) and the antibiotic resistant phenotype (ΔnfxB) due to the expression of the MexCD-OprJ efflux pump. The effect of AZM exposure for 24h and 72h of young (1 day-old) and mature (3 days-old) biofilms was investigated by establishing the minimal biofilm inhibitory concentration (MBIC₉₀) in the modified Calgary Biofilm Device.

**Results:** The AZM MBIC₉₀ in LB/RPMI1640 on young biofilms treated for 24h was 16/4 µg/ml for PAO1, 32/8 µg/ml for ΔmutS and 256/64 µg/ml for ΔnfxB. The effect of AZM was improved when the treatment was prolonged to 72h, the AZM MBIC₉₀ of young biofilm decreased to 8/1 µg/ml for PAO1, 8/1 µg/ml for ΔmutS and 32/4 µg/ml for ΔnfxB supporting the intracellular accumulation of AZM.

The AZM MBIC₉₀ in LB/RPM1640 on mature biofilms treated for 24h was 256/2 µg/ml for PAO1 and ΔmutS and 16/1 µg/ml for ΔnfxB, and decreased to 4/1 µg/ml for PAO1 and 8/1 for ΔmutS and was measured to 32/4 µg/ml for ΔnfxB with 72h treatment.

**Conclusions:** Our results show that AZM has a better effect on *P. aeruginosa* biofilms in RPMI 1640 than in LB medium and AZM effect is time and concentration-dependent in biofilms, suggesting that prolonged treatment at high dosages is recommended.

We show also that the production of MexCD-OprJ efflux pump is an important resistance mechanism for the in vitro efficacy of AZM on *P. aeruginosa* biofilms. Our results may have implications for susceptibility testing and for the dosing of AZM to CF patients.

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Abstract 1291

**Acinetobacter baumannii complex, the beast of the weakest**

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**Background:** We conducted surveillance for Acinetobacter baumannii (AB) blood isolates. Our objectives were: to describe the prevalence and trends of antimicrobial resistance; to characterize of colistin resistance; to identify risk factors and to provide data for policies and guidelines.

**Materials/methods:** Surveillance was conducted at 12 sentinel academic sites, in South Africa from September 2018 to 2019. Isolates were identified by MALDI-TOF MS. Susceptibility testing was performed on the MicroScan Walkaway System and broth microdilution assay for colistin. Results were interpreted by the CLSI guidelines. PCR assay for mcr 1-5 genes, followed by WGS on the MiSeq Instrument was completed for colistin resistant isolates. Genome assembly and single nucleotide polymorphism analysis, for the pmrCAB operon and the lpxA, lpxC, lpxD and lpxB genes was done in CLC Genomics workbench. Resistome prediction was done with ResFinder and the Comprehensive Antibiotic Resistance Database (CARD).

**Results:** We have received 1823 isolates (43%) with clinical information for 1409 (33%) patients from a total number of 4269 AB isolates. AB was more prevalent in male patients (54%) and in children less than 14 year (40%). Crude mortality was 34%. During hospitalization 54% patients received meropenem and 32% received colistin treatment. The majority of the patients had medical devices (83%); long stay in hospitals (67%); 20% had treatment with carbapenems and 14% with colistin prior to AB isolation. Amongst those with known HIV status (890) 20% were positive. Susceptibility to majority of antibiotic classes was extremely low, from 1 - 14% except for colistin (96%). Of the 45 colistin resistant isolates none harbored the mcr 1-5 genes. A subset of 21 isolates were established with chromosomal non-synonymous mutations in various genes [pmrCAB operon, lpxB, lpxD and lpxC]. Colistin resistance had no impact on patient outcome and no significant difference was noted in patients that died from susceptible versus resistant strains (p=0.689).

**Conclusions:** AB pathogen is a highly prevalent among children in South African hospitals. Low resistance to colistin was chromosomally mediated with no plasmid genes. Risk factors were duration of the stay in hospitals, prior antibiotic use and interventions. High crude mortality in patients with AB is of concern.

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Whole genome sequencing to detect antimicrobial resistance-associated determinants in Staphylococcus epidermidis

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Background: Staphylococcus epidermidis is a common cause of opportunistic nosocomial infections including prosthetic device-related infection. Nosocomial strains are commonly resistant to multiple antibiotics necessitating antimicrobial susceptibility testing of clinically significant isolates to guide treatment. Genotypic prediction of antimicrobial resistance from whole genome sequencing (WGS) has been successfully demonstrated in Staphylococcus aureus. We investigated the accuracy of this method for predicting antimicrobial resistance from WGS in S. epidermidis.

Materials/methods: Thirty nine isolates from orthopaedic device-related infection specimens and 48 carriage isolates (total 87) underwent disc diffusion phenotyping for 13 antibiotics routinely tested in our hospital microbiology laboratory against S. epidermidis. A panel of 27 resistance conferring genes and mutations in 11 housekeeping genes associated with staphylococcal antibiotic resistance was generated from previously published studies. All 87 isolates were sequenced on an Illumina HiSeq. Genomes were assembled de novo using Velvet 2.0 and interrogated using Basic Local Alignment Search Tool (BLASTn) for the presence of resistance conferring genes and mutations. Discrepant results were checked by repeat phenotypic testing and manual inspection of the relevant antimicrobial resistance genes.

Results: A total of 1131 comparisons (13 antibiotics in 87 isolates) were performed. There were 12 (1.06%) major errors (susceptible phenotype, resistant genotype) and 1 (0.09%) very major error (resistant phenotype, susceptible genotype). Overall the sensitivity and specificity of resistance genotype detection were 100% (95% CI 97% – 100%) and 99% (95% CI 98% - 99%) respectively.

Conclusions: These data demonstrate that detection of resistance conferring genes and mutations concord well with current routine phenotyping methods. Major error and very major error rates were within the acceptable limits of <3% and <1.5% respectively stipulated by the United States Food and Drug Administration Guidance for Antimicrobial Susceptibility Test Systems. A validation study is now required to determine if antimicrobial resistance of S. epidermidis is accurate and clinically viable as has been demonstrated previously for S. aureus.

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Transjugular intrahepatic portosystemic shunt and infections: a single-centre retrospective study

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Background: Transjugular intrahepatic portosystemic shunt (TIPS) is a procedure employed in advanced liver disease to reduce portal hypertension and its complications. Few data are available on infectious complications of TIPS, the best described of which being endotipsitis. However, uncertainties remain on the real incidence of other infectious events, including their prevalence and impact on the overall survival.

Materials/methods: We retrospectively identified infections occurred during a 2-year follow-up after TIPS placement in a cohort of patients who underwent this procedure between January 2010 and October 2019 in a large referral hospital. We recorded the microorganism isolates, the antimicrobial agents administered and the mortality rate during follow-up.

Results: Overall, we identified 42 patients subjected to TIPS placement, mostly males (62%) with a mean age of 61.5 years and a median baseline MELD score of 11. The hepatic venous pressure gradient was 23 mmHg before and 10 mmHg after the procedure. Forty (95%) patients received antibiotic prophylaxis concomitantly with TIPS placement: 17 (40%) received ceftriaxone, 16 (38%) cefotaxime, 2 (5%) meropenem, 2 (5%) piperacillin/tazobactam and 1 (2.5%) each ampicillin, amoxicillin/clavulanate and ciprofloxacin. During follow-up, infections occurred in 21 (50%) patients, for a total of 45 events. The most frequently observed were sepsis (33%) followed by urinary tract infections (29%). Pneumonia and acute bacterial skin and skin structure infections accounted for 9% of the events. The most frequently identified microorganisms were Enterobacteriales (39%) followed by Staphylococcus spp., Enterococcus spp. and Candida spp., each accounting for 14% of the events. Overall mortality rate was 19%, 16% in patients who developed infection(s) during follow-up, which was not significantly different from the 22% of those who did not (p=0.5, Fig.1A). The types of infection are shown in Fig.1B.

Conclusions: Infections, particularly sepsis and those caused by Enterobacteriales, were common in patients during the 2-years following TIPS placement. Occurrence of infections did not modify mortality rates.

Figure: Overall survival rates at 2-year and stratified according to the occurrence of infections. (A) Infections recorded during the follow-up period subdivided in 5 time periods (B).

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Development of intravascular microdialysis as a tool for therapeutic drug monitoring and intensive PK studies in children

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1Medical University of Vienna, Department of Clinical Pharmacology, Vienna, Austria, 2University of Vienna, Department of Clinical Pharmacy and Diagnostics, Vienna, Austria

Background: Pharmacokinetics (PK) of antibiotics in children differs considerably compared to adults. However, the limited blood volume of children and the ethical restrictions that are associated with repetitive blood sampling severely hamper PK studies and individualization of therapy by means of dense therapeutic drug monitoring (TDM) in children. Microdialysis (MD) overcomes the aforementioned obstacles of PK sampling in children. However, MD has rarely been used in children and the currently available MD probes do not fit the common intravenous lines used on pediatric wards.

Materials/methods: We conducted this study to develop and validate a method for PK measurements in blood of children using modified MD catheters that fit small intravenous lines. For this purpose, in-vitro and in-vivo experiments with cefturoxime (CEF) were performed.

In-vitro MD experiments were performed in triplicates with three sampling time-points of 1h and with CEF concentrations of 2.5, 25 and 250µg/ml.

For the in-vivo PK study, a single intravenous dose of CEF 1500mg was administered over 30minutes to ten healthy volunteers (HV). Two modified intravascular MD catheters were inserted and serial MD and blood samples were taken. The retrodialysis technique was employed to measure the in-vivo recovery.

Results: Mean recovery in the in-vitro experiments during forward dialysis ranged from 31% to 33% and mean loss during retrodialysis ranged from 30% to 41% for all sampling time-points and CEF concentrations. Mean recovery during the in-vivo MD experiments was 14.4±4.6%, markedly lower than the recovery found in the in-vitro experiments.

Figure 1 shows the representative concentration-time profiles of CEF and a scatter plot correlating the MD and plasma concentrations for one HV, demonstrating a strong linear correlation. Preliminary PK analysis of all samples yielded a mean half-life of 1.15±0.2h for MD and 1.3±0.26h for plasma.

Conclusions: We developed an innovative MD catheter that can be inserted into small intravenous lines, allowing PK measurements of free antibiotic concentrations in children and thereby enabling individualization of therapy through TDM. In our experiments with this new MD catheter we were able to correlate MD and plasma concentrations and show reproducibility over time and for different concentrations in-vitro and in-vivo.

Figure 1

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Background: Pre-prescription authorisation is a commonly employed carbapenem stewardship strategy however Tamma et al demonstrated that postprescription review with feedback (PPRF) had a greater impact in terms of carbapenem use. The introduction of the electronic prescribing record (EPR) to our institution enabled the development of a real time carbapenem list (RTCL) with robust identification of all carbapenem prescriptions in real-time. Our aim was to perform PPRF on all patients initiated on a carbapenem (outside of critical care) and to assess the safety, impact and efficiency of the system.

Materials/methods: A real-time carbapenem prescription list was designed using Cerner® electronic prescribing system that can be executed and updated by the antimicrobial stewardship (AMS) team. The PPRF was performed daily by the AMS team during the normal working week and consisted of a review of the patient EPR, microbiological results and a telephone consultation with patient’s clinician. Carbapenem use was measured in defined daily doses (DDD) per 100 bed days used (BDU).

Results: Over an 11-week period (June to August 2019), carbapenem PPRF was carried out on 163 patients (Table 1). The time required for the activity was 30 minutes of AMS pharmacist time and 90 minutes of consultant microbiologist time per day.

Conclusions: The design and implementation of a RTCL on EPR to perform carbapenem PPRF led to a safe and effective reduction in meropenem use and allowed for the identification of several areas to target for stewardship interventions. The group would recommend this approach be adopted by institutions with resource depleted AMS teams in which EPR is available.

Table 1.

<table>
<thead>
<tr>
<th>Median time to PPFR</th>
<th>2 Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median duration of carbapenem prior to de-escalation</td>
<td>1.45 days</td>
</tr>
<tr>
<td>Major Prescription Indications</td>
<td>Respiratory tract infection 40% Urinary tract infection 17% Intra-abdominal 11%</td>
</tr>
<tr>
<td>Carbapenem defined daily doses (DDD) per 100 bed days reduction</td>
<td>0.79</td>
</tr>
<tr>
<td>4.29 [Quarter 1 2019] – 3.5 [Jun-Aug 2019]</td>
<td></td>
</tr>
<tr>
<td>Prior infection specialist approval</td>
<td>63%</td>
</tr>
<tr>
<td>History of multi-drug resistant organisms (MDRO)</td>
<td>39%</td>
</tr>
<tr>
<td>Targeted therapy</td>
<td>30%</td>
</tr>
<tr>
<td>De-escalation advised</td>
<td>25.7%</td>
</tr>
<tr>
<td>De-escalation advice followed (reviewed at 48 hours)</td>
<td>76.1%</td>
</tr>
<tr>
<td>Subsequent re-escalation</td>
<td>3.1%</td>
</tr>
<tr>
<td>Crude mortality (30 day)</td>
<td>15.6% p=0.49</td>
</tr>
<tr>
<td>De-escalated group</td>
<td>15.6%</td>
</tr>
<tr>
<td>Non de-escalated group</td>
<td>21%</td>
</tr>
</tbody>
</table>

Presenter email address: hickeyca9@gmail.com
Abstract 1298

Effect of short-term antimicrobial therapy on the tolerance and antibiotic resistance of multidrug-resistant *Staphylococcus capitis*

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**Background:** Bacteria undergo adaptive mutation in the host under the selective pressure of an antimicrobial agent. However, the specific effect of clinical antimicrobial use on bacterial evolution and genome mutations related to bacterial survival within a patient is unclear.

**Methods:** Three *S.capitis* strains were continuously isolated from cerebrospinal fluid of a clinical inpatient. Antimicrobial susceptibility was determined by using agar dilution method. The growth rate and whole blood tolerance of the three *S.capitis* strains were measured and relative fitness were calculated. Biofilm formation were measured by crystal violet Staining. The virulence of the bacteria was examined in the *Galleria mellonella* model. Whole-genome sequencing(WGS) and in silico analysis was performed to explore the genetic mechanisms of the apparent changes in the antimicrobial resistance phenotype. Identification of hypothetical protein was done by molecular cloning.

**Results:** The first isolate was susceptible to rifampin (MIC=0.25 μg/ml), resistant to gentamicin (MIC=16 μg/ml), while the later two isolates were resistant to rifampin (MIC >64 μg/ml), susceptible to gentamicin (MIC=4 μg/ml). Growth curve showed the later two isolates grew faster than the first isolate with a relative fitness cost of 19.2%, and 15.0%, accordingly. Their ability to form biofilm and *in vitro* whole blood tolerance were enhanced. No significant differences of virulence in the *G. mellonella* model were observed.Genome SNPs analysis revealed three genes(*saeR*, *moaA*, and *rpoB*) harbored missense base substitution mutations and one hypothetical protein harbored frameshift mutation. The mutation of *rpoB* gene caused rifampicin resistance. Mutations in *saeR* *moaA* and hypothetical protein are associated with changes in other biological traits. Amino acid sequence-based structure and function identification the hypothetical protein indicated that a mutation in the encoding gene might be associated with altered aminoglycoside susceptibility.

**Conclusions:** We report here for the first time that short-term clinical antibiotic use causes resistance mutations, collateral sensitivity, and adaptive enhancement of *S. capitis*. The impact of clinical short-term antimicrobial use on bacterial ability to survive within the host should not be underestimated, and appropriate measures should be introduced to address the adaptive evolution of bacteria to antimicrobial agents.

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Cold plasma activated liquid reduces bacterial biofilm produced by Staphylococcus aureus and Escherichia coli
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Background: Hospital surfaces are a source of infection due to contamination by bacteria. A novel potential method of hospital surface decontamination is the use of cold atmospheric pressure plasma (CAPP) systems. CAPP has antimicrobial properties that can inactivate bacterial cells on surfaces directly but also through the use of plasma activated liquid (PAL). Although the mechanisms of action are not fully understood, it is thought to be due, in part, to the production of reactive oxygen and reactive nitrogen species (RONS) in the liquid. To be an effective hospital decontamination tool, CAPP must also inactivate bacteria within biofilms. Multi-cellular, biofilm structures confer a higher resistance to disinfectants than singular, planktonic bacteria. Here we aimed to assess the microbial inactivation by CAPP and to examine the possible mechanisms of the antimicrobial action of CAPP treated phosphate buffered saline (PBS) against bacteria in bacterial biofilms.

Materials/methods: PBS was treated with CAPP for 300 seconds to generate PAL. PAL was then evaluated for levels of RONS using colorimetric assays. Planktonic Staphylococcus aureus (S. aureus) and Escherichia coli (E. coli) were incubated with PAL and viability was assessed using colony forming unit (CFU) assays. S. aureus and E. coli biofilms were grown for 48 hours and inoculated with PAL. Biofilm viability was assessed using metabolic assays. Damage throughout the biofilm structure was assessed via imaging using LIVE/DEAD staining and confocal microscopy.

Results: RONS levels were greatly increased in PAL compared to untreated PBS. A seven-log reduction in CFU was achieved in planktonic S. aureus and E. coli after incubation with PAL. S. aureus and E. coli biofilm viability decreased by 48% and 64%, respectively, after PAL treatment. Confocal microscopy showed membrane damage in treated bacterial cells throughout the biofilm structure. The bacterial inactivation in treated biofilms could be, in part, due to the RONS present in PAL.

Conclusions: CAPP treated PBS results in PAL that has antimicrobial and anti-biofilm activity, probably mediated in part by RONS. Further research is required to confirm these findings with other pathogens and under different conditions to conform the potential of PAL as an effective decontaminant.

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Aztreonam-avibactam activity against carbapenemase-producing Enterobacterales collected in Europe, Asia and Latin America (2017-2019)

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\(^1\)JMI Laboratories, North Liberty, United States

**Abstract**

**Background:** Aztreonam-avibactam (ATM-AVI) is under clinical development for treatment of serious infections caused by Gram-negative bacteria and has demonstrated potent activity against Enterobacterales producing all types of clinically relevant β-lactamases, including metallo-β-lactamases (MBL). We evaluated ATM-AVI activity against a worldwide collection of carbapenemase-producing Enterobacterales (CPE).

**Materials/methods:** A total of 748 clinical CPE isolates were collected in Europe (n=504; 27 centres in 15 nations), Latin America (LATAM; n=152; 7 centres in 4 nations), and Asia-Pacific region (APAC; n=92; 8 centres in 7 nations) in 2017-2019. All isolates were tested for susceptibility against ATM-AVI and comparators by reference broth microdilution method and submitted to whole genome sequencing analysis for identification of β-lactamase genes.

**Results:** The collection included 636 Klebsiella pneumoniae, 51 Enterobacter cloacae, 20 Escherichia coli and 41 isolates of other species. The most common MBL (n=219) was NDM-type [193; 88.1% of MBLs] and the most common OXA-type (n=234) was OXA-48 [188; 80.3% of OXA-type]. Among KPC-producers (n=294), KPC-2 and KPC-3 represented 51.7% and 48.3%, respectively. ATM-AVI was very active against the entire collection of isolates with overall MIC\(_{90}\) values of 0.25/0.5 mg/L and 99.3% of isolates inhibited at ≤4 mg/L (Table). Isolates with ATM-AVI MIC >4 mg/L demonstrated additional resistance mechanisms, including PBP3 alterations. Among comparators, the most active agents overall were tigecycline [MIC\(_{90}\), 1/2 mg/L; 92.6% susceptible [S] at ≤2 mg/L] and colistin [MIC\(_{90}\), 0.12/≤8 mg/L; 77.5%S at ≤2 mg/L]. ATM-AVI [MIC\(_{90}\), 0.12/0.5 mg/L; 98.6% inhibited at ≤4 mg/L], tigecycline [MIC\(_{90}\), 1/2 mg/L; 92.7%S at ≤2 mg/L], and colistin [MIC\(_{90}\), 0.12/≤8 mg/L; 79.4%S at ≤2 mg/L] were the most active compounds against MBL producers. When tested against KPC-producers and OXA-producers, ATM-AVI (100.0% and 99.1% inhibited at ≤4 mg/L, respectively) and ceftazidime-avibactam (MIC\(_{90}\), 1/2 mg/L and 100.0%S for both subsets) were the most active agents.

**Conclusions:** ATM-AVI displayed potent activity against MBL-, KPC-, and OXA-producing Enterobacterales from Europe, LATAM, and APAC, inhibiting >99% of isolates at ≤4 mg/L. Our results support further clinical development of ATM-AVI for treatment of infections caused by CPE, including MBL-producing isolates.

<table>
<thead>
<tr>
<th>Carbapenemase Subtype</th>
<th>No. of Isolates (cumulative %) inhibited at ATM-AVI MIC (mg/L)</th>
<th>≤0.03</th>
<th>0.06</th>
<th>0.12</th>
<th>0.25</th>
<th>0.5</th>
<th>1</th>
<th>4</th>
<th>8</th>
<th>16</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBL-producers (219)</td>
<td>30 (13.7)</td>
<td>60 (26.6)</td>
<td>84 (36.6)</td>
<td>93 (40.6)</td>
<td>96 (41.6)</td>
<td>96 (41.6)</td>
<td>96 (41.6)</td>
<td>96 (41.6)</td>
<td>96 (41.6)</td>
<td>96 (41.6)</td>
</tr>
<tr>
<td>KPC-producers (254)</td>
<td>14 (4.6)</td>
<td>27 (8.6)</td>
<td>56 (18.8)</td>
<td>67 (23.9)</td>
<td>73 (25.1)</td>
<td>73 (25.1)</td>
<td>73 (25.1)</td>
<td>73 (25.1)</td>
<td>73 (25.1)</td>
<td>73 (25.1)</td>
</tr>
<tr>
<td>OXA-producers (234)</td>
<td>5 (2.6)</td>
<td>14 (6.8)</td>
<td>49 (20.7)</td>
<td>119 (50.8)</td>
<td>19 (7.9)</td>
<td>9 (3.9)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (0)</td>
</tr>
<tr>
<td>All (748)</td>
<td>50 (6.7)</td>
<td>72 (16.3)</td>
<td>169 (38.9)</td>
<td>310 (68.3)</td>
<td>119 (25.9)</td>
<td>15 (3.3)</td>
<td>7 (1.6)</td>
<td>1 (0.1)</td>
<td>4 (1)</td>
<td>1 (0)</td>
</tr>
</tbody>
</table>

\(^a\) Includes an MBL-producing E. cloacae with ATM-AVI MIC of 0.12 mg/L.

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Resistance to extended-spectrum β-lactams, aminoglycosides and quinolones in multidrug-resistance Enterobacterales isolated in patients receiving an allogeneic haematopoietic stem cell transplantation: the ENTHERE-SCT Study. PI16/01415

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Background: To analyze the mechanisms of resistance to extended-spectrum β-lactams, aminoglycosides and quinolones in MDRE isolated between June 2017 and August 2019 in 44 patients of the 127 recruited in the study, who receiving an Allo-SCT in four Spanish hospitals.

Materials/methods: Overall, 117 MDRE, (AmpC-hyperproducing and/or producers of extended-spectrum β-lactamases (ESBLs) or carbapenemases), isolated in rectal swabs [pretransplant, weekly during the first month post-transplant, biweekly up to 100 days post-transplant and monthly up to 180 days post-transplantation] and 8 MDRE isolated from different clinical samples, were studied. The minimum inhibitory concentrations (MICs) of 24 antibiotics were determined by broth-microdilution (EUCAST breakpoints). PCR was performed for ESBLs (SHV, TEM, CTX-M), plasmid-mediated AmpC β-lactamases, carbapenemases (KPC, IMP, VIM, NDM, GES, OXA-48), plasmid-mediated quinolone-resistance [PMQR] (qnrA, qnrB, qnrC, qnrD, qnrE, qepA, oqxAB) and aminoglycoside-modifying-enzymes [AMEs] (aac(3)-Ia, aac(3)-IIa, aac(6’)-Ib, ant(2’)-Ia, aph(3’)-Ia, aph(3’)-Ia) and AME-genes were detected in 45.9%, being aac(6’)-Ib the most prevalent (85.3%), 50.0% of strains harboured two AME-genes. PMQR-genes were detected in 35/60 (58.3%) isolates quinolone-resistant and qnrB was the most prevalent (51.4%).

Results: The microorganisms isolated were: E.coli 52 (41.6%), Enterobacter spp. 36 (28.8%), K.pneumoniae 16 (12.8%), Citrobacter spp. 13 (10.4%) and others species 8 (6.4%) [5 K.oxytoca, 1 H.alvei, 1 K.intermedia, 1 S marcescens]. PFGE analysis identified 19 clonal patterns in E.coli, 9 in E.cloacae, 5 in K.pneumoniae and 3 in C.freundii. The antimicrobial susceptibility, corresponding 74 MDRE (one isolate per REP-PCR pattern/antibiogram and patient) are shown in Table 1. In seven patients MDRE were detected in clinical samples, in all but one patient, the same MDRE was detected in different rectal swabs days on the follow-up. ESBLs were detected in 60.8% and CTX-M was (47.3%) the most prevalent, 29.7% isolates were AmpC-hyperproducers. Carbapenemases were detected in 8 (10.8%) isolates: VIM (2 E.cloacae, one S.marcescens and K.intermedia), GES (2 K.oxytoca and one E.cloacae) and IMP (E.aerogenes). AME-genes were detected in 45.9%, being aac(6’)-Ib the most prevalent (85.3%), 50.0% of strains harbour two AME-genes. PMQR-genes were detected in 35/60 (58.3%) isolates quinolone-resistant and qnrB was the most prevalent (51.4%).

Conclusions: In 6 of the 44 transplant patients who were colonized by MDRE, an infection by the same microorganism was documented. E. coli producing CTX-M was the MDRE most prevalent followed by Enterobacter spp. AmpC-hyperproducer.
Table 1. In vitro activity to 24 antibiotics in 74 multidrug-resistance *Enterobacterales* (MDRE) isolated from patients with Allo-SCT transplant.

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>MIC&lt;sub&gt;50&lt;/sub&gt;</th>
<th>MIC&lt;sub&gt;90&lt;/sub&gt;</th>
<th>% Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>&gt; 256</td>
<td>&gt; 256</td>
<td>100.0</td>
</tr>
<tr>
<td>Amoxicillin-Clavulanic acid</td>
<td>256</td>
<td>&gt; 256</td>
<td>82.4</td>
</tr>
<tr>
<td>Piperacillin</td>
<td>256</td>
<td>&gt; 256</td>
<td>89.2</td>
</tr>
<tr>
<td>Piperacillin-Tazobactam</td>
<td>32</td>
<td>&gt; 256</td>
<td>54.1</td>
</tr>
<tr>
<td>Cefoxitin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>32</td>
<td>&gt; 256</td>
<td>59.5</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>128</td>
<td>&gt; 256</td>
<td>93.2</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>32</td>
<td>256</td>
<td>79.7</td>
</tr>
<tr>
<td>Cefepime</td>
<td>8</td>
<td>&gt; 256</td>
<td>51.4</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>32</td>
<td>256</td>
<td>67.6</td>
</tr>
<tr>
<td>Imipenem</td>
<td>≤0.125</td>
<td>4</td>
<td>5.4</td>
</tr>
<tr>
<td>Meropenem</td>
<td>≤0.125</td>
<td>0.5</td>
<td>1.4</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>≤0.125</td>
<td>4</td>
<td>19.0</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>0.5</td>
<td>32</td>
<td>17.6</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>1</td>
<td>32</td>
<td>29.7</td>
</tr>
<tr>
<td>Amikacin</td>
<td>1</td>
<td>8</td>
<td>1.4</td>
</tr>
<tr>
<td>Netilmicin</td>
<td>0.5</td>
<td>16</td>
<td>17.6</td>
</tr>
<tr>
<td>Arbekacin</td>
<td>0.5</td>
<td>2</td>
<td>NA</td>
</tr>
<tr>
<td>Nalidixic acid</td>
<td>64</td>
<td>&gt; 256</td>
<td>NA</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>2</td>
<td>&gt; 256</td>
<td>60.8</td>
</tr>
<tr>
<td>Levofoxacin</td>
<td>2</td>
<td>32</td>
<td>55.4</td>
</tr>
<tr>
<td>Trimethoprim-Sulfamethoxazole</td>
<td>256</td>
<td>&gt; 256</td>
<td>78.3</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>0.5</td>
<td>4</td>
<td>36.5</td>
</tr>
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<td>Fosfomycin</td>
<td>8</td>
<td>256</td>
<td>25.7</td>
</tr>
<tr>
<td>Colistin</td>
<td>≤0.125</td>
<td>32</td>
<td>23.0</td>
</tr>
</tbody>
</table>

<sup>a</sup> for cefoxitin using ECOFF for EUCAST.  
NA. Not available (breakpoints have not been established for EUCAST)

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Abstract 1316

Antimicrobial activity of aztreonam-avibactam and comparator agents when tested against a large collection of contemporary Stenotrophomonas maltophilia isolates collected from medical centres worldwide

Hello S. Sader*, Cecilia Carvalhaes1, SJ Ryan Arends1, Leonard Duncan1, Robert Flamm1, Mariana Castanheira1

1JMI Laboratories, North Liberty, United States

Abstract third-party references: This study was performed by JMI Laboratories and supported by Pfizer, Inc., which included funding for services related to preparing this abstract.

Background: Stenotrophomonas maltophilia represents a major cause of hospital-acquired pneumonia (HAP) and bloodstream infections (BSI). There are very limited therapeutic options to treat S. maltophilia infections due to intrinsic production of metallo-β-lactamases (MBL) by these organisms. Aztreonam-avibactam (ATM-AVI) is under clinical development for treatment of serious infections caused by Gram-negative bacteria, including MBL-producers.

Materials/methods: A total of 1,839 isolates were collected in Western Europe (W-EU; n=388; 24 centres in 9 nations), Eastern Europe (E-EU; n=156; 15 centres in 12 nations), North America (NA; n=1,095; 77 centres), Latin America (LATAM; n=92; 12 centres in 9 nations), and Asia-Pacific region (APAC; n=108; 17 centres in 8 nations) in 2016-2019. The isolates were mostly from HAP (70.4%) and BSI (12.6%). Susceptibility testing was performed by reference broth microdilution method at a central laboratory and CLSI breakpoints were applied when available.

Results: ATM-AVI was very active against isolates from all geographic regions and infection types (MIC50/90, 2-4/4 mg/L), inhibiting 90.7-96.7% of isolates at ≤4 mg/L (92.1% overall) and 96.3-100.0% at ≤8 mg/L (97.8% overall), which are the current CLSI susceptible [S] and intermediate breakpoints, respectively, for ATM alone (Table). Trimethoprim-sulfamethoxazole (MIC50/90, ≤0.5-1/1 mg/L) and minocycline (MIC50/90, 0.5-1.2 mg/L) were active against 93.5-96.9% and 99.0-100.0% of isolates at the respective, current CLSI susceptible breakpoints. Moreover, 74.1%/84.7% of TMP-SMX-non-susceptible isolates were inhibited at ≤4/≤8 mg/L of ATM-AVI. Levofloxacin (MIC50/90, 1/4-4 mg/L/L) was active against 74.0-87.0% of isolates at the current CLSI breakpoint ≤2 mg/L). Ceftazidime (MIC50/90, >32/≥32 mg/L; 16.7-30.4%S at ≤8 mg/L) and colistin (MIC50/90, 4-8/>8 mg/L; 29.3-42.9% inhibited at ≤2 mg/L) exhibited limited activity, whereas tigecycline (MIC50/90, 1/2.4 mg/L) inhibited 82.7-90.7% (85.0% overall) of isolates at ≤2 mg/L. Ceftolozane-tazobactam, meropenem, imipenem, amikacin, and tobramycin exhibited very limited activity against these organisms.

Conclusions: ATM-AVI demonstrated potent in vitro activity against a large collection of S. maltophilia isolated from patients with HAP, BSI, and other systemic infections. ATM-AVI may represent a valuable option to treat S. maltophilia infections, addressing a major unmet medical need.

<table>
<thead>
<tr>
<th>Region (no. isolates)</th>
<th>ATM-AVI</th>
<th>TMP-SMX</th>
<th>Minocycline</th>
<th>Levofloxacin</th>
<th>Ceftazidime</th>
</tr>
</thead>
<tbody>
<tr>
<td>W-EU (388)</td>
<td>91.2/96.8</td>
<td>99.9/100.0</td>
<td>94.3/76.8</td>
<td>17.8/16.7</td>
<td></td>
</tr>
<tr>
<td>E-EU (156)</td>
<td>93.6/98.7</td>
<td>95.0/100.0</td>
<td>74.0/22.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NA (1,095)</td>
<td>90.7/98.1</td>
<td>99.0/99.2</td>
<td>88.0/30.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LATAM (92)</td>
<td>96.7/100.0</td>
<td>95.7/100.0</td>
<td>87.0/21.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>APAC (108)</td>
<td>90.7/96.3</td>
<td>95.3/99.0</td>
<td>76.0/20.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All (1,839)</td>
<td>92.1/97.8</td>
<td>95.4/99.5</td>
<td>87.0/20.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* % inhibited at ≤4/≤8 mg/L for comparison purpose.

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Abstract 1317

**Rapid detection of fungal feet infection by LED-UV light**

Ester Fusté1, Guadalupe Jimenez Galisteo2, M. Jesus Sanchez3, Mercedes Aguilar4, Teresa Vinuesa*2

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**Background:** Fungal feet infections are usually torpid diseases whose specific diagnostic is compulsory as similar clinical entities are treated with steroids that can worsen the mycotic infection. To avoid inaccurate therapies, a fast and accurate detection of fungi is needed. Potassium hydroxide (KOH) treatment of samples is used for clarifying specimens (rich in keratin), before examination by bright light microscopy but it requires skilled observers. Fluorescent brighteners absorbing UV light and emitting blue light, with affinities for polysaccharides with β-links, have been used to facilitate observation. Our group uses for this purpose Leucophor®, a disulphonated stilbene brightener along with KOH treatment. Based on the report of Denny G et al referent to hand held UV illumination, we aimed to evaluate an alternative easy to use, none-expensive method to fasten the time elapsed between the clinical suspicion and the confirmation of the presence of a fungal infection. We examined patients with clinical suspicion of mycotic infection as well as nail or skin samples, by means of a hand held LED UV, comparing it with the visualization by a fluorescence microscopy.

**Materials/methods:** 40 patients with clinical suspicion of fungal feet infection and 40 healthy individuals were analyzed in vivo by both methods. Their collected specimens were KOH digested, Leucophor® stained and examined in a fluorescence microscopy (Nikon E800). After switching the UV source off, they were observed under tangential illumination from a hand-held LED UV Flashlight (HAN-WYB75*4) at 395 nm. Also a 1418 90X Phone LED UV Light Magnifier 90 x and 60 X adapted to a Smart Phone Huawei with a Leica Camera was used. Culture in appropriate media was performed in all cases. Moreover, a series of 30 nails and scrapings of our collection were examined and imaged (15 positive: Aspergillus sp., Trichophyton rubrum, Scopulariopsis sp.and 15 culture negative).

**Results:** Even that the brightness of the conidia and hyphae using the hand-held LED UV Flashlight diminished slightly, it appears still clear permitting an accurate diagnosis of the presence of fungi.

![](Hand_held_LED_UV.png)  ![Nikon_Ellipse_800.png]

**Conclusions:** The use of low cost devices seems feasible for detection of fluorescence from samples containing fungi with reasonable resolution.

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Abstract 1319

MYCOPLASMA IST3, a new in vitro medical device to aid the diagnosis of urogenital mycoplasma infection: performance results from an international multi-centre trial

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**Background:** Mycoplasma hominis (Mh) and Ureaplasma spp (Uspp) are possible pathogens associated with urogenital infections. This study assessed performance of MYCOPLASMA IST3, a new in vitro diagnostic test designed to detect, identify, enumerate and test the susceptibility of Mh and/or Uspp to relevant agents (Levofloxacin, Moxifloxacin, Tetracycline, Erythromycin, Telithromycin and Clindamycin).

**Materials/methods:** 516 vaginal/cervical or urethral swabs, semen and urines were included. For detection/identification, performance was expressed as the positive (PPA) and negative agreements (NPA) between MYCOPLASMA IST3 and sample status defined using A7 agar and PCR. For indicative enumeration, performance was expressed as the agreement between MYCOPLASMA IST3 and A7 agar results. For Antimicrobial Susceptibility Testing (AST) application, Category Agreement (CA, %) Major Error rate (ME, %) and Very Major Error counts (VME, #) were calculated comparing MYCOPLASMA IST3 category (S or R) to Broth Micro Dilution Minimum Inhibitory Concentration (MIC) results interpreted using CLSI M43-A interpretive breakpoints.

**Results:** 312 samples were negative, 109 grew viable Uspp, 73 grew Mh and 22 grew both. 38% of the positive samples were contrived (spiked) samples. Regarding the detection/identification application, MYCOPLASMA IST3 had a PPA of 98.5% (129/131) and 92.6% (88/95) and a NPA of 99.7% (384/385) and 99.0% (410/414) with A7 agar for Uspp and Mh, respectively. Among the 22 mixed samples, MYCOPLASMA IST3 recovered both species for 18 samples while only the Uspp was recovered for the remaining samples. Indicative enumeration results were in agreement between MYCOPLASMA IST3 and A7 agar in 84.6% (99/117) and 83.7% (72/86) of the cases for Uspp and Mh, respectively. MYCOPLASMA IST3 AST application produced CA ranging from 96.0% to 100.0% and ME rates from 0.0% to 4.2% (Table). Three VMEs were observed (1 Uspp with tetracycline, 1 Mh with tetracycline, 1 Mh with Moxifloxacin), 2 of them originated from isolates with MIC within ± 1 doubling dilution from the CLSI breakpoint value.

**Conclusions:** MYCOPLASMA IST3 is an accurate aid in the diagnosis of urogenital infections related to Uspp or Mh, providing clinicians with valuable information to guide treatment.

**Table:** MYCOPLASMA IST3 Antimicrobial Susceptibility Testing performance.

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Abstract 1321

Comparison of the distribution of quinolone resistance markers in *Escherichia coli* in a human-animal health interface model

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**Background:** Quinolone action is the inhibition of DNA gyrase and topoisomerase IV DNA enzymes. However, two types of resistance are detected for these antibiotics: chromosome (modifications in gyrase and overexpression of efflux pumps) and PMQR (production of qnr proteins, acetylases, and efflux pumps). The aim is to know the distribution of quinolone resistance genetic markers in *E. coli* obtained from humans and porcine in a close model.

**Materials/methods:** Total of 1,407 *E. coli* isolates (982 from pigs and 425 from humans with diarrhoea) were obtained from a farm located in Morelos, Mexico (June 2015- April 2016). MIC was obtained for CIP and NAL. Phylogroup according to Clermont system and the genes gyrA and PMQRs were amplified by PCR. The plasmid was performed according to Kieser.

**Results:** Three different phenotype were identified: I (NALr/CIPr), II (NALr/CIPs), and III (NALs/CIPs); the most frequent in both population porcine (PEI) and human (HEI), was phenotype II (PEI 56.3%; HEI 50.1%). A representative sample of isolates was selected: 47/425 PEI, and 100/982 HEI. The major phylogroup was A (PEI 56%, HEI 44.6%), follow by B1 (PEI 31%, HEI 17%), D (PEI 11%, HEI 25.5%) and B2 phylogroup (PEI 2%, HEI 12.8%). ORDR region of gyrA gene was wild type (HEI 57.4%, PEI 54%) follow by S83L (HEI 19.4%, PEI 19%) and S83L/D87N (HEI 19.1%, PEI 18%) mutations. The major PMQR was qnrB in PEI (43%) and HEI (23.4%). Additionally, 39% of PEI and 59.6% of HEI, no qnr genes were identified. OqxA/OqxB, qepA and aac(6’)-Ib-cr were detected at low frequency (<7%). The phylogenetic tree shows three clades: 1) phenotype I/S83L/D87N, 2) phenotype II/S83L, and 3) phenotype II and III/wild ORDR region and qnrB. A plasmid of 150 to 160 kb was identified in most of the isolates.

**Conclusions:** No difference of qnrB was identified in both groups of *E. coli*. Eflux pumps and acetylation enzyme are more frequent in PEI than in HEI. A 150-160 kb plasmid was detected in most of the isolates. Further studies will be conducted to know the structure of the plasmids.

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Abstract 1322

Resistance mechanisms associated with pleuromutilins among Gram-positive clinical isolates from the worldwide surveillance programme for lefamulin in 2018

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Abstract third-party references: This study was performed by JMI Laboratories and supported by Nabriva Therapeutics, which included funding for services related to preparing this abstract.

Background: Lefamulin is a first-in-class, semi-synthetic pleuromutilin antibiotic that inhibits bacterial protein synthesis via a unique mechanism of action was approved by the United States Food and Drug Administration (FDA) in 2019 for the treatment of community-acquired bacterial pneumonia (CABP) in adults. This study characterized the resistance mechanisms associated with elevated lefamulin MICs in a global surveillance isolate collection from 2018.

Materials/methods: A total of 4,406 S. aureus, coagulase-negative staphylococci (CoNS), S. pneumoniae and β-haemolytic and viridans group streptococci were tested using reference broth microdilution. A total of 36 (0.8%) isolates met the criteria based on FDA breakpoints or MICs above the normal wildtype distribution. Bacterial genomes were sequenced (MiSeq Sequencer, Illumina) and screened in silico for possible lefamulin resistance genes and mutations in the 23S rRNA, L3, L4 and L22.

Results: 8 of 1,607 (0.5%) S. aureus harboured vga(A) (6/8; lefamulin MIC, 1–8 mg/L) or lsa(E) (2/8; lefamulin MIC, >32 mg/L). 20 of 270 (6.7%) CoNS carried either vga gene variants (18/20; lefamulin MIC, 2–>32 mg/L) or showed G2576T alterations in the 23S rRNA along L3 mutations at H146 and M156 or at position V154 (2/20; lefamulin MIC of 0.5 mg/L). Only 2 of 1,866 (0.1%) S. pneumoniae were non-susceptible to lefamulin (MIC, 1–2 mg/L); both isolates had mutations in ribosomal proteins (L4 or in L3 and L22). Among other streptococci, 3 of 522 (0.5%) β-haemolytic and 2 of 141 (1.4%) viridans group streptococci carried lsa(E) (lefamulin MIC, 2–32 mg/L), while one S. oralis (lefamulin MIC, 1 mg/L) did not show any resistance mechanisms. Other plasmid-mediated genes, such as cfr were not detected.

Conclusions: Gram-positive isolates from a global collection causing human infections exhibiting elevated lefamulin MICs are rare. The most common resistance mechanisms identified were vga and lsa(E); cfr was not detected. Longitudinal surveillance studies will monitor the stability of the in vitro activity of lefamulin.

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Abstract 1329

Efficacy of bacteriophage-antibiotic combinations on two different phenotypes of methicillin-resistant Staphylococcus aureus

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Background: The widespread use of antibiotics has generated selective pressures that have driven the emergence of multi-drug resistant strains. The antimicrobial of choice for invasive methicillin-resistant Staphylococcus aureus (MRSA) infections has been vancomycin; however, treatment failures have continued to be reported secondary to poor drug performance or the development of various resistant phenotypes. Bacteriophages (phages) have been suggested as a potential adjunctive/alternative therapy. These phages exhibit bactericidal activity by infecting bacterial cells, redirecting the cellular machinery to produce progeny virions and killing the bacterial cell upon lysis and release of those progeny phages. Staphylococcus aureus naturally releases extracellular vesicles (EVs) during growth, which are known to play important functions in bacteria-bacteria interactions and potentially transferring antibiotic resistance genes. Unfortunately, there is limited data on the use of phage-antibiotic combinations and bacterial response to these. The objective of this study was to test the in-vitro activity of various standard of care (SOC) antibiotics with phages and their effects on EVs formation.

Materials/methods: Phage-antibiotic exposure was tested on two different phenotypes of MRSA, isolates MW2 (daptomycin non-susceptible) and D712 (vancomycin intermediate resistant S. aureus). Phage, bacterial counts and EVs formations were performed during time-kill analysis (TKA) experiments. MRSA isolates were examined against an array of antibiotics alone (daptomycin, vancomycin, ceftaroline and cefazolin) and in combination with phages. Bacteriophage Sb-1 was used for experiments at ~10⁵ PFU/ml. Bactericidal activity was defined as a >3 log₁₀ CFU/ml reduction from baseline. Synergy between two agents was defined as a ≥2 log₁₀ CFU/ml reduction at 24 hours compared to either agent alone.

Results: In vitro 24-hour TKA experiments demonstrated bactericidal activity with phage-antibiotic combinations. While addition of ceftaroline or cefazolin to vancomycin or daptomycin was synergistic, both daptomycin-phage and vancomycin-phage combinations resulted in bactericidal activity against the D712 strain. In addition, emergence of EVs in presence of phages was suppressed in antibiotic-phage combination regimens for both MRSA isolates.

Conclusions: The combination of antibiotic-phages showed promising results against MRSA. If shown to be reproducible in vivo, this phenomenon would be valuable in the treatment of clinical cases that are treatment refractory or have failed SOC antibiotics.

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Vaccination Perception (VP) and Vaccination Coverage (VC) among healthcare students (HCS), a prospective French study: PERCEVAC Study

Aurelie Baldolli*, Anna Fournier1, Xavier Lecoutour1, Renaud Verdon1, Jocelyn Michon1

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Background: Vaccine hesitancy has been increasing and spreading throughout the world. However data are scarce regarding HCS. The aim of this study was to determine VC and VP among HCS.

Materials/methods: A self-reporting electronic questionnaire, related to VP and VC, was prospectively sent to HCS (physicians, nurse, pharmacist, midwives, physiotherapist students and 1st year of health sciences students [PACES]) of Normandy University (France) between 18/03/2019 and 8/04/2019. Global VC was defined as being vaccinated for French mandatory and recommended vaccines. VP was evaluated through various binary questions and numeric scales.

Results: Out of a population of 4546 HCS, 542 took part in this survey (12%, mean age 22.3 year, female 79%).

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>VC All students 542</th>
<th>VC Physicians 284</th>
<th>VC Nurses 86</th>
<th>VC Physiotherapists 14</th>
<th>VC Pharmacists 31</th>
<th>VC Midwife 10</th>
<th>VC PACES 117</th>
<th>p (compared to physician)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTP*</td>
<td>94%</td>
<td>95%</td>
<td>94%</td>
<td>93%</td>
<td>97%</td>
<td>100%</td>
<td>87%</td>
<td>0.08</td>
</tr>
<tr>
<td>Pertussis**</td>
<td>88%</td>
<td>92%</td>
<td>90%</td>
<td>71%</td>
<td>90%</td>
<td>80%</td>
<td>81%</td>
<td>0.03</td>
</tr>
<tr>
<td>HBV***</td>
<td>89%</td>
<td>96%</td>
<td>95%</td>
<td>100%</td>
<td>87%</td>
<td>90%</td>
<td>62%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HPV**</td>
<td>64%</td>
<td>66%</td>
<td>63%</td>
<td>73%</td>
<td>68%</td>
<td>50%</td>
<td>60%</td>
<td>0.85</td>
</tr>
<tr>
<td>MMR**</td>
<td>95%</td>
<td>96%</td>
<td>94%</td>
<td>79%</td>
<td>100%</td>
<td>90%</td>
<td>93%</td>
<td>0.2</td>
</tr>
<tr>
<td>Meningococcus C**</td>
<td>62%</td>
<td>61.2%</td>
<td>67%</td>
<td>50%</td>
<td>84%</td>
<td>70%</td>
<td>54%</td>
<td>0.03</td>
</tr>
<tr>
<td>Global VC</td>
<td>40%</td>
<td>44%</td>
<td>45%</td>
<td>36%</td>
<td>52%</td>
<td>40%</td>
<td>26%</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*mandatory, **recommended, *** mandatory in HCS

On multivariate analysis only being a PACES student is associated with a lower global VC (OR 1.9 [1.2-3.3] p=0.04).

Regarding VP, 98% of HCS think that vaccine are effective. On a 0-10 scale, 91% think that vaccine safety is ≥ 7 and 80% have vaccine hesitancy < 3, the benefit/risk balance is judged as always positive in 66%. 81% of HCS follow French recommendations. Not recommended vaccines are against Haemophilus influenza b (69%), HPV (63%), Influenza (71%), zona (82%) and meningococcus (46.4%). 92% agree with the recent French law increasing the mandatory vaccines for infants, and 62% with a flu mandatory vaccination for healthcare workers.

Conclusions: Despite the good VP, less than half HCS are well vaccinated. Some vaccines are not considered useful nor indicated. Information regarding these vaccines should be done with a focus on PACES students.

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Comparative in vitro activity of cefepime-enmetazobactam and other agents against 3rd-generation cephalosporin-resistant and extended-spectrum β-lactamase-producing clinical isolates of Enterobacterales collected between 2016-2018

Abstract 1331

Comparative in vitro activity of cefepime-enmetazobactam and other agents against 3rd-generation cephalosporin-resistant and extended-spectrum β-lactamase-producing clinical isolates of Enterobacterales collected between 2016-2018

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Background: Third generation cephalosporin (3GC)-resistant Enterobacterales are WHO critical priority pathogens in need of development of new agents. Enmetazobactam is a novel β-lactamase inhibitor targeting extended-spectrum β-lactamases (ESBL), the main resistance determinants in 3GC-resistant Enterobacterales. This study examined the in vitro activity of enmetazobactam combined with cefepime against clinical isolates of Enterobacterales collected between 2016-2018, including those resistant to 3GC or producing ESBL.

Materials/methods: µClinical isolates of Enterobacterales (n=7168) were collected from the US and Europe maintaining a proportion of clinically prevalent pathogens causing serious infections. Organisms were identified by MALDI-TOF mass spectrometry, and β-lactamase genotypes determined by multiplex PCR and sequencing for isolates with a ceftazidime or ceftriaxone MIC ≥ 1 mg/l. MIC and susceptibility were determined according to CLSI guidelines.

Results: Resistance to 3GC was 19.8% amongst the Enterobacterales collected, with 54.9% of those isolates expressing an ESBL with or without an AmpC and/or an OXA β-lactamase. The addition of enmetazobactam (fixed at 8 mg/l) to cefepime reduced the MIC90 >32-fold relative to cefepime alone against the Enterobacterales groups (table). Cefepime-enmetazobactam activity was comparable to meropenem against 3GC-resistant and ESBL-producing isolates and outperformed piperacillin-tazobactam and ceftolozane-tazobactam.

Conclusions: Cefepime-enmetazobactam may prove to be an important carbapenem-sparing therapy for serious infections caused by 3GC-resistant, ESBL-producing Enterobacterales.

<table>
<thead>
<tr>
<th>Antibacterial agent</th>
<th>MIC (mg/l)</th>
<th>% Susceptible</th>
<th>MIC (mg/l)</th>
<th>% Susceptible</th>
<th>MIC (mg/l)</th>
<th>% Susceptible</th>
<th>MIC (mg/l)</th>
<th>% Susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazidime</td>
<td>32</td>
<td>82.9</td>
<td>&gt;64</td>
<td>14.9</td>
<td>&gt;64</td>
<td>15.0</td>
<td>&gt;64</td>
<td>20.1</td>
</tr>
<tr>
<td>Cefepime²</td>
<td>16</td>
<td>87.089.9</td>
<td>&gt;64</td>
<td>35.549.8</td>
<td>&gt;64</td>
<td>12.026.1</td>
<td>&gt;64</td>
<td>11.925.5</td>
</tr>
<tr>
<td>Cefepime-enmetazobactam</td>
<td>0.25 (98.996.9)</td>
<td>2 (91.799.4)</td>
<td>0.5 (98.999.9)</td>
<td>0.25 (99.999.9)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>32</td>
<td>87.4</td>
<td>&gt;256</td>
<td>51.3</td>
<td>266</td>
<td>71.4</td>
<td>128</td>
<td>75.1</td>
</tr>
<tr>
<td>Meropenem</td>
<td>0.06</td>
<td>97.6</td>
<td>4</td>
<td>99.4</td>
<td>0.12</td>
<td>96.0</td>
<td>0.06</td>
<td>98.5</td>
</tr>
<tr>
<td>Cefazidime-avibactam</td>
<td>0.25</td>
<td>99.6</td>
<td>1</td>
<td>97.7</td>
<td>0.5</td>
<td>100</td>
<td>0.5</td>
<td>100</td>
</tr>
<tr>
<td>Ceftolozane- tazobactam</td>
<td>1</td>
<td>92.7</td>
<td>64</td>
<td>63.6</td>
<td>16</td>
<td>82.1</td>
<td>4</td>
<td>87.0</td>
</tr>
</tbody>
</table>

1ESBL group co-producing AmpC and/or OXA β-lactamases

2Cefepime susceptibility using CLSI breakpoints for susceptible (S; ≤2 mg/l)/susceptible, dose dependent (SDD; ≤8 mg/l).

3Breakpoints for cefepime-enmetazobactam have not been established. Values in (italics) represent the percent susceptibilities using cefepime CLSI breakpoints for S (≤2 mg/l)/SDD (≤8 mg/l).

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Abstract 1334

Administration of ceftazidime to patients undergoing haemodialysis: are trough levels consistently above the EUCAST breakpoints for Enterobacterales and Pseudomonas?

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Background: Patients undergoing haemodialysis should receive reduced ceftazidime doses. Based on a 6-patients study, a 1g interdialytic dose was considered sufficient to act on most frequent pathogens [Antimicrob Agents Chemother. 2013;57:5854-9]. Beta-lactams serum levels, however, are highly variable [Crit Care 2011;15:R137] while optimal PK/PD targets for beta-lactams are still under discussion [Expert Rev Anti Infect Ther. 2017;15:677-688]. Our aim was to measure actual ceftazidime trough serum concentrations in a larger cohort of haemodialysis patients to determine whether these would reach the current EUCAST ceftazidime R breakpoints for P. aeruginosa and Enterobacterales.

Materials/methods: Enrolment: 30 patients on long-term haemodialysis [3 times a week] suffering from infections justifying ceftazidime administration. Dosing: ceftazidime 1st dose: 2g, followed by 1g after each dialysis session. Sampling: serum obtained at approx. 44 or 68h after each administration, and after 1st and 4th dialysis session. Assay: validated HPLC-UV and UPLC-MS-MS. Calculations: since only trough levels were recorded, no pharmacokinetic model could be developed and data were used to fit [visual inspection and iterative optimization] a one-compartment decay model [k=0.032 h⁻¹; clearance 7.4 mL/min [non-renal clearance of ceftazidime]] to calculate values at two fixed standard post-administration times (44 and 68h).

Results: The Table shows the ceftazidime concentrations reached at 44 and 68h for each of the 4 successive administrations, and the number of evaluable patients for whom these concentrations were ≥ 8 or 4 mg/L. Levels were highly variable with significant correlation [simple and multivariate analysis] only demonstrable (i) with maintenance or not of a residual renal function and (ii) for 2d, 3d and 4th post-administration levels, with the 1st post-administration actual trough levels [multiple linear regression], suggesting larger inter-subject than within-subject variability. No correlation was seen with CRP, WBC, positive haemoculture, or clinical outcome of the infection. Ceftazidime concentration decrease by haemodialysis was 82.7±9.3%.

Conclusions: 2g of ceftazidime and post-administration times ≤44h are necessary to ensure > 73% of patients to have trough concentrations above the ceftazidime Pseudomonas R breakpoint. 1 g dosing and/or lengthening the post-administration time up to 68h will only ensure the same proportion of patients to show through concentrations up to 4 mg/L.

<table>
<thead>
<tr>
<th>Time (h)</th>
<th>Mean total ceftazidime concentration (mg/L ± SD) in evaluable patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>26.9±14.4 A.a (n=27)</td>
</tr>
<tr>
<td>68</td>
<td>12.5±6.8 B.b (n=27)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Threshold</th>
<th>Time (h)</th>
<th>Number of patients with concentration above threshold</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 8</td>
<td>44</td>
<td>23/26 B.a (79.3%)</td>
</tr>
<tr>
<td></td>
<td>68</td>
<td>19/27 B.a (70.3%)</td>
</tr>
<tr>
<td>&gt; 4</td>
<td>44</td>
<td>23/26 B.a (79.3%)</td>
</tr>
<tr>
<td></td>
<td>68</td>
<td>19/27 B.a (70.3%)</td>
</tr>
</tbody>
</table>

* After the end of ceftazidime infusion (and corresponding to the time of starting the dialysis session).
† Total concentrations (free concentrations are 83.9±20.4% [95% CI 79.2 to 88.6] of the corresponding total concentrations).
‡ EUCAST breakpoint (mg/L) for Pseudomonas and Enterobacterales, respectively.

Statistical analyses: differences with different letters are significantly different from each other (p<0.05) for (i) comparisons across each row (horizontal); upper case letters [A or B]; (ii) for comparisons across each column (vertical); lower case letters [a-b...]. For concentrations: (i) comparison across each row; ANOVA = with Tukey-Kramer Multiple Comparisons Test; (ii) comparison across each column; unpaired t-test. For number of patients: contingency tables (i) across each row; Chi square for all 4 entries (4x2 table) followed by Fisher exact test for successive comparisons between 2 entries (2x2 table); (ii) across each column but limited to pairs of entries corresponding to the same threshold (44 or 68h; 2x2 table); Fisher exact test.

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Abstract 1335

Human dirofilariasis in a changing world: evolving zoonosis just under the skin

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Background: Neglected tropical diseases are emerging in western countries due to migration routes, climate change and widespread access to travel for touristic or working reasons. Generally, clinicians are not aware of prevention measures linked to travel medicine outside vaccination schedules. Parasites are ubiquitous in the world and may mimic different medical conditions making diagnostic workup challenging.

Materials/methods: Case report.

Case report description: A 67-years old colleague, returning from 1-month fellowship in a rural hospital in Ethiopia, consulted our unit after three months of generalized pruritus and after the appearance of a palpable lump on his right forearm associated to intense generalized pruritus. His past medical history was unremarkable except for seasonal rhinitis well controlled by antihistamines. During his stay he remained asymptomatic except for a circumscribed arm swelling that progressed slowly in the following weeks. The lesion was evident at the time of consultation, appearing as a 20 mm swelling with intact superficial skin with no redness, warmness or pain. Baseline blood analysis showed normal leukocyte count without eosinophilia. All other laboratory parameters, including total IgE levels, tested within reference ranges. Ultrasonography found a well-circumscribed lesion, measuring 11x7x10 mm and containing anechogenic fluid with linear hyper echoic worm-like structures resting at the bottom of the cyst. Microscopic evaluation of three stool samples, blood specimens for microfilariae detection, as well as serologies for Filaria spp, Strongyloides spp, Trichinella spp. and Echinococcus spp. resulted negative. The nodule underwent excision and parasitological examination confirmed the presence of Dirofilaria repens [Figure attached].

Conclusions: Human dirofilariasis is currently considered a re-emerging mosquito-borne zoonosis caused by filarial worms of the genus Dirofilaria. Adults D. repens, the most significant Dirofilaria coupled with D. immitis, are commonly located in subcutaneous tissues, and the approach is primarily surgical. D. repens is currently found in Europe, Asia, and Africa, but has recently spread into colder regions; we are facing a continuous increase in the risk for humans to acquire dirofilariasis, because of climate changes, frequent travel and more extensive distribution of vectors outside tropical settings. The always evolving epidemiology should prompt physicians attention on neglected tropical diseases.

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Emergence of a mupirocin-resistant, methicillin-susceptible Staphylococcus aureus clone associated with skin and soft tissue infections in Greece

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Abstract 1336

Abstract 1336

Background: Staphylococcus aureus is associated with several infections, ranging from skin and soft tissue infections (SSTIs) to more invasive diseases. Various pathogenic factors are known, including methicillin resistance and virulent genes' carriage. In this study, S. aureus from SSTIs in patients among three tertiary care hospitals in different areas of Greece (Athens, Patras, Larisa) were compared in terms of antimicrobial resistance patterns, clonal distribution, toxins and adhesin genes’ carriage.

Materials/Methods: From a total of 10459 SSTIs recorded during five-year period 2014-2018, 5090 S. aureus were recovered. Of them, 4137 (81.28%) were methicillin-susceptible (MSSA). Antimicrobial resistance was determined by a gradient and the disk diffusion methods, according to EUCAST guidelines. Mupirocin-resistant were 1365/4137 (32.99%) of MSSA associated with SSTIs (mainly impetigo). Among 194 representative strains, genes encoding Panton-Valentine Leukocidin (PVL, lukS/lukF-PV), exfoliative toxins (eta, etb), adhesin FnB (fnbA) and the resistance genes mupA (mupirocin), fusB (fusidic acid), ermA, ermC (macrolides/lincosamides), were defined by PCRs with specific primers. Clones were determined by MLST.

Results: From 2014 to 2017, an increase of mupirocin-resistant isolates among MSSA causing SSTIs was observed, from 1.721% to 41.34%, followed by a decrease in 2018 [35.24%] (Figure 1). All tested isolates were mupA-positive with mupirocin MICs ranging from 64 to >1024 mg/L. Most strains were multi-resistant, with higher resistance observed against penicillin (100%), fusidic acid (92.78%) and tobramycin (89.95%). One major clone was identified, ST121, comprising of 192/194 (98.97%) tested strains. Most isolates carried eta (93.3%), etb (97.94%), fnbA (88.75%), and fusB (98.41%). The majority of erythromycin-resistant strains carried ermC (34/39, 87.18%). Only one MSSA out of 194 tested, classified as ST1, was PVL-positive. One more strain belonged to ST21 being negative for toxins’ genes.

Conclusions: An annual increase of mupirocin-resistant MSSA recovered from patients with SSTIs was observed from 2014 to 2017, with a decrease in 2018. The emergence of a predominant MSSA clone, ST121, resistant to mupirocin and highly resistant to tobramycin and fusidic acid was confirmed. This successful clone, comprised of PVL-negative isolates carrying resistance, exfoliative toxins and adhesin genes, predominated in SSTIs from patients in three different areas of Greece during the five-year period.

% MSSA among S. aureus from SSTIs
% Mupirocin-resistant among MSSA from SSTIs

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Abstract 1341

Community and nosocomial sepsis in older adults with bacteraemia: a retrospective study in a geriatric ward

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Background: Sepsis is a global medical emergency that involves not only Intensive Care Units, but also Internal and Geriatric Wards. The incidence of sepsis is disproportionately higher in elderly adults and age is an independent predictor of mortality. Despite this, there are few available data about sepsis in elderly patients in order to help physicians to promptly diagnose and manage it.

Materials/methods: Retrospective study about 149 patients consecutively admitted to Acute Geriatric Ward from 1 January 2017 to 30 June 2019 with positive blood cultures. We evaluated clinical characteristics, autonomies, parameters and blood tests at admission and calculate the main validated scores predicting mortality and diagnosis of sepsis. We divided patients in 2 groups: community bacteremia (CB, positive blood cultures within 48h from admission) and nosocomial bacteremia (NB). Epidemiology, site of infection, antibiotic resistance and therapeutic choices has been studied.

Results: We classified 107 patients as CB and 42 patients as NB. Overall median (IQR) age was 86 (81-91) years, 51% of patients were male. 65% of the sample came from home, but were defined as frail and with limited autonomies (median (IQR) CSF 7 (6-8)). 57% were diagnosed with dementia at admission, and 54% developed delirium at onset. Classic symptoms of sepsis (fever, hypotension, tachycardia) were absent in the majority of patients. qSOFA score was >2 only in 35% and 45% of CB and NB respectively. Polimicrobial bacteremia was significantly higher in NB compared to CB patients (23.8% and 11.2%, p=.014). 65% of CB cases were due to Gram – only, while 50% of NB to Gram + only. 49.5% of CB originated from urinary tract infection, while 42.9% of NB from blood stream infection. Duration of antibiotic therapy was significantly higher in CB patients compared to NB ones. Mortality due to sepsis at day 21 was 14.3% in CB patients compared to 21.1% in the NB (p=ns).

Conclusions: Elderly patients with sepsis have clinical peculiar characteristics. Symptoms at onset are often atypical and not specific. Delirium appears in many patients, and it is an early sign of severity that should be recognized to promptly treat the leading cause.

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Abstract 1346

Multinational performance evaluation of the BIOFIRE FILMARRAY Pneumonia plus (PNplus) panel
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Abstract third-party references: On behalf of the EMEA Evaluation Program Collaborative, Supported by bioMerieux/BioFire Diagnostics LLC

Background: Identification of pathogens causing community acquired, health-care and ventilated associated pneumonia can be problematic. The BioFire PNplus Panel detects 15 bacteria (with semi-quantification), three atypical bacteria, eight viral classes and seven antibiotic resistance markers (mecA/C/MREJ, CTX-M, KPC, VIM, IMP, NDM, OXA-48 like) directly from sputum-like specimens (induced or expectorated sputum; endotracheal aspirates), and bronchoalveolar lavage (BAL)-like specimens with results in about one hour.

Materials/methods: 52 laboratories from 13 countries across Europe and Israel compared the BioFire PNplus Panel results to standard of care (SOC) test results. SOC tests varied by site and included various combinations of culture, urinary antigen, molecular assays, and direct fluorescent antibody assays. A total of 2,501 samples (1,252 sputum-like and 1,249 BAL-like) were tested. Comparison of semi-quantification results for BioFire PNplus Panel and SOC bacterial pathogens were compared for 1,297 matched detections.

Results: A total of 3,278 bacterial analytes included on BioFire PNplus Panel were detected by at least one method. The BioFire PNplus Panel identified 3,128 (95%) analytes compared to 1,878 (54%) for SOC. The BioFire PNplus Panel detected 93 atypical bacteria and 618 viruses compared to 73 atypical bacteria and 135 viruses for SOC. Semi-quantitative values for the BioFire PNplus Panel were less than SOC values, equal to SOC values or greater than SOC values in 5.09%, 25.91% and 69.01% of the results, respectively. On average, BioFire PNplus Panel values were approximately 1 log higher than SOC values (57.75% 1-2 log; 11.26% 3-4 log). All resistance markers were detected at least once by the BioFire PNplus Panel and in various combinations, with mecA/C/MREJ the most prevalent in Staphylococcus aureus (20.35%), followed by CTX-M (8.0%) and KPC (4.3%) in applicable gram-negative bacteria.

Conclusions: Despite variations in laboratory testing methodologies across testing sites, BioFire PNplus Panel performed consistently with enhanced detection of all types of respiratory pathogens. In particular, limited SOC testing for viruses was shown to be a missed opportunity to define the potential cause of respiratory infection. Identification of the potential cause of pneumonia and associated resistance markers in approximately 1 hour could dramatically change antimicrobial selection and enhance patient outcomes.

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Abstract 1350

In vitro activity of ceftolozane/tazobactam against clinical isolates of carbapenem-resistant Pseudomonas aeruginosa from Japan hospitals

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Background: Ceftolozane/tazobactam [TAZ/CTLZ], a new-generation cephalosporins, is the first drug combined with a β-lactamase inhibitor, i.e., a cephalosporin antibacterial agent, to be effective against drug-resistant bacteria such as multi-drug-resistant Pseudomonas aeruginosa and ESBL-producing Enterobacteriaceae. In the present study, we examined its antibacterial activity against carbapenem-resistant P. aeruginosa and performed genetic analysis for resistant strains.

Materials/methods: Clinically isolated carbapenem-resistant P. aeruginosa strains (40 non-carbapenemase-producing strains) were tested. In the drug susceptibility test, an E-test (bioMérieux) was performed to measure the MIC50/90 and sensitivity (CLSI M100-S29). In addition, strains with a MIC of 16 mg/L were compared with a PAO1 strain for mRNA expression of the AmpC gene by sequencing and qRT-PCR.

Results: The MIC50/90 values (mg/L) of TAZ/CTLZ of all 40 strains were 2/16, with a susceptibility rate of 85%. The AmpC gene was sequenced, revealing V239A and A97V mutations. The expression levels of the AmpC gene increased 8-43-fold in all strains except one.

Conclusions: The antibacterial activity of TAZ/CTLZ for carbapenem-resistant P. aeruginosa is higher than that of the other β-lactams, and should be effective against strains with drug resistance involving outer membrane proteins. In addition, we found that resistant strains existed before the use of TAZ/CTLZ in Japan, and that such strains were caused by mutations and increased expression of the AmpC gene, although no highly resistant bacteria were detected.

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Abstract 1354

**Treatment status and prognosis of 203 cryptococcosis in non-human immunodeficiency virus-infected and nontransplant patients**

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**Background:** To learn the treatment status and prognosis of cryptococcosis in non-human immunodeficiency virus-infected and nontransplant patients.

**Materials/methods:** We retrospectively analyzed the gender, age, diagnosis, treatment and prognosis of 203 non-human immunodeficiency virus-infected and nontransplant patients of cryptococcosis from 2012 to 2018.

**Results:** There were 196 pulmonary cryptococcosis patients and 7 disseminated cryptococcosis patients of all the 203 non-human immunodeficiency virus-infected and nontransplant patients. 196 pulmonary cryptococcosis patients included 127 men (64.80%) and 69 women (35.20%) and the average age of men was 49.57 years old and the average age of women was 54.52 years old. 5 patients (2.55%) were diagnosed by culture, 112 patients (57.14%) were diagnosed by biopsy and 79 patients (40.31%) were diagnosed by latex agglutination test. 104 patients have finished the course of treatment among the 143 patients in the department of medicine, 74 patients were cured (71.15%), 27 patients were improved (25.96%), 1 patient was in persistence (0.96%) and 2 patients were treated surgically (1.92%); among the patients who have finished the course of treatment, 77 patients (6.04%) use fluconazole effectively, 9 patients (8.65%) used voriconazole effectively, 2 patients (1.92%) used itraconazole effectively and 13 patients (12.50%) used amphotericin B or amphotericin B liposome effectively. 53 patients were diagnosed by the surgical pathology, 27 patients (50.94%) used anti-fungal after the operation, 23 patients (43.40%) didn’t get any treatment and no recurrence was found, 3 patients (5.66%) were loss to follow up. Among 7 patients of disseminated cryptococcosis, 2 patients were cured, 2 patients were undergo treatment and 3 patients were withdrawn. The starting dose and maintenance dose were various in the 77 non-human immunodeficiency virus-infected and nontransplant patients who were cured by fluconazole. 8 patients (57.14%) got renal impairment among 14 patients of pulmonary cryptococcosis who used amphotericin B or amphotericin B liposome.

**Conclusions:** Triazoles is always effective in the pulmonary cryptococcosis in the non-human immunodeficiency virus-infected and nontransplant patients; few patients relapses and the prognosis is favorable.

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Abstracts 2020

Abstract 1357

Roles of the FadRACB system in formaldehyde detoxification and antibiotic susceptibility in Stenotrophomonas maltophilia

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Background: Formaldehyde toxicity is invariably stressful for microbes. Stenotrophomonas maltophilia, a human opportunistic pathogen, is widely distributed in different environments and has evolved an array of systems to alleviate various stresses. This study aimed to characterize the formaldehyde detoxification system FadRACB of S. maltophilia with respect to formaldehyde detoxification and antimicrobial susceptibility.

Materials/methods: Presence of fadRACB operon was verified by RT-PCR. Single or combined deletion mutants of fadRACB operon were constructed for functional assay. Formaldehyde quinolone susceptibilities were assessed by observing cell viability in formaldehyde- and quinolone-containing media, respectively. Agar dilution method was used to assess the bacterial susceptibilities to antibiotics. Expression of fadRACB was assessed by qRT-PCR.

Results: The fadR, fadA, fadC, and fadB genes are arranged in an operon. Mutants in fadA and/or fadB were more susceptible to formaldehyde than wild-type KJ. No significant difference was observed in the ability of fadC single mutant to defend formaldehyde; however, simultaneous inactivation of fadA, fadB, and fadC further enhanced the susceptibility toward formaldehyde. In addition, compared to wild-type KJ, the triple mutant KJΔFadACB was more susceptible to quinolone and more resistant to aminoglycosides. FadR functions as a repressor for fadRACB operon. FadRACB operon has a moderate expression in aerobically-grown wild-type KJ and is further de-repressed by formaldehyde challenge, but not by antibiotics.

Conclusions: FadACB system contributes to mitigation of formaldehyde toxicity and cross-protects S. maltophilia from attacks of quinolone.

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Abstract 1358

**Antifungal susceptibility profiles of olorofim (formerly F901318), and currently available systemic antifungals against mould and yeast phases of Talaromyces marneffei**

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**Background:** *Talaromyces marneffei* is a thermal dimorphic fungus and is the etiologic agent of talaromycosis, a life-threatening disease which affects immunocompromised host especially those with HIV infection. The fungus is endemic in Southeast Asia and is known to be associated with bamboo rats. Talaromycosis is initially treated with amphotericin B but its use is limited due to toxic side effects. Therefore, the need for new antifungals to treat talaromycosis is urgent. Olorofim is a novel fungicidal drug which targets dihydroorotate dehydrogenase in the de novo pyrimidine biosynthesis pathway. It is highly active against *Aspergillus* and other filamentous *Ascomycetes*. However, the *in vitro* efficacy of olorofim against *T. marneffei* has yet to be reported. We therefore aimed to evaluate the susceptibility of *T. marneffei* to olorofim and other currently available systemic antifungals in its yeast as well as in mold phases.

**Materials/methods:** We tested 32 clinical and environmental *T. marneffei* strains recovered from southern China against 8 different antifungals according to the Clinical and Laboratory Standards Institute M38-A2 and M27-A3 guidelines.

**Results:** The geometric means of the minimum inhibitory concentrations/minimum effective concentrations (MICs/MECs) of the antifungals against mold phase of all *T. marneffei* strains were (in increasing order): olorofim (0.0005 mg/mL), itraconazole and posaconazole (0.016 ug/mL), voriconazole (0.05 ug/mL), 5-flucytosine (0.08 ug/mL), terbinafine (0.1 ug/mL), caspofungin (0.4 ug/mL) and amphotericin B (2 ug/mL). The geometric means MICs/MECs against the yeast phase were, as follows: olorofim (0.0007 ug/mL), posaconazole (0.016 ug/mL), itraconazole (0.016 ug/mL), voriconazole (0.017 ug/mL), terbinafine (0.12 ug/mL), amphotericin B (0.13 ug/mL), 5-flucytosine (0.25 ug/mL), and caspofungin (4.5 ug/mL). Olorofim was the most active antifungal agent against both mold and yeast phases of all tested *Talaromyces marneffei* isolates, exhibiting an MIC range, MIC50, and MIC90 of 0.0005-0.002 ug/mL, 0.0005 ug/mL, and 0.0005 ug/mL, respectively.

**Conclusions:** In summary, olorofim demonstrated potent and consistent activity against all *T. marneffei* strains *in vitro*, and its activity was maintained in two different growth phases. Further studies are warranted to evaluate the *in vivo* efficacy of olorofim against this fungus.

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Bloodstream infections caused by strong biofilm-producing bacteria increase the risk of end-organ disease and mortality in patients with haematologic malignancies

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Background: Bacterial bloodstream infection (BSI) represents a major complication in patients with hematological malignancies (HM). However, factors leading to BSI, as well as progression to end-organ disease and death, are only partially understood. The study aims at analyzing host and microbial risk factors and assesses their predicted impact on the development of BSI and mortality.

Materials/methods: A total of 96 patients with HM and BSI were included in the study. Host-associated risk factors and all-causes of mortality were analyzed by multivariable logistic regression at 30 days after onset of the first BSI in the first neutropenic episode. The multidrug-resistant (MDR) profile and biofilm production of bacterial isolates were included in the analysis.

Results: The median age was 60 years [range 20-77 years]. The underlying diagnoses were acute leukemia n=53 (55%), lymphoma n=30 (31%) and myeloma n=13 (14%). Bacterial isolates from BSI were 96. Escherichia coli was the most common isolate [n=28, 29.2%], followed by Pseudomonas aeruginosa [n=16, 16.7%]. MDR [n=10] caused 10.4% of bacteremia episodes. Weak biofilm producers were significantly (P<0.0001) more abundant (72.2%) than strong (27.8%) biofilm-producers. Specifically, strong biofilm-producers were 9.6% for E. coli, 100% for P. aeruginosa, 50% for K. pneumoniae, and 23.3% for Coagulase-negative Staphylococcus spp. (CoNS). Mortality at day 30 was 8.3% [8/96], and all deaths were attributable to Gram-negatives. About 22% of all BSI were catheter-related (CRBSI). The mortality rate (P=0.62) and the level of biofilm production (P=0.75) were not correlated with CRBSI. Notably, strong biofilm-producing bacteria were found to be an independent risk factor (P=0.018) associated with the end-organ disease. Besides, multivariate analysis indicated that the presence of strong biofilm-producing bacteria (P=0.013) and MDR strains (P=0.006) were independent risk factors associated with 30-day mortality.

Conclusions: Strong biofilm-producing bacteria and MDR strains caused a limited fraction of BSI in patients with HM. Strong biofilm-producing bacteria present a high risk of end-organ disease and that, together with an MDR phenotype, are significantly and independently associated with an increased risk of death. The rapid identification of biofilm-producing bacteria from BSI can offer a key biomarker to predict the clinical and therapeutic outcomes in patients with HM.

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Abstract 1363

Genetic structure characteristics and treatment for Listeria monocytogenes infections
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Background: Invasive Listeria monocytogenes (Lm) carry a high mortality despite antibiotic treatment. The aim of this study was to investigate the mechanism of pathogenicity and resistance. In addition, the effect of existing treatment options against Lm were systematically evaluated as well.

Materials/methods: Three Lm isolates were collected and 15 antibiotics susceptibility tests were done. Subsequently, the genetic characteristics were investigated by genome sequencing and bioinformatics analysis. Furthermore, the effect of meropenem, linezolid, benzylpenicillin, vancomycin, trimethoprim/sulfamethoxazole were determined using the time-kill assay.

Results: Two sequence types (STs) were identified for isolate 23949 (ST87), 26530 (ST3), 34096 (ST87), respectively. All isolates were resistant to fosfomycin and daptomycin. The resistant genes fosX, mprF, norB and vgaALC were identified in all isolates. Furthermore, 80 virulence genes were detected and 72 genes were found in all three isolates. There were 26 virulent genes associated with the structure, biosynthesis, motor switch of flagellum. And other virulent genes were involved in chemotaxis, protease, internalin and metabolism. It is of note that 8 genes were only found in 26530 isolated from cerebrospinal fluid (CSF), 7 of which were associated with haemolysin. Further in vitro time-kill assay found trimethoprim/sulfamethoxazole at serum or CSF concentrations had bactericidal effect (>3.5 log10 CFU/ml) against three tested Lm strains at 24 h.

Conclusions: The involved virulence factors were mainly associated with bacterial pathogenicity. Notably, trimethoprim/sulfamethoxazole might be greater potential therapeutic option against Lm bloodstream infection or intracranial infection.

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Epidemiology of nosocomial candidaemia in paediatrics: a multi-centre study in Iran

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Background: Nosocomial bloodstream candidaemia is a life-threatening fungal infection with high morbidity and mortality, especially among paediatric patients undergoing intensive immunosuppressive therapy. Limited data on the epidemiology of candidaemia and susceptibility profiles are available in Iran. We aimed to characterize candidaemia epidemiology, comorbidity risk factors, species distribution, and antifungal susceptibility profiles among paediatric patients in Iran.

Materials/methods: A total of 26,189 hospitalized patients under 18 years old were involved. Blood samples from patients with suspected fungal bloodstream infection were analysed using the BACTEC culture system. Fungal isolates were identified using matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF) and DNA sequencing. Antifungal susceptibility testing was performed using the Clinical and Laboratory Standards Institute broth microdilution method.

Results: Overall, 109 episodes of nosocomial candidaemia, with an incidence of 4.1 cases per 1000 admissions, were observed among paediatric patients with or without immunosuppressive therapy. The most common healthcare-associated factor was the use of a central vascular catheter (97.24%). The all-cause mortality rate was 40.36%, of which 48% was attributable to candidaemia. While Candida albicans (49%) was the most frequent causative agent, emerging and uncommon Candida species were also isolated. The mortality of candidaemia caused by non-albicans Candida species were significantly higher from those of candidaemia caused by C. albicans (P < 0.05). All fluconazole resistant species were non-albicans Candida species.

Conclusions: Uncommon Candida species with reduced susceptibility to antifungal agents are likely to become the major agents of nosocomial candidaemia in high-risk patients in Iran, such as paediatric cancer patients. Appropriate source control, antifungal regimens, and strengthening of antifungal stewardship policies are all needed for the management and decrease of the burden of nosocomial candidaemia.

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Abstract 1367

Gentamicin-intercalated smectite as a new therapeutic agent against Helicobacter pylori infection and faecal microbiome analysis after eradication in mouse model

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Background: The eradication rate of Helicobacter pylori with conventional standard therapy shows a decreasing trend, because of antibiotics resistance especially clarithromycin. Thus, novel antibacterial strategies against H. pylori are needed. We evaluate the efficacy of a gentamicin-intercalated smectite hybrid [S-GM]-based treatment regimens including toxicity of S-GM using fecal microbiome analysis in a murine model of H. pylori infection.

Materials/methods: To evaluate anti-H. pylori efficacy, mice were divided into 8 groups, and H. pylori eradication was assessed by Campylobacter-like organism (CLO) test and H. pylori PCR of the gastric mucosa. For the test of toxicity of S-GM, four different model was designed. One week after the end of H. pylori eradication, the levels of proinflammatory cytokines and the atrophic changes of gastric mucosa were examined. In addition, stool specimens were collected, and analyzed for microbiome changes in each group.

Results: The S-GM-based triple regimen decreased bacterial burden in vivo, compared to that in untreated mice or mice treated with other regimens. The therapeutic reactions in the CLO test from gastric mucosa were 90, 90, 80, 80, 70, and 10% in Groups III-VIII, respectively. Those of H. pylori PCR in gastric mucosa of mice were significantly lower in Groups III-VIII than in the Group II. In the results of toxicity of S-GM, S-GM triple therapy also reduced the level of IL-8 and the atrophic change of gastric mucosa. In the analysis of stool microbiome, abundant microorganisms of phylum level were presented, and the diversity of microbiome was preserved in the S-GM triple therapy comparing the standard triple therapy.

Conclusions: These results suggest that S-GM is a promising and effective therapeutic agent for the treatment of H. pylori infection.

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Abstract 1370

Features and outcomes of tuberculosis among internally displaced people in East Ukraine
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Background: From the start of military conflict now there are about 1 500 000 officially confirmed internally displaced people (IDP) in Ukraine. In 2018 there were about 35,0 % of new and 62,0 % of re-treated confirmed cases of multiple and extensive drug resistant tuberculosis (MDR/XDR TB). This study aims to analyze the features and outcomes of TB among IDP in a given TB hospital.

Materials/methods: In 2014-2018 in a given TB hospital were treated 409 patients. Among them there were 51 cases of TB in IDP. Some patients were hospitalized more than one time – discharging from hospital was done mainly (85,0%) because of migration to and out of military conflict territory. Thus, 37 patients (IDP) with TB were treated in the hospital – 28 (75,7%) males and 9 (24,3 %) females. Patients` age was 23-87 years old, middle age 41,6.

Results: 22 (59,5 %) patients were without any temporary place of living, 7 (18,9 %) – HIV infected, 9 (24,3 %) – intravenous drug users. Medical help was provided according to national protocols. HIV-infected IDP had an opportunity to get antiretroviral therapy (ART), drug users – opioid substitutional therapy, as any other Kharkiv region citizens. 32 (86,4 %) patients had MDR/XDR TB. Treatment was prescribed by the results of drug susceptibility tests and previous case` s history (TB-manager – Ukrainian national TB database). Outcomes were analyzed according to WHO recommendations: 8 (21,6%) – treatment success (2 (5,4 %) – cured, 6 (16,2 %) – finished), 29 (78,4 %) – unsuccessful treatment (6 (16,2 %) – dead (2 (5,4 %)– brain stroke (elderly and senile aged IDP), 2 (5,4 %) – HIV-TB co-infection, 2 (5,4 %) – very severe cases of MDR-XDR TB), 15 (40,5 %) – lost to follow up, 8 (21,6 %) – treatment failure (all of them – MDR-XDR TB)).

Conclusions: Experience of working with IDP shows ways how to improve TB management: rapid diagnostics, social adaptation of TB patients, decreasing of stigma, availability of TB drugs, opioid substitution therapy and ART in all levels of medical support. National database as a TB-manager is very helpful to identify case even if it is from different territory and gives the mechanism to improve MDR/XDR TB epidemic.

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Abstract 1376

Nasal colonisation by Staphylococcus aureus in nursing home residents in Crete, Greece

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Background: About 25% of healthy persons are asymptptomatically colonized by in the anterior nares S. aureus and may spread the pathogen to other individuals, while they carry a higher risk of infection.

Materials/methods: This is a point-prevalence study detecting nasal colonization by S. aureus in nursing home residents conducted in 6 long-term care facilities (LTCFs) on the island of Crete, Greece. Nasal swabs were cultured in order to detect for S. aureus while risk factors for colonization were evaluated. Nasal swabs were also collected from healthy non-residents of LTCFs of the same age that were used as controls. Data collected included age, gender, duration of stay in LTCFs, comorbidities, antibiotic exposure, and recent hospitalization.

Results: A total of 290 LTCF residents aged 65 years or more were enrolled. Mean age was 83.1 years; 30.7% were male (89 residents). The median length of stay at the LTCF was 23 months. Residents with a Charlson comorbidity index ≥3 were 24.7% (82 residents). Recent hospitalization and recent antibiotic use were recorded in 8.6% (25 residents) and 13.4% (39 residents) respectively. Among the 290 residents, 28.6% (83) were colonized by S. aureus, while 66.5% of them (55 residents) were MRSA carriers. Analysis of S. aureus and MRSA prevalence among the LTCF residents and 43 healthy controls of the same age did not reveal statistically significant differences. Statistical analysis revealed that S. aureus colonization was more common in women (34.3%) than in men (21.7%) and that the only factor associated with MRSA colonization was recent antibiotic exposure (23.6% if recently on antibiotics vs 3.6% if not; p=0.028).

Conclusions: Colonization by S. aureus is quite common in LTCFs, but the rate may not differ from that in the community. Recent antibiotic exposure significantly increases the risk for MRSA colonization.

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Background: Pyogenic liver abscess (PLA) is a severe disease, whose unfavorable evolution may be categorized by primary treatment failure, recurrence or death. Our objective was to assess predictive factors of unfavorable courses in patients with PLA.

Materials/methods: We conducted a retrospective population-based study in Beaujon hospital, a single tertiary care center of Paris area. All patients admitted for a PLA episode between 2010 and 2018 were included. An unfavorable course was defined by the occurrence of a primary treatment failure (clinical worsening and/or increased radiological size despite appropriate treatment, requiring modification of antimicrobial therapy and/or new drainage), a recurrence occurring at least 28 days after an initial cure, or death within 3 months after diagnosis.

Results: Overall, 317 patients were included. Median age at diagnosis was 60 years (19-92); 208 (65.6%) patients were male. Healthcare-related and nosocomial infections accounted for 86 (27.1%) and 38 (12%) of cases, respectively. A biliary origin (179/317, 56.5%) was the main mechanisms of PLA occurrence. In patients with a biliary origin, hepato-biliary tumoral obstruction and ischemic cholangitis were retrieved in 70/179 (39%) and 32/179 (17.8%) patients, respectively. E. coli was the first pathogen isolated (104 patients, 24.5%), followed by Enterococcus spp. (55 patients, 17.4%); 46/424 (10.8%) microorganisms isolated from an initial PLA episode were multi-drug resistant organisms (MDRO). An unfavorable course occurred in 91 (28%) patients: primary treatment failure and recurrence were reported in 56 (17.6%) and 28 (8.8%) patients, respectively; 32 (10%) patients died within 3 months. Factors independently associated with an unfavorable course were a healthcare-related infection (HR=1.74, p=0.033), an underlying metastatic liver (HR=2.76, p<0.001), a portal thrombosis (HR=2.46, p=0.001), an ischemic cholangitis (HR=2.16, 0.008), presence of fungi (HR=3.08, p=0.008), enterococci. (HR=1.81, p=0.020) or MDRO (HR=1.88, p=0.020); PLA drainage versus no drainage was associated with a better outcome (HR=0.52, p=0.005).

Conclusions: Unfavorable course after an initial PLA episode remains frequent and likely occurs in a healthcare setting. Identification of risk factors may help to improve management of PLA and to elaborate targeted recommendations according to patient and disease's characteristics.

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Abstract 1378

**Infection incidence among patients colonised with carbapenem-resistant Enterobacteriaceae (CRE) and microbial aetiology**

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**Background:** CRE are important pathogens in Hospital Acquired Infections (HAI). Intestinal colonization with CRE precedes infection and has negative effects on the morbidity and mortality. There are conflicting data in the literature on the percentage of patients developing infection after intestinal colonization. The purpose of this study is to analyze the incidence of infection in colonized subjects detected through surveillance with rectal swab and hospitalized at ASST Lariana, also considering different bacterial species involved.

**Materials/methods:** A retrospective research is carried out evaluating the annual and cumulative incidence of CRE infection in rectal swab-positive patients, from January 2016 to June 2019. Isolation sites, hospitalization wards and bacterial etiology are considered. The surveillance first involved the patients admitted to intensive care, but was later extended to patients from long-term care, patients with hospitalization lasting more than 30 days, patients with hospitalization in the 60 days before. Furthermore, all patients admitted to Geriatrics and Neurorehabilitation are screened. Samples taken by rectal swab are seeded on chromogenic medium, with incubation at 24 hours; bacterial identification and antimicrobial susceptibility are performed with MALDI-TOF and VITEK2 (bioMerieux).

**Results:** From 2016 to June 2019, respectively: 60, 74, 72 and 30 (first six months) cases of carriers of CRE were identified. The wards were: Medicine (61%), Surgery (11%), Rehabilitation (12%) and Intensive care (16%). The total incidence of CRE infection in colonized patients was 23.7%. The most involved sites of infection were the urinary tract (56.2%) followed by the lower respiratory tract. The bacterial etiology was K. pneumoniae with the following percentages: 96.6% in 2016, 94.4% in 2017, 93.2% in 2018 and 80% in the first six months of 2019, with a growing finding of E. coli KPC.

**Conclusions:** Our study showed a 23.7% incidence of CRE infection in colonized patients, higher than verified in other research, suggesting the need for further longitudinal and epidemiological investigations. The bacterial etiology was found to be in line with the literature data, showing however a tendency towards an increase in the finding of bacterial species different from K. pneumoniae.

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**Abstract 1381**

**Antibiotic use in French hospitals 2012-2018: improvements to be confirmed!**

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**Background:** Surveillance of antibiotic consumption is at the core of mandatory antimicrobial stewardship programmes in hospitals. A national standardized method was developed to describe antibiotic consumption at hospital level. In order to assess the impact of antibiotic stewardship activities, namely guidelines on broad spectrum antibiotics, changes in antibiotic consumption between 2012 and 2018 were described.

**Materials/methods:** Antibacterials for systemic use (J01class, WHO Anatomical Therapeutic Chemical classification, ATC-DDD system), oral imidazole derivatives and fidaxomicin were surveyed for inpatients in voluntarily participating hospitals and expressed in number of defined daily doses (DDD) per 1 000 patient-days (PD). Data were retrospectively collected from pharmacy records and administrative services each year.

**Results:** The number of participating hospitals increased from 1 411 in 2012 to 1 630 in 2018 covering 73% of national PD in 2018. Antibiotic use increased between 2012 and 2015 (+1.8%) and decreased from 2016 (-8.5%) to reach 288 DDD/1000PD in 2018. Despite an overall increase in third generation cephalosporin use (+13% between 2012 and 2018), ceftriaxone use was 10% lower in 2018 compared to 2013; carbapenem use tended to remain stable since 2015. By contrast, the consumption of piperacillin-tazobactam, linezolid and daptomycin steadily increased from 2012 (+76%, 92% and 379% respectively). Proportion of broad spectrum antibiotics (ECDC secondary indicator for hospitals) was 32% in 2012 and 34% in 2018.

**Conclusions:** Recent surveillance data tend to show a stabilisation and even a decrease in antibiotic consumption, namely for antibiotics targeted by guidelines (ceftriaxone in 2014, carbapenems in response to increase in carbapenem-resistant Enterobacteriaceae cases), highlighting the usefulness of specific recommendations with clear messages. However, attention should be given to the increasing use of other antibiotics, namely in the context of emergence of linezolid-resistant staphylococci. To better inform next steps in promotion of prudent antibiotic use and antimicrobial resistance control, a new national project for surveillance and prevention of antimicrobial resistance in hospitals (SPARES) was set up in 2018. Hospitals are provided with standardized methods and webtools allowing 1) a more comprehensive antimicrobial resistance surveillance and 2) cross-transmission prevention audits in order to allow identification of areas for improvements at both local and national levels.

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Whole genome sequencing and comparative analysis of echinocandin susceptible and resistant sequential *Candida glabrata* clinical isolates

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**Background:** *Candida glabrata* ranks as the second most common cause of candidemia in many countries. Echinocandin resistance in *C. glabrata* is emerging. The aim of this study was to compare the genomes of two sequential echinocandins susceptible and resistant *C. glabrata* related isolates.

**Materials/methods:** Two bloodstream *C. glabrata* isolates were serially recovered from a 72-year-old female patient with candidemia post contrary artery bypass grafting procedure (CABG) before and after caspofungin treatment (<3 months interval). Whole-genome sequencing (WGS) was performed on these two isolates to determine genetic changes using 2x250bp paired-end sequencing using MiSeq system (illumina).

**Results:** In vitro antifungal susceptibility testing showed an increase in MIC against caspofungin and anidulafungin for the post-treatment isolate (8 mg/L, 2 mg/L respectively) compared to the pre-treatment isolate (0.03 mg/L for both), indicating the acquisition of echinocandins resistance. Isolates confirmed to be genetically related with same MLST type. Genomic analysis of pre-treatment isolate with post-treatment isolate identified 17 nonsynonymous SNVs, including a novel undescribed F1113C substitution in FKS2 gene in addition to the previously described F625S substitution in FKS1 gene. One novel SNV was detected in ERG2 gene (G92D substitution) that belongs to the ergosterol biosynthesis-related family which is known to mediate antifungal resistance in *C. glabrata*. Multiple SNVs were present in genes related to transcriptional and translational activation in response to cellular stress such as: MSS11, MIT1, FIR1, RNR1, DNA2, RPN9, BRE2, ROX3, and CMP2, while others were found in genes related to cell wall components and have functions in membrane transportation and localization such as: SECS, WSC4, and VMAS. Two SNVs were found in genes of unknown function.

**Conclusions:** *C. glabrata* has the ability to rapidly acquire echinocandin resistance. The genomic changes observed in the resistant isolate highlight the diverse mechanisms by which *C. glabrata* can adapt to the pressure of echinocandin therapy and host environment.

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Abstract 1384

The ultrastructural visualisation of Severe Fever with Thrombocytopenia Syndrome (SFTS) virus in human PBMC sample

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Background: Severe Fever with Thrombocytopenia Syndrome (SFTS) virus was first discovered in China. In Korea, it was first discovered in Gangwon-do in 2013 and the number of patients has been steadily increasing and has a high mortality rate of more than 30%. Before April 2017, symptoms of SFTS appeared only in humans by ticks as a medium, but since then, animals such as dogs and cats have developed symptoms of SFTS.

Materials/methods: We infected human-derived SFTS virus and dog-derived virus with vero cells and HEK cells, respectively, and then analyzed by Quantitative Real-Time PCR (qRT-PCR) analysis to identify genetic differences. Transmission electron microscopy (TEM) was also performed to confirm the morphology and composition of both cells. Furthermore, the ultrastructure of SFTS virus in human PBMC sample which is provided by Chonbuk national university hospital in Korea has been observed using TEM.

Results: SFTS is sphere and a dense nucleocapsid core of 90-120 nm which is characteristic of enveloped viruses, phleboviruses, commonly known as colonies. We also found the viral particles in monocytes from human samples.

Conclusions: The findings will help to provide a structural basis for the detection and diagnosis of SFTS infections.

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Abstract 1388

Results of an outpatient parenteral antimicrobial therapy programme in Spain

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Background: Outpatient parenteral antimicrobial therapy (OPAT) is an alternative for the conventional therapy to infectious diseases. The main advantages it offers are the reduction of the complications of conventional hospitalization, better quality of life for the patient and his family and the saving of hospital stay, with the consequent reduction of the economic cost for the health system. The results of an OPAT program are described.

Materials/methods: A retrospective, observational study of all patients attended between 2018-2019 in OPAT program of University Hospital of Cabuñes, Spain were performed. Demographics, therapy characteristics, pathogens, adverse events (AEs), and clinical outcomes were evaluated. Effectiveness was assessed by analyzing readmissions to hospital for inadequate control of underlying infection. Safety was assessed by analyzing adverse events, catheter-related complications and readmission to hospital before 30 days after the end of treatment.

Results: Eighty-six patients (55.8% females, mean age: 73 years) were included. The most frequent underlying diseases were neoplasm (25.6%), respiratory diseases (16.3%), cardiovascular diseases (14%), and diabetes (9.5%). Urinary tract infections (39.5%) were the most frequent infection followed by respiratory infections/pneumonia (30.2%), intra-abdominal infections (7%), endocarditis, septic arthritis, hepatobiliary diseases (4.7% each), prosthesis joint infection and cellulitis (3.5% respectively) and catheter-related sepsis (2.3%). Twenty-five percent of patients had bacteremia. The most frequent microorganisms were Escherichia coli (24.2%), Pseudomonas aeruginosa (15%) Staphylococcus aureus (7%), Klebsiella pneumoniae (4.7%), Staphylococcus epidermidis, Citrobacter freundii, Streptococcus group viridans (3.5% each) among others. In thirty cases the microorganism produced extended spectrum beta-lactamases. The most frequent treatment was ertapenem (34.8%) followed by piperacillin-tazobactam (23.3%), ceftriaxone (19.8%) and daptomycin (7.5%). Only six patients (7%) patients had a recurrence Six patients dead due to the infection. There are not significantly differences in sex, age, or underlying diseases between relapses or not. Catheter-related complications occurred in 3 patients. Mean duration of treatment was 13 days. Twenty days of antibiotic treatment was saved.

Conclusions: OPAT programs are a safe and effective alternative that saves hospital stay even in patients with bacteremia. The readmission rate is low and the level of patient satisfaction high.

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Extreme levels of diversity of *Mycobacterium tuberculosis* across a large genomic dataset: a map to disease pathogenesis and stress survival

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**Background:** *Mycobacterium tuberculosis* (*M*. *tuberculosis*) is a bacterial pathogen causing tuberculosis (TB), an ancient disease, which is one of the biggest infectious “killers” worldwide. It is almost 20 years since the first *M*. *tuberculosis* genome sequence. Many landmark studies have been undertaken, but have mainly focussed on phylogenetic analysis, drug resistance and outbreak investigation. However, a deeper understanding of the diversity present across all *M*. *tuberculosis* genes at a population level is required, especially in the future discovery of novel drug targets or vaccine candidates. We performed an unbiased gene-by-gene analysis of 8535 *M*. *tuberculosis* genomes by studying the extremes of nucleotide sequence diversity distribution - i.e. genes with low and high levels of nucleotide sequence diversity across the sequenced population.

**Materials/methods:** Public genomic data covering all seven *M*. *tuberculosis* lineages was retrieved and curated. A total of 8535 genome sequences were mapped against the reference *M*. *tuberculosis* genome, H37Rv, in order to identify single nucleotide polymorphisms (SNPs). The results of the initial mapping were further processed and a diversity frequency distribution of all the genes was identified.

**Results:** We show that levels of diversity across genes are not normally distributed and that there are genes with extreme levels of diversity and others with extreme levels of conservation. In highly variable genes, variants were found to occur at hotspots, and largely encoded functions related to disease pathogenesis and drug resistance. Such diversity may make it problematic to create a vaccine or drug that successfully targets the known diversity of *M*. *tuberculosis* strains. Conversely, very conserved genes are associated with the protection of the *M*. *tuberculosis* under stress conditions, intra-macrophage infection and the latent stage of the disease. This suggests that these genes are highly important in the TB infection cycle, and may constitute more preferential drug and vaccine targets to combat TB.

**Conclusions:** This study can be used as a “map” of the evolutionary trajectory of *M*. *tuberculosis* genes across all lineages and might inform the development of future vaccine candidates and novel anti-TB medication.

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Abstracts 2020

Abstract 1395

**Pathogen Box screening identifies novel antimicrobials that target *Mycobacterium chimaera***

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**Background:** *Mycobacterium chimaera* is a slow growing nontuberculous mycobacterium that is part of the *Mycobacterium avium* complex (MAC). *M. chimaera* infection has been identified in patients having previously undergone cardiac surgery and it is also increasingly being detected in patients with chronic lung disease. Like many mycobacterial infections, *M. chimaera* is recalcitrant to antimicrobial therapy and require long treatment regimens. There is an urgent need to both identify novel antimicrobials and to re-purpose drugs to treat *M. chimaera* as current treatment regimens are inadequate with patient mortality as high as 50%.

**Materials/methods:** In this study, we screened the Pathogen Box library, which consists of 400 drug-like molecules against *M. chimaera* using a resazurin based microtiter plate assay to determine cell survival that was validated with Z-factor analysis. Selected hits were characterised with dose response curves and time kill kinetics.

**Results:** A total of 21 hits were identified based on a cut off of 70% or more *M. chimaera* growth inhibition when screened at the single concentration of 20 µM. Dose response curves of four compounds (MMV02248, MMV675968, MMV688179 and MMV688271) showed favourable activity against *M. chimaera*, with MMV675968 exhibiting activity similar to clarithromycin which forms part of front line treatment of *M. chimaera*. In addition, one of the hits identified was doxycycline, which is a broad-spectrum antimicrobial drug. Doxycycline generated a minimum inhibitory concentration of 6.25 µg/mL against *M. chimaera* and is bacteriostatic, based on time kill kinetic studies. Three oxazolidinone compounds linezolid, sutezolid and radezolid were also identified as hits against *M. chimaera*.

**Conclusions:** Here, we identified new chemical entities as well as oxazolidinone compounds that show good activity against *M. chimaera* that could lead promising new antimicrobials with further drug development. As well as identifying new compounds, we have identified the currently licensed antimicrobial doxycycline as showing efficacy against *M. chimaera*. Doxycycline is a commonly used and well-tolerated antimicrobial that should be investigated further as part of treatment regimens for *M. chimaera* infection.

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**Abstract 1397**

Anaplasmosis in Poland: underestimated disease?

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Background: Human cases of *Anaplasma phagocytophilum* infection are not frequently reported in Europe. However, the disease may be underdiagnosed due to the nonspecific nature of presenting symptoms. The aim of our study was to clarify the clinical picture of anaplasmosis through analysis of the symptoms and clinical signs displayed by infected patients in a cohort of tick-bitten individuals.

Materials/methods: The study included 1375 patients after a tick bite. Finally, 120 patients (8.7%) were diagnosed with anaplasmosis. Routine laboratory tests, serological and molecular microbiologic investigations were performed. Blood samples were examined by PCR for *A. phagocytophilum*, *Candidatus Neoehrlichia micurcensis*, *B. burgdorferi*, *Babesia* spp., *Coxiella burnetii* and *Bartonella* spp. Positive samples were confirmed by sequencing. Serological analyses for tick-borne encephalitis virus and thin blood smears for detection of *Anaplasma* morulae were performed.

Results: Among 120 patients with HGA, there were 66 men (55%) and 54 women (45%). All patients had *A. phagocytophilum* DNA in blood samples that was detectable by standard PCR and confirmed by sequence analysis. 40 (33.3%) of patients were co-infected with *Borrelia burgdorferi*, 20 (17%) of patients were co-infected with TBEV, and one patient (0.83%) was co-infected with a *Babesia* spp. and 40 (33.3%) with *Borrelia burgdorferi*. Anaplasmosis patients presented with headaches, vertigo, nausea, vomiting, muscle pain, joints pain, and fever. Comparison of differences between patients with mono- and co-infection showed differences in symptoms and higher CRP concentration and AST activity in patients with co-infection. All patients recovered after doxycycline therapy.

Conclusions:

1. Anaplasmosis is not as rare in Europe, as it is thought to be.
2. Anaplasmosis often appears as a co-infection with other tick-borne pathogens.
3. Co-infection of *A. phagocytophilum* with *Borrelia burgdorferi* or TBEV may influence symptoms frequency.
4. PCR together with anamnesis, clinical picture and basic laboratory tests is a sufficient method for anaplasmosis diagnosis.
5. Doxycycline is an effective drug leading to complete recovery.

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Abstract 1403

**Toxocariasis in children in south Russia: epidemiological and laboratory features**

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**Background:** Clinical features of toxocariasis depend on geographic localization and age of patients. Aim: to investigate: epidemiological, clinical and laboratory features of toxocariasis in children in the South of Russia.

**Materials/methods:** We analyzed official statistical data in the period from 2014 to 2018 and implemented a retrospective analysis of 57 medical records of patients (40 children and 17 adults) who received treatment and were under observation in the clinic of infectious and parasitic diseases of the Rostov Scientific Research Institution of Microbiology and Parasitology, Rostov-on-Don, Russia.

**Results:** According to official statistics, the proportion of children aged 0 to 17 ranged from 33% to 37%. Based on clinical and laboratory examination, the diagnosis was established in 26 patients (45.6%). Among patients with a verified diagnosis of toxocariasis, the proportion of children from 2 years and 5 months to 9 years old was 96.0%. An analysis of epidemiological data showed that 76.0% of children had close contact with the soil. The invasion occurred in the form of latent toxocariasis in 9 (35%) patients. In more than half of the children, the invasion was clinically manifested by geophagy (54.0%). A permanent laboratory indicator in patients with toxocariasis was the leukemoid eosinophilic type reaction. Peripheral blood eosinophilia ranged from 15.66 ± 9.31 with latent toxocariasis to 25.5 ± 15.0 with visceral. In some cases, this figure exceeded 60%. The coefficient of positivity (CP) in ELISA with toxocariasis antigen in patients with latent toxocariasis was higher than in the group of patients with visceral toxocariasis. No correlation between the level of eosinophilia and CP in ELISA with toxocariasis antigen was established in the each of group (r = 0.1).

**Conclusions:** The results of our analysis of the epidemiology of toxocariasis showed that preschool children (68.0%) who are in close contact with the soil (76.0%) are most susceptible to invasion, which does not correspond to the official statistical reporting data. Infestation in children is often asymptomatic (36% according to our data). If peripheral blood eosinophilia is detected, an ELISA test with a toxocariasis antigen is recommended.

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A clinical predictive model of multidrug resistance in neutropenic cancer patients with bloodstream infection due to Pseudomonas aeruginosa (IRONIC study)

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Abstract third-party references: On behalf of the IRONIC study group

Background: We aimed to assess the rate and predictive factors of bloodstream infection (BSI) due to multidrug-resistant (MDR) Pseudomonas aeruginosa (PA) in neutropenic cancer patients.

Materials/methods: We performed a multicenter, retrospective cohort study including onco-hematological neutropenic patients with BSI due to PA conducted across 34 centers in 12 countries from January 2008 to May 2018. A mixed logistic regression model was used to estimate a predictive model for developing multidrug resistance.

Results: A total of 1217 episodes of BSI due to PA, 309 episodes (25.4%) were caused by MDR strains. The rate of multidrug resistance increased significantly over the study period (p=0.033). Predictors of MDRPA BSI were prior therapy with piperaci-
lin/tazobactam [odds ratio [OR], 3.48; 95% confidence interval [CI], 2.29-5.30], prior antipseudomonal carbapenem use [OR, 2.53; 95% CI, 1.65-3.87], fluoroquinolone prophylaxis [OR, 2.99; 95% CI, 1.92-4.64] underlying hematological disease [OR, 2.09 95% CI, 1.26-3.44] and the presence of a urinary catheter [OR, 2.54; 95% CI, 1.65-3.91], whereas older age [OR, 0.98, 95% CI, 0.97-0.99] was found to be protective.

Conclusions: Our prediction model achieves good discrimination and calibration thereby identifying neutropenic patients at higher risk of BSI due to MDRPA. The application of this model using a web-based calculator may be a simple strategy to identify high-risk patients, who may benefit from the early administration of a broad-spectrum antibiotic coverage against MDR strains in accordance with the local susceptibility patterns, thus avoiding the use of broad-spectrum antibiotics in patients at low risk of resistance.

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Abstract 1408

**Long-term suppressive treatment of cardiac surgery-related *Mycobacterium chimaera* disseminated infection**

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**Background:** *M. chimaera* infections after cardiac surgery are characterized by high morbidity and mortality rate due to dissemination of infection and high affinity of mycobacteria to form biofilm on the prosthetic devices. Prolonged anti-mycobacteria treatment and removal of all cardiovascular prosthetic material (redo-operation) are suggested to obtain source control and avoid breakthrough infection. Nevertheless, in some patients, owing to comorbidities redo-operation is not feasible. The management of inoperable patients remains undefined especially regarding the number of drugs, the regimen and the length of anti-mycobacteria treatment. We report our experience on long term treatment of inoperable patients.

**Materials/methods:** We retrospectively reviewed all cases of *M. chimaera* infection following cardiac surgery diagnosed in our hospital.

**Results:** Nine patients were diagnosed with disseminated *M. chimaera* infection. Two females and 7 males, mean age 59 years. All patients were treated with an initial combination therapy: clarithromycin, ethambutol and a rifamycin in addition to clofazimine or linezolid. Three underwent redo-operation, one died 48 hours after surgery owing to septic shock, the other had a breakthrough infection 9 months after surgery. One underwent redo-operation owing to a life-threatening periaortic abscess, before the diagnosis of *M. chimaera* infection was established. Among the six non re-operated patients three experienced a breakthrough infection, two of them died. Three are on long-term suppressive antibiotic therapy (clarithromycin+ethambutol) after respectively 8, 14 and 18 months of four drugs, lead-in, anti-mycobacteria treatment. The blood, urine and stool culture are persistently negative, the clinical condition and quality of life are good, the therapy is well tolerated, no side effects occurred after respectively 21, 26 and 27 months of follow up.

**Conclusions:** The long follow up of our non re-operated patients suggests that control of *M. chimaera* infection, in selected cases, is feasible with a long-term suppressive anti-mycobacteria therapy alone. We suggest that further studies should investigated the optimal timing and the criteria for redo-surgery and the final impact on patients survival. More clinical data are need to identify patients who will most benefit a conservative approach instead of implanted device substitution and to define the optimal medical therapy for inoperable patients.

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Abstract 1409

**Usefulness of the 16S rRNA gene PCR and sequencing in the diagnosis of prosthetic joint infections**

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**Background:** Microbiological cultures of prosthetic joint infections (PJI) often yield false negative results. We performed a prospective, comparative study to evaluate the usefulness of 16S RNA gene polymerase chain reaction and sequencing in the diagnosis of PJI.

**Materials/methods:** Patients older than 18 years who underwent surgery for a suspected joint prosthesis infection according to 2012 IDSA definitions were included as cases and primary arthroplasties as controls. We analyzed all surgical samples using conventional cultured (identification was performed using phenotypic methods and MALDI-TOF MS) and 16S PCR and sequencing. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for both methods.

**Results:** Twenty cases and 38 controls were included. Average age for cases 69.5 years (23-91) and 70 (24-90) for controls. We included 12 hips and 8 knees as cases and 19 hips and 19 knees as controls. Microorganisms were isolated by culture in 11/20 cases (S. epidermidis 3, S. hominis 3, S. aureus 2, E. coli 1, E. cloacae 1 and Streptococcus viridans group 1) and negative in 9. 16S PCR was positive in 18/20 cases (S. epidermidis 3, S. aureus 3, S. hominis 3, Cutibacterium acnes 3, Streptococcus viridans group 1, E. faecalis 1, E. coli 1, E. cloacae 1 and non-culturable microorganisms 2). Of the 9 negative cultures 16S PCR was positive in 2: Cutibacterium acnes 3, E. faecalis 1, S. aureus 1 and non-culturable microorganisms 2. In one case Cutibacterium acnes was detected by PCR in addition to the microorganism isolated by culture. Cultures and PCR were negative in 100% of the controls. For 16S PCR sensitivity was 90 %, specificity 100%, PPV 100 % and NPV 95%. For culture sensitivity was 55 %, specificity 100%, PPV 100 % and NPV 80.45.

**Conclusions:** In our study 16S PCR and sequencing was a useful tool in the diagnosis of PJI in cases with negative culture and in polymicrobial infections, allowing the identification of bacteria not detected in the culture.

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Hospital organisation, management and implementation of culture of excellence in infection control and prevention of hospital-acquired infections at Ziv medical centre, Israel

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Background: Infections associated with health-care institutes are a threat to the medical treatment safety and manifest in 5-10% of the hospitalized patients. During the last three years we implement culture of excellence on infection control. The intervention was based on the ministry of health incentive model on infection control in Israel which include 33 measurement elements stratified to 8 categories: Infection control team, hospital facility, hand hygiene training and compliance, computing support, quality parameters of microbiology laboratory, antibiotic stewardship, health care worker immunization and environmental cleaning and disinfection.

Materials/methods: Three years of implementation the culture of excellence and closing gaps in infection control elements supported by the hospital management. To achieve goals and excellence in infection control we empower nurses in infection control in each department, facility improvement, active surveillance of MDR bacteria, bacteremia and central line associated bloodstream infection (CLABSI) and hand hygiene, implementation of guidelines of antibiotic treatment and stewardship, immunization of health care worker, training of physicians and nurses on central line insertion, maintenance and infusion therapy including total parenteral nutrition.

Results: Comparing data from 2016 to 2019, the immunization coverage of health care workers (HCW) rise from 33% to 92% respectively. CLABSI declined from 6 per 1,000 line days to 0.8. Hospital acquired UTI decline from 2.4/1000 hospital days at 2018 to 1.2 at 2019, Carbapenemase producing Enterobacteriaceae (CPE) decline from 27.8/100K hospital days to 19.1, Carbapenem resistant Acinetobacter baumannii declined from 17.6/100k hospital days to 6.3. The score of excellence rise from 54.1% to 81.2%, being one of the higher score comparing with other governmental hospitals.

Conclusions: Management support and creating positive organization culture in infection control, bridging the facility gaps, training of staff, surveillance of processes and outcomes and monitor the quality of environmental cleaning are the main elements for hospital infection prevention of resistant bacteria and CLABSI, HCW protection from vaccine preventable diseases.

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Abstract 1419

**Dose optimisation of cefotaxime in critically ill patients: a population pharmacokinetic study**

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**Background:** Cefotaxime is a beta-lactam antibiotic used in critically ill patients to treat infections. Literature data on the pharmacokinetics (PK) of cefotaxime in these patients are lacking. A two-centre prospective, observational study in critically ill patients was undertaken. The aim of this study was to describe the PK of cefotaxime and propose a dosing regimen in critically ill patients.

**Materials/methods:** Critically ill patients treated with cefotaxime dosed 1g q6h or q4h were included. Five samples were drawn per patient during one dosing interval. PK parameters were estimated using NONMEM. Monte Carlo simulations (n=5000) were performed using Miclab 2.36 (Medimatics, NL) to determine Probability of Target Attainments (PTA). The percentage of patients reaching 100% T>MIC was used to compare different dosing regimens for Enterobacterales and S. aureus.

**Results:** 92 patients (57 males), median age (range) of 64 (23-85) years, weight 76 (45:150) kg and creatinine clearance 57 (4-347) ml/min were included. A total number of 437 observations were analyzed. The best structural model was a two-compartment model with a combined error, and interindividual variability (IIV) on clearance (CL), central volume (V1), and inter-compartmental clearance (Q). Correlations between IIV were included. CL increased with higher CKD-EPI (creatinine clearance) and higher albumin concentration and could explain 48% of IIV on CL. The estimates population parameters were 7.08 ml/min for CL; 15.7 L for V1; 25.0 L for V2 and 4.81 L/h for Q. For Enterobacterales (ECOFF 0.25 mg/L), 100% of patients reached the target with 1g q6h [15 minutes infusion time]. For S. aureus (ECOFF 4 mg/L) a PTA of 64.2% and 88.8% was reached for the regimen 1g q6h and 1g q4h, respectively. With an increased dose of 2g q4h 97.3% of critically ill patients reached the target for S. aureus.

**Conclusions:** In critically ill patients, cefotaxime PK is best described by a two-compartment model with CKD-EPI and albumin concentration as covariates influencing clearance. All dosing regimens are adequate to treat Enterobacterales. However, this study indicates that for S. aureus the dosing regimen needs to be increased to 2g q4h administered over 15 min.

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Abstract 1420

High-resolution influenza mapping of a city reveals socioeconomic determinants of transmission within and between urban quarters

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Background: With two-thirds of the global population projected to be living in urban areas by 2050, understanding the transmission patterns of influenza within cities is crucial for effective prevention strategies. Here, in unprecedented spatial resolution, we analysed the socioeconomic determinants of influenza transmission in a European city (Basel, Switzerland). We aimed to described the incidence rates of influenza cases and transmission patterns in context to socioeconomic determinants.

Materials/methods: Our dataset included all PCR confirmed influenza cases from 2013 to 2018. We conducted a large city-wide survey with more than 30,000 distributed questionnaires [2015/2016 season]. Whole genome sequencing (WGS) data of 663 viral isolates was used to analyse the transmission network [2016/2017 season]. We combined geographical and epidemiological data with WGS of influenza viruses at the scale of urban quarters and statistical blocks, the smallest geographic subdivisions within a city.

Results: We observed annually re-occurring geographic hotspots of influenza incidences, mainly associated with net income, and independent of population density and living space. In the questionnaire, vaccination against influenza was positively associated with household income and negatively linked to the likelihood of influenza-like illness within an urban quarter. Of WGS samples (n=663), a diverse set of 54 clusters (within 10 SNPs cut-off) were observed within the city. The phylogeny of isolates reflected the global diversity. A generally high exchange rate and complex transmission dynamic between different urban quarters was observed. Significant within quarter transmission was observed for two quarters with low socioeconomic scores and lower pre-seasonal herdimmunity as determined by heagglutination inhibition assays.

Conclusions: High-resolution city-level epidemiological studies combined with social science surveys such as this will be essential for understanding infectious disease transmission chains and delivering tailored public health information and vaccination programs at the municipal level.

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Abstract 1430

**Outcome impact of a highly bactericidal scheme as initial treatment of acute staphylococcal PJI**

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**Background:** S. aureus is one of the most common pathogens involved with acute PJI. Management usually involves DAIR and antibiotic treatment. Here we present the evaluation of our experience with a scheme of treatment that combines a high bactericidal combination followed by an antibiofilm combination.

**Materials/methods:** Between April 2011 and October 2018, 48 acute PJIs caused by S. aureus were treated with DAIR in our center, (15TKA and 33 THA). Time between index surgery and DAIR, antibiotic treatment scheme and follow-up were revised. We have compared the results between the new antibiotic scheme (5 days of daptomycin + cloxacillin followed by levofloxacin+rifampicin) with the previous combinations, based in the use of less-bactericidal combinations, mainly comprising vancomycin plus rifampicin or levofloxacin plus rifampicin.

**Results:** 23 patients were treated with DAIR diverse antibiotic combinations, after a mean period of 22.7 days after index surgery (range 12-39) and received a mean of 102.8 days of antibiotic treatment (range 35-180). 16 of them (63.6%) were free of infection after 30.6 months of follow-up (range 2-60). 25 patients were treated with DAIR and a new antibiotic scheme, which includes 5 days of daptomycin + cloxacillin (a combination with high bactericide power), followed by levofloxacin+rifampicin, with anti-biofilm properties, during a mean period of 101.4 days (range 45-180). 21 of them (84%) were free of infection after 11.3 months of follow-up (range 1.5-30). Although the limited sample size does not let us talk in terms of statistical significance, the difference in the healing rate depending on antibiotic treatment shows high clinical relevance. We have observed that this difference is higher when the period between index surgery and DAIR is less than 30 days (89.3% vs 63.2%).

**Conclusions:** The combination of daptomycin +cloxacillin plus levofloxacin+rifampicin, which combines an initial high bactericidal therapy followed by an antibiofilm activity, shows higher healing rates for treatment of acute PJIs caused by S. aureus and treated with DAIR.

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Diagnosis of acute dengue infection in Navarra

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Background: The aim of this study is to analyze the new diagnosis of dengue virus infection in our hospital from January 2016 to September 2019.

Materials/methods: Retrospective study of 255 samples from 227 different patients with possible dengue virus infection; 82 PCR and 173 serology tests were performed. Clinical history of each patient was studied to obtain clinical and epidemiological information. Cases of dengue were defined by clinical symptoms, epidemiological link and positive PCR and/or IgM detection and/or seroconversion. PCR was performed by TropicalFeverCore real-time PCR kit (FastTrack Diagnostics); for serology tests we used Dengue IgM and IgG capture ELISA kit (Panbio) and Dengue Virclia® IgM and IgG monitest (Vircell).

Results: Among all patients studied, 23 (10.1%) were diagnosed of dengue infection; mean age was 38.6 years (SD±11.4 years) and 13 were females (56.5%). Regions of birth were: Europe (60.9%), Africa (8.7%) and South America (30.4%). All patients had travelled to any dengue endemic country in Africa (17.4%), Asia (30.4%) and South/Central America (52.2%). In all cases the onset of symptoms happened during the journey or within 10 days after returning.

Main clinical manifestations were fever (100%), arthralgia/myalgia (60.9%), headache (43.5%) and cutaneous rash (34.8%); 10 cases (43.5%) presented thrombocytopenia and leukopenia. No clinically severe manifestations were observed.

Regarding diagnosis, 7 (30.4%) were performed by PCR and 15 (65.2%) were based on serology: 11 (73.3%) with IgM+/IgG+ and 4 (26.7%) with IgM+/IgG-. One case (4.3%) was confirmed by both PCR and serology. Different serum samples were available only in 2 patients (8.7%) and in both seroconversion was demonstrated.

Conclusions:

- All diagnosis were of imported dengue infection in travellers returning from endemic countries.
- Due to the short period of viremia the possibility of PCR based diagnosis is low. 65.2% of diagnosis were performed only by serological assays, 26.7% of which were based only on IgM reactivity.
- The availability of a second serum sample should be taken into account as an improvement in diagnostic procedure to allow confirmation of diagnosis in these cases by seroconversion.

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Abstract 1432

**Antimicrobial susceptibility of *Cutibacterium avidum* isolated from prosthetic joint infections: differences between biofilms and planktonic bacteria**

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**Background:** *Cutibacterium avidum* is a Gram positive anaerobic rod and known to colonize human moist skin such as the groin. Rarely, it causes abscesses, and hip and shoulder peri- prosthetic joint infections (PJI), and is usually susceptible to Penicillin. However, data about antibiotic susceptibility against planktonic and biofilm *C. avidum* are limited.

**Materials/methods:** We tested the activity of different antibiotics against planktonic and biofilm *C. avidum* in vitro (n=11 isolates from different PJI cases, identified by MALDI-TOF MS). Minimal inhibitory concentrations (MIC) and minimal bactericidal concentrations (MBEC) were evaluated according to the microdilution method by EUCAST, using Mueller Hinton cation adjusted broth with a final bacterial inoculums of 10⁴ CFU per well. The minimal biofilm inhibitory concentration (MBIC) and the minimal biofilm eradication concentration (MBEC) were assessed following the protocol previously described by Coenye et al. (Res Microbiol. 2007 May; 158(4):386-92). Plates were incubated at 37°C for 48 hours under anaerobic conditions.

**Results:** The MIC, the MBC, and MBIC were low for amoxicillin-clavulanic acid, clindamycin, levofloxacin, linezolid, rifampin, and vancomycin (table 1). However, the MBEC to eradicate the biofilm *C. avidum* were high with > 32mg/l except for rifampin with 0.5 mg/L.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC₉₀₀</th>
<th>MBC₉₀₀</th>
<th>MBIC₉₀₀</th>
<th>MBEC₉₀₀</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>0.125 mg/L</td>
<td>0.5 mg/L</td>
<td>0.125 mg/L</td>
<td>&gt; 32 mg/L</td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>0.5 mg/L</td>
<td>0.5 mg/L</td>
<td>1 mg/L</td>
<td>256 mg/L</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>0.5 mg/L</td>
<td>2 mg/L</td>
<td>2 mg/L</td>
<td>&gt;256 mg/L</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>0.25 mg/L</td>
<td>1 mg/L</td>
<td>0.5 mg/L</td>
<td>&gt;32 mg/L</td>
</tr>
<tr>
<td>Linezolid</td>
<td>0.5 mg/L</td>
<td>4 mg/L</td>
<td>0.25 mg/L</td>
<td>&gt;256 mg/L</td>
</tr>
<tr>
<td>Rifampin</td>
<td>0.03 mg/L</td>
<td>0.03 mg/L</td>
<td>0.03 mg/L</td>
<td>0.5 mg/L</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1 mg/L</td>
<td>2 mg/L</td>
<td>1 mg/L</td>
<td>256 mg/L</td>
</tr>
</tbody>
</table>

**Conclusions:** While all tested antibiotics showed bactericidal activity against planktonic *C. avidum* cells, eradication of biofilm *C. avidum* was only possible with rifampin. Currently, we are investigating the value of rifampin for cure of *C. avidum* PJs in a large multicenter study.

**Presenter email address:** jestebanmoreno@gmail.com
Abstract 1435

**Increased serum hydrogen sulfide as determinant of resolution of ventilator associated pneumonia caused by *P. aeruginosa***

Georgios Renieris*1, Konstantina Katrini1, Eleni Karakike1, Nikolaos Antonakos1, Athanasios Karageorgos1, Labros Sabrakos1, Evangelos Giamarellos-Bourboulis1

14th Department of Internal Medicine, National and Kapodistrian University of Athens, Medical School, Athens, Greece

**Background:** Previous data of our group in mice (Renieris G, et al. ECCMID 2018; abstract P0904) showed that host production of hydrogen sulfide (H2S) is modulating host defense against *Pseudomonas aeruginosa*. However, clinical data on the significance of host-derived H2S are lacking. This study investigated the role of host-derived H2S in the outcome of ventilator associated pneumonia (VAP).

**Materials/methods:** From a prospective cohort of 700 Greek patients with VAP, 219 cases caused by *P. aeruginosa* (group A, n=65), *Klebsiella pneumoniae* (group B, n=60) and *Acinetobacter baumannii* (group C, n=94) were selected. Pathogens grew at ≥ 105 cfu/ml in tracheobronchial secretions. H2S was measured by the blue methylene method in serum the first 24 hours.

**Results:** Serum levels of H2S were significantly higher in the resolved VAP cases of group A compared to the non-resolved cases (55.63 ± 10.93 vs 20.98 ± 4.30 μM respectively; p: 0.030). Respective values for group B were 16.03 ± 1.36 vs 16.15 ± 2.15 (p: 0.965) and for group C 17.90 ± 1.05 vs 17.16 ± 1.77 (p: 0.711). Further ROC curve analysis of group A indicated that serum H2S above 45μM could better discriminate resolved cases; 17 patients had more and 48 patients less than 45μM H2S. VAP resolved in 16 (94.1%) and in 27 (56.3%) patients, respectively (p: 0.004). Logistic regression analysis showed that serum H2S above 45μM was an independent protective factor for VAP resolution (Table).

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>95% CIs</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum H2S day 1 &gt; 45 μM</td>
<td>0.03</td>
<td>2.70 – 0.37</td>
<td>0.006</td>
</tr>
<tr>
<td>APACHE II day 1 &gt; 23</td>
<td>2.98</td>
<td>0.54 – 16.38</td>
<td>0.210</td>
</tr>
<tr>
<td>SOFA day 1 &gt; 10</td>
<td>7.05</td>
<td>1.37 – 36.32</td>
<td>0.020</td>
</tr>
<tr>
<td>Isolation of <em>P. aeruginosa</em> in blood</td>
<td>3.14</td>
<td>0.59 – 16.62</td>
<td>0.179</td>
</tr>
</tbody>
</table>

**Conclusions:** Circulating H2S in a novel independent determinant of the outcome of VAP caused by *P. aeruginosa*. This may open new boundaries in personalized therapeutics of VAP.

The study was funded by the ITN Horizon 2020 Marie-Curie European Sepsis Academy

**Presenter email address:** renierisg@yahoo.com
Abstract 1437

Multi-centre study of common pathogen epidemiology in hospitalised children with acute respiratory tract infection in winter from 2017 to 2018, China

Leijun Meng*, Hong Zhang2, Xuejun Shao3, Jun Zhou4

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Background: Acute respiratory tract infections (ARTIs) are a major public health problem and a leading cause of morbidity and mortality in children under the age of 5 years, with the highest number of deaths occurring in developing countries. This study aimed to analyze the epidemiological characteristics of pathogens among children hospitalized with ARTIs during the winter, with the aim of providing a reliable basis for clinical diagnosis and treatment and for rational antibiotics use.

Materials/methods: A total of 563 hospitalized children with ARTIs in the children's hospitals of Shanghai, Hangzhou, and Soochow were enrolled between November 2017 and February 2018, and nasopharyngeal aspirates were collected. Real time PCR assays were performed to detect 14 common pathogens, including Mycoplasma pneumoniae (MP), Chlamydia pneumoniae (CP), Legionella pneumophila (LP), Chlamydia trachomatis (CT), respiratory adenovirus (ADV), influenza virus A and B (IFV-A and IFV-B), human parainfluenza virus types 1-3 (HPIV 1-3), human rhinovirus (HRV), respiratory syncytial virus (RSV), and human metapneumovirus A and B (hMPV-A and hMPV-B).

Results: Of the 563 specimens obtained from the patients, 467 (82.95%) were positive for at least one pathogen. RSV was the most commonly detected pathogen (48.66%), followed by HRV (21.49%). The detection percentages for each of the respiratory pathogens varied considerably by age. RSV was the most common pathogen detected in the children aged less than 6 months. Co-infections were found in 20.6% of the patients. Of these coinfections, the combination of RSV and HRV was the most common.

Conclusions: The detection percentages of respiratory viruses and atypical bacteria in ARTI children was relatively high during the winter in the children's hospitals in Shanghai, Hangzhou, and Soochow. The pathogen incidence varied depending on patient age and ARTI manifestation.

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Abstract 1439

**Risk factors for hospital readmission following complicated urinary tract infection: a multinational, retrospective cohort study**

Tanya Babich*, Noa Eliakim - Raz¹, Adi Turjeman¹, Miquel Pujol², Jordi Carratalà², Evelyn Shaw², Aina Gomila², Cuong Vuong³, Ibironke Addy³, Irith Wiegand³, Sally Grier⁴, Alasdair P. Macgowan⁴, Christiane Vank⁵, Nienke Cuperus⁵, Leonardus Martinus Clemens Van Den Heuvel⁵, Leonard Leibovici¹

¹Beilinson Hospital, Rabin Medical Center, Petah-Tiqva, Israel, ²Hospital Universitari de Bellvitge, Institut d’Investigació Biomèdica de Bellvitge, Madrid, Spain, ³AiCuris Anti-infective Cures, Wuppertal, Germany, ⁴North Bristol NHS Trust, Bristol, United Kingdom, ⁵Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, Netherlands

**Background:** Patients surviving hospitalization are frequently readmitted. About 20% of patients are re-hospitalized during the first month after discharge. These readmissions have a vast implication by negatively influencing the patients’ quality of life and imposing a significant economic burden on the health care system. Understanding the avoidable risk factors for readmission may inform policy for optimal care during hospitalization and proper post-discharge ambulatory care. Therefore, we aimed to determine potentially preventable risk factors for 60-day readmission in patients surviving hospitalization for complicated urinary tract infection (cUTI).

**Materials/methods:** This was a multinational, multicentre retrospective cohort study conducted in Europe and the Middle East. Our cohort included survivors of hospitalization due to cUTI during the years 2013-2014. The primary outcome was 60-day readmission following index hospitalization. Patient characteristics that could have influenced readmission: demographics, infection presentation and management, microbiological and clinical data; were collected via computerized medical records from infection onset up to 60 days after hospital discharge.

**Results:** Overall, 742 patients were included. The median age of the participants was 68 years (interquartile range, [IQR] 55-80) and 43.3% (321/742) of patients were males. The all-cause 60-day readmission rate was 20.1% (149/742) and more than half were readmitted for infection [57.1%, (80/149)]. Recurrent cUTI was the most frequent cause for readmission [46.4% (65/140)]. A quarter of non-infection related readmissions were for urinary tract abnormalities or instrumentation. Statistically significant risk factors associated with 60-day readmission in the multivariable analysis were: older age (OR 1.02 for an one-year increment, CI 1.005-1.03), diabetes mellitus (OR 1.63, 95% CI 1.04-2.55), cancer (OR 1.7, 95% CI 1.05-2.77), previous UTI infection in the last year (OR 1.8, 95% CI: 1.14 - 2.83), insertion of an indwelling bladder catheter (OR 1.62, 95% CI 1.07-2.45) and insertion of percutaneous nephrostomy (OR 3.68, 95% CI 1.67-8.13). Length of hospital stay and discharge to long term facilities were not statistically associated with readmission.

**Conclusions:** Patients surviving hospitalization for cUTI are frequently re-hospitalized, mostly for recurrent urinary infections associated with a medical condition that necessitated urinary interventions. Interventions to avoid re-admissions should target these patients.

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Abstract 1442

Clinical impact of rapid susceptibility testing in Gram-negative bloodstream infections
Vanessa Antón Vázquez*1, Cristina Suarez1, Samuel Adjepong2, Timothy Planche1,2

1St George’s, University of London, Institute of Infection and Immunity, London, United Kingdom, 2St George’s NHS Foundation Trust, Medical Microbiology, London, United Kingdom

Abstract third-party references: St. George’s University of London, National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care (CLAHRC) South London, UK

Background: Rapid antimicrobial susceptibility testing (AST) might have the potential to improve patient care when results are available and communicated to clinicians in a timely manner. The aim of service evaluation is to assess the clinical impact of rapid susceptibility testing in patients with Gram-negative BSI.

Materials/methods: A prospective service-evaluation was conducted from March 2018 to December 2018 at St. George’s Hospital, London. Alfred 60AST system had been introduced to routine clinical management for AST of Gram-negative bacteria, directly from positive blood cultures. In routine practice, the Alfred 60AST was only run Monday-Friday before midday and results were communicated to clinicians in the same working day of positive blood culture. Patients in which the culture became positive after midday were tested by conventional AST (Phoenix). Times-to-antibiotic and clinical outcomes were compared between rapid and conventional AST. Odds ratio for discontinuation of antibiotics were generated.

Results: 191 patients were included, 93 in the rapid group and 98 in the standard group. The two groups did not differ with regard to co-morbidity, severity, source of infection, source control, multidrug-resistant organisms. The median time between blood culture collection and the reporting time of AST results was 36h (IQR; 16 – 123) in the rapid group and 63h (IQR; 34 – 5760) in the standard, p<0.001. Time to optimal antibiotic was shorter in the rapid group 43h (IQR; 3-339) vs 66.5h (IQR; 0-872), p=0.023. Aminoglycosides were stopped earlier in the rapid group 32h (IQR; 0-795) vs 54h (IQR; 4-216), p=0.002. Effective antibiotic escalation guided by AST results was initiated earlier in the rapid group 36h (IQR; 0-335) vs 51h (IQR; 2-408), p=0.028. Rapid AST and escalation of non-aminoglycosides by 48h were predictors for discontinuation of aminoglycosides at 48 hours [OR, 2.1; 95% [CI 1.1 - 3.9], p=0.03] and [OR, 3.4; 95% [CI 1.7 - 6.9], p<0.01] in binary logistic regression. No differences were found in 28-day mortality, length of stay, time to discharge, time to effective antimicrobial or time to stop all antibiotics.

Conclusions: Rapid susceptibility testing resulted in faster discontinuation of aminoglycosides and a shorter time to escalate beta-lactam therapy and to start optimal antibiotic.
### Demographics

<table>
<thead>
<tr>
<th></th>
<th>RAPID  n = 32</th>
<th>STANDARD n = 56</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>50 (54%)</td>
<td>49 (88.5%)</td>
<td>0.565</td>
</tr>
<tr>
<td>Age in years (Mean; SD)</td>
<td>66.4 (SD:20)</td>
<td>63.7 (SD:26)</td>
<td>0.607</td>
</tr>
<tr>
<td>Charlson index score (Mean; SD)</td>
<td>5.7 (SD:2.3)</td>
<td>5.6 (SD:2.9)</td>
<td>0.065</td>
</tr>
<tr>
<td>Pilt bacteraemia score ( &gt; = 2)</td>
<td>43 (43%)</td>
<td>49 (50%)</td>
<td>0.36</td>
</tr>
<tr>
<td>Escherichia coi in blood culture</td>
<td>62 (97%)</td>
<td>56 (97%)</td>
<td>0.142</td>
</tr>
<tr>
<td>Extended-spectrum-beta lactamase organism (ESBL)</td>
<td>18 (17%)</td>
<td>12 (12%)</td>
<td>0.773</td>
</tr>
<tr>
<td>Urinary source of blood stream infection</td>
<td>46 (52%)</td>
<td>49 (50%)</td>
<td>0.930</td>
</tr>
<tr>
<td>Empirical effective antimicrobial</td>
<td>86 (56%)</td>
<td>84 (88%)</td>
<td>0.378</td>
</tr>
</tbody>
</table>

### Antimicrobial outcomes*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>RAPID: 36 h [IQR: 16 - 123]</th>
<th>STANDARD: 63 h [IQR: 34 - 5760]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to AST communication results</td>
<td>38 h [IQR: 16 - 123]</td>
<td>63 h [IQR: 34 - 5760]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time to first effective antibiotic</td>
<td>2 h [IQR: 0 - 57]</td>
<td>3 h [IQR: 0 - 83]</td>
<td>0.205</td>
</tr>
<tr>
<td>Time to stop aminoglycosides</td>
<td>32 h [IQR: 0 - 785]</td>
<td>54 h [IQR: 4 - 218]</td>
<td>0.092</td>
</tr>
<tr>
<td>Time to effective escalation</td>
<td>36 h [IQR: 0 - 326]</td>
<td>51 h [IQR: 2 - 408]</td>
<td>0.965</td>
</tr>
<tr>
<td>Time to Optimal antimicrobial</td>
<td>43 h [IQR: 3 - 326]</td>
<td>57 h [IQR: 9 - 672]</td>
<td>0.923</td>
</tr>
</tbody>
</table>

### Clinical outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>RAPID: 7 (9%)</th>
<th>STANDARD: 13 (13%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality at 28 days</td>
<td>7 (9%)</td>
<td>13 (13%)</td>
<td>0.240</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome</th>
<th>RAPID: 11 [IQR: 0 - 47]</th>
<th>STANDARD: 10.5 [IQR: 0 - 71]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay</td>
<td>11 [IQR: 0 - 47]</td>
<td>10.5 [IQR: 0 - 71]</td>
<td>0.64</td>
</tr>
</tbody>
</table>

*(Time-to-event was measured from the time of blood culture collection)*

**Presenter email address:** vanesa.anton.v@gmail.com
**Abstract 1448**

**Antimicrobial susceptibility of bacteria isolated from patients with pneumonia in Brazil, Argentina, and Mexico: results from the SENTRY programme in Latin America (2015-2018)**

Ana Gales*, Ana Streling1, Carolina Silva Nodari1, Thais Rezende1, Cecilia Carvalhaes2, Helio S. Sader2

1Universidade Federal de São Paulo, São Paulo, Brazil, 2JMI Laboratories, North Liberty, United States

**Background:** The SENTRY Antimicrobial Surveillance Program monitors the frequency of occurrence and antimicrobial susceptibility of organisms from various infection types worldwide. We evaluated the frequency of occurrence and antimicrobial susceptibility results for organisms isolated from patients hospitalized with bacterial pneumonia in 3 Latin American countries.

**Materials/methods:** A total of 977 bacterial isolates were consecutively collected (1/patient) in 2015-2018 from 7 Latin American medical centres located in Brazil (n=427; 3 centres), Argentina (n=281; 2 centres) and Mexico (n=269; 2 centres). Organisms were tested for susceptibility by reference broth microdilution method in a central laboratory (JMI Laboratories). EUCAST and CLSI breakpoints were applied.

**Results:** The most common organism was *P. aeruginosa* in Brazil and Argentina, and *A. baumannii* in Mexico (Table). *P. aeruginosa, S. aureus, K. pneumoniae,* and *A. baumannii* represented the top 4 organisms in all 3 countries and accounted for 71.2-80.7% of the collection. Gram-negative bacilli (GNB) represented 75.6%, 81.9% and 92.6% of organisms; and non-fermentative (NF) GNB represented 45.4%, 43.8%, and 49.1% of organisms in Brazil, Argentina, and Mexico, respectively. *P. aeruginosa* susceptibility to ceftazidime, piperacillin-tazobactam, and meropenem were 87.0%, 79.7%, and 79.7% in Brazil, 72.3%, 69.1%, and 62.8% in Argentina, and 81.2%, 85.4%, and 79.2% in Mexico, respectively. Only 7.5% of all *A. baumannii* isolates (0.0-12.5%) were meropenem-susceptible. Besides colistin (96.9-100.0%), the most active agents tested against *A. baumannii* were minocycline and tobramycin, with susceptibility rates (CLSI) of 100.0% and 68.8% in Brazil, 56.0% and 36.0% in Argentina, and 69.2% and 33.8% in Mexico, respectively. Overall MRSA rates were 22.2% in Brazil, 25.0% in Mexico, and 40.4% in Argentina, and decreased during the study period. *K. pneumoniae,* susceptibility (EUCAST) to ceftriaxone and meropenem were 34.0% and 36.0% in Brazil, 44.1% and 73.5% in Argentina, and 49.3% and 84.9% in Mexico, respectively. CRE rates were 17.1%, 12.1%, and 12.0% in Brazil, Argentina, and Mexico, respectively.

**Conclusions:** GNB represented a large proportion (75.6-92.6%) and NF-GNB accounted for almost half of organisms isolated from patients with pneumonia, and resistance rates were extremely high among these organisms. In contrast, a decreasing trend was observed in MRSA rates.

<table>
<thead>
<tr>
<th>Rank</th>
<th>Frequency of top 7 organisms stratified by country</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Brazil (n=427)</td>
</tr>
<tr>
<td>1</td>
<td><em>P. aeruginosa</em> (32.3%)</td>
</tr>
<tr>
<td>2</td>
<td><em>S. aureus</em> (21.1%)</td>
</tr>
<tr>
<td>3</td>
<td><em>K. pneumoniae</em> (11.7%)</td>
</tr>
<tr>
<td>4</td>
<td><em>A. baumannii</em> (7.5%)</td>
</tr>
<tr>
<td>5</td>
<td><em>S. marcescens</em> (4.9%)</td>
</tr>
<tr>
<td>6</td>
<td><em>E. cloacae</em> (3.5%)</td>
</tr>
<tr>
<td>7</td>
<td><em>S. maltophilia</em> (3.3%)</td>
</tr>
</tbody>
</table>

**Presenter email address:** ana.gales@gmail.com
Do patients colonised by carbapenemase-producing *Klebsiella pneumoniae* have greater crude mortality? ANGEL-KpS Study

Angela Cano Yuste*1, Manuel García2, Marina Gallo-Marín1, Isabel Machuca1, Irene Gracia-Ahufinger3, Julián Torre-Giménez4, Azahara Frutos4, Lara Kindelán-Segador4, Elena Perez-Nadales4, Alejandra M.Natera4, Juan José Castón1, Jesús Rodríguez-Baño5, Luis Martínez-Martínez5, Julián De La Torre Cisneros3, Belén Gutiérrez-Gutiérrez2

1Hospital Universitario Reina Sofia-Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC)—Universidad de Córdoba, Córdoba, Spain, 2Hospital Universitario Reina Sofia, Córdoba, Spain, 3Microbiology Unit, Hospital Universitario Reina Sofia-IMIBIC, Universidad de Córdoba, Córdoba, Spain, 4Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC), Córdoba, Spain, 5Hospital Universitario Virgen Macarena—Instituto de Biomedicina de Sevilla (IBiS) and Department of Medicine, Universidad de Sevilla, Seville, Spain

**Background:** Carbapenemase-producing *Klebsiella pneumoniae* (KPC-Kp) infections are associated with high mortality rate. Colonization has been associated with higher risk of death. We evaluated the association of intestinal colonization by KPC-Kp with crude and attributable mortality and investigated the impact of infection in this association.

**Materials/methods:** Observational, prospective, longitudinal cohort study of patients at risk of colonization by KPC-Kp, at Reina Sofia University Hospital in Córdoba, Spain from July’2012 to November’2017. Patients were studied by rectal swab and followed-up for 90 days; rectal swab was repeated in negative patients during the follow-up (weekly in the intensive care and hematology units and before completing the follow-up in the rest of services). Cox regression was used to study variables associated with mortality from any cause. Survival curves were represented according to Kaplan-Meier. A competitive risk analysis was performed to study mortality risk factors specifically related to KPC-Kp infection.

**Results:** 1244 patients (1078 not colonized and 166 colonized) were included. None of the non-colonized patients developed KPC-Kp infection, while 74 (44.6%) of the colonized did. The crude 90-day-mortality was: 194/1078 (18%) in non-colonized and 69/166 (41.6%) in colonized. The variables associated with crude mortality in the Cox regression analysis were: KPC-Kp infection with INCREMENT score >7 (HR:1.84; 95%CI:1.19-2.86; p=0.006), hospitalization in a high-risk service (HR:3.16;95%CI:2.31-4.32; p<0.001), neutropenia (HR:2.49;95%CI:1.56-3.98; p<0.001), neoplasia (HR:1.42;95%CI:1.08-1.88; p=0.01), chronic kidney disease (HR:1.56;95%CI:1.14-2.14; p=0.005), age (HR:1.02; 95%CI:1.01-1.03; p<0.001) and mechanical ventilation (HR:2.37; 95%CI:1.83-3.06; p<0.001). Competitive risk analysis using a risk subdistribution model (SHR) found that infection with INCREMENT score >7 (SHR:66.13;95%CI:32.23-135.70; p<0.001) but not colonization was associated with attributable mortality. The period July’2012-August’2014 was also associated with attributable mortality (SHR:3.19; 95%CI:1.62-6.28; p<0.001). After this period, the attributable mortality decreased from 8.5% to 1.4%, coinciding with the onset of intestinal decontamination in patients at risk and treatment with cefazidime-avibactam.

**Conclusions:** Being colonized was a necessary, but not sufficient condition, to develop an infection due to KPC-Kp infection and die. Intestinal colonization by KPC-Kp was not associated with increased mortality by itself. The risk of death from KPC-Kp is increased when colonized patients develop severe KPC-Kp infection (INCREMENT >7), and the lower mortality observed since August 2014 could be due to changes in the clinical management.

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**Abstract 1452**

**Mandatory computerised decision support system is necessary for sustained control of carbapenems and piperacillin-tazobactam usage in a multi-faceted hospital antimicrobial stewardship programme: interrupted time series with segmented regression analysis**

Boon Hou Chua\(^1\), Shi Thong Heng\(^1\), LI Wei Ang\(^2\), Sock Hoon Tan\(^1\), Hui Lin Tay\(^1\), Min Yi Yap\(^1\), Jason Quek\(^1\), Christine Teng\(^1\), B.E. Young\(^1,2\), Ray Lin\(^1,2\), Brenda Ang\(^1,2\), Tau Hong Lee\(^1,2\), David Lye\(^1,2\), Tat Ming Ng\(^1\)

\(^1\)Tan Tock Seng Hospital, Singapore, Singapore, \(^2\)National Centre for Infectious Diseases (NCID), Singapore, Singapore

**Background:** As the use of piperacillin-tazobactam and carbapenems was rising in a public tertiary-care hospital in Singapore, antimicrobial stewardship (AMS) interventions targeting these two classes were introduced; empiric antibiotic guidelines and prospective review and feedback (PRF) in April 2009, and mandatory use of computerised decision support system (CDSS) in April 2011. Mandatory CDSS was lifted in March 2017 for half of the hospital’s wards for a 6-month cluster-randomised study. We aimed to examine the impact of the interventions on the utilisation of carbapenems and piperacillin-tazobactam.

**Materials/methods:** Monthly utilisation of carbapenems and piperacillin-tazobactam in defined daily doses [DDD] per 1,000 patient-days from January 2007 to December 2018 were obtained from the hospital’s database. The impact of AMS interventions was analysed by segmented regression analysis of interrupted time series.

**Results:** The starting level of the carbapenems and piperacillin-tazobactam utilization in January 2007 was 52.19 DDD/1,000 patient-days, and the average rate of increase was 1.17 per month prior to any interventions. When empiric antibiotic guidelines and PRF were implemented in April 2009, there was a reduction of 6.01 (95% confidence interval [CI]: -9.82, -2.20) in the same month, with an increase of 0.33 per month (95% CI: 0.18, 0.48) post-intervention. When mandatory CDSS usage was implemented, the utilisation level increased by 8.45 (95% CI: 2.82, 14.08) in the same month, followed by a reduction at a rate of 0.22 per month (95% CI: -0.33, -0.10). When mandatory CDSS usage was lifted in March 2017, the utilisation level increased by 8.29 (95% CI: 2.63, 13.94) in the same month, and the utilisation rate changed to an increase of 0.28 per month (95% CI: 0.02, 0.55).

By the end of the study period, we estimated an absolute reduction of 126.58 DDD/1,000 patient-days in the monthly utilisation of carbapenems and piperacillin-tazobactam due to the impact of the AMS interventions.

**Conclusions:** The AMS strategies led to a significant reduction of carbapenems and piperacillin-tazobactam utilisation over 10 years. However, the significant increase in utilisation when mandatory CDSS was lifted highlights the importance of having a mandatory CDSS combined with other strategies to ensure sustained control of antibiotic use.

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Development and implementation of an electronic admission-screening tool for Candida auris at a large healthcare system in Miami, Florida

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Background: Candida auris (C. auris), an emerging multidrug-resistant yeast, is considered an urgent public health threat worldwide. We describe the use of an electronic tool to screen all patients for risk factors associated with C. auris upon admission to all facilities within a large health system in Miami, Florida.

Materials/methods: Starting August, 2019, we implemented a mandatory questionnaire within the electronic medical record (EMR) applied to all patients at the time of triage to any of our facilities. The tool asked in a conditional branching fashion if the patient had: 1. History of C. auris; 2. Overnight hospital stay outside the continental USA in last 12 months; 3. Tracheostomy present on admission and transferred from a facility with high risk for C. auris; and 4. Recent history of extensively-resistant-organism. Answering “yes” to any of the questions automatically generated an order for contact precautions and requested notification to the infection control department (IPD). As follow up, the IPD verified placement in proper isolation precautions and coordinated collection of screening cultures from axilla and inguinal areas. Screening cultures were processed by the Antibiotic Resistance Laboratory Network in Tennessee, USA. If the screening culture was positive, the patient remained in enhanced contact precautions for the duration of admission; if the result was negative, isolation precautions were discontinued.

Results: A total 37390 patients (47428 encounters) were screened with the questionnaire from implementation to November 17th, 2019. Only 103 patients met criteria for isolation precautions and C. auris screening cultures; of those, four patients had previous history of C. auris, 23 had overnight hospital stay outside the USA (Bahamas, Canada, China, Colombia, Cuba, Dominican Republic, Haiti, Honduras, Jamaica, Nicaragua, Spain, US Virgin Islands, and Venezuela), and 76 had tracheostomy and were transferred from a facility with risk for C. auris. Of the 103 screening cultures collected, only the ones with previous history of C. auris were positive; all four cases were transferred from local long-term-care facilities.

Conclusions: Electronic screening tools incorporated in the EMR are effective means to detect carriers of highly resistant/transmissible organisms, thus facilitating early implementation of infection control interventions aimed to prevent the spread to such organisms within healthcare facilities.

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What are the risk factors associated with development of infection by carbapenemase-producing Klebsiella pneumoniae? ANGEL-KpS study

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Background: Carbapenemase-producing Klebsiella pneumoniae (KPC-Kp) infections are associated with high mortality risk. We previously reported that colonization by KPC-Kp is necessary but not sufficient for development of KPC-Kp infection. In this study, we analyzed the risk factors associated with development of infection during 90 days of follow-up.

Materials/methods: Observational, prospective, longitudinal cohort study of patients at risk of KPC-Kp colonization, from a tertiary hospital in the South of Spain from July'2012 to November’2017. All patients with risk factors for colonization were subjected to colonization study. Only those who became colonized by KPC-Kp at the beginning or during the follow-up were included in this analysis. Differences in the risk of infection were evaluated by CART analysis, according to different time periods. The infection risks were represented by Kaplan-Meier curves. Logistic regression was used to identify variables associated with the development of KPC-Kp infection after assessing that proportional hazard assumption for Cox regression was not fulfilled.

Results: 166 KPC-Kp colonized patients were included. Previously, CART established a high-risk period from July’2012 to August’2014, where the infection rate was 53% in comparison to the period from September’2014 to November’2017 in which it decreased to 38.5%. Among 118 patients who became colonized at the beginning of follow-up, 45 (38.1%) developed infection versus those colonized “during follow-up” (60.4%; 29/48). Through logistic regression, the variables associated with development of KPC-Kp infection were: colonization detection during follow-up (OR:2.68;95%CI:1.07-7.o0;p =0.04), Giannella risk score (OR:1.42;95%CI:1.27-1.62;p<0.001), high risk period (OR:3.60;95%CI:1.25-11.11;p =0.02), high risk ward (OR:4.97,95%CI:1.82-14.90;p=0.003) and urological manipulation after admission (OR:2.96;95%CI:0.95-10.75;p=0.07). A multivariate logistic regression analysis confirmed the same risk factors for developing KPC-Kp infection in patients with high risk of death [INCREMENT-CPE score>7].

Conclusions: According to our results, in addition to a high Giannella score, the moment in which the colonization occurs and the ward where the patient is admitted, would be factors to assess when considering empirical treatment to cover KPC-Kp in the case of a suspected infection.

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Abstract 1457

**Necrotising external otitis (NEO): analysis of risk factor for relapse in 66 patients managed during a 12 year period in a reference centre**

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**Background:** NEO is a complex bone and joint infection (BJI) of the skull base that occurred generally in the elderly and/or diabetic patients. There are few data in the literature about its therapeutic management. The aim of our study was to determine risk factor for relapse.

**Materials/methods:** Retrospective cohort study in a reference center for the management of complex BJI. Consecutive cases of NEO over 2006 to 2018 period were included. Diagnosis was done during otoscopy, supplemented by a dedicated imaging. Risk factor for relapse were analyzed by using Cox regression survival analysis with adjusted Hazard Ratio (aHR) and Kaplan Meier curve.

**Results:** Among the 66 patients included (median age, 74 years), most of them had diabetes (n=46, 72%), including 35 (53%) under insulin therapy. 11 (17%) had temporomandibular arthritis, 10 (15%) cranian nerve paralysis, 2 (3%) cerebrals thrombophlebitis, and 2 (3%) contiguity abscess. Samples were obtained during otoscopy: dedicated swab (n=49, 74%), 8 (12%) surgical biopsies, and 3 (4%) both of them. *P. aeruginosa* was involved in 44 patients (67%; all susceptible), 5 patients (7.5%) had fungal NEO at baseline (*A. fumigatus*; *C. albicans*). All patients were treated (average duration 13 weeks), orally and intravenously for 60 of them (91%), mostly with ceftazidime-ciprofloxacin. A subsequent surgery was required in 8 patients (12%), including 3 mastoidectomy. During a median follow-up of 27 months, 16 patients experienced a relapse (*P. aeruginosa* in cultures in 5 patients). Elevated ASA score, as endocranial complication, were potential risk factors for relapse: aHR 1.9 (CI, 0.9 to 3.9; P=0.07) and aHR 1.4 (CI, 0.4 to 4.9; P=0.6), respectively. Using a combination of antibiotics tended to have a protective effect: aHR 0.3 (CI, 0.1 to 1.2; P=0.08). Having a fungal infection at baseline was the only significant risk factor for relapse: aHR of 4.1 (CI, 1.1 to 15; P=0.03) (figure).

**Conclusions:** NEO is a severe BJI mainly due (but not exclusively) to *P. aeruginosa* in elderly and/or diabetic patients. Fungal infections at baseline significantly impact the outcome.

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A retrospective cohort study investigating the clinical features, outcomes and risk factors leading to a poor outcome in pyogenic liver abscesses (2017-2019)

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Background: The aim of this study was to describe the clinical features and outcomes of individuals with a pyogenic liver abscess (PLA) in a tertiary centre, and to identify factors associated with mortality.

Materials/methods: A retrospective analysis of data obtained from clinical records of patients was performed, followed by multivariable regression analysis of patient and treatment-related factors.

Results: Fifty-three patients were included, with a mean age of 69 years and a male preponderance. At presentation, symptoms had been present for a median of 7 days; 75% were febrile and 58% had sepsis. Initial blood tests revealed abnormal liver function tests in 87% and an elevated C-reactive protein in 98%. Diagnostic imaging was carried out a median of 2 days following admission; 69% had an abscess >5cm diameter, 41% had multiple PLAs and 11% had metastatic abscesses. An underlying cause was identified in 91%; with a contiguous spread from a biliary source the most common. A microbiological diagnosis was confirmed in 74%; E.coli and Streptococcus anginosus group bacteria were most commonly isolated, while 15% had multiple bacteria cultured. Treatment involved complex, prolonged antibiotic therapy (>4 weeks in 66%) combined with percutaneous drainage in 43% and source control surgery in 23% (mainly cholecystectomy). The patients that had percutaneous drainage had significantly larger abscesses but drainage was not associated with significant differences in clinical outcome or duration of either antibiotic therapy or hospital admission. Mortality was 19%, 11% suffered C.difficile infection and only 53% had an uncomplicated clinical course. Follow-up imaging was carried out in 92%; at the time of the final scan there was complete resolution of the abscess in only 45%. Non-survivors were more likely to have cancer than survivors, but no other factors significantly impacted on survival.

Conclusions: PLA is associated with a considerable morbidity and mortality and requires complex antibiotic treatment alongside selective percutaneous drainage. Further research is required to confirm features that can risk stratify patients at diagnosis and to define the optimal treatment strategies.

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Abstract 1459

Two novel fastidious anaerobes from the genus Bacteroides isolated from chicken gastrointestinal tracts

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Background: Anaerobic bacteria inhabiting digestive tract of humans or animals have been a challenging object of microbiological studies for years. Bacteroides spp. make up half of microbiome and majority of these species is hardly cultivated in laboratory conditions. Aim of this work was to thoroughly characterize three Bacteroides spp. (AN20, AN421 and AN502) isolated on media with rumen fluid from chicken gastrointestinal tracts that showed novel properties and that were assigned as candidates for novel species.

Materials/methods: A polyphasic taxonomic approach was applied to characterize isolated strains. All three were subjected to biotyping (micro-, and microscopy, Gram-staining, API 20A and RAPID 32A tests, fermentation products), chemotaxonomy based methods (analysis of proteins, fatty acids and menaquinones) and genomic methods (sequencing of the 16S rRNA gene, whole-genome sequencing and phylogenetic analyses).

Results: Initial analysis of the 16S rRNA sequences showed that the closest relative of AN20 is Bacteroides uniformis (90.3% similarity) and of AN421 and AN502 Bacteroides eggerthii (93.4%). These results suggested that cultivated strains may represent novel species of the genus Bacteroides. Phylogenetic analysis of 16S rRNA gene sequences showed that studied strains formed two separate clades within the genus Bacteroidetes, however they clustered along with Bacteroides coprophilus, Bacteroides coprocola and Bacteroides plebeius. Final confirmation of novelty was done by comparison of whole genomes based on ANI and dDDH values. ANI values between all three strains and B. coprophilus DSM 18228T, B. coprocola DSM 17136T and B. plebeius DSM 17135T were between 70.0-72.0%. Moreover, AN421 and AN502 showed 97.7% identity between each other, whereas AN20 showed 74.1 and 75.3% similarity to AN421 and AN502 confirming these belong to two different species. Biochemical and chemotaxonomy-based methods showed differences between novel strains as well as towards their closest relatives which is important for their proper identification.

Conclusions: In this study, novelty of two Bacteroides species was clearly proved. These two fastidious species were thoroughly described in order to characterize their unique properties. ANI values showing less than 95% genomes similarities as required for species delineation definitely confirmed two novel species for which the names Bacteroides pullorum (AN421T) and Bacteroides brunensis (AN20T) are proposed.

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Imported schistosomiasis in children: a French prospective multi-centre study of prevalence, clinical features and diagnostic methods

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**Background:** Data on imported schistosomiasis are scarce especially in children. Screening in at risk population is recommended but the best diagnostic strategy remains uncertain and not evaluated in children. The aim of the study was to estimate the prevalence of imported schistosomiasis in children at risk in Paris and suburbs, and to compare diagnostic methods.

**Materials/methods:** All children at risk of schistosomiasis who consulted in four hospitals in the region of Paris were prospectively included from June 2017 to June 2018. Clinical and biological data were collected anonymously using an online software after parental and child consent. Direct parasitological diagnosis was urinary and feces microscopy and real-time polymerase chain reaction. Serological diagnosis was performed by Western blot, ELISA, indirect hemagglutination, immunochromatography and rapid test diagnosis circulating cathogen antigen. The Western blot assay and the microscopy were the reference methods used to estimate schistosomiasis prevalence. A latent class model has been used to evaluate each test performances.

**Results:** A total of 114 patients were included [sex ratio: 2.9 and mean age: 13.2 years]. Most of the children were newly arrived migrants from Sub-Saharan Africa. The prevalence of schistosomiasis was 26.3%. Half of the positive patients were asymptomatic. The performances of ELISA and Western blot assays were equal [sensitivity: 83%; specificity: 99%] according to statistical analysis using latent class models. Serum immunochromatography had interesting performances [sensitivity: 100%; specificity: 89%].

**Conclusions:** Imported schistosomiasis is a common pathology in at risk children which confirms the need for systematic screening. Clinicians should be aware of such high prevalence in children at risk. And Serum immunochromatography seems to be the most cost/effective as a mass screening method.

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Utility of multiplex PCR in the screening, diagnosis and follow-up of malaria in patients attended in a tropical medicine referral centre

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Background: Due to the increase in trips to endemic zones and migrations, the diagnosis of malaria is on the rise in our setting. PCR with its high sensitivity (higher than immunochromatography and microscopy) is a widely used diagnostic tool, especially in non-endemic countries.

The objective of this work is to evaluate the usefulness of PCR in the detection of low parasitaemias (observed in semi-immune patients, in patients with incomplete prophylaxis / treatment and in post-treatment control) and in the identification of mixed infections in patients attended in a Tropical Medicine Referral Centre.

Materials/methods: Data from patients attended between July-2017 and July-2019 with a request for malaria PCR were reviewed. Two periods, July-2017 to June-2018 and July-2018 to July-2019 were established for the analysis. Results were evaluated together with those obtained by other techniques such as immunochromatography for antigen detection (SD Bioline®) and microscopic examination of thin and thick blood smears. During this period, two PCRs were used, an in-house Nested-Multiplex-PCR in the National Microbiology Centre and a commercial Multiplex-PCR (Bio-Evolution®) in our hospital.

Results: In the first period, a total of 203 PCRs were performed with a 11.82% positivity rate. 176 were screening PCRs in health exams (86.7%), 22 diagnostic PCRs (10.84%) and 5 follow-up PCRs (2.46%). 9.09% of the screening PCRs were positive (all non-mixed infections). 8 diagnostic PCRs were positive (36.36%), all of them also positive by microscopy.

In the second, a total of 290 PCRs were performed with a 15.52% positivity rate. 203 were screening PCRs (70%), 71 diagnostic PCRs (24.48%) and 16 follow-up PCRs (5.52%). 13.3% of the screening PCRs were positive (5 mixed and 22 non-mixed infections), 16 diagnostic PCRs were positive (22.54%), 9 of them (56.25%) being also positive by microscopy and 14 by antigen detection (87.5%).

In both periods, the agreement was total at species identification level between PCR and microscopy and the follow-up PCRs were always negative.

Conclusions: Malaria PCR has demonstrated its usefulness in post-treatment follow-up and in the detection of submicroscopic mixed and non-mixed malaria infections, with an increase in the positivity rate in the second period.

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**Abstract 1465**

**Plasmodium vivax diversity, population structuration and history of origin in Sudan**

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**Background:** *Plasmodium vivax* was less common in Sub-Saharan African countries due to the lack of Duffy antigen receptor for chemokine's (DARC) on red blood cells. In last year *P. vivax* emerged in Africa. In Sudan in the recent years the parasite is becoming widely distrusted and number of cases showed risen trend and can reach up to 20% of total positive malaria cases. It is not known whether this expansion is due to parasite evolution or population migration to Sudan. In this study use microsatellite DNA loci are polymorphic, neutral and distributed throughout the genome and have been useful for determining haplotypes diversity, population structure, history and ancestral origin of parasite population.

**Materials/methods:** *P. vivax* microsatellite typing was conducted on 113 field isolates collected from two districts in Sudan: 21 from Halfa [2013] and 92 from Khartoum [2013 and 2015]. Microsatellite DNA (MS) loci across the parasite genome were amplified and length variation of labeled PCR products was measured on an ABI PRISM 3730XL DNA Analyzer. MS data diversity, HE, haplotype across loci, Analysis of Molecular Variance (AMOVA) indexes and Principal Coordinate Analysis (PCoA) were generated with Gen AlEX. Linkage disequilibrium (LD) was obtained using LIAN software version 3.5. Geographical clusters and ancestral origin of Sudanese isolates were determined using STRUCTURE 2.2 software.

![Figure 1](image)

**Results:** Microsatellite DNA analysis showed multiple haplotype per locus varying in number from 9 to 22 (mean = 12.57). A total of 49 (62.1%) isolates revealed mixed clonal infection. The virtual heterozygosity (HE) values ranged from 0.71 to 0.88 (mean HE ± SE = 0.8450 ± 0.0460) while multilocus linkage disequilibrium (LD) showed ISA value of 0.1486 (P < 0.001). The AMOVA analysis showed that most of the genetic variation (96%) lies within parasite population. Clustering analysis of Sudanese versus Ethiopian population showed distinct different clusters for each population while clustering analysis of Sudanese versus worldwide isolates showed distinct signature and global pattern.

**Conclusions:** Microsatellite-based analysis of *P. vivax* parasites from Sudan showed extensive genetic diversity and ancestral origin of Sudanese *P. vivax* population represent the worldwide clusters and this seem to suggest a double origin from Africa [or Europe] and Asia.

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Abstract 1471

Relationship between intestinal microbiota and infantile colic
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Abstract third-party references: Supported by The Lebanese National Council for Scientific Research [CNRS]

Background: Infantile colic is a clinical condition in which a healthy infant suffers from paroxysms of excessive frequent crying that may be accompanied by irritability, flushing of the face, meteorism, drawing-up of the knees and arching the back. Approximately 10-30% of newborns will develop symptoms of infantile colic. In most cases, physicians are unable to determine the cause of the colicky behavior. An aberrant intestinal microbiota has been associated with infantile colic.

Materials/methods: This study compared 42 colicky infants with a control group composed of 46 non-colicky infants, all born at 37-42 weeks of amenorrhea, born by spontaneous delivery [n=33 newborns] or by caesarean section [n=54], exclusively breast fed [n=10] or exclusive formula fed [n=45] or receiving both feeding modes [n=33]. Fecal samples were collected in pediatric private clinics between January 2018 and September 2018 and microbiota was analyzed by 16S rRNA gene quantitative PCR (qPCR).

Results: Age was significantly higher in colicky infants [p=0.014], while other parameters such as, birth rank, number of siblings, birth weight and crowding index did not differ between both groups. Infants were mainly colonized by anaerobes such as Clostridium of cluster I, Bifidobacterium and Bacteroides/Prevotella group and facultative anaerobes such as Lactobacillus and enterobacterales. Differences were found by qPCR between colicky and non-colicky infants [figure 1]. Colicky infants are more colonized by Lactobacillus [p=0.015], enterobacterales [p=0.019], Klebsiella [p=0.002] and Clostridium of cluster XI [p=0.002]; whereas non colicky infants are more colonized by Bifidobacterium [p=0.005] and Clostridium leptum group [p=0.05]. Parents with depression and anxiety had 3 times more probability of having a colicky infant [p=0.03]. This could be bidirectional and can be the consequence of infantile colic and not the cause.

Conclusions: Our findings show that differences exist between the intestinal microbiota of colicky and non-colicky infants. On the long term, characterization of the intestinal microbiota in infants with colic may allow the implementation of prevention strategies to minimize the incidence and reduce crying in infants.

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Abstract 1474

Knowledge and awareness of inadvertent use of yellow fever vaccine among renal transplant recipients
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Background: Yellow fever (YF) is a vaccine-preventable disease but the live attenuated YF vaccine is contraindicated in immunosuppressed patients due to the increased risk of life-threatening YF vaccine-associated viscerotropic disease in this population. The objective was to (i) estimate the prevalence of renal transplant recipients (RTR) inadvertently vaccinated against YF; (ii) evaluate the evolution of these patients, (iii) awareness of those unvaccinated to not to be vaccinated, and (iv) evaluate the knowledge of those patients about the contraindication of YF vaccine to them.

Materials/methods: A cross-sectional telephone contact study was conducted with 200 RTR, selected from the highest risk of YF vaccine exposure based on state vaccination policies against the YF outbreak in Brazil in 2017/2018. A questionnaire with information on previous use of YF vaccine before or after transplantation was applied. If the patient did not receive the vaccine post-transplantation, he was instructed not to get vaccinated; if the patient was vaccinated post-transplant, a second questionnaire was conducted to check for possible adverse events potentially associated with inadvertent vaccination. For each patient, up to 3 telephone contact attempts were performed. If the patient was not available in either of them, the attempt to contact was terminated.

Results: There were 116 successful telephone contacts (58%). A total of 11 vaccinated patients were identified - 5 in the pre-transplant and 6 in the post-transplant period. All patients received the full dose of the vaccine. Among those vaccinated post-transplant, only 1 reported adverse events (nausea) after receiving the vaccine. 100% of post-transplant vaccinated patients reported not knowing the vaccine contraindication due to their clinical condition. Among the unvaccinated patients, this rate was 12.4%.

Conclusions: There is no specific antiviral treatment for YF, which makes vaccination the main tool for disease prevention and control. However, despite increasing evidence that transplant recipients have tolerated YF vaccine, data are not strong enough to recommend this vaccine in transplant recipients. Thus, counseling RTR on the contraindication of YF vaccine is important to prevent inadvertent use of the vaccine in this population, while additional studies on the real effects of YF vaccination on RTR are pending.

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Abstract 1475

An audit of latent tuberculosis management at a tertiary referral centre in Ireland

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Background: Ireland is a low-incidence Tuberculosis (TB) country. Effective treatment of patients at high risk of latent TB infection (LTBI) reactivation is important for low-incidence TB countries because TB due to ongoing transmission is thought to be less frequent compared to high incidence TB countries.

Materials/methods: Our aim was to evaluate the effectiveness of LTBI management at our tertiary referral outpatient department (OPD) using national guidelines as an audit standard. We included all patients seen in the infectious diseases OPD who were referred querying a diagnosis of LTBI. Patients had to have attended the OPD at least once in between the 01/07/2018-31/12/2018. A retrospective review of each patient’s electronic record was performed. Data extraction was performed independently by two auditors. A data collection tool was designed using Microsoft Excel. We calculated the cost of screening and managing the patients referred to our OPD. We calculated the cost considering the cost of investigations, staff and treatment using national costing guidelines.

Results: We identified 25 patients who met our inclusion criteria. 14/25 (64%) were male. The median age at time of first review was 52 years (IQR=24). All patients had a valid indication for LTBI screening, 22/25 (88%) were offered LTBI treatment, 22/22 accepted treatment, 17/21 (81%) completed treatment. The treatment used was isoniazid for a duration of 6 months for 12/21 (57%), isoniazid for 9 months 6/21 (29%) and rifampicin and isoniazid for 3 months in 3/21 (14%). A risk assessment for hepatotoxicity was documented in 20/21 (96%). 1 patient had gastrointestinal upset on rifampicin. There were no other adverse events. There were 109 appointments attended by these 25 patients. The median number of appointments attended was 4 (IQR=2.5). The cost of screening, testing and managing the 25 patients referred was €34,466.62. The lowest cost treatment was Isoniazid plus Rifampicin for 12 weeks. The mean cost per patient seen in the clinic was €1,378.66. The mean cost per LTBI successfully treated was €2,027.45.

Conclusions: Our TB clinic is effective in the assessment and safe management of latent TB in accordance with national guidelines.

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**Abstract 1479**

**Risk factors associated with daptomycin non-susceptible Staphylococcus aureus bloodstream infections**

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**Background:** Daptomycin (Dap) is being increasingly utilized for treatment of methicillin-resistant Staphylococcus aureus (MRSA) infections. Consequently, daptomycin non-susceptible (DNS) SA strains have recently emerged, leading to limited treatment options for complicated MRSA infections. The purpose of this study was to evaluate risk factors associated with DNS SA bloodstream infections (BSI) at Henry Ford Health System in Michigan.

**Materials/methods:** Retrospective case-control study was conducted from 07/07/2008 through 09/18/2019 to identify clinical characteristics and risk factors in hospitalized patients with DNS SA BSI using electronic medical records (EMR). Patients with daptomycin-susceptible (DS) MRSA were used as controls. Data were analyzed using univariate analysis. Multivariate regression analysis was constructed using the PROC LOGISTIC from the univariate analysis. Statistical analysis was done using SAS 9.4 software.

**Results:** Thirty-one patients with DNS SA BSI were identified during the study period and compared to 59 patients with DS MRSA BSI. There was no significant difference in baseline characteristics and risk factors between the 2 groups with the exception of nursing home (NH) residence (p = 0.01), presence of central venous catheter (CVC) (p = 0.004) foley catheter (p=0.02), diabetes mellitus with end-organ damage (p=0.01), hemodialysis (p=0.04) or MRSA in the past year (p=0.03). Open wounds were more common in the DS MRSA group (p=0.026). Antibiotic use within 90 days was not significant with the exception of vancomycin (p=0.02). There was significant daptomycin MIC change in the DNS SA group (odds ratio (OR)=15.67; 95% confidence interval, 3.19-76.89; p = 0.007). Mean bacteremia duration was 7.4 and 3.8 days (OR=1.2; 95% confidence interval, 1.07–1.35; p = 0.004) for case patients and controls, respectively. Multivariate analysis implicated NH residence (OR=13.03; 95% confidence interval, 2.24–75.57; p = 0.004) and CVC (OR=3.2; 95% confidence interval, 1.05–9.89; p = 0.04) as risk factors for DNS SA infection.

**Conclusions:** DNS SA is an emerging pathogen associated with indwelling devices, poorly controlled diabetes mellitus, hemodialysis, history of MRSA, vancomycin use and longer duration of bacteremia. NH residence and CVC use confer risk for DNS SA acquisition. Further studies to determine strain relatedness and identify resistance genes and virulence factors are warranted.

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Abstract 1480

A novel celecoxib-derivative kinase inhibitor, AR-12 (OSU-03012), is active against *Mycobacterium abscessus* complex *in vitro*

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**Background:** Therapeutic options for *Mycobacterium abscessus* (*M. abscessus*) infections are extremely limited and therapy outcomes often end in failures. New or repurposed drugs are in urgent need. AR-12 (OSU-03012), a novel celecoxib-derivative kinase inhibitor, has a broad spectrum of antibiotic activity against various pathogens. In this study, we investigated the *in vitro* and intracellular potency of AR-12 against *M. abscessus* complex.

**Materials/methods:** The susceptibility, stability and pre-exposure assays of AR-12 against *M. abscessus* complex were performed. We also conducted the minimum bactericidal concentration (MBC) and Time-kill kinetics assays to evaluate the bactericidal/Static activity of AR-12. Using checkerboard synergy assay, we tested in vitro synergistic interactions between AR-12 and five clinically important antimycobacterial agents against *M. abscessus*. Finally, we evaluated the effect of AR-12 on intracellular survival of *M. abscessus* complex in macrophage infection experiments.

**Results:** AR-12 exhibited high *in vitro* killing activity against *M. abscessus* isolates, with MIC50 of 4 and 8 mg/L for both subspecies. Stability testing showed that at 30°C AR-12 maintained its susceptibility within three days, and gradually lost its antimicrobial activity over time. MBC and Time-kill kinetics assays demonstrated AR-12 dominantly exhibited a bactericidal activity. Pre-exposure to AR-12 didn't induce more pronounced resistance of *M. abscessus* subspecies. There were no antagonistic interactions of AR-12 with clarithromycin, amikacin, imipenem, cefoxitin and tigecycline. Although AR-12 was inferior to amikacin in *in vitro* Time-kill kinetics assays, its intracellular cfu was significantly lower than that of amikacin.

**Conclusions:** AR-12 is active against *M. abscessus* *in vitro*, and showed excellent stability and compatibility with clinically important antimycobacterial agents. AR-12 may be a potential candidate for a novel treatment modality of *M. abscessus* complex infections.

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**Abstract 1481**

**Obstructive pyelonephritis associated with ureteral stones: microbiology, treatment and prognosis**

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**Background:** Acute pyelonephritis (APN) is often associated with obstruction of the upper urinary tract due to presence of urinary stones. It causes severe complications such as bacteraemia, sepsis, and septic shock. This study aimed to investigate the clinical outcomes and antibiotics susceptibilities of causative microorganisms in obstructive pyelonephritis associated with ureteral stones.

**Materials/methods:** This retrospective cohort study included female patients diagnosed with community-acquired APN at a tertiary care hospital from 2008 to 2017. A comparison between cases of APN associated with obstruction of the upper urinary tract due to presence of ureteral stones and cases of APN without complications was performed. Propensity score matching was used to adjust the heterogeneity within each group.

**Results:** Of the 588 female patients with community-acquired APN, 107 patients were diagnosed with obstructive pyelonephritis (OPU) and 481 patients were diagnosed with uncomplicated APN. *Escherichia coli* was the most common pathogen in both groups (61.7% vs. 65.5%, p = 0.502). *Proteus* species were determined as the causative agent in 9.3% OPU cases and 0.4% cases with uncomplicated APN (p < 0.001). After propensity score matching, Enterobacteriaceae strains isolated from OPU cases were more resistant to ciprofloxacin (51.9% vs. 16.0%, p < 0.001). In addition, extended-spectrum β-lactamase (ESBL) was detected in 22.2% and 21.0% of the Enterobacteriaceae strains isolated from OPU cases and cases with uncomplicated APN, respectively (p = 1.000). The overall in-hospital mortality (3.7% vs. 4.9%, p = 0.699) and urinary tract infection recurrence rates within 1 year were similar in OPU and uncomplicated APN groups (16.0% vs. 21.0%, p = 0.545).

**Conclusions:** Antibiotic treatment for patients with obstructive pyelonephritis associated with ureteral stones may be empirically selected in accordance with the treatment protocol for general pyelonephritis. Clinicians should exercise caution before prescribing ciprofloxacin for the treatment of obstructive pyelonephritis associated with ureteral stones.

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Abstract 1485

**Comparison of β-lactamase-producing Escherichia coli ST131 C1-M27 and ST131 non-C1-M27 by whole genome analysis using next-generation sequencing in Japan**

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**Background:** In recent years, ESBL-producing *Escherichia coli* ST131 has become prevalent worldwide. Recent studies using whole-genome sequencing (WGS) analysis revealed that since the 2000s, clade C has become the most dominant lineage among the ST131 isolates, and one report shows that clade C1-M27 is increasing. In the present study, to pursue factors that spread the epidemic strains globally, we conducted a genome analysis of the C1-M27 epidemic strain and the non-epidemic strain non-C1-M27 using WGS and attempted to detect the mutations.

**Materials/methods:** We used 99 strains isolated from West Japan. The clades determined using PCR were A (n = 7), B (n = 6), C1 (n = 18), C1-M27 (n = 34), and C2 (n = 34). We used SnpEff, which classifies proteins by the level of gene mutation, to extract specific proteins. We extracted those proteins that were classified as “HIGH”. We analyzed the protein mutation sites, functions, and protein interactions identified *in silico* using SeaView, S-VAR, and STRING.

**Results:** The proteins extracted were AMP nucleosidase and GABA permease. As a result, the 68th proline of the non-C1-M27 strain was a common amino acid in AMP nucleosidase, but it was mutated to serine in the C1-M27 strain. GABA permease, the 85th alanine, was mutated to threonine. AMP nucleosidase was predicted to have no effect on protein function by point mutation, whereas GABA permease was predicted to effect protein function. Although GABA permease is possessed by all *E. coli*, a p.Ala68Thr mutation was observed in all clade C1-M27 and C1 6 strains, whereas it was not observed in the other clades. We used STRING to analyze the protein-protein interactions of GABA permease. The results suggested that GABA permease is indirectly associated with acid-resistance systems.

**Conclusions:** GABA permease is a high-affinity uptake system for GABA. The prediction of protein function from point mutations suggests that the point mutation revealed here affects the function of GABA permease, and protein-protein interaction prediction suggested a relation with acid-resistance systems. We surmise that the specific point mutation extracted in this research may be related to the worldwide pandemic.

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Abstract 1486

**Colistin resistance increases fatality in bloodstream infections due to carbapenem-resistant Klebsiella pneumoniae**

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**Background:** Mortality due to K. pneumoniae bacteremia is on rise. Defining risk factors for colistin resistance and mortality is of paramount importance particularly in regions with high rates of carbapenem resistance.

**Materials/methods:** Patients diagnosed with "carbapenem-resistant K. pneumoniae (CRKp) bacteremia were divided into two groups as "colistin susceptible (ColS)" and "colistin resistant (ColR)". Retrospective casecontrol study was conducted to compare characteristics and outcomes. Multiple logistic regression model was used to define independent risk factors for acquired colistin resistance and mortality.

**Results:** A total of 82 patients (39 ColS and 43 ColR) were included. Mean age was 61.5 years and 50 (61%) were male. Colistin resistance was significantly increased with age (p = 0.074) and duration of hospitalization (p = 0.007). Prior colistin use was significantly higher (p = 0.007) in ColR group. Mortality rates at 14-day, 28-day and final follow up were 55%, 66% and 70% respectively. Colistin resistance significantly increased 28-day (p=0.009) and in-hospital (p = 0.040) mortality. PFGE analysis revealed an outbreak with K. pneumoniae ST78 and ST45 clones. OXA-48-like carbapenemase was positive in 60% of the strains and related with increased mortality. No significant difference was found between the outcomes of treatment modalities (monotherapy, double-triplequadruple combined therapy) in terms of 14th-day, 28th-day and total survival.

**Conclusions:** Colistin resistance increases 28-day and in-hospital mortality in CRKp bacteremia. Existing antibacterial combinations have no apparent superiority to each other. Clinical or microbiological response to treatment within seven days, along with prompt source control, favors survival.

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Abstract 1488

Geographical clustering of hantavirus isolates from Apodemus agrarius identified in the Republic of Korea indicates the emergence of a new hantavirus genotype

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Background: Several studies on hantavirus evolution have shown that genetic reassortment plays an important role in the evolution and epidemiology of this disease. Hantaan virus, a prototype hantavirus carried by Apodemus agrarius, is found throughout China, Russia, and Korea. The aim of this study was to investigate the distribution of hantaviruses in rodents in the Republic of Korea (ROK) and perform phylogenetic comparisons using the geographical distribution of their natural reservoir rodent hosts as a point of reference.

Materials/methods: To understand the genetic epidemiology of human pathogenic hantaviruses, we examined viral isolates from rodent reservoirs, captured at three different locations in the ROK, between 2017 and 2018. Each sample collected was subjected to reverse-transcription nested polymerase chain reaction (RT-N-PCR) targeting the L- and S-segments of the hantavirus genome. Positive isolates from Gwangju, Boseong-gun (Jeollanam-do Province), and Jeju Island were confirmed as Hantaan virus using DNA sequencing. Phylogenetic analysis showed that all isolates grouped together as Hantaan virus. The isolates from Jeju, Boseong-gun, and Gwangju tended to cluster together, but with each region forming a distinct cluster. In addition, these three clusters were distinct from other Hantaan isolates reported in previous studies from Korea and its neighboring countries China and Russia. This suggests the emergence of a new hantavirus genotype in southwestern ROK.

Conclusions: Hantaan viruses exhibit a considerable degree of geographical clustering, and there may be a novel Hantaan genotype in southwestern ROK. This study helps expand our knowledge regarding the emergence of new hantavirus strains and their degree of geographical variation.

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Abstract 1495

**Swiss Pathogen Surveillance Platform: development of a surveillance database for molecular epidemiology of multidrug-resistant pathogens**

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**Background:** Transmission of virulent and resistant pathogens can be described using molecular epidemiological methods. In particular, whole genome sequencing (WGS) allows high resolution typing. As the interactions between compartments (e.g. human, animal, food, and environment) are complex, molecular typing data alone often does not explain the route of transmission. Interoperable processes, standardized epidemiological vocabulary and metadata are key requirements for unmasking this complexity.

**Materials/methods:** Within a NRP72-funded project, we are developing and implementing a molecular surveillance platform for Switzerland allowing the integration of WGS typing and epidemiological data at high spatiotemporal resolution. Within the consortium framework (i) requirements are defined regarding the WGS workflows, data analysis and interpretation and (ii) a prototype for a web-based surveillance platform is established and (iii) the platform is tested using a set of methicillin-resistant *Staphylococcus aureus* (MRSA) isolates from all involved centers.

**Results:** The required functional specifications of the platform were agreed: minimal datasets on epidemiological data and visualization aspects of spatiotemporal information. Legal and governance frameworks were evaluated. Bioinformatics functionalities of the platform were determined and implemented based on open source software. These include whole genome typing methods (e.g. cgMLST, SNP-tree) and more classical methods such as MLST typing, that allow comparison to older datasets. A first prototype of the surveillance platform is hosted at a BioMedIT node of the Swiss Institute of Bioinformatics (SIB) to ensure secure data access and computational power. Data is managed and searchable through a user dashboard including visualization powered by an integrated version of Nextstrain. A current set of >200 MRSA isolates (genomic and metadata) will expand to >1000 isolates over the next few months.

**Conclusions:** Transferring powerful backend bioinformatic tools to an easily accessible and comprehensive frontend solution is critical for use by people with various knowledge backgrounds. The surveillance platform has been designed to be highly interactive and intuitive. The legal framework had to be carefully evaluated for epidemiological/research tools, as different laws are applicable. With this platform, we are increasing public health networking within Switzerland and enabling fast detection and real-time tracking of outbreaks on various scales. Expansion to other pathogens is planned.

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Abstract 1499

Antibiotic resistance of 34,539 Campylobacter spp. isolated from human sources: National Surveillance Data of Switzerland from 2007 to 2018

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Background: In Switzerland, acute gastroenteritis is commonly caused by bacteria, mainly, Campylobacter spp., with about 7,500 registered episodes annually, is of importance due to substantial healthcare costs. In recent years, more antimicrobial resistance (AMR) has been reported. However, little is known about temporal trends and geographical patterns of AMR within Switzerland.

Materials/methods: We used prospectively collected data from the ANRESIS antibiotic surveillance framework in Switzerland from 2007 to 2018. The network covers about two thirds of reported laboratory data. We conducted pre-defined, descriptive and exploratory statistical analyses. No a priori hypothesis was tested. For each year and geographic region the frequency of isolates resistant to specific antibiotics was calculated. Finally, we examined the association of AMR with demographic and epidemiological variables and invasiveness.

Results: The full dataset contained 34,539 human isolates of 11 Campylobacter spp. plus isolates identified to genus level only. The main analysis focused on C. jejuni (n=26,661) and C. coli (n=2,235) representing 99% of all isolates characterized on species level. A subset of 329 (1.1%) isolates was invasive. Per year, 2,273 to 3,308 isolates were collected for antibiotic resistance testing. Over time, we observed an increasing rate of resistance to ciprofloxacin and tetracycline in both species, to doxycycline in C. jejuni and to clarithromycin in C. coli. With exceptions, most geographic patterns of AMR were homogeneous. Noteworthy, in the South of Switzerland, as compared to the rest of Switzerland, a relatively higher rate of resistance to erythromycin was observed in C. coli. Further, in central-East and central-West Switzerland, as compared to the rest of Switzerland, a relatively lower rate of resistance to tetracycline was observed in both species. Our data provide no evidence for an association of AMR with demographic or epidemiological variables or in invasiveness.

Conclusions: We observed temporal and geographical differences in AMR patterns. As campylobacteriosis is epidemiologically often linked to handling and consumption of raw or undercooked chicken meat, travels abroad and no human-to-human transmission is known, these differences in AMR may be linked to practise changes outside of human medicine. Follow-up studies should include isolates from food samples.

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**Abstract 1501**

**HIV is a risk factor for death among persons with candidaemia in South Africa**

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**Background:** Mortality among critically-ill persons with candidaemia is high. We aimed to determine the effect of HIV on 30-day mortality risk among persons with candidaemia in South Africa.

**Materials/methods:** We included persons aged ≥18 months with an episode of culture-confirmed candidaemia at 29 sentinel hospitals, 1 January 2012 - 31 December 2017. Surveillance officers collected clinical data by interview/chart review. Candida isolates were identified at a reference laboratory. We used random-effects logistic regression to adjust for sentinel hospital and participant-level confounders, treating follow-up as a fixed length of time (30 days). We plotted Kaplan-Meier survival curves by HIV status.

**Results:** Of 2563 cases, clinical data were available for 1846 (72%). Of these, we retained 1040 cases with both HIV status and outcome data (56%). Of 1040 cases, 458 (44%) were HIV-seropositive. Among 404 with available data, 301 (75%) were antiretroviral treatment-experienced. Among 267 with a recorded CD4 count close to candidaemia diagnosis, the median CD4 count was 133 cells/µl [108, 42309]; 63% [166/267] had a CD4 count <200 cells/µl. The overall case-fatality ratio was 458/1040 (44%). The median age of 1037 participants was 37 years [IQR, 23-52 years] and 542/1040 [52%] were male. Overall, 50% [514/1023] were admitted to an intensive care unit [ICU] at time of diagnosis. The 30-day case-fatality was 37% [230/614] and 54% [228/426] for HIV-seronegative and -seropositive cases respectively (crude odds ratio [OR] 1.92, 95% compatibility interval [CI] 1.50-2.47, p<0.001). After adjusting for sentinel hospital, age, sex, year of diagnosis, ICU admission, receipt of systemic antifungal treatment and Candida species (n=907), the 30-day mortality was 1.89 times higher (95%CI 1.38-2.60; p<0.001) among HIV-seropositive vs. -seronegative participants. The stratum-specific mortality OR was higher among HIV-seropositive individuals not admitted to ICU [OR 2.27, 95%CI 1.47-3.52; p<0.001] than those who were [OR 1.56, 95%CI 1.00-2.43, p=0.05]. HIV-seropositive individuals had a 60% reduced adjusted odds of ICU admission than those HIV-seronegative [OR 0.40, 95%CI 0.25-0.64, p<0.001].

**Conclusions:** HIV-seropositive individuals had a two-fold increased adjusted risk of all-cause mortality within 30 days of candidaemia diagnosis, compared to their HIV-seronegative counterparts. HIV-seropositive individuals with candidaemia should be considered for ICU admission.

**Risk of death by HIV status**

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Abstract 1502

**Microbiological validation of the BIOFIRE FILMARRAY Pneumonia Panel plus: a single-centre experience**

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**Background:** Culture-based identification and AMR-testing requires up to 72h. In addition, respiratory samples may have low sensitivities due to (i) small sample amounts being cultured and (ii) background (over)growth of oropharyngeal flora. Broad-panel PCR assays may overcome these gaps. We aim to evaluate the microbiological performance of the Biofire® FilmArray® Pneumonia Panel plus (BFPP) compared to culture-based techniques.

**Materials/methods:** We used consecutive collected bronchoalveolar lavage (BAL) and tracheal secretion (TS) samples from February-August 2019. Detection rates of the BFPP (200uL per sample) was compared to culture (BAL: 1uL and TS: approx. 50uL; internal gold-standard) on 5% sheep blood agar, CNA, Haemophilus, and MacConkey plates. The BFPP covered 15 bacterial (semi-quantitative), 3 atypical bacterial and 9 viral and 7 AMR targets (qualitative) and was performed according to company instructions.

**Results:** We compared 690 respiratory samples, corresponding to 18,630 BFPP targets. BFPP detected 517 targets (347 bacteria, 2 atypical bacteria, and 168 viruses). In comparison to culture, the BDPP found significantly more bacterial targets (+114%, 347/690 vs. 162/690). Some species were more frequently detected with BFPP: *Haemophilus influenzae*, *Moraxella catarrhalis*, *Streptococcus agalactiae*, *Streptococcus pyogenes*, and *Staphylococcus aureus* with additional 375%, 533%, 100%, 250% and 89%, respectively. These were often detected at low quantities in PCR (10e4 to 10e5 CFUs/mL). Samples with higher background flora (>50,000 CFUs/mL) showed a higher mismatch between the culture and BFPP results. Overall specificity and sensitivity were 98.1% and 89.9%, respectively. We detected only 5 AMR genes (3x CTX-M/2x mecA), of which 3 were confirmed by culture (2x CTX-M/1x mecA).

**Conclusions:** BFPP allows a rapid assessment of most common pneumonia pathogens and AMR genes. The difference in detection rates is most likely due to substantial differences in the culture workup or small quantities of target bacteria overgrown by oropharyngeal flora. The question remains if *S. aureus* and *H. influenzae* are pathogens or bystanders at low concentrations or presence of substantial background flora. Careful evaluation of clinical evidence for infection should be considered to avoid overtreatment of patients. The BFPP may benefit from a background flora target.

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Abstract 1503

**Efficacy of pulsed xenon ultraviolet disinfection of multidrug-resistant bacteria and *Clostridioides difficile* spores**

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**Background:** Contamination of healthcare environments by multidrug-resistant organisms (MDRO) and *Clostridioides difficile* is a risk for healthcare-associated infections. The efficacy of pulsed xenon ultraviolet (PX-UV) disinfection in healthcare environments has mainly been studied in the United States. However, there are few reports about PX-UV disinfection in Japan. The aim of this study was to investigate in vitro the efficacy of PX-UV disinfection of MDRO and *C. difficile* spores commonly isolated in Japanese hospitals.

**Materials/methods:** We investigated reductions in microbial counts after exposure to PX-UV of the following clinically-isolated organisms on seeding agar plates: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus faecium*, carbapenemase-producing *Klebsiella pneumoniae*, extended spectrum β-lactamase-producing *Escherichia coli*, multidrug resistant *Acinetobacter baumannii*, and *C. difficile* spores. We also visually assessed the attenuation of sterilization by shielding of MRSA and carbapenemase-producing *K. pneumoniae* from PX-UV exposure. The left half of the plate was exposed to pulsed xenon ultraviolet light and the right half the plate was covered with aluminum foil during the exposure.

**Results:** PX-UV disinfection for 5 min induced >5-log growth inhibition of all the MDRO. PX-UV disinfection for 15 min induced >3-log growth inhibition of *C. difficile* spores. Where a plate was shielded from PX-UV exposure the bacteria showed confluent growth (Figure, the right side), but no colonies were observed on unshielded [exposed] parts of the plates [Figure, the left side].

**Conclusions:** PX-UV is a powerful disinfectant of clinical MDRO. *C. difficile* spores were more resistant to PX-UV disinfection than vegetative bacteria. Further evaluation for the efficacy of PX-UV disinfection on reducing the contamination of real-world surface and the incidence of healthcare-associated infection are needed.

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Abstract 1507

**Personalised production and administration of bacteriophages: lesson learned from a unique European academic collaboration to treat a patient with pandrug-resistant *Pseudomonas aeruginosa* spinal infection**

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**Background:** As lytic phages act synergistically with antibiotics on biofilms, they could be a potent adjunct treatment for bone and joint infections (BJI). Currently, phage Active Pharmaceutical Ingredients (APIs) production follows minimal requirements of quality and safety, which guarantee adequate composition and acceptable levels of residual contaminants.

**Materials/methods:** A 74-year-old man experienced *P. aeruginosa* bacteremia in January 2018. In summer 2018, spondylo-discitis with spinal abscess due to pandrug-resistant *P. aeruginosa* was diagnosed [panel A]. Industrial phages under development were inactive, but 3 active phages (Phi4029, Phi4032 and Phi4034) were identified by the laboratory of G. Resch [panel B, C]. Dedicated production of the APIs, in compliance with a monograph describing the production process and Quality Control (QC) system for incorporation in magistral preparations, was done at Queen Astrid military hospital in Brussels under the supervision of the French National authority (ANSM) in collaboration with the hospital pharmacist.

**Results:** The patient was treated by open debridement and one local application of the phage cocktail after magistral preparation [dilution in 7 mL; final titer of 10^7 PFU/mL]. Cefiderocol was started after the surgery for a duration of 6 weeks. One month after, a new surgery, using intersomatic cages for stabilization, was performed. The patient had no systemic (no fever, CRP 10 mg/L) nor clinical signs of infection. The same phage cocktail with same dilution and titer was locally used. Cefiderocol was pursued pending the culture results. Unfortunately, *P. aeruginosa* still grew in culture from bone biopsies with small colony variant phenotype [panel D], but remained susceptible to the phage cocktail and cefiderocol. Colistin was added and phages were administered intravenously in 3-hours infusions [30 mL, phage titers 10^8 PFU/mL] every day during 28 days. Antibiotics (cefiderocol and colistin) were stopped at 3 months. The outcome was favorable after 6 months, and the patient is walking without pain [video available].

**Conclusions:** Personalized phage therapy is a potential adjunct treatment for patients with complex BJI due to pandrug-resistant bacteria. In addition to industrial phages under development, academic collaborative research is crucial to develop personalized phage therapiu.

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Abstract 1508

**Serum active Granzyme A: a new biomarker that contributes to the pathogenesis of peritoneal sepsis**

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**Background:** Peritonitis is one of the most common leading cause of sepsis. Recent evidence suggests that Granzyme A (GzmA), a serine protease mainly expressed in NK cells and T cells, could act as a proinflammatory mediator and could play an important role in the pathogenesis of sepsis. This work aims to analyze the role of serum GzmA as a biomarker and therapeutic target in peritoneal sepsis.

**Materials/methods:** Concentration and enzyme activity of soluble GzmA were sequentially analyzed in serum from healthy donors and patients with peritonitis and were correlated with the Sequential Organ Failure Assessment (SOFA) score. Peritonitis was induced in C57Bl/6 (Wt) and GzmA-KO mice by cecal ligation and puncture (CLP). Mice were treated intraperitoneally with antibiotics and with serpinb6b, a specific GzmA inhibitor, for 5 days. Mouse survival was monitored during 14 days and the levels of serum proinflammatory cytokines and bacterial load in blood and spleen were analyzed at 6 and 24h from CLP.

**Results:** We have found high levels of GzmA in serum of patient with peritonitis. Most importantly, we observed that GzmA activity in serum correlates with SOFA score, suggesting that active GzmA could play an important role in sepsis development in peritonitis patients and could be a new biomarker of sepsis severity. In order to analyze the therapeutic potential of soluble GzmA in peritoneal sepsis, we used the CLP mouse model. After peritonitis induction, GzmA-KO mice exhibit increased survival compared with Wt mice, which correlated with reduced levels of proinflammatory cytokines in serum. The analysis of bacterial load in blood and spleen showed no differences between Wt and GzmA-KO mice suggesting that GzmA does not play an important role in bacterial control. Treatment with serpinb6b reduced mortality, which correlated with reduced cytokine serum levels in serum, confirming the therapeutical potential of gzmA to treat peritoneal sepsis.

**Conclusions:** Our findings confirm that soluble GzmA plays an important role in the pathogenesis of sepsis and could be a new therapeutic target and a biomarker for the treatment of peritoneal sepsis.

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Abstract 1513

First case of *Gemmiger formicilis* bacteraemia identified using partial 16S rRNA gene sequencing
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Background: *Gemmiger formicilis* is a Gram negative, strictly anaerobic, pleomorphic, budding-like organism previously isolated from human faeces and from chicken caecal contents. *G. formicilis* has not previously been reported as causing human infection. We report here the first case of *G. formicilis* bacteraemia.

Case report: A previously healthy 20 year old man was admitted with diarrhoea, abdominal pain, fever, chills, and rigors. On admission, he was febrile, with temperature 39.4°C, and inflammatory markers were raised. Blood cultures were taken. The anaerobic blood culture bottle taken on admission flagged positive after 42 hours of incubation. Gram stain of the positive blood culture broth showed microorganisms with an unusual morphology. The microorganisms appeared to be Gram variable cocci of varying sizes arranged in chains. The positive blood culture broth was sub-cultured onto solid media as per our laboratory’s routine processes, including incubating in anaerobic conditions. No growth was detected on sub-culture despite incubation for up to two weeks. A repeat sub-culture was also negative.

We extracted DNA directly from the positive blood culture bottle broth, and partial 16S rRNA gene sequencing identified the microorganisms as *G. formicilis*. This identity was in keeping with the distinctive Gram stain appearance, and with it being a fastidious, strictly anaerobic microorganism which may require stringent growth conditions. The patient had been treated with oral ciprofloxacin prior to admission, and was subsequently treated with intravenous ceftriaxone and oral moxifloxacin. He recovered well from this acute episode and was discharged on hospital day 11.

Conclusions: *G. formicilis* has not previously been reported as causing human infection. This might be because it is rarely pathogenic, but might also be because of difficulties with microbial growth and identification due to its fastidious, strictly anaerobic nature. This first case of *G. formicilis* bacteraemia highlights that this species may be able to cause clinically significant infection. Furthermore, direct partial 16S rRNA gene sequencing was necessary to identify the microorganisms in the blood culture broth. This case highlights the increasing need to integrate molecular diagnostics into routine clinical diagnostic bacteriology.

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Five versus seven days nitrofurantoin for urinary tract infections in women with diabetes: a non-inferiority study

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**Background:** In the Netherlands, the first choice therapy for cystitis in women with Diabetes Mellitus (DM) is seven days of nitrofurantoin. However, general practitioners often treat these patients as an uncomplicated cystitis with five days nitrofurantoin. The comparative effectiveness of either policy is unknown. The aim of this study was to compare the effectiveness between five and seven days of treatment.

**Materials/methods:** Data from the Julius General Practitioners’ Network, consisting of 75 GP practices, was retrospectively collected between January 2013 and June 2019. Inclusion criteria were nitrofurantoin prescription of five or seven days for cystitis, female sex, age > 12 and DM based on International Classification of Primary Care code T90. Patients with other reasons than DM for a seven day prescription were excluded, e.g. male gender, pregnancy, urologic abnormalities and immunosuppression. The primary endpoint early treatment failure was defined as a new prescription for a UTI within 28 days. The secondary endpoint was overall treatment failure within 90 days. Crude risk differences were estimated using linear regression. The adjusted risk differences were calculated by inverse probability weighting to account for confounders. The non-inferiority margin for the primary outcome was set at 2% absolute risk difference.

**Results:** We included 8,255 patients of whom 3,893 were treated for five days and 4,362 for seven days. Patients treated for seven days were overall older, used more co-medication and had more comorbidities. Treatment failure within 28 days occurred in 734 patients (18.9%) with five day treatment and 815 (18.7%) with seven day treatment (crude risk difference: 0.1% [95% CI -1.5 to 1.9]; adjusted risk-difference: -0.1% [95% CI -1.8 to 1.6]). Treatment failure within 90 days was 1239 (31.8%) and 1344 (30.8%) for five and seven day treatment, respectively (crude risk difference: 0.2% [95% CI -1.5 to 1.9]; adjusted risk-difference: 1.1% [95% CI -0.9 to 3.2]).

**Conclusions:** Five days treatment is non-inferior to seven days treatment with nitrofurantoin for early treatment failure in diabetic women with cystitis. Non-inferiority could not be demonstrated for overall treatment failure within 90 days, neither was there a statistically significant difference.

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Abstract 1518

Clinical and microbiological characteristics in men with non-obstructive acute pyelonephritis

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Background: Acute pyelonephritis (APN) is the most common cause of bacteremia in hospitalized patients. The objectives of this study were to investigate the differences in the clinical and microbiological features of hospitalized men with community-onset (CO) and healthcare-associated (HA) non-obstructive APN, as well as predictive factors associated with bacteremia.

Materials/methods: Five urological centers participated in this study. Men with non-obstructive APN as a discharge diagnosis were identified from January 2011 to December 2017 using an electronic medical records system. We compared the clinical and microbiological data in men with CO- and HA-APN.

Results: Of the 245 men with non-obstructive APN, 175 had CO- and 70 had HA-APN. The HA group was significantly older, had longer hospital stay and had a higher frequency of underlying disease, bacteremia, and ICU care than the CO group. Bacteria were identified in 154 of 245 patients (62.9%), and the most commonly cultured included Escherichia coli (41.7% and 50.0% in the CO and HA groups, respectively). The susceptibility of the cultured bacteria to fluoroquinolone was 68.7% in the CO group and 45.3% in the HA group (p=0.005). The proportion of ESBL-producing bacteria was 22.7% and 53.5% in the CO and HA groups, respectively (p<0.001). In the CO and HA groups, the sensitivity of piperacillin/tazobactam was 94.9% and 90.0%, respectively (p=0.297). Amikacin showed more than 95% sensitivity to bacteria isolated from both groups (p=0.555). The multivariate analysis revealed that age ≥65 years (p=0.043) and chronic liver disease (p=0.029) were independent predictive factors for bacteremia.

Conclusions: The HA group showed a higher incidence of antibiotic resistance and bacteremia than the CO group. However, the proportion of resistance for fluoroquinolone and ESBL-producing bacteria was high in both groups. Piperacillin/tazobactam and amikacin may be a feasible option as an empirical antibiotics for men with non-obstructive APN regardless of disease severity.

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Abstract 1519

Evaluation of the QIAstat-Dx Gastro-intestinal Panel at the University Hospital of Liege (Belgium)

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Background: The QIAstat-Dx Gastro-intestinal panel (QIAstat-Dx GI panel, Qiagen) detects the 24 most common gastro-intestinal pathogens by using qualitative real-time-PCR in stool samples. The system delivers results within 70 minutes with Ct values and amplification curves. The purpose of this study was to evaluate the QIAstat-Dx GI panel at the University Hospital of Liege (CHULiège) in comparison with the results obtained with the current techniques available in the laboratory.

Materials/methods: From 06/23/19 to 07/04/19, all stools addressed to the Microbiology lab for bacteriological, parasitological or virological analysis were tested with the QIAstat-Dx GI panel and the current diagnostic methods. These methods included bacteriological culture, Clostridium difficile antigenic tests (GDH and toxins A/B, Meridian), microscopy and rapid tests (Alere) for parasites.

Results: A total of 180 samples collected from 126 patients were included. Out of these samples, 51 (28%) were tested positive with the QIAstat-Dx panel with 61 pathogens detected in total. Co-infections were identified in 8 patients (4.5%). Four Campylobacter detected by PCR were not confirmed by culture nor by antigenic tests. Besides, 4 out of 13 C. difficile toxin-positive results detected by the GI panel were not confirmed by antigenic test or by culture. The results are summarized in the table 1.

Table 1. Summary of the results.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Positive GI panel N (%)</th>
<th>Positive detection by current methods N (%)</th>
<th>Discrepancies N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli (enteroaggregative, enteropathogen, enterotoxinogen and enteroinvasive) Campylobacter species</td>
<td>26 (43)</td>
<td>(0)*</td>
<td>26</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>13 (21)</td>
<td>9 (14)</td>
<td>4</td>
</tr>
<tr>
<td>Salmonella species</td>
<td>1 (2)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Virus (Norovirus, Adenovirus, Sapovirus)</td>
<td>6 (10)</td>
<td>6 (9)</td>
<td>0</td>
</tr>
<tr>
<td>Giardia lamblia</td>
<td>2 (3)</td>
<td>1 (1.6)</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>61 (34)</td>
<td>25 (40)</td>
<td>35</td>
</tr>
</tbody>
</table>

*not detectable by current methods

Conclusions: The QIAstat-Dx GI panel can detect many pathogens with higher sensitivity than the current non-PCR lab methods. The availability of Ct levels allows the evaluation of the nucleic acids content helping for differentiation between colonization and infection. The panel has a potential to improve the patient quality of care with reduction of turn-around time to result.

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Abstract 1521

Predictors of mortality in solid-organ transplant recipients with bloodstream infections due to carbapenemase-producing Enterobacteriales: the impact of cytomegalovirus disease and lymphopenia


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Abstract third-party references: This work was supported by Plan Nacional de I+D+i 2013-2016 and Instituto de Salud Carlos III, Subdirección General de Redes y Centros de Investigación Cooperativa, Ministerio de Ciencia, Innovación y Universidades, Spanish Network for Research in Infectious Diseases [REIPI R016/0016/0008; R016/0016/0001, R016/0016/0002, R016/0016/00010] - co-financed by European Development Regional Fund “A way to achieve Europe”, Operative program Intelligent Growth 2014-2020, ESCMID Study Group for Infections in Compromised Hosts [ESGICH grant to J.M.A.], Sociedad Andaluza de Trasplante de Órgano Sólido [SATOT grant to L.M.M.], ESCMID Study Group for Bloodstream Infections and Sepsis [ESGBIS], and ESCMID Study Group for Antimicrobial Resistance Surveillance [ESGARS].

Background: Treatment of carbapenemase-producing Enterobacteriales bloodstream infections (CPE-BSI) in solid-organ transplant recipients [SOT] is challenging. The objective of this study was to develop a specific score to predict mortality in SOT recipients with CPE-BSI.
**Materials/methods:** A multinational, retrospective (2004-2016) cohort study of CPE-BSI among SOT adult recipients (INCREMENT-SOT, ClinicalTrials.gov NCT02852902) was performed. The main outcome variable was 30-day all-cause mortality. The INCREMENT-SOT-CPE mortality score was developed using logistic regression and calculating the area under the ROC curve (AUROC). The impact of targeted therapy (monotherapy versus combination therapy) was analysed using Cox-regression.

**Results:** The INCREMENT-SOT-CPE score was developed using logistic regression. The global cohort included 216 patients. The final logistic regression model included the following variables: INCREMENT-CPE mortality score ≥8 (8 points), no source control (3 points), inappropriate empirical therapy (2 points), cytomegalovirus disease (7 points), lymphopenia (4 points), and the interaction between INCREMENT-CPE score ≥8 and CMV disease (minus 7 points, indicating that CMV disease does not further increase the risk of death if the INCREMENT-CPE-score is ≥8, but do so only if the score is <8). This score showed an area under the receiver operating characteristic curve of 0.82 [95% CI 0.76-0.88] and classified patients into three strata: 0-7 (low mortality), 8-11 (high mortality) and 12-17 (very-high mortality). We performed a stratified analysis of the effect of monotherapy versus combination therapy among 165 patients who received appropriate therapy. Monotherapy was associated with higher mortality only in the very-high [adjusted HR 2.82, 95% CI 1.13-7.06, P=0.03] and high [HR 9.93, 95% CI 2.08-47.40, P=0.004] mortality risk strata.

**Conclusions:** A mortality risk score of CPE-BSI in SOT recipients was developed. We propose a score-based algorithm (Figure 1), which can be used for therapy guidance.

Figure 1. Algorithm for clinical management of SOT patients with bloodstream infection due to carbapenemase-producing Enterobacterales (CPE-BSI), based on INCREMENT-SOT-CPE mortality risk score.

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**Abstract 1522**

**Do cytomegalovirus infection and valgancyclovir exposure increase the risk of BK viraemia and associated nephropathy after kidney transplantation?**

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**Background:** Both CMV and BK polyomavirus [BKV] adversely affect graft outcomes after KT. Indirect immunomodulatory effects attributable to CMV would predispose to non-CMV infections. Recent studies have suggested that VGCV prophylaxis may increase the risk of BKV viremia and BKV-associated nephropathy (BKPyVAN) due to a presumptive drug-specific immunosuppressive effect. However, these apparently contradictory associations remain controversial. We investigated whether KT recipients exposed to CMV replication and/or VGCV therapy experienced higher incidence of BKV infection.

**Materials/methods:** Prospective cohort study including 423 consecutive KT recipients from November 2014 to September 2019 in which CMV and BKV DNAemia were periodically monitored throughout the first year. VGCV prophylaxis was given for 6 months to D+/R- patients and for 3 months to R+ patients receiving antithymocyte globulin. The remaining patients were pre-emptively managed. The impact of CMV replication and VGCV therapy [prophylaxis or treatment] during the first 90 and 180 pos-transplant days on the subsequent occurrence of BKV viremia and BKPyVAN was analyzed.

**Results:** VGCV prophylaxis was administered to 235 patients [55.6%], whereas 188 [44.4%] were managed by preemptive therapy. In the latter group, 47 [25.0%] and 53 [28.2%] received VGCV treatment for CMV infection and/or disease during the first 90 and 180 days. One-year incidence rates for CMV and BKV DNAemia were 48.9% [n = 207] and 18.4% [n = 78]. Only one patient [0.2%] developed BKPyVAN. The incidence of BKV viremia beyond days 90 [17.7% vs. 14.2%; P-value = 0.355] and 180 [9.7% vs. 8.9%; P-value = 0.785] was not different between patients that had previously received or not VGCV therapy, respectively. Likewise, no significant differences were found in the occurrence of BKV viremia beyond days 90 [12.9% vs. 17.9%; P-value = 0.218] and 180 [8.4% vs. 10.2%; P-value = 0.542] between patients with or without CMV exposure over the preceding periods. The lack of impact of VGCV therapy or CMV exposure during the first 90 and 180 days was confirmed after adjusting for various clinical covariates by Cox regression.

**Conclusions:** This large prospective study does not support an association between previous CMV replication or VGCV exposure and subsequent BKV viremia after KT.

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High-resolution subtyping of *Escherichia coli* using optical DNA mapping

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**Background:** Typing of bacteria on the sub-species level generally requires sequencing, but there is a need for faster and easier methods for efficient infection control in clinics. We have previously demonstrated that optical DNA mapping (ODM) can differentiate bacterial species with high specificity, and here extend this approach to subtyping of *Escherichia coli*.

**Materials/methods:** The DNA extraction was carried out in agarose plugs to protect the DNA from fragmentation and generate ultra-long DNA molecules (>200 kb). The DNA was then stained with YOYO-1 and netropsin to generate an emission profile along the DNA that reflects the sequence: a DNA barcode. To visualize the barcode, the DNA was stretched in nanofluidic channels and imaged using fluorescence microscopy. The barcodes were aligned to a database of theoretical barcodes from >2000 bacterial species where the included *E. coli* genomes were typed using the Warwick MLST scheme. Only barcodes with high-quality matches to a single species were retained after quality filtering. Barcodes matching discriminatively to *E. coli* were further analyzed and reported if all high-quality matches were to the same sequence type (ST).

**Results:** ODM was performed for clinical *E. coli* isolates, including clinically important STs. Preliminary experiments on eight isolates, belonging to ST38, ST131, ST156, ST405, ST410, and ST648, comprised of on average 37 mapped molecules per sample. The proportion of barcodes that matched discriminatively to a single ST was on average 25%. Importantly, the proportion of discriminative barcodes that matched the correct ST – i.e. the true positive rate – was 100% for all samples, except one where nine out of ten discriminative barcodes matched the correct type.

**Conclusions:** We demonstrate how ODM can classify *E. coli* down to the ST level. Sample preparation and data collection are significantly faster than for sequencing methods, which opens up possibilities for clinical use, in particular in infection control. Importantly, the approach is general and can likely be transferred to other clinically relevant bacterial species.

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Abstract 1524

**Epidemiology of carbapenemase-producing Enterobacteriales in the Netherlands in 2018**

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**Abstract third-party references:** on behalf of the Dutch CPE Surveillance Study Group

**Background:** The current epidemiology of carbapenemase-producing Enterobacteriales (CPE) in Europe varies from sporadic imported cases, to sporadic hospital outbreaks, (inter-) regional spread between hospitals, and CPE being endemic in healthcare settings. Here, we describe the epidemiology of CPE in the Netherlands in 2018 based on the enhanced CPE surveillance system.

**Materials/methods:** All Dutch medical microbiological laboratories are requested to submit Enterobacteriales isolates with a MIC for meropenem >0.25 mg/L and/or MIC for imipenem >1 mg/L to the National Institute for Public Health and the Environment (RIVM). MALDI-ToF, MIC for meropenem, carbapenemase inactivation method (CIM), and PCR for carbapenemase-coding genes are performed on all isolates and whole genome sequencing (WGS) is done for all CIM+ isolates. An epidemiological questionnaire is requested for all CIM+ isolates. Reported data were based on the first unique CIM+ species-gene combination per person in 2018 and epidemiological data were analysed on person level.

**Results:** 578 Enterobacteriales isolates were submitted of which 306 were unique CPE isolates obtained from 266 persons (mean age 60 years and 53% male). *K. pneumoniae* was most frequently identified (40%), followed by *E. coli* (29%) and *E. cloacae* complex (12%), and 19% were other species. The genes most often detected coded for OXA-048 (40%), NDM (34%; 20% of all CIM+ isolates was NDM-5, 12% NDM-1), VIM (6%) and KPC (6%). Epidemiological characteristics were available for 161 persons (61%). Forty-five persons (28%) were sampled for diagnostic reasons. Screening because of presumed risk, usually upon admission, was the reason for sampling in 115 (71%) persons. Hospitalization abroad was the most common risk factor (n=93; 58%), with Turkey (n=20) and Morocco (n=14) most often reported. In 50 persons no risk factor was identified (31%). Risk factors reported in <4% of the persons include contact with a foreign country in a different way in the past year, relation with a known outbreak of CPE, work-related exposure to livestock animals, and already known carrier of CPE.

**Conclusions:** Genes coding for OXA-048 and NDM were most frequently detected in CPE isolates submitted to the RIVM. Recent hospitalization abroad is the main risk factor for CPE in the Netherlands.

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Impact of unrestricted movement of carbapenemase-producing Enterobacteriales (CPE) carriers on transmission of CPE in nursing homes: a prospective cohort study

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Background: In September 2018, the National Infection Prevention and Control Committee (NIPC) of Singapore recommended standard precautions and unrestricted movements for CPE carriers in NH. We studied the impact of this recommendation on Carbapenemase-producing Enterobacteriales (CPE) transmission among NH residents.

Materials/methods: This prospective cohort study was conducted in a 255-bedded nursing home in Singapore. Eligible consenting residents were followed for 3 months. Stool and environmental samples (sink steel traps and shower drain traps) were collected at baseline and weeks 2, 8 and 12. We collected demographic, comorbidity, hospitalization, antibiotics and travel history at baseline and during follow-ups. We used CHROMID® CARBA SMART to detect CPE, with environmental samples undergoing an additional selective broth enrichment step prior to culture. CPE were identified with MALDI-TOF and PCR for carbapenemase genes. CPE acquisition was defined as having a positive CPE stool sample after an initial negative screening at recruitment. Statistical analysis was done with STATA15.

Results: Between April and July 2019, 32 residents including 6 known CPE carriers (identified in a recent acute hospital stay): 5 blaNDM and 1 blaOXA-48] were recruited and followed-up. Among the known CPE carriers, only 1 remained persistently stool-positive for blaOXA-48, while the rest reverted to negative throughout the study. After a total follow-up of 2699 patient-days, one resident acquired blaNDM-producing Enterobacter cloacae at week 12, giving an acquisition rate of 0.37 per 1000 person-days (95%CI 0.05, 2.63). A total of 164 environmental samples were collected from 28 sink steel traps and 13 shower drains. Of the 28 sink steel traps, 6 were positive for CPE [5 were blaNDM and 1 was blaKPC]. The shower drain traps remained negative for CPE throughout the study.

Conclusions: The recommendation to allow standard precautions during patient care and unrestricted movement of CPE carriers in nursing home appears to be acceptable because we were unable to demonstrate patient-to-patient transmission in this study. However, larger studies with longer follow-up periods are necessary to definitively confirm this finding.

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Abstract 1528

Comparison of host immune responses in vivo versus ex vivo lipopolysaccharide stimulation in humans using an immune transcriptomic profiling panel

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Abstract third-party references: European Sepsis Academy, European Union’s Horizon-2020 research and innovation program grant agreement No. 676129

Background: Patients that suffer from sepsis exhibit an early hyper-inflammatory immune response which can lead to organ failure and death. In our study, we assessed the immune modulation in the human in vivo endotoxemia model and compared it to ex vivo lipopolysaccharide (LPS) stimulation using 38 transcriptomic markers.

Materials/methods: Eight volunteers were challenged with intravenous LPS in vivo. In parallel, blood from another 8 volunteers was challenged ex vivo. Blood was collected before and after 4 hours of LPS challenge and tested with the Immune Profiling Panel (IPP) using the FilmArray® system.

Results: The use of IPP showed that markers from the innate immunity dominated the response to LPS in vivo, mainly markers related to monocytes and neutrophils. Comparing the two models, in vivo and ex vivo, revealed that most of the markers were modulated in a similar pattern (68%). Some cytokine markers such as TNF, IFN-γ and IL-1β were under-expressed ex vivo compared to in vivo. T-cell markers were either unchanged or up-modulated ex vivo, compared to a down-modulation in vivo. Interestingly, markers related to neutrophils were expressed in opposite directions, which might be due to the presence of cell recruitment and feedback loops in vivo.

Conclusions: In both models, the majority of IPP markers showed similar patterns of expression post-LPS challenge, except for several markers related to neutrophils and T-cells. The IPP tool was able to capture the early immune response in the human in vivo endotoxemia model, which is a translational model mimicking the immune response observed in septic patients.

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First report of \textit{bla}\textsubscript{NDM-1} and \textit{bla}\textsubscript{OXA-181} harbouring \textit{P. vermicola} from Nepal

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\textbf{Background:} The genus \textit{Providencia} encompasses five common species i.e., \textit{P. alcalifaciens}, \textit{P. rettgeri}, \textit{P. stuartii}, \textit{P. rustigianii}, and \textit{P. heimbachae}. They are frequently isolated from wounds, respiratory tract, urinary tract, stool of humans, poultry, faeces from reptiles, throat, perineum, axilla and blood of humans. Other species and antimicrobial resistance in this genus are uncommon, especially in clinical samples. We executed whole genome analysis of a pan-drug resistant \textit{Providencia} spp. isolated from a septic patient in Nepal.

\textbf{Materials/methods:} In Nepal, the strain was isolated from urine sample and phenotypically identified as \textit{Providencia} spp. The strain was found resistant to 14 antimicrobials including colistin in disk-diffusion method. The pan-drug resistant \textit{Providencia} spp. was transported to our laboratory for further investigations. We cultured the bacteria on McConkey in 35\(^\circ\)C for overnight and prepared a pure stock. The susceptibility of the bacteria to 33 antimicrobials was measured by automatic microbiological system. We searched for ESBL and carbapenemase encoded genes in association with the isolate by disk-synergistic test and modified carbapenemase inactivation method (mCIM), respectively. Genomic DNA of the strain was extracted by boiling method and was sequenced using the PacBio RS II platform.

\textbf{Results:} Susceptibility test revealed that the isolate was susceptible only to monobactum and fosfomycin and was resistant to all other groups of antimicrobials including 3\(^{rd}\)-4\(^{th}\) generation cephalosporin, carbapenems, aminoglycoside, fluoroquinolone, colistin, etc. Disk synergistic test and mCIM conferred the isolate as non-ESBL encoded and carbapenemase producing isolate, respectively. 16S rRNA sequencing revealed the isolate is highly identical to the \textit{P. vermicola} (99.65%). A total of 13 resistance genes including \textit{qnrD}, \textit{aac(6')-Ib}, \textit{bla}_{\text{NDM-1}}, \textit{bla}_{\text{OXA-181}} etc. were detected in association with the isolate. No typable plasmid replicons, including IncF was detected.

\textbf{Conclusions:} To our knowledge, this is the first \textit{Providencia} strain concomitantly harboring \textit{bla}\textsubscript{NDM-1} and \textit{bla}\textsubscript{OXA-181} encoding genes. First clinical \textit{P. vermicola} was isolated in 2015 from India and we are reporting the second clinical and most resistant species in the genus \textit{Providencia} from Nepal. The findings suggest that the preparedness to emerging MDR organisms mandates more microbiological surveillances in Asia.

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Abstract 1531

Clinical and microbiological characteristics and outcomes for community-onset sepsis patients in a teaching hospital in Latvia: a retrospective, single-centre, cohort study

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Background: Sepsis is a complex life-threatening condition characterised by systemic inflammatory immune response, which may cause organ failure, septic shock and death. The objective of the study is to assess the mortality and associations between clinical and microbiological characteristics in patients with community-onset sepsis (COS) admitted to Pauls Stradins Clinical University Hospital (PSCUH).

Materials/methods: In retrospective cohort study we identified 395 adult patients with sepsis-related ICD-10 codes upon discharge, admitted to PSCUH between September 2017 and September 2018. Further analysis was performed on 289 COS cases, identified using consensus definitions (Sepsis-3). We collected demographic data, information on clinical presentation, risk factors, time-to-culture (TTC), blood culture (BC) turn-around-time (TAT) and mortality.

Results: The median age of the COS cohort patients was 74 years (IQR 59.0-82.5) with median Charlson Comorbidity Index of 6 points (IQR 4-8), 49.8% were male. The intrahospital mortality reached 47.2%. The reason of hospitalization was documented as infectious disease for 50.8% of COS cases; nevertheless, the BC were not taken in 12.2% of those patients. The most common sites of COS origin were pneumonia (22.7%) and urinary tract infection (16.3%). In 79.2% of cases BC were performed; furthermore, patients without BC were significantly older (p=0.004). Antimicrobials prior to the BC were administered in 36.2% of cases. From 173 BC performed 59.0% returned positive with Staphylococcus aureus MS, Escherichia coli and Streptococcus pneumoniae as the most common isolates – 47.1%, 27.5% and 14.7%, respectively. The rate of positive BC was significantly higher in COS survivor group (p=0.045). Median TTC was 4.8 hours (IQR 2.8-16.4). TTC was not dependent on age, comorbidities, previous exposure to long-term healthcare facilities, clinical presentation, source of infection or presence of septic shock. Median TTC in COS patients initially admitted for non-infectious reason was 5.4h (IQR 3.6-18.6). Median TAT was 93.7h (IQR 78.3-115.0).

Conclusions: Intrahospital mortality was remarkably higher than reported in other sepsis cohorts. Additional training is needed about the recognition of the community-onset sepsis and importance of blood cultures to improve outcomes, especially in the geriatric population. The data collection will be continued and larger cohort remains to be assessed.

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**Abstract 1532**

**Bacteriophages in real-life: positive and negative experience in a difficult to access old-new therapeutic**


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**Background:** Bacteriophages therapies as an alternative or in combination with antibiotics are regaining a place in the arsenal of occidental Infectious Diseases (ID) specialist’s after decades of neglect. In the last year bacteriophages as treatment increased in France with more than fifteen patients treated.

**Materials/methods:** Demographic and clinical data, bacteriophages indication, microbiological aspects including antibiotic susceptibility, procedure to obtain bacteriophages, health care authority statement and outcome after therapy are reported.

**Results:** Between November 2018 and November 2019, eight cases were discussed in our center. Four patients had bone and joint infection, two a central nervous system infection, one pulmonary abscess and one chronic sinusitis. After reviewing medical chart by a dedicated board, bacteriophages therapy was considered as an option for five patients out of eight. The three remaining cases could be treated with antibiotics optimization. These five cases were subsequently presented and validated by the French national drug agency (ANSM) who authorized compassionate use. Bacteriophages active against patient’s bacterial strains were available in three cases. In two cases, bacteriophages were provided by a French pharmaceutical biotech company. In the last case bacteriophages were available in a Swiss research lab. They were active *in vitro* but the patient’s family finally refused the treatment. Patients treated with Bacteriophages presented (i) a *Staphylococcus aureus* extradural empyema (ED) and osteitis and (ii) a prosthetic knee infection. Both previously experienced relapses despite adapted antibiotic treatment. Both patients received a combination of two different Bacteriophages through local instillation in association with active antibiotic therapy. The prosthetic infection relapsed one month after phage instillation while the patient with the ED is cured without relapse at one year follow up.

**Conclusions:** Bacteriophages therapy is a neglected therapy which came back in our therapeutic arsenal through the multi and pan resistance problem. One of the major limits for Bacteriophages use nowadays is the absence of bacteriophages active against clinical stains as experienced in our experience. Open source libraries of bacteriophages available for clinicians and patients might resolve this limitation. Finally bacteriophages were currently used as salvage therapy in desperate situation which might explain the experienced relapse.

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Abstract 1533

**Anakinra for the treatment of protracted paradoxical inflammation in HIV-associated tuberculosis**

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**Background:** Paradoxical inflammation including immune reconstitution inflammatory syndrome (IRIS), is well described in HIV-associated tuberculosis (TB). At the severe end of the disease-spectrum significant morbidity and mortality may occur particularly in TB of the central nervous system (CNS), or when protracted high dose corticosteroids are used. Interleukin-1 (IL-1) mediated inflammation has been implicated in the pathophysiology of IRIS. We describe two cases where anakinra (recombinant human IL1 antagonist) successfully controlled life-threatening protracted paradoxical inflammation.

**Materials/methods:** Case reports

**Results:**

Case 1: A 33-year-old woman from Ethiopia was diagnosed with HIV (baseline CD4 count of 60 cells/mm³) and fully-sensitive TB with cervical, thoracic and abdominal adenopathy and splenic micro-abscesses. She was treated with standard anti-TB therapy. Following antiretroviral therapy initiation, she had protracted IRIS with fever and massive adenopathy. No alternative infective, malignant or inflammatory cause was found. Pus from repeated lymphnode aspirations showed acid fast bacilli but no further growth of mycobacteria, consistent with IRIS. Over 3 years it was not possible to wean prednisolone below 20mg, nor achieve control of inflammation despite montelukast and colchicine. Protracted inflammation lead to nephrotic syndrome with AA amyloidosis on renal biopsy. This prompted initiation of anakinra, with rapid normalisation of inflammatory markers, proteinuria and quality of life.

Case 2: A 41-year-old man from Zimbabwe with known HIV (virologically suppressed with CD4 count of 275 cells/mm³) was diagnosed with isoniazid-monoresistant miliary TB. He had cerebral tuberculomata on magnetic resonance imaging (MRI). He was treated with rifampicin, moxifloxacin, pyrazinamide, ethambutol and dexamethasone. He had no neurological deficit at treatment initiation. Over 18 months had progressive episodic neurological deterioration whenever he weaned off corticosteroids with ataxia, aphasia, hemiparesis and inability to live independently. Serial MRI showed unstable tuberculomata in both hemispheres, cerebellum, pons and medulla. Brain biopsy demonstrated necrotizing granulomata with no mycobacterial growth consistent with a paradoxical inflammatory reaction. Anakinra was initiated after unsuccessful trial of thalidomide. Since anakinra initiation he had continual neurological and functional improvement with resolution of tuberculomata on MRI.

**Conclusions:** We describe, to the best of our knowledge the first reported usage of anakinra to control life-threatening paradoxical inflammation in HIV-associated TB.

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Abstract 1541

One Health surveillance of extended-spectrum beta-lactamase-producing Enterobacteriales in urban and rural Malawi

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Background: The greatest burden of drug-resistant infections is predicted to occur in low- and middle-income countries (LMICs). Given the limited availability of carbapenems and local resistance to 3rd generation cephalosporins, extended spectrum beta-lactamase (ESBL) bloodstream infections are often untreatable. It is therefore essential to understand the key drivers and environmental reservoirs of ESBL resistance within these settings to interrupt community transmission. We describe a one-health focused observational study of households in Malawi to describe the dynamics of ESBL E. coli (ESBL-E) and ESBL Klebsiella pneumoniae (ESBL-K) and their ecological niche.

Materials/methods: Longitudinal, microbiological surveillance of 195 households in urban (65), peri-urban (65) and rural (65) Malawi. Each household undergoes 3-4 visits over a 6-month period. At each visit human and animal stool, alongside an extensive environmental sweep of the household, and broader external environment are taken. Household sampling includes food, drinking water, clothing and key hand contact surfaces, whilst broader environmental sampling comprises nearby soil, drainage systems and local river water. Samples undergo concentration and enrichment culture (buffered peptone water), before plating onto ESBL chromogenic agar. ESBL-E and ESBL-K isolates are identified morphologically, and ESBL-K are confirmed with PCR.

Results: Microbiological surveillance of 112 households [1,700 samples] indicates a high prevalence of ESBL-E and ESBL-K within human stool [34.5% n=162], animal stool [26.4% n=43], on household food [17.1% n=29], in household drinking water [17.8% n=21], on participant clothing [8.2% n=8], on household environmental surfaces [8.6% n=38] and within the broader environment [71.6% n=53] (Figure 1).

Conclusions: In urban and rural Malawi there is a very high prevalence of ESBL Enterobacteriales in humans, animals and the environment. These data will be placed in the context of water sanitation and hygiene behaviour, human health and antimicrobial usage in order to develop a dynamical transmission model.

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Clinical factors associated with empirical antibiotics resistance in febrile patients with urinary tract calculus

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Background: To investigate the clinical and microbiological features in the febrile patients with urinary tract calculus, as well as factors that affect empirical antibiotics resistance.

Materials/methods: A retrospective analysis was performed of 203 patients hospitalized between January 2011 and December 2016 for antibiotic treatment of febrile urinary tract infection with urinary calculus at 3 institutions. We investigated patient age, sex, body mass index, underlying diseases, stone-related factors and results of urine and blood culture examination and antibiotic sensitivity test.

Results: Bacteria were identified in 152 of 203 patients (74.9%), and the most commonly cultured included Escherichia coli (44.1%), followed by Enterococci spp. (11.8%), Proteus (8.6%), S. agalactiae (6.6%), Klebsiella spp. (5.3%), Pseudomonas spp. (4.6%), coagulase-negative Staphylococci (4.0%), Staphylococcus epidermidis (4.0%), Enterobacter (0.7%), Acinebacter (0.7%), mixed infection (7.2%) and other spp. (5.4%). The multivariate analysis revealed that multiplicity of calculus was independent predictive factor for fluoroquinolone resistance (p=0.008). Recurrent infection was determined to be significant predictor of cefotaxime resistance on multivariable analysis (p=0.041).

Conclusions: Based on the results from the present study, fluoroquinolone should not be considered as the empirical treatment in febrile patients with urinary tract calculus. Also, combination antibiotic therapy is recommended in case with recurrent infection, because cefotaxime resistance can occur.

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Abstract 1545

Does iodine-impregnated incision drape prevent periprosthetic joint infection? One-year follow-up of 1187 patients in a randomised controlled trial

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Background: PJI is a devastating incident for the patients and in a population that is getting older and the incidence of arthroplasty surgery is rising it is vital to keep the infection rate as low as possible. Despite prophylactic measures as pre-operative decontamination, antisepsis and prophylactic antibiotics the infection rate has been constant at 1-2%.

The primary aim of this study was to examine whether the use of iodine impregnated incision drape (IIID) decreased the risk of periprosthetic joint infections (PJs). The secondary aim was to investigate whether intraoperative contamination could predict postoperative infection.

Materials/methods: We performed a prospective, randomized two arm study (IIID vs control group) of 1187 patients undergoing primary knee arthroplasty surgery. A database with patient demographics and surgical observations was established with the purpose of following the patients for ten years. Patients, who developed an infection within the first year of surgery were analysed for correlation with the intraoperative bacterial findings and the use of IIID.

Results: 31/1187 (2.6%) patients were re-operated during the follow-up period. 18/31 (58%) patients were deemed infected and received antibiotic treatment. 9/18 of infected patients were female. Of the 18 infected patients 2 were contaminated at primary surgery. 9 of the 18 infected patients were operated with IIID at the primary surgery. No correlation was found between the use of IIID at primary surgery and subsequent infection (OR 0.95, 95% CI 0.38-2.46, P=0.95) Chi square test showed no correlation between contamination and infection (OR 0.86, 95% CI 0.20-3.79, P=1).

Conclusions: We found no effect of the use of IIID and subsequent development of PJI. Nor did we find a correlation between the intraoperative contamination and development of PJI within the first year of follow-up. Longer follow-up time and larger studies are needed to determine if IIID can prevent postoperative infection.

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Abstract 1546

**Bronchial abundance of Streptococcus as a potential biomarker for lung cancer**


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**Background:** Lung cancer has been associated to dysbiosis of the lung microbiota, but available data are scarce. The aims of this work were: i) to define the microbiota of the central bronchial tumour, in comparison with the contralateral bronchus of the same patient and with a cohort of controls; ii) to analyse the differences between the oral and pulmonary microbiota, and iii) to find potential microbiota-related biomarkers for lung cancer.

**Materials/methods:** We obtained bronchial samples by bronchoscopy from tumour and from contralateral lung of 25 patients diagnosed of central lung cancer. Sixteen healthy controls were also included, each contributing with a biopsy of their healthy bronchi. One salivary sample per participant was also obtained. None received antibiotics within the month prior sampling. Bacterial composition was determined by PCR amplification and sequencing of the V3-V4 regions (16S rDNA) using a MiSeq platform (Illumina). Bioinformatics was performed using QIIME2. Differential abundance was assessed by Linear discriminant analysis Effect Size (LEfSe). ROC curves were plotted using SPSS (v.22).

**Results:** After quality evaluation of the sequencing process, 22 tumour tissue (affected bronchi), 25 contralateral bronchi, and 25 saliva samples from patients (n=25), and 12 bronchi and 16 saliva samples from controls (n=16) were finally included. Alpha-diversity analysis showed higher Chao1 and Shannon indices in patients’ bronchi than controls’ (p<0.001), whereas no significant differences were observed between patients’ and controls’ saliva (p>0.05). Beta-diversity analysis (UniFrac distance) showed that both affected and contralateral bronchial microbiota were different from controls (p<0.001). Saliva from patients and controls were also different (p<0.005). LEfSe analysis showed a higher density of Firmicutes (particularly Streptococcus), in detriment of Proteobacteria, in patients’ samples. ROC curves using the relative abundance of Streptococcus [Figure1] showed that >14.6% of Streptococcus in bronchus predicted lung cancer with 90.9% sensitivity and 83.3% specificity (AUC=0.848, using affected and control bronchi data). Otherwise, streptococcal abundance in saliva did not perform well as biomarker.

**Conclusions:** Lung and oral microbiota showed an enrichment of Firmicutes and a reduction of Proteobacteria in lung cancer patients. Streptococcal abundance in lung samples obtained by bronchoscopy could be a potential biomarker for lung cancer diagnosis.

![ROC curves](image)

Figure1. ROC curves to discriminate patients from controls using their relative abundance of Streptococcus.

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Abstract 1548

Comparison of antibiotic susceptibility of *Escherichia coli* between community-acquired and post-prostate biopsy acute bacterial prostatitis

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**Background:** To compare the antibiotic susceptibility of *Escherichia coli* (*E. coli*) between community-acquired acute bacterial prostatitis (CA-ABP) and ABP following transrectal ultrasound-guided prostate biopsy (Bx-ABP).

**Materials/methods:** A total of 4,383 patients underwent prostate biopsy from January 2005 to June 2014. Among these patients, 34 had Bx-ABP, of which 22 patients had *E. coli* identified in their urine or blood culture. *E. coli* was also identified in 91 out of 209 patients with CA-ABP in urine or blood culture. We investigated patient and microbiological characteristics.

**Results:** The Bx-ABP (50.1%) group showed a higher bacteremia prevalence than the CA-ABP group (13.2%) (p<0.001). Significant differences in the antibiotic sensitivity to *E. coli* between the two groups were observed for fluoroquinolone, cephalothin, and gentamicin. The antibiotic sensitivity of fluoroquinolone in the Bx-ABP group was only 27.3%. Amikacin, imipenem, meropenem, amoxicillin/clavulanic acid, and piperacillin/tazobactam showed more than 95% antibiotic sensitivity in both groups. Bx-ABP was an independent predictive factor for bacteremia by multivariate analysis.

**Conclusions:** *E. coli* in Bx-ABP showed a higher incidence of antibiotic resistance and bacteremia than those in CA-ABP. Carbapenem may be a treatment of choice for patients suspected of having sepsis. Considering the recent emergence of carbapenem-resistant bacteria, piperacillin/tazobactam or amikacin may be considered.

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Abstract 1556

**Rapid carbapenemase detection using the CARBA5 lateral flow device**

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**Abstract third-party references:** Supported by NG Biotech

**Background:** Colonisation and infection with carbapenemase-producing organisms is now frequently reported in the UK, with many diagnostic microbiology laboratories routinely screening for these organisms. Following validation of the NG-Biotech CARBA5 lateral flow device for the detection of the ‘Big 5’ carbapenemases, we implemented the test into our diagnostic service. Here, we report our carbapenemase detection rate for all rectal screens since March 2019.

**Materials/methods:** All Enterobacteriales recovered from rectal swabs, as part of our carbapenemase-producing organism screen, were identified by MALDI-ToF and underwent antibiotic susceptibility testing by disk diffusion. Isolates that matched our presumptive carbapenemase algorithm were tested on the CARBA5 according to the manufacturer’s instructions.

**Results:** Between March 2019 and October 2019, 3993 patient rectal swabs were screened for carbapenemase-producing organisms. Of these, 132 (3%) were positive for a carbapenemase-producing organism according to the CARBA5 device, including 12/132 that possessed two carbapenemase-producing organisms. Enzymes detected included OXA-48 (70%), NDM (21%), IMP (2%) and 6% of isolates possessed both OXA-48 and NDM. One presumptive carbapenemase-producer, that was resistant to ertapenem and meropenem, was negative on the CARBA5 device. This isolate was confirmed as negative for the common carbapenemases by the Public Health England reference laboratory.

**Conclusions:** The CARBA5 lateral flow device was successfully validated and implemented as part of our routine diagnostic service. Importantly, this test enables rapid identification of the most common carbapenemases in our Trust, and in the UK, which reduces the turnaround time for this test, as well as enabling prompt and appropriate infection control interventions.

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Abstract 1557

Incidence of bloodstream infection from multidrug-resistant bacteria in haematological patients with rectal colonization

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Background: Spread of multidrug-resistant (MDR) bacteria has a relevant impact on the clinico-therapeutic management in the hospital setting with epidemiological surveillance playing a crucial role in its containment. Patients with hematological malignancies are at high risk of infection due to deep immunodepression and long hospitalization periods. In Italy, approximately 5-10% of these patients are colonized by MDR bacteria (carbapenem-resistant [CR], extended spectrum beta-lactamase producers [ESBL] and vancomycin-resistant enterococci [VRE]); blood stream infection (BSI) develops in 25% of these patients with 60% of these infections being caused by colonizing MDR bacteria. In this study, the incidence of rectal colonization and subsequent MDR-BSI was evaluated in hematological adult patients referred to our laboratory.

Materials/methods: MDR-bacteria colonization was evaluated in 828 hematological patients referred to our laboratory over a two-year period (2017-18) by rectal swab screening; in these patients, blood cultures were analyzed for BSI development following MDR bacteria colonization.

Results: Overall, 43/817 patients (5.3%) were colonized by CR, 232/746 (31.1%) ESBL and 56/441 (12.7%) VRE. Thirty patients (3.6%) presented colonization by multiple MDR bacteria. Considering species, K. pneumoniae (KP) represented 78% of CR, E.coli (EC) 75.3% of ESBL (53% of all MDR bacteria) and E.faecium (EF) 98.2% of VRE. Over the study period, at least one episode of BSI developed in 223/828 patients (26.9%), with MDR bacteria in 17.9% of the cases (4.8% of all the patients). Among 43 MDR isolates, 30 were involved in BSI following colonization. Overall, the mean rate of BSI in colonized patients was 12% (3/32 KP CR, 16/174 EC ESBL, 9/45 KP ESBL).

Conclusions: Over the study period, at least one case of rectal colonization from MDR bacteria was found in 35.7% of patients with a high prevalence of ESBL producers (70.4%); this rate of colonization is higher than in other countries, in which however CR bacteria are prevalent (59%). The rate of BSI (26.9%) is similar to that reported in literature (25-26%), however BSIs from MDR bacteria following colonization result lower in comparison to those reported in literature (15-20%). Further studies are required to define the impact of colonization and subsequent BSI on the patient outcome.

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Abstract 1559

**Pooled saliva cytomegalovirus-PCR: a viable laboratory technique for universal cytomegalovirus screening of healthy newborns**

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**Background:** The vast majority of congenital CMV (cCMV) infected infants have no overt manifestations at birth; still, CMV-related sensorineural hearing loss (SNHL) may be present. Valganciclovir initiated to neonates with moderate-severe cCMV disease has the potential to ameliorate long-term hearing outcome, yet with the customary target screening, many neonates with SNHL cases are missed. Given its ease of collection, saliva is recommended as the preferred screening specimen. Accordingly, we aimed to investigate the screening of healthy full-term neonates employing a pooled saliva specimen technique.

**Materials/methods:** This was a prospective laboratory universal CMV PCR screening conducted at a secondary hospital in Northern Israel, March 2019 until June 2019. All neonates underwent saliva sampling upon arrival to the nursery. Specimens were extracted in pools of 10 and individually (40 μL and 400 μL, respectively) by the QiaCube (Qiagen) automated extractor. Specimen extracts were analyzed for the presence of CMV DNA by the RealStar® CMV-PCR Kit 1.0 (Altona Diagnostics) using the Rotorgene 6 plex real-time platform (Qiagen). In cases where the pooled specimen was positive, the pool was opened and the individual specimens evaluated to determine the source[s] of CMV. A definitive cCMV was defined only after confirmation with positive urine testing.

**Results:** Of the 1000 saliva samples, there were 6 urine-confirmed congenital CMV patients attained by both laboratory techniques. The specificity of both techniques, was high with the pooled specimen yielding 98.94% (95% CI: 94.2-99.97%) and the individual sampling 98.1% (95% CI: 97.0-98.8%), respectively. The rate of false positive results was statistically significantly higher in individual sampling in comparison to the pooled specimens, 19/25 (76.0%) versus 1/7 (14.3%; p<.003), respectively. Similarly the PPV of the individual sample was only 22.4% in comparison to 98.2% in the pooled specimens.

**Conclusions:** Pooled saliva CMV PCR of full-term healthy newborns appears to be an effective laboratory technique for identification of asymptomatic cCMV infection. The pooling technique affords a higher specificity by decreasing the rate of saliva false-positive samples and may have the potential to improve the laboratory workflow and decrease costs. Further studies are needed to evaluate the clinical correlation of this widespread cCMV screening technique.

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Abstracts 2020

Abstract 1562

**Acquired resistome of *Escherichia coli***

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**Background:** *Escherichia coli* is an ubiquitous bacterium found in the intestinal microbiota of vertebrates. Accordingly, *E. coli* is widely exposed to antibiotics and has evolved by acquiring different antibiotic resistance genes (ARGs). In the past, the exhaustive characterization of these genes was difficult because based on targeted PCRs. With the availability of next-generation sequencing, the identification of resistance genes has become easier. Here, we aimed at characterizing the census ARGs acquired by *E. coli*, leveraging a publicly available *E. coli* genome database.

**Materials/methods:** We downloaded the 82,084 genomes of Enterobase that includes *E. albertii*, *E. marmotae*, *Escherichia* clades, *E. fergusonii*, *E. coli*, *Shigella* or unspecified. *E. coli* genomes were identified by the ClermonTyper tool and in silico PCR. Plasmid incompatibility groups were determined by PlasmidFinder and ARGs by the Diamond tool using both the AMRFinder and ResFinderFG databases [minimum 80% nucleotide identity and/or 80% coverage]. In order to reduce selection bias of the strains in the database, the proportions of ARGs were normalized within each phylogroup. The different associations were studied with R.

**Results:** We identified 70,307 *E. coli* genomes that carried 311,348 antibiotic resistance genes: 382 genes sharing 100% identity with known genes (n = 164,534) and 328 genes for which variants of known genes were identified (n = 146,814). *bla TEM-1* was the most recovered gene (n = 16,766). We observed limited beta-lactamase diversity with only 22 different families.

However, we have identified a gene encoding a class A beta-lactamase from *Bacteroides* in a strain isolated in Germany. In addition, we observed the frequent presence of ARGs conferring resistance to antibiotics used in Gram-positive bacterial infections: rifampin (*arr*) and macrolide-lincosamines (*lnu, mef, mphA, erm, vga* and *msr*). Finally, we observed associations between ARGs as well as correlations between ARGs and plasmid incompatibility groups.

**Conclusions:** Using a substantial set of *E. coli* genomes, we could describe the acquired resistome of *E. coli*. While the diversity of acquired beta-lactamases – encoding genes was low, we could observe the frequent presence of ARGs conferring resistance to antibiotics not primarily targeting *E. coli*, reflecting the selective pressure exerted on *E. coli* in the gut.

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Abstract 1563

Risk factors for readmission among OPAT patients in the Netherlands

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Background: In the Netherlands, home treatment with intravenous antimicrobial therapy is a relatively new concept. Although several studies have shown that outpatient parenteral antimicrobial therapy (OPAT) can be administered safely, people receiving antimicrobials at home remain at risk for adverse events. The Infectious Disease Society of America (IDSA) guidelines recommend weekly follow-up of all OPAT patients, to monitor and reduce adverse events. The aim of our retrospective study is to determine rates of OPAT-related complications and to identify risk factors for readmission in patients discharged with OPAT.

Materials/methods: Electronic patient records from all patients, age > 18 years and discharged with OPAT during the period of 2016-2018 were included. Complications consisted of antibiotic-related adverse drug events (ADE) or catheter-related (infection, thrombosis, mechanical). Multivariate analysis was performed to identify demographic risk factors for readmission.

Results: A total of 247 patients were included in the analysis; mean age was 60 years. Most common reason for OPAT was bone and joint infections (17%). Penicillins (40%), cephalosporins (28%) and vancomycin (13%) were the most commonly prescribed antimicrobials. A total of 37 patients (15%) were discharged with aminoglycosides or vancomycin. The overall complication rate was 16%. Forty-one percent of readmission was OPAT-related (ADE, catheter- or mechanical complications). The overall readmission rate was 10%, respectively. Among the patients receiving aminoglycosides or vancomycin, 51% (19/37) received weekly therapeutic drug monitoring (TDM). The readmission rate in this group was 32%. Receiving aminoglycosides or vancomycin was found to be an independent predictor of readmission (p<0.05, OR 5.7; CI, 2.46-13.78). Age, gender, indication and discharge to skilled nursing facility were not found predictive for readmission in multivariate analysis.

Conclusions: OPAT patients receiving aminoglycosides or vancomycin have a higher risk of readmission, compared to the general OPAT population. Further research needs focus on the prevention of readmission by performance of weekly TDM and monitoring according to IDSA guidelines.

Table 1. Complications and readmission rate in patients discharged with OPAT from 2016 until 2018 at the VU Medical Center.

<table>
<thead>
<tr>
<th>Complications</th>
<th>Total n=247</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter-related</td>
<td>22 (55%)</td>
</tr>
<tr>
<td>Adverse drug events (ADE)</td>
<td>15 (38%)</td>
</tr>
<tr>
<td>Other (not-OPAT related)</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Readmission</td>
<td>25 (10%)</td>
</tr>
</tbody>
</table>

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Abstract 1564

**Bordetella holmesii in suspected cough: a frequent pathogen?**
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**Background:** *Bordetella holmesii* is responsible for bacteremia in asplenic or sickle cell patients. *B holmesii* can also be found in nasopharyngeal samples of patients with a symptomatology compatible with whooping cough. Diagnostic PCR kits typically target IS1001 and IS481, which does not distinguish *B. pertussis* from *B. holmesii*. This lack of distinction leads to biases in vaccine efficacy analyzes, as the vaccine does not protect against *B. holmesii*. We investigated the frequency of detection of *B. holmesii* from March to August 2019, in outpatients (93%) and hospitalized patients (7%), following the implementation of PCR assays targeting IS481 and IS1001 but also hIS1001, which allows distinction between *B. holmesii* and *B. pertussis*.

**Materials/methods:** Automated DNA extraction from nasopharyngeal samples was performed on the Janus Chemagic 360 from 1 mL of sample with an elution volume of 100 μL. Automated amplification was performed using a CFX 96 ™ with the Viasure Bordetella kit. The absence of *B. pertussis* DNA in the 10 samples was controlled by the National Reference Center of whooping cough.

**Results:** Of the 7,161 nasopharyngeal samples analyzed, we detected *B. holmesii* in 10 samples, (0.14%), *B. pertussis* in 819 (11.4%) and *B. parapertussis* in 34 (0.47%). No co-infection was identified. The age of patients infected with *B. holmesii* was 24.7 years, whereas mean age was 27.5 and 14.9 years for *B. pertussis* and *B. parapertussis*, respectively. Cases were evenly distributed over time. The geographical origin of the *B. holmesii* cases was Paris, Ile de France outside Paris, South East, Aquitaine, Loire Valley and Great East.

**Conclusions:** *B. holmesii* was rarely found in the population studied, and represented only 2% of *Bordetella* infections among adults and adolescents, consistent with recent reports from Spain, Switzerland, Australia and Japan.

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Abstract 1566

A mock-outbreak of carbapenem-resistant *Klebsiella pneumoniae*: using whole genome sequencing to correlate clinical and environmental samples and provide clues to improve infection control in real-time

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Background: ONEIDA is a Portuguese consortium of research institutions aiming to collaborate with hospitals to integrate bacterial real-time genotyping based on whole genome sequencing (WGS) to support infection control.

In Portugal, the incidence of nosocomial infections due to carbapenem-resistant *Klebsiella pneumoniae* (CRKP) is increasing exponentially.

We conducted a pilot study to simulate the investigation of a CRKP outbreak in a Portuguese hospital with two main goals: to test the capacity to obtain and interpret WGS data in a short period of time; to evaluate the relevance of concomitant analysis of hospital environmental samples to unveil potential routes of transmission.

Materials/methods: Ten CRKP clinical strains routinely isolated in the hospital microbiology laboratory were provided to simulate an outbreak situation. In parallel, 40 environmental samples (from sinks and sink drains) were obtained from the wards where the infected patients had stayed.

Environmental samples were plated in selective media and pure cultures suggestive of CRKP were isolated. DNA was extracted from clinical and environmental isolates and sequenced (Illumina NextSeq). Genomes were assembled using INNUca v3.1. MLST, cgMLST and antimicrobial resistance were determined using Pathogenwatch.

Results: The first conclusions were obtained within 48 hours: eight clinical samples were confirmed to be CRKP; the other two were *K. aerogenes*. The eight CRKP were of ST13 (n=6, all harboring *bla*<sub>KPC-3</sub>), ST14 (n=1, *bla*<sub>OXA-181</sub>) and ST111 (n=1, *bla*<sub>OXA-181</sub>).*

Results regarding the 40 environmental samples were obtained within six days: half of the samples yielded colonies compatible with CRKP. By WGS, eight were confirmed to be CRKP: five were ST13, one was ST117 and two were ST323. All harbored the *bla*<sub>KPC-3</sub> gene. Environmental CRKP were isolated mostly from sink drains (n=6). Importantly, ten out of the 11 clinical and environmental ST13 CRKP clustered closely together by cgMLST differing from each other in 0-19 alleles (out of 1927 core genes).

Conclusions: This pilot study demonstrated the ability of ONEIDA academic researchers and health care professionals to work closely together to investigate an outbreak in real time. The results further indicate that concomitant environmental sampling is informative to determine transmission routes allowing for rapid implementation of targeted infection control measures.

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Transcriptome analysis of pneumococci isolated from meningitis patient’s cerebrospinal fluid identifies multiple genes important for pathogenesis, including a novel operon of unknown function

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Background: Pneumococcal meningitis (PM) remains a significant cause of mortality and long-term morbidity, despite antibiotics and corticosteroids. We sequenced the S. pneumoniae transcriptome in patient CSF during PM, to investigate which highly expressed genes are implicated in damaging inflammatory responses.

Materials/methods: CSF from adults with PM was collected prior to antibiotics and stored at -80ºC in PAXgene®. Total RNA was isolated and sequenced after ribodepletion on the Illumina Nextseq platform. Transcripts were mapped against multiple S. pneumoniae genomes, normalised and quantified. The clinical transcriptome was analysed against infection-relevant conditions in the in-vitro D39 transcription model PneumoExpress. Gene-deletion mutant bacteria were generated by targeting selected genes that were highly expressed during PM in a serotype 1 (ST5316) S. pneumoniae meningitis isolate. The mutant phenotypes were investigated using in-vitro models of neutrophil phagocytosis, growth in human CSF (hCSF), and in a murine model of PM.

Results: CSF transcriptomes were available for 11 adults with PM (median age 32 years, 60% male, 70% HIV-1 co-infected, 10/11 non-survivors, median bacterial load 1.6x10⁷ copies/ml CSF (IQR 4.1x10⁶ – 7.0x10⁷)). Transcripts mapping was optimal against Serotype 1 strains (gamPN10373, P1031). Genes with very high expression included multiple genes encoding proteins involved in avoidance of opsonophagocytic killing (BgaA, PsaA, PspC, CiaRH, NanA, ply, pepO, Pbp1A, CbpA) as well as several genes with unknown function. Highly upregulated genes were clustered and tested against a set of in-vitro conditions mimicking different infection models. Clinically expressed genes most closely correlated with S. pneumoniae D39 gene expression in the presence of A549 epithelial cells. Gene deletion mutants were constructed in two highly upregulated genes not previously described to be involved in PM, bgaA (encodes a betagalactosidase) and the operon SP_1800-5 (no previous published data). Neither mutant strain grew in ex-vivo human CSF, opsonophagocytic killing of both mutants was enhanced compared to WT bacteria, murine data pending.

Conclusions: S.pneumoniae expresses multiple virulence proteins in the CNS compartment during meningitis. Expression of an operon with previously unknown function implies that S.pneumoniae may invoke meningitis-specific responses in CSF. Further investigation of the meningitis-specific bacterial response may present novel therapeutic targets for this devastating disease.

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Abstract 1569

Effectiveness of chlorhexidine-impregnated dressing and a bundle of interventions for prevention of central line-associated bloodstream infections
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Background: The aim of this study was to assess the effectiveness of chlorhexidine-impregnated dressing and bundle practice to reduce the rate of central line associated bloodstream infections (CLABSIs).

Materials/methods: We performed a bundle of interventions to reduce the CLABSIs by the year 2012. As one component of the bundle, we started using the chlorhexidine impregnated catheter dressing. We used a form describing how to apply central venous catheter for the practicing physicians and nurses, and we organized several information meetings. Then we have compared the rate of CLABSI before and after the intervention.

Results: In total 76 CLABSI events were detected between January 1, 2011 and June 31, 2019. Twenty-six cases were detected before the intervention period which was between January 1 2011 and December 31 2011, and 50 cases were detected after the intervention period in seven and a half years (January 1, 2012 and June 31, 2019). Following interventions, the annual CLABSI rate was 2.60/1000 catheter days in pre-intervention period and 0.49/1000 catheter days (p=0.037) in post-intervention period. Additionally, the CLABSI rate among hematology-oncology inpatients decreased from 3.39 to 0.76 (p=0.010) in the same term.

Conclusions: The use of chlorhexidine impregnated dressing and bundle form decreased the rate of CLABSIs significantly. This protocol became the standard of care in our hospital.

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Abstract 1571

**Effect of hybrid organo-inorganic sol-gel coating loaded with antifungals on Candida strains**

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Abstract third-party references: Funded by a grant from the Mutua Madrileña Foundation

**Background:** *Candida albicans* and *C. parapsilosis* are the major etiological agents of fungal prosthetic joint infections (PJIs). Although infrequent, these infections are difficult to diagnose and treat and display high recurrence rates. Here we evaluate two sol-gel coatings loaded with fluconazole and anidulafungin in order to treat fungal biofilms formed during PJIs.

**Materials/methods:** A hybrid organo-inorganic sol-gel coating was fabricated from a mixture of two organopolysiloxanes: 3-methacryloxypropyltrimethoxysilane and tetramethoxysilane in a molar ratio of 1:2, and the addition of tris (trimethylsilyl) phosphite in a molar ratio of 52:1 (organopolysiloxanes:phosphorus compound). Control coatings without additions of antifungal (P2) and three coatings loaded with three saturation percentages [50, 75 and 100%] of anidulafungin (A) or fluconazole (F) were used.

Biofilm formation of *C. albicans* ATCC 10231 (Cal ATCC) and *C. parapsilosis* ATCC 22019 (Cpar ATCC) was induced in a 96-well plate using 0.5 McFarland of yeasts in RPMI 1640 + 2% glucose for 48 h. After incubation, medium was renewed and the lid of the plate was replaced by a MBEC™ biofilm Incubator lid whose pegs had been coated a day before by dipping it in wells filled with 200 µL of each treatment, followed by incubation at 37 °C for 48 h. Biofilm viability was determined by adding 10 µl of Alamar Blue per well and measuring the fluorescence after 3 h. Experiments were performed in triplicate. Comparisons of the viability percentage were performed by using t-Student test with a level of statistical significance of 0.05.

**Results:** The presence of P2 was sufficient to produce a significant decrease (between 10-15%) of *C. albicans* ATCC 10231 biofilms, while the addition of antifungal contributed slightly to this effect. P2 alone did not affect biofilm viability of *C. parapsilosis* ATCC 22019 and the presence of antifungal decreased viability by up to 99% in the case of fluconazole.

![Graph A](image1.png) **Figure 1.** Biofilm viability after treatment with fluconazole-loaded (F50, F75, F100) (A) or anidulafungin-loaded (A50, A75, A100) (B) sol-gels. *P<0.05.*

**Conclusions:** The sol-gel coating loaded with antifungals is able to reduce fungal biofilm viability, being a promising tool for locally treating *Candida* PJI.

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Abstract 1573

Prevalence and outcome of ampicillin-susceptible but penicillin-resistant Enterococcus faecalis bacteraemia: a multi-centre retrospective study

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Background: Ampicillin-susceptible but penicillin-resistant Enterococcus faecalis (PRASEF) strains have been recently related to higher mortality in enterococcal bacteremia. The primary purpose of this study was to assess the prevalence and outcome of PRASEF bacteremia.

Materials/methods: This observational, retrospective, multicenter study was conducted between January 2010 and July 2019 in two Italian and one Spanish hospital. All hospitalized patients with monomicrobial bacteremia caused by ampicillin-susceptible E. faecalis were enrolled. Penicillin-susceptibility was defined based on CLSI criteria. Primary endpoint was clinical failure, defined as composite outcome consisting of a) modification of antibiotic therapy due to lack of efficacy, b) relapse, endocarditis or mortality within 90 days from the index blood culture.

Results: Study population consisted of 204 patients: median age was 73 years (IQR 60-81), 69% of the patients were male and median Charlson comorbidity index was 10 (IQR 10-12). Main bacteremia sources were urinary tract (32%), primary (29%), and gastro-intestinal tract (18%). PRASEF were observed in 28 (14%) cases. There were no differences in terms of demographics, source and severity of bacteremia among PRASEF and non-PRASEF groups. Median (IQR) length of hospitalization was significantly longer [18 (9-31) vs 28 (13-45), p 0.02] in PRASEF vs. non-PRASEF groups. Clinical failure occurred in 61% and 37% of patients in the two groups (p 0.033), respectively. Mortality at 90 days was also significantly higher in the PRASEF population (46% vs 26%, p 0.004). No differences were found among the other elements of composite outcome. Multivariate logistic regression analysis adjusted for Charlson comorbidity index, diabetes, sepsis or septic shock, isolation of PRASEF, immunosuppression, source of bacteremia, showed that isolation of PRASEF [OR 2.46 (95% CI 1.04-5.81) p 0.04], Charlson comorbidity index [OR 1.143 (95% CI 1.05-1.23) p 0.001], and sepsis or septic shock [OR 2.84 (95% CI 1.32-6.09) p 0.007] were independent risk factors for clinical failure.

Conclusions: Our study confirms the unfavorable outcome of bacteremia due to PRASEF strains and emphasizes the need for a timely evaluation of minimum Inhibitory concentrations [MICs] for penicillin and ampicillin. Further studies are needed in order to assess ad hoc therapeutic regimens for this peculiar resistance phenotype.

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Abstract 1574

**Nontoxicogenic Clostridioides difficile strains against C. difficile colonisation: an experimental study**

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**Background:** Nontoxicogenic *Clostridioides difficile* strains (NTCD) are non-pathogenic and cannot acquire the toxin A and B genes. Their role in preventing *C. difficile* recurrence was demonstrated among hospitalized patients (Gerding et al., JAMA 313(17):1719-1727).

In a previous study we described a high *C. difficile* intestinal colonization rate of preterm neonates, mostly due to two NTCD. We hypothesized that these strains could be protective against *C. difficile* colonization and conducted an *in vivo* experiment in a hamster caecitis model to determine their potential protective role.

**Materials/methods:** 40 hamsters were treated by clindamycin to induce an intestinal dysbiosis (D-5). They were divided into 5 groups: 1 positive control group (n=8, A) was infected only by a toxigenic strain (PCR-ribotype 027), 2 groups (n=7, B and C) were administered only one NTCD each, and 2 groups (n=9, D and E) were administered one NTCD each (D-3), followed by the 027 strain (D0). Animals were daily monitored for 19 days (clinical activity score and weight). Stool colonization was determined from D-1 until death or sacrifice. After sacrifice (if euthanasia criteria were met or at D19), caeca were collected for histological analysis.

**Results:** All animals (8/8) in group A died within 2 days. The survival rate was significantly increased in groups D (4/9 deaths, p=0.029) and E (1/9 death, p=0.0004). The mean colonization rate of the toxigenic strain in the group A was 1.6x10⁷ CFU/g of stool, and was equivalent in the other groups. At D2, the colonization rate of NTCD in groups B, C, D and E was 2.3x10⁷, 2.4x10⁷, 1.5x10⁸ and 6.2x10⁷, respectively. In the group D, the toxigenic strain was steadily detectable at a lower rate in 4 animals [10⁶-10⁸ CFU/g], whereas in the group E, only 2 animals were colonized and only at D2. Histological analysis of the caeca revealed that co-infected animals with no clinical signs had no tissular alterations.

**Conclusions:** Both NTCD provide a potential protection against *C. difficile* colonisation. *In vitro* studies and genome analysis are ongoing to try to elucidate the protective mechanisms.

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Abstract 1576

Ceftolozane/tazobactam for multidrug-resistant Pseudomonas aeruginosa in a swine model of severe pneumonia

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Abstract third-party references: BITRECS, IDIBAPS, Barcelona, Spain, CIBERES, Madrid, Spain, Merck & Co, Kenilworth, NJ, USA

Background: Nosocomial pneumonia is one of the most common hospital-acquired infections, associated with high morbidity and mortality. Gram-negative pathogens, particularly Pseudomonas aeruginosa, cause life-threatening infections specifically in hospital settings. Ceftolozane/tazobactam (C/T) is a novel antibiotic with activity against multidrug resistant (MDR) P. aeruginosa but still not fully characterized against other first-line antibiotics for nosocomial pneumonia.

Materials/methods: Twenty-one pigs (32.9±1.7 kg) were anesthetized and mechanically ventilated up to 76h. Severe pneumonia was developed by intra-bronchial inoculation of a clinical P. aeruginosa, intermediate to piperacillin/tazobactam (TZP) but susceptible to C/T. Following clinical pneumonia diagnosis, animals were randomly assigned into three groups: placebo (control), 50/25 mg/kg C/T and 200/25 mg/kg TZP. Antibiotic doses had previously been humanized. Ceftriaxone was administered to avert endogenous colonization. Inflammatory markers were measured throughout the study. P. aeruginosa was cultured in tracheal secretions and bronchoalveolar lavage (BAL) fluid and development of antibiotic resistance compared among groups. Upon autopsy, P. aeruginosa was cultured in lungs and histopathology injury scored.

Results: Development of pneumonia and treatment substantially affected systemic cytokines. In particular, IL-1β was significantly downregulated by C/T and returned to baseline levels after 48h of treatment, in comparison with control and TZP animals (p=0.031). Bacterial burden in tracheal secretions and BAL fluids varied among study groups (p<0.001) and times of assessments (p<0.001) [Figure 1A-B]. Specifically, C/T-treated animals achieved the greater eradication in both matrices. In contrast, P. aeruginosa burden in lung tissue was 5.30[4.00-6.30], 4.04[3.64-4.51], and 4.04[3.05-4.88] CFU/g in the control, C/T, and TZP groups, respectively (p=0.299), without histopathological differences (p=0.556) [Figure 1C-D]. An increase in resistance to TZP was found in 3 animals.

Conclusions: In a swine model of MDR P. aeruginosa severe pneumonia, C/T decreased respiratory secretions’ bacterial burden, while averting development of resistance and possibly reducing systemic inflammation. Yet, after only 2 days of treatment, P. aeruginosa tissue concentrations were moderately affected.

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Efficacy of beta-lactam/beta-lactamase inhibitors to treat extended-spectrum beta-lactamase-producing Enterobacteriaceae bacteraemia secondary to urinary tract infection in kidney transplant recipients


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Abstract third-party references: This work was supported by Plan Nacional de I+D+i 2013-2016 and Instituto de Salud Carlos III, Subdirección General de Redes y Centros de Investigación Cooperativa, Ministerio de Ciencia, Innovación y Universidades, Spanish Network for Research in Infectious Diseases [REIPI R016/0016/0008; R016/0016/0001, R016/0016/0002, R016/0016/00010] - co-financed by European Development Regional Fund “A way to achieve Europe”, Operative program Intelligent Growth 2014-2020, ESCMID Study Group for Infections in Compromised Hosts [ESGICH grant to J.M.A.]; Sociedad Andaluza de Trasplante de Órgano Sólido [SATOT grant to L.M.M.]; ESCMID Study Group for Bloodstream Infections and Sepsis [ESGBIS]; and ESCMID Study Group for Antimicrobial Resistance Surveillance [ESGARS].
Background: Urinary tract infection (UTI) is the most common source of bloodstream infection (BSI) in kidney transplant recipients (KTR). Episodes caused by extended-spectrum β-lactamase-producing Enterobacterales (ESBL-E) are particularly frequent in these patients. We sought to evaluate risk factors for therapeutic failure and examine the impact of regimens based on carbapenems versus β-lactam/β-lactamase inhibitors (BLBLI) in a large multinational cohort of KTR diagnosed with BSI secondary to UTI.

Materials/methods: We retrospectively evaluated 306 KTR with BSI secondary to UTI caused by ESBL-E, admitted to 30 centers from January 2014 to October 2016 (INCREMENT-SOT, ClinicalTrials.gov NCT02852902). Therapeutic failure [lack of cure or clinical improvement and/or death from any cause] at days 7 and 30 from BSI onset were primary and secondary study outcomes, respectively. Univariate and multivariate logistic regression models were applied to identify factors predicting therapeutic failure. A propensity score (PS) was used to control the therapy indication bias.

Results: Carbapenem monotherapy (68.6%, primarily meropenem) was the most frequent active therapy used, followed by BLBLI monotherapy (10.8%, mostly piperacillin-tazobactam). Therapeutic failure at day 7 was 9.0% (13.8% at day 30) with carbapenems and 3.0% (9.1% at day 30) with BLBLI. Mortality at days 7 and 30 was 1% and 3%, respectively. Hospital-acquired BSI [adjusted OR (aOR): 3.89; 95% CI: 1.41-10.76] and Pitt bacteremia score at BSI onset [aOR: 1.53; 95%CI: 1.24-1.88] were independently associated with therapeutic failure at day 7. Age-adjusted Charlson Index [aOR: 1.25; 95%CI: 1.05-1.48], Pitt score [aOR: 1.72; 95%CI: 1.35-2.17] and lymphocyte count ≤500 cells/μL at presentation [aOR: 3.16; 95%CI: 1.42-7.06] were independently associated with therapeutic failure at day 30. In PS-adjusted analysis, BLBLI could not be found to be associated with increased risk of failure at day 7 or 30 (PS-adjusted OR: 0.79; 95%CI: 0.23-2.64 and PS-adjusted OR: 0.64; 95%CI: 0.23-1.77, respectively).

Conclusions: Significant differences in the risk of therapeutic failure at 7 and 30 days, according to the use of active therapy with BLBLI versus carbapenem-containing regimens, could not be identified in this large multinational cohort of KTR diagnosed with BSI secondary to UTI due to ESBL-E.

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Abstract 1578

Aspirin reduces cardiovascular events in patients with pneumonia: a prior events rate ratio analysis in a large primary care database

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Abstract third-party references: NIHR, NIHR HPRU

Background: Ischaemic stroke and myocardial infarction are common after pneumonia, and are associated with mortality. Aspirin may attenuate this risk, leading to significant reduction in post-pneumonia complications. Limited evidence from secondary care suggests that aspirin may have a beneficial effect, but studies so far have been small, and none have focussed on primary care.

Materials/methods: A prior event rate ratio (PERR) analysis, performed in the Clinical Practice Research Datalink (CPRD), a large UK primary care database, from inception until January 2019, linked to Office for National Statistics (ONS) mortality data. All patients over 50 with a coded diagnosis of pneumonia and adequate data quality, with follow-up data for at least one year after pneumonia, were included. The study period covered from one year before to 6 months after the pneumonia date. The PERR approach allows for control of measured and unmeasured confounding, as the ratio of events prior to and after a given event is considered, and each participant is a self-control. Diabetes, smoking, hypertension, previous cardiac and cerebral ischaemic events, age, gender, and socioeconomic deprivation were included as covariates. Time-to-event analysis was performed. The primary outcome was the combined outcome of ischaemic stroke and myocardial infarction. Secondary outcomes were ischaemic stroke and myocardial infarction individually.

Results: 48,260 patients were included in the final analysis. 8,099 of these were aspirin users, with 35,197 non-aspirin users, and 4,964 patients censored for intermittent aspirin use. Despite being older and more comorbid, aspirin users had a reduced risk of the primary outcome (adjusted hazard ratio, HR 0.68; 95% confidence interval 0.55 - 0.83) in the PERR analysis. For both secondary outcomes, aspirin use was also associated with a reduced risk (HR 0.52 (0.34 – 0.77) and 0.7 1 (0.55 – 0.94) for myocardial infarction and stroke respectively).

Conclusions: Aspirin use is strongly associated with reduced ischaemic events after pneumonia, in a primary care setting. Further work should explore the prophylactic benefits of aspirin prescription in pneumonia, in a prospective, randomised fashion.

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Abstract 1580

Optimising the use of triazole therapeutic drug monitoring using quality improvement methodology

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Background: Posaconazole and voriconazole are triazole antifungals indicated for prophylaxis and treatment of mycotic infections. Therapeutic drug monitoring (TDM) and individualised dosing are recommended to ensure clinical efficacy and prevent toxicity. Local audit data revealed 38% (n=8) of haematology inpatients administered triazoles received TDM at our tertiary London hospital. We undertook a Quality Improvement (QI) project to optimise triazole TDM.

Materials/methods: Haematology inpatients administered posaconazole or voriconazole were identified retrospectively from pharmacy dispensing records to calculate baseline TDM compliance over 16 weeks. Compliance was calculated by dividing the number of patients who received TDM by the number of patients eligible for TDM based on local guidelines: 1) 3-7 days post-treatment initiation, 2) repeated week 2, and 3) repeated every 4 weeks. Therapeutic ranges were taken from ESCMID guidelines (Ullman et al. Clin Microbiol Infect; 2018).

QI methodology was used to improve compliance with Trust guidelines. This included the development of a driver diagram and questionnaire to identify barriers to conducting TDM appropriately. Interventions were designed to prompt TDM when indicated.

- Intervention 1 (week 17): a pharmacist prospectively identified patients on triazoles from the electronic prescribing system (Cerner PowerChart) for discussion on a joint infection-haematology ward round. Additionally, a text reminder was built into Cerner.
- Intervention 2 (week 27): patients requiring TDM were sent directly to the haematology consultant.

Results: 111 encounters (n=38 patients) were prospectively reviewed over the course of 16 weeks. 51 levels were taken out of 87 recommended (59%). Subtherapeutic levels (n=13) and potentially toxic levels (n=4) were managed by dose adjustment (n=10). Remaining deviations were managed with repeat levels or alternative treatment.

Following the first intervention, compliance remained above the mean, demonstrating a shift (figure 1). Mean compliance was recalculated at almost three-times baseline (24% to 65%).

Conclusions: This QI project has improved appropriate use of TDM. Future work will focus on expanding to outpatient areas and other specialties such as respiratory medicine. Pharmacist-led TDM clinics incorporating other tests (e.g. liver function) could be used to ensure outpatients are effectively monitored and doses optimised.

Figure 1. Week 21 excluded (no referrals due to Bank Holiday).

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Abstract 1581

The difficulties of differentiating central nervous system infection from disease relapse in a cohort of adult patients with haematological malignancy: 10 years’ experience from a central London hospital

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Background: CNS infections occur in up to 15% of patients with haematological malignancy undergoing allogenic haemopoetic stem cell transplant (HSCT). Delays to identification of causative pathogens may contribute to worse outcomes, however diagnostic samples can be difficult to obtain. We sought to describe MRI head (MRH) features seen in a cohort of adult patients with haematological malignancy in who CNS infection was suspected.

Materials/methods: We undertook a retrospective case review of patients with haematological malignancy undergoing MRH for suspected CNS infection between 2007-2017. Cases were identified through electronic MRH database using a text search. MRI images were classified according to anatomical disease, reports divided into either high or low/equivocal suspicion of CNS infection by two radiologists (unaware of the final diagnosis). Laboratory and clinical records were subsequently searched for definitive diagnostic data.

Results: 5887 MRH scans were identified, 1855 in patients with haematological malignancy, of which 147 were for suspected CNS infection. After duplicate scan removal, 110 patients were included. Median age 52 years (13-81), 51% were female, 81% were inpatients. 50% were <12 months post bone marrow transplant (BMT) including allo-HSCT. Leukaemia (46%) and lymphoma (44%) predominated. 20/20 (100%) of extra-dural lesions were caused by disease relapse, other anatomical patterns were equally split between infection and relapse. Of 31 patients with MRH reports of high clinical suspicion of infection on MRH, 24/31 (77%) had proven infection, the remainder had tissue diagnosis of disease relapse or no cause found. Of those with low/equivocal suspicion of infection on MRH, seven had subsequently proven infection. CNS infection was diagnosed in 30 (26%) patients, disease relapse in 15 (14%) and alternative diagnosis/no cause found in 65 (59%). Of patients with proven CNS infection, viruses were identified in 15/30 (50%) (CMV 7/15, HSV 1, JC 3 and HHV6 4), bacteria and fungi were rare (6). Patients with CNS infection more frequently presented within 12 months of BMT (50%) than those with disease relapse (20%).

Conclusions: Reported imaging finding on MRH are relatively non-specific in patients with subsequently proven CNS infection. Multi-centre prospective data are required to confirm these findings and inform treatment guidelines.

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Abstract 1583

**Evaluation of the filmarray GI panel in the microbiological diagnosis and management of the patient with infectious gastroenteritis**

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**Background:** To evaluate the usefulness of a molecular diagnostic panel for the diagnosis and management of patients with gastrointestinal infections.

**Materials/methods:** Retrospective observational study of molecular panels for syndromic diagnosis of infectious gastroenteritis (GEI) Filmarray™ GI Panel, Biofire diagnostics (Biomérieux) conducted from January to October 2019. The results of the traditional microbiological techniques and variables obtained from the clinical history were also reviewed.

**Results:** RT-CRP was performed on 54 non-shaped feces, one sample per patient. The age range was from 10 months to 92 years with a median of 33.30 years. Thirty of them were men and 24 women. Cultures were performed in 94% of the cases, viral antigens in 50%, parasites in 26% and *Clostridioides difficile* toxins in 48%. The indications for requesting the microarray were the severity of the condition (invasive diarrhea and/or dehydration) in 50% of the cases, base immunosuppression in 30%, travel history in the previous week in 7% and others in 13%.

The panel was negative in 57% of cases, detected *Campylobacter sp* in 21%, *C. difficile* toxin in 8%, *Salmonella sp* 4% and other enteropathogens (8%). Seven coinfections were detected by the molecular panel (13%) and none by traditional techniques.

There was an agreement between the results of the microarray and traditional microbiological methods in 84% of cases (kappa 0.687).

**Table 1: Distribution of positive tests by classical techniques and by CRP**

<table>
<thead>
<tr>
<th>Tests</th>
<th>Number of traditional tests*</th>
<th>Positive traditional test n (%)</th>
<th>Positive CRP tests n (%)</th>
<th>n total=54</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture</td>
<td>51</td>
<td>13 (25%)</td>
<td>21 (39%)</td>
<td></td>
</tr>
<tr>
<td>Viral antigens</td>
<td>27</td>
<td>0 (0%)</td>
<td>3 (6%)</td>
<td></td>
</tr>
<tr>
<td>Parasites</td>
<td>15</td>
<td>0 (0%)</td>
<td>1 (2%)</td>
<td></td>
</tr>
<tr>
<td><em>C. difficile</em> toxin</td>
<td>25</td>
<td>3 (12%)</td>
<td>7 (13%)</td>
<td></td>
</tr>
</tbody>
</table>

* CRP was performed in all cases (54) but traditional tests only when expressly requested under clinical criteria (the table reflects the total of tests of each type performed)

There was a therapeutic modification in 63% of the cases in which the panel was requested due to the severity of the diarrhea, in 54% of the cases in which the CRP was performed due to travel history, in 40% when the cause was immunosuppression and when the cause was unknown, no therapeutic change was assumed.

The filmarray results had an average delay of 1 hour vs an average of the traditional techniques of 26 hours (range: 2-72).

**Conclusions:** The agreement between traditional techniques and CRP is substantial (kappa 0.6) although it is far from perfect. The average time saved by CRP, its greater range of potential diagnoses per test and the possibility of detecting coinfections can allow effective and faster clinical decisions.

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Abstract 1587

The pharmacodynamics of omadacycline against Escherichia coli and Acinetobacter baumannii studied in an in vitro pharmacokinetic model of infection

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Background: Omadacycline (OMC) is a broad spectrum aminomethylcycline tetracycline antimicrobial. OMC is approved for clinical use by the US FDA in community-acquired bacterial pneumonia and skin and skin structure infections as intravenous and oral formulations. The pharmacodynamics (PD) of OMC have been extensively studied against Gram-positive pathogens but less information is available for Gram-negatives. Here we describe the pre-clinical PD of OMC against E. coli and A. baumannii.

Materials/methods: An in vitro dilutional single compartment PK model was used. Exposure ranging experiments - freedrug Area Under Curve to MIC ratio (fAUC/MIC) 0-1200 were performed. Five strains of E. coli and 5 strains of A. baumannii were used. In addition, time-kill curves were conducted with a single strain of either E. coli or A. baumannii over a concentration range 0-80 mg/L OMC. 2% oxyrase was added to broth to stabilise OMC. The primary endpoint was - log change in viable count at 24h.

Results: E. coli OMC MICs ranged from 0.25-2 mg/L and A. baumannii OMC MICs ranged from 0.5-1 mg/L. In time-kill experiments with both E. coli and A. baumannii, OMC showed concentration dependant killing up to 80 mg/L: OMC was less bactericidal against A. baumannii than E. coli. The fAUC/MIC for 24h static, -1 log and -2 log reduction in E. coli bacterial load were 22.5±15.9, 38.1±28.3 and 83.6±64.4. For A. baumannii the fAUC/MIC for 24hr static and -1 log drop in bacterial load were 108.1±38.6 and 266.3±27.1. Emergence of resistance was observed with both E. coli and A. baumannii strains. OMC MICs of strains recovered at the end of 24-48h exposure to OMC were increased 2-32 fold.

Conclusions: The size of the OMC fAUC/MIC for static effect against E. coli is in alignment with published in vivo data from a murine thigh infection model. fAUC/MIC targets are higher for A. baumannii than E. coli. These OMC fAUC/MIC targets may be useful for translational modelling of possible OMC doses for therapy of these Gram-negative pathogens.

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Abstract 1591


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**Abstract third-party references:** Malaria Atlas Project [MAP]

**Background:** Monitoring spatiotemporal variation in antimalarial drug efficacy and effectiveness is of importance to understand and sustain the gains in reducing malaria burden globally. Therapeutic efficacy studies (TES) are the gold-standard for measuring drug efficacy and appropriate for characterizing global variations. This study utilizes data from 232 TES comprised of 89,713 individuals to estimate the effectiveness of artemisinin-based and non-artemisinin-based antimalarials in malaria-endemic countries between 1991 and 2019.

**Materials/methods:** Bayesian spatiotemporal models were fitted separately for the artemisinin-based and non-artemisinin-based antimalarial drugs, and used to predict effectiveness at the pixel-level [5km x 5km]. Median and interquartile range (IQR) of the effectiveness are presented.

**Results:** The global effectiveness levels of artemisinin-based antimalarials were high: 87.3% (IQR: 75.4-93.9) in 1994 and 94.6% (IQR: 89.2-97.4) in 2019. However, country-to-country variations exist. In Africa, the Democratic Republic of the Congo, Republic of Congo, Uganda, and parts of the Central African Republic face challenges of relatively low effectiveness. In Asia, effectiveness of these drugs remained >90% for an extended period. However, effectiveness fluctuations were observed from the mid-1990s to 2008/2009 with Cambodia, Malaysia, and Indonesia being the most affected countries. Use of artemisinin-based combination therapies (ACTs) with a competent partner drug and having multiple ACTs as first-line treatment were associated with sustained high levels of effectiveness. High levels of access to healthcare, human resource capacity, education, and proximity to cities were associated with increased effectiveness. Global effectiveness of non-artemisinin drugs remained low over time, 69.9% (IQR:48.5-89.3) in 1994 and 71.6% (IQR: 57.9-91.5) in 2019. These drugs are not effective in several Sub Saharan African countries and Asia but remained effective in Central and South America.

**Conclusions:** This study provides evidence that ACTs are effective for treating uncomplicated *Plasmodium falciparum* malaria. Other antimalarial drugs such as chloroquine and sulphadoxine-pyrimethamine remain useful for *P. falciparum* malaria in only a few locations. Low effectiveness is driven by type of drug, health system performance and climate factors. These results are useful to guide countries’ treatment policies and as critical inputs for malaria prevalence and incidence models utilized to estimate national levels of malaria burden.

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Beyond the contact precaution: what does the surveillance culture tell us about multidrug-resistant microorganisms in critically ill patients? Data of the Public Hospital of São Paulo City, Brazil

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Background: Surveillance cultures (SC) are routinely used to screen multidrug resistant microorganisms (MDR). The purpose of this study was to evaluate the epidemiological and molecular aspects between events of colonization and healthcare-associated infection (HAI) caused by the same MDR in critically ill patients.

Materials/methods: Study was performed in two ICUs (clinical and surgical) of a public tertiary hospital between January 2016 and May 2018. All patients had SC collected for institution of contact precautions in positive cases of MDR. The healthcare associated infections are notified according to CDC criteria. The bacterial identification was performed using mass spectrometry and the minimal inhibitory concentration of antibiotics was determined using the Vitek 2 System. The detection of the carbapenemases, VanA and VanB genes were determined by real time PCR and the genetic relatedness of the strains were characterized by Pulsed-Field Gel Electrophoresis (PFGE) only for available strains at the time.

Results: Thirty six patients colonized by MDR developed HAI by MDR, the mean between MDR colonization and HAI was 2.19 days. The most prevalent HAI was central line-associated bloodstream infections (CLABSI) in clinical ICU and surgical site infection (SSI) in surgical ICU. Twenty eight HAI episodes were caused by the same colonizing bacteria with identical antimicrobial susceptibility profile (ASP) (Table 1), 14 episodes could be analyzed by PFGE and the concordance rate was 100%. Other eight HAI episodes were caused by non-concordant MDR.

Conclusions: MDR colonization prevention measures are essential and must be performed prior to colonization in critically ill patients. The presence of colonization should be valued by the clinician to an appropriate choice of initial empirical therapy and stewardship in critically ill patients.

Table 1: Concordant microorganism distribution between colonization and infection

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Colonized patients</th>
<th>HAI concordant by ASP</th>
<th>HAI concordant by PFGE</th>
<th>PFGE concordant HAI topography</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Klebsiella pneumoniae</em> (KP-KPC)</td>
<td>28</td>
<td>24</td>
<td>10</td>
<td>CLABSI 6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>VAP 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>UTI 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SSI 1</td>
</tr>
<tr>
<td><em>Vancomycin resistant Enterococcus</em> (VRE)</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>CLABSI 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>IE 1</td>
</tr>
<tr>
<td><em>Carbapenem resistant Acinetobacter baumannii</em></td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>CLABSI 1</td>
</tr>
<tr>
<td><em>Carbapenem resistant Pseudomonas aeruginosa</em></td>
<td>1</td>
<td>1</td>
<td>1</td>
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Presenter email address: cely.saad@gmail.com
Abstract 1594

Ceftobiprole compared with vancomycin plus aztreonam in the treatment of acute bacterial skin and skin-structure infections: results of a phase III, randomised, double-blind trial (TARGET)

J. Scott Overcash1, Charles Kim2, Richard Keech3, Ilia Gumenchuk4, Borislav Ninov5, Yaneicy Gonzalez-Rojas6, Michael Waters7, Simeon Simeonov7, Marc Engelhardt5, Mikaël Saulay8, Daniel Ionescu8, Jennifer Smart8, Mark Jones8, Kamal Hamed8

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Abstract third-party references: Supported by Basilea, Submitted on behalf of J. Scott Overcash and co-authors

Background: The development of novel, broad-spectrum antibiotics with efficacy against both Gram-positive and Gram-negative bacteria has the potential to enhance treatment options for acute bacterial skin and skin structure infections (ABSSSI). Ceftobiprole, the active moiety of the prodrug ceftobiprole medocaril, is an advanced-generation cephalosporin with broad in vitro activity against Gram-positive (including methicillin-resistant Staphylococcus aureus) and Gram-negative pathogens, and is approved in many European and several non-European countries for the treatment of pneumonia. The present study (TARGET) evaluated the utility of ceftobiprole in patients with ABSSSIs.

Materials/methods: TARGET was a randomised, double-blind, active-controlled, parallel-group, multicentre, phase 3, non-inferiority study that compared ceftobiprole with vancomycin plus aztreonam (NCT03137123). Main efficacy endpoints were: early clinical response 48–72 hours after therapy initiation ≥20% reduction in primary lesion area, survival, no concomitant antibacterials, and no unplanned ABSSSI surgery; and investigator-assessed clinical success [complete or near complete resolution of baseline signs and symptoms, with no further antibacterial treatment] at the test-of-cure (TOC) visit 15–22 days after randomisation. Non-inferiority was defined as the lower limit of the 95% confidence interval for the difference in success rates [ceftobiprole minus vancomycin/aztreonam] >10%. Safety was also assessed through adverse event and laboratory data collection.

Results: 679 patients were randomised to ceftobiprole (n=335) or vancomycin/aztreonam (n=344), of whom 676 received ≥1 dose of study medication. Median treatment duration was 6.0 and 7.0 days, respectively, with a median duration of 3.0 days for aztreonam in the comparator group. Main efficacy endpoint results are shown in the figure. Documented or presumed microbiological eradication rates at the TOC visit were similar between treatment arms [90.2% vs 86.6%]. The proportion of patients experiencing ≥1 treatment-related adverse events [n [%]: 66 [19.8%] vs 62 [18.1%]) was also similar between treatment arms. Treatment-related serious adverse events were uncommon, reported in only 1 and 2 patients in the ceftobiprole and vancomycin/aztreonam arms, respectively.

Conclusions: TARGET demonstrated that ceftobiprole is non-inferior to vancomycin/aztreonam in the treatment of ABSSSIs, both in terms of early clinical response and investigator-assessed clinical success at the TOC visit. Both treatment arms displayed similar microbiologic success and had similar safety profiles.

Figure: Main efficacy endpoint analyses

Abbreviations: CE, clinically evaluable; CI, confidence interval; ITT, intention-to-treat

*Proportion differences (95% CI) (ceftobiprole minus vancomycin/aztreonam) were computed using the Cochran–Mantel–Haenzel weights method adjusted for geographical region and actual type of ABSSSI.

1Secondary endpoint. The objective for the FDA-defined primary endpoint was based on a non-inferiority assessment of the ITT population only. The EMA-defined primary endpoint was based on a non-inferiority assessment in both the ITT and CE populations.
Routine use of whole genome sequencing for Salmonella Enteritidis surveillance in the Netherlands in 2019

Maaike J.C. Van Den Beld*1, Roan Pijnacker1, Anjo Verbruggen1, Kim Van Der Zwaluw1, Sjoerd Kuiling1, Eelco Franz1

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In the Netherlands, national laboratory surveillance for Salmonella Enteritidis was based on conventional serotyping and Multi Locus Variable Number Tandem Repeat Analysis (MLVA). In January 2019, whole genome sequencing (WGS) was implemented as routine typing method for S. Enteritidis. Here we describe the relation between WGS-based cluster detection and MLVA types, and the presence of genetic and phenotypic β-lactamase resistance in S. Enteritidis isolates from Dutch national surveillance in 2019.

Submitted Salmonella isolates were serotyped using Luminex and conventional methods, minimum inhibitory concentrations (MIC) for antibiotics were determined on a selection of isolates. For those serotyped as S. Enteritidis, MLVA type was determined and WGS was performed using Illumina technology. An in-house pipeline based on SPAdes 3.10.0 was used for quality control, trimming and de novo assembly. Detection of resistance genes was performed using the bacterial analysis pipeline of the Center for Genomic Epidemiology. WGS Clustering was investigated with core genome multi-locus sequence type (cgMLST) using the Enterobase S. enterica cgMLST V2 scheme.

From January until October 2019, 1,171 Salmonella isolates were received, of which 399 S. Enteritidis (35%). A total of 377 isolates were from unique patients, resulting in 349 sequences (93%) of good quality. A β-lactamase gene was detected in 45 S. Enteritidis isolates (13%), in one isolate coding for extended spectrum β-lactamase. For 35 of these isolates the MIC for ampicillin was determined, for which 29 (83%) were phenotypically resistant according to EUCAST breakpoints. Using a threshold of five alleles distance in cgMLST, 43 clusters of ≥ 2 isolates were detected, containing a total of 254 isolates (73%). With MLVA, 60 types were found comprising 23 clusters of ≥ 2 isolates, 312 isolates (89%) were part of these clusters. Using WGS, clusters ranged from 2-36 isolates, and 15 clusters (35%) contained multiple MLVA types ranging from two to five types within the same cluster.

WGS showed a higher discriminatory power than MLVA. This is especially important during outbreak investigation to avoid misclassification of outbreak-related cases. Moreover, WGS allows us to monitor resistance and virulence genes.

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Abstract 1599

High levels of resistance to recommended antimicrobial agents in *Pseudomonas aeruginosa* from patients with bronchiectasis

Roberto Cabrera*, Laia Fernandez Barat1, Nil Vázquez Burgos1, Ruben López-Aladid1, Victoria Alcaraz1, Leticia Bueno1, Rosanel Amaro1, Patricia Elena Oscanos1, Laura Muñoz1, Antoni Torres1

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**Background:** Non-cystic fibrosis bronchiectasis (BE) is a chronic structural lung condition that facilitates chronic colonization by different microorganisms and courses with frequent exacerbations and recurrent infections. One of the main pathogens involved in chronic colonization and acute exacerbations is *Pseudomonas aeruginosa*. When not eradicated during early infection *P. aeruginosa* can accumulate high rates of resistance to the most antipseudomonal agents.

**Materials/methods:** A prospective observational study was carried out in Hospital Clinic. A total of 44 strains of *Pseudomonas aeruginosa* were isolated and characterized from sputum of BE patients. The antimicrobial susceptibility to: Aztreonam, ciprofloxacin, meropenem, imipenem, amikacin, tobramycin, pipertaz, ceftazidime and colistin was performed using the Kirby-Bauer method with the ATCC 27853 strain as a control. Interpretation of results was carried out according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Molecular characterization of each resistance mechanism was screened by PCR, electrophoresis in 2% agarose gels and sequencing.

**Results:** The frequency of *Pseudomonas aeruginosa* resistant isolates was: Aztreonam (68,18%), ciprofloxacin (45,45%), meropenem (31,81%), imipenem (31,81%), amikacin (20,45%), tobramycin (20,45%), pipertaz (11,36%), ceftazidime (11,36%) and colistin (2,27%). The strains showed different antimicrobial profiles: PS (9,09%), MR (6,1,37%), MDR (20,45%) and XDR (9,09%). Mutations in *gyrA*, *gyrB*, *ParC* and *ParE* genes were found in ciprofloxacin resistant *P. aeruginosa* strains. The most frequent mutation in *gyrA* was A33G, in *gyrB* S466F, in *ParC* S87W and in *ParE* D539E. Our study showed that a higher number of mutated genes was related to the increased of MIC in the ORDR. The presence of different β-lactamases was detected: *oxa50* (95,45%), *ges* (90,74%), *imi* (23,8%), *gim* (4,76%) and *sim* (4,76%), in the strains resistant to β-lactams. The *aac(3)*-la, *aac(3)*-lc, *aac(6'')*-Ib and *ant(2'')*-la genes were related to aminoglycoside resistance.

**Conclusions:** the high level of resistance to first-line antimicrobials recommended in BE guidelines and the great diversity of mechanisms of resistance found, threatens the treatment of BE and the eradication of *P. aeruginosa*.

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Abstract 1603

In vitro Activities of ceftazidime-avibactam and comparator agents against Enterobacterales and Pseudomonas aeruginosa from Turkey collected through the ATLAS global surveillance programme 2013-2018

Samantha Pacha1, Meredith Hackel*1, Greg Stone2, Dan Sahm1

1IHMA, Schaumburg, United States, 2Pfizer, Inc., Groton, United States

Background: Avibactam (AVI) is a non-β-lactam, β-lactamase inhibitor that can restore the activity of ceftazidime (CAZ) against organisms that possess Class A, C, and some Class D enzymes. This study examined the in vitro activity of CAZ-AVI and comparators against Enterobacterales and Pseudomonas aeruginosa collected in Turkey through the ATLAS global surveillance program from 2013 to 2018.

Materials/methods: A total of 2,205 non-duplicate, clinically isolated Enterobacterales and 567 P. aeruginosa were collected from six sites in Turkey during 2013-2018. Susceptibility testing was done using broth microdilution according to CLSI guidelines and interpreted using EUCAST 2019 breakpoints. CAZ-AVI was tested with a fixed concentration of 4 mg/L AVI. The presence of genes encoding resistance mechanisms was previously assessed via multiplex PCR, followed by amplification of the full-length genes and sequencing.

Results: Susceptibility data are provided in the table. CAZ-AVI exhibited potent activity against all Enterobacterales (MIC90, 0.5 mg/L; 98.2% susceptible). When MBL-positive isolates were removed from analysis, susceptibility to CAZ-AVI was 100%. CAZ-AVI showed consistently higher % susceptibilities than all comparators against MBL-negative meropenem-nonsusceptible isolates (CRE) and isolates positive for OXA-48. CAZ-AVI also showed good activity against the majority of P. aeruginosa isolates (MIC90, 8 mg/L; 94.2% susceptible).

Conclusions: CAZ-AVI showed potent in vitro activity against Enterobacterales and P. aeruginosa collected in Turkey, including isolates resistant to last-in-line agents.

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<table>
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<tr>
<th>Organism (n)</th>
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<th>%susceptible</th>
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<td>CAZ-AVI (0.5/98.2)</td>
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</table>

*colistin not tested in 2013; colistin tested vs. 16/76 Enterobacterales in 2014-2018
CAZ-AVI, ceftazidime-avibactam, CAZ, ceftazidime, MEM, meropenem, AMK, amikacin; CST, colistin; MBL, metallo-β-lactamase. % susceptible defined using EUCAST 2019 breakpoints

Conclusions: CAZ-AVI showed potent in vitro activity against Enterobacterales and P. aeruginosa collected in Turkey, including isolates resistant to last-in-line agents.

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Abstract 1607

Evaluating prophylactic post cardiac transplantation amphotericin B treatment by simulation

Camille Mane*1, Véronique Duhalde2, Isabelle Labadens2, Olivier Cointault2, Didier Concordet1, Peggy Gandia1,2

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Background: Antifungal treatment is recommended to prevent invasive aspergillosis, a condition which occurs frequently and is associated with a poor prognosis in the first 3 months following cardiac transplantation. Current recommendations do not include a once a week administration of liposomal amphotericin B (L-AmB), despite its favorable safety profile. The objective of the current study was to simulate the efficacy of a once a week administration of L-AmB using a pharmacokinetic-pharmacodynamic (PK-PD) approach.

Materials/methods: Based on the population PK model published by Würthwein et al., 1000 plasma and tissue kinetic profiles were simulated over a 7-day period after administration of a single dose of 7.5 mg / kg of L-AmB as a 1-hour infusion. For each simulated plasma profile, the Area Under the Curve (AUC) for total concentrations over 24 hours was calculated from D1 to D7. These AUCs were compared with L-AmB PK-PD efficacy target (AUC / MIC > 167) to determine the percentage of simulated profiles achieving this target (i.e. probability of target attainment). The theoretical duration of effectiveness was determined using both the simulated tissue kinetic profiles and a concentration higher than the MIC for more than 90% of the profiles.

Results: At D1, more than 90% of the plasma profiles met the PK-PD target for Minimum Inhibitory Concentrations (MICs) ≤ 0.5 mg/L. This percentage dropped to 80.2% when the MIC was increased to 1 mg/L (i.e. Aspergillus breakpoint). At D7 and for a MIC corresponding to the breakpoint, only 3.3% of the plasma profiles achieved the PK-PD target. The treatment efficacy assessed at tissue level does not extend to 7 days regardless of the MICs tested. Indeed, efficacy is theoretically maintained during 3.2 and 1.3 days for MICs of 0.25 to 0.75 mg/L. For MICs ≥ 1 mg/L, less than 90% of the simulated profiles reached tissue concentrations ≥ 1 mg/L.

Conclusions: Regardless of plasma or tissue PK-PD target, our simulations suggest that a once a week administration of L-AmB does not guarantee antifungal efficacy throughout the entire one-week period. These results need to be confirmed in clinical practice.

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Identification of host-specific genetic elements of Campylobacter jejuni in Germany based on whole genome data

Lennard Epping*, Rosario Piro2,3, Marie-Theres Knüver4, Maria Borowiak4, Charlotte Huber1, Andrea Thürmer6, Burkhard Malorny7, Kerstin Stingl7, Angelika Fruth8, Lothar H. Wieler6, Torsten Semmler1

1Robert Koch-Institut, Microbial Genomics, Berlin, Germany, 2Free University Berlin, Department of Mathematics and Computer Science, Berlin, Germany, 3Charité – Universitätsmedizin Berlin, Institute of Medical Genetics and Human, Berlin, Germany, 4Bundesinstitut für Risikobewertung, National Reference Laboratory for Campylobacter, Berlin, Germany, 5Robert Koch-Institut, Advanced Light and Electron Microscopy, Berlin, Germany, 6Robert Koch-Institut, Methodology and Research Infrastructure, Berlin, Germany, 7Bundesinstitut für Risikobewertung, Study Centre for Genome Sequencing and Analysis, Berlin, Germany, 8Robert Koch-Institut, National Reference Centre for Salmonella and other Bacterial Enterics, Wernigerode, Germany

Background: The zoonotic pathogen Campylobacter jejuni is the leading cause of bacterial food-borne infections in humans worldwide. Campylobacter are most commonly transmitted through the consumption of undercooked poultry meat or raw milk products. In silico multi locus sequence typing (MLST) of C. jejuni strains from different sources has revealed association of certain sequence types (STs) with specific hosts or a host-generalism lifestyle. While host restriction of C. jejuni lineages is known, the survival mechanisms allowing them to adapt to gut environments of different hosts have not been completely understood.

Materials/methods: To generate more in-depth knowledge about these mechanisms, 330 C. jejuni strains from different hosts (100 each from human, chicken, cattle and 30 from pig) across Germany were randomly selected, and whole genome sequencing (WGS) was performed. Additionally, 166 isolates from a Canadian study were included to extend the dataset and compare it with international samples. Host-specificity was investigated by a stratified random sampling approach on top of a k-mer based genome-wide association study (GWAS) to increase the accuracy of the identification of host specific determinants.

Results: We discovered that a strong host association can be observed in the core genome as well as in the accessory genome. The identified genetic elements encode for proteins, which play important roles in mobility, energy metabolism and genetic information processing. Although, we could discover a strong recombination barrier between C. jejuni lineages within the same host, identical allelic gene variants could be found amongst those genes.

Conclusions: Our research shows, that host-adaptation in C. jejuni takes place in a wide range of cellular functions within the whole pan-genome. This indicates that the adaptation towards a specific host niche is most likely a long evolutionary and multifactorial process rather than a spontaneous evolution or selection pressure.

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Abstract 1610

An international quality control pilot programme for the measurement of antimicrobial drugs
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Background: There is an increased interest in developing assays to determine plasma concentrations of antimicrobial drugs; used for pharmacokinetic research purposes as well as in clinical practice when performing TDM. Participation in an interlaboratory quality control (QC) program is an essential component of quality assurance. Therefore, we developed the first international QC program for the measurement of antimicrobial drugs.

Materials/methods: Antimicrobial drugs involved in the first two rounds of this pilot program were ceftazidime, ciprofloxacin, flucloxacillin, piperacillin, tazobactam, sulfamethoxazole, n-acetyl sulfamethoxazole and trimethoprim. Two QC samples (one sample per round) were prepared by spiking drug-free plasma with all eight antimicrobial drugs in either low or high concentrations. All participants were provided feedback anonymously on their performance. All weighed-in concentrations were considered true values. Acceptable accuracy was defined if measurements were within the 80-120% limits of the true weighed-in concentrations. A one-tailed unpaired t test was performed on the absolute inaccuracies to determine a difference between the high versus low concentrations.

Results: A total of 143 laboratories were approached. Seventeen laboratories participated in the first round and 22 laboratories in the second round. A total of 129 analyses were performed in both rounds. A total of 81% of the measurements was determined accurately. The measurements of flucloxacillin showed the best performance; 100% (21 out of 21) of the samples was determined accurately. The measurements of ceftazidime showed the worst performance; 56% (14 out of 25) of the samples was determined accurately. The measurements of the higher antibiotic concentrations showed a trend towards better performance than of the lower concentrations (p=0.052).

Conclusions: The initial results of this pilot program showed a relatively good performance of the participating laboratories compared to previous program initiated by us (HIV, TB and fungal). Nevertheless, still one out of five (19%) measurements was inaccurate. By participating in the program these laboratories were alerted, which may help them to improve their methods. Our results emphasize the importance of an ongoing QC program. In future rounds we will consider incorporating other antimicrobial drugs as well as the possibility the report free concentrations.

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Review of enquiries to the UK national travel advice line by healthcare professionals regarding immunocompromised travelers

Blair Merrick*1, Sanch Kanagarajah2, Dipti Patel2

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Background: Overseas travel is rising; UK residents made >70 million trips abroad in 2017. Concurrently, there has been a rise in individuals with primary/ acquired immunosuppression. The National Travel Health Network and Centre (NaTHNaC) offers a nurse-led telephone advice line for clinicians to discuss travellers with special health needs. A cohort of immunosuppressed patients from 2013 was described previously – we aimed to update this.

Materials/methods: Retrospective review of advice line data collected between January 2016 and December 2018 involving immunosuppressed travellers.

Results: 2107/17250 (12.2%) calls involved immunosuppressed travellers; a proportionate rise since 2013 [8.1%]. On review, 1085/2107 individuals [51.5%] did not fulfil CDC/ green book criteria for immunosuppressive condition/ treatment. The majority of enquiries originated from General Practice [82.1%], concerned male patients [55.7%], aged 21-59 [50%]. The majority of travel was to Africa [40%], and overall, most trips were 1-4 weeks duration [60.7%]. The most common purpose of travel was tourism [49%]. 792 callers [77.5%] asked for advice on vaccinations, most frequently Yellow fever [431, 54.4%]. A significant number of callers also asked about malaria prophylaxis [404, 39.5%]. There were 147 travellers with a diagnosis of HIV in the cohort; CD4 count was available for 44 [29.9%]. 123 patients had asplenia/ splenic dysfunction, 63 patients had renal failure, 128 chronic liver disease/ diabetes (or both), and 642 were severely immunocompromised, most frequently due to an immunosuppressive treatment [403, 62.8%].

Conclusions: Findings were broadly similar to 2013. As might be expected, there was a rise in travellers receiving monoclonal antibodies or small molecule inhibitors and individuals post solid organ/ stem-cell transplant. Criteria for immunosuppressive states and the risks facing these travellers do not appear be well understood. The majority of enquiries regarded live vaccinations [e.g. Yellow Fever] which account for a small minority of the total risk encountered by these individuals. Information provided [e.g. CD4 count, drug dose, timing of stem-cell transplant] by referring healthcare professional was frequently incomplete limiting advice that could be offered. A checklist of information to collect prior to contacting the NaTHNaC advice line may help to identify immunocompromised travellers and tailor guidance.

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Suitability of citrate buffered piperacillin/tazobactam via continuous infusion in outpatient parenteral antimicrobial chemotherapy (OPAT)

Felicity Drummond1, Conor Jamieson*1, Laima Ozolina2, Alan-Shaun Wilkinson2

1British Society for Antimicrobial Chemotherapy, Birmingham, United Kingdom, 2BioPharma Stability Testing Laboratory, Nottingham, United Kingdom

Abstract third-party references: On behalf of Members of the BSAC Working Group on Drug Stability Testing

Background: Piperacillin/tazobactam is a broad-spectrum penicillin/beta-lactamase inhibitor combination antibiotic with activity against a wide range of pathogens including multi-drug-resistant Gram-negative organisms. Optimal administration of piperacillin/tazobactam is at 6-8 hourly intervals, which is unfeasible for OPAT services. This study assessed the stability of piperacillin/tazobactam solution for injection for up to 13 days followed by continuous 24-hour infusion in two different commercially available elastomeric devices. The stability for both actives must comply with the UK National Health Service (NHS) Yellow Cover Document (YCD) requirements throughout the study.

Materials/methods: Piperacillin/tazobactam was diluted in 0.3% w/v citrate-buffered saline (pH 7.0). Two clinically useful concentrations of drug (25 mg/mL and 90 mg/mL) were compounded into two different elastomeric devices (FOLFusor, Baxter and Easypump®II, B.Braun). Devices were refrigerated for 13 days at 2-8°C, followed by 2-3 hours at room temperature and 24 hours at 32°C (representing a simulated infusion period). All testing was in accordance with NHS YCD requirements.

Results: Results show piperacillin/tazobactam diluted in 0.3% w/v citrate-buffered saline pH 7.0 is stable for 13 days at 2-8°C, plus a 24-hour administration period in both elastomeric devices tested.

Conclusions: This study confirms piperacillin/tazobactam solutions for injection when prepared in buffered saline at both concentrations has the potential to allow for single infusion at 32°C over a 24-hour period following extended storage at 2-8°C, making this practical for use in OPAT.

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**Abstract 1620**

*In vitro Activities of ceftazidime-avibactam and comparator agents against Enterobacterales and *Pseudomonas aeruginosa* from Israel collected through the ATLAS global surveillance programme 2013-2018*

Mary Person1, Meredith Hackel2*, Greg Stone2, Dan Sahm3

1IHMA, Schaumburg, United States, 2Pfizer, Inc., Groton, United States

**Background:** Avibactam (AVI) is a non-β-lactam, β-lactamase inhibitor that can restore the activity of ceftazidime (CAZ) against organisms that possess Class A, C, and some Class D enzymes. This study examined the *in vitro* activity of CAZ-AVI and comparators against Enterobacteriaceae and *Pseudomonas aeruginosa* collected in Israel through the ATLAS global surveillance program from 2013 to 2018.

**Materials/methods:** A total of 2,585 non-duplicate, clinically isolated Enterobacterales and 663 *P. aeruginosa* were collected from five sites in Israel during 2013 to 2018. Susceptibility testing was done using broth microdilution according to CLSI guidelines and interpreted using EUCAST 2019 breakpoints. CAZ-AVI was tested with a fixed concentration of 4 mg/L AVI. The presence of genes encoding resistance mechanisms was previously assessed via multiplex PCR, followed by amplification of the full-length genes and sequencing.

**Results:** Susceptibility data are provided in the table. CAZ-AVI exhibited potent activity against all Enterobacterales (MIC₉₀, 0.5 mg/L; 99.7% susceptible). When MBL-positive isolates were removed from analysis, susceptibility to CAZ-AVI was 100%. CAZ-AVI showed consistently higher % susceptibilities than all comparators other than colistin against MBL-negative meropenem-nonsusceptible isolates (CRE) and isolates positive for KPC. CAZ-AVI also showed excellent activity against the majority of *P. aeruginosa* isolates (MIC₉₀, 4 mg/L; 98.8% susceptible).

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<th>% susceptible</th>
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<td>Enterobacterales (2,585)</td>
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<td>Enterobacterales, MBL-negative (2,205)</td>
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*colistin not tested in 2013; colistin tested vs. 2,173 Enterobacteriaceae in 2014-2018.
CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; AMK, amikacin; CST, colistin; MBL, metallo-β-lactamase. % susceptible defined using EUCAST 2019 breakpoints.

**Conclusions:** CAZ-AVI showed potent *in vitro* activity against Enterobacterales and *P. aeruginosa* collected in Israel, including isolates resistant to last-in-line agents.

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Abstract 1625

Effects of prospective review and feedback and mandatory computerised decision support system for carbapenems and piperacillin-tazobactam on other broad-spectrum antibiotic use: interrupted time series with segmented regression analysis

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Background: As the use of piperacillin-tazobactam and carbapenems was rising in a public tertiary-care hospital in Singapore, antimicrobial stewardship (AMS) interventions targeting these two classes were introduced; empiric antibiotic guidelines and prospective review and feedback (PRF) in April 2009, and mandatory use of computerised decision support system (CDSS) in April 2011. Mandatory CDSS was lifted in March 2017 for half of the hospital’s wards for a 6-month cluster-randomised study. We aimed to examine if AMS interventions targeting piperacillin-tazobactam and carbapenems impacted the utilisation of other broad-spectrum antibiotics.

Materials/methods: In addition to piperacillin-tazobactam and carbapenems, monthly utilization of other broad-spectrum antimicrobials (co-amoxiclav, 3rd and 4th generation cephalosporins, fluoroquinolones and vancomycin) in defined daily doses (DDD) per 1,000 patient-days from January 2007 to December 2018 were obtained from the hospital’s database. We investigated the impact of AMS interventions using segmented regression analysis of interrupted time series.

Results: The baseline of other broad-spectrum antibiotic use was 1424.51 DDD/1,000 patient-days in January 2007. When empiric antibiotic guidelines and PRF were implemented in April 2009, there was an increase in the level of utilisation by 103.46 (95% confidence interval [CI]: 49.23, 157.68) in the same month, followed by a reduction at a rate of 11.1 per month (95% CI: -15.12, -7.08). Co-amoxiclav accounted for most of the changes in the broad-spectrum antibiotic use. After the implementation of mandatory CDSS, the reduction rate of other broad-spectrum antibiotic utilisation slowed to 2.10 per month (95% CI: -3.13, -1.07). When mandatory CDSS usage was lifted in March 2017, there was an increase in the level of other broad-spectrum antibiotic use by 109.20 (95% CI: 57.79, 160.61) in the same month with no significant changes in the monthly utilisation rate. By the end of the study period, we estimated absolute reductions of 126.58 DDD/1,000 patient-days in monthly utilisation of carbapenems and piperacillin-tazobactam, and 264.70 DDD/1,000 patient-days of other broad-spectrum antibiotic use due to the impact of the AMS interventions.

Conclusions: Despite AMS interventions being centred on piperacillin-tazobactam and carbapenems, unexpected reduction of other broad-spectrum antibiotic utilisation was observed.

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Abstract 1626

Epidemiological aspects of ascariasis in the south of Russia
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Background: More than a quarter of the world’s population is at risk of invasion with the soil-transmitted helminths. Ascaris lumbricoides is the main species infecting people and it is represent a significant public health problem. Aim: to assess the epidemiological situation of ascariasis and determine the risk factors for invasion with Ascaris lumbricoides of the population in the South of Russia based on serological and parasitological investigations.

Materials/methods: Over the past 5 years a serological screening was carried out of 2600 serum samples of conditionally healthy residents of the southern Russia. Human samples were analyzed with a commercial ELISA test to detect anti Ascaris lumbricoides IgG antibodies. For the same period, 7800 parasitological studies of environmental objects (wastewater and their sediments, soil, sand, surface water) were carried out by the flotation method.

Results: According to official statistics the incidence rate of ascariasis in Russia ranges from 12.7 to 18.4 per 100 000 population over the past 5 years. Also, it is worth noting that about 70% of patients are children. As a result of the research, it was found that the detection rate of anti Ascaris lumbricoides IgG antibodies in the serum of residents of the South of Russia in average 19.8% for the period from 2014 to 2018. Parasitological investigation of environmental objects found that the intensive indicators of contamination by ascaris eggs amounted from 2 to 15 eggs per liter/kg for wastewater and their precipitation and 1-10 eggs per kg/liter for soil, sand and surface water.

Conclusions: Significant proportions of seropositive individuals, as well as the presence of facts of detection of ascaris eggs in environmental objects indicate the maintenance of a potential risk of infection of the population of southern Russia with ascariasis. In addition, the results mean the necessity to continue monitoring for ascariasis.

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**Abstract 1627**

*In vitro activity of aztreonam-avibactam and comparator agents against Enterobacterales from Europe collected during the ATLAS global surveillance programme 2015-2018*

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**Background:** β-lactamase-producing Enterobacterales frequently co-carry resistance to antimicrobials from other classes, limiting treatment options. Avibactam inhibits class A, class C, and some class D serine β-lactamases, including extended-spectrum β-lactamases and KPC-type and OXA-48-like carbapenemases, while aztreonam is refractory to hydrolysis by metallo-β-lactamases (MBL). Aztreonam-avibactam is being developed for use against drug-resistant isolates of Enterobacterales, especially those co-producing MBLs and serine β-lactamases. This study evaluated the *in vitro* activity of aztreonam-avibactam and comparators against Enterobacterales collected in 2015-2018 in Europe as part of the Antimicrobial Testing Leadership and Surveillance (ATLAS) program.

**Materials/methods:** Non-duplicate clinical isolates were collected from 134 medical centres in 25 countries. Susceptibility testing was performed by CLSI broth microdilution and interpreted using EUCAST 2019 breakpoints. Aztreonam-avibactam was tested at a fixed concentration of 4 mg/L avibactam. PCR and sequencing were used to determine the β-lactamase genes present in all isolates with meropenem MIC >1 mg/L, and *Escherichia coli*, *Klebsiella* spp. and *Proteus mirabilis* phenotypically positive for ESBL activity (2015) or with aztreonam or ceftazidime MIC >1 mg/L (2016-2018).

**Results:** Aztreonam-avibactam was active *in vitro* against Enterobacterales isolates (MIC₉₀, 0.12 mg/L), with 99.9% (31 230 of 31 252) of isolates inhibited by ≤8 mg/L of aztreonam-avibactam. Aztreonam-avibactam tested with MIC₉₀ values of 0.5 mg/L against subsets of cephalosporin-resistant, aminoglycoside-resistant, colistin-resistant, and MBL-positive Enterobacterales and MIC₉₀ of 1 mg/L against meropenem-resistant isolates and those resistant to three last-line agents [meropenem, amikacin and colistin] (Table). In most cases, the tested comparators showed susceptibility of <80% against these subsets of resistant isolates.

**Conclusions:** Based on MIC₉₀ values, aztreonam-avibactam was the most potent agent tested against resistant and MBL-positive subsets of Enterobacterales collected in Europe, including isolates resistant to one or multiple last-resort agents from different drug classes. The promising *in vitro* activity of aztreonam-avibactam warrants further development of this combination for treatment of infections caused by drug-resistant Enterobacterales.

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Abstract 1629

**Cardiovascular Disease risk in liver transplant recipients for hepatitis B, C and delta virus-associated cirrhosis**

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**Background:** Cardiovascular disease (CVD) is a cause of morbidity and mortality after liver transplantation (OLT), mostly in patients transplanted for NASH, obesity and diabetes-associated liver disease. Few data exist on CVD among patients transplanted for viral hepatitis. Our aim is to clarify the CVD risk and subclinical vascular damage among OLT recipients for HCV, HBV, HDV-associated liver disease.

**Materials/methods:** OLT patients due to viral hepatitis admitted for follow-up to University of Campania in the period June-July 2019 were prospectively enrolled. An estimation of cardiovascular risk was assessed using the main risk charts (Framingham, ASCVD, Heart Score), and by performing the ecocolordoppler of epiaortic vessels to assess subclinical endothelial damage. A Intima-Media Thickness [IMT] ≥1 mm was considered pathological. A carotid was classified as being affected by atherosclerotic plaque if the localized thickening was ≥1.3 mm.

**Results:** An overall of 76 patients were considered of whom 31 (40.8%) were transplanted for HCV, 14 (18.4%) for HBV, 24 (31.6%) for dual infection HBV-HDV, 5 (6.6%) for dual infection HBV-HCV and 2 (2.6%) for triple infection HBV-HDV-HCV. 30 patients (39.5%) had a familiarity for CVD, 39 (51.3%) for diabetes mellitus and 19 (25.2%) for dyslipidemia; 27 (35.5%) patients had diabetes and 19 (25%) were active smokers. More than half of the patients (63.1%) were taking antihypertensive therapy and 19.7% a lipid-lowering drugs. An overall of 43 patients (56.6%) were considered at high cardiovascular risk according to Framingham, 28 patients (36.9%) to ASCVD and 10 (13.1%) to Heart Score. Only 4 patients (5.3%) showed a normal carotid ultrasound, while 27 patients (35.5%) had a IMT and 45 (59.2%) an atherosclerotic plaque.

**Conclusions:** OLT recipients for HCV, HBV±HDV-associated liver disease are at high risk of CVD. Comparing the high percentage of subclinical carotid lesions with data of the risk charts, the latter seem to underestimate the real extent of the endothelial damage. In the pathogenesis of CVD in these patients, a chronic inflammatory status, could play a key role. It’s important to raise the awareness of CVD risk in OLT patients to prevent CVD and improve the timing of early diagnosis of premature vascular lesions.

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Abstract 1630

Knowledge about transmission and determinants of tuberculosis among Pakistani adults: evidence from demographic and health survey

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Background: Knowledge about symptoms and transmission of tuberculosis determines health-seeking behavior and helps in the prevention of tuberculosis transmission in the community. Such data is useful for policymakers to formulate information, education and communication strategies for tuberculosis control.

Materials/methods: A secondary data analysis of Pakistan demographic and health survey, 2017/18 was carried out. Questions about self-reported tuberculosis, transmission, and curability of tuberculosis were analyzed. Correct knowledge (without misconceptions) about tuberculosis transmission was used as a dependent variable and the explanatory variables tested were demographic data, education, wealth quintiles, frequency of exposure to media and the curability of tuberculosis. Determinants of correct knowledge without misconceptions were tested by univariate and multivariate analyses.

Results: The percent of correct knowledge of tuberculosis (TB) was 51.7. The 'Correct knowledge about TB transmission' was TB transmission "Through the air when coughing or sneezing" but had no misconceptions about TB transmission. The number of respondents who had "heard of an illness called tuberculosis" was 13,596 (90.2%). Of these 3015 (20.0%) participants did not know the correct mode of TB transmission. The common misconceptions about transmission were "Through food" (31.7%), "Sharing utensils" (35.7%), and "Touching a person with tuberculosis" (9.1%). Only 7793 (51.7%) participants had correct knowledge about TB transmission. Being rich (aOR 1.39, 95% CIs 1.26-1.52), urban residence (aOR 1.22, 95% CIs 1.12-1.32), age (25-49 years) (aOR 1.48, 95% CIs 1.35-1.62), education (secondary and higher) [(aOR 1.53, 95% CI 1.37-1.70) and (aOR 3.08, 95% CI 2.68-3.50)], and "Tuberculosis can be cured" (aOR 3.33, 95% CIs (2.89-3.83) were significantly associated with correct knowledge without misconceptions.

Conclusions: Knowledge about TB transmission is considerably poor, and misconceptions remain persistent. Among the traditional mass media, the frequency of watching television was associated with correct knowledge about TB transmission. Strategies to deliver information, education and communication campaigns could be improved.

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**Abstract 1631**

**Insights into vaginal metabolic profiles throughout pregnancy**
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**Background:** During pregnancy, the vaginal microbiome plays an important role in both maternal and neonatal health outcomes. The vaginal microbiome undergoes significant changes during pregnancy, including a significant decrease in overall diversity, increased stability, and enrichment with *Lactobacillus* spp.

Since the changes in the microbial profiles are usually associated with significant shifts in the composition of vaginal metabolites, the aim of this study was to characterize the vaginal metabolic profiles throughout pregnancy at two different gestational ages, correlating them with a microscopic evaluation of the vaginal bacterial composition.

**Materials/methods:** A total of 67 Caucasian pregnant women, with a mean age of 31.3 years, and presenting to the Family advisory health Centres of Ravenna for prenatal care were enrolled. After a clinical examination, a vaginal swab was collected at gestational ages 9-12 weeks (first trimester) and 20-24 weeks (second trimester) from each woman. The composition of the vaginal microbiome was evaluated by a Gram stain scoring system (Nugent score), assessing for the presence of different bacterial morphotypes (*Lactobacillus* spp., *Gardnerella vaginalis* and *Mobiluncus* spp.). Based on this score, women were divided into 3 groups: 'H' [normal lactobacilli-dominated microbiota], 'I' [intermediate microbiota], 'BV' [bacterial vaginosis].

Starting from the cell-free supernatants of the vaginal swabs, a metabolomic analysis was performed by means of a 1H-NMR spectroscopy. Differences among experimental groups were assessed via PCoA and a two-ways ANOVA test.

**Results:** From the first to the second trimester of pregnancy, a greater number of women showed a normal lactobacilli-dominated microbiota (33 vs 45 women), with a reduction of cases of dysbiosis. These microbial shifts were clearly associated with profound changes in the vaginal metabolic profiles. Globally, over the weeks, a significant reduction in the levels of BV-associated metabolites [e.g. putrescine, acetate, propionate, methylamine, butyrate, formate, cadaverine] was observed. At the same time, the vaginal metabolome was characterized by higher concentrations of leucine, isoleucine, serine and phenylpropionate, typically found in healthy vaginal conditions.

**Conclusions:** Throughout pregnancy, the vaginal metabolic composition became less diverse and more homogeneous, reflecting the shift towards a lactobacilli-dominated microbiome.

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Abstract 1632

**In vitro activity of tigecycline and comparator agents against Gram-negative and Gram-positive isolates from China in 2018**

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**Background:** The TEST (Tigecycline Evaluation and Surveillance Trial) global surveillance program monitors *in vitro* activities of tigecycline and a panel of marketed antimicrobial agents against clinically significant Gram-negative and Gram-positive bacterial pathogens. In this analysis we review recent TEST program data for Gram-negative and Gram-positive isolates tested by clinical laboratories in China.

**Materials/methods:** Clinically significant Gram-negative (*n=2,999*) and Gram-positive (*n=989*) isolates were cultured from multiple infection sites by 24 clinical laboratories in China in 2018. Isolates were identified to species level and MICs determined in each clinical laboratory using broth microdilution panels (supplied by IHMA, Schaumburg, IL, USA) following CLSI guidelines. Isolates were limited to one per patient. Data were submitted to IHMA for analysis. MICs were interpreted using current EUCAST [2019, v 9.0] and US FDA [tigecycline] MIC breakpoint criteria.

**Results:**

<table>
<thead>
<tr>
<th>Organism (n)</th>
<th>TGC</th>
<th>AMK</th>
<th>FEP</th>
<th>CAZ</th>
<th>CRO</th>
<th>LVX</th>
<th>MEM</th>
<th>TZP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacterales (2,549)</td>
<td>97.4</td>
<td>90.2</td>
<td>53.8</td>
<td>52.8</td>
<td>47.8</td>
<td>52.0</td>
<td>67.1</td>
<td>73.6</td>
</tr>
<tr>
<td>CRE (329)</td>
<td>95.4</td>
<td>46.8</td>
<td>0.3</td>
<td>1.2</td>
<td>0</td>
<td>9.1</td>
<td>0</td>
<td>2.4</td>
</tr>
<tr>
<td>Acinetobacter spp. (410)</td>
<td>NA²</td>
<td>29.3</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>14.9</td>
<td>15.9</td>
<td>NA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Organism (n)</th>
<th>TGC</th>
<th>AMC</th>
<th>AMP</th>
<th>LVX</th>
<th>LNZ</th>
<th>VAN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococcus spp. (370)</td>
<td>90.0</td>
<td>60.3</td>
<td>45.1</td>
<td>98.4</td>
<td>97.8</td>
<td></td>
</tr>
<tr>
<td>S. aureus (619)</td>
<td>96.6</td>
<td>NA</td>
<td>NA</td>
<td>72.0</td>
<td>99.8</td>
<td>100</td>
</tr>
</tbody>
</table>

CRE, carbapenem-resistant Enterobacterales (meropenem MIC >2 mg/L); NA, MIC breakpoints not available; TGC, tigecycline; AMK, amikacin; FEP, cefepime; CAZ, ceftazidime; CRO, ceftriaxone; LVX, levofloxacin; MEM, meropenem; TZP, piperacillin-tazobactam; AMC, amoxicillin-clavulanate; AMP, ampicillin; LNZ, linezolid; VAN, vancomycin.

* US FDA MIC breakpoints applied. 91% (670/736) of *Escherichia coli* had tigecycline MICs ≤0.5 mg/L (EUCAST tigecycline-susceptible MIC breakpoint).

Conclusions: *In vitro* susceptibility of Enterobacterales was highest to tigecycline (97.4%); isolates were less susceptible to amikacin, meropenem, and the other agents tested. 12.9% of Enterobacterales isolates in China were CRE; 95.4% of CRE were susceptible to tigecycline. >90% of enterococci and *S. aureus* were susceptible to tigecycline; linezolid and vancomycin were slightly more active *in vitro* than tigecycline against common Gram-positive cocci. Country specific monitoring of susceptibility patterns among common bacterial pathogens provides useful information for determining empiric treatment strategies.

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Abstracts 2020

Abstract 1633

Utilising the full potential of model-based dosing tables: an interprofessional collaboration to develop and integrate meropenem dosing tables into clinical routine

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Background: Meropenem is an antibiotic used to treat infections in intensive care patients. Pharmacokinetic [PK] variability observed in critically ill patients leads to a high risk of suboptimal exposure. Recent observational data at the Charité-Universitätsmedizin Berlin shows that >70% of patient’s exposure is outside the C_{min} target range (1x-5x MIC). Consequently, improvement of current dosing practices is urgently needed. Model-based Bayesian dosing software for dose optimization have been suggested [1] to improve dosing practices, however several barriers exist [2] hindering implementation in clinical practice. We aimed to develop easy-to-use model-based dosing tables to optimise meropenem treatment at intensive care units (ICU) at Charité. To ensure suitability and user-friendliness a close collaboration with the antimicrobial stewardship (AMS) and ICU teams of the hospital was pursued.

Materials/methods: A previously developed meropenem PK model was used to perform Monte Carlo simulations considering PK parameter uncertainty [3]. In close discussion with the AMS and the ICU teams multiple clinically relevant dosing regimen (n=15) were evaluated with respect to target attainment (f_{T>MIC}=98%) and its probability (PTA≥90%). Dosing regimen reaching a PTA≥90% were further discriminated with regards to probability of reaching the predefined target range (1x-5x MIC) and potentially toxic \(C_{min}\) values (>16 mg/L or >64 mg/L).

Results: Optimised and easy-to-use model-based dosing tables are now available for clinical routine dosing at Charité-Universitätsmedizin Berlin. Dosing regimen stratified for a patient’s creatinine clearance and determined/assumed MIC are summarised in one concise table. Our result showed that for the same daily dose, (i) prolonged (4h) or continuous infusions reached higher PTA than short-time infusions and (ii) four-times-daily dosing was superior in PTA to three-times-daily dosing. Both can easily be integrated into clinical routine. 2-g meropenem loading doses provided little further benefit over 1-g loading doses and consequently were not further considered.

Conclusions: Model-derived dosing tables are a promising tool to improve dosing in ICU patients. To fully utilise their potential and integrate them into clinical routine a close collaboration between all parties of an interprofessional team is needed. The developed dosing tables are currently prospectively evaluated.


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Abstract 1635

Feasibility studies of the WHO practical toolkit for antimicrobial stewardship programmes in healthcare facilities in low-and middle-income countries

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Background: The overuse and misuse of antimicrobials are a main driver for development of antimicrobial resistance [AMR]. Antimicrobial stewardship (AMS) has emerged as a systematic approach to optimize antimicrobial use. To meet the increasing need for practical guidance on how to implement effective AMS programmes, the World Health Organization (WHO) developed a draft toolkit for AMS programmes in hospitals in low- and middle-income countries (LMIC). In this study, we evaluated the feasibility of implementing the toolkit in four LMIC settings.

Materials/methods: The study used a descriptive qualitative study design with semi-structured interviews with national- and hospital-level stakeholders. Four countries were included: Bhutan, the Federated States of Micronesia, Malawi, and Nepal. A total of 12 national policy makers, 20 hospital administrators and managers, and 64 hospital staff were interviewed.

Results: All study participants identified AMS as an important priority and responded that the AMS toolkit would be helpful in improving AMS programmes within their countries and hospitals. Key facilitators for implementing AMS included strong national and hospital leadership and support, and hospital staff engagement in AMS committees. Key barriers included lack of human and financial resources, limited access and supply of medicines particularly in remote regions, difficulty enforcing regulations for prescription only antibiotic sales, and inadequate AMS competencies training. Key recommendations to strengthen AMS included dedicated AMS financial resources, identification of dedicated hospital AMS leaders and champions, stepwise approach for AMS implementation based on country and hospital context, establishing mechanisms for reporting and feedback, and initiating AMS training workshops and AMS curricula. Key recommendations to improve the draft WHO toolkit included the need for guidance to prioritize AMS activities based on available resources, stronger linkage between existing programmes e.g. Infection Prevention and Control, and further guidance on establishing AMS committees.

Conclusions: The draft toolkit was well received throughout the four study countries. The overall consensus was that the toolkit will be an important asset as countries and hospitals move forward to combat AMR and implement AMS programmes. However, many barriers will need to be addressed at both the national and hospital levels in order to facilitate implementation.

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Abstract 1636

HPV OncoPredict: analytical performance of a novel diagnostic tool allowing accurate determination of sample cellularity and normalised high-risk human papilloma virus genotype-specific viral load

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Abstract third-party references: This Project is conducted in collaboration with GeneFirst as part of the EU funded programme (SME Instrument Grant GA 806551)

Background: Cervical cancer (CC) kills 330,000 people annually and requires persistent infection with high-risk Human Papillomavirus [hrHPV] for its development. Type-specific hrHPV viral load has been suggested to be a useful risk triage indicator for the development of high-grade squamous intraepithelial lesion (≥HSIL) as well as a clinically useful marker to monitor post treatment (“test-of-cure”). Most presently commercially available hrHPV tests do not provide type-specific hrHPV viral load or quantitative sample cellularity assessment as a measure of sample adequacy.

HPV OncoPredict is a new in-vitro diagnostic tool allowing accurate sample adequacy assessment and hrHPV type-specific viral load (E6/E7 DNA) determination. The aim of this study is to evaluate the intra- and inter-laboratory analytical performance of HPV OncoPredict prototype using international standards and reference samples.

Materials/methods: HPV OncoPredict prototype analytical performance has been evaluated using NIBSC [National Institutes of Biological Standards and Controls] standards for HPV16 [06/202] and HPV18 [06/206], WHO LabNet Proficiency Panels as well as commercially available Verification/Validation standards [Microbix] for HPV 16, 18, 31, 33, 39, 45 and HPV 67 [negative control].

Results: HPV OncoPredict was able to quantitatively assess and correctly identify hrHPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 as well as a human gene, used to normalize viral load and assess sample adequacy. HPV OncoPredict assigned type-specific viral loads and human Genomic Equivalents [hGE] comparable to those indicated in the WHO LabNet 2018 report. Moreover, HPV OncoPredict demonstrated 100% accuracy in genotyping all 12 hrHPV types, as defined by IARC, on testing both NIBSC and Microbix control standards. Inter-laboratory performance is presently under evaluation in 2 external University Laboratories using 2019 WHO LabNet Proficiency Panel.

Conclusions: HPV OncoPredict analytical performance has demonstrated accurate assessment of sample’s cellularity and hrHPV type-specific viral loads, using both international standards and commercial controls. These promising results will support HPV OncoPredict future clinical validation studies aimed at evaluating the correlation between normalized viral loads and cervical lesions. References: This project is conducted in collaboration with GeneFirst as part of a EU funded Horizon 2020 SME Instrument Project (SME Instrument Grant GA 806551).

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Abstract 1644

Prediction of antibiotic resistance in *Helicobacter pylori* by whole genome sequencing and open-source bioinformatics tools

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¹Royal Navarre Hospital, Pamplona, Spain, ²CatLab (Parc Logístic de Salut), Viladecavalls, Spain, ³UCM Faculty of Veterinary Medicine, Madrid, Spain, ⁴University Hospital 12 de Octubre, Madrid, Spain, ⁵Karolinska Institute, SOLNA, Sweden, ⁶Hospital de La Princesa, Madrid, Spain

**Background:**

Increasing antimicrobial resistance in *Helicobacter pylori* (Hp) is a worldwide problem. Whole genome sequencing (WGS) has recently emerged as a diagnostic tool in clinical microbiology for drug resistance prediction in bacteria. The aim of this study was to compare phenotypic drug susceptibility testing results with the presence of genetic resistance determinants identified in Hp genome using two open-source bioinformatics tools.

**Materials/methods:**

20 Hp strains isolated from gastric biopsies were selected. Antimicrobial susceptibility testing was performed on blood agar plates using the following E-tests: clarithromycin (CLA), metronidazole (MTZ), levofloxacin (LEV), amoxicillin (AMX) and tetracycline (TET). EUCAST breakpoints were used. After DNA extraction, WGS was performed using Illumina-MiSeq platform. Resistance Gene Identifier (RGI) 5.1 and ResFinder 3.2 were used to identify resistance mutations.

**Results:**

The following table shows the results from susceptibility testing (susceptible=S, resistant=R) and the resistance mutations found:

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<th>Nº OF STRAINS</th>
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<th>CLA</th>
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<th>TET</th>
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<td>R</td>
<td>S</td>
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<td>A2147G</td>
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<tr>
<td>5</td>
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<td>S</td>
<td>S</td>
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<td>A2147G</td>
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</tr>
<tr>
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<td>S</td>
<td>S</td>
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<td>S</td>
<td>R</td>
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<td>1</td>
<td>R</td>
<td>R</td>
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**Conclusions:** Both tools detected a clarithromycin resistance mutation in all clarithromycin-resistant strains, except in one. The most frequent clarithromycin mutation was A2147G. Metronidazole resistance is due to a combination of various complex mechanisms, so it is difficult to predict it with genotypic data. No resistance was detected in the amoxicillin-resistant strain. Hp WGS and open-source bioinformatics tools can be useful to predict clarithromycin resistance.

**Presenter email address:** talarcon@helicobacterspain.com
Distinct effectiveness of oritavancin against tolerance-induced Staphylococcus aureus

Lauren Harven1, Victoria Bingley1, Pushkar Kulkarni1,2, Sanket Khaire1, Somrita Dey1, Paula Smolenski1, Andrew Berti*1,3

1Wayne State University, College of Pharmacy, Pharmacy Practice Dept, Detroit, United States, 2Wayne State University, College of Engineering, Detroit, United States, 3Wayne State University, College of Medicine, Biochemistry Microbiology and Immunology Dept, Detroit, United States

Background: Within a sufficiently large bacterial population, some of the members will naturally adopt an alternate, metabolically-active state that favors small molecule synthesis over cell division. In Staphylococcus aureus this process can be sharply accelerated by multiple factors present during infection including nutrient limitation, host cationic peptide exposure and polymorphonuclear neutrophil internalization. These isogenic “tolerant” subpopulations have variable responses during antibiotic exposure and can remain viable in the presence of typically bactericidal concentrations. Survivors of the antibiotic exposure can restart cell division upon cessation of antibiotics and cause relapse or recurrent infection. In this study we determine the ability of typical and atypical antistaphylococcal therapies to reduce the viability of tolerant Staphylococcus aureus bacteria.

Materials/methods: S. aureus strain ATCC29213 as well as four clinical isolates (two MSSA, two MRSA) were selected for analysis. Overnight cultures were diluted in pre-warmed broth (MHB50) to approximately 1×10^6 cfu/mL. Tolerance was induced by exposure to mupirocin (low [0.032 µg/mL] or high [3.2 µg/mL]) for 30 min. Tolerant cultures were exposed to vancomycin (35 µg/mL), cefazolin (25 µg/mL), daptomycin (7 µg/mL), telavancin (10 µg/mL), dalbavancin (6 µg/mL) or oritavancin (14 µg/mL) and viability was assessed by dilution plating at pre-defined time points (0, 2, 6, 24, 48 h). The minimum duration for 3-log viability reduction from baseline (MDK99.9) and culture viability at 48h were calculated independently for each of three biological replicates.

Results: The rate of bacterial killing (MDK99.9) was reduced for all study antibiotics by the addition of mupirocin in a dose-dependent manner. In contrast to all other regimens, including lipoglycopeptide comparators, oritavancin was the only antimicrobial agent that maintained a similar extent of bacterial killing against tolerant staphylococci.

Conclusions: Antimicrobial tolerant staphylococci exhibit a decreased rate of killing by antistaphylococcal agents. However, oritavancin remained effective at maintaining a similar extent of killing. Further studies to investigate the role of oritavancin against recurrent or relapse staphylococcal infection is warranted.

Presenter email address: andrew.berti@wayne.edu
Abstract 1651

CANDIMAD study: a prospective multi-centre laboratory based survey of antifungal resistance in Candida spp. causing invasive candidiasis in Madrid

Judith Diaz-Garcia1,2, Aina Mesquida1,2, María Ángeles Meléndez Carmona3, Fernando González-Romo4,5, Cuetara María Soledad6, Nelly Daniela Zurita Cruz7, María Muñoz Algarra8, Maria Del Coral Garcia9, Aída Sánchez10, Inmaculada Quiles11, María Teresa Duran-Valle12, Carlos Sanchez-Carrillo1,2,13, Patricia Muñoz1,2,6,13, Pilar Escribano1,2, Jesus Guinea Ortega1,2,13

1Gregorio Marañón Hospital, Madrid, Spain, 2Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain, 3University Hospital 12 de Octubre, Madrid, Spain, 4Hospital Clínico Universitario San Carlos, Madrid, Spain, 5Universidad Complutense de Madrid, Madrid, Spain, 6Hospital Severo Ochoa, Leganés, Spain, 7Hospital de La Princesa, Madrid, Spain, 8Hospital Puerta de Hierro-Majadahonda, Majadahonda, Spain, 9Hospital Universitario de Getafe, Getafe, Spain, 10Hospital Infanta Sofía, San Sebastián de los Reyes, Spain, 11University Hospital La Paz, Madrid, Spain, 12Hospital de Móstoles, Móstoles, Spain, 13CIBER Enfermedades Respiratorias-CIBERES, Madrid, Spain

Background: Active surveillance studies are necessary to know local epidemiology and help clinicians start appropriate empirical antifungal treatment. Resistance rates in Candida spp. come mainly from isolates causing candidaemia and figures in Spain are relatively old (CANDIPOP study, 2014). We assessed the epidemiology and antifungal resistance of recent yeast isolates causing invasive infections in patients at hospitals located in Madrid, Spain.

Materials/methods: We studied 312 isolates from 282 patients (23 presented ≥2 isolates and 19 showed mixed cultures) admitted to 15 hospitals located in the Madrid metropolitan area from January 2019 to October 2019. Isolates sourced from blood (52.6%), abdominal samples (29.8%), peritoneal samples (10.9%) and other digestive tract samples (6.7%) were identified by MALDI-TOF and antifungal susceptibility to amphotericin B, azoles, micafungin, anidulafungin and investigational agent, ibrexafungerp (previously SCY-078) was tested according to EUCAST EDef 7.3.1 (Breakpoints table v.10.0). FKS genes were sequenced in echinocandin-resistant Candida isolates.

Results: The species distribution of isolates was C. albicans (48.7%, n=152), C. glabrata complex (19.2%, n=60), C. parapsilosis complex (17.6%, n=55), C. tropicalis (7.1%, n=22), C. krusei (2.9%, n=9), other Candida spp. (3.2%, n=10), and non-Candida yeasts (1.3%, Rhodotorula mucilaginosa [n=2], and Trichosporon inkin [n=2]). Overall, triazoles, candins and ibrexafungerp showed high activity. Ibrexafungerp was more active against C. parapsilosis than candins. Fluconazole resistance was detected in 6.1% of Candida isolates (n=19; C. krusei [n=9], C. glabrata [n=4], C. parapsilosis [n=2], C. albicans [n=1], C. tropicalis [n=1], C. guilliermondii [n=1], and C. inconspicua [n=1]) sourcing from blood (n=11), abdominal samples (n=6), and peritoneal samples (n=2). Rate of echinocandins resistance was lower than 1% and was found in isolates sourcing from blood (n=2) and abdominal samples (n=1): C. krusei (n=2; L701M FKS1) and C. glabrata (n=1, WT). Resistant isolates were from patients from nine out of the 15 hospitals. Non-Candida yeasts showed intrinsic echinocandin resistance. No resistance to amphotericin B was detected (Figure).

Conclusions: We found a low percentage of overall resistance (<7%), with anecdotal echinocandin resistance rate. Resistant isolates sourced from blood (4%), abdominal samples (2%), and peritoneal samples (0.6%), and were distributed across different hospitals. No multi-drug resistant species were found.
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Values shaded in grey indicate either resistant isolates or non-wild type isolates according to clinical breakpoints or tentative ECOFF's (EUCAST Breakpoints table v 10.0, November 2019).

ND: Not done as either breakpoints or ECOFFs were not available. R: Resistant. NWT: Non-wild type.

Presenter email address: judithdiaz5@gmail.com
Abstract 1653

High diagnostic yield of splenic core biopsy in patients with pyrexia or inflammation of unknown origin: a descriptive analysis of imaging (including FDG-PET) and pathological findings at a major tertiary centre

Yee Ting Nicole Yim*1,2, Gabriel Wallis1, Jawad Saeed3, Stefan Voo4, Ian Proctor5, Christopher Mcnamara3, Michael Brown1,2

1Hospital For Tropical Diseases, University College London Hospital, London, United Kingdom, 2London School of Hygiene & Tropical Medicine, London, United Kingdom, 3Department of Haematology, University College London Hospital, London, United Kingdom, 4Department of Radiology, University College London Hospital, London, United Kingdom, 5Department of Histopathology, University College London Hospital, London, United Kingdom

Background: A proportion of patients with pyrexia and/or inflammation of unknown origin (PUO) are without a diagnosis following clinical and laboratory evaluation. Imaging, including with FDG-PET, may identify and characterise splenic abnormalities. Many specialists are reticent to undertake splenic biopsies because of the perceived risk. We aim to report on the diagnostic yield of targeted splenic biopsy in patients with febrile or inflammatory presentations showing splenic abnormalities, and explore predictors of definitive diagnosis.

Materials/methods: Cases were identified by searching the pathology archive at University College London Hospital over the 10 year period 2009-2019. We combined search terms ‘biopsy’ and ‘spleen’ and excluded non-core biopsy samples. We used electronic patient records to identify those investigated for unexplained fever or inflammation and collated data on prior and subsequent diagnostic tests, final diagnosis, complications and 6 month survival.

Results: 20 patients meeting these criteria were identified. All patients had splenomegaly. Microbiological diagnoses were made by culture or PCR. A diagnosis was made from splenic biopsy in 15 (75%) cases. Of the remaining cases, 1 biopsy showed reactive features only and responded to steroids; 2 were diagnosed at subsequent splenectomy, and 2 received a delayed final diagnosis from prior investigations. An infectious cause was found in 20%. 15 patients had a FDG-PET scan. While diagnostic yield was higher in those with the most abnormal splenic PET findings, biopsies were diagnostic even among those with mild FDG avidity. There were no complications.

Conclusions: We demonstrate the high utility of splenic core biopsy in diagnosing patients with inflammatory/infectious presentations and splenic imaging abnormalities who have undergone extensive investigation on other laboratory and imaging. In patients with splenomegaly, FDG-PET features cannot classify those for whom biopsies were non-diagnostic.

Presenter email address: nicole_yim90@hotmail.com
Abstract 1655

Comparison of prognostic capacity of presepsin and procalcitonin in adult septic patients: results from a prospective observational study in two university clinical centres

Ajete Aliu Bejta*1,2, Sadije Namani2, Bahrie Halili2, Donjeta Plana-Hajdari3, Bruno Baršić4, Anita Atelj4

1University Clinical Center of Kosovo, Clinic of Infectious Diseases, Prishtina, Kosovo, 2University Clinical Center of Kosovo, Clinic of Infectious Diseases, Prishtina, Kosovo, 3National Institute for Public Health, Department of Molecular Microbiology, Prishtina, Kosovo, 4University Clinical Center of Zagreb, Hospital for Infectious Diseases, Zagreb, Croatia

Background: Sepsis is a life-threatening condition that causes millions of death worldwide each year. Early recognition of disease is crucial for better outcome. Sepsis biomarkers are widely used for rapid diagnosis of sepsis. We evaluated a prognostic value of presepsin concentrations in patients with sepsis.

Materials/methods: A prospective observational study was conducted on 100 adult septic patients admitted at the Clinic of Infectious Diseases in Prishtina, Kosovo, and University Hospital for Infectious Diseases in Zagreb, Croatia. New Sepsis-3 definitions were used for disease stratification. Based on the disease outcome patients were grouped as survivors and non-survivors. During the disease course, sepsis biomarkers (presepsin and procalcitonin) were measured four times: on admission, after 24 hours, 72 hours, and on day 7. Multivariate generalized linear model (glimix) was performed to test the association of presepsin and procalcitonin levels during the course of the disease with outcome and multivariate logistic regression analysis was performed to test the association of initial sepsis biomarkers (presepsin and procalcitonin) with disease outcome.

Results: There were 68 survivors and 32 non-survivors. In Figure 1 are presented the differences in trends of presepsin and procalcitonin during disease course between two outcome groups. Initial and subsequent measurements of presepsin concentrations significantly differ between survivors and non-survivors. In non-survivors presepsin levels were significantly higher throughout the disease course. Procalcitonin concentrations did not differ in two outcome groups.

Figure 1. Concentration of presepsin and procalcitonin in two outcome groups

On the left side association of presepsin concentration with disease outcome. On the right side association of procalcitonin with disease outcome. Black line-survivors, black spotted line-non-survivors. Hosmer-Lemeshow test p=0.6226, with satisfactory explanatory value c=0.675.

Presepsin values but not procalcitonin values on admission were significantly associated with death. Procalcitonin didn’t show any prognostic value.

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<td>1.002 1.020</td>
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<td>PCT on admission</td>
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<td>0.970 1.003</td>
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Conclusions: Initial presepsin concentrations and their non-decreasing trend over the time suggests poor disease outcome.

Presenter email address: ajete.aliu@gmail.com
Abstract 1658

**Accurate differentiation of carbapenemases by MALDI-TOF MS-typing: employment of bioinformatics**

Eva Gato1, Jorge Arca Suárez1, Bruno Kotska Rodiño1, Gema Méndez2, Manuel Arroyo2, Luis Mancera Pascual2, Germán Bou Arevalo1, Marina Oviñaño García*1

1Complejo Hospitalario Universitario A Coruña, a Coruña, Spain, 2Clover BioSoft, Granada, Spain

**Background:** Detection of Carbapenemase-Producing Enterobacterales (CPE) is one of the main goals of microbiology laboratories, as they constitute a health alarm worldwide. Rapid methods to detect resistance mechanisms and strain typing as part of routine data analysis could therefore greatly benefit infection control efforts. MALDI-TOF MS has demonstrated substantial utility for rapid organism identification. Here, we demonstrate that real-time, direct tracking of CPE is possible using MALDI-TOF MS and artificial intelligence in a manner that could be implemented for routine screening in clinical microbiology laboratories.

**Materials/methods:** A total of 102 previous molecular characterized CPE (20 KPC-2, 26 KPC-3 and 56 OXA-48) with different sequence types, were submitted to two different standard operating procedures, an in-target and a full formic acid-ethanol extraction. All isolates were spotted four times on the MALDI target plate and measured three times each. Thus, 12 spectra were acquired per sample using the automated functionality of FlexControl 3.3 software (Bruker Daltonik). Raw data was submitted to baseline subtraction using Top-Hat filter and smoothing via Savitzky-Golay filter (Clover BioSoft software). All replicates were aligned with a tolerance factor of 0.0002. The processed data set was submitted to Principal Component Analysis (PCA) and hierarchical clustering. Technical reproducibility was analyzed, along with the best extraction method in terms of spectral quality, discrimination against the gold standard (molecular characterization) and simplicity of the method.

**Results:** Both extraction methods provided similar results, so we chose the in-target extraction for further studies. KPC-3 strain was correctly classified by hierarchical clustering after applying PCA to the processed dataset and was accurately differentiated from OXA-48 and KPC-2 isolates (Image 1). Besides, potential biomarkers have been identified to classify OXA-48 different clones. In particular, the peaks 9831, 9845, 9857 y 9872m/z ± 1.5 Da discriminate ST 307, whereas 9342m/z ± 1.5Da identify ST 147.

**Conclusions:** Accurate differentiation of CPE by MALDI-TOF MS-typing was accomplished in as little as 10 min from isolated colonies, demonstrating the potential clinical utility for real-time screening in clinical practice. This software can be implemented in all currently available MALDI-TOF MS systems.

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Abstract 1662

Approaches to identify new onset diarrhoea among hospitalised patients and the frequency of stool sample collection for *Clostridioides difficile* infection: a pilot for the CLOUD Louisville study

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Abstract third-party references: On behalf of the CLOUD Louisville Study Group. This study was sponsored by Pfizer, Inc.

**Background:** Population-based surveillance studies defining the incidence of *Clostridioides difficile* infection (CDI) are important to inform policy makers. One challenge to perform these studies is the identification of all hospitalized patients with new onset diarrhea. Additionally, CDI may be underestimated if stool specimens are not collected from patients with diarrhea and tested for *C. difficile*. We conducted a pilot study to inform the development of a protocol for a population-based incidence study in all hospitals in Louisville, Kentucky. The objectives of this pilot study were to define the optimal approach to identify adult patients with new onset diarrhea and the frequency of stool collection for CDI testing.

**Materials/methods:** This was a cross-sectional pilot study conducted in all nine adult hospitals in Louisville, Kentucky. For seven consecutive days in December 2018, all adult Louisville inpatients were evaluated for new-onset diarrhea (≥3 loose stools within 24 hours, Bristol stool form scale 5-7) using a 3-level approach: 1) medical record review; 2) nurse interview; and 3) patient interview. The frequency of stool specimen collection for CDI testing according to local standard of care was ascertained.

**Results:** A total of 7,540 Louisville adult in-hospital patient days were evaluated (Figure 1). Patients with diarrhea were identified either by medical record review (50%), nurse interviews (42%) or patient interviews (8%). All cases identified by patient interviews were identified by nurses the following day. New onset diarrhea was identified in 167 patients (47% male; median age 64 years). Stool samples were submitted for *C. difficile* testing in 32% (53/167) of patients.

**Conclusions:** Medical record review and nurse interviews were the most effective approaches to identify inpatients with new onset diarrhea. Considering that stool specimens were collected from only one-third of the inpatients with new onset diarrhea, it is likely that CDI is underdiagnosed and the burden of CDI may be underestimated. Results were used to inform the design of the CLOUD Louisville study, an ongoing, prospective population-based surveillance study to define the incidence of CDI among hospitalized adults in the United States.

**Figure 1. Study Flow Chart**

[Diagram showing the flow of the study with patient days, cases of new onset diarrhea, and stool sample testing]

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Abstract 1663

**Bacterial DNA promotes tau and beta-amyloid aggregation and is suggested as a novel therapeutic target for Alzheimer’s disease**

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**Background:** Different bacteria (including facultative intracellular parasites) and fungi have been detected in the cerebrospinal fluid and postmortem brains of individuals with Alzheimer’s disease (AD). We hypothesize that DNA from these microorganisms can act as an efficient promoter for protein misfolding and AD pathogenesis. In this study, we evaluated the effect of DNA extracted from diverse prokaryotic and eukaryotic cells in tau and beta-amyloid misfolding and aggregation. Our results show that DNA from various, unrelated gram-positive and gram-negative bacteria may play a previously overlooked role, in triggering the propagation of protein misfolding and AD pathogenesis.

**Materials/methods:** We used a protein misfolding cyclic amplification method, electron microscopy, sedimentation analysis and cell culture methods to evaluate the effects of DNA from different Gr+/- bacteria, fungi and human cells on Tau and beta-amyloid aggregation. 3xTG mouse model of AD was used to evaluate the effect of bacterial extracellular DNA destruction on tau and beta-amyloid deposition.

**Results:** The results showed that DNA from various (but not all) bacterial species significantly promoted tau and beta-amyloid aggregation. Thus, both ThT fluorescence and lag phase were over 5 times higher compared to untreated control (p<0.001). Conversely, addition of eukaryotic DNA, such as from yeast or human cells, had no effect in promoting tau aggregation. Data received indicate that the largest promoting effect was obtained in the presence of DNA from *Escherichia coli* and *Porphyromonas gingivalis*. Animal studies confirmed that the destruction of extracellular DNA decreased tau and beta-amyloid deposition in 3xTG mouse model.

**Conclusions:** Here we report the first evidence for the capacity of extracellular DNA from certain bacterial species to substantially promote tau and beta-amyloid misfolding, for the first time suggesting its role in AD.

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Validation of a machine learning model for prediction of mortality among patients with community-acquired pneumonia

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¹Treat Systems, Aalborg, Denmark, ²Hospital Universitario y Politécnico La Fe, Pneumology Department, Valencia, Spain, ³Hospital Clinic of Barcelona, Respiratory Institute, Barcelona, Spain, ⁴Center for Biomedical Research Network in Respiratory Diseases, Madrid, Spain

Background: Scoring systems such as the PSI and CURB-65 predict short-term mortality and are useful tools in guiding the diagnostic workup and initial therapy for patients with suspected community-acquired pneumonia (CAP). To be operational, scores should be able to be calculated automatically based on routine clinical data available in the electronic health record. We assess the generalizability of a previously developed mortality prediction score based on a machine-learned causal probabilistic network (CPN).

Materials/methods: Retrospective observational study. Data were collected prospectively for consecutive patients 18 years or older admitted with CAP at Hospital Universitario y Politécnico La Fe, Valencia, Spain from January 2012 to December 2018. Pneumonia diagnosis was based on a new radiological infiltrate with at least two compatible clinical symptoms. Exclusion criteria were admission in the previous 15 days, immunosuppressive treatment or human immunodeficiency virus (HIV+). The SepsisFinder CPN (SF) was extended to include common respiratory variables; respiratory rate, pH, PaO₂, SaO₂, supplement oxygen flow rate or FiO₂ where available, using data collected at the Hospital Clinic of Barcelona. Results of learning were described previously (O0421, ECCMID 2019).

The updated SF was used to calculate the probability of death within 30 days. Discriminatory performance for predicting 30-day mortality was assessed using the area under the ROC curve (AUC) and compared with commonly used clinical scores: PSI and CURB-65. Mortality rates were also compared for risk cut-offs defined for SF according to the percentiles associated with each PSI risk class.

Results: 1034 patients were included in the study. 30-day mortality was 4.2%. The AUC was 0.803 for SF, which did not differ significantly from that obtained for the training data (0.811). For the validation data, the AUC for SF was not significantly different to that for PSI: AUC=0.830 (p=0.42) or CURB-65: AUC=0.763 (p=0.20). When cut-offs were set to stratify the patients into groups of the same size as the PSI risk classes, the SF-selected groups had similar mortality, as shown in the table.

Conclusions: SepsisFinder shows potential for improving mortality prediction among patients with CAP using structured health data. Additional external validation studies should be conducted to support generalizability.

<table>
<thead>
<tr>
<th>PSI Risk Class</th>
<th>Patients, n (%)</th>
<th>30-day Mortality</th>
<th>SF – matched N patients, 30-day mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>113 (10.9)</td>
<td>1 (0.9)</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>2</td>
<td>186 (18.0)</td>
<td>0 (0.0)</td>
<td>2 (1.1)</td>
</tr>
<tr>
<td>3</td>
<td>300 (29.0)</td>
<td>5 (1.7)</td>
<td>6 (2.0)</td>
</tr>
<tr>
<td>4</td>
<td>337 (32.6)</td>
<td>16 (4.7)</td>
<td>12 (3.6)</td>
</tr>
<tr>
<td>5</td>
<td>98 (9.5)</td>
<td>21 (21.4)</td>
<td>22 (22.2)</td>
</tr>
</tbody>
</table>

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Development of a user-friendly clinical decision support system (TREAT-Essential) for antimicrobial stewardship

Mads Lause Mogensen*, Logan Ward, Peter Leutscher1,2, Henrik Carl Schønheyder4, Marc Ludwig5, Christoffer Madsen6, Steen Andreassen7

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Background: Clinical decision support systems (CDSS) for antimicrobial stewardship can reduce unnecessary antimicrobial use and change prescribing patterns away from resistance-promoting drugs without compromising coverage, thereby improving the quality of empiric therapy and reducing costs. Despite purported benefits, CDSS are faced with a number of barriers to successful implementation. Our aim was to overcome key barriers identified for the previously developed TREAT CDSS, which provided guidance for antimicrobial therapy. The barriers were incomplete integration into the clinical workflow and interface with IT systems, limited physician acceptance of the CDSS intervention and limited management commitment.

Materials/methods: We developed a new version of TREAT, TREAT-Essential. This involved a series of four workshops concerning functionality, user-friendliness, IT architecture and calibration/clinical relevance. Workshops were conducted with relevant stakeholders including specialists in infectious diseases, clinical microbiology, and IT management.

Results: The result of the workshops was a redesigned graphical user interface and simplified decision engine. By modifying the decision engine to take the physician’s diagnosis as an input rather than determining this from entered signs and symptoms, the data entry burden was reduced to a range of 5 clicks with a minimized loss of physician autonomy. Additional patient information is automatically extracted from the electronic health record and summarized as it pertains to the current infection. Keeping the detailed information out of view provided the clinician an easier overview, but easily displayed when required. Likewise, the recommended therapy is presented as a single recommendation, while probabilities for causative pathogens and expected coverage for the chosen treatment are hidden by default (Figure). The workshops also identified opportunities for deeper integration (thus less manual data input) and locations for activation within the current workflow with minimum interruption of current workflows.

Conclusions: Involving key stakeholders across disciplines [clinicians and IT developers] uncovered additional opportunities for improving the design that may have been missed with separate workshops. TREAT-Essential has improved integration into workflow and IT infrastructure and requires less user input. Whether this will improve clinical acceptance must be validated in clinical trials.
TREAT Essential is activated directly in the electronic prescription module at the time of prescribing.

1. Add background information

1a. (optional) Inspect summary of patient data

2. Select diagnosis

2a. Depending on diagnosis, severity, answer questions to confirm indication for antimicrobial therapy

3. View recommendation, select treatment (or no treatment), approve

3a. (optional) Inspect decision support output

User returns to the prescription module where the selected treatment is pre-filled. Audit-trail includes the recommendation and its basis for quality assurance.

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Abstract 1669

First report of the discovery of amurin peptides: direct lytic agents with broad activity against carbapenem-resistant Enterobacteriaceae, Acinetobacter, and Pseudomonas, including colistin-resistant strains

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Background: DLAs are new modalities in development to address antimicrobial resistance (AMR). Lysins, cell wall hydrolases enzymes, are at the vanguard of this field, with recently reported clinical Proof of Concept of the antistaphylococcal lysin, ex-ebacase to treat MRSA bacteremia. Here, we describe amurin peptides, previously unidentified bacteriophage-encoded DLAs, distinct from lysins, with bactericidal activity against a wide range of pathogenic Gram-negatives (GN) including CDC urgent threat/WHO critical priority pathogens: colistin-resistant CRE, CRA, and CRP.

Materials/methods: Amurin were identified in the viral genome database (NCBI) and synthesized by GenScript (Piscataway, NJ). In vitro characterization of bactericidal activity, antibiofilm effects, synergy with antibiotics, and resistance profile was conducted using standard methodologies. MICs were determined against MDR/XDR clinical isolates (n=188) from 5 CDC Antibiotic Resistance Panels.

Results: We identified a novel class of DLAs comprised of amurin peptides with antimicrobial activity against all GN ESKAPE pathogens, as well as E. coli, P. mirabilis, A. xylosidans, and S. maltophilia. Hallmark features of amurins include rapid bactericidality (>3-log10 kill), synergy with >13 antibiotics, antibiofilm activity (MBEC values of ≤2 µg/mL), and no detectable resistance in spontaneous. Strikingly, an MIC90 of 1 µg/mL (range=0.125-2 µg/mL) was demonstrated for several peptides against all CDC resistance panel isolates, including XDR strains of P. aeruginosa, K. pneumoniae, E. cloacae, A. baumannii, and E. coli with both carbapenem and colistin resistance (examples in Table 1).

Table 1: MIC (µg/mL) analysis of amurin peptides [AM1-3] and comparator antibiotics against select colistin-resistant CRE, CRA and CRP isolates from CDC resistance panel isolates.

<table>
<thead>
<tr>
<th>Strain</th>
<th>Strain/Resistance type</th>
<th>AM1</th>
<th>AM2</th>
<th>AM3</th>
<th>AMI</th>
<th>CIP</th>
<th>COL</th>
<th>LEV</th>
<th>MEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>K. pneumoniae AR522 (CRE)</td>
<td>0.5 0.5 0.5</td>
<td>8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
</tr>
<tr>
<td>A. baumannii AR303 (CRA)</td>
<td>1 1 0.5</td>
<td>&gt;64</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
</tr>
<tr>
<td>P. aeruginosa AR239 (CRP)</td>
<td>1 0.5 0.5</td>
<td>&gt;64</td>
<td>8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
</tr>
</tbody>
</table>

Key: AMI, amikacin; CIP, ciprofloxacin; COL, colistin; LEV, levofloxacin; MEM, meropenem

Conclusions: Newly discovered amurin peptides are highly active DLAs against CRE, CRA, and CRP including colistin resistant strains, and are potential "game changers" in the efforts to combat AMR and treat pathogens for which there are no current therapeutic options.

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Abstract 1671

**Imported malaria: overview of the diagnosed and suspected cases of malaria in a Spanish city (15 years of experience)**

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**Background:** In our city, paludism is the first imported tropical disease. It is suffered all about in visiting friends and relatives (VFR). We describe 287 malaria cases and 367 suspected but not confirmed cases of malaria attended in the last 15 years.

**Materials/methods:** It is a retrospective, comparative and populational study of all malaria cases and not confirmed cases diagnosed during 2004-2018 period. We have used media or median values, chi square test and median test to describe and to compare both groups.

**Results:**

Malaria group: 287 cases of malaria were diagnosed. 72.6% VFR, 10.8% travelers VFR, 15.6% immigrants, 0.3% travelers. September (16%) and August (13.2%) were the two most frequent periods of diagnosis in front of March (2.1%) and April (3.5%). 53% were men. 47.6% came from Guinea Ecuatorial, 45.1% from Nigeria. *P. falciparum* 89.6%, *P. vivax* 1.4%, *P. ovale* 3.1%, *P. malariae* 1% mixed infections 2.4%.

Median values: age 33 years, days in risk areas 30, days in Spain to diagnosis 7, days with symptoms to diagnosis 4, Leucocytes 5450/mcl, Plaquets 109000/mcl, Hemoglobin 12.2 g/dl, Bilirrubin 2 mg/dl, C reactive protein (CRP) 9.1 mg/dl, LDH 281 mg/dl, and amount of parasitation 1%. Of all patients, 73.6% had thrombopenia, 52.2% had anemia and 95.7% had high values of CRP. 14.9% had splenomegaly, 94.8% fever, 50.3% headache, 51.4% digestive symptoms.

14 cases (4.9%) had submicroscopic malaria, the rest of them were diagnosed with antigenic test or gross gout. 11 patients (3.8%) needed an intensive care unit treatment. 14 cases were on pregnant (10.6% of all women). 12 cases were HIV positive (2 false positive 6 were new diagnosis of HIV infection, and 4 were known HIV positive. Median of CD4 364/mcl, and 75% under 500/mcl CD4, and 30% under 250/mcl CD4. 18 (6.3%) patients were diabetics.

Of all patients only 4.9% did appropriate prophylaxis. One death in all series.

Comparative values with confirmed and not confirmed Malaria (Figure).

**Conclusions:** Malaria is a prevalent imported infectious diseases. There are important prevalent groups as HIV, pregnant, and diabetic patients. Different clinical, and analytic characteristics could help us to diagnose risk patients with and without malaria.

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Abstract 1674

**Georeferencing patients infected by Gram-negative bacteria producing extended-spectrum beta-lactamase, Pereira city, Colombia, 2012-2017**

Julián Andres Hoyos Pulgarín*, Deving Arias², Alexander Alzate³, Germán Moreno³, Juan Olaya³, Isabella Cortés³, Camila Vargas³

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**Background:** Knowledge about the geographic distribution patterns of resistant Gram Negative Bacteria (GNB) is potentially valuable information that could help establish ecological factors associated with transmission and resistance acquisition in the community level. The aim of this study was to establish the existence of patterns of geographic distribution of patients with positive isolation for gram-negative bacilli resistant to third-generation cephalosporins with phenotype producing Extended Spectrum Beta lactamase (ESBL), in the city of Pereira, Colombia. Study period: 2012 to 2017.

**Materials/methods:** A georeferencing study was carried out. We took the database of a tertiary Hospital and a reference laboratory in the city on the isolates with phenotypic pattern of ESBL production. Ethical endorsement was obtained from the bioethics committee of the Universidad Tecnológica de Pereira Pereira. The georeferencing was done with the KOSMO GIS and QGIS open access programs.

**Results:** We obtained 1246 records of subjects with GNB ESBL infection. After applying the inclusion and exclusion criteria, the geographical distribution of 415 subjects with isolation from the community, from Pereira, was established (Figure 1). The highest concentration of events was found in the San Joaquin, Perla del Otún, Río Otún, Centro, Oriente, Villavicencio, Boston and Universidad districts.

**Conclusions:** The geographic distribution patterns of resistant GNB infections with ESBL producing phenotype are shown. The existence of local transmission foci is proposed mainly in the central and eastern areas of the city. We highlight the importance of controlling the sources of microbial resistance not only at the hospital level but also at different actors in the community.

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Abstracts 2020

Abstract 1675

Low horizontal transfer rate of mcr-8 may constrain the spread of mcr-8 genes
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Background: Colistin has been regarded as a highest priority important antimicrobial for human medicine by World Health Organisation since 2017. Plasmid-borne mcr- genes are one of the main contributors for the success of the global spread of colistin resistance bacterial pathogens. This study aims to characterize a novel plasmid harbouring a mcr-8 gene in Klebsiella pneumoniae isolated from blowflies in Thailand, and examine the fitness effect of mcr-8 gene on plasmid maintenance and competitiveness.

Materials/methods: Hybrid assembly of Illumina and Oxford Nanopore sequencing was performed to identify a novel mcr-8-carrying plasmid and strain. The transferability of both co-existed mcr-1 and mcr-8 plasmids were investigated by conjugation experiments and qPCR. To assess the fitness effect of mcr-8 expression on bacterial growth, plasmid constructs and growth assays were conducted. Furthermore, the competition and persistence between mcr-1 and mcr-8 were investigated via 30-day passage experiments.

Results: The mcr-8 gene was identified in previous reported 17 mcr-1-positive K. pneumoniae strains isolated from blowflies in Thailand. The mcr-8 gene is located in an IncFII:FiB plasmid (pKP100-mcr8) that co-harboured with qnrS1, tet(A), blaTEM-1b and ampC. pKP100-mcr8 shares low sequence similarity (less than 60% coverage) of other plasmids in the NCBI database. The plasmid pKP100-mcr8 can be transferred from K. pneumoniae to Escherichia coli J53Azr, with significantly lower transfer frequency (as low as 3.4x10^-13) than that of mcr-1-IncX4 plasmid co-existed in the K. pneumoniae strains (approx.1x10^-4). The expression of mcr-8 did not affect bacterial growth rate, suggesting that there is no significant fitness burden conferred by the expression of mcr-8 gene. Furthermore, both mcr-1 and mcr-8 are very stable in an in-vitro competition model over a period of 330 generations.

Conclusions: The emergence of this newly identified mcr-8.1-positive plasmid from blowflies raise a great concern to our public health. Our data show that mcr-8 has fitness advantage and ability of maintenance and persistence, however, when comparing to its co-existed mcr-1 gene, its rate of horizontal transfer is relatively low, which explain the low occurrence of mcr-8 in the global level. It further suggests that horizontal transfer is a key factor for the global dissemination of AMR genes.

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ESwab collection device allows both detection of human papilloma virus with molecular assays and culture with WASP automation

Raluca Gatej, Mihaela Giuca, Sabrina Constanda*, Roxana Musat, Mihaela Dinescu

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Background: A multitasking specimen collection device that supports different testing methods is an asset for a centralized microbiology laboratory. Copan ESwab™ kit, consists of a FLOQSwab® and a tube with 1 ml Amies liquid medium for the collection of clinical specimens, resulting in a homogeneous sample suspension suitable for gram smear, antigens detection, bacteria culture, and molecular assays for the detection of microbial infectious agents. The objective of this study was to validate the performance of genital specimens collected with ESwab™ for the detection HPV genotypes with the Roche Linear Array and the detection of bacteria culture processed on the WASP™ automated system.

Materials/methods: In this study were analysed 427 genital samples, [383 females, 44 males] received in the SANADOR Molecular Laboratory from Gynecology, Dermatology and Urology Departments for HPV genotyping. ESwab™ codes 490CE for females and 491CE for males were used for sample collection. Nucleic acids were extracted from 200 ul of each ESwab™ sample using the High Pure PCR Template Preparation kit. Fifty µL of the extracted DNA were used for PCR amplification and analyzed for HPV genotyping with Roche Linear Array assay. HPV genotypes were visualised after reverse hybridisation in a Beeblot automated system. All ESwab™ samples were processed on the WASP™ for bacteria culture on Columbia and Sabourand agar plates.

Results: In the 427 samples investigated, 241 were negative and 186 were HPV positives. At least one HPV genotype was detected in 44% of patient’s samples. Most prominent HPV HR, present, in single or multiple co-infections, were HPV 16 [44/186], 51 [35/186], 52 [27/186], 31 [25/186], 39 [23/186], 58 [19/186], 18 [18/186], 35 [12/186]. HPV53 was most prominent [38/186] for the possible HR and 54 [33/186] for the LR. In the males 20/44 HR genotypes, and 10/44 possible HR were detected. In the 241 HPV negative samples, culture detected 13 Candida spp, 10 Streptococcus B, 4 Candida spp+Streptococcus B and 1 E. coli.

Conclusions: Data generated in this study demonstrated that ESwab™ is a versatile collection device that can be used for both the detection of HPV genotypes with molecular assay and bacteria culture with WASP™ automation.

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Abstract 1678

**Decreasing reporting time of blood cultures by workflow optimisation with the WASPLab system**

Sylvie D’Haese*, Karolien Claeys, Marc Van Ranst, Katrien Lagrou, Melissa Depypere, Kirsten Jeuris, Katty Standaert, Ann Verdonck, Stefanie Desmet

1UZ Leuven, Leuven, Belgium

**Background:** One of the goals of lab automation is fast reporting to clinicians while maintaining high quality and efficiency. We describe the impact of WASPLab® and consecutive extension of the working hours of lab technicians in the bacteriology laboratory on reporting time of identification (ID) and antimicrobial susceptibility testing (AST) results of blood cultures (BC).

**Materials/methods:** At the University Hospitals Leuven, positive BCs are streaked manually on at least a blood and MacConkey agar and incubated afterwards. Based on tracking in the laboratory information system, the time from BC positivity to ID and AST results reporting to the clinician were calculated. Three 5-months periods were compared: period 1 with conventional incubation and reading at 8.30h, 14h and 17h; period 2 with WASPLab® incubation and reading at 8.30h, 14h and 17h of BCs positive during the day [same staff and working hours as period 1] and period 3 with WASPLab® incubation of all plates and reading at 8.30h, 14h, 17h and 21h [extended working hours]. Plates are photographed in WASPLab® at 4, 6, 10, 16, 24 and 48 hours of incubation. ID is performed with MALDI-TOF MS and AST with Vitek2® or disk diffusion.

**Results:** Median time between BC positivity and reporting of ID decreased from 19h50min in period 1 to 17h41min and 12h55min in respectively period 2 and period 3 (Table). The percentage of IDs reported within 8 hours increased from 0.7% to 7.2% and 16.5% in the consecutive periods. In period 3, 83.5% of IDs were reported within 24 hours compared to 63.4% in period 1. Also a decrease in median time between BC positivity and reporting of AST was seen from 40h32min in period 1 to 37h07min and 33h17min in respectively period 2 and 3.

**Conclusions:** Introduction of WASPLab® without change in staff and working hours resulted in a decreased reporting time of blood cultures. Extending the working hours of the bacteriology lab from 8:30-17:30 to 7:00-23:00, made it possible to further optimize the use of WASPLab®, which altogether resulted in a decrease of median reporting time of ID and AST of 7 hours compared to conventional workup.

**Table 1: Comparison of time to results for identification (ID) and antimicrobial susceptibility testing (AST) of blood culture isolates in periods 1 (conventional incubation and reading), period 2 (use of WASPLab® system) and period 3 (use of WASPLab® system with extended opening hours) for incubation and reading of agar plates.**

<table>
<thead>
<tr>
<th>Method of incubation and reading of BC</th>
<th>Period 1 June – October 2017</th>
<th>Period 2 June – October 2018</th>
<th>Period 3 June – October 2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>Working hours of technician in bacteriology lab</td>
<td>8.30h - 17.30h</td>
<td>8.30h - 17.30h</td>
<td>7h - 22h</td>
</tr>
<tr>
<td>Reading moments of the plates</td>
<td>4905</td>
<td>4310</td>
<td>4269</td>
</tr>
<tr>
<td>Number of positive BC</td>
<td>9405</td>
<td>8310</td>
<td>7429</td>
</tr>
<tr>
<td>Reporting of ID results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Median time between BC positivity and reporting ID</td>
<td>19h 50min</td>
<td>17h 41min</td>
<td>12h 55min</td>
</tr>
<tr>
<td>- Percentage of samples reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Within 8 hours</td>
<td>0.7%</td>
<td>7.2%</td>
<td>16.5%</td>
</tr>
<tr>
<td>- Within 12 hours</td>
<td>10.0%</td>
<td>20.1%</td>
<td>40.2%</td>
</tr>
<tr>
<td>- Within 16 hours</td>
<td>33.6%</td>
<td>43.9%</td>
<td>65.3%</td>
</tr>
<tr>
<td>- Within 24 hours</td>
<td>63.4%</td>
<td>70.9%</td>
<td>83.5%</td>
</tr>
<tr>
<td>Reporting of AST results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Median time between BC positivity and reporting AST</td>
<td>46h 32min</td>
<td>37h 07min</td>
<td>33h 17min</td>
</tr>
<tr>
<td>- Percentage of samples reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Within 24 hours</td>
<td>3.0%</td>
<td>7.7%</td>
<td>15.1%</td>
</tr>
<tr>
<td>- Within 36 hours</td>
<td>38.2%</td>
<td>47.4%</td>
<td>50.3%</td>
</tr>
<tr>
<td>- Within 48 hours</td>
<td>70.7%</td>
<td>72.9%</td>
<td>78.5%</td>
</tr>
</tbody>
</table>

**Presenter email address:** sylvie.dhaese@uzleuven.be
Abstract 1679

First evidence of systemic efficacy of a pathogen-targeted, engineered lysin (GN-370) against carbapenem-resistant Pseudomonas aeruginosa in a rabbit pneumonia model

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Background: Lysins are direct lytic agents which have shown efficacy against gram-positive bacteria in vivo and in a recent Phase 2 clinical study in MRSA bacteremia. However, lysins were considered to be inactive against gram-negative (GNs) pathogens when administered systemically in vivo. GN-370, a novel engineered lysin, was evaluated as systemic treatment for P. aeruginosa alone or in addition to meropenem, in a rabbit pneumonia model.

Materials/methods: Pneumonia was induced in New Zealand White rabbits by endotracheal inoculation with PA20 (3x10⁹ CFU). At 6h post-infection, rabbits were randomized to receive: no therapy (pretreatment); vehicle alone; meropenem alone (20 mg/kg, 3 doses x q8h, subcutaneously); GN-370 alone (3 or 10 mg/kg, single intravenous dose); or GN-370 plus meropenem at the same doses. Lung, kidney, and spleen tissues were collected 24h after the last dose of meropenem, were quantitatively cultured (log₁₀ cfu/gram of tissue; and mean counts (+/- SD)) and compared in the various groups.

Results: GN-370 was well tolerated. All GN-370-treated animals survived until end of study, whereas only ~40% of vehicle-controls survived. In animals receiving either meropenem or GN-370 alone, the mean bacterial lung counts decreased by ~1.5-2-log₁₀ CFU/g vs pretreatment or vehicle-treated controls, p ≤ 0.0016. GN-370 (10 mg/kg) in addition to meropenem was synergistic, with bacterial counts in all target tissues decreasing by an additional ~2 log₁₀ CFU/g vs meropenem or GN-370 alone (p ≤ 0.02).

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Lungs (log₁₀ CFU/g)</th>
<th>Kidney (log₁₀ CFU/g)</th>
<th>Spleen (log₁₀ CFU/g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6hr pretreatment control (n=4)</td>
<td>7.77±0.55</td>
<td>4.13±0.59</td>
<td>4.57±0.70</td>
</tr>
<tr>
<td>Vehicle control (n=5)</td>
<td>7.86±0.62</td>
<td>6.41±0.90</td>
<td>6.39±0.59</td>
</tr>
<tr>
<td>Meropenem 20mg/kg, SC X 3doses every 8hrs. (n=6)</td>
<td>5.88±0.98</td>
<td>3.92±0.63</td>
<td>3.62±0.21</td>
</tr>
<tr>
<td>GN-370 (3mg/kg, IV, once) (n=8)</td>
<td>6.36±1.04</td>
<td>5.06±1.05</td>
<td>5.23±1.25</td>
</tr>
<tr>
<td>GN-370 (3mg/kg) + Meropenem (n=9)</td>
<td>6.11±1.17</td>
<td>3.90±1.06</td>
<td>4.16±0.98</td>
</tr>
<tr>
<td>GN-370 (10mg/kg, IV, once) (n=6)</td>
<td>6.08±1.47</td>
<td>3.46±0.78</td>
<td>3.76±0.44</td>
</tr>
<tr>
<td>GN-370 (10mg/kg) + Meropenem (n=8)</td>
<td>3.97±1.62</td>
<td>1.99±1.00</td>
<td>1.89±1.01</td>
</tr>
</tbody>
</table>

Conclusions: These data represent the first evidence that GN-targeted lysins can be engineered to result in systemic efficacy in vivo. GN-370 was well tolerated and effective against P. aeruginosa when administered intravenously alone, and had marked synergy with meropenem in the rabbit pneumonia model. P. aeruginosa causes serious, life-threatening and ever-increasing antibiotic-resistant invasive infections, especially nosocomially. This study provides in vivo proof-of-concept for the further development of GN-370 to treat invasive P. aeruginosa infections. Moreover, these data represent a key proof of principle for GN-targeted lysins as new modalities to combat antimicrobial resistance in such pathogens.

Presenter email address: dlehoux@contrafect.com
Total knee and hip arthroplasty after septic arthritis: retrospective analysis of 53 cases managed in a reference centre for bone and joint infections

Elodie Portier1,2, Valérie Zeller*1,2, Sophie Godot1,2, Y. Kerroumi1,4, Beate Heym1,5, Vanina Meyssonnier1,3, Simon Marmor1,4, Pascal Chazerain1,2


Background: Arthroplasty after or during treatment of septic arthritis (SA) raises diagnostic and therapeutic questions. The objective was to describe characteristics of patients undergoing total knee (TKA) or hip arthroplasty (THA) after SA, results of cultures taken at implantation, management of antibiotic therapy and outcome after arthroplasty.

Materials/methods: Retrospective monocentric study from January 2005 to May 2019, including all the patients undergoing TKA or THA with a history or SA or current SA on the same joint.

Results: 51 patients, 31 men (61%), with a median age of 64 years, operated on 53 joints (32 knees, 21 hips) were included. SA occurred after joint infiltration (n=13), surgery (n=8), hematogenous spread (n=12), from a contiguous source (n=9) or was of undetermined origin (n=11). Median time between SA and arthroplasty was 31 [0-832] weeks. It was ≤2 years in 47 and ≤6 months in 21 cases. Arthroplasty was performed in 6 cases while the patient was still on SA treatment. Synovectomy and one-stage arthroplasty was carried out in 47 cases, two-stage arthroplasty in 8 cases. Intraoperative cultures were positive in 8 cases (15%) with the same microorganism in 3, a different one in 4, and SA was diagnosed on these cultures in one case. No antibiotic prophylaxis was administered, but all the patients received postoperative antibiotic therapy, targeting the SA microorganism and the skin flora. Median duration of treatment was 10 days, if cultures remained sterile, 82 days, if they confirmed an infection. To date, 32 patients (60%) were followed for ≥ 12 months. No SA relapse was observed. Five patients (3 TKA, 2 THA) developed a prosthetic joint infection with a different microorganism 5 months to 7 years after arthroplasty.

Conclusions: Arthroplasty may be considered after or during SA, even within a short period of time. Intraoperative cultures were positive in 15% of the cases. One-stage arthroplasty was performed if a thorough synovectomy is realized, intraoperative samples are taken systematically, and an antibiotic therapy is administered until the cultures results are available. We observed no SA relapse, but new prosthetic joint infections occurred.

Presenter email address: vzeller@hopital-dcss.org
Abstract 1681

Clinical utility of syndromic meningitis/encephalitis testing in children
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Background: Rapid diagnosis and treatment of central nervous system infections is critical. The BioFire FilmArray Meningitis/Encephalitis Panel (FA-M/E) is a molecular syndromic test that can rapidly detect 14 pathogens in cerebrospinal fluid (CSF). Here, we sought to analyze the clinical utilization and impact of FA-M/E in children.

Materials/methods: Between June 2016-December 2017, FA-M/E was tested on 449 patients [Test group] and 412 patients received no FA-M/E testing [Control group]. Chart abstraction was conducted to compare patient medical history, antimicrobial course, and length of stay (LOS).

Results: FA-M/E testing in the Test group detected 62/449 (14%; 14 bacteria, 48 virus) targets compared to 8/412 (2%; 5 bacteria, 3 virus) in the Control group. The top three most common targets detected by FA-M/E were Enterovirus (n=25), HHV-6 (n=14), and Streptococcus agalactiae (n=7). The number of immunocompetent patients were slightly lower in the Test group compared to Control (57.9% vs 66.5%). The median time to discontinuation (TTD) of key antibiotics in patients with negative test results was shorter by 21.8 hours [32.7 vs 54.5 hrs, P=0.0002] in Test group. These drugs include gentamicin [32.2 vs 54.4 hrs, P=0.03], ampicillin [34.4 vs 54.4 hrs, P=0.0002], cefepime [28.9 vs 55 hrs, P=0.002], and meropenem [154 vs 215 hrs, P=0.52]. For a positive viral result, the median TTD of antibiotics in the Test group was 34.7 hours from time of test ordered. Results were not compared to Control group due to the low number of viral positives. Patients previously not placed on antibiotic therapy but tested positive for bacterial target were started on appropriate antibiotics 69 hours earlier in the Test group [14.5 vs 83.5 hrs, P=0.2]. Rapid FA-M/E results in the Test group resulted in a decrease in LOS by 4 days [2.7 vs 6.7 days, P<0.001] in positive patients. In the Test group, patients positive for viral targets were discharged 11.2 days [2.6 vs 13.8 days, P=0.002] earlier than those positive for bacterial targets.

Conclusions: FA-M/E significantly reduced time to identification of M/E pathogens. Use of FA-M/E was associated with accelerated optimization of therapy and decreased LOS in pediatric patients.

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Rapid molecular diagnosis of Neisseria meningitidis, Streptococcus pneumoniae, Listeria monocytogenes, Enterovirus and parechovirus from blood in patients of the pediatric emergency department of a tertiary hospital

Mikel Urrutikoetxea-Gutierrez*, David Montero Vazquez, Manuel Imaz Perez, Estibaliz Ugalde Zarraga, Elisa Garrote Llanos, Gonzalez Hermosa Andres, José Luis Diaz De Tuesta

1Basurto University Hospital (Microbiology Department), Osakidetza, Bilbao, Spain, 2Basurto University Hospital (Pediatric Department), Osakidetza, Bilbao, Spain

Background: Early microbiological diagnostic of febrile illness in children under 3 years may be challenging, especially when no infectious focus is identified. New molecular techniques allow us to detect the most common pathogens in short time. The objective of this study was to evaluate the performance of molecular detection of Neisseria meningitidis, Streptococcus pneumoniae, Listeria monocytogenes, Enterovirus and Parechovirus from blood in patients of the pediatric emergency department of a tertiary hospital.

Materials/methods: We selected children under 3 years with fever (≥38ºC) without focus attending to the pediatric emergency department from January to October 2019. In addition to the routine analyses a 5ml whole blood tube was collected. Nucleic acids were extracted on MagNaPure® system under standard conditions and two different Progenie-Molecular® assays (bacterial and viral) were conducted on the SmartCycler®. We compared the results of the bacterial PCR to the gold standard blood culture and to the clinical manifestations

Results: 202 patients (123 male 79 female) were included on the study with a mean age of 0.96 years. There were 26 patients with positive samples (12.9%).

<table>
<thead>
<tr>
<th>Total patients</th>
<th>Streptococcus pneumoniae</th>
<th>Neisseria meningitidis</th>
<th>Listeria monocytogenes</th>
<th>Enterovirus</th>
<th>Parechovirus</th>
</tr>
</thead>
<tbody>
<tr>
<td>202</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>12</td>
<td>8</td>
</tr>
</tbody>
</table>

Only one patient with a positive assay for Streptococcus pneumoniae had a positive blood culture, one was contaminated, and the rest were negative. Three were clinically significant and two were doubtful about having also another infectious cause. There was no previous record of antibiotic consumption. All of them but one were vaccinated. The patient with a positive Neisseria meningitidis assay had also a positive blood culture. There were no positive blood cultures for the detected bacterial agents in the patients with negative bacterial assay or positive blood cultures when any of the viral targets were positive.

Conclusions: This diagnostic approach may be useful in this kind of patients when combined with the standard procedures, especially when an early viral diagnosis, which were almost a 10% in our series, may reduce the antibiotic burden at childhood. This molecular assay may outperform the blood culture particularly if the sample is from the early stages of the illness.

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Abstract 1684

A retrospective study of pyogenic liver abscess caused by *Klebsiella pneumoniae* as a primary pathogen: computed tomography and clinical differentiation

Shinhee Hong¹, Young-Rock Jang*¹, Joong Sik Eom², Yong Kyun Cho¹

¹Gachon University Gil Medical Center, Incheon, South Korea

**Background:** The incidence of *Klebsiella pneumoniae* pyogenic liver abscesses (KP-PLA) is increasing. However, its diagnosis and treatment are often delayed, leading to complications. To retrospectively compare computed tomographic (CT) features of KP-PLAs with those of abscesses caused by other bacterial pathogens (non-KP-PLA) and to further identify prognostic factors for PLA.

**Materials/methods:** Data of 219 study patients including clinical presentation, comorbid conditions, metastatic infection, treatment duration, and mortality were retrospectively collated. CT characteristics of abscesses were recorded. Etiology was established by pus and/or blood culture. The differentiating CT features and clinical findings were compared between the monomicrobial KP-PLA and non-KP-PLA groups. Furthermore, factors related to in-hospital case fatality were analyzed.

**Results:** Our study identified thin-walled abscesses, absent rim enhancement, metastatic infection, and absence of underlying biliary tract disease as significant predictors of KP-PLA. With 3/4 criteria applied in combination, a specificity of 96.5% was achieved for KP-PLA diagnosis. The in-hospital mortality rate was 3.7%. In present study, multivariate analysis revealed that diabetes mellitus (P=.031), multiple abscesses (P=.026), internal gas bubbles (P=.041), metastatic infection (P=.004), and septic shock (P=.002) were significantly associated with mortality.

**Conclusions:** Our study suggested that thin-walled abscess, metastatic infection, absence of rim enhancement, and absence of underlying biliary tract disease are potentially useful CT findings for early KP-PLA diagnosis.

**Presenter email address:** ilmagnifico112@gmail.com
Abstract 1685

Comparing outcomes and clinical characteristics associated with carbapenemase-producing and non-carbapenemase-producing carbapenem-resistant Enterobacteriaceae bacteraemia

Michael Hovan*, Navaneeth Narayanan†, Vanessa Cedarbaum‡, Tanaya Bhowmick§, Thomas Kirn¶

*Rutgers Robert Wood Johnson Medical School, New Brunswick, United States

Background: Carbapenem-Resistant Enterobacteriaceae (CRE) bacteremia is associated with significant morbidity and mortality. CRE are classified as either carbapenemase-producing (CP-CRE) or non-carbapenemase-producing (non-CP-CRE). There are limited studies comparing the outcomes and characteristics of patients with each type of infection.

Materials/methods: We performed a chart review of 146 patients with CRE bacteremia from January 2010-July 2019. CRE was defined using the current CDC definition. The modified carbapenem inactivation method was performed on each CRE isolate to determine carbapenemase production. Electronic medical records were reviewed to obtain clinical characteristics and outcomes including prior antibiotic use, comorbidities, prior location, treatment, hospital course, and outcomes including in-hospital mortality, recurrence of bacteremia, and readmission.

Results: Of 145 cases included in our analysis, 87/145 (60%) were CP-CRE and 58/145 (40%) were non-CP-CRE. Patients with CP-CRE had a higher median Pitt Bacteremia score (4 vs. 2, p=<.001), were more likely to have been admitted from a healthcare facility (49.4% vs. 27.5%, p=.008), and to have received antibiotics in the 90 days prior to bacteremia onset (89.7% vs. 72.4%, p=.007). Patients with CP-CRE were less likely to receive active empiric therapy (19.54% vs. 51.72%, p=<.005) and active targeted therapy (74.4% vs. 86.2%, p=.08). Non-CP-CRE was associated with a 2.6 times higher hazard of death within 30 days compared to CP-CRE (hazard ratio, 2.6; 95% CI, 1.4, 4.9). Additional outcomes data are presented in Table 1.

Table 1. Outcomes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non-CP-CRE (n=58)</th>
<th>CP-CRE (n=87)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Survival until hospital discharge</td>
<td>38 (65.5%)</td>
<td>51 (58.6%)</td>
<td>0.403</td>
</tr>
<tr>
<td>Survival until 14 days after bacteremia</td>
<td>39 (67.2%)</td>
<td>66 (75.9%)</td>
<td>0.255</td>
</tr>
<tr>
<td>Survival until 30 days after bacteremia</td>
<td>39 (67.2%)</td>
<td>54 (62.1%)</td>
<td>0.525</td>
</tr>
<tr>
<td>Time to death, days</td>
<td>5 (1-9.5)</td>
<td>12 (2-20)</td>
<td>0.029</td>
</tr>
<tr>
<td>Time to discharge alive, days</td>
<td>8.5 (5-17)</td>
<td>16 (9-29)</td>
<td>0.005</td>
</tr>
<tr>
<td>LOS, days</td>
<td>13.5 (7-43)</td>
<td>25 (15-52)</td>
<td>0.009</td>
</tr>
<tr>
<td>LOS post positive blood cx, days</td>
<td>7.5 (4-13)</td>
<td>14 (8-25)</td>
<td>0.002</td>
</tr>
<tr>
<td>Recurrence of CRE BSI within 90 days</td>
<td>2 (5%)</td>
<td>8 (13.8%)</td>
<td>0.158</td>
</tr>
</tbody>
</table>

Conclusions: Patients with CP-CRE were more likely to have exposure to healthcare facilities and antibiotics, have more severe illness at bacteremia onset and were less likely to receive active therapy. There was no significant difference in mortality between groups but non-CP-CRE was associated with a higher likelihood of death within 30 days.

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Abstract 1693

Imipenem/relebactam pharmacokinetic/pharmacodynamic analyses from an in vivo neutropenic murine thigh infection model

Munjal Patel1*, Naveen Daryani1, Hwa-Ping Feng1, David W. Hilbert1, Maria J. Melchers2, Eleftheria Mavridou1, Katherine Young1, Matthew L. Rizk1

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Background: Relebactam is a small molecule beta-lactamase inhibitor. The combination of relebactam with imipenem [in vitro] and imipenem/cilastatin [in vivo] showed significant antibacterial activity against imipenem nonsusceptible strains. We conducted pharmacokinetics/pharmacodynamics (PK/PD) analyses utilizing data from an in vivo neutropenic murine thigh infection model to derive relebactam PK/PD targets associated with stasis, 1-log kill and 2-log kill.

Materials/methods: Previously conducted PK/PD murine thigh studies were used for generation of the pooled PK/PD dataset. This dataset was obtained using two isolates of Klebsiella pneumoniae and four isolates of Pseudomonas aeruginosa at imipenem doses within two-fold of the humanized dose with varying total daily doses and dosing frequency of relebactam. Correlation analyses using the pharmacokinetic (PK) exposure and response (change in log_{10} colony-forming unit at 24 hours post-dose) was plotted against fAUC, fAUC/MIC, fCmax, fCmax/MIC, %fT>C at 1, 2 and 4 mg/L for both Pseudomonas aeruginosa and Klebsiella pneumoniae. Imipenem MICs in the presence of 4 mg/L of relebactam were used to derive the fAUC/MIC and fCmax/MIC for each strain. An Emax model with Hill coefficient was used to fit the data. Stasis, 1-log kill, and 2-log kill PK/PD targets were derived from this model.

Results: The PK/PD parameter fAUC/MIC was best correlated with response in this analysis. The derived stasis, 1-log kill, and 2-log kill fAUC/MIC PK/PD targets for Pseudomonas aeruginosa were 3.3, 4.3 and 7.0 respectively. This 2-log kill PK/PD target is consistent with previous analyses in an in vitro hollow fiber infection model.

Conclusions: PK/PD analyses using pooled data from four isolates of Pseudomonas aeruginosa and two isolates of Klebsiella pneumoniae demonstrated that fAUC/MIC is the best PK/PD driver for relebactam. The derived 2-log kill target can be used for dose justification and probability of target attainment (PTA) assessments for the fixed dose combination of imipenem/cilastatin/relebactam.

Figure. PK/PD Relationship of relebactam in the neutropenic mouse thigh infection model at imipenem 8 mg/kg and 15.9 mg/kg for Pseudomonas aeruginosa

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Abstract 1697

**NK cell deficiency and cryptococcosis**


*Hôpitaux Civils de Colmar, Colmar, France, **Hopital de la Conception, Marseille, France, #University of Calgary, Calgary, Canada, AP-HM Timone, Marseille, France, #immunopole, Marseille, France*

**Background:** Human NK deficiency (NKD) is a rare primary immunodeficiency, characterized by less than 50 NK cells and < 1% of circulating lymphocytes and usually associated with *Herpesviridae* infections. We described a new phenotype of NK deficiency in a healthy 28-year-old man characterized by a predominant Dim NKD associated with a pulmonary cryptococcosis.

**Materials/methods:** The patient was admitted in December 2008 for a nonproductive cough and the discovery of non-calcified nodules on chest X rays. The patient had no medical history. He had no fever and medical examination was normal. The standard biological results were in the normal values including a normal leukocyte count and a CRP of 2mg/l. A broncho-alveolar lavage revealed the presence of many *Cryptococcus neoformans var. grubii* (serotype A). Cryptococcal antigenemia and/or fungal culture were negative in Cerebrospinal fluid, blood and urine. The patient was successfully treated by fluconazole 400mg per day for 12 months. The patient remains healthy 11 years after the diagnosis without relapse or new infection.

**Results:** Immune system evaluation revealed an isolated NKD with $7/mm^3$ [0.3%] CD3⁻CD56⁺ natural killer (NK), and $1943/mm^3$ [88%] CD3⁺ T cells stable during the 10 years follow up. Related to the NKD two adaptative immunological abnormalities were noted 1) an in vitro impaired lymphocyte proliferation assays after challenge with *Cryptococcus* antigens and 2) a stable TCD8 Vβ14 expanded population accounting for 50% of circulating TCD8 lymphocytes (figure). Cryptococcosis was therefore linked to a complex immunodeficiency via a lack of direct killing of *Cryptococcus neoformans* by NK cells, an inability to mount a Th1 response normally shaped by NK cells and a possible inhibition of anti-*Cryptococcus* TH1 lymphocytes response in relation to the huge TCD8 Vβ14 clonotype. This case illustrates the central role of NK cells in immunity against *Cryptococcus* and confirms the tight interplay between NK cells and adaptative immunity via TH1 modulation and regulation of CD8 expansion.

**Conclusions:** Two practical medical conclusions can be drawn: the need to perform NK cells determination in cases of idiothemic cryptococcosis, and the need to screen the Vβ repertoire in cases of NKD in other to better understand NKD.

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Abstract 1699

**One day detection of live *Mycobacterium tuberculosis* from sputum by measuring heat-induced MPT64 secretion with ultra-sensitive ELISA**

Rikiya Takeuchi*1, Wen-Hung Wang2, Shu-Huei Jain3, Yong-Huang Jiang1, Sonoko Watanuki1, Yoshiharu Ohtaki1, Kazunari Nakaishi1,5, Satoshi Watabe3,5, Po-Liang Lu2, Etsuro Ito3,5,6

1TAUNS laboratories, Inc., R&D department, Izunokuni-shi, Japan, 2Kaohsiung Medical University Chung-Ho Memorial Hospital, Sanmin, Taiwan, 3TAUNS laboratories, Inc., R&D headquarters, Izunokuni-shi, Japan, 4Waseda University, Waseda Research Institute for Science and Engineering, Shinjuku, Japan, 5Waseda University, Department of Biology, Shinjuku, Japan, 6Kaohsiung Medical University, Graduate Institute of Medicine, Sanmin, Taiwan

**Background:** Although nucleic acid amplification tests (NAATs) are now widely used, they cannot discriminate live bacilli from dead ones because nucleic acids exist in dead bacilli. Detection of only live bacilli can be achieved by only a time-consuming culture test. In the present study, we propose a de novo TB diagnosis method for the detection of only live bacilli that has the same high-detection sensitivity as a culture test and can be performed within a day.

**Materials/methods:** TB patient sputum was pretreated, and the specimen was heated at 46°C for 1 h to induce secretion of MPT64 protein from live *M. tuberculosis*. This protein was detected with our new ultrasensitive diagnosis method that was based on an enzyme-linked immunosorbent assay (ELISA) coupled with thionicotinamide-adenine dinucleotide (thio-NAD) cycling. We compared our data with those of a culture test (MGIT), a smear test (Kinyoun staining) and a NAAT (Xpert).

**Results:** The limit of detection for MPT64 in our ultrasensitive ELISA was 0.2 amoles/assay. We confirmed that heat-induced MPT64 secretion was not observed when BCG was exposed with 8 μg/mL rifampicin. Using the cutoff value of the measuring absorbance at 17 mAbs, which corresponded to ca. 330 CFU/mL in a culture method, the sensitivity was 86.9% [93/107, 95% CI: 79.0 - 92.7%), and the specificity was 92.0% [770/837, 95% CI: 89.9 - 93.7%] compared to that of MGIT. These were better than those obtained from Kinyoun staining tests and were not significantly different from those of Xpert tests. Further, the validity for drug susceptibility examination was shown by our ultrasensitive ELISA tests better than by Xpert tests because our tests detected only live bacilli.

**Conclusions:** A de novo, culture-free, same-day TB diagnosis method detects only live *M. tuberculosis* with a high-detection sensitivity. This method is especially useful for the patients under TB-treatment to evaluate whether it is effective or not.

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Abstract 1702

**Evaluation of voriconazole therapeutic drug monitoring practice: experience of a tertiary referral centre**

Yee Chin Kwang¹, Angela Netluch², Tony Lai³, Sharon Chen⁴,⁵,⁶, Hannah Yejin Kim*¹,², Indy Sandaradura⁴,⁵,⁶, Jan W. C. Alffenaar¹,⁷,⁸

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**Background:** Therapeutic drug monitoring (TDM) is used to optimise the dosing of voriconazole. To maximize the benefit of TDM, evaluation of current TDM practice is needed. This study had three objectives: 1) to evaluate current voriconazole TDM practice by identifying patient characteristics that were associated with TDM being performed, 2) to identify potential barriers to the optimal conduct of TDM and 3) to make recommendations for practice improvement.

**Materials/methods:** This retrospective study was undertaken at Westmead hospital, an Australian tertiary hospital, and was approved by the local ethics committee. Medical records of inpatients who started voriconazole therapy with or without TDM between January 2017 and December 2018 were reviewed. TDM was evaluated for sample collection, turnaround time and actions taken for trough concentrations which were outside the therapeutic range of 1-5 mg/L. On-site and off-site sample analyses were compared with respect to turnaround time and costs in a scenario analysis.

**Results:** In total, 112 patients (median age 57 years) were included. A longer duration of voriconazole therapy rather than patient characteristics was found to predict the performance of TDM. TDM was initiated in 91 (81%) patients on a median of day 6 of voriconazole therapy with a median follow-up TDM interval of 5 days. Sample collections were frequently mistimed (n=101/253, 40%). Half (n=34/68) of the first trough concentrations were within the therapeutic range. Voriconazole dosages were adjusted for 20% (n=16/80) of trough concentrations which were outside the therapeutic range, with a follow-up measurement performed in 69% (n=11/16) of patients. Off-site sample analysis resulted in a median turnaround time of 7 days with a cost of AUD 37.10 per sample analysed. On-site implementation of immunoassay can potentially shorten the turnaround time to 3 hours and reduce the cost of TDM by up to 53%.

**Conclusions:** Mistimed sample collections, prolonged turnaround time and lack of recommendations when reporting results were barriers to the optimal conduct of TDM. On-site sample analysis, Bayesian software to guide dosing and antifungal stewardship are required to improve the current practice. Periodical evaluation of TDM practice should be established to ensure sustainable improvement in TDM practice.

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Abstract 1706

Extended spectrum beta-lactamase producing Enterobacteriaceae urinary tract infections: is cefoxitin an effective therapy?

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Background: Cefoxitin is a β-lactam antibiotic derived from substrate produced by Streptomyces lactamdurans. Cefoxitin resistance to β-lactamase hydrolysis is attributed to a 7α-methoxy group in the nucleus conferring activity against various bacteria including extended spectrum beta-lactamases (ESBL) producers. There is a growing interest in cefoxitin as a carbapenem-sparing agent; however, there is paucity in outcome data. Our study aim is to evaluate clinical and microbiologic cure rates for non-complicated Urinary Tract Infections [UTIs] caused by ESBL Enterobacteriaceae in which cefoxitin was used.

Materials/methods: We conducted a retrospective study to review all patients who were diagnosed with a UTI and received cefoxitin at our quaternary care hospital over 3 years. The primary end points were; clinical cure [defined as the resolution of urinary symptoms as documented by the treating physician] and microbiologic cure [negative repeat urinary culture if done at the end of therapy]. Relapse and recurrence data were documented and defined as repeat positive urine culture and/or clinical symptoms within 2 to 4 weeks and three months respectively.

Results: During the study period we identified 26 patients with 27 infection encounters who were diagnosed with UTI secondary to ESBL producing Enterobacteriaceae and received cefoxitin. The sample was comprised of 18 males, mean age 66.9±18.7 years, mean weight 76.8±18.7 kg, 22 patients had UTIs with an indwelling Foley catheter, and 16 were diabetic. Identified organisms were E.coli (n=17) and Klebsiella Pneumoniae (n=10). Minimum Inhibitory Concentration [MIC] was ≤4 mg/L for all isolates except for two [MIC was 8mg/L]. Cefoxitin doses ranged from 1-2 g IV q6-12 hours for mean therapy duration of 5.9±2 days. Clinical Cure was achieved in 24 of the treatment encounters (85%), and microbiological cure was confirmed in all 11 repeat cultures (100%). Five patients relapsed. Four patients had recurrence within 3 months. Mortality occurred with one patient.

Conclusions: Cefoxitin is an effective treatment for non-complicated UTIs causes by ESBL producing enterobacteriaceae. Randomized controlled studies are required to determine the efficacy of cefoxitin as a carbapenem-sparing agent.

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Replication of MERS and SARS Coronaviruses in bat cells offers insights to their ancestral origins

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Background: The Middle East Respiratory Syndrome coronavirus (MERS-CoV), which first emerged in Saudi Arabia 2012, has caused >2,000 cases including >800 deaths in 27 countries. Previous findings of MERS-CoV-related viruses in bats, and the ability of Tylonycteris-BatCoV HKU4 spike protein to utilize MERS-CoV receptor, human dipeptidyl peptidase 4 (hDPP4), suggest a bat ancestral origin of MERS-CoV.

Materials/methods: We developed 12 primary bat cell lines from 7 bat species, including Tylonycteris pachypus, Pipistrellus abramus and Rhinolophus sinicus (hosts of Tylonycteris-BatCoV HKU4, Pipistrellus-BatCoV HKU5, and SARS-related-CoV respectively), and tested their susceptibilities to MERS-CoVs, SARS-CoV, and human coronavirus 229E (HCoV-229E). Effort in constructing more cell lines from more relevant species and organs are on-going.

Results: 5 cell lines, including P. abramus and R. sinicus but not T. pachypus cells, were susceptible to human MERS-CoV EMC/2012. However, 3 tested camel MERS-CoV strains showed different infectivities, with only 2 strains capable of infecting 3 and 1 cell lines, respectively. SARS-CoV can only replicate in R. sinicus cells, while HCoV-229E cannot replicate in any bat cells. Bat dipeptidyl peptidase 4 (DPP4) sequences were closely related to those of human and non-human primates but distinct from dromedary DPP4 sequence. Critical residues for binding to MERS-CoV spike protein were mostly conserved in bat DPP4. Of the 5 bat cells susceptible to MERS-CoV DPP4 expression was detected, with significantly higher mRNA expression levels than those in non-susceptible cells, supporting that DPP4 expression is critical for MERS-CoV infection in bats. However, overexpression of T. pachypus DPP4 failed to confer MERS-CoV susceptibility in T. pachypus cells.

Conclusions: Our study suggested that a number of bat cell lines were susceptible to human MERS-CoV, and within those, some for camel MERS-CoV. There seems to be a correlation between susceptibility and DPP4 mRNA expression, yet other factors are at play. The broad cellular tropism of MERS-CoV should prompt further exploration of host diversity of related viruses to identify its ancestral origin. Further work is being conducted to illustrate other determinants for susceptibility and characterize the cellular response during an infection in these cell lines.

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Abstract 1713

Mass PCR testing and targeted treatment for malaria in a low transmission area in Amazonia, French Guiana

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Background: Plasmodium vivax (Pv) and Plasmodium falciparum (Pf) are the main species found in French Guiana. The major difficulty for malaria elimination in the area is the prevalence of Pv, which causes relapses and asymptomatic gametocyte carriers. The aim of this study was to assess the impact of PCR-based mass screen and treat (MSAT) campaigns for malaria control in the general population of a malaria endemic area.

Materials/methods: A before-after study was conducted in 13 of 16 most affected neighborhoods (2,727/4,033 inhabitants) of the most impacted municipality of French Guiana, Saint Georges de l’Oyapock. Two MSAT interventions were implemented at a one-year interval relying on PCR for malaria detection followed by treatment of malaria positive individuals. RDT or PCR-positive consenting participants received artemether-lumefantrine against Pf or chloroquine and, in the absence of contraindication, primaquine against Pv. Symptomatic malaria incidence was passively monitored through the health center from one year before the first intervention until the end of the second intervention.

Results: More than half targeted inhabitants (1,566/2,727, 57.4%) were included in the study and 1,501 participated in the first screening, of which 1,276 (81.5%) also participated in the second screening. Overall, there were 1,231 individuals with complete PCR results. During the first MSAT, the PCR-positivity rate was 6.7% [6.0% Pv, 0.7% Pf with 73% of asymptomatic carriage], compared to 2.9% [2.4% Pv 0.5% Pf with 88% of asymptomatic carriage] during the second intervention (p<0.005). All positive participants received treatment and any severe side effect was reported. During the first intervention a large seasonal malaria epidemic was reported. A significant decrease of incidence was observed by passive monitoring among study participants (95 to 43/1566 person-years, p<0.005) but not in the non-participating population (38 to 59/2467 person-years p=0.24).

Conclusions: In French Guiana, a mass PCR screening and treatment intervention was operationally feasible and could reduce Plasmodium sp. carriage and incidence. Limitations of this study include seasonal variations and villager mobility, which may have limited the impact of the intervention. Strategies that only target populations with RDT testing and symptomatic cases treatment alone are likely to overlook a large part of the reservoir.

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Abstract 1716

**Ceftobiprole and daptomycin concentrations in valve tissue in a patient with aortic native valve endocarditis**

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**Background:** A main determinant of clinical response to antibiotic treatment is drug concentration at the infected site. Data on ceftobiprole (CFB) valve penetration are lacking. We measured CFB and daptomycin (DPT) concentrations in a native infected valve to verify their pharmacokinetic penetration and relationship with pharmacodynamic microbiological markers.

**Materials/methods:** One patient undergoing surgical valve substitution for native valve endocarditis (NVE) with lung and brain embolism and receiving intravenous CFB and DPT was studied. Valve and plasma specimens were collected at a variable time in the operatory day (4.00pm and 8.00pm, respectively) after CFB (500mg 8.00am and 4.00pm) and DPT (500mg 8.00am) administration. Drug concentrations were measured by high-performance liquid chromatography with tandem mass spectrometry kit for plasma (CoQua Lab srl) and a modified-method for the valve tissue evaluation. The valve tissue quantifications were performed in triplicate [in two different days], from 3 different positions on valve.

**Results:** The isolated microorganism was a MRSA with CFB and DPT MIC<2 mg/L and <1 mg/L, respectively. The CFB and DPT plasma concentrations were 36.2 and 14.1 mg/L, respectively and the extrapolated concentration at the operatory time were 16.4 and 19.1 mg/L for CFB and DPT, respectively; the corresponding median CFB and DPT valve concentrations were 2.26 (IQR 1.44-2.69) and 12.9 mg/L (IQR 5.51-20.9), respectively. The estimated tissue/plasma ratios for CFB and DTP were 0.14 and 0.67, respectively.

**Conclusions:** NVE is a serious infection with potentially fatal consequences. From the data available, we can suppose that the time above the minimum inhibitory concentration (T>MIC) was probably near to 24h in all compartments. CFB valve penetration (>14%) is not high but seems to be enough to cover MRSA CFB MIC (the patient has had a good clinical and microbiological response). For DTP, valve penetration (>67%, 12.9 mg/L) and plasma concentration (12h post-infusion) 14.1 mg/L, seems to be enough to cover MRSA sensitivity both in plasma and in tissue. DTP tissue concentration has a very high variability, probably influenced by tissue blood irroration. This is the first data on CFB valve tissue penetration, and it needs to be confirmed in other patient valve tissues.

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Abstract 1717

The effectiveness of nitrofurantoin, fosfomycin and trimethoprim for cystitis in relation to renal function

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Background: Nitrofurantoin, fosfomycin-trometamol and trimethoprim are recommended for the treatment of cystitis in primary care in the Netherlands. In patients with impaired renal function, lower urinary concentrations have been reported for all three antibiotics, which may be associated with a higher risk of treatment failure. We evaluated the effects of renal function on clinical failure rates of treatment with nitrofurantoin, fosfomycin-trometamol and trimethoprim in cystitis patients in primary care.

Materials/methods: Data was retrospectively obtained from the Julius General Practitioners’ Network, consisting of 78 Dutch general practitioner (GP) practices between 2013 and 2019. Episodes were classified as uncomplicated or complicated cystitis if antibiotics were prescribed according to Dutch guideline. The estimated glomerular filtration rate (eGFR) was calculated using plasma creatinine, age and gender. Clinical failure was defined as a second antibiotic prescription for cystitis or pyelonephritis within 28 days post-prescription. We used mixed effects regression analysis, with patient and GP practice as random effects and demography, comorbidity, cystitis history as fixed effects.

Results: In 21,891 unique patients 42,473 episodes were included consisting of 31,014 uncomplicated cystitis, treated with 5 days nitrofurantoin (NF5, n=24,591), 1 dosage fosfomycin-trometamol (FT1, n=5,359) and 3 days trimethoprim (TMP3, n=1,064), and 11,459 complicated cystitis, treated with 7 days nitrofurantoin (NF7, n=10,628) and 7 days trimethoprim (TMP7, n=831). An eGFR below 60 mL/min was observed in 3,757 of 42,473 episodes (8.8%). Adjusted odds ratios (aOR) for clinical failure per 10 mL/min decrease in eGFR were 1.05 (95%CI:1.01-1.09) for NF5, 0.96 (95%CI:0.92-1.01) for FT1, 0.98 (95%CI:0.89-1.08) for TMP3, 1.05 (95%CI:1.02-1.09) for NF7 and 1.02 (95%CI:0.93-1.14) for TMP7. In patients with uncomplicated cystitis and normal renal function (eGFR ≥60 mL/min), FT1 or TMP3 resulted in more clinical failures than NF5, with aOR of 1.37 (95%CI:1.18-1.59) and 1.42 (95%CI:1.07-1.87), respectively. In patients with uncomplicated cystitis and impaired renal function (eGFR<60 mL/min), FT1 was associated with less clinical failures than NF5 (aOR 0.61,95%CI:0.39-0.95).

Conclusions: In patients with uncomplicated cystitis and impaired renal function treatment with nitrofurantoin was associated with more clinical failure than fosfomycin-trometamol. In patients with uncomplicated cystitis and normal renal function treatment with fosfomycin-trometamol or trimethoprim was associated with more clinical failure than nitrofurantoin.

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Abstract 1720

Current use of baseline chest CT in haematology patients at high risk for invasive fungal infection

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Background: Baseline chest computed tomography (BCT) in high-risk hematology patients appears to allow early diagnosis of invasive pulmonary aspergillosis (IPA) since recent studies found CT abnormalities close to admission in 36% and 31%, respectively. Distribution of BCT implementation in hematology units and the impact on patient outcome is unknown.

Materials/methods: A web-based questionnaire was designed and disseminated via www.clinicalsurveys.net. Members of twelve international scientific bodies were invited. Estimated numbers of annually treated high-risk hematology patients, chest imaging timepoints and techniques, IPA rates, and follow-up imaging were assessed. BCT was defined as chest CT performed upon diagnosis of malignancy or hospital admission.

Results: Ninety-two of 142 participants (64%) from 43 countries answered all questions. Medical specialties included infectious diseases (n=69; 49%), hematology (n=68; 48%), microbiology (n=15; 11%), and other (n=26, 18%). Numbers of patients treated per year were estimated 5,505 acute myelogenous leukemia, 2,641 acute lymphoblastic leukemia, and 5,287 allogeneic hematopoietic stem cell transplantation.

Baseline CT was performed in 57% (n=54) of 92 hospitals. Upon diagnosis of malignancy or admission, 48% and 24% centers performed BCT, respectively. Overall, HSCT was the most frequent BCT indication (44.2%, n=42) and BCT was more frequently performed in relapsed than in de novo leukemia.

European centers performed BCT in 59%, whereas non-European centers did in 53%. CT was predominantly low-dose and contrast-enhanced in 38% of centers. Median estimated IPA rate was 8% and did not differ significantly between BCT centers [9%; IQR 5 - 15%] and non-BCT centers [7%; IQR 5 - 10%] (p=0.69). Follow-up CT after diagnosed IPA was performed in 98% (n=90), while only three (3.3%) centers did this at guideline-recommended timepoints.

Conclusions: In high-risk hematology patients baseline chest CT at diagnosis or admission became a standard-of-care. Randomized, controlled studies are needed to investigate its impact on patient outcome.

![Figure 1. Baseline CT timepoints](image)

#may be super-additive

**Figure 1. Baseline CT timepoints**

**ABSTRACT BOOK – 30th ECCMID 2020**

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Abstract 1722

A rocky road: lessons learned from a case of disseminated Rhodococcus hoagii infection
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Background: Rhodococcus species are gram-positive bacilli that primarily infect immunocompromised patients. Rhodococcus equi, reclassified as R. hoagii, is the major pathogenic species that usually affects the pulmonary system, whereas bloodstream infections (BSI) are often catheter-related. We describe a case of BSI where the source was a soft tissue infection mimicking Actinomycosis. The identification was established by 16S rRNA sequencing. This case underscores how Rhodococcus infections may be undiagnosed or misdiagnosed due to identification challenges in the routine laboratory.

Clinical presentation: A 46 year old HIV-infected man (CD4+ count of 42 cell/mm³; defaulted antiretrovirals) was admitted to hospital due to progressive dysphagia. CT scans revealed extensive necrosis of the mouth floor and neck lymphadenitis with abscesses draining via sinus tracts. C. pseudotuberculosis and unidentified gram-positive bacilli were initially isolated from the affected site. Follow-up culture revealed an unidentified gram-positive bacillus – confirmed by 16S rRNA sequencing as Rhodococcus species. TB cultures yielded Mycobacterium intracellulare and only anti-mycobacterial therapy was initiated at this stage.

On a subsequent admission for C. neoformans meningitis, a Bacillus species was cultured from blood. Shortly afterwards, re-admission for pneumonia occurred. He developed a nosocomial BSI with K. pneumoniae. Other blood cultures during this admission showed Bacillus species and Corynebacterium species, respectively. Dysphagia and failure of clinical improvement persisted. Multiple specimens from the neck and blood cultured Turicella otitidis. However, molecular methods identified them all as R. hoagii.

On the basis of in-vitro antibiotic susceptibility testing performed on the R. hoagii, the patient was commenced on imipenem, levofloxacin and rifampicin. He improved and was discharged on levofloxacin, rifampicin and other M. intracellulare treatment. Antiretroviral therapy was re-initiated.

Conclusions: Our case represents a disseminated infection with R. hoagii, with co-infection of M. intracellulare. Before molecular diagnostics, Rhodococcus was often misidentified as Mycobacterium species based on its acid-fast staining properties. The patient responded to combination therapy – recommended for at least nine months. R. hoagii was unidentified, misidentified or not identified to species level. This led to a significant delay in diagnosis and initiation of appropriate treatment.

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Risk factors and mortality in invasive Rasamsonia spp. infection: an analysis of cases in the FungiScope registry and from the literature

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Background: The Rasamsonia spp. complex comprises filamentous fungi causing pneumonia and occasionally disseminated disease in immunocompromised patients. To provide a knowledge base of risk factors and for therapeutic decisions in invasive Rasamsonia spp. complex infection.

Materials/methods: A literature search was performed in PubMed aiming at all reported cases of invasive infection due to Rasamsonia spp. (formerly Geosmithia spp./Penicillium spp.) since data base inception. These were complemented by cases from the FungiScope® registry. Cases of mere colonization were excluded.

Results: We identified 23 invasive infections due to Rasamsonia spp., six (26.1%) in the FungiScope® registry and 17 (73.9%) in the literature. Main risk factors were chronic granulomatous disease (n=12, 52.2%), immunosuppressive treatment (n=10, 43.5%), hematopoietic stem cell transplantation (n=7, 30.4%), graft-versus-host disease, and major surgery (n=4, 17.4%, each). Predominantly affected organs were the lungs (n=21, 91.3%), disease disseminated in seven cases (30.4%). Initial misidentification of the fungus occurred in 47.8% (n=11) and sequencing was used in 69.6% of patients (n=16) to establish definite diagnosis. Breakthrough infection occurred in 13 patients (56.5%). All patients received antifungal treatment, mostly with posaconazole (n=11), caspofungin (n=10) or voriconazole (n=9). Combination therapy was administered in 13 patients (56.5%). Susceptibility testing showed high minimum inhibitory concentrations for azoles and amphotericin B, but not for echinocandins. No preferable treatment influencing favorable outcome was identified. Overall mortality was 39% (n=9) at last patient contact while attributable mortality to Rasamsonia spp. was 17.4% (n=4).

Conclusions: Rasamsonia spp. are emerging fungi causing life-threatening infections, especially in immunocompromised and critically ill patients. Breakthrough infection occurs frequently and sequencing methods are necessary for diagnosis. Mortality is high. Treatment is challenging and clinicians dealing with this patient population should become aware of this infection.

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Abstract 1724

Emergence of novel recombinant Coxsackievirus A6 in Hong Kong

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Background: Coxsackievirus A6 (CV-A6), a member of enterovirus A in the genus Picornaviridae, has recently emerged globally as serious public health threats. Since 2008, CV-A6 arose and replaced enterovirus A71 (EV-71) and CV-A16 as the main causative agents responsible for hand, foot and mouth disease (HFMD) outbreaks worldwide. Recombination is an important mechanism for genetic evolution in RNA viruses, and CV-A6 recombinant strains were reported in China, Thailand, United Kingdom and Spain. To determine whether recombination events play a role in the evolution of the emergence of CV-A6 strains in Hong Kong, CV-A6 strains isolated from hospitalized patients were sequenced. Potential recombinant CV-A6 strains were further proceed with complete genome sequencing and recombination analysis.

Materials/methods: Nasopharyngeal aspirates (NPAs) were collected from patients from regional hospitals in Hong Kong. All specimens were confirmed positive for CV-A6 by RT-PCR and partial 5' untranslated region (5' UTR) sequencing. The partial VP1, 2C and 3D regions were sequenced, and phylogenetic trees were constructed. Five CV-A6 were selected for complete genome sequencing and recombinant analysis.

Results: CV-A6 were detected positive in 40 NPAs collected from January 2010 to December 2018, and partial VP1 gene of 28 CV-A6 strains were amplified for genotyping. The phylogenetic analysis of VP1 gene revealed that CV-A6 strains circulating in Hong Kong were divided into two subgenotypes: D5 (n=24) and D4 (n=4). Subsequently, the phylogenetic analyses of 2C and 3D gene analysis showed that eight CV-A6 strains are potential recombinant strains. Complete genome sequencing was performed and four recombinant CV-A6 strains were identified. Recombination between CV-A6 and CV-A4, and recombination between CV-A6 and EV-A71 were observed in three and one recombinant CV-A6 strains, respectively. 3D gene was identified as the frequent recombination site for CV-A6 strains.

Conclusions: Recombination plays an important role in the emergence and evolution of CV-A6 strains in Hong Kong. Recombinant CV-A6 strains are generally recombinant with CV-A4 and EV-A71 strains at 3D gene.

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Abstract 1725

Interim analysis: a large-scale clinical evaluation of QMAC-DST for rapid drug susceptibility testing of {\textit{Mycobacterium tuberculosis}}

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**Background:** The effective management of TB and MDR/XDR-TB relies upon rapid diagnosis and appropriate treatment of resistant infections. Culture-based phenotypic drug susceptibility testing (DST) methods are currently the gold standard for drug resistance detection. In the previous study, we examined the accuracy of QMAC-DST which is an automated rapid phenotypic DST system based on imaging technology. The results of the QMAC-DST for MDR/XDR-TB showed a high agreement rate compared to a conventional method, and the QMAC-DST could provide the fast result within around 1-week turnaround time. In the present study, we have been evaluating the accuracy and speed of the QMAC-DST system through a large number of clinical strains isolates collected from multi-centers. As an interim analysis, the result from 555 samples is presented.

**Materials/methods:** The Korean Institute of Tuberculosis (KIT, Osong, Republic of Korea) has provided laboratory services for public health centers. We conducted the conventional DST and the QMAC-DST for the 555 clinical strains which were sent to the KIT for DST from July 2019 to September 2019. Those strains were positive cultures in liquid or solid medium. The conventional DST was performed by the absolute concentration method with Lowenstein-Jensen (L-J) medium. And the QMAC-DST was performed by the automatic imaging and analyzing system with QMAC-DST panel. We compared the results of both methods and calculated the accuracy of QMAC-DST.

**Results:** Except for strains suspected of contamination or growth failure, The QMAC-DST for 480 clinical samples for 13 anti-tuberculosis drugs were showed a high agreement rate (98.73\%) compared to conventional DST. The average time required for QMAC-DST was 7.9 days, which was much faster than conventional DST (21 days).

**Conclusions:** The QMAC-DST was evaluated with 555 samples out of 3000 targets. The interim results of QMAC-DST were reported 2\textsuperscript{2}3 weeks earlier than conventional DST and showed a high concordance rate. In this study, we confirmed that the QMAC-DST can provide a rapid and accurate diagnosis for effective TB treatment so that it can be an alternative DST method replacing slow conventional DST methods.

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Abstract 1726

Reactive hyperaemia measured by peripheral arterial tonometry correlates with glycocalyx degradation and the presence of sepsis in the critically ill patient

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Background: Sepsis is a life-threatening condition whose diagnosis relies on markers of organic damage in the presence of infection. The endothelium is virtually present in every organ and is highly influenced by the circulating cytokines and may be responsible for the microvascular organic damage seen in sepsis. We investigated if reactive hyperaemia correlates with the presence of sepsis and whether it may be used to distinguish between septic and non-septic patients in the Intensive Care Unit (ICU).

Materials/methods: We performed a prospective study of a cohort of ICU admitted patients. Patients were assessed for endothelial dysfunction quantifying the Reactive Hyperaemia Index (RHI) using peripheral arterial tonometry and biomarkers of glycocalyx degradation. Patients with infection were compared to a control group of patients without evidence of infection.

Results: Eighty-six patients were included in the study, 58 (67.4%) in the septic group and 28 (32.6%) in the control group. There were no significant clinical differences between groups except for age. The natural logarithm of RHI (Ln_RHI) was negatively correlated with cardiovascular comorbidities, disease severity and plasma levels of soluble E-selectin (p=0.024) and Syndecan-1 (p<0.001). Ln_RHI was lower in septic patients when compared with controls (0.53±0.48 vs 0.69±0.42, respectively) and multivariate analysis adjusted for age predicted that within each age group, each 0.1 unit decrease in the Ln_RHI increased the odds for infection by 14.6%.

Conclusions: Reactive hyperaemia measured by peripheral arterial tonometry seems to be closely related to endothelial glycocalyx degradation and endothelial activation. Sepsis is associated with lower RHI in critically ill patients when compared to non-septic patients and RHI may be a useful tool for the diagnosis of infection in this setting, especially in an older population.

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Evaluation of the Aptima BV assay for detection of bacterial vaginosis by comparison with the BD MAX vaginal panel assay

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Background: Bacterial vaginosis (BV) is one of the most common lower genital tract conditions, of which the diagnosis is challenging due to its complex polymicrobial nature. To study the performance of the Aptima® BV assay (Hologic), 238 genital swabs were tested in parallel with the BD MAX™ Vaginal Panel (Beckton Dickinson). Both assays are nucleic acid target amplification-based, fully automated -sample in answer out- and include an internal control. Microbiome-based algorithms are used to determine BV test results.

Materials/methods: Two hundred thirty-eight swabs (97 cervical, 85 vaginal, 55 introitus, and 1 fluor) were from women ≥ 18 years (mean age 38, range 18-94) being seen by their general practitioner (symptomatic women, n=198) or for routine obstetric / gynaecological care (symptomatic and asymptomatic women n=40). Swabs were analysed by parallel testing on the same day. Two-hundred µl (BD Max) or 400 µl (Aptima) of Eswab medium were transferred to BD MAX™ UVE tubes or Aptima Specimen Transfer tubes, respectively, and tubes were placed directly on the BD MAX™ or the Panther system. At the same time, aliquots were frozen for discrepancy evaluation with the AmpliSens® Florocenosis / Bacterial vaginosis-FRT PCR kit (ATRiDA). If at least two tests were positive or negative for BV the sample was considered true positive or negative, respectively.

Results: Seventy-two samples tested positive in both assays, 133 samples negative, while 33 samples showed discordant test results. Further analysis of the discordant samples with the AmpliSens® kit yielded a BV-positive or BV-negative test result for 27 samples.

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<thead>
<tr>
<th>BD MAX™ Vaginal Panel</th>
<th>Aptima® BV assay</th>
<th>Discrepancies analysis</th>
<th>AmpliSens® assay</th>
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For the Aptima assay for BV detection the number of true positives was 84, false positives 5, true negatives 136 and false negatives 7, yielding a sensitivity, specificity, PPV and NPV of 92.3%, 96.45%, 94.4% and 95.1%. For the BD MAX™ Vaginal Panel assay these values for BV were 86.8%, 92.9%, 96.3% and 92.0%, respectively. One sample yielded an invalid test result in the Aptima test, 10 samples in the BD test [6 indeterminate, 4 unresolved].

Conclusions: We conclude that the Aptima® BV assay is an easy to carry out test, suitable for the reliable detection of bacterial vaginosis.

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Abstract 1730

**Effects of penicillin V on the intestinal microbiota in patients with pharyngo-tonsillitis**

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**Background:** Increasing antimicrobial resistance is a growing threat to human health. The commensal microbiota, in particular the rich intestinal microbiota, may function as a reservoir of antibiotic resistance genes. Studies on the ecological impact of penicillin V with current dosage regimens are lacking. The objective of the present investigation was to evaluate potential impact on the faecal microbiota with focus on beta-lactam resistance.

**Materials/methods:** Thirty-one patients, a subset from a recent study, treated with penicillin V for 5 days (n=14, daily dose 3.2g) or 10 days (n=17, daily dose 3.0g), contributed each with 3 faecal samples. The specimens were collected before penicillin V administration, directly after the last dose and 7-10 days after discontinuation of treatment. Samples were inoculated semi-quantitatively on non-selective and selective screening chromogenic agar plates, to study beta-lactam resistance, shift in Enterobacteriales, overgrowth and shift among enterococci, colonisation with candida and Clostridoides difficile. Susceptibility testing was performed on resistant isolates. Results were analysed by Wilcoxon paired-rank sum test and Mann-Whitney U-test.

**Results:** The amount of Enterobacteriales resistant to ampicillin and third generation cephalosporins, mainly Amp C producers, increased significantly from baseline (sample 1) to after the last dose of penicillin V (sample 2), p<0.01 and p<0.05, respectively. At follow-up (sample 3), the increase from baseline was no longer significant. There was a non-significant shift from E. coli to non-E. coli, between samples 1 and samples 2. Eight patients were newly colonised by unusual gram negative rods in sample 3. Three patients had new colonisation with Candida albicans in sample 2. One patient had moderate growth of toxin-positive C. difficile in sample 3 and symptoms consistent with C. difficile infection. No significant differences were seen between the two study groups (penicillin V for 5 or 10 days).

**Conclusions:** Treatment with penicillin V caused marked ecological impact on the faecal microbiota. The amount of beta-lactam resistant Enterobacteriales increased significantly during the treatment period. Ecological disturbances in the microbiota were still seen 7-10 days after treatment discontinuation. These results challenges the general perception that penicillin V is an "ecological safe" agent that can be prescribed without inducing resistance.

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Abstract 1735

Genome-based surveillance of clinical vancomycin-resistant Enterococcus faecium reveals increased prevalence of vanB-type isolates of ST117/CT71 in German hospitals, 2010-2016

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Background: Enterococci are considered as common cause of nosocomial infections, where treatment options are limited due to intrinsic and acquired resistances. Particularly vancomycin-resistant E. faecium (VRE) represent a burden, since well-adapted lineages are widespread established in healthcare facilities. In recent years, the upcoming resistance to linezolid diminishes this last-line treatment option. For this study, microbiological and genome-based analyses of VRE clinical isolates were realized. VRE were collected as part of the tri-annual resistance studies of the Paul-Ehrlich-Society at 25 medical laboratories in Germany, Austria and Switzerland in 2010, 2013 and 2016.

Materials/methods: A total of 166 VRE isolates was collected. Susceptibility to 18 antibiotics was tested by applying the broth microdilution method. Resistance breakpoints were assessed according to EUCAST guidelines (v. 9.0). Whole genome sequencing was realized with Illumina technology. For high-resolution genotyping and to determine phylogenetic relations, cgMLST analyses were performed with the generated data.

Results: In 2010, 38 isolates were collected, in 2013 52 and in 2016 a total of 76. From 2010 to 2016, a change in vancomycin-resistance type from vanA to vanB was observed. 62 Different genotypes were identified and were assigned to distinct clusters in phylogenetic analysis, showing individual population composition for each study year. In total, the most abundant genotype was ST117 [45%]. In 2016, the predominant lineage was genotype ST117/CT71 [n=23], showing the vanB-type; the predominant genotype detected in 2010 (ST192, vanA) was almost absent in 2016, while ST203 with vanA-type was present in all study years. Additionally for 2016, 8 linezolid-resistant isolates were identified, so in 2016 LVRE (vanA and vanB) had a prevalence of about 10%.

Conclusions: Structured surveys like the PEG resistance studies allow a snapshot of hospital pathogens’ prevalence within a given time frame and geographical coverage. We observed the fluctuation of genetic lineages over time, like the rise of ST117 showing the vanB-type. cgMLST analyses determined various subtypes within ST117 such as CT71, which in turn ascertained a cross-hospital, regional or country-wide spread of distinct VRE strain types. At the same time, some lineages were present in all cohorts.

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Abstract 1743

Risk for antibiotic resistance in patients hospitalised with urinary tract infection: a matched case-control study using the French health insurance database

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Background: Antibiotic resistance rates are increasing among urinary pathogens, both in community and hospital infections, leading to increased therapeutic difficulties, and resulting in worse clinical and economic outcomes. Several risk factors of acquiring antibiotic-resistant urinary tract infections (UTIs) have been highlighted by previous studies, but few are universally accepted. This study aims to assess the risk factors for infection due to antibiotic-resistant bacteria (ARB) in patients hospitalised for an UTI, using the comprehensive French national health insurance database (SNDS).

Materials/methods: Incident hospitalizations for UTI diagnosis, due to an Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, Pseudomonas aeruginosa or an Enterococcus were identified from Jan 1st 2015 to Dec 31 2017. Only stays for which bacteria could be determined were included. Cases (UTIs due to ARB) were matched to controls (UTIs without ARB) according to age (± 5 years), gender, infection code, year of admission, and bacterial species. Healthcare-associated (HCAI) and community (CAI) infections were studied separately, and conditional multivariate logistic regressions were stratified by gender.

Results: For all three years, 9759 cases were identified from which 6606 CAIs and 3001 HCAIs were matched with controls. For all infections, consumption of antibiotic in the last 3 months was a risk factor for ARB UTI, with an OR reaching 3.84 [3.04−4.85] for men with CAI who had received ≥ 3 antibiotics. The risk increased when the last antibiotic taken was broad spectrum, whether associated with a previous UTI or not [OR 2.59 [2.15−3.11] vs. 1.35 [1.18−1.53], respectively]. Having undergone a surgical procedure on the urinary tract during the last 3 months increased the risk for men with CAIs (OR 1.39 [1.14−1.69]) and for women with HCAIs (OR 1.72 [1.37−2.17]). Staying in ICU > 7 days in the past 3 months increased slightly the risk for men with HCAIs [OR 1.44 [1.03−2.02]]. Diabetes, immunosuppression, neurological disease, urinary tract diseases, and pregnancy had no impact on ARB infection.

Conclusions: This study confirms the importance of broad antibiotic consumption on the risk of UTI with ARB, and the importance of prevention during surgical procedure on the urinary tract, and long ICU stays.

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**Abstract 1744**

**Characterisation of the microbial community in patients with pharyngeal gonorrhoea infection**

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**Background:** Pharyngeal gonorrhoea is a common sexually transmitted infection among ‘men having sex with other men’ (MSM). To appropriately survive and persist in the oro-pharynx, Neisseria gonorrhoeae (NG) has to compete with the local commensal bacteria. The aim of this study was to characterize the pharyngeal bacterial community profiles during an ongoing NG infection in a well-selected cohort of MSM.

**Materials/methods:** A total of 70 HIV-negative MSM reporting condomless oral intercourse were enrolled: in particular 45 non-infected subjects and 25 patients with pharyngeal gonorrhoea were considered. Starting from pharyngeal swabs, the pharyngeal microbiome composition was analysed through sequencing of hypervariable V3-V4 regions of the 16S rRNA gene. Bacterial biodiversity and distribution were characterized via alpha and beta diversity evaluations. A functional prediction of the bacterial metabolic pathways was performed using PICRUSt software and KEGG pathways database. Differences in abundances of bacterial taxa and functional pathways among experimental groups were analyzed by Mann-Whitney t-test, using MATLAB software (Natick, MA, USA). p-values < 0.05 were considered as significant for each statistical analysis.

**Results:** The pharyngeal microbiome of all subjects was dominated by Prevotellaceae, Veillonellaceae and Streptococcaceae families. Patients with pharyngeal gonorrhoea exhibited significantly higher levels of Spirochaetaceae [in particular, bacteria belonging to Treponema genus] compared to non-infected individuals. Considering low-abundance bacterial genera, an imbalance between aerobe and anaerobe microorganisms was observed: the pharyngeal microbiome of NG-positive patients was richer in several anaerobes (e.g. Porvimonas, Peptococcus, Clostridiales, Prevotellaceae) and poorer in various aerobe genera (i.e. Pseudomonas, Escherichia). The metabolic functional prediction indicated a more abundant involvement of D-glutamine and D-glutamate metabolism, carbohydrate metabolism, as well as a greater activation of the energy metabolism in patients with pharyngeal gonorrhoea.

**Conclusions:** Information about the bacterial composition of the pharyngeal microbiome in case of gonorrhoea could shed light on the pathogenesis of the infection and open new perspectives for the prevention and control of this condition.

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Abstract 1745

**Associations of HLA genotypes with adverse events of hepatitis and skin rash during treatment of latent tuberculosis infection**

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Abstract third-party references: This study was supported by a grant from the Taiwan Centers for Disease Control [MOHW108-CDC-C-114-000109 and MOHW-107-CDC-C-114-000104].

**Background:** Treatment of latent tuberculosis infection (LTBI) is a cornerstone strategy for control of TB. Drug adverse events (AE) leading to treatment interruptions compromise treatment of LTBI. Considerable progress has been made in identifying genetic risk factors for idiosyncratic adverse drug reactions. This study aims to identify human leucocyte antigen (HLA) risk alleles associated with serious drug AE, hepatotoxicity and skin rash, which may be used as a tool to predict AE prior to treatment.

**Materials/methods:** We prospectively recruited patients who received LTBI treatment from Jan 2018 to Dec 2019, in Taiwan, across 7 hospitals. Whole blood was drawn for HLA typing using the HLAssure SE SBT Kit (TB Diagnostics Ltd) using DNA-based methods for determination of HLA alleles using PCR amplification with sequence based typing. Patients were followed up at baseline, week 2, 4, 8 and 12 for adverse events and liver function testing, while under 3 months isoniazid-rifapentine treatment (3HP) and followed monthly after 8 weeks while under 9 months of isoniazid (9H) or 4 months of rifampin (4R) treatment.

**Results:** 216 patients were enrolled, 106 women, 110 men, average age 54.3 ± 15.5 years. 131 were TB contacts, 36 were candidates for transplantation and 23 were candidates for anti-TNF alpha blocker treatment. Treatment regimens were 3HP in 166 (76.9%), 9H in 45 (20.8%) and 4R in 5 (2.3%). AE occurred in 134/216 (62.0%), of which 117 were on 3HP and 16 on 9H and 1 was on 4R. AE of at least grade 2 occurred in 37 (17.1%). The most common AE include fatigue (31.5%), dizziness (27.3%), nausea (12.7%), fever (13.0%), myalgia (11.1%), hepatitis (10.2%), anorexia (7.4%), pruritis (10.2%), skin rash (9.3%), gastrointestinal upset (5.1%), limb numbness (5.1%) and diarrhea (2.3%). Associated genotypes for hepatitis included HLA-A*0101, A*0201, A*0203, B*4006. Associated genotypes for skin rash included HLA-A*0101, A*3501.

**Conclusions:** Several HLA genotypes are associated with serious adverse events of hepatitis and skin rash in patients undergoing treatment of LTBI. Further investigations are required to validate these risk alleles to predict AE in a larger population undergoing treatment for LTBI.

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**Abstract 1750**

**Diversity and therapeutic potential of Klebsiella pneumoniae bacteriophages and their depolymerases: genomics and enzymatic activity**

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**Background:** *Klebsiella pneumoniae* has become a significant health threat in hospital settings. The rampant use of antibiotics has promoted the emergence of multidrug resistance (MDR) strains, particularly carbapenem-resistant and extended-spectrum-beta-lactamases (ESBL) producers. The unavailing use of current antibiotic treatments have prompted great interest in alternative treatments such as phage therapy. Lytic bacteriophages are considered an effective antidote against MDR pathogens for their ability to precisely adhere and degrade bacterial capsular polysaccharide, which acts as a protective layer to the bacterial cell and contributes to its pathogenicity. In this study, we have isolated and identified a large collection of obligately lytic *K.pneumoniae* phages that produce capsule depolymerases, enzymes that hydrolyse *Klebsiella* capsules. We conducted genotypic and phenotypic analyses to characterise these phages by studying their putative depolymerases genes against published homologues and over-expressing these enzymes to study their efficacy against MDR *K.pneumoniae*, respectively.

**Materials/methods:** The genomic DNA of *K.pneumoniae* phages (n=59) extracted by PCI/SDS extraction were sequenced by Illumina NexteraXT technology and assembled using various bioinformatics tools. The putative depolymerase genes were identified against published genomes of *K.pneumoniae* phages using a custom, in-house phage protein database. Homologues were identified using HHsearch which conducts a profile similarity searching based on protein function prediction. To examine the activity of these enzymes, the identified genes were cloned into pEXP5/TOPO vector and over-expressed using the Expressway cell-free *E.coli* expression system. The His-tagged proteins were analysed by SDS-PAGE and then purified using the HisPur-NiNTA purification kit.

**Results:** We successfully isolated and characterised 59 Caudovirales, obligately lytic *K.pneumoniae* phages consisting of the most common tailed phages *Siphoviridae, Podoviridae* and *Myoviridae*. We identified 33 putative depolymerase genes in 26 of our phages using stringent HHsearch criteria which showed similarity to several distinct capsular depolymerases such as hydrolases and lyases. Subsequently, eight putative structures were selected and five successfully cloned and over-expressed. SDS-PAGE analysis showed clear bands at expected sizes. The recombinant proteins were purified using nickel-affinity spin columns and the eluted fractions analysed by SDS-PAGE gel were pooled for further studies.

**Conclusions:** Characterization of novel depolymerases from our collection of *K.pneumoniae* phages may prove useful for effective treatment against MDR strains.

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Abstract 1755

Evaluation of a new commercial disc susceptibility kit for detection and differentiation of carbapenemases produced by Enterobacterales

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Background: The MASTDISCS® Avibactam Combi set for OXA-48 detection and carbapenemase screen is a kit comprising 3 discs. Disc A contains temocillin with KPC and MBL inhibitors; Disc B contains temocillin plus avibactam and Disc C contains a penem antibiotic. The kit is intended to allow detection of carbapenemase-producing Enterobacterales (CPE) and differentiation of isolates with OXA-48-like enzymes from those with KPC or metallo-ß-lactamase (MBL). We describe here the first evaluation of this assay using standard EUCAST / CLSI methodology.

Materials/methods: The kit was evaluated with a diverse collection of 208 well characterised Enterobacterales including carbapenemase-producers [CPE; n = 159], isolates with ESBL and/or AmpC ß-lactamase [n = 47] and two control strains. Susceptibility testing was performed using EUCAST methodology on Mueller-Hinton agar. After overnight incubation, inhibition zone diameters were measured and the presence of carbapenemases was inferred following the kit instructions.

Results: All of the CPE isolates (n = 159) were correctly assigned as being carbapenemase-producers [sensitivity: 100%; specificity: 92%]. 4/49 other isolates were incorrectly assigned as carbapenemase-producers including isolates with TEM-10, LAT and two isolates with DHA-1. 61 out of 62 isolates with OXA-48-like enzymes were correctly assigned as OXA-48-like producers with one isolate inferred to be a producer of KPC or MBL. Of 97 isolates with KPC or MBL, all but one were correctly assigned as KPC/MBL producers. A single isolate with a combination of carbapenemases [VIM and OXA-48] was assigned as an OXA-48 producer. Finally, one isolate of CPE with NMC-A carbapenemase was falsely assigned as KPC/MBL.

Conclusions: The kit performed very well as a screening test with a challenging set of bacterial isolates. Most importantly, the presence of a carbapenemase was predicted with absolute sensitivity (100%) and high specificity (91.8%). Only 4 out of 49 non-CPE would require additional investigation as possible CPE – and the vast majority of these 49 isolates expressed ESBL or AmpC activity. This combination of 3 discs could be included with other antimicrobials for routine testing of Enterobacterales in clinical laboratories using EUCAST methodology.

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Impact of corticosteroids on alveolar macrophage interaction with mucorales

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Background: Alveolar macrophages (AM) are lung first line of defence against moulds from the Mucorales order. They are able to control inhaled spore growth. Since corticosteroid use is a known risk factor for mucormycosis, the aim of this study was to decipher the role of corticosteroids on AM phagocytic and killing functions using a new ex vivo model.

Materials/methods: Male BALB/c mice were untreated or treated with 500 mg/kg of cortisone acetate at day 1 and 3 before AM collection through bronchoalveolar lavage. AM from untreated and corticosteroid-treated mice were then exposed to Lichtheimia corymbifera spores at a ratio of 1:5 in DMEM without phenol red in a 96-well plate at 37°C with 5% CO2. Fungal growth was assessed using optical densities measured by spectrophotometer each hour for 48 hours at 800 nm. Flow cytometry was used for phagocytosis assay. After 1 hour of co-incubation, AM and spores were labelled with antibodies anti-CD11c+ and FITC, respectively. AM CD11c+FITC+ were considered having phagocytized spores. Statistical comparisons were performed using Mann-Whitney and Fisher tests.

Results: Absorbance of wells containing corticosteroid-treated AM was significantly higher than wells with untreated AM from 24h of coinoculation with spores (0.219 ± 0.007 vs. 0.200 ± 0.003, p=0.023). The difference in fungal growth persisted at 48h (p=0.001). Corticosteroid-treated AM showed a lower proportion of AM CD11c+FITC+ compared to that of untreated AM (7.6% vs 21.5%, p<0.001, figure 1.).

Conclusions: Corticosteroids enhanced fungal growth of L. corymbifera through AM phagocytosis alteration in our ex vivo model. Further studies are ongoing assessing killing functions of AM in this model.

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Abstract 1758

Is strongyloidiasis currently endemic in Croatia?
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Background: Due to its low prevalence and various clinical presentations, the Strongyloides stercoralis infection in temperate zones can be easily overlooked. As the majority of symptomatic cases are diagnosed during the stage of chronic infection reactivation in immunosuppressed hosts, with unknown time of primoinfection, current endemicity in European countries is difficult to assess. The epidemiological and clinical burden of the disease in Europe has not been well studied and there have been no such studies in Croatia yet. Knowing local epidemiological circumstances is important in managing immunosuppressed persons and in transplant medicine. This study explored the epidemiological and clinical features of patients with strongyloidiasis, with particular aim to find elements for current endemicity of the disease.

Materials/methods: A retrospective descriptive study was performed that included patients of both genders and all ages treated for strongyloidiasis from January 2010 to May 2019 at the University Hospital for Infectious Diseases in Zagreb, Croatia. The diagnosis was made directly [by light microscopy of fecal samples after salinic provocation, three stool samples for parasites and ova, and/or tissue or duodenal aspirate samples], or indirectly by blood serology (in 83.1 and 16.9% of patients, respectively). Statistical analysis was done.

Results: Among 65 patients with strongyloidiasis, 60% were men, and 78.5% were aged 50-79 (range 17-82 y.; average: 62 y.). The number of patients significantly increased over the study period (p=0.013). Clinical presentations were: asymptomatic eosinophilia [41.5%], chronic symptomatic disease [33.9%], hyperinfection [6.1%] and acute primoinfection [18.5%]. Altogether 20 patients [30.8%] were immunosuppressed [9 by corticosteroids, 4 cytostatic drugs, 7 immune-debilitating illness]; four developed hyperinfection, with two lethal outcomes. The initial therapy was: albendazole in 71.7% of patients, 13.3% thiabendazole, 13.3% ivermectin, 1.7% mebendazole. Six patients [9.2%] received repeated treatment. The parasitologic cure rate between albendazole and ivermectin group was equal (p=0.0878) [lost to follow up: 48.8% in albendazole and 25% in ivermectin group].

Conclusions: Records of patients with acute primary infection confirm current endemicity for strongyloidiasis in continental Croatia, and immunosuppressed travellers to this region should be advised to take precaution measures. Patients undergoing immunosuppression and organ donors from Croatia should be screened.

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Abstract 1764

Epidemiology of *Clostridioides difficile* infections among hospitalised community-acquired pneumonia patients who received empiric treatment with ceftriaxone plus a macrolide

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**Background:** *Clostridioides difficile* infection (CDI) among hospitalized community-acquired pneumonia (CAP) patients receiving ceftriaxone + macrolide (CTX+M), the most commonly prescribed CAP regimen, is under-researched.

**Materials/methods:** This is a retrospective study (2012–2015) of hospitalized patients (≥18 years) in the MedAssets database with primary discharge diagnosis of CAP; patients received CTX+M on Days 1–2, had no CDI admitting diagnosis, and had ≥1-year enrollment before index date. Patients with an ICD-9 code for CDI ≤60 days from index admission for CAP were identified and further stratified by Charlson Comorbidity Index (CCI)/Pneumonia Severity Index (PSI) risk scores from diagnosis codes. CDI incidence was tabulated across CCI/PSI categories.

**Results:** In total 278/33,173 (0.8%) identified patients had a CDI diagnosis ≤60 days after index admission. CDI incidence among CTX+M CAP patients was similar to CAP patients who received a fluoroquinolone on Days 1–2 of hospitalization (1.1%). Among CTX+M patients, CDI incidence in bivariate analyses was: age ≥65/<65 (1.0%/0.5%), prior/no prior CAP (1.3%/0.8%), cancer/no cancer (1.5%/0.7%), coronary heart disease (CHD)/no CHD (1.1%/0.6%), congestive heart failure (CHF)/no CHF (1.4%/0.7%), acute respiratory failure (ARF)/no ARF (1.5%/0.7%), dementia/no dementia (1.2%/0.8%), immunocompromising conditions (IC)/no IC (1.4%/0.9%), renal failure (RF)/no RF (1.4%/0.7%), and prior versus no hospitalization in past year (1.5% versus 0.8%). CDI incidence increased with increasing CCI [0 [0.4%], 1 [0.6%], 2 [0.9%], and ≥3 [1.2%]], and PSI class [≤2 [0.2%], 3 [0.9%], 4 [1.2%], and 5 [2.2%]]. In multivariate analyses, PSI class, ARF, and CHD were independently associated with CDI; in a multivariate analysis that excluded PSI, age ≥65, ARF, and CHD, IC, and RF were independently associated with CDI (P<0.05, all analyses).

**Conclusions:** Certain CAP patient populations empirically receiving CTX+M may be at elevated risk for CDI. High-risk populations identified in this analysis are consistent with those identified in prior CDI risk-factor studies. Whether alternative antibiotics with a lower propensity to cause CDI than CTX-M can reduce this observed risk of CDI warrants further investigation.

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Abstract 1765

Clinical feasibility of simultaneous microdialysis of voriconazole and its N-oxide metabolite at target site demonstrated by in vitro investigations

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Background: Antifungal resistance is globally rising and the demand for rational and effective dosing regimens with antifungals such as voriconazole (VRC) thus intensifies. Currently, detailed knowledge of VRC pharmacokinetics (PK) is lacking, resulting in inadequate exposure or adverse events in patients. Application of microdialysis (µD), a minimally invasive sampling technique, in clinical studies, allows for determination of unbound drug concentrations at target site. However, metabolite concentrations are frequently of equal interest, as they contribute to efficacy, alter the PK of the parent drug or cause adverse events. Therefore, in this in vitro study, VRC and its N-oxide (NO) metabolite were chosen to investigate the feasibility of simultaneous µD of drug and drug metabolite prior to in vivo studies.

Materials/methods: CMA63 µD catheters (n=4) were placed in a static in vitro microdialysis system and perfused with Ringer’s solution (RS). The medium consisted of RS containing (i) VRC, (ii) NO or (iii) VRC and NO combined at different concentrations ranging from 0.010 to 3.0 µg/mL. Relative recovery (RR) was determined as the ratio of the respective VRC or NO concentration in microdialysate and medium. Quantification was performed using a LC-MS/MS assay.

Results: Overall, mean RR of (i) VRC was 87.8% (95% CI: 87.0 – 88.7%, n=85) and did not change significantly when simultaneous µD with NO was performed ((iii) 88.4% (95% CI: 87.2 – 89.6%, n=82)). Non-significant were also the differences in the mean RR of NO with (ii) 91.7% (95% CI: 90.3 – 93.1%, n=85) in the absence and (iii) 89.8% (95% CI: 88.6 – 91.1%, n=82) in the presence of VRC.

Conclusions: The RR of VRC and NO were high, reproducible and independent of each other in vitro. Thus, the results provide a solid basis for unbiased measurements of target site concentrations in vivo. Since metabolites cannot be administered to humans, the substance-specific catheter calibration using retrodialysis must be replaced. In this regard the comparable RR of VRC and NO indicate the feasibility of VRC retrodialysis as surrogate to back-calculate the tissue fluid concentrations of NO. Ultimately, incorporating knowledge of target site PK into clinical decisions will contribute to the optimisation of dosing regimens.

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Prevalence and risk factors of inappropriate use of intravenous and urinary catheters in surgical and medical patients

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Background: Inappropriate use of catheters is common and associated with adverse patient outcomes, such as healthcare-associated infections. We previously conducted a successful project, entitled the RICAT-study, to reduce inappropriate use of intravenous and urinary catheters in medical wards. Broad-scale implementation should be started if inappropriate use is a hospital-wide problem. The current objective was to compare surgical and medical wards, and determine risk factors for inappropriate catheter use.

Materials/methods: We performed a prospective observational study from October, 2017 to May, 2018 in surgical wards of two university hospitals. We observed patients every other week for seven months, and assessed inappropriate use of intravenous and urinary catheters. Inappropriate use was compared with non-surgical wards of the RICAT-study. Primary outcomes were the percentages of inappropriate use of peripheral intravenous catheters (PIVCs) and urinary catheters on the days of data collection.

Results: We included 409 surgical patients [mean age 59.2 years; SD 15.3, 151 (37%) female] and compared this with 1781 medical patients [mean age 64.8 years; SD 17.6, 842 (47%) female]. Inappropriate use occurred in 36 (8.5%) of 425 peripheral intravenous catheters in 373 surgical patients, compared to 400 (22.9%) of 1747 peripheral intravenous catheters in 1665 medical patients. This represents a difference of 14.4% [95% CI 11.1% to 17.8%; P < 0.001]. Inappropriate use of urinary catheters occurred in 14 (10.4%) of 134 surgical patients, compared to 105 (32.4%) of 324 medical patients, a difference of 22.0% [95% CI 14.7% to 29.2%; P < 0.001]. The main risk factor for inappropriate use of peripheral intravenous catheters was admission to medical wards; odds ratio 3.50 [95% CI 2.15 to 5.69], which was also one of the main risk factors for urinary catheters; odds ratio 2.75 [95% CI 1.36 to 5.55].

Conclusions: Inappropriate use of catheters is more common in medical wards compared to surgical wards. Prevention strategies to reduce healthcare-associated infections should primarily focus on sites with high prevalence of inappropriate use.

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Dalbavancin provides a second-line option for patients who fail conventional on outpatient parenteral antimicrobial therapy (OPAT): a case series in Aberdeen

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Abstract third-party references: Supported by NHS Grampian and NHS Scotland.

Background: Aberdeen Royal Infirmary’s outpatient parenteral antimicrobial therapy (OPAT) service treats a variety of infections across specialties. Although OPAT is effective for many patients, some do fail on first-line therapy and so require further antibiotics. Dalbavancin, a second-generation lipoglycopeptide bactericidal antibiotic that is active against susceptible Gram-positive pathogens and can be administered as just two doses on days 1 and 8, provides a second-line option.

Materials/methods: The OPAT team report a cohort of 15 patients from a larger case series of 202 patients with skin and soft tissue infections, in whom dalbavancin was used as second-line therapy after previous antibiotic failure (Table 1).

Results: The 15 patients had failed on a variety of previous antibiotics, including teicoplanin (n=1), daptomycin/ceftazidime (n=1), flucloxacillin/tigecycline (n=1), daptomycin (n=4), clindamycin (n=2), ceftriaxone/teicoplanin (n=1), doxycycline (n=2), co-trimoxazole (n=2) and daptomycin/ciprofloxacin (n=1). Fourteen patients were given 1,500 mg dalbavancin as two doses – alone or in combination with clindamycin (n=2), ciprofloxacin (n=1) or doxycycline (n=1). One patient received 1,000 mg dalbavancin. In all 15 cases, the infection resolved, with three admissions prevented.

Conclusions: For patients with skin and soft tissue infections who fail on first-line antibiotics in the OPAT setting, dalbavancin provides an effective, convenient and potentially cost-saving second-line option.

Table 1 Case series: patient histories.

<table>
<thead>
<tr>
<th>Patient</th>
<th>History</th>
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<tbody>
<tr>
<td>9</td>
<td>Leg cellulitis</td>
</tr>
<tr>
<td>13</td>
<td>Bilateral leg cellulitis</td>
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<tr>
<td>18</td>
<td>Apron infection and leg cellulitis</td>
</tr>
<tr>
<td>54</td>
<td>Enterococcal bacteraemia</td>
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<tr>
<td>55</td>
<td>Staphylococcus aureus bacteraemia</td>
</tr>
<tr>
<td>83</td>
<td>Skin and soft tissue infection (flare up of pyoderma gangrenosum)</td>
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<tr>
<td>85</td>
<td>Right groin abscess</td>
</tr>
<tr>
<td>105</td>
<td>Skin and soft tissue infection</td>
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<tr>
<td>108</td>
<td>Skin and soft tissue infection</td>
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<tr>
<td>128</td>
<td>Skin and soft tissue infection (left foot ulcer)</td>
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<tr>
<td>136</td>
<td>Skin and soft tissue infection</td>
</tr>
<tr>
<td>148</td>
<td>Skin and soft tissue infection (apron cellulitis)</td>
</tr>
<tr>
<td>156</td>
<td>Skin and soft tissue infection (multiple infected pressure sores; Group C streptococci and Pseudomonas)</td>
</tr>
<tr>
<td>177</td>
<td>Skin and soft tissue infection</td>
</tr>
<tr>
<td>196</td>
<td>Skin and soft tissue infection</td>
</tr>
</tbody>
</table>

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Multiple evaluation of surgical antimicrobial prophylaxis in Japanese university hospitals

Hiroshi Morioka*, Hiroki Ohge¹, Miki Nagao¹, Hideaki Kato¹, Ryoshei Kokado¹, Koichi Yamada², Takahiro Yamada³, Nobuyuki Shimo¹, Yoko Nukui⁴, Shingo Yoshihara⁵, Ippei Sakamaki⁶, Kisato Nosaka⁷, Yoko Kubo⁸, Hideki Kawamura⁹, Yuji Fujikura¹⁰, Tsuyoshi Kitaura¹¹, Mitsuhiro Sunakawa¹², Tetsuya Yagi¹³

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Abstract third-party references: On behalf of the Sectional Meeting of Clinical Research and Data Collection, Japan Infection Prevention and Control Conference for National and Public University Hospitals.

Background: Optimal surgical antimicrobial prophylaxis (SAP) can reduce surgical site infections, cost, and adverse events. In Japan, overall evaluation of SAP have not been performed. The purpose of this study was to reveal the adherence of Japanese Clinical Practice Guidelines for antimicrobial prophylaxis in surgery (JCPGL-AP), which was published in 2016, and to extract problems about SAP in Japanese university hospitals.

Materials/methods: This study was performed at 16 university hospitals (including 1 dental hospital). A total of 18 surgeries performed to over 18 year-old patients were selected to evaluate adherence of JCPGL-AP. Maximum 3 cases per each surgery within 4 weeks were collected from September to December 2018. To evaluate appropriateness of SAP, following items were surveyed: choice of antimicrobials during/after surgery, timing of administration before/during surgery, and duration of SAP. Surgeries were defined as appropriate SAP when all items were adhered to JCPGL-AP. Ophthalmologic- and neuro-surgeries were not listed in JCPGL-AP, thus open craniotomy and cataract surgery were excluded to evaluate the antibiotics choice and duration of SAP.

Results: A total of 688 cases were included in this study. Collected cases ranged from 22 to 45 (median 42) by the surgery, and 3 [dental hospital] to 54 (median 47) by the hospital, respectively. Percentage of appropriate items were as follows: choice of antimicrobials during surgery (467/601, 77.7%) / after surgery (475/601, 79.0%), timing of administration before surgery (632/664, 95.1%) / during surgery (612/665, 92.0%), and duration of SAP (375/601, 62.4%). Figure shows the percentage of appropriate SAP (281/601, 46.8%), duration of SAP over 3 days (115/688, 16.7%), and oral antimicrobial use after surgery (57/688, 8.3%). Percentage of appropriate SAP of general university hospitals ranged from 20.0% to 76.9% (median 48.8%).

Conclusions: Adherence rate of JCPGL-AP were significantly differed among surgeries and university hospitals. Oral Antimicrobial use after surgery and longer duration of SAP were seen in specific surgeries. Data of SAP about more surgeries and from community hospitals are necessary to reveal real-world SAP in Japanese hospitals.
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Abstract 1774

Contact effect of a Methylobacterium sp. extract on biofilm of a Mycobacterium chimaera strain isolated from a 3T heater-cooler system

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Abstract third-party references: Funded by a grant from the Instituto de Salud Carlos III (PI18/01068).

Background: Mycobacterium chimaera is an opportunistic, slowly growing, non-tuberculose mycobacterium currently gaining in importance due to the rise in mycobacteremia cases provoked by a strain that contaminates the 3T heater-cooler device (HCD) extracorporeal membrane oxygenator (ECMO). The aim of this study was to evaluate the effect of pre-treating a surface with a Methylobacterium sp. CECT 7180 extract to inhibit the biofilm development of M. chimaera ECMO strain.

Materials/methods: The extract of the Methylobacterium sp. CECT 7180 was performed according to García-Coca et al. (J Antimicrob. 2019 Sep 3). The effect of this extract on biofilm development of M. chimaera ECMO was evaluated at 24, 48, 72, 96, and 120 h using hydrophobic uncoated sterile slide 24-well plates (Ibidi GmbH, Martinsried, Germany) according to the methodology described previously by Muñoz-Egea et al. (Appl. Environ. Microbiol. 2013 Feb; 79(3):1065–1067). Pretreatment consisted of treating at room temperature for 15 min with 0.3 ml of PBS (control) or with 0.3 ml of Methylobacterium sp. CECT 7180 extract. After 15 min, the supernatant was removed and each well was washed once with PBS. Four parameters were studied: covered surface (%), thickness (μm), viability (%) and relative autofluorescence (%). Each condition was performed by triplicate.

The statistical data were analyzed by nonparametric pairwise comparisons using the nonparametric Mann-Whitney test with a level of statistical significance of p<0.05. The values are cited as median and interquartile range.

Results: The results obtained are represented in Figure 1.

![Figure 1. M. chimaera ECMO biofilm development over time on a control surface (gray) and on a surface treated with Methylobacterium extract (black). The four parameters evaluated were mycobacterial viability (A), biofilm height (B), biofilm covered surface (C), and relative autofluorescence (D). Bars indicate tenth and ninetieth percentiles. #: P-value < 0.001 for Wilcoxon test between control surfaces and surfaces treated with Methylobacterium extract. The bar represent 10th and 90th percentile.](image)

Conclusions: In conclusion, exposing a surface to the Methylobacterium sp. Extract inhibits M. chimaera ECMO biofilm development. This extract could be used as a pre-treatment prior to disinfection protocols for equipment contaminated with mycobacteria.

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NDT80 transcription factor acts as a repressor of Candida parapsilosis virulence attributes

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3CNC-Centre for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal, Coimbra, Portugal
4FMUC-Faculty of Medicine, University of Coimbra, Coimbra, Portugal, Coimbra, Portugal
5UniC –Cardiovascular R&D Center, Faculty of Medicine, University of Porto, Porto, Portugal., Porto, Portugal
6Burnit Unit, São João Hospital Center, Porto, Portugal

Background: Candida parapsilosis is a predominant species within non-albicans yeast responsible for invasive candidosis among immunocompromised patients. In fact, the prevalence of C. parapsilosis results from its notorious capacity to persist in the hospital environment for long periods. This ability is associated with its propensity to adhesion and form biofilm. In C. albicans, Ndt80 is one of the transcription factors that controls biofilm formation, hyphal growth and expression of genes related with cell wall organization. In C. parapsilosis, Ndt80 was associated with biofilm formation, however, its mechanistic role remain unveiled. This study aimed to understand the role of NDT80 - CPAR2-213640 in C. parapsilosis virulence attributes.

Materials/methods: From C. parapsilosis BC014S strain two independent lineages lacking one (ndt80Δ – NG2 strain) or both (ndt80ΔΔ - EF16 strain) copies of CpNDT80 gene were generated using the SAT1-Flipper cassette. ndt80Δ and ndt80ΔΔ adherence to polystyrene microspheres (as a representative of abiotic surface) was quantified using a flow cytometric adhesion assay. Biofilm formation was also quantified by two independent methods: CV staining and dry weight. Gene expression of a set of transcription factors recognized as regulators of virulence factors (ALS7, ALS3, CZF1, UME6, GZF3, CPH2, EFG1, BCR1, ACE2, STP3, CWH41, OCH1, RHR2 and MKC1) in C. parapsilosis were assessed by RT-qPCR. Using the murine macrophage cell line RAW264.7, the interaction of fungal-host immune system was characterized through macrophage fungal internalization and macrophage killing.

Results: Deleting NDT80 substantially changed colony and cell morphologies from smooth and yeast-shaped to crepe and pseudohyphal elongated forms. Adherence to polystyrene microspheres and biofilm formation were enhanced in both ndt80Δ and ndt80ΔΔ mutants comparatively to wild type strain. Additionally, we identify NDT80 as a repressor of ALS7, UME6, CPH2, CWH41, ACE2 and MKC1 transcription factors, being overexpressed in ndt80ΔΔ strain and associated with the trigger of virulence attributes exhibited by this strain. Ultimately, ndt80ΔΔ mutants, in their natural pseudohyphae phenotype, were more efficient in macrophage killing.

Conclusions: Our findings clearly demonstrate Ndt80 as a repressor of Candida parapsilosis virulence attributes (morphogenesis, adhesion and biofilm formation). Interestingly, phenotypes exhibited by ndt80ΔΔ mutants also confer enhanced ability to neutralize immune system response.

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Abstract 1779

Cross-platform comparison of one qPCR assay with four leading technologies and six master mixes for the detection of Pneumocystis jirovecii

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Background: Pneumocystis jirovecii is a fungus responsible for severe pneumonia in immunocompromised patients. Quantitative real-time PCR (qPCR) performed on respiratory samples is essential to detect and quantify this non-cultivable pathogen. Many molecular assays have been developed and lack of standardization results in significant differences among assays/centers. Studies initiated by the Fungal PCR Initiative evaluated 20 assays in 16 diagnostic centers pointing out the superiority in sensitivity of the mitochondrial small subunit (mtSSU) target. To further promote standardization, we compared four thermocyclers and six master mixes for the detection of P. jirovecii.

Materials/methods: Whole nucleic acid (WNA) from three qPCR-positive and ten qPCR-negative broncho-alveolar lavages were extracted on QiaSymphony with the Virus Kit Pathogen (Qiagen). Positive and negative extracts were pooled to provide sufficient homogeneous material. The positive pool was extemporaneously diluted at 1:5, 1:10, 1:50, 1:100 and 1:1000 in the negative pool. Three master mixes were tested to detect DNA by qPCR and three to detect WNA by reverse transcriptase qPCR (Table 1). All tests targeted mtSSU using the same primers and probes. Experiments were performed on four thermocyclers (LightCycler 480, ABI7500, QuantStudio and Rotorgene).

Results: Comparison of quantitative cycle (Cq) values between the methods targeting WNA and the methods targeting DNA showed lower Cq values with WNA independently from thermocycler and mix. For high (pure extract) and low (1:1000 dilution) fungal loads, ∆Cq values were 6.97 (± 2.95) and 5.81 (± 3.30) respectively (p<0.0001). Regarding DNA detection, lower Cqs were obtained with Mix1 compared to Mix2 and Mix3 with median ∆Cq of 2.6 (p=0.015) and 2.9 (p=0.039) respectively. Regarding WNA detection, no mix was superior to the others. The mean efficiency of PCR reactions was similar. PCR efficiency was not significantly different according to the qPCR equipment (p=0.14).

Conclusions: This study confirms that amplifying WNA is more sensitive than DNA alone to detect P. jirovecii nucleic acids. Variability observed due to enzyme/kit and thermocycler is a hurdle to harmonizing PCR protocol and producing comparable data among centers. Further studies should focus on developing a calibration method for accurate assessment of fungal load.

Materials and methods:

<table>
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<tr>
<th>Mix</th>
<th>Probes Master Mix</th>
<th>Manufacturer</th>
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<tbody>
<tr>
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<td>2</td>
<td>MasterMix Plus Low ROX</td>
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<td>LightCycler Multiplex RNA Virus Master</td>
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Association between susceptibility to quinolones in *Escherichia coli* and tetracycline use in the community: analysis of 9 communities with a single model

Marie-Anne Vibet1,2, François Javaudin1,2, Marcelo Low1, Batseahe Gottesman1, José-María López-Lozano4, Emmanuel Montassier1,2, Eric Batard*1;2

1University of Nantes, Microbiotas Hosts Antibiotics bacterial Resistances [MiHAR], Nantes, France, 2Nantes University Hospital, Nantes, France, 3Clalit Health Services, Tel Aviv, Israel, 4University of Murcia, Murcia, Spain

**Background:** Tetracyclines are extensively used in the community. We previously found that tetracycline use was associated with resistance to quinolones in *E. coli* in a French community, but this association was not described in other communities. Pharmaco-epidemiological studies are usually conducted with arima models, that only apply to a single site. However, results of a model derived from a given site may not be extrapolated to another site. Our aim was to assess the association between tetracycline use and quinolone susceptibility in *E. coli* isolates of several communities, using a single model.

**Materials/methods:** Monthly time series of proportions of quinolone susceptible *E. coli* and uses of quinolones and tetracyclines [in DDD/1000 inhabitants/month] were obtained from 9 communities (France, n=1; Israel, n=7; Spain, n=1), between 2009 and 2018. A single linear mixed effects model was used to assess the relationship between antimicrobial use and resistance in different sites, with site as a random effect, including a 1st order auto-correlation. Results were provided as estimate (95% confidence interval) of fixed effect (FE) and range of random effects (RE).

**Results:** Median (range) population was 434,000 (190,000 to 1,346,000). The proportion of susceptible isolates increased significantly with time [time FE, +0.032 (+0.012 to +0.052); RE range, -0.041 to +0.036]. Quinolone use significantly decreased [time FE, -0.21 [-0.30 to -0.11]; RE range, -0.30 to +0.15], but tetracycline use showed no significant temporal trend [time FE, 0.01 [-0.06 to +0.07]; RE range, -0.12 to +0.18]. In multivariate analysis, quinolone susceptibility was associated with both quinolone use [lag, 7 months; FE, -0.040 [-0.074 to -0.004]; RE range, -0.022 to +0.006] and tetracycline use [lag, 8 months; FE, -0.073 [-0.140 to -0.007]; RE range, -0.198 to +0.094].

**Conclusions:** A single linear mixed effects model with autocorrelation can be used to assess the relationship between antimicrobial use and resistance in several communities. Both community uses of tetracycline and quinolones were associated with decreased susceptibility to quinolones in *E. coli*, with high variability across communities. These results suggest that decreasing tetracycline use in the community may decrease quinolone resistance in community isolates of *E. coli*.

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**Abstract 1782**

**A mortality prediction model for adult intensive care unit patients infected with Klebsiella pneumoniae in a tertiary hospital: a retrospective cohort study**

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**Background:** Klebsiella pneumoniae (K. pneumoniae) infections, especially infections with multidrug-resistant strains, can be life-threatening and are a critical public health concern. K. pneumoniae infections are even more critical and the antibiotic resistance rate is much higher in intensive care unit (ICU) patients. This study aimed to develop and evaluate the accuracy of a prediction model and risk score to predict 14-day mortality in adult ICU patients infected with K. pneumoniae in a tertiary hospital.

**Materials/methods:** For this retrospective cohort study, data were extracted from the medical records of adult patients admitted to the ICU of a 1900-bed tertiary hospital in Vietnam in 2016-2018 and in whom K. pneumoniae was isolated. We used univariable and multivariable logistic regression analyses to develop a valid prediction model and a simplified risk score for 14-day mortality. We assessed their discriminative ability by optimism-corrected area under a receiver operating characteristic curve (AUC) and their calibration by calibration plots and Hosmer-Lemeshow test statistics.

**Results:** In total, 249 patients were included in the analysis. Their 14-day mortality was 28.9%. Out of 18 prognostic determinants, the final prediction model comprised of route of referral, Sequential Organ Failure Assessment score and Charlson comorbidity index at infection onset, presence of central venous catheter, intracerebral haemorrhage operation within 72 hours before infection onset, and the absence of adjunctive treatment to remove the probable focus of infection [see Table 1; AUC (95% CI): 0.80 (0.76-0.82); Hosmer-Lemeshow test: p=0.165, after bootstrapping]. The simplified risk score corresponded to a very low (0%), low (7.8%), moderate (18.2%), high (50.6%) and very high (100%) risk of mortality for scores 0-1, 2-3, 4-5, 6-8 and 9-13, respectively.

**Table 1.** Independent predictors of 14-day mortality, the corresponding odds ratios and contribution to risk score

<table>
<thead>
<tr>
<th>Prediction model</th>
<th>Regression coefficients (95% CI)</th>
<th>OR (95% CI)</th>
<th>Contribution to risk score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>-4.76 (-6.27, -3.45)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Route of referral</td>
<td>0.87 (0.19, 1.83)</td>
<td>2.65 (1.21, 6.21)</td>
<td>1</td>
</tr>
<tr>
<td>SOFA score 4-11</td>
<td>1.50 (0.39, 2.36)</td>
<td>3.68 (1.47, 10.83)</td>
<td>2</td>
</tr>
<tr>
<td>SOFA score ≥12</td>
<td>2.20 (0.95, 5.34)</td>
<td>8.99 (2.58, 34.90)</td>
<td>3</td>
</tr>
<tr>
<td>Charlson index ≥1</td>
<td>0.72 (0.28, 1.74)</td>
<td>2.06 (0.76, 6.67)</td>
<td>1</td>
</tr>
<tr>
<td>Charlson index ≥2</td>
<td>0.64 (0.05, 1.08)</td>
<td>2.32 (1.05, 5.37)</td>
<td>1</td>
</tr>
<tr>
<td>Central venous catheter</td>
<td>1.40 (0.66, 2.30)</td>
<td>4.28 (1.95, 9.01)</td>
<td>2</td>
</tr>
<tr>
<td>Intracerebral haemorrhage</td>
<td>1.29 (0.19, 2.64)</td>
<td>4.03 (1.21, 14.05)</td>
<td>2</td>
</tr>
<tr>
<td>Operation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absence of adjunctive treatment</td>
<td>2.75 (1.67, 3.97)</td>
<td>15.65 (5.33, 52.90)</td>
<td>4</td>
</tr>
</tbody>
</table>

OR = Odds Ratio; 95% CI = 95% Confidence Interval; SOFA = Sequential Organ Failure Assessment

* Simplified risk score: Total score = 1*Intra-hospital referral + 2*SOFA score 4-11 + 3*SOFA score ≥12 + 1*Charlson index ≥ 1 + 2*Presence of Central venous catheter + 2*Intracerebral haemorrhage operation + 4*Absence of adjunctive treatment

**Conclusions:** We constructed a prediction model and risk score for 14-day mortality in adult ICU patients with K. pneumoniae infection in a tertiary hospital which could support patient risk stratification and clinical decision making in this setting.

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Abstract 1786

**Temporal and regional prevalence of carbapenemase-producing Enterobacterales in Switzerland from 2013 to 2018**

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**Background:** Increasing rates of carbapenemase-producing Enterobacterales (CPE) have been observed in Europe and all over the world. CPE represent a great concern since they are frequently associated to resistance to multiple antibiotics thus reducing therapeutic options.

**Materials/methods:** Data on human CPE isolates from 2013 to 2018 were collected by the Swiss Centre for Antibiotic Resistance (ANRESIS) and analysed for temporal and regional trends. A statistical detection of regional clusters was performed with the SaTScan software embedded in WHONET.

**Results:** From 2013 to 2018, yearly detection of CPE isolates has increased considerably from 65 to 212. The most frequently isolated species were *Klebsiella pneumoniae* (54% of the cases), followed by *Escherichia coli* (28%). The most frequent carbapenemase genotypes were OXA-48-types (43%), KPC (21%), and NDM (14%). At the regional level, highest numbers of CPE isolates per 100'000 inhabitants were identified in the Geneva and the Ticino regions. Multivariable analyses of regional and temporal trends of CPE cases confirmed an increase in total number, higher prevalence in the Geneva region and in male patients. In contrast to the French speaking parts (Western and Geneva regions) where OXA-48-types were the predominant genotypes (55% and 60%, respectively), KPC was the most frequently detected genotype in the Italian speaking region of Ticino (62%). SaTScan outbreak detection analysis identified a total of seven clusters in five different regions of Switzerland.

**Conclusions:** In a first continuous surveillance of CPE in Switzerland it was shown that the epidemiological situation aggravated nationwide and that regional patterns of CPE genotypes mirror the situations in neighbouring European countries.

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Abstract 1788

**Characterisation of immune response of patients with rheumatic disorders and latent tuberculosis infection**

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**Background:** The use of antitumor necrosis factor agents (anti-TNF) (biologics) for the treatment of inflammatory rheumatic disorders has reopened the tuberculosis (TB) problem also in countries with low TB incidence, due to the increased risk of TB reactivation in subjects with latent tuberculosis infection (LTBI). This study aims to evaluate the effect of biologics on acquired immunity to Mtb, at enrolment and at the end of preventive treatment.

**Materials/methods:** We enrolled 11 RD-LTBI at the baseline and at the end of preventive treatment. LTBI subjects started the biological agent after the first month of TB-therapy. As controls, we enrolled 11 LTBI subjects without RD. Cells were stimulated with antigens contained in TB1 and TB2 tubes of QFT-Plus. We characterized the cytokine (IFNγ, TNFα, IL2) and phenotypic profile (CD45RA, CD27) of Mtb-specific T-cells by cytometry. Wilcoxon signed rank test was performed.

**Results:** We found that the use of biological drugs does not reduce the ability of CD4 and CD8 T-cells to respond to Mtb stimulation. Moreover, we found an increased CD8 T-cell response at the end of TB preventive therapy in both LTBI groups.

Regarding the CD4 T-cell response, LTBI subjects had higher proportion of IFNγ+TNFα+IL2+CD4+ T-cells [p=0.04] and IFNγ+TNFα+IL2+CD4+ T-cells [p=0.01] at the baseline compared to end of therapy. Differently, RD-LTBI subjects had a similar cytokine profile of CD4 T-cells before and after TB-therapy.

Regarding the CD8 T-cell response, this response was characterized by a high proportion of IFNγ producing T-cells both before and after TB-therapy, independently of the RD status.

Regarding the phenotype, the Mtb-specific CD4 T-cells showed predominantly a central memory phenotype before and after TB-therapy, independently of the RD status.

**Conclusions:** The increased risk to develop active-TB disease is an emerging aspect in the use of biological drugs of patients with rheumatic disorders. These preliminary data show that the use of biological agents does not reduce the ability of CD4 and CD8 T-cells to respond to Mtb-stimulation. This study is helpful to understand the immunological safety of the biological drugs and to identify new candidate biomarkers of Mtb-infection.

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Background: Distinctive characteristics of *Strongyloides stercoralis* are its ability to persist and replicate within a host for life and its potential to cause life-threatening infection in an immunocompromised host as HIV patients. The aims of this cross-sectional study were to describe the results of a systematic serological screening program for strongyloidiasis in HIV positive patients.

Materials/methods: Between 2009 and 2018, a prospective serological screening program for strongyloidiasis in all immigrant patients diagnosed of HIV infection with infection confirmed by Western-Blot, in Asturias, a region in the north of Spain was conducted. Three formalin-ether concentrated stool samples and an enzyme-linked immunosorbent assay for anti-*S. stercoralis* antibodies were used as screening tools. We considered that infection exists if the microscopic visualization of larvae in stool sample and/or the ELISA was positive. In positive patients was discarded the presence of other nematodes or filarias.

Results: Of the 83 screened patients (average age 39 [10] years, 61.8% of them female, average time in Spain 760 days), Twelve patients (13.5%) had a positive serological test for *S. stercoralis* and in only four of them was the microscopic visualization of larvae of *S. stercoralis* by formalin-ether concentration of faeces positive. The areas of origin were Central Africa (61.4%), South America (26.5%), West Africa (7.2%), North Africa and Mexico and Central America (2.2% respectively). Fifty percent of *Strongyloides* positive patients come from Central Africa (6/51, prevalence 11.7%) and the rest from South America (6/22; prevalence 27.2%; P= 0.0550; OR 3.4375 [0.9739 - 12.1325]). Infection was significantly more frequent in patients from Paraguay (P = 0.0042 OR 81 [4.0066 – 1637]). There is not differences in CD4+ count, viral load, sex, age or time in Spain between infected and no infected patients. No patients had HTLV-I co-infection. Fifty-two percent of patients were asymptomatic at the moment of diagnostic. *Strongyloides* positive patients had higher levels of eosinophilia (842,42 ±724,989 cells/mm$^3$ versus 280,91 ± 428,765 cells/mm$^3$; p=0.003)

Conclusions: Strongyloidiasis is frequent in immigrant HIV positive patients, specially proceeding from Equatorial Guinea and Paraguay. Screening for Strongyloidiasis, even in asymptomatic patients should be taken fully into account. Serological test are useful in screening programs.

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Anidulafungin-loaded hybrid organo-inorganic sol-gel coating can prevent the prosthetic joint infections provoked by Candida albicans

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Abstract third-party references: Funded by a grant from the Mutua Madrileña Foundation

Background: Prosthetic joint infections occur infrequently, but they represent the most devastating complication. Nowadays, yeast belonging to Candida genus, mainly C. albicans, are gaining relevance. These PJIs are infrequent, they use to show high recurrence rates. Local antibiotic therapy is a desired feature which would allow locally preventing or treating these infections. In order to overcome prosthetic joint infection, sol-gel technology allows loading the coating with antifungal and osteointegrative molecules such as organophosphate compounds. The aim of this work was to evaluate the prophylactic effect of coatings loaded with anidulafungin using an in vivo murine model of candidal prosthetic joint infection.

Materials/methods: Sol-gel coating was produced using a molar ratio of 1:2 (MAPTMS:TMOS) and an organophosphate dispersed in ethanol. The unloaded coating was loaded with 20 mg of anidulafungin per 20.3 mL and was used to coat chemical polished Ti6Al4V samples (CP+A). Chemical polished Ti6Al4V samples without coating were used as control (CP). The surgical procedure was performed as described previously by Lovati et al. (PLoS One. 2013 Jun 20;8(6):e67628) using only one of two femurs of each mouse treated ad libitum with 4 mg/mL of dexametasone and 100 mg/mL of enrofloxacin from a week before surgery and upwards and infected with a C. albicans isolated from a hip PJI (Cal 35). During five weeks, weight, limping and piloerection of animals were monitored. After five weeks, the animals were sacrificed and the bacterial load was estimated and confirmed in the peri-implant bone tissue and the implant using the methodology described by Esteban et al. (J. Clin. Microbiol. 2008 vol. 46 no. 2 488-492). Each treatment was performed five times

Results: The results are shown in the Figure 1. Fifty percent (3/6) of Cal 35-infected CP group were positive culture and 100% percent Cal 35-infected CP+A group were negative culture (0/6) (p-value=0.0228).
Figure 1. Median weight (A), limping (B), piloerection (C), and survival (D) in different noninfected group (black), and Cal 35-infected group (green) with CP (left column) and CP+A (right column) over time.

Conclusions: Anidulafungin-loaded hybrid organo-inorganic sol-gel coating can prevent at local level PJII provoked by C. albicans.

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Seredagnosis of Lyme borreliosis: is IgM in serum more harmful than helpful?

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Background: Interpretation of serological findings in suspected Lyme borreliosis (LB) may be challenging in endemic areas and IgM antibodies in serum are often associated with false positive reactivities. There is a risk for over-diagnosis of LB, inadequate use of antibiotics and potential delay of proper diagnosis. The clinical value of IgM analysis in serum in LB diagnosis is therefore questioned. The aims of this study were to investigate how well the clinical recommendations for the diagnosis of LB and when to test for borrelia-specific antibodies were followed in Jönköping County, Sweden, and to evaluate the clinical value of IgM antibodies in serum.

Materials/methods: In total, 4428 borrelia-specific antibody tests in serum were analyzed in Jönköping County during 2017. Of these, 643 individual patients had positive results (IgM and/or IgG), of which we had to exclude 33 patients due to inaccessible medical records. The remaining patients (n=610) with positive test results were then divided into separate groups of either IgM and/or IgG-positivity. Based on current European recommendations, we defined the criteria for correct indication for serological testing and how to evaluate the diagnosis made by the clinician. Medical records and laboratory test results for each patient were then assessed according to these criteria.

Results: Only 183/610 (30%) of patients were tested according to the European recommendations. The groups positive for either isolated IgG or both IgM and IgG antibodies showed a similar pattern with high number of diagnoses assessed as being confident or doubtful. Isolated detection of IgM (without concomitant IgG) was only helpful in 50% of the diagnoses assessed as being confident or doubtful. Thus, 50% of the LB diagnoses in patients with isolated IgM reactivity in serum were assessed as incorrect (LB unlikely).

Conclusions: Isolated IgM positivity in serum shows limited clinical value in LB diagnostics and needs further assessment before being reported by the laboratory.

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Abstract 1800

Application of a new molecular biology method for carbapenem-resistant Enterobacteriaceae detection in rectal swabs

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Background: The extreme ease with which the CPEs (Carbapenemase Producing Enterobacteriaceae) spread, requires the implementation of an effective screening program that allows the rapid identification of resistant strains. In this study we evaluated the diagnostic utility of an innovative molecular biology method for CPE detection in rectal swabs. Furthermore, we verified the percentage of rectal colonization as a predictive event for CPE bacteremia in the patients.

Materials/methods: In February-March 2019, 153 rectal swabs from intensive care unit (36%), hematology (19%), cardiology (17%), and other departments (28%) were examined. All the samples were analyzed by phenotypic method on McConkey with Ertapenem disk and E-test on MH for Meropenem (Biomerieux) and examined by Real-time PCR multiplex, using Allplex Entero-DR Assay kit (Allplex, Seegene, Republic of Korea) on automatic system Nimbus IVD (Seegene) which allows to identify simultaneously 8 resistance genes: KPC, VIM, NDM, IMP, OXA-48; van-A, vanB; CTX-M. Blood cultures were analyzed with automatic Bactec FX (BD) system, subcultures from positive vials and identification by mass spectrometry (MALDI-TOF Bruker). Antibiograms were performed with Phoenix instrument (BD) and interpreted according to EUCAST criteria.

Results: The results obtained by phenotypic method and molecular screening indicate a perfect agreement between the two tests for 135 samples (88%). In particular, 20 (13%) were positive for the molecular method only, for CPE resistance genes, 115 samples (75%) agreed on negativity and positivity to resistance genes for ESBL and VRE genes, 59% (10 of 17) of patients with positive molecular analysis and negative culture had already been positive before. We also evaluated how many of the examined patients, positive for CPE rectal colonization, subsequently developed bacteremia: 25% (39 patients) of patients tested were affected by bacteremia caused by the same micro-organism.

Conclusions: The application of new molecular biology techniques in surveillance allows the rapid detection of CPE and given the extreme sensitivity of the method, is able to detect the presence of resistance genes early even in conditions of low bacterial load. This approach offers the clinician useful information for patient management and the possibility of promptly administering the most appropriate antibiotic therapy to counteract a possible bacteraemia.

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Abstract 1801

**Impact of ribotype on *Clostridioides difficile* diagnostics**

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**Background:** *Clostridioides difficile* infection (CDI) is one of the most common health-care associated infections worldwide. The ability of a strain to produce toxins is crucial for clinical disease. An accurate diagnosis of CDI remains a challenge, and underdiagnosis is an issue in Europe. A wide variety of diagnostic tests are available and the choice of reference method or gold standard is crucial in order to assess the accuracy of a test. One drawback of many studies comparing diagnostic techniques is that the local epidemiology is not taken into consideration, and several studies have been carried out in high prevalence or outbreak settings. This prospective study investigates the performance of diagnostic methods for detection of *C. difficile* infection in Sweden, including impact of PCR ribotype on diagnostic performance.

**Materials/methods:** Between 2011 and 2016, a total of 17,878 stool samples from 26 laboratories were tested by either well-type enzyme immunoassays (EIAs), membrane bound EIAs, cell cytotoxicity neutralization assay (CTA) or nucleic acid amplification tests (NAATs) and subsequently cultured for *C. difficile*. Roughly half of the samples (9,454/17,878) were subjected to diagnostic testing both on the fecal sample and on the 1,323 isolated *C. difficile* strains. All *C. difficile* isolates were typed by PCR ribotyping, and classified as toxigenic or non-toxigenic based on the empirical knowledge of the association between toxin-positivity and ribotype.

**Results:** The overall sensitivity, specificity, and positive and negative predictive values were highest for NAATs and membrane EIAs. Ribotype specific sensitivity varied greatly between methods and ribotypes. All methods had 100% sensitivity against ribotype 027 and 013. For other types the sensitivity ranged from 33% to 85% in fecal samples and from 78% to 100% on isolates. For the most prevalent ribotypes (014, 020 and 001) the sensitivity varied between 38% and 100% in the fecal samples, with the lowest sensitivity observed for well-type EIAs and CTA.

**Conclusions:** The large variation in diagnostic sensitivity implies that type distribution significantly affects the outcome when evaluating diagnostic performance. Furthermore, performing comparative studies of diagnostic tests in settings with high prevalence of ribotype 027 will overestimate the general performance of diagnostic tests.

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Abstract 1802

Changes in the gut microbiota due to smoking in patients with inflammatory bowel disease

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Abstract third-party references: Smoking Research Foundation

Background: Smoking is one of the important factors affecting the onset and pathogenesis of inflammatory bowel disease (IBD). The effects of smoking are different depending on the disease types, and it is thought to promote the aggravation and relapse of Crohn’s disease (CD), but to suppress those of ulcerative colitis (UC). However, the underlying mechanisms by which smoking affects IBD has not been fully studied. In this study, we investigated the effects of smoking on the composition of oral and intestinal microbiota.

Materials/methods: Saliva, feces, and colonoscopy aspirates from 77 UC (smokers 10, ex-smokers 28, non-smokers 39) and 12 CD (smoker 3, ex-smoker 3, non-smoker 6) patients. The gut microbiota was analyzed by 16S rRNA gene sequencing.

Results: The subjects were classified into 4 clusters (Cluster A to D) from the microbial composition of colonoscopy aspirates rich in mucoadhesive bacteria. Smokers were predominantly classified (8 out of 13), whereas non-smokers were not (19 out of 76), in Cluster D. Co-abundance groups analysis revealed that patients clustered in Cluster D had increased abundance of oral bacteria, including Streptococcus, in the colonic aspirates. Streptococcus and Megasphaera were also increased in the saliva of smokers.

Conclusions: Smoking seems to facilitate the colonization of oral bacteria in the colonic mucosa. This might affect the mucosal immune system and the pathology of IBD.

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Abstract 1804

Comparison of Cutibacterium acnes biofilm formation between strains isolated from prosthetic joint infection and healthy skin microbiota

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Background: Cutibacterium acnes is a Gram-positive facultative anaerobe rod. It colonizes human skin and can causes invasive infections such as periprosthetic joint infection (PJI). C. acnes causes disease through a number of virulence factors, such as biofilm formation during implant infection. In this study, we compared the biofilm formation of C. acnes isolates recovered from healthy skin with isolates recovered from deep tissue in PJI patients.

Materials/methods: We used the modified in-vitro biofilm test by Stepanovic et al. (APMIS 2007, 115 (8): 891-9) as a static biofilm assay, using BHI+ 2% glucose with a bacterial inoculum of 10⁷ CFU/mL at 37°C for 48h in anaerobic conditions and crystal violet for staining. One hundred and twenty-five C. acnes isolates recovered from PJI (n=89) from eight European centers, and healthy skin from face (HS) volunteers (n=36) were used. Biofilm formation of isolates was based on the optical density (OD) of each strain and the optical density control (ODc) measured at 570 nm, and classified into weak (ODc<OD<2xODc), moderate (2xODc<OD<4xODc), and strong (OD>4xODc) biofilm-former. The statistical data were analyzed by using a comparison test of proportions with a level of statistical significance of p<0.05.

Results: All isolates were biofilm-former types (Table 1). There was no statistical significant difference in between the biofilm-forming ability of strains isolated from these different sources.

<table>
<thead>
<tr>
<th>Biofilm-former type (%)</th>
<th>PJI  [n]</th>
<th>HS  [n]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate</td>
<td>57.30 [51]</td>
<td>72.22 [26]</td>
<td>0.120</td>
</tr>
</tbody>
</table>

Table 1.

Conclusions: Although some reports suggest that C. acnes strains isolated from PJI produce more biofilm in vitro [Holmberg et al. Clin Microbiol Infect. 2009; 15 (8): 787-95], according with our data, both infection-associated and skin commensal isolates of C. acnes have the potential to form a static biofilm in vitro independently of the source of isolation.

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Abstract 1805

Prevalence of non-tuberculous mycobacteria in a tertiary hospital in Beijing, China, January 2013 to December 2018

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Background: In China, patients diagnosed with tuberculosis (TB) or suspected of having TB, are referred to a thoracic specialist hospital for further treatment. However, clinical manifestations of non-tuberculous mycobacteria (NTM) diseases and TB are quite similar. A considerable number of patients TB or suspected TB, are lost in tertiary hospitals. This study retrospectively analyzed the identification data of NTM samples to provide a general outline of the prevalence of NTM in a tertiary hospital in China.

Materials/methods: Clinical data of patients who tested positive/negative for Mycobacterium tuberculosis (MTB) or NTM using a screening test (Real-time fluorescent PCR detection) from January 2013 to December 2018 at Peking Union Medical College Hospital [Beijing], were collected. Data on Mycobacteria species identification, which was carried out by DNA microarray chip, was also collected. Trend analysis of annual constituent ratio was carried out by trend Chi-square tests using SPSS 22.0 and a P value < 0.01 was considered statistically significant.

Results: Mycobacterial species were detected in 1514 specimens from 1508 patients, among which NTM accounted for 37.3% (565/1514), increasing from a prevalence of 15.6% in 2013 to 46.1% in 2018 (P<0.001). Among the 565 NTM positive specimens, the majority (55.2%) were from female patients. Furthermore, patients aged 45-65 years accounted for 49.6% of the total patients tested. Among 223 NTM positive specimens characterised further, the majority (86.2%) were from respiratory tract, whilst 3.6% and 3.1% were from lymph nodes and pus, respectively. Mycobacterium intracellulare (31.8%) and Mycobacterium chelonae / Mycobacterium abscessus (21.5%) were the most frequently detected species, followed by M. avium (13.5%), M. gordonae (11.7%), M. kansasii (7.6%), and others.

Conclusions: The proportion of NTM among mycobacterial species detected in a tertiary hospital in Beijing, China, increased rapidly from year 2013 to 2018. Middle-aged patients are more likely to be infected with NTM, especially females. Mycobacterium intracellulare and Mycobacterium chelonae/ Mycobacterium abscessus were the most frequently detected NTM pathogens. Accurate and timely identification of NTM is important for diagnosis and treatment.

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Novel organism verification and analysis (NOVA) study: identification of potentially novel bacterial species from a diverse spectrum of clinical isolates

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Background: During routine diagnostic work, a small number of bacterial isolates may not be identified reliably using the conventional identification method MALDI-TOF MS, due to insufficient reference data or the presence of a novel organism. We have established an algorithm to identify and characterize such strains using 16S rRNA gene sequence analysis and whole genome sequencing (WGS) in a prospective and systematic manner. Here we present preliminary data.

Materials/methods: Bacterial isolates from diverse clinical specimens which could not be identified definitely by MALDI-TOF MS (Bruker Daltonics, database version 4.1) were subject to partial 16S rRNA gene sequencing (approx. 800bp). All strains with 16S rRNA sequence identities ≤99.0% compared to validly described species were analyzed by WGS (MiSeq/NextSeq, Illumina) in our institution, for full 16S rRNA gene, rMLST, and digital DNA-DNA-hybridization (dDDH) analysis. Isolates are stored to enable further characterization.

Results: Since 2016, 28 novel clinical isolates were collected (19 Gram-positive, nine Gram-negative). Twenty represent aerobic or facultatively anaerobic organisms and eight are anaerobic strains. Among the aerobic bacteria 12 are Gram-positive rods, four Gram-negative rods, three Gram-negative cocci, and one a Gram-positive coccus. The anaerobic bacteria include four Gram-positive cocci, two Gram-positive rods, and two Gram-negative rods. The strains were isolated from 11 biopsies and 11 swabs with localization of extremities [8], ear [6], miscellaneous [10] as well as three blood cultures, one urine and two with unknown source. Identities of the 28 corresponding 16S rRNA gene sequences ranged from 90-98.5% and 24/28 have a dDDH of <70%, as determined by WGS data. Two novel species were detected repeatedly: three independent isolates belonging to the Microbacteriaceae family; and an unknown Corynebacterium sp. was detected in two patients. Clinical relevance of the isolates has not yet been investigated.

Conclusions: Our preliminary data indicate a diverse spectrum of hitherto undescribed cultured bacterial organisms from various body sites. We have defined an algorithm for rapid characterization of these isolates, within a well-equipped clinical microbiological laboratory. Publications arising to date include an emendation of Auritidibacter ignavus (Bernard K et al. IJSEM, 2019) and description of Mycobacterium basiliense (Seth-Smith, Frontiers in Microbiology, 2019).

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Abstract 1812

**Once-daily dose ceftriaxone plus ampicillin: an alternative for Enterococcus faecalis infective endocarditis OPAT treatment**

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**Abstract third-party references:** on behalf of the Grupo Andaluz para el estudio de las infecciones Cardiovasculares de la Sociedad Andaluza de Enfermedades Infecciosas (GAEICV-SAEI)

**Background:** Ceftriaxone 2g/12 hours plus ampicillin 2g/4 hours is a safe and effective strategy for the treatment Enterococcus faecalis infectious endocarditis. Ceftriaxone administration as 4g once-daily short infusion allows its inclusion in outpatient parenteral antibiotic therapy programs (OPAT), avoiding the use of two infusion pumps simultaneously. Given the importance of ceftriaxone exposure to obtain the synergistic effect with ampicillin, an examination of ceftriaxone high once-daily dose pharmacokinetic profile is warranted.

**Materials/methods:** This Phase II, open-label, crossover, pharmacokinetic study, enrolled healthy adult volunteers, who underwent two sequential treatment phases. During Phase A all volunteers received 2g of ceftriaxone each 12 hours during 24 hours followed by 7-day washout. Then, all the participants received Phase B medication, which consisted on 4g single dose of ceftriaxone. Throughout both phases each volunteer underwent intensive PK sampling over 24 hours. For concentrations lower than 100 mg/L, ceftriaxone unbound plasma concentrations were estimated assuming 10% of total drug. Ceftriaxone total concentrations were measured using validated LC-MS/MS methods, following FDA criteria.

**Results:** Twelve participants were enrolled and completed both phases. Five were female and median age and BMI were 28 years and 26.1 kg/m2. Mean concentration (GM±SD) 24 hours after the first dose (C24h) and estimated unbound C24h (uC24h) were 83.39±25.90 mg/L (range 47.98-135.73) and 8.34±2.59 mg/L (range 4.80-13.57) in phase A and 34.60±11.16 mg/L (range 18.50-51.07) and 3.46±1.12 mg/L (range 1.85-5.11) in phase B, respectively. In both cases mean uC24h were superior to 2 mg/L, the concentration required to maintain ceftriaxone synergistic activity. All patients achieved estimated unbound plasma concentrations superior to the concentration suggested to maintain ceftriaxone synergistic activity at least 20 hours, and most of them (>80%) 24 hours. Ceftriaxone total exposure, measure by AUC0-24, was similar in both phases and mean values were (GM±SD) 3319.6±573.3 mg.h/L in phase A vs 3035.4±573.3 mg.h/L in phase B (p=0.266). No grade 3 or 4 adverse events or laboratory abnormalities were observed.

**Conclusions:** Ceftriaxone plasma concentrations 24 hours after 4g single-dose administration are adequate to maintain the synergistic activity with ampicillin during 24 hours, allowing patient inclusion in OPAT programs without risk of inadequate exposure.

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Abstract 1813

**Does automated susceptibility testing overcall temocillin resistance?**

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**Background:** Temocillin is a semi-synthetic penicillin with narrow spectrum activity against *Enterobacteriaceae*, including AmpC and extended spectrum beta-lactamase (ESBL) producing organisms. Temocillin has the potential to be an important tool in clinical practice to treat serious infections caused by multi-resistant organisms and for antimicrobial stewardship purposes, including reducing use of critical antibiotics such as carbapenems. Common current clinical microbiology laboratory practice involves use of automated susceptibility testing methods such as the Becton-Dickinson (BD) Phoenix™. However, reported resistance rates to temocillin for *Enterobacteriaceae* isolates at our clinical microbiology laboratory far exceeds that expected by our knowledge of temocillin’s stability in the presence of beta-lactamase enzymes, leading to a hypothesis that Phoenix is overcalling temocillin resistance. This potentially poor quality data may lead to greater reluctance to utilise the antibiotic in clinical practice and give incorrect antimicrobial resistance epidemiology data.

**Materials/methods:** Prospective data was collected on *Enterobacteriaceae* blood culture isolates at our clinical microbiology laboratory from July 2017 to October 2018. Isolates were routinely tested for susceptibility on Phoenix and results recorded. Isolates that were deemed temocillin resistant on Phoenix had the temocillin susceptibility test repeated using an alternative method, for example a temocillin E-test and the concordance of the results was investigated.

**Results:** 87% (117/134 isolates) of *Enterobacteriaceae* blood culture isolates initially reported to be temocillin resistant, were found to be susceptible when re-tested using an alternative method. This reduced the overall reported temocillin resistance rate from 26% (209/805 isolates) to 2% (17/730 isolates).

**Conclusions:** Temocillin resistance in *Enterobacteriaceae* blood cultures isolates reported using automated susceptibility testing on BD Phoenix was only confirmed to be true using a second susceptibility testing method in 13% of cases. Phoenix overcalls temocillin resistance. All laboratories relying on BD Phoenix for temocillin susceptibility testing should confirm initial resistant results using a 2nd susceptibility testing method, such as a temocillin Etest. Becton-Dickinson should consider withdrawing temocillin from their Phoenix automated susceptibility testing panels until more reliable resistance results can be obtained.

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Abstract 1816

Burden of surgical site infections after solid organ transplantation in the Swiss transplant cohort study

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Background: Surgical site infections (SSI) after solid organ transplantation (SOT) result in increased morbidity due to antibiotic therapy and surgical revision, and have been associated with a negative impact on graft function and patient survival. Studies addressing this important hospital-acquired infection after SOT are very limited and mostly derived from retrospective studies.

Materials/methods: The Swiss Transplant Cohort Study prospectively collects clinical data of lung, heart, kidney, liver, pancreas, and combined [e.g. kidney-pancreas, kidney-liver] transplant recipients. We analyzed SSIs occurring within 90 days post-transplant that were related to all transplant surgical procedures in Switzerland between June 2008 and October 2018. We excluded patients that received serial transplants.

Results: A total of 193 SSIs were observed in 4794 transplantations [378 heart, 449 lung, 1052 liver, 2564 kidney, 195 kidney-pancreas, 149 other combined transplants], corresponding to an incidence of 4.0%. Median time from surgery to SSI was 18 days [interquartile range [IQR] 10-32 days]. The incidences of SSIs were 6.9%, 4.7%, 4.9%, 2.2%, 1.4%, 2.7% after heart, lung, liver, kidney, pancreas, combined kidney pancreas and other simultaneous transplantations, respectively. In 161 (83.4%) SSIs a causative pathogen was identified, whereas in 16.5% diagnosis was established based solely on clinical findings. The majority of SSIs was caused by bacteria [n= 131, 67.9%] and presented in 19 cases with concomitant bacteremia. SSIs were most frequently caused by gram-positive bacteria [n= 105, 80.2%], with enterococcal infections being most common [n= 54, 41.2%, 12 polymicrobial infections] (Figure). Fungal SSIs were identified in 15.5% of transplant recipients. Candida spp. were the main cause of fungal SSIs [n= 30, 6 SSIs with detection of more than one fungal pathogen] with a predominance of Candida albicans [n= 21, 70.0%].

Conclusions: In our cohort of SOT recipients we found a SSI rate of 4.0%. The highest SSI rate was observed after combined kidney pancreas transplantations and the lowest SSI rate after kidney transplantation. Most SSIs were caused by gram-positive bacteria, with enterococci being most frequent.

Figure: Frequency of detected pathogens in surgical site infections

a) Gram-positive pathogens
b) Gram-negative pathogens
c) Fungal pathogens

Abbreviation: CNS coagulase-negative Staphylococcus spp.

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Abstract 1817

Epidemiological investigation of newly detected highly lethal Borna disease virus 1 cases reinforcing indirect shrew contact as possible source of infection: results from in-depth interviews, Germany, 2019

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Background: In 2018, Borna disease virus 1 (BoDV-1) was first confirmed as a zoonotic pathogen causing severe human encephalopathy in Germany with an extremely high case fatality (15/16). Bicoloured white-toothed shrews (Crocidura leucodon) have been identified as reservoir hosts shedding virus in urine, saliva and faeces in endemic areas. Clinical presentation, risk factors and transmission routes for human infection are unknown. We aimed to generate hypotheses about transmission routes and provide evidence to guide prevention.

Materials/methods: We defined cases as BoDV-1-confirmed by pro- or retrospective nucleic acid detection. Viruses were sequenced. We conducted interviews with family members at patients´ homes in 2019 using a standardized semi-qualitative questionnaire covering a broad spectrum of clinical presentation and pre-existing conditions. Queried exposures included housing environment, profession, animal contacts, outdoor activities, travel, and nutrition.

Results: We identified family members of five patients deceased 1996 through 2019 [4/5 female, median age 25 years, range 13-56]. Immunosuppression was known for none. Four had presented with fulminant encephalitis starting with headache and fever, the fifth had initially shown signs of Guillain-Barré-syndrome. All had developed confusion, deep coma and had died within a median of 2.5 (range 1 - 11) months after symptom onset. All had lived their whole life in rural areas of Germany. Other than private gardening no communalities were identified. Three families kept domestic or farm animals [cat, dog, hare, duck, chicken]. Family members did not know of any direct contact to shrews, but all had observed irregular peridomestic presence of shrews. Three families reported domestic cats bringing home shrews. All human BoDV-1 sequences clustered with animal BoDV-1 sequences from the respective regions.

Conclusions: Rural residence is a common denominator of all five patients but transmission routes remain poorly understood. Phylogenetic analysis and shrew presence suggest peridomestic infection from the local reservoir. In the absence of direct shrew contact, most likely transmission may be via indirect contact. Interviews with other patients´ families are ongoing. To prevent cases of this fatal zoonosis, we recommend against avoidable contact to shrews and their secretions and published an online-handout on prevention measures targeting the public in endemic areas.

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**Abstract 1822**

### T2 magnetic resonance technology in the diagnosis of sepsis and clinical impact in patient management

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**Background:** Rapid and effective antimicrobial therapy is crucial to improve septic patient outcome, while inappropriate empirical therapy is a well-known, strong, independent predictor of mortality. Multidrug resistant organisms (MDRO) have reached pandemic level during the last two decades. A delay of 3-5 days has been found for effective therapy of systemic infections by MDRO. Thus, a rapid identification of pathogens, especially of bacterial species known to be multi-drug resistant, is a major goal in the diagnosis of sepsis.

Differently from technologies applicable on positive blood culture, dependent on the time of positivization of the sample, molecular tests performed directly on whole blood samples allow rapid identification of the etiological agents and are supposed to dramatically impact on patient outcome. Recently, the T2 Magnetic Resonance technology (T2Dx®) has been approved by FDA for laboratory diagnosis of sepsis by ESKAPEc organisms, with high sensitivity and specificity.

**Materials/methods:** The aim of this study was to evaluate the accuracy and the clinical impact of T2Bacteria Panel of T2Dx® system in comparison with the standard blood culture protocol in the early detection of ESKAPEc pathogens in patients with sepsis. Blood samples for culture and T2 testing were collected from 61 patients and diagnostic accuracy was evaluated. Duration of empirical therapy, and switch to target therapy were compared in patient with positive or negative T2 results.

**Results:** T2Bacteria Panel sensitivity and specificity were 100% (panel targets) and 94.6%, respectively. Time to report of positive T2Bacteria results was significantly lower than that of positive blood cultures [4.24 h ± 3.4 h vs 24.2 h ± 33.4 h, *p* < 0.001]. The percentage of patients in which antibiotic therapy was switched to target therapy the same day of sample collection was significantly higher in patients with positive T2 results [37.5% vs 11.4%, *p* = 0.031 2]. Duration of empirical therapy was shorter in these patients [34.11 h ± 23.87 h vs 80.48 h ± 73.40 h].

**Conclusions:** T2Bacteria Panel, allowing rapid detection of ESKAPEc pathogens, significantly impacts on the switch from empiric to target therapy, and represents a novel, valuable tool to improve the management of septic patients.

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Abstract 1823

Marine organisms from Yucatán Peninsula (México) as a potential natural source of new antimicrobial compounds against multidrug-resistant pathogens

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Background: Antibiotic resistance has become a global health emergency and new therapeutic options to treat multidrug-resistant pathogen infections are indisputably needed. Oceans constitute an important natural source of bioactive molecules mainly due to their high biological diversity. Porifera (sponges) and Cnidaria (soft coral) are the most productive phyla regarding this aspect. Here we report the antimicrobial activity found in organic extracts of marine invertebrate species collected along the coasts of the Yucatan Peninsula and selected according to chemotaxonomical criteria.

Materials/methods: Samples were collected in different coastal zones of the Yucatan Peninsula, during three different periods of time [2016-2018]. Taxonomic identification of sponges was performed and the organic extracts were prepared. In vitro antimicrobial screening of sixty-three marine organisms (50 sponges and 13 ascidians) against four bacterial species of multidrug-resistant pathogens, three gram-negative (Acinetobacter baumannii, Klebsiella pneumoniae, Pseudomonas aeruginosa) and the gram-positive Staphylococcus aureus, was conducted in this study. MICs were evaluated through microdilution assay.

Results: Eight out of sixty-three species displayed activity against the bacteria tested (TABLE 1), being the organic extracts of Agelas citrina and Haliclona curacaoensis the most active, and reflecting respectively MICs of 0.5-8 and 32 mg/L. Four extracts (A. dilatata, A. citrina, H. curacaoensis and A. compressa) showed antibacterial activity against all pathogenic species tested, while the rest exhibited a narrow-spectrum antibiotic activity. Other extracts of marine organisms did not present antimicrobial activity (MICs ≥512 mg/L).

Conclusions: This work constitutes the first wide antimicrobial screening report of the marine sponges and ascidians collected from the Yucatan Peninsula, México. Extracts of some marine species showed a relevant antimicrobial activity. Purification and identification assays of the active compounds are currently being developed.

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<th>Pseudomonas aeruginosa ATCC 27823</th>
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**Abstract 1824**

**Influence of empirical piperacillin-tazobactam on 30-day mortality in bacteraemia due to ESBL-producing versus non-ESBL-producing non-AmpC Enterobacteriaceae**

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**Background:** The comparative efficacy of piperacillin-tazobactam (PTZ) against non-ampC Enterobacteriaceae depending on the production of ESBL is unclear. The aim of the study was to assess the possible influence of empirical therapy with piperacillin-tazobactam (PTZ) on 30-day mortality in patients with bacteraemia due to susceptible non-ampC ESBL-producing compared with non-ESBL-producing *Escherichia coli*, *Klebsiella* spp. and *Proteus mirabilis* (EKP).

**Materials/methods:** Retrospective analysis of a prospectively collected database of patients with bacteraemia diagnosed at a 750-bed university hospital in Barcelona (Spain) from January 2003 to December 2018. Monomicrobial episodes due to EKP susceptible to PTZ (MIC≤ 8 mg/L) and empirically treated with PTZ were selected. Multivariate analysis was performed by a step backward logistic regression procedure.

**Results:** A total of 1323 EKP bacteraemia episodes were included of which 109 (14.7%) were due to ESBL-producers. In univariate analysis, 30-day mortality was associated with ESBL-producers in episodes with a urinary tract infection source (7/42 [16.7%] vs. 26/412 [6.3%]; OR 2.9, 95%CI 1.2-7.3, p=0.02) but not in those with other sources (9/67 [13.4%] vs. 89/802 [11.1%]; OR 1.2, 95%CI 0.5-2.5, p=0.5). In episodes with a urinary source, ESBL-producers remained an independent predictor of 30-day mortality (OR 3.1, 95%CI 1.1-9.1) along with age over 65 (OR 3.8, 95%CI 1.3-10.5), an ultimately/rapidly fatal prognosis of underlying disease (OR 3.6, 95%CI 1.5-8.4), chronic corticosteroid therapy (OR 6.8, 95%CI 2.7-16.9), neutropenia (OR 5.3, 95%CI 1.4-19.1) and shock (OR 5.2, 95%CI 2.2-12.3).

**Conclusions:** In patients with PTZ-susceptible *E.coli*, *Klebsiella* spp. or *P.mirabilis* bacteraemia receiving empirical therapy with PTZ, a very good outcome (30-day mortality below 10%) seems to be a reasonable expectation only for those with a urinary tract infection due to non-ESBL producers.

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Abstract 1826

**Respiratory ß-2-microglobulin exerts direct antimicrobial activity**

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**Background:** The respiratory tract is a major entry site for pathogens into the human body. To combat bacterial infections, the immune system has a large variety of host defense mechanisms at its disposal. Part of the innate immune system and a first line of defense are antimicrobial peptides (AMPs). To search for novel AMPs from the human respiratory tract, a peptide library established from human broncho-alveolar-lavage (BAL) fluid was screened for antimicrobial activity against Gram-positive and Gram-negative bacterial pathogens.

**Materials/methods:** The peptide library was prepared from 20 liter of pooled human BAL. Peptides and small proteins were extracted by acetic acid and separated through ultrafiltration (cut-off 20 kDa). Employing reversed phase chromatography 76 different peptide fractions were generated from the BAL pool. Antimicrobial activity was determined by agar diffusion assays allowing the efficient detection of antibacterial activity within a small sample size. Bacterial membrane integrity was measured by sytox green uptake and bacterial cells were visualized by transmission electron microscopy (TEM).

**Results:** After three testing-cycles and subsequent purification of active BAL fractions we identified ß-2-microglobulin (B2M) for its antimicrobial activity. B2M is a subunit of the MHC-1 receptor complex present at the surface of every nucleated cell. It is known to inhibit the growth of *Listeria monocytogenes* and *Escherichia coli* and to facilitate phagocytosis of *Staphylococcus aureus*. Using commercially available B2M we could confirm a dose-dependent inhibition of *Pseudomonas aeruginosa* as well as *L. monocytogenes*. To localize AMP activity within the B2M sequence, peptide fragments of the molecule were tested for antimicrobial activity. Sytox green uptake into bacterial cells following the exposure to B2M was determined and revealed a dose-dependent loss of bacterial membrane integrity. TEM analysis showed areas of disrupted bacterial membranes in *L. monocytogenes* incubated with B2M and high amounts of lysed bacterial cells.

**Conclusions:** In conclusion B2M as part of an ubiquitous cell surface complex may represent a potent antimicrobial agent by interfering with bacterial membrane integrity.

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**Abstract 1828**

**Improved detection of van-B bearing *E. faecium* isolates in a German hospital laboratory by a modified routine workflow for antimicrobial susceptibility testing**

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**Background:** Vancomycin-resistant *E. faecium* (VRE) are an emerging problem in the German health care system. Various factors are under discussion to enhance VRE-spread. One factor that may contribute to the spread of VRE is the low expression of Vancomycin-resistance. Facing a significant increase of VRE in the past two years, our hospital laboratory started to improve the detection of Vancomycin-susceptible Van-B positive isolates in developing a new workflow for antimicrobial susceptibility testing (AST) adding a Van-A/Van-B-PCR and chrome agar plates to the routinely performed AST.

**Materials/methods: Routine workflow:** AST was performed with VitekII AST-611 (biomerieux) alternatively with agar diffusion (biorad) following EUCAST standard procedures and breakpoint interpretation guidelines. First time isolated VRE in a patient underwent Van-A/Van-B-PCR (TiBMol). **Modified workflow:** Every Vancomycin susceptible *E. faecium* isolate underwent Van-A/Van-B-PCR-testing (TiBMol). *E. faecium* isolates from material other than VRE-screening material were streaked on chromagar (bioMerieux) in parallel to the purity control. Data analysis was performed with hybase®-system to eliminate copy-strain counts of isolates.

**Results:** From 01.03. to 31.08.19 a total amount of 686 *E. faecium* AST from 361 patient was carried out. 186 isolates were tested Vancomycin resistant, 175 Vancomycin susceptible. From the Vancomycin susceptible strains 35 (20%) beared the Van-B-Gene detected by PCR, none show a Van-A gene. The parallel to AST streaked chromagar showed a positive VRE result in 32 cases.

**AST result for Vancomycin**

<table>
<thead>
<tr>
<th></th>
<th>resistant</th>
<th>susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total Number of patient isolates</strong></td>
<td>186</td>
<td>175</td>
</tr>
<tr>
<td><strong>Van-A positive isolates</strong></td>
<td>n.o.</td>
<td>0</td>
</tr>
<tr>
<td><strong>Van-B positive isolates</strong></td>
<td>n.o.</td>
<td>35 (20.0%)</td>
</tr>
<tr>
<td><strong>Chromagar (modified workflow)</strong></td>
<td>n.o.</td>
<td>32 (2 negative, one not evaluable)</td>
</tr>
</tbody>
</table>

**Conclusions:** We found a remarkable 20% proportion of phenotypically Vancomycin-susceptible and Van-B-positive *E. faecium* -isolates after modification of the AST-workflow. Those isolates would normally be undetected by routine AST and therefor escape surveillance and further hygiene measures. VRE chromagar additionally streaked out to the purity control may help to detect these strains. Further investigation has to be done on the performance on other automated or manual AST systems. Of further interest would be the genomic analysis of these strains in comparison to phenotypically vancomycin resistant strains to understand their role in VRE-epidemiology.

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Human endogenous retroviruses as markers of severity in sepsis

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Abstract third-party references: bioMerieux, Hospices Civils de Lyon

Background: Sepsis is defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. The heterogeneity of the disease present a major clinical challenge with regard to the therapeutic coverage, and this day the proposed markers are not enough to stratify patients. The human endogenous retroviruses (HERVs) could be relevant markers, due to their expression in inflammatory and autoimmune diseases and their emerging immunological properties (envelopes and non-coding sequences).

Materials/methods: In order to determine to what extent the HERVs are expressed and modulated in the blood compartment, in inflammatory and immunocompromised contexts in vitro and in vivo, we used a custom high density DNA chip allowing the transcription analysis of 360,689 HERVs. The HERVs expression was objectified in endotoxin tolerance (ET) ex vivo model in peripheral blood mononuclear cells (PBMCs) of healthy volunteers and in whole blood of healthy volunteers and 120 septic shock patients, stratified or not according to the immune status determined by mHLA-DR level.

Results: About 7% of HERVs are expressed in the blood compartment including notably hundreds of identified HERV-H and PRI-MA-41 loci. The HERV transcriptome is modulated in ex vivo ET model, letting appear two major transcriptional phenotypes. Major differences in HERVs expression was observed between septic patients and healthy volunteers. More, the HERVs transcriptome was modulated between septic patients, according to their immune status. Using a signature of modulated elements, we have been able to stratify an independent validation cohort with a clear difference in severity between two clusters of patients.

Conclusions: We illustrated the importance of addressing both the exome and repetitive DNA repertoires to increase our understanding of sepsis pathophysiology. The added value of these newly identified HERVs markers should be evaluated in a larger cohort of septic patients. If they prove to be robust, they could further serve as a stratification tool prior to immunostimulatory treatment and to monitor drug efficacy, which could contribute to the reduction of mortality in sepsis patients.

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Detection of rifampin and isoniazid resistance using molecular testing to initiate an ethambutol-free 3-drug regimen in pulmonary tuberculosis: a French non-inferiority multi-centre randomised clinical trial

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Background: Current guidelines recommend initiation of a 4-drug regimen (rifampin RIF, isoniazid INH, pyrazinamide PZA and ethambutol EMB) for drug- susceptible tuberculosis [TB]. The rationale behind the use of EMB is to prevent the emergence of resistance to RIF in case of primary resistance to INH (5% prevalence in France in 2018). Early detection of INH resistance using molecular testing may allow to initiate treatment with an EMB-free 3-drug regimen. This strategy has not been evaluated in settings with low incidence INH resistance.

Materials/methods: FAST-TB, a phase 4 French multicenter, open-label non-inferiority trial, compared two strategies: (i) PCR-based detection of INH and RIF resistance at baseline using Genotype MTBDR Plus v2.0® and then start a 3-drug containing TB regimen without EMB if no resistance detected [PCR arm], vs. (ii) standard 4-drug combination and treatment initiation, pending phenotypic drug-susceptibility testing results [C arm]. Adult patients with acid-fast bacilli [AFB+] on respiratory samples were enrolled; patients with previous TB treatment were excluded from the study. The primary endpoint was the proportion of patients with treatment success defined as bacteriological and clinical cure within the first year after enrollment. A non-inferiority margin of 10% was used.

Results: 201 patients were randomized, 104 in the PCR arm and 99 in the C arm: 27% were female, median age was 37 [IQR: 27-51] years, 72% were born in Africa, and 5.4% were HIV-infected. Chest X-ray showed excavations in 64% of the cases and half of the participants had bilateral abnormalities. We detected 7 [3.5%] patients with INH phenotypic resistance, 2 in the PCR arm and 5 in the C arm. Overall, 167 patients met criteria of treatment success: 86/104 (82.7%) in the PCR arm and 81/99 (81.8%) in the C arm with a difference of +0.87% (95%IC: -9.64; 11.39), meeting non-inferiority criteria.

Conclusions: In a setting with low incidence of TB and INH resistance, the use of a 3-drug combination with RIF, INH and PZA based on early detection of INH and RIF resistance using MTBDR Plus® test on AFB+ sputum samples was non-inferior to a 4-drug containing regimen.

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Bacterial profile associated with oral cancer: metagenomic analysis in oral micro-niches
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Background: Oral microbiota is associated with Oral Squamous Cell Carcinoma (OSCC), mainly by persistent inflammatory processes and production of acetaldehyde. Variation of bacterial communities within the oral cavity depending on anatomical location [niches] is well established. Studies with high-throughput sequencing describe the composition and abundance total bacteria in the oral micro-niches. However, at present no studies have characterized different oral micro-niches in OSCC. The objective of this study was to determine and compare tumoral tissue, saliva and dental plaque bacterial profiles, in patients with OSCC.

Materials/methods: A total of nine OSCC patients were included. Samples included saliva, dental plaque and tumor tissue. DNA was extracted from all samples. Subsequently, libraries were prepared using Illumina Nextera XT®. For sequencing paired-end MiSeq of Illumina® was used. Trimmomatic software was used to evaluate quality. Moreover, identification of bacteria in each sample was performed with Kraken Aligner V1.0. Initially, bacteria associated with tumoral tissue was identified. Subsequently, intra and inter-patient samples where bacteria in saliva and dental plaque samples were statistically significant (p-value < 0.05) were compared.

Results: In tumoral tissue of patients with OSCC, eighteen species of bacteria were identified. The more characteristic bacteria in OSCC were a profile of nine species of bacteria Riemerella anatipestifer, Chlorobium phaeobacteroides, Yersinia enterocolitica, Proteus mirabilis, Mycoplasma hyorhinis, Flavobacterium psychrophilum, Streptococcus pyogenes, and Mycoplasma hyopneumoniae in a sub-group of patients, and Alteromonas mediterranea in other sub-group of patients. After saliva and dental plaque comparison high similarity was observed, where the more abundant bacteria were Prevotella melaninogenica, Capnocytophaga ochracea, Fusobacterium nucleatum and Haemophilus influenzae, nevertheless no sub-groups were observed. Last, bacterial profile associated which OSCC in saliva and dental plaque was scarce or absent representing less than 3% of the total bacteria in those samples.

Conclusions: A profile of nine species of bacteria were predominant in tumoral tissue. Saliva and dental plaque samples do not contain bacteria associated with OSCC.

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Abstract 1834

Vancomycin pharmacokinetics in patients undergoing extracorporeal membrane oxygenation after 48 hours of treatment

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Background: Extracorporeal membrane oxygenation (ECMO) could affect drug pharmacokinetics (PK), which is critical for antimicrobial effectiveness. Vancomycin PK during ECMO has been previously studied, but only in the first 48 hours of treatment (Initial-48h). The aim of this study was to assess vancomycin PK during ECMO after 48 hours of treatment (After-28h) and compare with those estimated from the complete cohort and initial-48h.

Materials/methods: A retrospective observational study was carried out in patients under simultaneous treatment with vancomycin and ECMO between January 2016 and January 2019 whose vancomycin serum concentrations were measured. The variables recorded were: ECMO type and indications, renal replacement therapy, dose, creatinine, exitus, vancomycin serum concentration and day of the analysis. The PK analysis was performed using Abbottbase Pharmacokinetics Systems software (Abbott Diagnostics Division, Irving, TX, USA), adjusting experimental data according to a compartmental linear model using Bayesian estimates. Two-sided t-student test was used for comparing vancomycin PK parameters (PKp) obtain from i48h, a48h and the complete cohort.

Results: Six patients were excluded for lack of data and 13 patients were analyzed. Most patients 84.6%(11) underwent venoarterial ECMO. ECMO indications were 7(53.8%) cardiogenic shock, 3(23%) ventricular dysfunction and others 3(23%). Exitus occurred in 6(46.2%) patients, and 3(23%) underwent concomitant renal replacement therapy. Vancomycin was measured in 38 samples, 28(73.7%) after 48 hours of treatment.

Vancomycin PK-p estimated from a48h, i48h and the complete cohort are depicted in table 1. No significant differences were observed in any case (p>0.05), but a48h, a tendency towards higher Vd, Cl and T1/2 and lower AUC were detected.

Table 1

<table>
<thead>
<tr>
<th>PKp</th>
<th>After-48h</th>
<th>Initial-48h</th>
<th>Complete cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vd [L/kg]</td>
<td>0.864±0.304</td>
<td>0.799±0.1</td>
<td>0.847±0.267</td>
</tr>
<tr>
<td>Cl [L/h/kg]</td>
<td>0.039±0.017</td>
<td>0.036±0.010</td>
<td>0.039±0.015</td>
</tr>
<tr>
<td>AUC [mg*h/L]</td>
<td>605.6±165.6</td>
<td>831.4±402.3</td>
<td>671.1±270.6</td>
</tr>
<tr>
<td>T1/2 [h]</td>
<td>18.38±11.64</td>
<td>1786±6.9</td>
<td>18.24±10.5</td>
</tr>
</tbody>
</table>

Vd: Volume of distribution, Cl: Vancomycin clearance, AUC: Area under the curve, T1/2: Half-life

Conclusions: Vancomycin PKp estimated from our population are similar to those previously described, including high variability. Vancomycin PKp after-48h were not previously described, and despite being similar to other populations, the tendencies observed warranted further studies in bigger populations to detect finest variations.

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Tuberculosis impacts immune-metabolic pathways resulting in perturbed cytokine responses

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Background: Tuberculosis (TB) is a major public health problem for which host-directed therapeutics are proposed as novel treatment strategies. However, their successful development still requires a more comprehensive understanding of how Mycobacterium tuberculosis (M.tb) infection impacts immune and metabolic host responses.

Materials/methods: To address this challenge we applied standardised immunomonitoring tools to compare induced immune responses between individuals with latent M.tb infection (LTBI) and active TB disease (n=50). Whole blood was collected and stimulated with TB antigens (TB Ag), Bacillus Calmette-Guérin (BCG), IL-1β, and a Null control. Immune responses were analyzed at proteomic, transcriptomic, metabolomic and cellular levels. The TB patients were analyzed both prior to, and after, successful antibiotic treatment.

Results: This approach revealed multiple differential immune responses in active TB disease at transcriptomic, proteomic, metabolomic and cellular levels. These immune differences were absent after successful antibiotic treatment highlighting their disease-specific nature. Integrative analysis of these different datasets permitted a detailed characterisation of the perturbed IFNγ response in TB disease. Specifically TB patients had different IFNγ responses as compared to LTBI controls, at the proteomic, but not transcriptomic level. We also identified dysregulated IL1 responses to BCG stimulation in TB patients, for both agonist (IL1a/b) and antagonist (IL1RA) responses. Furthermore, the combination of novel digital ELISA readouts with Mass Spectometry identified novel immune-metabolic drivers of IL1RA secretion.

Conclusions: This study improves our knowledge of how M.tb alters key immune responses, and will support the design of improved diagnostic, prophylactic and therapeutic tools.

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Abstract 1839

**Actinotignum schaalii in breast abscesses, an emerging pathology? Report on five cases**

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**Background:** *Actinotignum schaalii* are Gram-positive rod-shaped bacteria known to be responsible for urinary tract infection in elderly and patient with urological conditions. Breast abscesses caused by *A. schaalii* are rare (only two cases previously described), so few clinical or microbiological data were available. This review of five cases describes the clinical profile of patients with breast abscesses caused by *A. schaalii*, as well as the antimicrobial susceptibility.

**Materials/methods:** From 2017 to 2019, clinical isolates of *A. schaalii*, isolated from breast abscesses from patients hospitalized in the University Hospital of Poitiers were included. Culture identification was performed by MALDI-ToF (Vitek-MS, bioMérieux). Antimicrobial susceptibility was assessed by the E-test method (bioMérieux), on Brucella Blood Agar media plates (bioMérieux). MICs were interpreted using the EUCAST 2019 v9.0 breakpoint table. In order to determine the analytical performance of culture to identify *A. schaalii*, 20 breast abscess samples with similar clinical presentation were tested. The presence of *A. schaalii* DNA was challenged using a specific qPCR assay targeting the *gyrB* gene, as previously described [1].

**Results:** Among the five patients, the median age was 46 years (from 37 to 50 years). All patients had a polymicrobial infection, 80% were active smokers, 60% had an underlying immunodepressive condition (diabetes, cancer, immunodepressive therapy) and 40% had a chronic abscess. Evolution was favorable in every case, without recurrence at six months. Treatment was based in all cases on surgical drainage of the abscess. Three out of five patients also received a short course of antibiotics. Antimicrobial susceptibility is detailed in Table 1. *A. schaalii* DNA was detected in all samples with positive *A. schaalii* culture. The qPCR assay was negative for all *A. schaalii* negative breast abscess samples (*n*=20). These latter included negative and positive bacterial cultures.

**Table 1: In vitro activity of 11 antimicrobial agents against 5 clinical isolates of *A. schaalii* recovered from breast abscesses.**

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Case 1 (mg/L)</th>
<th>Case 2 (mg/L)</th>
<th>Case 3 (mg/L)</th>
<th>Case 4 (mg/L)</th>
<th>Case 5 (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin G</td>
<td>0.012</td>
<td>0.016</td>
<td>0.016</td>
<td>0.012</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>0.094</td>
<td>0.064</td>
<td>0.094</td>
<td>0.094</td>
<td>&lt;0.016</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>4</td>
<td>0.38</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0.125</td>
<td>0.19</td>
<td>0.094</td>
<td>0.094</td>
<td>0.047</td>
</tr>
<tr>
<td>Linezolid</td>
<td>0.25</td>
<td>0.19</td>
<td>0.25</td>
<td>0.25</td>
<td>0.125</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>0.5</td>
<td>0.38</td>
<td>0.5</td>
<td>0.5</td>
<td>0.25</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>1.5</td>
<td>1.5</td>
<td>4</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>0.125</td>
<td>0.064</td>
<td>0.125</td>
<td>0.094</td>
<td>0.094</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>&gt;32</td>
<td>0.047</td>
<td>&gt;32</td>
<td>0.25</td>
<td>0.064</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>0.023</td>
<td>&gt;256</td>
<td>&gt;256</td>
<td>0.032</td>
<td>24</td>
</tr>
<tr>
<td>Quinupristin-Dalfopristin</td>
<td>0.19</td>
<td>0.19</td>
<td>0.125</td>
<td>0.094</td>
<td>0.125</td>
</tr>
</tbody>
</table>

**Conclusions:** *Actinotignum schaalii* breast abscesses occur mainly in young patients with a smoking history. Infection can be diagnosed with standard culture methods and are frequently polymicrobial. Resistance to clindamycin, ciprofloxacin and cotrimoxazole were frequent.


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Abstract 1840

Comparison of early effects of *Streptococcus pneumoniae* vaccination policies on nasopharyngeal carriage in a Palestinian population

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Abstract third-party references: my abstract supported by Al-Quds University

**Background:** *Streptococcus pneumoniae* can asymptptomatically colonize the nasopharynx and cause a various range of illnesses. Pneumococcal conjugate vaccines (PCVs) are at present used in different countries. The aim of the study is to determine the effect of different vaccination policies PCV7/13 to that PCV10 on the carriage rates and comparing the impact of different vaccination policies in East Jerusalem and West Bank region.

**Materials/methods:** Five cross-sectional surveillances of *S. pneumoniae* were carried out in East Jerusalem and Palestinian authority (PA), where two Palestinian populations with different vaccination policies were screened, with an annual average of 348 and 616 children, respectively, were performed during 2009-2016. Nasopharyngeal swabs and data were collected from children less than 5 years old. In East-Jerusalem (EJ), PCV7 was implemented in 2009 and replaced by PCV13 in late 2010, while in Palestine (PA), PCV10 was implemented in 2011.

**Results:** A total of 4686 children were screened in EJ (n=1615) and PA (n=3070), the overall rate of *S. pneumoniae* carriage did not change significantly during the 5 first years of the study, in either population. The pediatric subjects from EJ were determined to carry *S. pneumoniae* during the 5 years study, 2009, 2010, 2011, 2014, and 2016 as 28.9%, 29.3%, 28.6%, 30.7% and 16.9%, respectively. In addition 35.9%, 33.6%, 28.8%, 28.6% and 32.9% of the pediatric subjects from PA were shown to carry *S. pneumoniae* in 2009-2016, respectively. By year 2016, *S. pneumoniae* carriage was reduced significantly in EJ from ~29% on average to ~17%, following seven years application of PCV7/13. In PA, where follow-up included only 5 years after PCV10 application, *S. pneumoniae* carriage remained ~30%.

Interestingly, VT7 strains gradually decreased following PCV implementation. Following vaccine implementation, during the study period, there was a significant decrease in carriage of *S. pneumoniae* in the EJ between 2009 and 2016. No significant variation was seen in the overall carriage of *S. pneumoniae* between 2009 to 2016 in PA. PCV10 was introduced to PA late in 2011, but *S. pneumoniae* carriage was approximately [160/566] 28% in 2011, prior to vaccine introduction, and [216/656], 32.9% in 2016, five years following vaccine implementation.

**Conclusions:** Following PCV implementation, a decrease in the prevalence of VT strains was observed in EJ, and PA.

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Abstract 1842

**A selective culture medium for screening ceftazidime/avibactam resistant Gram-negative isolates**

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**Background:** The emergence of carbapenemases in Enterobacterales, in particular of the Klebsiella pneumoniae carbapenemases (KPCs) that are associated to multidrug resistance, represent a high priority for the development of novel antibacterials. Avibactam, a non-β-lactam inhibitor, is able to restore the efficacy of ceftazidime against KPC producers. However, resistance to the novel ceftazidime-avibactam (CAZ-AVI) association is increasingly reported among clinical strains expressing KPC variants. Taking in account the increasing isolation of those CAZ/AVI-resistant enterobacterales, a selective culture medium for screening CAZ-AVI-resistance in Gram-negative bacteria (Enterobacterales, Pseudomonas aeruginosa) was developed.

**Materials/methods:** This medium (SuperCAZ/AVI) contains ceftazidime, avibactam, zinc sulfate, daptomycin, and amphotericin B. It was evaluated with 50 CAZ/AVI-susceptible (40 Enterobacterales including Enterobacter cloacae, Klebsiella pneumoniae, and Escherichia coli, 10 Pseudomonas aeruginosa), and 42 CAZ/AVI-resistant (20 Enterobacterales including Enterobacter cloacae, Klebsiella pneumoniae, and Escherichia coli, 22 Pseudomonas aeruginosa) Gram-negative isolates. In addition, testing was performed by spiking stools with a series of resistant isolates, at different concentrations.

**Results:** Sensitivity and specificity of detection of the SuperCAZ/AVI medium were ca. 100%. By testing stools spiked with CAZ/AVI-resistant or -susceptible Gram-negative bacteria (92 isolates), an excellent performance of the medium was observed, with a lowest detection limit ranging from $10^1$ to $10^2$ CFU/ml.

**Conclusions:** The Super CAZ/AVI medium constitutes a screening medium aimed to detect CAZ/AVI-resistant bacteria regardless of their resistance mechanism. This Super CAZ/AVI medium may be used for prospective screening, and epidemiological surveys that may contribute to rapidly detect carriers of CAZ/AVI resistant isolates, and consequently to rapidly implement infection control measures in order to limit their spread.

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Is it realistic to offer an antibiotic susceptibility bonus to developers?

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Background: Return on investment for antibiotic development needs to be amended, without jeopardizing the future efficacy of novel compounds through high volume sales. This study explores the feasibility of a financial bonus that depends on levels of antibiotic susceptibility over time after approval. This bonus is intended to align pharmaceutical industry interests with public health interests through prolongation of efficacy through time. But how could such a bonus scheme work, with regards to magnitude and eligibility?

Materials/methods: This multidisciplinary (business, economics and microbiology) study utilized literature study, market analyses, Delphi consultation, informal interviews, and investment analysis.

Results: Findings from this (public-sector funded) project show that a suitable bonus magnitude should be sufficiently high to deter profit-driven mass marketing, low value or riskier sales, but not so high that the company would prevent access to their product where there is justified need. To be effective it must be clear that it is not intended as a traditional R&D incentive (indeed a large-scale monetary reward is needed independently from this scheme). What is proposed here is a proper bonus paid for strong product performance -- i.e. proven ability to stave off resistance. Since not all factors contributing to resistance will be under company control, falling below the susceptibility threshold does not imply being penalized – it is simply that the product did not perform to this higher standard. With regard to the susceptibility criterion, there are advantages in utilizing epidemiological cut-offs to determine bonus eligibility rather than MIC break points to avoid gaming strategies. Linear eligibility thresholds could run from 100% wild type (weight=1) to ≤50% (weight=0). Additional binary weights can be applied to ensure that only useful and accessible products are eligible.

Conclusions: The theory underlying an Antibiotic Susceptibility Bonus and its different components is backed by market dynamics and experts in the field, and can be facilitated by on-going efforts in microbiology and lab quality standardization and widespread AMR surveillance initiatives. The bonus could be considered alongside -- or as a performance-related component of -- a pull-based R&D reward such as a market entry reward or an insurance/supply contract.

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Abstract 1844

**Clinical and laboratory features of mixed invasive mycoses in adult haematologic patients with invasive aspergillosis**

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**Background:** We investigated the features of mixed invasive mycoses (IM) in hematologic patients.

**Materials/methods:** Retrospective study in 1998-2019 y.y. Diagnostic criteria EORTC/MSG, 2008 were used.

**Results:** In group I we included 72 adult hematologic patients with combination of invasive aspergillosis (IA) and non-Aspergillus caused mycoses, median age – 41 years (18 - 75), males – 71%. The comparison group consisted of 519 hematologic patients with IA, median age – 46.5 years (18 – 79), males – 56%.

The predominant underlying diseases were acute leukemia (51% vs 44%) and lymphomas (35% vs 34%). Mixed IM less often developed in patients with chronic leukemia (6% vs 9%) and multiple myeloma (3% vs 8%). The main risk factors were severe neutropenia (79% vs 73%), and steroid therapy (72% vs 69%). Mixed IM occurred significantly more frequently in patients with lymphocytopenia (63% vs 52%, p = 0.01), immunosuppressive therapy (33% vs 23%, p = 0.04), ICU stay (29% vs 7%, p = 0.0001), and after allo-HSCT (33% vs 23%, p = 0.04).

In patients with mixed IM ≥ 2 organs (29% vs 5%, p = 0.001), CNS (15% vs 2%, p = 0.03), and paranasal sinus involvement (10% vs 4%) were more often observed; respiratory failure (51% vs 34%, p = 0.0001), hemoptysis (13% vs 5%, p = 0.005), and hydrothorax (9% vs 3%) were more often noted. The main causative agents of IA were *A. fumigatus* (40% vs 43%) and *A. niger* (34% vs 33%). Non-Aspergillus pathogens were: mucormycetes – 35%, *Pneumocystis jirovecii* – 25%, *Candida* spp. – 22%, hyalohyphomycetes – 9%, *Cryptococcus neoformans* – 4%, rare yeasts – 4%, and pheohyphomycetes – 1%. Overall 12-week survival in the mixed-infection group was significantly lower (52% vs 84%, p = 0.0001).

**Conclusions:** Mixed invasive mycoses occurred in patients with persistent lymphocytopenia (63%), long-term immunosuppressive therapy (33%), ICU stay (29%), and after allo-HSCT (33%). Non-Aspergillus etiological agents were mucormycetes – 35%, *Pneumocystis jirovecii* – 25%, and *Candida* spp. – 22%. In patients with mixed invasive mycoses, ≥ 2 organs (29% vs 5%, p = 0.001) and CNS involvement (15% vs 2%, p = 0.03) were more often observed. Overall 12-week survival: 52% vs 84%, p = 0.0001.

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Abstract 1848

Investigation and control of measles outbreak in Balkh province, Afghanistan, Dec 2016-2017

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**Background:** Measles is a most contagious infection known to humans, and ranks among the top four childhood killers worldwide. Despite immunization progression, unfortunately Afghanistan is still an endemic country for measles outbreaks. Over 20 of the 34 provinces in Afghanistan, of the 25,000 reported cases in 2017, 1235 cases reported by Balkh province.

**Materials/methods:** On December 2016 the index suspected measles case reported by surveillance focal point from an internally displaced people (IDP) encampment in Dehdadi District of Balkh province. Outbreak investigation conducted, a measles case defined as any person with fever, maculopapular rash, conjunctivitis and cough or coryza in the affected area since 3rd Dec 2016. Rapid assessment conducted in the area for vaccine coverage and active case finding. Blood serum specimen collected and shipped to Central Public Health Laboratory in Kabul and confirmed by ELISA-IgM test.

**Results:** Of the 546155 population 359 suspected measles cases identified attack rate AR = 6.6/10000 and male to female ratio 1.3:1. Of the 173 cases tested for measles IgM, 131 (75.7%) [95% CI 68.6, 81.9] confirmed. There were 17 deaths that indicated case fatality rate (CFR) (4.7%) [95% CI 2.5, 6.9]. The mean age of cases was 30.6 months and ranged 1 month -29 years. One dose of vaccination coverage among the IDP population was 18%, while only 6 (1.67%) of all cases had received one dose of measles vaccine. We conducted two rounds village-wide immunization campaign and vaccinated 61084 children, subsequently, cases ceased.

**Conclusions:** To eradicate measles, high vaccination coverage must be maintained, and this must be the focus of local and national authorities. Low vaccination coverage looks likely caused of the outbreak. The high contagiousness of measles requires initial widespread supplemental vaccination to stop a large epidemic; small efforts will not be successful.

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Abstract 1851

**An ultrasensitive test for the detection of Clostridiodes difficile toxins in stool samples using a single-molecule counting method**

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**Background:** Clostridiodes difficile infection is considered an urgent antibiotic resistance threat by the CDC, accounting for ≈225,000 hospitalizations, 12,800 deaths, and ≈$1B in healthcare costs in the US in 2017. The presence of the secreted toxins A and B, that cause the devastating symptoms of this gastrointestinal infection are diagnostic of C. difficile infection (CDI). However, the rapid testing methods currently used to detect CDI lack accuracy: Enzyme immunoassays are specific but lack sensitivity and nucleic acid amplification tests (NAAT) are sensitive but lack specificity. This has resulted in the adoption of complex algorithms for C. difficile diagnosis. We present results for a new toxin test that demonstrate both high sensitivity and specificity for C. difficile toxins A and B on a fully automated benchtop platform.

**Materials/methods:** The detection technology uses non-magnified digital imaging to count single toxin molecules that are tether together target-specific magnetic and fluorescent particles. The 30 minute method includes the use of a dye-cushion to eliminate wash steps and the need for time consuming specimen preparation steps. We determined analytical performance characteristics of the test using negative clinical stool samples spiked with purified toxin. To assess clinical performance, we tested 787 stool samples from 5 clinical sites and compared the results with the cellular cytotoxicity neutralization assay (CCNA).

**Results:** The test’s LoD for toxin B was 60 pg/mL. Comparison of the new test to the CCNA reference method gave 95% positive percent agreement (PPA) (83/87 samples) and 95% negative percent agreement (NPA) (667/700 samples).

**Conclusions:** The results presented demonstrate the potential of the C. difficile toxin test to aid in the diagnosis of CDI and reduce the need for testing algorithms that require multiple assays.

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Activity of the β-lactamase inhibitor LN-1-255 against plasmid-mediated Class C cephalosporinases enzymes from Enterobacteriaceae

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**Background:** Class C β-lactamases are clinically relevant cephalosporinases encoded on the chromosomes or plasmids of many Enterobacteriaceae. Overexpression can confer resistance to broad-spectrum cephalosporins, such as cefotaxime or ceftazidime. Classical inhibitors such as clavulanic acid, sulbactam, and tazobactam have a very limited effect on AmpC β-lactamases. Avibactam, approved in 2015, was the first β-lactamase inhibitor that provide activity against these enzymes. The aim of the study was to evaluate the inhibition ability of the experimental inhibitor LN-1-255 against plasmid-mediated AmpC enzymes.

**Materials/methods:** bla<sub>DHA-1</sub>, bla<sub>DHA-7</sub>, bla<sub>CMY-2</sub>, bla<sub>CMY-54</sub> and bla<sub>FOX-4</sub> genes encoding plasmid-mediated class C enzymes were cloned to pBG18S and transformed into Escherichia coli TG1. MICs were performed to cefoxitin (FOX), ceftazidime (CAZ) and the combinations cefoxitin/LN-1-255 and ceftazidime/LN-1-255. bla<sub>CMY-2</sub> and bla<sub>CMY-54</sub> genes were cloned into the p-GEX-6P-1 plasmid, electropored into E. coli BL21 and encoded proteins were then purified. For inhibition kinetics, IC<sub>50</sub> for tazobactam, avibactam and LN-1-255 was calculated.

**Results:** The inhibitor LN-1-255 displayed a relevant ability to decrease the MICs to cephalosporins, decreasing 2-32 and 8-2056-fold the MICs to FOX and CAZ, respectively. The IC<sub>50</sub> of LN-1-255 was in the nanomolar range, 24 and 17 nM for the CMY-2 and CMY-54 β-lactamases, showing excellent hydrolysis efficiency. Avibactam showed a similar efficacy inhibiting CMY-2, being less efficient against CMY-54. Tazobactam displayed an inhibition efficacy 68 and 22-fold lower than LN-1-255 against CMY-2 and CMY-54, respectively.

**Conclusions:** We describe the inhibitory activity of LN-1-255 against the plasmid-mediated AmpC of Enterobacteriaceae. Cephalosporins in combination with LN-1-255 were effective against cephalosporins-resistant strains. LN-1-255 displayed better IC<sub>50</sub> than tazobactam or avibactam. Therefore, LN-1-255 represents a potential new therapeutic option in combination with cephalosporins against plasmid-mediated AmpC Enterobacteriaceae. A complete analysis of kinetic and microbiological assays for all enzymes and inhibitors are currently being developed.

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Abstract 1854

**Infection and mortality rates due to carbapenem-resistant organisms in infants admitted to the neonatal unit**

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**Background:** Healthcare-associated multidrug resistant bacterial infections, particularly due to carbapenem resistant organisms (CRO), has been on the rise globally. Most studies on CRO prevalence are from high-income countries, with very few from low-middle income countries (LMIC). Although limited, the reported prevalence of infections and mortality due to CRO in LMIC has been alarmingly high. This study evaluated the rates of infection and all-cause mortality due to CRO in infants admitted in a hospital from a low-middle income country.

**Materials/methods:** Positive bacterial cultures from sterile sites in infants admitted to the neonatal unit at Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa, in 2018, was retrieved from the microbiology laboratory and reviewed retrospectively. Type of organism, susceptibility results and outcomes were recorded. Among these, the Gram-negative isolates, including the CRO, were extracted. Rates and outcomes were analysed.

**Results:** There were 804 positive cultures (excluding coagulase-negative Staphylococci) from sterile sites, giving an infection rate of 12.6/1000 patient days. Of these 539 (67%) were Gram-negative isolates. The common Gram-negatives were *Acinetobacter baumannii* (225/539; 42%) and *Klebsiella pneumoniae* (229/539; 42%). 176 (78%) of the *Acinetobacter baumannii* isolates and 75 (33%) of the *Klebsiella pneumoniae* isolates were CRO, accounting for 47% of all Gram-negatives. The rate of carbapenem resistant *Acinetobacter baumannii* (CRAB) was 2.8/1000 patient days and carbapenem resistant *Klebsiella pneumoniae* (CRE) was 1.2/1000 patient days. The rates of CRAB varied from a trough of 0.8/1000 patient days to a peak of 5.8/1000 patient days per month, and those of CRE varied from 0.2/1000 patient days to 2.5/1000 patient days per month. The all-cause mortality rate in infants with Gram-negative isolates was 20%. The mortality was 26% in infants with CRAB and 40% in infants with CRE. The all-cause mortality rate in infants with CRO was 30%. The mortality rate in infants with CRO was higher than those with non-CRO (30% vs 11%; p <0.05).

**Conclusions:** There was a high rate of positive cultures from sterile sites in 2018. Gram-negative organisms predominated, and among these carbapenem resistance was high. Rates of CRO varied over the months, suggesting outbreaks. CRO were associated with high mortality rate.

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Abstract 1855

Colonisation and infection with ESBL-producing and carbapenem-resistant Enterobacteriaceae in kidney transplant recipients: risk factors, impact on renal graft function and use of hospital resources

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Background: ESBL-producing and carbapenem resistant (CR) Enterobacteriaceae are a common cause of severe infection, morbidity and mortality in kidney transplant recipients (KTR). Few studies have investigated the risk factors for ESBL-producing/CR Enterobacteriaceae colonization and infection in this group of patients, the effect of colonization and infection on KTR's renal graft function, and the use of hospital resources.

Materials/methods: Retrospective follow-up study on a consecutive series of patients undergoing kidney transplantation at Parma University Hospital (Italy) between January-2016 and December-2018. We examined the difference in risk factors by two-sample Mann-Whitney test, and Fisher's exact test for continuous and categorical variables. Crude and adjusted (donor's/recipient's age, recipient's gender) renal function (eGFR) decline was compared by mixed-effects random-coefficients models, hospital resources by negative binomial regression.

Results: We enrolled 180 KTR (mean recipient's age: 52.42 [SD 12.40]; males 65%; mean donor's age: 54.59 [SD 15.57]) and followed them up for 2-years post transplantation. Cumulative prevalence of colonization 3-months post-transplantation and cumulative incidence of infection were 26.1% and 9.4% for ESBL, and 4.4% and 1.6% for CR. ESBL colonization was associated with hemodialysis vs peritoneal dialysis (93% vs 70% non-colonized), dialysis vintage (mean months: 65.00 vs 41.93) and retention of ureteral stent for more than one month after transplant (28% vs 12%) (p<0.05 for all); ESBL infection was associated with retention of ureteral stent (47% vs 13%; p=0.002) whereas CR colonization was associated with surgical complication during transplant admission (50% vs 15% p=0.027). Two patients (both with CR) died over the study follow-up, whereas none of the patients lost the graft. There was a non-statistically significant trend of eGFR yearly decline, being sharper (up to -5mL/min/year) in patients with CR colonization compared to non-colonized. In comparison with non-colonized patients, adjusted mean days of carbapenem treatment in ESBL/CR colonized/infected was 5.6 vs 0.7 (p=0.002); length-of-hospital stay 5.6 vs 0.7 (p=0.002); days on drug-resistant-infection intravenous-outpatient-therapy 1.6 vs 0.07 (p=0.005).

Conclusions: The study shows that ESBL and CR colonization and infection in KTR are associated with longer hemodialysis vintage, urological procedures, and surgical complications, and that they cause an increase in the hospital resources use.

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Abstract 1865

Risk score for non-ventilator-associated hospital-acquired pneumonia (nvHAP)
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Background: Pneumonia is one of the most common healthcare-associated infections, and the burden of disease is higher in non-ventilated than in ventilated patients. Identifying patients at high risk for non-ventilator-associated hospital-acquired pneumonia [nvHAP] allows targeting prevention measures to high-risk patients. We derived and validated a risk score to predict nvHAP in a broad patient collective.

Materials/methods: We included all inpatients ≥18 years of age, discharged during a 2.5-year period from the University Hospital Zurich, Switzerland. The derivation cohort consisted of patients from the first two years; the remainder of patients was included in the validation cohort. The derivation cohort was used to identify distinct and easily available risk factors for nvHAP by applying uni- and multivariable Cox proportional hazards models. These risk factors were used to compute a risk score. Receiver operator characteristics (ROC) analyses were performed in the derivation and validation cohort to evaluate the nvHAP risk score’s ability to predict pneumonia incidence ≥2 days, ≥4 days, and ≥6 days after the assessment of risk factors.

Results: The derivation and validation cohort comprised 69,608 and 17,642 patients with an nvHAP rate of 0.69% (n=483) and 0.61% (n=107), respectively. After assessing 18 risk factor candidates, eight risk factors were incorporated in a simple ‘nvHAP risk score’ ranging from 0 to 11 points (age ≥60 = 1 point; male sex = 1 point; severely impaired activity and mobility = 2 points; acute problems with breathing = 1 point; impaired orientation = 1 point; moderate/severe pain = 1 point; affiliation to high risk clinic = 1 point; swallowing difficulties or tube feeding = 3 points). The areas under the ROC in the derivation and validation cohort were 0.78 and 0.72 to predict nvHAP ≥2 days in advance, 0.77 and 0.70 ≥4 days in advance, and 0.76 and 0.69 ≥6 days in advance.

Conclusions: We developed a simple risk score for nvHAP that is applicable on a very broad acute care patient population. It allows identification of patients at high risk for nvHAP ≥6 days in advance with a fairly good predictive accuracy.
Figure 1

a) Forest plot of hazard ratios of potential risk factors for nvHAP

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>HR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (≥25)</td>
<td>0.90 (0.75, 1.09)</td>
</tr>
<tr>
<td>Age ≥60</td>
<td>2.09 (1.72, 2.54)</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>1.96 (1.62, 2.38)</td>
</tr>
<tr>
<td>Abdominal or thoracic injuries or surgeries</td>
<td>1.57 (1.27, 1.93)</td>
</tr>
<tr>
<td>Severely impaired activity and mobility</td>
<td>4.46 (3.56, 5.58)</td>
</tr>
<tr>
<td>Acute problems with breathing</td>
<td>3.65 (2.97, 4.47)</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>1.66 (1.33, 2.07)</td>
</tr>
<tr>
<td>Impaired orientation</td>
<td>4.82 (3.70, 6.14)</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>1.23 (0.97, 1.55)</td>
</tr>
<tr>
<td>Psychotropic substances</td>
<td>2.73 (2.24, 3.33)</td>
</tr>
<tr>
<td>Nausea</td>
<td>4.52 (3.54, 5.76)</td>
</tr>
<tr>
<td>Moderate/severe pain</td>
<td>1.85 (1.51, 2.26)</td>
</tr>
<tr>
<td>Current stay on ICU</td>
<td>4.75 (3.64, 6.20)</td>
</tr>
<tr>
<td>Analgesedation</td>
<td>1.36 (0.98, 1.90)</td>
</tr>
<tr>
<td>General anesthesia</td>
<td>1.26 (1.05, 1.50)</td>
</tr>
<tr>
<td>High risk clinics *</td>
<td>1.80 (1.48, 2.17)</td>
</tr>
<tr>
<td>Swallowing difficulty but no tube feeding</td>
<td>3.78 (2.81, 5.08)</td>
</tr>
<tr>
<td>Tube feeding</td>
<td>6.11 (4.77, 7.84)</td>
</tr>
</tbody>
</table>

b) ROC curves for nvHAP risk score to predict nvHAP ≥ 2 days in advance

**Derivation cohort, ≥2-day prediction**

**Validation cohort, ≥2-day prediction**

Abbreviations: AUC, area under the curve; BMI, body mass index; CI, confidence interval; HR, hazard ratio; ICU, intensive care unit; nvHAP, non-ventilator-associated hospital-acquired pneumonia; ROC, receiver operator characteristics

* High risk clinics: Internal medicine and all subspecialties, clinics performing major surgical procedures on chest, abdomen, or extremities.

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Abstract 1873

**Spatiotemporal mapping of Bartonella bacilliformis in Peru and qualitative analysis of local perceptions and understanding of the disease**

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**Background:** Carrion’s disease is a biphasic illness caused by *Bartonella bacilliformis* and is endemic to parts of Peru. Understanding its spatiotemporal behavior is a key factor to improve pre-emptive measures. This study aims to identify spatiotemporal clusters of disease in Peru and elucidate local perceptions about the disease, to provide the basis for further research to guide elimination strategies.

**Materials/methods:** Spatial autocorrelation, hotspot and spatiotemporal analysis were carried out using ArcGIS and SatScan software to identify disease clusters over time. Data from the department of Ancash [Peru], showing absolute number of cases of Carrion’s disease was analysed to look for trends in the data between January 2000 and June 2019. Focus group discussions took place among health workers and community members in Ancash and core themes were identified.

**Results:** The departments of Ancash and Cajamarca contained significant hotspots of disease and were part of the eight clusters identified by spatiotemporal analysis. Clusters were also identified in previously non-endemic departments, with one significant secondary spatiotemporal cluster identified in the department of Puno from 2006 to 2007. In general, within Ancash, males and females were similarly affected (most commonly in the youngest age group), with similar number of cases of acute and chronic forms of the disease reported each year. Five core themes emerged from the focus groups – presentation, aetiology, prevention, diagnosis, treatment. Community members were aware of the disease and most would visit the clinic if unwell. Health workers discussed preventive interventions and the influence of experience and antibiotic availability on treatment.

**Conclusions:** This study provides evidence supporting the theory that Carrion’s disease is spreading into previously non-endemic areas and highlights the beliefs of local health workers and communities regarding this disease. Carrion’s disease could still be targeted for elimination, but further research is needed for this to occur, before the window of opportunity closes.

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Abstract 1876

**Reduced production of bacterial membrane vesicles predicts mortality in ST45/USA600 methicillin-resistant Staphylococcus aureus bacteremia**

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**Background:** Staphylococcus aureus is one of the major causes of infection-related morbidity and mortality in humans. Prognostic biomarkers such as IL-10 and TNFα produced after manifestation of symptoms are not routinely orderable tests in standard clinical microbiology. Therefore, identification of a prognostic microbial factor may pave ways for early identification. We hypothesize that membrane vesicles (MV), detached portions of the staphylococcal membrane enriched with multiple immunomodulatory effectors, may represent a microbial factor that can be detected early in infection and predict clinical outcome. In the present study we establish that clinical isolates from survivors of endovascular ST45/USA600 staphylococcal infection produce significantly more MV than from decedents.

**Materials/methods:** Forty-four well-characterized sequential ST45/USA600 isolates were selected for this study. Of these 44 isolates, 21 were isolated from patients who survived the infection and 23 were isolated from decedents. Isolates were confirmed to be ST45 by multi-locus sequence typing. Pertinent clinical data along with calculated clinical risk scores were recorded. Phenotypic and genomic strain characterization was performed. MV were isolated by three different methods and detected using a vesicle membrane-specific styryl dye (FM1-43). Descriptive data was expressed as mean and standard deviation, median and interquartile range, or frequencies and percentage. Univariable analysis was performed using Student’s t-test, Wilcoxon rank sum, or Fisher’s exact. Classification and Regression Trees (CART) were used to determine an RFU breakpoint for mortality.

**Results:** In ST45/USA600 clade, low MV production *ex vivo* is strongly associated with 30-day mortality. Preliminary targeted genome sequence analysis does not identify any significant differences between isolates in agrABDC, sigAB, sle1 or psmα1-4 sequence suggesting some other, unknown factor is responsible for differences in MV production. Therefore, the genetic differences between strains that result in differential MV production remain unclear.

**Conclusions:** Low production of MV is associated with an increased risk of mortality in staphylococcal bacteremia caused by ST45/USA600 MRSA. MV can be rapidly quantified allowing for facile integration into existing clinical microbiology workflows.

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Abstract 1879

Prevention of pneumocystis pneumonia by Ibrexafungerp in a murine prophylaxis model

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Abstract third-party references: Supported by SCYNEXIS, Inc.

Background: Pneumocystis pneumonia (PCP) is an opportunistic fungal infection that affects immunocompromised patients. Ibrexafungerp (IBX) is an oral and intravenous antifungal from a novel class of glucan synthase inhibitors, triterpenoids, and has shown activity against Candida, Aspergillus, and PCP in a murine therapy model. We evaluated the ability of IBX to prevent PCP in a prophylaxis model of murine PCP.

Materials/methods: Experiment 1: Balb/c mice (10 mice/group) were infected by intranasal inoculation with Pneumocystis murina, immune-suppressed with dexamethasone in acidified drinking water and treated with 30-, 15- and 7.5 mg/kg, IBX/BID. Control groups treatment included TMP-SMX (50/250 mg/kg QD) and vehicle. After 6 weeks, mice were sacrificed and prevention was determined by organism burdens (asci and total nuclei).

Experiment 2: Balb/c mice were immune-suppressed and infected as in Exp. 1. Treatment groups included: 1) 30 mg/kg BID x 6wk; 2) 30 mg/kg/BID x 6wk followed by cessation of treatment with IBX but with immune-suppression for 3 additional weeks; 3) 15 mg/kg BID 1 week prior and 6 wks after infection and immune suppression; 4) 15mg/kg BID for 8 wks; 5) 15 mg/kg BID for 6 wks then IBX was discontinued but with immune suppression; 6) untreated, vehicle control.

Results: Experiment 1: No P. murina nuclei or asci were observed after 6 weeks of treatment at a dose of 30 mg/kg/BID in the prophylaxis mouse model of PCP, similar to positive control, TMP/SMX. Some nuclei and asci were observed in the lower dose IBX groups. Experiment 2: To investigate whether any P. murina remained after different regimens of prophylaxis, treatment of IBX was withdrawn at both doses for an additional 3 wks of immune suppression to provoke the growth of any remaining fungi. Group 1 showed reduction in total nuclei and asci to undetectable. Group 2 did not result in any recrudescence of infection. Group 3 and 4 showed similar reduction in organism burden. Group 5 was similar to untreated control.

Conclusions: These results demonstrate that 30 mg/kg BID IBX prevented PCP in a murine model. We suggest that IBX could be a viable option for preventing PCP in immunocompromised patients.

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Impact of chemoprophylaxis on the outcomes of Plasmodium vivax and Plasmodium ovale imported malaria cases among civilian travellers

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Background: Malaria prophylaxis aims at reducing infection with Plasmodium. In those infected with Plasmodium vivax or Plasmodium ovale, it may alter the clinical course since it does not target hepatic forms. This study aimed at describing the clinical course of P. vivax or P. ovale malaria in travelers, based on chemoprophylaxis use.

Materials/methods: We conducted a case-control analysis of the outcomes of P. vivax and P. ovale infections nested in the cohort of imported malaria cases in civilian travelers reported to the French National Reference Center for Malaria from January 2006 to December 2017. We assessed the effect of chemoprophylaxis on the incubation period, delay between symptoms and diagnosis, type of medical care, biological findings at admission, type of symptoms and duration of hospitalization using adjusted logistic regression. As only infected travelers were observed, we assessed prophylaxis effect on post-infection outcomes using a counterfactual approach.

Results: Among 360 P. vivax and 756 P. ovale civilian travelers cases, 33% and 48%, respectively, reported a chemoprophylaxis use. There were 16 and 7 severe cases respectively, one patient died. Eighty percent of patients had symptoms less than 6 months after return. Chemoprophylaxis users had a greater risk to present symptoms more than 2 months after returning for both species (P. vivax OR: 3.40, 95% CI: [1.76-6.56], p<0.001, P. ovale OR: 2.42, 95% CI: [1.74-3.36], p<0.001), and those infected by P. ovale had a greater risk of having diagnosis more than 3 days after onset of symptoms (OR: 1.52, 95% CI: [1.07-2.17], p<0.05). Attributing these changes to prophylaxis was possible as long as the proportion of overall travelers to endemic areas under prophylaxis was less than 50%. There was no impact on the other studied characteristics.

Conclusions: Civilian travelers infected by P. vivax or P. ovale reporting chemoprophylaxis use had a greater risk of delayed onset illness after infection (probably first relapse). The full impact of chemoprophylaxis on infection with relapse-causing species should consider both reduction in infection and delay onset of symptoms, hence the need of new recommendations of chemoprophylaxis for travelers exposed to these species, acting against both erythrocytic and liver stages.

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Abstract 1882

**Murine typhus, a step beyond the clinic: how does it affect us in the 21st century? Epidemiology in Spain (1997-2015)**

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**Background:** Murine typhus (MT) is a zoonosis caused by Rickettsia typhi. Its main host is the rat and its vector to the human is the rat flea. The clinical picture is characterized by headache, fever, skin rash and liver function alteration. The severe pattern affects up to 10% of patients with pulmonary or renal involvement and even admission to Intensive Care Units. The prevalence of MT is considered underestimated since most cases are mild and self-limited. The aim of our study is to analyze the epidemiological impact of MT in patients who required hospitalization in the Spanish National Health System (NHS) between 1997 and 2015.

**Materials/methods:** Retrospective longitudinal descriptive study of in-patients diagnosed with Rickettsia typhi in Spanish public hospitals between 1997 to 2015. We obtained the data from the Minimum Basic Data Set of patients admitted to the NHS with a diagnosis of Rickettsia typhi: International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM), 081.0, provided by the Health Information Institute of the Ministry of Health and Equality.

**Results:** A total of 99 cases were registered. Most cases were men (63, 63.6%). Mean age (±SD) was 46.4 years (±19.0). 85 (85.9%) cases were an urgent hospital admission. The period incidence rate (IR) was 0.12 (95% CI, 0.09-0.14) cases per million person-years. An irregular distribution was observed throughout the study period, although there was a slight upward trend between 2013 and 2015. Canary Islands had the highest IR (2.17), followed by Andalusia (IR: 0.07). Esporadic cases were evenly distributed without other clear geographical aggregates. The average (±SD) hospital stay was 11 days (±9.9). Only 1 (1%) case died.

**Conclusions:** Despite of the small sample, our data suggests that MT is an emerging disease in Spain, as literature reflects. Regardless of its low incidence, all the authors agree with the huge underestimation of this zoonosis, due to the self-limited nature of most cases and the low clinical suspicion. In our study, the highest number of cases is recorded in the Canary Islands and Andalusia. The mortality rate remains very low. The control of MT should focus on primary prevention.

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Abstract 1883

Post-transplant lymphoproliferative disorders and association of antiviral prophylaxis in a nationwide cohort study

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Background: Post-transplant lymphoproliferative disorder (PTLD) is a serious complication of transplantation. Most PTLD in solid organ transplant recipients (SOT) are induced by Epstein-Barr virus (EBV) infection. However, the role of antiviral prophylaxis in the prevention of EBV-associated PTLD is controversial.

Materials/methods: SOT recipients enrolled in the Swiss Transplant Cohort Study (STCS) transplanted from 2008 to 2018 were included. We assessed incidence, presentation and outcome of histologically proven PTLD. In addition, we assessed the impact of anti-viral prophylaxis (Val-)Acyclovir, (Val-)Ganciclovir) on the incidence of PTLD using adjusted stratified Cox regression models.

Results: We included 4'811 patients with a follow-up duration of 24'455 patient-years (py) (median follow-up time 4.68y/patient, IQR 2.35-7.74). 54 histology proven PTLD-cases were identified, 36 were EBV positive (EBV-PTLD). Median age at transplantation was 54 years overall (IQR 42-62), 61y (IQR 54-63) for non-EBV-PTLD cases and 41y (IQR 24-60) for EBV-PTLD. Histopathological-classification revealed early lesions in 6 (11%), polymorphic in 15 (28%) and monomorphic PTLDs in 33 (61%) of cases. Extra-nodal sites were common (74%), CNS involvement was present in 7 cases (13%). PTLD incidence rate was 2.21/1000py and 1.47/1000py for EBV-PTLD. Highest incidence was found among lung transplant recipients with 4.47/1000py (4.19/1000py for EBV-PTLD). Incidence for EBV-PTLD at 1, 2 and 3 years post-transplantation were 2.81;1.94;1.71/1000py respectively vs. 0.43;0.35;0.28/1000py for non-EBV-PTLD (Figure1), median time post-transplantation to EBV-PTLD was 14.5 months vs. 61 months to non EBV-PTLD (p <0.001). We did not find a significant effect of antiviral prophylaxis ((Val-)Acyclovir or Val-)Ganciclovir) on EBV-PTLD incidence, however some evidence towards lower risk for early EBV-PTLD (<2y post-transplantation) was seen for patients with ganciclovir prophylaxis (HR 0.34 [95%CI: 0.12-1.02, p=0.054). Overall mortality during follow-up was 14.45%, in patients with PTLD, related mortality was 31% for EBV-PTLDs, and 33% for non-EBV-PTLDs.

Conclusions: PTLD incidence in our cohort was low, although associated with high mortality. Incidence of EBV-PTLD declined over time and was highest in the first 2 years post-transplantation, while non-EBV-PTLD incidence did not decline. Antiviral prophylaxis had no significant effect on EBV-PTLD occurrence.

Figure 1. EBV- and non-EBV-PTLD Incidence per 1000 patient-years
Symbols represent point-estimates, whiskeys 95% confidence intervals.
EBV, Epstein-Barr Virus. PTLD, Post Transplant Lymphoproliferative Disorder. PY, patient-years.

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Viral meningitis in adults: what are we missing? The use of viral capture sequencing to detect pathogens in the cerebrospinal fluid of adults with meningitis

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**Background:** Many patients with meningitis never have an aetiology identified, leading to unnecessary courses of antibiotics and antivirals, prolonged hospitalisation, and uncertainty for patients. Viruses are the most common cause of meningitis where a pathogen is found. Therefore, we used new viral capture sequencing methods to identify any viruses present in cerebrospinal fluid (CSF) from patients with meningitis and no pathogen identified.

**Materials/methods:** CSF from 76 adults was tested by VirCapSeq-VERT, an oligonucleotide probe set designed to capture viral targets using high throughput sequencing. Patients were categorised as either a) suspected viral meningitis – CSF pleocytosis and no pathogen found on routine molecular testing with a suspicion of viral aetiology based on validated clinical scores and/or negative 16s rRNA PCR testing (n=38), b) proven viral meningitis – CSF pleocytosis and virus identified on routine molecular testing (n=17), or c) not meningitis – symptoms and signs of meningitis but no CSF pleocytosis (n=21).

**Results:** VirCapSeq-VERT detected twelve individual viruses in 16/38 (42%) CSF samples from patients with suspected viral meningitis. Most viruses detected [58% (7/12)] were clinically relevant and included - *Herpes simplex virus* type 2, *Enteroviruses*, *Varicella zoster virus*, HIV, *Toscana virus*, *Rotavirus* and *Saffold virus*. Other viruses detected, unlikely to be clinically relevant, were *Epstein barr virus*, *Human herpes virus 6*, *Human pegivirus*, *Merkel cell polyomavirus* and *Human papillomavirus*. In the proven viral meningitis group one virus, additional to what had previously been found, was detected in one sample – *Human pegivirus* – not thought to be clinically relevant. 14% (3/21) of samples from patients without meningitis had a virus detected. The only viruses detected in this group were *Human pegivirus* (x2) and *Merkel cell polyomavirus*, neither of which are clinically relevant.

**Conclusions:** Sequencing methods enable the detection of a wide variety of pathogens. VirCapSeq-VERT increases the chances of detecting a virus due to its agnostic approach. This study shows that new diagnostic methods can allow more patients with meningitis to have an aetiological cause identified. Further work is needed to determine the prevalence of atypical viral candidates in meningitis and the clinical impact of using sequencing methods in real time.

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ABSTRACTS 2020

Abstract 1885

**Optimising the combination of ceftazidime/avibactam and gentamicin against KPC-producing Klebsiella pneumoniae (KPC-Kp) with aminoglycoside-modifying enzymes**

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**Background:** Although the β-lactam/β-lactamase inhibitor ceftazidime/avibactam is active against KPC-Kp, treatment failure rates up to 45% have been reported. Combinations with ceftazidime/avibactam and an aminoglycoside may be synergistic, however, ~90% of KPC-Kp harbor the aminoglycoside-modifying enzyme aac(6′)-Ib, which partially inactivates gentamicin. An alternate allele, aac(6′)-Ib′, is also harbored by some KPC-Kp and fully inactivates gentamicin. The purpose of this study was to evaluate bacterial killing by combinations of ceftazidime/avibactam with gentamicin against KPC-Kp with aac(6′)-Ib or aac(6′)-Ib′.

**Materials/methods:** Clinical KPC-Kp isolates containing aac(6′)-Ib [KPC-Kp-085 and -213] and aac(6′)-Ib′ [KPC-Kp-061 and -078] were used in all experiments. Ceftazidime/avibactam and gentamicin MICs were determined using broth microdilution. Time-kills were performed using a starting inoculum of ~10^8 CFU/mL and viable bacterial counts were quantified at 0, 1, 2, 4, 6, 8, and 24 hours, to examine clinically relevant concentrations of ceftazidime/avibactam [5/0.94, 20/3.75, and 80/15 mg/L] and gentamicin [0.625, 1.25, 2.5, 5, and 10 mg/L] alone and in combination. Synergy was defined as a ≥2log₁₀ CFU/mL reduction by the combination compared to each agent alone.

**Results:** Each isolate was susceptible to ceftazidime/avibactam and gentamicin according to CLSI. KPC-Kp-085, -213, -061, and -078 ceftazidime/avibactam MICs were 0.5, 0.03, 0.25, and 0.5 mg/L and gentamicin MICs were 0.25, 0.25, 4, and 4 mg/L, respectively. Ceftazidime/avibactam concentrations of 5/0.94, 20/3.75, and 80/15 mg/L achieved ≤1, 1 - 3, and >3log₁₀ CFU/mL reductions at 24 hours, respectively against all isolates. For aac(6′)-Ib containing isolates, gentamicin concentrations ≥2.5 mg/L were bactericidal [≥3log₁₀ CFU/mL reduction] whereas no gentamicin concentration was bactericidal for aac(6′)-Ib′ containing isolates. For aac(6′)-Ib containing isolates, ceftazidime/avibactam 20/3.75 mg/L combined with gentamicin ≥2.5 mg/L achieved ≥7log₁₀ CFU/mL reductions, whereas gentamicin ≥10 mg/L was needed for aac(6′)-Ib′ containing KPC-Kp. Gentamicin combined with ceftazidime/avibactam was synergistic for all isolates. However, lower gentamicin concentrations were required to achieve synergy against aac(6′)-Ib containing KPC-Kp.

**Conclusions:** Ceftazidime/avibactam failed to eradicate susceptible KPC-Kp as monotherapy. Combinations of gentamicin and ceftazidime/avibactam were synergistic but displayed more activity against isolates with aac(6′)-Ib than aac(6′)-Ib′. Using rapid diagnostics to differentiate between aac(6′)-Ib and aac(6′)-Ib′ may be useful to quickly optimize combination therapy for KPC-Kp infections.

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Abstract 1886

**Longitudinal (2011-2018) activity of oritavancin against Gram-positive isolates causing bacteraemia and endocarditis in Europe, including enterococcal infections requiring adjusted daptomycin dosing**

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**Abstract third-party references:** This study was performed by JMI Laboratories and supported by A. Menarini Farmaceutica Internazionale s.r.l (AMFI), which included funding for services related to preparing this abstract.

**Background:** Oritavancin is a long-acting lipoglycopeptide antibiotic with rapid bactericidal activity. This study assessed oritavancin activity against *Staphylococcus aureus* (SA), *Enterococcus faecalis* (EF), and *E. faecium* (EFM) causing bloodstream infection (BSI), including infective endocarditis (IE) and vancomycin-resistant enterococci (VRE) displaying elevated-daptomycin (EDAP) MIC values (≥2 mg/L). The longitudinal activity of oritavancin was also evaluated.

**Materials/methods:** A total of 4,198 SA, 1,211 EF, and 953 EFM were recovered from BSI in 44 European medical centres [2011-2018], including 146 SA isolates causing IE and 111 EDAP-VRE isolates. Species identification was confirmed by MALDI-TOF MS, when necessary, and susceptibility testing were performed by broth microdilution method following CLSI/EUCAST guidelines.

**Results:** Overall, oritavancin showed similar MIC₅₀ (0.03 mg/L) and MIC₉₀ results (0.06 mg/L) against MRSA, MSSA, and SA isolates causing IE (28.1% MRSA). Oritavancin displayed potent activity against EF regardless of susceptibility to daptomycin (MIC₅₀/₉₀, 0.015/0.03-0.06 mg/L; Table). Only 15 (1.2%) EF isolates were resistant to vancomycin, and 84.7% of those displayed VanA phenotypic profile. In contrast, VRE were observed in 19.8% of EFM isolates, among which VanA was also the predominant phenotype (84.7%). Although, EFM isolates displaying VRE and EDAP MIC phenotypes showed slightly higher oritavancin MIC values (MIC₅₀/₉₀, 0.015/0.06 mg/L) than VSE-EFM with daptomycin MIC ≤1 mg/L (MIC₅₀/₉₀ ≤0.008/≤0.008 mg/L), all isolates but one [oritavancin MIC, 0.25 mg/L] were inhibited by oritavancin at MIC of ≤0.12 mg/L. MRSA rates were 27.0% in 2011, 22.8% in 2018 and varied from 20.9% to 29.4% during the 8-year period. Yearly oritavancin MIC₅₀ results were 0.015 mg/L or 0.03 mg/L and MIC₉₀ results varied from 0.03 mg/L to 0.12 mg/L against MRSA. Against EF, yearly oritavancin MIC₅₀ results remain at 0.015 mg/L and MIC₉₀ results were 0.03-0.06 mg/L. No variation was observed on oritavancin MIC₅₀ results (≤0.008 mg/L) against EFM isolates and MIC₉₀ were 0.015-0.03 mg/L.

**Conclusions:** Oritavancin showed potent activity against this collection of isolates causing BSI and IE in Europe, including enterococci with decreased susceptibility to daptomycin. In addition, oritavancin maintained stable *in vitro* potency throughout the 8-year study period with no apparent temporal trends.

**Organism / Phenotype (No. of isolates) | Cumulative % inhibited by oritavancin at (mg/L): | MIC₂₅/₉₀**
---|---|---
S. aureus (4,198) | ≤0.008 | 0.015 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 0.03/0.06
MSSA (3,124) | 3.0 | 37.4 | 80.2 | 95.1 | 99.9 | 100.0 | 0.03/0.06
MRSA (1,074) | 3.0 | 35.9 | 80.0 | 95.1 | 100.0 | 0.03/0.06
SA-IE (146) | 3.4 | 35.3 | 76.7 | 93.8 | 99.3 | 100.0 | 0.03/0.06
*E. faecalis* (1,211) | 32.4 | 72.5 | 90.0 | 96.1 | 99.9 | 100.0 | 0.015/0.03
Non-EDAP (1,142) | 33.3 | 73.0 | 90.3 | 96.2 | 99.9 | 100.0 | 0.015/0.03
EDAP (69) | 17.4 | 63.8 | 85.5 | 94.2 | 98.8 | 100.0 | 0.015/0.06
*E. faecium* (953) | 82.0 | 91.9 | 96.6 | 99.0 | 99.9 | 100.0 | =0.008/0.015
Non-EDAP / VSE (316) | 63.7 | 90.1 | 100 | 100 | =0.008/0.008
EDAP / VRE (110) | =0.008 | 0.015/0.03

MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*; EDAP, elevated daptomycin MIC (≥2 mg/L); non-EDAP, non-elevated daptomycin MIC (<1 mg/L); VSE, vancomycin-resistant enterococci; VRE, vancomycin-resistant enterococci.

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**Abstract 1887**

**Delafloxacin activity against drug-resistant Streptococcus pneumoniae, Haemophilus influenzae, Haemophilus parainfluenzae, and Moraxella catarrhalis from European medical centres (2014-2018)**

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**Abstract third-party references:** This study was performed by JMI Laboratories and supported by A. Menarini Farmaceutica Internazionale s.r.l (AMFI), which included funding for services related to preparing this abstract.

**Background:** Delafloxacin (DLX) is an anionic fluoroquinolone (FQ) that has been approved in the United States and in Europe for the treatment of acute bacterial skin and skin structure infections and was recently approved in the US for the treatment of community-acquired bacterial pneumonia (CABP). In the present study, in vitro susceptibility (S) results for DLX and comparator agents were determined for CABP pathogens including *Streptococcus pneumoniae* (SPN), *Haemophilus influenzae* (HI), *H. parainfluenzae* (HP) and *Moraxella catarrhalis* (MC) clinical isolates from European hospitals participating in the SENTRY Program during 2014-2018.

**Materials/methods:** A total of 2,111 SPN, 1,087 HI, 701 MC, and 17 HP isolates were collected from community-acquired respiratory tract infections (CARTI) during 2014-2018 from European hospitals. Sites included only 1 isolate/patient/infection episode. Isolate identifications were confirmed at JMI Laboratories. Susceptibility testing was performed according to CLSI broth microdilution methodology, and EUCAST (2019) breakpoints were applied where applicable. Other antimicrobials tested included levofloxacin (LEV) and moxifloxacin (MOX; not tested in 2015). Multidrug-resistant (MDR) SPN isolates were categorized as being nonsusceptible (NS) to amoxicillin-clavulanate, erythromycin (ERY), and tetracycline; other SPN phenotypes were ERY-NS, or penicillin (PEN)-NS. β-lactamase (BL) presence was determined for HI, HP, and MC.

**Results:** The activities of the 3 FQs are shown in the table. The most active agent against SPN was DLX, with the lowest MIC<sub>50</sub> values of 0.015/0.03 mg/L. DLX activities were similar when tested against the MDR or PEN-NS for SPN phenotypes. ERY-NS isolates had DLX MIC<sub>50</sub> results of 0.015/0.03 mg/L. DLX was the most active FQ against HI, HP, and MC. BL presence did not affect FQ MIC values for HI or MC; only 1 HP isolate was BL-positive.

**Conclusions:** DLX demonstrated potent in vitro antibacterial activity against SPN, HI, HP, and MC. DLX was active against MDR SPN that were NS to the agents commonly used as treatments for CABP. These data support the utility of DLX in CABP including when caused by antibiotic resistant strains.

<table>
<thead>
<tr>
<th>Organism/Phenotype</th>
<th>Delafloxacin MIC&lt;sub&gt;50/90&lt;/sub&gt; (mg/L)</th>
<th>Levofloxacin MIC&lt;sub&gt;50/90&lt;/sub&gt; (mg/L)</th>
<th>Moxifloxacin MIC&lt;sub&gt;50/90&lt;/sub&gt; (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. pneumoniae</em> (2,111)</td>
<td>0.015/0.03</td>
<td>0.015/0.03</td>
<td>0.03/0.06</td>
</tr>
<tr>
<td>MDR (177)</td>
<td>0.015/0.06</td>
<td>1/2</td>
<td>≤0.12/0.25 (151)</td>
</tr>
<tr>
<td>PEN-NS (591)</td>
<td>0.015/0.03</td>
<td>1/2</td>
<td>≤0.12/0.25 (554)</td>
</tr>
<tr>
<td>ERY-NS (476)</td>
<td>0.015/0.03</td>
<td>1/2</td>
<td>≤0.12/0.25 (445)</td>
</tr>
<tr>
<td><em>H. influenzae</em> (1,087)</td>
<td>≤0.001/0.002</td>
<td>≤0.015/0.03</td>
<td>0.03/0.06 (1,003)</td>
</tr>
<tr>
<td>BL-positive (200)</td>
<td>≤0.001/0.002</td>
<td>≤0.015/0.03</td>
<td>0.03/0.03 (186)</td>
</tr>
<tr>
<td><em>H. parainfluenzae</em> (17)</td>
<td>0.008/0.06</td>
<td>0.03/0.6</td>
<td>0.06/0.25 (11)</td>
</tr>
<tr>
<td><em>M. catarrhalis</em> (701)</td>
<td>0.004/0.008</td>
<td>0.03/0.06</td>
<td>0.06/0.06 (610)</td>
</tr>
<tr>
<td>BL-positive (591)</td>
<td>0.004/0.008</td>
<td>0.06/0.06</td>
<td>0.08/0.06 (591)</td>
</tr>
</tbody>
</table>

*Number of isolates tested for moxifloxacin, not tested in 2015.*

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**Abstract 1891**

**Typing of emm1 Group A streptococci using MALDI-TOF MS**

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**Background:** In recent years, invasive infections caused by group A streptococcus (GAS) are increasing. Among them, emm1-type GAS are highly pathogenic, and it is said that the invasive infections are significantly more cases of fulminant type, and the mortality rate and the persistence survival rate are high. Here, we propose a new technique which is able to discriminate highly pathogenic emm1 type and other types using MALDI-TOF MS and statistical analysis software.

**Materials/methods:** We searched biomarkers that were able to discriminate emm types using frequently isolated types of the invasive infectious disease-derived GAS strain, emm1 strain, emm12 strain, emm28 strain, and emm89 strain. The above four types of emm strains were cultured on sheep blood agar plate for 24 hours. MALDI mass spectra were observed by positive linear mode for m/z 4000-20000. Biomarkers were selected by using eMSTAT Solution statistical analysis software (Shimadzu, Japan). To evaluate the selected biomarker, a blind test was conducted using 379 strains derived from pharyngitis / tonsillitis, including B, C, and G hemolytic streptococci.

**Results:** We used eMSTAT Solution to search marker peaks that contribute to discriminate emm1 from other types. As a result of the search, it can be confirmed that the peak of m/z 10932 was detected in all samples of emm1 while the peak was not detected in other types. Next, a blind test of 379 clinical isolates was performed using the peak of m/z 10932 as a biomarker. In the gene analysis of the conventional method, 97 out of 379 strains were typed to emm1. Similarly, 92 (94.8%) of the 97 strains were typed to be emm1 using the biomarker. Both methods showed a high positive concordance rate. In this method, three emm1 strains were typed to be non-emm1 strains [emm11 strain (n = 1) and emm28 strain (n = 2)], and the negative concordance rate was 98.9%.

**Conclusions:** This is the first result that discriminates emm1 type of GAS by MALDI-TOF MS. This new MALDI-based method is easier and faster than conventional methods like DNA sequencing.

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Background: universal screening for tuberculosis (TB) before anti-TNFα therapy and treatment of those who have latent TB (LTB) resulted in a significant reduction of active TB. However, we still diagnose TB in this population. We aimed to review severe TB cases in patients treated with anti-TNFα admitted to a tertiary hospital ID department between 2013-19.

Materials/methods: clinical records from patients with active TB were reviewed with data pertaining the inflammatory immunemediated disease, anti-TNFα treatment, TB screening and TB episode collected.

Results: ten cases of TB were documented (mean age 42.6 years, 7 men), 5 were under adalimumab, 3 under infliximab and 1 under golimumab and certolizumab pegol each. Five patients had a diagnosis of Inflammatory Bowel Diseases, 5 rheumatologic immune disease (2 psoriatic arthritis, 2 ankylosing spondylitis, 1 rheumatoid arthritis). All underwent LTB screening prior to anti-TNFα therapy with average time between screening and therapy of 4.8 months [range: 1-15]. Eight were negative and TB screening during anti-TNFα therapy was not repeated. LTB diagnosis was made in the remaining: one was treated with rifampicin [6 months], the other with isoniazid [9 months]. In these two cases, active TB was diagnosed, respectively, 4 and 3 years after LTB screening and treatment. Time between anti-TNFα therapy onset and TB diagnosis was 55 months [range: 3-138] and between TB symptoms and its diagnosis 1.6 months [range: 1-5]. Six patients had disseminated TB (involvement of central nervous system 2, lymphatic 5, hepatic 4, pleural 2), 2 pulmonary tuberculosis (PTB) with hepatic and pleural involvement each, and 2 PTB. Multisensitive Mycobacterium tuberculosis was recovered from biological samples in 9 patients, the remaining case being a presumptive diagnosis. All patients were treated with a 4-drug regimen with average treatment duration of 10.1 months [range: 9-15] and overall favorable evolution. Immunosuppressive therapy was resumed without anti-TNFα.

Conclusions: TB under anti TNFα therapy remains an important diagnosis despite TB screening. As before, 60% of our cases comprise disseminated forms. A high level of TB suspicion should be maintained, regular screening of TB under anti-TNFα therapy is probably worth being done and better tests for TB screening are welcomed.

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Abstract 1893

Comparison of the microbiological efficacy of disinfection using ultraviolet and aerosolised hydrogen peroxide system for carbapenemase-producing Enterobacteriaceae in a healthcare setting

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Background: Carbapenemase-producing Enterobacteriaceae (CPE) are a growing problem in the worldwide. Environmental cleaning is important strategy to prevent CPE transmission and "no-touch" methods including ultraviolet C (UV-C) and aerosolized hydrogen peroxide (aHP) system have been evaluated to overcome the shortcomings of manual cleaning. However, data regarding efficacy of UV-C and HP system against CPE are limited. We thus compared the microbiological efficacy of disinfection using UV-C and aHP as area decontamination in a healthcare setting.

Materials/methods: This study was conducted in empty single patient rooms with dimension of 48.3 m3 at a tertiary hospital, Seoul, South Korea from May to October, 2019. We ran 4 rooms with 2 UV-C and 2 aHP, respectively and 30 formica sheets contaminated with KPC-producing Klebsiella pneumoniae \(10^6 \text{CFU}\) were placed in the room, both direct and indirect sites. After intervention, median log reduction and decontamination rate were assessed using Rodac plates.

Results: We observed median 5.52 log reduction after UV-C (n=60) and median 5.37 log reduction after aHP (n=60) (P=0.86), and 50% decontamination rate after UV-C and 45% decontamination rate after aHP (P=0.71) (Table 1). At direct sites, UV-C showed higher median log reduction (5.91 vs. 5.61, P=0.002) and decontamination rates (83% vs. 53%, P=0.03) than aHP. Conversely, at indirect sites, aHP showed higher median log reduction (4.63 vs. 5.07, P=0.02) and decontamination rate (17% vs. 37%, P=0.01) than UV-C.

Conclusions: Both UV-C and aHP reduced bacterial contamination in a single room. aHP was significantly more effective at indirect sites, and UV-C was significantly more effective at UV direct sites. Depending on the shadow area, healthcare facilities might choose between UV-C and aHP.

Table 1. Microbial efficacy of UV-C and aHP

<table>
<thead>
<tr>
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<th>UV-C</th>
<th>aHP</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median log reduction (IQR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (n=60)</td>
<td>5.52 (4.65-5.91)</td>
<td>5.37 (4.78-5.91)</td>
<td>0.86</td>
</tr>
<tr>
<td>Direct (n=30)</td>
<td>5.91 (5.91-5.91)</td>
<td>5.61 (4.97-5.91)</td>
<td>0.002</td>
</tr>
<tr>
<td>Indirect (n=30)</td>
<td>4.63 (4.20-5.19)</td>
<td>5.07 (4.55-5.91)</td>
<td>0.02</td>
</tr>
<tr>
<td>Decontamination rate*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (n=60)</td>
<td>30 (50%)</td>
<td>27 (45%)</td>
<td>0.71</td>
</tr>
<tr>
<td>Direct (n=30)</td>
<td>25 (83%)</td>
<td>16 (53%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Indirect (n=30)</td>
<td>5 (17%)</td>
<td>11 (37%)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*It was defined as the ratio of the number of less than 2.5 CFUs per plate to the total number of plates

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Identification of novel mobile colistin resistance gene mcr-10

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**Background:** Mobile colistin resistance (mcr) genes represent an emerging challenge. We found and characterized a gene that is likely a new variant of mcr.

**Materials/methods:** An *Enterobacter roggenkampii* (a member of *Enterobacter cloacae* complex) clinical strain with a mcr-like gene encoding a new phosphoethanolamine transferase was subjected to whole genome sequencing using both Illumina short-read and MinION long-read platforms. This gene was cloned on pBC SK and then transferred into a colistin-susceptible *E. roggenkampii* strain. Conjugation and electroporation experiments were performed to examine the location of the mcr-like gene. The prevalence of mcr-10 was screened for depositions of GenBank. The 3D and secondary structures of this MCR-like protein were predicted using Phyre2 and ESPript 3 and were compared with known MCR proteins (MCR-1 to 9) and chromosomally encoded MCR-like phosphoethanolamine transferases [designated MCR-B here] of various *Buttiauxella* species.

**Results:** Here we describe a novel mcr gene, mcr-10, on an non-self-transmissible IncFIA plasmid of an *E. roggenkampii* clinical strain. mcr-10 has the highest nucleotide identity (79.69%) with mcr-9 and encodes MCR-10 with 82.93% amino acids identical to MCR-9. mcr-10 confers 4-fold increase of colistin MIC (from 1 to 4 mg/L) when cloned into a colistin-susceptible *E. roggenkampii* strain. By screening GenBank, mcr-10 was found in various *Enterobacteriaceae* species of countries in four continents, suggesting that this gene has widely spread. MCR-10 shows 79.04% to 83.67% amino acid identity and highly conserved predicted protein structures with MCR-Bs. MCR-10, MCR-9 and MCR-B proteins may therefore originate from a common ancestor. mcr-10 was adjacent to a site-specific recombinase-encoding gene and was bracketed by IS903 and may be mobilized by site-specific recombination or composite transposon (Fig).

**Conclusions:** Our results indicate that mcr-10 is a novel plasmid-borne colistin resistance gene and warrants immediate monitoring and further studies.

**Figure.** Genetic context of mcr-10 on pMCR10 090065. Gene int encodes a XerC-type tyrosine recombinase, which may mediate mobilization of adjacent genetic components via site-specific recombination. Δ represents truncated insertion sequences. Two copies of IS903 are located at upstream and downstream of int-mcr-10 and the 9-bp abutting sequences are indicate.

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Abstract 1895

**Dalbavancin as definitive therapy for Gram-positive infections in patients with haematologic malignancies and haematopoietic cell transplant recipients**

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**Background:** Patients with hematologic malignancies and hematopoietic cell transplants (HCT) are at an increased risk of infection due to the use of immunosuppressive agents, neutropenia, and central venous catheters. These infections are frequently caused by Gram-positive bacteria and are often complicated requiring extended courses of intravenous (IV) antibiotics. Dalbavancin is an IV lipoglycopeptide antibiotic with unique pharmacokinetics allowing for once weekly dosing. The aim of this study was to assess the efficacy of dalbavancin for definitive treatment of Gram-positive infections in patients with hematologic malignancies and HCT recipients at an academic medical center.

**Materials/methods:** This was a retrospective, single-center observational study from January 2016 – May 2019 of patients receiving dalbavancin at West Virginia University Hospitals. Patients were included if they were greater than 18 years of age, active hematologic malignancy or HCT recipient, and received at least one dose of dalbavancin for a Gram-positive blood stream infection (BSI) or skin and soft tissue infection (SSTI). The primary outcome was to evaluate clinical resolution of infection. Secondary outcomes were to determine infection recurrence within 30 days after dalbavancin completion, difference in efficacy for indication, and length of inpatient stay prior to outpatient dalbavancin.

**Results:** Fifty-seven patients met inclusion criteria, 24 (42%) were HCT recipients. Most patients were male (65%) with a median age of 60 years and weight of 87.4 kg. Acute myeloid leukemia was the most common malignancy (28.3%). BSIs were the most common dalbavancin indication, (52.6%). Overall, the clinical resolution rate was 78.9% (95% CI 0.6656 – 0.8767). Resolution was observed in 80% of BSIs versus 77.8% of SSTIs \( P = 0.8372 \). In patients without resolution, failure occurred in 10% of BSIs versus 7.4% of SSTIs \( P = 0.7297 \) and recurrence was observed in 10% of BSIs versus 14.8% of SSTIs \( P = 0.7014 \). The most frequent dosing regimens were 1,000 mg weekly and one 1,500 mg dose for BSIs and SSTIs, respectively. The median length of stay was seven days.

**Conclusions:** Dalbavancin appears to be an adequate treatment option for Gram-positive BSIs and SSTIs in this population. Using dalbavancin allows for outpatient treatment and may allow for earlier hospital discharge.

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Excess length of acute inpatient stay attributable to acquisition of hospital-onset Enterobacteriaceae bloodstream infection with and without antimicrobial resistance: a multistate model analysis

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Background: Hospital length of stay (LOS) is an important outcome impacted by healthcare-associated infections (HAIs) and antimicrobial resistance (AMR). However, measurement of excess LOS can be subject to survival bias when considering death as a censoring event due to variable timing of HAI onset and high mortality. We aimed to estimate unbiased change in LOS attributable to hospital-onset (HO) Enterobacteriaceae bloodstream infections (BSI) using multistate models without considering death as a censoring event.

Materials/methods: We analyzed a retrospective matched-cohort that included all case patients who developed HO BSI due to Escherichia coli or Klebsiella spp. (BSI onset >48 hours after the admission) during the period 2003 to 2013 at 130 hospitals within the US Veterans Health Administration System. Up to three uninfected control patients per case were identified and matched at patient-level based on gender, hospital and LOS before the onset of BSI. Case patients were further categorized by the resistance profile to fluoroquinolones (FQ) and extended-spectrum cephalosporins (ESC). A multistate model (Figure) was utilized, and change in LOS was estimated as an effect of the intermediate state (HO BSI: State 1 in Figure). We stratified analyses by isolate susceptibilities to FQ (FQ-S and FQ-R) and ESC (ESC-S and ESC-R) and assessed extra LOS for each category.

Results: 5,964 patients who had HO BSI due to E. coli (2,663/44.7%) or Klebsiella spp. (3,301/55.3%) and 15,213 uninfected patients were analyzed. 957 patients (16.9%) and 1,638 patients (28.9%) had organisms resistant to FQ and ESC, respectively. AMR was associated with larger change in LOS for both FQ (FQ-S: 12.13 days [95% CI: 6.25-17.88] vs. FQ-R: 12.94 days [95% CI: 2.35-24.31], difference: 0.81 days [95%CI: 0.56-1.05], p<.001) and ESC (ESC-S: 11.57 days [95%CI: 6.25-17.42] vs. ESC-R: 16.56 days [95%CI: 3.63-30.38], difference: 4.99 days [95%CI: 4.75-5.24], p<.001).

Conclusions: In this large matched cohort study, HO Enterobacteriaceae BSI with or without resistance to FQ or ESC was associated with attributable excess LOS. Resistance to FQ or ESC was associated with longer increases in LOS than seen in cases infected with susceptible isolates, and the impact was greater in ESC resistance compared to FQ.

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De-escalation of carbapenems to ciprofloxacin in the treatment of bacteremia caused by extended spectrum beta-lactamase-producing Enterobacteriaceae

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Background: Carbapenems are recommended for the treatment of bacteremia caused by extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae. However, increased use also selects for carbapenem resistance. Alternatives to carbapenem have yielded conflicting results in recent studies, with limited data evaluating fluoroquinolones (FQ) as carbapenem-sparing options. This study aimed to evaluate the use of ciprofloxacin as step-down from carbapenems in the treatment of bacteremia due to ESBL-producing Enterobacteriaceae.

Materials/methods: Patients with ESBL-producing Enterobacteriaceae bacteremia were evaluated in a retrospective cohort study. We compared patients who received definitive carbapenem therapy throughout (carbapenem group) versus those who were switched from carbapenem to ciprofloxacin (ciprofloxacin group) within 8 days of definitive therapy. The primary outcome evaluated was 30-day all-cause mortality. Secondary outcomes included re-infection and readmission rates, incidences of Clostridioides difficile and carbapenem-resistant infections, and length of hospitalisation. Factors influencing mortality were analysed via logistic regression.

Results: A total of 179 patients were included. There were 148 patients in the carbapenem group and 31 patients in the ciprofloxacin group. Median age was 74 years old and 52% were males. Patient demographics and treatment-related characteristics were similar between groups. Duration of carbapenem use prior to ciprofloxacin switch was 5 days (interquartile range [IQR] 3-6 days). The 30-day mortality were not statistically different between groups (0/31 [0%] vs. 16/148 [10.8%]; p=0.07). The median total duration of antibiotic treatment was longer in the ciprofloxacin group (16 vs.15 days; p=0.01). However, the median duration of hospitalisation was significantly shorter for the ciprofloxacin group [8 [IQR 8-13] vs. 15 days [IQR 9-19]; p=0.01]. Other secondary outcomes were not statistically different between both groups. Failure to reach clinical stabilisation by day 5 was associated with mortality (adjusted odds ratio 7.95% confidence interval 1.66-29.4).

Conclusions: Ciprofloxacin can be an effective carbapenem-sparing therapy for the treatment of bacteremia caused by ESBL-producing Enterobacteriaceae. Switching from carbapenem to ciprofloxacin can be considered when the patient achieved clinical stabilisation, and may result in shorter hospital stay.

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Abstract 1901

**Evaluation of rapid extraction methods coupled with recombinase polymerase amplification assay for point-of-need diagnosis of post-kala-azar dermal leishmaniasis**

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**Background:** Post kala-azar dermal leishmaniasis (PKDL) usually develops as sequelae of visceral leishmaniasis (VL) and can manifest in multiple dermatological forms. Since PKDL patients harbor Leishmania donovani parasites and can potentially trigger inter-epidemic transmission of the disease, the success of kala-azar elimination programme could be jeopardized by these cases. Although several molecular methods with promising diagnostic efficacy have been developed to detect PKDL cases, albeit complicated and expensive DNA extraction methods limit their application in resource poor settings. To address this, in comparison to a reference DNA extraction method (Qiagen), we evaluated two rapid DNA extraction methods and determined their impact on the detection of the parasite DNA using our newly developed recombinase polymerase amplification (RPA) assay.

**Materials/methods:** Thirty suspected PKDL cases were enrolled after diagnosis by clinical examination and a positive rk39 strip test. DNA was extracted from three skin biopsy samples using either a spin column-based method (Qiagen) or one of two rapid DNA extraction methods, (Boil & Spin (B&S) and SpeedXtract (SE)). RPA and qPCR were subsequently performed with the extracted samples to detect L. donovani DNA.

**Results:** Using DNA extracted by Qiagen method, the qPCR and RPA assays exhibited sensitivities of 86.7% and 93.3% respectively. In contrast, the sensitivity of RPA assay dropped to 76.7% and 63.3%, respectively, when the B&S and SE rapid extraction methods were performed. Despite this compromised sensitivity, B&S-RPA technique yielded an excellent agreement with both 0-qPCR (k = 0.828) and 0-RPA (k =0.831) techniques. Moreover, SE-RPA showed good agreement with 0-qPCR (k = 0.755), 0-RPA (k =0.692) and B&S-RPA (k =0.635) assays. As expected, with all of the three DNA extraction methods, both qPCR and RPA assay showed absolute specificity.

**Conclusions:** This study finding substantiates the superior diagnostic efficacy of Qiagen DNA extraction method over B&S and SE method in detecting LD DNA through RPA assay from skin biopsy of PKDL patients. To apply these rapid DNA extraction methods in resource-constrained settings, further methodological refinement is warranted to improve DNA yield and purity through rigorous experiments.

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Abstract 1902

Application of matrix-assisted laser desorption ionisation: time of flight mass spectrometry for Mycobacterium tuberculosis Beijing and Non-Beijing genotyping

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Background: The widely prevalent and highly virulent Mycobacterium tuberculosis (MTB) Beijing genotype strains were closely related to tuberculosis outbreaks and multiple drug resistance. Therefore, rapid and accurate preliminary diagnosis of the MTB Beijing strains is crucial.

Materials/methods: Recently, the advanced proteomic profiling method by matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) in identifying a variety of pathogenic microorganisms has shown promising results. Our study was to evaluate the performance and feasibility of the MALDI-TOF MS for genotyping MTB Beijing and Non-Beijing strains using a panel of 263 MTB isolates with the most reliable MALDI-TOF MS identification scores of ≥ 1.8.

Results: As a standard method, RD207 gene fragment deletion assay classified 263 MTB isolates into Beijing (195/263) and Non-Beijing (68/263) genotypes. The MS fingerprints of 133 MTB isolates (98 Beijing and 35 Non-Beijing strains) were used for modeling with various machine learning such as Genetic algorithm (GA), Supervised Neural Network (SNN) and Quicker Classifier (QC) in ClinProTools 3.0 software of MALDI-TOF MS. The GA model showed the best diagnostic performance with 90.31% sensitivity and 70.98% specificity and was externally validated by correctly identifying 130 MTB strains (97 Beijing and 33 Non-Beijing strains) into 82.47% Beijing strains (80/97) and 63.64% Non-Beijing strains (21/33), which showed 77.69% accuracy (101/130) and 95%CI (70.40%-84.90%). The GA model identified 2 characteristic mass peak biomarkers (4485.05 Da, AUC=0.74; 5785.67 Da, AUC=0.73) for the identification of MTB Beijing and Non-Beijing strains.

Conclusions: MALDI-TOF MS technology with ClinProTools software is easy and suitable to distinguish the MTB Beijing and Non-Beijing genotypes and has a promising application in homology analysis of Mycobacterium tuberculosis complex (MTBC).

Graph 1 Comparison of the average spectral characteristic peaks of Beijing (1) and non Beijing (2) strains (a: 4485.05 Da; b: 5785.67 Da)

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Abstract 1904

The positive impact of infectious diseases consultation on antimicrobial appropriateness in hospitalised patients with antimicrobial stewardship oversight: a propensity-score matched study

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Background: Hospital-based antibiotic stewardship (AS) programs provide oversight and guidance for appropriate antimicrobial use in acute care settings. Infectious Diseases expertise is beneficial in the care of hospitalized patients with infection. The impact of Infectious Diseases consultation (IDC) on antibiotic appropriateness in a large tertiary hospital with an established AS program was investigated.

Materials/methods: This was a cross-sectional study from 10/2017 to 3/2019 at a large, academic hospital with an AS-directed prospective audit and feedback process and multiple IDC services. Antimicrobial appropriateness was adjudicated by an AS team member at 3-6 days after antimicrobial start. Antimicrobial appropriateness was compared among antimicrobial orders with and without IDC using propensity-score matching and multivariable logistic regression. Analyses were stratified by primary services caring for the patients.

Results: There were 10,508 antimicrobial orders from 6,165 unique patient encounters. Overall appropriateness was 92% with higher appropriateness among patients with IDC vs. without IDC, (94% vs 84%, p<0.0001). After propensity-score matching and adjustment for certain antibiotics, organisms, syndromes and locations, IDC was associated with greater antimicrobial appropriateness odds ratio (OR) 2.4 (95% confidence interval (CI) 1.9, 3.0). Stratification by primary service showed OR of 4 (95% CI 1.3,12) for vascular surgery and OR of 1.5 (95% CI 0.9,2.4) for medicine.

Conclusions: Even with a high overall antimicrobial appropriateness rate, patients with IDC had greater odds of antimicrobial appropriateness than those without IDC with greatest impact in vascular surgery and least in medicine. Infectious disease consultation can be synergistic with antimicrobial stewardship programs.

<table>
<thead>
<tr>
<th>Primary Service</th>
<th>Appropriate (N)</th>
<th>Unadjusted OR (95% CI)</th>
<th>p-value ($\chi^2$)</th>
<th>Appropriate (N)</th>
<th>PS matched OR (95% CI)</th>
<th>p-value ($\chi^2$)</th>
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<tr>
<td>Orthopedics</td>
<td>445</td>
<td>7.8 (3.8-17)</td>
<td>0.0001</td>
<td>92</td>
<td>1.9 (0.74,7)</td>
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<td>7.3 (2.9-19)</td>
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<td>146</td>
<td>4.0 (1.3,12)</td>
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<td>1.9 (1.1,3.4)</td>
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<td>619</td>
<td>1.5 (0.9, 2.4)</td>
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</tbody>
</table>

CT cardiothoracic, PS propensity score ¹ Cardiology, Otolaryngology, General Surgery, Neurology, Neurosurgery, Obstetrics, Oncology, Pulmonary, Transplant, Trauma, ²Unadjusted

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Abstract 1906

**Hantavirus registry (HantaReg): a novel worldwide platform for epidemiological and clinical studies of hantavirus diseases**

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**Background:** Frequent outbreaks of globally emerging hantavirus infections emphasize the substantial threat to patients due to hantavirus associated diseases. Increasing incidence rates, worrisome trends of changing distribution of hantaviruses and new insights into clinical course of hantavirus diseases call for multinational surveillance.

**Materials/methods:** HantaReg serves as a novel worldwide registry project facilitating multinational research of hantavirus caused diseases, such as nephropathia epidemica, hemorrhagic fever with renal syndrome (HFRS) and hantavirus cardiopulmonary syndrome (HCPS). HantaReg includes an electronic Case Report Form (eCRF) and is accessible via the General Data Protection Regulation (GDPR) compliant platform clinicalsurveys.net. Data entry is carried out via any internet browser and is spontaneously encrypted. All documented cases are automatically collected into the database. To assess attributable mortality, HantaReg partly uses matched case-control design. HantaReg has a modular structure, as the registry platform is designed to display or hide questions and items according to the documented case (e.g. patient with HFRS vs. control patient). For quality control, each case entered is reviewed by a team of physicians for consistency and completeness.

**Results:** HantaReg facilitates the straightforward and standardized documentation of hantavirus diseases. Information categories documented into HantaReg are demographics, pre-existing diseases, clinical signs and symptoms, diagnostic and therapeutic approaches, as well as outcome. Details on management of hantavirus diseases include virology findings, imaging procedures, admission to the intensive care unit, diuretic treatment, renal replacement therapy and treatment response. Documented information on outcome of hantavirus diseases contains the development of kidney function and both overall and attributable mortality.

**Conclusions:** HantaReg is a novel, ready to use platform for clinical and epidemiological studies, as well as outbreak situations. Therefore, HantaReg enables the monitoring of changing epidemiological trends and of outbreak situations of hantavirus diseases locally and globally over time. HantaReg facilitates the worldwide, standardized documentation of disease course associated with hantavirus infections. HantaReg is a novel worldwide registry project promoting international collaboration and contributes to improving patient management by analysis of diagnostic and treatment approaches for hantavirus diseases.

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Epidemiology, clinical characteristics and outcomes of central nervous system infections in solid organ transplant recipients: a nationwide cohort study

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Background: The epidemiology and clinical presentation of central nervous system (CNS) infections after solid organ transplantation [SOT] has not been systematically assessed in the current era.

Materials/methods: Patients from the Swiss Transplant Cohort Study [STCS] transplanted from 05/2008 to 12/2017 with a CNS-infection were included. Epidemiological, microbiological, and clinical data were extracted from the STCS database and patients’ medical records. Descriptive statistics were used to characterize the patient population, diagnostic and therapeutic management. We analysed the incidence rate of CNS-infections and 90-day patient survival, according to presenting clinical syndrome.

Results: 37 cases of CNS-infection in 36/4249 (0.8%) SOT recipients were included in this study, with an overall incidence rate of 2.12 per 1000 patient-years. Incidence did not differ by transplanted organ. There were 13 space-occupying lesions and 24 meningoencephalitis cases. 2/13 (15.4%) space-occupying lesions were bacterial, 4/13 (30.8%) viral and 7/13 (53.8%) fungal infections [all invasive aspergillosis]. 2/24 (8.3%) of meningoencephalitis cases were bacterial, 15/24 (62.5%) viral, 3/24 (12.5%) fungal, and 4/24 (16.7%) cases were of unknown etiology (Fig.1). Median time of CNS-infection onset following SOT was 17 months [0.8-97]. Most fungal infections occurred <6 months after transplant [7/10, 70%]. Median time from symptoms onset to diagnosis was 8 days [IQR 3-25]. Most patients [75.6%] had a Glasgow Coma Scale >14 at presentation. The majority of space-occupying lesions had a histopathologic and/or culture-proven diagnosis obtained from biopsy or post-mortem samples. Patients with meningoencephalitis had more frequently a viral etiology documented by PCR performed on cerebrospinal fluid [CSF]. In 30% of meningoencephalitis cases CSF cellular count was normal with mild elevation of protein. In 16 [43%] cases, infection was disseminated involving the respiratory tract or the skin. Notably, 32.4% of infections required intensive-care-unit hospitalization. The majority of patients with a treatable etiology [20/23, 86%] received an effective antimicrobial treatment and in 48.6% at least one immunosuppressive drug was withdrawn. 90-day mortality was 29.7% [8.3% for meningoencephalitis, and 69.2% for space-occupying lesions, p<0.0002].

Conclusions: In the STCS, a low incidence of CNS-infections was observed, with viral meningoencephalitis being the most common presenting syndrome. Space-occupying lesions were associated with an elevated mortality rate.

Fig.1 Etiology of CNS infections

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Abstract 1908

Burden and impact of carbapenem resistance caused by Enterobacterales in a Bangladeshi hospital: an epidemiological, clinical and molecular study

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Background: Despite the high prevalence of antimicrobial resistance (AMR) in developing countries, limited data is available informing the actual health burden. We undertook a prospective cohort study at Dhaka Medical College Hospital (DMCH) to investigate the impact of AMR on health.

Materials/methods: Microbiology of Enterobacterales included minimum inhibitory concentration of antimicrobials and whole genome sequencing. Both unadjusted and adjusted logistic regression and Cox proportional subdistribution hazard model were performed to analyse risk and outcome for infections caused by carbapenem-resistant Enterobacterales (CRE) compared to carbapenem-sensitive Enterobacterales (CSE).

Results: Patients positive for at least one CRE from any clinical specimen were considered as ‘CRE infections’ and patients without any CRE positive clinical samples were included as ‘CSE infections’. Crude mortality was 26% (64/246) with CRE infections and 11.7% (29/248) with CSE infections. CRE infections were significantly associated with in-hospital mortality ($p<0.0000001$) and significant inverse correlation with discharge alive ($p<0.0000001$) in both baseline model with time from infection as the timescale (time 0 is infection) by adjusting time from admission (time 0 is admission) and adjusted for the subdistribution hazard model. E. coli and K. pneumoniae were significantly responsible for mortality compared to other infections ($p<0.01$), but carbapenem resistance did not change p value for the mortality due to E. coli or K. pneumoniae in adjusted logistic regression. There was a trend towards prolonged hospital stay in patients with CRE; however, result was not statistically significant. Demographic and clinical parameters for CRE acquisition were mostly insignificant except the CREs recovery from urine ($p<0.0001$). Epidemiological evidence of CRE dissemination in Bangladeshi clinical setting was apparent: A. carbapenem resistance in E. coli was prevalent in ST167 ($p<0.0000001$) B. outbreak of K. pneumoniae ST23 (n=35) was detected and carbapenem resistance was associated with this particular clone ($p<0.05$) C. CRE faecal colonization was higher among inpatients than outpatients ($p<0.0001$) D. plasmids with identical backbone, IncFIA, IncFIB, IncFIIC and IncX3 were found in association with blaNM5 among the species of Enterobacterales.

Conclusions: Our data suggests that the magnitude of the impact of AMR associated with CRE on health outcomes in Bangladesh is worrying and needs immediate attention.

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Abstract 1918

**Tuberculosis in renal failure: clinical presentation and outcome from a TB endemic area**

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**Background:** Tuberculosis (TB) is a major cause of morbidity and mortality. Patients with renal failure are 6 to 25 times more likely to develop TB than the general population. The diagnosis of TB disease is difficult because of lack of classic symptoms and extra-pulmonary involvement. The atypical presentation, delay in diagnosis and difficulty in management may be cause of increase mortality, ranging from 17% to 75% in different studies. Our aim is to find out the clinical presentation and treatment outcome of TB in renal failure from a TB endemic country.

**Materials/methods:** A retrospective cohort study was done at Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan. SIUT is a 700 bedded tertiary care hospital mainly caters to renal and urological diseases. It runs the country's largest renal transplantation and dialysis unit and a very busy nephrology and urology department. All patients diagnosed as tuberculosis are included in the study from May 2017 till May 2019. Tuberculosis was diagnosed on, clinical features and/or sputum smear, culture and/or PCR, biopsy specimens or on radiological grounds. Renal failure was defined as creatinine clearance <30ml/min, needing dosage adjustment of ATT. The presentation, diagnosis and outcome till the end of the treatment was noted.

**Results:** A total of 286 patients were diagnosed as TB, out of whom 70 (24.4%) had renal failure. Around 64% were male. Out of 70, 46 (66%) had extra pulmonary (EPTB) among which 9 (19.5%) patients had genitourinary, 11 (24%) lymphadenitis, 5 (10.8%) central nervous system disease, 7 (15%) abdominal. The diagnosis of genitourinary and lymph node TB was made through histopathology (18/20, 90%). A total of 24 (34%) were pulmonary TB in whom 75% were diagnosed on microbiologic grounds [smear or GeneXpert for MTB or TB culture]. All-cause mortality was 17.1% in renal failure having tuberculosis where as it was 9.7% in patients who did not have renal failure.

**Conclusions:** We found that majority of patients having renal failure have extra pulmonary tuberculosis, of which lymphadenitis and genitourinary were more common. Among pulmonary, majority were diagnosed microbiologically. All-cause mortality was slight more in patients having renal failure.

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Abstract 1919

**Anti-apoptotic role of human cytomegalovirus miRNAs, miR UL-70-3p and UL-148D on hydrogen peroxide-induced apoptosis in HEK 293T cells**

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**Background:** Human Cytomegalovirus (HCMV), an ubiquitous human pathogen, belongs to the family Herpesviridae, exhibits more than 70% seroprevalence in adult population. It is reported to encode 26 mature miRNAs from 16 precursors. The viral miRNAs garnered attention by the scientific community for their spectacular biological roles, as they can regulate both the viral as well as cellular pathways. Most of the reports indicate that these molecules play an augmentative role in making the conducive environment for viral survival in their host by subverting the antiviral responses of the host besides the viral proteins. By using various bioinformatic tools we predicted the HCMV miRNAs which inhibit the cellular apoptosis. Further, these results were validated in *in vitro* by using HEK 293T cell lines.

**Materials/methods:** miRNA sequence homology between human and HCMV miRNAs were evaluated through T-Coffee (global alignment) by using the URL: http://tcoffee.vital-it.ch/apps/global/tcoffee/do:regular. The potential binding sites in 3'UTR regions of the apoptotic genes for HCMV miRNAs were probed through the online algorithms, i.e., RNA hybrid and RNA 22 by using the URL's http://www.bibiserv.cebitec.uni-bielefeld.de; http://cm.jefferson.edu/rna22/interactive respectively. The *in vitro* studies were performed in HEK293T cells, apoptosis was induced through H2O2 and the antiapoptotic effect of the HCMV miRNAs were evaluated through fluorescent microscopy and flow cytometry. Further, the potential genes targeted by these miRNAs were examined through qRT PCR.

**Results:** The sequence homology studies between human and HCMV miRNAs show there was no single HCMV miRNA shares sequence homology with the Human miRNAs. The mRNA:miRNA binding studies reveals that the 3'UTR of cellular proapoptotic genes such as MOAP1 and ERN1 has potential binding sites for the HCMV miR UL-70-3p and UL-148D. Further, the *in vitro* results augmented the *in silico* findings that these HCMV miRNAs inhibit the H2O2 induced apoptosis in HEK293T cells by targeting the MOAP1.

**Conclusions:** The study shows that no HCMV miRNA shares sequence homology with the human miRNAs. HCMV uses its miRNA machinery to inhibit the cellular apoptosis. The HCMV miR's UL-70-3p and UL-148D inhibit the H2O2 induced apoptosis. Fig. Antiapoptotic effect of HCMV miR UL 70-3p on H2O2 induced apoptosis

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Leptospirosis registry: LeptoScope. A novel global registry for emerging leptospirosis infections

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Background: Leptospirosis is a worldwide zoonotic disease caused by pathogenic Leptospira spp. During bacteremia, Leptospira spp. may lead to invasive, deep-seated leptospirosis often with infection of kidney, liver, heart and the central nervous system. Incidence of invasive leptospirosis is rising and there have been frequent outbreak situations in many parts of the world. Therefore, a global surveillance in epidemiology and species distribution is needed.

Materials/methods: The leptospirosis registry – LeptoScope is a novel worldwide registry project for invasive leptospirosis facilitating multinational research. LeptoScope consists of an electronic Case Report Form (eCRF) and it uses the General Data Protection Regulation (GDPR) compliant platform clinicalsurveys.net. LeptoScope can be accessed from any browser and it uses highly-encrypted communication for data entry. Cases documented are collected into the LeptoScope database automatically. A team of physicians reviews each case entered for completeness and consistency for quality control.

Results: LeptoScope is a novel registry project enabling fast, but standardized documentation of invasive leptospirosis using a modular structure. Items categories are patient characteristics, pre-existing diseases, clinical signs and symptoms, microbiological diagnostics, imaging procedures, admission to the intensive care unit, complications including acute kidney injury, acute liver failure and acute respiratory distress syndrome, as well as antibiotic, diuretic and renal replacement therapies and outcome. Additionally, LeptoScope facilitates the monitoring of changing epidemiological trends and outbreak situations locally and globally.

Conclusions: LeptoScope is a novel global, ready to use registry platform for invasive leptospirosis enabling worldwide, standardized documentation of disease course and outcome. LeptoScope may be employed for a variety of epidemiological and clinical studies including outbreaks. LeptoScope promotes international collaboration and may contribute to improve patient management by the standardized analysis of clinical course, prognostic factors, as well as diagnostic and treatment pathways.

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Abstract Book – 30th ECCMID 2020

Abstract 1925

**Preliminary results of microRNA expression profile in patients with cystic echinococcosis and identification of possible cellular pathways**

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**Background:** Although CE can be diagnosed with imaging techniques such as ultrasonography (US) and magnetic resonance imaging (MRI), these modalities may be insufficient to diagnose some cysts especially young CE1. However, differential diagnosis is crucial as WHO-IWGE recommends a stage-specific approach for treatment of CE. Recently discovered microRNAs (miRNAs) are small, stable, tissue specific RNA molecules encoded by the genome that are not translated into proteins. Circulating miRNA expression profiles vary in health and disease. The aim of this study is to determine the altered cellular pathways in CE by comparing miRNA profiles of CE patients having active cysts with either CE patients having inactive cysts or control group.

**Materials/methods:** Following abdominal US examination 20 patients diagnosed with active or inactive cystic echinococcosis and three healthy individuals were included in the study. Total RNA extraction and DNA (cDNA) synthesis were performed from plasma of the patients/controls by miRNeasy Mini Kit (Qiagen) and miScript II RT system (Qiagen) respectively following the manufacturer’s instructions. Detection and quantitation of miRNAs were performed using miScript SYBR Green PCR Kit and miScript miRNA HC PCR Arrays with a LightCycler 480 instrument II (Roche, Germany), according to the manufacturers’ instructions. Data analysis was performed using online Geneglobe data analysis center. For miRNA target prediction miRDB, Targetscan and DIANA databases were used. p< 0.05 was considered as statistically significant.

**Results:** Compared to control group, expression of 5 miRNAs (hsa-miR-4659a-5p, hsa-miR-4518, hsa-miR-3977, hsa-miR-4692, hsa-miR-181b-3p) and 2 miRNAs (hsa-miR-4522, hsa-miR-4687-5p) were found to be down regulated in CE patients with active and inactive cysts respectively [p<0.05]. For down-regulated miRNAs, predicted targets were found to be associated mainly with biological membrane lipids.

**Conclusions:** These results indicate that in CE miRNA expression profiles of inactive and active cysts of the liver differ from each other. In the future, miRNA profiles of the patients will possibly provide accurate diagnosis of the nature of CE cysts by eliminating the necessity of US.

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Abstract 1926

**Spectrophotometric MICs reading of azoles and amphotericin B shows high agreement with visual reading MIC interpretation using EUCAST 9.3.1 methodology**

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**Background:** EUCAST 9.3.1 procedure recommends visual MIC reading (complete fungal growth inhibition) with azoles and amphotericin B against *Aspergillus* spp. As visual MIC setting may be challenging, we obtained spectrophotometric MICs readings of azoles and amphotericin B against *A. fumigatus* complex isolates and compared them with visual method to overcome subjectivity.

**Materials/methods:** A total of 848 *A. fumigatus* complex clinical isolates collected in a 30-hospital survey conducted in Spain were studied. *A. fumigatus* sensu stricto isolates included 45 azole-resistant isolates with the following cyp51A gene mutations: TR34-L98H [n=24], G54R [n=5], TR46/Y12F/T289A [n=1], F46Y/M172V/N248T/D255E/E427K [n=2], F46Y/M172V/N248T/D255E/E416Q/E427K [n=1], F165L [n=1], S496L [n=1], and wild type [n=10]. Antifungal susceptibility to amphoter, itraconazole, voriconazole, posaconazole, and isavuconazole was performed according to EUCAST 9.3.1 methodology. Visually-set MICs were compared with spectrophotometrically-obtained MICs (fungal growth reduction >95% compared to control and read at 540 nm); essential (±1 twofold dilution) and categorical agreement were calculated. Errors were classified as very major (isolate classified as resistant by visual MIC and as susceptible by spectrophotometric reading) and major (isolate classified as susceptible by visual MIC and as resistant by spectrophotometric reading).

**Results:** Overall, essential agreement was 97%, with amphotericin B and posaconazole showing the highest agreement [%Table]. Categorical agreement was very high [98%] as well, with a total of 1.8% very major errors found in six *A. fumigatus* sensu stricto isolates that were resistant to either voriconazole and isavuconazole [n=3] or to isavuconazole [n=3], and four cryptic species (*N. udagawae* [n=2], *A. fumigatioaffinis* [n=2]). No very major errors were found with amphotericin B or itraconazole. Major errors were scarce and exclusively found with voriconazole and posaconazole against *A. fumigatus* sensu stricto (<1%; n=5 isolates). All cyp51A gene mutants were correctly classified as resistant. Most of errors occurred in MICs just one two-fold dilution above the breakpoint.

**Conclusions:** MICs of azoles and amphotericin B against *A. fumigatus* obtained either by spectrophotometer or visually showed very high agreement. Cyp51A mutants were correctly classified as resistant and most misclassifications occurred in MICs just one two-fold dilution above the breakpoint.

<table>
<thead>
<tr>
<th>Antifungal agents</th>
<th><em>A. fumigatus</em> sensu stricto (%)</th>
<th>Cryptic species (%)</th>
<th><em>A. fumigatus</em> complex (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Essential Agreement</td>
<td>Categorical agreement</td>
<td>VME</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>99 100 0 0</td>
<td>90 100 0 0</td>
<td>99 0 0 0 0</td>
</tr>
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<td>Itraconazole</td>
<td>95 100 0 0</td>
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<td>95 0 0 0 0</td>
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<td>Voriconazole</td>
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<td>95 90 10 0</td>
<td>98 98.5 0.94 0.47</td>
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<td>100 95 5 0</td>
<td>97 99.7 0.12 0.12</td>
</tr>
<tr>
<td>Isavuconazole</td>
<td>96 99.6 0.36 0</td>
<td>90 85 15 0</td>
<td>96 99.3 0.71 0</td>
</tr>
</tbody>
</table>

*A. fumigatus* sensu stricto (n=828 isolates); cryptic species distribution (n=20 isolates); *A. lentulus* (n=6), *A. fumigatioaffinis* (n=6), Neosartoria tsunetiae (n=3), *N. udagawae* (n=2), *A. novofumigatus* (n=2), *A. thermomutatus* (n=1).

VME: very major error; ME: major error

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Abstract 1929

Antifungal cost in the patients with febrile neutropaenia episodes due to haematological malignancies
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Background: The aim of this study was to assess the cost of antifungal drugs used in the treatment of febrile neutropenic episodes of patients with hematological malignancies.

Materials/methods: The cost of antifungal drugs used in the treatment of adult patients who were followed at the department of Hematology of Ministry of Health Okmeydani Research Hospital between November 2010 and November 2012 due to hematological malignancies and had febrile neutropenia attacks (FNA) were assessed, retrospectively.

Results: The cost of antifungal drugs was calculated and evaluated in 126 patients, who had 282 FNA were evaluated. The mean age of patients, who 60 patients were female, was 51.73 ± 14.4 years (range: 17–82 years). The mean MASCC score was 17.18 ± 8.27. The mean duration of FNA was 29.38 ± 6.95 days. During 282 febrile episodes of 126 patients, systemic antifungal drugs were administered to 23 patients with 31 culture-proven invasive fungal infection (IFI), 19 patients with probable invasive pulmonary aspergillosis (IPA) in 25 febrile neutropenia episodes, 38 patients with possible IPA in 42 febrile neutropenia episodes, and 30 patients with suspected IFI in 31 febrile neutropenia episodes, respectively.

Liposomal amphotericin B (L-AmB) was calculated to cost $29322.98 per month, $366537.43 per year with 0.21 patient daily dose/100 patient days as the most costly antifungal drug. Total cost were calculated to be $1,271,789.08/year and $18039/patient for antifungal drugs. The costs of antifungal drugs were found to be $3857.85 for voriconazole (VOR), $15783.34 for caspofungin, $21561.02 for L-AmB per febrile neutropenic episode, respectively. The cost of posaconazole was $32167.39/patient for the prophylaxis use.

Conclusions: Antifungal drugs pose a serious cost in the treatment of IFI. The costs could be reduced with those measures, including an accurate and fully implemented infection control measures, an administration of preemptive antifungal treatment instead of empirical antifungal treatment, switching from intravenous form of VOR to tablet form when it is possible, an administration of VOR for the secondary prophylaxis of invasive aspergillosis, and use of L-AmB as a secondary choice or in the salvage therapy.

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**Abstract 1933**

**Nasal methicillin-resistant Staphylococcus aureus colonisation among adults and children in Russia: predominance ST22-subclone “Gaza Strip”**

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Abstract third-party references: The Russian Science Foundation [Grant No. 18-75-10114] supported this study.

**Background:** S. aureus nasal carriage can be considered as a risk factor for subsequent invasive staphylococcus infections. Carriage of MRSA poses the greatest potential threat. In the present study we characterize molecular epidemiology of MRSA colonizing healthy adults and children in Russia.

**Materials/methods:** For the present study, healthy adult individuals (2,000) and children (14,026) in Moscow and Saint Petersburg were sampled with nasal swabs during routine medical screening from 2016 to 2019. S. aureus isolation, identification and susceptibility testing was performed using conventional methods, PCR was used for detection of mecA gene. Selected isolates were sequenced on the MiSeq platform.

**Results:** MRSA carriage rate of was 0.84% (118) among children, and 0.85% (17) among adults. Several lineages were predominant: ST22-t223-SCCmec IVa (32.6%), ST8-t008-SCCmec IVce (10%), ST59-t1950-SCCmec V (7%) and ST1-t321-SCCmec IVa (7%). PVL genes were identified in 4.4% isolates which belonging to different STs and seb were identified in 4% and associated with ST59. Isolates of ST22 lineage (n=44) were tsst-positive and harbored chp, sak, scn and selK virulence genes. Phylogenetic tree for ST22 was constructed using 18,546 core-SNPs in 1,514 core genome loci from 1,252 public available genomes of ST22. Russian ST22 genomes (Figure, red color nodes) were located among tsst-positive “Gaza Strip” clade which was described recently (Chang et al, 2018). We found that ST22 isolates shared high-level similarity, all Russian ST22 isolates had only 14±4.3 SNPs in spite of differences in host age, geographic region and time of collection. Comparing two clades EMRSA-15 and “Gaza Strip” the number of SNPs were also low: 41.4±4.5. Most of carriers isolates demonstrated susceptibility to non-β-lactam antibiotics and 29% were oxacillin susceptible (MIC≤2 mg/L). We compared (PCR mecA as reference) several susceptibility tests for detection oxacillin-susceptible MRSA, high positive predicative value [PPV] were for chromogenic agar [PPV = 0.94] and cefoxitin test based on disk diffusion or broth dilution methods [PPV = 0.88].

**Conclusions:** Overall rate of MRSA carriage in healthy children and adults coincides with the global data. In adults and children ST22, subclone “Gaza Strip” was the most prevalent. High prevalence of oxacillin susceptibility was detected among carrier isolates.

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**Abstract 1935**

**Differential innate immune responses of human macrophages and bronchial epithelial cells against Talaromyces marneffei**

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**Abstract third-party references:** This work was supported by the General Research Fund [No. 17104318], Research Grants Council, University Grants Committee, Hong Kong; Health and Medical Research Fund [No. HKM-15-M07 [commissioned project]], Food and Health Bureau, Government of the Hong Kong Special Administrative Region, Hong Kong; Seed Fund for Basic Research, The University of Hong Kong, Hong Kong; as well as the Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Ministry of Education, China. We thank Dr PJ Punt and Dr ML Yeung for generously providing us the plasmids pAN7-1 and pEGFP-C1, respectively. We are also grateful to the staff members from the Centre for Genomic Sciences and Faculty Core Facility of Li Ka Shing Faculty of Medicine, The University of Hong Kong, for their technical support in RNA–Seq and image analyses, respectively.

**Background:** *Talaromyces marneffei* is a thermally dimorphic fungal pathogen endemic in Southeast Asia. As inhalation of airborne conidia is believed as the major infection route, airway epithelial cells followed by pulmonary macrophages are the first cell types which the fungus encounters inside the host. However, there is a lack of knowledge on how the fungus interacts with host cells during infection.

**Materials/methods:** Human peripheral blood-derived macrophages [hPBDMs] cultured with the supplementation of autologous plasma were used as the *in vitro* infection model for the study of innate immune response to *T. marneffei* infection. Transcriptomic changes of hPBDMs upon infection were profiled by RNA–sequencing and mRNA expression changes in immune-related genes were confirmed by reverse-transcription–quantitative polymerase chain reaction [qRT–PCR]. Differential cytokine responses in human bronchial epithelial cells [hBECs] were also determined and compared to macrophages. A green fluorescent protein-tagged *T. marneffei* strain [GFP-PM1] was constructed to visualise the interactions between *T. marneffei* and hBECs using confocal microscopy and live cell imaging.

**Results:** *T. marneffei* infection could activate hPBDMs to the M1-like phenotype and trigger a potent induction of chemokine (CXCL8, CXCL10, CCL5 and CCL20) and pro-inflammatory cytokine (TNF) production as well as the expression of other immunoregulatory genes (SOD2, CCL3, STAT1, CLEC4E, IL1B, IER3, PIK3R2 and L3). In contrast to hPBDMs, there was no detectable innate cytokine response (CXCL8, CXCL10, IFNA2, IFNB1, IFNL1, IFNL2, IL1B, IL6, and TNF mRNA expression) against *T. marneffei* in hBECs. Under confocal microscopy, internalisation of *T. marneffei* by hBECs was confirmed. Live cell imaging further demonstrated that the infected cells exhibited normal cellular physiology, especially that the process of cell division could be observed.

**Conclusions:** Our results illustrated a potential role of hBECs to serve as reservoir cells for *T. marneffei* to evade immunosurveillance by phagocytes, from which the fungus reactivates when the host immunity is weakened and causes infection. Such immunoevasion and reactivation may also help explain the long incubation period observed for talaromycosis, in particular the travel-related cases.

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Abstract 1936

Comparison of clinical findings and risk factors of community-acquired and nosocomial Legionella pneumonia cases in Konya, Turkey

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Background: Legionella pneumophila is an important cause of community and hospital-acquired pneumonia. The aim of this study was to compare the clinical findings and risk factors retrospectively in 20 nosocomial and 26 community-acquired cases with the diagnosis of L. pneumophila pneumonia.

Materials/methods: Twenty patients with nosocomially acquired Legionella pneumonia (NALP), and twenty six patients with community-acquired Legionella pneumonia (CALP) were included in the study. We applied to the Centers for Disease Control and World Health Organization criteria for diagnosis both of nosocomial infection and Legionella pneumonia. The diagnosis was based on the positivity of urinary antigen test for Legionella pneumonia Acro Biotech, USA). Statistical analysis was performed using chi-square and independent student t test using SPSS Statistics 25.0 program.

Results: Among the risk factors, the older age was more common in the NALP group than in the CALP group, whilst chronic lung disease and cancer were more common in the NALP group than in the CALP group. The difference for other risk factors, such as cardiopathies, chronic renal failure, diabetes, smoking habit, corticosteroid therapy was not statistically significant [p>0.05]. Some of the most common clinical manifestations are shown in the table. Statistical analysis showed that myalgia was more common in the CALP group than in NALP group [p<0.05]. The difference among other common clinical manifestations, such as fever, cough, expectoration, chest pain, dispnea, headache, confusion, abdominal pain, fatigue, diarrhea, loss of appetite was not statistically significant [p>0.05].

Conclusions: The mean age of the patients in the NALP group was higher than the CALP group. Chronic lung disease and cancer were found to be risk factors in NALP group. In conclusion, other demographic and clinical data of Legionella pneumonia in our nosocomial and community-acquired patients were quite similar.

Table: Statistical analysis of risk factors and clinical data of 20 NALP and 26 CALP patients

<table>
<thead>
<tr>
<th></th>
<th>NALP (n=20)</th>
<th>CALP (n=26)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>72±18</td>
<td>67±16</td>
<td>0.01*</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>13/7</td>
<td>12/14</td>
<td>0.20</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>11/20</td>
<td>4/26</td>
<td>0.04*</td>
</tr>
<tr>
<td>Cancer</td>
<td>3/20</td>
<td>0/26</td>
<td>0.04*</td>
</tr>
<tr>
<td>Cardiopathies</td>
<td>2/20</td>
<td>3/26</td>
<td>0.86</td>
</tr>
<tr>
<td>Fever</td>
<td>15/20</td>
<td>25/28</td>
<td>0.76</td>
</tr>
<tr>
<td>Cough</td>
<td>16/20</td>
<td>22/26</td>
<td>0.68</td>
</tr>
<tr>
<td>Chest pain</td>
<td>1/20</td>
<td>6/26</td>
<td>0.09</td>
</tr>
<tr>
<td>Myalgia</td>
<td>2/20</td>
<td>12/26</td>
<td>0.008*</td>
</tr>
</tbody>
</table>

*p<0.05

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Abstract 1940

**Pattern of osteoarticular infections caused by non-tuberculous mycobacteria: 9 years’ experience**

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**Background:** Non-tuberculous mycobacteria (NTM) are ubiquitous organisms associated with various types of infection and reports of osteoarticular NTM infection (OAI-NTM) remain infrequent. We aimed to describe OAI-NTM over a 9-year period in a French Reference Center for OAI and for Mycobacterial infection.

**Materials/methods:** Case identification and ascertainment was done through laboratory and clinical file review between January 2010 and December 2018. The American Thoracic Society/Infectious Disease Society of America criteria were used to define cases of OAI-NTM.

**Results:** A total of 11 patients (3 females and 8 males) were identified: 7 with slow growing NTM, i.e. *Mycobacterium avium* complex (n=4), *M. xenopi* (n=2), and *M. marinum* (n=1); and 4 with rapidly growing NTM, i.e. *M. chelonae* (n=2), *M. fortuitum* (n=1), and *M. wolinsky* (n=1). Locations were solely OA in most of the cases (n=9), including one associated with prosthesis. All patients were immunocompromised (4 autoimmune diseases, 3 HIV, 1 solid organ transplant, 1 cancer), except one (*M. marinum* infection related to aquarium use) and information was lacking for the remaining case. Infected sites were: spine (n=4), wrist (n=1), hand (n=1), knee joint (n=2), hip (n=1), and elbow (n=2). Eight patients had delayed NTM infection diagnosis because of wrong initial diagnosis. Treatment regimens were retrieved for 8 patients: five tri-therapies and 3 bi-therapies, a majority containing both clarithromycin and rifamycins. Eight patients underwent surgery. With regard to outcome, 6 patients achieved healing with a two year follow up without relapse, 1 patient experienced relapse, 3 were lost for follow up but alive and 1 patient died during the treatment course.

**Conclusions:** Pattern of NTM infections is diverse, and difficult to diagnose. Awareness about NTM as a causative organism of OAI should be brought to clinicians and laboratories, especially in immunosuppressed patients in order to reduce the diagnosis delay.

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Involvement of walK gene mutations in antibiotic resistance increase in daptomycin-unsusceptible methicillin-resistant Staphylococcus aureus

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Background: Resistance to peptide antibiotics (daptomycin (DAP), dalbavancin (DLV)) in Staphylococcus aureus is uncommon. DAP non-susceptibility is a complex process, in which several genes may be involved. WGS studies allow to complete the map of genes involved in these processes, and help to understand the importance of different genes in DAP resistance. Otherwise, since vancomycin (VAN) is the most used peptide antibiotic, is useful to know how the exposition to different concentrations of VAN can affect susceptibility to other newer peptide antibiotics. We exposed a previously DAP non-susceptible MRSA clinical isolate to increasing VAN concentrations, in order to obtain mutants with higher VAN MICs and study their genetic changes and their behavior against other peptide antibiotics.

Materials/methods: A clinical MRSA isolate [St6] was grown in a serial VAN gradient (1-32 mg/l). A mutant growing on 1 mg/l VAN plates was obtained. MICs of VAN, DLV, DAP and oxacillin (OXA) were determined by E-test. The DNA was extracted, and the whole genome of the parent isolate and the mutant obtained were sequenced by using Illumina Miseq.

Results: Parent clinical isolate harbored several mutations in the genes mprF, cls1, cls2, rpoB and rpoC. Moreover, this isolate showed mutations in the region mw1109, coding for a hypothetical protein. The MICs of both isolates appear in Table 1. The genome of the mutant was identical to the parent isolate in terms of protein translation, with the only significant modification of a Leu10Phe change in the gene walK, coding for a sensor protein kinase that regulates genes involved in cell wall metabolism.

Table 1. MICs of VAN, DLV, DAP and (OXA).

<table>
<thead>
<tr>
<th>MICs (mg/l)</th>
<th>VAN</th>
<th>DLV</th>
<th>DAP</th>
<th>OXA</th>
</tr>
</thead>
<tbody>
<tr>
<td>St 6 (parent isolate)</td>
<td>1</td>
<td>0.032</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>St 6.1 (mutant obtained)</td>
<td>2</td>
<td>0.2</td>
<td>6</td>
<td>0.75</td>
</tr>
</tbody>
</table>

Conclusions: Mutations in walK gene seems to increase VAN, DAP and especially DLV MICs, at least in microorganisms harboring previous mutations affecting cell membrane and/or cell wall metabolism. The loss of the methicillin resistant phenotype has been associated to a highly modified bacterial wall, whose alteration in structure and fluidity might prevent PBP2a from anchoring properly to the membrane.

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Abstract 1945

Alterations in the gut microbiome of HIV-infected patients under antiretroviral therapy
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Background: Millions of individuals currently living with HIV globally are receiving antiretroviral therapy (ART) that suppresses viral replication and improves host immune responses. The crucial involvement of gut microbiome during HIV infection has been extensively studied; correlating microbiome changes with immune deficiency and inflammation. However understanding the direct effect of ARTs on gut commensals of HIV infected individuals has been mostly overlooked in microbiome studies.

Materials/methods: The microbiota composition was determined by 16s rRNA sequencing (Illumina MiSeq) of stool samples from 16 patients before and during ART. We also tested the direct effect of 15 antiretrovirals on predominant gut microbes of high clinical relevance namely, Escherichia coli, Enterococcus faecalis, Bacteroides and Prevotella spp. to assess their individual antibacterial effect. Thus, we screened 35 isolates of E. coli, 20 isolates of E. faecalis, 22 isolates of Bacteroides spp and 10 isolates of Prevotella spp. which were cultured from patient samples received at Karolinska University Hospital.

Results: Our 16s rRNA analysis showed that effective ART does not reestablish the microbiome diversity within HIV infected patients, thereby showing moderate reduction in α-diversity and β-diversity (NMDS2 and NMDS1) for clustering of microbial communities before and after ART. Escherichia genus (phylum Proteobacteria) showed enrichment under therapy. On the contrary, the relative richness of Prevotella (phylum Bacteroidetes) was significantly reduced after ART. Our study also found the direct effects of antiretrovirals on gut microbes, where the thymidine analog zidovudine showed in vitro antibacterial activity with an MIC of 0.5-1 mg/l against E. coli, 4-8 mg/l against Bacteroides fragilis and 4 mg/l against Prevotella spp. Efavirenz also showed a consistent MIC of 32 mg/l against E. faecalis, 32 mg/l for Prevotella spp. and 32-128 mg/l against Bacteroides spp.

Conclusions: HIV infection induces gut microbiome dysbiosis and ART does not reverse these changes after one year follow-up. In this study, we found that the antivirals directly have a broad effect on the gut bacteria, which in HIV infected individuals might aggravate microbiota alterations. Therefore restructuring the microbiota could be a potential therapeutic target in HIV-1 patients since effective ART itself may not be sufficient to reverse the microbiota dysbiosis.

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**Characterisation of the kinetics and LPS dose-response profiles of presepsin, procalcitonin and sTREM-1 as potential biomarkers for severe infections and sepsis in a human endotoxemia model**

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**Background:** Sepsis constitutes a major healthcare challenge associated with high mortality. Specific and sensitive new clinical biomarkers are required for personalized antibiotic treatment. Current sepsis biomarkers, such as interleukin-6, white blood cell count, and C-reactive protein, are non-specific or suffer from a delayed onset of production and slow half-life, making them poorly suitable for guiding treatment decision making. Procalcitonin (PCT), presepsin, and soluble triggering receptor expressed on myeloid cells-1 (sTREM-1) are important new biomarkers with clinical potential to guide treatment. However, even though several studies in critically ill patients have been conducted, the kinetics of these biomarkers are poorly characterized. There is a lack of quantitative understanding of the relationship between infection burden and biomarker kinetics, which is crucial for allowing biomarker guided treatment. To this end, we characterized the kinetics and LPS dose-response of PCT, presepsin, and sTREM-1 in a human endotoxemia model and in an ex vivo incubation experiment.

**Materials/methods:** Ten healthy volunteers received a single dose (1 or 2 ng/kg bodyweight) of LPS. In parallel, blood samples collected prior to LPS injection were incubated with LPS (0.01 – 40 ng/mL). The concentration-time profiles of PCT, presepsin, and sTREM-1 were quantified in plasma samples after the in vivo and ex vivo LPS challenges.

**Results:** The median in vivo C_max for presepsin, sTREM-1, and PCT were 274, 182, and 1500 pg/mL, respectively, with a corresponding T_max of 3, 8, and 9 hours. The median in vivo elimination half-lives for presepsin, sTREM-1, and PCT were 9.13, 39.2, and 139 hours. A dose-response relationship between LPS and presepsin was observed both in vivo (Mann-Whitney-Wilcoxon test, p<0.05) and in the ex vivo incubation experiments (E_max 1373 pg/mL, EC_50 2.82 pg/mL, likelihood ratio test, p<0.05). No dose-response relationship was found for PCT and sTREM-1.

**Conclusions:** This is the first study that quantitatively describes the kinetic and dose-response profiles for novel immune response biomarkers after administration of LPS to healthy volunteers and in ex vivo incubation experiments. The rapid pronounced induction and short half-life of presepsin and its distinct LPS dose-response relationship support further studies of presepsin as biomarker for severe infections and sepsis.

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Abstract 1950

Retrospective evaluation of appropriate dosing of cefmetazole for invasive urinary tract infection due to ESBL-producing Escherichia coli

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Background: Cefmetazole (CMZ) is active against most ESBL-producing E. coli (ESBLEC) strains. Previous reports suggest it to be a potential candidate for carbapenem-sparing regimen for the treatment of invasive urinary tract infection (iUTI) due to ESBLEC. However, information regarding appropriate dosing is limited.

Materials/methods: We reviewed records of adult patients with iUTI due to ESBLEC who were treated with CMZ > 4 days at two tertiary hospitals in Japan. iUTI was defined as UTI with fever ≥ 37.5°C, or low back/flank/renal pain. Patients who received prior active antibiotic therapy, who were on renal replacement therapy, and who had ESBLEC without known CMZ MICs were excluded. Microbiological efficacy was defined as ≥ 1-log reduction of post-treatment CFU from pre-treatment in the urine. Clinical efficacy was defined as complete resolution or improvement of symptoms compared with the baseline.

Results: Thirty-nine patients were included (Table). CMZ was clinically efficacious in 38 (97.4%) cases. Among 18 cases with available follow-up urine cultures, CMZ was microbiologically efficacious in 16 (88.9%) cases. For cases with CrCl > 60 ml/min, 13 case received CMZ 1g every 8 hours, and CMZ was clinically efficacious in 12 (92.3%) with median time above MIC (TAM) of 93%.

Conclusions: "Three time a day" dosing of CMZ was shown to be effective against majority of iUTI due to ESBLEC.

**Table. Characteristics of patients, number (%)**

<table>
<thead>
<tr>
<th>Age*</th>
<th>Complicated UTI</th>
<th>ESBLEC CFU ≥10^6</th>
<th>MIC (mg/L)</th>
<th>PKPD of clinically efficacious cases with CrCl &gt; 60ml/min</th>
</tr>
</thead>
<tbody>
<tr>
<td>74 (58-81)</td>
<td>22 (56.4)</td>
<td>35 (89.7)</td>
<td>1g q8hr</td>
<td>≤4</td>
</tr>
<tr>
<td>26 (66.7)</td>
<td>ESBLEC Bacte remia</td>
<td>17 (44.7)</td>
<td>9 (23.1)</td>
<td>2g q12hr</td>
</tr>
<tr>
<td>8 (20.5)</td>
<td>Time to CMZ (days)*</td>
<td>2 (0-3)</td>
<td>1g q12hr</td>
<td>≤1</td>
</tr>
<tr>
<td>10 (25.6)</td>
<td>Duration of CMZ (days)*</td>
<td>8 (2-13)</td>
<td>1g q6hr</td>
<td>4</td>
</tr>
<tr>
<td>3 (7.7)</td>
<td>Body weight*</td>
<td>54 (44-63)</td>
<td>4</td>
<td>9 (23.1)</td>
</tr>
<tr>
<td>2 (5.1)</td>
<td>CrCl*</td>
<td>61.7 (42-87)</td>
<td>8</td>
<td>1.1 (2.6)</td>
</tr>
<tr>
<td>3 (7.7)</td>
<td>BPH</td>
<td>16</td>
<td>1 (2.6)</td>
<td></td>
</tr>
</tbody>
</table>

*median [IQR]

*infused over 1hr[n=9] and 0.5hr[n=3].

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**Abstract 1952**

**A comparative prospective study for the qualitative detection of Helicobacter pylori specific antigens in stool samples at Sheffield Teaching Hospitals Foundation Trust, England**

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**Background:** Helicobacter pylori (H. pylori), a Gram negative spiral shaped bacterium found in the human gastric mucosa of around 25% of people living in the UK, is linked to the development of significant gastrointestinal disease including chronic gastritis, gastric ulcers and gastric malignancy. Successful eradication of H. pylori is shown to significantly reduce the incidence of gastric symptoms including gastric cancers, highlighting the importance of rapid and reliable detection. Current methods employed for the detection of H. pylori include; stool antigen test, urea breath test, culture, histopathology, immunohistochemistry and serological testing. At Sheffield Teaching Hospitals Foundation Trust (STHFT), stool antigen EIA is routinely used as a primary, non-invasive, method of detection. In this small prospective study, we aimed to assess the accuracy and usability of three palette tests through comparison with our current methodology (Amplified IDEIA™ HP Star) as reference.

**Materials/methods:** 250 stool samples received for routine H. pylori testing using Amplified IDEIA™ HP Star were tested in parallel with; RIDA®QUICK Helicobacter, Proflow™ and ImmunoCard STAT!® HpSA® palette tests. Any discrepant results produced were repeated using all four tests. Stool samples were excluded if they were greater than 2 days old, had not been stored at 4-8°C and if there was not sufficient sample to complete all tests plus required repeats.

**Results:** Testing showed RIDA®QUICK Helicobacter to have the highest sensitivity and specificity (98% and 100% respectively pre repeat testing) in comparison to the reference method. All three test kits showed discrepancies when compared against the reference, with PPV and NPV of 97.0% and 99.2% (RIDA®QUICK Helicobacter), 89.5% and 97.2% (Proflow™) and 88.9% and 97.2% (ImmunoCard STAT!® HpSA®). Overall, compared to the reference method, RIDA®QUICK Helicobacter was shown to produce the most comparable results and performed well on repeat testing.

**Conclusions:** RIDA®QUICK Helicobacter was shown to produce the best results in comparison to the reference method. Repeat testing, although initially used for the confirmation of discrepant results, highlighted difficulties in reproducibility for all kits including Amplified IDEIA™ HP Star.

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Molecular and clinical characterisation of methicillin-resistant Staphylococcus aureus isolates carrying Panton-Valentine leucocidin in Northern Bavaria, Germany, 2009-2016

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Background: The spread of community-acquired MRSA carrying Panton-Valentine-leukocidin [PVL] as a distinctive virulence factor has been recognized as a worldwide threat, causing recurring and persistent human infections. The following study investigated the epidemiology as well as clinical characteristics of PVL-positive MRSA-strains in Northern Bavaria, Germany over the course of 8 years.

Materials/methods: 131 PVL-positive MRSA were collected between 2008-2016 from different hospitals in Northern Bavaria, Germany. Identification was performed by MALDI-TOF mass spectrometry, susceptibility testing by VITEK-II or agar diffusion. The presence of mecA and PVL genes was confirmed by PCR, the isolates were then subjected to genotyping by using a DNA microarray (Alere), and assigned to clonal complexes (CC)/sequence types (ST) accordingly. Furthermore, the molecular characteristics of the isolates were correlated to the clinical presentation of the patients.

Results: The predominant strains overall were „ST8-MRSA-[IV+ACME] [PVL+], USA300“ (27/131; 20,6%), followed by „CC30-MRSA-IV (PVL+)“, Southwest Pacific Clone“ (26/131; 19,8%) and „CC80-MRSA-IV (PVL+)“ (25/131; 19,1%). Whereas detection of CC80 followed no clear tendency, the percentage of CC30 per year showed a slight increase. ST8 was declining over the last three years of observation. Other clonal complexes (CC5, CC1, CC722, CC22, CC59, CC88, CC152 and CC93) were detected in smaller numbers. Notably, CC1 (n=7) was not detected before 2015, and clinical data indicate that migration could be a major factor leading to its emergence in this area.

The majority (77.9%) of the collected specimens were skin swabs and swabs taken from surgical sites. In total, 100 cases (76.3%) were causally linked to an infection (mostly skin and soft tissue) in the respective patients, with the department of dermatology ranking first in terms of samples provided (23/131; 17.6%). Resistance rates aside from penicillins fluctuated over the years, being the highest for erythromycin (48/125 tested isolates; 38.4%), levofloxacin (14/47; 29.8 %) and clindamycin (29/125; 23.2%). Resistance against vancomycin, linezolid and mupirocin was not found.

Conclusions: This study demonstrated the molecular epidemiology and variability of clones of PVL-positive MRSA in Northern Bavaria, Germany. Migration, travel and evolutionary factors could lead to further diversification and change in the landscape of PVL-positive MRSA in the region.

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Healthy people in Zanzibar are frequently colonised at intestinal level with MDR Enterobacterales identical to those detected in poultry and retailed chicken meat

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Background: Extended-spectrum cephalosporin- (ESC-R) and colistin-resistant (COL-R) Enterobacterales [Ent] can colonize the intestinal tract of people in the community posing an important health issue. This phenomenon can be driven by contamination of the food chain and contact with colonized animals. However, studies analyzing simultaneously human and non-human settings are scarce. Here, we evaluated the prevalence and molecular characteristics of ESC-/COL-R-Ent colonizing healthy people (HP) and poultry (P), as well as contaminating chicken meat (CM) in Zanzibar (Tanzania).

Materials/methods: During June-July 2018, we collected rectal swabs from HP (n=59) and P (n=62), together with retailed CM (n=37). Samples were plated on ChromID ESBL/Carba/Colistin-R. Species ID was achieved using the MALDI-TOF/MS. Strains were characterized with microarray, multiplex PCRs for mcr-1/-8, rep-PCR, and Illumina WGS (Res/PlasmidFinder and MLST).

Results: The prevalence of ESC-R-Ent, COL-R-Ent, and mcr-1-positive E. coli [Ec] were, respectively: 91.5%, 66.1%, 18.6% in HP; 88.7%, 48.4%, 25.8% in P; 43.2%, 18.9%, 18.9% in CM. In total, we collected 124 ESC-R-Ec (3 COL-R), 67 ESC-R-K. pneumoniae [1 COL-R], 41 non-ESC-R but COL-R-Ec, and 38 non-ESC-R but COL-R-K. pneumoniae. The following main resistance mechanisms were found: ESC-R-Ec [CTX-M-15-like, 61.8%; CTX-M-1-like, 21.6%; mcr-1, 2%], ESC-R-K. pneumoniae [CTX-M-9-like, 46.6%; CTX-M-15-like, 29.3%; no mcr-1/-8], 41 non-ESC-R but COL-R-Ec [mcr-1, 80.5%], 38 non-ESC-R but COL-R-K. pneumoniae [no mcr-1/-8]. Several clones of Ec were found in the three settings: ST46 carrying mcr-1 in an IncX4 plasmid (43.5%, HP; 34.8% P; 21.7%, CM) and ST361 possessing CTX-M-15 (46.2%, HP; 15.4%, P; 38.4%, CM). This was also observed for K. pneumoniae: ST17 possessing CTX-M-14/-15 (64.7%, HP; 29.4%, P; 5.9%, CM) and ST1741 harboring CTX-M-15 (50%, HP; 37.5%, P; 12.5%, CM).

Conclusions: Identical clones of ESBL-producing and/or COL-R-Ent were concomitantly detected in the three settings. We therefore speculate that the frequent gut colonization observed in community people might be favored by contamination of the food chain and/or colonization of food animals in direct contact with humans. However, it cannot be excluded that human subjects are actually responsible for the spread of MDR-Ent in the non-human settings. Further studies with a One-Health approach should be planned to investigate this overall phenomenon.

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Abstract 1958

Detection of viable microorganisms and molecular Gram categorisation from whole blood in less than 4 hours
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Background: Diagnosis of bloodstream infections (BSI) and successful treatment with appropriate antimicrobials are reliant upon rapid and accurate information about the causative pathogens. The time required for positive blood cultures, subsequent microbial identification and antimicrobial susceptibility testing (AST) can lead to poor antimicrobial stewardship outcomes. A large proportion of antimicrobial change decisions are based on Gram stain results, as these are the first blood results to be available. Results from a rapid direct-from-blood test can confirm BSI and provide Gram information, thus providing a clear advantage in improving patient care, whilst also benefitting antimicrobial stewardship.

Materials/methods: MagRAPID is a molecular test, developed by Momentum Bioscience Ltd, that uses whole blood for the detection and molecular Gram delineation of BSI. The test involves microbial capture by magnetic beads together with Enzymatic Template Generation and Amplification (ETGA®) for ultra-sensitive, universal detection of viable bacterial and fungal species. Simultaneously, molecular testing provides key information about Gram status and genus/species identification of the organism. This assay was used to identify analytical detection limits for a broad panel of microorganisms, comprising 97% of BSI reported to Public Health England (2018 report).

Results: Here we present results demonstrating detection down to 1 cfu/mL of blood, with a time-to-result of less than 4 hours, including a 1.5-hour qPCR. Importanty, the most prevalent microbes associated with sepsis, such as E. coli, S. aureus and S. pyogenes were detected at these low levels.

Conclusions: MagRAPID has been shown to have the performance to detect microbes in low numbers, with a turnaround time substantially faster than traditional blood culture. With the aim of further shortening the time of detection to less than 3 hours, the assay is able to benefit both identification of BSI and antimicrobial selection and stewardship. Future studies in a clinical setting will seek to further demonstrate the efficacy and rapid turnaround time of the assay.

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**Abstracts 2020**

**Abstract 1969**

**Candida parapsilosis...not so "candid"! The burden of Candida parapsilosis bloodstream infections and azole-resistance pattern in a tertiary care university hospital**

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**Background:** The rate of Candida spp. bloodstream infections (BSI) remains high, especially in critically ill patients. A recent shift of invasive candidiasis from *C. albicans* to non-*albicans* species was reported worldwide. *C. parapsilosis* has emerged as an important antifungal-resistant pathogen because of its ability to form biofilm and to survive in hospital environment.

**Materials/methods:** A retrospective study of *C. parapsilosis* BSI episodes was carried out from January 1st, 2015 to August 31th, 2019 in a tertiary referral University Hospital, northern Italy. Data regarding clinical characteristics, risk factors and antifungal resistance rate were collected. Molecular and MALDI-TOF analyses have been performed to better identify *C. parapsilosis* subspecies and to evaluate the possible phenotypical correlation between isolates.

**Results:** A total of 77 episodes of *C. parapsilosis* BSI were reported. The isolation rate for *C. parapsilosis* in Intensive care unit (ICU) was greater than that in medical and surgical wards (41.15%, 34/77). The incidence rate ranged to 0.96 to 12.2 cases/10^4 admissions, with a 12-fold increase [p=0.001]. Fluconazole resistance rate was 56% [43/77]. Presence of solid neoplasms, tracheostomy, urinary catheter, *Candida* spp. multifocal colonization, mechanical ventilation and previous 30-day azole therapy were significantly associated with BSI due to resistant *C. parapsilosis*. Molecular and MALDI-TOF analyses classified strains as *C. parapsilosis sensu stricto*. Y132F mutation of ERG11 gene was the major mechanism of azole resistance among 13/14 analyzed strains. In 2018 and 2019, ICU resistant isolates (87.5%, 23/34) were grouped in the same MALDI-TOF cluster, showed a similar resistant profile and belonged to patients recovered during the same period and in nearby beds. Overall 30-day mortality was 25%.

**Conclusions:** Nosocomial transmission of *C. parapsilosis* should be considered in the clinical practice, especially among ICU patients. Patient’s treatment history and periodic evaluation of colonization may predict the development of *C. parapsilosis* BSI in patients at risk. Local epidemiology reports and infection control policies are also fundamental to monitor the incidence trend and the antifungal susceptibility profiles. MALDI-TOF appears to be a reliable technique for the identification of *C. parapsilosis* subspecies and for evaluate the possibility of interstrains relationship during outbreak.

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**Abstract 1970**

**The role of Staphylococcus aureus surface protein G (sasG) and its allelic variants in biofilm formation**

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**Background:** Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most frequent causes of nosocomial infections and may persist for long periods colonizing the host, due to biofilm formation. This study describes the distribution of *S. aureus* surface protein G (*sasG*) and its allelic variants, along with their putative connection with biofilm formation.

**Materials/methods:** 80 MRSA bloodstream isolates representative of the endemic (CC5, CC8, CC22) and sporadic clones (CC1, CC30, CC45, CC72, CC88, CC398) isolated in Spanish hospitals (2000-2015) were studied by DNA-microarray methodology (*S. aureus* Genotyping Kit 2.0, Alere Technologies) to detect *sasG* and its allelic variants (alleles 1 and 2, described in NCTC8325 and MW2 strains, respectively). Biofilm formation was assessed by crystal violet staining. *S. aureus* closed genomes available on NCBI (n=429), were classified in endemic and sporadic clones according the in silico MLST, and analysed to determine the distribution of *sasG*.

**Results:** Regarding the MRSA collection, all the endemic clones carried *sasG*, while only some sporadic clones (CC1, CC72, CC88) presented the gene. Isolates belonging to endemic clones, except CC22, carried allele 1, while sporadic clones, and CC22, carried allele 2. The analysis of *S. aureus* closed genomes confirmed the distribution of *sasG* and its allelic variants by clone, observed in the selected MRSA bloodstream isolates (Table), in spite of being resistant or susceptible to methicillin.

Clones with *sasG* developed stronger biofilms than clones without *sasG* (p-value=0.001 2). Specifically, strains carrying allele 1 formed significantly stronger biofilms than those without *sasG* (p-value=0.0002). Differences in biofilm formation were not statistically significant among strains carrying allele 1 and 2; nevertheless, those with allele 1 tended to produce more biofilm than strains carrying allele 2 (p-value=0.1166).

**Conclusions:** *sasG* is strongly associated with biofilm formation, being more common in endemic than in sporadic clones. Specifically, *sasG* allele 1 has a direct connection with endemic clones and high biofilm formation, while allele 2 is associated with sporadic clones and lower biofilm production.

<table>
<thead>
<tr>
<th></th>
<th>Endemic clones</th>
<th>Sporadic clones</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Clones</td>
<td>227</td>
<td>202</td>
<td></td>
</tr>
<tr>
<td><em>sasG</em> positive clones (%)</td>
<td>226 (99.6%)</td>
<td>70 (34.7%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Allele 1</td>
<td>215 (95.1%)</td>
<td>14 (20%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Allele 2</td>
<td>11 (4.9%)</td>
<td>56 (80%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

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**Abstract 1976**

**In silico identification of host-associated genomic determinants in Escherichia coli using bacterial genome-wide association study**

Sumeet Kumar Tiwari*, Boas Van Der Putten2;3, Vinh Trung Nguyen*, Martin Bootsma3, Roberto La Ragione6, Sébastien Matamoros1, Thi Hoa Ngo9, Christian Berens8, Joy Leng8, Julio Alvarez10;11, Marta Ferrandis-Vila8, Jenny Ritchie9, Angelika Fruth12, Stefan Schwarz10, Lucas Dominguez20;13, Maria Ugarte-Ruiz10, Astrid Bethe13, Charlotte Huber14, Vanessa Johanns15, Ivonne Stamm12, Rik Oldenkamp2, Lothar H. Wieler16, Christian Berens8, Julio Alvarez10;11, Marta Ferrandis-Vila8, Jenny Ritchie9, Angelika Fruth12, Stefan Schwarz10, Lucas Dominguez20;13, Maria Ugarte-Ruiz10, Astrid Bethe13, Charlotte Huber14, Vanessa Johanns15, Ivonne Stamm12, Rik Oldenkamp2, Lothar H. Wieler16, Christian Menge8, Constance Schultsz2;3, Torsten Semmler1

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**Background:** The prevalence of antimicrobial resistance [AMR] is increasing globally not only in pathogenic bacteria causing infections, but also in commensal bacteria. Commensal bacteria, such as *Escherichia coli*, may serve as reservoir for AMR genes in both humans and animals. Antimicrobial resistant *E. coli* strains can be transmitted within or between host species and can disseminate resistance genes via horizontal gene transfer. However, there is a paucity of information regarding whether lineages of *E. coli* are adapted/restricted to certain host or if they have lost such specialization. Furthermore, genomic determinants contributing to either a narrow or a broad host range are unknown.

**Materials/methods:** 1,198 *E. coli* strains from different hosts (cattle, chicken, pig, human and wild-boar, both healthy and diseased) and geographical locations [Germany, Spain, UK, and Vietnam], isolated between 2003 and 2018 were randomly picked from existing strain collections for whole genome-sequencing. The core-genome phylogeny and accessory gene profiles were analysed. The presence of genes enriched in strains isolated from a specific host was determined by bacterial Genome-Wide Association Study (GWAS).

**Results:** The strains are randomly distributed over the core-genome phylogeny as well as on accessory gene profiles but appeared to be partially host-restricted at sub-population level. We identified adaptation of ST131 and ST117 lineages to human and chicken hosts, respectively. Neither the geographical origin of the strains nor AMR genes were associated with either a specific host or phylogenetic lineage. The GWAS resulted in k-mers associated with chicken, human and cattle hosts, but not for pigs. Genes involved in molecular functions such as sialic-acid catabolism, iron acquisition, outer-membrane proteases were found to be associated with these host species.

**Conclusions:** In general, strains were randomly distributed throughout the entire *E. coli* phylogeny, but various phylogenetic clusters were observed which exhibited a significant enrichment of strains from specific hosts. Mapping of k-mers significantly associated with a host to reference genomes showed different gene sets enriched in *E. coli* isolates from different hosts. In silico analysis of gene functions revealed a potential role in adaptation to or colonization of different hosts, which may determine broad or narrow host range adaptation.

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Variable anti-Hepatitis B surface titres in vaccinated birth-cohorts: a cross-sectional population based study in northwestern Romania

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Background: After the introduction of hepatitis B (HB) vaccination in 1995 in newborns, two catch-up campaigns targeted unvaccinated 9 years old children in 1999-2008 [born in 1990-1998] and 18 years old adolescents in 2004-2008 [born in 1986-1990], resulting in 4 unique birth-cohorts [Lexis diagram]. More than expected vaccinated young people have inadequate protection against HB. Our objective was to assess the anti-AgHBs titres in each birth-cohort.

Materials/methods: We included outpatients [78.5%] and hospitalized patients with measured anti-AgHBs titres, the Teaching Hospital of Infectious Diseases in Cluj-Napoca, Romania, during 2014-2018. Exclusion criteria were: repeated examinations, confirmed HB history during the study period and infants. We compared the anti-AgHBs titres in all birth-cohorts using the Lexis surface visualization [titres by age, time period and cohort patterns]. We also evaluated the number of acute cases of hepatitis B in corresponding inpatient birth-cohorts.

Results: Please We included 2968 participants, mean age=31.0 ±14.2, 64.0% women. The birth-cohort [1998-2006], vaccinated at birth (n=330, 3-dose HB vaccine coverage >90%), had significantly lower protective titres [31.2% >10 PEI/L] compared to other birth-cohorts vaccinated at birth: >2006 [67.0%, n=106] or later: [1990-1995] [74.5%, n=941], [1986-1990] [74.8%, n=-481]. In the unvaccinated cohort [few independently vaccinated, n=1105, mean age=45.5 ±12.4] protective titres were found in 44.7%, probably after self-limited HB infection. Concordant results were found using median titres [PEI/L]: [1998-2006] - 3, >2006 - 29.8, [1990-1995] - 53, [1986-1990] - 108, <1986 - 4. Despite low protective levels in the birth-cohort [1998-2006], no acute HB cases were identified in the corresponding inpatient cohort. Only 4 and 35 acute HB cases were found in inpatients corresponding to all the other vaccinated and unvaccinated cohorts, respectively. Data on a few tested infants [n=47, not included in the main study] demonstrated good protection levels: 89.4%.

Conclusions: Please A sub-cohort vaccinated at birth had lower protection against HB with no clear explanation. However, very few cases occurred in vaccinated cohorts, suggesting that the vaccine is capable of sustained immune memory.

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Abstracts 2020

Abstract 1980

Rapid identification of uropathogens by combining Alfred 60 system with matrix-assisted laser desorption ionisation-time of flight mass spectrometry technology

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Background: Urinary tract infections can lead to life-threatening sepsis. Rapid identification of uropathogens is needed to determine appropriate antimicrobial therapy. This study evaluated performance of the Alfred 60 system combined with matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) technology for rapid identification of uropathogens.

Materials/methods: The Alfred 60 system was used to screen urine cultures, followed by identifying the microbial pathogen in positive cultures using MALDI-TOF MS. The Alfred 60 detected positive cultures by measuring the turbidity of urine samples, which were transferred automatically to vials containing liquid medium and incubated for 3.5 hours at 35°C in the Alfred 60 system. Vials that showed growth were removed and centrifuged. The pellet was subjected to MALDI-TOF MS identification. In parallel, positive urine samples were inoculated onto Agar plates for identification by conventional culture.

Results: The time required to detect positive urine cultures with Alfred 60 and identify the uropathogens with MALDI-TOF MS ranged from 15 minutes to 3.5 hours. Among 146 positive urine samples tested, conventional cultures showed three culture groups. Group 1, 101 samples with growth of a single type of microorganism, group 2 included 34 samples with 2 types of microorganisms, and group 3 included 11 samples with ≥3 types of microorganisms. Direct identification by MALDI-TOF MS was concordant with 95% of the samples in group 1, 100% of the principal microorganism in group 2, but could not identify microorganisms in group 3.

Conclusions: This combination of methods provides rapid, reliable microbial identification for most positive urine cultures.

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Abstract 1981

**BacterialTyper: a bioinformatics pipeline for the integrative analysis of bacterial whole genome sequencing**

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**Background:** Recent advances in bacterial whole genome sequencing (WGS) methodology make it feasible to consider its implementation for deep molecular characterization of isolates in clinical research laboratories and public health agencies. Here we present BacterialTyper, a pipeline for the analysis of bacterial WGS data that integrates and facilitates the interpretation of results generated from multiple software analyses.

**Materials/methods:** The pipeline is written in Python with a modular architecture and based on open-source software and databases engines (Figure 1). Multiple tasks are performed by each of several modules including: preparation of raw data; assembly and annotation; bacterial strain identification; mobile genetic elements identification (plasmids, putative pathogenicity islands or phage insertions regions); generation of a virulence and resistance profile; clustering based on sequence similarity; phylogenetic analysis and integration of metadata. The tool allows the comparison of obtained results with those previously generated (internal database) but it also uses and updates periodically external databases from different sources.

**Results:** We analyzed a set of 22 *Staphylococcus aureus* clinical strains that underwent WGS using Illumina HiSeq4000. We recovered DNA microarray results [Clondiag] reported as presence/absence of a list of genes as well as phenotypic results regarding drug susceptibility testing and virulence factor secretion. We found a high correlation between the tests. Interestingly, we identified novel resistance and virulence genes that could not be detected by previous DNA microarray results. WGS data allowed to more easily and clearly cluster samples according to sequence similarity with high precision and sensitivity, enhancing outbreak analysis capabilities in relation to classical methods. Also, the data generated from the virulence and resistance profiling and the mobile genetic elements analysis enabled a richer interpretation and better inference of clinical implications for each bacterial isolate tested.

**Conclusions:** We report the development of a bioinformatic pipeline capable of processing and identifying bacterial species, identifying resistance and virulence genes, and generating data for outbreak analysis using WGS results from microbial cultures. WGS analysis results agreed with conventional tests used with improved resolution. This encourages the use of this tool to support WGS analysis for clinical diagnostics and outbreak analysis settings.

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Spatial and temporal genomic homogeneity among *Haemophilus influenzae* serotype f

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**Background:** *Haemophilus influenzae* is an opportunistic pathogen highly adapted to the human respiratory tract which is often reported as the etiologic agent of infectious diseases. After the introduction of serotype b vaccine, non-typeable *H. influenzae* (NTHi) has become the most frequent cause of respiratory infection, followed in frequency by serotype f strains (Hif). The aim of this study was to analyze the genomic diversity among invasive and colonizing Hif isolates by whole genome sequencing (WGS).

**Materials/methods:** Thirty-seven Hif isolated from Spain (n=16), The Netherlands (n=18) and Portugal (n=3) between 2004 and 2016 were characterized by WGS. A core-based phylogenetic tree was constructed with Parsnp from the Harvest suite, followed by a core and accessory genome analysis with Roary and roProfile. The MLST was determined in silico and single nucleotide analysis was done through Snippy to detect polymorphisms (SNPs) among bacterial genomes. To better understand the phylogenetic diversity in this species, all available genomes on RefSeq were downloaded and included in the analysis.

**Results:** Among 37 *H. influenzae*, four were collected from the oropharynx of healthy children and the remaining were from adult invasive infection. All isolates belonged to ST124 or a single locus variant. Although all strains were closely related, two major clusters were observed in the phylogenetic tree, one of them contained the four colonizer strains. The estimated core genome was 92% and 12,825 core-SNPs were detected. A total of 1,853 genes were predicted, of them, 1,691 were present in more than 95% of the strains. From 732 *H. influenzae* genomes available on NCBI, 8 were Hia, 56 Hib, 4 Hic, 1 Hid, 20 Hie and 9 Hif and the remaining were NTHi. Duplicated NTHi were removed to construct a phylogenetic tree of 347 *H. influenzae* that revealed a very low core genome (21%) compared to the Hif values (92%).

**Conclusions:** In contrast to the high genomic heterogeneity described in NTHi, capsulated Hif strains presented very low variability suggesting genomic stability conferred by the presence of the capsule. No genomic variation was observed among countries or the colonizing strains.

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Additional testing and prevalence of Enterobacterales with elevated carbapenem MIC in the Netherlands, 2014-2018

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Abstract third-party references: ISIS-AR study group

Background: Carbapenem-resistant Enterobacterales (CRE) and carbapenemase-producing Enterobacterales (CPE) have been reported globally. Because carbapenems represent a last-resort drug for treatment of many enterobacterial infections, they pose significant challenges for patient care. Measured prevalence of CRE/CPE is influenced by test procedures and methods, and the Dutch national guideline suggests a gradient test as the first step in further investigation of isolates with automated elevated MIC. We assessed practices of additional testing by Dutch laboratories, and determined the prevalence of Enterobacterales with gradient test confirmed elevated MIC.

Materials/methods: We searched the Dutch surveillance system for antimicrobial resistance (ISIS-AR) for diagnostic and screening E. coli and K. pneumoniae isolates (years 2014-2018). Based on crude automated test values, we categorized them as either having elevated MIC for meropenem (>0.25 mg/L) and/or imipenem (>1 mg/L), as defined by the national guideline ‘Laboratory detection of highly resistant microorganisms’, or not. Subsequently, we searched the ISIS-AR database and the bacteriological typing network (Type-Ned) database for data on additional tests (gradient tests and tests for carbapenemase production and carbapenemase genes). Including one isolate per patient per species and based on data from 28 laboratories, we assessed the percentage of isolates with 1) elevated automated MIC that underwent further testing, and 2) gradient test confirmed elevated MIC, by year.

Results: The use of gradient tests increased between 2014 and 2016 but decreased thereafter, to 73% (E. coli) and 64% (K. pneumoniae) in 2018 (Figure). There was an increase in tests for carbapenemase production (E. coli: 2%-10%, K. pneumoniae: 5%-32%) and carbapenemase genes (E. coli: 1%-7%, K. pneumoniae: 5%-19%) in the past five years. The prevalence of gradient test confirmed strains increased slightly between 2014 and 2018 (E. coli: 0.02%-0.05%, K. pneumoniae: 0.25%-0.52%).

Conclusions: The percentage of isolates with a gradient test performed has not increased further since 2016. This is probably partly compensated by an increase in tests for carbapenemase production or carbapenemase genes in the past five years. Our data show a slight increase in E. coli and K. pneumoniae with gradient test confirmed elevated MIC between 2014 and 2018, which is worrying although it is still low.

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Host adaptative changes of *Staphylococcus aureus* through respiratory colonisation and bloodstream infection

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**Background:** Prolonged persistence of *Staphylococcus aureus* in biofilms or inside the host’s cells may cause adaptative bacterial changes, modifying host interaction. This study aimed to explore differences in biofilm formation and intracellular invasion that may induce a commensal respiratory *S. aureus* strain into progression to cause invasive disease.

**Materials/methods:** The study included *S. aureus* isolated from respiratory colonization episodes that caused a later bacteremia (Hospital Universitari de Bellvitge, 2013-2017). The genetic profiles were compared by PFGE to select persistent strains with the same clonal origin. Lung epithelial cells (A549) were infected to determine *S. aureus* intracellular invasiveness and host cells viability by flow cytometry. Biofilm formation was determined by crystal violet staining. Whole genome sequencing (Illumina MiSeq) was performed to analyze single nucleotide polymorphisms (SNPs) by Snippy.

**Results:** Three patients (P5, P7, P9) presented persistent *S. aureus* isolates in respiratory samples that progressed into a bacteremic episode (Table). The last respiratory and the first bacteremic strains were phenotypically compared. Intracellular invasion analysis revealed that bacteremic strains had significant lower capability to invade A549 cells in comparison with the respiratory isolates. Regarding the viability of A549 cells and biofilm formation, only strains from patient 9 showed significant differences among isolates: the respiratory strain caused higher cell mortality and weaker biofilm formation than the bacteremic strain. Genetic changes were observed between respiratory and bacteremic strains. A few SNPs and open reading frame (ORF) modifications were found (Table), such as the alteration of fibronectin-binding protein in patient 5.

**Conclusions:** *S. aureus* persist intracellularly or within biofilms for long-periods of time. Despite the host’s condition, some phenotypic changes occur, which may lead to facilitate the entrance of the microorganism into the bloodstream.

<table>
<thead>
<tr>
<th>Strain characterization</th>
<th>P5</th>
<th>P7</th>
<th>P9</th>
</tr>
</thead>
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<td>Colonization time (days)</td>
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<tr>
<td>Number of strains</td>
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<td>MLST/CC</td>
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<td>125/5</td>
<td>3207/398</td>
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<td>Last colonization isolate (date)</td>
<td>(Nov-2016)</td>
<td>(July-2013)</td>
<td>(Jan-2014)</td>
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<td>Bacteraemia isolate (date)</td>
<td>(Jan-2017)</td>
<td>(Aug-2013)</td>
<td>(Jan-2014)</td>
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<td>Invasion (cfu/A549)</td>
<td>1.25:0.02 (p=0.0004)</td>
<td>1.96:0.69 (p=0.004)</td>
<td>0.92:0.34 (p=0.0006)</td>
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<td>Viability (% dead cells)</td>
<td>781.616 (NS)</td>
<td>12.71:11.35 (NS)</td>
<td>0.92:5.023 (p&lt;0.0001)</td>
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<td>Biofilm (A370)</td>
<td>2.64:2.03 (NS)</td>
<td>2.41:2.79 (NS)</td>
<td>0.6:1.15 (p=0.021)</td>
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<td>SNPs/ORFs differences</td>
<td>50/7</td>
<td>1/3</td>
<td>2/3</td>
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</table>

**Presenter email address:** acarrera@idibell.cat
Abstract 1986

Testing EEG-LORETA and CSF Biomarkers in patients with HIV-associated neurocognitive disorders
Alessandro Lazzaro1, Veronica Pirriatore1, Giacomo Stroffolini1, Ambra Barco*, Giuseppe Noce2, Daniela Vai3, Giovanni Di Perri1, Stefano Bonora1, Andrea Calcagno1

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Background: HIV-associated neurocognitive disorders (HAND) are diagnosed in people living with HIV (PLWH) successfully treated with antiretroviral therapy. Brain function can be probed estimating cortical sources of resting state EEG (rsEEG) rhythms. Our aim was to test whether rsEEG markers are related to specific cognitive domains and cerebrospinal fluid (CSF) biomarkers in a novel cohort of HIV-positive patients with HAND.

Materials/methods: Patients diagnosed with HAND according to the Frascati’s criteria, without significant comorbidities and with plasma HIV RNA < 50 copies/mL were enrolled. Statistical analysis compared rsEEG (LORETA freeware) source estimates with scores of 10 neuropsychological tests and CSF biomarkers including tTau, pTau, βAmyloid42, neopterin, S100β [thresholds validated in HIV-negative subjects]. Data are described with median values (IQR) and analysed through non-parametric tests.

Results: 42 patients were included: 31 (73,8%) were male, with median age and BMI of 56,3 years (48-63.2) and 24.48 Kg/m² (22.17-24.82), respectively. Current and nadir CD4+ cell count were 724 (496-863) and 299 (152-441) cells/µL; 12.3 (4-14) years of virological suppression were recorded. All but five patients (11.9%, MND) were diagnosed with ANI. Abnormal tTau, pTau, βAmyloid42, neopterin and S100β were observed in 7.1%, 14.3%, 11.9%, 16.6% and 7.1% individuals, respectively.

Occipital delta source activity (< 4 Hz) and parietal delta source activity (< 4 Hz) were associated with longer executive functions (Trail making B and AB test) (p values <0.05, rho >0.5).

Parietal delta source activity (< 4 Hz) and alpha3 source activity (10-12 Hz) were strongly associated with CSF neopterin (p values <0.05), with an opposite trend: neopterin directly correlated with delta source activity (rho 0.544) while inversely correlated with alpha3 source activity (rho -0.405).

Conclusions: rsEEG source activity at delta and alpha rhythms may reflect brain dysfunction in HIV patients with HAND and were specifically related to altered executive functions. The association of rising neopterin CSF levels with a parallel rise in delta activity and a decay in alpha activity, in both occipital and parietal areas, might reflect an impairment of cortical activity, suggesting that electrical cortical activity registration could be used to assume CSF alteration. Further studies are needed to assess neurotoxicity and ageing among PLWH.

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Abstract 1987

**Seroepidemiology of Helicobacter pylori infection in different regions of Croatia: new perspective after 20 years**

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**Background:** The aim of the study was to analyze the seroprevalence of *Helicobacter pylori* infection in four different Croatian regions. The last time the data about seroprevalence in different Croatian regions were published, was in 1997 and 1998 by other Croatian authors. Therefore, the goal was also to compare our results with those published 20 years ago.

**Materials/methods:** The sera were collected in the period from 2015 to 2017 from the patients without the symptoms of peptic or other chronic diseases in four different Croatian regions - central, north-adriatic, south-adriatic and eastern Croatia. Informed consent with demographic data was completed for each patient. The sera were tested for specific IgG antibodies by ELISA method.

**Results:** A total of 306 patients, 142 (46.4%) male and 164 female (53.6%), were analyzed. The age range was 20-89 years and the mean age was 49.9. *H. pylori* IgG was detected in 141 (46.7%) patients, out of which 73 (51.8%) were male and 86 (48.2%) female. The highest prevalence (70.0%) was found in the age group of 60-69 years and the lowest (16.0%) in the age group of 20-29 years. Seroprevalence according to the geographic region was as follows: central (54/138, 39.0%), north-adriatic (20/40, 50.0%), south-adriatic (28/68, 41.1%) and eastern Croatia (39/60, 65.0%).

**Conclusions:** Overall seroprevalence of *H. pylori* infection in Croatia decreased in the last 20 years from 60.0 – 68.0% to 46.0% which is in concordance with the decreasing trend in recent decades worldwide. This change is also characteristic for the transition from a developing to a developed country.

The seroprevalence of *H. pylori* infection varied among studied geographic areas of Croatia and is higher in eastern region. In comparison to data 20 years ago, the seroprevalence in central and south-adriatic region decreased from 58.4% to 39.0% and from 66.0% to 41.1%, respectively. Regarding the seroprevalence in north-adriatic and eastern Croatia, our study is the first one analyzing the seroprevalence in these two regions so far. Further investigation is needed that will include larger population from different regions of Croatia.

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Optimisation of a series of salicylamide derivatives of niclosamide as potent antiviral agents against human adenovirus

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Background: The effective treatment of human adenovirus (HAdV) infections in immunocompromised patients still poses great challenges. Despite the significant clinical impact, there remains no specifically approved antiviral therapy for HAdV infection to date. Accumulated studies indicated that niclosamide, an FDA-approved anthelminthic drug used in humans to treat tapeworm infections, can modulate multiple signaling pathways and biological processes and it has great antiviral potential against various viruses, including HAdV, Zika virus, Ebola Virus, or influenza. Herein, we reported the optimization of a series of salicylamide derivatives of niclosamide as potent inhibitors of HAdV infection.

Materials/methods: The anti-HAdV activity of 54 niclosamide analogues has been evaluated in vitro. Inhibition of HAdV infection was evaluated by plaque assay. The cytotoxicity (CC₅₀) of compounds which showed significant HAdV inhibition was measured using the AlamarBlue Kit (Invitrogen). The effect of the selected compounds on HAdV genome accessibility to the nucleus was evaluated by qPCR and their effect on the virus yield was evaluated in a burst assay.

Results: Nine out of the 54 derivatives showed IC₅₀ values at sub-micromolar concentrations, ranging from 0.05 to 0.68 µM, and with CC₅₀ values ranging from 10.9 to 200 µM. They showed yield reductions of the HAdV progeny ranging from 1.8 to 989-fold. As for their mechanism of action, our results showed that compounds 1, 3, 62 and 70 exerted their activities in the HAdV entry pathway, while compounds 11, 17, 20 and 58 inhibited later steps after DNA replication. With regard to compounds 14 and 60, they seem to be targeting the HAdV DNA replication process.

Conclusions: The niclosamide derivatives evaluated here have great potential for the development of new anti-HAdV drugs. In addition, considering the broad antiviral activities of niclosamide, these salicylamide derivatives could be repurposed to treat other viral infections, including influenza, Zika, or Ebola virus, among others. The next step in the development of these new antiviral drugs will be the in vivo evaluation of their efficacy and safety in the animal model of infection of the immunosuppressed Syrian hamster.

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### Abstract 1993

**Characterisation of differences in infectious disease events between first liver transplantation and re-transplantation in the STCS**

Peter W. Schreiber*1, Katharina Kusejko¹, Dionysios Neofytos¹, Hans H. Hirsch³, Pascal Meylan⁴, Oriol Manuel⁵, Katia Boggian⁶, Cédric Hirzel⁶, Christian Garzoni⁶, Roger Kouyos¹, Nicolas Mueller¹, Swiss Transplant Cohort Study⁷

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**Background:** Re-transplantation after graft failure has become a valuable option, but graft survival, patient survival and quality of life is decreased after liver re-transplantation. Data describing the role of infectious disease (ID) events on this worse outcome is scarce. We analyzed ID events after first liver transplantation and re-transplantation in the Swiss Transplant Cohort Study (STCS).

**Materials/methods:** All liver transplant recipients that experienced a liver re-transplantation were included. We required at least 30 days between the transplantations and follow-up after re-transplantation. Symptomatic bacterial, viral or fungal infections and probable infections (suspected infections prompting empiric antimicrobial treatment without pathogen identification) were included. We performed a survival analysis to compare the time to the first infection after first transplantation and re-transplantation and a Poisson regression to test whether the number of ID events after the first transplantation is predictive of the number of ID events after the re-transplantation.

**Results:** 29 patients were included (male: 69%, median age at first transplantation: 56). The most common underlying diseases resulting in first transplant were viral hepatitis (14, 29.2%), malignancies (9, 18.8%) and chemical cirrhosis (5, 10.4%). Median time between first and re-transplantation was 1.4 years [range: [0.1, 7.2]]. The 29 patients had 255 ID events, 132 (51.8%) after the first and 123 (48.2%) after re-transplantation (Figure). Bacterial infections were most prevalent (159, 62.4%) with enterococci, *Escherichia coli* and *Klebsiella* spp being most common, viral (24, 9.4%) and fungal infections (20, 7.8%) were less frequent. The median time to first infection was 33 days after the first transplantation and 60 days after re-transplantation (hazard ratio = 0.68, confidence interval: [0.36, 1.3]). The number of infections in the first 30 days after the first transplantation was predictive of the number of infections in the first 30 days after re-transplantation (p=0.0005).

**Conclusions:** On the patient-level, ID events after first transplantation were predictive of ID events after liver re-transplantation. Overall, a comparable number of infections were observed after first liver transplantation and re-transplantation. The time period until the first incident infection was slightly, albeit not significant, longer after re-transplantation. Hence, in this cohort, infections did not contribute to the reported worse outcome after re-transplantation.

**Infecions after 1st liver transplantation and re-transplantation**

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Prevalence, correlates and outcomes of plasma cryptococcal antigen postivity among HIV-infected patients with a CD4+ T-cell count under 100/mm3, diagnosed in Spain

María Asunción Pérez-Jacoiste Asín1, Otilia Bisbal1, Jose Antonio Iribarren Loyarte2, Santiago Moreno Guillén3, Rafael Rubio1

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Background: Cryptococcal meningitis (CM) is a major cause of AIDS-related mortality. WHO recommends routinely screening HIV-infected patients with CD4+-count<100/mm3 for cryptococcal infection, to prevent CM among infected. This recommendation is based on studies in regions where the prevalence of positive cryptococcal-antigen (CrAg) is ≥3%, mainly Sub-Saharan Africa. There are no available data about such prevalence in Spain and Spanish AIDS-Study Group (GESIDA) guidelines do not recommend routinely screening. Our objective is to determine the prevalence of cryptococcal infection in HIV-infected patients with CD4+-count≤100/mm3 diagnosed in Spain, through detection of CrAg in plasma.

Materials/methods: We determined CrAg using lateral-flow-assay (CryptoPS, Biosynex, France) in stored plasma samples from participants in the Cohort of Spanish AIDS-Research Network, a multicenter-prospective cohort of HIV-seropositive patients diagnosed in Spain, >18 years-old and naïve to antiretroviral treatment when included. Eligible patients were those with CD4+-count ≤100/mm3 when plasma sample was collected, with a follow-up>4 weeks, unless death.

Results: 576 patients fulfilled the inclusion criteria and had available stored plasma, from June 2004 to December 2017. The overall prevalence of CrAg-positivity (CrAg+) was 7.5% [CI95% 5.35%-9.65%]. There were no differences in prevalence depending on birthplace: Spain 7.4%, other European countries 5.9%, Latin-America 6.8%, sub-Saharan Africa 9.8% (p=0.951). When comparing the group with CrAg+ with those with CrAg-negativity (CrAg-), there were no differences by age, education level, CD4-/mm3-count and HIV-viral load. CrAg+ was more common among injecting-drug users than those with sexually-transmitted HIV (17.9% vs 5.7%, p=0.003). Those with CrAg+ had a reduced survival compared to those with CrAg- (Figure). CM was reported in 10 of the 43 cases with CrAg+ (23.25%), in five when plasma-sample was collected and in the remaining during follow-up, after a median-time of 35 days [0.1-0.3=11.5-60.5].

Conclusions: The prevalence of CrAg+ in HIV-infected patients with CD4+-count≤100/mm3 diagnosed in Spain, including those born in Spain, is >7%. There are no identifiable factors associated with CrAg+, apart from injected-drug use. According to these results, it seems necessary to update GESIDA-guidelines and recommend routinely screening cryptococcal infection in this group of patients in Spain. Future studies should explore if this recommendation could apply to other European countries.

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Abstract 1995

Evaluation of a fully automated prototype version of the BD Kiestra ID/AST system

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1University of Louisville, Louisville, United States, 2University of Louisville Hospital, Louisville, United States, 3University of Lou-
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Abstract third-party references: BD Diagnostics

Background: The BD Kiestra™ TLA automates specimen processing, plate streaking, incubation and digital visualization of cul-
tures prior to a technologist initiating manual or semi-automated identification and antibiotic susceptibility (AST) procedures [current system]. This study aimed to compare the performance of the current system to that of a fully automated research use only prototype BD Kiestra™ IdentifA/SusceptA [automated system] in a clinical setting.

Materials/methods: Five hundred twenty three isolates from culture-positive de-identified, remnant/left-over urines, lower respiratory tract specimens, wounds, abscesses, blood cultures and miscellaneous specimens were processed for microbiological identifications and AST by both systems. Colonies were selected manually [current system] and from digital images [automated system] for Bruker MALDI-TOF (MALDI) identification and BD Phoenix™ AST system. The current system required separate inocula for identification and AST. The automated system used an onboard automated colony picker to prepare a single inoculum suspension for identification and AST. Results were extracted from BD EpiCenter™ and evaluated to determine agreement between the systems. Tests were repeated if MALDI scores were below 1.7 or identifications differed or if categorical differences existed in susceptibility results.

Results: On initial testing 89.0% and 92.4% of identifications yielded acceptable MALDI log scores ≥ 1.7 for the automated and current identification systems respectively. Problems encountered included rare instances of inaccurate automated MALDI target spotting, and difficulties in handling mucoid and Streptococcus isolates. By managing these issues on repeat testing, the respective acceptable MALDI scores were 97.1% and 98.1%. On initial testing, the automated and current systems yielded 97.5% categorical agreement for 7,325 drug-organism tests. After omitting discrepant MICs that differed by only one dilution and categorical discrepancies that were not reproducible, 0.2% unresolved discrepancies remained thus yielding 99.8% categorical agreement.

Conclusions: The high agreement between the systems indicated that the automated prototype offers potential for develop-
ment into an accurate, fully automated ID/AST system which could be integrated with BD Kiestra™ TLA. This walkaway system could optimize workflow and offer benefits such as reduced hands-on time and associated cost savings, improved efficiency, improved ergonomics and better standardization.

* Components of system are under development and not for sale or use.

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Abstract 1996

**New polysaccharide capsule identification in urogenital *Haemophilus parainfluenzae* related to capsular locus present in *Haemophilus* spp.**

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1Microbiology Dept. Hospital Universitari Bellvitge. IDIBELL-UB, Barcelona, Spain, 2Research Network for Respiratory Diseases (CIBERES), Madrid, Spain

**Background:** *Haemophilus parainfluenzae* is part of the human oropharyngeal and genitourinary microbiota. This bacterium is increasingly recognized as an opportunistic pathogen causing invasive, chronic or recurrent diseases frequently associated with antibiotic resistance. The polysaccharide capsule is one of the most important virulence factors and has been used for vaccine development in important pathogens, including the *Haemophilus influenzae* serotype b

**Materials/methods:** The detection of the capsular gene *bexA* was done by PCR in 154 *H. parainfluenzae* strains isolated in Hospital de Bellvitge from urogenital samples between 2013 and 2017. Whole genome sequencing (WGS) was performed in *bexA* positive samples. All *Haemophilus* spp. genomes available on NCBI were downloaded for *in silico* detection of capsular operon using hicap. The *bexA* positive *H. parainfluenzae* were compared to the *Haemophilus* spp. capsular operons. The visualization of the new capsular operon was done by Transmission electron microscopy (TEM).

**Results:** Nine different capsular operons were found within the *Haemophilus* spp; the six well known types [a-f] of *H. influenzae*, two types in *H. sputorum* [HSBU-type 1 and 2] and one type in *H. haemolyticus* [HHAE-type 1]. In the *H. parainfluenzae* collection, a total of 18 urogenital isolates were *bexA* positives. After WGS, 17 *bexA* positive isolates presented a capsular operon close to *H. influenzae* serotype c [HPAR-type 1] and one similar to *H. sputorum* type 2 [HPAR-type 2]. One HPAR-type 1 presented one specific gene truncated by the insertion of a transposase. To visualize the presence of the polysaccharide capsule, one representative HPAR-type 1, one *H. influenzae* serotype b [positive control] and one *H. parainfluenzae bexA* negative [negative control] were analyzed by TEM. The cellular visualization revealed that the non-encapsulated *H. parainfluenzae* was surrounded by a defined bacterial cell membrane, which was significantly thinner than that of the encapsulated *H. influenzae* serotype b and *H. parainfluenzae* HPAR-type 1.

**Conclusions:** This study identified the presence of capsular operon in urogenital *H. parainfluenzae*. Since the capsule is a relevant virulence factor, the presence of capsulated *H. parainfluenzae* isolates among urogenital samples highlights its putative role as cause of sexually transmitted diseases. Nevertheless, further surveillance studies should be considered.

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Abstract 2000

Report of the national reference centre for multidrug-resistant Gram-negative bacteria on carbapenemases in Germany in 2019

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Background: Multidrug-resistance in Enterobacterales, Pseudomonas aeruginosa and Acinetobacter baumannii is of utmost therapeutic importance since hardly any innovative antimicrobial drug against gramnegative bacteria will be introduced into clinical practice within the next years. Among all resistance mechanisms the worldwide spread of carbapenemases is the most worrisome development. However, the correct identification of carbapenemases is still challenging for the microbiological laboratory.

Materials/methods: The National Reference Centre for Multidrug-Resistant Gramnegative Bacteria offers the free service of carbapenemase detection in bacterial isolates with elevated carbapenem MICs. All isolates are tested by a wide array of phenotypic and molecular methods. A bioassay based on cell-free extracts and WGS methods allow the detection of still unknown \(\beta\)-lactamases.

Results: A total of 5993 isolates were investigated for carbapenemases in the National Reference Centre in 2019 until November 6th. Carbapenemases were found in 1724 Enterobacterales strains, 428 of A. baumannii and 325 of P. aeruginosa. The most frequent carbapenemases in Enterobacterales were OXA-48 \(n = 468\), VIM1 \(n = 292\), KPC-2 \(n = 184\), NDM1 \(n = 163\), OXA-244 \(n = 135\), NDM5 \(n = 134\), OXA-181 \(n = 67\) and KPC-3 \(n = 62\). OXA-162, OXA-232, VIM-4, GIM-1 and others were found in less 30 isolates each. In P. aeruginosa, VIM-2 was the most frequent carbapenemase \(n = 228\), followed by GIM-1 \(n = 20\), GES-5 \(n = 12\), VIM-1 \(n = 11\) and VIM-4 \(n = 10\). IMP-13, IMP-7, NDM-1 and others were found in less than 10 isolates each. OXA-23 was the most frequent carbapenemase in A. baumannii \(n = 287\), followed by OXA-72 \(n = 92\) and NDM-1 \(n = 25\). GIM-1, OXA-143, OXA-58 and others were found in less than 10 isolates each.

Conclusions: A variety of different carbapenemases is detected in Germany. The molecular epidemiology in Germany differs significantly from observations made in other countries like Greece, Italy or the USA with a predominance of OXA-48. Compared to previous years, variants of OXA-48, especially OXA-244, are again on the rise.

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**Abstract 2001**

**Streptococcus pneumoniae: an uncommon possible cause of male urethritis?**

Francesca Menotti1, Sara Comini1, Cristina Crocillà1, Rosaria Sparti1, Giuseppina Amarù2, Carmela Solimine2, Anna Maria Cuffini1, Valeria Allizond1, Giuliana Banche*1

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**Background:** Streptococcus pneumoniae is not a common agent of urinary tract infections (UTIs); indeed, literature data about its isolation in genitourinary samples of both adults and children are limited. In this study, we report cases of S. pneumoniae isolated from male urethral samples

**Materials/methods:** From June 2018 to October 2019, a total of 408 urethral swabs, transferred to the ASL-TO3 Microbiology Laboratory of the Infermi Hospital (Rivoli, Turin, Italy), was examined for suspected urethritis. Specimens were analyzed for the presence of opportunistic bacteria, fungi, Mycoplasma spp and Trichomonas spp with cultural examination and for Chlamydia trachomatis and gonococci by strand displacement amplification. All the isolates were tested for antimicrobial susceptibilities to many widely used antibiotics. Resistant ones were confirmed by manual susceptibility testing

**Results:** 42.7% of male patients was microbiologically positive: in details, bacteria or fungi were isolated in pure culture in 87.5% of samples, whereas the remaining 12.5% was characterised by coinfections. Remarkably, S. pneumoniae was detected in 10.83% of men with symptoms of urethritis. Examination of their urethral specimens revealed the presence of Gram-positive cocci, confirmed as S. pneumoniae. In three patients microscopy and cultural analysis highlighted a polymicrobial infection caused by S. pneumoniae with Staphylococcus haemolyticus, or Streptococcus agalactiae, or Ureaplasma urealyticum, respectively. The majority of analyzed S. pneumoniae was resistant to erythromycin and clindamycin. In some isolates, further resistance was noted; in particular, one case presented multi-resistance to different classes of antibiotics

**Conclusions:** This study described an unusual high number of male urethritis cases caused by S. pneumoniae in a relatively short period (16 months) in an enclosed area (ASL-TO3), confirmed by its isolation in pure culture in the majority of cases. As pneumococci are commensal of the upper respiratory tract, orogenital sexual contact has been suggested to be responsible for their direct inoculation in the male urethral mucosa. With the increase in sexually transmitted diseases and variable human sexual behaviors, the significance of S. pneumoniae as a sexually transmitted pathogen should be more considered and it would be useful to look for S. pneumoniae during routine screening for UTIs

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Whole genome analysis of non-PCV13 emergent serotypes 8, 12F, 9N and 22F causing invasive pneumococcal disease in Spain

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Background: Invasive pneumococcal disease (IPD) is a major cause of morbidity and mortality. Although conjugated vaccines (PCVs) are highly effective preventing the serotype associated disease, their introduction changed the epidemiology of IPD mainly due to serotype replacement.

Materials/methods: Invasive episodes in adults from three periods 2008-2009 (pre-PCV13), 2012-2013 (early-PCV13) and 2015-2016 (late-PCV13) were collected from 6 Spanish hospitals. After serotyped (Quellung) and genotyped (PFGE and/or MLST), 10 representative strains of major clonal complexes (CC) of emergent non-PCV13 serotypes [S] (S8-CC53, S8-CC404, S12F-CC989, S9N-CC67 and S22F-CC433) were selected for WGS analysis (n=50).

Results: A total of 2187 IPD episodes were collected (949, 609 and 639, respectively). In the last period the most frequent non-PCV13 serotypes were S8 (n=92, 15.6%), S12F (n=48, 7.8%), S9N (n=33, 5.4%) and S22F (n=25, 4.1%). Within CC, the WGS analysis showed an identical capsular operon. Among S8, the operon was almost identical (identity >99%) in the two major CC. Acquired resistance genes were only found among S12F-CC989: six isolates had cat (pC194) and seven isolates presented a Tn916-like transposon carrying tet(M). No amino acids changes were observed among resistance-associated determinants (PBPs, ParC, ParE, GyrA and DHFR) with the exception of one S12F strain presenting T338A in PBP2X and another S12F with I100L in DHFR. Pan-genome analysis revealed a total of 3,022 genes, of them 1,537 were present in all genomes (core-genomes). Among accessory genome, 21 genes were only present in S8-CC53, 21 in S8-CC404, 50 in S12F-CC989, 62 in S9N-CC67 and 51 in S22F-CC433. The zinc metalloprotease C (ZmpC) was found only in S8-CC53 whereas neuraminidase B (NanB) was absent only in S8-CC404. Within clonal complexes, the core-genome accounted for 54% of genome for S8-CC53 and S8-CC404; and 87% for S12F-CC989, S22F-CC433 and S9N-CC67. In addition, the core-genome of S9N-CC67 had the highest number of SNPs (2449 SNPs).

Conclusions: Emerging CC linked to non-PCV13 serotypes balanced the previous decline of IPD in adults. In general these CC were genetically highly homogenous, a hallmark of highly invasive clones. The highest diversity CC was S9N-CC67 and the presence of acquired resistance was only seen in S12F-CC989.

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In vitro efficacy of miltefosine on chronic cutaneous leishmaniasis compared to meglumine antimoniate

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Background: Cutaneous Leishmaniasis (CL) is the most common form of leishmaniasis. CL can be divided into two major groups: acute CL (ACL) and chronic CL (CCL). CL lesions are called CCL if they do not heal by treatment or spontaneously within 2 years. The aim of this study is to compare the efficacy of miltefosin and pentavalent antimony compounds in vitro with the CCL patient samples.

Materials/methods: Five isolates previously isolated from 5 CCL patients were included in this study. Following genotyping, in vitro drug efficacy tests were applied to these five isolates to determine their activity against meglumine antimoniate (MA) and miltefosine. Serial dilutions (512, 256, 128, 64, 32, 16, 8 and 4 µg/ml) prepared from MA and miltefosine were prepared in 96-well flat-bottom cell culture plates with 100 µL leishmania culture (RPMI 1640; 15% FCS and 1x10^6 promastigotes/ml) in every well and incubated at 24 °C for 48 hours. The efficacy of the drug on leishmania promastigotes after 24 and 48 hours was evaluated by counting with the hemocytometer slide and XTT cell viability test.

Results: All of the samples were genotyped as L. tropica. In the first 24 hours, 128 µg/ml and 256 µg/ml concentrations of miltefosine and MA were enough to kill all the promastigotes respectively. After 48 hours, 32 µg/ml and 64 µg/ml of miltefosine and MA were enough to kill all the parasites respectively. The results of hemositometer slide and XTT were consistent.

Conclusions: There are no studies investigating the in vitro efficacy of miltefosine with the CCL patient group. In order to overcome the treatment challenges experienced in this special patient group, more studies are needed. According to our results, it is concluded that miltefosine is an efficient treatment option for the treatment of CCL and further clinical studies with miltefosine will reveal valuable data.

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Abstract 2005

Single-shot azithromycin in treatment of Legionella pneumophila: 18-year experience at the Vienna General Hospital, Austria

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Background: Pneumonia caused by the intracellular atypical pathogen Legionella (L.) pneumophila remains a life-threatening infection despite fast point of care diagnostic tools and specific antimicrobial treatment with mainly fluoroquinolones or macrolides. The overall mortality in Europe in 2015 was 8.1%, according to the data of the European Centre of Disease Prevention and Control (ECDC).

A recent study by Garcia-Vidal et al. (2017) demonstrated an equal efficiency of levofloxacin, clarithromycin and azithromycin when treated for a median of 3-5 days intravenously. Given concerns regarding adverse effects of fluoroquinolones, low bioavailability of oral macrolides and the costs of long hospital stays we demonstrate a feasible treatment option of Legionnaires’ disease with an intravenous single-shot of 1500mg azithromycin (diluted in 1000mL Ringer’s lactated solution; duration of infusion: 4 hours).

Materials/methods: In this single-centre retrospective analysis at the Vienna General Hospital 74 patients with L. pneumophila infections, confirmed by urinary antigen test and/or serology and/or PCR from respiratory tract specimens were included between 2000 and 2018.

Results: Five patients (6.8%) died during the observation period due to sepsis and/or multi-organ failure. These five patients either received a combination therapy with fluoroquinolones and macrolides or fluoroquinolones alone. Twelve patients (16%) only received a single-shot of 1500mg azithromycin without any additional L. pneumophila active therapy.

Neither adverse events, nor treatment failures were observed in those patients treated with azithromycin single-shot. The median hospital stay was 6.5 days [Q1-Q3: 5-8] in the single-shot group, in contrast to 12.5 days [Q1-Q3: 7-26] in patients with other therapy regimes.

Conclusions: This retrospective data provides a safe and feasible treatment alternative for patients with L. pneumophila infections, which could also be administered as outpatient parenteral antimicrobial therapy (OPAT), while avoiding potential adverse events of fluoroquinolone antibiotics.

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Abstract 2007

**Association of the prophage BTP-1 with anti-virulence of *Salmonella* typhimurium sequence type 313**

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**Background:** The prophage BTP-1 is highly conserved among strains of the human invasive lineage *Salmonella* Typhimurium (*S. Typhimurium*) ST313. Little is known on the influence of BTP-1 on fitness of the host-bacterium during infection. The aim of the current study was to determine the virulence effect of the full prophage BTP-1 and the gene bstA encoded from the phage in the ST313 reference strain D23580. The gene bstA was previously found to play a role in virulence of a strain of *S. Typhimurium* ST313 from Congo-Africa, and in a strain of the human invasive serovar *S. Dublin.*

**Materials/methods:** D23580 mutants lacking bstA (D23580ΔbstA) and BTP-1 (D23580ΔBTP-1) were constructed and tested during infection of THP-1 human macrophages [where uptake, survival and net replications were estimated] and mice [single and competition assays]. Cytokines expression by macrophages and cytotoxicity towards these cells were also analyzed. CFU counts in the liver, spleen and mesenteric lymph nodes (MLNs) together with analysis of organs enlargement, and histology studies were performed during mice infections.

**Results:** The mutant D23580ΔbstA showed significantly higher survival and net replication rates within the human macrophages than the wild-type [WT] strain, while the mutant D23580ΔBTP-1 did not significantly differed from the WT. Interestingly, both mutants displayed an hypervirulent phenotype during infection of mice. Thus, D23580ΔBTP-1 yielded significantly higher counts in all tested organs than the WT, and all three organs were significantly enlarged indicating higher cell infiltration. D23580ΔbstA significantly out-competed the WT during competitive infection of mice, and yielded significantly enlarged spleens and MLNs compared to WT-infected animals during single infection. Besides, significant histopathological changes [increased cellular infiltration and focal necrosis] were observed in the liver samples of mice infected with D23580ΔbstA and D23580ΔBTP-1 compared to WT-infected animals.

**Conclusions:** The presence of the prophage BTP-1 is associated with anti-virulence since a hyper-virulent phenotype was observed for the mutants lacking bstA and BTP-1 during mice infection. Removal of the gene bstA in *S. Typhimurium* ST313 led also to increased virulence during macrophages infection. These results agree with a previous study on *S. Dublin* where the gene was regarded as an anti-virulence gene.

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**Abstract 2009**

**Tuberculosis screening among newly arrived asylum seekers in Denmark**

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**Background:** Asylum seekers are in high risk of tuberculosis (TB) due to both the precarious conditions they are escaping from, and to the often dangerous conditions faced during migration such as overcrowding, imprisonment and poor access to health care. Upon arrival in host countries, TB screening programmes among asylum seekers tend to focus on chest radiography (CXR), whereas knowledge on spot sputum screening is limited. Among other high-risk groups spot sputum screening including *M. tuberculosis* culture has proven useful in identifying cases earlier and at a less infectious stage. We evaluated active TB screening including both spot sputum and CXR among asylum seekers arriving in Denmark. In addition, we assessed the coverage of a voluntary health assessment.

**Materials/methods:** Between February 1st 2017 and March 31st 2019, all newly arrived asylum seekers in Denmark ≥ 18 years from TB high-risk countries or risk groups, who attended a voluntary health assessment, were offered active TB screening with CXR and spot sputum including culture for *M. tuberculosis*.

**Results:** The coverage of the voluntary health assessment was 65.1%. Among 1154 referred for active TB screening, 923 (80.0%) attended. 34.1% were from countries with a WHO incidence ≥100/100,000 population. Among 854 screened by CXR, one case of active TB was identified equivalent to a yield of 0.12%. Sputum samples were collected from 758 and one *M. tuberculosis* culture-positive case (also identified by CXR) was identified, equivalent to a yield of 0.13%. No cases were found by spot sputum culture only.

**Conclusions:** CXR and spot sputum screening identified one case of active TB. Sputum screening did not identify additional TB cases compared with CXR in our study. However, sputum screening may be relevant among asylum seekers from TB high-incidence countries. In general, TB screening among asylum seekers should focus on asylum seekers from TB high-incidence countries. Furthermore, encouragement of health assessment attendance should be of high priority among newly arrived asylum seekers.

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Evaluation of sample preparation method by the liquid nitrogen for identification of Aspergillus fumigatus and Schizophyllum commune in matrix-assisted laser desorption ionisation-time of flight mass spectrometry analysis

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Background: Filamentous fungi have a robust cell wall that requires particular sample preparation to ensure good-quality mass spectra for matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS). In this study, we compared five unique sample preparation methods to obtain extracted protein from filamentous fungi.

Materials/methods: Seven strains of Aspergillus fumigatus including ATCC 204305 and three of Schizophyllum commune were isolated in clinical samples from our hospital. These strains were grown at 30°C on Sabouraud dextrose broth. Then, the following five protein extraction methods were performed: ethanol/formic acid standard extraction, freezing in liquid nitrogen, cell disruption with silica beads, combination of liquid nitrogen and silica beads, and homogenization by non-freezing. We compared the number of common specific peaks used for identification in A. fumigatus/S. commune databases (Microflex version 3.1, Bruker Daltonics Inc.) with the number of peaks obtained by the five methods.

Results: Thirteen specific peaks were found in the mass spectra of A. fumigatus and 9 specific peaks were found in those of S. commune. In the ethanol/formic acid standard extraction method, the average appearance rates in A. fumigatus and S. commune were 66% and 4%, respectively. The methods with the best rates were the combination of liquid nitrogen and silica beads method and the freezing in liquid nitrogen method. In the combination of liquid nitrogen and silica beads method, the rates were 74% and 59% for A. fumigatus and S. commune, respectively, whereas the rates with the freezing in liquid nitrogen method were 74% and 54%, respectively.

Conclusions: The two methods using liquid nitrogen obtained a larger number of mass spectra than the other methods including the ethanol/formic acid standard extraction method. These methods have high protein extraction efficiency and increase the identification accuracy of A. fumigatus and S. commune.

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Abstract 2015

External validation of the NOVA and DENOVA scores for clinical prediction of endocarditis in patients with Enterococcus faecalis bacteraemia

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Background: Enterococcus faecalis (Ef) is a frequent cause of bacteraemia, and between 10 and 15% of patients with Ef bacteremia are diagnosed with endocarditis. Several scores have been developed in order to estimate the clinical probability of endocarditis in Ef bacteraemia, including the NOVA score, which carries a sensitivity (Se) of 97% and a specificity (Sp) of 23%. The recently developed DENOVA score could have enhanced diagnostic performances but has not been validated. The objective of this study was to compare the diagnostic performances of the NOVA and DENOVA scores in an external cohort of Ef bacteremia and endocarditis.

Materials/methods: In this retrospective study, we included all cases of Ef bacteraemia diagnosed in two French hospitals between January 2015 and October 2019, as well as additional cases of Ef endocarditis diagnosed in four other French hospitals during the same period. Only endocarditis cases classified as “definite” according to Duke criteria were included. NOVA and DENOVA scores were determined for each case based on data collected during hospitalization. Patients with missing data precluding calculation of the scores were excluded.

Results: The study population comprised 490 patients, including 128 endocarditis cases. Median age was 74 years (IQR 62-83), and 70% of patients were males. Diagnostic performances of the NOVA and DENOVA scores are presented in Table 1.

In a theoretical cohort of 100 patients with Ef bacteremia including 13 with an endocarditis, use of the NOVA score for selection of patients at risk of endocarditis would lead to the realization of 52 echocardiograms, versus 25 with DENOVA. The number of false negative would be 0.2 and 0.7, respectively.

Conclusions: These results confirm the excellent sensibility of the DENOVA score for screening of patients at risk for Ef endocarditis, with an improved specificity compared with the NOVA score. Use of the DENOVA score could markedly reduce the number of unnecessary echocardiograms.

Table 1

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<thead>
<tr>
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<th>DENOVA</th>
<th>NOVA</th>
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<tbody>
<tr>
<td>Sensibility</td>
<td>95% (90%-98%)</td>
<td>98% (94%-100%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>84% (80%-88%)</td>
<td>54% (49%-59%)</td>
</tr>
<tr>
<td>Positive likelihood</td>
<td>6.1 (4.8-7.7)</td>
<td>2.1 (1.9-2.4)</td>
</tr>
<tr>
<td>Negative likelihood</td>
<td>0.06 (0.03-0.13)</td>
<td>0.03 (0.01-0.12)</td>
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<tr>
<td>Area under the ROC curve</td>
<td>0.94 (0.92-0.96)</td>
<td>0.92 (0.90-0.95)</td>
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</table>

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Evaluation of the performance of three chromogenic culture media for the detection of carbapenemase producing Enterobacterales to manage healthcare-associated infections

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Background: The increasing incidence of infections caused by Carbapenemase-Producing Enterobacterales [CPE] emerging worldwide at an alarming rate becomes a significant clinical and public health concern.

The aim of the study was to compare the performance of three chromogenic media: CHROMID® CARBA SMART agar [bioMérieux], a bi-plate for the screening of CPE, Brilliance™ESBL/Brilliance™ CRE agar [Thermofischer], a bi-plate for the detection of ESBL producers and carbapenem-resistant Enterobacterales, and BD BBL™CHROMagar™ CPE agar for CPE screening.

Materials/methods: A total of 54 strains: 42 Enterobacterales (10 Escherichia coli, 23 KESC [Klebsiella, Enterobacter, Serratia, Citrobacter] and 9 Proteae) harboring various types of carbapenemase [11NDM, 6 KPC, 8 OXA 48 or OXA48 like, 4 VIM], 5 resistant to carbapenems but carbapenem-negative, 7 ESBL producers and 1 carbapenem-susceptible were selected to evaluate the performances of each carbapenemase medium. Seven non-fermenting Gram negative bacilli (NFGNB): 6 carbapenemase and 1 ESBL producers and 5 other species (3 enterococci, 1 S.aureus and 1 C.albicans) were added. Strains were diluted in saline solution at 1.5x10^5 CFU/mL and inoculated on each medium. After 18h and 24h of incubation the presence of growth and coloration of colonies were recorded for each medium.

Results: The overall sensitivity of each medium [all species] for the detection of CPE was respectively 76.9%, 68.3% and 61.5% for CHROMID® CARBASMART, Brilliance™ CRE, and BD BBL™CHROMagar™ CPE at 18h of incubation and 82.1%, 83.7% and 64.1% at 24h of incubation. Regarding the performance of each medium for the claimed species only (E.coli and KESC for CHROMID® CARBASMART, E.coli, KESC and NFGNB for Brilliance™ CRE, and E.coli, KESC, proteae group for BD BBL™CHROMagar™ CPE), the sensitivity reached respectively 95.8 %, 75%, and 57.6% for the three media. The specificity of each medium was respectively 80% for CHROMID® CARBASMART and BD BBL™CHROMagar™ CPE and 100% for Brilliance™ CRE agar at 18h and 24h.

Conclusions: CHROMID® CARBASMART shows a better sensitivity of detection of Carbapenemase Producing Enterobacterales compared to Brilliance™ CRE and BD BBL™CHROMagar™ CPE at 18h and 24h. Specificity of Brilliance™ CRE is higher than CHROMID® CARBASMART and BBL™CHROMagar™ CPE agar which remains acceptable due to the number of specimens tested.

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Miltefosine as a promising agent for chronic cutaneous leishmaniasis: an in vivo model
Varol Tunali*1,2, Ibrahim Cavus3, Ahmet Yildirim1, Orcun Zorbozan2, Mehmet Harman4, Cumhur Gunduz5, Ahmet Ozbilgin3, Nevin Turgay2

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Background: Cutaneous Leishmaniasis (CL) is the most common form of leishmaniasis. CL can be divided into two major groups: acute CL (ACL) and chronic CL (CCL). The aim of this study is to compare the efficacy of miltefosin and pentavalent antimony compounds in vivo with the CCL patient samples.

Materials/methods: Three study groups were formed, each consisting of 5 male Mus musculus (Balb/C) mice. In this model, promastigotes from the culture of a CCL patient was utilized. 100 μL L. tropica promastigote suspension with a density of 10^8 promastigotes/ml were injected into the rear-right sole of each experimental animal intradermally. Soles of the mice were measured every two weeks until 24th week. From the 13th week following the inoculation, miltefosin 50 mg/kg/day was administered orally using gavage for 21 days, Meglumin antimoniate (MA) was administered by intramuscular (IM) injection daily for 21 days at 50 mg/kg/day and Saline was administered IM for 21 days for the miltefosine, MA and control group respectively. The mice were sacrificed at the 24th week and tissue suspensions were prepared from the infected foot and the visceral organs of the mice.

Results: The sole measurements of the miltefosine group were lower than the control group statistically. Between the miltefosine group and the MA group and MA group and the control group, there was no statistically significant difference. Giemsa stained slides revealed amastigotes in one, two and all of the slides for the miltefosine, MA and control group respectively. Molecular tests were performed with the Rotor Gene (Qiagen GmbH, Hilden, Germany) device using prepared tissue suspensions and L. tropica consistent peaks were obtained in one of the miltefosin group, four in the MA group and all mice in the control group.

Conclusions: Demonstration of both clinical and laboratory improvement in four of the five experimental animals provides strong evidence that miltefosine is an effective drug in the treatment of CCL compared to MA. In the literature, no clinical or laboratory studies using miltefosine have been reported with CCL patient groups. We conclude that miltefosine can be a valuable treatment option for CCL patient group.

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**Abstract 2020**

**In vitro dynamics and mechanisms of resistance development to imipenem and imipenem/relebactam in Pseudomonas aeruginosa**

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**Background:** Pseudomonas aeruginosa is a major cause of nosocomial and chronic infections, being considered a paradigm of antimicrobial resistance development. The main objective of this study was to analyze the dynamics and mechanisms of resistance development to imipenem alone or combined with the novel β-lactamase inhibitor relebactam in P. aeruginosa wild type (PAO1) and mutator (PAOMS; ΔmutS) strains.

**Materials/methods:** In vitro resistance development assays started by incubating PAO1 and PAOMS in Müller-Hinton Broth (MHB) for 24 h with 0.125 to 64 µg/mL of imipenem alone or plus relebactam at a fixed concentration of 4 µg/mL. Tubes from the highest antibiotic concentration showing growth were reinoculated in fresh medium containing concentrations of imipenem up to 64 µg/mL or imipenem with relebactam for 7 days. The susceptibility profiles for PAO1 and PAOMS mutants were determined by MHB microdilution. The mutants were further characterized by whole-genome sequencing (WGS) and those mutations related to ampC and efflux pumps hyperexpression were tested by RT-PCR. Finally, the virulence of the mutants was studied in a Caenorhabditis elegans infection model.

**Results:** As shown in the figure, imipenem/relebactam combination reduced imipenem resistance development for both strains, although resistance emerged much faster for PAOMS, as expected. Moreover, WGS indicated that imipenem resistant mutants showed mutations in the carbapenem porin OprD and regulators of ampC expression, while the mutations in imipenem/relebactam resistant mutants were located in oprD and regulators of the expression of the efflux pump MexAB-OprM. Moreover, high-level imipenem/relebactam resistance was only documented in the PAOMS strain, and was associated with additional mutations in penicillin-binding proteins (PBPs) and with reduced virulence in the C. elegans model.

**Conclusions:** Our results suggest that imipenem/relebactam could be a useful alternative for the treatment of MDR P. aeruginosa infections, potentially reducing resistance development during treatment. Moreover, this work deciphers the potential resistance mechanisms that may emerge upon the introduction of this novel combination in the clinical practice.

![In vitro dynamics resistance development](image)

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The impact of transport media, shipping time and DNA extraction kits on the absolute abundance of key vaginal bacterial species
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Background: A variety of different commercially available kits exists for both microbial specimen collection as well as for microbial DNA extraction. Sample preparation with the chelating resin Chelex-100 is a simple, cheap and universal method for DNA extraction, whereas newer more complex and more expensive DNA extraction methods might yield more optimal DNA extraction – especially in Gram positives - by using mechanical lysis with bead-beating. Previously, it has been reported that different methods could yield different results. Hence, this study aimed to evaluate two commercially available transport systems, two DNA extraction methods and shipping/storage time effect on the qPCR bacterial abundance of key vaginal bacterial species.

Materials/methods: A total of 20 Caucasian women were recruited for vaginal swab collection. Three swabs were collected from the same woman and stored in two different tubes, 1 sample in ESwab™ and 2 samples in eNAT™ (Copan, Brescia, Italy). One eNAT was stored at room temperature for 7 days until analysis, whereas the other samples were stored -80 degrees Celsius until analysis. The bacterial abundance of common vaginal Lactobacillus spp., A.vaginae and G.vaginalis was analyzed using qPCR. Bacterial DNA was extracted from the ESwab™ and the eNAT specimens using Chelex DNA extraction and Fast DNA™ SPIN Kit for Soil (© MP biomedicals).

Results: In the present study, we did not observe significant differences in bacterial abundance [counts/mL] by qPCR analysis of L.crispatus (P=0.92), L. iners (P=0.60), G. vaginalis (P=0.86) and A. vaginae (P=0.62) comparing Eswab and eNAT samples when the MPbio DNA extraction method was used. Moreover, the bacterial abundance in Eswab samples was non-significantly different with a Chelex DNA extraction compared to MP bio extraction. Chelex DNA extraction method was not compatible with eNAT resulting in inhibition. A storage time of 7 day at room temperature yielded similar results to immediate freeze at -80°C and dry-ice shipment of vaginal specimens.

Conclusions: In conclusion, qPCR analysis of Eswab and eNAT vaginal samples yield comparable copies/mL for L.iners, L. crispatus, A. vaginae and G. vaginalis when the MPbio extraction method was used. Only, Eswab was compatible with Chelex extraction and this method was non-inferior to MPbio extraction.

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The sink as source of transmission of VIM metallo-β-lactamase-producing Pseudomonas aeruginosa in the intensive care unit

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Background: Hospital-acquired infections, caused by multi-drug resistant, Verona Integron-encoded Metallo-β-lactamase (VIM)-producing P. aeruginosa, are a major problem in intensive care units (ICU). A previous study conducted in our hospital revealed that sinks drains of the ICU were a possible source of various multi-drug resistant pathogenic germs and suggested that transmission from these drains could indeed play a role in nosocomial infections colonized/infected by germs present in the sink drains.

Materials/methods: Thirty-six sinks located in the ICU of the UZ Brussel were sampled on 28/10/2019 with Eswabs® (Copan, Italy). Samples were inoculated on MacConkey agar (Biomérieux, France) and identification of suspicious colonies was performed by MALDI-TOF (Bruker, US). Twenty sinks were found to be positive and isolates were analyzed by whole-genome sequencing (WGS) together with 83 P. aeruginosa strains from 31 patients in the hospital, positive for P. aeruginosa between 01/2019 and 09/2019, in order to investigate the relationship between those strains. DNA-purification was done with a Maxwell® RSC Instrument (Promega, US) and WGS was performed on a NovaSeq® 6000 (Illumina, US) by Brussels Interuniversity Genomics High Throughput core (BRIGHTcore). The sequencing data was analysed using the wgMLST schema for P. aeruginosa of the BioNumerics software v.7.6 3 (Applied Maths, Biomérieux, Belgium).

Results: Twenty-five % of the P. aeruginosa strains found in the sink drains carried the VIM2-gene. 9.6% of the 83 patient samples carried the VIM2-gene and 2.4% carried the VIM4-gene. Twenty-two different P. aeruginosa sequences types (ST) were identified among 83 isolates, of which 15 belong to 22 ICU-patients. Seven of these were also found in strains recovered from the sink samples. WgMLST- analysis of all VIM2-positive isolates showed that isolates within each ST were very closely related. Transmission in both directions is suspected: patients who contaminated the sink drains with P. aeruginosa strains, but also patients who became infected over time by VIM-producing P. aeruginosa strains present in the sink drains.

Conclusions: This study points out that sink drains are a possible source of VIM-producing P. aeruginosa strains after contamination with patients’ materials. We also show that patients could get infected from sink drains containing VIM-producing P. aeruginosa.

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Systematic validation of blood transcriptional biomarkers for active pulmonary tuberculosis in a high-burden setting: a prospective diagnostic accuracy study
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Background: Blood transcriptional signatures are candidates for non-sputum triage or confirmatory tests of tuberculosis (TB). Prospective head-to-head comparison of their performance in real-world settings is necessary to evaluate their clinical utility.

Materials/methods: Consecutive, symptomatic adults presenting to a TB clinic in Cape Town, South Africa, provided blood for RNA sequencing, and sputa for liquid culture and molecular testing using Xpert MTB/RIF and Xpert MTB/RIF Ultra (Ultra). We assessed the diagnostic accuracy of 27 candidate signatures identified by systematic review, compared to culture or Xpert MTB/RIF positivity as the standard reference.

Results: Among 181 patients, 54 (30%) had TB. Four signatures achieved the highest diagnostic accuracy with comparable area under receiver operating characteristic curves of 86.8% (95% confidence interval 80.6-93.1%-90.6% (85.6-95.6%), independent of age, sex, HIV, previous TB, or sputum smear result. At test thresholds that give 70% specificity, these signatures achieved sensitivities of 83.3% (71.3-91%-90.7% (80.1-96%), thus meeting or approximating the minimum World Health Organization target product profile (WHO TPP) for a triage test. No signature met the optimum criteria for a triage test at any threshold, or the minimum criteria for a confirmatory test, but all four correctly identified Ultra-positive, culture-negative patients.

Conclusions: Four blood transcriptional signatures achieved minimum target criteria for a triage test. None were suitable for confirmatory tests, but they may be used to identify false-positive Ultra results. Further development of the signatures is warranted for these applications, in order to test their impact on clinical and health economic outcomes.

Performance metrics of the four best-performing signatures, benchmarked against minimum WHO TPP criteria. 95% confidence intervals are indicated in brackets.

| Sensitivity at 70% specificity (= minimum specificity for a triage test) |
|-----------------|-----------------|
| BATF2           | 88.9% [77.8-94.8%] |
| Kaforou25       | 83.3% [71.3-91%]  |
| Roe3            | 90.7% [80.1-96%]  |
| Sweeney3        | 90.7% [80.1-96%]  |

| Specificity at 65% sensitivity (= minimum sensitivity for a confirmatory test) |
|-----------------|-----------------|
| BATF2           | 85.8% [78.7-90.8%] |
| Kaforou25       | 92.1% [86.1-95.7%] |
| Roe3            | 92.1% [86.1-95.7%] |
| Sweeney3        | 93.7% [88.1-96.8%] |

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Abstract 2030

Microbiological factors of *Escherichia coli* from adult patients with bacteraemia and sepsis/septic shock from 21 hospitals in Spain: PROBAC-EC study

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Abstract third-party references: Supported by Instituto de Salud Carlos III (PI16/01432), On behalf of PROBAC REIPI/GEIH-SEIMC/SAEI Group

Background: Bacteraemia due to *Escherichia coli* presenting with sepsis/septic shock is associated with considerable morbidity and mortality. The objective of this study was to analyze the presence of microbiological factors of *E. coli* that may be related to the presentation of sepsis/septic shock in adult patients with bacteremia.

Materials/methods: 143 *E. coli* isolates from blood cultures of patients with sepsis/septic shock (2016 criteria) from 21 Spanish hospitals were included. Clinical data were collected prospectively. *E. coli* isolates were sent to the Microbiology Service of the University Hospital Virgen Macarena where Whole Genome Sequencing (WGS) (MiSeq, Illumina Inc) was performed. The assembly was done with the CLC Genomic WorkBench (Qiagen) software. Sequence type, WGS-based serotyping, virulence factors and antibiotic resistance genes were assessed in MLST 2.0, SerotypeFinder 2.0, VirulenceFinder 2.0, and ResFinder 3.2 databases, respectively. Phylogenetic group was determined using the Clermont scheme.

Results: Isolates were grouped into 60 clonal groups; ST131 (n=21; 14.7%), ST69 (n=17; 11.9%), ST73 (n=14 9.8%) and ST95 (n=9; 6.3%) were the most frequent. Overall, the virulence genes most frequently detected were the serum survival increase (*iss*) gene (124/143; 86.7%) and the glutamate decarboxylase (*gad*) enzyme gene (117/143; 81.8%). Among the most frequent clones, ST73 had the highest virulence score (median: 11 factors, range 7-14), while clone ST131 had the lowest value (median 5, range 4-7). Clones ST131, ST73 and ST95 were included in the phylogenetic group B2, and clone ST69 belonged to the phylogroup D. The most common types of polysaccharide (O) antigen and flagellar (H) antigen were O25 (27/143; 18.9%) and H4 (38/143; 26.6%), respectively. ST131 comprised the 95.4% of isolates with serotype O25:H4 (21/22); and 86.3% of ST131 isolates [19/21] presented the type 1 fimbrae fimH30 allele. In 17 (11.8%) isolates the presence of ESBL genes was detected, especially *bla*<sub>CTX-M-15</sub> (n=10; 6.9%) and *bla*<sub>CTX-M-14</sub> (n=4; 2.8%).

Conclusions: *E. coli* isolates from patients with severe sepsis/septic shock showed high clonal variability, although ST131, ST69, ST73 and ST95 were detected more frequently. Different profiles of virulence were observed for each sequence type. ESBL genes were detected in 11.8% of the isolates.

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Abstract 2037

In vitro Activities of ceftazidime-avibactam and comparator agents against Enterobacterales from Europe stratified by region, ATLAS global surveillance programme 2018

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Background: Ceftazidime-avibactam (CAZ-AVI) is a cephalosporin combined with a diazabicyclooctane β-lactamase inhibitor for treatment of Gram-negative infections. CAZ-AVI is active against Enterobacterales (Eba) isolates that produce Class A, C and some Class D β-lactamase, but not Class B metallo-β-lactamases (MBLs). The in vitro activity of CAZ-AVI and comparators against Eba isolated from different countries in Europe in 2018 is evaluated herein.

Materials/methods: 9,179 non-duplicate Eba isolates were collected from 103 sites in 23 countries in Europe during 2018 for the ATLAS global surveillance program. Antimicrobial susceptibility testing was by broth microdilution using CLSI guidelines and EUCAS 2019 breakpoints. CAZ-AVI was tested with a fixed concentration of 4 mg/L AVI. Isolates with meropenem MICs >1 mg/L were genetically screened for β-lactamases.

Results: CAZ-AVI was active against more isolates than comparator agents in Northern/Western and Central/Eastern Europe (MIC₉₀ 0.5 and 1 mg/L; 99.2% and 96.1% susceptible, respectively). CAZ-AVI was the most active agent among meropenem-non-susceptible MBL-negative isolates in both regions (MIC₉₀ 8 and 2 mg/L; 97.3% and 100% susceptible, respectively). 12/16 meropenem-non-susceptible and MBL-negative isolates with CAZ-AVI MICs >128 mg/L were KPC-positive and collected in Italy. Comparator agents were active against fewer isolates than CAZ-AVI in Northern/Western and Central/Eastern Europe (≤97.7% and ≤90.8% susceptible respectively).

Conclusions: CAZ-AVI demonstrated potent in vitro activity against Eba isolates collected in 2018 from Northern/Western Europe and Central/Eastern Europe. MBL-positive isolates were responsible for a modest decrease in the percentage of CAZ-AVI-susceptible isolates in both regions, but more notably Central/Eastern Europe where more of them were collected.

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<table>
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<tr>
<th>Region/Phenotype</th>
<th>CAZ AVI</th>
<th>CAZ</th>
<th>FEP</th>
<th>MEM</th>
<th>CST</th>
<th>TZP</th>
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<tr>
<td></td>
<td>MIC₉₀</td>
<td>%S</td>
<td>MIC₉₀</td>
<td>%S</td>
<td>MIC₉₀</td>
<td>%S</td>
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<td>Northern/Western Europe, All (n=8,294)</td>
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<td>5.6</td>
<td>&gt;32</td>
<td>3.5</td>
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<td>97.3</td>
<td>&gt;128</td>
<td>9.1</td>
<td>&gt;32</td>
<td>4.6</td>
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<td>Central/Eastern Europe, All (n=2,855)</td>
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<td>96.1</td>
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<td>61.8</td>
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<td>8.9</td>
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<td>MEM-non-susceptible, MBL-negative (n=149)</td>
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<td>100</td>
<td>&gt;128</td>
<td>15.7</td>
<td>&gt;32</td>
<td>11.4</td>
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</tbody>
</table>

Abbreviations: CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; FEP, cefepime; MEM, meropenem; CST, cefotaxime; TZP, piperacillin-tazobactam; %S, percent susceptible; MBL, metallo-β-lactamase.

*Percent susceptible determined using EUCAS 2019 breakpoints

1Northern/Western Europe includes Belgium (n=567), Denmark (n=91), Finland (n=43), France (n=923), Germany (n=916), Ireland (n=242), Italy (n=162), Latvia (n=80), Lithuania (n=184), the Netherlands (n=142), Portugal (n=375), Spain (n=384), Sweden (n=87), Switzerland (n=182), and the United Kingdom (n=572).

2Central/Eastern Europe includes Croatia (n=308), the Czech Republic (n=381), Greece (n=266), Hungary (n=362), Poland (n=32), Romania (n=351), Russia (n=668), and Ukraine (n=197).
**Streptococcus pneumoniae: the chameleon of ocular diseases**
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**Background:** *Streptococcus pneumoniae*, an inhabitant of the upper respiratory tract, is a leading cause of invasive infections as well as ocular surface infection. We previously reported that *S. pneumoniae* conjunctivitis is mainly caused by unencapsulated strains that form a specialized clade termed Epidemic Conjunctivitis Cluster (ECC). To determine whether the pathogenicity of ECC is limited to the conjunctiva or extends to other ocular tissues, and to determine the influence of the Pneumococcal Conjugate Vaccine (PCV-13) on the etiology of ocular infection, we determined the identity and relatedness of *S. pneumoniae* isolated from all ocular infections from 2014 to 2017 at Massachusetts Eye and Ear.

**Materials/methods:** *S. pneumoniae* isolated from 46 separate ocular infections were characterized by genome sequencing. We used CLC Genomics workbench to trim and assemble the sequences. We used the Center for Genomic Epidemiology pipeline to obtain species identification, sequence type (ST) and to identify antibiotic resistance genes present. STs were grouped into clonal complexes using goeBURST. Capsule serotype was predicted from genome sequence using Pneumocat.

**Results:** *S. pneumoniae* were mainly isolated from keratitis (n=22, 47.8%) or conjunctivitis (n=13, 28.2%). The remaining isolates were recovered from endophthalmitis and dacryosystitis. Strains from conjunctivitis generally lacked capsule operons (88.9%) and grouped within the ECC (53.8%). On the contrary, 90.9% of the *S. pneumoniae* responsible for keratitis possessed capsule operons. Most of these (96.8%) had an inferred capsule type not covered by the PCV-13. Inferred encapsulated strains were highly diverse with 22 different STs found with 3 most common STs: ST199 (16.2%), ST558 (6.6%) and ST100 (6.6%). Overall, 41.3% of the isolates were resistant to erythromycin, with no significant differences between unencapsulated and encapsulated strains (33.3% and 45.2%, respectively). All isolates were susceptible to levofloxacin.

**Conclusions:** Our study demonstrates that the tropism of ECC *S. pneumoniae* is limited to the conjunctiva, and does not extend to the cornea or other ocular tissues. In contrast to conjunctivitis, keratitis is caused by a highly diverse population of *S. pneumoniae* that escape the current vaccine. These data will be useful in the designing of next generation vaccines that cover common and sometimes sight-threatening ocular *S. pneumoniae* infections.

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Abstract 2041

**Real-world experience of bictegravir/emtricitabine/tenofovir alafenamide in a diverse Dublin cohort**

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**Background:** Biktarvy contains Bictegravir, a potent Integrase Inhibitor, co-formulated with emtricitabine/tenofovir alafenamide. The aim of this analysis was to review the characteristics, indications and outcomes of those switching to or initiating Biktarvy.

**Materials/methods:** All PLWH who attended the Guided clinic in St James’s Hospital, Dublin who were commenced Biktarvy between January - June 2019 were identified via the Pharmacy Dispensing system. A retrospective case notes analysis of these patients was undertaken and information regarding demographics, treatment experience, ART history, switch indication, virological response, and tolerability was determined.

**Results:** 144 Patients were commenced on Biktarvy. Five were lost to follow up and excluded from the analysis. 6 were ART naïve and 132 (95%) were switched to Biktarvy from another regimen. 111 (80%) were White, 19 (14%) were Black. 107 (77%) were male, mean age was 46 years, and mean time on prior ART was 9.3 years.

Reasons for switching included: simplification to a Single tablet regimen 44 (32%), side effects 43 (31%), and drug interactions 31 (22%).

Analysis of viral load was divided into 3 groups.

**Treatment Naïve patients:**

Of the 6 (4%) Naïve patients: 5 (83%) were virally suppressed at week 4 and 100% at week 12.

**Patients Virally suppressed pre switch:**

115 (87%) were virally suppressed at the time of switch. At the time of analysis the VL was available for 113 patients: 112 (99%) remained Virally suppressed at week 4 with 100% suppressed at week 12.

**Patients Virally detectable pre switch:**

17 (13%) were detectable at the time of switch.

Of the 16 for whom a VL was available 4 weeks post switch, 10 (63%) were suppressed. Of the 15 for whom a VL was available at 12 weeks 100% were suppressed.

Most patients tolerated Biktarvy, 5 (3.4%) patients discontinued, due to GI upset, weight gain and joint pain.

**Conclusions:** Biktarvy has shown to be effective in both treatment naïve and experienced patients. It has the potential to effectively suppress and maintain viral suppression, with 99% of treatment experienced patients remaining virally suppressed 4 weeks post switch. It is well tolerated with 3% of patients discontinuing treatment due to side effects.

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Abstract 2042

In vitro activities of ceftazidime-avibactam and comparator agents against Pseudomonas aeruginosa from Europe stratified by region: ATLAS global surveillance programme 2018

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Background: Avibactam (AVI) is a non-β-lactam, β-lactamase inhibitor that can restore the activity of ceftazidime (CAZ) against organisms that possess Class A, C, and some Class D enzymes. The aim of this study was to investigate the in vitro activity of ceftazidime-avibactam (CAZ-AVI) and comparators against contemporary Pseudomonas aeruginosa (Paer) collected in Europe during 2018 with isolates divided into two geographic regions, North/Western and Central/Eastern Europe.

Materials/methods: 2517 non-duplicate Paer isolates were collected from 103 sites in 23 countries in Europe as part of the ATLAS surveillance study in 2018. Susceptibility testing was by broth microdilution according to the ISO standard method and interpreted using EUCAST 2018 breakpoints. CAZ was tested with a fixed concentration of 4 mg/L AVI. When meropenem MIC values were >2 mg/L, the β-lactamase gene content was assessed by PCR and sequencing.

Results: CAZ-AVI demonstrated potent in vitro activity against the collection of 1715 Paer isolates from North/Western Europe (MIC90, 8 mg/L, 95.5% susceptible), but was less effective against the collection (n=802) from Central/Eastern Europe (MIC90, 64 mg/L, 79.6% susceptible). When metallo-β-lactamase (MBL)-positive isolates were removed from this latter set, the activity of CAZ-AVI increased marginally (MIC90, 32 mg/L, 82.9% susceptible). The in vitro activity of CAZ-AVI was the highest among all comparators for both regions except for colistin.

Conclusions: The in vitro activity of CAZ-AVI against the Paer isolates collected in North/Western Europe was higher than that against isolates from Central/Eastern Europe. Some of this difference can be attributed to the large percentage of MBL-carrying isolates originating from Central/Eastern European countries. However, much of the resistance apparently stems from other mechanisms. More isolates were susceptible to CAZ-AVI than to any comparator except colistin, suggesting that it remains an effective treatment versus Paer infection.

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Abstract 2043

**Effective control strategies for cutaneous leishmaniasis after Syrian influx in Turkey**

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**Background:** Turkey hosts the largest refugee population in the world, which may carry some potential risk on public health. Infectious diseases are the first one to be considered. Cutaneous leishmaniasis (CL) is also known as a disease emerging among migrants and travelers. Although, CL has been seen in Southeastern part of Turkey for years, strict control strategies implemented by Ministry of Health decreased the incidence significantly. These strategies include; vector control, raising awareness and knowledge of health staff and public, early diagnosis and prompt treatment of cases, and active and passive case detection. House to house search, index case approach and screening are major strategies implemented for active case detection. After the huge number of migrants influx from Syria, Ministry of Health adopted CL control strategies in order to cover migrants’ needs. However, Syrians are mostly living in Southeastern Anatolian cities, they are living in all cities. All the services provided to Turkish citizens are also being delivered to migrants. The objective of this study is to evaluate the influence of migration on CL epidemiology in Turkey and the efficiency of control strategies.

**Materials/methods:** CL is a mandatorily notifiable disease since 2004, and health care facilities are obliged to report all the cases compatible with the case definition. Incidence of CL and geographical distribution of cases were analysed seven years prior and after the migrants’ influx.

**Results:** In total, 34,643 CL cases were identified between 2005 and 2018. The incidence (per 100 000) was mostly increase in Marmara (0.03/0.20), Black Sea (0.02/0.10), Central Anatolia (0.11/1.13) and Southeastern Anatolia (11.95/24.28) compared between 2005-2011 and 2012-2018 due to Syrians population. The total number of CL cases increased two-fold in 2013 and gradiently decreased since then (Graphic 1).

**Conclusions:** Increase in the incidence of CL cases in 2013 seems to be attributable to massive Syrian influx, however steady decrease of incidence in both Syrian and Turkish citizens can only be explained by the efficiency of control measures. It is clear that internationally acknowledged strategies pave the way to success if implemented thoroughly.

Graphic 1. Distribution of CL cases by years and by nationality, Turkey, 2005-2018

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Are *Pseudomonas aeruginosa* biofilms a major issue in non-cystic fibrosis bronchiectasis?

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Abstract third-party references: FIS (ISCIII) PI1800145, Icrea Academy, SEPAR 624, Ciberes [P101/2018]

**Background:** During chronic infection in Cystic Fibrosis (CF) an adaptation of *Pseudomonas aeruginosa* (PA) to different lung niches occurs through biofilms which are associated to worse outcomes and mortality. However, scarce information exists on whether PA biofilms are also a major issue in non-CF bronchiectasis (BE). Thus, the diagnostic methods applied in BE are not those applied during biofilm associated infections. **Aim:** To determine whether PA biofilms are a major issue in BE patients with PA chronic infection and to evaluate the early diagnostic of PA by applying recommended diagnostic methods for CF biofilm infections compared to standard methods.

**Materials/methods:** Prospective collection of sputum and serum samples every 3 months; Use of DTT (1:1) and sonication; >72h incubation, non-mucoid and mucoid PA isolation and MALDI-ToF. Biofilms imaging by Gram-staining and Fluorescent in situ Hybridization and Confocal Laser Scanning Microscopy (FISH+CLSM), respectively. Quantification of specific serum antibodies against PA (precipitins) by crossed immunoelectrophoresis. Metagenomics 16SrRNA sequencing was carried out to analyze the microbiome diversity by PA-phenotype.

**Results:** Three-hundred and sixty-five BE patients were screened. Of those, 46 vs 19 were chronically or intermittently colonized by PA, respectively. Comparison between standard vs biofilm recommended methods increased the sensitivity of PA cultures, specifically 29/103 (28%) sputa were false negative PA by standard but true positive PA by recommended (p<0.001). The mucoid PA was difficult to detect by standard cultures and a marker of decreased biodiversity in sputum (Figure). Biofilms were identified by Gram (Figure) and FISH+CLSM and the presence of alginate in images was associated to the mucoid phenotype (p>0.001) and ≥5 years of chronic PA (p=0.040). Precipitins were higher in BE patients with chronic vs those with intermittent PA 11.0 [6.3-17.0] vs 0.5 [0-3.2], p<0.001, respectively. Compared to the chronic, the intermittently PA colonized patients had higher number of exacerbations during the follow up.

**Conclusions:** *Pseudomonas aeruginosa* biofilm is a major issue in BE since mucoid PA, that produces alginate and biofilms, is a marker of decreased sputum biodiversity and chronic respiratory infection. Applying recommended methods for biofilm infections allows an earlier PA diagnostic which may have clinical implications.

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Quality of care indicators in the management of bloodstream infections caused by Enterobacteriaceae: systematic review (MAMBOO-E study)

Pietro Malosso*1, Luigia Scudeller1, Stefano Ianniruberto1, Linda Bussini1, Renato Pascale1, Livia Pancaldi2, Michele Bartoletti3, Milo Gatti3, Pierluigi Viale1, Mical Paul4, Maddalena Giannella1

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Background: Evidence-based care bundles have received increasing attention in recent years to improve the outcome of patients with infectious diseases. However, an evidence-based bundle for the management of patients with Enterobacteriaceae BSI (E-BSI) does not exist. To investigate the impact on outcome of five interventions in patients with E-BSI aimed at drawing a bundle.

Materials/methods: We searched for randomized controlled trials (RCTs) and observational studies, published in all languages from January 2008 to March 2019 on PUBMED, EMBASE and COCHRANE library. Five searches corresponding each to a population-intervention-control-outcome (PICO) were performed. In all of them population consisted of patients with microbiologically confirmed E-BSI. Interventions were: i. performance of imaging to assess BSI source and/or complications; ii. follow-up blood culture (BCs); iii. use of loading dose followed by extended/continuous infusion (E/CI) of beta-lactams; iv. short treatment duration; and v. infectious disease (ID) consultation. Patients without intervention were considered as controls. Main outcome for all PICOs was all-cause 30-day or nearest mortality. RoB 2.0 and ROBINS-I tools were used for bias assessment.

Results: For PICO 1, 2 and 5 there were no RCTs, observational studies included together bacteremic and non-bacteremic patients; separate data for E-BSI and adjustment for confounders were not provided. Thus, no qualitative or quantitative synthesis for these PICOs could be done. PICO 3: Three RCTs were included, comprising 263 patients with E-BSI. No study evaluated the impact of intervention on mortality. Lower relapse and higher microbiological cure rates among patients receiving intervention were observed in one and two studies, respectively. PICO 4: Five studies, one RCT and four observational studies, were included comprising 3036 patients with E-BSI. Treatment duration was classified as short (7 or 10 days) and long groups. We found no significant difference between short and long treatment groups for all-cause mortality (OR 1.10, 95% CI 0.83-1.44, p=0.41) (see Figure).

Conclusions: There is a gap in the literature regarding the optimal management of patients with E-BSI. In particular regarding the need of systematic imaging, follow-up BCs, and ID consultation. Current data seem to support the use of beta-lactams by E/CI and a short treatment duration. CRD42019127225.

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Performances comparison between rapidly growing mycobacteria medium for direct-isolation of non-tuberculous mycobacteria, and its industrial version

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Background: Pulmonary nontuberculous mycobacteria (NTM) represent an increasing threat. Consideration of NTM pathogenicity has increased but diagnosis remains difficult due to slow growth of mycobacteria and to pulmonary flora that can be abundant, especially in the case of cystic fibrosis (CF) patients. RGM medium has been designed at the Freeman Hospital (Newcastle Upon Tyne, UK). This medium shows increased specificity and sensitivity compared to reference methods. NTM Elite agar [bioMérieux] is the industrial version derived from RGM medium dedicated to the isolation of NTM from respiratory specimen without prior decontamination. RGM and NTM Elite agar have been compared with pure strains and sputum specimens.

Materials/methods: Pure strains (51 NTM; 46 non-mycobacteria) and 83 sputa (77 patients including 70 with CF) were inoculated on both RGM and NTM Elite agar. Media were incubated at 30°C for 28 days with regular readings, minimum once a week. The number of colonies isolated on both media were then compared. Clinical isolates were identified by MALDI-ToF MS.

Results: Among the 51 NTM strains inoculated, 46 grew on RGM (90%) and 47 on NTM Elite agar (92%) after 28 days incubation. Among the 46 non-mycobacteria strains, 34 were inhibited on RGM (74%) and 36 on NTM Elite agar (78%). From 83 sputa, respectively 5 and 6 isolates belonging to Mycobacterium avium complex were isolated on NTM Elite agar and RGM media. 7 isolates belonging to Mycobacteroides abscessus were isolated on both media. A higher number of Mycobacteroides chelonae isolates were recovered on NTM Elite agar, but this may be artefactual since an important proportion grew only after 21 days of incubation. Among the 83 sputa tested, no overwhelming growth of pulmonary flora was observed at final reading. 15 non-mycobacteria were isolated on both media (17 recovered in total). 4 NTM were isolated in the presence of contaminants.

Conclusions: NTM Elite agar, industrial version of RGM, appears as efficient as RGM for the culture of NTM. These media enable a simple, sensitive and highly selective screening of NTM in sputa without prior decontamination. Therefore, they have a real contribution to the diagnosis of NTM pulmonary infection.

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Abstract 2048

**Formation of enterobacterial aggregates in presence of bovine synovial fluid**

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**Abstract third-party references:** AM was funded by a SEIMC grant for a short-term visitor scholar, Funded by NIH R01 GM124436-(PS)

**Background:** Septic arthritis (SA) and prosthetic joint infection (PJI) are mostly caused by Gram-positive cocci, but an increase of cases provoked by Enterobacteria has been recently reported. Once bacteria invade synovial joints, they can form free-floating clumps or aggregates in synovial fluid which are more resistant to antimicrobial treatments in comparison to the single cells. Thus, we evaluated the formation of enterobacterial aggregates and their size in presence of synovial fluid.

**Materials/methods:** Two bacterial strains of *Klebsiella pneumoniae*, *Escherichia coli*, *Proteus mirabilis* and *Enterobacter cloacae* isolated from PJI in Hospital Universitario Fundación Jiménez Díaz were used. All PJI were diagnosed according to internationally accepted criteria. One antibiotic susceptible strain and another antibiotic multidrug-resistant strain (resistant to at least three antibiotic families) of each species were used. 25 μL of bacterial overnight tryptic-soy broth culture were added to 100 μL of Ringer solution with or without 10% bovine synovial fluid. After 24-h incubation at 37ºC and 5% CO₂, images of the aggregate formation were taken using the SpectraMax i3x plate-reader. The images were analyzed using ImageJ. Data were examined using non-parametric Wilcoxon test. The values are represented as median and interquartile range.

**Results:** Results obtained are shown in Figure 1.

![Figure 1](image-url)

**Conclusions:** The presence of synovial fluid increases the size of aggregates of *E. cloacae*, *P. mirabilis* and susceptible *E. coli* strain. The size of aggregates increased over time in *P. mirabilis* and susceptible *E. coli*. Further studies and a higher number of strains are necessary. Research about aggregate size by enterobacteria will lead to greater understanding of SA and PJI pathogenesis and to develop new treatment strategies.

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Antimicrobial treatment and treatment duration for urinary tract infections in adult males

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Abstract 2049

Background: Male urinary tract infections (UTIs) represent up to 20% of UTI consultations in primary care, however, little research has been done into the most appropriate antimicrobial regimen. Most of the knowledge is focused on urological patients with prostatitis, pyelonephritis/urosepsis, infections related to surgery and hospitalised patients. Generally, male UTIs are considered complicated, which implies longer antimicrobial treatment duration. However, some UTIs can be considered uncomplicated in otherwise healthy males. Uncertainties exist with regard to clinical diagnosis as well as the type and duration of antimicrobial use for male UTIs including the consideration of adverse effects, risk of relapse and emergence of resistance. The aim of this systematic review and meta-analysis is to review randomised controlled trials (RCTs) evaluating the effectiveness of different antimicrobial treatments and duration of treatment for UTIs in adult males.

Materials/methods: We searched MEDLINE, EMBASE, PubMed, Cochrane Register of Controlled trials (CENTRAL), Cochrane library and Wiley) and CINAHL EBSCOhost using selective search strategies, detailing interventions and randomised controlled trials (RCTs) in primary care focusing on UTIs in adult males. Eligible studies compared oral administration of any type of antimicrobial with either no treatment (placebo) or other (antimicrobial) treatment and/or different duration in primary care/non-hospitalised patients.

Results: 1,052 references were imported to Covidence for title and abstract screening of which 115 studies were included in full-text screening [101 were subsequently excluded]. There were fourteen papers selected for data extraction of which six had to be dismissed due to lack of male specific data and/or inability to contact the authors. The remaining eight papers include two with a specific focus on males and six reporting on both males and females for which data for males only are requested by contacting the authors. The antimicrobials used to treat male UTIs were quinolones, trimethoprim/co-trimoxazole and cephalosporins. Few similarities are observed between papers, which makes meta-analysis challenging.

Conclusions: Research on antimicrobial treatment for male UTIs is scarce and few RCTs exist to determine the best treatment. Further research is needed to examine the effectiveness of antimicrobial treatment for male UTIs in primary care.

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Abstracts 2020

Abstract 2050

Pharmacokinetic model for intravenous vancomycin in pregnant rats and pups
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Background: Vancomycin can be used to treat methicillin-resistant Staphylococcus aureus in pregnant patients. Literature suggests maternal vancomycin crosses the placental barrier into the fetus. Thus, during pregnancy, describing the mass transit of vancomycin to the fetus is important in the design of dosing regimens. We employed a translational rat model to: 1) identify a relevant physiological based pharmacokinetic (PK) model of vancomycin in pregnancy, 2) estimate PK parameters and describe the mass transit of vancomycin from mother to pup.

Materials/methods: Pregnant female Sprague-Dawley rats were divided randomly into 3 groups: Trimester 1, Trimester 2, and Trimester 3 (T1, T2, and T3). All dosages were administered via double jugular vein catheters. Rats from each group received doses of 250 mg/kg daily for three days. Dams delivered pups vaginally after completion of the pregnancy term. Vancomycin levels in plasma and homogenized pup kidneys were quantified via LC-MS/MS. Population PK analyses were conducted using Pmetrics for R. PK parameters for trimester comparison were calculated from Bayesian posteriors utilizing noncompartmental analysis (NCA).

Results: Sixteen vancomycin treated rats and 10 pups contributed PK data. A 3-compartment model fit the data well [serum Bayesian: observed vs. predicted R²=0.918, pup Bayesian: observed vs. predicted R²=0.999] shown in Figure 1. The median rate constant for vancomycin mass transit to the pup kidney was 9.14 hr⁻¹. The fourteen population PK parameters exhibited shrinkages less than 14%. NCA of the Bayesian posteriors revealed similar median clearance [T1: 0.39L/hr vs. T2: 0.35L/hr vs. T3: 0.25L/hr, P-value: 0.32] and volume of distribution between trimesters [T1: 0.47L vs. T2: 0.73L vs. T3: 0.80L, P-value: 0.12].

Conclusions: The model is an explanatory PK model for the transfer of vancomycin through the placenta. Vancomycin transit to the fetus from the mother is rapid and predictable in the rat model. This model can be highly useful for understanding the distribution of vancomycin in pregnancy to ensure efficacious and safe doses for mother and fetus.

Figure 1. Log-scale observed concentrations versus Bayesian predicted concentrations. Fetus concentrations are in orange (R²=0.999). Mother concentrations are in blue (R²=0.929). Line of unity is shown in black.

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Comparison of genetic diversity in *Streptococcus pyogenes* isolates from Gambia and United Kingdom causing skin and soft tissue infections

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**Background:** *Streptococcus pyogenes* causes diseases ranging from mild superficial skin infections to severe invasive disease. Despite having a high burden of disease, few isolates from sub-Saharan Africa have been included in large-scale *S. pyogenes* genetic diversity studies. Furthermore, the leading 30-valent M-protein *S. pyogenes* vaccine candidate in development is based primarily on dominant emm genotypes circulating in high income countries (HIC). We investigated the diversity and genetic variation of *S. pyogenes* isolates causing skin and soft tissue infection (SSTI) from The Gambia and UK, and compared these with an existing global *S. pyogenes* whole genome sequence dataset.

**Materials/methods:** *S. pyogenes* isolates causing SSTI were collected during a community prevalence study of skin disease in The Gambia and routine clinical isolation in a UK clinical microbiology laboratory. WGS data was generated using the Illumina Miseq platform. Spades and Prokka were used for genome assembly and annotation, and emm type determined using the CDC typing tool. Roary was used to determine the core genome and RAxML used to infer phylogenetic relatedness by maximal likelihood.

**Results:** 105 *S. pyogenes* genomes from The Gambia and 160 from the UK were newly generated. We identified 44 different emm genotypes in Gambian isolates but, unlike in HIC, there was no dominant genotype. Unusually, there were no emm1, emm3 or emm12 genotypes which typically dominate in HIC among the Gambian isolates. Overall, there was only 26.67% coverage of Gambian emm types in the 30-valent M vaccine, much lower than that of the UK collection. We also identified a high number of multilocus sequence types, which indicated high chromosomal diversity within the Gambian collection compared to UK isolates, which was confirmed by whole genome comparisons. A similar pattern was observed when contextualised within the global collection of >5000 genomes. Although isolates belonging to HIC clustered distinctly by emm-type, higher diversity was observed when isolates from low/middle income countries, including The Gambia, were included.

**Conclusions:** Our study provides insights into *S. pyogenes* diversity and generates much needed data from neglected areas of high disease burden. Understanding this diversity will enable better vaccine development to provide greater coverage and efficacy.

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Screening and management of Chagas disease in at-risk blood donors in a non-endemic country: experience of a north-western tertiary care centre in Italy

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Background: Chagas Disease (CD) represents an emerging health concern in non-endemic countries due to migration and vector-free routes of transmission, including blood transfusion. Since 2016 international guidelines recommend CD screening protocols for first-time donors from or who recently travelled to endemic countries (at-risk blood donors).

Aim of the study: to report CD seroprevalence and management of individuals tested positive for CD in a north-western Italian Hospital.

Materials/methods: Retrospective monocentric study. From 2016 to 2019 serological screening for CD was performed in at-risk blood donors and patients with likelihood of CD symptoms by using a specific chemiluminescent microparticle immunoassay (CMIA) Trypanosoma cruzi serology. For those tested positive, a second serological assay was performed at a reference centre. Subjects with two different positive serology were considered CD confirmed cases and underwent screening for evaluating the extent of disease (acute, chronic indeterminate or symptomatic). Screening included ECG, chest X-ray, echocardiography and, for those with gastrointestinal symptoms, oesophageal manometry. CD treatment was then proposed according to current guidelines.

Results: Of 4327 blood donors tested, 16 (0.37%) had a positive CMIA serology. Nine blood donors and 6 patients tested for clinical suspicion (three achalasia, two suspected cardiomyopathies, a mother of CD confirmed case) were referred to our outpatient’s department. Overall, 6 subjects (40%) resulted positive at confirmatory serology, four of them were blood donors. All CD confirmed cases had chronic indeterminate stage of disease. They were all females, born in endemic country (three from Bolivia, one from Ecuador, Paraguay and Mexico), with a mean age of 38.8 years [range 24-48]. Three of them (50%) reported relatives with CD. Five patients received benznidazole at standard dose -150 mg bid for 60 days, weight-based prolongation of treatment-, three of them developed side effects [1 peripheral neuropathy, 2 skin rash]. One patient still has to start treatment.

Conclusions: Despite low prevalence rates, implementation of T. cruzi screening in blood donors led to identification of 4 CD cases, while none of clinically suspected subjects had symptomatic disease. Scaling-up screening protocols in low-endemic countries is crucial to prevent iatrogenic transmission and identify positive individuals before the onset of symptomatic disease.

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Comparative efficacy of piperacillin-tazobactam versus third-generation cephalosporins or carbapenems against susceptible ampC-bearing Enterobacteriaceae

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Background: The comparative efficacy of PTZ versus 3-CEF or carbapenems against susceptible ampC-bearing Enterobacteriaceae is unknown. The aim of the study was to assess the possible influence of empirical therapy with PTZ vs. 3-CEF or a carbapenem on 30-day mortality in patients with bacteraemia due to ampC Enterobacteriaceae.

Materials/methods: Retrospective analysis of a prospectively collected database of patients with bacteraemia diagnosed at a 750-bed university hospital in Barcelona (Spain) from January 2003 to December 2018. Episodes due to ampC-bearing Enterobacteriaceae susceptible to PTZ (MIC≤ 8 mg/L), 3-CEF (≤2 mg/L) and carbapenems and empirically treated with these antibiotics were selected. Multivariate analysis was performed by a step backward logistic regression procedure.

Results: Among 599 episodes of monomicrobial bacteraemia due to ampC-bearing Enterobacteriaceae, 182 (30.3%) were empirically treated with PTZ, 171 (28.5%) with a 3-CEF and 246 (41%) with a carbapenem. In comparison with PTZ, 30-day mortality was not significantly different in episodes treated with a 3-CEF (13/182 [7.1%] vs 14/171 [8.2%]; OR 0.86, 95%CI 0.3-1.8, p=0.7) but was higher in those receiving a carbapenem (40/246 [16.3%]; OR 2.5, 95%CI 1.3-4.8, p=0.005) regardless of the source. In episodes empirically treated with a carbapenem or PTZ, the best predictors of 30-day mortality were to receive a carbapenem (OR 1.5, 95%CI 1.06-2.2), an ultimately/rapidly fatal underlying disease (OR 4, 95%CI 1.9-8.5), indwelling urinary catheter (OR 2.2, 95%CI 1.1-4.5), chronic corticosteroid therapy (OR 3.1, 95%CI 1.5-6.3), shock (OR 5.2, 95%CI 2.5-10.7), cirrhosis (OR 3.6, 95%CI 1.4-10.2), chronic pulmonary disease (OR 3.1, 95%CI 1.4-8.6), and a non-urinary source (OR 7.2, 95%CI 1.8-28).

Conclusions: In terms of 30-day mortality, empirical use of PTZ for patients with susceptible ampC-bearing Enterobacteriaceae bacteraemia was not worse than that of other active beta-lactams and may even perform better than a carbapenem.

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**Abstract 2058**

**Arthroscopic debridement, antibiotic and implant retention (DAIR) with local administration of Exebacase [Lysin CF-301] (LysinDAIR) followed by suppressive tedizolid as salvage therapy in elderly patients for relapsing multidrug-resistant *Staphylococcus epidermidis* prosthetic knee infection**

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**Abstract third-party references:** on behalf of the Lyon BJ1 study group

**Background:** Exebacase, a recombinantly-produced lysin has recently: (i) reported Proof of Concept data from a phase II study in *S. aureus* bacteremia; and (ii) demonstrated activity *in vitro* against embedded-biofilm *S. epidermidis*. In patients with relapsing MDR *S. epidermidis* prosthetic knee infection (PKI), the only surgical option is prosthesis exchange. In elderly patients who have undergone several revisions, prosthesis explantation could be associated with definitive loss of function and mortality. Arthroscopic DAIR is considered to be not appropriated, as this procedure is associated with a considerable failure rate.

**Materials/methods:** We proposed in our BJ1 reference regional center ”CRIOAc Lyon” to perform arthroscopic DAIR with local administration of exebacase [LysinDAIR] followed by suppressive tedizolid as salvage therapy in elderly patients with recurrent MDR *S. epidermidis* PKI with no therapeutic option or therapeutic dead-end (for whom revision or transfemoral amputation was not feasible, and for whom no other oral option was available). Each use was decided in agreement with French health authority (ANSM) and in accordance with the local ethics committee. A written consent was obtained for each patient. Exebacase (75 mg/mL; 30 mL) was administered directly into the joint during arthroscopy.

**Results:** Four patients (79 to 89 yo) were treated with the LysinDAIR procedure. All had several previous prosthetic knee revisions, without prosthesis loosening (panel A). Three had relapsing PKI despite suppressive antibiotics following open DAIR. Two had clinical signs of septic arthritis (panel B); the two others had fistula. No adverse events occurred during arthroscopy; all patients received daptomycin (8 mg/kg) and linezolid (600 mg bid) for 4 to 6 weeks, followed by tedizolid 200 mg/day as suppressive therapy. At 6 months, recurrence of the fistula occurred in the two patients with fistula at baseline. After 1 year follow up, the outcome was favorable for the two last patients, with disappearance of clinical signs of septic arthritis (panel C).

**Conclusions:** Exebacase has the potential to be used as salvage therapy during arthroscopic DAIR in patients with relapsing MDR *S. epidermidis* PKI, to improve the efficacy of suppressive antibiotics, and to avoid considerable loss of function.

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In vitro activity of ceftazidime-avibactam and comparators against isolates of Enterobacterales and Pseudomonas aeruginosa collected from pediatric patients as part of the ATLAS global surveillance program: 2013-2018

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Background: Ceftazidime-avibactam (CAZ-AVI) is a β-lactam/non-β-lactam β-lactamase inhibitor combination with in vitro activity against Enterobacterales and Pseudomonas aeruginosa isolates carrying Class A, C and some Class D serine β-lactamas. CAZ-AVI is approved in Europe and the United States (US) for treatment of adults with complicated intra-abdominal (cIAI), complicated urinary tract (cUTI), and lower respiratory tract (LRTI) infections, and in the US for treatment of pediatric patients 3 months and older with cIAI and cUTI. We examined the in vitro activity of CAZ-AVI and comparators against isolates collected from pediatric patients (newborn to 17 years old) as part of the ATLAS surveillance program in 2013-2018.

Materials/methods: Isolates were collected from 272 medical laboratories in 52 countries located in Europe (EUR; n=3561), Middle East/Africa (MEA; n=834), Asia/Pacific (AP, excluding China and India; n=745), and Latin America (LA; n=1175) from patients with LRTI (n=2414), IAI (n=1395), and UTI (n=2506). Susceptibility testing was performed by CLSI broth microdilution and values were interpreted using EUCAST 2019 breakpoints. CAZ-AVI was tested at a fixed concentration of 4 mg/L AVI.

Results: The in vitro activity of CAZ-AVI was comparable to or greater than that of meropenem against Enterobacterales and P. aeruginosa collected globally from pediatric patients with LRTI, IAI and UTI (Table).

<table>
<thead>
<tr>
<th>Organism/Drug</th>
<th>Enterobacterales</th>
<th>P. aeruginosa</th>
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<tbody>
<tr>
<td></td>
<td>CAZ-AVI</td>
<td>MEM</td>
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<tr>
<td><strong>Region/Source</strong></td>
<td><strong>N</strong></td>
<td><strong>MIC90 (mg/l) % Susceptible</strong></td>
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</tr>
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</table>

|     | EUR, Europe; MEA, Middle East/Africa; AP, Asia/Pacific; LA, Latin America; LRTI, lower respiratory tract infection; IAI, intra-abdominal infection; UTI, urinary tract infection; CAZ-AVI, ceftazidime-avibactam; MEM, meropenem. % Susceptible was determined using EUCAST 2019 breakpoints. |

MIC90 values ranged from 0.25-0.5 mg/L (98.6-100% susceptible) against Enterobacterales collected in the four geographic regions surveyed, while MIC90s ranged from 4-8 mg/L (90.9-97.5% susceptible) against P. aeruginosa collected from LRTI in LA and from all examined infection sources in EUR, MEA and AP. MIC90 values were higher against P. aeruginosa collected from IAI and UTI in LA, which included an elevated proportion of isolates carrying Class B metallo-β-lactamas. Overall, 99.2%, 99.2% and 99.4% of Enterobacterales collected from pediatric patients with LRTI, IAI and UTI, respectively, and 92.7%, 93.0% and 94.3% of P. aeruginosa, respectively, were inhibited by ≤8 mg/L of CAZ-AVI; higher percentages of susceptibility were only observed for colistin tested against P. aeruginosa isolates (not shown).

Conclusions: CAZ-AVI demonstrated potent in vitro activity against the majority of Enterobacterales and P. aeruginosa isolates collected globally from pediatric patients in 2013-2018, regardless of infection source.

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Abstracts 2020

Abstract 2063

In vitro activities of ceftazidime-avibactam and comparator agents against Enterobacterales from Europe stratified by infection type from the ATLAS global surveillance programme 2016-2018

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Background: The global spread of multi-drug resistant (MDR) Enterobacterales (Eba) has limited the number of options available to treat Gram-negative infections. Ceftazidime-avibactam [CAZ-AVI] is a β-lactam-β-lactamase inhibitor combination developed for treatment of carbapenem-resistant and MDR infections caused by β-lactamase-producing Gram-negative bacteria. CAZ-AVI has activity against Eba that carry Class A, C and some Class D β-lactamases, but not Class B metallo-β-lactamases (MBLs). The in vitro activity of CAZ-AVI against Eba collected from patients in Europe from various body sites for the ATLAS Global Surveillance Program in 2016-2018 is evaluated herein.

Materials/methods: 23,655 non-duplicate Eba isolates were collected from 123 sites in 24 countries in Europe from patients with lower-respiratory-tract infections (LRTI), urinary-tract infections (UTI), skin/soft-tissue infections (SSTI), intra-abdominal infections (IAI), and blood infections. Antimicrobial susceptibility was determined by broth microdilution according to CLSI guidelines and EUCAST 2019 breakpoints. Avibactam was tested at a fixed concentration of 4 mg/L. β-lactamase carriage was determined by PCR and sequencing for isolates with meropenem MIC values >1 mg/L.

Results: CAZ-AVI was active against more Eba isolates from LRTI, UTI, SSTI, IAI, and blood than any other comparator (98.5%-99.1% susceptible; Table). Meropenem was also active against these isolates, however when compared to other sources, relatively fewer isolates from LRTI and blood were meropenem-susceptible [95.3% and 95.2% susceptible, respectively]. Among isolates from all sites, ≤82.5% were susceptible to other comparator agents.

Conclusions: CAZ-AVI demonstrated in vitro potency against Eba isolates collected from different infection sites from 2016-2018 in Europe. In contrast to comparator agents, the percentage of isolates susceptible to CAZ-AVI did not vary greatly by infection site.

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**Abstract 2065**

**Mycobiome-microbiome cross-talk analysis during acute pulmonary exacerbation: focus on climax-attack model in cystic fibrosis**

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**Background:** Lung infections play a critical role in cystic fibrosis (CF) pathogenesis, especially in CF pulmonary exacerbation (CFPE) and decreases in respiratory function (i.e., FEV1 decline). CF respiratory tract is now considered as a polymicrobial ecosystem that NGS allowed to analyze deeply in terms of mycobiome and microbiome. To the best of our knowledge, no data have been generated in regards of the mycobiome and the microbiome together during CFPE.

**Materials/methods:** Thirty-three sputa isolated from patients with and without CFPE underwent targeted metagenomics, based on analysis of bacterial and fungal rRNA regions (16S and ITS2 regions). Inter-kingdom network and adapted Phy-Lasso method were used to highlight correlations in compositional data. Given the limited number of samples, we chosen to apply a penalized regression method with bootstrap (bootstrap-enhanced Phy-Lasso) for examining associations between microbial genera and clinically relevant features (here CFPE and/or FEV1 decline).

**Results:** As previously described, the decline in respiratory function (FEV1) was associated with a decrease in bacterial diversity. The inter-kingdom network revealed three main clusters organized around Aspergillus, Candida, and Scedosporium genera. We confirmed by in vitro experimentations the cross-domain positive interactions between Aspergillus and Streptococcus predicted by the correlation network. We identified Aspergillus and Malassezia to be associated with CFPE. Scedosporium plus Pseudomonas were associated with a decline in FEV1. Collectively, our findings (inter-kingdom network analysis, in vitro co-culture results, and feature selection based on bootstrap-enhanced Phy-Lasso) pave the way for deciphering the role of fungi in CF lung disease at the ecological level by proposing a new version of the recently-described Climax-Attack Model (CAM).

**Conclusions:** Altogether, these results highlighted the complexity of the microbial community interacting within the CF respiratory tract, and suggested the suitability of developing ecological models such as CAM. For the first time, we included documented mycobiome data into CAM that opens new lines of thoughts about the physiopathology of CF lung disease and future perspectives to improve its therapeutic management.

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Abstract 2068

Effects of a strict postoperative glycaemic control on surgical site infection’s incidence following liver transplantation: a randomised clinical trial

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Abstract third-party references: São Paulo Research Foundation (FAPESP) Brazil, Comissão de Aperfeiçoamento de Pessoal de Nível Superior (CAPES - Ministry of Education) Brazil

Background: Hyperglycemia is an independent risk factor for the development of surgical site infections among liver transplantation recipients. We compared the effects of a postoperative strict blood glucose control protocol against a conservative protocol on the incidence of surgical site infection among liver transplantation recipients.

Materials/methods: In this open-label, two-arm controlled clinical trial we recruited liver transplant recipients in a Brazilian referral centre. Eligible patients were 18 years or older whose allograft came from a deceased donor. We excluded patients who had undergone any kind of surgery in the 30 days before the transplantation. Patients were randomly assigned into two groups: 21 with a conservative blood glucose of 180 mg/dL and 20 with a strict blood glucose of 130 mg/dL. Subcutaneous insulin or continuous intravenous insulin therapy were employed. A blinded adjudication committee analysed the endpoint adopting the surgical site infection criteria given by the CDC. The analysis was by intention to treat.

Results: 41 patients were assigned to either the conservative or strict groups and followed up until 30 days after the liver transplantation. At baseline, the median age was 55.2 years (IQR 49.6-69.4), 31 (75.6%) were male, 30 (75.0%) were white and the median of the model of end-stage liver disease was 18 (IQR 13-21). Within the conservative and strict groups, we have observed: 8 (38.0%) and 6 (30.0%) had diabetes, and the median glycaemia immediately before the anaesthesia was 117.5 mg/dL (IQR 82.5-132.5) and 98 mg/dL (IQR 81-123), respectively. Participants enrolled to strict control presented lower glycaemia median in the first 24 hours after liver transplantation in comparison to those in the conservative group (145 mg/dL [IQR 130-160.3] versus 221.9 mg/dL [IQR 181.3-235.8]; p<0.001). Furthermore, the length of stay was higher among recipients enrolled on the conservative compared to the strict group (17 days [IQR 13-29] versus 15 days IQR 10-19; p<0.05). Five (23.8%) patients in the conservative group developed surgical site infection in contrast to three (15%) from the strict group (RR 0.63 [95% CI 0.17-2.29]; p=0.48).

Conclusions: Using intravenous strict insulin protocol did not reduce the occurrence of surgical site infections among liver transplant recipients.

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Safety and efficacy of fumagillin for the treatment of intestinal microsporidiosis: a French prospective cohort study

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Background: Intestinal microsporidiosis due to Enterocytozoon bieneusi is a rare cause of chronic diarrhea in immunocompromised patients. Fumagillin has been approved in France since 2005 for its treatment. We report on the real-life use of fumagillin.

Materials/methods: As required by the French Medicine Agency, all patients receiving fumagillin were enrolled in a prospective study to assess its safety and parasitic efficacy. Fumagillin was given orally at a dose of 20 mg tid for 14 days. At baseline patients demographics and comediations were collected. Stool examination for the detection of microsporidial spores and identification of E. bieneusi by PCR was performed at baseline, end of treatment [with a window of -5 to + 20 days], and monthly thereafter for 6 months. Safety was monitored up to the 6-month follow-up visit. The primary endpoint was safety. Parasitic clearance and relapse were secondary endpoints. Descriptive statistics were used.

Results: From July 2007 to October 2018, 169 patients from 40 sites received fumagillin. Ninety-nine (59%) were males; median age: 49 years (range: 5-81), 139 (82%) were recipients of solid organ or hematopoietic stem cell transplants, 21 (12%) had HIV-infection, and 9 (5%) other causes of immunosuppression. More than 90% had comediations [antiretrovirals or immunosuppressive drugs]. Median duration of treatment was 14 days (range: 5-23) and treatment was prematurely discontinued in 58 patients (35%). Forty-five patients (26.6%) presented at least one AE, mainly thrombocytopenia (15.4%), neutropenia (4.1%), anemia (1.8%), hepatic disorder (3%) and cutaneous rash (1.8%). Thrombocytopenia (<150 G/L) occurred in 13 patients (81%) with spontaneous recovery after treatment discontinuation. Thirty-five patients (21%) presented a serious AE, mainly thrombocytopenia (13%), and neutropenia (4%), and one patient died of peritoneal hemorrhage following a liver biopsy. At the end of treatment, 122/128 patients (95%) who had a stool examination in the window had no spore detected. Three patients presented a parasitic relapse during follow-up, and 3 patients were treated twice (2 failures and one relapse) with parasitic clearance.

Conclusions: E. bieneusi microsporidiosis was mainly diagnosed in transplant recipients. Fumagillin was associated with hematological toxicity but showed high efficacy with a low relapse rate.

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In vitro Activities of ceftazidime-avibactam and comparators against Pseudomonas aeruginosa from Europe stratified by infection type: ATLAS global surveillance programme 2016-2018

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Background: The non-β-lactam β-lactamase inhibitor avibactam (AVI) is active against class A, class C and some class D β-lactamases, and in combination with ceftazidime (CAZ) has been approved by the FDA and EMA for treatment of infections caused by Gram-negative bacteria including Pseudomonas aeruginosa (Paer). This study reports susceptibility data for CAZ-AVI and comparators for recent (2016-2018) clinical Paer isolates from Europe stratified by infection source.

Materials/methods: From 2016-2018, 6574 non-duplicate Paer isolates were collected from 123 sites in 24 countries in Europe as part of the ATLAS surveillance study from lower respiratory tract infections (LRTI), urinary tract infections (UTI), intra-abdominal infections (IAI), skin and soft tissue infections (SSTI) and blood infections. Susceptibility testing was by broth microdilution according to the ISO standard method and interpreted using EUCAST 2019 breakpoints. CAZ-AVI was tested with a fixed concentration of 4 mg/L avibactam. When meropenem MIC values were >2 mg/L, the β-lactamase gene content was assessed by PCR and sequencing.

Results: Among the various infection sources, CAZ-AVI susceptibility percentages ranged from 90.7% (UTI and blood) to 93.5% (SSTI). The addition of AVI to CAZ increased its activity against Paer from all infection sources, with the most dramatic being LRTI isolates (% susceptibility increasing from 73.7% to 90.7%, and MIC90 falling to 8 mg/L from 64 mg/L for this population). Among the comparators, only colistin exhibited superior activity against Paer.

<table>
<thead>
<tr>
<th>Source (n)</th>
<th>CAZ-AVI</th>
<th>CAZ</th>
<th>MEM</th>
<th>TZP</th>
<th>LVX</th>
<th>CST</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (6574)</td>
<td>91.5%</td>
<td>8%</td>
<td>76.9%</td>
<td>64%</td>
<td>73.1%</td>
<td>&gt;8</td>
</tr>
<tr>
<td>LRTI (2877)</td>
<td>90.8%</td>
<td>8%</td>
<td>73.7%</td>
<td>64%</td>
<td>69.5%</td>
<td>&gt;8</td>
</tr>
<tr>
<td>UTI (886)</td>
<td>90.7%</td>
<td>8%</td>
<td>79.0%</td>
<td>64%</td>
<td>75.1%</td>
<td>&gt;8</td>
</tr>
<tr>
<td>IAI (460)</td>
<td>90.9%</td>
<td>8%</td>
<td>80.0%</td>
<td>64%</td>
<td>75.0%</td>
<td>&gt;8</td>
</tr>
<tr>
<td>SSTI (1792)</td>
<td>93.5%</td>
<td>8%</td>
<td>80.4%</td>
<td>32%</td>
<td>78.2%</td>
<td>&gt;8</td>
</tr>
<tr>
<td>Blood (559)</td>
<td>90.7%</td>
<td>8%</td>
<td>76.2%</td>
<td>64%</td>
<td>70.8%</td>
<td>&gt;8</td>
</tr>
</tbody>
</table>

*CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; TZP, piperacillin-tazobactam; LVX, levofloxacin; CST, colistin.

Conclusion: CAZ-AVI continues to demonstrate good in vitro activity against Paer isolates in Europe regardless of infection site. It was the second most active agent tested, eclipsed only by colistin, a last-resort agent with known toxic side effects.

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**Abstract 2074**

**In vitro activities of ceftazidime-avibactam and comparator agents against Gram-negative isolates from China as part of the ATLAS global surveillance programme 2018**

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**Background:** Avibactam (AVI) is a β-lactamase inhibitor with potent inhibitory activity against Class A, Class C, and some Class D serine β-lactamases. The combination of ceftazidime (CAZ) with AVI has been approved in Europe and in the United States for several indications. This study evaluated the *in vitro* activity of CAZ-AVI and comparators against Enterobacterales (Eba) and *Pseudomonas aeruginosa* (Pae) isolates collected from patients in China as part of the ATLAS surveillance program in 2018.

**Materials/methods:** A total of 1,425 Eba and 386 Pae non-duplicate clinically significant isolates, were collected by 24 clinical laboratories in China in 2018. Organism identification was confirmed by MALDI-TOF mass spectrometry and susceptibility testing was performed by broth microdilution following CLSI guidelines at a central laboratory [Peking Union Medical College Hospital, Beijing, China] using broth microdilution panels [supplied by IHMA, Schaumburg, IL, USA]. CAZ-AVI was tested at a fixed concentration of 4 mg/L AVI. MICs were interpreted using current EUCAST [2019, v 9.0] MIC breakpoint criteria.

**Results:** Susceptibility data are shown in the Table. CAZ-AVI showed potent *in vitro* activity against all Eba isolates, including CAZ-NS and colistin-resistant (CST-R) subsets (87.2% and 95.8% S, respectively), with reduced activity against MEM-NS Eba (66.5% S). CAZ-AVI also showed good *in vitro* activity against all Pae isolates (MIC90, 8 mg/L, 90.7% S). Activity was reduced against CAZ-NS, MEM-NS and CST-R subsets (70.8%-87.5% S), but exceeded the activity of CAZ and MEM against these subsets. CST and amikacin were the only tested comparators that demonstrated comparable or greater activity against Pae isolates.

<table>
<thead>
<tr>
<th>Organism/Phenotype (n)</th>
<th>CAZ-AVI</th>
<th>CAZ</th>
<th>MEM</th>
<th>AMK</th>
<th>CST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enterobacterales, all (1,425)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>94.0</td>
<td>&gt; 128</td>
<td>52.7</td>
<td>&gt; 16</td>
<td>85.1</td>
</tr>
<tr>
<td>CAZ-NS (674)</td>
<td>64</td>
<td>87.2</td>
<td>&gt; 128</td>
<td>0</td>
<td>&gt; 16</td>
</tr>
<tr>
<td>MEM-NS (212)</td>
<td>&gt; 64</td>
<td>66.5</td>
<td>&gt; 128</td>
<td>1.4</td>
<td>&gt; 16</td>
</tr>
<tr>
<td>CST-NS (96)*</td>
<td>2</td>
<td>95.8</td>
<td>128</td>
<td>56.3</td>
<td>&gt; 16</td>
</tr>
<tr>
<td><strong>P. aeruginosa, all (386)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>90.7</td>
<td>128</td>
<td>68.9</td>
<td>&gt; 16</td>
<td>64.5</td>
</tr>
<tr>
<td>CAZ-NS (120)</td>
<td>32</td>
<td>70.8</td>
<td>&gt; 128</td>
<td>0</td>
<td>&gt; 16</td>
</tr>
<tr>
<td>MEM-NS (137)</td>
<td>32</td>
<td>74.5</td>
<td>&gt; 128</td>
<td>40.9</td>
<td>&gt; 16</td>
</tr>
<tr>
<td>CST-NS (56)</td>
<td>16</td>
<td>87.5</td>
<td>128</td>
<td>57.1</td>
<td>&gt; 16</td>
</tr>
</tbody>
</table>

CAZ-AVI, ceftazidime-avibactam; CAZ, ceftazidime; MEM, meropenem; AMK, amikacin; CST, colistin; NS, non-susceptible; R, resistant; % Susceptible was determined using CLSI 2019 breakpoints

*Excludes isolates of Proteaeae and Serratia spp., which are intrinsically resistant to colistin

**Conclusions:** CAZ-AVI demonstrated potent *in vitro* activity against Eba and Pae isolates collected in China in 2018 as a part of the ATLAS global surveillance program.

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Neurological manifestations of rickettsiosis

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Background: Rickettsiosis, a relatively benign disease, typically manifests with fever, skin rash, and headache. Neurological complications may occur, changing the prognosis and could even become permanent. In this perspective, the aim of this work was to determine the clinical, biological and therapeutic characteristics of neurorickettsiosis.

Materials/methods: We conducted a retrospective study including all patients hospitalized for rickettsiosis in infectious diseases department between 1998 and 2018. The diagnosis was confirmed by serological tests.

Results: During the study period, 410 patients with rickettsiosis were identified, among whom 48 patients (11.7%) had neurological manifestations. There were 28 male (58.3%). The median age was 25 years [9-82 years]. Thirty-three patients had a close contact with dogs (68.7%). The majority of cases occurred during the hot season, between May and October (44 cases; 91.6%). The most common revealing symptoms was fever and headache, noted in all cases, followed by arthralgia, noted in 35 cases (72.9%). Vomiting was noted in 33 cases (68.7%). Physical examination showed meningeal syndrome in 31 cases (64.5%) and maculopapular skin rash in 16 cases (33.3%). Laboratory investigations revealed thrombocytopenia (37.5%) and liver cytolysis (35.4%). The most common clinical presentation was meningitis, noted in 42 cases (87.5%). There were 29 cases of lymphocytic meningitis (69%) and 13 cases of meningitis with neutrophil predominance (31%). Meningoencephalitis was noted in 6 cases (12.5%). The patients received doxycycline in 39 cases (81.2%) and fluoroquinolones in 9 cases (18.8%). The mean duration of treatment was 10 ± 2 days. The disease evolution was favorable in all cases. Complications such as epileptic seizure were noted in 2 cases (4.1%).

Conclusions: Rickettsiosis is a benign disease once diagnosed and treated on time. It should be bearded in mind in front of acute fever and maculopapular rash, especially during hot season.

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Abstract 2080

Differential drug susceptibility patterns of Mycobacterium avium complex isolates recovered in Greek university hospitals

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Background: Mycobacterium avium complex (MAC) includes a group of mycobacterial pathogens that causes disease in susceptible hosts. Current treatment recommendations for MAC infections include a macrolide, a rifamycin (rifampin or rifabutin) and ethambutol with or without a fourth agent such as amikacin. In this study, we investigated the in vitro drug susceptibility patterns of individual MAC species for antimicrobial agents commonly used to treat MAC infections.

Materials/methods: We studied 73 M. avium and 55 M. intracellulare clinical strains recovered from 128 different patients. The minimum inhibitory concentrations (MICs) for clarithromycin, amikacin, moxifloxacin, linezolid, streptomycin, ethambutol, rifampicin and rifabutin were determined using a commercial broth microdilution method (SLOMYCOI, TREK Diagnostic systems), according to the CLSI recommendations and MICs were interpreted based on CLSI breakpoints for clarithromycin (S ≤ 8 mg/l) and amikacin (S ≤ 16 mg/l) and tentative breakpoints for moxifloxacin [S ≤ 8 mg/l] and linezolid (S ≤ 8 mg/l) (CLSI documents M24 and M62, 2018). Also, the MIC50 and MIC90 were determined and finally “tentative” epidemiological cutoff (ECOFF) values were determined by the ECOFFinder algorithm.

Results: Clarithromycin wild-type populations were mostly classified as susceptible, with MIC90 of M. avium and M. intracellulare to be equal to ECOFF (8 mg/l and 4 mg/l respectively). Overall, 121 MAC strains (94.5%) were susceptible to clarithromycin, while only 4 (3.5%) M. avium and 3 (5.5%) M. intracellulare strains were resistant (MIC > 64 mg/l). For amikacin, the CLSI breakpoints split the wild-type populations for both species (MIC90 = MIC50 = 32 mg/l). Thirty-eight (70.4%) of M. intracellulare but only 32 (43.8%) M. avium strains were categorized as susceptible to amikacin. Tentative moxifloxacin and linezolid CLSI breakpoints split also the wild-type populations. Only 2.3% (3/128) of MAC strains were categorized as susceptible to moxifloxacin and linezolid. Rifabutin MICs for both species were lower than those of rifampicin. No ECOFFs could be set for rifampicin, ethambutol and streptomycin due to truncation of MIC distributions.

Conclusions: The in vitro drug susceptibility patterns of the different MAC species studied are comparable to each other. Except for clarithromycin, current breakpoints for MAC categorization should be reevaluated.

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Drain water as a potential source of in-hospital room-to-room transmission of carbapenemase-producing Klebsiella pneumoniae

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Background: Carbapenemase-producing Enterobacterales [CPE] have rapidly emerged in Europe with OXA-48 producing Klebsiella pneumoniae as one of the prominent causes of nosocomial outbreaks. Toilets may produce potentially infectious aerosols during flushing to which subsequent toilet users may be exposed. The study of an outbreak suggests that CPE can also be transmitted between patients staying in different hospital rooms via toilet plume aerosols.

Materials/methods: A total of 14 OXA-48 producing K. pneumoniae isolates collected over 4 months’ time were sequenced, including 12 isolates involved in an outbreak at the burn center (containing six linearly positioned rooms with open bathrooms) of Ghent University Hospital and two random strains. The outbreak isolates were five isolates obtained from rectal swabs [patients residing in rooms 1,3,6], four from toilet water [rooms 2,3,4,6], two from toilet water after 2 months of daily disinfection with bleach [rooms 3,4], one from drain water [between rooms 4 and 5]. Whole genome sequencing was performed on a HiSeq300 instrument (Illumina,USA) in single-end mode generating 50-bp reads. FASTQ files were quality-trimmed and de novo assembled using CLC Genomics Workbench [CLC Bio,Denmark]. Whole-genome Multilocus Sequence Typing was performed to determine phylogeny by using Ridom SeqSphere+ [Ridom GmbH,Germany].

Results: A coverage of 262 to 485-fold was obtained with 196 to 260 contigs per isolate. Phylogenetic analysis revealed isogenicity (<15 allele differences) of all isolates obtained from the outbreak (Figure 1). This suggests that the isolate persisted despite disinfection and may have spread between different rooms by drain water. Unexpectedly, one random isolate obtained from a patient who became colonized whilst residing at the geriatric ward in another building belonged to the same genetic cluster, suggesting the outbreak to be larger than expected. There was no obvious link between this patient and the burn center.

Conclusions: Drain water may be a potential source of hospital room-to-room transmission of carbapenemase-producing K. pneumoniae. Further research is needed to map the actual size of the hospital outbreak.

Figure 1:Phylogenetic tree of Klebsiella pneumoniae isolates with isogenic isolates indicated in blue, the non-isogenic isolate in red, control isolates underlined and number of allele differences presented on the branches.

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Abstract 2086

Imipenem/relebactam pharmacokinetic/pharmacodynamic analyses from an in vivo neutropenic mouse delayed lung infection model

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**Background**: Relebactam (REL) is a small molecule beta-lactamase inhibitor which has shown significant antibacterial activity against imipenem-resistant strains in combination with imipenem/cilastatin. Based on previous analyses using an in vitro hollow fiber model and an in vivo mouse thigh infection model, we assumed the REL PK/PD driver was $\frac{AUC_{0-24hr}}{MIC}$. We conducted PK/PD analyses utilizing data from an in vivo neutropenic mouse delayed lung model to derive REL $\frac{AUC_{0-24hr}}{MIC}$ associated with stasis, 1-log kill and 2-log kill targets.

**Materials/methods**: Previously conducted PK/PD murine delayed lung model studies were used for generation of the pooled PK/PD dataset. This dataset consisted of nine isolates of *Pseudomonas aeruginosa* at imipenem doses thirteen-fold below the humanized dose with varying total daily doses of REL. A Population PK model was used to estimate the $AUC_{0-24hr}$ for each mouse from measured concentrations in each respective study. Correlation analysis using the pharmacokinetic (PK) exposure and response [change in log$_{10}$ CFU at 24 hours post-dose] was plotted against $\frac{AUC_{0-24hr}}{MIC}$. Imipenem MICs in the presence of 4 mg/L of REL were used to derive the $\frac{AUC_{0-24hr}}{MIC}$ for each strain. An Emax model with Hill coefficient was used to fit the data. Stasis, 1-log kill, and 2-log kill PK/PD targets were derived from this model.

**Results**: There appeared to be a relationship between $\frac{AUC_{0-24hr}}{MIC}$ and change in log$_{10}$ CFU at 24 hours in the murine delayed lung model data. The derived stasis, 1-log kill, and 2-log kill $AUC/MIC$ PK/PD targets for *Pseudomonas aeruginosa* were 0.1, 0.3 and 8.0 respectively. This 2-log kill PK/PD target is consistent with previous analyses in an in vitro hollow fiber infection model and an in vivo mouse thigh model.

**Conclusions**: PK/PD analyses using pooled data from nine isolates of *Pseudomonas aeruginosa* confirmed that $\frac{AUC_{0-24hr}}{MIC}$ is the PK/PD driver for REL. The derived 2-log kill target can be used for dose justification and probability of target attainment (PTA) assessment for fixed dose combination of imipenem/cilastatin/relebactam.

Figure. PK/PD Relationship of REL in the Neutropenic Mouse Lung Infection Model at imipenem 5 mg/kg for *Pseudomonas aeruginosa* [Left] and overlaid with observed mouse thigh infection model [Right]

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Abstract 2088

Evaluating the usefulness of whole genome sequencing in tuberculosis treatment decisions in a low-incidence clinical setting

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Abstract third-party references: This work is funded by the National Institute for Health Research (NIHR) Imperial Biomedical Research Centre (BRC).

Background: Whole genome sequencing (WGS) has been implemented in the UK as part of routine diagnostics for the detection of Mycobacterium tuberculosis and susceptibilities. No study has yet described the impact of WGS on clinical decision making for TB drug treatment regimens in a real-life clinical setting.

Materials/methods: A retrospective analysis of 189 cases from January 2018 to March 2019 in London. Demographics and clinical data were collected. Susceptibility results by WGS and turn-around times (TAT) were correlated to alterations in drug treatment.

Results: 80/189 cases had positive culture and WGS results. The median age was 40 years (IQR 28-53.5), Male:Female was 46:34, 3 patients with HIV and 3 had previous TB.

50/80 had fully sensitive TB to 1st line treatment on WGS. In the remaining 30/80 cases, WGS showed drug resistance, failed or unknown results for 1st line treatment and required additional phenotypic drug sensitivity testing (DST).

20/80 had treatment decision changes but only 12 were defined by WGS. 9/12 were due to isoniazid resistance (excluding the 2 MDR-TB cases). For these 12 cases the median time for culture positivity was 16 days (IQR 13.5-19.5). Median TAT from collection to WGS results in the centralised lab was 35 days (IQR 32.5-36.25) resulting in the median time on the incorrect treatment of 42 days (IQR 27-59). The median time for DST results was 86 days (IQR 70.5-94.25).

63/80 had rapid TB PCR of which 50 cases were positive. 4/9 of the isoniazid resistant cases were PCR positive with an additional 2/9 with ‘Trace’ readings. Both MDR-TB cases were positive on PCR with rifampicin resistance being identified.

Conclusions: WGS is helpful in determining the correct treatment regimen but in our cohort this took over a month. We highlight the important issue of isoniazid resistance and delayed identification of this. This stresses the need for an extended panel of susceptibilities using rapid PCR at the point-of-care [in addition to rifampicin] in order to inform immediate treatment choices and reduce the number of days on suboptimal treatment. WGS continues to have a valuable role especially for transmission data and outbreak detection.
Abstract 2089

In vitro antimicrobial susceptibility testing of rapidly growing mycobacteria isolated in a university hospital, Athens, Greece

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Background: Several species of rapidly growing mycobacteria (RGM) are now recognized as human pathogens and antimicrobial susceptibility testing is important since susceptibility pattern is variable within RGM species. In this study we recorded the antibiotic susceptibilities of clinical RGM strains recovered over 13 years (1/2007-10/2019) in a University Hospital in Athens, Greece.

Materials/methods: We studied 25 Mycobacteroides abscessus (16 M.abscessus subsp. abscessus, 6 M.abscessus subsp. bolletii, and 3 M.abscessus subsp. massiliense), 23 Mycolicibacterium fortuitum, 9 Mycobacteroides chelonae, 7 Mycolicibacterium peregrinum, 3 Mycolicibacterium mucogenicum, 4 Mycolicibacterium neoaurum, 2 Mycolicibacterium canariense and 1 Mycolicibacterium phlei non-duplicate clinical strains recovered from 73 different patients. Identification was performed with sequencing of hsp65 gene. The minimum inhibitory concentrations [MICs] for clarithromycin, amikacin, ciprofloxacin, moxifloxacin, linezolid, cefoxitin, imipenem, trimethoprim-sulfamethoxazole, doxycycline, tigecycline, minocycline and tobramycin were determined using a commercial broth microdilution assay (RAPMYCOI, TREK Diagnostic systems), according to the CLSI recommendations and MICs were interpreted based on CLSI breakpoints (documents M24 and M62, 2018), except for tigecycline and minocycline, for which only MIC90 were determined. To investigate possible inducible clarithromycin resistance that is common among M.abscessus isolates, the incubation period was extended up to 14 days.

Results: The RGM species tested were commonly susceptible to amikacin and linezolid (susceptibilities 77.8-100%) and resistant to doxycycline (susceptibilities 4-34%) and cefoxitin (susceptibilities 8-29%). Only 20% of the M.abscessus strains were susceptible to clarithromycin, 18 (72%) strains had inducible and 2 (8%) acquired resistance. On the other hand, 90% of M.chelonae, and 57% of M.fortuitum strains were susceptible to clarithromycin. The M.abscessus and M.chelonae strains were highly resistant to ciprofloxacin, moxifloxacin, imipenem and trimethoprim-sulfamethoxazole (resistances 88-96%), while M. fortuitum strains (susceptibilities 64-87%) were susceptible to these drugs. Of the M.chelonae strains, 80% were susceptible to tobramycin, while 84% of M.abscessus and 68% of M.fortuitum strains were tobramycin-resistant. The MIC50/MIC90 values for tigecycline were 0.5/1 μg/ml for M.abscessus and 0.1 2/0.5 μg/ml for M.fortuitum while the respective values for minocycline were >8 μg/ml for both species.

Conclusions: The high variation of susceptibility profiles within RGM species confirms the need for accurate identification and susceptibility testing for clinically relevant strains.

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Abstract 2091

**Which HIV-positive men who have sex with men patients benefit of anal cancer screening?**

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**Background:** Our main objective was to analyze the incidence of HSILs and ASCC (HSIL+) in anal mucosa of HIV+ MSM, and the risk factors related.

**Materials/methods:** The study included consecutive HIV-infected MSM between May 2010 and December 2018. Data were gathered at baseline and annually on their sexual behavior, CD4 and CD8 levels, HIV VL, and anal cytology, HPV PCR, and high-resolution anoscopy (HRA). Patients with normal HRA and LSIL were evaluated annually with cytology, HPV PCR, and HRA besides in case of LSIL. There were two options for HSIL: mucosectomy with electrosurgical procedure (from May 2010 onwards); or self-administration of 5% imiquimod 3 times/week/16 weeks (from November 2012 onwards). When ASCC was detected, patients were sent to the oncology Service. Between May 2012 and May 2014, the qHPV vaccine was administered to 66 patients.

**Results:** Among the 405 patients, 87.2% had at least two control HRA with a median follow-up of 36 months (IQR: 12-69). During this period, there were 38 new cases of HSIL (incidence of 30.86/1,000 patient-years) and 1 new case of ASCC (incidence of 81.22/100,000 patient-years). One ASCC was resolved with wide local surgery; another was treated with abdominal-pelvic amputation, chemotherapy, and radiotherapy and has been in remission for 12 months; and the third patient with ASCC died at 15 months post-diagnosis after chemotherapy and radiotherapy. 49 HSILs were treated by mucosectomy and 34 with intra-anal 5% imiquimod. None of HSIL progressed to ASCC. We found significant reductions in HSIL+ between 2010 and 2018 (42.9% vs. 4.1%, p=0.034). Risk factor related to HSIL+ were HPV 11 (OR 4.153; CI95% 1.85-9.3), HPV 16 (OR 2.74, CI 95% 1.189-6.34), HPV 53 (OR 3.67, CI95% 1.141-11.79); HPV 61 (OR 13.98, CI 95% 3.74-52.2); HPV 68 (OR 2.773 CI 95% 1.121-6.86); presence of mixture infection by Low and High-Risk HPV (OR 1.058; CI95% 1.003-1.116), and low CD4 nadir (OR1.002; CI95% 1-1.004).

**Conclusions:** The reduction in HSIL+ rate observed in our patients may be attributable to the bundle of measures adopted at our center. The chronic mixture infection by HPV and low level of CD4 nadir were related to HSIL

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Abstract 2092

**Blood culture contamination is commonly associated with divergent blood culture sets**

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**Background:** Contamination of blood cultures by nonpathogenic bacteria is associated with diagnostic uncertainty and health care costs. Diversion of the initial blood specimen during venipuncture, potentially containing skin organisms, is suggested to reduce contamination. Since blood culture sets include two bottles taken sequentially directly from the Vacutainer device (used for all blood cultures in our institution), the first bottle could act as a "diversion device" for the second bottle. If diversion is effective in reducing blood culture contamination, it might be expected that contaminated sets would be positive in only one bottle, whereas both bottles would grow true pathogens.

**Materials/methods:** We retrospectively reviewed all blood cultures drawn over 15 years. Blood isolates were defined prospectively as pathogens or contaminants. Blood culture sets were **convergent** if both culture bottles were positive for the same organism and **divergent** if only one bottle was positive. Convergent and divergent sets of blood cultures were compared. Growth patterns in aerobic or anaerobic media were not taken into account.

In order to test the results in a homogeneous bacterial population, we assessed the subgroup of blood cultures growing only *Staphylococcus aureus* (SA) or *Coagulase-negative Staphylococci* (CoNS). These bacteria have similar growth patterns in aerobic and anaerobic media, and yet commonly represent a true pathogen and a common contaminant.

**Results:** From 2004 to 2019, blood cultures sets were collected on 384,284 occasions. Most culture sets were sterile (n=332,510, 87%). One or both bottles were positive in 51,774 (13%) sets and overall 55,247 isolates were identified. Pathogens grew in 29,088 (7.6%) of all sets taken. Of these sets 12,577 (43%) were divergent. Contaminants grew in 26,159 (6.8%) of all sets taken. Of these sets 19,591 (75%) were divergent (p<0.001 vs pathogens, Figure). Amongst sets positive for SA and CoNS, 14,605/54,455 (27%) and 11,700/18,148 (64%) were divergent, respectively (p<0.001).

**Conclusions:** Blood culture sets growing contaminants are much more frequently divergent than sets growing pathogens. This may support the theory that diversion is a tool to reduce culture contamination.

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Epidemiology of *Pneumocystis jirovecii* pneumonia in HIV-negative patients from 2005-2014 in the United States

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**Background:** *Pneumocystis jirovecii* pneumonia (PJP) is an opportunistic infection seen in patients with immunosuppressive conditions. Systematic studies to identify patients at greatest risk are lacking.

**Materials/methods:** Using the Nationwide Inpatient Sample, a 20% stratified sample of hospital discharges in the United States, we performed a cross-sectional study from 2005-2014 to estimate relative risk of PJP. Human Immunodeficiency Virus (HIV)-negative patients with hospital admission for PJP were identified using International Classification of Diseases, 9th Edition (ICD-9) codes. All ICD-9 and Disease Related Group (DRG) codes were reviewed and ranked to identify the most common associated conditions. Relative risk of PJP was calculated using all other adult non-obstetric hospitalizations as a comparator group.

**Results:** Among 77,177,931 hospitalizations, a total of 14,245 HIV-negative patients with PJP were identified (1.84 PJP cases / 10,000 admissions). Relative risk for PJP was greatest among nonmalignant hematologic conditions and autoimmune conditions (RR = 26.8 and 25.6, respectively) (Figure 1). Elevated risk was also observed for solid organ transplant (RR = 17.1), hematologic malignancy (RR 14.6), and disorders affecting cortisol (RR 14.1). Solid organ malignancy demonstrated only slight increased risk (RR = 3.7). Zero patients with multiple sclerosis, muscular dystrophy, or myasthenia gravis required hospital admission for PJP over this 10-year period, despite prolonged high-dose corticosteroid administration to many of these patients.

**Conclusions:** Among all immunosuppressive conditions, risk for PJP varies widely and is likely affected by corticosteroid use, T-cell and B-cell function, and provider awareness of PJP risk and prophylaxis. However, neurologic conditions associated with high-dose prolonged corticosteroid use confer no increased risk of PJP.
Abstracts 2020

ABSTRACT BOOK – 30th ECCMID 2020

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**Abstract 2096**

**Occurrence, susceptibility profiles, evaluation of synergistic activity of isavuconazole or voriconazole plus anidulafungin and genetic characterisation of Candida auris detected in a surveillance programme**

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**Abstract third-party references:** This study was performed by JMI Laboratories and supported by Pfizer, Inc., which included funding for services related to preparing this abstract.

**Background:** C. auris have recently emerged worldwide as a cause of nosocomial outbreaks. This organism often displays high fluconazole MIC values and some strains also have high MIC results for echinocandins and amphotericin B. We evaluated the occurrence of C. auris in 13 years of surveillance, performed synergy testing for an echinocandin and 2 azoles and genetically characterized these isolates using whole genome sequencing analysis.

**Materials/methods:** A total of 15 C. auris isolates were identified in the SENTRY Program and susceptibility tested by CLSI reference broth microdilution. These and other 21 isolates from other collections were tested for synergy against anidulafungin plus voriconazole or isavuconazole using checkerboard CLSI panels. Surveillance isolates were analyzed for genetic relatedness and resistance mechanisms described in C. auris.

**Results:** During 2006-2018, 15 C. auris isolates were collected among 16,273 Candida species consecutively collected from invasive infections (0.09%). Only 1 isolate was recovered before 2013 (2009) and 1-2 isolates were recovered in 2013-2017, but 7 (0.4%) isolates were collected in 2018. Applying the CDC tentative breakpoints, all isolates were susceptible to echinocandins, 2 were resistant to amphotericin B and 12 were resistant to fluconazole. Among the fluconazole-resistant, 10 had an Erg11 K143R alteration, 1 had the Y501H and no resistance mechanism was observed in the remaining isolate. Synergy or partial synergy was noted in 4 (11.1%) and 16 (44.4%) of the isolates with the combination of anidulafungin plus voriconazole and 13 (36.1%) and 24 (66.6%) isolates for the combination anidulafungin plus isavuconazole. Noteworthy, synergy was not observed among the surveillance isolates but only among isolates from other collections and antagonism was not noted. MLST analysis was performed based on ITS, D1/D2, RPB1 and RPB2 sequences showed that isolates from US were genetically related, but different from isolates from Latin America (Panama and Colombia) that were related and Germany.

**Conclusions:** The increase in C. auris worldwide was also captured by the SENTRY Program. Isolates collected from invasive candidiasis were not as resistant as the ones described in the literature, with exception of fluconazole. Combinations of echinocandins and azoles displayed synergy/partial synergy against C. auris.

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Abstract 2100

Particularities of brucellar spondylodiscitis

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Background: Osteoarticular involvement is the most frequent complication of brucellosis. A delayed diagnosis of brucellar spondylodiscitis (BSD) may lead to serious complication and neurologic sequelae. We aimed to study the epidemiological, clinical and evolutionary features of BSD.

Materials/methods: We conducted a retrospective study including all cases of spondylodiscitis hospitalized in infectious diseases department between 2001 and 2017. The diagnosis of BDS was based on positive Brucella seroagglutination test (100%) or the isolation of Brucella species from blood culture (21%) associated to signs of spondylodiscitis on imaging.

Results: During the study period, we enrolled 160 cases of spondylodiscitis, among whom 44 patients had BSD (27.5%). There were 34 males (77.3%). The mean age was 50 ±16 years. Thirty-nine patients (88.6%) came from rural area and 40 patients (90.9%) consumed non-pasteurized milk. Six patients had a history of treated brucellosis (13.6%). Patients consulted after a median duration of 4 months [1-13 months]. All patients presented back pain, which was associated to fever in 35 cases (79.5%) and night sweats in 32 cases (72.7%). Thirteen patients had neurologic deficit (29.5%). Laboratory tests investigations revealed an elevated erythrocyte sedimentation rate in 29 cases (65.9%) and an elevated C-reactive protein in 25 cases (56.8%). Lumbar involvement was the most common level of involvement, noted in 30 cases (68.1%). Fine-needle aspiration biopsy was performed in 10 cases (22.7%). All patients were treated with doxycycline and rifampicin. Cotrimoxazole was associated in 20 cases (45.4%). The mean duration of treatment was 8 ±4 months. Immobilisation was required in 26 cases (59%). The disease evolution was favourable in all cases. However, 16 patients had persistent back pain (36.3%).

Conclusions: Brucellar spondylodiscitis is not rare. It can lead to severe sequelae. In front of back pain and fever, Brucella seroagglutination test and imaging should be performed in order to rule out the diagnosis of BSD.

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Abstract 2105

**Tuberculous spondylodiscitis: diagnostic and therapeutic approach**

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**Background:** Tuberculous spondylodiscitis (TSD) is one of the most common forms of extrapulmonary tuberculosis. Surgical treatment might be associated with antitubercular therapy. The aim of this work was to identify the diagnostic and the therapeutic approach of TSD.

**Materials/methods:** We conducted a retrospective study including all cases of TSD hospitalized in infectious diseases department between 2001 and 2017.

**Results:** In total, we identified 70 cases of TSD. There were 40 females (57.1%). The mean age was 48 ± 19 years. Consumption of non-pasteurized milk was noted in 34 cases (48.6%). Fifty-two patients came from rural area (74.3%) and 4 patients (5.7%) had a history of tuberculosis. The most common clinical presentation was back pain (64 cases; 91.4%) associated to weight loss (36 cases; 51.4%) and night sweats (33 cases; 47.1%). Twenty-two patients had neurologic deficit (31.4%). Abnormal laboratory investigations included elevated inflammatory markers such as elevated erythrocyte sedimentation rate (58 cases; 82.8%), an elevated C-reactive protein level (49 cases; 70%) and leukocytosis (13 cases; 18.6%). Tuberculin intradermal reaction was positive in 55.7% of the cases. Fine-needle aspiration biopsy of vertebral and intervertebral disc lesions was performed in 45 cases (64.3%). It confirmed the diagnosis showing caseous granuloma (71.1%) and/or the presence of *Mycobacterium tuberculosis* (22.2%). The mean duration of antitubercular therapy was 13 ± 6 months. Besides medical treatment, immobilization was required in 54 cases (77.1%). Abscess drainage was performed in 14 cases (20%) and surgical treatment in 13 cases (18.5%). The outcome was favourable in 67 cases (95.7%). Three patients (4.3%) were dead. Sequelae were noted such as persistent back pain in 27 cases (40.2%) and spinal deformity in 18 cases (26.8%).

**Conclusions:** Tuberculous spondylodiscitis was a severe form of tuberculosis requiring antitubercular therapy for the appropriate duration and a regular follow up in order to avoid significant complications.

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Abstract 2106

**Application of whole genome sequencing analysis to detect the azole-resistance mechanisms in Aspergillus fumigatus in a global surveillance programme**

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**Abstract third-party references:** This study was performed by JMI Laboratories and supported by Pfizer, Inc., which included funding for services related to preparing this abstract.

**Background:** Azole-resistance is uncommon among *A. fumigatus* clinical isolates and is mainly associated with mutations in *cyp51A* and its promoter region or its homologue *cyp51B*. We evaluated 35 *A. fumigatus* isolates nonwildtype (NWT) to isavuconazole, itraconazole or voriconazole collected during a 2-year surveillance using whole genome sequencing (WGS) to detect alterations in the genes involved in the ergosterol biosynthesis and others associated with azole resistance.

**Materials/methods:** Among 297 *A. fumigatus* isolates collected worldwide in 2017-2018, 35 isolates displayed NWT MIC values to isavuconazole, itraconazole or voriconazole when tested by the CLSI reference broth microdilution method. These 35 isolates were submitted to WGS and data analysis using previously described tools.

**Results:** Among the 35 NWT isolates, 29 were NWT to isavuconazole, 16 to itraconazole and 9 to voriconazole (M59Ed2 criteria). A total of 9 isolates carried 

Cyp51A L98H/TR34 alterations: 8 from different patients hospitalized in a single Italian hospital and 1 from Belgium. All 9 Cyp51A L98H/TR34 isolates were NWT to both isavuconazole and itraconazole and 8 were voriconazole-NWT. Cyp51A L98H/TR34 isolates belonged to sequence type (ST) 6, ST26 or its single loci variant ST1. None of the other azole-NWT isolates belonged to these STs. Five isolates were NWT to itraconazole alone, 3 of 5 containing Cyp51A I242V. A Cyp51B O42L mutation was detected in 3 isolates, 1 voriconazole-NWT and 2 isavuconazole-NWT of which 1 also harboured multiple mutations in Cyp51A (F46Y, M172V, N248T, D255E and E427K). Two isolates NWT to isavuconazole and itraconazole possessed F46Y, M172V, E427K ± N248T, D255E. Among the 29 isavuconazole-NWT strains, 16 contained alterations in other ergosterol biosynthesis or efflux genes that have not been implicated in azole resistance.

**Conclusions:** Cyp51A L98H/TR34 were noted in 9 isolates that were NWT to both isavuconazole and itraconazole and 8 were NWT to all azoles tested. Other alterations, including F46Y, M172V, E427K± N248T, D255E that have been reported in 10% of the azole-NWT isolates worldwide, were only detected in isolates NWT to isavuconazole and itraconazole. Mutation driven azole resistance mechanisms were not detected in 16 isolates displaying isavuconazole-NWT MIC values that had WT MIC values for other azoles.

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Abstract 2108

Pre-emptive therapy utilisation after haematopoetic cell transplantation

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Background: Preemptive therapy for CMV after HCT is effective in preventing CMV end organ disease but requires antiviral utilization, is associated with toxicities and may require hospitalization. Objectives 1) describe patterns of preemptive therapy (type, duration, setting) 2) describe frequency of toxicities at discontinuation of first PET: 3) impact of letermovir on antiviral days

Materials/methods: Study cohort comprised of adults, CMV R+ HCT recipients of first peripheral blood or marrow allograft at Memorial Sloan Kettering Cancer Center (MSKCC) from 3/2013 to 12/2017. HCT recipients were routinely monitored for CMV using quantitative PCR assay and administered PET as per the standards of care. Data on clinical characteristics, CMV outcomes, PET administration and all-cause and CMV-related inpatient hospitalization were extracted from the electronic medical records/databases.

Results: Of 368 HCT recipients, 176 (48%) received unmodified graft from matched related or unrelated donors [low CMV risk], and 192 (52%) received either ex vivo T-cell depletion or convention graft from mismatched donors [high CMV risk]. Overall, 208 (57%) HCT recipients received PET; and 72% of them were high risk. PET started a median XX (range ) post HCT. The median duration of PET by D180 was x days (Figure 1). Of x antiviral days x [%] were vGCV, x(%) fosc. X(%) days were given before D100 and x(%) were given as outpatient. PET recipients had more readmissions compared to NO PET recipients, and x(%) readmissions were due to CMV at discontinuation of first PET neutropenia (ANC<100 ) was observed t 11.2% and 2% of vGCV and FCN recipients respectively. AKI was observed in nx% and X% of vGCV and FCN recipients respective. After letermovir implementation the incidence of CMV reactivation bD100 was 5.1% compared to PET 53%. There was an overall 95% reduction in antiviral days bD100, including 94% of vGCV days and 88% reduction FCN days.

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Abstract 2109

Tuberculosis prevalence and latent tuberculosis infection management in solid organ transplantation recipients: a part of national snapshot


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Background: Since May 2019 “National Tuberculosis Diagnosis and Treatment guidelines” have been established, active and latent tuberculosis infection (LTBI) screening is recommended in the pretransplant evaluation of the solid organ transplant (SOT) recipients. However, there is still a lack of routine tuberculosis (TB) risk stratification in most of the transplant centers in our country. Therefore, we decided to investigate the pretransplant TB risk evaluation, posttransplant follow up, registry rates, and TB prevalence in a given period.

Materials/methods: Adult (1 > 18) SOT recipients who were evaluated in the pretransplant period between January 2015 and December 2018 and who had undergone tuberculin skin test (TST) and/or interferon gamma releasing assay (IGRA) were included in the study. Five mm induration of TST was accepted positive. Demographic characteristics, prior TB exposure, LTBI screening method and treatment, pre/posttransplantation TB history were recorded from the electronic database of each transplantation unit nationwide and collected in single center for a united database. The findings were shared with “Ministry of Health, General Directorate of Public Health, and Department of Tuberculosis” and checked from the national registry.

Results: In this period, 2266 SOT patients from 14 centers were included. TST and/or IGRA was administered to 766 (33.8%) of them. LTBI screening rate varied according to different centers (2.2-100%). Within these 766 patients, 485 (63.4%) were kidney, 206 (26.8%) liver, 45 (5.9%) lung, and 30 (3.9%) heart transplantation recipients. Isoniazid was given to 203 (26.5%) patients, 104 (51.2%) of whom started treatment post transplantation first day. Among the patients who were under LTBI treatment, 112 (55.2%) were registered in the national registry and 82 (73.2%) of them completed the treatment. We did not observe active...
TB in patients who had undergone LTBI treatment, however within 563 patients who were not treatment for LTBI, 6 (1.06%) of them developed TB.

Conclusions: In our country, we found that only one third of SOT recipients has been evaluated for TB risk, depending on the transplantation units’ pretransplant procedures and transplanted organs. Only one out of four SOT recipients had received LTBI treatment and half of them were registered. As we showed the compliance to national guidelines is low, we suggest performing pretransplant TB risk stratification as a national imperative.

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Characterising clinical and bacterial factors of community-associated carbapenem-resistant Enterobacteriaceae infections

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Background: While most carbapenem-resistant Enterobacteriaceae (CRE) infections are healthcare-associated, community-associated (CA) CRE infections are increasing worldwide. Our goal is to define CA-CRE epidemiology.

Materials/methods: CRACKLE-2 is a prospective, multicenter study of hospitalized patients with CRE. Patients with possible CA-CRE (pCA-CRE) were admitted from home with a CRE culture within 48 hours, not immunocompromised, and had no history of malignancy, renal failure, or liver disease. Patients not meeting the pCA-CRE criteria were classified as having non-CA-CRE with either home origin (HO-non-CA-CRE) or non-home origin (nHO-CRE). Clinical outcomes at 30 days post-culture date were compared by Desirability of Outcome Ranking (DOOR) analysis adjusted for culture source. Outcomes were categorized as clinical response with 0 events (readmission, renal failure, or Clostridioides difficile infection), no clinical response with 1 event, no clinical response with > 1 event, or death. Genetic diversity between strains was characterized by a comparative gene analysis.

Results: Between 06/2016 to 08/2017, 807 patients in the US with CRE were included; pCA-CRE (n=83), HO-non-CA-CRE (n=362), and nHO-CRE (n=362). Klebsiella pneumoniae was the most common CRE; pCA-CRE (72%), HO-non-CA-CRE (58%), and nHO-CRE (76%). Patients with pCA-CRE were more likely to have bacteriuria (65%) than HO-non-CA-CRE (36%) and nHO-CRE (37%; p<0.001, Chi-Square). Of note, pCA-CRE strains, versus HO-non-CA-CRE and nHO-CRE, were less likely to be susceptible to gentamicin (46% vs 62% vs 56%; p=0.031), tigecycline (54% vs 82% vs 73%; p=0.006) and ciprofloxacin (10% vs 25% vs 15%; p<0.001). Overall, CRE genomes had similar distributions of adhesin, virulence and biofilm-associated genes and plasmid types. Using DOOR analysis, where 50% indicates equivalence between groups, the probability that a randomly selected person with pCA-CRE had a better clinical outcome versus HO-non-CA-CRE or nHO-CRE was 65% [95% CI: 56-74%] and 67% [95% CI: 58-76%], respectively.

Conclusions: In this cohort of patients with CRE, 10% had pCA-CRE. The percentage of true CA-CRE is likely lower. Interestingly, while resistance rates to non-carbapenem antibiotics were higher, patients with pCA-CRE had better overall clinical outcomes. Identifying characteristics important for CA-CRE strains will improve early detection of strains with the potential to cause community outbreaks.

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Abstract 2113

Activity of novel β-lactamase inhibitor QPX7728 combined with various β-lactams against Enterobacterales collected from urinary tract infections, including β-lactamase-producing isolates

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Abstract third-party references: This project has been funded in whole or in part with Federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority (BARDA), under OTA number HHSO100201600026C.

Background: Gut colonization by antimicrobial-resistant bacteria have been pointed as the culprit for the increasing prevalence of urinary-tract infections (UTIs) caused by antimicrobial-resistant organisms. Isolates producing β-lactamases that include ESBL and less frequently carbapenemases have been reported as a cause of community-acquired UTIs and are often resistant not only to β-lactams, but also quinolones and aminoglycosides. We tested several IV and oral β-lactams in combination with QPX7728, a novel β-lactamase inhibitor (BLI) active against all β-lactamate classes, against a collection of 407 β-lactam-resistant UTI Enterobacterales isolates collected from a global surveillance study.

Materials/methods: A total of 407 UTI Enterobacterales isolates displaying an MIC ≥2 mg/L for ceftazidime, ceftriaxone, and/or aztreonam were susceptibility tested by reference broth microdilution against various β-lactams ± QPX7728. Among the isolates tested 234 were screened for β-lactamases using whole genome sequencing analysis and included 7 isolates producing KPC, 174 producing CTX-M, 86 oxacillinases with cefepime activity and 24 producing transferrable AmpC enzymes.

Results: Cefepime [MIC50/90, 16/32 mg/L, 25.3% susceptible [EUCAST breakpoints]], ceftriaxone [MIC50/90, 16/>32 mg/L, 23.6%], and ceftolozane [MIC50/90, 8/>32 mg/L] had limited activity against these isolates [Table]. MIC50/MIC90 values for these agents in the presence of QPX7728 at 4 or 8 mg/L were ≤0.015/0.06 or ≤0.015/0.03 mg/L for cefepime, 0.12/0.25 mg/L or 0.03/0.25 mg/L for ceftolozane, 0.06/0.25 mg/L or ≤0.015/0.12 mg/L for ceftriaxone with QPX7728 at 2 or 4 mg/L, respectively. Tebipenem [oral carbapenem; MIC50/90, 1/8 mg/L] combined with QPX7728 at 2 or 4 mg/L had MIC50/MIC90 values at 0.06/0.5 mg/L or ≤0.015/0.25 mg/L. Ertapenem [MIC50/90, 0.06/0.5 mg/L] and meropenem [MIC50/90, 0.03/0.12 mg/L] inhibited all isolates at 1 or 0.5 mg/L, respectively, in the presence of 4 or 8 mg/L of QPX7728. Among comparator agents, the susceptibility rates were lowest for levofloxacin (33.9%) and highest for amikacin (92.9%).

Conclusions: QPX7728 tested at 2 [tested for ceftriaxone and tebipenem only], 4 or 8 mg/L lowered the MIC values for all agents tested to clinically achievable levels where these agents could be active for most isolates tested, including isolates producing common β-lactamases detected worldwide.

<table>
<thead>
<tr>
<th>Agent/combination</th>
<th>% of isolates inhibited at MIC (mg/L):</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.12</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>8.0</td>
</tr>
<tr>
<td>Ceftazidime + QPX7728 at fixed 4 mg/L</td>
<td>95.6</td>
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<td>Ceftazidime + QPX7728 at fixed 8 mg/L</td>
<td>98.0</td>
</tr>
<tr>
<td>Ceftolozane</td>
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<td>Ceftolozane + QPX7728 at fixed 8 mg/L</td>
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</tr>
<tr>
<td>Ceftriaxone</td>
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</tr>
<tr>
<td>Ceftriaxone + QPX7728 at fixed 2 mg/L</td>
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</tr>
<tr>
<td>Ceftriaxone + QPX7728 at fixed 4 mg/L</td>
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<td>Tebipenem</td>
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<td>Meropenem + QPX7728 at fixed 8 mg/L</td>
<td>99.3</td>
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</tbody>
</table>

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Abstract 2114

Incidence of medically-attended influenza and influenza-related hospitalisations by co-morbidities among a commercially insured population in the United States

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Background: Despite broad availability of vaccination, influenza poses a substantial clinical and economic burden, contributing to morbidity, mortality, and healthcare utilisation. This study describes medically-attended influenza incidence and hospitalisation rates among patients with underlying medical conditions.

Materials/methods: All patients enrolled in a health plan in IQVIA’s Real-World Data Adjudicated Claims – US database at the beginning of any of 4 influenza seasons (October 1, 2014 – May 31, 2018) were included in analyses of medically-attended influenza incidence. The seasonal incidence proportion was calculated for patients with ≥1 diagnosis for a medical condition of interest before the start of the influenza season, categorized by Agency for Healthcare Research and Quality (AHRQ) and Centers for Disease Control and Prevention (CDC) definitions. Medically-attended incident influenza cases were defined as an influenza diagnosis with a record of influenza testing within ±14 days or an influenza diagnosis in the primary position during an influenza season. For analyses of influenza-related hospitalisation, the index date was the date of the earliest influenza diagnosis during an influenza season between October 1, 2014 – May 31, 2018. Patients were required to have ≥12 months continuous enrolment before (baseline) and ≥30 days after (follow-up) index. The outcome of interest was hospitalisation during the 30-day follow-up period with a diagnosis of influenza or a pre-defined influenza-related complication in any position.

Results: The average medically-attended influenza incidence proportion over the 2014-2017 influenza seasons was 1.7% and varied by medical conditions of interest (from 2.2% for immunodeficiency/HIV/AIDS, 2.1% for B-cell deficiency, 1.7% for chronic obstructive pulmonary disease, 1.7% for congestive heart failure/valvular disease, and 1.6% for leukaemia/lymphoma/metastatic cancer) and by age. Medically-attended influenza rate was higher in young children than the elderly. Average influenza incidence among all patients ≥65 years of age was 0.8%. Of 1,601,367 influenza patients, 18,509 (1.2%) had ≥1 influenza-related hospitalisation; hospitalisation rates were higher among patients ≥65 years (9.4%) and patients with the above comorbid conditions (7.7%, 15.2%, 13.3%, 9.3%, 13.7%, respectively).

Conclusions: Patients with specific underlying conditions have elevated risks of influenza-related hospitalisation. Additional research is needed to address and alleviate influenza burden in these high-risk populations.

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Abstract 2116

Whole genome sequencing investigation of iGAS outbreak in elderly care

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Background: In the UK, cases of invasive group A streptococcal (iGAS) disease are reported to local Health Protection Teams (HPT) and isolates sent to PHE reference laboratory for emm typing. emm 94.0 is the 6th most common type identified, comprising 5.6% of all typed iGAS isolates in 2019. Six cases in London developed iGAS sepsis due to emm 94.0 strain over a 7-month period in 2019. Prior to disease onset, all six had received care from a community district nursing (DN) team in a care home setting, where it was initially detected, and in the community. We investigated whether there was microbiological evidence to support the epidemiological link identified among these six cases.

Materials/methods: Whole genome sequence (WGS) data was obtained using the Illumina Nextera protocol and run on HiSeq platforms. The analysis included the iGAS emm 94.0 isolates from the six individuals in the cluster, four sporadic cases from same geographical region (1) and four from bordering region (2), all received since January 2019, and 3 isolates (2 patients and 1 staff) linked to a cluster investigated in 2014. These data were used to generate a SNP-based phylogenetic tree of isolates using an in-house pipeline.

Results: Six of the cases from region 1 were within 0-3 SNP (average 1.3 SNP, Cluster 1), and all were cared for by the same DN team. A second cluster (Cluster 2) with 3 isolates from 2019 was identified, with average 3.3 SNP (2-4SNPs), and separate from Cluster 1 by 8-12 SNPs. An average of 28.8 SNPs (0-52 SNPs) was observed for the 18 remaining isolates.

Conclusions: WGS SNP analysis is a powerful method to discriminate between iGAS isolates of the same emm type. In Cluster 1, WGS provided strong microbiological evidence to confirm the outbreak and led to institution of GAS screening and chemoprophylaxis to all members of the DN team. WGS also identified Cluster 2 that was previously undetected and led to further investigations to identify epidemiological links. The large genetic diversity among remaining cases provided evidence to infer that they were sporadic and no further investigations of these cases undertaken.

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**Abstract 2117**

*Lawsonella clevelandensis: an emerging cause of vascular graft infection*

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**Background:** Vascular graft infections (VGI) pose a significant risk of morbidity and mortality. In up to 50% of VGI cases, the causative organism is not established by conventional culture. With the incorporation of 16S ribosomal (r) RNA gene PCR methods, a causative agent may be identified from clinical samples of extracted vascular grafts. We report the first case of VGI due to *Lawsonella clevelandensis*, an anaerobic Gram-positive, partially acid-fast, fastidious organism identified using 16S ribosomal rRNA gene PCR approach.

**Materials/methods:** We reviewed medical records of a 65-year old patient with inferior abdominal aortic aneurysm, status post endovascular aneurysm repair with stent graft who presented with a one-month history of progressive bilateral inguinal pain, fever, chills, night sweats and unintentional weight loss of 30 pounds.

**Results:** Labs revealed leukocytosis of 17.5 x10⁹/L, elevated C-reactive protein at 132.8 mg/L, erythrocyte sedimentation rate at 100mm/hr, and thrombocytosis of 758x10⁹/L. Positron emission tomography showed high fluorodeoxyglucose avidity within the aneurysm wall and graft, along with bilateral psoas abscesses. Vascular graft was removed and replaced with cryopreserved aortobi-iliac graft. Operative specimens including aortic aneurysm sac fluid and aortic tissue were obtained. Aerobic and anaerobic bacterial cultures, fungal culture, and mycobacterial cultures, along with corresponding direct smears, were negative. Histopathology revealed mild to moderate acute inflammatory infiltrate and a cluster of weakly acid-fast, Gram-variable bacilli [Figure 1]. A 16S rRNA gene PCR identified *L. clevelandensis*. As the organism did not grow on cultures for susceptibility testing, the patient was treated with a six-week course of intravenous vancomycin and oral doxycycline therapy, followed by chronic suppression with cefadroxil. The patient’s symptoms resolved, and he recovered well since surgery.

**Conclusions:** *L. clevelandensis* is a highly fastidious anaerobic organism, primarily detected by molecular methods. Clinical infection due to this organism appears to be characterized by localized abscess formation. Cases of disseminated infection have not been reported in the literature. Our case highlights the importance of incorporating molecular methods in cases of vascular graft infection, where conventional cultures are negative.

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Figure 1. Fite stain, 100X magnification demonstrating weakly acid-fast bacilli
Abstracts 2020

Abstract 2118

ESBL-producing *Enterobacteriaceae* in patients with travellers’ diarrhoea: a prospective cohort study

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**Background:** Patients with traveller’s diarrhoea frequently acquire extended spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae* (EPE) upon return from endemic areas. The aim of this study was to investigate the rate and characteristics of EPE carriage in Swedish travellers.

**Materials/methods:** Clinical samples sent for culture of *Campylobacter, Salmonella,* *Yersinia* or *Shigella,* for which the referral stated foreign travel, were included in the study and selectively cultured for EPE on chromogenic selective media (Chrom ID® ESBL and Uri-Select agar with vancomycin). Antimicrobial susceptibility testing was done according to the EUCAST disk diffusion test methodology. Patients positive for EPE were asked to provide cultures after 1, 3, 6 and 12 months to determine prolonged EPE colonization. EPE strains were subjected to WGS on a HiSeq (Illumina) platform, followed by in silico mapping of sequence types, as well as known virulence and resistance genes in the microSAL T pipeline.

**Results:** Eighty-four of 303 patients (28%) carried a total of 92 ESBL-producing *Enterobacteriaceae*. The majority (85; 92%) were *Escherichia coli* and the remaining 7 (8%) were *Klebsiella pneumoniae*. ESBL acquisition was highest for isolates from Africa (54%, 26/49), Asia (45%, 43/95) and North America and the Caribbean (25%, 4/18). For specific countries, highest ESBL acquisition rates were seen for India (100%, 8/8), Egypt (78%, 7/9), Tanzania/Zanzibar/Kenya (78%, 7/9), Cuba (57%, 4/7) and South Africa (50%, 5/10). No imipenem, meropenem, ceftazidime-avibactam or amikacin-resistant strains were found. Out of 82 strains available for WGS, 48 different sequence types were identified, of which 2 were novel. Only 5 strains belonged to ST131. Out of the 75 *E. coli* isolates, 76% carried at least one type 1-fimbriae gene, 29% carried at least one *pap* (encoding p-fimbriae) gene and 31 (41%) were ExPEC/UPEC. Out of 27 EPE positive patients submitting a culture after one year, 8 patients (30%) were positive for EPE.

**Conclusions:** A relatively high proportion of patients with travellers' diarrhoea carry EPE with a broad diversity of sequence types. A comparatively high proportion of the strains were ExPEC/UPEC, many expressing virulence genes *pap* and/or *fim*. Continuous EPE carriage one year after travel was common but with heterogeneity in EPE strains.

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Abstract 2121

Bloodstream infection survey in high-risk oncology patients (BISHOP) with fever and neutropenia (FN) in the United States: Gram-negative susceptibility and treatment patterns

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Abstract third-party references: Supported by Merck

Background: Gram-negative (GN) bloodstream infections (BSI), that occur during febrile neutropenia (FN), cause significant morbidity and mortality in high-risk (HR) patients receiving chemotherapy for HSCT or hematologic malignancy (HM). Antibiotic regimens to empirically treat FN should be driven by BSI microbiological epidemiology in this population, yet no recent U.S. data exists. The BISHOP study aimed to describe contemporary BSI profiles among HR patients at U.S. cancer centers. Herein we describe GN BSI data to aid rational development of empirical antibiotic recommendations.

Materials/methods: In a prospective survey (12/2016-06/2019) at 14 high-volume US cancer center, bacterial isolates and 30-day clinical data were collected from consecutive HR FN patients with BSI with first fever after cytotoxic chemotherapy. UNMC laboratory determined MICs using broth microdilution susceptibility panels. Isolates were coded as Susceptible (S) or Non-susceptible (NS) using breakpoints defined by CLSI. NS included both intermediate and resistant.

Results: Among 442 patients, 478 aerobic GNR, were identified, including polymicrobial BSIs. 460 were available for testing, including most commonly, E. coli (49%), Klebsiella pneumoniae (18%), Pseudomonas aeruginosa (15%), and Enterobacter cloacae (9%). The most frequent initial antibiotic regimen (IAR) was cefepime (63.3%). Susceptibility to common IARs and fluoroquinolone prophylaxis is displayed (figure). Notably, 22% and 74% of E. coli isolates are NS to cefepime and levofloxacin respectively. Carbapenems retain excellent activity against the Enterobacteriaceae, but piperacillin-tazobactam susceptibility is reduced among Enterobacter spp. Variability in carbapenem susceptibility was noted in Pseudomonas aeruginosa; 29% of Pseudomonas are levofloxacin-resistant. Overall, 82% of patients were treated with IAR that was active against identified isolates, with modifications increasing coverage to 88% in the first 24 hours.

Conclusions: BISHOP data represents the only contemporary multicenter profile of GNR BSI in HM or HSCT patients in the US. Reduced in vitro susceptibilities (<80%) of some organisms to mainstage IAR agents are observed. However, clinicians chose antibiotic regimens with in vitro activity against bloodstream isolates in 88% of cases within 24 hours of presentation. Correlations of drug susceptibility and clinical outcomes are planned. Finally, the limited activity of fluoroquinolones against E. coli underscores concerns about utility of FQ prophylaxis.

GN Susceptibilities

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Abstract 2123

**Activity of meropenem-vaborbactam and single-agent comparators against Enterobacterales isolates, including KPC-producing isolates, from European patients hospitalised with pneumonia (2014-2018)**

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**Abstract third-party references:** This study was performed by JMI Laboratories and supported by A. Menarini Farmaceutica Internazionale s.r.l (AMFI), which included funding for services related to preparing this abstract.

**Background:** Meropenem-vaborbactam (MVB) was recently approved in Europe for the treatment of complicated UTIs, including acute pyelonephritis, complicated intra-abdominal infections [cIAI], hospital-acquired bacterial pneumonia [HABP], ventilator-associated pneumonia [VABP], and bacteremia. KPC-producing Enterobacterales [ENT] isolates have disseminated worldwide and are considered endemic in various countries and several hospitals. We evaluated the activity of MVB and single-agent comparators against 5,648 ENT isolates from patients hospitalised with pneumonia [PHP] in European hospitals from 2014–2018.

**Materials/methods:** Among 5,648 ENT clinical isolates from PHP collected in 40 European hospitals located in 20 countries that were susceptibility [S] tested using reference broth microdilution methods, Of the carbapenem-resistant isolates submitted to whole genome sequencing, 59 carried *bla*<sub>KPC</sub>. ENT isolates were also characterized for an extended spectrum beta-lactamase (ESBL) phenotype as described (CLSI, 2019). EUCAST (2019) interpretive criteria were used. %S from intensive care unit (ICU) and non-ICU isolates were also analysed.

**Results:** The most common ENT pathogens isolated from PHP were *Klebsiella pneumoniae* [KPN; n=1,539] and *Escherichia coli* [EC; n=1,344]. The %S of MVB and comparators to ENT, ICU, and non-ICU are shown in the table. Overall, 98.2% of ENT were S to MVB. For 2,663 ENT isolates from ICU patients, MVB %S was 97.5% and for 2,187 non-ICU isolates MVB %S was 98.6%. The %S of comparators for ICU vs non-ICU isolates were similar, except for levofloxacin (76.3%S ICU/70.1%S non-ICU). 21 KPC-producing isolates were from ICU patients, 38 from non-ICU. KPC-producing isolates were mainly KPN [n=55] and included 44 *bla*<sub>ESBL</sub>, 14 *bla*<sub>KPC-3</sub>, and 1 *bla*<sub>KPC-2</sub> from 6 countries. 4 EC contained *bla*<sub>KPC-3</sub>. Italy had the highest number of KPC-producing isolates at 38 (64%). MVB inhibited 100% of KPC-producing isolates. Against isolates with an ESBL-phenotype, MVB inhibited 91.4%. Amikacin was the most active comparator against all ENT (94.3%S); colistin was the most active comparator against KPC-producing isolates (79.7%S).

**Conclusions:** These results demonstrate MVB has potent activity against ENT isolates from PHP including those producing KPC enzymes and suggest MVB is a useful treatment option for ICU and non-ICU PHP.

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<th>Organisms and organism groups (n)</th>
<th>% susceptible using EUCAST breakpoints</th>
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<tr>
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<td>Meropenem-vaborbactam</td>
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<td>Enterobacterales (5,648)</td>
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<td>KPC-producing (52)</td>
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<td>ICU isolates (2,663)</td>
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<td>non-ICU isolates (2,167)</td>
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<td>ESBL producing (438)</td>
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<td>KPC-producing (38)</td>
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Abstract 2125

Evaluation of the cobas MTB and MTB RIF/INH assays on samples from Sierra Leone and Germany at a supranational reference laboratory for tuberculosis serving both low-incidence and high-burden settings

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Abstract third-party references: Supported by Roche Molecular Diagnostics/Submitted on behalf of Dr. F. Maurer

Background: Rapid and sensitive detection of Mycobacterium tuberculosis complex (MTBC) DNA from clinical samples is critical for tuberculosis management. The Roche cobas® MTB and MTB-RIF/INH assays use PCR for the direct detection of MTBC DNA from inactivated human respiratory specimens. Samples positive for MTBC DNA are subsequently tested for rifampicin (RIF) and isoniazid (INH) resistance-associated mutations in the rpoB, katG and inhA genes, respectively. The objective of this study was to evaluate sensitivity and specificity of these assays at the German National Reference Center using specimens from low and high burden settings.

Materials/methods: Sensitivity, specificity and overall percent agreement (OPA) were determined on 326 sputum samples (smear-positive n=94 [28.8%]; smear-negative n=232 [71.2%]; MTBC culture-positive n=103 [31.6%]; MTBC culture-negative n=223 [68.4%]; 18 NTM culture-positive) collected from treatment-naïve, non-duplicate patients with presumptive TB in Germany (n=280) and Sierra Leone (n=46). MTBC PCR was compared to culture as reference. RIF and INH-resistance were compared to a combined reference standard (phenotypic DST and HAIN MTBDRplus, with sanger sequencing on selected isolates). Whole-genome sequencing was used to resolve discrepancies.

Results: In MTBC culture-positive samples, the overall sensitivity of the cobas MTB assay was 89.3% (95%CI, 81.8-93.9%). The majority of culture-positive samples were smear-positive (n=76) for which the cobas MTB assay demonstrated a sensitivity of 98.6% (92.9-99.8%) compared to 63% (44.2-78.5%) in smear-negative samples (n=27). Overall specificity of the cobas MTB assay was 98.6% (96.1-99.5%). OPA for RIF-resistance was 90.9% (85.4-96.7%) (n=44/85 with RIF-resistance). OPA for INH-resistance was 86.0% (77.2-91.8%) (n=48/86 with INH-resistance). Discrepant results for RIF and INH were mainly due to uncommon mutations in the Sierra Leone group not included in the intended target mutations for the cobas assays. When removing the Sierra Leone data the RIF-resistance OPA was 95.1% (83.9-98.7%).

Conclusions: The Roche cobas MTB and RIF/INH assays provide rapid, sensitive and specific detection of MTBC DNA and resistance-associated mutations in clinical specimens. The large capacity of the cobas 6800/8800 instruments makes the assays particularly suited to high-throughput laboratories. The local prevalence of undetectable/uncommon resistance mutations should be investigated before implementation of PCR-based rapid molecular tests.

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Evaluation of a novel high-definition PCR multiplex assay to identify nine genetic targets associated with multidrug-resistant organisms

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Abstract third-party references: Supported by ChromaCode, Inc

Background: Multidrug-resistant organisms (MDROs) are an emerging threat requiring immediate attention. Screening to identify asymptomatic carriers aids in preventing the spread of MDROs within healthcare facilities, and accurate identification of resistance mechanisms can inform early therapy. High-definition PCR (HDPCR) uses limiting-probe chemistry and data analytics to enable detection of multiple targets in a single fluorometric channel. This approach increases the multiplexing capabilities of existing 4 channel PCR instruments by 3 to 5-fold. We evaluated the performance of the HDPCR Multi-Drug Resistance (MDR) Panel RUO (ChromaCode, Carlsbad, CA) to identify nine genetic targets commonly associated with MDROs.

Materials/methods: The MDR Panel specifically identifies carbapenemases (KPC, NDM, VIM, IMP, OXA-48), the ESBL CTX-M groups 1 and 9, \textit{mcr-1} (colistin resistance), \textit{vanA} (vancomycin resistance), and \textit{tcdB} (toxigenic \textit{C. difficile}). A total of 131 genetically characterized isolates of Enterobacteriaceae, \textit{P. aeruginosa}, and \textit{A. baumannii} obtained from the CDC Antibiotic Resistance Isolate Bank were used to challenge the MDR Panel. This included 89 isolates containing ≥1 on-panel target and 42 isolates containing resistance genes not detected by the MDR Panel. Isolates were tested as pure 0.5 McFarland suspensions following 10 min. heat lysis step (n=67) or as contrived stool specimens in ESwab (final concentration of 4 log\textsubscript{10} CFU/mL) requiring nucleic acid extraction (eMag, bioMerieux) prior to HDPCR.

Results: Among 67 isolates tested from pure suspension, MDR Panel demonstrated 100% sensitivity and 99.5% specificity. This included accurate identification of 55/55 unique targets in 42 unique isolates including 13 isolates containing multiple MDR targets. Three false-positive results included one each for \textit{tcdB}, NDM, and CTX-M in isolates lacking these markers. Among 64 contrived stool specimens, MDR Panel demonstrated 98.5% [66/67] sensitivity and 100% specificity. This included 29 specimens containing a single MDR target, 16 containing two targets, and 2 containing three targets. The single false-negative result was failed detection of NDM in a specimen containing NDM and CTX-M.

Conclusions: MDR Panel provides a sensitive and specific method for detection of 9 common targets associated with MDROs. It can be applied for characterization of pure bacterial isolates or as a method to screen for MDROs in stool specimens.

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Background: Clostridioides difficile infection (CDI) is the most common cause of infectious health-care associated diarrhea in hospitalized patients, affecting primarily elderly patients with comorbidities and antibiotic exposure. Large scale patient level data sets including information on symptoms, diagnosis, treatment, response and recurrence, as well as the associated cost of treating CDI within the German health care system are missing.

Materials/methods: Using an observational, retrospective/prospective, multi-center study design, we collected data from 9 hospitals in Germany through the epidemiological research platform www.ClinicalSurveys.net.

Results: Out of 288 patients with CDI analyzed, 162 (56.3%) patients were male and the median age was 71 years (range 20-96 years; IQR 19). The most common comorbidities were cardiovascular (72.3%), endocrine (45.0%) and kidney (44.6%) diseases. Overall, 34 (11.8%) received hemodialysis and 88 (30.6%) patients were immunocompromised at study inclusion. Immunosuppression was defined by current neutropenia (<500 neutrophils/mm³), a history of allogenic stem cell transplantation, prolonged use of corticosteroids or inherited severe immunodeficiency. Median Charlson comorbidity index was 6 (range 1-19; IQR 4) and median Karnofsky score was 50% (range 20-100%; IQR 30%). At the time of CDI diagnosis, 37 patients (12.8%) were treated in an intensive or intermediate care unit. After initial diagnosis of CDI, 209 (72.6%) patients received vancomycin, 70 (24.3%) metronidazole, 2 (0.7%) fidaxomicin, 2 (0.7%) metronidazole + vancomycin and 2 (0.7%) received no treatment. If treated, the median duration of treatment of CDI was 10.0 days (range 1-26 d; IQR 3). At day 10+/-2 d 92 patients (31.7%) were discharged, 188 patients (65.5%) were still hospitalized and 8 patients (2.8%) had died during treatment. Overall, 228 (79.2%) patients responded to CDI treatment. When compared to treatment with metronidazole, response to vancomycin treatment at day 10+/-2 d was significantly higher (70.0% vs 83.3%; p<0.05). At follow up on day 45+/-4 d, 98 (34.0%) patients were lost to follow up. Among patients that were followed-up, 8 (15.2%) presented with first recurrence of CDI.

Conclusions: These preliminary results from the IBIS study provide valuable epidemiological information on the incidence, treatment and clinical outcomes of hospitalized patients diagnosed with CDI in the German health care system.

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Specific antibody responses to recombinant UB05 and MSP3 proteins displayed through the surface of Coliphage Qβ in mother-neonate couples

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Background: Malaria blood stage parasite is a main causal pathogen of adverse outcomes in pregnant women and their babies. However, Immunoglobulin G (IgG) specific responses against the antigens of this parasite stage were associated with malaria control, although with law efficiency. Hence, we assessed the profile of antibody responses specific to MSP3 and UB05 antigens displayed Qβ phage system of in mother-neonate couple.

Materials/methods: Plasmodium infection was screened in mother’s peripheral blood and Placental impression smears. Mother-neonate paired plasma samples were collected at delivery and used to determine the levels of IgG and IgG subclasses specific to recombinant phages QβUB05, QβMSP3 and, QβUB05MSP3.

Results: Irrespective of malaria status, both mothers and neonates had significantly higher IgG responses to QβUB05 and QβUB05MSP3 phages compared to anti-QβMSP3 IgG (P < 0.05). A significant negative correlation was shown between IgG levels specific to the three antigens and parasitaemia. anti-QβUB05 and anti-QβUB05MSP3 IgG in neonates showed a significant positive correlation with the corresponding mothers’ antibodies (rs = 0.25 with P= 0.04; rs = 0.31 with P= 0.01 respectively). QβUB05MSP3 specific IgG3 and IgG1 responses were significantly higher than IgG4 subclass (p<0.01). The neonates IgG1 and IgG3 levels positively correlated with the corresponding antibody subclasses of mothers.

Conclusions: These findings suggest an association between QβUB05 and QβUB05MSP3 specific antibody responses and malaria control during pregnancy. Maternal-foetal transfer of MSP3 and UB05 specific IgG occurs during pregnancy, suggesting the development of future malaria vaccination strategies for pregnant women required for early baby protection to malaria.

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Abstract 2136

Predicting phenotypic polymyxin resistance in *Klebsiella pneumoniae* through machine learning analysis of genomic data

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**Background:** Polymyxins are treatments of last resort for Gram-negative infections but increased use has led to emerging polymyxin resistance (PR). Phenotypic polymyxin susceptibility testing is resource-intensive and difficult to perform accurately. We therefore aimed to use machine learning (ML) on *Klebsiella pneumoniae* clonal group (CG)258 whole genome sequencing (WGS) data to predict phenotypic PR.

**Materials/methods:** We classified 619 *K. pneumoniae* genomes with broth microdilution polymyxin susceptibility data as phenotypically susceptible (MIC ≤ 2 mcg/ml) or non-susceptible (MIC > 2 mcg/ml). We assessed performance of a non-ML rule-based approach that predicted phenotypic PR if variants were present in known PR genes. We then implemented an ML pipeline in Python Sci-kit Learn and compared performance using a reference-based representation of genomic data with a reference-free representation as k-mers. We also assessed performance when a bacterial genome-wide association study (GWAS) was used to prioritize genes prior to ML, and clinical polymyxin exposure data were added.

**Results:** Using a reference-based representation of WGS with ML outperformed the rule-based approach (area under receiver operator curve [AUROC] 0.894 vs 0.791, P=0.006). Using a GWAS to filter relevant genes and integrating clinical polymyxin exposure led to modest increases in performance. Conversely, reference-free representation of WGS as k-mers decreased performance (AUROC 0.692 vs 0.894, P=0.015). Choice of ML algorithm (logistic regression, Support Vector Machine, Gradient Boosted Trees and Random Forests) did not impact performance. When ML models were interpreted to extract genomic features, 6/7 known PR genes were correctly identified without prior programming and several genes were identified as potential novel PR determinants.

**Conclusions:** These findings are a proof-of-concept that WGS can accurately predict PR in *K. pneumoniae* CG258 and may be applicable to other forms of complex antimicrobial resistance. Use of ML for resistance prediction may need to be tailored to specific organisms and antimicrobial agents.

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Rapid detection of ceftazidime/avibactam-resistant Enterobacteriaceae by VITEK MALDI-TOF mass spectrometry using direct-on-target microdroplet growth assay

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Abstract 2137

**Background:** We evaluated the direct-on-target microdroplet growth assay for rapid detection of ceftazidime-avibactam resistant CRE (carbapenem resistant Enterobacteriaceae)

**Materials/methods:** In our study, a total of 47 non-duplicate CRE isolates were used to evaluate the performance of ceftazidime-avibactam resistance detection, including 19 *Klebsiella pneumoniae*, 8 *Escherichia coli*, 6 *Enterobacter cloacae*, 5 *Serratia marcescens*, 4 *Klebsiella aerogenes*, 3 *Citrobacter freundii* and 2 *Klebsiella oxytoca* clinical isolates. These isolates were incubated for 3h, 4h, 5h, and 6h with and without 16 µg/ml ceftazidime-avibatam in broth as microdroplets directly on matrix-assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) target spots. The microdroplet volume was 6µl. After the incubation period, the broth is separated from microbial cells by pipette. MALDI-TOF MS was used to determine the growth of the isolates in each spot and identify the microorganism at the same time. The micro-broth dilution method recommended by the European Committee on Antimicrobial Susceptibility Testing (EUCAST) was used as a reference method. Polymerase chain reaction based assay were used to determine the carbapenem-resistance mechanisms by screening the presence of β-lactamase-encoding genes, including Ambler class A (SME, IMI, KPC and GES), class B (NDM, IMP and VIM), and class D (OXA-48).

**Results:** We observed that incubation duration of 3 h was not sufficient for isolates. At that time, the identification valid results of the growth control were only 25.0%. Therefore, this time-point was not carried in further experiments. For CRE strain detection, 83.7% of growth controls were successfully detected after 4 hours incubation. At this time point, sensitivity and specificity for resistance detection were both 100%. 5 h of incubation droplets resulted in 98.0% of valid tests with 100% sensitivity and 100% specificity. However, 6 h of incubation droplets resulted in 100% of valid tests with 100% sensitivity and 100% specificity.

**Conclusions:** Newly developed MALDI-TOF MS-based direct-on-target microdroplet growth assay is a rapid, convenient and accurate tool which is able to detect ceftazidime-avibactam resistant CRE within 5 hours. This assay can determine the susceptibility status of the isolate and the underlining resistance mechanisms could also be revealed.

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Breakthrough blood culture isolates whilst on broad spectrum antimicrobial therapy for high-risk neutropenic fever: more common and resistant that previously thought

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Background: We aimed to review the frequency and spectrum of breakthrough positive blood cultures (BT-BC) during broad spectrum antimicrobial therapy (BS-AMT) for neutropenic fever (NF) in those with acute leukaemia receiving induction/consolidation chemotherapy (CTx), autologous (autoHCT) or allogeneic haematopoietic cell transplant (alloHCT).

Materials/methods: The PIPPIN study (Clinicaltrials.gov identifier: NCT03429387) is a prospective, multicentre, randomised trial of conventional CT versus PET/CT for prolonged or recurrent NF in adults with acute leukaemia receiving CTx or conditioning for alloHCT or autoHCT. First-line empiric NF BS-AMT was piperacillin-tazobactam, with ceferpine or ciprofloxacin/vancomycin in penicillin allergy. Participants had BCs (Bactec) collected at the clinician’s discretion plus at three timepoints: (1) at onset of NF (temp≥38.0, neutrophils≤0.5 cells/L), (2) persistent NF (>72 hours), (3) recurrent NF (new fever beyond 72 hours of initial onset, with 48 hours defervescence). A BT-BC was defined as a positive BC >72 hours after commencement of BS-AMT. An isolate was deemed resistant if it was intrinsically resistant or had an acquired resistance mechanism (e.g. ESBL). The data of the first 120 participants consented were analysed.

Results: Participants were enrolled between January 2018 and March 2019 (n=120: 57 acute leukaemia CTx, 63 alloHCT, 4 autoHCT). NF occurred in 128/140 cycles observed. During these NF episodes, 154 of 1,574 (9.8%) BCs collected were positive. Eighty-one unique isolates were identified (Figure 1). There were 45 BT-BC isolates: 25 initial BC negative and BT-BC positive, 4 persistent positive BC with same isolate, 16 initial BC positive and BT-BC positive with different pathogen. BT-BC occurred at 14.5 days median duration of neutropenia [IQR 8-26 days] and 12 days median continuous BS-AMT [IQR 8-18]. Of the 39 gram negative isolates, 17 were BT-BCs, and 12/17 (70.6%) were resistant to BS-AMT used, compared to 3/22 (13.6%) of the non-BT-BCs (p=0.003 by chi-square test).

Conclusions: Rates of BT-BC are high in the setting of prolonged neutropenia. Repeat BCs are indicated in prolonged and/or recurrent NF as a different causative pathogen is likely, which in turn is likely to be resistant to the current antimicrobials. Continuing BS-AMT in the setting of defervescence may have selected out for such resistance.

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Multidisciplinary treatment model led by infectious physician reduce the unreasonable use of antibiotics and improve the efficacy in the treatment of patients with diabetic foot infection

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Background: Diabetic foot infection (DFI) is common cause of hospitalization and nontraumatic amputation in patients with diabetic mellitus. In this study, we aimed to explore the effectiveness of antibiotic management implementation in multidisciplinary collaborative therapies (MDT) led by infectious physicians. We hypothesized that this treatment model could make rational use of antibiotics and improve patient prognosis.

Materials/methods: This is a historical cohort study to assess antibiotic use and prognosis in patients with DFI between the two intervention models. One cohort received a multidisciplinary collaborative treatment model led by infectious physicians, in conjunction with surgeons and pharmacists, from October 2018 to September 2019. The control cohort was patients who were treated in the traditional mode from September 2017 to August 2018. In this mode, the surgeon led the treatment, and infectious physician was consulted if necessary. Data for the control group included demographic, clinical, laboratory, and surgical data, all from electronic medical records.

Results: There were 32 patients in the control cohort and 35 patients in the intervention cohort. Patients in intervention cohort present higher percentage of peripheral neuropathy (80.5% vs 53.1%, p=0.016) and polymicrobial infections (47.2% vs 12.5%, p=0.002), longer duration of diabetic foot ulcer (120 days vs 30 days, p=0.002) and more site of osteomyelitis involved (p=0.031). The rate of correct initial empirical treatment in MDT group was 100%, compared with 48% in the control group (p<0.001). The median duration of fever persistance decreased from 7 days to 1 day (p=0.004). The median intravenous antibiotic treatment time in the intervention and control groups was 12 days and 13.5 days (p = 0.692), with median hospital stay of 22 days and 21 days (p = 0.425) respectively. There was no significant difference in the number of surgical debridements between the two groups (p = 0.224).

Conclusions: Multidisciplinary treatment model led by infectious physician can reduce the unreasonable use of antibiotics and improve the efficacy in the treatment of patients with diabetic foot infection.

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Abstract 2154

Sub-inhibitory concentrations of mupirocin stimulate Staphylococcus aureus biofilm formation by up-regulating cidA

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Background: Previous studies have shown that the administration of antibiotics at sub-inhibitory concentrations stimulates biofilm formation by the majority of MRSA strains. Here, we investigated the effect of sub-inhibitory mupirocin concentrations on biofilm formation by the community-associated (CA) mupirocin-sensitive MRSA strain USA300 and highly mupirocin-resistant clinical S. aureus SA01-SA05 isolates.

Materials/methods: Cell lysis and eDNA quantification studies were used to investigate whether mupirocin increased the ability of S. aureus to attach to surfaces and form biofilms, which was correlated with eDNA production. The RNA-Seq and RT-qPCR were used to evaluate the expression of different genes in the mupirocin-treated and untreated strains in more detail. As follow-up functional analysis, we generated a cidA knock out mutant to form biofilms comparable to that formed by the parent strain in presence of antibiotic.

Results: We found that mupirocin increased the ability of MRSA cells to attach to surfaces and form biofilms. Confocal laser scanning microscopy (CLSM) demonstrated that mupirocin treatment promoted thicker biofilm formation, which also correlated with the production of extracellular DNA (eDNA). Furthermore, RT-qPCR results revealed that this effect was largely due to the involvement of holin-/antiholin-like proteins (encoded by the cidA gene), which are responsible for modulating cell death and lysis during biofilm development. We found that cidA expression levels significantly increased 6.05-35.52 fold (P < 0.01) on mupirocin administration. We generated a cidA-deficient mutant of the USA300 S. aureus strain. Exposure of the ΔcidA mutant to mupirocin did not result in thicker biofilm formation compared with that in the parent strain.

Conclusions: The increase in biofilm formation mediated by mupirocin was due to cell death and lysis. Mupirocin-induced stimulation of S. aureus biofilm formation may involve the upregulation of cidA. Our study supports the recommendation to clinicians regarding the prudent usage of sub-concentrations of antimicrobials agents, which may possibly contribute to poor prognosis of MRSA infections.

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Viral and immunologic factors associated with fatal outcome of patients with severe fever with thrombocytopenia syndrome in Korea

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Background: Severe fever with thrombocytopenia syndrome (SFTS), which is caused by a novel phlebovirus SFTS virus (SFTSV), is an emerging tick-borne disease in East Asia with a high fatality (16.2-32.6%). Significant progress has been made on the molecular biology of the virus, however, many parts of pathophysiological mechanisms of mortality in SFTS remain unclear. In the present study, we investigated virologic and immunologic factors for fatal outcomes of patients with SFTS.

Materials/methods: We prospectively enrolled 34 confirmed cases of SFTS admitted to 5 university-affiliated hospitals in South Korea from July 2015 to September 2018. SFTSV infection was confirmed by real-time reverse transcription polymerase chain reaction for the detection of viral RNA; segment S and M. We simultaneously measured the levels of cytokines in the plasma samples by multiplex-microbead immunoassay for 18 cytokines selected. Serological testing for the presence of anti-SFTSV IgG titer was tested by immunofluorescence antibody assay.

Results: A total of 34 patients with SFTS were enrolled, including 31 (91.2 %) survivors and 3 (8.8 %) non-survivors. Sixteen (47.1%) patients were previously healthy but the others had a broad range of underlying diseases. Non-survivors had 4 log copies/mL higher plasma SFTSV load than survivors at admission [seg S; median 6.40 vs 2.54 log, p = 0.001, seg M; median 6.87 vs 2.73 log, p = 0.001] and the viral load in non-survivors increased progressively during the hospitalization. In addition, non-survivors did not develop adequate anti-SFTSV IgG response, whereas survivors exhibited anti-SFTSV IgG during the hospitalization. Among the cytokines measured in this study, the plasma concentrations of IL-10, IFN-α, MIP-1α, IP-10, MCP-1, IL-6, IL-8 and G-CSF were significantly elevated in non-survivors than survivors and not reverted to normal ranges during the hospitalization [p < 0.05]. Of note in particular, the plasma IL-10, IFN-α, MIP-1α concentrations were markedly higher in non-survivors throughout the disease course.

Conclusions: Our findings suggest that high plasma concentrations of cytokines, uncontrolled viremia and failure of the antibody response were critical determinants of fatal outcomes of SFTSV infection.
Figure 1. Plasma SFTSV load, antibody titer, interleukin-10, interferon-α, and macrophage inflammatory protein 1α concentrations in patients with SFTS.

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Abstracts 2020

Abstract 2157

Rising clarithromycin resistance in *Helicobacter pylori* in a Hong Kong regional hospital and molecular characterisation by next-generation sequencing

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**Background:** Helicobacter pylori, which causes chronic stomach infections and associated with gastric malignancies, infects one-third to half of the population in Hong Kong. Current recommended eradication therapy is a standard 7-day amoxicillin-clarithromycin-containing triple therapy, given the low prevalence of clarithromycin resistance in the locality (<15%). Antibiotic susceptibility testing prior to eradication therapy is not commonly performed in Hong Kong due to reported low resistant rate (7.8%-14%). This study aims to report the increasing prevalence of antibiotics resistance in *H. pylori* in a Hong Kong regional hospital and the potential use of molecular methods in resistance prediction.

**Materials/methods:** A total of 503 *H. pylori* strains, which were isolated from patient gastric biopsies during a 22-month period, were included in this study. Susceptibility testing on clarithromycin, metronidazole, amoxicillin, levofloxacin, tetracycline and rifampicin were performed. Forty-seven clarithromycin-resistant strains were selected in the preliminary study for whole genome sequencing using Illumina MiSeq system.

**Results:** The resistance rates of *H. pylori* to clarithromycin, metronidazole, amoxicillin, levofloxacin, tetracycline and rifampicin were 46.7%, 60.2%, 12.3%, 39.2%, 2% and 19.1% respectively. Among the clarithromycin-resistant strains, 89.4% (42/47) carried resistant genotype in 23S rRNA gene; 10.6% (5/47) of them did not contain any mutations. Mutations in *gyrA* or *gyrB* genes, which were responsible for fluoroquinolone resistance, were identified in 70.8% (17/24) of resistant strains and 39.1% (9/23) of susceptible strains. Mutations in *rdxA* and/or *frxA*, which were responsible for metronidazole resistance, were observed in 78.8% (26/33) of resistant strains and 35.7% (5/14) of susceptible strains. Among the rifampicin-resistant strains, 25% (2/8) carried resistant genotype in *rpoB* gene and none of these mutations was detected in susceptible strains. Although none of the sequenced strains was amoxicillin or tetracycline-resistant, resistance-associated mutations in *pbp1A* and 16S rRNA were observed in 23.4% (11/47) and 21.3% (10/47) of strains respectively.

**Conclusions:** The prevalence of clarithromycin-resistant *H. pylori* was higher than previously reported and exceeded the 15% threshold level. Antibiotic resistance profiling is recommended to be performed prior to eradication therapy prescription. Further studies are necessary for studying the association of antibiotic resistance and mutations and the usefulness of molecular testing in resistance prediction.

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Abstract 2163

**Chagas disease in Japan, 2012-2019: clinical presentation and diagnostic delay**

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**Background:** Chagas disease, caused by *Trypanosoma cruzi*, is the neglected tropical disease in both endemic and non-endemic countries. Chagas disease was considered a public health problem in non-endemic countries because the epidemiology of Chagas disease has radically changed in accordance with the increasing numbers of immigrants from Latin America to non-endemic countries. There is little information of clinical characteristics of Chagas disease in non-endemic countries, although the 3,000 patients were estimated to live in Japan. The current study aimed to clarify the clinical characteristics of Chagas disease in Japan.

**Materials/methods:** Twenty nine patients with suspected Chagas disease between 2012 and 2019 were included in the study. Patients were diagnosed with Chagas disease based on the two different serological tests for antibodies to *T. cruzi*. The real-time PCR assay and blood culture technique were performed to confirm the parasitemia of *T. cruzi*. The discrete typing units (DTUs) of clinical isolates were determined by PCR-RFLP method.

**Results:** Of the 29 patients, 23 were immigrants from Latin America. Finally, 13 patients were diagnosed with Chagas disease. Of the 13 patients, median age was 51 years, 12 patients were immigrants from Latin American [Brazil, 5; Bolivia, 7], and 1 was Japanese case of congenital infection. Nine patients developed chronic phase (Chagas cardiomyopathy, 8; megacolon, 1). A patient died from Chagas cardiomyopathy. Six had confirmed parasitemia of *T. cruzi*, and 2 were positive for blood culture. DTUs of 2 clinical isolates were identified as *T. cruzi* DTUs I. Finally, 4 patients were initiated treatment with Benznidazole.

**Conclusions:** Our study demonstrated that patients of Chagas disease living in Japan have developed chronic phase when they diagnosed with the disease because of diagnostic delays. This study indicates an urgent need for the Chagas disease screening program for the Latin American immigrants in non-Chagas disease-endemic countries, including Japan.

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Systematic assessment of available data on the incidence of bloodstream infections and hospital-acquired pneumonia caused by carbapenem-resistant Acinetobacter baumannii in Europe: the ABOUT-MDRO-CRAB study

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Background: Acinetobacter baumannii (AB) is an important cause of hospital-acquired and ventilator-associated pneumonia (HAP, VAP) and bloodstream infection (BSI). Carbapenem-resistant AB (CRAB) is increasing worldwide. However, a precise assessment of the incidence of HAP/VAP and BSI due to CRAB is not available and current figures are mainly based on modelling methodologies using proportion of resistant isolates. The aim of this study is to estimate the correlation between incidence of HAP/VAP and BSI due to CRAB and the proportion of carbapenem-resistance in Europe.

Materials/methods: A systematic review (following PRISMA recommendations) was performed for data on incidence of CRAB and proportion of carbapenem-resistance in AB data for BSI, HAP and VAP in Europe from 2005-2018, from scientific literature and European surveillance systems in SUSPIRE/EPI-NET databases. Correlations between incidence data and proportion of carbapenem-resistance in AB were analysed by linear regression.

Results: Overall 2,687 and 5,537 articles containing data for BSI or HAP/VAP, respectively were identified. Finally, 32 and 20 studies were included. Incidence of CRAB BSI, HAP and VAP were extracted from 13, 22 and 14 studies, respectively, from 5 countries. Incidence of HAP/VAP ranged 2.38-2.52/100 ICU admissions in Greece (2 studies), 0.45-3.76 in Italy (2 studies), 0.3-1.66 in Spain (2 studies), 0.70-23.30 in Poland (7 studies) and 0.16-3.5 in Turkey (2 studies). Incidence of BSI/100 ICU admissions ranged: 0.35-0.87 in Greece (2 studies), 0.41 in Italy (1 study), 1.49 in Spain (1 study), 0.94-1.84 in Poland (2 studies) and 4.08 in Turkey (1 study). No statistically relevant correlation was found between incidence and resistance proportion for CRAB \([R^2=0.197\text{ for BSI in ICU}, 0.010\text{ for HAP in ICU and 0.170 for VAP, respectively}]\) in the 5 countries analysed.

Conclusions: This systematic review on European data showed: [a] scarce data on incidence of BSI and HAP/VAP due to CRAB; [b] high heterogeneity in incidence and resistance proportions within countries; [c] lack of correlation between incidence and proportion of carbapenem-resistance in AB. These data strongly call for improved surveillance systems to inform burden assessment and drive infection control and antibiotic policy decisions.

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Abstract 2166

Risk factors of severe dehydration among children under five
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Background: Dehydration is the leading cause of hospitalization from diarrhea among children under five years old. The degree of dehydration is measured using capillary refill time, skin turgor, respiratory rates and signs of shock. According to demographic and health survey 2010, the prevalence of diarrhea was 9% among under-five children in Armenia and 7% of all infant deaths were related to diarrheal diseases.

Objective: The aim of this study was to identify the risk factors of moderate-to-severe dehydration among children under five years old hospitalized because of acute diarrhea.

Materials/methods: The study utilized a case-control study design to identify the risk factors of severe/moderate dehydration among children under five years old. Cases (n=62) were under-five children admitted to “Nork” infectious clinical hospital with the initial diagnosis of acute diarrhea and with severe or moderate dehydration at the admission. Controls (n=125) were under-five children admitted to “Nork” infectious clinical hospital with the initial diagnosis of acute diarrhea and with no or mild dehydration at the admission. Face to face interviews were conducted with mothers of the children.

Results: From all 187 children, 105 (56.1%) were males and 82 (43.9%) were females. The mean age of children of cases was 14.8 (14.6) and 24.4 (15.4) for controls. Mother’s higher KAP (knowledge, attitude and practices) score was negatively associated with the child’s dehydration status (OR0.68, CI 0.53; 0.87). Being vaccinated against rotavirus (OR 0.29, CI 0.08; 0.61), child’s good general health rating by the mother (OR0.23, CI 0.09; 0.62), child’s age (OR0.94, CI 0.90; 0.97) and high socioeconomic status score (OR (0.70, CI 0.49; 1.01) of the family were among factors protecting from severe/moderate dehydration, while higher birth order OR(2.21, CI 1.10; 4.42) and repeating vomiting during the disease (OR 5.10 CI 1.84; 14.08) were among its risk factors.

Conclusions: The study recommends increasing mother’s KAP on diarrhea home management through public education interventions. The coverage of under-five children with rotavirus vaccination and mothers’ awareness about diarrhea danger signs should be increased.

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**Abstract 2167**

**Sensitivity of C-reactive protein and procalcitonin to diagnose urinary tract infections in nursing home residents**

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**Background:** Urinary tract infections (UTI) are common in elderly nursing home residents. Diagnosis of UTI is complex since signs and symptoms are often nonspecific, especially in residents with cognitive impairments. The high prevalence of asymptomatic bacteriuria (ASB) limits the usefulness of bacterial culture or dipstick-based diagnostics, and potentially leads to antibiotic overuse. The aim of this study is to assess the sensitivity of blood C-reactive protein (CRP) and procalcitonin (PCT) measured by Point-of-Care tests (POCTs) for UTI diagnosis, thereby potentially providing supportive diagnostics to distinguish ASB from true UTIs.

**Materials/methods:** In an 18-month prospective study in three nursing home organizations in the Netherlands, residents with a suspected UTI were included. The target sample size was 440 to detect a minimal clinically relevant sensitivity of 65% of either tests and a 10% difference between tests, with a power of 90% and two-sided p-value of 0.05. CRP and PCT sensitivities were derived empirically from Receiver Operator Curves, using a predefined stringent definition of ‘true’ UTI which included microbial culture results and symptom resolution during adequate antimicrobial treatment.

**Results:** After enrolment of 293 residents (66.6% of planned sample size) a previously unplanned and funder-mandated interim analysis was performed. In residents with suspected UTI 41% of CRP and 47% the PCT POCT results were below the lower limit of detection (similar in UTI and ASB). The sensitivities of CRP (cut-off 6.5 mg/L) and PCT (cut-off 0.025 μg/L) were 49% and 45% respectively. To achieve the required minimal sensitivity of 65%, POCT sensitivities in remaining study participants would have to be at least 96%. Based on these results, the study was discontinued prematurely for futility.

**Conclusions:** Sensitivities of CRP and PCT POCTs to diagnose UTIs in nursing home residents are low. Our results indicate that CRP and PCT are not suitable to distinguish UTI and ASB in this setting.

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Abstract 2168

Systematic assessment of available data on the incidence of hospital-acquired pneumonia and bloodstream infections due to carbapenem-resistant *Pseudomonas aeruginosa* in Europe: the ABOUT-MDRO-CRPA project

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**Background:** *Pseudomonas aeruginosa* (PA) is a leading cause of bloodstream infections (BSI), hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP). Carbapenem-Resistant *P. aeruginosa* (CRPA) is a “critical” priority pathogen, nonetheless, most available data are obtained from proportion of resistant isolates, and the incidence of infections is not precisely characterized. The aim of this study is to provide data on incidence of BSI and HAP/VAP by CRPA in European countries, and its correlation with carbapenem-resistance among PA isolates.

**Materials/methods:** A systematic review (following PRISMA recommendations) was performed for data on incidence of CRPA and proportion of carbapenem resistance in PA for BSI and HAP/VAP in European countries from 2005-2018, from scientific literature and available data from European surveillance systems from SUSPIRE/EPI-NET databases. Correlations between incidence data and proportion of carbapenem resistance in PA were analyzed by linear regression.

**Results:** Literature review identified 12,960 and 4,223 articles containing data for BSI and HAP/VAP, respectively; 20 studies for BSI and 17 for HAP/VAP were finally included. BSI and HAP/VAP incidence for CRPA were measured as cases per 100 admissions, 1,000 patient-days (PD), and 1,000 ventilator-days (VD). Incidence of HAP/VAP ranged from 0.62 to 0.65/100 admissions in Poland, 1 to 1.7 in Italy, and 1.11 and 2.0 in Turkey and Greece, respectively; for BSI, incidence ranged from 0.0015 in Sweden, from 0.02 to 0.6 in Italy, from 0.71 to 3.8 in Turkey, and 0.64 and 0.71 in Greece and Spain, respectively. HAP/VAP incidence in cases per 1,000PD ranged from 0.57 in Poland to 15.4 in Serbia, and CRPA incidence in BSI ranged from 0.013 in Italy to 2.1 in Turkey. Carbapenem-resistance in *P. aeruginosa*, ranged from 31.5%-100% in HAP/VAP, and 6.3%-88.9% in BSI. No statistically significant correlation was found between incidence and carbapenem-resistance in PA ($R^2=0.433$ and 0.317 in BSI and pneumonia, respectively).

**Conclusions:** Data on incidence of BSI and HAP/VAP due to CRPA are scarce and showed heterogeneous results within countries. No correlation was found between available data on incidence of CRPA infections and proportion of carbapenem resistance in PA. These data suggest that improved surveillance data are needed to inform burden assessment of CRPA infections.

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How an inflammatory marker Point-of-Care test can reduce inappropriate antibiotic use in urinary tract infections: perceptions of physicians and nurses in Dutch nursing homes

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Abstract third-party references: This study is funded by The Netherlands Organization for Health Research and Development (ZonMW) grant 541001003. ZonMW, Laan van Nieuw Oost Indië 334, 2593 CE Den Haag, The Netherlands.

Background: Diagnosing Urinary tract infections (UTI) in nursing home residents is challenging. Due to the high prevalence of non-specific symptomatology and asymptomatic bacteriuria (ASB), current urine tests have limited usefulness and often result in inappropriate antibiotic use. A sufficiently sensitive blood inflammatory marker Point-of-Care test (POCT) could help verifying the presence of a UTI. However, apart from its sensitivity, the effectiveness of a POCT highly depends on its correct use in practice. We explored the perceptions of physicians and nurses in Dutch nursing homes how to use a POCT in practice.

Materials/methods: In this multicenter multiple case study, we used 18 semi-structured face-to-face interviews to identify physicians’ and nurses’ intended use of POCT in diagnosing UTI in nursing home residents. Both the development of the interview guide and the analysis of the interview transcript were based on the Consolidated Framework for Implementation Research (CFIR).

Results: Most respondents acknowledged positive POCT results could decrease the diagnostic uncertainty in residents presenting non-specific symptoms and reduce inappropriate antibiotic use. However, most respondents also expected that new diagnostic uncertainties would arise. First, other infections with non-specific symptoms causing positive POCT results might be overlooked. Second, the respondents were not sure how to deal with negative POCT results. These new uncertainties could again provoke inappropriate antibiotic use. Furthermore, many respondents intended – improper – use of POCT, such as diagnosing other infections, assessing infection severity, monitoring infections and deciding about emergency referrals.

Conclusions: In order to effectively contribute to diagnosing and properly treating UTI in nursing homes, practical guidelines on POCT use are needed, when sufficient sensitivity of POCT is demonstrated. These guidelines should include the indications for testing and guidance on interpretation of results, to prevent inappropriate use and consequently inappropriate antibiotic use.

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Severe Plasmodium falciparum malaria in non-immune travellers admitted to the intensive care unit: assessment of parasite clearance in response to antimalarial medication and exchange transfusion

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Background: Most of the Severe P. falciparum malaria complications occur in non-immune subjects and involves damage to multiple organ systems. To optimize the management of severe P. falciparum we developed an algorithm which includes exchange transfusion (ET) methods [continuous venovenous hemodiafiltration and plasmapheresis] and mechanical ventilation under medically induced coma as preventive measures for cerebral forms. ET was implemented not only to reduce parasite load in cases of high parasitaemia but also to reduce the mortality of severe cases. Jinfeng Lin, Xiaoying Huang et al. 2018 conducted a recent study in which the authors did not identify substantial evidence supporting the use of exchange transfusion in severe P. falciparum malaria.

Materials/methods: 72 patients treated for severe P. falciparum malaria, admitted to the intensive care unit (ICU) at the Infectious Diseases Clinical Hospital №2, Moscow, Russia between 2002 and 2019 were included in this retrospective study. Parasite clearance was determined using the Worldwide Antimalarial Resistance Network’s parasite clearance estimator. The primary end point was the parasite clearance time.

Results: All patients had obtained antimalarial medication in accordance with the World Health Organization treatment guidelines. Data from 54 patients were suitable for estimation of parasite clearance. 38 (71%) patients were managed with parenteral antimalarial medication and ET as an adjunct treatment while 16 (29%) patients received only intravenous (IV) antimalarial treatment. The median parasite clearance time was 37.50 (95% CI 36.21 to 38.18) hours for patients who received ET under antimalarial treatments and 47.56 (95% CI 46.26–48.70) patients managed with antimalarial drugs only, p value < 0.05. The median parasite clearance rate in the ET intervention group had a slope half-life of 3.12 (95% CI 1.91–4.88) hours and 4.00 (95% CI 2.14–5.20) hours for patients who received antimalarial drugs only, p = 0.671. Majority of mortality cases was observed in the group of patients managed with antimalarial drugs only.

Conclusions: Our investigation does reveal ET contributes significantly to parasite clearance in ICU patients treated with antimalarial drugs, although the slope half-life did not differ significantly. Extensive investigations would be conducted to reveal the accurate scope of ET intervention in severe malaria

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Outcomes of the antibiotic stewardship programme in a teaching hospital of southern Italy: an interrupted time-series analysis

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Background: The widespread of antimicrobial resistance is a global health problem, significantly increasing the hospital mortality, the need for Intensive Care Units (ICUs) admission, the length of stay, and the healthcare costs. The antimicrobial resistance is hugely accelerated by the selective pressure exerted by antibiotics overuse. The implementation of the “Antibiotic Stewardship Programme” (ASP) is essential to improve the appropriateness of antibiotic prescriptions. In the present study we aimed at evaluating the impact of an ASP in selected departments of 3 different clinical areas (medical, surgical and intensive areas) of an acute-care teaching hospital in Naples, Italy.

Materials/methods: We conducted a prospective, interventional, before and-after study, based on prospective audit and feedback in 3 surgical units, 4 medical units and 2 ICUs (January 2017-April 2019). The outcomes were the difference in the antibiotic consumption (as DDD/100 patient-day), the mean length of stay and the antibiotic costs. Additional outcomes in critical area were the difference in incidence of bloodstream infections (BSI) caused by multidrug-resistant (MDR) bacteria (as cases/100 patients-day) and the hospital mortality rate.

Results: During the study period, 231 audit were performed in ICUs, 210 in medical units and 184 in surgery units, evaluating a total of 4,312 patients. The program led to a significant reduction in the use of fluoroquinolones (p<0.001), teicoplanin and azoles (p=0.04) in ICUs, of carbapenems (p<0.001) and tygecilcline (p=0.01) in medical units and of third-four generation cephalosporins (p=0.002) in surgical units (Figure 1); in these latter a simultaneous increase in the use of cefazolin (p<0.001) and metronidazole (p=0.01) was observed. The antibiotic costs were reduced in medical units and ICUs. No significant differences were found on length of hospital stay in all three areas and on hospital mortality in ICUs. Instead, we registered in ICUs a significant decrease in BSI due to MDR Gram-negative bacteria (p=0.043) (Figure 1).

Conclusions: Our study demonstrated that the implementation of an ASP in a teaching hospital induced a significant reduction in high impact antibiotic use and a positive ecologic impact in the incidence of BSI due to MDR Gram-negative bacteria, without impact on the mortality rate.

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Whole genome sequence of a pan-resistant Klebsiella pneumoniae sequence type 11 harbouring an IncR-F33:A-B-plasmid carrying multiple resistance determinants identified in Japan in 2016

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**Background:** Klebsiella pneumoniae carbapenemase (KPC)-producing Klebsiella pneumoniae has expanded rapidly and is associated with severe nosocomial infections. Last-line antibiotics such as colistin and tigecycline remain the only treatment option. Here, we describe the genetic background of a novel pan-resistant KPC-producing K. pneumoniae isolate from Tokyo, Japan.

**Materials/methods:** The antibiotic susceptibility of clinical isolates from a patient hospitalized in 2016 was tested using a MicroScan WalkAway instrument and the broth microdilution method. Susceptibility was defined according to breakpoints provided by the Clinical and Laboratory Standards Institute (CLSI). Whole-genome sequencing was performed to detect acquired resistance genes and gene mutations, using Single-Molecule Real-Time (SMRT) sequencing.

**Results:** The isolates were identified as part of a laboratory stool and swab surveillance-screening program for infection control. The carbapenem-resistant strain was resistant to β-lactams, including broad-spectrum cephalosporins and carbapenems, and to aminoglycosides, chloramphenicol, fosfomycin, fluoroquinolones, polymyxins (colistin and polymyxin B), tetracyclines (minocycline and tigecycline), and trimethoprim/sulfamethoxazole. The K. pneumoniae isolate harbored an IncR-F33A-B-plasmid carrying catA2, fosA3, rmtB, blaCTX-M-65, blaTEM-1, blaSHV-1, and blaKPC-2 in a non-Tn4401 mobile element (NTE). Colistin and tigecycline resistance was associated with mutations in mgrB gene, which regulates the PhoP/PhoQ two-component system, and ramR gene, respectively. The K. pneumoniae isolate belongs to sequence type (ST) 11, a successful epidemic-type strain.

**Conclusions:** We identified molecular resistance markers in a pan-resistant isolate and provided a genomic description of the pan-resistance and the origins of the isolate and plasmid. The isolate is closely related to a recent highly pathogenic carbapenem-resistant K. pneumoniae identified in China; however, it lacks a virulence plasmid (but it could still act as a reservoir for a virulence plasmid). This K. pneumoniae isolate is of concern in hospital and community care settings. Whole-genome sequencing would be useful for detection and prevention of the spread of newly emerging K. pneumoniae.

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**Abstracts 2020**

**Abstract 2186**

**Evaluation of QuantiFERON-TB Gold Plus test in the diagnosis of Mycobacterium tuberculosis infection**

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**Background:** The aims of this study were to evaluate the sensitivity of QuantiFERON®-TB Gold Plus (QFT) test and to investigate possible factors associated with indeterminate QFT test results and to explore the relationship between latent tuberculosis infection (LTBE) prevalence and the rate of tuberculosis (TB) cases in our region.

**Materials/methods:** 750 cases with QFT test performed in Ege University Faculty of Medicine Hospital in 2016 were included in the study. The QFT results of the cases were compared according to their gender, age groups and clinical characteristics.

**Results:** Among 750 cases, 250 (33.3%) were QFT positive and 33 (4.4%) had an indeterminate QFT result. When the indeterminate results were excluded, QFT positivity was found as 34.9%. The highest indeterminate results were determined among 0-4 year-old group as 11.5% and lowest among the 25-34 age group as 0%. Immunosuppressive patients had nearly two times more indeterminate QFT results when compared with cases without any cellular immunity defect. Among 10 culture-positive cases, 8 had QFT positive, two negative results. The sensitivity of the test was 80% (8/10) among culture-positive active TB cases. The ratio of QFT positivity has increased as the age increased. Interestingly, QFT positivity was higher among females than males in the 15-34 age group and higher among males in the other age groups. The rates of QFT positivity were lower among immunocompromised patients. When QFT positivities were compared with the rate of TB cases among age groups, QFT positivity was observed as parallel to the rate of TB cases.

**Conclusions:** In conclusion, although the sensitivity of QFT was, 80% in culture-positive active TB cases, it was found that it could not be considered as a gold standard in LTBE diagnosis. As active TB cases originate from the LTBE pool, QFT test results might be considered a better indicator of active TB development risk.

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**Abstract 2187**

**Risk factors for developing BK virus associated nephropathy: a single-centre retrospective cohort study of kidney transplant recipients**

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**Background:** BK virus (BKV) infection after kidney transplantation leads to BKV associated nephropathy (BKVAN) in up to 10% of recipients, and is associated with an increased risk of allograft dysfunction or loss. There is no established antiviral therapy available for BKV infection but a pre-emptive strategy to reduce immunosuppression when BK viremia is detected, has been shown to lower the incidence of BKVAN. The objective of this study was to analyse whether the sub-group of patients receiving enhanced immunosuppression have an increased risk of BKVAN, justifying more intensive surveillance.

**Materials/methods:** This was a single centre retrospective cohort study. All patients aged ≥18 years who underwent kidney transplantation or simultaneous pancreas/kidney transplantation at the Uppsala University Hospital in Sweden between 2005 and 2014 were included, a period when BKV screening was not yet implemented at our centre. Most patients received basiliximab and methylprednisolone as induction and a combination of prednisone, mycophenolate mofetil and tacrolimus as maintenance immunosuppression. Enhanced immunosuppression was defined as treatment with thymoglobulin, rituximab, ecuizumab, IVIG, glycosorb and/or plasmapheresis/apheresis. Other risk factors included in the multivariate Cox proportional hazards model were sex, age, cytomegalovirus (CMV) mismatch (donor +/recipient -) and rejection treatment.

**Results:** 44 out of 928 (4.7%) patients developed a biopsy verified BKVAN 4.8 (1.5-35.0) months after transplantation. 141 (15.2%) patients received enhanced immunosuppression. Only male sex showed to be a significant risk factor (Table 1). Patients who presented with BKVAN experienced a significantly higher risk of early graft loss than patients without BKVAN (hazard ratio 4.4).

**Conclusions:** Male sex, but not enhanced immunosuppression, is a significant risk factor for developing BKVAN after kidney transplantation.

**Table 1. Multivariate Cox proportional hazards model of risk factors for BK virus nephropathy after kidney transplantation**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Hazard ratio</th>
<th>95 % Confidence interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.09</td>
<td>0.88-1.35</td>
<td>0.440</td>
</tr>
<tr>
<td>Male sex</td>
<td>2.02</td>
<td>1.02-4.00</td>
<td>0.044*</td>
</tr>
<tr>
<td>Enhanced IS</td>
<td>1.10</td>
<td>0.48-2.55</td>
<td>0.820</td>
</tr>
<tr>
<td>CMV mismatch</td>
<td>0.92</td>
<td>0.42-2.01</td>
<td>0.835</td>
</tr>
<tr>
<td>Rejection treatment</td>
<td>1.22</td>
<td>0.59-2.51</td>
<td>0.593</td>
</tr>
</tbody>
</table>

IS=Immunosuppression, CMV=Cytomegalovirus. * A p-value of ≤ 0.05 was considered statistically significant

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Abstract 2188

Decontamination strategies used for AFB culture significantly reduce the viability of Mycobacterium abscessus in sputum samples from patients with cystic fibrosis

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Background: Nontuberculous mycobacteria (NTM) are important respiratory pathogens in patients with underlying lung diseases and particularly in patients with cystic fibrosis (CF). For diagnosis, international guidelines recommend culture of sputum that has been decontaminated via chemical treatment e.g. using 2% N-acetyl L-cysteine with 2% sodium hydroxide (NALC-NaOH). RGM medium is a highly selective agar-based culture medium allowing isolation of NTM without decontamination of sputum samples. RGM medium therefore provides a convenient tool to quantitatively assess the impact of various decontamination strategies on the viability of NTM.

Materials/methods: Sputum samples from 41 distinct patients known to be colonized with NTM were subdivided and the aliquots were subjected to six different decontamination strategies followed by quantitative culture for NTM using serial dilutions inoculated onto RGM medium. 38 samples were from patients with CF. Thirty sputum samples contained Mycobacterium abscessus complex (MABSC) and 11 contained Mycobacterium avium complex (MAC). Decontamination strategies included treatment with NALC-NaOH, 4% NaOH, 1% chlorhexidine, N/2 sulfuric acid, 5% oxalic acid and double decontamination with NALC-NaOH followed by 5% oxalic acid. As a control, a further aliquot was treated with sterile saline (0.85%). The sputum samples were also cultured directly with no treatment.

Results: The standard NALC-NaOH treatment resulted in an average reduction in colony count of 85% for MABSC when compared with saline-treated controls. 4% NaOH, which is commonly used in the UK, caused a 98% average reduction in colony count. All treatments that included NaOH resulted in colony counts that were statistically lower than the saline-treated control (P <0.05). Standard treatments using sulfuric or oxalic acids were less deleterious but still resulted in an average reduction in colony count of at least 30%. The viability of MAC was much less affected by most decontamination treatments with the biggest impact caused by 1% chlorhexidine, which caused a 66% reduction in viability (Fig.1).

Conclusions: The viability of MABSC was severely compromised by the standard decontamination regimen recommended by international guidelines. This supports an abundance of recently acquired evidence to show that optimal recovery of MABSC is achieved by culture on selective agar media without decontamination of sputum samples.

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Is it safe to use rapid molecular tests for the detection of microorganisms in blood to optimise antimicrobial therapy in septic patients?

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Background: Sepsis is a healthcare problem worldwide with high mortality rate even in intensive care unit. In the era of antimicrobial resistance [AMR], rapid detection of microorganisms in septic patients associated with antimicrobial stewardship program should be used to avoid inappropriated antimicrobial prescription.

Materials/methods: Prospective randomized study including 200 heart disease adult patients with nosocomial sepsis and septic shock. Outcomes and antimicrobial consumption were measured comparing early optimize antibiotic therapy guided by rapid molecular test results or convencional blood culture.

Results: 25% of patients had positive rapid molecular test (group A) and 21% positive blood culture (group B) to detect microorganisms in blood. Antimicrobial de-escalation was performed after 8 hours in group A and 54 hours in group B (p<0.001). There was a 25% decrease in antimicrobial consumption (measured by DOT-days of therapy /1000 patients-day) comparing groups A and B (p 0.017). Hospital mortality was similar in both groups (42% vs 64% in groups A and B respectively) (p=0.149). We also observed that antimicrobial de-escalation suggested by the stewardship team was easily accepted by the physicians in group A patients (results available after 6 to 8 hours) compared to group B (results after 48 hours).

Conclusions: The use of a rapid molecular test to guide antimicrobial therapy in septic patients allowed for earlier de-escalation with clinical evolution similar to conventional blood culture. This strategy could be used safely in stewardship antimicrobial programmes.

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Background: Coagulase-negative staphylococci (CoNS) are frequently isolated in clinical specimens and are important reservoirs of resistance genes. The clinically defined Staphylococcus epidermidis-like group include S. epidermidis, S. haemolyticus and others distinguished from S. saprophyticus, S. lugdunensis and animal associated species. Some strains are frequently associate with resistance to anti-staphylococcal agents and the resistance to methicillin/oxacillin mediated by a modified penicillin-binding protein (PBP2a) encoded by the meca gene is a severe concern.

Materials/methods: The study included CoNS species of S. epidermidis-like group, except S. epidermidis, obtained from clinical specimens between March to August 2018 in south of Brazil. The isolates were identified at species level by MALDI-TOF/MS and a PCR were conducted to determine the presence of meca gene. For methicillin/oxacillin resistance screening, the disk-diffusion with cefoxitin disc was done according with EUCAST (version 9.0) recommendations for Staphylococcus spp.. The institutional Ethics committee approved the research procedure (2.649.105).

Results: We tested 22 isolates (16 S. haemolyticus, 4 S. warneri, 1 S. cohnii and 1 S. caprae) and evaluate the results of disk-diffusion screening using the criteria for CoNS others than S. epidermidis and the criteria for S. epidermidis. The screening criteria recommended by EUCAST for CoNS others than S. epidermidis correctly spotted one isolate (4.5%) meca positive but failed in detected eight isolates (36.4%) carrying meca, with sensitivity of 11% (5.8 – 49.3%) and specificity of 100% (71.6 – 100%). When adopting the criteria for S. epidermidis, seven isolates (31.8%) were correctly identified as resistant, two (9.1%) showed high inhibition zones and were incorrectly classified as susceptible and three (13.6%) meca negative meted the criteria of technical uncertainty (ATU), showing sensitivity and specificity of 77.8% (40.1 – 96.1%) and 76.9% (45.9 – 93.8%). Of all CoNS, nine (40.1%) were positive for meca.

Conclusions: The prevalence of meca in CoNS is high and the screening by disk-diffusion is recommend by EUCAST. In our sample, we observed a low sensitivity of screening criteria to CoNS species others than S. epidermidis. But applying the current criteria available for S. epidermidis, including the ATU, to all species of S. epidermidis-like group we observed increased sensitivity with acceptable specificity.

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Proof of concept: efficacy of surgical titanium implants coated with linear gentamicin against osteomyelitis in pigs

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Abstract third-party references: The project was managed and supported by Rescoll, and funded by FUI, INRA and Rescoll.

Background: Implant infections in human surgery are serious clinical conditions that result in high mortality rates. The treatment of these infections almost systematically requires the combination of long-term antibiotic treatment and concomitant surgical treatment, as well as implant replacement. However, standard antibiotic treatment protocols have a low efficacy for this type of infection and the surgical procedure is often complex. These practices represent a high risk to the patient and a significant cost to society. It is necessary to find alternative solutions, such as using a surface treatment on titanium to deliver antibiotics locally only in case of infection. To meet this objective, it is therefore essential to develop an animal model for the surgical placement of titanium implants with bone infection and to measure the antibiotic efficacy of coated implants.

Materials/methods: The objective of this study is therefore to demonstrate the concept of the efficacy of gentamicin-coated surgical implants against S. aureus osteomyelitis in pigs. We have defined two sizes of titanium cylinder implants (4 and 8 mm length by 4 mm diameter). Double and bilateral partial osteotomy surgery of the porcine tibia was performed, followed by local bone infection with S. aureus SAHOS (human bone clinical isolate) at two different concentrations (10^2 CFU and 10^6 CFU). Once the bacteria have been deposited in the bone hole, the 4 mm and/or 8 mm titanium implant with or without coated gentamicin were deposited.

Results: Clinical and bacteriological results from implants with or without gentamicin confirmed local bone infection at both concentrations tested, as early as 7 days post-infection. However, a significant reduction in bacterial load is observed in the presence of gentamicin-coated implants. In both cases, inflammation of the implanted bone area was observed through clinical and medical imaging (MRI) follow-up and confirmed by the increase in cytokines. As with bacteraemia, the results show that the clinical condition of the pigs is better and inflammation is less spread in the presence of gentamicin coated implants.

Conclusions: This porcine model therefore validates the proof of concept on the therapeutic efficacy of biomedical implants coated against acute postoperative osteomyelitis for human use.

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Biochemical characterisation of GPC-1, a novel class A carbapenemase from a clinical Pseudomonas aeruginosa isolate

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Background: The increasing number of multidrug-resistant Gram-negative bacteria constitutes a serious threat to healthcare systems. Strains of P. aeruginosa are already known to exhibit intrinsic and acquired resistance to many antibiotic classes, including β-lactams. Especially carbapenemase producers are of great concern because they are generally able to hydrolyze many β-lactams. Masked by the intrinsic resistance of Pseudomonas aeruginosa, novel carbapenemases with only low sequence identity to known carbapenemases and an unknown substrate spectrum are difficult to detect and therefore pose a serious challenge for carbapenemase detection by routine diagnostic laboratories. Here we describe the biochemical characterization of GPC1, a novel class A carbapenemase found in a clinical P. aeruginosa isolate from Germany.

Materials/methods: The GPC-1 encoding gene was cloned into the pASGIBA103 vector, that promotes expression of Twin-Strep-tag®-fusion-proteins. The thus-obtained recombinant plasmid was expressed heterologously in Escherichia coli TOP10. Cells were lysed by sonication and the crude lysate was prepared for purification by centrifugation and desalting. Purification of the enzyme was performed by a two-step-Fast Protein Liquid Chromatography (FPLC), including affinity chromatography and gel filtration. The catalytic behavior of GPC-1 was analyzed by in vitro hydrolysis assays through photometrical measurement of the absorbance decrease during β-lactam hydrolysis, followed by determination of the kinetic parameters $K_m$ and $k_{cat}$ using the Michaelis Menten equation. The 50 % inhibitory concentration (IC$_{50}$) for clavulanic acid, tazobactam and avibactam were determined using penicillin G as an indicator substrate.

Results: Determination of kinetic parameters of GPC1 showed that the enzyme was able to hydrolyze penicillins, oxyimino-cephalosporins, monobactams and imipenem. For meropenem and ertapenem an absorbance decrease was only observed under unsaturated conditions indicating that GPC1 seems to bind and capture these carbapenems but without hydrolyzing them efficiently. GPC-1 was inhibited most efficiently by avibactam, followed by tazobactam and clavulanic acid.

Conclusions: The biochemical characterization of GPC-1 illustrates that it shows only weak carbapenemase activity. In strains with various resistance mechanisms, the expression of such a weak carbapenemase might be difficult to detect by routine laboratories. This could also increase the risk of inadequate hygiene measures for patients infected or colonized with bacteria expressing those carbapenemases.

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Impact of combining vancomycin with piperacillin/tazobactam or with meropenem on vancomycin-induced nephrotoxicity

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Background: The major adverse effect of vancomycin (VAN) is nephrotoxicity especially in patients administered large doses. VAN is a broad-spectrum antibiotic against Gram-positive cocci and is used empirically with other broad-spectrum antibiotic such as piperacillin/tazobactam (TZP), cepham, or meropenem (MEM). Literature on the incidence of acute kidney injury (AKI) of VAN with MEM is limited. Therefore, this study aimed to evaluate the incidence of AKI in patients receiving VAN with either TZP or MEM.

Materials/methods: A retrospective cohort study of patients who received either VAN-TZP or VAN-MEM for ≥72h. Patients with a baseline serum creatinine (SCr) of ≥1.5 mg/dL were excluded. The primary outcome was the incidence of AKI [increase in SCr by ≥0.3 mg/dL or ≥1.5-time baseline, whichever is greater]. SCr was recorded at baseline and 3-5 days post antibiotics initiation. Secondary outcomes included all-cause mortality, and length of stay.

Results: A total of 164 patients were included, 81 in the VAN-TZP group vs. 83 in the VAN-MEM group. No difference in baseline characteristics was observed between the two groups in terms of age, sex, race, hospital location, Charlson comorbidity index, diabetes, nephrotoxic drugs, and baseline SCr levels. Change in SCr at day 3-5 was not significantly different between the two groups [-9.4 vs. -6.1%; P=0.78]. While the percentage of patients meeting the definition of AKI was higher in the VAN-MEM group, this difference did not meet statistical significance [11.1 vs. 20.5%; P=0.1]. All-cause mortality was higher in the VAN-MEM group [39.8 vs. 23.5%; P=0.03] possibly because this combination was used in more critically ill patients [31.1% of VAN-MEM patients were admitted to the intensive care unit vs. 18.5% of VAN-TZP patients]. Median length of stay did not differ between the groups [20 vs. 22 days; P=0.64].

Conclusions: This study shows that combining MEM with VAN did not offer the benefit of a lower incidence of acute kidney injury compared with a combination with TZP. Therefore, patients with no risk factors for infections resistant to TZP can continue to receive TZP with VAN without risking AKI development. Hence, conserving MEM and reduce the risk of emergence of carbapenem resistance.

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Abstract 2200

**Long-term immune response to yellow fever vaccination in HIV-infected and non-infected adults: ANRS EP46 study**

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**Abstract third-party references:** For the ANRS EP46 Study Group

**Background:** Duration of immune response after yellow fever (YF) vaccination in HIV-infected patients has been questioned. We evaluated the persistence of YF vaccine antibodies in HIV-infected and HIV-uninfected primary vaccine recipients from the NDVAA-ANRS EP46 prospective study up to 5 years post-vaccination.

**Materials/methods:** The long-term study included 30 of 41 YF vaccine-naïve HIV-infected adults under antiretroviral therapy (ART) with CD4 >350/mm3 and HIV-RNA<50 cp/ml for 6 months minimum, and 20 of 30 healthy adults. All received one YFV17D full dose vaccine. Neutralizing antibody responses were measured by a reference 80% Plaque Reduction Neutralization Test (PRNT) and by a West Nile Virus-YFV17D pseudotype neutralization assay.

**Results:** Up to month 60 (M60) post-vaccination, YF neutralizing antibodies remained above the level for protection of 1:10 in 100% of HIV-infected and uninfected vaccinees. PRNT titers declined significantly at M60 vs M12 in both groups [see Table]. PRNT Geometric Mean Titers (GMT) of HIV-infected and non-infected were not statistically different. With the pseudotype assay, median neutralizing activities were 94% [IQR:86-99] and 99% [93-100] at M12, decreased at 80% [54-98] and 94% [84-97] at M36 and 83% [47-97] and 90% [75-97] at M60 in HIV-infected and non-infected respectively. At M60, no significant association was seen with baseline characteristics of HIV-infected patients [age, CD4, CD8, CD4/CD8, CD4 nadir and zenith, duration of ART, duration of HIV infection]. No SAEs related to vaccination were reported.

**Conclusions:** After a single dose of YF vaccine, the persistence of protective antibodies up to 5 years was similar in HIV-infected patients with CD4 counts >350/mm3 and suppressed viral replication and in healthy subjects. The decrease in neutralization titers over time suggests surveillance over a longer period regardless of the HIV status of participants.

<table>
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**Presenter email address:** christine.durier@inserm.fr
Abstract 2202

Exclusive oral post-surgical antibiotherapy is effective for infectious flexor hand tenosynovitis: a study of 127 patients

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Background: Infectious flexor hand tenosynovitis (IFHT) are frequent conditions with serious consequences in the absence of adequate treatment. Several surgical modalities are possible but antibiotic therapy is not well codified.

Materials/methods: We retrospectively reviewed IFHT managed at Caen University Hospital Center between 01/01/2013 and 01/01/2018. The inclusion criteria were: confirmation of the clinical diagnosis during surgery and a post-antibiotic follow-up of at least 6 months. We evaluated patient’s demographics, type of surgery, antibiotic therapy modalities (molecule, route of administration oral [O] or intra venous [IV] and duration) and the clinical outcome at 6 months.

Results: 127 patients were included. From the classification of Michon we found 62 Stage I, 36 stage II, 1 stage III and 28 unclassified due to missing data. Comorbidities were present in 46.5%, 34.6 % had negative culture due to pre-operative antibiotherapy, the most common bacteria was Staphylococcus (54.2%). The surgery was open-air in 32.3% cases and minimally invasive for 58.3%. All patients received postoperative antibiotic therapy. The most commonly used was Amoxicillin + Clavulanic Acid, it covered 94.5% of the identified organisms.

116 (91.3%) patients were cured of their infection and 11 (8.7%) had a recurrent infection. In multivariate analysis, administration of IV or IV + Oral antibiotic therapy was of no benefit compared to exclusively oral treatment (p = 0.65). Treatment for less than 7 days in comparison with treatment for 7 to 14 days appeared to be associated with a 4.5 times greater risk of failure, although not significant (p = 0.07). We didn’t find any significant difference of outcome according to the duration of antibiotic therapy less than 7 days, 7 to 14 days or more than 14 days (p = 0.14). Diabetes, smoking, surgical technic or immunosuppression were not associated with infectious relapse. The unique factor associated to recurrence was a positive surgical bacteriological sample (p= 0.03).

Conclusions: For stage 1 and 2 IFHT surgical management followed by an exclusive post-operative oral treatment with Amoxicillin + Clavulanic Acid 7 to 14 days seems effective, thus allowing outpatient management. The duration of antibiotic treatment should be better defined by prospective studies.

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Abstract 2203

Stx2k-producing Escherichia coli in China
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Background: Shiga toxin (Stx) is the key virulence factor in Shiga toxin-producing Escherichia coli (STEC), which can cause mild diarrhea to fatal hemolytic uremic syndrome (HUS). Stx comprises two toxin types, Stx1 and Stx2. Several Stx1/Stx2 subtypes have been identified, which are variable in sequences, toxicity and host specificity. Here, we report the wide distribution of our newly-identified Stx2k subtype in E. coli strains from diarrheal patients, animals, and raw meats. A comprehensive whole genome sequence (WGS) analysis was performed to characterize the Stx2k strains and to elucidate the evolution of new STEC variant.

Materials/methods: STEC strains from animals, foodstuffs, patients and healthy carriers were collected through our systematic STEC investigation conducted in China. All strains were sequenced by Illumina platform to obtain the draft genomes, and further molecularly characterized by WGS analysis. Stx subtype was confirmed by a phylogeny scheme based on holotoxin amino acid sequences of Stx. The production and cytotoxicity in vitro of Stx was assessed by Vero cell assay. The complete genomes of specific strains were sequenced by PacBio platform. In-depth comparative genomics analysis was performed to assess the genetic variations in relation to pathogenic capacity, and to identify mobile genetic elements (MGE) impacting the molecular evolution of new STEC variants.

Results: Stx2k was widely identified from STEC strains from diarrheal patients, animals and raw meats, with particularly high prevalence in goats-derived strains. Stx2k exhibits diverse cytotoxicity in vitro among strains from different hosts. The Stx2k converting prophages displayed considerable heterogeneity in terms of insertion site, genetic content and structure. Phylogenomic analysis showed that Stx2k strains formed two major phylogenetic clusters closely with strains belonging to STEC, enterotoxigenic E. coli (ETEC), and STEC/ETEC hybrid. Interestingly, one stx2k-containing strain harbored one plasmid-encoded heat-stable enterotoxin stA gene and two identical copies of chromosome-encoded stb gene, which were virulence determinants of another pathotype, ETEC.

Conclusions: Our findings highlight the extraordinary genomic plasticity of E. coli strains. Given the wide distribution of the Stx2k-producing strains in diverse sources and their pathogenic potential, Stx2k should be taken into account in global epidemiological STEC surveillance and clinical diagnosis of STEC infections.

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Abstract 2206

**Development of novel inhibitors of metallo-β-lactamases in carbapenem-resistant Gram-negative pathogens**

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**Background:** Metallo-β-lactamases (MBLs) are rapidly becoming a major mechanism to carbapenem resistance in Gram-negative bacteria. These enzymes hydrolyse the majority of β-lactam antibiotics (including carbapenems) and the organisms carrying them are frequently multidrug resistant, owing to co-carriage of multiple resistance determinants on transferable genetic elements. Indeed, they have been categorized as a critical threat to human health according to the World Health Organisation. MBL-positive pathogens represent an urgent medical need as there is currently no effective MBL inhibitor (MBLI), meaning treatment options are often few to none. The AMR Centre has identified and optimised an MBLI (AMRC-835) for use with β-lactam antibiotics in MBL-positive infections.

**Materials/methods:** Susceptibility testing and time of kill analysis was performed according to CLSI guidelines. Enzyme assays were performed using nitrocefin and recombinant NDM-1, VIM-2 and IMP-1. Off-target activity was evaluated in a human receptor and enzyme panel (SafetyScreen44, Cerep) and a panel of Matrix metallopeptidases (MMPs). Cytotoxicity, cardiotoxicity and genotoxicity were investigated using standard methods. Resistance frequencies and serial passage were also performed to standard methods. *In vivo* efficacy was assessed in a mouse thigh infection model using *E. coli* (NDM-1). *In vivo* safety was determined in a rat 3-day repeat-dose toxicology study.

**Results:** MBLIs demonstrated broad spectrum activity versus NDM, IMP and VIM enzymes; no inhibition of human matrix metallopeptidases (MMPs) was observed. A representative compound from the series restored meropenem activity in Enterobacterales and *Acinetobacter baumannii*; Enterobacterales (n=115) MIC\textsubscript{90} = 0.12 µg/mL (from 128 µg/mL) and *A. baumannii* (n=6) MIC\textsubscript{90} = 2 µg/mL (from >128 µg/mL). The resistance profile of the series was equivalent to meropenem alone. Addition of MBLI to meropenem restored efficacy in time of kill assays and a mouse thigh infection model (*E. coli* NDM). An excellent safety profile was established *in vitro* [no flags identified in SafetyScreen44, cardiotoxicity or genotoxicity assays] and the lead MBLI (AMRC-835) was safe in a 3-day repeat-dose rat toxicology study up to 900 mg/kg.

**Conclusions:** Evaluation of this series has led to nomination of AMRC-835 as a preclinical candidate for development towards a novel combination therapy for the treatment of MBL-positive Gram-negative infections.

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**Necrotising otitis externa: a retrospective cohort study and treatment protocol proposal**

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**Background:** In England, the incidence of Necrotising otitis externa (NOE) has increased 6.3 times increase over 14 years. The most common pathogen is *Pseudomonas Aeruginosa*, and patients are often diabetic and frail. No randomized controlled trials are available in the current literature, and case series include 5-88 patients. Hence no consensus on the most effective treatment protocol for NOE has been agreed. We aim to produce local NOE treatment protocol using a a retrospective cohort study in our hospital.

**Materials/methods:** A retrospective cohort study on the treatment of patients with NOE in Hull University Hospitals Trust was done according the STROBE criteria. Case notes coded for NOE from December 2013 to December 2018 were reviewed. There were no exclusion criteria. Relevant data on demographics, risk factors, diagnosis, microbiology results, morbidity and mortality and follow-up were extracted from the paper notes and electronic hospital systems.

**Results:** Twenty-nine patients aged 47-94 years were included; Eighteen patients (62%) had diabetes or were immunosuppressed. *Pseudomonas aeruginosa* was the most commonly identified micro-organism (64%); other organisms included MSSA, and *E.Coli; Aspergillus Niger and Candida spp* were only encountered in polymicrobial infections. In 12.5% no growth was seen possibly reflecting prior topical antibiotic use. Ceftazidime or meropenem monotherapy was mostly used, with ciprofloxacin as an oral step-down option. There were no relapses, but one patient died directly due to NOE related sepsis. Daily microsuction of the ear was performed in 82.8% of patients and hyperbaric oxygen treatment was used in 25%. Treatment lasted for an average of 6 weeks, which is in keeping with other treatment protocols for osteomyelitis. Based on our findings we proposed a local treatment protocol as described in figure 1.

**Conclusions:** To the best of our knowledge, this study is the second UK based large case series on the management of NOE. Extrapolating these results, we proposed a practical management protocol for necrotizing otitis externa in the UK focusing on identification of the causal pathogen, culture tailored antibiotics and supportive measures. This protocol will need further validation.
Figure 1 – Suggested treatment algorithm for Necrotising Otitis Externa based on a case series of 29 patients in Hull and East Yorkshire Hospitals. Side boxes – optimisation of patient outcomes

Suspicion of Necrotising Otitis Externa (NOE)

Ear and Pus Swab for culture and sensitivity analysis (MC/S)

Empirical IV Ceftazidime monotherapy antibiotics

Pre-diagnosis

CT Scan via radiologist for confirmation

Modify IV antimicrobials according to MC/S result

Negative culture from MC

Punch Biopsy

Hickman Line/PICC Line

Modify for combinational therapy or antifungals

Post Diagnosis

Absence of presenting symptoms and signs of infection

Post discharge Oral antibiotics, typically Ciprofloxacin for at least 4/52

Follow up via outpatients

Post Discharge

Clinical Resolution of NOE

- Control BMs
- Microsuction daily
- Topical drops antibiotics
- Correction of immunosuppression
- Analgesia
- CRP

- Surgery - debridement, polypectomy
- Hyperbaric oxygen Chamber
- CRP

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Relation of risk factors and mortality in carbapenem-resistant *Klebsiella pneumoniae* ST11 bloodstream infections

Tingting Xiao*, Xiao Yonghong†

†Zhejiang University, Zhejiang, China

**Background:** Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) is rapidly emerging as a life-threatening nosocomial infection. It is valuable to identify the clinical characteristics, particularly the outcomes and antibiotic therapy for CRKP infections.

**Materials/methods:** A retrospective, comparative analysis of data from patients treated for CRKP bloodstream infections (BSIs) at a single tertiary teaching hospital during 18 months. All statistical analyses were executed by using the SPSS version 23.0.

**Results:** Data from 90 patients with CRKP BSI were included, 84.4% (N=76) with ST11. Among ST-11 CRKP, 82.9% (N=63) were K64. There were no significant differences in 30-day mortality among patients with ST11-CRKP and nonST11-CRKP (56.6% versus 35.7%, P=0.087). Univariate analysis showed that hemodialysis within 30 days prior to BSI, lower total protein, lower platelet, high Pitt score, prior exposure to corticosteroid, and inappropriate empirical treatment after BSI, tigecycline therapy after BSI were associated with mortality. Prior exposure to corticosteroid (OR=7.300, P=0.027) and lower total protein (OR=0.909, P=0.002) were identified as independent risk factors for the 30-day mortality of CRKP BSI patients.

**Conclusions:** There was not significantly different in mortality of patients with BSI caused by ST11-CRKP or non-ST11 CRKP during the study period. Exposure to corticosteroid and lower total protein were strong risk factors for mortality of CRKP-BSI.

**Figure 1.** Kaplan–Meier survival curves for patients with Non-ST11 and ST11 carbapenem-resistant *Klebsiella pneumoniae* (CRKP) bloodstream infection.

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Abstract 2211

Monitoring of difficult-to-treat tuberculosis patients in Ghana identifies additional pre-XDR and XDR cases

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1Noguchi Memorial Institute of Medical Research, University of Ghana, Accra, Ghana, 2Swiss Tropical And Public Health Institute, University of Basel, Basel, Switzerland

Abstract third-party references: The West African Network for TB, AIDS, Malaria (WANETAM), National Tuberculosis Control Program, Ghana, Swiss-African Research Cooperation (SARECO)

Background: Emergence of drug resistant TB (DR-TB) threatens to make TB untreatable. Early identification of the causation of TB and its drug susceptibility profile are essential for appropriate treatment regimen. We report here preliminary findings of our monitoring of difficult to treat TB-cases (DTT-TB) in Ghana.

Materials/methods: Sputum samples obtained from DTT-TB (i.e treatment failures, relapsed, retreatment and known drug resistant TB) from health facilities across Ghana were processed for rapid diagnosis using the Genotype MTBDRplus, Genotype MTBDRsl, direct smear-microscopy and culture.

Results: A total of 244 (73.7%) out of the 331 sputum samples processed gave interpretable bands out which 54 (22.1%), 48 (19.7%) and 78 (31.9%) were INH-mono-resistant (INHr), RIF-mono-resistant (RIFr) and MDR respectively. Two (1.3%) of the MDR samples were resistant to second line fluoroquinolones (FQs) and aminoglycosides (AMGs) hence termed XDR-TB whereas 16 (20.5%) were resistant to either drugs and termed pre-XDR-TB. More so, 8 samples (6 RIFr and 2 INHr) were additionally resistant to at least one of the second line AMGs or FQs hence termed poly-drug-resistant samples. Eighty-two (62.1%) of INH-resistant samples had katG-mutations where as 34 (25.7%) had inhA-pro-mutations. The remaining 16 (12.1%) had mutations at both loci. Out of the 26 samples with resistance to at least one second-line drug, 16 (61.5%) and 3 (11.5%) were resistant to FQs (gyrA mutations) and AMGs (rrs mutations) respectively whereas 7 (26.9%) were resistant to both. With the exception of the 2 XDR samples and 3 RIF-poly-resistant samples, no sample had eis mutations.

Conclusions: Detection of additional XDR and pre-XDR TB cases in Ghana following the first report from our lab last year calls for intensified monitoring of TB patients to ensure compliance

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Abstract 2212

**Efficacy of memory B lymphocytes in experimental model of pneumonia caused by Pseudomonas aeruginosa**

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**Background:** There is an urgent need for new alternatives to treat infections multidrug-resistant (MDR) *P. aeruginosa* infections. Immunotherapy as adjuvant to antibiotics might be a good option by increasing the host innate immunity. In this study we evaluate the efficacy of memory B lymphocytes in the treatment of a pneumonia murine model by clinical strains of *P. aeruginosa*.

**Materials/methods:** Two MDR clinical strains of *P. aeruginosa* (Pa147, colistin-susceptible and PaM1, colistin-resistant) were used. C57BL/6J male mice, 20g were inoculated with the minimum lethal dose calculated for each strain. Antimicrobial treatment was initiated 4h post-infection and lasted 72 hours, while memory B lymphocytes therapy was a single dose 30 minutes after infection. Treatments groups were: a) controls (infected, untreated); b) memory B lymphocytes (2x10⁶ B lymphocytes, intravenously) c) colistin; 20mg/kg/8h/intraperitoneally and d) Ceftazidime; 100mg/kg/12h/intraperitoneally. After death or sacrifice, bacterial counting in lung and blood was performed, and percentages of bacteremia and survival were analyzed. The two-tailed Fisher’s test, analysis of variance (ANOVA), and the Dunnet and Tukey *post hoc* tests were used. *P*<0.05 was considered significant. The SPSS v22.0 was used (SPSS Inc).

**Results:** Efficacy results of antimicrobials and B lymphocytes.

<table>
<thead>
<tr>
<th>Strains</th>
<th>Treatments</th>
<th>N</th>
<th>Lung (Log CFU/g)</th>
<th>Blood (Log CFU/mL)</th>
<th>Bacteremia (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pa 147</td>
<td>CTL</td>
<td>19</td>
<td>9.15±1.21</td>
<td>6.71±0.89</td>
<td>100 [19]</td>
<td>100 [19]</td>
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<tr>
<td></td>
<td>Memory B lymph</td>
<td>10</td>
<td>6.56±3.57</td>
<td>3.76±3.29</td>
<td>60 [6][^a]</td>
<td>50 [5][^a]</td>
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<tr>
<td></td>
<td>CMS</td>
<td>16</td>
<td>8.98±0.72</td>
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<td>100 [16]</td>
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<tr>
<td></td>
<td>CAZ</td>
<td>12</td>
<td>7.16±1.72[^a]</td>
<td>2.78±2.58[^a]</td>
<td>67 [8][^a]</td>
<td>58 [7][^a]</td>
</tr>
<tr>
<td>Pa M1</td>
<td>CTL</td>
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<td>9.80±0.47</td>
<td>6.18±1.36</td>
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<td>100 [13]</td>
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<tr>
<td></td>
<td>Memory B lymph</td>
<td>9</td>
<td>9.75±0.57</td>
<td>5.64±2.44</td>
<td>100 [9]</td>
<td>78 [7]</td>
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<td>CMS</td>
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<td>5.24±2.05</td>
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<td>70 [7]</td>
</tr>
<tr>
<td></td>
<td>CAZ</td>
<td>10</td>
<td>8.21±0.97[^a,^c]</td>
<td>5.24±1.70</td>
<td>100 [10]</td>
<td>60 [6][^a]</td>
</tr>
</tbody>
</table>

CTL: Control, CMS: Colistin methate sodium, CAZ: Ceftazidime. * P≤0.05 compared to CTL, ^ P<0.05 compared to CMS and ^ P<0.05 compared to memory B lymphocytes.

**Conclusions:**

1) Memory B lymphocytes reduced bacterial concentration and improved survival and bacteremia compared to controls and colistin in a murine model by a MDR *P. aeruginosa* colistin-susceptible strain.

2) Immunotherapy as adjuvants to antimicrobials might be an option for these infections, nevertheless further studies must be done.

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Abstract 2215

A novel spectrophotometric assay for rapid detection and differentiation of KPC-, MBL- and OXA-48-producing Enterobacteriaceae

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Background: The augmented prevalence of carbapenemase-producing enterobacteriaceae (CPE) in hospitals and healthcare facilities has made crucial the development of more rapid tests for the specific detection of multidrug-resistant pathogens. The present study focused on the development of a simple methodology that is based on the measurement of hydrolytic activity of β-lactamases through UV-visible spectrophotometry.

Materials/methods: In the present analysis a total of 86 CPE clinical isolates were tested, while CPE isolates were characterized as KPC, VIM, NDM and OXA-48 producers through phenotypic disc testing and PCR assay, as well. Moreover, detailed susceptibility test was conducted in all tested clinical isolates. The hydrolysis of imipenem was measured through spectrophotometry in bacterial extracts. The initial absorbance of imipenem was measured immediately after the insertion of the antibiotic in bacterial extracts. Phenylboronic acid (PBA) and EDTA were also incorporated in the newly developed spectrophotometric assay in order to identify the different groups of carbapenemase producers.

Results: The spectrophotometric assay enables the sufficient differentiation of CPE and non CPE strains in 45 minutes of incubation (t test, P < 0.0001). Moreover, the presence of PBA and EDTA in the reaction mixtures inhibited the hydrolytic capacity of KPC and MBLs, respectively [P<0.001], while OXA-48 producers were not affected in the presence of the respective inhibitors. The outcomes of spectrophotometric assay were compared with that of phenotypic disc test and PCR [gold standard] and it was suggested that the newly developed assay demonstrates 100% sensitivity and specificity in detecting KPC, MBLs and OXA-48 producers.

Conclusions: In conclusion, the newly established spectrophotometric methodology can be considered as a highly sensitive and specific diagnostic tool that offers healthcare providers in short time considerable information concerning the proper antimicrobial therapy.

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Abstract 2220

**Effective antimicrobial combination testing: linking rapid microcalorimetry screening to in vivo efficacy**
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**Background:** The emergence of antibiotic resistant bacterial strains worldwide calls for an effective exploitation of existing antibiotics. A possible approach is combination of antibiotics with different modes of action, which can synergize and allow for successful treatment. This approach must involve rapid testing to ensure effective treatment at the initial stages of serious infections.

Here we present a study of the use of a microcalorimetry-screening platform for protagonistic combination treatment, against clinical multi-drug-resistant (MDR) strains of *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, and the verification in a murine in vivo model.

**Materials/methods:** 98 resistant clinical isolates were screened for protagonistic effectiveness of meropenem in combination with either colistin, rifampicin or amikacin, compared to single drug treatment, in a calScreener micro calorimeter based on metabolic activity.

One *E. coli*, 4 *K. pneumoniae*, 2 *P. aeruginosa* and 3 *A. baumannii* strains expressing either antagonistic or protagonistic effect of combination treatment were chosen and further tested in a murine peritonitis/sepsis model. MNRI mice where inoculated intraperitoneally with approx. 10E7 CFU. After 1-hour mice were treated with either saline, drug X, drug Y or both antibiotics. After 4 hours of treatment mice where sacrificed and the quantity of bacteria determined by CFU count in both blood and peritoneal fluid.

**Results:** Several (8) strains exhibited drastically reduction in MICs for drugs when used in combination, with fractional inhibitory concentration index’s (FICI) <1. Together with 5 strains with increased MIC in combination FICI >2 these were tested in vivo. There was a significant negative correlation (P = 0.0296) between FICI-value found in the microcalorimetry-screening and log-reduction in peritoneal fluid from mice treated with the combination treatment compared to the best mono-drug treatment, indicating that microcalorimetry could effectively predict the possible antimicrobial synergy in vivo.

**Conclusions:** These data support the ability of the calScreener micro calorimeter to predict protagonistic or synergistic effect of combinations of antibiotics for the treatment of MDR infections and therefore be used as a viable tool for screening for new treatment regimen.

**Fractional inhibitory concentration index**

**Peritoneal fluid**

\[ R^2 = 0.47, P = 0.0296 \]

**Blood**

\[ R^2 = 0.35, P = 0.0702 \]

**Log-reduction of combination treatment better than best mono-treatment**

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Abstract 2221

Microbiome analysis of samples from patients with idiopathic pulmonary fibrosis in the A Coruña University Hospital, Spain: a pilot study

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Background: Idiopathic pulmonary fibrosis (IPF) is a chronic lung disease with an unknown etiology which causes progressive loss of pulmonary function showing high mortality. Previous works linked the presence of Streptococcus, Staphylococcus, Haemophilus, Neisseria and Veillonella in the lungs with the IPF. The aims of this work were: (i) to perform a metagenomic analysis of samples from both the oropharyngeal cavity and lungs of IPF patients, (ii) to know if the lung colonization could be due to microaspirations from the oropharyngeal cavity harboring the infectious agents.

Materials/methods: Oropharyngeal samples, obtained by scraping (OS), and lung samples, obtained from bronchoalveolar lavage (BAL), from IPF patients of the Hospital of A Coruña (HUAC, Spain), were collected. After an enzymatic treatment, samples were subjected to DNA extraction. DNA was used for the PCR-amplification of a hypervariable region of the bacterial 16S rRNA gene. PCR products were used for metabarcoding libraries preparation and sequencing was performed using a MiSeq equipment, following Illumina procedures. Bioinformatic analysis were done using QIIME 2. The taxonomic assignment was performed by querying the representative sequence variants against the SILVA reference database.

Results: Streptococcus [6-36% BAL, 10-79% OS], Veillonella [4-8% BAL, 0.1-16% OS], Haemophilus [3.8-4.6% BAL, 0-4.6% OS] and Neisseria [1.9-17% BAL, 21-27% OS] genus were found both in BAL and in OS samples, whereas Staphylococcus was not present in any sample. A significant abundance of other bacteria such as Fusobacterium, Porphyromonas, Prevotella, Granulicatella, Rothia, Gemella, Orobacterium and Parvimonas were found in both the oropharyngeal and the broncoalveolar regions.

Conclusions: The great abundance of bacteria previously associated with IPF, found in lungs and in the oropharyngeal region of IPF patients, suggested that these microorganisms living on the oral and the pharyngeal cavities could be recruited through microaspirations, causing secondary lung colonization and, consequently, disturbing the internal pulmonary environment leading to IPF. Other bacteria, some of them being oral inhabitants previously described as important infectious agents, such as Fusobacterium or Porphyromonas, were also detected in both BAL and OS samples. We suggest that these bacteria could be involved in IPF development, although major studies are needed to confirm it.

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Abstract 2224

Increased carriage of *Streptococcus pneumoniae* serotype 19A three years after a PCV13 to PCV10 vaccine switch in Belgian children

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**Background:** The predominantly "2+1" Belgian infant pneumococcal conjugate vaccine (PCV) programme changed from PCV13 to PCV10 in 2015-2016. Nasopharyngeal carriage of PCV13 pneumococcal serotypes (STs) was evaluated by real-time PCR in children (6-30 months) attending day-care centres (DCC) or seeking care for acute otitis media (AOM) over a three year period between March 2016 and April 2018.

**Materials/methods:** Nasopharyngeal swab samples were obtained from 2615 DCC and 366 AOM children in Belgium, stored in STGG medium at -80°C and analysed by real-time PCR targeting *lytA*. All *lytA*-positive samples were screened by pooled, singleplex real-time PCRs for presence of PCV13 STs. For serogroup 6, analysis of the *wciP* and *wciN* gene was carried out by three real-time PCRs targeting, respectively, the single nucleotide polymorphism at codon 195 (Ser for ST6A/6C; Asn for ST6B/6D) and the *wciN* gene which is 200 bp shorter (*wciNβ*) for ST6C/6D. Pearson's Chi square test was used for statistical analysis.

**Results:** Total pneumococcal carriage remained at a high and stable level during the three year study period, ranging between 75.7% and 80.0% in DCC and 77.9% and 82.1% in AOM. Carriage of PCV13 STs among *lytA*-positive samples (n=2329) increased from 4.6% to 10.4% in DCC (P<0.001) and from 6.3% to 9.8% in AOM. This increase could be attributed to the increase in PCV13-non-PCV10 STs, which was in turn almost completely due to the rise in carriage of ST19A from 0.5% to 8.0% in DCC (P<0.001) and 0.0% to 5.5% in AOM. Meanwhile, prevalence of PCV10 STs decreased from 3.3% to 1.7% in DCC and 6.3% to 2.5% in AOM, the most prevalent among PCV10 STs was 19F. Finally, increased prevalence of ST6C was noted in the third year for both DCC and AOM, respectively from 1.3% to 6.1% (P<0.001) and 3.2% to 8.0%. Even though ST6C is not part of PCV13, it has been shown that cross-protection might occur based on its close relation to ST6A.

**Conclusions:** Following a switch in the PCV programme from PCV13 to PCV10, we have shown a rise of ST19A and ST6C among pneumococcal carriage in children.

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Impact of antibiotic stewardship programme in an intensive care unit in Brazil

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Background: In an intensive care unit (ICU), the multiple drug-resistant (MDR) pathogens present challenges for patients’ survival. The antimicrobial stewardship programs (ASP) aim to improve and measure antibiotic use, but also to decrease the MDR’s incidences. With this context in mind, the present study analyzed the impact of ASP at the MDR’s incidence and global mortality in an Intensive Care Unit in Brazil.

Materials/methods: Data from 4 ICUs (68 beds) from a private hospital in Rio de Janeiro city, Brazil, were analyzed. Data from the first period (May 2015 to May 2017) and from the second period (June 2017 to June 2019) were retrospectively and prospectively collected, in this order. Since June 2017, the ASP group focused activities on infection control and daily antimicrobial prescription audits. Data of antimicrobial consumption were obtained from the hospital pharmacy and expressed as defined daily doses (DDD) per patients-days; MDRs were expressed as density of incidence (DI) for carbapenem-resistant Enterobacteriaceae (CRE) and carbapenem-resistant Pseudomonas (CRP). Global mortality at the ICU was also evaluated.

Results: 3,074 and 3,733 patients were hospitalized and reviewed at 1st and 2nd periods, respectively. The consumption of meropenem decreased between the two periods from 48.58 [95% CI 9.63 – 9.80] to 17.32 DDD per pts-days [95% CI 3.41 – 3.52]. The density of incidence of CRE decreased through the study period from 6.45 [95% CI 5.74 – 7.21] to 4.56 cases per 1,000 pts-days [95% CI 3.96 – 5.22]. The density of incidence of CRP also decreased from 5.24 to 3.09 cases per 1,000 pts-days [95% CI 4.61 – 5.93]; [95% CI 2.60 – 3.64], respectively. The mortality rate decreased during the study period. In the 1st period was 30.03 per 1,000 pts-days [95% CI 2.85 – 3.16] and in the 2nd period was 22.45 [95% CI 2.11 – 2.40]; the rate ratio was 1.34 [95% CI 1.23 – 1.45].

Conclusions: Despite all the difficulties in implementation, ASP in the ICU setting resulted in the decrease of antimicrobial consumption, MDR incidence and mortality.

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Efficacy of immunoglobulin enriched in IgM, alone and in combination, in experimental model of pneumonia caused by Pseudomonas aeruginosa

Tania Cebrero Cangueiro, Gema Labrador Herrera, Marta Claudia Carretero Ledesma, Younes Smani, Jeronimo Pachon-Diaz, María Eugenia Pachon-Ibáñez

1Institute of Biomedicine of Seville (IBiS), University of Seville/CSIC/University Hospital Virgen del Rocio, Sevilla, Spain

Background: New therapeutic alternatives for the treatment of multidrug-resistant (MDR) P. aeruginosa infections. The aim of this study was to evaluate the efficacy of immunoglobulin enriched in IgM [IVIG-IgM], as adjuvant to antimicrobials in a pneumonia murine model by clinical MDR P. aeruginosa strains.

Materials/methods: Two clinical MDR P. aeruginosa strains were used, Pa147, colistin-susceptible and PaM1, colistin-resistant. C57BL/6J mice were inoculated intratracheally with the minimum lethal doses of each strain. Antimicrobial therapy was initiated 4h post-infection, while an only dose of IVIG was given 30 minutes post-infection. Therapy groups were: a) controls (infected, untreated); b) IVIG-IgM, 430mg/kg/intravenously; c) colistin, 20mg/kg/8h/72h/intraperitoneally; d) Ceftazidime, 100mg/kg/12h/72h/intraperitoneally; e) IVIG-IgM+CMS and d) IVIG-IgM+CAZ. After death or sacrifice, bacterial counts in lung and blood, and bacteremia and mortality percentages were analyzed. The two-tailed Fisher’s, ANOVA, and the Dunnet and Tukey post hoc tests were used. P<0.05 was considered significant. The SPSS v22.0 was used.

Results: Efficacy results of immunoglobulin (IVIG-IgM) enriched in IgM and antimicrobials. Controls animals and IVIG-IgM treated group had high bacterial concentrations and 100% bacteremia and mortality with both strains.

<table>
<thead>
<tr>
<th>Strains</th>
<th>Treatments</th>
<th>N</th>
<th>Lung (Log CFU/g)</th>
<th>Blood (Log CFU/mL)</th>
<th>Bacteremia (%)</th>
<th>Mortality (%)</th>
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<tr>
<td>Pa 147</td>
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<td>16</td>
<td>8.98±0.72</td>
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<td>CMS+IVIG-IgM</td>
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<td>6.75±2.06</td>
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<tr>
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<td>CAZ+IVIG-IgM</td>
<td>11</td>
<td>6.95±1.33</td>
<td>1.89±1.10</td>
<td>80 [9]</td>
<td>36 [4]</td>
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<tr>
<td>Pa M1</td>
<td>CMS</td>
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<td>8.94±1.06</td>
<td>5.24±2.05</td>
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<tr>
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<td>CAZ</td>
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<td>8.21±0.97</td>
<td>5.24±1.70</td>
<td>100 [10]</td>
<td>60 [6]</td>
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</tbody>
</table>

Conclusions: 1. IVIG-IgM in combination with colistin and ceftazidime reduced bacterial concentration and improved bacteremia and survival in a pneumonia model by MDR P. aeruginosa strains. 2. IVIG-IgM as adjuvants to antimicrobials might be a good option to treat these kind of infections, further studies are necessary.

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Abstract 2227

**Chlamydia psittaci /C. abortus detection in respiratory samples (England and Wales, 2012-2018)**

Sanaa Mayet*, Jessica Day¹, Lalita Vaghji¹, Alice Peace¹, Derren Ready¹, Victoria Chalker¹, Meera Chand¹, Baharak Afshar²

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**Background:** Human psittacosis is caused by *Chlamydia psittaci* from inhalation of urine/faeces from infected birds via occupational or recreational exposure in the home or workplace. Infection presents as a non-specific flu-like illness or community-acquired pneumonia (CAP). Psittacosis is not often tested for in cases of CAP. The proportion of CAP caused by *C. psittaci* remains unclear with 1% attributed by meta-analysis¹. *Chlamydia abortus* infection is associated with human contact and inhalation of infected material from livestock such as foetal loss in sheep, cattle and goats.

**Materials/methods:** Respiratory specimens referred to RVPBRU PHE from 2012-2018 by laboratories from England and Wales for psittacosis investigations were tested using a *C. psittaci*/abortus qPCR assay. However, this assay is not able to distinguish between the two species.

**Results:** A total of 59 respiratory specimens were received between August 2012 and October 2018, from patients ranging in age from 8-80 years. 29 specimens (49.2%) were from males. *C. psittaci /abortus* was detected in 9/59 (15.2%) specimens. Positive specimen types included bronchoalveolar lavage; BAL [5], sputum [2], throat swab [1] and one nucleic acid extract [sample type unspecified]. Referral documentation from positive cases indicated three had recent exposure to birds, two of these regularly handled parrots and one case worked in a wildlife centre, with no reference to sheep, cattle or goat exposure. Seven of the cases required intensive care/high dependency with severe respiratory signs, with two requiring extracorporeal membrane oxygenation.

**Conclusions:** Of the samples tested, 15.2% had detectable *C. psittaci /abortus* DNA. The increased use of the qPCR assay could support detection of further cases. Psittacosis is not a common cause of CAP, however in patients with relevant animal exposures, such as those with exposure to avian species, faecal matter, occupational or recreational exposure, it is an important differential diagnosis. The cases detected herein are presumed to represent the more severe spectrum of disease, stimulating clinical suspicion of *C. psittaci /abortus* infection with subsequent specimen collection and testing.

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**Abstract 2232**

**In vitro virulence of Staphylococcus schweitzeri**

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**Background:** Although *Staphylococcus schweitzeri* is part of the *Staphylococcus aureus* complex, it is not considered a human pathogen. The aim of this work was to assess the virulence of *S. schweitzeri*.

**Materials/methods:** Whole genome sequencing was done to screen for virulence factors and to assess the population structure of *S. schweitzeri* (n=58) from Gabon, DR Congo, Nigeria and Côte d’Ivoire. The invasion, induction of cell death, cytotoxicity, phagosomal escape, coagulase activity and host cell activation of *S. schweitzeri* was compared with *S. aureus* comparator isolates representing the most common clonal complexes (CC) in Africa (CC15, CC121, CC152) using different host cells (Vero, A549). A collection of clinical isolates from Gabon provisionally identified as *S. aureus* (n=159) were screened for *S. schweitzeri*.

**Results:** *S. schweitzeri* were grouped into five geographical clusters and isolates from humans were found in two different clades within the Gabonese cluster. The comparison of *S. schweitzeri* vs. *S. aureus* comparator isolates showed a similar host cell invasion (0.9 vs. 1.2 CFU/ml), host cell activation (4.1 vs. 1.7 normalized fold expression of CCL5 and 7.3 vs. 9.9 normalized fold expression of IL8) and intracellular cytotoxicity (31.5% vs. 25%). The extracellular pathogenicity (52.9% vs. 28.8%) was higher for *S. schweitzeri* than for *S. aureus*. All tested *S. schweitzeri* were able to escape from phagosomes. *S. schweitzeri* was not detected in clinical samples.

**Conclusions:** *S. schweitzeri* is as virulent as *S. aureus* in the applied in-vitro assays. Its transmission to humans was demonstrated on two occasion but clinical infections were not detected.

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Abstract 2233

Impact of immunosuppressive agents on clinical manifestations and outcome of Staphylococcus aureus bloodstream infection: a propensity-score matched analysis in two large, prospectively evaluated cohorts

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Background: Staphylococcus aureus bloodstream infection (SAB) is a common, life-threatening infection. Several factors associated with poor clinical outcome have been previously identified. However, large studies examining mortality and long-term complications in patients under immunosuppressive agents are lacking.

Materials/methods: Data from two prospective, multicentre cohort studies (INSTINCT and ISAC) conducted in 20 tertiary care hospitals in 6 countries (Germany, Korea, Spain, Taiwan, United Kingdom, USA) between 2006 and 2015 were analysed. Patients taking immunosuppressive agents (defined as >40mg/day prednisolone-equivalent, calcineurin or mTOR inhibitors, MMF, cyclophosphamide, high dose DNA biosynthesis inhibitors and newer biological agents) were identified. A 1:2 propensity score matched analysis was performed to adjust for baseline characteristics of patients. Overall survival and time to SAB-related late-complications (SAB relapse, infective endocarditis, osteomyelitis or other deep-seated manifestations) were analysed by Cox regression models, properly adjusting for competing risks.

Results: Of 3,191 analysed patients, 174 were under immunosuppressive treatment according to our definitions. 173 were successfully matched to 344 non-immunosuppressed patients. Median age of 517 included patients was 58 years and 345 (67 %) were male. After propensity score matching, baseline characteristics were well balanced. In the Cox regression analysis we observed no significant difference in survival between the two groups [death during follow-up: 27.9% non-immunosuppressed vs. 29.5% in immunosuppressed patients, hazard ratio 1.02 [0.70; 1.48]]. However, a trend towards higher survival within the first 30 days after SAB onset among immunosuppressed patients was noticed [Fig. 1]. Competing risk analysis showed a cause-specific hazard (CSH) of 3.95 [1.21; 12.82] for SAB-related late-complications in patients under immunosuppressive agents.

Conclusions: While immunosuppression was not associated with an overall higher mortality during follow-up, we observed lower mortality rates early in the course of SAB. Conversely, patients under immunosuppressive agents were more likely to develop SAB-related late-complications. Immunosuppressive agents might prevent hyperinflammation early in the course of (severe) SAB cases (and are therefore associated with a transiently lower mortality), but may also lead to inefficient pathogen clearance and relapsing or disseminated disease.
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Clinical features of acute Q fever in Réunion Island: a retrospective cohort study

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Background: Q fever is an underreported and underdiagnosed zoonotic disease due to Coxiella burnetii, an intracellular bacterium. In Reunion Island, a French department under the tropics, which has known a rapid epidemiologic transition, zoonoses are believed to be more common than in temperate regions. Among these, the situation of Q fever has been well characterized in ruminants with seroprevalence as high as 13.4% in goats, the most likely contributors to transmission with shedding rate as high as 20% in vaginal fluids. In human, the seroprevalence has been estimated at 6.8% in the community, which prefigures Reunion Island as an endemic setting. The aim of this study was to report clinical and first incidence data of acute Q fever in Réunion Island from 2004 to 2017.

Materials/methods: Cases were retrieved from hospital databases using "Q fever" or "Coxiella burnetii" as search terms and enrolled in a retrospective regional cohort study conducted from the chart reviews of the four hospitals of the Island. Inclusion was based either on a positive Coxiella burnetii serology (defined as phase IgG II ≥ 200 and phase IgM II ≥ 50), or a seroconversion or a positive PCR of hospitalized patients. Given the retrospective nature of the study design, the regional cumulative incidence over the study period was estimated from municipalities where cases had been observed in order to limit underreporting.

Results: One hundred and forty-five patients were screened during the study period. Forty-two patients matched the case definition. Cumulative incidence was estimated at 9.3 per 100,000 inhabitants (95%CI: 6.4-12.1) with cases diagnosed yearly all throughout the study period except in 2006. Ninety percent of the cases were dwelling in the south (n=38). Most common manifestations were pulmonary [n=26 with 45.24% pneumonia], digestive [n=11] and cardiac [endocarditis, n=2].

Conclusions: Together with some previously known seroprevalence figures [Bouche du Rhône, French Guiana], these data suggest that Q fever reaches low to moderate endemic levels on Réunion Island. As previously reported, pulmonary symptoms are on the foreground.

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Abstract 2240

The novel resistance mechanism of tigecycline in Acinetobacter baumannii
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Background: Tigecycline is a potent antibiotic for treating infections with multi-drug resistant Acinetobacter baumannii (MDR-AB). With the increasing usage of tigecycline, isolates resistant to tigecycline have constantly been reported. However, the definitive mechanism of tigecycline resistance in MDRAB has not been fully determined. This study aimed to explore the molecular mechanisms of tigecycline resistance in A. baumannii.

Materials/methods: Spontaneous mutants with reduced susceptibility to tigecycline were selected both in liquid and solid medium by serial passage experiments. Mutations were identified by illumina sequencing and bioinformatics analysis, then confirmed using PCR and Sanger sequencing. Complementation experiments were performed to evaluate the contribution of the mutations to decreased susceptibility to tigecycline. The significance of mutations were further investigated in terms of growth rates, antibiotic susceptibilities, and RNA-seq.

Results: Four mutations were identified, including three non-synonymous substitutions in adeS, rrf, rpoB and one insertion mutation in adeS. The rpoB and rrf gene were confirmed to cause decreased susceptibility to tigecycline by reconstruction experiments and antimicrobial susceptibility tests. Two types of mutations were observed in adeS gene (adeS::ISAba1 and adeS E51K) and both of them were confirmed to cause tigecycline resistance. By constructing an ISAba1 knockout strain on XH354, we demonstrated that the insertion of ISAba1 in adeS was correlated with tigecycline resistance. By measuring the relative growth rate, two adeS mutants exhibited faster growth than the parental strain with or without tigecycline and the ISAba1 knockout strain showed slower growth than XH354 with tigecycline. RNA-seq analysis was performed to determine the role of rpoB and rrf on the transcriptomes of A. baumannii MDR-ZJ06, and the result showed that hundreds of genes were upregulated or down-regulated.

Conclusions: Two kinds of mutations were found in adeS and both had been confirmed to cause decreased susceptibility to tigecycline. Besides, rrf and rpoB might play important roles in decreased susceptibility to tigecycline in A. baumannii.

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Abstract 2241

Isoquinolinesulfonamide H89 reduces the intestinal inflammation and promotes Candida albicans clearance from the gut

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Background: The gastrointestinal microbiota acts a natural barrier to colonization and proliferation of opportunist pathogens. Deregulation of the dynamic crosstalk between the microbiota, intestinal epithelial cells and immune cells is critically involved in the development of inflammatory bowel disease. Clinical and experimental studies have shown that Candida albicans overgrowth aggravates the intestinal inflammation induced by dextran sulfate sodium (DSS) in mice, and, conversely, that DSS colitis promotes the fungal colonization. Candida albicans is an opportunistic yeast pathogen that has adapted to colonize all segments of the human gut. Recently, we showed that blocking of P2X7R by pyroglutamide-based P2X7 antagonists attenuate the intestinal inflammation. The isoquinolinesulfonamide H89 molecule is thought to compete with ATP at its binding site within the protein kinase A and to some purinergic receptors including P2X7R. In the present study, we investigated the impact of H89 on the intestinal inflammation and C. albicans clearance from the gut and determined the diversity of the gut microbiota in a dextran sulfate sodium (DSS)-induced colitis model.

Materials/methods: Mice were administered a single inoculum of C. albicans and were exposed to DSS treatment for 2 weeks in order to induce acute colitis. For H89, mice were administered with H89 orally and daily, for 5 days, starting on day 1. The number of C. albicans colonies and changes in microbiota diversity were assessed in freshly collected stool samples from each tagged mouse, using traditional culture methods based on agar plates.

Results: We showed that H89 reduced the clinical and histological scores of inflammation and promoted the elimination of C. albicans from the gut. An increase in Escherichia coli and Enterococcus faecalis populations and a reduction in Lactobacillus johnsonii and Lactobacillus reuteri populations were observed during colitis development. H89 administration to mice decreased the overgrowth of aerobic bacteria while L. johnsonii and L. reuteri populations increased significantly.

Conclusions: In conclusion, H89 reduced the intestinal inflammation and promoted the elimination of C. albicans from the gut. Further studies are ongoing to understand the direct effect of H89 on C. albicans and the aerobic bacteria.

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Abstract 2242

Prevalence of carbapenemase-producing Gram-negative bacilli in a health area of southern Spain

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Background: Carbapenemase-producing Gram-negative bacilli (CPGNB) represent a threat. There is considerable heterogeneity across EU countries and across different regions. To assess the burden of CPGNB in our hospital, we report the cases studied during a 4 year period.

Materials/methods: Isolates from 1st October 2015 to 30th June 2019 were included. Only the first isolate for each patient was considered. Species identification was confirmed by MALDI-TOF (Bruker Biotyper). Detection of carbapenemase-production was performed by immunocromatography (NG-Test CARBA 5, NG Biotech) and PCR (Xpert Carba-R, Cepheid). All isolates were sent to the Andalusian Reference Centre “PIRASOA” (Sevilla, Spain) for molecular genotyping (XbaI-PFGE, MLST) and characterization (MiSeq, Illumina).

Results: 104 isolates from 102 patients were included. Seventy-two (70.5%) were obtained from clinical samples: urine (36/50%), respiratory tract (16/22.2%), blood (11/15.2%) and exudates (9/12.5%), and remaining were for colonization studies (30/29.4%). Main CPGNB were K. pneumoniae (49/47.1%), P. aeruginosa (24/23%), E. cloacae (17/16.3%), and K. oxytoca (11/10.5%). Overall, the most common carbapenemases were VIM-type (32/30.4%), followed by the KPC-type (31/29.5%), IMP-type (24/22.2%) and OXA-48-type (18/17.1%). For Enterobacteriaceae the most common carbapenemase was KPC-type (31/38.2%), followed by VIM-type (30/37%), and OXA-48-type (18/22.2%). The most common carbapenemase in P. aeruginosa was IMP-type (22/91.6%). KPC-3 variant from K. pneumoniae was obtained in 26 (83.8%) isolates and they belonged to the hyperendemic ST258 clone. The main VIM variant was VIM-1 (29/90.6%), and the most common ST clone was ST78 (12/37.5%). The most prevalent IMP variant from P. aeruginosa was IMP-8 (12/50%), followed by IMP-16 and IMP-23 (6/25%, each one). The main ST clone for IMP variants was the ST348 (9/37.5%). Regarding OXA-48, the main ST clone was ST307 (14/77.7%).

Conclusions: Among Enterobacteriaceae, the most prevalent carbapenemases were KPC-3 and VIM-1. KPC-3 was associated with the K. pneumoniae high-risk clone ST258, whereas VIM-1 with the K. oxytoca ST36 clone and the E. cloacae ST78 clone. Among P. aeruginosa, the most prevalent carbapenemase was IMP-8, which were associated with the ST348 clone. These data contrast with those previously reported from Spain, where OXA-48 is the most prevalent carbapenemase, and reinforce the need for epidemiological control at the regional level.

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Exploration of gonococcal MtrE-based antigens as prophylactic and therapeutic vaccines
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Background: Neisseria gonorrhoeae has become a global public health problem due to the high burden of disease and the rise in multidrug resistance. No vaccine is available due to antigenic and phase variability of surface-expressed proteins and the absence of clear correlates of protection.

Materials/methods: An in silico approach was used to predict surface-expressed proteins and analyze sequence conservation and phase variability. The most conserved protein, MtrE, and its surface-exposed Loop 2, which was displayed as both a structural and linear epitope on an established immunogenic protein, were used to immunize mice. Immunogenicity was subsequently analyzed by determination of antibody titers and serum bactericidal activity. To further define whether Th1 polarization is beneficial for the development of a vaccine against N. gonorrhoeae, MtrE and Loop 2 containing proteins were formulated with various Th1-stimulating adjuvants and investigated for polarizing in vitro dendritic cell stimulation and T cell activation assay. The best Th1 stimulating adjuvant, CpG, was used in immunogenicity and infection studies with MtrE and Loop 2 containing proteins in mice.

Results: MtrE and its surface exposed Loop 2 were identified as the most conserved surface-expressed antigens. Furthermore, MtrE and both Loop 2 containing proteins raised high specific antibody titers with good bactericidal activity. The vaccine formulations again raised high IgG titers against both MtrE protein and Loop 2 peptide and displayed a clear Th1-polarized IgG1/IgG2a ratio. In addition, immune sera showed stronger bactericidal activity compared with vaccine formulated with Alum, a well-established Th2-polarizing adjuvant. Finally, MtrE and Loop2 containing proteins formulated with CpG showed protection against a gonococcal challenge in a mouse vaginal tract infection model, as well strong therapeutic activity in this model when used as a therapeutic vaccine to clear an already established infection.

Conclusions: MtrE and Loop 2 are promising novel fully conserved surface-expressed antigens for vaccine development against N. gonorrhoeae and formulated with the Th1-polarizing adjuvant CpG provided both prophylactic and therapeutic activity in a mouse challenge model.

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Complementary inhibition of penicillin binding proteins by cefepime and zidebactam in presence of VIM-1 results in potent in vitro and in vivo bactericidal action against metallo-β-lactamase producing Pseudomonas aeruginosa

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Background: WCK 5222 is a combination of cefepime and a novel β-lactam enhancer, zidebactam. Zidebactam, a high-affinity PBP2 binding antibiotic, inhibits class A, and C β-lactamases but not metallo-β-lactamases (MBLs). Against MBL-producing pathogens, WCK 5222 triggers bactericidal action at sub-minimal inhibitory concentrations of cefepime and zidebactam suggesting effective PBP3 and PBP2 inhibition. The objective of this study was to establish PBP binding assay-based mechanistic evidence for cefepime-zidebactam mediated bactericidal effect against MBL P. aeruginosa in vitro and in vivo.

Materials/methods: VIM-1 was purified from E. coli BL21 harbouring pGEXVIM-1. PBP binding affinities were determined using Bocillin-FL assay. The activity of cefepime-zidebactam combination against MBL-expressing P. aeruginosa was assessed using time-kill and neutropenic mouse lung and thigh infection studies. Neutropenic animals were infected (inoculum ~6-log_{10} CFU/mL in lung/thigh), treatment regimens were initiated 2h post-infection. Bacterial loads (CFU/lung or thigh) were determined before and after treatment. Doses and regimens that generated human simulated exposures in mice (q2h for cefepime, zidebactam and q4h for carbapenems) were selected.

Results: Cefepime showed effective binding to PBP3 amidst cefepime-hydrolyzing concentrations of VIM-1 with minimal IC_{50} change in absence or presence of VIM-1 (PBP3 IC_{50} = 0.07/0.13 mg/L). Zidebactam binding to PBP2 remained intact (IC_{50} = 0.3/0.27 mg/L); however, imipenem binding to its target PBPs was adversely affected (PBP2 IC_{50} = 0.04/1.64 mg/L). Kinetic studies showed fast cefepime PBP3 binding rates with slight IC_{50} changes (IC_{50} 5' = 0.22 mg/L; IC_{50} 30' = 0.07). Imipenem PBP2 IC_{50} lowered significantly only after 30 min (IC_{50} 5' = 0.59 mg/L; IC_{50} 30' = 0.03), showing slower binding. Effective PBP inhibition amidst MBL translated in potent bactericidal activity of cefepime-zidebactam combination in time-kill study (ff1.5-log_{10} kill in 8h) against P. aeruginosa isolates expressing VIM. In vivo studies showed that although standalone cefepime, zidebactam and imipenem were not bactericidal, cefepime-zidebactam combination resulted in potent bactericidal activity (ff2.5-log_{10} bacterial killing in lung/thigh CFU).

Conclusions: The results show that cefepime and zidebactam effectively bind to respective target PBPs in the presence of MBL; presumably, as a result of cefepime faster rate of PBP binding which helps evade β-lactamase mediated hydrolysis.

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Abstract 2250

Efflux pump inhibitors based on novel cyclic peptides as an approach against ESKAPE pathogens
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Background: Multidrug resistant Gram-negative pathogens represent a global health threat and overexpression of multidrug efflux pumps is one of the most prevalent resistance mechanisms. Therefore, efflux pump inhibition arises as a promising strategy for new auxiliary therapies to restore antibacterial potency and cyclic peptides (CPs) could be used as a powerful tool to develop this approach.

A library of 27 CPs was screened for its ability to inhibit efflux pumps in the presence of antibiotics.

Materials/methods: Antibiotic susceptibility profiles of a collection of Acinetobacter baumannii (8 strains) and Pseudomonas aeruginosa (8 strains) presenting RND efflux pump overexpression were determined using broth microdilution assay for netilmicin, norfloxacin, chloramphenicol, nalidixic acid, gentamicin and tigecycline. This assay was also performed in the presence of constant concentrations of the reported Efflux Pump Inhibitor (EPI) phenyl-arginine β-naphthylamide (PAβN) for the sake of comparing its activity against that of the CPs library.

Results: After phenotypic characterization of the efflux pump overexpression, one strain of each pathogen was selected to assess the EPI activity of the CP library since they showed the greatest PAβN inhibitory activity for chloramphenicol and netilmicin in A. baumannii, and norfloxacin in P. aeruginosa.

Out of 27 CPs, 3 presented putative efflux pump inhibition on the selected A. baumannii strain. These exerted a reduction of the MICs of chloramphenicol and netilmicin of at least 2 folds when compared to their MICs when tested alone against that strain as shown below:

<table>
<thead>
<tr>
<th>Component</th>
<th>Chloramphenicol MIC (µg/mL)</th>
<th>Netilmicin MIC (µg/mL)</th>
<th>Fold change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alone</td>
<td>128</td>
<td>128</td>
<td>2X</td>
</tr>
<tr>
<td>+ CP1*</td>
<td>32</td>
<td>128</td>
<td>8X</td>
</tr>
<tr>
<td>+ CP3*</td>
<td>32</td>
<td>256</td>
<td>1X</td>
</tr>
<tr>
<td>+ CP14*</td>
<td>64</td>
<td>8</td>
<td>4X</td>
</tr>
<tr>
<td>+ PAβN*</td>
<td>32</td>
<td>64</td>
<td>1X</td>
</tr>
</tbody>
</table>

*Tested at a constant concentration of 100 µg/mL.

Conclusions: These preliminary results suggest that CP1, CP3 and CP14 have potential auxiliary activity in vitro when tested with chloramphenicol and netilmicin in A. baumannii overexpressing efflux pumps.

Further studies regarding the characterization of the strains and compounds are being performed to disclose if the active compounds found in our study act as EPIs in A. baumannii.

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Abstract 2252

**Influence of inflammation on pharmacokinetics and protein binding of tedizolid in healthy volunteers**

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**Background:** For combating bacterial infections a complex interplay between pathogen, host and antibiotic is decisive for treatment success. Most commonly the focus of infection models is put on the “pathogen-antibiotic” interaction, especially the intrinsic antimicrobial activity. In the following study pharmacokinetics and protein binding of the reserve antibiotic tedizolid (TZD), a second-generation oxazolidinone with strong activity against multi-resistant gram-positive bacteria, was investigated. Further, by introducing an endotoxin (LPS) based sepsis model, the impact of inflammation on TZD pharmacokinetic parameter was studied for the first time.

**Materials/methods:** Fourteen healthy volunteers received 3 single oral doses of 200 mg TZD phosphate, followed by an intravenous infusion of the same dose once a day over 60 minutes on 3 consecutive days (study days 1 to 6). Additionally, on day 6 subjects received an intravenous bolus of LPS (2 ng/kg body weight). Blood collections were performed at given time points at baseline and after drug application during study day 5 and 6. Free TZD concentration was obtained by ultrafiltration, total and unbound TZD was assayed using a validated HPLC-UV method. Pharmacokinetic parameters were compared between normal and artificial "septic" condition, validated by a significant increase in heart rate (p < 0.001), body temperature (p < 0.001) and c-reactive protein (p = 0.002).

**Results:** Under steady state conditions mean concentration-time profiles of total and unbound TZD in plasma showed almost identical concentration-time courses before and after LPS application (fig. 1). Further, for TZD plasma C_max was 2.96 prior and 2.94 mg/L after "sepsis" induction and for free plasma concentration 0.64 mg/L and 0.63 mg/L, respectively. AUC_{0-10} was 13.6 and 2.91 mg*h/ml before and 13.91 and 2.98 mg*h/ml after LPS for total and free TZD in plasma, respectively. Unbound fractions at 1 and 8 hours delivered similar values before (21.6 vs. 21.64%) and after (21.48 vs. 21.66%) LPS treatment, without statistical significant difference (p = 0.90).

**Conclusions:** The induction of inflammation by application of LPS did not have a significant effect on TZD pharmacokinetic data or protein binding.

![Mean concentration-time profile of TZD for total and free plasma before and after inflammation (LPS)](image)

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Abstract 2253

Prevalence and clinical characteristics of *Mycoplasma pneumoniae* in Navarra (Spain), 2014-2018

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**Background:** *M. pneumoniae* (MP) is one of the main pathogens of atypical pneumonia. It affects all ages, especially children under 14 years. Infections appear at any time of the year and usually have cyclic episodes every 4-8 years. The aim of our work is to know the characteristics of MP infection in Navarre in the period 2014-2018.

**Materials/methods:** Prospective study of cases of MP infection in Navarra during the period 1/1/2014-31/12/2018. All patients with positive MP PCR (Atypical CAP, FastTrack) are included. Clinical history was consulted to know the clinical characteristics

**Results:** There were 136 patients with positive PCR MP (136/1426; 9.53%). The distribution of cases/year was: 2014: 21.4% (25/117), 2015: 7.7% (14/182), 2016: 5.7% (18/318), 2017: 5.9% (19/318), 2018: 12.2% (60/492).

We had access to 123 patients (123/136; 90.4%). 56% of the population with MP infection were males with a mean age of 11 +/- 2.2 years. 65% (80) were between 5-14 years old and 19.5% (24) were <5 years old.

Clinical manifestations: 92.7% (114) cough, 66.7% (82) fever, 28.4% (35) upper respiratory symptoms and 18.7% (23) gastrointestinal symptoms. The only comorbidity detected was asthma, 14.6% (18) patients, which 77.7% (14) were male. 82.9% (102) had clinical and radiological diagnosis of pneumonia, 8.9% (11) with acute bronchitis, 4.9% (6) with upper respiratory tract infection and 3.2% (4) had no respiratory symptoms (1 diarrhea, 2 fever, 1 nausea and 1 urticaria).

A 3.2% (4) developed extra-respiratory complications: 2 dermatological (rash and urticaria) and 2 neurological (encephalitis and S. Guillén Barré).

44.7% (55) of the patients required hospitalization, with an average stay of 3.4 +/- 1.7 days.

47.1% (58) of the episodes developed during the warm months (June, July and August).

**Conclusions:**

- An epidemic situation was not clearly observed during the study period, although in 2014, 21.3% of the samples studied were positive.
- The main symptomatology is respiratory and the most frequent diagnosis is pneumonia.
- Forty-five percent of confirmed cases required hospital admission.
- CNS complications, although infrequent, may be important.
- Infections caused during this period are predominantly stationary, with half of cases occurring in warm months.

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Polyarginine nanocapsules carry and deliver genetic material inside bacteria

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Background: Acinetobacter baumannii is considered one of the most challenging pathogens partly due to its antimicrobial resistance profile, having developed resistance to almost all the antibiotics. This feature, added to the lack of new antibiotics, highlights the urgent demand for alternative antimicrobial strategies. Nanocapsules (NCs) can be used as nanocarriers for controlled delivery of different molecules inside the cells, such as polynucleotides. The aims of this study were to design a nanosystem able to internalize into bacteria and to evaluate the potential role of NCs in vehiculation and delivery of genetic material inside the bacterial cell.

Materials/methods: NCs with different polymer composition such as polyarginine (PArg NCs), protamine (Pr NCs) and octoarginine (R8 NCs) were designed to be internalized into bacterial cells. pAcGFP2 oriAb plasmid containing the green fluorescent protein (GFP) was used as a control to demonstrate the capacity of DNA-vehiculization of the NCs. Two different strategies were used to associate the plasmid to the NCs: a) association to the nanoemulsion and coating with the external polymer, and b) association to the outer shell of the NCs. A. baumannii ATCC 17978 cultures were incubated in the presence of NCs loaded with pAcGFP2 oriAb (20 µg/mL) in 0.9% NaCl from 30 min to 20 h. Confocal microscopy was used to visualize the NCs internalization and plasmid release by GFP expression.

Results: Confocal microscopy images revealed that, among all the NCs tested, only PArg NCs were able to penetrate into bacterial cells after 2 h of incubation. These NCs, with the pAcGFP2 oriAb entrapped between the nucleus and the outer polymeric shell, were able to pass through the bacterial membrane and to release the plasmid inside bacterial cells. These bacteria were cultured and the GFP expression was detected by confocal microscopy.

Conclusions: This study revealed that it is possible to internalize polyarginine nanocapsules inside bacteria and represents a proof of concept of genetic material mobilization inside the bacteria using these NCs as a vehicle. This finding opens the door to future studies dealing with the blocking of messenger RNA via the release of antisense molecules contained within NCs.

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Abstract 2257

Clonal attack: number of vancomycin-susceptible, -variable and -resistant E. faecium clones in individual rectal swabs

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Background: Rectal swabs are routinely used in hospitals to screen for vancomycin resistant Enterococcus faecium during outbreaks. Today the most detailed molecular typing is derived from whole-genome sequencing of the isolates. For a successful sequencing it is important that the sample only contains a single clone. Today, the number of (VSE, VVE and VRE, respectively) clones within a swab is unknown.

Materials/methods: We investigated 43 rectal swabs to determine the number of E. faecium clones within each swab. From VSE swabs we picked 20 colonies on a chromogenic agar, without antibiotics. From VRE swabs we picked ten VRE colonies from a chromogenic VRE agar plate. To describe the VSE population in a VRE swab we picked ten colonies from a chromogenic agar plate similar to the VSE swabs. All isolates [N=846] were tested for antibiotic phenotype [vancomycin, linezolid, ampicillin, gentamicin, ciprofloxacin and tigecycline] and RAPD PCR to estimate the number of clones in each sample. Any differences in RAPD fingerprint or antibiogram resulted in whole-genome sequencing of the isolate [N=232]. Determination of number of clones in each sample was based on individual phylogenetic trees with SNP distance calculations [same clone= <40 SNPs] combined with phenotypic antibiogram.

Results: The number of VRE/VVE containing swabs was 22 of which 17 contained a single VRE/VVE clone (77%) whereas five swabs [white triangles] contained >1 VRE/VVE clone [23%] [figure]. In 28/43 swabs we observed a single clone and in 15/43 swabs we identified ≥2 distinct clones [N=15]. In two swabs we observed identical clones according to SNP distance, however, with different phenotype - VVE and VRE as well as VSE and VRE.

Conclusions: The results show that 23% of swabs contain more than one VRE/VVE clone, which makes molecular typing during outbreaks less efficient in predicting spread of VRE/VVE infection between patients based on phylogenetic relationship. A combination of clonal relationship and transposon typing could be proposed to overcome this.

Figure: Rectal swabs [one per patient, N=43] stratified according to classification of E. faecium and number of different clones/swab. White triangles represent swabs with more than one VRE/VVE clone.

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Abstract 2258

Community-acquired and hospital-acquired Clostridioides difficile infections in the context of a trans-sectoral antibiotic stewardship intervention in Berlin, Brandenburg and Thuringia

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Abstract third-party references: On behalf of the RAI study group

Background: The association between antibiotic use and Clostridioides difficile infections (CDI) is well known. Within the RAI project (Rational Antibiotic Use via Information and Communication), we simultaneously carried out knowledge- and communication-based interventions in the outpatient and inpatient sector to reduce unnecessary antibiotic prescriptions. Aim of this study was to investigate effects on the occurrence of community-acquired and hospital-acquired CDI.

Materials/methods: RAI intervention tools were introduced in 271 GP practices, as well as intensive care units (ICU) and surgical departments from 29 hospitals in Berlin, Brandenburg and Thuringia between August 2016 and July 2017. The tools had been tailored to the specific needs of general practitioners and hospital physicians. CDI admission prevalences (proxy for community-acquired CDI) were measured in hospitals in Berlin, Brandenburg and Thuringia, which continuously joined the CDI module of the German Hospital Infection Surveillance System (KISS; n = 39, I-hospitals). The 356 CDI-KISS participating hospitals from the rest of Germany served as comparison group (C-hospitals). The effect of the inpatient intervention was investigated in those RAI participants whose wards participated continuously in the ICU module of KISS before and during intervention (n = 6, I-wards). The comparison group consisted of 3 times the number of structurally similar ICU-KISS participants from Germany (C-wards).

Results: The prevalence of CDI cases per 1000 admissions in the I-hospitals dropped significantly by 20% from 1.78 in the year 2016 to 1.42 in 2017 [rate ratio (RR) 0.80; 95% confidence interval (CI) 0.73–0.86]. Whereas the admission prevalence in the C-hospitals dropped only by 8% from 1.98 to 1.83 [RR 0.93; CI 0.90–0.95]. The incidence density of hospital-acquired CDI per 1000 patient days in the I-wards decreased statistically significant by 75% from 0.64 in the pre-intervention period to 0.16 in the intervention period [RR 0.25; CI 0.08–0.76] whereas in the C-wards it stayed nearly the same [0.41 pre-intervention versus 0.39 intervention period [RR 0.94; CI 0.54–1.64]].

Conclusions: Both, the outpatient and inpatient parts of the RAI intervention appear to have had an effect on the occurrence of CDI, although the study design of course, is not able to demonstrate causality.

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Abstract 2259

Dual therapy with aztreonam & ceftazidime/avibactam against multi-drug resistant Stenotrophomonas maltophilia on tricuspid valve endocarditis

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Abstract 2259

Background: Antimicrobial resistance in Stenotrophomonas maltophilia is one of the most complex among Gram-negatives. Presence of regulating non-specific antimicrobial class efflux pumps and chromosomal encoded L1 metallo-beta-lactamase (Ambler Class B) and L2 beta-lactamase (Ambler Class A) are responsible for few clinically active antimicrobials and the rapid raise of pan-drug resistant strains.

Materials/methods: A 38-year old male with a history of IV drug use, chronic hepatitis C, and recent MSSA endocarditis was admitted with sepsis. Workup revealed tricuspid valve endocarditis with pulmonary septic emboli due to Stenotrophomonas maltophilia. Initial antibiotics were levofloxacin, metronidazole, and piperacillin/tazobactam followed by levofloxacin and minocycline. He had valve replacement on day 6. Repeat blood cultures and valve tissue culture revealed Stenotrophomonas maltophilia had become pan-drug resistant (resistant: ceftazidime, levofloxacin, minocycline, trimethoprim/sulfamethoxazole, chloramphenicol; intermediate: minocycline; eravacycline MIC 8 μg/mL; tigecycline MIC 16 μg/mL). Microbiology Department was consulted for additional antimicrobial options based on susceptibility patterns. In vitro testing for a combination of aztreonam (AZT) and ceftazidime/avibactam (C/A) was recommended.

Results: Synergy testing between AZT and C/A was performed by positioning AZT strip (bioMerieux®, Inc.) over the area where C/A (bioMerieux®, Inc.) had been previously placed and removed after 10 minutes of incubation. The interception of the growth with the AZT strip was read. In presence of avibactam, AZT MIC was 4 μg/mL, 6 two-fold dilutions lower than AZT without C/A. MIC for AZT (256 μg/mL), ceftazidime (256 μg/mL) and C/A (32 μg/mL) were tested individually. AZT with C/A was recommended as a salvage treatment based on in vitro result. Patient completed 6 weeks of AZT with C/A along with minocycline. He achieved microbiologic clearance and clinical recovery from infection. At the end of treatment, he experienced episodes of refractory ascites. With complex cardiac, renal, and hepatic disease, patient was not a transplant candidate and transitioned to hospice two weeks later.

Conclusions: Although the surgical excision was key in the management, antimicrobial therapy with AZT and C/A provided effective antimicrobial treatment in the setting of persistent positive blood culture. AZT with C/A should be considered for cases of pan-drug resistant Stenotrophomonas maltophilia with limited treatment options.

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Abstract 2261

Genomic analysis of cardiac surgery-associated Mycobacterium chimaera infections in Italy
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Background: A clonal outbreak of over 150 cases of Mycobacterium chimaera (M. chimaera) infections were notified, linked to contaminated heater-cooler units (HCUs) used during cardiac surgery. We report the results of whole genome sequencing (WGS) analysis conducted on M. chimaera isolates from cardiac surgery (CS) related and unrelated patients and from HCUs in different centers in Italy.

Materials/methods: We investigated 122 Italian isolates of M. chimaera from HCUs (n=79), cardiothoracic surgery (CS-related) (n=23) and CS-unrelated patients (n=14) collected between 2015-2019. WGS was performed on the Illumina NextSeq500 platform and the reads were mapped on M. chimaera DSM-44623 as reference genome. The combined set of detected high quality SNP positions was used to construct a maximum likelihood phylogenetic tree using RAxML Version8 with a general time reversible substitution model, 1,000 re-samples and Gamma20 likelihood optimization to account for rate heterogeneity among sites. In order to detect the mixed populations in the samples we reduced the threshold of variant detection (at least 2-fold coverage and 5% allele frequency).

Results: Out of 122 strains only three belonged to groups other than Group 1. All M. chimaera isolates from CS-related patients grouped within Group 1; of these, 19 belonged to Subgroup 1.1, 3 to Subgroup 1.8 and 1 to Branch 1. Moreover, Subgroups 1.1 and 1.8 included 51 out of 79 isolates from HCUs. The isolates from CS-unrelated patients were heterogeneous and were distributed across the phylogenetic tree, mostly belonging to Branch 1. Overall, the isolates within Subgroup 1.1 showed comparatively little diversity, with a median pairwise distance of only 4 SNPs (range 0-20).

Conclusions: A common source of M. chimaera infection has been recognized on the basis of the remarkable similarity between almost all the isolates from patients with a history of cardiac surgery and the ones recovered from most HCUs. Three distinct strains of M. chimaera, belonging to Subgroups 1.1, 1.8, and 2.1, have been reported responsible of contamination of LivaNova HCUs at the production site. This finding is in agreement with our results showing large prevalence of Subgroups 1.1 and 1.8 among the isolates from CS-related patients and HCUs.

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Initiation of an immunisation and catch-up programme in schools in a country with a high vaccine hesitancy: yes we can!

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Background: Childhood immunization programs in schools are attractive because of their ability to reach large numbers of children in a short period of time. Such programs were stopped in France in 1998 after a controversy about a link between HBV vaccine and multiple sclerosis. Vaccine hesitancy has recently increased, leading to low vaccine coverage (VC) and outbreaks such as measles. A school immunization program was launched in Normandy in April 2019 to improve VC. We performed a study to identify factors associated with VC and vaccine acceptance (VA).

Materials/methods: We performed a prospective study to describe acceptability of a proposal for free vaccine catch-up or initiation of vaccination, if needed, for all pupils of 12 year old in high school by two vaccination teams in Normandy between April and October 2019.

An information letter and a consent form were sent to parents one month before the vaccination meeting. Parents could choose for each of the mandatory (diphtheria tetanus poliomyelitis [DTP], pertussis) and recommended vaccines (hepatitis B virus [HBV], human papilloma virus [HPV], meningococcus C, measles mumps rubella [MMR]) those they allowed. All children who’s parents allowed one vaccine were evaluated. During the meeting the doctor checked the vaccination notebook and the child was vaccinated when needed and authorized. We prospectively collected VC and VA for each vaccine. Two multivariate analysis were performed to identify factors associated to the need for an update of vaccination and VC.

Results: We intervened in 34 high schools located in 3 departments. Out of 3296 pupils, 879 (27%) accepted at least one vaccine. M/W ratio was 0.47, 689 (78%) pupils were vaccinated, they received a mean of 1.66 vaccine.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>DTP+Pertussis</th>
<th>MMR</th>
<th>Meningococcus C</th>
<th>HPV</th>
<th>HPV</th>
<th>Global</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA</td>
<td>63%</td>
<td>73%</td>
<td>77%</td>
<td>67%</td>
<td>69%</td>
<td>73%</td>
</tr>
<tr>
<td>Acceptance with a vaccine indication</td>
<td>62%</td>
<td>50%</td>
<td>62%</td>
<td>67%</td>
<td>53%</td>
<td>58%</td>
</tr>
<tr>
<td>Final VC with a vaccine indication</td>
<td>6%</td>
<td>12%</td>
<td>24%</td>
<td>31%</td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>VC (%) before-after intervention</td>
<td>46-60 (+65%)</td>
<td>84-89 (+5.9%)</td>
<td>41-73 (+78%)</td>
<td>42-66 (+57%)</td>
<td>8-59 (+637%)</td>
<td>52-52 (+60%)</td>
</tr>
<tr>
<td>Vaccine shot</td>
<td>366</td>
<td>44</td>
<td>286</td>
<td>211</td>
<td>236</td>
<td>1142</td>
</tr>
</tbody>
</table>

In multivariate analysis boys had a better VC (OR=0.38, IC95% 0.27-0.54), one of the 2 teams had a better post intervention VC (OR=0.65, IC95% 0.46-0.94). Post meeting VC was higher in low income area (OR=4.04, IC95% 1.5-10.91).

Conclusions: In high school pupils, despite a low VA, this program helped increase the VC. Further researches are needed to increase VA.

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Abstract 2268

Prosthetic joint infections treated with two-stage revision procedure: a case series

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Abstract third-party references: CRIOGO study group

Background: Two-stage revision procedure is the gold standard surgical treatment for the most complicated prosthetic joint infection (PJI), as it allows a window period with no prosthetic material. However, optimal duration of antimicrobial regimen after reimplantation of a new prosthesis remain poorly standardized. We aimed to characterize patients with PJI managed by a two-stage revision procedure in our institution, and identify prognosis factors.

Materials/methods: We performed a retrospective study in Rennes University Hospital, a referral center for complex PJI in western France. We identified all cases of PJI managed by two-stage procedures during years 2015-2018. Patient management was designed by a multidisciplinary team according to international guidelines. Standard follow-up included systematic consultation at 3, 6, 12 and 24 months after treatment discontinuation. Failure was defined as microbiologically documented relapse, the need for unplanned surgery or antibiotic treatment for PJI during follow-up. A Cox regression model was performed to identify risk factors for treatment failure.

Results: Fifty patients fulfilled inclusion criteria (18 women, 32 men, mean age 67±14 years), with PJI involving the hip (n=24), knee (n=22), or shoulder (n=4). PJI occurred as a relapse in 27 patients (54%), and was mostly classified as late (>12 months, n=35, 70%). Most common microorganisms were Staphylococcus aureus (n=18), coagulase-negative staphylococci (n=12) and streptococci (n=9). Twenty-three patients (46%) received antibiotic before prosthesis removal. The mean duration of antibacterial treatment after prosthesis removal was 10±4 weeks, the mean duration of antibiotic-free period was 16±7 weeks. Microbiological samples obtained during the second-stage were positive in 14 patients (28%), for Staphylococcus aureus (n=4), coagulase-negative Staphylococcus (n=8), and Cutibacterium acnes (n=2), after a median of 2 [min-max: 1-12] days. The mean duration of antimicrobial regimen after prosthesis reimplantation was 24.4±19.9 weeks. With a mean follow-up of 26.8±11.9 months after reimplantation, 5 patients (10%) presented criteria for failure. No variable associated with failure were identified, including microorganisms, second-stage antimicrobial treatment duration, and positive cultures at the second-stage.

Conclusions: Two-stage revision procedure was successful in most cases of complex PJI.

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Abstract 2270

**Colistin, turns active an otherwise ineffective rifampicin-linezolid combination in Gram-negatives**

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**Background:** The emergence of antimicrobial resistance is currently one of the most relevant healthcare concerns worldwide and the WHO has included it among its most urgent priorities. Combinations of already known antimicrobials offer a strategy to combat antimicrobial resistance, together with the design and development of new antimicrobials. Cationic antimicrobial peptides (CAMPs) are thought to induce alterations in membrane permeability through different mechanisms, as described by barrel-stave, toroidal pore, carpet, aggregate models, increasing fluidity, and some others, thus facilitating the entry of other antimicrobials into the bacterial cell. Synergies between different (C)AMPs and between CAMPs and classical antibiotics may therefore offer a method for the re-sensitization of bacteria that have become resistant to several antibiotics. This work deals with the effect on *Escherichia coli* clinical strains of sub-inhibitory concentrations of colistin administered together with combinations of linezolid-rifampicin, otherwise inactive in these bacteria.

**Materials/methods:** A checkerboard method was used to compare the effect of sub-inhibitory concentrations of colistin on the activity of the linezolid-rifampicin combinations. The effect of the linezolid-rifampicin combination was compared in presence and absence of ½ MIC colistin.

**Results:** Linezolid alone was absolutely inactive against *E. coli*, evidenced by its minimum inhibitory concentration (MIC) of 256 mg/L, while the MIC of rifampicin was much lower (8 mg/L). The combination of the two antimicrobials linezolid-rifampicin did not lead to their interaction (0.5< FICI [fractional inhibitory concentration index] >4), but in the presence of sub-inhibitory concentrations of colistin the interaction between linezolid-rifampicin was highly synergistic (FICI < 0.5).

**Conclusions:** Our results demonstrate that colistin either enhances the activity of linezolid-rifampicin combinations or re-sensitizes bacterial cells to these drugs. Thus, a triple antibiotic combination that includes colistin may be a promising alternative treatment of infections caused by multidrug resistant bacteria.

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Pharmacokinetic/pharmacodynamic analysis of tedizolid phosphate compared to linezolid for the treatment of infections caused by Gram-positive bacteria

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\textbf{Background:} Tedizolid phosphate (TZD) is a novel oxazolidinone launched into the market for the treatment of acute bacterial skin and skin-structure infections (ABSSSIs) caused by Gram-positive bacteria. Pharmacokinetic (PK) and pharmacodynamic (PD) properties of TZD allow its once-daily administration, either orally or intravenously, at equivalent dosage. This study aimed to evaluate the probability of attaining targeted pharmacodynamic exposure of TZD compared to linezolid (LNZ) at standard dosing regimens against different clinical isolates using Monte Carlo simulation.

\textbf{Materials/methods:} PK/PD parameters of TDZ and LNZ and minimum inhibitory concentrations (MIC) for Staphylococcus aureus, coagulase negative staphylococci (CoNS) and Enterococcus spp. were retrieved from published studies. All strains had been isolated either in Europe or in the United States. Using Monte Carlo simulation, PK/PD target attainment (PTA) by MIC and cumulative fraction of response (CFR) were determined for each bacterial collection for TDZ (200 mg q24h) and LNZ (600 mg q12h) in simulated patients with normal renal function.

\textbf{Results:} Table 1 shows the CFR values obtained for both antibiotics against staphylococci and enterococci. For all microorganisms studied, TDZ provided higher CFR values than LNZ. Regarding staphylococci, CFR values obtained for TDZ were always higher than 95% except for methicillin- and LNZ-resistant S. aureus (MLRSA) (CFR of 62%). However, CFR>80% was only obtained with LNZ against methicillin-resistant S. aureus [MRSA] and CoNS. For enterococci, both TDZ and LNZ provided CFR values higher than 80% except for LNZ- and vancomycin-resistant (LVR) E. faecium.

\textbf{Conclusions:} For both staphylococci and enterococci, TDZ provided higher CFR values, indicative of higher probability of empirical treatment success. Differences were more relevant for staphylococci.

Table 1. Cumulative fraction of response (CFR) for tedizolid (TZD) and linezolid (LNZ) against staphylococci and enterococci. In bold, CFR≥80%.

\begin{tabular}{|c|c|c|c|}
\hline
\textbf{Organism (number of isolates)} & \textbf{Staphylococci} & \textbf{Enterococci} & \\
\hline
\textbf{S. aureus (7187)}\textsuperscript{1} & 99 & 76 & 98 & 83 \\
\textbf{MSSA (2729)}\textsuperscript{2} & 99 & 76 & VS-Enterococcus spp (705)\textsuperscript{2} & 100 & 88 \\
\textbf{MRSA (1770)}\textsuperscript{2} & 99 & 79 & \textbf{VR-Enterococcus spp (163)}\textsuperscript{2} & 98 & 83 \\
\textbf{MRSA (18)}\textsuperscript{3} & 99 & 83 & \textbf{LVR E. faecium (30)}\textsuperscript{2} & 4 & 0 \\
\textbf{LNZ-resistant S. aureus (5)}\textsuperscript{4} & 96 & 4 & & \\
\textbf{MLRSA (18)}\textsuperscript{3} & 62 & 1 & & \\
\textbf{CoNS (674)}\textsuperscript{1} & 99 & 94 & & \\
\hline
\end{tabular}

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Abstract 2274

Molecular characterisation of methicillin-resistant Staphylococcus aureus isolates from the United Arab Emirates: emergence of novel strains and variants

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Background: Although recent reports on methicillin resistant Staphylococcus aureus (MRSA) from Arabian Gulf countries have demonstrated an emergence of novel strains and variants, data from the United Arab Emirates (UAE) are insufficient. This study aimed to determine the clonal distribution and genetic characteristics of MRSA in the UAE.

Materials/methods: MRSA [associated with clinical infections] identified between December 2017-January 2019 in four hospital laboratories were studied. Molecular characterisation was done using DNA microarray-based assays.

Results: The 466 MRSA isolates investigated belonged to 22 clonal complexes (CC) and 80 distinct strains as defined by CC affiliation, SCCmec type and Panton-Valentine leukocidin (pvl) genes carriage. The predominant CCs were CC30 (n=69), CC6 (n=65), CC5 (n=63) and CC22 (n=62), CC1 (n=34), CC772 (n=31), CC8 (n=27) and CC361 (n=26). There were 18 isolates each for CC60, CC97, with CC88 (n=15), CC239 (n=9), CC15 (n=7) and the rare CC121 (n=6). Other CC were CC152 (n=5), ST72, CC45, CC398, CC1153 [two isolates each], CC9 (ST834), CC96 MRSA and CC2250 S. argenteus (single isolates). A strain with a novel SCC-element was CC5-MRSA-[V/VT+cas+fus+ccrA/B-1]. Other variant/rare MRSA strains were CC5-MRSA-V (edinA+), CC5-MRSA-[V/VT+fus], CC5-MRSA-V (tst1+). CC8-MRSA-V, CC45-MRSA-[IV+fus+tr]; CC121-MRSA-V/VT; CC152-MRSA-[V/VT+fus] (PVL+), CC361-MRSA-V (SCCmec V/cos composite element). Our findings also demonstrate the emergence of ST5/ST22-MRSA-II, Rhine-Hesse EMRSA/New York-Japan Clone, CC5-MRSA-IV (sed/j/r+, PVL+), “Sri Lanka Clone”, CC398-MRSA-V/VT (PVL+); CC772-MRSA-V (PVL+), “Bengal Bay Clone” in this region. Another emerging clone was a CC22-MRSA-IV harbouring pvl and tst1 genes. A variant CCBD-MRSA-IV strain uncharacteristically with SCCmec IVa, harboured enterotoxin genes and was negative for the pvl genes. Two variants of the pandemic CC8-MRSA-[IVA+ACME1] (PVL+), USA300 – one putative PVL-deletion mutant and one with SCCmecIVa+ACMEIII were detected. The pvl genes were present in 221 (47.4%) isolates while 124 (26.6%) harboured fusC [SCC-borne fusidic acid resistance] gene.

Conclusions: An extensive MRSA repertoire which includes CCs previously unreported in the region, plus rare and novel strains are present in the UAE. Some strains detected occur in other countries, so a travel connection is possible. Others which have not been described elsewhere, probably evolved locally. Continued surveillance and further studies to understand the drivers of MRSA evolution are needed.

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Colonisation dynamics of *Streptococcus pneumoniae* in a remote African population: a prospective cohort study

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**Background:** Increased exposure to the outside world can change the microbiome of isolated communities. We aimed at analyzing the population dynamics of *Streptococcus pneumoniae* in a remotely living African Pygmy population in a time of increasing contact with foreigners.

**Materials/methods:** We conducted a prospective cohort study to analyze the nasopharyngeal *S. pneumoniae* in the same Babongo pygmy population in Gabon in 2011 (n=103), 2013 (n=104) and 2017 (n=107). Only non-duplicate isolates were included (n=126), serotyped and tested for antimicrobial resistance (broth microdilution, EUCAST clinical breakpoints).

**Results:** Resistance rates were highest for tetracycline (36–58%), followed by penicillin (parenteral, meningitis-breakpoints, 6–39%) and chloramphenicol (3–15%). Resistance rates increased for tetracycline and chloramphenicol while self-reported contact to foreigners increased as well from 6.8% (2011) to 17.8% (2017). The majority of isolates was non-typeable (NT, n=18/126, 14.3%) followed by serotype 6B (n=17/126, 13.5%), 21 and 15A (n=9/126, 7.1%, each). The distribution of serotypes was highly dynamic as only three serotypes (14, 17F, NT) were detected during all three visits.

**Conclusions:** Resistance rates and serotypes of nasopharyngeal *S. pneumoniae* markedly changed in the remote Babongo population. This rapid change in serotypes could challenge the selection of pneumococcal vaccine.

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Abstract 2279

Evaluation of faecal calprotectin as a predictor of severity and relapse in *Clostridioides difficile* infection

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**Background:** The assessment of fecal calprotectin (FCp) has been applied to rule out organic gastrointestinal diseases. Its potential value as predictive biomarker of outcome in *Clostridioides difficile* infection (CDI) remains unknown.

**Materials/methods:** A stool sample was collected at CDI diagnosis during a 10-month period and frozen at -80°C until analysis. Epidemiological and clinical variables were prospectively recorded. The fCAL® ELISA kit with the CALEX® Cap Extraction Device (both from Bühlmann Laboratories, Switzerland) were used for assessing FCp values. According to manufacturer's recommendations, cut-off values of 50 and 200 µg/g were used to define assay positivity, as well as alternative thresholds at the second (Q2) 741.5 µg/g and third (Q3) 2,194.7 µg/g quartiles. Study outcomes were severity of the index CDI episode and CDI relapse within the first 8 weeks.

**Results:** Overall, 170 samples (146 first CDI episodes and 26 relapses) were included. The presence of FCp values below Q2 was more common among patients with diabetes mellitus (64.3% [27/42] vs. 44.5% [57/128]; P-value = 0.03), solid organ transplantation (65.6% [21/32] vs. 45.6% [63/138]; P-value = 0.04) and chronic renal failure (63.8% [30/47] vs. 43.1% [53/123]; P-value = 0.02), whereas solid cancer was associated with FCp values above this threshold (73.3% [22/30] vs. 45.0% [63/140]; P-value = 0.005). Patients with non-severe CDI had more frequently FCp values below 50 µg/g (12.5% [14/112] vs. 3.4% [2/58]; P-value=0.05) or 200 µg/g (27.7% [31/112] vs. 15.5% [9/58]; P-value=0.07) than those with severe or fulminant episodes. Patients with FCp values >200 µg/g exhibited higher leukocyte count at diagnosis (median of 9,050 [IQR: 6,650-14,075] vs. 7,700 [IQR: 5,350-12,250] cells/µl). When we analysed the subset of 146 first episodes, we also found a higher proportion of patients with a non-severe CDI with FCp values <50 µg/g (13.7% [14/102] vs. 2.3% [1/44]; P-value = 0.03), whereas the rate of relapse was similar between patients with FCp values below or above 200 µg/g (5.9% [2/34] vs. 11.6% [13/112]; P-value = 0.52).

**Conclusions:** In our single-center study, patients with non-severe CDI showed lower FCp values, although none of the cut-off points explored appeared to be useful to predict CDI relapse.

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Laboratory stewardship initiative on repeat blood culture collection practices led to reduction of collection rates but electronic best practice alerts are needed to sustain reduction rates

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Background: Blood cultures (BCs) remain the gold standard and the first line tool for detecting blood stream infections. Indiscriminate repetition, after an initial culture is positive, is unnecessary and is associated with excessive use of resources, unnecessary additional testing and puts patients at risk for adverse effects. In our health system, we calculated the number of BCs during the first 48 hours of admission and implemented a laboratory stewardship initiative with the goal to reduce the number of repeat blood cultures by 5% within a year.

Materials/methods: The number of BCs, positivity rates and repeat BCs in the first 48 hours were calculated during a pre-implementation period from January- June 2018. From July 2018-June 2019, a large educational initiative was put in place detailing the significance of BCs and best practices regarding their recollection. The three parameters followed during the pre-implementation period were also recorded for 12 months following the educational efforts. The data were collected from the hospital's electronic medical record system (EPIC) as part of the quality improvement project.

Results: From January-June 2018 there were 74,760 BCs collected with an average BC positivity rate of 11.04%±0.01. At the initial site of collection, 2 sets were obtained. Depending on the collection site throughout the system 50.2-76.5% of BCs were repeated within the first 48hrs. Educational efforts starting in August 2018 resulted in an average decrease in BCs of 1.86%±4.24 during July 2018- June 2019. Initially, there was a big decrease up to 12.4% but six months following the educational efforts there was an increase of BC collection reaching 3.51%. During these 12 months the average BC positivity rate was 11.79%±0.01.

Conclusions: The educational efforts helped with the reduction of BCs recollection and did not affect positivity rates. However, the stewardship initiative was partially effective demonstrating the need for continuous reminders of best practices. To effectively impact practice the introduction of best practice alerts at the point of ordering through the hospital electronic system would be a permanent solution in addition to learning initiatives.

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**Abstract 2283**

**Vaccination perception and factors influencing MMR vaccination decisions during a university measles outbreak in a country with a high vaccine hesitancy**

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**Background:** Recent MO found a low vaccine coverage in young adults, including university students. Few studies evaluated VP and factors influencing MMR vaccination decisions during a MO in country with a high vaccine hesitancy.

**Materials/methods:** We performed a prospective cohort study in a French university during a MO. The 13/05/19 a measles case occurred in the University of Caen. Informations about the disease and a recommendation to check vaccination was sent by mail to all students, apprentices and university staff, and broadcasted on video screens. The 27/05/19 a second case occurred; leading to an oral presentation by an infectious disease specialist. The 28/05/19 a medical consultation was proposed to all university members to up-to-date MMR vaccination according to their vaccination notebook. They were then proposed to complete a questionnaire to assess their perception of the information and of the vaccination. A logistic regression was performed to identify the factors that influence their willingness to accept a MMR vaccine and factors associated to a positive perception of global vaccination (coted >6 on a scale of 0 to 10).

**Results:** Out of 331 university members, 268 (81%) were included. Immunization was demonstrated in 81%, negative in 14% and doubtful in 5%, 13% received immediate vaccine shot. 184/268 (69%) answered the questionnaire: 148 (65%) students, 17 (33%) apprentices and 19 (33%) staff. 63% were men, mean age was 22.5 years. Mean VP before the outbreak was of 7.9 and increased to 8.5 after the intervention, 37% of participants with negative perception before outbreak changed their perception positively. 87% accepted vaccination if needed, 91% of students, 63% of apprentices and 69% of staff.

In multivariate analysis: acceptance of MMR vaccination was correlated to the global VP (OR=1.5, IC95% 1.2-2.0), it was lower for apprentice and staff members compared to students [respectively, OR=0.13; IC95% 0.02-0.78 and OR= 0.14; IC95% 0.03-0.63]. The positive perception of vaccination after the MO was proportional to the level of understanding of the presentation (OR=1.7; IC95% 1.2-2.4).

**Conclusions:** A rapid human intervention seems efficient for vaccine implementation and improvement of vaccine perception during MO, with focus on staff and apprentices.

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Abstract 2284

**Temporal acquisition of IS1548 in Streptococcus agalactiae clonal complexes**
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**Background:** Insertion sequences (ISs) play a critical role in the evolution and the plasticity of *Streptococcus agalactiae* genomes. Fourteen different ISs were identified in this species. Among them, IS1548 was found to be linked with strains of clonal complex (CC) 19, associated with neonatal meningitis and endocarditis. Thereby, IS1548 was proposed to serve as a marker of this lineage. In this work, we took advantage of the release of the genome sequences of a huge number of epidemiologically unrelated *S. agalactiae* strains of various origins to better understand the prevalence and the temporal acquisition of IS1548 in *S. agalactiae* strains.

**Materials/methods:** To identify strains with an IS1548 genomic insertion, nine hundred and eleven *S. agalactiae* genomes, available as whole genome contigs or as complete genome sequences at the NCBI database, were blasted with the IS1548 complete DNA sequence of strain Mc1. A sequence type (ST), based on the allelic profile of seven housekeeping genes, was assigned to each strain possessing IS1548 by submitting the complete genome sequence or all of the contigs sequences of each strain to the *S. agalactiae* MLST databases. Strains were then grouped into clonal complexes (CCs) with the eBURST software.

**Results:** One hundred and twenty-two of the analyzed strains (13.3 % of the strains) possess IS1548 in their genome. These strains belong to twenty-nine different STs and to ten CCs. The majority of them were clustered within ST19 (55.3% of the strains) and ST22 (15.5% of the strains), belonging to CC19 and CC22, respectively. The fact that strains possessing IS1548 are not in equivalent proportion in each of the identified STs suggests that IS1548 was not acquired by a common ancestor of the main clonal complexes of *S. agalactiae*, but that independent integration occurred firstly in CC19, then in CC22 and later in the eighth other CCs. This hypothesis is strengthened by the finding that the average number of IS1548 insertion sites is twelve in CC19 strains, whereas it is eight and six in CC22 and CC10 strains, respectively.

**Conclusions:** IS1548 is expanding from CC19 to other lineages of *S. agalactiae*.

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Abstract 2286

**Destruction of Staphylococcus aureus biofilm matrix by innovative combination therapies between antibiotic and non-antibiotic substances**

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**Background:** Staphylococcus aureus forms biofilms in which bacteria are embedded in a matrix of extracellular polymeric substances (EPS). Due to the tolerance of biofilms to many antimicrobial drugs, we aimed at selecting innovative therapies on clinical S. aureus isolates leading to EPS destruction and to biofilm bacteria detachment.

**Materials/methods:** A collection of 14 MSSA and 10 MRSA originating from bovine mastitis were selected from 73 isolates based on the biofilm mass (OD value) and cultured in BHI (1% glucose). Ca2+ and subtilisin A selected from 8 non-antibiotics (proteinase K, Subtilisin A, DNase I, lactorrefin, EDTA, Phyto sphingosine, Chlorhexidine, and Calcium gluconate), as well as eight antibiotics, were tested on 24h mature biofilm of each isolate. The OD value and the detachment of biofilm bacteria after treatments were assessed after crystal violet staining and by bacteria counting, respectively.

**Results:** According to the OD values obtained from 73 isolates, the bacteria were classified into three levels (low, medium or high) of biofilm mass. A minimal decrease of OD values was observed after antibiotic monotherapies, whereas Ca2+ (1.25 mMol/mL) and subtilisin A (0.01U/mL) led to most effectively and significantly decline of the OD values in 2 1/24 isolates. Based on their MIC and MBC, Ca2+ (11.2.5mMol/mL) and subtilisin A (0.05U/mL) had no killing effect on the 24 isolates and the counting of biofilm bacteria shown no significant detachment effect. However, when Ca2+ or subtilisin A were combined with oxytetracycline (10 μg/mL), the detachment effect of biofilm bacteria was significantly enhanced.

**Conclusions:** Since Ca2+ and subtilisin A have no killing effect and no significant effect of detachment on biofilm bacteria, the low OD values obtained after both monotherapies suggest a destruction of EPS. In addition, we first demonstrated that the combination of oxytetracycline with Ca2+ or subtilisin A produced synergistic effects on biofilm bacterial detachment. The effect of two combinations is currently being evaluated by confocal laser scanning microscopy and studied in a dynamic system.

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Abstract 2289

**Increasingly limited options for the treatment of enteric fever in travelers returning to England, 2014-2017**

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**Abstract third-party references:** Public Health England

**Background:** Enteric fever (caused by *Salmonella enterica* serovar Typhi or Paratyphi) frequently presents as an acute, febrile illness in returning travellers, requiring timely empirical antibiotics. More than 90% of enteric fever in England occurs in travellers returning from South Asia. Characterising risks of antibiotic resistance associated with travel destination helps guide treatment.

**Materials/methods:** All English isolates of *S*. *Typhi* and *S*. *Paratyphi* between 2014-2017 underwent antimicrobial susceptibility testing; results were compared to a previous survey in London 2005-2012 by chi-squared test. Risk factors for antimicrobial resistance were analysed for each organism, constructing a stepwise, subtractive multivariate logistic regression model to predict adjusted odds ratios (aOR) for resistance to individual antibiotics and multi-drug resistance.

**Results:** We identified 584 isolates of *S*. *Typhi*, 442 *S*. *Paratyphi A*, 56 *S*. *Paratyphi B*, and one *S*. *Paratyphi C*. Overall, 87% of *S*. *Typhi* and 97% of *S*. *Paratyphi* isolates were resistant to ciprofloxacin; 21% of *S*. *Typhi* were resistant to ciprofloxacin, amoxicillin, co-trimoxazole, and chloramphenicol (MDR4). No isolate was resistant to azithromycin; a single *S*. *Paratyphi A* isolate was resistant to azithromycin; a single *S*. *Paratyphi A* isolate was resistant to third-generation cephalosporins. Comparison with the previous survey (Figure 1) indicates substantial increases in resistance of *S*. *Typhi* isolates to ciprofloxacin among travellers to Pakistan (from 79% to 98% resistant; P<0.001) and Africa (from 12% to 63% resistant; P<0.001). For *S*. *Typhi* isolates, resistance to ciprofloxacin was associated with travel to Pakistan (aOR 27.6, 95%CI: 9.2-83.0), India (aOR 5.3, 95%CI: 2.8-9.9), and Bangladesh (aOR 3.2, 95%CI: 1.3-8.3) compared to travel elsewhere. After adjustment for confounding by sex, MDR4 multi-drug resistance in *S*. *Typhi* isolates was associated with travel to Pakistan (aOR 3.1, 95%CI: 1.8-5.4) and less likely with travel to India (aOR 0.15, 95%CI: 0.07-0.33) compared with other travel areas.

**Conclusions:** Third-generation cephalosporins and azithromycin remain appropriate choices for empirical treatment of enteric fever in returning travellers. Prescribing guidelines should reflect high rates of ciprofloxacin resistance for travellers from South Asia and Africa and potential multi-drug resistance in travellers to Pakistan. Results will be reflected in forthcoming national treatment guidelines.

![Salmonella Typhi resistance to Ciprofloxacin](image)

Figure 1. Changing patterns of Ciprofloxacin-resistant *Salmonella Typhi*.

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Abstracts 2020

Abstract 2291

**Rapid molecular screening for vancomycin-resistant Enterococcus faecium (VRE) allows to expedite evaluation of VRE-exposed patients and is cost saving**

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**Background:** Outbreaks of Vancomycin-resistant E. faecium (VRE) are an emerging problem. The SwissNoso national guideline recommends to contact-isolate VRE-colonized patients, as well as those after VRE-exposure. Preemptive contact isolation often leads to lack of rooms and adds to cost. Culture-based screening may take up to 4 days to determine the VRE status and three weekly negative screenings are recommended before termination of contact isolation. Our study aimed to shorten the clinical turn-around-time using molecular testing and to estimate the saving costs of the shortened contact isolation.

**Materials/methods:** During two outbreaks with VRE vanB and vanA in 2019, we prospectively evaluated a subgroup of patients exposed to VRE-colonized patients with molecular screening. We used Xpert vanA/vanB (Cepheid) 24h after enrichment in broth medium (bioMérieux) in comparison to a full culture-based detection algorithm consisting of first broth enrichment, followed by 48h subculture on selective plates (bioMérieux) as current internal standard. Preemptive contact precautions were lifted after a first negative PCR result, but we continued culture-based screening for VRE by three rectal swabs. The primary outcome variable was the number of pre-emptive contact isolation days with cultures compared to PCR.

**Results:** Index patient samples were used to validate the PCR-based screening method. All index patients could be detected. A total of 848 contact patients at risk were identified. Of those, we performed in 111 patients the Xpert vanA/vanB PCR. 107 of 111 patients were screened negative by PCR and all of those had negative follow-up cultures saving a total of 639 isolation days. The saving costs were estimated 93,000 Euros calculated on a 145 Euros saving per isolation day. Four PCRs showed vanB, which were later confirmed to be false positive, since follow-up cultures remained negative.

**Conclusions:** A negative PCR can reliably identify patients without VRE colonization. The implementation of the procedure based on PCR and the linked reduction of isolation days leads to high cost savings. Our study is limited by the fact that no real transmission occurred and the sensitivity assay could not be extensively analysed. Nevertheless, we recommend the fast procedure with a molecular method for lifting of contact precautions.

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Abstract 2295

Epidemiological, clinical and prognostic comparison of Gram-positive cocci (GPC) and Gram-negative bacilli (GNB) in native bone and joint infections (BJI): a multi-centre retrospective study of 538 patients

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**Background:** The majority of BJI are due to GPC, while GNB are responsible of less than 15%. The aim of this study was to compare these BJI from an epidemiological, clinical and prognostic point of view.

**Materials/methods:** We performed a multicenter, retrospective study on the patients hospitalized for a BJI in 2 tertiary hospitals between 2007 and 2017. Inclusion criteria were: more than 18 years old, native BJI, positive microbiological culture on blood, synovial fluid or biopsy for GPC or GNB and at least one blood culture performed. Polymicrobial infections with GPC and GNB were excluded. Statistical analysis was performed using Fisher and Mann-Whitney tests.

**Results:** 538 patients met the inclusion criteria. 64% of patients presented a comorbidity with: diabetes (21%), connective tissue disease (10%), immunosuppression (9%), renal failure (11%) and liver cirrhosis (4%).

<table>
<thead>
<tr>
<th></th>
<th>Total n=538</th>
<th>GNB n=73</th>
<th>GPC n=465</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>64.7 (63.7-66.7)</td>
<td>69 (71-73.5)</td>
<td>64.1 (63-66.2)</td>
<td>0.005</td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>1.9 (1.7-2.1)</td>
<td>2.2 (1.5-2.6)</td>
<td>1.6 (1.4-2.1)</td>
<td>0.2</td>
</tr>
<tr>
<td>Immunosuppressive treatment</td>
<td>51 (8%)</td>
<td>11 (12%)</td>
<td>40 (8%)</td>
<td>0.09</td>
</tr>
<tr>
<td>Fever at presentation</td>
<td>309 (55%)</td>
<td>32 (44%)</td>
<td>277 (60%)</td>
<td>0.051</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>365 (60%)</td>
<td>37 (51%)</td>
<td>329 (71%)</td>
<td>0.02</td>
</tr>
<tr>
<td>CRP</td>
<td>178 (164-191)</td>
<td>118 (105-182)</td>
<td>184 (170-199)</td>
<td>0.01</td>
</tr>
<tr>
<td>Surgery</td>
<td>130 (24%)</td>
<td>13 (18%)</td>
<td>117 (25%)</td>
<td>0.2</td>
</tr>
<tr>
<td>Death</td>
<td>36 (7%)</td>
<td>4 (6%)</td>
<td>32 (7%)</td>
<td>0.8</td>
</tr>
</tbody>
</table>

The infection developed in the limbs in 50% (knee 33%, shoulder 22%, wrist and hand 12%, hip 11%), and in the spine in 57% (lumbar 64%, thoracic 26%, cervical 14%). Multifocal infections (20%) were more frequent in the GPC group [23 vs 7% p=0.02]. The joint puncture culture was positive in 55%. Bacteria identified in the GPC group were: *Staphylococcus* (56%), *Staphylococcus aureus* (47%), Coagulase negative staphylococci (8%), *Streptococcus* (27%), *Streptococcus pneumoniae* (5%), *Enterococcus spp* (4%). In the GNB group we identified: *Escherichia coli* (52%), *Pseudomonas aeruginosa* (18%), other enterobacteriae (11%), and other GNB (19%).

In multivariate analysis parameters associated to a GNB BJI were: monoarticular involvement (OR=3.02; IC95% 1.14-8), polymicrobial infection (OR=5.15; IC 95% 1.41-18) and older age (OR=2.59; IC95% 1.48-4.5). The parameters associated with a GPC BJI were: bacteriemia (OR=1.86; IC95% 1.07-3.2), and higher level of C-reactive protein (OR=2.43; IC95% 1.2-4.7).

**Conclusions:** This large retrospective cohort permits to identify the characteristics of GNB BJI and to compare them to GPC BJI. The GNB BJI symptomatology differs (less fever) and occurs in older patients, but no differences in mortality or management were observed.

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Abstract 2297

Genetic diversity evident from comparative genome analysis of ESBL-producing Escherichia coli isolated from swine microbiomes in Cameroon and South Africa

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Abstract third-party references: College of Health Sciences UKZN, Supported by the National Research Foundation, Supported by South African Medical Research Council

Background: In a multicentre comparative study conducted in pig abattoirs in Cameroon and South Africa, extended spectrum beta-lactamase producing Enterobacterales (ESBL-PE) were screened from pooled nasal and rectal samples of 432 pigs and nasal and hand swabs of 82 humans. An overall high ESBL-PE prevalence (>70%) was observed in both sample types. Of the total of 162 Enterobacterales isolates, 11 phenotypic ESBL-producing E. coli isolates and clonally related were selected for whole genome sequencing (WGS). The purpose of this study was to characterize the resistome, virulome, mobilome and phylogenetic diversity of these presumptive and clonally related ESBL-producing E. coli using WGS.

Materials/methods: The E. coli isolates were de novo assembled using the Qiagen CLC Genomics Workbench and SPAdes. The assembled contigs were annotated using RAST and PROKKA. Prediction of antibiotic resistance genes, virulence factors, plasmids, bacteriophages, and CRISP/Cas system was performed using ResFinder, VirulenceFinder and PlasmidFinder, PHASTER and CRISP/CasFinder, respectively. Enterobase server (http://enterobase.warwick.ac.uk/species/ecoli) was used for serotypes, phylogroups, fimH and multilocus sequence types (STs) prediction.

Results: Diverse STs were detected within the circulating E. coli isolates but sequence type (ST) 2144 and 88 dominated. blaAmpC (73%), blaCTX-M-15 (55%) and blaTEM-1B (45%) were the most common β-lactamase genes identified. Additionally, several genes encoding for resistance to aminoglycosides, phenicols, fosfomycin, fluoroquinolones and polymyxins were identified, the latter including the mcr-1 gene. The isolates were assigned to phylogroups A/B1 (45/28.3%), C/D (18.18/9.09%). The serotype O-:H49 (18.18%), O-:H9 (18.18%), O-:H18 (18.18%) were the principal serotypes detected while the fimH1250 (18.18%) and fimH89 (18.18%) were the predominant fimH gene observed. At least one (100%) and up to nine virulence factors (27.27%) were detected in the isolates. Forty-five percent of the isolates harboured IncFIB and IncY plasmid incompatibility groups, while IncX (18.18%) and IncHI2 (27.27%) were also detected.

Conclusions: This Sub-Saharan multicentre survey shows that the gut microbiota of swine is colonized by ESBL-producing E. coli predominantly CTX-M-15. Although the phylogenetic diversity observed precludes any suggestion for clonal dissemination, the resistance and high pathogenicity potential demonstrate the urgent need to implement effective strategies to contain the dissemination of antibiotic resistant bacteria in Cameroon and South Africa.

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Too much of a good thing? Evaluation of respiratory viral panel usage in paediatric bone marrow transplant patients

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Background: Viral upper respiratory tract infections (URIs) are a significant cause of morbidity in pediatric bone marrow transplant (BMT) patients. The speed and increased sensitivity of the FilmArray Respiratory Viral Panel (FA-RVP) is valuable but may prompt inappropriate testing. We investigated FA-RVP usage, test outcomes, and clinical response in our pediatric BMT population to determine whether implementation of testing restrictions are warranted.

Materials/methods: Retrospective data was collected for 682 respiratory specimens tested by FA-RVP from 214 unique BMT patients between 01/01/2016–01/01/2019. Information including age, underlying conditions, and frequency of FA-RVP testing were recorded. Data on patients with multiple specimens tested within a 14-day period were also examined to determine consistency of target detection, the presence of URI symptoms, and modifications in management.

Results: 312/682 (45.8\%) specimens were positive by FA-RVP. Detection of rhinovirus/enterovirus (179, 57.3\%) was most common, followed by coronaviruses (40, 12.8\%), parainfluenza (33, 10.6\%), and respiratory syncytial virus (19, 6.1\%). 66 patients had multiple specimens tested within a 14-day period, consisting of 105 repeat tests on 195 total specimens; of these, the same target was detected in 79 (75.3\%) cases. In contrast, 26 (24.7\%) patients with additional specimens tested yielded a different result: 13 (6.7\%) positive patients became negative and 13 (6.7\%) negative patients became positive. In the negative to positive group, the most common target detected was rhinovirus/enterovirus and only five patients were symptomatic during original test and retest. 27\% (53/195) of specimens were collected from asymptomatic patients, of these four cases of rhinovirus/enterovirus were detected. FA-RVP result informed addition of antiviral agents. No de-escalation of antimicrobial therapy was observed regardless of FA-RVP result. Influenza detected in one patient prompted chemotherapy suspension and there were no recorded instances in which FA-RVP results delayed BMT.

Conclusions: There is a high incidence of inappropriate FA-RVP testing in asymptomatic BMT patients and results seldom influence patient management. Moreover, testing of additional specimens over a 14-day period infrequently provides useful information. These findings support implementing diagnostic stewardship measures including potentially limiting repeat testing within a 14-day period without negatively affecting patient outcome.

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Abstract 2299

Characterisation of the vaginal DNA virome in health and dysbiosis: an opening study in patients with non-female factor infertility

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Background: Bacterial vaginosis (BV) is characterised by a reduction in the abundance of Lactobacillus spp. and a subsequent increase in the abundance of facultative anaerobes, such as Gardnerella vaginalis. Despite recent advances, the BV aetiology is not fully understood, but bacteriophages could play a pivotal role during perturbations of the vaginal bacterial community. Here we investigate the viral community of the vagina, including bacteriophages, and its association to the bacterial community.

Materials/methods: Vaginal samples collected in Eswab (Copan™) from 48 patients undergoing IVF treatment for non-female factor infertility were subjected to metagenomic sequencing of purified virus-like particles. The overall composition of the vaginal viral community was characterized and correlated with bacterial vaginosis (BV) status (Nugent score), bacterial community by 16S rRNA sequencing and presence/absence of key vaginal bacterial species by qPCR. Correlation between bacterial and viral abundance was performed using the mixOmics R package with CSS-normalized OTU-tables.

Results: A total of 773 viral vOTUs were retained after de novo assembly and filtering, sized from 3 to 85 kb with a median of 7.5 kb in length. The majority of identified vaginal viruses belonged to the class of double-stranded DNA bacteriophages, with eukaryotic viruses constituting 4% of total reads. Clear links between viral community composition and BV (q = 0.006, R = 0.26) as well as presence/absence of qPCR L. crispatus (q = 0.001, R = 0.43), L. iners, Gardnerella vaginalis and Atopobium vaginae were found (q < 0.002, R > 0.15). Interestingly, also the eukaryotic viral community was significantly correlated with BV-status (q = 0.018, R = 0.20).

Conclusions: This study provides the first in-depth characterization of the vaginal DNA virome based on virus like particle purification followed by metagenomic sequencing and de-novo assembly. We found that the composition of both the prokaryotic and the eukaryotic viral communities varied strongly between BV-negative and BV-positive samples. Further, clear co-abundance patterns between certain bacteria and vOTUs indicate that these two components of the vaginal microbiome are strongly interlinked. Interestingly, the eukaryotic viral component differed significantly between BV-positive and negative samples although these viruses are not directly interacting with the bacterial community.

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Abstract 2300

**Multi-centre evaluation of cephalexin MIC results for Enterobacterales using EUCAST breakpoints on MicroScan dried Gram-negative MIC panels**

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**Background:** A multicenter study was performed to evaluate the accuracy of cephalexin on a MicroScan Dried Gram-negative MIC (MSDGN) Panel when compared to a frozen ISO/CLSI broth microdilution reference panel.

**Materials/methods:** An evaluation was conducted at three U.S. sites by comparing MIC values obtained using the MSDGN to MICs utilizing an ISO/CLSI broth microdilution reference panel. A total of 450 Enterobacterales clinical isolates were tested using the turbidity and Prompt® methods of inoculation during the efficacy phase. A subset of 12 organisms was tested on MSDGN panels at each site during reproducibility. MSDGN panels were incubated at 35 ± 1°C and read on the WalkAway System, the autoSCAN-4 instrument, and read visually. Read times for the MSDGN panels were at 16-20 hours. Frozen reference panels were prepared according to ISO/CLSI methodology, incubated for 16-20 hours and read visually. All frozen reference panels were incubated at 35 ± 2°C for 16-20 hours and read visually. EUCAST breakpoints (mg/L) used for interpretation of MIC results were: Enterobacterales ≤ 16 S, > 16 R.

**Results:** Essential and categorical agreement when compared to frozen reference panel results, for all isolates tested in efficacy as follows:

<table>
<thead>
<tr>
<th>Read Method</th>
<th>Essential Agreement %</th>
<th>Categorical Agreement %</th>
<th>Very Major Error (VMJ)* %</th>
<th>Major Error (MAJ)* %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P</td>
<td>T</td>
<td>P</td>
<td>T</td>
</tr>
<tr>
<td>WalkAway</td>
<td>98.0</td>
<td>(441/450)</td>
<td>96.4</td>
<td>(443/450)</td>
</tr>
<tr>
<td>autoSCAN-4</td>
<td>97.8</td>
<td>(440/450)</td>
<td>98.7</td>
<td>(444/450)</td>
</tr>
<tr>
<td>Visually</td>
<td>98.0</td>
<td>(441/450)</td>
<td>96.0</td>
<td>(444/450)</td>
</tr>
</tbody>
</table>

T = Turbidity inoculation method, P = Prompt inoculation method

*Calculation of MAJ and VMJ excluding 1 well errors

**Conclusions:** This multicenter study showed that cephalexin MIC results for Enterobacterales obtained with the MSDGN panel correlate well with MICs obtained using frozen reference panels using EUCAST interpretive criteria. PROMPT® is a registered trademark of 3M Company, St. Paul, MN USA. Beckman Coulter, the stylized logo and the Beckman Coulter product and service marks mentioned herein are trademarks or registered trademarks of Beckman Coulter, Inc. in the United States and other countries.

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Abstract 2301

**Multiplex PCR for the detection of traveller’s diarrhoea: a nested case-control study**

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**Background:** Traveler’s diarrhea (TD) can cause high morbidity among travelers. Multiplex methods have been developed recently for the molecular detection of causative agents of TD. However, these approaches are not yet sufficiently validated. The aim of this study was to test a multiplex-PCR approach in patients with TD and asymptomatic controls.

**Materials/methods:** A total of 91 travelers (61 TD cases, 30 asymptomatic controls) prospectively collected stool samples during travel and documented gastrointestinal symptoms. Samples were analysed using the BioFire® FilmArray® Gastrointestinal Panel, which covers 13 enteric bacteria (e.g. diarrheagenic Escherichia coli), four protozoan parasites (*Cryptosporidium* spp., *Cyclospora cayetanensis*, *Entamoeba histolytica*, *Giardia lamblia*) and five viruses (adenovirus, astrovirus, norovirus, rotavirus, sapovirus).

**Results:** TD cases had more likely a positive test compared to controls (75 vs. 57%, p=0.07). The most common enteric pathogens were enteroaggregative *E. coli* (36/91, 40%), followed by enterotoxigenic *E. coli* (31/91, 34%) and enteropathogenic *E. coli* (EPEC, 29/91, 32%). The only pathogens significantly associated with TD were EPEC (p=0.01) and ETEC (p=0.047). Others were detected both in TD cases and asymptomatic controls without a clear association with disease. Protozoan parasites were not detected.

**Conclusions:** The results challenge the use of multiplex-approaches covering numerous enteric pathogens in the diagnostic workup of TD because only few (i.e. diarrheagenic *E. coli*) were related to symptoms of TD.

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Visual antibiogram of *Staphylococcus aureus* using machine learning demonstrates multidrug resistance as associations between individual antimicrobials

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**Background:** Phenotypic antimicrobial susceptibility testing (AST) data, generated in clinical settings, can be used as surveillance for co-antimicrobial resistance or cross-resistance that could lead to co-selection of antimicrobial resistance; i.e., the use of one antimicrobial selects for resistance to multiple antimicrobials. We created an antibiogram using association mining, an unsupervised machine learning method, to identify and measure high-order relationships between antimicrobial resistance in *Staphylococcus aureus*.

**Materials/methods:** We examined 1,091 isolates collected from one New York hospital between 2008 and 2018 and performed AST using reference broth microdilution. Methicillin-resistant *S. aureus* (MRSA) and methicillin-susceptible *S. aureus* (MSSA) isolates were examined separately. The Apriori algorithm was used to identify patterns of antimicrobial resistance that occurred in at least one isolate. We only included patterns that were unlikely to occur due to random chance by using the expected cross-support ratio (P value < 0.05 in simulation study) and conditional lift (bootstrap 95 percentile interval excluding the null value of 1).

**Results:** Overall, 39% of isolates were MRSA and 39.5% of all isolates were MDR (resistant to ≥3 antimicrobial classes). There were more non-MDR MRSA isolates than expected if all the antimicrobial resistances were independent. Resistance associations were visualized by connecting all antimicrobials in each pattern and overlaying them, revealing distinct subnetworks of resistance associations at the antimicrobial class level (Figure 1). The MRSA sub-networks are connected through β-lactam resistance although different β-lactams are involved in each subnetwork: ceftaroline resistance is associated with aminoglycoside, tetracycline and sulfonamide resistance; whereas penicillin and ertapenem resistance are associated with fluoroquinolone resistance.

**Conclusions:** The antibiogram suggests a potential for co-selection of ceftaroline resistance with tetracycline or sulfonamide treatment, although antimicrobial use data was unavailable to confirm this hypothesis. MRSA and MSSA isolates demonstrated dissimilar antimicrobial resistance associations, suggesting different co-resistance mechanisms. An antibiogram created with association mining can uncover clinically-relevant antimicrobial resistance patterns.

**Figure 1:** Resistance patterns decomposed into nodes (antimicrobials) connected by edges (e.g. pattern {A,B,C} decomposes into A—B, B—C, A—C). Darker edges, stronger association; thicker edges, more frequent pattern. Node pie chart represents resistance prevalence: color, non-susceptible; gray, susceptible; white, not-tested.

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**Luminogenic phosphatase substrate for rapid susceptibility testing of Gram-positive strains**

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**Background:** Antibiotic susceptibility testing (AST) using fluorogenic and colorimetric reporters are well-established methods. Despite the superior sensitivity of luminescence, AST based on bioluminescence remains unexploited due to the need for addition of reagents addition and its limitations with respect to end-point analysis. Chemiluminescence detection is limited by the lack of stable luminogenic substrates compatible with microorganisms in an aqueous medium. The AquaSpark™ substrates recently commercialized by BIOSYNTH are claimed to fulfill these criteria. We evaluated a luminogenic substrate of this range for AST. The study was focused on the AST of Gram positive bacteria using the broad range phosphatase substrate.

**Materials/methods:** 40 strains (30 staphylococci and 10 enterococci) were tested by broth microdilution with 10µM of broad range phosphatase substrate [BIOSYNTH]. Cefoxitin, ciprofloxacin, erythromycin, gentamicin, levofloxacin, tetracycline and vancomycin were tested with appropriate strains. Medium, inoculum and antibiotic dilutions were based on CLSI standard M07 method. Incubation at 35°C, absorbance (OD660nm) and luminescence (LUM) measurements were performed using a micro-plate reader (TECAN). Kinetics of OD660nm and LUM signals were compared to the MIC obtained visually.

**Results:** LUM and OD660nm signals were correlated at 96% [16/16 antibiotic/strain tests for enterococci; 57/60 for staphylococci]. All discordances were observed in presence of ciprofloxacin: no luminescence was detected while growth of resistant strains was obvious at high concentrations [above 8 mg/L].

For rapid MIC determination, analysis criteria were calculated for both OD660nm and LUM. Average time gain using LUM was 415 minutes for enterococci and 290 minutes for staphylococci. Application of these criteria led to 3 major errors for LUM [previous discordances with ciprofloxacin] and 4 very major errors [VME] for both OD660nm and LUM when comparing to the MIC obtained visually. VME were obtained for vancomycin and could be resolved by modifying the interpretation criteria for this drug.

**Conclusions:** AquaSpark™ broad range phosphatase substrate can be used for chemiluminescence detection in kinetics in the presence of antibiotics and bacterial strains. LUM signal correlates to growth detection and can predict MIC with confidence. Its optimized use for AST requires definition of interpretation criteria which is challenging due to the diversity of resistance mechanisms.

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Impact of respiratory panel PCR assay on antibiotic use in patients with community-acquired pneumonia admitted to intensive care unit

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Background: Community-acquired pneumonias (CAP) hospitalized in intensive care units (ICU) are a common cause of antibiotic prescriptions. The recent availability of respiratory multiplex PCR assays, that identify a panel of viral and intracellular pathogens in less than 2 hours, could be a useful tool for antimicrobial stewardship and thus optimize and reduce antibiotic consumption. Nevertheless, data concerning the real-life impact of those tools are lacking.

Materials/methods: We performed a monocentric retrospective study including all patients admitted to the ICU for a CAP with a positive FilmArray® respiratory panel, from September 2018 to July 2019. This test detects 15 virus and 4 bacteria (Mycoplasma pneumoniae, Chlamydia pneumoniae, Bordetella pertussis, Bordetella parapertussis). Definition of CAP for inclusion in this study was: at least one respiratory clinical symptom and temperature ≥38 or <36°C or leucocyte ≥10 or <4 G/L and radiological image compatible with CAP. All medical charts were reviewed by 2 infectious-disease specialists and 1 intensive care specialist.

Results: During the period study, 70 respiratory multiplex PCR assays were performed among patients hospitalized in the intensive care unit, 33 were excluded because they did not meet inclusion criteria. Among the 37 patients included, sex ratio was 0.46 and mean age was 69.9. The mean IGS II score was 43 (median: 41, IQR: 13) and the mean Fine score was 125 (median: 122, IQR: 73). Thirty-five PCR test results (94.6%) were positive for viral agents (15 influenza viruses, 2 respiratory syncytial viruses and 22 other viruses) and 2 for Mycoplasma pneumoniae. Regarding usual bacterial respiratory samples, 26/37 (70.3%) cultures were positive for bacteria. Modification of the antibiotic treatment was assessed for the 2 cases with a PCR positive for Mycoplasma. For every other patient (n=35), antibiotherapy was not modified, even for patients with no microbiological identification of bacterial infection (n=9).

Conclusions: In our experience, the impact of respiratory PCR assays on antibiotic use in patients hospitalized for CAP in ICU is weak. Only flu and intra cellular bacteria detection seem useful for patient management. Cost effective study should evaluate more precisely the interest of those tests.

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In vitro activity of ceftazidime-avibactam against Enterobacterales and Pseudomonas aeruginosa from central Europe and Israel: ATLAS global surveillance programme 2018

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Abstract third-party references: Supported by Pfizer, On behalf of Katalin Kristóf

Background: Ceftazidime-avibactam is a cephalosporin/beta-lactamase inhibitor combination for use in Gram-negative infections. The ATLAS study compares its in vitro activity with comparator agents.

Materials/methods: In vitro antimicrobial susceptibility of Gram-negative isolates collected during 2018 from 28 sites in 9 countries (Croatia, Czech Republic, Hungary, Israel, Poland, Romania, Ukraine, and Latvia/Lithuania combined) was determined using CLSI broth microdilution methodology and EUCAST 2019 breakpoints. Ceftazidime-avibactam was tested with a fixed concentration of 4 mg/L avibactam.

Results: The table shows the in vitro activity of ceftazidime-avibactam and comparators for isolates across all countries.

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Enterobacterales (N=2,585)</th>
<th>Pseudomonas aeruginosa (N=707)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIC90 (mg/L),</td>
<td>MIC90 (mg/L),</td>
</tr>
<tr>
<td>Amikacin</td>
<td>8</td>
<td>4–52</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>32</td>
<td>2–32</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>126</td>
<td>30–250</td>
</tr>
<tr>
<td>Ceftriaxone-avibactam</td>
<td>1</td>
<td>0–2</td>
</tr>
<tr>
<td>Colistin</td>
<td>1</td>
<td>0–1</td>
</tr>
<tr>
<td>Colistin (N=2,113)*</td>
<td>1</td>
<td>0–1</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>126</td>
<td>16–128</td>
</tr>
<tr>
<td>Meropenem</td>
<td>0.12</td>
<td>0.12–4</td>
</tr>
</tbody>
</table>

*Excludes Morganella, Proteus, Providencia and Serratia spp. due to intrinsic colistin resistance.

Susceptibility among Enterobacterales was highest to ceftazidime-avibactam, followed by colistin, meropenem, and amikacin. For Klebsiella pneumoniae (N=607) and E. coli (N=713), susceptibility rates were high to ceftazidime-avibactam (98.5%, 99.3%) and colistin (94.9%, 99.7%). Colistin was the most active agent for P. aeruginosa [see Table].

Susceptibility of Enterobacterales isolates in each country was ≥94.9% to ceftazidime-avibactam and ≥94.7% to colistin [excluding intrinsically-resistant organisms]. Among K. pneumoniae, ceftazidime-avibactam and colistin susceptibility was ≥93.7% and ≥84.0%, respectively, in all countries, including Ukraine (N=50), which had the lowest susceptibilities to amikacin (64.0%) and meropenem (66.0%). Among P. aeruginosa, ceftazidime-avibactam susceptibility was >90% in 5 countries, and susceptibility to all agents except colistin (100%) was lowest in Ukraine (N=53).

Conclusions: Ceftazidime-avibactam demonstrated potent in vitro activity against Enterobacterales and P. aeruginosa isolates collected from each of 8 countries in Central Europe and Israel.

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Abstract 2309

Microbiology and molecular characterisation of Enterobacterales from children enrolled in global, prospective, controlled paediatric clinical trials for complicated intra-abdominal and urinary tract infections for ceftazidime-avibactam

Rodrigo E. Mendes1, Timothy Doyle1, Greg Stone2, Annie Gardner2, Mariana Castanheira1, John Bradley3

1 JMI Laboratories, North Liberty, United States, 2 Pfizer Inc., Groton, United States, 3 Rady Children’s Hospital/UCSD, San Diego, United States

Abstract third-party references: This study was performed by JMI Laboratories and supported by Pfizer, Inc., which included funding for services related to preparing this abstract.

Background: The efficacy, safety and tolerability of ceftazidime-avibactam (CAZ-AVI) were demonstrated in several clinical trials for adult patients. Randomized, prospective, comparative trials for complicated urinary tract infections (cUTI) and complicated intra-abdominal infections (cIAI) evaluated, respectively, CAZ-AVI and CAZ-AVI plus metronidazole for treating these infections in infants/children. This study characterized the baseline Enterobacterales recovered from the microbiological intended-to-treat (Micro-ITT) population.

Materials/methods: These single-blind, randomized, multicenter, active-controlled, studies (NCT02497781 and NCT02475733) were conducted to evaluate the safety, tolerability, efficacy and pharmacokinetics of CAZ-AVI in children (≥3 months to <18 years) diagnosed with cIAI or cUTI, including acute pyelonephritis. Isolates were tested for susceptibility by broth microdilution. Isolates that met pre-defined MIC criteria were molecularly characterized by genome sequencing and in silico analysis.

Results: A total of 77 and 69 subjects (both study arms) were included in the Micro-ITT populations of cUTI and cIAI trials, respectively. Among these patients, 72 (5 species; 91.7% E. coli) Enterobacterales were recovered at baseline during the cUTI trial and 57 (4 species; 91.2% E. coli) baseline Enterobacterales in the cIAI trial. CAZ-AVI (Table) inhibited all cUTI Enterobacterales at ≤0.5 mg/L and cIAI isolates at ≤0.25 mg/L. Four (5.6%) baseline cUTI E. coli from Taiwan (2), Turkey (1) and Czech Republic (1) met the MIC screening criteria and carried bblaCTX-M-15 or bblaCMY-2, except for 1 isolate that had high transcriptional levels of bblaTEM-1 based on promoter configurations (called Pa/Pb). This latter isolate had low MICs for extended-spectrum β-lactams, but met the screening criteria due to a ceftazidime MIC of 2 mg/L. Three (5.3%) baseline cIAI E. coli from Turkey (2) and Taiwan (1) met the MIC screening criteria and carried bblaCTX-M-15, bblaCMY-2 or bblaDH A-1. These 7 isolates belonged to distinct MLST types, including 1 ST131.

Conclusions: E. coli predominated among Enterobacterales recovered from the Micro-ITT populations in the cUTI and cIAI clinical trials. CAZ-AVI (100.0% susceptible) was active against these baseline pathogens, as were comparator agents (94.4–100.0% susceptible). A small percentage (7.5%) of isolates with distinct genetic backgrounds showed non-wildtype susceptibility phenotypes and, in general cUTI isolates carried bblaTEM-1 variants, while cIAI isolates had plasmid AmpC genes.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Agent</th>
<th>cUTI</th>
<th>Agent</th>
<th>cIAI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIC5000</td>
<td>%S</td>
<td></td>
<td>MIC6000</td>
</tr>
<tr>
<td>CAZ-AVI</td>
<td>0.12/0.12</td>
<td>100.0</td>
<td>CAZ-AVI</td>
<td>0.12/0.12</td>
</tr>
<tr>
<td>CEP</td>
<td>0.03/0.12</td>
<td>94.4</td>
<td>MER</td>
<td>0.016/0.03</td>
</tr>
<tr>
<td>CAZ</td>
<td>0.12/0.5</td>
<td>94.4</td>
<td>CAZ</td>
<td>0.25/0.25</td>
</tr>
</tbody>
</table>

a cUTI, complicated urinary tract infections; cIAI, complicated intra-abdominal infections
b CAZ-AVI, ceftazidime-avibactam; CEP, ceferpine; MER, meropenem

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Abstract 2310

Deciphering the biochemical features of PDC-315, a ceftolozane-hydrolyzing Pseudomonas-derived cephalosporinase selected in vivo

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Background: Resistance to ceftolozane/tazobactam (CTZ) may occur in Pseudomonas aeruginosa through the selection of mutations in ampC. These mutants typically exhibit rearrangements on the ampC Ω loop that confer increased MICs toward CTZ and ceftazidime-avibactam (CZA), but mitigated effects over penicillins and carbapenems. However, the contribution to the substrate profile of the enzyme of specific mutations is still largely unknown. Here we aim to characterize PDC-315, a novel ampC selected during CTZ therapy which exhibited a previously undescribed D245N substitution in the Ω loop.

Materials/methods: A pair of CTZ susceptible/resistant isolates of MDR P. aeruginosa recovered before and during CTZ therapy from a patient admitted to the ICU of Puerta del Mar University Hospital (Cádiz) were evaluated. Minimum inhibitory concentrations were determined by broth microdilution. Resistance mechanisms were depicted through whole genome sequencing on an Illumina MiSeq benchtop (Illumina INC, USA). bla ampC genes from the clinical isolates were cloned in parallel into the PAO1 ampC knock-out mutant (PAODC) to evaluate the resistance profiles, and in E. coli BL21 for protein purification. Steady-state kinetics and the IC50 values were determined using a Nicolet Evolution 300 spectrophotometer (Thermo Fisher Scientific, Waltham, MA, USA).

Results: A CTZ MIC elevation from 2/4 mg/L to >32/4 mg/L was observed between the two isolates. WGS revealed oprD loss and ampC upregulation in both isolates, but the CTZ-resistant isolate additionally harbored a mutation in ampC (D245N). PAODC transformants proved that this mutation caused resistance [CTZ MIC=16 µg/mL]. Kinetic assays revealed that the new ampC variant, designated PDC-315, exhibited a Kcat/Km ratio 10-fold higher than the WT ampC for ceftolozane, but impaired hydrolysis of piperacillin and imipenem (Kcat/Km ratios of 0.3 and 0.2 compared to WT ampC, respectively). Inhibition kinetics showed that PDC-315 was efficiently overcomed by avibactam but poorly inhibited by cloxacillin compared to WT ampC (IC50 ratios of ≈1 and ≈ 318, respectively).

Conclusions: PDC-315 exhibited enhanced catalytic efficiency towards ceftolozane, impaired hydrolysis of penicillins and carbapenems, and was potently inhibited by avibactam. Thus, piperacillin/tazobactam, carbapenems and ceftazidime/avibactam may play a role in the treatment of certain strains with evolved resistance to CTZ.

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Descriptive epidemiological analysis of antimicrobial resistance in strict anaerobes in Scotland, 2013-2018

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Background: Antimicrobial resistance in anaerobic bacteria has been recognised to be increasing globally, with growing resistance to metronidazole and carbapenems being of particular concern. Health Protection Scotland receives clinical microbiology results, including susceptibility data from all Scottish diagnostic laboratories via a national database [ECOSS].

Materials/methods: Data from 2013 to 2018 relating to strict anaerobes isolated from clinical samples was extracted from ECOSS (de-duplicated based on a 14 day episode definition). Predominant species, sample types and susceptibility to a variety of antibiotics was assessed. A literature review was conducted to compare resistance in Scottish isolates, to that reported globally.

Results: The most commonly reported organisms were Cutibacterium acnes (n = 2433), Bacterioides fragilis (n= 2253) and Clostridium perfringens (n = 2252). The most frequently associated sample type varied by species. Of the clinically relevant antibiotics, susceptibility testing was performed most commonly for metronidazole (ranging from 54-76%, depending on species). Reported resistance varied by agent and species.

Conclusions: Nationally, limited susceptibility testing is carried out for the majority of anaerobic bacteria. Where tested, resistance to most antibiotics including metronidazole was broadly comparable to that reported in the published literature, although comparatively higher resistance to clindamycin was observed for several species including C. perfringens. Work is ongoing in Scotland to improve identification of anaerobes and standardisation of susceptibility testing for isolates from sterile sites. It is anticipated that this will support more targeted treatments for individual patients and antimicrobial stewardship programmes.

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Abstract 2316

**Optimisation of blood components sterility testing: impact of small volumes in analytical sensitivity**

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**Background:** sterility testing of blood components is pivotal to prevent bacterial and/or fungal transfusion-transmitted infections. This is particularly challenging for lymphocyte apheresis, hematopoietic stem cells, platelet concentrates, cord blood and serum, for which very small volumes (from 0.5 to 1 ml) are inoculated into culture bottles. Aim of this study was to find and validate the most effective and rapid method in detecting a possible contamination of blood components.

**Materials/methods:** 15 strains were used, 13 from ATCC®: *Aspergillus brasiliensis* 16404; *Aspergillus niger* 16888; *Candida albicans* 10231; *Bacillus subtilis* subsp.*spizizenii* 6633; *Bacteroides fragilis* 25285; *Campylobacter jejuni* 33560; *Clostridium sporogenes* 19404; *Cutibacterium acnes* 11827; *Haemophilus influenzae* 49247; *Neisseria gonorrhoeae* 49226; *Pseudomonas aeruginosa* 9027; *Staphylococcus aureus* subsp.* aureus* 6538; *Streptococcus pyogenes* 19615; and two strains from clinical samples: *Corynebacterium striatum*; *Micrococcus luteus*; Colonies of each strain grown on chocolate agar were resuspended in separate tubes containing sterile saline solution until a standard turbidity of 1.0 McFarland (equivalent to about 3x10⁸ CFU/ml) was obtained. From these tubes, a series of four 1:100 dilutions were made, resulting in a final concentration of ~3x10⁶ CFU/ml (3 CFU/ml) of inoculum. The final suspension was inoculated into BD Bactec plus Aerobic, Anaerobic, Pediatric and Mycosis (the latter only for *Candida albicans* and *Aspergillus* spp.), with a volume of 1 ml and 0.5 ml.

**Results:** among bottles inoculated with 1 ml: 6/15 (40%) Aerobic, 5/15 (33.3%) Anaerobic and 8/15 (53.3%) Pediatric were positive. In the 0.5 ml group: 3/15 (20%) Aerobic, 4/15 (26.6%) Anaerobic and 5/15 (33.3%) Pediatric were positive. Time to positivity: for the 1 ml group: the 6 Aerobic bottles flagged positive in a mean time of 60.1 hours with a standard deviation of ±43.1 hours; the 5 Anaerobic bottles in 58.8 ±51.9 hours; the 8 Pediatric bottles in 31.9 ±27.6 hours. For the 0.5 ml group: 81.3 ±78.4 hours for the 3 Aerobic bottles; 50.8 ±45.9 hours for the 4 Anaerobic bottles; 24.2 ±15.2 hours for the Pediatric bottles.

**Conclusions:** this study showed how the combined use of both pediatric and anaerobic bottles improves detection of possible contamination even dealing with small volumes of blood components.

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Abstract 2319

The impact of consolidating molecular sexually transmitted infections screening and viral load testing on a new fully automated platform

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Background: Our laboratory processes 100,000 STI screens and viral load tests (HIV-1, HBV and HCV) annually, all of which are batched and performed on the Abbott m2000 System. The Alinity m System (Abbott Molecular) is the new fully automated, random and continuous access molecular diagnostics analyser. This platform performs multiple assays in parallel, eliminating the need for sample batching, resulting in a fast turn-around-time (TAT), streamlined workflow and reduced staff requirements. This platform also offers a STAT function.

Materials/methods: To investigate the impact of workflow consolidation to a single Alinity instrument from batch testing, currently performed on four m2000 instruments, we replicated seven days of routine testing on the Alinity using archived clinical samples, comparing TAT and assay results to our current system. Testing included 162 HIV-1, 92 HBV, 240 HCV viral loads and 1608 STI tests.

Results: Consolidated testing on Alinity lead to significant savings in TAT. Results for all four assays were reported in an average of 4:12 to 4:35 hours, with all results reported within 7:45 hours of sample arrival. Samples tested using the STAT function were available within an average of 3 hours (Table 1.).

Quantified viral load results from HIV-1 (n=9), HBV (n=42) and HCV (n=51) assays tested on both platforms were highly correlated (R² = 0.981, 0.964, 0.961, respectively). PPV and NPV for Chlamydia trachomatis were 100% and 99.8% respectively, for Neisseria gonorrhoeae (NG) PPV and NPV were 73.7% and 99.9% respectively. Five samples tested NG positive by Alinity and negative by m2000, however all had low cycle numbers and two of these samples were unvalidated sample types.

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<th>Assay</th>
<th>Platform</th>
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Table 1.

Conclusions: Consolidation of workflow from batch testing onto the Alinity m System considerably improved sample TAT, whilst producing test results comparable with the m2000. The improvements in TAT should lead to tangible clinical benefits to patients.

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**Abstract 2323**

**In vivo acquisition of oxacillinase-mediated resistance to ceftolozane/tazobactam and ceftazidime/avibactam in *Pseudomonas aeruginosa***

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**Background:** Narrow-spectrum oxacillinases such as OXA-2 and OXA-10 are disseminated among *Pseudomonas aeruginosa* strains worldwide. The contribution of these enzymes to the β-lactam resistance profile of *Pseudomonas aeruginosa* is limited. However, point-mutation derivatives may be selected during therapy upon exposure with certain β-lactams, resulting in new variants able to compromise the clinical utility of multiple antipseudomonalbs, including the recently marketed cephalosporin/β-lactamase inhibitor combinations ceftolozane/tazobactam (CTZ) and ceftazidime/avibactam (CZA). Here we describe the emergence of different extended-spectrum OXA-10 variants conferring resistance to CTZ and CZA in multiple patients during treatment with cephalosporins.

**Materials/methods:** Four pairs of CTZ and CZA-susceptible/resistant *P. aeruginosa* isolates recovered from 4 patients treated with ceftazidime at Hospital Universitario Puerta del Mar (Cádiz, Spain) between September 2018 – February 2019 were evaluated. Minimum inhibitory concentrations of ticarcillin, piperacillin/tazobactam, aztreonam, ceftazidime, ceftazidime/avibactam, cefepime, ceftolozane, ceftolozane/tazobactam, imipenem, imipenem/relebactam, meropenem, tobramycin, amikacin, ciprofloxacin and colistin were determined by broth microdilution. Clonal relatedness was assessed by REP-PCR and MLST. Characterization of chromosomal and acquired β-lactamases was performed by PCR and sequencing. The different *bla*_{OXA-10} alleles detected were cloned in parallel in plasmid pUCP24 and electroporated into reference strain PAO1 to evaluate their impact on β-lactam resistance.

**Results:** All isolates exhibited multidrug resistance. However, whereas all initial isolates exhibited wide susceptibility to ceftazidime, CTZ and CZA, the isolates obtained after treatment exhibited a substantial increase in the MIC of ceftazidime, CTZ and CZA. Imipenem partnered with relebactam retained activity against all strains (MIC=1-2 µg/mL). All isolates yielded similar REP-PCR patterns, were assigned to the ST253, and yielded positive results for *bla*_{OXA-10}. DNA sequencing demonstrated that the isolates obtained after treatment had additionally developed mutations in the *bla*_{OXA-10} gene, resulting in four OXA-10 derivatives: the classic OXA-14 (G157D) and three new variants, designated OXA-794 [W154C], OXA-795 [Δ(F153-W154)] and OXA-824 [N143K]. PAO1 transformants proved that the new variants conferred high-level resistance to CTZ (MIC≥8 µg/mL) and CZA (MIC≥32 µg/mL).

**Conclusions:** Selection of extended-spectrum mutations in narrow-spectrum OXA-type β-lactamases is an emerging mechanism of resistance to CTZ and CZA in *P. aeruginosa*. Imipenem-relebactam may represent a therapeutic option when this kind of resistance emerge in the clinical setting.

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Abstract 2324

Modelling the impact of antibiotic use and infection control agents on the incidence of methicillin-resistant Staphylococcus aureus incidence rates in hospital, informed by identifying antibiotic usage thresholds utilising non-linear time series analysis

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Background: Evidence has shown the relationship between antibiotic use and antimicrobial resistance to be linear; the more antibiotics consumed the higher the resistance levels seen, irrespective of the intensity of antimicrobial use. However mathematical models have suggested that the relationship between antibiotic use, infection control agents and antimicrobial resistance is non-linear and that there is a threshold level of drug, above which the persistent selection of the antibiotic in the environment will lead to the development and spread of antimicrobial resistance. These thresholds may define safe usage levels for antibiotic stewardship activities, avoiding over restriction and bringing restricted antibiotics back into practice.

Materials/methods: We applied a NLTS model to identify thresholds in population antibiotic use and infection control agent use that influence MRSA incidence rates within a secondary care hospital in Northern Ireland in order to inform an antibiotic stewardship policy (ASP).

Results: The NLTS model identified critical thresholds for hospital consumption of fluoroquinolones, co-amoxiclav and alcohol-based hand rub (ABHR). The thresholds identified for fluoroquinolones and co-amoxiclav were 6.1 Defined Daily Doses (DDDs)/100 Occupied Bed Days (OBDs) and 37.17 DDDs/100 OBDs respectively, the consumption of both was identified to be above the thresholds. An inverse relationship was observed with increases in hospital consumption of ABHR up to 0.81 Litres/100 OBDs, above which further increases were not associated with further declines in MRSA. The identified thresholds were then translated into ASP suggestions, based on consumption in the previous 12 months. Fluoroquinolone and co-amoxiclav consumption should be reduced by 30% and 10% respectively in order to reduce consumption below the identified thresholds, ABHR levels need to be maintained.

Conclusions: NLTS can provide quantitative goals for antibiotic stewardship interventions by identifying critical thresholds in antimicrobial consumption. An ASP has been devised that restricts fluoroquinolone and co-amoxiclav consumption to a level below threshold to determine if the reduction in consumption has an effect on MRSA incidence within the hospital.

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Insights into reservoir and pathogenicity of *Escherichia coli* ST83: role of haemolysin A operon duplication in severity of urinary tract infections

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**Background:** The characterization of the virulence genes content of *Escherichia coli* populations causing urinary tract infections (UTI) has been the subject of intensive research to find critical features for pathogenesis. However, genetic determinants conditioning severe forms of disease are poorly understood. We used comparative genomics, histological and clinical data to support the origin and pathogenicity of an aggressive *E. coli* strain causing a feline acute pyelonephritis and glomerulonephritis that resulted in kidney damage.

**Materials/methods:** An *E. coli* strain (Ec_151217) was identified in purulent fluid and urine. In vitro antibiotic susceptibility testing was performed for 17 antibiotics (EUCAST/CLSI). Genomic DNA was sequenced by Illumina MiSeq system, and this information was used to characterize phylogenetic group, serotype, sequence type, virulence potential and virulence gene content (n=49 ExPEC genes in-house database) (CGE in silico tools). The genome was compared with 27 ST83 *E. coli* genomes retrieved from NCBI and EnteroBase public databases to generate a SNP-based phylogeny (CSI phylogeny 1.4).

**Results:** Strain Ec_151217 (B2, ST83, O83:H5:K5) was susceptible to all antibiotics tested. High virulence score was detected (n=28/49), including adhesins (pap, fim, sfa/foc, matB, yfcV), toxins (hly, cnf1, vat), siderophores (fyuA, iroN), invasins (ibeA, gimB) amongst others (e.g. malX, usp, upaH), many important to urinary epithelium adhesion. The SNP-based ST83 phylogeny showed a high relatedness with ST83 O83:H5 and O6:H5 genomes carrying a similar array of virulence genes, from animals and human infections [including bacteremia] further supporting their pathogenic potential and the risk of host-to-host transmission. Interestingly, Ec_151217 strain contains two copies of the hemolysin A operon (hlyCABD). Though they encode highly similar HlyA proteins, they can be discriminated by their highly dissimilar 1.6 Kb upstream regions (~50% homology). Comparative genomics and epidemiological data showed that the presence of these hlyA paralogues is sporadic in ExPEC population (1%) but in strains that caused acute pyelonephritis [e.g. *E. coli* 536], supporting preliminary experimental data that the presence of two operons conditions higher pathogenicity.

**Conclusions:** Our data support a higher pathogenic potential for specific serotypes within ST83 *E. coli*, potentially associated with a duplication of hlyA operon conditioning higher virulence and severe forms of UTI.

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Increases in environmental cleaning and reduction in in-hospital mortality in multi-patient rooms with single-use disinfection wipes hung at the patient bed: a prospective, crossover trial

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Background: The hospital environment, particularly high-touch surfaces, plays an established role in mediating human pathogen transmission between patients. In resource-limited facilities with multi-patient rooms, this mode of transmission is enhanced, but environmental cleaning initiatives are challenging to implement. We evaluated the impact of hanging cleaning/disinfecting wipes at patient bedside in improving patient outcomes.

Materials/methods: A crossover-prospective trial was conducted at four medical departments in Shamir (Assaf Harofeh) Medical Center, Israel. We compared the effect of installing single-use quaternary ammonium-based wipes (Clinell®) at patient bedside and in close proximity to medical care areas in the unit to the standard practice of using reusable cloths with bleach. Each department was randomly assigned to an intervention (six months) and control period (six months) separated by a one month washout period. The patient environment (five predefined high-touch surfaces) was tested for cleaning indicators (fluorescent markers) twice weekly. Patient outcomes, including rates of in-hospital mortality, central line-associated bloodstream infections (CLABSI) and catheter-associated urinary tract infection (CAUTI), and cleaning frequency were compared between intervention and control departments using Poisson regression and generalized estimating equations, respectively.

Results: Among 7,725 patients (47,670 person-days) followed, 3,932 (23,792 person-days) were in intervention rooms and 3,793 (23,878 person-days) were in control rooms. In-hospital mortality rate among patients in intervention units was significantly lower, with 92.0 deaths/10,000 person-days versus 111.9 deaths/10,000 person-days in control units [IRR=0.8; 95% CI=(0.69, 0.98)]. No significant incidence rate differences of CLABSI [IRR=1.8; 95% CI=(0.7, 4.3)], CAUTI [IRR=1.4; 95% CI=(0.8, 2.4)] or CLABSI and CAUTI combined [IRR=1.4; 95% CI=(0.9, 2.3)] were noted. Effective environmental cleaning of all five tested locations occurred in 34% of intervention rooms versus 12% of control rooms [OR=3.7; 95% CI=(1.9, 7.1)].

Conclusions: By increasing their proximity to end users, easily accessible single-use quaternary ammonium-based wipes significantly increased the frequency in which high-touch surfaces cardinal to transmission were being cleaned in departments with multi-patients rooms while in-hospital mortality was significantly reduced in intervention departments. Single-use cleaning/disinfecting wipes may provide a more effective and acceptable alternative to bleach for reducing environmental transmission of pathogens.

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Abstract 2330

**Antibiotic with novel lipid A pathway target shows activity against Gram-negative bacteria**

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**Background:** Gram negative bacteria such as *Acinetobacter baumannii*, *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* cause a wide range of infections and pose a significant risk to human health. Additionally, resistance to commonly used first line treatments represent a significant clinical problem which is compounded by a lack of new development compounds. Using a computational model involving the biogenesis of the *E. coli* cell envelope, Oppilotech identified a novel target enzyme within the Lipid A biosynthetic pathway. Lipid A is an essential component of the outer membrane and is involved in virulence and cellular integrity. To date only engineered strains of *Neisseria* and *Acinetobacter* can survive without this important physical barrier. Defects in lipid A synthesis often lead to cells with compromised membrane integrity and increased permeability making enzymes within this pathway attractive to drug discovery and development efforts.

**Materials/methods:** Gram negative bacterial isolates taken from HAP/VAP patients were tested against the OPT molecule in combination with various antimicrobials, following standard broth microdilution checkerboard methods.

**Results:** Fractional inhibition concentration indices (FICI) were calculated from inhibitory values taken from a antimicrobial checkerboard assay and interpretations from Odds (2003). Activity of the Oppilotech compound was seen in combination with other antimicrobials against MEM and AMC *E. coli*, CT and AMC *P. aeruginosa* and ESBL positive *K. pneumoniae* isolates.

**Conclusions:** OPT200 5/37, an early ‘hit to lead’ stage molecule, shows direct acting activity against various Gram-negative species as well as potentiating activity with other antimicrobials. This data is consistent with the essentiality of Lipid A enzymes along with the chemical protection provided by the LPS barrier. Importantly, activity of the Oppilotech compound was also seen against MEM and AMC *E. coli*, CT and AMC *P. aeruginosa* and ESBL positive *K. pneumoniae* isolates.

HAP- Hospital Acquired Pneumonia, VAP- Ventilator Acquired Pneumonia, LPS- Lipopolysaccharide, MEM – Meropenem, AMC – Amoxicillin clavulanate, R- Resistant, CT- Colistin

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Detection and genotyping Lymphogranuloma venereum in Tenerife, Spain

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Background: Chlamydia trachomatis (CT) is the world's leading sexually transmitted infection (STI) and is increasing every year. The serovars L1, L2 and L3 invade the connective tissue and can produce Lymphogranuloma venereum (LGV) that is characterized by a genital ulcer at the site of inoculation. A secondary stage can be presented with an inflammatory reaction in the inguinal nodes and proctocolitis can also be present with rectal discharge, anal pain and/or tenesmus.

The aim of this study was to assess LGV infection prevalence and investigate genotype distribution in our region.

Materials/methods: A total of 460 samples from the routine screening of sexual transmitted infections (STI) patients were submitted to the Microbiology Laboratory from August 2019 to November 2019. Those samples were processed by a multiplex Real-time PCR Allplex STI-7 (Seegene®) that detects simultaneously CT, Neisseria gonorrhoeae (NG), Mycoplasma hominis (MH), Mycoplasma genitalium (MG), Ureaplasma urealyticum (UU), Ureaplasma parvum (UP), Trichomonas vaginalis (TV).

In case of a CT positive result, pmpH-real-time PCR was used to discriminate between LGV and non-LGV genotypes and ompA amplification and sequenced was used to identify the different genotypes.

Results: During the study period we found 47 positive samples for CT. The prevalence of CT infection was 10%, with a significant difference between genders (infected males 64% [30/47] vs infected female 36% [17/47]). NG co-infection was detected in 15% of CT positive patients.

Only 41 of 47 samples could be analyzed for LGV detection. Two percent (9/451) of samples were positive for LGV and all of them were male. Most of positive samples (5/9) were rectal swabs. The study of ompA gene was possible in only four samples, and the most common genotype in our population was L2 (75% [3/4]), followed by D (25% [1/4]).

Conclusions: In the present study we found that genotype L2 was the most frequent in our region. Considering sexual behavior, LGV infection was more prevalent in men who have sex with mean (MSM) population. It should be underlined that CT genotyping is fundamental in order to rule out LGV infection, often underdiagnosed, since the treatment for LGV is different from that for non-LGV Chlamydia.

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Proposing the spike gene of Coronavirus OC43 as a target for nosocomial outbreak investigation in long-term care facilities

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Background: Viral genome sequencing for the investigation of respiratory virus outbreaks has been described, but data remains limited, particularly for non-influenza respiratory viruses. Coronaviruses are frequently implicated in long-term care home (LTC) respiratory outbreaks, coinciding with increased levels of viral activity in the community. Here, we propose the spike (S) gene as a sequencing target to determine relatedness between isolates of coronavirus OC43 during outbreaks at a veteran’s LTC.

Materials/methods: A total of 54 outbreak samples from ten distinct outbreaks through 2015 to 2017 were collected using traditional infection prevention and control (IPC) criteria. The S gene from these isolates were sequenced after amplification using multiple primer combinations. Near-complete (>99% coverage) spike gene sequences were obtained for 48 samples.

Results: Sequencing results demonstrated that the S gene was sufficient to resolve epidemiologically-related viruses into their respective outbreak classifications. A phylogenetic tree showed that clades were distinctive to the year in which the outbreak occurred [see figure]. That is, the sequences from the one presumed outbreak in 2015 were highly dissimilar from sequences of 2016 and 2017 outbreaks. Although four outbreaks were called in 2016, phylogenetic analysis revealed near-identical sequences across outbreaks in the different wards, suggesting either inter-unit transmission, or a limitation to using the spike gene as a candidate reference gene for outbreak investigation. Additionally, S gene phylogenetic analysis of isolates from 2017 outbreaks was sufficient to distinguish between the four unique outbreaks identified by traditional IPC. Moreover, sequencing results linked strains that were retrospectively epidemiologically-associated, though initially classified as unrelated by conventional outbreak definitions. In some instances, epidemiologically-unassociated isolates from the same catchment area shared identical or near-identical S gene sequences with outbreak strains.

Conclusions: Although whole genome sequencing or genotyping may be advantageous for outbreak investigation, spike gene sequencing paired with epidemiological classification has the potential to provide additional insight compared to epidemiological investigation alone.

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Abstract 2334

Multi-centre evaluation of meropenem/vaborbactam MIC results for Enterobacterales and Pseudomonas aeruginosa using EUCAST breakpoints on MicroScan dried Gram-negative MIC panels

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Background: A multicenter study was performed to evaluate the accuracy of testing meropenem/vaborbactam on a MicroScan Dried Gram-negative MIC (MSDGN) Panel when compared to a frozen ISO/CLSI broth microdilution reference panel

Materials/methods: An evaluation was conducted at three U.S. sites by comparing MIC values obtained using the MSDGN to MICs utilizing an ISO/CLSI broth microdilution reference panel. A total of 775 Enterobacterales and P. aeruginosa clinical isolates were tested using the turbidity and Prompt® methods of inoculation during the efficacy phase. A subset of 14 organisms for reproducibility was tested on MSDGN panels at each site. MSDGN panels were incubated at 35 ± 1°C and read on the WalkAway System, the autoSCAN-4 instrument, and read visually. Read times for the MSDGN panels were at 16-20 hours. Frozen reference panels were prepared according to ISO/CLSI methodology, incubated for 16-20 hours and read visually. EUCAST breakpoints (mg/L) used for interpretation of MIC results were: Enterobacterales ≤ 8/8 S, > 8/8 R and P. aeruginosa ≤ 8/8 S, > 8/8 R.

Results: Essential and categorical agreement when compared to frozen reference panel results, for all isolates tested in efficacy as follows:

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<td>0.3 (2/769)</td>
</tr>
<tr>
<td>Visually</td>
<td>99.5 (771/775)</td>
<td>99.1 (768/775)</td>
<td>99.5 (773/775)</td>
<td>99.6 (772/775)</td>
</tr>
<tr>
<td></td>
<td>0.0 (0/6)</td>
<td>0.0 (0/6)</td>
<td>0.1 (1/769)</td>
<td>0.3 (2/769)</td>
</tr>
</tbody>
</table>

T = Turbidity Inoculation method, P = Prompt Inoculation method
*Calculation of MAJ and VMJ excluding 1 well errors

Conclusions: This multicenter study showed that meropenem/vaborbactam MIC results for Enterobacterales and P. aeruginosa obtained with the MSDGN panel correlate well with MICs obtained using frozen reference panels using EUCAST interpretive criteria.

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Presenter email address: jchau@beckman.com
Abstract 2335

Antibiotic exposure and the risk of CRE acquisition

Nasreen Hassoun Kheir1,2, Khetam Hussein1,2, Maram Saffuri2, Sally Badaan2, Shani Peleg2, Yuval Geffen1,2, Mical Paul1,2

1Rambam Health Care Campus, Infectious diseases institute, Haifa, Israel, 2Technion - Israel Institute of Technology, The Ruth and Bruce Rappaport Faculty of Medicine, Haifa, Israel

Background: Carbapenem Resistant Enterobacteriaceae (CRE) are increasingly prevalent worldwide. In this study, we aimed to examine the association between CRE acquisition in hospitalized patients and exposure to different classes of antibiotics.

Materials/methods: We conducted a matched case:control 1:2 study in Rambam-healthcare campus (RHCC) between Jan 2014 – Jun 2017. Enrolled cases included adult patients who acquired CRE in RHCC, both colonized and infected. Controls were matched from negatively screened-CRE hospitalized patients by age, hospitalization unit and number of hospital days in the 90 days prior to swab date. Antibiotic exposure was measured as sum of treatment days to a certain class of antibiotics during the preceding 90 days. We analyzed the data using univariate and multivariate analysis controlling for matching, adjusting other significant clinical risk factors for CRE acquisition found in our study.

Results: we included 267 patients: 90 cases and 177 matched controls. Mean age was 64±18 years, and 118 patients were female (44.2%). Exposure to carbapenems, cephalosporins vancomycin and piperacillin/tazobactam were significantly associated with the risk for CRE acquisition on univariate analysis (Table).

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>univariate analysis</th>
<th>adjusted multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR [95% CI]</td>
<td>Sig</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>1.111 (1.029-1.199)</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>1.054 (0.948-1.171)</td>
<td>0.333</td>
</tr>
<tr>
<td>Quinolones</td>
<td>1.027 (0.989-1.067)</td>
<td>0.166</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>1.099 (1.016-1.189)</td>
<td>0.019</td>
</tr>
<tr>
<td>Cephalosporins</td>
<td>1.071 (1.071-1.128)</td>
<td>0.009</td>
</tr>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>1.058 (1.003-1.116)</td>
<td>0.039</td>
</tr>
<tr>
<td>Other Penicillins</td>
<td>1.021 (0.991-1.053)</td>
<td>0.175</td>
</tr>
</tbody>
</table>

Other significant risk factors for CRE acquisition included anemia, referral from another facility and number of non-invasive imaging procedures before acquisition. Adjusted to these and all significant antibiotics, carbapenem and cephalosporins were significantly associated with CRE acquisition (Table).

Conclusions: Exposure to carbapenems and cephalosporins is significantly associated with CRE acquisition. Antibiotic stewardship targeting these classes can selection pressure for CRE. We plan to increase the cohort and conduct separate analyses for CPE and non-CPE, assuming that associations will be stronger for non-CPE.

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Abstract 2337

**Drug repositioning as a possible strategy to combat bacterial infections: evaluation of non-antibiotic human therapeutics as quorum-sensing inhibitors**

Márió Gajdács*1,2, Gabriella Spengler3

1University of Szeged Faculty of Pharmacy, Department of Pharmacodynamics and Biopharmacy, Szeged, Hungary, 2Hungarian Society for Clinical Microbiology and Infectious Diseases, Budapest, Hungary, 3University of Szeged - Faculty of Medicine, Department of Medical Microbiology and Immunobiology, Szeged, Hungary

**Background:** Since the 21st century, antibacterial drug development has been slow to keep up with the developing bacterial resistance. Quorum sensing (QS) is a distinct mechanism of bacterial cell-cell communication, during which bacteria sense the density of cells in the surrounding environment by the detection of various signal molecules. The influence of QS on the expression of bacterial virulence determinants has been described. Drug repositioning is a promising drug development strategy, during which novel pharmacological applications are identified for drugs already approved for human therapeutic uses.

**Materials/methods:** Forty-five pharmacological agents, encompassing a wide range of chemical structures and mechanisms of action were screened for their antibacterial and QS-inhibitory activity. Screening for QS-inhibition was carried out using the cross-inoculation method, while quantitative assessment of compounds was performed by the parallel inoculation method. *Chromobacterium violaceum* wt85, *C. violaceum* CV026 and *Serratia marcescens* AS-1 were utilized as acyl-homoserine lactone (AHL) sensory strains, while *Enterobacter cloacae* 31298, *Sphingomonas paucimobilis* Ezf 10-17 and *Novosphingobium* spp. Rr 217 were used as AHL-producers. QS-inhibition experiments were performed on a modified Luria-Bertani agar supplemented with 2 g/L glucose and a microelement stock solution. Acridine orange was used as a positive control during QS-experiments. MIC determination was performed using broth microdilution, according to CLSI standards. *Staphylococcus aureus* ATCC 25923 and *Escherichia coli* ATCC 25922 were used as control strains.

**Results:** Among the tested pharmaceutical agents, fourteen (namely celecoxib, mebendazole, ivermectin, verapamil, promethazine, chlorpromazine, thioridazine, methotrexate, doxorubicin, bleomycin, atorvastatin, simvastatin, clotrimazole and fluconazole) showed antibacterial activity on various bacterial strains in the tested concentration range (0.25-250 µg/mL). Eight drugs (namely 5-fluourouracil, metamizole-sodium, cisplatin, methotrexate, bleomycin, promethazine, chlorpromazine and thioridazine) presented with concentration-dependent (3.12-50 µg/mL) QS-inhibitory activity on the tested bacterial model systems.

**Conclusions:** Compared to antibiotics, the use of virulence inhibitors may be advantageous as the selection pressure exerted by these drugs [and the consequent development of resistance] is expected to be much lower. Currently marketed pharmaceutical compounds can be considered as potential sources of QS inhibitory agents, as the pharmacokinetic parameters and tolerability of these compounds have already been verified in vivo.

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Evaluation of tedizolid and comparators activity against Gram-positive bacterial isolates causing skin and skin structure infections from paediatric patients in Europe and surrounding countries (2015-2019)

Cecilia Godoy Carvalhaes1,2, Helio S. Sader1, Jennifer Streit1, Robert Flamm1, Rodrigo E. Mendes1

1JMI Laboratories, North Liberty, United States

Abstract third-party references: This study was performed by JMI Laboratories and supported by Merck, which included funding for services related to preparing this abstract.

Background: Tedizolid is approved in many European and non-European countries for treating acute bacterial skin and skin structure infections (SSSI) in adults. The efficacy, safety and tolerability of tedizolid was evaluated in phase 3 clinical trials for treating complicated SSSI caused by Gram-positive organisms in paediatric patients. The activity of tedizolid and comparators was evaluated against clinical surveillance isolates collected from paediatric patients with SSSI in Europe and surrounding countries during a 5-year period.

Materials/methods: A total of 861 Gram-positive isolates were collected from paediatric patients with SSSIs in 36 medical centres in European countries and surrounding regions (2015–2019). Bacterial identification was confirmed by MALDI-TOF MS and susceptibility testing applied reference broth microdilution method. CLSI and EUCAST interpretive criteria followed current guidelines.

Results: The major Gram-positive bacterial species and pathogen groups causing SSSI included S. aureus (73.5%) and β-haemolytic streptococci (BHS; 16.4%), followed by small numbers of Enterococcus faecalis (2.9%), and other microorganisms (7.2%). Similar frequency was also observed in both age groups (<12 and 12-18 years of age). Tedizolid was highly active against S. aureus [MIC50/90, 0.12/0.25 mg/L; 100% susceptible by EUCAST criteria]. Equivalent tedizolid MIC50/90 values were observed (100% susceptible) against methicillin-resistant S. aureus (MRSA; n=12.5%; MIC50/90, 0.12/0.25 mg/L) and methicillin-susceptible [MSSA; MIC50/90, 0.12/0.25 mg/L] isolates. Tedizolid was also very active against BHS [MIC50/90 values, 0.25/0.25 mg/L]. Susceptibility rate of 100% was obtained for tedizolid, linezolid, vancomycin and daptomycin against the main Gram-positive species and organism groups (Figure). Ceftaroline and clindamycin showed susceptibility rates of >90% against MRSA, MSSA, S. pyogenes and S. dysgalactiae, but lower susceptibility rates were observed for clindamycin tested against VGS (85.0%) and S. agalactiae (62.5%).

Conclusions: Tedizolid was highly active against Gram-positive clinical isolates responsible for SSSI in paediatric patients from hospitals located in European and surrounding countries recovered in a 5-year period. Tedizolid was equipotent or more potent than comparators against MSSA and MRSA isolates.

<table>
<thead>
<tr>
<th>Organism (no. tested)</th>
<th>Tedizolid</th>
<th>Linezolid</th>
<th>Ceftaroline</th>
<th>Daptomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIC (mg/L)</td>
<td>%S1</td>
<td>MIC (mg/L)</td>
<td>%S1</td>
</tr>
<tr>
<td>MSSA (554)</td>
<td>0.12</td>
<td>0.25</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>MRSA (75)</td>
<td>0.12</td>
<td>0.25</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>E. faecalis (25)</td>
<td>0.25</td>
<td>0.25</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>BHS (141)</td>
<td>0.12</td>
<td>0.25</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>S. pyogenes (116)</td>
<td>0.12</td>
<td>0.25</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>S. agalactiae (12)</td>
<td>0.25</td>
<td>0.25</td>
<td>100.0</td>
<td></td>
</tr>
<tr>
<td>VGS (21)</td>
<td>0.12</td>
<td>0.12</td>
<td>100.01</td>
<td></td>
</tr>
</tbody>
</table>

1 MSSA = methicillin-susceptible S. aureus; MRSA = methicillin-resistant S. aureus; BHS = β-haemolytic streptococci; VGS = Viridans group streptococci.

1 S. pyogenes (116) | 0.12 | 0.25 | 100.0 | 0.25 | 0.25 | 100.0     | 0.25 | 0.25 | 100.0     | 0.25 | 0.25 | 100.0

2 using other than pneumonia breakpoints.

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**Prevalence of *Mycoplasma genitalium* and frequency of resistance to macrolides and fluoroquinolones in Tenerife, Spain.**

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1Hospital Universitario Nuestra Señora de Candelaria, Santa Cruz de Tenerife, Spain

**Background:** Information of macrolide and fluoroquinolone resistance in *Mycoplasma genitalium* (MG) is limited in certain geographic areas in Spain. MG is a common cause of non-gonococcal urethritis, cervicitis, pelvic inflammatory disease, preterm birth and spontaneous abortion. An increasing incidence of treatment failure suggests the emergence of antibiotic resistance associated to mutations in the 23S rRNA gene (Azithromycin, the recomended treatment) and in parC and gyrA genes (Moxifloxacin, alternative treatment).

The aim of this study is to establish the current prevalence of resistant strains in our region.

**Materials/methods:** The study was conducted retrospectively/prospectively with a total of 1842 samples from the routine screening of sexual transmitted infections (STI) patients. Between December 2018 and November 2019, samples where MG was detected using PCR (Allplex® STI-7, Seegene) were also studied for susceptibility to macrolides and fluoroquinolones.

Resistant was investigated by sequencing the 23S rRNA studying changes in positions A2058TCG, A2059CG, A2062GCT, A2098C, C2055G considered to be associated with resistant to macrolides and point mutations in the quinolone resistante determining region (QRDR) of the topoisomerase IV gene parC and mutations in the DNA gyrase gene gyrA for quinolones.

**Results:** Forty-four patients, most of them male (59% [26/44]) with a median age of 32 years (19-59) were studied. The specimens with a positive result were: 38% (17/44) endocervical swabs, 50% (22/44) urethral swabs, 7% (3/44) pools of different samples and 2% (1/44) of a rectal and ulcer specimen. The prevalence of MG was 3.9% (70/1772). A total of 41% (16/39) of MG strains had at least resistant to one antibiotic. Macrolide resistant strains were detected in 25% (10/39) patients. The most frequent single nucleotide polymorphism (SNP) was at position A2059G (Escherichia coli numbering) with 60% (6/10). We identified point mutations in QRDR of gyrA or parC in 15% (6/39) patients. Five percent (2/39) of patients had a multiresistant strain. Regarding patients follow-up, the test of cure have been performed, only in 25% (11/44) of patients.

**Conclusions:** Mutations associated with first line treatment are present in a high percentage (25%). Resistant test should be done in order to adjust antibiotic treatment and prevent spread of resistant strains. According to the current guidelines a test of cure have to be done in all patients due to high prevalence of macrolide resistant.

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Antimicrobial use for asymptomatic bacteriuria: first, do no harm

Yana Shpunt1, Inna Estrin1, Hodaya Saadon1, Galit Ben-Yossef1, Lilly Goldstein1, Dan Klafter1, Yossi Levi1, Shani Zilberman-Itskovich1, David Katz1, Tzilia Lazarovitch1, Ronit Zaidenstein1, Shani Zilberman-Itskovich1, David Katz1, Tzilia Lazarovitch1, Ronit Zaidenstein1, Dror Marchaim*1

1Shamir Medical Center, Zerifin, Israel

Background: Antimicrobials administered to patients with asymptomatic bacteriuria (ASB) is a common medical error that can lead to devastating clinical and fiscal outcomes. However, controlled analyses quantifying the commonality and impact of this practice are lacking. Our study aims were to conduct an epidemiological investigation to define the characteristics of patients with ASB, to identify independent risk factors for instituting antimicrobials for this population, and quantify the impact of this practice on clinical and fiscal outcomes.

Materials/methods: A retrospective cohort study for calendar year 2017 was conducted at the Shamir Medical Center, Israel. All adults’ urine cultures were reviewed, and ASB was determined according to CDC criteria. Pregnant women, renal transplant recipients, and patients who underwent urologic procedures, were excluded. Multivariable logistic regression models were constructed in order to analyze the predictors and outcomes associated with use of antimicrobials for ASB.

Results: In our study population, we identified 1,530 patient-unique positive urine cultures, of which 610 (40%) patients were determined to have ASB. Of the 696 offending isolates, 219 (36%) were MDROs: i.e., mainly extended-spectrum beta-lactamase-producing Enterobacteriaceae (n= 143, 23.4%) and Pseudomonas aeruginosa (n= 33, 5.4%). There were 178 patients (29%) who received antimicrobials for ASB. Independent predictors for improper administration of antimicrobials for patients with ASB were male sex (aOR=2; p<0.001) and dependent functional status upon hospital admission (aOR=2.3; p<0.001). In three separate multivariable outcome models, “treatment” for ASB was independently associated with longer length of stay (p=0.04), with additional hospitalization (aOR=1.7; p=0.02) and with acute Clostridioides difficile infection (i.e., CDI) in the following 90 days (aOR=4.5; p<0.001).

Conclusions: ASB is a common condition, frequently resulting from MDROs. Approximately one-third of patients in our study population were improperly treated for ASB. This futile usage of antimicrobials was independently associated with longer length of stay, with re-hospitalization, and with later acute CDI. Future research and focus should be directed towards men with poor functional status.

Presenter email address: drormarchaim@shamir.gov.il
Abstract 2342

Comparative effectiveness of macrolides, fluoroquinolones or combination therapy for the treatment of Legionnaires’ disease in the US Department of Veterans Affairs health system

Vanessa Stevens*1,2, Shantini Gamage3,4, Annie Jasper5,6, Gary Roselle3,4,7, Nasia Safdar5,6

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Background: The incidence of Legionnaires’ Disease (LD) is increasing worldwide. Scant data are available to guide the selection of optimal antimicrobial therapy. We evaluated the impact of treatment with macrolides, fluoroquinolones, or both on the risk of mortality and other clinical outcomes among patients with LD.

Materials/methods: Retrospective cohort study of patients diagnosed with LD reported to VA Inpatient Evaluation Center October 2013 - March 2019. Patients with no record of treatment in VA were excluded. Treatment was classified as macrolides only, fluoroquinolones only, or both. The primary outcome was 30-day all-cause mortality. Secondary outcomes included new onset acute renal failure or dialysis and apyrexia. Propensity scores were fit using generalized boosted models and included age, history of hospitalization, comorbidities, setting of diagnosis, and abnormal laboratory values as defined by the pneumonia severity index. Relative risks (RR), risk differences (RD) and 95% confidence intervals (CI) were estimated with propensity-weighted modified Poisson regression using generalized estimating equations clustered at the facility level.

Results: There were 718 LD patients; 96.7% were male and 63.5% were white. One-third of patients received fluoroquinolones, 37.3% received macrolides, and 30.1% received both. Before weighting, patients treated with fluoroquinolones were more likely to be diagnosed as outpatients than those treated with macrolides or both drugs (53.0% vs 42.9% and 40.7%, respectively). A comparison of the risks of primary and secondary outcomes across treatment groups is shown (Table). Outcomes were similar, with small increases in the risk of mortality and dialysis for patients treated with fluoroquinolones compared to both drugs.

Conclusions: We found no difference between fluoroquinolones, macrolides, or the combination in the risk of mortality or other clinical outcomes among this large cohort of patients with LD. Given the known adverse event profile of fluoroquinolones, macrolides may be preferred therapy for LD.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Fluoroquinolones</th>
<th>Macrolides</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR*(95% CI)</td>
<td>RD*(95% CI)</td>
</tr>
<tr>
<td>30D Mortality</td>
<td>1.42(0.79–2.56)</td>
<td>0.02(-0.03–0.07)</td>
</tr>
<tr>
<td>Acute Renal Failure</td>
<td>0.92(0.58–1.48)</td>
<td>-0.01(-0.06–0.04)</td>
</tr>
<tr>
<td>New Dialysis</td>
<td>1.75(0.63–4.85)</td>
<td>0.03(-0.01–0.06)</td>
</tr>
<tr>
<td>Apyrexia</td>
<td>0.92(0.79–1.07)</td>
<td>-0.06(-0.16–0.03)</td>
</tr>
</tbody>
</table>

*Compared to combination

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Abstract 2344

Organisation of an ID consultation: are medical reports more important than patients?

Jonathan Tschopp*1, Benoit Guery1

1 University Hospital of Lausanne, Service of Infectious diseases, Lausanne, Switzerland

Background: The clinical practice of an infectious diseases' (ID) specialist mostly consists in a transversal activity as a consultant for physicians of other specialties. The daily workload may be highly variable, depending on the number of demands, and therefore difficult to plan. Accordingly, the needed number of fellows and attending physicians (AP) to allow a smooth functioning of the ID clinic is hard to predict. The aim of this study was to better understand the global workload and time needed to fulfill key daily tasks and improve the overall efficiency of our ID clinic.

Materials/methods: Lausanne University Hospital is a 1500-bed tertiary care hospital in Switzerland. ID consultations are provided 24 hours/day, 7 days/week either by ID fellows or internal medicine (IM) fellows. All clinical cases are overseen by an AP. Data from all ID consultations were collected from our hospital’s electronic medical database over a 12-month period (August 2018 to July 2019), excluding pediatrics, orthopedics, and immunosuppressed patients (solid organ transplant, haematology-oncological, HIV/AIDS). A smartphone app was created to monitor the time for each consultation. Fellows reported the time needed to answer phone calls, visit patients and write medical reports. AP reported the time to oversee each clinical case, visit patients and validate fellows’ reports. Only working days/hours were considered for this part of the study.

Results: 3242 ID reports were made during this period, of which 1360 (41.2%) during working hours (8am – 6pm), 1208 (37.3%) out of working hours (6pm – 8am), and 674 (20.1%) during weekends. Reports were classified as first consultations (39.3%) and follow-up consultations (60.7%). According to the smartphone app, mean time for each clinical case was 109.9 minutes for the fellows and 60.5 minutes for the AP, including a shared supervision time (Table 1).

Conclusions: Offering ID consultations 24/7 seems to be essential in our hospital as only 41% of all consultations were made during working days/hours. ID fellows spent more time with patients than IM fellows but were more efficient in writing medical reports, which was the longest task of each clinical case.

Table 1.

<table>
<thead>
<tr>
<th></th>
<th>IM fellows</th>
<th>ID fellows</th>
<th>ALL fellows</th>
<th>Junior AP</th>
<th>Senior AP</th>
<th>ALL AP</th>
</tr>
</thead>
<tbody>
<tr>
<td>First consultation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Answering phone calls</td>
<td>5.6 ± 4.5</td>
<td>7.6 ± 5.7</td>
<td>6.4 ± 5.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supervision (min)</td>
<td>20.5 ± 8.7</td>
<td>24.3 ± 7.6</td>
<td>21.9 ± 8.5</td>
<td>17.5 ± 7.4</td>
<td>5.1 ± 4.5</td>
<td>12.5 ± 8.5</td>
</tr>
<tr>
<td>Visiting patients (min)</td>
<td></td>
<td></td>
<td></td>
<td>14.3 ± 12.0</td>
<td>4.1 ± 5.0</td>
<td>9.9 ± 11.9</td>
</tr>
<tr>
<td>Writing reports (min)</td>
<td>37.8 ± 30.2</td>
<td>59.8 ± 8.9</td>
<td>53.8 ± 24.5</td>
<td>9.6 ± 6.1</td>
<td>3.0 ± 3.0</td>
<td>6.7 ± 6.0</td>
</tr>
<tr>
<td>Total (min)</td>
<td>63.8 ± 31.8</td>
<td>61.7 ± 11.7</td>
<td>63.0 ± 26.5</td>
<td>41.5 ± 15.8</td>
<td>13.2 ± 9.7</td>
<td>25.1 ± 15.8</td>
</tr>
<tr>
<td>Fellowship consultations</td>
<td>4.9 ± 3.7</td>
<td>7.6 ± 5.7</td>
<td>6.9 ± 4.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Supervision (min)</td>
<td>18.8 ± 11.6</td>
<td>22.0 ± 9.8</td>
<td>20.1 ± 10.9</td>
<td>15.9 ± 7.4</td>
<td>5.7 ± 4.7</td>
<td>10.9 ± 7.4</td>
</tr>
<tr>
<td>Visiting patients (min)</td>
<td>29.5 ± 9.6</td>
<td>27.1 ± 15.7</td>
<td>21.0 ± 12.2</td>
<td>17.4 ± 10.8</td>
<td>8.1 ± 7.9</td>
<td>13.7 ± 10.7</td>
</tr>
<tr>
<td>Writing reports (min)</td>
<td></td>
<td></td>
<td></td>
<td>5.5 ± 4.8</td>
<td>3.9 ± 2.5</td>
<td>7.1 ± 5.1</td>
</tr>
<tr>
<td>Total (min)</td>
<td>44.2 ± 15.5</td>
<td>61.4 ± 19.2</td>
<td>46.9 ± 17.0</td>
<td>41.1 ± 13.9</td>
<td>16.8 ± 8.5</td>
<td>31.4 ± 14.1</td>
</tr>
</tbody>
</table>

Presenter email address: jonathan.tschopp@gmail.com
Opportunistic screening for sexually-transmitted infections in young men with leukocyturia and negative urine culture in primary care

Itziar Angulo López1, Ander Gonzalez Sarria*,1, Julia Aragón-Díez1, Manuel Imaz Perez1, Leonora Hernandez Ragpa1, Jose Angel Alava Menica1, José Luis Díaz De Tuesta1

1Hospital Universitario Basurto, Bilbao, Spain

Background: Conventional midstream urine culture is usually the only microbiological test ordered at primary care when lower urinary tract symptoms are the chief complaint in young men, despite urinary tract infections (UTI) being rare in this population and sexually transmitted infections (STIs) increasingly prevalent. The aim of this study was to assess the impact of screening for STIs on sexually active men with clinical diagnosis of suspected UTI and sterile pyuria.

Materials/methods: A prospective study was conducted since June 2019 with the midstream urine samples received in the Microbiology Laboratory in men between 15-59 years old. Negative urine cultures with leukocyturia (≥20/µL) detected by flow cytometry (UF-1000i®), with no other clinical condition that could have justified it, were tested with a real-time PCR assay, Anyplex™II STI-7 (Seegene), which detects 7 pathogens: Chlamydia trachomatis, Neisseria gonorrhoeae, Trichomonas vaginalis, Mycoplasma hominis, Mycoplasma genitalium, Ureaplasma urealyticum, and Ureaplasma parvum.

Results: A total of 107 urine samples were subject to PCR, with a positive result in 47 cases (43.9%). Among them, 12 patients (25.5%) had admitted an unprotected sexual intercourse at the first consultation. The microorganisms detected and the variables of study are shown in Table 1.

<table>
<thead>
<tr>
<th>Microorganisms detected by PCR (n=47)</th>
<th>Mean age (years) (SD)</th>
<th>Mean bacteria/µL (SD)</th>
<th>Median Leukocytes/µL (IQR)</th>
<th>Nitrile test (n = 28)</th>
<th>Chief complaint (n = 45)</th>
<th>Sexual preference (n = 30 )</th>
<th>Previous STI (n = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neisseria gonorrhoeae (n = 11) 23.4%</td>
<td>28.2 (6.6)</td>
<td>184 (126.3)</td>
<td>2091.0 (5006.0)</td>
<td>Negative 6 (85.8%) 1 (14.2%)</td>
<td>8 (65.0%) 9 (61.8%) 1 (6.1%)</td>
<td>Heterosexual 5 (62.5%) 3 (37.5%)</td>
<td>2 (16.2%)</td>
</tr>
<tr>
<td>Chlamydia trachomatis (n = 26) 55.3%</td>
<td>32.5 (8.5)</td>
<td>108.9 (60.5)</td>
<td>240.5 (749.3)</td>
<td>Negative 16 (100%)</td>
<td>16 (61.5%) 9 (31.3%) 1 (3.8 %)</td>
<td>Heterosexual 9 (69.2%) 5 (37.5%)</td>
<td>7 (56.9%)</td>
</tr>
<tr>
<td>Mycoplasma genitalium (n = 6) 12.8%</td>
<td>39.8 (9.7)</td>
<td>260.8 (494.8)</td>
<td>111.5 (97.3)</td>
<td>Negative 3 (100%)</td>
<td>3 (100%) 2 (66.7%) 2 (33.3%)</td>
<td>Heterosexual 4 (80.0%) 1 (20.0%)</td>
<td>3 (90.0%)</td>
</tr>
<tr>
<td>Coinfection: N. gonorrhoeae + C. trachomatis (n = 4) 8.5%</td>
<td>19.3 (2.8)</td>
<td>196 (62.7)</td>
<td>3398.0 (8044.0)</td>
<td>Negative 2 (100%)</td>
<td>2 (100%) 1 (50.0%) 1 (25.0%)</td>
<td>Heterosexual 4 (100%) 0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

Table 1. Variables studied for each microorganism detected by PCR. SD: standard deviation; IQR: interquartile range; MSM: men who have sex with men. Antibiotic treatments were optimized in 32 cases (68.1%) because of these results, and 28 (59.6%) were referred to specialized STI centers, where 6 patients (21.4%) had an additional finding: 1 HIV positive serology result to be confirmed, 3 cases of lack of immunity for HVA and 1 for HVB (who were advised to get vaccinated), 1 N. gonorrhoeae proctitis and 1 C. trachomatis detection in a semen sample.

Conclusions:

- Analyzing the midstream urine samples from men with genitourinary tract symptoms and sterile pyuria improves the diagnostic yield for STIs.
- Promotion of a greater awareness of clinical presentation forms of STIs is needed among primary care practitioners.
- An STI diagnosis should involve referring the patient to a specialized center for correct management and systematic screening.

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Abstract 2347

Evaluating the effectiveness of current microbiological tools on time to diagnosis of pulmonary tuberculosis

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Background: Early diagnosis of pulmonary TB is essential for limiting infection transmission and relies heavily on the availability of sputum. However only 65% of patients in England have a recorded sputum result, suggesting a significant proportion are unable to provide sputum, leading to additional investigation and consequent diagnostic delay.

Leicester City is a UK TB hotspot (incidence 40 per 100,000) providing a rapid access pathway for accelerated assessment of pulmonary TB suspects. The pathway incorporates clinico-radiological triage with systematic microbiological investigation of respiratory tract samples using Xpert MTB/RIF (Xpert) and mycobacterial culture (MGIT). Our objective was to evaluate factors influencing time from referral and symptoms onset to microbiological diagnosis and start of treatment respectively.

Materials/methods: A retrospective cohort study of 290 consecutive incident pulmonary TB patients diagnosed and treated at Leicester between 2016-2018. Data was collected from the University Hospitals of Leicester health informatics warehouse.

Results:

- 113 patients [41.8%] required invasive respiratory tract sampling with bronchoscopy due to either no or inadequate sputum [89 and 24 patients] expectorated.
- Compared with sputum producers, the requirement for bronchoscopy was associated with a significant delay (mean difference [95% CI]) in time to microbiological diagnosis from referral [25.1 (13.7 – 36.5) days] and time to treatment from symptom onset [28.8 (8.9 – 48.6) days].
- Concomitant Xpert and mycobacterial culture was performed on respiratory tract samples from 170 [59%] patients. The culture confirmation rate was 80% and increased to 84% with combined Xpert testing. A positive Xpert result was associated with shorter time to treatment from symptom onset [94 days], compared with not performing the test [106 days].

Conclusions: The predominant delay in pulmonary TB diagnosis occurs prior to accessing healthcare review. However, in a high-income setting with optimized referral and diagnostic pathways, time to microbiological diagnosis and treatment is significantly reliant upon sputum expectoration. However, this is achievable in less than 60% of patients of our population. Xpert testing provides a modest improvement in microbiological confirmation and time to treatment commencement but significant improvements will require novel non-invasive diagnostic tools, targeting universally accessible tissue.

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Co-trimoxazole resistance in Stenotrophomonas maltophilia

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Background: Stenotrophomonas maltophilia (Sm) is an environmental bacterium naturally resistant to many broad-spectrum antibiotics (including all carbapenems). The drug of choice for treating Sm is Co-trimoxazole. We aimed to evaluate the amount of Co-trimoxazole resistance in our clinical setting, further we aimed at elucidating whether the prevalence of Co-trimoxazole resistant strains of SM has increased over time.

Materials/methods: We extracted all samples with Sm from our local clinical database for our tertiary referral hospital, from Jan 1 2002 – Oct 1 2019. Patients were divided into time-groups based on the first available Sm isolate (2002-2005, 2005-2010, 2010-2014 and 2014-2019). We calculated time to Co-trimoxazole resistant Sm and used Kaplan-Meier plots to compare differences in the different time-periods.

Results: We identified 3,497 patients with a total of 14,482 samples. 2,740 (18.9%) samples were obtained from cystic fibrosis patients. Most samples 9,693 (67%) were from the lower respiratory tract, 515 (3.6%) samples were from blood cultures and 4,277 samples were obtained from other sites. 252 (7.2%) individuals and 552 (3.8%) samples contained Co-trimoxazole resistant SM strains. 6 individuals (2.2%) had positive blood cultures containing resistant Sm strains. When we compared different time periods, we did not find any statistically significant differences in the rates of resistant Sm strains.

Conclusions: In this large series of Sm we found that Co-trimoxazole resistance rate was generally low. For invasive Sm infections, we found only 2.2% resistant strains in blood cultures. We did not find evidence to suggest substantial changes of resistance over time.

Time to resistant strain

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Abstract 2352

Molecular epidemiology of carbapenem-resistant Acinetobacter baumannii in the United States, 2013–2017

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Background: Acinetobacter baumannii has emerged as an important healthcare-associated pathogen worldwide. Carbapenem-resistant A. baumannii (CRAB) are increasingly common and found to be associated with epidemic global clones and different classes of carbapenemase genes. Here we describe the molecular epidemiology of CRAB collected through public health efforts in the United States.

Materials/methods: From 2013-2017, CDC received CRAB isolates from sixteen sites via reference testing and surveillance activities. Testing was performed to assess antimicrobial susceptibility profiles and identify carbapenemase genes. Whole genome sequencing (WGS; Illumina MiSeq® System) was performed on select, nonredundant isolates to determine sequence type and identify antibiotic resistance genes.

Results: Of 94 isolates characterized by WGS, nearly all (n=92, 98%) carried an OXA-type carbapenemase gene, among which we identified a total of 20 blaOXA variants. While 90 isolates (96%) had an intrinsic blaOXA51-like gene, 67 isolates (71%) harbored an additional acquired blaOXA gene, most commonly blaOXA-23 (n=45). Compared to intrinsic oxacillinases, acquired OXA-type carbapenemases were associated with a higher prevalence of imipenem nonsusceptibility (70 vs 100%) and higher median imipenem MIC (8 vs 64ug/ml). Isolates harboring acquired blaOXA carbapenemase genes were also more likely to be resistant to other drug classes including aminoglycosides, cephalosporins, and polymyxins.

Twenty-nine STs were identified using the Oxford MLST scheme, with the majority of isolates (n=59, 63%) representing STs belonging to the international clonal complex 92 (CC92). Among these, ST208 (n=21) and ST281 (n=20) were the most common and each displayed unique epidemiology. ST208 was widely distributed and associated with six different acquired blaOXA variants. Conversely, ST281 isolates were largely restricted to the Mid-Atlantic region (n=15, 75%) and only found associated with the blaOXA-23 variant.

Conclusions: Taken together these data illustrate the wide distribution of CC92 in the United States and high prevalence of acquired blaOXA carbapenemase genes among CRAB. Previous work has identified ST281 as an emerging ST that is rapidly replacing STs from established clades such as ST208, the predominant ST in the United States. Our data provide a snapshot of the dynamic epidemiology of CRAB and identify ST-antibiotic resistance gene combinations that may warrant further attention through detection and containment activities.

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Abstract 2359

**Tedizolid activity against a global collection of Gram-positive bacterial isolates causing bone and joint infections (2017-2019)**

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Abstract third-party references: This study was performed by JMI Laboratories and supported by Merck, which included funding for services related to preparing this abstract.

**Background:** Despite the advances in current health care, bone and joint infections (BJI) remain difficult-to-treat infections that frequently involve prolonged systemic antibiotic use. Tedizolid has been considered as a candidate for therapy in adults and children with BJI. This study assessed the in vitro activity of tedizolid and comparator agents against a contemporary global collection of Gram-positive isolates causing BJI.

**Materials/methods:** A total of 523 Gram-positive cocci, including 379 S. aureus (SA), 81 β-hemolytic streptococci (BHS) isolates, 25 CoNS, 20 E. faecalis and 11 Viridans group streptococci (VGS), were collected from patients with BJI from the United States (USA; n=224 isolates), Europe (EUR; n=200), Asia-Pacific (n=47), and Latin America (n=52) during 2017–2019. Bacterial identification was confirmed by MALDI-TOF MS and MIC obtained by broth microdilution method according to current CLSI and EUCAST guidelines and interpretation criteria.

**Results:** Tedizolid was active against S. aureus isolates (MIC<sub>50</sub>/MIC<sub>90</sub>, 0.25/0.25 mg/L) and retained potent in vitro activity against methicillin-resistant S. aureus (MRSA; MIC<sub>50</sub>/MIC<sub>90</sub>, 0.12/0.25 mg/L). Tedizolid, linezolid, vancomycin and daptomycin inhibited all S. aureus isolates at the respective susceptible breakpoints (Table). MRSA rates varied among regions (17.2%-35.1%); however, based on MIC<sub>90</sub>, tedizolid showed consistent potencies (MIC<sub>90</sub>, 0.25-0.5 mg/L), regardless of geographic region. Tedizolid (MIC<sub>50</sub>/MIC<sub>90</sub>, 0.25/0.5 mg/L) was also active against E. faecalis isolates, as well as linezolid (100% susceptible) and vancomycin (100% susceptible). All BHS isolates were inhibited at ≤0.5 mg/L of tedizolid (MIC<sub>50</sub>/MIC<sub>90</sub>, 0.25/0.25 mg/L; 100% susceptible). Linezolid, vancomycin, and daptomycin were also active against BHS. Among the entire collection, only 1 CoNS isolate [S. cohnii] was resistant to linezolid (MIC, 8 mg/L) and/or tedizolid (MIC, >1 mg/L). Tedizolid and vancomycin inhibited all VGS isolates at the respective susceptible breakpoints. No differences on tedizolid activity against BHS or VGS were observed among geographic regions.

**Conclusions:** Tedizolid demonstrated potent in vitro activity against this worldwide collection of contemporaneous Gram-positive isolates causing BJI. High susceptibility rates were observed by tedizolid and comparators agents against the most frequent organisms and organism groups, including MRSA. These findings support the clinical development of tedizolid for treating BJI infections caused by Gram-positive pathogens.

<table>
<thead>
<tr>
<th>Organism (no. tested)</th>
<th>MIC&lt;sub&gt;50&lt;/sub&gt;/MIC&lt;sub&gt;90&lt;/sub&gt; in mg/L (%S, EUCAST)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenotype</td>
<td>Tedizolid</td>
</tr>
<tr>
<td>MSSA (276)</td>
<td>0.25/0.25 (100)</td>
</tr>
<tr>
<td>MRSA (103)</td>
<td>0.12/0.25 (100)</td>
</tr>
<tr>
<td>CoNS (25)</td>
<td>0.12/0.25 (98)</td>
</tr>
<tr>
<td>E. faecalis (20)</td>
<td>0.25/0.5 (-)</td>
</tr>
<tr>
<td>BHS (81)</td>
<td>0.25/0.25 (100)</td>
</tr>
<tr>
<td>VGS (11)</td>
<td>0.25/0.25 (100)</td>
</tr>
</tbody>
</table>

S. susceptible; MRSA, methicillin-resistant S. aureus; BHS = β-haemolytic streptococci; VGS = viridans group streptococci * breakpoint not available.

* Tedizolid breakpoint for S. anginosus group used for VGS

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**Abstract 2360**

**In vitro activities of aztreonam-avibactam and comparator agents against carbapenemase-producing Enterobacterales collected during the ATLAS global surveillance programme 2015-2018**

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**Background:** Carbapenemase-producing Enterobacterales (CPE) cause significant morbidity and mortality. Aztreonam-avibactam is a β-lactam/β-lactamase inhibitor combination with activity against both serine carbapenemases and metallo-β-lactamases (MBL) in development for treatment of infections caused by CPE. We evaluated the *in vitro* activity of aztreonam-avibactam against CPE collected in 2015-2018 through the ATLAS global surveillance program.

**Materials/methods:** Non-duplicate, clinically significant isolates of Enterobacteriaceae, Proteaceae and *Serratia* spp. were collected from 237 medical centres in 51 countries in Europe, Latin America, Asia/Pacific (excluding China and India), and the Middle East/Africa region. Susceptibility testing was performed by CLSI broth microdilution and results were interpreted using EUCAST 2019 breakpoints. Avibactam was tested at a fixed concentration of 4 mg/L. All organisms with meropenem MIC >1 mg/L and *Escherichia coli*, *Klebsiella* spp. and *Proteus mirabilis* phenotypically positive for ESBL activity (2015) or with aztreonam or ceftazidime MIC >1 mg/L (2016-2018) were screened for the presence of β-lactamase genes.

**Results:** A total of 2290 isolates (1733 *Klebsiella pneumoniae*, 181 *Enterobacter cloacae*, 124 *E. coli*, and 252 isolates of 17 other species) were CPE. Of these, 69.6% (n=1594) carried serine carbapenemases (KPC, OXA-48-like, GES), 26.6% (n=610) carried MBLs (NDM, VIM, IMP), and 3.8% (n=86) carried both serine- and metallo-carbapenemases (Table). Aztreonam-avibactam tested with MIC₉₀s of 0.5 mg/L against the overall collection of CPE, CP-*K. pneumoniae*, and subsets of KPC-positive, OXA-48-like-positive and MBL-positive isolates. The MIC₉₀ was 4 mg/L against the subset of CP-*E. coli*, which included isolates harboring a YRIX insertion in PBP3. 99.9% (2288/2290) of CPE were inhibited by ≤8 mg/L of aztreonam-avibactam. The tested comparators showed reduced activity against subsets of CP organisms stratified by carbapenemase type and by species except for GES-positive isolates (100% susceptible to all agents but aztreonam) and CP-*E. cloacae* (98.9% susceptible to colistin) and CP-*E. coli* (99.2% susceptible to colistin).

**Conclusions:** Based on MIC₉₀ values, aztreonam-avibactam demonstrated potent *in vitro* activity against CPE, including MBL-positive isolates and those carrying multiple carbapenemases, and retained activity against isolates resistant to the last-resort agent colistin. The promising *in vitro* activity of aztreonam-avibactam warrants further development of this combination for use against infections caused by CPE.

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**Abstract 2362**

**Acute cystitis symptom score questionnaire for patient-reported outcome measure in female patients with acute uncomplicated cystitis: clinical validation as part of a phase III trial comparing antibiotic versus non-antibiotic therapy**

Jakhongir Alidjanov¹, Andre Overesch², Dimitri Abramov-Sommariva³, Martina Höller², Hubert Steindl², Florian Wagenlehner¹, Kurt G. Naber*³

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Abstract third-party references: The study was supported by Bionorica SE, Neumarkt, Germany

**Background:** Since non-antibiotic therapy has become an alternative approach to treat uncomplicated acute cystitis (AC) in women, clinical criteria for diagnostics and patient-reported outcome measure (PROM) become more important as main study objectives. The Acute Cystitis Symptom Score (ACSS) was developed as a standardized self-reporting diagnostic questionnaire, which has proven its efficacy in the clinical diagnosis of AC in women and in monitoring possible changes after therapy.

**Materials/methods:** In a double-blind, randomized, multicentre, clinical Phase-3 trial including a total of 657 patients with AC in 51 centres in Europe, 325 women with AC were treated with the phytodrug Canephron®N (BNO-1045) for 7 days and 332 patients with a single oral 3g-dose of fosfomycin trometamol (FT). The main aim of the study was to compare the number of patients using any additional antibiotics. The ACSS used in this study was evaluated as a PROM in this post-hoc analysis.

**Results:** Between Days 1 and 38, 238 (83.5%) patients in the BNO-1045 group and 272 (89.8%) patients in the FT group received no additional antibiotic. At a 15% non-inferiority margin, BNO-1045 was non-inferior to FT in treating AC [non-AB rate difference: –6.26%; 95%CI –11.99 to –0.53%; 2-sided p = 0.0014]. The mean sum-scores of the six typical symptoms (ACSS typical domain) were comparable between the groups on Day 1 (BNO 1045: 10.2; FT: 10.1), and decreased at Day 4 (BNO-1045: 5.1, FT: 4.5), to the end of treatment at Day 8 (BNO 1045: 2.1; FT: 2.1) and to late follow-up at Day 38 (BNO-1045: 0.8; FT: 0.9). Predefined thresholds using the scoring system of the ACSS could be established and validated to define „clinical cure“.

**Conclusions:** In this post hoc evaluation, it could be demonstrated that the ACSS questionnaire, now translated and validated in several languages [www.acss.world], has the potential to be used as a suitable instrument for diagnostics and PROM in well-designed clinical studies investigating different treatment modalities of AC.

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A single dose of gentamicin in patients with sepsis in the emergency department is safe with regard to renal function

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Background: Aminoglycosides are frequently used in the empirical treatment of sepsis. Since aminoglycosides can cause acute kidney injury (AKI), it is questioned whether it is safe to administer aminoglycosides in patients with sepsis visiting the emergency department (ED). With increasing antibiotic resistance the options for appropriate empirical antibiotic therapy are becoming fewer. Therefore, our aim was to evaluate the renal safety of aminoglycosides.

Materials/methods: We retrospectively enrolled 1573 patients with sepsis in the ED in three hospitals. Local antibiotic guidelines recommended gentamicin as part of empirical therapy in one hospital, whereas the other two hospitals did not. Patients with and without gentamicin were compared. Subsequently, the effect of gentamicin and other potential risk factors on the incidence of AKI was evaluated. AKI was defined according to the KDIGO-criteria.

Results: Of 1573 patients, 32.9% received a single-dose of gentamicin. At admission, 32.6% of the gentamicin, and 23.3% of the non-gentamicin patients had AKI (p<0.001). After admission, AKI occurred in 12.4% of the gentamicin, and in 9.1% of the control group (p=0.06). Multivariate analysis showed that shock (OR 2.72 [95%CI, 1.31-5.67]), diabetes mellitus (OR 1.49 [95%CI, 1.00-2.23]), and higher baseline (i.e. pre-admission) serum creatinine (OR 1.007 per point increase [95%CI, 1.005-1.009]) were associated with the development of AKI after admission, but not gentamicin (OR 1.29 [95%CI, 0.89-1.86]). Persistent AKI was rare (6.6% in the gentamicin, compared to 3.3% in the non-gentamicin group, p=0.09). No differences were seen in the median serum creatinine concentrations over a 14-day period between those with, and without gentamicin and AKI on admission (p=0.85) (Figure).

Conclusions: Our study shows that a single-dose of gentamicin in patients with sepsis in the ED is safe with regard to renal function, as gentamicin was not associated with AKI after admission. The development of AKI after admission was associated with shock, diabetes mellitus, and a higher baseline creatinine.

Median serum creatinine levels [IQR] during 14 days follow up.
Baseline: most recent creatinine value prior to admission; Admission: creatinine value on admission; 1-2 days: 1-2 days after admission; 3-7 days: 3-7 days after admission; 8-14 days: 8-14 days after admission.

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In vitro activities of ceftaroline and comparator agents against bacterial pathogens frequently causing community-acquired respiratory tract infections in patients from Latin America: ATLAS surveillance programme 2016-2018

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Background: Community-acquired bacterial pneumonia (CABP) is a frequent cause of patient morbidity and mortality. *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* are frequent etiologic agents of CABP. Ceftaroline fosamil is a parenteral cephem approved for treatment of patients with CABP caused by *S. pneumoniae* (including cases with concurrent bacteremia), methicillin-susceptible *Staphylococcus aureus* (MSSA), *H. influenzae*, and some species of Enterobacteriales. Published data reporting the in vitro activity of ceftaroline against current isolates of bacterial pathogens causing community-acquired respiratory tract infections in patients in Latin America are limited.

Materials/methods: Clinically relevant, non-duplicate, isolates cultured from respiratory specimens by clinical laboratories in 9 countries in Latin America in 2016-2018 were collected by the ATLAS Surveillance Program central laboratory (IHMA, Inc., Schaumburg, IL, USA). In total, 436 isolates of *S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, MSSA, and methicillin-resistant *S. aureus* (MRSA) were tested. The isolates (n) originated from Argentina (73), Brazil (79), Chile (116), Colombia (23), Costa Rica (4), Dominican Republic (15), Guatemala (21), Mexico (79), and Venezuela (26). Ceftaroline and comparator agent MICs were determined by CLSI broth microdilution methodology. MICs were interpreted using current EUCAST MIC breakpoints.

Results: Ceftaroline and comparator agent in vitro activities are summarized below.

<table>
<thead>
<tr>
<th>Bacterial Pathogen</th>
<th>% Susceptible / MIC&lt;sub&gt;50&lt;/sub&gt; (mg/L) / (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CPT&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><em>H. influenzae</em></td>
<td>95.7/0.03/(117)</td>
</tr>
<tr>
<td><em>M. catarrhalis</em></td>
<td>NA/0.25/(21)</td>
</tr>
<tr>
<td>MSSA</td>
<td>100/0.25/(127)</td>
</tr>
<tr>
<td>MRSA</td>
<td>80.9/2/(68)</td>
</tr>
<tr>
<td>PS <em>S. pneumoniae</em></td>
<td>100/0.015/(48)</td>
</tr>
<tr>
<td>PNS <em>S. pneumoniae</em></td>
<td>100/0.015/(55)</td>
</tr>
</tbody>
</table>

PS, penicillin-susceptible; PNS, penicillin-nonsusceptible; NA, MIC breakpoints not available; CPT, ceftaroline; CRO, ceftiraxone; LVX, levofloxacin; AMC, amoxicillin-clavulanate; ERY, erythromycin.

* Ceftaroline MIC range for *M. catarrhalis* was 0.06-0.25 mg/L.

Conclusions: All isolates of *S. pneumoniae* and MSSA were susceptible to ceftaroline, including penicillin-nonsusceptible *S. pneumoniae*. 13 MRSA were ceftaroline-resistant (12 isolates with MICs of 2 mg/L; 1 isolate with an MIC of 4 mg/L); 9 of the 13 isolates were from Chile. 95.7% of *H. influenzae* isolates were susceptible to ceftaroline. Ceftaroline demonstrated potent in vitro activity against current pathogens associated with CABP in patients in Latin America.

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Abstract 2365

**Treatment of Erythema migrans with doxycycline for 7 days versus 14 days: a non-inferiority randomised open-label study**

Maša Velušček¹, Anja Gomišček², Rok Blagus³, Tjasa Cerar Kišek⁴, Katarina Boršič⁵, Mirijam Nahtigal Klevišar⁶, Eva Ruzic-Sabljic⁷, Dasa Stupica*⁶

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**Background:** With awareness of increasing bacterial resistance globally, it is important to re-evaluate the duration of therapies needed for particular infections. Doxycycline for 10 days is the shortest treatment duration recommended for adult patients with erythema migrans, but shorter regimens have not been assessed.

**Materials/methods:** In an open-label randomized clinical trial, performed at the University Medical Centre Ljubljana, Slovenia, the efficacies of 7-day versus 14-day of oral doxycycline therapy were compared on a noninferiority premise in adult patients with solitary erythema migrans. The efficacy of treatment was assessed based on clinical and microbiologic parameters, as assessed at 14 days and at 2, 6, and 12 months after enrolment.

**Results:** Out of 300 randomized patients, 147 patients (50.5%) completed treatment with doxycycline for 7 days, and 144 patients (49.5%) received doxycycline for 14 days. Patients in the two treatment groups did not differ regarding basic demographic, clinical, and microbiologic characteristics at enrolment. The proportion of patients with incomplete response decreased during follow-up, and was comparable between 7-day and 14-day treatment groups [14 days: 25/144 [17.4%] vs 29/141 [20.6%]; P=0.295; 2 months: 27/136 [19.9%] vs 23/132 [17.4%]; P=0.638; 6 months: 15/118 [12.7%] vs 14/124 [11.3%]; P=0.557]. At the 12-month visit, 8/101 [7.9%] patients in the 7-day vs 9/102 [8.8%] patients in the 14-day group showed incomplete response [difference -0.9 percentage points; 1-sided 95% CI, –1 to 0.06 percentage points; P=0.5]. None of the patients developed new objective manifestations of Lyme borreliosis during follow-up and none had positive skin re-biopsy culture result for borreliae.

**Conclusions:** The 7-day regimen of oral doxycycline was noninferior to the 14-day regimen for treating adult European patients with solitary erythema migrans. At 12 months post-enrolment, only a minority of patients had incomplete response, manifested as post-Lyme borreliosis symptoms.

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Using T2Bx and rapid AST with blood culture pre-sampling for combined ID and AST before blood culture positivity

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Abstract

Background: Rapid diagnostic methods are important for antibiotic stewardship and for improving quality of care in severe disease like sepsis. New culture-independent methods for identification (ID) within hours directly from blood are becoming available, such as T2Bacteria – however, blood cultures (BC) remain necessary for bacteria isolation and follow-up analysis such as antibiotic susceptibility testing (AST). QuickMIC is a rapid diagnostic tool under development, capable of AST at very low bacterial concentrations. Here we evaluate a combined rapid ID+AST diagnostic workflow using T2Bacteria and the QuickMIC AST system.

Materials/methods: Two diagnostic workflows were simulated, “standard” using blood culture followed by MALDI-TOF MS (ID) and AST by broth microdilution (BMD); or “rapid” using T2Bacteria followed by AST using QuickMIC. Escherichia coli (n=5), Klebsiella pneumoniae (n=9), Acinetobacter baumannii (n=6), Pseudomonas aeruginosa (n=5), and Staphylococcus aureus (n=13) clinical strains were inoculated in horse blood and BC started simultaneously with T2Bacteria. After T2Bacteria positive identification, the BC bottle was presampled for rapid AST. After BC positivity, samples were subcultured and MSID was performed. Specificity, sensitivity and turnaround time were compared between the two workflows, and QuickMIC results were compared to BMD with regards to categorical agreement.

Results: The rapid diagnostic workflow was significantly faster than the standard workflow (9.5±2.5h vs. 52.9±0.4h, p<0.001), and significantly faster for Gram-negative (GN) compared to Gram-positive (GP) bacteria (7.4±0.6h vs 12.2±0.4h, p<0.001). For 68% of the samples, the rapid ID+AST result was available before BC positivity (86% for Gram-negatives, 45% for Gram-positives). For 100% of the samples, rapid ID+AST was available before MSID. Diagnostic sensitivity/specificity at the species level were 94.7%/99.5% and 97.4%/100% for T2ID and MSID, respectively. QuickMIC (GN/GP panel) results took on average 167±15 min, and categorical agreement to BMD was 82% (GN) and 83% (GP).

Conclusions: We conclude that QuickMIC has the potential to be a suitable companion diagnostic to T2Bacteria for delivering rapid ID+AST results. The value of same-shift results for improved antibiotic stewardship and quality of care is high, and further evaluation beyond this pilot study will be conducted.

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Abstract 2367

European regional analysis of the in vitro activities of ceftaroline and comparator agents against bacterial pathogens frequently isolated from patients with community-acquired respiratory tract infections: ATLAS surveillance programme 2015-2018

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1University of Manitoba, Winnipeg, Canada, 2IHMA, Schaumburg, United States, 3Pfizer, Inc., Groton, United States

Background: Regional variation in resistance to many antimicrobial agents is widely appreciated. Ceftaroline fosamil, the prodrug of ceftaroline, is a parenteral cephem approved by both EMEA and the US FDA for the treatment of patients with community-acquired bacterial pneumonia caused by susceptible isolates of Staphylococcus aureus, Streptococcus pneumoniae, and Haemophilus influenzae as well as susceptible isolates of Escherichia coli and Klebsiella spp. The current analysis intended to determine whether regional variation in susceptibility to ceftaroline existed amongst its indicated respiratory pathogens in Europe.

Materials/methods: From 2015 to 2018, 118 clinical laboratories in Europe submitted 4,457 bacterial isolates cultured from respiratory samples of patients diagnosed with community-acquired respiratory tract infections to IHMA, Inc., (Schaumburg, IL, USA), the coordinating laboratory for the ATLAS (Antimicrobial Testing Leadership and Surveillance) program. At IHMA the identities of all isolates were confirmed using MALDI-TOF mass spectrometry and antimicrobial susceptibility testing was performed following standardized CLSI broth microdilution methodology [M07, 2018; M100, 2019]. Percent susceptibilities were determined using current EUCAST MIC breakpoints (2019, v. 9.0) where available.

Results: The in vitro activity of ceftaroline against respiratory pathogens is summarized below.

<table>
<thead>
<tr>
<th>Bacterial Pathogen*</th>
<th>Ceftaroline % Susceptible/MIC90**(No. of Isolates Tested)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Europe (n=4,457)</td>
</tr>
<tr>
<td>Streptococcus pneumoniae, PSSP</td>
<td>100/0.015(1,255)</td>
</tr>
<tr>
<td>Streptococcus pneumoniae, PNSSP</td>
<td>96.4/0.25(496)</td>
</tr>
<tr>
<td>Staphylococcus aureus, MSSA</td>
<td>100/0.25(823)</td>
</tr>
<tr>
<td>Staphylococcus aureus, MRSA</td>
<td>94.8/1/(767)</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>97.5/0.03(831)</td>
</tr>
<tr>
<td>Moraxella catarrhalis</td>
<td>NA/0.25(285)</td>
</tr>
</tbody>
</table>

* PSSP, penicillin-susceptible S. pneumoniae; PNSSP, penicillin-nonsusceptible S. pneumoniae; MSSA, methicillin-susceptible S. aureus; MRSA, methicillin-resistant S. aureus; NA, MIC breakpoints not available

** mg/L

*** NW Europe, Northern and Western Europe

**** CE Europe, Central and Eastern Europe

Conclusions: Ceftaroline demonstrated potent in vitro activity against a 2015-2018 European collection of bacterial pathogens commonly associated with community-acquired respiratory tract infections. All isolates of MSSA and PSSP were susceptible to ceftaroline; overall, 94.8% of MRSA and 98.4% of PNSSP were susceptible to ceftaroline. A statistically significant (P<0.5) difference between NW Europe and CE Europe in vitro susceptibility to ceftaroline was only identified for MRSA [7.9% difference]. PNSSP susceptibility to ceftaroline only differed by 1% for isolates from NW Europe and CE Europe.

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Abstract 2368

**Prolonged versus intermittent infusion of beta-lactam antibiotics: a systematic review and meta-regression of bacterial killing in preclinical infection models**

Sofie Dhaese*1,2, Aaron Heffernan1,4, David Liu4, Mohd Hafiz Abdul Aziz4, Veronique Stove2, Vincent Tam5, Jeffrey Lipman4,6,7, Jason Roberts4,6,7, Jan De Waele2

1AZ Sint-Jan Brugge, Brugge, Belgium, 2Ghent University Hospital, Ghent, Belgium, 3Griffith University, Brisbane, Australia, 4University of Queensland, Brisbane, Australia, 5University of Houston, Houston, United States, 6Royal Brisbane and Women’s Hospital, Brisbane, Australia, 7Nîmes University Hospital, Nîmes, France

**Background:** Administering beta-lactam antibiotics using prolonged infusions in critically ill patients have been proposed to improve efficacy but is mainly based upon preclinical evidence. Preclinical data on this topic have not been systematically reviewed before. Our objectives were to describe the pharmacokinetic/pharmacodynamic (PK/PD) indices and targets reported in preclinical models and to compare the bactericidal efficacy of intermittent and prolonged beta-lactam infusions.

**Materials/methods:** The Medline and EMBASE databases were searched from their inception until the 15th of April 2019. To compare the bactericidal action of beta-lactam antibiotics across different modes of infusion, the reported PK/PD outcomes of individual studies were recomputed relative to the area-under-the-curve of free drug to MIC ratio, ($fAUC_{0-24}/MIC$) for an equal reduction in CFU/mL. An $E_{max}$ model was then fitted and the mean and standard error (SE) $fAUC_{0-24}$ for a 1 log10 reduction in CFU/mL was predicted. A linear mixed effects meta-regression was performed to evaluate the impact of the antibiotic exposure (expressed as $fAUC_{0-24}$/MIC), the beta-lactam class, the initial inoculum, the host immune system, the gram-stain, and infusion-type on the reduction in the number of bacteria after 24 h of antibiotic treatment. The study protocol was published online with the PROSPERO (CRD42018085202) and CAMARADES database.

**Results:** Overall, 32 articles were included for review, of which 7 provided enough data for the simulation of a stable $E_{max}$ model and were included in the meta-regression. For maximal bactericidal activity, intermittent experiments reported a PK/PD target of 40%-70%$f_{MIC}$ while continuous experiments reported a steady-state concentration to MIC ratio ($C_{ss}$/MIC) of 4-8. The results of the metaregression indicated that the adjusted effect of a prolonged infusion on bacterial killing was small [coefficient and 95% CI of 0.81 [-0.47;2.10]].

**Conclusions:** Beta-lactam antibiotic PK/PD indices and targets are different for intermittent and continuous infusion. The additional effect of a prolonged infusion for enhancing bacterial killing on bactericidal action could not convincingly be demonstrated.

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Abstract 2369

Turnaround time for pathogen identification and antimicrobial susceptibility testing of bronchoalveolar lavage specimens in U.S. acute care hospitals

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Background: Identification of respiratory pathogens and antimicrobial susceptibility testing (AST) results are fundamental to the diagnosis and management of patients hospitalized with pneumonia. Here, we examine the turnaround time (TAT) for reporting of results of the most prevalent bacterial pathogens among bronchoalveolar lavage (BAL) from patients hospitalized with suspected or confirmed pneumonia.

Materials/methods: Using the Premier Healthcare Database, a comprehensive database of U.S. hospitals, BAL samples from in-patient encounters with microbiology culture data were identified. BALs were excluded if they were from patients age < 18 years old, diagnosis of cystic fibrosis, time to organism identification > 7 days, and > 3 pathogens. Time from collection to reporting of gram stain, first organism identification (ID), and first organism AST were summarized descriptively.

Results: From June 2015 through May 2018, a total of 43,129 BALs met all study criteria, of which 28.6% were no growth, 43% were normal respiratory flora (including yeast), and 0.7% molds. Bacterial pathogens were recovered from 11,956 (27.7%) BALs. S. aureus and P. aeruginosa were recovered in 3,391 (7.9%) and 2,184 (5.1%) of all BALs, respectively and were the most common bacterial pathogens, followed by Haemophilus spp. (2.6%), Klebsiella spp. (2.1%), S. pneumoniae (1.8%), E. coli (1.6%), and Enterobacter spp. (1.3%). Median (interquartile range) TAT from specimen collection for bacterial pathogens were 10.6 (4.1-20.4), 41.0 (22.6-52.9), and 63.8 (46.5-72.4) hours for Gram stain, ID, and AST respectively. Median TAT for major respiratory pathogens is shown in Figure 1, ranging from 32.0 (S. aureus) to 47.3 (S. pneumoniae) hours for ID and from 47.9 (Klebsiella spp.) to 72.9 (S. pneumoniae) hours for AST. ID for BALs with bacterial pathogens was reported during the day shift (7:00 A.M. to 2:59 P.M.) for 75% of samples and 16% during the evening (3:00 P.M. to 10:59 P.M.). Similarly, AST was reported during the day shift for 74% of samples and 6% during the evening.

Conclusions: The average BAL TAT from specimen collection to ID and AST were approximately 40 and 65 hours, respectively. Most ID/AST results are reported during the day shift. BALs represent an area of interest for improved TAT.

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Abstract 2371

**In vitro activity of ceftaroline and comparator agents against bacterial pathogens collected from patients with skin and soft tissue infections in Europe: a regional analysis of results from the ATLAS surveillance programme 2015-2018**

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1University of Manitoba, Winnipeg, Canada; 2IHMA, Schaumburg, United States; 3Pfizer, Inc., Groton, United States

**Background:** Ceftaroline fosamil, the prodrug of ceftaroline, is a parenteral cephem approved by the EMA for the treatment of adults and children aged ≥2 months with complicated skin and soft tissue infections (SSTIs) caused by susceptible isolates of *Staphylococcus aureus* [including methicillin-resistant isolates], β-hemolytic streptococci, *Streptococcus anginosus* group, and members of Enterobacterales. The current analysis intended to determine whether regional variation in susceptibility to ceftaroline existed amongst its indicated SSTI pathogens in Europe.

**Materials/methods:** From 2015 to 2018 the ATLAS (Antimicrobial Testing Leadership and Surveillance) program received 17,445 bacterial isolates (130 laboratories; 25 countries) from samples of European patients diagnosed with SSTIs. All isolates were transported to IHMA (Schaumburg, IL, USA) where their identities were confirmed using MALDI-TOF mass spectrometry and CLSI broth microdilution antimicrobial susceptibility testing performed against ceftaroline and comparator agents. MICs were interpreted using EUCAST breakpoints (2019, v. 9.0) where available. *Streptococcus pyogenes* MICs were interpreted using the CLSI M100 breakpoint (≤0.5 mg/L; 29th edition, 2019) because EUCAST does not publish criteria for this organism-antimicrobial agent combination. Phenotypic ESBL screening was performed using the CLSI M100 method.

**Results:** The *in vitro* activity of ceftaroline is summarized below.

<table>
<thead>
<tr>
<th>Bacterial Pathogena</th>
<th>Ceftaroline % Susceptible/MICb (No. of Isolates Tested)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Europe</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em>, MSSA</td>
<td>100/0.25/(4,269)</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em>, MRSA</td>
<td>96.5/1/(4,622)</td>
</tr>
<tr>
<td><em>Streptococcus pyogenes</em></td>
<td>100/0.0006/(1,572)</td>
</tr>
<tr>
<td>Enterobacterales, All isolates</td>
<td>66.6&gt;128/(6,982)</td>
</tr>
<tr>
<td>Enterobacterales, ESBL-negativee</td>
<td>87.7/0.5/(3,198)</td>
</tr>
</tbody>
</table>

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a MSSA, methicillin-susceptible *S. aureus*; MRSA, methicillin-resistant *S. aureus*  
b mg/L  
c NW Europe, North and Western Europe  
d CE Europe, Central and Eastern Europe  
e ESBL-negative Enterobacterales: 1,578 *Escherichia coli*, 763 *Klebsiella pneumoniae*, 361 *Klebsiella oxytoca*, 496 *Proteus mirabilis*

**Conclusions:** All isolates of MSSA were susceptible to ceftaroline as were 96.5% of MRSA isolates. Of the 160 ceftaroline-non-susceptible isolates of MRSA, 154 (96%) had MIC values of 2 mg/L (intermediate). Statistically significant regional differences (P<0.05) in *in vitro* susceptibility of isolates to ceftaroline were observed for MRSA (4.6% higher in NW Europe) and for all isolates of Enterobacterales (7.5% higher in NW Europe). Ceftaroline demonstrated potent *in vitro* activity against a 2015-2018 European collection of bacterial pathogens commonly associated with SSTI.

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Abstract 2372

Using the Antibiotic Spectrum Index (ASI) score to assess antibiotic exposure for patients with Bloodstream Infections (BSI): an analysis of the Accelerate PhenoTest BC Kit (AXDX) IOAS study

Shawn Macvane*, Amira Bhalodi1, Margie Morgan1, Michael Ben-Aderet2, Meghan Madhusudhan2, Johann Kolev2, Ryan Dare3, Eric Rosenbaum3, Kaleb Wolfe3, Bradley Ford4, Dilek Ince4, Patrick Kinn4, Kelly Percival4, Romney Humphries1

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Background: Rapid diagnostic tests (RDTs) that expedite organism identification (ID) and antimicrobial susceptibility testing (AST) allow clinicians to optimize antibiotic therapy sooner. Measuring antibiotic use is essential to assessing an RDT’s effectiveness. The purpose of this study to investigate the impact of fast ID/AST on antibiotic exposure in the early course of BSI.

Materials/methods: Antibiotic exposure received during the initial 96 hours following blood culture positivity from the IOAS study were assessed using the antibiotic spectrum index (ASI). This multicenter, quasi-experimental study compares clinical and antimicrobial stewardship metrics among patients with BSI before and after implementation of AXDX. Total ASI scores for each patient were calculated using the Gerber et al scoring system [with a lower score representing a shorter duration and/or narrower spectrum of antibiotic exposure] and compared between pre-AXDX and post-AXDX groups. To objectively measure antibiotic exposure, the ASI scoring system assign points to each antibiotic based on the antibiotic’s spectrum of activity against clinically relevant pathogens, ranging from a score of 1 to 13. Antibiotic exposure was calculated by multiplying duration of antibiotic exposure (days) by the ASI. All hospitals had antimicrobial stewardship programs throughout the study period.

Results: There were 462 patients with BSI who contributed ASI scores; 238 pre-AXDX, 224 post-AXDX. Patient demographics, comorbidities, and severity of illness were similar between groups, as were distributions of gram-negative (~60%) and gram-positive (~35%) BSI. The most prevalent gram-negative and gram-positive organisms were E. coli and S. aureus, respectively. The average total ASI score for pre-AXDX was 36.7 [SD 16.6] compared to post-AXDX 32.8 [SD 15.0], an overall reduction in ASI of 3.9 [95% Confidence Interval, 1.0 to 6.7; P=0.009] in the post-AXDX group.

Conclusions: In this study, implementation of the AXDX improved antibiotic prescribing among patients with BSI as evident by a reduction in the ASI score of approximately 4 units [equivalent to a day of ceftazidime or clindamycin exposure]. Use of antibiotic spectrum index scoring in patients with BSI can enhance the understanding of the impact of RDTs on antibiotic use, particularly when compared across several institutions that may have differing formulary or antibiotic prescribing practices.

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Can MALDI-TOF MS provide enough discrimination between *Aspergillus fumigatus* sensu stricto and cryptic species?

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1Gregorio Marañón Hospital, Madrid, Spain, 2Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain, 3University Hospital La Paz, Madrid, Spain, 4Complejo Hospitalario Universitario de Albacete, Albacete, Spain, 5Hospital Toledo, Toledo, Spain, 6Hospital Universitario Puerta del Mar, Cádiz, Spain, 7Hospital Virgen de Valme, Sevilla, Spain, 8Hospital General Universitario de Elche, Elche, Spain

**Background:** Accurate species identification is of particular interest in the case of *A. fumigatus* complex given that sibling species show systematically low susceptibility to antifungal agents. MALDI-TOF could be a good alternative for the discrimination of *A. fumigatus* sensu stricto and cryptic species but information about this topic is limited.

**Materials/methods:** Morphologically identified *A. fumigatus* complex isolates (*n*=617) collected in a multicentre surveillance study conducted in Spain were further submitted to antifungal susceptibility testing. Resistant species were also molecularly identified by β-tubulin sequencing. All isolates, cultured on Sabouraud agar plates during 2-3 days, were identified by MALDI-TOF. Conidia were mechanically disrupted by vortexing for 5 min. The sample was centrifuged and the pellet was dried thoroughly and submitted to a standard protein extraction. 1µl of the supernatant was spotted on the MALDI target plate and covered with 1µl of matrix. All isolates were analysed in duplicates.

**Results:** MALDI-TOF accurately identified all *A. fumigatus* sensu stricto isolates (*n*=592) as such, showing score values ≥2.0 in 87.7% of them. The remainder isolates were identified as cryptic species (*n*=25); in 14/25 of them, identification was concordant with β-tubulin sequencing: *A. lentulus* (*n*=10), *Neosartoria pseudofisheri* (*n*=1) and *N. udagawae* (*n*=3) isolates. However, *A. fumigataffinis* (*n*=7) were consistently misidentified as *A. lentulus* [CBS 117267 strain] with score values ≥1.8; the remaining cryptic species isolates – *A. novofumigatus* (*n*=2) and *N. tsurutae* (*n*=2) – were also misidentified as *N. pseudofisheri*. The latter misidentifications could be detected since they were considered as unreliable reports due to their low scores and inconsistency through the top ten identifications provided by MALDI-TOF.

**Conclusions:** MALDI-TOF proved high reliability to discriminate between *A. fumigatus* sensu stricto and cryptic species within the *A. fumigatus* complex. Although the identification of cryptic species was poor (53.8%), particularly for non-*A. lentulus* species, the presence of cryptic species may be suspected by low scores and inconsistent results by MALDI-TOF. Inclusion in the databases and/or peak analysis may improve identification of cryptic species in the near future.

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Abstract 2374

Detection of dengue virus antibodies in febrile patients suspected of malaria attending a health centre in Jos, Nigeria

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1University Of Jos, Jos, Nigeria, 2University Of Jos, Jos, Nigeria, 3Plateau State Virology Research Center, Jos, Nigeria, 4National Veterinary Research Institute, Jos, Nigeria

Background: Despite the public health importance of dengue infections, it is less investigated by clinicians and rarely considered in the differential diagnosis of febrile illnesses in Nigeria. This study was aimed at determining dengue seroprevalence and malaria infection.

Materials/methods: We conducted a cross sectional study on ninety four (94) consenting febrile patients suspected of malaria in Jos. Detection of dengue antibodies (IgG/IgM) were determined by Enzyme Linked Immunosorbent Assay technique. Total RNA and DNA was extracted from patient serum with a commercial kit and quantified to determine concentration and quality of the extraction process. Malaria was detected by the amplification of a conserved region of 18S rRNA gene in a Real Time Polymerase Chain Reaction. Ethical clearance and consent were obtained accordingly before study was conducted on human subjects.

Results: Dengue antibodies were detected in 55.3% (52/94) of the febrile patients. The mean age was 29.9±1.2. Highest dengue seroprevalence of 75% (39/52), 50% (26/52) and 59.6% (31/52) were recorded among females, students and non-users of mosquito nets, respectively.

Only 11.7% (11/94) tested positive for malaria. Dengue and Malaria co-infection recorded 5.3% (5/94). There was a significant difference in the prevalence of dengue and malaria among febrile subjects. No association of dengue infection with gender and use of Insecticide Treated Nets.

Conclusions: The lower prevalence of Malaria as compared to Dengue suggests that, febrile illnesses in our study population are more associated with dengue infection than malaria infection. The co-infection of dengue and malaria reported in this study is of clinical importance, and deserves more investigation. An inclusion of dengue in the differential diagnosis of febrile illnesses should be given consideration. We recommend a continuous surveillance of dengue infection and a determination of the circulating serotypes in this population.

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**Abstract 2375**

**In vitro activity of imipenem/relebactam against Gram-negative organisms collected globally from patients with different infection types: SMART 2018**

Sibylle Lob¹, Krystyna Kazmierczak¹*, Katherine Young³, Mary Motyl¹, Fakhar Siddiqui², Dan Sahm¹

¹IHMA, Schaumburg, United States, ²Merck & Co., Inc., Kenilworth, United States

**Background:** Relbeactam (REL) inhibits class A and C β-lactamases and was approved in the USA in combination with imipenem (IMI) and clastatin for the treatment of complicated intraabdominal and urinary tract infections. We evaluated the activity of IMI/REL against non-Morganellaceae Enterobacterales (NME) and *Pseudomonas aeruginosa* (PA) isolates collected globally as part of the SMART surveillance program from patients with various infection types.

**Materials/methods:** In 2018, 195 clinical laboratories in 54 countries each collected up to 250 consecutive aerobic or facultative gram-negative pathogens from bloodstream (BSI), intraabdominal (IAI), lower respiratory tract (LRTI), and urinary tract infections (UTI). MICs were determined using CLSI broth microdilution and interpreted with EUCAST breakpoints for all agents except IMI/REL for which FDA breakpoints were used. Isolates testing with IMI MIC ≥2 mg/L (NME) or ≥4 mg/L (PA) were screened for β-lactamase genes.

**Results:** The three most common species found among all gram-negative isolates collected from BSI (n=8472), IAI (n=7939), and UTI (n=9424) were *E. coli* (EC; 42.4%, 44.3%, and 51.7%, respectively), *K. pneumoniae* (KP; 18.9%, 15.0%, 16.4%, respectively), and PA (8.7%, 10.5%, 8.0%, respectively). The ranked order was different for LRTI isolates, with PA being most common (27.7%), followed by KP (18.9%) and EC (12.2%). All NME combined composed 77.7%, 78.4%, 51.1%, and 79.7% of gram-negative isolates collected from BSI, IAI, LRTI, and UTI. Among NME, 1.4% [393/28265] were metallo-β-lactamase (MBL)-positive; among *P. aeruginosa*, 4.8% [318/6642] were MBL-positive. Excluding these MBL-positive isolates, the table shows susceptibility to IMI/REL among the three most common species, combined isolate collections, and carbapenem-resistant subsets.

<table>
<thead>
<tr>
<th>Organism/phenotype</th>
<th>BSI</th>
<th>IAI</th>
<th>LRTI</th>
<th>UTI</th>
<th>All sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBL-negative EC</td>
<td>99.8 (3561)</td>
<td>99.8 (3506)</td>
<td>99.6 (1887)</td>
<td>99.7 (4851)</td>
<td>99.7 (13815)</td>
</tr>
<tr>
<td>IMI-resistant EC</td>
<td>95 of 7²</td>
<td>95 of 6²</td>
<td>95 of 2²</td>
<td>95 of 5²</td>
<td>95.0 (20)</td>
</tr>
<tr>
<td>MBL-negative KP</td>
<td>95.0 (1545)</td>
<td>95.5 (1147)</td>
<td>95.0 (2644)</td>
<td>95.6 (1487)</td>
<td>95.2 (7023)</td>
</tr>
<tr>
<td>IMI-resistant KP</td>
<td>67.0 (109)</td>
<td>62.6 (88)</td>
<td>62.6 (235)</td>
<td>55.7 (79)</td>
<td>62.4 (511)</td>
</tr>
<tr>
<td>All MBL-negative NME</td>
<td>98.4 (6498)</td>
<td>98.6 (6149)</td>
<td>98.9 (7823)</td>
<td>98.7 (7462)</td>
<td>98.1 (27387)</td>
</tr>
<tr>
<td>IMI-resistant NME</td>
<td>69.3 (127)</td>
<td>56.6 (104)</td>
<td>60.6 (277)</td>
<td>54.3 (92)</td>
<td>61.3 (669)</td>
</tr>
<tr>
<td>MBL-negative PA</td>
<td>93.5 (706)</td>
<td>93.9 (790)</td>
<td>91.2 (4142)</td>
<td>92.3 (606)</td>
<td>91.9 (6324)</td>
</tr>
<tr>
<td>IMI-resistant PA</td>
<td>68.3 (142)</td>
<td>71.5 (165)</td>
<td>66.5 (1150)</td>
<td>58.7 (126)</td>
<td>68.0 (1583)</td>
</tr>
<tr>
<td>Meropenem-resistant PA</td>
<td>41.1 (73)</td>
<td>48.6 (70)</td>
<td>46.9 (580)</td>
<td>29.2 (72)</td>
<td>44.9 (795)</td>
</tr>
<tr>
<td>All MBL-negative NME and PA</td>
<td>98.0 (7204)</td>
<td>98.1 (6939)</td>
<td>94.9 (11965)</td>
<td>98.2 (8088)</td>
<td>97.0 (34196)</td>
</tr>
<tr>
<td>IMI-resistant NME and PA</td>
<td>68.8 (269)</td>
<td>66.9 (269)</td>
<td>67.0 (1427)</td>
<td>56.9 (218)</td>
<td>66.2 (2183)</td>
</tr>
</tbody>
</table>

²Percent susceptible not shown when n<10: number of susceptible isolates is shown instead

IMI/REL maintained activity of >99%, ≥95%, >96%, and >91% against MBL-negative EC, KP, NME, and PA, respectively, regardless of infection source. IMI/REL maintained susceptibility rates of 54-72% against IMI-resistant isolates across infection sources, with lower rates of 29-49% among meropenem-resistant PA. Among molecularly characterized IMI/REL-susceptible isolates of IMI-resistant MBL-negative NME (n=367) and PA (n=1071), 94.0% and 0.1%, respectively carried KPC, 2.2% and 2.5%, respectively, carried only ESBL±AmpC, and in 3.3% and 97.3%, respectively, no acquired β-lactamases were detected.

**Conclusions:** IMI/REL could provide an important treatment option against antimicrobial-resistant gram-negative pathogens from BSI, IAI, LRTI, and UTI.

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Abstract 2380

An imported case of West Nile virus neuroinvasive disease in the UK
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Background: Since its discovery in 1937, West Nile Virus (WNV) has rapidly emerged as the commonest cause of arboviral neurological disease worldwide. Neuro-invasive disease accounts for less than 1% of presentations but carries a significant 10% mortality rate. There is currently no cure or human vaccine available. There have been large human outbreaks in Europe and North America since the 1990s and the disease is now endemic in the USA with over 24000 cases of neuro-invasive disease since WNV first crossed the Atlantic in 1999.

Materials/methods: An imported case of WNV infection with neuro-invasive disease in the UK is discussed.

Results: A 59 year-old British male, resident in Philadelphia, USA, presented with confusion and fever, four days after arrival to London to visit family. He deteriorated within 48 hours with reduced Glasgow Coma Scale (GCS) to 9/15, neck stiffness and flaccid paralysis requiring intubation and ventilation. Magnetic resonance imaging showed high-signal intensity within the left thalamus and right frontal parietal subcortical region. Cerebrospinal fluid (CSF) showed white cell count 252/mm3 with lymphocytic predominance and extensive tests for infection were negative. A diagnosis of West Nile Virus (WNV) was established with assistance from the Rare Imported Pathogens Laboratory based on strongly positive serum and CSF IgM. Patient had a long period of supportive management, spending a total of three months in the intensive care unit, with slow and limited recovery of function.

Conclusions: There have been increasing reports of imported cases of WNV neuro-invasive infection in the UK. There are limited treatment options with highest efficacy of treatment likely in early phase of the disease, warranting early recognition. There is a clear need for increased awareness, early recognition and further development of treatment and preventative strategies for WNV.

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Abstract 2381

Cost-effectiveness analysis of pneumococcal vaccines in older adults in Argentina
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Background: In 2017, the Argentine Ministry of Health implemented a sequential vaccination scheme with pneumococcal conjugate vaccine 13 serotypes [PCV-13] plus 23 valent pneumococcal capsular polysaccharide vaccine [PPSV23] for adults ≥ 65 years with the purpose of reducing pneumonia burden of disease, complications, and related mortality. Previously in 2012, PCV13 was introduced in the national immunization program for infants in a 2+1 schedule. During 2020, Argentinean NITAG will reassess this recommendation for older adults. Objective: The aim of this study was to perform a cost-effectiveness analysis of the pneumococcal vaccines, PCV-13 plus PPSV23 for adults ≥ 65 years old in Argentina.

Materials/methods: A cost-effective Markov model was developed to quantify the impact of pneumococcal vaccination based on a cohort of 314,690 people ≥ 65 years old. The model considered outpatient pneumonia, hospitalized pneumonia in patients with low risk/at risk of comorbidities, immunsupression [high risk] and invasive pneumococcal disease [IPD]. Updated local cost data, pneumococcal burden of disease and serotype coverage were incorporated into the model. The vaccine efficacy/effectiveness were obtained from a systematic review. With the aim of minimizing the uncertainty, alternative scenarios, univariate and probabilistic sensitivity analyses were developed. The Microsoft Excel program was used to perform the model of effectiveness adjustment by serotypes and drop in effectiveness over the time. Results were described as life years gained; event and cost of illness averted at a time horizon of 15 years.

Results: PCV13 in sequential schedule with PPSV23 vaccine resulted cost saving for Argentina in the main scenario with, 2,308 life years gained, 1,021 outpatient pneumonia, 2,977 hospitalized pneumonia, 1,072 IPD, and 707 related deaths averted, saving USD 4,304,808. Additionally, results were cost saving and highly cost effective in additional scenarios. Conditions associated with pneumonia incidence, lethality and serotype coverage inputs, were some of the most important factors that support these results.

Conclusions: The sequential schedule turned out to be cost saving for Argentina in the population of adults ≥ 65 years old in many of the assumptions.

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Cidofovir-associated nephrotoxicity in adult allogeneic haematopoietic cell transplant recipients
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1Memorial Sloan Kettering Cancer Center, Infectious Diseases service, New York, United States, 2Hospital Clínic de Barcelona, Barcelona, Spain, 3Beth Israel Deaconess Medical Center (BIDMC), Harvard University, Boston, United States, 4Universität zu Köln, Faculty of Medicine and University Hospital Cologne, Department I of Internal Medicine, Center for Integrated Oncology Aachen Bonn Cologne Duesseldorf (CIO ABCD), Excellence Center for Medical Mycology (ECMM), Köln, Germany, SÜniversität zu Köln, Cologne Excellence Cluster on Cellular Stress Responses in Aging-Associated Diseases (CECAD), Köln, Germany, 5Universität zu Köln, Clinical Trials Centre Cologne (ZKS Köln), Köln, Germany, 6German Centre for Infection Research, Partner Site Bonn-Cologne, Cologne, Germany, 7Stanford, Stanford University, Stanford, United States, 8Hôpitaux Universitaires de Genève (HUG), Genève, Switzerland

Background: Concerns about nephrotoxicity may limit cidofovir (CDV) use in allogeneic hematopoietic cell transplant recipients (allo-HCTr). In this multi-center study, we aimed to assess real-life use and nephrotoxicity of CDV in allo-HCTr.

Materials/methods: Data on all consecutive adult allo-HCTr treated with intravenous CDV (2011-2018) were retrospectively collected in six centers. We report preliminary descriptive data on CDV nephrotoxicity.

Results: We included 123 allo-HCTr (5% bone marrow, 77% peripheral blood stem cells, 15% cord blood), from a matched-related (16%), mismatched/matched-unrelated (76%) or haploidentical (7%) donor. Seventy-three (59%) patients received a T-cell depleted HCT, mostly by ex-vivo CD34-selection (61%) and 54 (44%) patients had acute graft-versus-host disease at CDV initiation. CDV was administered for: adenovirus (58, 47%), cytomegalovirus (54, 44%), BK-virus (35, 28%), human herpes virus 6 (7, 6%), herpes simplex virus (5, 4%) or JC-virus (1, 1%) infections. In 24 (20%) patients >1 viral indication was present. Patients received a median of 3 (interquartile ratio, IQR 2-4) CDV doses. CDV doses were 5 mg/kg/week, 3 mg/kg/week, 1 mg/kg in various frequencies in 88 (71.5%), 11 (8.9%), and 19 (15.4%) patients, respectively. Median time from HCT to CDV initiation was 90 days [IQR 59-163]. Mean creatinine was 0.9 mg/dL (±0.42, N=123) at baseline, 1.07 mg/dL (±0.71, N=103) at end-of-treatment (EOT; p-value=0.0001) and 1.34 mg/dL (±0.98, N=54) at EOT+14D (p-value baseline-EOT+14D=0.002, p-value EOT-EOT+14D=0.023; Figure 1). Out of 62 patients with reported glomerular filtration rate (GFR), 52 (83.9%) and 46 (74%) patients had GFR>60 mL/min at baseline and EOT, respectively (p-value=0.11). Using the RIFLE-criteria, ≥50% creatinine increase and ≥25% GFR decline by EOT compared to baseline were observed in 19/105 (18.4%) and 13/62 (21%) patients, respectively. Patients receiving 5 mg/kg/week CDV were more likely to develop acute kidney injury (AKI) by EOT compared with those receiving 1-3 mg/kg/week (32.8% versus 4.5%, p-value=0.032). None of the patients developed end-stage-renal-disease. No significant associations were found between AKI and CDV number of doses or cumulative dose.

Conclusions: Based on preliminary analyses, renal impairment developed in 20% of allo-HCTr treated with CDV. CDV dose of 5 mg/kg/week appeared to be associated with a higher rate of AKI.

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Abstract 2385

Unravelling the potential utility of novel β-lactam/β-lactamase inhibitors against Enterobacter cloacae complex

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Background: Enterobacter cloacae complex are genetically diverse pathogens increasingly reported as resistant to cefepime and/or carbapenems. Our objective was to investigate the in vitro activity of novel β-lactam/β-lactamase inhibitor (BL/BLI) combinations against E. cloacae.

Materials/methods: Isolates non-susceptible to cefepime or a carbapenem by automated testing methods were selected. Minimum inhibitory concentrations (MICs) were determined by broth microdilution methods and interpreted using CLSI breakpoints. β-lactamases were identified by PCR and/or whole-genome sequencing.

Results: 86 isolates from unique patients were included; 50%, 63%, and 24% were resistant to cefepime, ertapenem, and meropenem, respectively. Carbapenemases were detected in 17 isolates (15 KPC, 2 VIM); 41%, 6%, and 53% of carbapenemase-producing (CP) isolates were susceptible to cefepime, ertapenem, and meropenem, respectively. Rates of susceptibility were 12%, 91%, 88%, and 95% to ceftolozane-tazobactam, ceftazidime-avibactam, imipenem-relebactam, and meropenem-vaborbactam, respectively (Table). Ceftolozane-tazobactam susceptibility rates were similar to piperacillin-tazobactam (13%). Median fold-reductions in ceftazidime, imipenem, and meropenem MICs following the addition of avibactam, relebactam, and vaborbactam for all isolates were 128, 4, and 4, respectively. Against CP isolates the corresponding fold-reductions were 128, 32, and 16. 51% and 62% of meropenem-resistant isolates demonstrated imipenem-relebactam or meropenem-vaborbactam MICs ≥ 2µg/mL, respectively. Conversely, 52% of meropenem-resistant isolates had meropenem MICs ≤8 µg/mL. Only 38% of meropenem-resistant isolates were CP. Against non-CP meropenem-resistant isolates, the addition of relebactam and vaborbactam to imipenem and meropenem, respectively, lowered median MICs by 4-fold; median ceftazidime MICs were lowered 1.28-fold with the addition of avibactam. 8 isolates were resistant to ceftazidime-avibactam, 2 produced VIM and 6 had substitutions in the R2 or Ω-loop of AmpC. 3 isolates were resistant to meropenem-vaborbactam, 2 harbored substitutions in R2 loop of AmpC and OmpC/OmpF, 1 produced VIM.

Conclusions: Against diverse E. cloacae, ceftazidime-avibactam, imipenem-relebactam, and meropenem-vaborbactam demonstrated susceptibility rates ranging from 88–95%; however, novel resistance mechanisms were identified. >50% CP-E. cloacae were susceptible to meropenem. Against non-CP E. cloacae, relebactam and vaborbactam both lowered carbapenem MICs suggesting possible β-lactamase inhibition beyond stability of carbapenems. In the setting of β-lactam resistance, most novel BL/BLIs provide excellent in vitro activity, but the preferred treatment approach merits further investigation.

Table. Percentage of isolates susceptible to novel BL/BLI or harboring KPC by phenotype

<table>
<thead>
<tr>
<th></th>
<th>All isolates (n=86)</th>
<th>Cefepime-R (n=43)</th>
<th>Ertapenem-R (n=54)</th>
<th>Cefepime and Ertapenem-R (n=13)</th>
<th>Cefepime, Ertapenem, and Meropenem-R (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftolozane-tazobactam</td>
<td>12%</td>
<td>12%</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Ceftazidime-avibactam</td>
<td>91%</td>
<td>61%</td>
<td>67%</td>
<td>85%</td>
<td>76%</td>
</tr>
<tr>
<td>Imipenem-relebactam</td>
<td>88%</td>
<td>81%</td>
<td>81%</td>
<td>100%</td>
<td>52%</td>
</tr>
<tr>
<td>Meropenem-vaborbactam</td>
<td>90%</td>
<td>93%</td>
<td>91%</td>
<td>100%</td>
<td>81%</td>
</tr>
<tr>
<td>Presence of carbapenemase</td>
<td>20%</td>
<td>23%</td>
<td>26%</td>
<td>23%</td>
<td>38%</td>
</tr>
</tbody>
</table>

Presenter email address: mccrearye3@upmc.edu
Abstract 2386

**T2Bacteria panel in diagnostics of sepsis: the first experience at the University Hospital Centre Zagreb**

Ivana Mareković*1,2, Zrinka Bosnjak1,2, Sanja Pleško1, Vesna Tripkovic1

1University Hospital Centre Zagreb, Zagreb, Croatia, 2School of Medicine, University of Zagreb, Zagreb, Croatia

**Background:** T2Bacteria® Panel (T2 Biosystems®) is the first and only FDA and CE-marked test to identify sepsis-causing bacteria directly from whole blood in 3 to 5 hours, which would aid in prescribing earlier appropriate antimicrobial treatment. The aim of the study was to show our first experience with this unique new technology in septic patients.

**Materials/methods:** From December 2018 to March 2019 T2Bacteria® Panel (T2BP) was used in the following groups of septic patients: medical and surgical intensive care unit (ICU), hematology and solid organ transplant. Four mL of blood for T2BP was collected in a K2EDTA tube and one set of blood cultures (BC) was simultaneously obtained. T2BP results were compared against concomitant drawn blood cultures and additional microbiological results within 14 days of T2BP sample.

**Results:** A total of 29 patients, 21 (72,4%) male and 8 (27,6%) female, were included with age ranging from 0 – 83 years and twenty-six (89,6%) of them at the ICU. T2BP was positive in 13 (44,8%) and BC in 6 (20,7%) of patients. When T2BP results were compared to BC (on panel bacteria only), 2 patients were T2BP+BC+, 11 patients T2BP+BC-, 16 patients T2BP-BC-, and no patients T2BP-BC+. Average time to positive result with T2BP was 4 hours and 40 minutes and in two patients with concomitantly positive BC for panel organisms 86 hours and 30 minutes. Average time to negative result was 5 hours and 6 minutes with T2BP and 120 hours with BC. When analyzing the significance of 13 T2BP+BC- results in the context of all other available microbiological data, 11 additional results otherwise missed by BC were identified, one was probably false-positive and for one there were no data available. Statistical analysis showed 100,0% positive percent agreement (PPA), 90,0% negative percent agreement (NPA), 100,0% negative predictive value (NPV) and 84,6% positive predictive value (PPV).

**Conclusions:** Our first experience with T2Bacteria® Panel showed this is highly promising molecular method reducing time to species identification as well as to negative result. It demonstrated high PPA and NPV as well as proving etiology of additional cases otherwise missed with conventional diagnostics.

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Built environment microbiological surveillance in a large intensive care unit revealed abiotic reservoirs of highly persistent clones of *Klebsiella* species (*K. pneumoniae, K. oxytoca, K. variicola*)

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**Background:** Extended-Spectrum Beta-Lactamase (ESBL) or carbapenemase-resistant (CR) *Klebsiella* spp. (Ki) are increasing in hospitals, environmental Kl reservoirs being often detected in built hospital environment (BE) during ESBL/CRKl outbreaks. We screened Kl in abiotic surfaces of an ICU-Intensive Medicine ward fully enrolled in infection control programs of antimicrobial resistance.

**Materials/methods:** 5 samples/patient room (sinks-SK; ventilator’s-touchscreen-VT; washbasin-WB; bedrails-BR) and 2 samples from staff-areas (keyboards) were weekly collected using EZ-Reach-Sponges [April-October 2019]. 1,728 samples were plated [(5x14rooms+2)x24weeks] on ChromagarOrientation and bacterial colonies were characterized [1/morphotype; 10,180 colonies]. Identification (MALDI-TOF-MS), antimicrobial-susceptibility (disk-diffusion, Hodge-test, PCR-bla) and clonal typing (FT-IR spectroscopy, XbaI/S1 -PFGE, whole genome sequencing, WGS) were analysed. REDCap [Research Electronic Data Capture] application was used to integrate and further exploit comprehensive metadata [clinical records, IC, BE surveillance]. ICU-metrics for this period include 95%-ICU occupancy, 244 patients, 27.9%-MDR colonization-rate (23% ESBLKP, 6.8% CRKP).

**Results:** We detected Kl in BE of 9/14 rooms [K. pneumoniae (KP), K. oxytoca (KO), K. variicola (KV)] in 7, 4 and 1 rooms, respectively. KP appears in all samples, KO in SK+BR while KV was confined to SK. BE-KP isolates clustered in 11 clones [1ESBL+/-, 3CRs (OXA-48), 7 non-ESBL and non-CR]. All CRKP were collected from BR of rooms with patients colonized by CRKP. A KP clone (ESBL+/- variants), together with other ESBL-producing species, was detected in a SK for ≥3 months. Some KP were high-risk lineages (CG258,CG405)/K-types (K19, K24, KL151), often recovered from inpatients. All non-ESBL/non-CRKP clones were sporadically detected [1-2 weeks in SKs]. KO clustered in 6 clones [5 capsular types], one being an ESBL producer recovered in a single SK for 4-months. All KV isolates belong to a single clone [different variants] for 6months. Preliminary WGS confirms different transmission routes within and between abiotic and biotic samples.

**Conclusions:** BE surveillance revealed hidden and persistent KP, KO and KV reservoirs in SK of specific rooms able to occasionally acquire and retain *bla*<sub>ESBL</sub>, and also the ability of some KP and KO human clones for transiently colonize surfaces. Analysis of metadata from different human and BE surveillance programs improves risk assessment analysis for the transmission of multidrug resistant pathogens.

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Abstract 2390

Improving Outcomes and Antibiotic Stewardship for patients with bloodstream Infections (IOAS): a quasi-experimental multi-centre analysis of time to optimal therapy

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Background: Measuring impact of diagnostic technologies on patient care can be complex. For hospitals with established antimicrobial stewardship programs, initiatives focused on improving quality of care are key and can be demonstrated by measuring the impact on time to optimal therapy. Effect of antibiotic optimization for patients with bloodstream infections (BSI) was evaluated in the Accelerate PhenoTest™ BC kit (AXDX) registry program, with emphasis on time to optimal therapy (TTOT).

Materials/methods: This multicenter, quasi-experimental study compares clinical and antimicrobial stewardship metrics, prior to and after implementation of AXDX, to evaluate the impact this technology has on patients with BSI. Laboratory and clinical data from hospitalized patients with BSI (excluding contaminants) were compared between two groups, one that underwent testing on AXDX (post-AXDX) and one that underwent alternative organism identification and susceptibility testing (pre-AXDX). Interim analysis of data collected from 3 centers was performed. Pre-AXDX methods for each of the 3 sites were: Verigene®, MALDI-TOF MS, and BD Phoenix™ at Hospital A; MALDI-TOF MS and VITEK® 2 at Hospital B; and MALDI-TOF MS, VITEK® 2, and Sensititre™ at Hospital C. All institutions had active antimicrobial stewardship programs throughout the study period. Primary outcome was TTOT; multiple linear regression analysis was performed to identify clinical factors associated with TTOT.

Results: 464 patients with BSI (239 pre-AXDX, 225 post-AXDX) were included in this analysis. Patient demographics, comorbidities, and severity of illness (median Pitt bacteremia score of 2) were similar between groups, as were distributions of gram negative (~60%) and gram positive (~35%), with polymicrobial (~11%) BSI. The most prevalent gram-negative and gram-positive organisms were E. coli and S. aureus, respectively. Median TTOT was 42.0 hours [interquartile range [IQR], 20.5 - 65.3] in the pre-AXDX group and 28.2 hours [IQR, 12.8 - 49.2] in the post-AXDX group (p=0.003). Independent factors associated with shorter TTOT were BSI with AXDX on-panel organisms (p=0.01), absence of intravenous vasopressors (p=0.01), and post-AXDX group (p=0.01).

Conclusions: Implementation of AXDX improves antimicrobial stewardship in patients with BSI reducing both TTOT and unnecessary antimicrobial exposure.

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Abstract 2392

High burden and undetected clusters of pneumococcal disease in long term care in Ontario, Canada

Allison Mcgeer1, Wallis Rudnick1, Walter Demczuk1, Wayne Gold3, Ian Kitai4, Sigmund Krjaden5, Reena Lovinsky6, Irene Martin2, Matthew Muller7, Jeff Powis1, Neil Rau5, Greg Tyrrell10, Andrew E. Simor11, Toronto - Tibdn12

1Sinai Health System, Toronto, Canada; 2National Microbiology Laboratory, Winnipeg, Canada; 3University Health Network, Toronto, Canada; 4The Hospital for Sick Children, Toronto, Canada; 5St. Joseph’s Health Centre, Toronto, Canada; 6The Scarborough Hospital, Toronto, Canada; 7Unity Health, Toronto, Canada; 8Toronto East Health Network, Toronto, Canada; 9Halton Healthcare, Oakville, Canada; 10Alberta Public Laboratories, Edmonton, Canada; 11Sunnybrook Health Sciences Centre, Toronto, Canada; 12Toronto Invasive Bacterial Diseases Network, Toronto, Canada

Abstract third-party references: Toronto Invasive Bacterial Diseases Network

Background: Despite PPV23 and herd immunity from pediatric PCV, there are reasons to be concerned about persisting burden of illness in long-term care residents (LTCR), as pneumococcal carriage and congregate living may reduce herd protection. We analyzed invasive pneumococcal disease (IPD) in LTCR in Toronto/Peel region, Canada, post PCV13 implementation.

Materials/methods: TIBDN conducts population-based surveillance for IPD in Toronto/Peel, Canada (Pop=4.5M). Serotyping and antimicrobial susceptibility testing are performed. Incidence in LTCR was calculated per 1000-bed-days. The odds of occurrence of >1 case of a particular serotype in any one LTC home was calculated by comparing incidence in that home due to that ST from first to last case to incidence in all other homes due to that ST during the same period; P<.0005 was considered statistically significant.

Results: From 1995-2018, 566 episodes of IPD occurred in LTC; incidence decreased from 224 to 70/1000 bed-days after adult PPV23 (1996)/infant PCV (2005/2010) programs; but 37% of 2014-18 isolates were of PCV13 STs. In cases of IPD, LTCR were more likely than age-matched community controls to have received PPV23 (55v44%, P=.002), but case fatality was higher (49 vs 14%, P<.0001), and isolates more resistant to penicillin (20 vs 14%, P=.03) and levofloxacin (4.9 vs 1.0%, P<.001). Although no outbreaks were reported, 29 clusters of ≥3 cases (total 134/500, 27% of IPD) were retrospectively identified in which the serotype incidence in the affected home was significantly higher than in other homes at the same time (P<.0005). The largest clusters are in the Table; clusters were more likely of serotypes 14, 3, 38 and 31.

Conclusions: The burden of IPD in LTC is high. Unrecognized transmission appears to contribute to this burden.

Table: Largest case clusters in LTC, 1995-2018

<table>
<thead>
<tr>
<th>Serotype</th>
<th>Home code</th>
<th>Total cases</th>
<th>Year of first case</th>
<th>Time 1st to last case</th>
<th>Incidence, affected home</th>
<th>Incidence, other homes</th>
<th>IRR (95% CL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>A</td>
<td>12</td>
<td>1995</td>
<td>22yrs</td>
<td>0.37</td>
<td>0.041</td>
<td>9.2 (4.5, 17)</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>6</td>
<td>2000</td>
<td>3.3yrs</td>
<td>2.1</td>
<td>0.092</td>
<td>23 (7.5, 59)</td>
</tr>
<tr>
<td>3</td>
<td>C</td>
<td>13</td>
<td>2005</td>
<td>10.4yrs</td>
<td>1.7</td>
<td>0.020</td>
<td>85 (37, 190)</td>
</tr>
<tr>
<td></td>
<td>D</td>
<td>8</td>
<td>1995</td>
<td>8.1yrs</td>
<td>1.8</td>
<td>0.034</td>
<td>53 (20, 128)</td>
</tr>
<tr>
<td>23F</td>
<td>E</td>
<td>5</td>
<td>2000</td>
<td>2.7yrs</td>
<td>4.1</td>
<td>0</td>
<td>und (94, -)</td>
</tr>
<tr>
<td>38</td>
<td>G</td>
<td>7</td>
<td>2001</td>
<td>12mos</td>
<td>1.8</td>
<td>0.0029</td>
<td>620 (79, 28000)</td>
</tr>
<tr>
<td>31</td>
<td>H</td>
<td>9</td>
<td>2004</td>
<td>22mos</td>
<td>0.92</td>
<td>0.0050</td>
<td>183 (51, 815)</td>
</tr>
</tbody>
</table>

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Abstract third-party references: ALK Abello

Background: Nearly 90% of self-reported penicillin allergies are negative upon assessment or skin testing. Allergy assessment and penicillin skin testing (PST) are useful tools to increase use of beta-lactams (BL), which are frequently the antibiotic of choice for many infectious syndromes. PST has been successfully implemented in both inpatient and outpatient care settings; however, longitudinal effects of PST have not been evaluated.

Materials/methods: This was a retrospective, observational study of adult patients who had a negative PST between August 2014 and October 2019 across one academic medical center and one community hospital. Time period assessed per patient was defined as the twice the number of days between PST and most recent day of discharge. Primary outcome was percent of antimicrobial courses containing a BL before and after PST in patients who received at least one antimicrobial course before and after PST. Secondary outcomes were percent of antibiotic days containing a beta-lactam, percent of beta-lactam days of penicillin, and percent antibiotic days of penicillin. Results were considered significant if p ≤0.05.

Results: In total, 337 patients with a negative PST completed per protocol over the study time period were included. One hundred thirty-nine patients received at least one antibiotic course during any readmission after PST, and 64 received at least one course before and after PST. The proportion of patients that received a BL course after PST was 50% higher than before PST. (Table 1)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Before</th>
<th>After</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent Courses BL</td>
<td>28.1 ± 40.5</td>
<td>78.4 ± 34.7</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Percent Antibiotic Days BL</td>
<td>19.9 ± 30.0</td>
<td>52.0 ± 30.5</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Percent BL Days PCN</td>
<td>0.1 ± 0.5</td>
<td>43.4 ± 38.3</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>Percent Antibiotic Days PCN</td>
<td>0.04 ± 0.3</td>
<td>21.3 ± 26.3</td>
<td>p&lt;0.0001</td>
</tr>
</tbody>
</table>

Data presented as Mean ± SD; PCN: penicillin

Conclusions: Negative PST leads to sustainable improvements in patient care, as patients received significantly more BL days of therapy, including penicillins, after negative PST. Our results confirm the importance of allergy assessment and intervention for patients labeled as penicillin allergic.

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Abstract 2395

Shorter duration of antibiotherpy in super-infection pneumopathy occurring in viral infection
Simon Bessis*1, Martin Trichet1, Alina Beresteanu1, Morgan Matt1, Benjamin Davido1, Aurélien Dinh1

1Raymond Poincaré University Hospital - [AP-HP], Garches, France

Background: Bacterial superinfections during respiratory viral infections are common. In this situation, the optimal antibiotic treatment duration is unknown. We aimed to demonstrate that a short treatment duration [3 days] is as effective as a longer duration [>3 days].

Materials/methods: We performed a retrospective cohort study including all patients hospitalized for respiratory viral infection with bacterial superinfection.

Our case definition was:
- adult hospitalized patient with positive PCR assay for respiratory viruses
- and fever (≥38°C) + at least one clinical symptom of pneumonia (dyspnea, cough, muco-purulent sputum, crackles)
- and bacterial superinfection defined as the presence of: muco-purulent sputum + hyperleukocytosis [with high neutrophil count] + elevated CRP and/or PCT levels + a new infiltrate on chest X-ray compatible with bacterial infection + positive bacterial sputum culture + antibiotic treatment prescribed by the physician in charge.

Cure was assessed at hospital discharge. It was a composite criterion: no resumption of antibiotic therapy and/or extension of the initially planned duration, associated with apyrexia and improvement of initial clinical symptoms. Death from any cause was considered as failure.

Results: From January 1st to April 1st 2019, 36 patients were included. The mean age was 74.7 years with a sex ratio (M/F) of 1.4. Overall, 17/36 (47.2%) patients had a chronic respiratory disease, 17/36 (47.2%) were smokers, 9/36 (25.0%) were immunocompromised. At admission, 21/36 (58.3%) patients presented fever, 14/36 (38.9%) needed oxygen supplementation. Main positive results of the multiplex PCR assay were: influenza A H3N2 [28/36], rhinovirus [4/36], and Respiratory Syncitial Virus [2/36].

Finally, 19 patients received 3 days of antibiotic treatment and 17 patients were treated more than 3 days. There was no significant difference regarding clinical and therapeutic characteristics between the 2 groups. The cure rate was 84.2% [16/19] in the group treated 3 days and 70.6% [12/17] in the group treated more than 3 days, with no significant difference (p=0.43).

Conclusions: A short duration [3 days] of antibiotic seems to be sufficient for bacterial superinfections of respiratory viral infections. Larger sample size study and randomized controlled trials are needed to confirm these preliminary data.

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Abstracts 2020

Abstract 2396

Elucidation of environment-dependent antibiotic resistance mechanisms
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Background: The propensity of pathogens to evolve resistance to antibiotics used in clinical infectious disease therapeutics has been an increasing concern in recent decades. Acquisition of resistance often translates into treatment failure and puts patients at risk of serious adverse outcomes. Current laboratory testing of antibiotic susceptibility does not account for the different microenvironments that bacteria encounter within the human body, providing results that often do not translate into the clinic. Our goal is to better understand evolutionary strategies employed by the major human pathogen Staphylococcus aureus in development of resistance in distinct environments.

Materials/methods: We used adaptive laboratory evolution (ALE) to generate isogenic strains resistant to several antibiotics (nafcillin, vancomycin, and azithromycin). Different media were used to mimic distinct environments and multi-omics approaches applied in the understanding of resistance mechanisms.

Results: Evolved strains were able to grow in the presence of higher concentrations of the antibiotic under study, and corresponding phenotypes were similar to those observed in clinical resistant isolates. Mutational analysis indicated that mutations conferring antibiotic resistance were specific and condition-dependent. Distinct mutations led to resistance phenotypes under a particular environmental condition, but these mutations did not necessarily translate into resistance under a different environmental condition. In particular, resistant strains possessed distinct transcriptional landscapes, even when the same systems were mutated, suggesting that similar evolutionary paths translate into distinct resistance mechanisms.

Conclusions: We identified several resistance mechanisms employed by S. aureus that were not only environment-dependent, but also environment specific. Additionally, we showed that ALE can be applied in pathogens of interest to study antibiotic resistance evolution and prediction of clinical resistance mechanisms, as supported by the significant overlap of mutations identified via ALE and those reported in clinical isolates.

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Meso-2,3-dimercaptosuccinic acid in combination with a carbapenem against metallo-β-lactamase-producing Escherichia coli in murine peritonitis: a proof-of-concept

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Background: Carbapenemase-producing Enterobacteriales (CPE) represent a major therapeutic challenge. Among carbapenemases, metallo-beta-lactamases (MBL) require the presence of zinc at their active site to inactivate carbapenems. Meso-2,3-dimercaptosuccinic acid (DMSA), a heavy metal chelator, may have a chelating activity on the zinc/carbapenemases binding, restoring carbapenems’ activity against MBLs.

Materials/methods: Six isogenic derivatives of wild-type E. coli CFT073 strain producing the MBL NDM-1, VIM-2, IMP-1 and the serine carbapenemases OXA-48 and KPC-3 were constructed. Minimum inhibitory concentrations (MICs) of imipenem, meropenem and ertapenem were determined alone or in combination with DMSA. Time-kill assays were performed to evaluate the existence of a synergy between imipenem and DMSA. Mice infected with CFT073, NDM-1 and KPC-3 strains were treated intra-peritoneally every 4h for 24h with imipenem 100 mg/kg, DMSA 200 mg/kg, or both. Bacterial counts in peritoneal fluid (PF) and spleen were determined at 24h. DMSA concentrations in plasma of uninfected mice were measured.

Results: DMSA alone had no antibacterial effect against any of the tested strains. DMSA in combination with each carbapenem permitted a significant decrease of the MICs against all MBL-producing strains, but not the non-MBL strains, in a concentration-dependent manner, and a full recovery of susceptibility to carbapenems for MBL-producing strains at a maximum concentration of 6 mM. A synergistic bactericidal effect between imipenem at the MIC and DMSA 6 mM was observed in vitro only against the NDM-1 strain, with a reduction in bacterial load superior to 3 log10 colony forming units (CFU)/mL at 24h. No benefit was observed against non-MBL strains. In mice infected with NDM-1 strain, combination of imipenem and DMSA significantly reduced bacterial counts in PF and spleen as compared with imipenem alone (P<0.001), with no benefit against CFT073 and KPC-3. This in vivo benefit of DMSA was achieved with a dose of 200 mg/kg, generating peak serum levels of 21 to 85 µmol/L, in the range of those obtained in human with therapeutic doses of DMSA.

Conclusions: DMSA is highly effective in restoring carbapenems’ activity against MBL and appears as a promising strategy in combination with carbapenems for the treatment of NDM-1 E. coli related infections.

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Abstract 2398

Outpatient clinic for tuberculosis screening: an opportunity to promote healthcare access among applicants for international protection

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Background: In a global context, the health of migrants remains a huge and often neglected medical and political challenge. In March 2017 we implemented an Outpatient Clinic (OC) at our hospital for second-level screening of latent tuberculosis infection (LTBI) among refugees and asylum-seekers.

Materials/methods: We retrospectively analysed data from all subjects who accessed the OC.

Results: 150 subjects [all Mantoux test-positive] were sent to our OC. They were mostly males (98%), with a mean age upon arrival in Italy of 25 years. They came mainly from Sub-Saharan Africa (83%), less frequently from Asia (14%). Only 44 subjects reported having stayed in Libya. First access to the OC dated on average 10 months after entering Europe. A mean of 3 visits and 2 blood panels were performed for each subject.

Upon first visit, we detected respiratory symptoms in 16 cases (11%), gastrointestinal in 11 (7%) and itching in 9 (6%). Blood tests showed hypereosinophilia in 36 subjects (24%), polycythemia/thrombocytopenia in 8 (6%). Twenty-five subjects (17%) refused to have their blood drawn, discontinuing all clinical follow-up.

After performing an Interferon-Gamma Release Assay, 76/150 subjects (51%) were diagnosed with LTBI: 69 of them (91%) agreed to start prophylaxis, which was completed in 36 cases (52%). We observed 5 cases (3%) of scabies, 2 of diabetes and 1 of arterial hypertension (all treated accordingly).

Since August 2018 a wider serological screening was introduced (Table 1). In 19/38 patients (50%) a schistosomal infection was identified and treated. All patients found positive for chronic HBV infection were taking care and regularly followed up, whereas HBV-negative subjects were referred to our Vaccine Centre.

Conclusions: Through our OC we were able not only to diagnose and treat several LTBI, but also to diagnose and treat other chronic diseases and neglected tropical infections, guaranteeing an acceptable compliance to therapies and managing to promote healthcare access among a very fragile population, such as immigrants.

Table 1

<table>
<thead>
<tr>
<th>Serologies</th>
<th>Performed (N)</th>
<th>Positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schistosoma</td>
<td>38</td>
<td>19 (50)</td>
</tr>
<tr>
<td>Syphilis</td>
<td>42</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>HIV</td>
<td>106</td>
<td>0 (0)</td>
</tr>
<tr>
<td>HCVAb</td>
<td>58</td>
<td>0 (0)</td>
</tr>
<tr>
<td>HBsAg</td>
<td>61</td>
<td>5 (8.1)</td>
</tr>
<tr>
<td>HBCAb</td>
<td>43</td>
<td>19 (44.2)</td>
</tr>
<tr>
<td>HBsAb</td>
<td>47</td>
<td>18 (38.2)</td>
</tr>
</tbody>
</table>

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Examining discordance in blood culture and T2 positivity in the detection of candidaemia: modelling the odds of blood culture and T2 discordance as a function of candidaemia risk factors

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Background: The T2Candida® Panel (T2) is a rapid molecular diagnostic that detects 5 Candida species (C. albicans/C. tropicalis, C. glabrata/C. krusei, and C. parapsilosis) directly from whole blood samples in patients candidemia with excellent sensitivity and negative predictive value. Henry Ford Health System implemented both T2 in 2015 and BacT/Alert Virtuo® (bioMérieux, Inc., Durham, NC) blood culture (BC) system in 2019 for the detection of pathogens, including Candida causing bloodstream infection (BSI). In practice, there are discrepancies in test results when employing both tests simultaneously. We evaluated the potential factors associated with discordance between these two tests for the detection of candidemia.

Materials/methods: We screened all patients who had a T2 performed since implementation of the Virtuo system in February 2019 through August 2019, focusing on patients who had discordant results between the two testing methodologies. This study reports the types of discrepancy seen between the two tests, the turn-around times (TAT), and frequency of risk factors for candidemia in these patients. Finally, we performed a univariate analysis modeling the odds of discordant T2/BC results as a function of risk factors for candidemia.

Results: A total of 675 T2 tests were performed during the study period. Only 33 (5%) T2s were positive. Of these, 23 (70%) were discordant (T2+/BC-) and 10 (30%) concordant (T2+/BC+). Three patients had T2-/BC+. The most common Candida species found in blood by both culture and T2 were C. albicans (5), followed by C. glabrata (4). Blood culture TAT was 15 hours faster detecting bacteria than yeast, on average (P=0.3918). T2 was 40 hours faster than BC in detecting candidemia. The vast majority of our patients presented in septic shock (72%), had intravascular devices (94%), were exposed to broad spectrum antimicrobials (92%), or had corticosteroids administered (50%). Univariate analysis showed no statistical association between candidemia risk factors and discordant test results.

Conclusions: Discordant T2/BC results were mostly a function of T2 being more sensitive than BC, despite the implementation of an enhanced BC system to increase yield. Traditional risk factors for candidemia did not predict discordance in testing results.

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Appropriacy of empirical antibiotic therapy in percutaneous endoscopic gastrostomy site infection among head and neck cancer patients: a 15-year retrospective study

So Yeon Park*, Jihyu Oh, Jungok Kim, Eun-Jeong Joo, Jin Seo Lee

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Abstract

Background: Wound infection is the most common complication associated with Percutaneous endoscopic gastrostomy (PEG) placement, with an incidence between 4% and 30%. In this study, we compare characteristics of PEG site infection between head and neck cancer group and non-head and neck cancer group.

Materials/methods: We retrospectively collected data on patients who underwent PEG insertion from October 2003 through May 2019 at Kangdong Sacred Heart Hospital, Seoul, Korea. A total 314 cases with PEG insertion, 129 cases in head and neck cancer group and 187 in non-head and neck cancer group, were included in this study.

Results: A total of 314 patients were eligible for this study, 187 for non-head and neck cancer patients and 129 for head and neck cancer patients. PEG site infections were significantly higher rate in head and neck cancer group than non-head and neck cancer group (32.6% vs. 13.4%; p<0.001). In head and neck cancer group, PEG wound isolates included Pseudomonas aeruginosa in 33.3% (14/42) of patients, MRSA in 26.2% (11/42) of patients and Klebsiella pneumoniae in 21.4% (9/41) of patients. Pseudomonas aeruginosa is most common pathogen of PEG site infection. 31 of 42 head and neck cancer patients with PEG infection (73.8%) were chronic infection. 40.6% of these patients were isolated P. aeruginosa, but only 21.4% of these patients had proper antibiotics for empirical treatment. In the 25 clinical isolates of P. aeruginosa, the overall drug resistance to all anti-pseudomonal drugs tested was higher in the head and neck cancer group compared with in the non-head and neck cancer group (fig1).

Conclusions: PEG site infection is more prominent on head and neck cancer patients than non-head and neck cancer patients. Unlike other skin and soft tissue infection, gram negative bacteria, especially P. aeruginosa, were major causative pathogen in PEG site infection in Head and neck cancer patients. For appropriate treatment, we should consider P. aeruginosa when start empirical therapy of PEG site infection on head and neck cancer patients.

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Abstract 2402

Rethinking the involvement of patients in infection prevention and control and antimicrobial stewardship

Holly Seale* 1

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Background: Interventions developed to date to support patient participation in hand hygiene advocacy have failed to meaningfully transition patients from 'being willing to participate' to actively speaking up. To inform the development of a new hospital-based strategy to improve patient participation in infection prevention and control activities (including those focused on reducing the risk of antimicrobial resistance), our team undertook a series of studies to examine the current landscape around patient participation.

Materials/methods: A multi method study involving three major public hospitals in Sydney, Australia was undertaken that involved in-depth interviews with patients and healthcare providers, a survey of patients and a co-design workshop to understand the current landscape around strategies to promote and involve patients, as well as the understanding and attitudes of patients and healthcare providers toward the concept. We also explored the perceptions of participants towards new ways that could be used to improve patient involvement.

Results: We identified that: (1) the health system focuses on information provision as the primary strategy (generally reactive not proactive); (2) there is a level of misunderstanding about what patient involvement entails amongst providers and patients; and (3) that both healthcare workers and patients acknowledge that 'everybody has a role to play in IPC' but are not sure about activities. In support of the need to renew the focus on patient participation in infection control, is our finding that 88% (449/511) of patients surveyed want to partner with healthcare providers to help prevent infections while at hospital.

Conclusions: While building awareness about healthcare associated infections has been the traditional approach to date, this is an outdated model. If we are going to move towards a patient centered system for IPC, we need to start focusing more on the enablers of participation. We need to support change using theory-driven behavioral change interventions that are grounded in an understanding of the enablers and barriers impacting on patient participation.

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Abstracts 2020

Abstract 2403

Examining factors impacting influenza vaccination amongst healthcare workers in Asia and the Pacific
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Background: Despite clear recommendations from leading health organisations, hospital healthcare workers (HCWs) continue to reject the influenza vaccine. Research has focused on the perceptions towards influenza and the influenza vaccine have centered on HCWs in high- and middle-income countries. Understanding the factors impacting on acceptance amongst HCWs located within Asia and the Pacific is important for the development of relevant strategies.

Materials/methods: A cross sectional survey was undertaken with HCWs from nine countries across the Asia/Pacific region in 2014-2015. A 9-item measure of cognitive empowerment towards flu vaccination (MoVac) and an 11-item measure of cognitive empowerment towards vaccination advocacy (MovAd) was used.

Results: One thousand and forty-eight HCWs were included. A high mean motivation (mean=77) and advocacy score (mean=84) was shown from these countries. HCWs scored high on individual items of vaccination motivation and advocacy score. In the regression model: males (P<0.01 OR: 1.54; 95% CI 1.19-2.01), being a paediatrician (P=0.002), GP (P<0.001), perceived severity of getting the flu if unvaccinated (P=0.009, OR:1.12; 95% CI=1.01 - 1.21) and having a high vaccine motivation score (P<0.001, OR=1.27; CI=1.12-1.47) were the strongest predictors of getting the flu vaccine.

Conclusions: There has been a lot of focus on monitoring vaccine acceptance amongst the general community but very little work on using validated measures for HCWs. Using this MoVac/MovAd tool we have not only been able to identify the factors that are predicting vaccination acceptance within a population that doesn't usually get a lot of focus but also can compare these results to HCWs in other countries.

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Evaluation of the antimicrobial activity of ridinilazole and six comparators against Chinese, Japanese and South Korean isolates of \textit{Clostridioides difficile}

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Background: \textit{Clostridium (Clostridioides) difficile} is the most common cause of antibiotic-associated diarrhoea in high-income countries. Risk of recurrent infection is high, occurring in up to 25% of cases, due to slow recovery of the gut microflora following broad-spectrum antimicrobial treatment. Fluoroquinolone resistance facilitated the emergence and spread of the ribotype (RT) 027 strain of \textit{C. difficile} in the early 2000s. Despite frequent inappropriate antimicrobial use in Asia, RT027 is rarely isolated in the region, but other strains of global importance, including the often fluoroquinolone- and clindamycin-resistant RT017 strain, predominate. The aim of this study was to evaluate the antimicrobial activity of ridinilazole, a novel antimicrobial agent with highly specific activity for \textit{C. difficile}, against isolates of \textit{C. difficile} from Asia.

Materials/methods: A collection of 140 \textit{C. difficile} isolates from Japan (n=64), South Korea (n=32), and China (n=44) were tested by the agar dilution method for susceptibility to ridinilazole and six comparators (Table 1) according to the Clinical and Laboratory Standards Institute guidelines.

Results: Overall resistance rates and minimum inhibitory concentrations (MICs) are shown in Table 1. All isolates were susceptible to ridinilazole with low MICs. Several RTs showed enhanced resistance profiles, particularly RT017 (100% clindamycin-resistant, 91.3% moxifloxacin-resistant, 82.6% rifaximin-resistant) and RT369 (94.4% clindamycin-resistant, 100% moxifloxacin-resistant). Rifaximin resistance was absent in all isolates from Japan. Multi-resistance to clindamycin, moxifloxacin and rifaximin was found in 19 RT017 isolates from China and Korea, two RT001 isolates (Korea) and one RT046 isolate (Korea).

Conclusions: Ridinilazole showed potent activity against a range of Asian \textit{C. difficile}, which otherwise displayed resistance to several comparator antimicrobial agents. Ongoing surveillance of antimicrobial resistance profiles is required to monitor and control spread of resistant strains.

Table 1. Overall susceptibility of 140 \textit{C. difficile} isolates to test antimicrobial agents.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Resistant n (%)</th>
<th>MIC range (mg/L)</th>
<th>MIC\textsubscript{50}</th>
<th>MIC\textsubscript{90}</th>
<th>Geometric mean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ridinilazole</td>
<td>0</td>
<td>0.03-0.25</td>
<td>0.125</td>
<td>0.25</td>
<td>0.12</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>0</td>
<td>0.06-0.5</td>
<td>0.25</td>
<td>0.25</td>
<td>0.18</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0</td>
<td>0.08-4</td>
<td>1</td>
<td>2</td>
<td>1.13</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>99 (70.7)</td>
<td>0.125-&gt;32</td>
<td>&gt;32</td>
<td>&gt;32</td>
<td>13.03</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>86 (61.4)</td>
<td>1-&gt;32</td>
<td>16</td>
<td>32</td>
<td>7.96</td>
</tr>
<tr>
<td>Rifaximin</td>
<td>23 (16.4)</td>
<td>0.002-&gt;32</td>
<td>0.03</td>
<td>&gt;32</td>
<td>0.08</td>
</tr>
<tr>
<td>Fidaxomicin</td>
<td>0</td>
<td>0.015-0.25</td>
<td>0.125</td>
<td>0.25</td>
<td>0.07</td>
</tr>
</tbody>
</table>

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Abstracts 2020

Abstract 2411

Co-evolutionary adaptations of Acinetobacter baumannii and an OXA-23-encoding plasmid under carbapenem pressure

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Background: The carbapenemase OXA-23 is the predominant cause for carbapenem-resistant Acinetobacter baumannii [CRAB], with the conjugative plasmid pAZJ221 being a vehicle for the horizontal transmission of OXA-23 in China. However, the resistance phenotype comes with a reduction in growth when pZAJ221 is introduced to hosts. We aimed to investigate the co-evolutionary adaptations between pAZJ221 and A. baumannii ATCC 17978 under carbapenem pressure.

Materials/methods: Four colonies of the ancestor strain XH565 (ATCC 17978 pAZJ221) were daily passaged independently in media containing 16 mg/L imipenem for 60 days. Every ten days stocks were generated for each of the populations. Grow rates of evolved populations were measured. Whole-genome sequencing and breseq were employed to detect the mutations occurred during the evolution. We re-constructed mutants to demonstrate the impact of mutations on growth rates in A. baumannii. OXA-23 copy number was estimated by quantitative PCR and verified by Nanopore sequencing.

Results: We observed genetic adaptations in both plasmid and the chromosome over 400 generations. Fluctuating growth rates with dynamic mutational changes in populations were observed during the evolution process. Common adaptational mutations were found in internal or intergenic regions of global regulation genes. When reconstructing six such mutations in ATCC 17978, we observed increased growth rates only in the presence of the plasmid pAZJ221 (all P<0.001). Interestingly, in all lineages, the OXA-23 copy number in the plasmid doubled in the early phase but decreased back to a single copy in three out of four lineages (Fig.1A). We confirmed the existence of two copies of Tn2009 containing OXA-23 in the evolved plasmid pAZJ221 evolved (pAZJ221E) (Fig.1B). The introduction of pAZJ221E into ATCC 17978 led to a growth rate higher by 19.45%±3.84% compared to XH565 (P=0.0173).

Conclusions: Our study described the co-evolution pathway of pAZJ221 and its A. baumannii host, via OXA-23 duplication on plasmid at the early stage and genetic adaptations on chromosome conferring a fitness advantage in the presence of the plasmid. The results provide a possible explanation for the widespread of pAZJ221 among CRAB in China.

Fig.1 (A) changes of OXA-23 copy number in four lineages during evolution. (B) Two copies of OXA-23 in pAZJ221E.

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Comparison of the clinical features of human metapneumovirus infections in children between paediatric patients with severe mental and physical disabilities and those without underlying diseases at a children’s hospital in Japan

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Background: Human metapneumovirus (HMPV) is a common etiologic pathogen of respiratory tract infections in children. This study describes the differences in clinical characteristics of HMPV infection in children with severe mental and physical disabilities (SMPD) and those without underlying diseases.

Materials/methods: This was a retrospective, single-center cohort study of HMPV infection at Gunma Children’s Medical Center. All of the HMPV cases were detected in respiratory tract samples between January 2015 and August 2018 and identified from the Medical Center’s database. The patients’ demographic and clinical data were analyzed in order to compare the characteristics of HMPV infection between the two groups.

Results: Seventeen patients with SMPD and 20 without underlying diseases were included. The patients with SMPD were significantly older than those without underlying diseases [Median months; 68.9 vs. 17.0, p=.002]. Median length of stay was longer in the patients with SMPD (11.5 days vs. 6.0 days, p=.002). The proportion of supplemental oxygen, systemic steroids and antibiotics administration was higher in the patients with SMPD (oxygen; 82% vs. 35%, p=.007, systemic steroids; 35% vs. 0%, p=.005, antibiotics; 88% vs. 40%, p=.005).

Conclusions: HMPV infection was proved to be a substantial burden for children with SMPD.

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<tr>
<th></th>
<th>Children without underlying diseases (n=20)</th>
<th>Children with severe mental and physical disabilities (n=17)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>10 (50%)</td>
<td>8 (47%)</td>
<td>0.500</td>
</tr>
<tr>
<td>Median age, months (IQR)</td>
<td>17.0 (12.0–26.1)</td>
<td>68.9 (27.1–102.3)</td>
<td>0.002</td>
</tr>
<tr>
<td>Lymphocytes (x10^3/L) (IQR)</td>
<td>9200 (7200–11200)</td>
<td>9900 (7900–11200)</td>
<td>0.601</td>
</tr>
<tr>
<td>C-reactive protein (mg/dL) (IQR)</td>
<td>0.9 (0.46–1.85)</td>
<td>3.9 (1.80–6.63)</td>
<td>0.007</td>
</tr>
<tr>
<td>Supplemental oxygen</td>
<td>7 (35%)</td>
<td>14 (82%)</td>
<td>0.007</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>8 (40%)</td>
<td>15 (88%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>0</td>
<td>6 (35%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Length of stay, days (median)</td>
<td>6</td>
<td>11.5</td>
<td>0.02</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>0</td>
<td>1 (6%)</td>
<td>0.459</td>
</tr>
</tbody>
</table>

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Clinical evaluation of a novel rapid test for Aspergillus galactomannan

He Wang*1, Jie Peng1, Yuan Zhang1, Kevin Sun1, Junli Wen1, Yan Su1, Zeqi Zhou1

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Background: Invasive Aspergillosis (IA) is a life-threatening complication in patients with hematological malignancy, early and rapid diagnosis is crucial for the treatment. Aspergillus Galactomannan (GM) has been proved as a biomarker for detection of IA. Recently, GM Lateral Flow Assay (QuicGM™, Dynamiker, China) was released as a screening test of IA. It is a fluorescent immunochromatographic cassette test which using a monoclonal antibody against GM and Europium nanoparticles (Eu NP). After pretreatment of serum samples, pretreated supernatant was added into the pad and then read the fluorescent signal after 15 mins (Fig). It is a semi-quantitative test as compared with the traditional GM ELISA assay (Bio-Rad, USA).

Fig: Diagram of a rapid fluorescence LFA for the detection of GM

Materials/methods: A total of 209 serum samples were collected according to the revised EORTC/MSG guideline [2008], and tested by QuicGM™ (Dynamiker, China). Those included 82 IA samples (proven, n=30; probable, n=52) and 127 negative samples. Those samples were compared with Platelia™ GM ELISA (Bio-Rad, USA).

Results: A total of 209 serum samples were analyzed by ROC, the sensitivity and specificity of QuicGM™ was 87.8% and 90.6%, respectively. The positive coincidence rate, negative coincidence rate and total coincidence rate of QuicGM™ compared with Platelia™ was 87.8%, 90.55% and 89.47%, respectively. The Kappa value was 0.821>0.75.

Conclusions: The Dynamiker QuicGM™ was significantly consistent with Bio-Rad Platelia™ GM ELISA. It could be used as an aid for the early rapid screening test for the IA. Additionally, the Dynamiker QuicGM™ test was showed significant consistency with that Bio-Rad Platelia™ GM.

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Abstract 2419

Impact of a continuous improvement programme on central venous catheter care in reducing the incidence of primary bloodstream infection in neonatal intensive care unit

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Abstract third-party references: United Health Group - Amil

Background: Healthcare-Related Infections, particularly central venous catheter-associated bloodstream infections (CVC), are recognized as one of the most important causes of morbidity and mortality in hospitalized neonates.

Materials/methods: A cohort study was conducted in the neonatal intensive care unit (ICU) during the period from January to December 2017. The study was divided into two periods: first: January to June 2017 (reference period); second: July to December 2017 (period of continuous improvement). During the period of continuous improvement, the process of exchanging spray alcohol for alcohol gel was finalized, the disinfectant product was exchanged in terminal and concurrent cleanings, and a group of peripherally inserted central catheters (PICC) was formed. From August 2017, the CVC bundle and dressing film change were revised due to difficulty in adhering and intensifying hand hygiene campaigns. Beginning in November 2017, a multi-professional working group was set up with weekly meetings to evaluate bloodstream infection prevention practices, 2% chlorhexidine liquid soap exchange and daily catheter maintenance and passage audits. A specific professional for the neonatal ICU for guidance on hand hygiene of family members and employees.

Results: The incidence density of CVC-associated bloodstream infection in the reference period (1) was 21.59 (32/1482) per 1000 CVC / day and in the period of continuous improvement (2) was 5.74 (7) / 1218) per 1000 CVC / day (p = 0.0021). In 2018 it was 5.50 (12/2181) per 1000 CVC / day and in 2019 (January to August) it was 3.53 (5/1414) per 1000 CVC / day. The consumption of alcohol gel in period 1 was 34.61 mL / pct-day and in period 2, implantation of good quality alcohol gel in place of alcohol spray, 56.43 mL / pct-day. In 2018 it was 76 mL / pct-day and in 2019 it was 106 mL / pct-day.

Conclusions: We have evaluated that effective infection prevention bundle implementation measures and measures to encourage the use of alcohol in hand hygiene are effective measures to reduce bloodstream infection in hospital units.

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Abstract 2420

**Carbapenem resistance development in an OXA-499-harbouring, non-resistant *Acinetobacter pittii* isolate under imipenem selective pressure**

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**Background:** Carbapenem-resistance in *Acinetobacter pittii* poses crucial challenges to clinical treatments. Understanding the resistance development in carbapenem non-resistant strains could complement mechanisms for carbapenem resistance in *A. pittii*.

**Materials/methods:** *A. pittii* A1254 is an OXA-499-harboring clinical strain which is susceptible to imipenem (MIC, 2 mg/L) and intermediate to meropenem (MIC, 4 mg/L). Four colonies of the A1254 were passaged in media supplemented with 0.75 mg/L imipenem for 9 days. Breseq was employed to detect the mutations in four evolved populations at 9th day. Expression levels of *bla*OXA-499* were measured by quantitative reverse transcription PCR in two mutants. *bla*OXA-499* with its promoter (original or mutated) from A1254 and two mutants were respectively cloned into a vector pYMAb2-hyg* and transformed into *A. baumannii* ATCC17978, *A. pittii* LMG 1035 and A1254. MICs were evaluated by the broth microdilution method.

**Results:** Two carbapenem-resistant mutants (CAB009 and CAB010) with mutations at the promoter region of *bla*OXA-499* were isolated from two independently evolved populations. The mutation at position -14 (A to G) in CAB009 resulted in higher imipenem MIC (32 mg/L) and a higher *bla*OXA-499* expression level (4.53±0.19 fold relative to A1254) than another mutation at position -42 (G to A) in CAB010 (imipenem MIC, 8 mg/L). However, all transformed strains with either initial or mutated promoter were resistant to imipenem (16-64 mg/L) and meropenem (64-128 mg/L). Compared with transformed strains with the original promoter, *bla*OXA-499* with promoter from CAB009 (P009) conferred the highest MICs of imipenem (32-64 mg/L) among *A. baumannii* and *A. pittii* strains, but the increase of meropenem MIC (128 mg/L) was only observed in A1254 and LMG 1035, indicating that mutations at the promoter region were not indispensable for carbapenem resistance in transformed strains, but essential to the development of higher carbapenem resistance.

**Conclusions:** We demonstrated that carbapenem non-resistant *A. pittii* A1254 could turn carbapenem-resistant by a single base substitution at the promoter region of *bla*OXA-499* under imipenem pressure, indicating the need to monitor potential development of carbapenem-resistance when treating infections caused by non-resistant strains.

![Locations of mutations (blue), the start codon (red), the transcription initiation site (grey), -10 and -35 boxes (green) in CAB009 and CAB010.](image)

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Abstract 2424

Molecular evidence of bacteria with medical relevance in fleas parasitising cats and dogs
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Background: Even though a few microbial species are recognized as flea-borne human pathogens, a multitude of microbes may be identified in the microbiome of fleas. In this study we present medically relevant bacteria identified in the microbiome of cat and dog fleas in Greece.

Materials/methods: Fleas were collected in pools from individual cats and dogs presenting in small-animal clinics in Attica, Greece, during the period 2016-2017. The per pool extracted DNA was screened with 16s metagenomics for bacterial genera and/or species associated with human disease based on the International Statistical Classification of Diseases and Related Health Problems by WHO (ICD-10, 2016 version).

Results: Among the 100 flea-pools, collected from 67 cats and 33 dogs and stratified by flea species to 96 Ctenocephalides felis, two C. canis and two Pulex irritans pools, 19 phyla, 319 genera and 439 species of bacteria were recognized; 19 bacterial genera with potential medical relevance according to ICD-10 were identified in 93 flea-pools; a median of two bacterial genera were identified per flea-pool in cats [IQR=1;min=0,max=12] and a median of three in dogs [IQR=3;min=0,max=11] without significant difference between the two animal species (Mann-Whitney test, \( p=0.95 \)). The detected bacterial genera were Brucella spp., Coxiella spp., Legionella spp., Mycobacterium spp., Campylobacter spp., Salmonella spp. Bartonella spp., Clostridium spp., Corynebacterium spp., Haemophilus spp., Klebsiella spp., Nocardia spp., Pasteurella spp., Proteus spp., Pseudomonas spp., Rickettsia spp., Spirochaeta spp., Staphylococcus spp. and Streptococcus spp. Significantly increased prevalence was noted in Bartonella spp. from cat-borne flea-pools \( [OR=276, p<0.001] \) with no difference of the occurrence rate of the other bacterial genera between fleas collected from cats and the ones collected from dogs. Species identified included Clostridium perfringens, Haemophilus parainfluenzae, Klebsiella pneumoniae, Pasteurella multocida, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella enterica and Streptococcus suis.

Conclusions: The vectorial capacity and potential human health implications for many bacterial genera and species identified in fleas with molecular methods such as 16s metagenomics, is not meticulously investigated. DNA occurrence of medically important bacteria supports the rationale of more study about the potential role of fleas as vectors or disseminators of pathogens.

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**Abstract 2425**

**Assessing the impact of using sepsis bundle to salvage critically sick patients admitted with sepsis in a tertiary care hospital in India**

Malvika Srivastava¹, Summy Kumari², Rashmi Datta³

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**Background:** Advances in our understanding of heterogeneity of sepsis pathogenesis have made it clear that any single therapeutic intervention is ineffective in salvaging the affected patients. Bundles are a group of “therapies” built around the best evidence-based guidelines, which, when implemented together, produce greater benefit in terms of outcome than the individual therapeutic interventions.

**Materials/methods:** A prospective observational study was conducted in a new multi-speciality hospital over twenty months from February 2018 to October 2019 to demonstrate the impact of complying to the six sepsis bundle elements within the first six hours of presentation to the hospital. The six elements were as follows:

1. Measuring serum lactate
2. Obtaining Blood cultures prior to administration of antibiotics
3. Broad spectrum antibiotics administered within 3 hours of admission
4. Treat hypotension and elevated lactate (>4mmol/l) with fluids [Crystalloids at 30ml/kg]
5. Vasopressors [to maintain Mean Arterial Pressure (MAP) more than 65 mmHg]
6. Central venous pressure (CVP) to be maintained more than 8mmHg and Central venous oxygen saturation (ScvO2) of more than 70%

A total of 758 patients, more than eighteen years of age admitted to ICU and emergency with proven or suspected features of septic shock were included in the study.

**Results:** Among 758 patients admitted, 492 could be salvaged in ICU. Out of 492, complete compliance to 6 hours sepsis resuscitation bundle was seen in 340 patients. In 152 of 492 patients, partial or no compliance to sepsis bundle was seen. Of 266 who died, compliance to sepsis bundle was seen in 86 and non-compliance in 180 patients. Patients compliant to sepsis bundle got the mortality benefit. (odds ratio: 4.68, C.I. 3.4,6.45, p value < 0.5)

<table>
<thead>
<tr>
<th></th>
<th>Number of patients salvaged</th>
<th>Number of patients not salvaged</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis bundle applied:</td>
<td>400</td>
<td>152</td>
</tr>
<tr>
<td>Sepsis bundle not applied:</td>
<td>26</td>
<td>180</td>
</tr>
</tbody>
</table>

**Conclusions:** Critical Care Units should develop management strategies to ensure compliance with the sepsis bundles in order to decrease hospital mortality due to severe sepsis.

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Detection of norovirus major capsid protein using M-class UPLC/MSE

Pei-Yu Chu*, Michittra Boonchan*, Hui-Wen Huang*, Kazushi Motomura*, Liang-Yin Ke*

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Background: Norovirus is the most common foodborne pathogen, and norovirus-associated disease is a worldwide economic burden. Noroviruses are still uncultivable in the clinical laboratory, so specimens are usually detected using variable polymerase chain reaction. However, the high amplification sensitivity of RT-PCR can obtain false-positive results, and sequence-dependent amplification of RNA viruses with high mutation rates may obtain negative results in variant strains. Alternatively, M-class ultra-performance liquid chromatography (UPLC) with quadrupole time-of-flight (Q-TOF) MSE is a promising tool for high sensitivity and coverage in viral typing and identification.

Materials/methods: The GII.4 2006b VP1 proteins were constructed and used for peptide mapping and post-translational modification detection using UPLC/Q-TOF MSE for proteomic analysis of tryptic digests. The best region for identification was estimated using the Tree-Puzzle program.

Results: More than 95% total coverage of the 2006b of VP1 and each functional sub-domain was shown in VP1 digests. The missing residues were located at the N- and C-termini. The dominant peptide signal was located at P2-P1b, but it highly accumulated at the S domain. The phosphorylation sites accumulated in four of the five strongest peptide signals, especially in the hinge region. The full VP1 and S domains show the best identification signal based on tree-puzzle analysis.

Conclusions: The results of this study suggest that M-class UPLC combined with Xevo G2 Q-TOF/MS outperforms provide high sensitivity and sequence coverage. The P2-P1b and S domains were efficient targets for high-throughput diagnostic methods. Interestingly, the detected phosphorylation sites had a strong peptide signal, especially in the hinge region. This suggests an essential role of hinge region in the viral life cycle.

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Abstract 2429

The clinical and economic burden of mucormycosis in Japan

Rie Ueno*, Shinichi Nishimura1, Go Fujimoto1, Dilinuer Ainiwaer2, Seok-Won Kim2

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Abstract third-party references: MSD K.K., IQVIA Solutions Japan K.K.

Background: Mucormycosis is an uncommon but life-threatening infection that occurs in immunocompromised patients which may lead to high mortality and morbidity. Mounting evidence demonstrates an increasing economic burden attributed to mucormycosis. However, the majority of mucormycosis studies conducted in Japan are case reports or studies with small sample sizes with limited information. This study analyzed data evaluating clinical outcomes, resource utilization and costs associated with mucormycosis among inpatients in Japan.

Materials/methods: A descriptive, retrospective study was conducted including all patients, within a commercially available database (the MDV database), who were hospitalized with a diagnosis of mucormycosis [ICD-10 code (B46.x)] between January 1, 2010, and January 31, 2019 in Japan. Patient baseline characteristics and clinical information was collected as well as outcomes which included length of stay, mortality, readmission, utilization of IV antifungals, and costs. During the study period, data from a total number of 126 patients (main group) who had a record of hospitalization on the same month as the diagnosis, and a subgroup of 105 patients received L-AMB or AMPH-B treatment were analyzed.

Results: Approximately half of the patients were over 65 years old, of which 68.2% were male. The most common comorbidities were hematological malignancies (61.9%), followed by diabetes mellitus (46.0%). Mean duration of the index stay was 94 days for the main group, and 106 days for the subgroup. Mortality during the index stay was 35.7% in the main group, and 41.9% in the subgroup. The 30-day readmission rate in the main group and in the subgroup was 19.8% and 18.03%, respectively. The mean duration of IV amphotericin-containing regimen was around 37 days. For the main group, median total costs exceeded US $55,000 which included around US $37,000 in drug costs. Similar or even higher costs were observed in the subgroup who received LAMB or AMPH-B treatment during the index hospitalization.

Conclusions: This study demonstrated a high mortality rate based on the database results, and the considerable clinical and economic burden of mucormycosis in Japan.

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Abstract 2431

Performance of two rapid influenza diagnostic testing compared to real-time PCR
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Background: Influenza viruses cause acute respiratory diseases which is associated with morbidity and in some cases mortality. Since it is easily transmitted between human, rapid and accurate diagnosis is important for optimal patient care. At present, rapid influenza diagnostic testing (RIDT) is widely used in clinical setting due to its faster turn-around-time for results and its ease of use. However, test performance varies widely. In this study, we evaluated the performance two RIDT compared to real-time reverse transcription (RT)-PCR, using nucleic acid amplification test (NAAT) as the gold standard.

Materials/methods: Total 431 nasopharyngeal swabs were randomly collected from March, 2017 to March, 2019 (Influenza A, n=173; Influenza B, n=115; negative, n=143). Two RIDT, QuickNavi-Flu (Denka Seiken, Tokyo, Japan) and Genedia Greencare Flu A&B Antigen (Green Cross Corp., Korea) were compared to Allplex Respiratory Panel 1 (Seegene, Korea) real-time reverse transcription (RT)-PCR. Interpretation was done according to the manufacturer’s instructions.

Results: For influenza A, the sensitivities and specificities of the QuickNavi-Flu were 72.8%, 100% and Genedia Greencare Flu A&B Antigen were 75.7%, 98.1%, respectively. For influenza B, the sensitivities and specificities of the QuickNavi-Flu were 58.3%, 100% and Genedia Greencare Flu A&B Antigen were 57.4%, 99.4%, respectively. The agreement between QuickNavi-Flu and Genedia Greencare Flu A&B Antigen was 96.5% for influenza A and 98.6% for Influenza B. The Kappa ratio for those were 0.92 and 0.96, respectively.

Conclusions: This study indicates that RIDT has suboptimal sensitivity for both influenza A and influenza B, despite high specificity. The key advantage of RIDT is the production of quick result, in less than 10 minutes, which can help making clinical decision at that time. However, due to the limited sensitivities, negative results of RIDTs do not exclude influenza virus infection in patients with symptoms suggestive of influenza. Thus, confirmatory testing is always recommended.

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Genomic and environmental investigation of hospital room occupied by an imported case of meningitis due to extensively drug-resistant (XDR) *Pseudomonas aeruginosa*

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**Background:** Importation of highly resistant bacteria from high prevalence foreign countries is a major global public health concern. To prevent further spread, we investigated environmental contamination of a hospital patient room in Japan that was occupied by an imported case of meningitis due to extensively drug-resistant *Pseudomonas aeruginosa* (XDR-PA) who had undergone craniotomy in southeast Asian country with known colonization of XDR-PA and extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* (ESBL-KP) using whole-genome sequencing (WGS), and conducted room decontamination using ultraviolet-C (UV-C) device.

**Materials/methods:** Five XDR-PA and 2 ESBL-KP isolates were obtained from the patient. A total of 76 environmental cultures were taken from 19 sites in the patient's room, including 13 high-touch surfaces, 2 medical devices, and 4 sink components at following 4 different time points: before and after daily cleaning/disinfection, after discharge cleaning/disinfection, and after UV-C decontamination. UV-C decontamination was performed using Optimum UV™ with three 10-minute cycles. WGS was performed to determine the relatedness of clinical and environmental isolates with multiple resistance genes.

**Results:** Among the 19 sampling sites, XDR-PA and ESBL-KP isolates were detected in 2 sites (a bedside table and a sink surface) and 6 high-touch surfaces respectively before daily cleaning/disinfection (Figure). A sink surface and 3 high-touch surfaces (right bed rail, infusion pump control panel, spinal drain unit) were positive for XDR-PA and ESBL-KP, respectively, even after discharge cleaning/disinfection. After UV-C decontamination, these isolates were not detected from targeted environmental sites. WGS analysis revealed XDR-PA isolates from the patient and a bedside table and ESBL-KP isolates from the patient and 6 high-touch surfaces belonged to ST2613 and ST29 with similar resistance genes, respectively. XDR-PA isolates also harbored *bla*<sub>IMP-26</sub> carbapenemase that is rarely found in Japan.

**Conclusions:** Sink and high-touch surfaces were heavily contaminated with XDR-PA and ESBL-KP from an imported case despite standard terminal cleaning/disinfection, highlighting the need for enhanced disinfection methods to reduce a risk of acquiring these pathogens in patients subsequently admitted to the room. The use of UV-C device in addition to standard cleaning/disinfection was effective for decontamination of hospital room environment surfaces and medical equipment that were contaminated with XDR bacteria.
Abstracts 2020

Figure. (A) Sampling sites. Red and blue circles indicate XDR-PA-positive and ESBL-KP-positive respectively. Four boxes below the circle respectively indicate organism positive before and after daily cleaning/disinfection, after discharge cleaning/disinfection, and after UV-C decontamination from left to right. (B) Characteristics of resistance genes among isolates from the patient and environment.

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Abstract 2441

Short-term environmental contamination with MRSA explained by in-room activity of MRSA-colonised patients
Aline Wolfensberger*, Nora Mang1, Kristen Gibson2, Marco Cassone2, Kyle Gontjes2, Hugo Sax1, Lona Mody2,3

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Background: Rooms with methicillin-resistant Staphylococcus aureus (MRSA) colonized patients are often contaminated with MRSA. Little is known about influence of in-room patient activity on short-term hand and environmental contamination.

Materials/methods: An observational study was conducted at two hospitals, Hospital 1 in Zurich, Switzerland, and Hospital 2 in Michigan, USA. Inpatients with an MRSA infection and/or colonization were included. At first visit, groin, axilla, and nares were swabbed to assess the patient’s ‘colonization status’. Additionally, cultures were taken from the patient’s dominant hand and his environment. After disinfection of all sampled areas, microbiological cultures of hands, environment, and air (Hospital 1) were taken every 90 minutes for 5 hours, always followed by disinfection of sampled sites. Patient activity was assessed by questioning patients (Hospital 1) or by videotaping (Hospital 2).

Results: Ten patients were included in the study, of whom six received an MRSA-active antibiotic due to MRSA infection. The majority (7/10) was female, the average age was 52.8 years. In total, 360 patient and environmental swabs were obtained over 40 visits. MRSA was detectable in the groin, axilla, and nares in six, two, and four patients, respectively. At the first visit, a mean of 1.2 of six environmental sites were contaminated with MRSA. During the 90 minutes time intervals, 27% (95% Confidence interval: 12–46%) of patient hands newly acquired MRSA. Environmental sites were contaminated with a frequency of 6% (95%CI: 3–10%), with toilet seats being the most frequently contaminated site (17%, 95%CI: 6–35%), followed by the bed rail (13%, 95%CI: 2–40%). Patient activity explained the majority of environmental contaminations (8/10), e.g. all six toilet seat contaminations were preceded by toilet use. Conversely, not all toilet uses lead to seat contamination. Air samples were positive in 27% (95%CI: 8–55%), but we were not able to clearly identify a causative activity for this result.

Conclusions: Contamination of patient’s hands and environment with MRSA changes over short periods of time. Environmental MRSA can mostly be explained by patient activity and seems to correlate with the patient’s ‘colonization status’. The significance of frequently found airborne MRSA remains unclear.

Figure 1. Depiction of patient colonization status, hand and environmental contamination, and description of patient activity

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Abstract 2444

Clinical evaluation of a novel chemiluminescent microparticle immunoassay of Aspergillus galactomannan in diagnosis of invasive aspergillosis

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Background: Aspergillus galactomannan (GM) ELISA assay has been proved as an important indicator of probable invasive aspergillosis (IA), and it has been widely used especially for patients with haematological malignancy. The disadvantage of ELISA includes cumbersome procedures, false positive problems and numerous interference factors. Other proposed manual or semi-automatic strategies cannot meet the large-scale requirement either. Therefore, developing a specific, sensitive and automatic detection and quantitation strategy for clinical diagnosis and therapeutic monitoring of GM is in urgent demand. In this study, we used galactomannan monoclonal antibodies to establish a chemiluminescent quantitative detection method based on an automatic chemiluminescent analyzer (Fig). The clinical assessment was also carried out.

Fig: Schematic of the magnetic microparticle-based automatic chemiluminescent immunoassay for GM

Materials/methods: A total of 321 serum samples were collected according to the revised EORTC/MSG guideline (2008), and tested by Automatic Chemiluminescent microparticle immunoassay for GM (Dynamiker, China). All the samples from the Shan-dong and Tianjin Provincial Chest Hospital. Those including 126 IA samples (proven, n=43; probable, n=83) and 195 negative samples. Those samples were compared with PlateliaTM GM ELISA (Bio-Rad, USA).

Results: Through the analysis of 321 serum samples, the Automatic Chemiluminescent microparticle immunoassay sensitivity and specificity was 83.33%, 82.05%, respectively. The positive coincidence rate, negative coincidence rate and total coincidence rate of automatic chemiluminescent microparticle immunoassay compared with PlateliaTM was 91.03%, 96.30% and 95.02%, respectively.

Conclusions: The Dynamiker automatic chemiluminescent microparticle immunoassay for GM, with competent specificity and sensitivity, is highly consistent with Bio-Rad PlateliaTM GM ELISA. It could be used as a rapid test to support the diagnosis of IA.

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Abstract 2445

Molecular epidemiology and clinical features of human adenovirus: a 20-year retrospective observational study in Bern, Switzerland

Joyce Odeke Akello* 1;2;3, Richard Kamgang1, Maria Teresa Barbani1, Franziska Suter-Riniker1, Stephen L. Leib1, Alban Ramette1

1University of Bern, Institute for Infectious Diseases, Bern, Switzerland, 2Spiez Laboratory, Spiez, Switzerland, 3Graduate School for Cellular and Biomedical Sciences, University of Bern, Bern, Switzerland

Background: Human adenovirus (HAdV) is an important viral pathogen, especially in young children. It is often implicated in keratoconjunctivitis, pharyngoconjunctival and various respiratory illnesses.

Materials/methods: In this retrospective observational study, we analysed data of HAdV positive patients who presented at the University Hospital of Bern, one of the largest hospitals in Switzerland. Various biological samples (conjunctivitis swabs, respiratory tract, stool, urine, blood, or genital swab) were tested for HAdV positivity using routine diagnostic methods including PCR, immunofluorescence, virus culture, or ELISA. Multivariate analysis was used to identify epidemiological trends and risk factors associated with increased number of HAdV cases over the study period. HAdV genotyping was performed by sequencing PCR amplicons targeting the hexon gene. Phylogenetic comparison of the obtained sequences with HAdV reference strains was performed to determine genotype relatedness.

Results: HAdV infection was confirmed in 1,302 samples that were collected between 1998 and 2017. Cases of HAdV infection were reported throughout the years with no clear seasonality, with the exception of reoccurring peaks in HAdV cases occurring every four years among young children. Increased number of HAdV cases were observed in years 2009 [n = 110] and 2010 [n = 112]. Upper respiratory tract samples, conjunctivitis swabs, and stool were associated with the highest positivity rates, with 56.2%, 18.7% and 14.2% of the cases, respectively. HAdV infection was highest among young children (on average 57.2%). HAdV genotyping for 145 positive samples from years 2009 and 2010 identified HAdV8 as the predominant genotype contributing to HAdV infection among young adults (20-44 years), middle aged (45-64 years), and elderly (65-100 years) patients. Predominant genotypes among young children were HAdV1, HAdV2, and HAdV3. The most prevalent genotypes circulating among young children in the 20-year period belonged to HAdV species C. Phylogenetic analysis showed close relationship among the identified genotypes and international reference strains.

Conclusions: Our study gives novel insights on long-term epidemiological trends and genotypic relatedness among HAdV strains causing infections in patients from one of the largest hospitals in Switzerland, country in which little data on HAdV prevalence and diversity was so far available.

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Abstracts 2020

Abstract 2447

Molecular epidemiological survey of Staphylococcus lugdunensis isolates with different copies of the repeat region in the gene encoding the von Willebrand factor-binding protein

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Background: The von Willebrand factor binding protein (vWbl) is a surface protein and a virulence factor of staphylococcus lugdunensis. The vWbl gene has 4 major regions, including S (signal peptide), A (non-repetitive region), R (repeat-region), and W (wall-associated region). Previous studies demonstrated that the R region of the vWbl gene contains ten copies of repeated sequences, referred to as vWbl repeats. Our preliminary study revealed that the number of vWbl repeats vary among different clinical isolates. In this study, we conducted an epidemiological surveillance of S. lugdunensis to determine whether the copy number of vWbl repeats correlates with the types of infections caused by the isolates.

Materials/methods: Two hundred and nine isolates including 164 oxacillin sensitive and 45 oxacillin resistant S. lugdunensis were collected during the period of 2003 to 2014 from different patients in Taiwan. SCCmec typing and MLST were performed on each isolate, and the copy number of vWbp repeats in each isolate was determined based on the sizes of PCR products.

Results: Approximately 50% (105 of 209) of the isolates were from blood, and most of them contained thirteen (36, 34%), nine (30, 28.5%), or twelve (20, 19%) copies of vWbl repeats. The 45 oxacillin resistant isolates were found to have nine (28, 62%) or thirteen (14, 31%) vWbl repeats. Twenty-seven of the 28 isolates with 9 vWbl repeats were SCCmec V or Vt and belonged to ST3, and all isolates with 13 vWbl repeats were SCCmec II and of ST6. Most isolates (49 of 55) with 9 vWbl repeats had a stop codon at the codon in the third repeat, suggesting the production of a nonfunctional vWbl. None of the isolates from endocarditis patients had 9 vWbl repeats.

Conclusions: The number of vWbl repeats varied among Staphylococcus lugdunensis isolates from different patients. None of isolates from patients with endocarditis contained 9 vWbl repeats. Results of this study suggest that the number of vWbl repeats in S. lugdunensis may correlate with its pathogenicity.

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Characterisation of a fibronectin binding protein in the virulence of Streptococcus parasanguinis FW213

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Background: Streptococcus parasanguinis is a dominant isolate and a primary colonizer of the dental biofilm. Upon gaining entrance to bloodstream, S. parasanguinis could potentially cause life-threatening subacute endocarditis and other systemic infections. By using BLASTP, a fibronectin binding protein (Fbp) homolog, Spaf_1 409 was identified from the genome of strain FW213. As fibronectin exists widely on host tissues and in bloodstream, Fbps are known to play important roles in establishing infection by many pathogens. Thus, this study was designed to investigate the function of Spaf_1 409 in the pathogenicity of S. parasanguinis FW213.

Materials/methods: By using a Spaf_1 409 knockout strain (MPH4) and various in vivo and in vitro analyses, including ELISA, western blotting, a flow-cell biofilm system couple with CLSM examination, macrophage survival assays, flow cytometry analysis, and the the Galleria mellonella larva model, the binding specificity and location of Spaf_1 409, and the role of Spaf_1 409 in biofilm formation, survival within macrophages and systemic infections were determined.

Results: Spaf_1 409 is the key ligand of S. parasanguinis FW213 for fibronectin and could be found both on the cell-wall fraction and growth supernatant of S. parasanguinis cultures. Inactivation of Spaf_1 409 reduced the ability of S. parasanguinis to withstand the shearing force from the medium flow in a flow-cell biofilm system, suggesting that Spaf_1 409 mediates bacterial cell-cell interaction. The phagocytic rate of MPH4 by RAW264.7 macrophages was lower than that of wild-type FW213, and less viable MPH4 cells could be detected within RAW264.7 macrophages. Thus, the reduced survival rate of MPH4 compared to wild-type FW213 may result from a reduced phagocytic rate and/or intracellular survival ability. Suprisingly, MPH4 exhibited an enhanced virulence in G. mellonella larvae.

Conclusions: Spaf_1 409 mediates the binding of S. parasanguinis FW213 to fibronectin and cell-cell interaction during the development of biofilm. Spaf_1 409 is also a target for RAW264.7 macrophages during phagocytosis, but inactivation of Spaf_1 409 increased the virulence of S. parasanguinis FW213 in G. mellonella larvae. Thus, inactivation of Spaf_1 409 may reduce the killing by macrophages due to reduced phagocytosis, but Spaf_1 409-null S. parasanguinis is more virulent in systemic infections.

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Abstract 2449

Risk factors for healthcare-associated infections caused by cefepime resistant Pseudomonas aeruginosa in a tertiary care hospital in Serbia

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Background: Cefepime can be considered as one of the agents of potential choice for treatment of moderate to severe healthcare-associated infections (HAIs) causing Pseudomonas aeruginosa. However, new reports point to growing frequency of cefepime resistant P. aeruginosa (CRPA) as a causative agent of mentioned infections and associated poorer treatment outcomes. Previous research has tried to identify some of the risk factors for the onset of HAIs caused by this pathogen, but there is still a gap in clinical knowledge regarding the risk factors, especially those associated with fatal outcome. The aim of our study was to identify risk factors associated with HAIs caused by CRPA, not only in whole population of patients with HAIs, but also in the subgroups of patients who died in hospital.

Materials/methods: The study was conducted as combination of two nested case/control studies within the cohort of patients with HAIs caused by P. aeruginosa, regardless of localization, prospectively followed from January 2009 to December 2017 in a tertiary care hospital in Serbia. Influence of risk factors on specific outcomes was estimated by adjusted odds ratios calculated from multivariate logistic regressions.

Results: Six independent risk factors for CRPA infections were identified: the existence of another HAI (aOR=2.257; p=0.001), hospitalization in ICU longer than one month (aOR=2.440; p=0.007), longer stay in hospital until infection (aOR=1.049; p=0.004), longer use of mechanical ventilation (aOR=1.035; p=0.036), administration of antibiotics before infection (aOR=1.755; p=0.001) and previous use of fluoroquinolones (aOR=2.024; p=0.030). Further, independent risk three independent risk factors have been identified for the fatal outcome: traumatic injury (aOR=12.639; p=0.020), existence of another HAI (aOR=4.599; p=0.001) and long-term use antibiotics before HAI (aOR=1.118; p=0.034).

Conclusions: Risk factors for HAIs with CRPA are primarily linked to pre-infection use of systemic antibiotics, which is a common pathway for selection of multi, extensive or pan-resistant strains of P. aeruginosa that invade tissues and cause infection or to increased use of antibiotics, which is common way for induce HAI in general, including that caused by CRPA. Implementation of adequate corrective measures in order to improve the actual situation in healthcare associated infections area is necessary.

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Impact of Point-of-Care testing on the surveillance of respiratory viral infections in West Midlands, England

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**Background:** Respiratory viruses cause 44% of hospital admissions due to acute respiratory illness in central England. To support clinical management of these cases, Point-of-Care Testing (PoCT) for selected respiratory viruses is being introduced into hospitals in the UK.

In England, routine laboratory surveillance of infections is via Public Health England's Second Generation Surveillance System (SGSS), which is based on electronic reports from Laboratory Information Management Systems (LIMS). Reports generated from this system are a key component of national and local NHS winter planning. If PoCT devices are not interfaced with LIMS, these results may be excluded from routine surveillance. We therefore undertook a survey and case study in August 2019 to determine the extent of PoCT’s in West Midlands hospitals and identify potential gaps in surveillance.

**Materials/methods:** We sent a questionnaire to all microbiology laboratories in West Midlands to determine whether PoCT was being planned or already implemented; and whether these data are captured in LIMS. PoCT data was provided by one hospital during the 2018/19 influenza season to compare with PHE SGSS surveillance data for the same period.

**Results:** All thirteen West Midlands microbiology laboratories responded. Three hospitals reported using PoCT, with two performing influenza A & B and RSV and one performing just RSV tests. Four hospitals plan to introduce PoCT for respiratory virus infections for the 2019/2020 season. The two hospitals performing PoCT for influenza A & B and RSV did not send results to their LIMS; however, the hospital performing only RSV PoCT entered their positives cases into their laboratory system.

PoCT data from one hospital collected between December 2018 and May 2019 showed 461 positive records (433 influenza A, 6 influenza B and 22 RSV). Only 8 (2%) of these records were found in the PHE SGSS database.

**Conclusions:** PoCT testing has major implications for current surveillance systems. Our finding highlights the need for healthcare organisations to ensure UK statutory reporting obligations are met to prevent the serious misrepresentation of the incidence of key public health infections, and consequent loss of utility for public health functions such as winter planning.

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Benzimidazole SPR719/720 is a potent new candidate for treatment of non-tuberculous mycobacterial infections
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Background: The outcomes of antibiotic treatment of nontuberculous mycobacterial (NTM) disease are very poor and new drugs and regimens are urgently needed. A novel benzimidazole SPR719, the active moiety of SPR720, showed low minimum inhibitory concentrations (MIC) against Mycobacterium abscessus, Mycobacterium avium complex (MAC) and Mycobacterium kansasii. Therefore we aimed to explore the potential role of SPR719/720 in the treatment of NTM disease.

Materials/methods: MICs and minimum bactericidal concentrations (MBC) of SPR719 against clinical and reference strains of M. avium complex, M. kansasii and M. abscessus were determined by broth microdilution, according to CLSI guidelines. Synergy between SPR719 and key antimycobacterial drugs was assessed using checkerboard microdilution assays. To study pharmacodynamics, time-kill assays with SPR719 alone were performed and in the combination with drugs that proved to have the most synergistic effect.

Results: The MIC50 and MIC90 for SPR719 were 1 and 2 mg/L, respectively for MAC and M. kansasii and 2 and 8 mg/L, respectively for M. abscessus. SPR719 was bacteriostatic against all tested NTM strains (MBC/MIC ratio ≥8). SPR719 had no interaction with other anti-mycobacterial drugs, but showed low fractional inhibitory concentration index values with ethambutol (∑FIC =0.8) for M. avium and M. kansasii and with clarithromycin for M. abscessus (∑FIC =0.8). SPR719 as monotherapy displayed significant concentration-dependent activity in time-kill assays (Figure 1) and the combination of SPR719 with ethambutol (for M. avium and M. kansasii) and clarithromycin (for M. abscessus) showed more killing over time than SPR719 alone.

Conclusions: SPR719 exhibits potent antimycobacterial activity against the NTM strains of MAC, M. kansasii, and M. abscessus evaluated. Time-kill assays indicate SPR719 is a potent monotherapy against M. avium and displays increased activity when used in combination with ethambutol. For M. abscessus SPR719 in combination with clarithromycin outperformed either agent alone. These data confirm that SPR719 is active against key NTM pathogens and that SPR-720 could serve an important role as a new oral agent for the treatment of NTM pulmonary disease.

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Abstract 2457

Clinical impact of ceasing isolation procedure using a single molecular test for suspected pulmonary tuberculosis in The Royal Melbourne Hospital

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Background: Active pulmonary tuberculosis (aPTB) transmission in health care centers is concerning and infection prevention policies previously recommended isolation in airborne precautions until three daily samples of sputum became acid-fast bacilli (AFB) negative. Recently, the use of molecular testing was assessed regarding accuracy and cost-effectiveness in hypothetical situations. Newer guidelines recommend using Xpert MTB/RIF testing in strategies around patient isolation, however, few studies examine the real impact of this. Since November 2018, our hospital changed procedure to follow these recommendations in patients with a low index of suspicion of aPTB.

Materials/methods: We performed an observational retrospective study examining all cases admitted with suspected aPTB in airborne precautions during two 4-month periods: Period A, when the three negative AFB sputum were required and Period B, requiring only one single Xpert MTB/RIF negative sputum to cease isolation in patients with a low index of suspicion of active disease. We used infection prevention software to detect cases and reviewed electronic medical records to collect clinical and microbiological data.

Results: 76 cases were isolated for suspected aPTB (40 vs. 36), from which 15 confirmed cases were excluded (8 vs. 7). Six patients in period A and 16 in period B had Xpert MTB/RIF performed on the first sputum. There was no significant difference in the mean isolation days between the periods (3.9 vs. 4.7 days, P=0.4). Time taken to de-isolate was shorter in the infectious diseases and respiratory units compared with other units overall (3.4 vs. 5.1 days, P=0.01), although the time stayed the same for the infectious diseases/respiratory units in each time period (3.5 vs. 3.4 days, P=0.90) and lengthened in the other units (4.3 vs. 5.82 days, P=0.25).

Conclusions: We did not find the expected reduction in isolation time in our hospital using a new protocol including molecular testing. This may be because the decision and practicalities around de-isolation are affected by a range of logistic issues as well, for example the workflow on ward. The impact of a new test needs more than just change of policy, so future work could be more explicit about the ‘cascade of management’ needed around this.

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Abstract 2459

**Comparison of two commercial platforms for identification of bacteria and Candida isolates at species-level by MALDI-TOF MS in Shenzhen, China**

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**Background:** MALDI-TOF mass spectrometry is a revolutionary technology for identification of microorganisms. We aim to compare the performance of two commercial MALDI-TOF MS Systems.

**Materials/methods:** A total of 541 clinical isolates including 448 clinical specimens collected from patients who admitted to an accredited hospital in Shenzhen, China from November 2018 to January 2019 and 93 archived strains stored at -80°C were identified by MicroIDSys system (ASTA, Korea) and Microflex LT system (Bruker Daltonics, Germany). Direct transfer-formic acid and/or ethanol-formic acid extraction procedures with α-cyano-4-hydroxycinnamic acid matrix solution were used to acquire the peptide profiles by the systems, and subsequently analyzed using Biotyper and MicroIDSys database softwares respectively. The identification scores ≥2 and ≥140 were considered to be reliable at species-level for Microflex LT and MicroIDSys systems respectively. 16S rRNA gene sequencing were applied to verify the discrepancies between the two systems and the protein spectra with scores <2.0 (Microflex LT) and/or <140 (MicroIDSys).

**Results:** Among the 541 isolates involving 90 strains, 95.7% (518/541) obtained the identical results achieving species-level with scores ≥2 for Microflex LT and ≥140 for MicroIDSys. The top twenty frequently isolated strains were Escherichia coli (n=40), Klebsiella pneumoniae (n=37), Pseudomonas aeruginosa (n=32), Staphylococcus aureus (n=29), Acinetobacter baumannii (n=26), Enterococcus faecalis (n=21), Streptococcus agalactiae (n=19), Streptococcus pneumoniae (n=19), Staphylococcus epidermidis (n=18), Enterococcus faecium (n=16), Stenotrophomonas maltophilia (n=15), Haemophilus influenzae (n=14), Moraxella catarrhalis (n=14), Proteus mirabilis (n=12), Streptococcus pyogenes (n=12), Enterobacter cloacae (n=11), Citrobacter koseri (n=10), Candida albicans (n=9), Serratia marcescens (n=9), Candida tropicalis (n=9), Klebsiella oxytoca (n=8), Staphylococcus hominis (n=8) and Streptococcus mitis (n=8). Except for A. baumannii (96.2%), the agreement rate with identical results achieving species-level with scores ≥2 for Microflex LT and ≥140 for MicroIDSys for other 19 top twenty strains were 100%. Nine rare strains including Actinomyces euopeuse (n=1), Achromobacter mucicolens (n=1), Bacillus velezensis (n=1), Burkholderia ambifaria (n=1), Comamonas terrigena (n=1), Enterobacter xiangfangensis (n=1), Neisseria cinerea (n=2), Pantoea agglomerans (n=1), and Streptococcus tigurinus (n=1) were not identified or misidentified by both platforms.

**Conclusions:** The ASTA MicroIDSys system has comparable identification performance to the Bruker Microflex LT system.

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Abstract 2460

**Encephalitis in French travellers, 2016-2019**

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**Abstract third-party references:** French public health agency [Santé publique France], French Infectious Diseases Society

**Background:** Encephalitis diagnosis in travelers is challenging, especially when they return from areas with different vectors and animal reservoirs. However, they might also be exposed to very common infectious agents, or be infected before they travel. Therefore, solid data is needed to prioritizing the etiological investigation in returning travelers presenting with encephalitis. Our study aimed at describing returning travelers enrolled in the ENCEIF cohort with regards to their cause of encephalitis, destination, and reported at-risk exposures.

**Materials/methods:** Patients matching the case definition of encephalitis [Venkatessan et al. CID 2013] were prospectively enrolled. Demographic data, medical history, clinical and diagnosis characteristics were gathered in a standardized manner. Travelers were defined as people who reported a travel out of France during the 6 months before onset, or who were resident of another country and diagnosed during a stay in France.

**Results:** As of 16th October 2019, 69/ 476 [15%] enrolled patients were travelers. They had visited or lived in Europe [n=34], Africa [n=20], Asia [n=5], Middle-East [n=4], North America [n=4], South America [n=1], and South Pacific [n=1]. With regards to visited countries, 18/69 [26%] had stayed in a tropical area. The most frequent diagnosis in travelers were HSV [13%] and tuberculosis [9%], but 13 [19%] had an arboviral encephalitis (West Nile, Japanese Encephalitis, Tick-borne Encephalitis, Chikungunya, Toscana and Zika). Arboviruses accounted for 20% of travelers returning from a European country. On discharge, 66% had minor or no sequelae on Glasgow outcome scale, and none died. 4 reported being bitten by a carnivore during their travel, but none were diagnosed with rabies or another zoonotic infection.

**Conclusions:** In our cohort, travelers were more frequently infected with a flavivirus or alphavirus than with HSV. However, HSV accounted for 13% of cases and tuberculosis for 9%. Our results suggest that specific arboviruses should be investigated early in travelers, even those visiting Europe, but the usual culprits should not be excluded. In our cohort, only few patients were exposed to animals during their travel, making it impossible to discuss this as an at-risk exposure.

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Performance evaluation of the BD Kiestra ID/AST prototype for automatic colony picking, Bruker MALDI Biotyper target plate spotting and Phoenix AST panel preparation and loading

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Background: The emergence of automation in bacteriology opens a new era in clinical diagnostic laboratories. The development of additional automated solutions is required to provide a fully automated solution from sample to results. We thus evaluated in this study the performance of a Becton Dickinson Kiestra™ IdentifA/SusceptA prototype for automatic colony picking, bacterial suspension preparation, MALDI-TOF target plate spotting and Phoenix AST panels preparation and loading.

Materials/methods: The performance of the IdentifA/SusceptA prototype controlled by dedicated research software designed for this study was compared to conventional manual processing (direct spotting on the MALDI target plate) for MALDI-TOF identification (ID) and Phoenix M50 antibiotic susceptibility testing (AST). The evaluation was performed on 1305 clinical microbial isolates for ID and 336 isolates for AST representing 66 species isolated from 22 different clinical specimen types.

Results: The IdentifA exhibited a higher performance than manual processing for Gram-negative bacteria with an ID at the species level (score >2) of 96.3% and 86.8%, respectively. A significant better performance (score >2) was observed with the IdentifA (95.3%) compared to manual spotting (75.3%) from colonies on MacConkey agar. Compared to manual processing, the IdentifA exhibited a lower ID performance at the species level (score >2) for streptococci, coagulase-negative staphylococci (ConS) and yeasts with 76.2% and 92%, 73.4% and 90%, 41.3% and 73.2%, respectively. Staphylococcus aureus and enterococci were similarly identified by the two approaches with 92% ID rate (score >2).

For AST, the SusceptA exhibited an overall essential agreement and category agreement of 98.8%, 0.22% (14/6295) major errors (ME) and 1.23% (7/570) very major errors (VME) compared to the reference Phoenix M50 manual AST checked and corrected by Etest MICs for discrepant results. ME and VME were reported for 7 and 5 antibiotics, respectively.

Conclusions: The IdentifA prototype exhibited a high identification performance for the majority of isolates. The reduced performance with streptococci and ConS was observed with tiny colonies on CHROMagar. Similarly, the SusceptA prototype showed a high performance for AST with only 14 ME and 7 VME out of 6950 antibiotics tested. Five VME would have been corrected due to unusual profiles, natural resistance or laboratory routine confirmatory procedures.

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Abstract 2466

Duration of colonisation with vancomycin-resistant Enterococcus faecium in a large ST796 vanB hospital outbreak: a cohort study

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Background: During a large hospital outbreak with predominantly vanB vancomycin-resistant Enterococcus faecium (VRE), ST 796, we identified more than 500 VRE-carriers. Colonized patients are placed on contact isolation precautions, including upon subsequent admissions. As these measures are resource-intensive, we aimed at determining the optimal interval for rescreening to document VRE clearance.

Materials/methods: Cohort study from January 2018 to November 2019 in the six Insel Group hospitals (~1600 beds), Bern, Switzerland. We included newly identified VRE carriers with at least one follow-up rectal swab. Testing was PCR-based with prior enrichment in selective broth and subsequent culture-based confirmation. Follow-up swabs were collected (not systematically) during subsequent hospitalizations. VRE clearance was defined as a VRE-negative rectal PCR; however, for the definitive discontinuation of contact precautions we required a minimum interval of six months after the last VRE detection in addition to confirmatory negative screenings. We predicted VRE clearance at given time points with a generalized additive model.

Results: We included 77 VRE-carriers with a median of one (interquartile range [IQR] 1-2) follow-up swabs, 67/77 (87.0%) being VRE vanB. Follow-up screenings were conducted at a median of 85 days (IQR 8-232) after initial VRE detection. The predicted likelihood of a VRE carrier to remain colonized (Figure 1) at 30 days was 67.8% (95% confidential interval [CI] 51.5-84.1), at 90 days 26.1% (95% CI 6.1-46.0) and at 180 days 20.6% (95% CI 4.2-36.9). We observed no VRE recolonization once a follow-up was negative.

Conclusions: VRE colonizations halved within 50 days and were reduced substantially [by roughly 80%] within 3-6 months. Depending on the availability of isolation rooms and the lab capacity during a VRE outbreak, follow-up swabs of VRE-carriers should be taken earliest at 3 months after the last VRE detection.

Figure 1: Probability of persistent VRE carriage as a function of time interval since detection (bright blue dots = PCR positive, dark blue dots = PCR negative).

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Prevalence of carriage and characterisation of extended-spectrum beta-lactamase-producing Escherichia coli in healthy pregnant women living in Madagascar

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Background: ESBL dissemination in the community is a major public health concern worldwide. WHO has developed a one-health surveillance project called «Triycle» focusing on ESBL -E. coli in humans, the environment and the food chain. Here we present the first results from the human component in Madagascar.

Materials/methods: Rectal swabs were collected prospectively in 2018 from Malagasy pregnant women close to delivery from two maternity wards in the capital (Antananarivo) and one in province (Mahajanga). Samples were plated on MacConkey agar supplemented with 4 mg/L cefotaxime in the laboratories of the RESAMAD network [Madagascar]. Isolates were then shipped to France for identification on a Vitek2 system and antibiotic susceptibility testing by disk-diffusion according to EUCAST guidelines. Whole genome sequencing was performed on an Illumina NextSeq system.

Results: In all, 299 pregnant women [mean age = 27 year old] were sampled, of those 93 (31.1%) were ESBL -E. coli positive. Prevalence was 23% (45/199) in women from the capital and 48% (48/100) in province [p<0.01]. 16% of the strains were resistant to piperacillin/tazobactam, 10% to amikacin, 39% to gentamicin, 68% to ciprofloxacin and 80% to co-trimoxazole. All isolates were susceptible to colistin and fosfomycin. A single one was resistant to carbapenems. Whole genome sequencing was performed on 86 of 111 isolates. blaCTX-M-15 was the most frequent ESBL gene, observed in 86% (n=74) of the isolates, followed by blaCTX-M-27 (8%, n=7). One strain harboured the blaCMY-2 plasmid-borne cephalosporinase gene and the carbapenem resistant strain carried the blaNDM-5 gene. Most isolates belonged to commensal phylogenetic groups: A (73%), B1 (14%) and C (1%) and to a lesser extent to extra-intestinal virulent groups B2 (5%), D (6%) and F (1%). Multi locus sequence typing showed 42 different sequence types (ST) gathered in 24 clonal complexes (CC), the most frequent being CC10 (37% of the isolates), CC155 and CC450 (6.7% each) and CC131 (4.5%).

Conclusions: Prevalence of ESBL-E. coli in the community in Madagascar is high, especially in province and is consistent with the ESBL global epidemiology with the predominance of blaCTX-M-15 and E. coli CC10. The detection of carbapenemase producing E. coli in the community is worrying.

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Abstract 2471

Predictors of mortality of influenza virus infections in a Swiss hospital during four influenza seasons: role of quick sequential organ failure assessment

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Background: Influenza infections have been associated with high morbidity. The aims were to determine predictors of mortality among patients with influenza infections and to ascertain the role of quick Sequential Organ Failure Assessment (qSOFA) in predicting poor outcomes.

Materials/methods: All adult patients with influenza infection at the Hospital of Jura, Switzerland during four influenza seasons (2014/15 to 2017/18) were included. Cepheid Xpert Xpress Flu/RSV was used during the first three influenza seasons and Cobas Influenza A/B and RSV during the 2017/18 season.

Results: Among 1684 influenza virus tests performed, 441 patients with influenza infections were included (238 for influenza A virus and 203 for B). The majority of infections were community onset (369; 83.7%). Thirty-day mortality was 6.0% (25 patients). Multivariate analysis revealed that infection due to A virus (P 0.035; OR 7.1; 95% CI 1.1-43.8), malnutrition (P<0.001; OR 25.0; 95% CI 4.5-138.8), hospital-acquired infection (P 0.003; OR 12.2; 95% CI 2.3-65.1), respiratory insufficiency (PaO2/FiO2<300) (P<0.001; OR 125.8; 95% CI 9.6-1648.7) and pulmonary infiltrate on X-ray (P 0.020; OR 6.0; 95% CI 1.3-27.0) were identified as predictors of mortality. Among 287 patients requiring hospitalization, mortality was independently associated with infection due to A virus (P 0.035; OR 7.1; 95% CI 1.1-43.6), malnutrition (P<0.001; OR 24.0; 95% CI 4.5-137.8), hospital-acquired infection (P 0.003; OR 12.1; 95% CI 2.3-64.7), respiratory insufficiency (PaO2/FiO2<300 mmHg) (P<0.001; OR 123.7; 95% CI 9.4-1635.2) and pulmonary infiltrate on X-ray (P 0.021; OR 5.9; 95% CI 1.3-26.8). qSOFA showed a very good accuracy (0.89) equivalent to other more specific and burdensome scores such as CURB-65 and Pneumonia Severity Index (PSI).

Conclusions: qSOFA was equivalent to specific severity scores (PSI, CURB-65) in predicting mortality. Infection by influenza A virus, respiratory insufficiency and malnutrition were associated with worse prognosis.

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Comparative analysis of diagnostic utility of microbial metagenomic next-generation sequencing among different sample types

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Background: Microbial metagenomic sequencing was suggested to potentially replace traditional microbiological methodology because of its comprehensiveness and sensitivity. Here we aim to systematically compare the sensitivity and specificity of various clinical sample types for maximizing its diagnostic performance.

Materials/methods: From April 2017 to October 2019, 2,725 clinical biospecimen were collected, with 2419 samples were retrospectively diagnosed as infectious disease (1647, 68.1%), non-infectious (467, 19.3%) and unknown causes (305, 12.6%). 2,206 specimens were tested on-site with a fast turnaround time of 48h. using BGI platform localized in Zhongshan Hospital in Shanhgai, China. 583 of these patients were collected with multiple specimens for diagnosis The positivity rate of various sample types was compared, including plasma (n=757, 27.8%), sputum (n=515, 18.9%), bronchoalveolar lavage fluid (BALF) (n=460, 16.9%), tissue (n=430, 15.7%), body fluid (n=379, 13.9%), cerebrospinal fluid (CSF) (n=85, 3.1%), and the other (99, 3.6%). The pathogen biomass level in different sample types was also assessed.

Results: In infectious diseases, the positive rate of metagenomic test was higher in sputum (254/515, 55.2%), followed by BALF (206/460, 44.8%), plasma (202/757, 43.9%), while the least detection rate was shown in CSF (5.9%). In most cases, plasma was inferior to samples from primary infectious site, even in infectious endocarditis (22.2% vs 52.6%, p<0.01) and intra-abdominal infection (36.0% vs 52.4%, p<0.05) where blood stream infection is common. Importantly, for some microbes such as virus and Pneumocystis carinii, plasma shared the same detection rates with other specimen. Interestingly, a higher positivity in BALF than that in sputum and tissue (82.4 vs 50.0%, p<0.01) were observed for non-tuberculosis mycobacteria but not mycobacteria tuberculosis or fungus.

Conclusions: In most cases, a higher sensitivity for pathogen identification could be obtained by testing samples from primary infectious sites, and by choosing appropriate specimen depending on potential microbes consideration. Therefore, sample selection of metagenomic sequencing, not the technique itself, needs hypothesis.

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**Serotype is associated with high rate of colistin resistance among clinical isolates of Salmonella from China**

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**Background:** To investigate the reason that the ratio of colistin resistant clinical isolated *Salmonella* (MIC >2 mg/L) were significantly higher than other Enterobacteriaceae, such as *Escherichia coli* and *Klebsiella pneumoniae* in China.

**Materials/methods:** *Salmonella* isolates were collected from fecal and blood samples of patients. Serotyping was conducted according to the White–Kauffmann–Le Minor scheme. Broth microdilution was used for colistin MIC determination. Representative isolates were subjected to detailed characterization and phylogenetic analysis by whole genome sequencing (WGS).

**Results:** In this study, 42.77% (136/318) clinical isolated *Salmonella* were resistant to colistin. *mcr-1* gene and mutations in PmrAB confer little for high rate of colistin resistant *Salmonella* isolated from human patients, because only two of the 136 colistin resistant isolates were *mcr-1* positive (both serotype Typhimurium) and other two possessed PmrAB mutations (serotype Gallinarum and Goldcoast). MIC distribution for colistin at serotype level among the two most prevalent serotypes originating from humans in China indicated that *Salmonella* Enteritidis (83.9% resistance, 125/149) were significantly less susceptible than *Salmonella* Typhimurium (15.3% resistance, 9/59, P<0.01). The high isolation rate of *S.* Enteritidis and high rate of colistin resistance in *Salmonella* bloodstream infection indicated that not only was *S.* Enteritidis more likely to be colistin-resistant compared to *S.* Typhimurium, but also more frequently cause severe infections. Phylogenetic tree based on core-genome single nucleotide polymorphisms (SNPs) was separately by the serotypes but not MICs and implied a diffused distribution of MICs in the same serotype isolates.

**Conclusions:** Colistin susceptibility of clinical isolated *Salmonella* not only associated with *pmrAB* and *mcr-1* genes, but more importantly, were closely associated with specific serotypes. We suggest clinical microbiology laboratory interpreting *Salmonella* colistin MIC results in the serotype level.

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Abstract 2479

**Impact of universal infectious diseases consultation on the management of Staphylococcus aureus bloodstream infection in a Swiss community hospital**

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**Background:** Due to the complexity of *Staphylococcus aureus* bacteraemia (SAB), an infectious diseases (ID) consultation is usually recommended to improve diagnostic work-up and treatment. The aim of this study was to identify adherence to IDSA guidelines before and after implementation of a systematic ID consultation in a community hospital in Switzerland.

**Materials/methods:** This retrospective study was conducted at the Hospital of Jura, Switzerland during 54 months (June 2014 to December 2018). During the pre-intervention period (June 2014 to September 2016), infectious diseases consultation was at the discretion of the treating physician and obtained by telephone from the university hospital of Basel. During the post-intervention period (September 2016 to December 2018), an on-site infectious disease specialist was notified by email for each *S. aureus* positive blood cultures.

**Results:** A total of 107 episodes of SABs were included: 60 during the pre-intervention period and 47 in the post-intervention period. The most commonly identified sources of bacteremia were skin and soft tissue infections (23 episodes; 21%), primary bacteremia (19; 18%) and lower respiratory tract infection (18; 17%). Endocarditis accounted for 7% (7 patients). Only two (2%) methicillin-resistant *S. aureus* (MRSA) were detected. Patients in the post-intervention period were more likely to benefit from a transthoracic echocardiography, have follow-up blood cultures drawn, receive appropriate anti-staphylococcal agent and intravenous antibiotics for at least 14 days (Table). Thirty-day mortality was 22%. Multivariate analysis revealed that septic shock (\(P<0.001\); OR 7.1, CI 2.4-20.8) and lower respiratory tract infection (\(P=0.022\); OR 4.4, CI 1.2-15.8) as independent predictors of mortality.

**Conclusions:** The addition of a universal bedside consultation for all SAB in a community hospital led to a better adherence to IDSA guidelines. However, no difference in mortality was detected. Our study reinforces the growing number of published evidences exhibiting the importance of an ID consultation in the complex background of SAB, especially in community hospitals were adherence to guidelines is low.

<table>
<thead>
<tr>
<th>Pre-intervention (n=60)</th>
<th>Post-intervention (n=47)</th>
<th>(P)</th>
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</thead>
<tbody>
<tr>
<td>Follow-up blood cultures until sterilization</td>
<td>23 (38%)</td>
<td>40 (85%)</td>
</tr>
<tr>
<td>Transthoracic echocardiography</td>
<td>15 (25%)</td>
<td>37 (79%)</td>
</tr>
<tr>
<td>Transeosophageal echocardiography</td>
<td>3 (5%)</td>
<td>13 (28%)</td>
</tr>
<tr>
<td>Source control(^a)</td>
<td>25 (89%)</td>
<td>20 (81%)</td>
</tr>
<tr>
<td>Duration of intravenous antibiotics for at least 14 days(^b)</td>
<td>30 (52%)</td>
<td>35 (85%)</td>
</tr>
<tr>
<td>Appropriate definitive anti-staphylococcal agent</td>
<td>46 (77%)</td>
<td>42 (96%)</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>11 (18%)</td>
<td>13 (27%)</td>
</tr>
<tr>
<td>Recurrence of <em>S. aureus</em> bacteraemia (90 days)</td>
<td>4 (7%)</td>
<td>0 (0%)</td>
</tr>
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</table>

\(^a\) among 28 (pre-intervention) and 22 patients (post-intervention)

\(^b\) including patients that survived until day 14 from first positive blood cultures; 58 (pre-intervention) and 41 patients (post-intervention)

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Abstract 2481

Self-reported health status in ambulatory acute bacterial skin and skin structure infection patients who inject drugs, who received oral therapy with omadacycline or linezolid

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Background: Persons who inject drugs (PWID) are at elevated risk for acute bacterial skin and skin structure infections [ABSSSI]. Literature regarding health-related quality-of-life (HRQoL) outcomes for PWID with ABSSSI are scant, and these outcomes are not well understood. This study investigated PWID-reported outcomes in OASIS-2 (ClinicalTrials.gov NCT02877927), a randomized, double-blind Phase 3 clinical study comparing oral omadacycline versus oral linezolid for treatment of adults with ABSSSI.

Materials/methods: Participants were asked to complete the 36-item Short Form Health Survey Version 2 [SF-36v2R; Optum Inc., MN, USA] at screening and post-treatment evaluation [PTE; 7–14 days after last dose]. Responses to each item within the eight domains [physical functioning, social functioning, role physical, role emotional, bodily pain, mental health, vitality, and general health] were combined to generate a score from 0 to 100, where 100 indicates best health. Results were analysed in accordance with established norm-based standards for the survey, where each scale is scored to have the same mean [50 points] and the same standard deviation [10 points]. Analysis was performed for the intent-to-treat (ITT) population [all randomized participants].

Results: In total, 68.6% of participants in OASIS-2 had ABSSSI that was a result of intravenous drug use. Among PWID, improvement in patient-reported health status and HRQoL measures at PTE were greater for omadacycline than for linezolid-treated PWID [Table]. Improvement in role physical and role emotional were significantly higher for omadacycline than for linezolid-treated PWID [95% CI 0.63–9.45 and 1.1–10.59, respectively].

Conclusions: In this exploratory analysis, PWID with ABSSSI who received omadacycline experienced a greater improvement in patient-reported health status than PWID with ABSSSI who received linezolid. Greatest improvement was in performance of self-maintenance and social functions impacted by physical and mental health status. Further research among the population of PWID, including real-world studies, are warranted to determine the short- and long-term impact of ABSSSI treatments in improving patient physical and social role functioning, and whether treatments can have a differential effect on such functioning.

**TABLE:** Treatment effect at post-treatment evaluation in the intent-to-treat population – PWID subgroup

<table>
<thead>
<tr>
<th>HRQoL outcome</th>
<th>Post-treatment evaluation score (95% CI)</th>
<th>Change from baseline score (95% CI); P-value</th>
<th>Difference in score (95% CI); P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OMADACYCLINE (N ≥ 222) *</td>
<td>OMADACYCLINE (N ≥ 222) *</td>
<td>OMADACYCLINE vs LINEZOLID P-value</td>
</tr>
<tr>
<td></td>
<td>(N ≥ 212) *</td>
<td>LINEZOLID (N ≥ 212) *</td>
<td></td>
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<tr>
<td>Physical Functioning</td>
<td>76.6 (73.4, 78.7)</td>
<td>75.0 (71.8, 78.3)</td>
<td>7.40 (4.23, 10.57); &lt;0.0001</td>
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<td></td>
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<td>5.05 (2.61, 9.1); 0.0004</td>
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<td></td>
<td></td>
<td></td>
<td>1.54 (–2.99, 6.08); 0.50</td>
</tr>
<tr>
<td>Bodily Pain</td>
<td>51.4 (48.4, 54.4)</td>
<td>50.3 (47.2, 53.3)</td>
<td>9.46 (8.49, 12.47); &lt;0.0001</td>
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<td></td>
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<td>6.36 (5.3, 11.42); &lt;0.0001</td>
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<td></td>
<td>1.12 (–3.16, 5.4); 0.61</td>
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<tr>
<td>Role Physical</td>
<td>69.0 (65.9, 72)</td>
<td>63.9 (60.8, 67.1)</td>
<td>7.98 (4.9, 11.06); &lt;0.0001</td>
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<td></td>
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<td>2.04 (–0.22, 6.09); 0.07</td>
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<td></td>
<td>5.04 (0.63, 9.45); 0.03</td>
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<tr>
<td>General Health</td>
<td>59.9 (57.7, 62.1)</td>
<td>58.6 (56.3, 60.8)</td>
<td>0.88 (–1.35, 3.11); 0.4369</td>
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<td></td>
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<td>−0.47 (−2.74, 1.8); 0.6834</td>
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<td></td>
<td>1.35 (–1.83, 4.53); 0.40</td>
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<tr>
<td>Vitality</td>
<td>52.1 (49.9, 54.3)</td>
<td>51.1 (48.9, 53.4)</td>
<td>2.46 (0.25, 4.67); 0.0293</td>
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<td></td>
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<td></td>
<td>1.50 (−0.78, 3.76); 0.19</td>
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<td></td>
<td></td>
<td></td>
<td>0.95 (−2.21, 4.11); 0.55</td>
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<tr>
<td>Role Emotional</td>
<td>70.1 (66.8, 73.4)</td>
<td>64.3 (60.9, 67.6)</td>
<td>5.22 (1.9, 8.53); 0.0021</td>
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<tr>
<td></td>
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<td></td>
<td>−0.63 (−4.02, 2.76); 0.72</td>
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<tr>
<td></td>
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<td></td>
<td>5.64 (1.1, 10.59); 0.02</td>
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<tr>
<td>Mental Health</td>
<td>61.0 (50.7, 64.1)</td>
<td>61.0 (58.8, 63.3)</td>
<td>1.88 (−0.31, 4.07); 0.0923</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>1.00 (−1.24, 3.24); 0.39</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>0.88 (−2.25, 4.01); 0.58</td>
</tr>
<tr>
<td>Social Functioning</td>
<td>66.2 (63.4, 69.1)</td>
<td>64.7 (61.8, 67.6)</td>
<td>4.16 (1.31, 7.01); 0.0044</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>2.66 (−0.25, 5.58); 0.07</td>
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<td></td>
<td></td>
<td></td>
<td>1.49 (−2.58, 5.57); 0.47</td>
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</tbody>
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Norm-based SF-36v2 summaries:

| Mental Component Summary | 43.9 (42.7, 44.1) | 42.5 (41.2, 43.7) | 0.8 (−0.34, 2.13); 0.15 | −0.53 (−1.78, 0.72); 0.41 |
| Physical Component Summary | 44.7 (43.7, 45.6) | 44.4 (43.4, 45.3) | 2.84 (1.86, 3.78); <0.0001 | 2.05 (1.59, 3.5); <0.0001 |

*NS vary slightly for each of the scale parameters

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Molecular diagnosis of toxoplasmosis: impact of sample storage duration for five types of biological samples

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1Academic Hospital of Grenoble Alpes, Parasitology-Mycology Laboratory, Grenoble, France, 2 Academic Hospital of Montpellier, Parasitology-Mycology Laboratory, Montpellier, France, 3Academic Hospital of Rennes, Parasitology-Mycology Laboratory, Rennes, France, 4Academic Hospital of Strasbourg, Parasitology-Mycology Laboratory, Strasbourg, France, 5 Saint-Antoine Hospital, AP-HP, Parasitology-Mycology Laboratory, Paris, France, 6 Cochin Hospital, AP-HP, Parasitology-Mycology Department, Paris, France

Background: Toxoplasma-PCR is essential to diagnose disseminated, cerebral and congenital toxoplasmosis. As samples may travel for more than 24 hours before arriving in proficient laboratories, it seems important to evaluate the impact of the delay between sampling and technical support. This multicentric study evaluated the impact of samples storage at +4°C on Toxoplasma-PCR performances, aiming at proposing guidelines for the shipment and the delay before DNA extraction is performed.

Materials/methods: Five matrices, amniotic fluid (AF), cerebrospinal fluid (CSF), bronchoalveolar lavage fluid (BAF), whole blood (WB) and buffy coat (BC), were artificially spiked with various amounts of Toxoplasma gondii (20, 100 and 500 tachyzoites of RH strain/mL of sample). Moreover, blood was also spiked with the PRU strain and with THP1 cells previously infected with a Type II strain. Each spiked sample was made in triplicate at each parasite concentration. Sample processing and DNA extractions were performed at day 0 and after 2, 4 and 7 days of storage at +4°C using routine diagnostic techniques in each centre. Each extract was amplified at least in duplicate by real-time PCR assays targeting the ‘rep529’ DNA target. Results were analyzed using Fisher’s exact and Wilcoxon rank tests.

Results: 252 spiked samples were amplified by PCR. No increase in Ct was observed and 100% of PCR reactions were positive for AF, BAF, BC and WB plus infected-THP1, up to 7 days at 4°C. For CSF with low T. gondii concentrations, the number of positive PCR reactions decreased with time and only 50% of reactions were positive at D7 (p<0.05). For WB + PRU strain, amplification was significantly delayed from D2 but all reactions remained positive; for WB + RH strain, the number of positive reactions decreased for the three concentrations at D7.

Conclusions: T. gondii parasites appear robust in routine samples. The diversity of samples, extraction and PCR methods used in this multicentric study allows us proposing guidelines for good laboratory practices: sample storage at +4°C is possible up to 7 days; for CSF and whole blood, particularly from the 5th day at +4°C, we recommend to perform the PCR at least in triplicate.

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Abstract: Rate of IE was high among patients with *S. aureus* BSI. Presence of embolic events and prosthetic valves were the best predictors of IE.

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Abstract 2484

**Encephalitis in elderly patients in France, 2016-2019**

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Abstract third-party references: French Infectious Diseases Society, French public health agency (Santépublique France)

**Background:** Infections are challenging diseases in elderly patients due to immune senescence, and to their increased incidence and prevalence of chronic diseases. Moreover, elderly patients can experience cognitive decline making the detection and management of encephalitis more complicated. In France, the ENCEIF cohort enrolled encephalitis patients from 2016 to 2019. The present work aimed at describing the characteristics of enrolled elderly patients.

**Materials/methods:** Patients matching the case definition of encephalitis (Venkatessan et al. CID 2013) were prospectively enrolled. Demographics, medical history, clinical and diagnosis characteristics were gathered in a standardized manner. Elderly patients were defined as patients aged 65 y.o. or older. They were compared to patients younger than 65 y.o., using Pearson’s chi square, Student t-test and when needed, non-parametric tests.

**Results:** As of 16th October 2019, among 476 enrolled patients 251 (52%) were elderly including 120 (25%) 75 y.o. or older and 29 (6%) 85 y.o. or older. Among 251 elderly patients, 82 (32%) were being treated for another disease at the time of onset of encephalitis, vs 27 in non-elderly patients (12%, p<10⁻⁴). The most frequent causes of encephalitis in elderly patients were HSV (26%), VZV (18%) and L. monocytogenes (8%). Elderly patients were less likely to be admitted in ICU than younger patients (37% vs 47%, p=0.03), but more likely to die during hospitalization (12% vs 2%, p<10⁻³). The case-fatality rate increased to 14% in patients 75 y.o. or older, and to 18% in patients 85 y.o. or older. On discharge, 122/204 (60%) elderly patients had minor sequelae or no sequelae on Glasgow outcome scale, but 29 (14%) had severe disability or were in vegetative state. 108/203 (53%) were discharged home and 85/203 (42%) to a rehabilitation facility.

**Conclusions:** Elderly patients represented more than half of the ENCEIF cohort. Like younger patients, the most frequent causes of encephalitis were HSV and VZV, but listeriosis was more frequent than in younger patients. Elderly patients experienced a high case-fatality rate during hospitalization but the majority of those surviving the acute phase of the disease had a favorable outcome on discharge.

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**Abstract 2488**

**Community outbreak of OXA-48-producing Escherichia coli linked to a food premises: New Zealand, 2018-19**

Craig Thornley*, Matthew Kelly, Maxim Bloomfield, Annette Nesdale, Xiaoyun Ren

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**Background:** Carbapenemase-Producing Enterobacterales (CPE) are a serious threat to healthcare. CPE transmission is well described in hospitals and long-term care facilities (LTCFs) however little is known about community outbreaks.

**Materials/methods:** CPE are infrequently detected in New Zealand with almost all cases linked to international travel. Between August 2018 and June 2019, an OXA-48 and CTX-M-174-producing ST131 *Escherichia coli* was detected in 14 people from routine diagnostic testing of urine (11) or faecal (3) specimens. One case had urosepsis; the remainder had uncomplicated infection or asymptomatic colonisation. An outbreak investigation collected data on hospital, LTCF, travel and community exposures during the 12 months before CPE detection. A closed reference genome was generated for the index case using minION; whole-genome sequencing and pair-wise core SNP distances were used to estimate relatedness.

**Results:** The 14 cases were aged 44-94 years (median 74y). Nine were female. None had travelled internationally. Ten had prior admission (>4 hours) to Hutt Hospital, in 8 different wards; none of the remaining 4 had been admitted to the hospital or had household contacts who had been admitted. Three pairs of cases had concurrent ward admissions involving 2 different wards. Extensive screening of other ward contacts did not detect the organism. Ten cases had visited a particular food premises (Premises A), at which food hygiene concerns were identified. The outbreak organism was detected in faecal specimens from 4 Premises A food-handlers; one of these had a prior concurrent admission with a case. The organism was not detected in Premises A environmental samples. Isolates from the 14 original cases and 2 food-handlers had pair-wise core SNP distances of <8; the remaining 2 food-handlers' isolates had SNP distances of 49 and 21 compared to the index case. Action was undertaken to improve hygiene standards at Premises A.

**Conclusions:** These findings suggest probable community transmission of OXA-48 CPE at a food premises, with additional hospital transmission. Improvements in hygiene standards at the premises appear to have halted further transmission related to the premises. Clusters of OXA-48 CPE may have community origins; guidelines for investigation and control of community transmission are important.

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Effectiveness and safety of a dual therapy with boosted darunavir and dolutegravir in patients with an advanced HIV infection

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Background: The benefits of new antiretroviral drugs (ARV) allow treatment simplification and a reduction of potential toxicity associated to antiretroviral treatment (ART) in patients who have previously been exposed to many ART combinations and have a long-term, difficult-to-manage HIV infection. The objective of this study was to analyze the effectiveness and safety of a dual therapy (DT) with dolutegravir and boosted darunavir (DTG+bDRV) in these patients.

Materials/methods: Observational, retrospective, multicenter study to analyze the effectiveness of DTG+bDRV, defined as the ability to achieve or maintain complete viral suppression, i.e. viral load (VL) <50 copies/mL. Three analyses were carried out: "ITT-Snapshot" (proportion of patients with VL<50 copies/mL at week 48 of all patients with complete follow up, including treatment discontinuations), "Per Protocol" (PP) (excluding non virological-related drops-out) and "Observed Data" (OD) (proportion of last VL<50 copies/mL of all patients with any VL determinations after switch to DT).

Results: We analyzed 163 patients with a median age of 52 years, with a CD4 nadir of 171 cells/μL, 49.4% had a history of AIDS and 58.7% had a history of virological failures (VF) (31.3% had VF with protease Inhibitors and 60.7% to at least, 2 different ARV families).

Baseline VL was >50 copies/mL in 40.5% of patients and >200 copies/mL in 26%. The reason for switch was simplification/optimization in 53%, VF in 30.2%.

From the initial 163 patients 19 were discontinued: 6 were lost to follow-up, 4 discontinuations due to adverse events [1 insomnia, 2 digestive issues and 1 non-specified], 2 were non-related exitus [both virologically suppressed in their last VL] and 7 VF [associated to bad adherence and without resistance mutation appearance]. 43 haven’t completed 48 weeks yet.

At week 48 ITT analysis, the virological success (lack of VF) and virologically suppressed was 84.2% (101/120) and 93.5% (101/108) at PP analysis. At week 48 OD analysis, 149/156 subjects, with a global exposition to DT of 162 patients-year, has their last VL<50 copies/mL (95.5%), with a VF rate of 4.3 x 100 patients-year.

Conclusions: Dual therapy with DTG+bDRV is an attractive and highly effective simplification/rescue strategy for patients with an advanced and difficult-to-treat HIV infection.

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Abstract 2494

Clinical performance of a novel Point-of-Care testing automation of fungus (1-3)-β-D-glucan assay

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Background: At present, Invasive fungal diseases [IFD] have been emerging globally, especially in immunocompromised patients. Diagnostic of IFD still remains a big challenge due to the limit of conventional methods like culture and microscopy. Fungus [1-3]-β-D-Glucan (BDG) had been proved as a useful biomarker for Panfungal detection, except for cryptococcus and zygomycetes. However, the current version of BDG assay needs to pool samples and is easy to be contaminated due to complicated operation. We evaluated a novel POCT Automation of Fungus BDG assay (Dynamiker Funguy D240, China). By using of Funguy D240, the result could be reported within 30mins after adding the sample [only one step operation]. The monotest card is based on MICRO-FDSPHERES technology, which could achieve POCT for each sample due to internal standard curve. It contains 24-test channels and allow emergency test. Funguy D240 provides a rapid, flexible and POCT solution for Fungus BDG assay (Fig).

25μl Serum

30min

Fig: Dynamiker Funguy D240

Materials/methods: In total, 210 clinical serum samples previously defined according to revised EORTC/MSG guideline, including 30 proven Invasive Candidiasis [proven IC], 52 Invasive Aspergillosis [probable IA], and 128 negative samples from patients without IFD. All the samples were tested in parallel using Funguy D240 (Dynamiker, China) and Fungitell BDG assay (Associate of Cape Cod, USA).

Results: Through the analysis of 210 serum samples, the sensitivity and specificity of Funguy D240 was 82.92%, 85.15%, respectively. The positive coincidence rate, negative coincidence rate and total coincidence rate of Funguy D240 compared with Fungitell was 87.21%, 96.77% and 92.86%, respectively.

Conclusions: The Dynamiker Funguy D240 is a rapid and flexible POCT to detect Fungus BDG Glucan and could be used as an adjunct diagnostic for IFD.

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Proof of concept of a low-cost tropicalised device to detect bacterial growth in equipment-free blood cultures: results from the Turbidimeter pilot study

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Background: Bloodstream infections (BSI) are an important cause of mortality and their misdiagnosis/mistreatment is an important factor in the rise of antimicrobial resistance, in particular in low resource settings (LRS). Diagnosis of BSI in LRS is done using manual blood culture bottles (BCBs), visually checked for signs of growth. The most consistent parameter of growth is broth turbidity, but visual inspection of turbidity is inaccurate. To overcome this inaccuracy, we have developed the open-access, tropicalized Turbidimeter, that objectively assesses BCB broth turbidity.

Materials/methods: The Turbidimeter is built using cheap off-the-shelf electronics components and a customizable 3D-printed holder. Because of bacterial growth in the BCB, the turbidity of the broth increases. This causes a change in light intensity: transmitted light decreases while scattered light increases. The graph of OD versus time represents the bacterial growth curve. In addition to the detection of turbidity, a colour sensor is built in the bottom of the Turbidimeter to measure the color change at the bottom of the commercially available BacT/ALERT BCBs. To demonstrate the Turbidimeter performance, we compared time-to-positivity between BCBs spiked with Escherichia paracoli (clinical isolate from DR Congo) in the BacT/ALERT automate (reference) and the Turbidimeter incubated in a conventional incubator. Turbidimeter measurements were done every 10 minutes for 48 hours in total.

Results: The average time-to-positivity of the reference was 12.27 hours. Using the Turbidimeter, we found a comparable shift in signal from both the colour sensor and the turbidity sensor (Example given in figure 1). For the tested strain, we could demonstrate a steep growth curve, with both sensors, that reached a plateau after 2 to 3 hours. On average over four measurements, the increase in signal started after 10.07 hours (colour sensor) and 10.93 hours (turbidity sensor) and reached a plateau after 12.45 hours and 13.07 respectively.

Conclusions: Pilot results of the Turbidimeter demonstrate that the system was performant and that time-to-detection was comparable to the reference test. More testing is needed to validate the system.

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Comparison of 28-day mortality rates of recently completed prospective, randomised treatment studies of adult patients with carbapenem-resistant Gram-negative bacterial infections

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Background: Several randomised, prospective treatment studies of adult patients with serious CR-GNBIs have been conducted in the past 6 years. Recently, the CREDIBLE-CR study assessed the efficacy and safety of cefiderocol, a novel siderophore cephalosporin, for the treatment of patients with serious CR-GNBIs versus best available therapy (BAT). This analysis compares 28-day mortality rates observed in CREDIBLE-CR versus other recent CR-GNBi-focused treatment studies.

Materials/methods: Six open-label and one double-blind trials assessing antibiotics for the treatment of patients with CR-GNBIs were included. Two trials focused on carbapenem-resistant Enterobacteriaceae [CRE] [CARE, n=37; (primary analysis population); TANGO II, n=47]; 3 primarily included non-fermenters [NF] CR-GNBIs [AIDA, n=406; Durante-Mangoni, n=209; Sirijatuphat, n=94]; and 2 included both CRE and CR-NF-GNBIs [RESTORE-IMI, n=31; CREDIBLE-CR, n=118]. Participants were adults with hospital-acquired pneumonia, ventilator-associated pneumonia, bloodstream infections, complicated intra-abdominal or urinary tract infections caused by CR-GNB. Data were obtained from publicly disclosed information including FDA documents, publications, or presentations at congresses. Antibiotic treatments included: plazomicin, colistin, meropenem-vaborbactam, imipenem-relebactam, cefiderocol, meropenem, rifampicin, fosfomycin, and BAT. 28-day all-cause mortality (ACM) per study was collated and compared with ACM in CREDIBLE-CR by Forest plot.

Results: In the analysis, 824 patients were included with patient numbers varying from 37 to 406. Mortality at day 28 was 23.8% [20/84] for patients in studies of CREs and 45.0% [319/709] in NF studies. Day 28 ACM rates in CREDIBLE-CR and CR-GNBi-focused studies by CRE and NF and treatment are shown in the Figure. In studies with CRE and mixed pathogens [CRE or Pseudomonas aeruginosa], mortality rate for cefiderocol aligned with plazomicin, meropenem-vaborbactam, and imipenem-relebactam. For patients with NF, the mortality rate for cefiderocol-treated patients (35.3%) was similar to that seen for the treatment arms in comparator studies (45.0%). Mortality for the BAT in CREDIBLE-CR was lower (18.5%) than would be expected based on contemporary comparator studies.

Conclusions: Mortality rates in recently completed CR-GNBi-focused studies were high and consistent, particularly for patients with infections caused by CR NFs. Mortality rates for cefiderocol among patients with infections due to CRE and NFs were comparable to that reported with other investigational treatments in recently completed prospective, randomised trials.

Clinical Trial and Antibiotic | ClinicalTrials.gov Identifier | All-case Mortality % (95% CI) | 28-day Mortality Rate
--- | --- | --- | ---
**CRE infections**
CARE: Plazomicin | NCT01970371 | 11.8% [2/17] | 11.8% [2/17]
CARE: Colistin | NCT02168946 | 40.0% [6/15] | 40.0% [6/15]
TANGO II: Meropenem-vaborbactam | NCT01749459 | 33.3% [5/15] | 33.3% [5/15]
TANGO II: BAT | NCT02714597 | 13.8% [4/29] | 13.8% [4/29]
CREDIBLE-CR: Cefiderocol | NCT02445247 | 27.3% [9/33] | 27.3% [9/33]
**CR Pseudomonas aeruginosa**
RESTORE-IMI: Imipenem + colistin | NCT02978994 | 30.0% [1/3] | 30.0% [1/3]

**Non-Fermenter Infections**
CRE: Cefiderocol | NCT02714597 | 35.3% [10/57] | 35.3% [10/57]
TANGO II: CRE | NCT02151530 | 43.4% [38/88] | 43.4% [38/88]
AIDA: Colistin | NCT01732250 | 46.2% [9/20] | 46.2% [9/20]
AIDA: Colistin + meropenem | NCT01573662 | 43.3% [40/93] | 43.3% [40/93]
Durante-Mangoni: Colistin + rifampicin | NCT01749459 | 42.9% [45/105] | 42.9% [45/105]
Sirijatuphat: Colistin + fosfomycin | NCT01749459 | 48.6% [22/46] | 48.6% [22/46]
Sirijatuphat: Colistin | NCT01749459 | 57.7% [27/47] | 57.7% [27/47]

*Inhibitor: Plazomicin, Daptomycin, Phthiocerulin, Baxilactam, Tobramycin, Teicoplanin*

**Abstract 2497**

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Abstract 2501

**MixinYeast: a multi-centre survey on mixed yeast infections**


**Background:** Invasive candidiasis (IC) is one of the most prevalent mycoses worldwide. Infections caused by mixed yeast species may increase the risk of recurrence; despite this possible consequence, the incidence is mostly unknown. This analysis describes the epidemiological, clinical and microbiological characteristics of mixed yeast infections (Miy) isolated in several centers over a period of six months.

**Materials/methods:** A prospective study was conducted at 34 medical centers in 14 countries between April and September 2018. Miy were defined as the isolation of more than one yeast species in the same sterile specimen. Clinical data of these patients were recorded with denominators in all centers. Miy isolates were sent to a Reference Center (CNM-ISCIII) to confirm identification by ITS sequencing and to perform antifungal susceptibility testing, according EUCAST procedures.
Results: During the study period, 325,809 samples were processed. A total of 6553 positive cultures for yeasts were obtained; 150 (2.3%) involved MIY. The patients mean age was 53.7 years; 80 (53.3%) were males. Frequent risk factors were major surgery (85, 56.6%), use of central venous catheters (72, 48%), ICU stay (69, 46%) and hematological underlying disease (53, 35.3%). The principal sites of infections were blood (57, 38%) and peritoneum (50, 33.3%). Antifungal information was available for 94 (62.6%) cases; of whom 25 (26.6%) had previously received antifungal agents. Among MIY cases listed, 145 had available isolates; the mixed species most frequently found were *Candida albicans/C. glabrata* 42 (28.9%), *C. albicans/C. parapsilosis* 16 (11%), and *C. glabrata/C. tropicalis* 8 (5.5%). *C. albicans* was involved in 85 (58.6%) cases and *C. glabrata* in 64 (44.1%). The rest of the cases presented high diversity species combinations. All isolates were susceptible to amphotericin B, and 7.3% were fluconazole-resistant. Two isolates, *C. albicans* and *C. tropicalis*, were resistant to echinocandins, with *fks*1 hot spot 1mutations.

Conclusions: We documented a 2.3% of MIY in a six-month study. While *C. albicans* and *C. glabrata* were frequently identified, a high diversity of combinations was found; hence, it is important to accurately identify the species involved. Fluconazole-resistance was observed in 7.3% of the isolates; echinocandins resistance was uncommon but present.

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Abstract 2507

**On non-tuberculous mycobacteria in human alveolar macrophages**

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**Background:** Despite growing relevance of nontuberculous mycobacteria (NTM) infections, namely pulmonary infections, accurate data on incidence and pathogenesis is lacking. Here, we evaluated the intracellular persistence of three NTM species in a human alveolar macrophages model in order to get insight on the contribution of innate immune mechanisms to mycobacteria intracellular fate. The NTM genome diversity was also explored.

**Materials/methods:** *M. smegmatis* mc²155, reference strains (*M. avium* ATCC25291; *M. fortuitum* ATCC6841) and clinical isolates (*M. avium* 60/08; *M. fortuitum* 747/08) were used. Mycobacteria intracellular persistence was assessed via: 4x10⁴ THP-1 cells plated/well and incubated for 72h with 100nM PMA. Then fresh medium without PMA was added and the cells incubated for further 24h. The cells were infected for 1h (fast) or 3h (slow growers). Intracellular persistence was evaluated by CFU enumeration at different time points. NO production was evaluated using the Griess reagent, phagosome acidification and apoptosis was followed by confocal microscopy. Persistence ability of mycobacteria at different pHs was evaluated using BACTEC-MGIT960. NTMs virulence factors were characterized by whole-genome sequencing.

**Results:** NTMs experienced different intracellular fates: *M. smegmatis* and *M. fortuitum* ATCC6841 were cleared within 24h; whereas the remaining strains replicated. Still, unexpectedly, high percentages of acidified phagosomes were found harbouring Rab7, but not CD63. All NTM were able to survive in vitro at acidic pHs, with the exception of *M. smegmatis*. Our data further suggest a minor role for NO in intracellular persistence and that apoptosis mediated by caspase 8 and 3/7, but not necrosis, is triggered during NTM infection. Insights on the genomic backbone corroborated the virulence potential of *M. avium* and *M. fortuitum*.

**Conclusions:** Phagosome maturation arrest plays a secondary role in intracellular survival of *M. avium* and *M. fortuitum* in comparison to *M. tuberculosis*. NO seems to play a minor role in NTM intracellular persistence. Contrarily, apoptosis mediated by the caspase 8- caspase 3/7 pathway influences survival probably by promoting mycobacteria spread to neighboring cells. Our insights on the genomic traits underlying virulence further emphasized the importance of carrying out multidisciplinary studies in the NTM field.

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Abstract 2509

**Hospital-acquired pneumonia in liver transplant recipients**

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**Background:** Pneumonia is a serious complication in liver transplantation (LT) recipients. The pre, intra and post operative condition of the recipients influence the risk of developing pneumonia, especially, during the early period. Hence this study was taken up to determine the incidence, aetiology and outcomes of bacterial and fungal pneumonia in liver transplant recipients.

**Materials/methods:** This study was conducted from January 2018 to January 2019. Patients undergoing LT were followed up for 30 days post operatively for signs & symptoms of pneumonia. Respiratory samples were sent for microbiological analysis. Bacteriological identification and antibiotic susceptibility testing was performed using VITEK2 system.

**Results:** 89 patients underwent LT. 87.6% were males with age ranging from 4-65 years. The most common indication for transplantation was alcoholic liver disease. 31 (34.8%) had developed pneumonia during the study period, with the median time to development being 6 days post operatively. Ventilator associated pneumonia was seen in 8 (25.8%).

51 samples were sent for microbiological analysis, which included 16 endotracheal aspirates (ET), 10 broncho alveolar lavage (BAL), 9 blind BAL (b-BAL), 9 sputum and 7 pleural fluid samples. 58.8% were culture positive. The most common bacterial isolates were *Klebsiella pneumoniae* (21.56%), *Pseudomonas aeruginosa* (7.8%) & *Stenotrophomonas maltophilia* (7.8%). There was high level of multi drug resistance amongst isolates with colistin and fosfomycin being the drug of choice. There were 3 isolates of *Aspergillus flavus* from ET aspirate and BAL, 2 isolates of *Candida auris* from ET and 1 isolate of *Aspergillus niger* from BAL, isolates of *Rhizopus* from ET aspirate was confirmed with the same growth from BAL.

Patients who had pneumonia had greater need for non invasive ventilation (74.2%, p=<0.01), mechanical ventilator support (48.4%, p=<0.01) and tracheostomy (19.4%, p=<0.01). Post operative development of sepsis (74.2%, p=<0.01), requirement for vasopressors (71%, p=<0.01) and mortality (32.3%, p= 0.003) was observed more frequently in patients with pneumonia than those without.

**Conclusions:** Hospital acquired organisms and multi drug resistant Gram negative bacteria are frequently associated with the causation of pneumonia in the immediate post transplant period. Pneumonia is a significant cause of morbidity and mortality.

**Distribution of isolates amongst samples (n=51)**

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Clinical and echocardiographic predictors of embolism in infective endocarditis

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Background: Systemic embolization remains an important complication of infective endocarditis (IE) leading to high morbidity and mortality. The aim of the present study was to determine the factors associated with systemic emboli among patients with IE.

Materials/methods: This prospective observational study included all patients with suspected IE hospitalized at the University Hospital of Lausanne, Switzerland during a 21-month period (January 2018 to September 2019). IE was defined according to modified criteria of 2015 European Society of Cardiology Guidelines and patients with definite or possible IE were further evaluated.

Results: Among 453 patients with suspected IE, 121 were included (84 were categorized as definite IE and 37 as possible). Most commonly isolated pathogens included Staphylococcus aureus (40; 33%), Streptococcus spp. (27; 22%) and Enterococcus spp. (9; 7%). Surgical treatment was performed in 20 patients (17%). The most common area of embolization was the central nervous system (17 patients; 14%). Embolic events were observed in 63 patients (52%). The most common areas of embolization were the central nervous system (39 patients; 32%) and the limbs (23; 19%). Surgical treatment was performed in 49 patients (41%). Embolic events were more common in patients with fever (81% vs 62%; P 0.026), bacteraemia due to S. aureus (43% vs 22%; P 0.021), mitral valve (51% vs 16%; P<0.001), left heart vegetation >10mm (41% vs 12%; P<0.001), confusion upon admission (9% vs 25%; P 0.017), younger age (60 vs 65 years; P 0.046). Multivariate analysis found that S. aureus (P 0.038; OR 3.0, CI 1.1-8.6), mitral valve (P 0.005; OR 4.4, CI 1.6-12.3) and left heart vegetation >10mm (P 0.037; OR 3.4, CI 1.1-10.5) were independently associated with systemic emboli. The accuracy of the size of left heart vegetation in the prediction of embolic events was 0.708 (Figure 1).

Conclusions: Rate of systemic embolization was high among IE patients. S. aureus was the most commonly isolated pathogen and was independently associated with systemic embolization. Large vegetation (>10 mm) and involvement of the mitral valve put the patient at increased risk from embolic episodes.

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Abstracts 2020

Abstract 2513

Role of enteroaggregative Escherichia coli in people with diarrhoea in Gipuzkoa

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Background: Enteroaggregative Escherichia coli (EAEC) is one of the most recently identified diarrheagenic Escherichia coli. Nowadays EAEC infection is increasingly recognised as a cause of acute and persistent diarrheal illness among infants and young children worldwide. It has also been linked with travellers of industrialised regions who visited developing countries. On the contrary, some authors question the clinical relevance of these pathogens. The pathogenesis of EAEC infection is not fully understood. The aim of this study is to examine the role of EAEC in children and adult patients from Gipuzkoa suffering from acute and persistent diarrhea

Materials/methods: This study was conducted in the microbiology department of Donostia University Hospital (Spain) from November 2018 to October 2019. Overall, 10344 stool samples were analysed by multiplex pcr [allplexTM GI-bacterial (II) assay, seegene], which includes the detection of the aggR gene.

Results: A total of 10344 stool samples were analysed, EAEC was detected in 360 (3.5%) of them. Altogether, 126 patients (35%) were children under 3 years of age, of which 82% had acute diarrhea. The majority of patients in whom EAEC was detected had a self-limited diarrhea, not associated with outbreaks. 245 patients (68%) were reported to have had acute diarrhea (lasting less than 15 days). Only 16% of cases would be associated with traveller’s diarrhea. 248 patients (69%) were not only infected with EAEC, but also with an additional microorganism. The following table shows the characteristics of EAEC-positive patients.

<table>
<thead>
<tr>
<th>DIARRHEA TYPE</th>
<th>No. of episodes (n=360)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-term (≤15 days)</td>
<td>245</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Long-term (&gt;15 days)</td>
<td>115</td>
<td></td>
</tr>
<tr>
<td>Travellers’ diarrhea</td>
<td>59</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Nontravellers’ diarrhea</td>
<td>301</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Coinfection</td>
<td>248</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>No coinfection</td>
<td>112</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: EAEC was regularly identified in diarrhea episodes and the identification of truly pathogenic strains is difficult. The presence of EAEC was more frequent in children under 3 years of age than in adults, and the rate of coinfections was high. In our region this pathogen does not seem to have a great impact on health. It appears to cause subclinical infection or only intestinal colonization. Further investigation of the clinical relevance of these putative pathogens would be needed.

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Empiric treatment with fluconazole, as compared to echinocandins or amphotericin B, was associated with lower mortality among intensive care unit patients with sepsis due to candidaemia

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Background: Candidaemia is associated with high mortality, with echinocandins being associated with better outcome as compared to fluconazole. The aim of the present study was to identify predictors of mortality of candidaemia among critically ill patients.

Materials/methods: During a 9-year period (2010-18), all candidaemias among Intensive Care Unit (ICU) patients, at University Hospital of Patras, Greece, were studied. Susceptibility of antifungals was assessed by Etest and was evaluated according CLSI.

Results: Among 2780 ICU hospitalized patients, 150 (5.4%) candidaemias were observed (133 patients). Non-albicans species predominated (97 patients; 64.7%) with C. parapsilosis being the most commonly isolated species (66; 44.0%), followed by C. tropicalis (16; 10.7%) and C. glabrata (13; 8.7%); C. albicans was the cause of candidaemia for 53 patients (35.3%). Fluconazole resistance was found in 34 isolates (22.7%), whereas, resistance to at least one echinocandin was found in 15 (10.0%); no isolate was resistant to amphotericin. The most common cause of candidaemia was catheter-related (68 episodes; 45.3%), followed by primary (56; 37.3%). 14-day mortality was 25.3% (38 patients). Appropriate empiric antifungal treatment was administered in 122 patients (81.3%); fluconazole was administered in 33 patients (22.0%), echinocandins in 76 (50.7%) and liposomal amphotericin B in 13 (8.7%). Fluconazole administration was associated with better outcome (P<0.014) as compared to echinocandins, liposomal amphotericin B or no appropriate empiric treatment (Figure 1). Multivariate analysis identified septic shock (P=0.010; OR 6.1, CI 1.5-23.9) and SOFA score upon BSI onset (P<0.001; OR 1.6, CI 1.3-2.0) as independent predictors of mortality, whereas treatment with at least one appropriate antifungal was a predictor of survival (P=0.002; OR 0.108, CI 0.026-0.448). Among septic shock patients (68; 45.3%), multivariate analysis revealed SOFA score upon BSI onset (P=0.024; OR 1.3, CI 1.0-1.6) as independent predictor of mortality, whereas treatment with at least one appropriate antifungal was a predictor of survival (P=0.018; OR 0.066, CI 0.007-0.624).

Conclusions: Most candidaemias were catheter-related, which can explain the predominance of non-albicans species. Empirical administration of an appropriate antifungal, especially fluconazole, was associated with better survival probably due to the high prevalence of C. parapsilosis.

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Abstract 2517

**Surveillance for epidemic of Mycoplasma pneumoniae and macrolide resistance (A2063G and A2064G) using consecutive multiplex real-time PCR in Korea**

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**Background:** Pneumonia caused by *Mycoplasma pneumoniae* is a major cause of community-acquired pneumonia (CAP) in children. Three epidemics of *M. pneumoniae* pneumonia have occurred in Korea in 2006-2007, 2011 and 2015. Molecular diagnostic method is now replacing a Mycoplasma IgM/IgG Ab test. The macrolide-resistant *M. pneumoniae* is reported in worldwide and the resistance rate was very high (50-70%) in Korea. Detection of *M. pneumoniae* and macrolide resistance at same time is very important for appropriate antibiotics treatment during epidemic. We tested respiratory pathogens multiplex PCR and validated multiplex real-time PCR assay for reporting macrolide resistance related mutations (A2063G and A2064G in 23S rRNA) in *M. pneumoniae*.

**Materials/methods:** The Seegene Medical Foundation (SMF) has a nationwide network of 43 province local offices that collect and transport specimens in Korea. More than 200 pediatrics clinics and children's hospitals send nasopharyngeal swabs and respiratory specimens every day, and the results are reported the next working day. From January 2019 to November 2019, 56,103 samples were tested and analyzed at SMF using Seeplex PneumoBacter (Seegene, Seoul, Korea). This multiplex PCR could detect six respiratory infection causing pathogens including *M. pneumoniae*. In cases of *M. pneumoniae* were detected, macrolide resistance PCR was done consequently.

**Results:** The overall prevalence of first half year 2019, *M. pneumoniae* was 2.4% (633 from 26,590). However epidemic and outbreak was noticed from early July. The positive rate was increased to 8.5% in July and 32.5% in October. Macrolide resistance of *M. pneumoniae* was also increased in epidemic season. The prevalence rate of A2063G mutation positive cases was 61.3%. However, this positive rate was increased up to 68.7% in October.

**Conclusions:** We conclude this epidemic is fourth epidemic in Korea after 2006. The prevalence of *M. pneumoniae* in different by province in Korea and by season (usually high in winter and recent epidemics). Macrolide resistance rate is also increased in epidemic season in Korea. In clinical independent laboratory, high throughput multiplex real-time PCR is very convenient and these epidemiologic data of resistance pattern could be indicator of finding epidemics and also helpful guide for selecting antibiotics to clinicians.

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Abstract 2519

Whole genome sequence-based PCR for the rapid identification of *Pseudomonas aeruginosa* ST175 high-risk clone isolates directly from clinical samples

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**Background:** *Pseudomonas aeruginosa* is a major nosocomial pathogen frequently showing MDR/XDR profiles associated with world-wide disseminated high-risk clones (HRC). ST175 HRC is widespread in European countries and especially in Spain, where it is the most frequent HRC. Current approaches for the detection of HRC include MLST, that is expensive and time consuming, or other simple but less reliable techniques such as serotyping or Maldi-TOF. All these approaches require cultured isolates, delaying their detection in the clinical laboratory. Thus, the objective of this work was to develop of a specific PCR assay, based on whole genome sequence data analysis, for the fast diagnosis of infections caused by isolates belonging to ST175 HRC.

**Materials/methods:** Whole-genome sequence was obtained for one ST175 isolate by a PacBio RSII sequencer and then assembled and annotated to be used as consensus reference genome. Available PAO1 whole-genome data was used as comparator, and sequenced isolates from diverse clones from previous works were used to verify the adequacy of the designed tool. Reads from multiple isolates belonging to ST175, and PAO1 reference strain were mapped against ST175 consensus genome to comparatively identify potentially specific regions. Once curated, using the blast database to search for presence of those regions in any other organism, we designed a specific PCR for the identification of infections caused by ST175 isolates.

**Results:** We analysed the presence/absence of 4 potentially specific regions in 229 fully sequenced isolates from previous works. All ST175 isolates (73/229) were identified and there was no misidentified isolate. Furthermore, we tested blindly a PCR assay to identify ST175 directly from 69 clinical samples (17 positive blood cultures, 27 urine samples and 25 respiratory samples), compared with culture results followed by MLST analysis. All 5 clinical samples yielding ST175 isolates were identified correctly, whereas none of the negative clinical samples were misidentified as ST175.

**Conclusions:** A PCR assay showing high sensitivity and specificity for the fast detection of ST175 HRC directly from clinical samples was developed, and thus could become a useful tool for guiding infection control and treatment strategies in areas with high prevalence of this clone, such as Spain.

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Abstract 2525

Disease course, management and predictors of fatality in hospitalised patients with real-time PCR confirmed Lassa fever in Nigeria: a prospective cohort study

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1Inserm 1219, Université de Bordeaux, Bordeaux, France, 2CHU de Bordeaux, Department of Infectious Diseases and Tropical Medicine, Bordeaux, France, 3Alliance for International Medical Action, Dakar, Senegal, 4Federal Medical Center Owo, Owo, Nigeria, 5University of Oxford, Nuffield Department of Medicine, Oxford, United Kingdom, 6Irrua Specialist Teaching Hospital, Institute for Lassa Fever Research and Control, Irrua, Nigeria, 7Bernhard Nocht Institute for Tropical Medicine, Department of Virology, Hamburg, Germany

Abstract third-party references: Supported by Institut National de la Santé et de la Recherche Médicale (Inserm)

Background: Lassa fever (LF) is a viral haemorrhagic fever that is endemic in West Africa. As the risk benefit ratio of ribavirin is debated and promising agents are available for evaluation in humans, we need robust data to inform the design of future trials. We set up a prospective cohort study in Nigeria to: i) estimate in-hospital mortality of LF under the best available standard of care, ii) identify key prognostic factors, iii) build capacities needed for the implementation of clinical trials.

Materials/methods: Patients with RT-PCR confirmed LF hospitalised at the Federal Medical Centre, Owo, Nigeria, were eligible. Data concerning habits, exposure, disease history and presentation, management and outcomes were collected during hospitalisation. Patients had free access to optimized standard of care (including ribavirin, oxygen and dialysis), routine biology and Lassa RT-PCR. This analysis focus on participants included between April 2018 and August 2019.

Results: Among 2 1 7 patients with confirmed LF, mortality was 15.7%. 193 signed consent, of whom 78% were aged between 18 and 59; 47 % were female, 20% of them being pregnant. The median delay from first symptom to presentation was 9 days (IQR 7 – 14). On admission, the most frequent symptoms were fever (74%), headache (27%), dizziness (25%), vomiting (20%), abdominal pain (26%) and watery diarrhoea (20%). During follow-up, the following warning signs were noticed: tachycardia (30%), systolic BP < 90 mmHg (21%), SpO2 < 92% (19%), impaired consciousness (14%) and bleeding (31%). Regarding management: 100%, 21% and 25% received intravenous ribavirin, oxygen and transfusion respectively; 11% developed acute kidney failure (AKF) and 9% were dialysed. Baseline factors most associated with death were: AKF (58% vs. 2.5%, p<0.0001), AST ≥ 3 times the upper limit of normal (ULN) vs. < 3 ULN (18.9% vs 0%, p<0.0001), ALT ≥ 3 ULN vs. < 3 ULN (33% vs 3.1%, p<0.0001), RT-PCR cycle threshold (Ct) value < 30 vs. ≥ 30 (25 vs. 0.9%, p<0.0001).

Conclusions: The observed 15.7% mortality suggests that a composite primary endpoint, rather than mortality alone, should be considered for future efficacy trials. AKF, hepatitis and Ct value, should also be considered as randomisation stratification factors.

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New freeze-dried multiplex one-step real-time qPCR assay with room temperature storage for hepatitis A virus and norovirus detection in clinical and food/environmental samples

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**Background:** Food-borne diseases are an important worldwide public health issue. Their main cause are diarrheal disease agents, in particular Norovirus GI and GII, which cause 120 million cases/year and 200,000 deaths; among other food-borne hazards, HAV is responsible for 14 million cases/year. The majority of these cases occurs in low-resource countries, where food-borne diseases management is hampered by many limitations. Rapid detection is crucial for timely infection source identification and therapy. Bioside developed freeze-dried multiplex One-Step RT-qPCR assay with room temperature (RT) storage for HAV and NoV detection in clinical and food/environmental samples. The objective of this study was to validate the performance of this RT-qPCR assay for the concurrent detection of HAV, NoV GI and GII in fecal/food/environmental samples.

**Materials/methods:** In this study 56 analyses were performed on naturally/artificially HAV/NoV-contaminated samples and on negative samples. We developed a workflow for extraction and detection of HAV and NoV GI-GII in fecal/food/environmental samples according to ISO 15216-1 for food/environmental sources and to clinical guidelines for fecal samples. All samples were processed as per kit procedure’s with qualyfast® RNA extraction kits, based on starting volume [200ul-1ml], and analyzed with freeze-dried multiplex One-Step RT-qPCR assay qualyfast® HAV, NoV GI and GII for detection/discrimination of these viruses. Study analysis and stability tests were performed on 3 different batches.

**Results:** qualyfast® HAV, NoV GI and GII, validated with WHO standards on different matrices, allows simultaneous detection/discrimination of HAV [all genotypes], NoV GI and GII in positive samples, with LOD of 10 copies/reaction for HAV and NoV GI and 3 copies/reaction for NoV GII [see graph], with 100% specificity. Shelf-life testing confirmed the freeze-dried format performance up to 12 months.

**Conclusions:** Data generated in this study demonstrated that this RT-qPCR assay accurately detected samples for HAV [all genotypes], NoV GI and GII with 100% specificity and a 12 months RT storage stability. This freeze-dried assay is easy to use, fast and suitable device for HAV, NoV GI and GII detection in fecal/food/environmental samples especially in areas with limited technological/instrumental resources.

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Abstract 2527

**Imported malaria: the innovative approach of machine learning on clinical management and severity prediction**

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**Background:** Malaria is currently a major clinical problem with high risk of unfavourable outcome. A prompt identification of patients with a poor prognosis is a challenge. Machine Learning (ML) approaches represent a new frontier in medicine. ML uses datasets to recognize complex connections between several patient characteristics, make predictions and provide personalized treatment. The aim of this study is to design ad hoc ML approaches to predict clinical outcome in all patients with imported malaria and therefore to identify the best clinical setting.

**Materials/methods:** In this single-centre cross sectional study, 259 patients consecutively hospitalized with confirmed malaria were retrospectively recruited at the National Institute for Infectious Diseases, Lazzaro Spallanzani, Rome, Italy, from January 2007 to December 2017. Demographical, epidemiological, travel history, clinical, laboratory and parasitological data, anti-malarial and supportive treatment and clinical outcome were collected. Different machine learning approaches were used to perform the analysis of this dataset: support vector machines, random forests, feature selection approaches and clustering analysis.

**Results:** From 2007 to 2017, a total of 259 patients with malaria were enrolled. Out of them, 111 had severe malaria. Four baseline parameters, aspartate aminotransferase (AST), platelet count, total bilirubin and parasitemia, were all independently associated to an unfavorable outcome. At the clustering analysis, two groups were identified (19 and 92 patients, respectively). The consistency of the cluster analysis among severe cases was confirmed by the evidence that all the 19 patients clustered in the smallest group has the prolonged hospital stay complicated by comorbidities, bacterial infections and/or ICU admissions. In this cluster, baseline AST, acute renal and respiratory failures were strongly associated to the unfavorable outcome.

**Conclusions:** ML is a new challenge to solve health problem and its applicability could help physicians to improve diagnosis and the specific management. In particular, an early assessment of the severity status is required in patients with malaria. In this setting, ML can help to identify unknown parameters as shown in our preliminary data in which AST and platelet are associated to severe malaria but are not included in the current list of WHO severe malaria criteria.

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In vitro evaluation of ceftolozane/tazobactam-aztreonam and ceftolozane/tazobactam-fosfomycin combinations by time-kill assays against SPM-1-producing Pseudomonas aeruginosa clinical strains

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Background: Carbapenem-resistant Pseudomonas aeruginosa (PSA) is a pathogen with critical priority for research and development of new antibiotics. Metallo-beta-lactamase (MβL) producing PSA is associated with extremely drug resistance, and effective treatment options against MβL PSA are still scarce. Previous study showed synergistic activity of ceftolozane/tazobactam (C/T) with fosfomycin (FOS) and aztreonam (ATM) against the locally endemic São Paulo MβL (SPM-1) producing PSA.

We evaluated the in vitro activity of C/T+ATM and C/T+FOS combinations by time-kill assays using clinically relevant concentrations against SPM-1-producing PSA clinical isolates.

Materials/methods: Six genetically unrelated SPM-1-producing PSA clinical strains were studied. C/T, FOS, and ATM MICs were determined by epsilometric test. Time-kill assays were performed with C/T, FOS, and ATM alone and in combinations, at plasmatic peak and through concentrations. Viable colonies were determined at 3, 6, and 24h of exposure to the drugs. A reduction of the original inoculum ≥3log_{10} CFU/mL when the combination was compared to the most active compound was considered bactericidal, and a ≥2log_{10} CFU/mL reduction was considered synergistic.

Results: C/T MICs were of 512 mg/L for all strains, and ATM and FOS MICs varied between 3-16 and 1-28 mg/L, respectively. Peak ATM concentrations (with or without C/T) provided a ≥2log_{10} CFU/mL reduction at 6h and a ≥3log_{10} CFU/mL reduction at 24h to all strains, but addition of C/T did not improve the extent of bacterial killing. Trough ATM (with or without C/T) concentrations provided ≥2log_{10} CFU/mL reduction at 6h for all isolates, with regrowth at 24h for 4 of 6 isolates. C/T+FOS and FOS peak concentrations exhibited a mean growth reduction of 1.93 and 1.41 log_{10} CFU/mL at 6h, respectively, but a marked regrowth was observed at 24h for 4 of 6 isolates. No inoculum reduction was observed with FOS trough and C/T+FOS trough concentrations at any time.

Conclusions: Plasmatic peak concentration of C/T+FOS combination were synergistic by time-kill assay for one tested isolate. Bactericidal reduction at ATM peak and trough concentrations was observed in all SPM-1-producing PSA. These findings suggest that the use of such clinical combinations may be applicable under certain circumstances.

Table 1 – Mean log_{10} CFU/ml variation from starting inoculum by antimicrobials against six SPM-1 producing PSA

<table>
<thead>
<tr>
<th></th>
<th>6h bacterial</th>
<th>change from 0h control (log_{10})</th>
<th>24h bacterial</th>
<th>change from 0h control (log_{10})</th>
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<tr>
<td>ATM peak</td>
<td>4.45</td>
<td>-2.74</td>
<td>3.54</td>
<td>-3.29</td>
</tr>
<tr>
<td>ATM peak + C/T peak</td>
<td>4.34</td>
<td>-2.85</td>
<td>3.87</td>
<td>-3.32</td>
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<tr>
<td>ATM trough</td>
<td>5.20</td>
<td>-1.91</td>
<td>7.90</td>
<td>0.79</td>
</tr>
<tr>
<td>ATM trough + C/T trough</td>
<td>5.29</td>
<td>-1.94</td>
<td>7.72</td>
<td>0.53</td>
</tr>
<tr>
<td>FOS peak</td>
<td>5.46</td>
<td>-1.41</td>
<td>8.74</td>
<td>2.05</td>
</tr>
<tr>
<td>FOS peak + C/T peak</td>
<td>4.94</td>
<td>-1.93</td>
<td>8.74</td>
<td>0.98</td>
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<tr>
<td>FOS trough</td>
<td>9.62</td>
<td>2.75</td>
<td>10.00</td>
<td>3.12</td>
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<tr>
<td>FOS trough + C/T trough</td>
<td>9.29</td>
<td>2.42</td>
<td>10.00</td>
<td>3.04</td>
</tr>
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</table>

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Abstract 2532

**Cascade of HIV care in three different settings in Morrumbene, Mozambique**

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Abstract third-party references: Medicus Mundi Italia ONLUS ONG, University of Brescia

**Background:** Mozambique estimates 2 million people being HIV-positive. In 2013, the UNAIDS set the target of 90-90-90 to be reached by 2020. Aim of our study was to evaluate the state of the retention in care of HIV patients in a country with high prevalence of HIV infection.

**Materials/methods:** This is a retrospective, observational study. We collected data on patients diagnosed with HIV infection in 2017 in three health services in Morrumbene: Centro de Saúde de Morrumbene (CSM), Centro de Saúde de Mahangue (MAH) and TARV Movel service (TM). Demographic, clinical, immunological and therapeutic data were retrieved. The follow-up period lasted until the 31st of December 2018. Data on follow-up were collected at 6 and 12 months. Data were analyzed by Epi-Info 7. Descriptive statistics were obtained for all variables; for group comparison, for categorical variables chi square test or exact Fischer test, for numeric variables ANOVA test, when appropriate, were applied. Two tailed tests were used. Only p-values <0.05 were considered statistically significant. Uni and multivariate analysis were performed by logistic regression.

**Results:** In 2017, 960 patients were diagnosed with HIV infection. At 6 months, 49% of patients showed up at medical visit, where only 34% of them were still on follow-up after one year. In the multivariate analysis, factors associated with being lost after one year were male sex (OR 0.41, IC95% 0.26-0.63, p<0.001) and an advanced WHO status (OR 0.54, IC95% 0.32-0.92, p=0.024). Adherence to ART was observed in 157 (25%) patients in the first 6 months, where only 72 patients have been adherent to ART for one year. Interestingly, being prescribed an ART regimen the same day of the diagnosis correlated with an early loss at follow-up (AOR 1.8, IC95% 1.15-2.7, p=0.009).

**Conclusions:** Our study shows that only one third of patients resulted adherent to follow-up after one year, where as little as 13% of patients resulted adherent to ART. Male sex and a late diagnosis led to poor outcome, showing that more efforts are needed for diagnosis and follow-up in this population. Interestingly, the test-and-threat strategy correlated with an early loss at follow-up.

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The cost-effectiveness of isavuconazole compared to voriconazole, the standard of care in the treatment of patients with invasive fungal infection prior to differential pathogen diagnosis in Spain

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Background: Invasive mold diseases are associated with high morbidity, mortality, and high economic impact. Isavuconazole is an antifungal azole approved for the treatment of invasive aspergillosis (IA), a systemic infection caused by Aspergillus spp., and for invasive mucormycosis (IM) when amphotericin-B is not indicated. This model designed to evaluate the cost-effectiveness of isavuconazole vs. voriconazole for the treatment of adult patients with possible IA prior to differential pathogen diagnosis was adapted to the Spanish context.

Materials/methods: The analysis consisted of a decision tree (Figure 1) using the Spanish Healthcare System perspective, with 7.81% possible IA patients having mucormycosis, in order to reflect that in clinical practice differential diagnosis between IA and mucormycosis can be extremely challenging. Inputs for the model were obtained from Spanish publications, clinical guidelines and from a panel of experts. Direct medical resources and effects considered were: costs for laboratory analysis, management of adverse events, hospitalization and drugs per patient, deaths and long-term effects in life years (LYs) and quality-adjusted life years (QALYs). Efficacy data were obtained from clinical trials and utilities from the literature. Local unitary costs (€, 2019) were applied. Costs and outcomes were discounted at 3%. Deterministic and probabilistic sensitivity analyses (PSA) were conducted.

Results: In patients with possible IA, isavuconazole was found to be more costly (+2,175€) and effective (+0.49 LYs and +0.41 QALYs per patient) than voriconazole, with an Incremental Cost Effectiveness Ratio (ICER) of 4,398€ per additional LY gained and 5,363€ per additional QALY gained. The higher cost of isavuconazole is mainly due to drug acquisition costs since the rest of direct costs considered (management of adverse events, laboratory tests and hospitalization days) are reduced when using isavuconazole in comparison to voriconazole. Main parameters influencing results were mortality, treatment duration and hospitalization days. The PSA results showed that isavuconazole has a probability of being cost-effective of 75%, being dominant in 34.4% of cases.

Conclusions: Isavuconazole is a cost-effective treatment compared to voriconazole for patients with possible IA for a Willingness to Pay (WTP) threshold of 25,000€ per QALY.
Figure 1. Decision tree.

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Target attainment and pharmacokinetics of frequently used antimicrobials in surgical patients (TAPAS study)

Peter Declercq*, Eric Van Wijngaerden1, Greet Van De Sijpe1, Roxanne Poncelet1, Stefaan Nijs4, Willem-Jan Metsemakers4, André D’hoore4, Albert Wolthuis5, Joost Wauters2, Isabel Spriet1;6
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Background: Despite the high prevalence of bacterial infection and the broad scale use of antibiotics in surgery patients, few attention is paid in literature whether optimization of antimicrobial exposure is necessary in this setting. The primary objective was to document pharmacokinetic/pharmacodynamic (PK/PD) target attainment (TA) of frequently used β-lactam antibiotics in adult non-critically surgery patients.

Materials/methods: A prospective single-centre PK point-prevalence study was conducted in adult non-critically ill abdominal, trauma orthopaedic patients. Per patient, six blood samples were obtained during a single dosing interval. The PK/PD target was defined as unbound antibiotic concentrations above the minimum inhibitory concentration (MIC) of the pathogen for at least 40% of the dosing interval (40% fT>MIC). Both European Committee on Antimicrobial Susceptibility Testing (EUCAST) susceptibility breakpoints and local MIC90 values were applied as target MICs.

Results: Eighty-one non-critically ill surgery patients receiving amoxicillin [-clavulanic acid], flucloxacillin, piperacillin-tazobactam or meropenem were included. Overall, 81 % [66/81] did attain 40% fT>MIC when EUCAST susceptibility breakpoints were applied as target MICs. When local MIC90 values were applied, 93% [75/81] did attain 40% fT>MIC.

<table>
<thead>
<tr>
<th></th>
<th>EUCAST</th>
<th>Local MIC90</th>
<th>EUCAST</th>
<th>Local MIC90</th>
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<tr>
<td>P. aeruginosa</td>
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<td></td>
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<tr>
<td>Amoxicillin, number [%]</td>
<td>n.a.</td>
<td>n.a.</td>
<td>21/25 (84%)</td>
<td>21/25 (84%)</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Flucloxacillin, number [%]</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td>11/15 (73%)</td>
<td>15/15 (100%)</td>
<td>15/15 (100%)</td>
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</tr>
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<td>Meropenem, number [%]</td>
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<td>13/13 (100%)</td>
<td>13/13 (100%)</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>Piperacillin, number [%]</td>
<td>21/28 (75%)</td>
<td>26/28 (93%)</td>
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<td>26/28 (93%)</td>
<td>ND</td>
<td>ND</td>
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<td>ND</td>
</tr>
</tbody>
</table>

n.a., not applicable; ND, not determined; *Staphylococcus aureus, lugdunensis, saprophyticus; **CNS, Coagulase-negative Staphylococci (except Staphylococcus lugdunensis and Staphylococcus saprophyticus)

Conclusions: Implications for clinical practice in our hospital are limited as TA is 93% when considering our local susceptibility data. On the contrary, when MIC values would increase to the extent of the EUCAST breakpoints, TA will decrease towards 81%. Further population PK modelling and simulations might reveal the optimal dosing regimen and covariates explaining variability in PK parameters.

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Abstract 2538

A retrospective matched cohort study evaluating the rate of acute kidney injury in patients with severe Gram-negative infections treated with colistin or new β-lactam + β-lactamase inhibitor antibiotics

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Background: Colistin is a polymyxin class antibiotic originally discovered in the 1950's and was one of the first antibiotics with significant activity against Gram-negative bacteria. However, concerns over toxicity led to limited use. With the rise of antibiotic resistance, colistin has been used as a "last-line" or "salvage" therapy for multidrug-resistant Gram-negative infections, including infections caused by carbapenem-resistant Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacterales spp. Despite recent increased usage, there are an increasing number of anecdotal reports describing the rates of acute kidney injury (AKI) in patients treated with colistin, but few are population based.

Materials/methods: Electronic healthcare records from 2016 to 2018 in the US Premier Healthcare Database were used to identify adult hospitalised patients with confirmed Gram-negative infections that were treated with colistin or one of the three recently approved β-lactam + β-lactamase inhibitor antibiotics (ceftazidime-avibactam, ceftolozane-tazobactam, and meropenem-vaborbactam). Patients with acute renal failure (ARF), identified by ICD-9 code 584.X or ICD-10 code N17.X, or evidence of haemodialysis prior to initiation of study antibiotic were excluded from analysis. Rates of AKI, defined as ARF or haemodialysis after initiation of study drug, were compared between the two cohorts using 1:1 propensity score matching. Results were further stratified by baseline status of renal disease and treatment duration.

Results: Rates of AKI for the matched population are displayed in the Table. Median duration of treatment was 6 vs. 7 days, respectively, for colistin cohort and the new agents’ cohort. Neither cohort was observed to have an increased incidence of AKI as treatment duration increased. Observed rates of AKI were higher in the colistin cohort, for both patients with baseline renal disease (55.6% versus 40.8%, P=0.153) and patients without (17.1% versus 6.8%, P=0.001).

Conclusions: This real-world database confirms expectations that for the treatment of severe Gram-negative bacterial infections, colistin is associated with a higher risk of AKI in comparison to new β-lactam + β-lactamase inhibitor antibiotics.

<table>
<thead>
<tr>
<th></th>
<th>Colistin (N=256)</th>
<th>New agents (N=256)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARF, n (%)</td>
<td>52 (20.3%)</td>
<td>28 (10.9%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Haemodialysis, n (%)</td>
<td>14 (5.5%)</td>
<td>8 (3.1%)</td>
<td>0.191</td>
</tr>
<tr>
<td>Acute Kidney Injury (ARF or Haemodialysis), n (%)</td>
<td>61 (23.8%)</td>
<td>34 (13.3%)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

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Quantifying the intestinal load of genes of antibiotic resistance among two paediatric patient populations: not all “positives” are equal

Elias Dahdouh*, Fernando Lázaro Perona1, Emilio Cendejas1, Guillermo Ruiz-Crrascoso1, Jesus Mingorance1

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Abstract third-party references: Supported by the European Commission through a Marie Curie Individual Fellowship (Grant Number: P96084), Supported by Instituto de Salud Carlos III, PI16-01209

Background: Intestinal colonization with Multi-Drug Resistant (MDR) organisms carries a risk of developing difficult-to-treat infections, and could be a source of dangerous hospital outbreaks. Though numerous studies have aimed at detecting resistant organisms in the intestinal microbiome, few have quantified the load of resistance genes.

Materials/methods: Four-hundred-thirty-four rectal swabs were collected from 51 transplanted and 70 non-transplanted paediatric patients in the Hospital Universitario La Paz. Total DNA was extracted and qPCRs targeting the 16SrDNA, the blaCTX-M1-Family ESBL, blaOXA-1, and the carbapenemases blaOXA-48 and blaVIM genes were performed. The loads of the antibiotic resistance genes were calculated relative to the 16SrDNA (i.e. total bacterial load) using the △Ct method.

Results: The loads of the investigated genes in the positive swabs ranged from 0 to -5.9, representing ≈100% to ≈0.0001% of the bacterial population, respectively. The average load for the carbapenemases blaOXA-48 and blaVIM was higher for transplanted patients, and had an asymmetric distribution that is aggregated around loads similar to those calculated for pure MDR bacterial cultures (△Ct ≈ 0). In comparison, the loads of these genes for non-transplanted patients had a broad but more uniform distribution (Figure 1). Clinically relevant samples of MDR organisms harbouring the same gene(s) as those detected in the intestine were collected from other body sites (including urine, bloodstream, and biliary ducts) in 12 patients, 9 of which have high loads.

Conclusions: The intestinal loads of blaOXA-48 and blaVIM were higher among transplanted patients (that typically consume more antibiotics), and closer to loads calculated from pure MDR bacterial cultures. Clinically significant MDR bacterial isolates in extra-intestinal sites were isolated from 9 patients with high loads. These findings highlight the possible usefulness of stratifying patients based on the intestinal load of antibiotic resistance genes.

Figure 1: Intestinal loads of blaOXA-48 and blaVIM among transplanted versus non-transplanted patients.

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**Abstract 2541**


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**Background:** Urinary tract infections (UTIs) complicated by bacteraemia exacerbate the burden of illness in hospitalised patients. We aimed to evaluate the risk factors of UTIs developing into bacteraemia and the impact of UTI on readmission.

**Materials/methods:** Data from the US Premier Healthcare Database of adults hospitalised between 2014 and 2018 with UTIs (defined as positive urine culture and receipt of antibiotics for a Gram-negative infection within –2 to 3 days) with bacteraemia (blood culture positive for the same pathogen as index urine culture) or without bacteraemia, caused by carbapenem-resistant (CR) or -susceptible (CS) Gram-negative bacteria were analysed retrospectively. We used univariate analysis to select potential risk factors and a multivariable logistic regression model to identify risk factors for bacteraemia development among patients hospitalised with UTI. We also described patients who were readmitted with the same pathogen as that identified at index hospitalisation, and evaluated the time to readmission by CR and urosepsis status.

**Results:** A total of 46,076 patients had index UTI; 11,212 (24.3%) developed concomitant bacteraemia. Urosepsis patients were more likely to have a positive urine culture on the day of the admission than UTI patients without bacteraemia (93.0% [10,428/11,212] vs. 74.8% [26,078/34,864], P<0.001, respectively. Multivariable logistic regression analysis (OR; 95% confidence interval) showed that patients who had ICU admission (2.118; 2.012–2.23), urinary catheter (1.238; 1.164–1.316) or surgery (1.449; 1.352–1.554), *E. coli* infection (1.552; 1.45–1.662), CS infection (1.669; 1.431–2.011), male sex (1.972; 1.88–2.069), non-white race (1.233; 1.171–1.297) and aged 46–65 years vs 18–45 years (1.19; 1.094–1.294) were strongly associated with urosepsis versus UTI without concomitant bacteraemia. Patients with UTI >3 days of admission (0.231; 0.21–0.254), *Acinetobacter* (0.423; 0.251–0.711), *Pseudomonas* (0.44; 0.388–0.499), or *Stenotrophomonas* (0.301; 0.155–0.585) were significantly less likely to develop urosepsis. Patients with CR infections were more likely to be readmitted within 30 days (Table).

**Conclusions:** Urosepsis patients were more likely to be male, non-white, developed a UTI within 3 days, admitted to the ICU, had urinary surgery, and urinary catheter. CR pathogens increased the risk of readmission, but not the risk of bacteraemia.

<table>
<thead>
<tr>
<th></th>
<th>Urosepsis, n (%)</th>
<th>UTI only, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CR N=171</td>
<td>CS N=10,342</td>
</tr>
<tr>
<td>First readmission with same pathogen, n (%)</td>
<td>34 (19.9)</td>
<td>1,243 (12.0)</td>
</tr>
<tr>
<td></td>
<td>CR N=1,727</td>
<td>CS N=31,695</td>
</tr>
<tr>
<td>Time to readmission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Within 30 days</td>
<td>12 (7.0)</td>
<td>249 (2.4)</td>
</tr>
<tr>
<td>Within 31–60 days</td>
<td>9 (5.3)</td>
<td>197 (1.9)</td>
</tr>
</tbody>
</table>

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Abstract 2544

**Evaluation of difficult-to-treat resistant Gram-negative bacilli from European respiratory isolates: SIDERO-WT-2014–2018**

Melinda Soriano*1, Sean Nguyen2, Meredith Hackel1, Daniel Sahm3, Roger Echols3, Miki Takemura4, Yoshinori Yamano4

1Shionogi Inc, Florham Park, United States; 2IHMA, Inc., Schaumburg, United States; 3Infectious Disease Drug Development Consulting LLC, Easton, United States; 4Shionogi & Co., Ltd., Osaka, Japan

**Background:** Cefiderocol (CFDC) is a novel siderophore cephalosporin with potent activity against Gram-negative pathogens. Among resistant Gram-negative bacteria, difficult-to-treat resistant (DTR) pathogens represent a subset of organisms demonstrating non-susceptibility (NS) to first-line antibacterials. This analysis evaluated the in vitro activity of CFDC and contemporary broad-spectrum Gram-negative antibiotics against DTR pathogens collected over four years (2014–2018) from the SIDERO-WT study.

**Materials/methods:** Gram-negative non-duplicate clinical isolates were collected as part of the multinational SIDERO-WT surveillance study and underwent susceptibility testing at a central laboratory (IHMA, Schaumburg, IL). European respiratory isolates collected from 2014 to 2018 were included in this analysis. Pathogens were defined as DTR if they were non-susceptible to cefepime (FEP), ciprofloxacin (CIP), and meropenem (MEM) according to CLSI breakpoints. Minimum inhibitory concentrations (MIC) were determined for CFDC, ceftazidime-avibactam (CZA), ceftolozane-tazobactam (C/T), and colistin (CST). For SIDERO-WT Year 4 (i.e. 2018) isolates, aztreonam-avibactam (ATM/AVI, ATM in the presence of 4 µg/mL AVI) and meropenem-vaborbactam (MVB) were added as comparators. CFDC was tested in iron-depleted cation adjusted Mueller-Hinton broth (ID-CAMHB), while comparators were tested in CAMHB.

**Results:** Of 7,179 Gram-negative European respiratory isolates collected from 2014 to 2018, 22.4% [n=1,611] were DTR. DTR was most frequently observed in *Acinetobacter* spp. (55.6%), followed by *Stenotrophomonas maltophilia* (15.3%), *Burkholderia cepacia*-complex spp. (24%), *Pseudomonas aeruginosa* (15.0%) and *Enterobacterales* (1.6%). The MIC₅₀/₉₀ of tested compounds are shown in the Table. CFDC demonstrated the most potent in vitro activity relative to comparators against DTR *Acinetobacter* spp. with MIC₅₀/₉₀ of 0.25/2 µg/mL versus MIC₅₀ of >8 µg/mL for ATM/AVI and CST, and >64 µg/mL for CZA, C/T, and MVB. Against DTR *P. aeruginosa*, CFDC MIC₅₀/₉₀ was 0.25/2 µg/mL and was several fold lower than the MIC₅₀/₉₀ of 16/>64 µg/mL for CZA and C/T. CFDC was the most potent tested antibiotic against *S. maltophilia* [MIC₅₀/₉₀ of 0.06/0.25 µg/mL].

**Conclusions:** In a subset of DTR European respiratory isolates from a multinational collection of Gram-negative bacteria, cefiderocol demonstrated potent in vitro activity relative to contemporary broad-spectrum β-lactam/β-lactamase inhibitor combinations.

![Table](Table.png)

* Only included in Year 4 of SIDERO-WT; NA: not available

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Staphylococcus aureus intestinal colonisation in patients undergoing bowel preparation for colonoscopy

Julie Gagnaire*1,2, Leslie Rinaldi2, Florence Grattard1,2, Anne Carricajo1,2, Emilie Del Tedesco1, Nicolas Williet1, Josselin Rigaill1,2, Elisabeth Botelho-Nevers1,2, Xavier Robin2, Paul Verhoeven1,2, Philippe Berthelot1,2

1GIMAP EA 3064, University Jean Monnet, University of Lyon, Saint-Etienne, France, 2University hospital of Saint-Etienne, Saint-Etienne, France

Background: Staphylococcus aureus intestinal colonization investigated by using perineal, stools or rectal samples has been reported in various populations. However data about this reservoir in the gut are scarce. The aim of this study was to estimate the prevalence of intestinal S. aureus carriage and to investigate the dynamics of S. aureus colonization before and after bowel cleansing preparation.

Materials/methods: Prospective study in community patients undergoing a colonoscopy for cancer screening. The bowel preparation was based on polyethylene glycol or sodium picosulfate administration. Nasal, throat, groin and rectal swabs were screened for S. aureus, by a semi quantification on a chromogenic medium, before and at the day of colonoscopy. Colonic biopsies from the right and the left colon were cultured with or without broth enrichment.

Results: Among the 113 enrolled patients, according to the screening of 4 colonization sites, the overall prevalence of S. aureus carriage, was estimated at 41.6 % [CI 95% 32.5 – 50.7] with only one methicillin resistant S. aureus carrier. At the inclusion, 11 (9.7 %) and 12 (10.6%) patients were identified as groin and rectal carriers, respectively. Among S. aureus carriers, at the day of colonoscopy, 3 (8.8 %) patients were identified as S. aureus intestinal carriers with positive colonic biopsies. After the bowel preparation, there was a significant decrease of S. aureus carriage in the studied population (p = 0.02, McNemar test), a significant decrease of nasal S. aureus carriage (p = 0.004, McNemar test) and a trend to a decrease for groin S. aureus carriage (p = 0.06, McNemar test). As a whole, the S. aureus load decreased significantly for the nose, throat and the groin sites (p=0.01, p=0.04, p=0.06, respectively for the three sites, Wilcoxon signed-rank test).

Conclusions: We report for the first time in community patients the identification of S. aureus in colonic biopsies. Interestingly, we document the decolonizing effect of bowel preparation on 4 S. aureus colonization sites including the nose.

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In vitro antibacterial activity of cefiderocol against a multinational collection of difficult-to-treat resistant Gram-negative bacteria from respiratory and bloodstream infections: SIDERO-WT-2014–2018

Sean Nguyen*, 1, Melinda Soriano1, Meredith Hackel2, Daniel Sahm2, Roger Echols3, Miki Takemura4, Yoshinori Yamano4

1Shionogi Inc, Florham Park, United States; 2IHMA, Inc., Schaumburg, United States; 3Infectious Disease Drug Development Consulting LLC, Easton, United States; 4Shionogi & Co., Ltd., Osaka, Japan

Background: Cefiderocol (CFDC) is a novel siderophore cephalosporin with in vitro activity against a broad range of Gram-negative pathogens, including carbapenem non-susceptible strains. Difficult-to-treat resistant (DTR) organisms are defined as being non-susceptible to all high-efficacy and low-toxicity antibiotics (e.g. penicillins, cephalosporins, carbapenems, and quinolones). This study evaluated the in vitro activity of CFDC and contemporary broad-spectrum Gram-negative antibiotics against clinical DTR respiratory and bloodstream infection (BSI) isolates collected from 2014 to 2018 as part of the multinational SIDERO-WT surveillance program.

Materials/methods: Clinical non-duplicate, respiratory and BSI isolates of Gram-negative bacteria collected in Europe and North America from 2014 to 2018 were tested for antimicrobial susceptibility. MICs were determined for CFDC, ceftazidime-avibactam (CZA), ceftolozane-tazobactam (C/T), colistin (CST), cefepime (FEP), meropenem (MEM), and ciprofloxacin (CIP) by broth microdilution according to CLSI guidelines. For SIDERO-WT Year 4 (i.e. 2018) isolates, aztreonam-avibactam (ATM/AVI, ATM in the presence of 4 µg/mL AVI) and meropenem/vaborbactam (MVB) were added. CFDC was tested in iron-depleted cation adjusted Mueller-Hinton broth (ID-CAMHB), while all other comparators were tested in CAMHB. DTR pathogens were defined as being non-susceptible to FEP, MEM, and CIP according to CLSI breakpoints. For SIDERO-WT Year 4 *S. maltophilia* isolates, DTR was defined as NS to MEM, CIP, and TMP/SMX to account for the absence of FEP as a comparator.

Results: Among 18,863 Gram-negative respiratory and BSI isolates collected, 15% were defined as DTR. DTR strains were most frequently observed in *Acinetobacter* spp. (86.3%), followed by *Stenotrophomonas maltophilia* (45.7%), *Burkholderia* spp. (23.6%), *Pseudomonas aeruginosa* (11.6%) and Enterobacterales (3.3%). The MIC90 of tested compounds are shown in the table. CFDC was the most active antibiotic tested against DTR isolates as 93.6% DTR *A. aeruginosa* and 96.7% DTR Enterobacterales had an MIC ≤4 µg/mL, which has been shown to be effective in non-clinical in vivo models under humanised pharmacokinetics.

Conclusions: In a subset of respiratory and BSI isolates from a multinational collection of Gram-negative bacteria, CFDC demonstrated potent in vitro activity against DTR Gram-negative pathogens with limited first-line treatment options.

<table>
<thead>
<tr>
<th>DTR organism</th>
<th>N</th>
<th>CFDC</th>
<th>ATM/AVI*</th>
<th>CZA</th>
<th>C/T</th>
<th>CST</th>
<th>MVB*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacteriales</td>
<td>374</td>
<td>4</td>
<td>2</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;8</td>
<td>&gt;64</td>
</tr>
<tr>
<td><em>P. aeruginosa</em></td>
<td>424</td>
<td>1</td>
<td>&gt;8</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>2</td>
<td>&gt;64</td>
</tr>
<tr>
<td><em>A. baumannii</em></td>
<td>1443</td>
<td>2</td>
<td>&gt;8</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;8</td>
<td>&gt;64</td>
</tr>
<tr>
<td><em>S. maltophilia</em></td>
<td>538</td>
<td>0.25</td>
<td>NA</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;8</td>
<td>NA</td>
</tr>
<tr>
<td><em>B. cepacia-complex spp.</em></td>
<td>56</td>
<td>16</td>
<td>8</td>
<td>16</td>
<td>&gt;64</td>
<td>&gt;8</td>
<td>4</td>
</tr>
</tbody>
</table>

*Only included in Year 4 of SIDERO-WT; NA: not available

Presenter email address: Sean.nguyen@shionogi.com
Abstract 2551

Ceftaroline for severe community-acquired pneumonia: a real-world two-centre experience in Italy and Spain
Matteo Bassetti¹, Alessandro Russo*¹, Catia Cilloniz Campos¹, Daniele Roberto Giacobbe¹, Antonio Vena¹, Rosanel Amaro³, Elena Graziano⁴, Alex Soriano³, Antoni Torres³

¹Genoa, Genoa, Italy, ²Pisa, Pisa, Italy, ³Barcelona, Barcelona, Spain, ⁴Udine, Udine, Italy

Background: Ceftaroline is one of latest additions to the armamentarium for the treatment of community-acquired pneumonia (CAP). In this study, we aimed to describe the outcome of SCAP in a cohort of hospitalized patients treated with ceftaroline.

Materials/methods: Retrospective, observational study of patients with SCAP treated with ceftaroline in two hospitals in Spain and Italy. The primary objective was to describe 30-day mortality after the diagnosis of SCAP. Secondary objectives were: (i) to identify predictors of 30-day mortality; (ii) to identify predictors of clinical failure; (iii) to describe the rate of clinical success.

Results: During study period we observed 89 cases of SCAP treated with ceftaroline, used in combination with other antibiotics in 53 cases (60%). The causative agent was identified through blood cultures (n = 11) or respiratory specimens (n = 20), with the most frequently involved pathogen being Streptococcus pneumoniae (39%), followed by MRSA (29%). A concomitant laboratory-confirmed influenza was reported in 33 (37%) patients. Ceftaroline was used as first line and salvage therapy in 36% (32/89) and 64% (57/89) of cases, respectively. Overall, 30-day mortality and clinical failure were 20% (18/89) and 36% (32/89), respectively. Independent predictors of 30-day mortality were increasing age (odds ratio [OR] for one year increase 1.0, 95% confidence intervals 1.0 - 1.1, P = 0.043), presence of solid neoplasm (OR 4.0, 95% CI 1.0 - 15.1, P = 0.044), and concomitant therapy with oseltamivir (OR 8.5, 95% CI 1.2 - 57.3, P = 0.029). The only independent predictor of clinical failure was the time elapsing from SCAP diagnosis to ceftaroline therapy (OR for each passing day 1.5, 95% CI 1.1 - 1.9, P = 0.003). The clinical success rate was 64% (57/89). In the subgroups of patients with proven S. pneumoniae, methicillin-susceptible Staphylococcus aureus, and methicillin-resistant S. aureus (MRSA) infection, clinical success was 83% (10/12), 75% (3/4), and 56% (5/9), respectively.

Conclusions: Ceftaroline could represent an important therapeutic option for SCAP, especially if initiated early during the course of the disease. Further studies are needed to delineate the precise clinical success rate against MRSA in a larger cohort of patients.

Figure 1. Clinical success in patients with confirmed Streptococcus pneumoniae, MSSA, or MRSA infection

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Abstract 2553

**Evolution and adaptation of *Pseudomonas aeruginosa* in biofilms exposed to ciprofloxacin: beyond the resistance to antibiotic**

Marwa Ahmed\(^1\), Ahmed Abdelsamad\(^1\), Tina Wassermann\(^3\), Andreas Porse\(^4\), Janna Becker\(^1\), Morten Sommer\(^4\), Niels Heiby\(^1\), Oana Ciofu*\(^1\)

\(^1\)University of Copenhagen, Costerton Biofilm Center, Copenhagen, Denmark, \(^2\)University of Cairo, Faculty of Agriculture, Department of Genetics, Copenhagen, Denmark, \(^3\)Rigshospitalet, Department of Clinical Microbiology, Copenhagen, Denmark, \(^4\)Technical University of Denmark, Novo Nordisk Foundation Center for Sustainability, Lyngby, Denmark

**Background:** Ciprofloxacin is widely used to treat *P. aeruginosa* intermittent colonization and chronic biofilm infection in the lungs of cystic fibrosis (CF) patients. We have recently shown in experimental evolution studies of *P. aeruginosa* (PAO1) wild-type (WT) and \(\Delta katA\) in the presence of sub-inhibitory levels of ciprofloxacin (CIP) that biofilm mode of growth promote the development of low-level resistant mutants and that oxidative stress increases the mutagenesis and the development of resistance.

**Materials/methods:** Growth curves, competition studies with ancestor colonies, cross-resistance to other anti-pseudomonal antibiotics, swimming, swarming and twitching motility as well as whole-genome sequencing were performed on CIP-resistant isolates from the previous evolution experiments.

**Results:** We report here that the CIP resistance was due to mutations in negative regulators of the efflux pumps in biofilm isolates (\(nfxB, mexR, nalC, nalD\)) and in target genes (\(gyrA, gyrB, parC\)) in planktonic PAO1 isolates as well as in \(\Delta katA\) biofilm isolates with hypermutable phenotype. In addition, mutations in genes involved in cell-wall recycling (\(ftsZ, murC\)) could explain the cross-resistance to beta-lactams aztreonam and ceftazidime. Mutations in arginine catabolism leading to a metabolic rewiring to anaerobic metabolism and in the TCA cycle (\(sdhA\)) were also identified and might contribute to increased tolerance to other antibiotics which bactericidal effect depends on reactive oxygen species formation. Maintenance of swarming and loss of twitching motility was observed in colonies from CIP-exposed populations. Prolonged lag-phase of the growth curves of CIP-resistant colonies from the CIP-exposed populations was observed and might represent an additional mechanism for persistence of these colonies. In spite of the high fitness-cost, the CIP-resistant colonies persisted in the biofilms in competition with the WT in the absence of antibiotics and were selected by exposure to ciprofloxacin.

**Conclusions:** Overlapping to a large number of the published patho-adaptive genes in *P. aeruginosa* CF isolates was observed suggesting the important role of the antibiotic stress in shaping the bacterial evolution in biofilms in vivo that leads to the so-called chronic phenotype which becomes well adapted to the conditions of the respiratory tract of CF patients and therefore persists in spite of antibiotic therapy.

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Abstract 2554

Fatal babesiosis in a non-HIV immunocompromised host
Uli Schwab*1
1Royal Victoria Infirmary, Department of Infection and Tropical Medicine, Newcastle upon Tyne, United Kingdom

Background: Human Babesiosis is a protozoan intra-erythrocytic-infection. We report a fatal infection with Babesia microti complicated by haemophagocytic-lymphohistiocytosis (HLH).

Materials/methods: Case report

Results: A 83 year old man presents with a 3 day history of malaise, anorexia, rigors and a dry cough to a peripheral hospital following a cruise along the Scandinavian coastline (Copenhagen, Oslo, Stavanger, Bergen) and the British Isles (Shetland, Orkney). He is febrile at 38.7°C, tachycardic but haemodynamically stable, with a marked thrombocytopenia (41), abnormal PT (15), renal impairment (Creatinine 199) raised CRP 117 but normal white cells including differential. CXR, throat swab, serial blood cultures, MSU were culture-negative. Despite receiving iv fluids, broad spectrum antibiotics for presumed lower respiratory tract infection with AKI and delirium his pyrexia persists, his CRP rises to 223, and he develops abdominal pain with jaundice (Bilirubin 158, AST 249, ALT 94, AlkP 277), worsening renal function (Crea 543) oliguria, anaemia (Hb 7.6, haptoglobin <0.03g/l) with worsening confusion and bruising suggestive of a hepato-renal syndrome with DIC prompting transfer to the regional ID-unit. PMH includes AVR/TAVI, PUD, Waldenstroem’s macroglobulinaemia previously receiving IVIG’s and Rituximab, last 3 months prior. Extensive travel history; Nigeria (‘60ties,’90 and 2003), Kenya, Malaysia/Taiwan, Indian Subcontinent (‘70ties), South Africa (‘97) Korea (2011). A blood film suggest malaria parasitaemia (20-30%) posing speciation difficulty. Of note he spent most summers on the Great pond in Belgrade (Maine/USA), most recently 4 weeks before presentation, pointing towards epidemiological babesiosis exposure particularly in a immunocompromised individual with a negative RDT for P.falciparum, later confirmed as 22% parasitaemia, B.microti ELISA+ve, IFAT+ve 1:320 (negative blood-borne-virus-screen, leptospira-DNA, hantavirus-IF, B.burgdorferi and anaplasma-IF). A pan-reactive auto-Ab panel, prevented exchange-transfusion. Despite iv cefotaxime, artesunate, po doxicicline, atovaquone/azithromycin together with iv clindamycin/quinine, he deteriorates rapidly despite full organ support and dies due to multiorgan failure. Ferritin elevation >16,000 suggests HLH confirmed on post-mortem. Epidemiology, diagnosis, prognosis and treatment of Babesiosis will be discussed.

Conclusions: Diagnosis of Babesiosis requires a high index of suspicion, in part because the clinical manifestations are non-specific. In the age of increasing immunomodulators and global travel, early diagnosis and treatment are essential to reduce mortality from babesiosis.

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Antibiotic and biocide resistance among staphylococci causing skin and soft tissue infections in companion animals in Portugal

Sofia Santos Costa*, Rute Ribeiro¹, Valéria Oliveira¹, Maria Serrano², Carolina Ferreira¹, Catarina Morais¹, Maria Constança Pomba², Isabel Couto¹

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Background: Skin and soft tissue infections (SSTIs) are among the most frequent pathologies affecting companion animals. Staphylococci other than *S. pseudintermedius* account for 10-15% of these infections. The increasing prevalence of methicillin-resistant staphylococci (MRS) and multiresistant strains in animals has become an emerging problem.

Materials/methods: We studied a collection comprising all *S. aureus* (n=55), *S. schleiferi* (n=28) and *S. epidermidis* (n=14) isolates associated with SSTIs in companion animals from two laboratories in Lisbon, collected between 1999 and 2018. Identification was confirmed by species-specific nuc gene PCR. Antibiotic and biocide susceptibility profiles were established by disk diffusion or determination of minimum inhibitory concentrations (MICs). The distributions of biocide MICs were used to identify non-wild-type (NWT) populations. Biofilm production was evaluated by the crystal violet method. Strain clonality was evaluated by SmaI-PFGE and MLST.

Results: Methicillin resistance (mecA⁺) was identified in 31 *S. aureus* (56.4%, 31/55), two *S. schleiferi* (7.1%, 2/28) and eight *S. epidermidis* (57.1%, 8/14), often associated with multidrug resistance (MDR). Resistance was most frequently observed for beta-lactams (*blaZ* and/or *mecA*), fluoroquinolones and macrolides/lincosamides [linked with *erm*(A)/*erm*(C) in *S. aureus*, *erm*(B) in *S. schleiferi* and several genes in *S. epidermidis*]. We also detected resistance to fusidic acid, tetracycline and/or aminoglycosides, mostly linked to carriage of *fusC*, *tet*(K)/*tet*(M), and *aadD*, respectively. For *S. aureus* and *S. epidermidis*, we identified NWT populations towards biocides linked with several efflux pump genes (e.g., quaternary ammonium compounds, arsenate and cadmium associated with *qacA/B* or *smr; orsB* cadA or *cadB*, respectively). Several *S. epidermidis* isolates and one methicillin-resistant *S. schleiferi* were strong biofilm-producers. SmaI-PFGE revealed high heterogeneity among *S. aureus* and *S. epidermidis* isolates, contrary to *S. schleiferi*. The CC22 lineage was predominant amongst *S. aureus* isolates, whereas CC5 was the most frequent *S. epidermidis* lineage.

Conclusions: We demonstrate a high prevalence of antimicrobial resistant staphylococci, particularly MRS and MDR strains, associated with SSTIs in companion animals, evidencing a growing limitation of available therapeutic options for the management of these infections.

Funding: BIOSAFE projet – LISBOA-01-0145-FEDER-03713,PTDC/CAL-EST/30713/2017 (FEDER/Fundação para Ciência e a Tecnologia, FCT); GHTM-UID/Multi/04413/2013 (FCT).

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In vitro antibacterial activity of cefiderocol against a multinational collection of Gram-negative bacteria from urinary isolates: SIDERO-WT-2014–2018

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Background: Cefiderocol (CFDC) is a siderophore cephalosporin with potent activity against a wide range of Gram-negative pathogens including carbapenem non-susceptible (CarbNS) strains of Enterobacterales and non-fermenting bacteria. This study evaluated the in vitro activity of CFDC and comparator agents against Gram-negative clinical isolates collected from urinary sources of infection as part of the multinational SIDERO-WT surveillance studies [a pool of 4 consecutive years/studies from 2014 to 2018, totalling >30,000 recent clinical isolates].

Materials/methods: A total of 8,549 clinical non-duplicate urinary isolates of Gram-negative bacteria from Europe and the USA were collected and underwent susceptibility testing at a central laboratory (IHMA, Schaumburg, IL). MICs were determined for CFDC, cefepime (FEP), ceftazidime-avibactam (CZA), ceftolozane-tazobactam (C/T), ciprofloxacin (CIP), colistin (CST), and meropenem (MEM) by broth microdilution and interpreted according to CLSI guidelines. For SIDERO-WT Year 4 (i.e. 2018) isolates, aztreonam-avibactam (ATM/AVI, ATM in the presence of 4 µg/mL AVI), meropenem/vaborbactam (MVB) and sulfamethoxazole/trimethoprim (SXT) were added. As recommended by CLSI, CFDC was tested in iron-depleted cation-adjusted Mueller-Hinton broth.

Results: CFDC exhibited potent in vitro activity with MIC90 values ranging from 0.25 to 1 µg/mL for isolates of P. aeruginosa, Acinetobacter spp., S. maltophilia, and Enterobacterales, and 1 to 4 µg/mL for CarbNS subsets. Against CarbNS P. aeruginosa, CFDC MIC90 was 1 µg/mL and was lower than the MIC90 of 64 and >64 µg/mL for CZA and C/T, respectively. CFDC demonstrated potent in vitro activity against CarbNS Acinetobacter spp. with MIC90 of 2 µg/mL versus MIC90 of >8 µg/mL for ATM/AVI, CZA, C/T, and MVB. Against S. maltophilia, CFDC was the most potent tested antibiotic with an MIC90 value of 0.25 µg/mL, including SXT with an MIC90 of 0.5 µg/mL.


<table>
<thead>
<tr>
<th>Organism</th>
<th>N</th>
<th>CFDC</th>
<th>FEP</th>
<th>CZA</th>
<th>C/T</th>
<th>CIP</th>
<th>CST</th>
<th>MEM</th>
<th>ATM/AVI*</th>
<th>MVB*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacterales, CarbNS</td>
<td>167</td>
<td>4</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;64</td>
<td>2</td>
<td>64</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>949</td>
<td>0.5</td>
<td>16</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;64</td>
<td>2</td>
<td>64</td>
</tr>
<tr>
<td>S. maltophilia</td>
<td>181</td>
<td>1</td>
<td>64</td>
<td>64</td>
<td>&gt;64</td>
<td>&gt;8</td>
<td>8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;64</td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
<td>564</td>
<td>1</td>
<td>64</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;8</td>
<td>8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;64</td>
</tr>
<tr>
<td>Acinetobacter spp., CarbNS</td>
<td>219</td>
<td>2</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>&gt;8</td>
<td>8</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;64</td>
</tr>
<tr>
<td>S. maltophilia</td>
<td>103</td>
<td>0.25</td>
<td>64</td>
<td>64</td>
<td>64</td>
<td>8</td>
<td>8</td>
<td>&gt;64</td>
<td>4</td>
<td>32</td>
</tr>
</tbody>
</table>

*Only included in Year 4 of SIDERO-WT

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Abstract 2560

In vitro activity of cefiderocol against Stenotrophomonas maltophilia clinical isolates in Europe and North America: multinational surveillance SIDERO-WT-2018 study

Naoki Ishibashi*1, Meredith Hackel2, Hideki Maki1, Takafumi Satou1, Roger Echols3, Daniel Sahm2, Yoshinori Yamano1

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Background: Cefiderocol (CFDC) is a novel siderophore cephalosporin with activity against a wide range of Gram-negative bacteria. In this study, we analysed the in vitro activity of CFDC against Stenotrophomonas maltophilia clinical isolates collected in 2018 in the multinational surveillance study SIDERO-WT-2018 and compared it with the activity of comparator agents.

Materials/methods: A total of 392 S. maltophilia isolates were collected from 79 medical centres in Europe (n=192) and North America (n=200). Minimum inhibitory concentrations (MICs) were determined for CFDC, ceftazidime-avibactam (CZA), ceflozane-tazobactam (C/T), meropenem (MEM), meropenem-vaborbactam (MVB), ciprofloxacin (CIP), colistin (CST) and trimethoprim-sulfamethoxazole (SXT) by broth microdilution according to Clinical and Laboratory Standards Institute (CLSI) guidelines. The MIC for aztreonam (ATM) in the presence of 4 µg/mL of avibactam (AVI) was also determined. Susceptibility rates of comparators were calculated based on the breakpoint by European Committee on Antimicrobial Susceptibility Testing (EUCAST) or CLSI, and the breakpoint against P. aeruginosa was used when the breakpoint against S. maltophilia is not available. Susceptibility to ATM/AVI was provisionally calculated using breakpoints of AZT.

Results: CFDC showed an MIC90 of 0.5 µg/mL, which was the lowest among the tested compounds [Table]. 389 among 392 S. maltophilia isolates showed MIC of ≤2 µg/mL, against which cefiderocol has been shown to be effective in non-clinical in vivo studies under humanised PK profile. Among 392 isolates, 17 isolates were non-susceptible to SXT, and only two isolates had CFDC MIC >4 µg/mL. Among the 17 SXT non-susceptible isolates, one isolate showed CFDC MIC >4 µg/mL. Six ATM/AVI non-susceptible isolates based on ATM breakpoint showed CFDC MIC ≤4 µg/mL.

Conclusions: CFDC was active against S. maltophilia isolates, with in vitro activity against SXT and ATM/AVI non-susceptible isolates. CFDC has favourable potency that is similar to SXT, which is a standard therapeutic agent for S. maltophilia infection.

<table>
<thead>
<tr>
<th>Agent(s)</th>
<th>MIC90 (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFDC</td>
<td>0.5</td>
</tr>
<tr>
<td>ATM/AVI*</td>
<td>8</td>
</tr>
<tr>
<td>CZA*</td>
<td>&gt;64</td>
</tr>
<tr>
<td>C/T†</td>
<td>&gt;64</td>
</tr>
<tr>
<td>MEM</td>
<td>&gt;64</td>
</tr>
<tr>
<td>MVB‡</td>
<td>&gt;32</td>
</tr>
<tr>
<td>CIP</td>
<td>8</td>
</tr>
<tr>
<td>CST</td>
<td>&gt;8</td>
</tr>
<tr>
<td>SXT</td>
<td>1</td>
</tr>
</tbody>
</table>

*Avibactam fixed concentration: 4 µg/mL; †Tazobactam fixed concentration: 4 µg/mL; ‡Vaborbactam fixed concentration: 8 µg/mL.

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Abstract 2564

**Single dose cefazolin is feasible in orthopaedics: behavioural change success with collaborative working**

Fatma Şebnem Erdinç¹, Necla Tülek*,¹, BahadırAlemdaroğlu², Serkan İltar¹, Gunay Ertem¹, S. Kinikli¹, Çiğdem Ataman Hatipoğlu¹

¹Ankara Training and Research Hospital, Infectious Diseases and Clinical Microbiology, Ankara, Turkey, ²Ankara Training and Research Hospital, Orthopedics and Traumatology, Ankara, Turkey

**Background:** Compliance to surgical antibiotic prophylaxis recommendations is an essential problem and duration of antibiotic use has a priority for improvement. Each centre may have its own surgical infection prevention priorities and strategies. The aim of this study was to evaluate the change in appropriateness of antibiotic prophylaxis after a collaborative work with orthopaedists in the hospital.

**Materials/methods:** The study was performed in a 468-bed tertiary care teaching hospital in Ankara, Turkey. Surgical prophylaxis appropriateness in selected categories of surgical procedures has being followed by infection control team routinely since 2006. The first hospital-specific surgical prophylaxis guideline had been published in 2013. That guideline was introduced and explained to the surgeons of the hospital in a general information meeting after publication. To update the existing guideline in 2018, infection control team of the hospital performed a collaborative study with the related surgeons according to current international guidelines and scientific articles. After a series of meetings with participation of surgeons, the updated guideline was published in May, 2018. Surgical prophylaxis appropriateness percentages of Orthopaedic and Traumatology department, one year before and one year after the “2018 Hospital-specific Surgical Prophylaxis Guideline” publication were evaluated retrospectively. Time intervals were June 2017-May 2018 for the before and June 2018-May 2019 for the after groups.

**Results:** Selected orthopaedic surgery categories for surveillance were knee prosthesis, open reduction of fracture and hip prosthesis. Total number of those procedures were 555 in the before group and 665 in the after group. Appropriateness of surgical prophylaxis percentages are shown in the figure. Single dose cefazolin percentage was less than 1% in the before group while more than 70% in the after group. Prophylaxis more than 24 hours was the most frequent reason for inappropriate prophylaxis.

**Conclusions:** Although both hospital-specific guidelines [2013 and 2018] did include almost the same recommendations, dramatic increase in the compliance after collaborative work emphasized that being involved in the process has an important effect on behaviour change.

Figure. Percentages of single dose cefazolin appropriateness

<table>
<thead>
<tr>
<th></th>
<th>Before Updated Guideline</th>
<th>After Updated Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knee prosthesis</td>
<td>0,83</td>
<td>78,72</td>
</tr>
<tr>
<td>Open reduction of fracture</td>
<td>0,65</td>
<td>71,17</td>
</tr>
<tr>
<td>Hip prosthesis</td>
<td></td>
<td>75,59</td>
</tr>
</tbody>
</table>

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Abstract 2566

Rapid increase in occurrence of carbapenem-resistant Enterobacteriaceae in healthy rural residents in Shandong province, China, from 2015 to 2017

Baoli Chen¹, Björn Berglund², Shuang Wang¹, Stefan Börjesson²,³, Hong Yin⁴, Zhenwang Bi¹, Maud Nilsson², Zhenqiang Bi¹, Lennart E. Nilsson*²

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Background: The rapid increase of carbapenem-resistant Enterobacteriaceae (CRE) globally during the last decade has led to the World Health Organization listing the prevention and control of CRE in health care facilities as a priority. Infections caused by CRE are associated with increased mortality and length of hospital stays, emphasizing the health and economic burden posed by these pathogens. Although CRE can inhabit the human gut asymptomatically, colonisation with CRE is associated with increased risk of CRE infection and mortality. Monitoring the carriage rates of healthy individuals is therefore relevant for assessing the epidemiological situation regarding CRE.

Materials/methods: In 2015 and 2017, we investigated carriage rates of CRE in a rural region of Shandong province, China, by collecting faecal samples from healthy individuals of 12 villages in the region. In July 2015, 758 households in the study region were selected and in 2017, 628 of these households where sampled again. One individual from each household was sampled on each occasion. Samples were screened for CRE by cultivation on selective agars and suspected CRE-isolates were verified as Enterobacteriaceae with MALDI-TOF and MICs of meropenem by using agar dilution. Isolates were defined as CRE by using the EUCAST recommended meropenem-screening cut-off of >0.125 mg/L and subsequently whole-genome sequenced.

Results: A total of 18 and 86 individuals were positive for CRE in 2015 and 2017 respectively, corresponding to an increase of CRE occurrence ratios from 2.4% in 2015 to 14% in 2017. Most isolates were of Escherichia coli (>90% at both sampling occasions) and all isolates carried blaNDM genes, with blaNDM-5 (71%) being the most common.

Conclusions: This study shows a worrying and rapid five-fold increase in colonisation rates of CRE carrying blaNDM genes among rural residents in Shandong, China, indicating an increased risk of severe and difficult-to-treat infections and the potential for further dissemination of carbapenemase-encoding genes. Further studies and monitoring are essential to understand the rapid increase. Interventions may also need to be considered in China to prevent a further worsening of the epidemiological situation.

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Abstract 2567

In vitro activity of cefiderocol against carbapenem non-susceptible Enterobacterales from multiple countries in Europe and North America: multinational surveillance SIDERO-WT-2018 study

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1Shionogi & Co., Ltd., Osaka, Japan, 2IHMA, Inc., Schaumburg, United States, 3Infectious Disease Drug Development Consulting, LLC, Easton, United States

Background: Cefiderocol (CFDC) has demonstrated potent activity against Gram-negative pathogens including carbapenem non-susceptible (NS) Enterobacterales strains. We conducted a multinational surveillance study (SIDERO-WT-2018) to evaluate in vitro activity of CFDC against clinical isolates collected in 2018 from Europe and North America. In this study, we evaluated in vitro activity of CFDC and comparator agents against carbapenem NS Enterobacterales.

Materials/methods: A total of 145 carbapenem NS Enterobacterales isolates from a total of 5046 Enterobacterales isolates from SIDERO-WT-2018 were studied (115 from Europe, 30 from North America). Minimum inhibitory concentrations (MICs) were determined for CFDC, cefepime (FEP), ceftazidime-avibactam (CZA), cefotaxime-tazobactam (C/T), ciprofloxacin (CIP), colistin (CST), meropenem (MEM) and meropenem-vaborbactam (MVB) by broth microdilution according to Clinical and Laboratory Standards Institute (CLSI) guidelines. CFDC was tested in iron-depleted cation-adjusted Mueller–Hinton broth according to CLSI guidelines. The MIC for aztreonam (ATM) in the presence of avibactam 4 µg/mL (AVI), which can be used clinically in combination, was also determined. Carbapenem-NS isolates were defined using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints for MEM.

Results: The MIC90 values for CFDC and comparators for all isolates, MEM-NS isolates and ATM/AVI-NS isolates of Enterobacterales are shown in the Table. CFDC MIC90 was 4 µg/mL against MEM-NS isolates and ATM/AVI-NS isolates. 93.8% of MEM-NS isolates had CFDC MIC of ≤4 µg/mL, against which CFDC has been shown to be effective in non-clinical in vivo studies under humanised PK profile. Among 145 MEM-NS isolates, nine isolates were found with CFDC MIC >4 µg/mL (six from Russia and one each from Spain, UK and USA) and 20 isolates showed ATM/AVI MIC >1 µg/mL (seven from USA, six from Greece, four from Russia, two from Italy, and one from UK).

Conclusions: CFDC showed potent antibacterial activity with low MIC values against carbapenem NS Enterobacterales isolates, indicating that CFDC has high potential for treating infections caused by these difficult-to-treat strains.

<table>
<thead>
<tr>
<th>Agent</th>
<th>All isolates (n=5046)</th>
<th>MEM-NS isolates (n=145)</th>
<th>ATM/AVI-NS isolates (n=76)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFDC</td>
<td>1</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>FEP</td>
<td>16</td>
<td>&gt;64</td>
<td>&gt;64</td>
</tr>
<tr>
<td>CZA</td>
<td>0.5</td>
<td>&gt;64</td>
<td>64</td>
</tr>
<tr>
<td>C/T</td>
<td>1</td>
<td>&gt;64</td>
<td>&gt;64</td>
</tr>
<tr>
<td>MEM</td>
<td>≤0.06</td>
<td>NA</td>
<td>64</td>
</tr>
<tr>
<td>MVB</td>
<td>≤0.06</td>
<td>64</td>
<td>16</td>
</tr>
<tr>
<td>CIP</td>
<td>&gt;8</td>
<td>&gt;8</td>
<td>&gt;8</td>
</tr>
<tr>
<td>CST</td>
<td>1 (n=4018)</td>
<td>8 (n=134)</td>
<td>4 (n=57)</td>
</tr>
<tr>
<td>ATM/AVI</td>
<td>0.25</td>
<td>2</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA, not applicable.

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Abstract 2568

**Genomic characterisation of multidrug-resistant Klebsiella michiganensis strains**

Preetha Shibu¹, Frazer Mccuaig², Magdalena Kujawska¹, Lindsay Hall³, Anne Mccartney⁴, Lesley Hoyles*²

¹University of Westminster, London, United Kingdom, ²Nottingham Trent University, Clifton Campus, Clifton, United Kingdom, ³Quadram Institute Bioscience, Norwich, United Kingdom, ⁴University of Reading, Reading, United Kingdom

**Background:** While much attention has focused on the clinical relevance of *K. pneumoniae*, bacteria identified as *K. oxytoca* in clinical laboratories have received little attention. *K. oxytoca* represents 17% of all *Klebsiella*-positive blood culture isolates in UK clinical settings, and the bacterium is becoming increasingly associated with nosocomial infections, particularly in immunocompromised patients.

**Materials/methods:** Whole-genome sequences were generated for three carbapenem-resistant outbreak strains identified by MALDI-TOF and API 20E as *K. oxytoca*. Antimicrobial susceptibility profiles were determined according to EUCAST guidelines, with ertapenem resistance confirmed by E-test. Average nucleotide identity (ANI) and phylogenetic analyses of genome data, by comparison to type strains, were used to determine the strains’ species affiliation. Capsule and O antigen types of the strains were determined using Kaptive. Multilocus sequence typing was done via the online *Klebsiella oxytoca/Klebsiella michiganensis* MLST databases. Antibiotic resistance and virulence gene profiles of the strains were determined using BLASTP with the Comprehensive Antibiotic Resistance Database and Virulence Factor Database, respectively. BLASTP was also used to determine whether the strains encoded the tilimycin biosynthetic gene cluster (BGC) thought to be unique to *K. oxytoca* isolates associated with non-*C. difficile*-antibiotic-associated haemorrhagic colitis. Over 7000 publicly available *Klebsiella* spp. genome sequences were also screened to determine the prevalence of the BGC.

**Results:** The strains were resistant to a range of antimicrobials, including ertapenem. Genomic analyses revealed the three strains to be *K. michiganensis* ST138 (unknown capsular and O antigen types), encoding SHV-66 and GES-5, and the complete tilimycin BGC. Only 1% of all publicly available *Klebsiella* genomes screened encoded one or more genes of the BGC, with all belonging to the *K. oxytoca* complex of six species.

**Conclusions:** Whole-genome sequence data are required to allow accurate taxonomic classification of strains identified as *K. oxytoca* using MALDI-TOF and/or API 20E. This is the first report of *K. michiganensis* encoding SHV-66 and GES-5, and the tilimycin BGC. We also demonstrate that the tilimycin BGC is represented in a minority of strains belonging to representatives of the *K. oxytoca* complex (*K. oxytoca*, *K. michiganensis*, *K. grimontii*, *K. huaxiensis*, ’*K. pasteurii’* and ’*K. spallanzanii’*).

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Abstract 2569

Baseline resistance to ceftazidime-avibactam and aztreonam-avibactam in carbapenemase-producing Enterobacterales from Argentina mediated by the co-expression of PER ESBL: role of imipenem-relebactam and aztreonam-relebactam as therapeutic alternatives

Fernando Pasteran1,2, Juan Manuel De Mendieta1, Melina Rapoport1, Soledad Ramirez1, Diego Faccone1, Celeste Lucero1, Paola Ceriana1, Alejandra Corso1

1Servicio Antimicrobianos, Laboratorio Nacional de Referencia, INEI ANLIS “Dr. Malbran”, buenos aires, Argentina, 2Cza working group, buenos aires, Argentina, 3Center for Applied Biotechnology Studies, Department of Biological Science, College of Natural Sciences and Mathematics, Fullerton, United States

Background: Carbapenemase-producing Enterobacterales (CPE) isolates have reached 20% during 2018 in Argentina, with KPC nationwide endemicity and outbreaks of NDM and OXA-48-like. PER is the second most frequent ESBL in Argentina and have a weak inhibition by avibactam, significantly lower than other class A enzymes. We describe the emergence of CPEs with baseline resistance to ceftazidime-avibactam (CAZ-AVI) and aztreonam-avibactam (ATM-AVI) mediated by the co-expression of PER and explore therapeutic alternatives, such as imipenem-relebactam (IPM-REL) and aztreonam-relebactam (ATM-REL).

Materials/methods: Since 2017, susceptibility to CAZ-AVI and ATM-AV was prospectively monitored against CPE submitted to the NRL. Strains non-susceptible to AVI combinations were tested for IPM-REL and ATM-REL. AVI and REL (4ug/ml final concentration), with the indicated beta-lactams, were tested by reference dilution methods, while susceptibility to other agents was performed either by disk diffusion or MIC methods (CLSI/EUCAST criteria). Due to the absence of breakpoints for ATM-AVI/ATM-REL, we used the EUCAST criteria for ATM. Molecular characterization of β-lactamases genes was carried out by PCR/sequencing.

Results: 606 CPE isolates (119 Hospitals) were analyzed: i) KPC: 18/365 (4.9%) were ATM-AVI non-susceptible, of which 9/365 (2.5%) were also CAZ-AVI resistant, being 16/18 PER co-producers. CAZ-AVI resistant strains harbored KPC-2 allele. ii) OXA-48-like: 6/119 (2.5%) were ATM-AVI non-susceptible, of which 3/119 (0.8%) were also CAZ-AVI resistant, being 4/6 PER co-producers. iii) MBLs (107 NDM, 11 IMP, 4 VIM): 5/122 (4.1%) were ATM-AVI non-susceptible, all PER co-producers (Figure-A). Additionally, 14 (7 KPC, 1 OXA, 6 MBL) and 17 (14 KPC, 3 OXA) CPE+PER remained susceptible to ATM-AVI and CAZ-AVI, respectively, with MIC values shifted towards higher levels compared to PER non-producers (Figure-A). IPM-REL and/or ATM-REL were the most active agents for CPE+PER (Figure-B).

Conclusions: The co-expression of PER in CPEs was a determining factor for the MIC creep of avibactam combinations. PER seems to be the cause of non-susceptibility to CAZ-AVI and ATM-AVI in KPC and MBL, respectively. An ATM-AVI MIC >=1.0ug/ml was selected as an ECOFF for further screening of PER co-production among CPE. Rellebactam combinations resulted key alternatives for CPE+PER. Considering the dissemination potential of PER, IPM-REL should be part of the therapeutic armamentarium.
Figure A: MIC distributions for CAZ-AVI and ATM-AVI for CPEs. Number of isolates with the indicated MIC value (in μg/ml) according to the type of carbapenemase and the co-production of blaPER. The dotted line indicates the cutoff values:

- Non PER coproducers
- PER coproducers

Figure B: Susceptibility to different antimicrobial agents against the indicated subgroups of CPE + blaPER clinical isolates:

<table>
<thead>
<tr>
<th>Group</th>
<th>Species (n)</th>
<th>% of susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CAZ-AVI</td>
<td>ATM-AVI</td>
</tr>
<tr>
<td>KPC+PER (n=23)</td>
<td>ECI (14), KOX (5), KPN (2), MMD (1), CFR (1)</td>
<td>61 30 91 57 82 87 57 74 39 30</td>
</tr>
<tr>
<td>MBL+PER (n=11)</td>
<td>ECI (4), KPN (3), PHE (2), ECO (1), PAN (1)</td>
<td>0 55 0 91 55 64 64 27 27 27</td>
</tr>
<tr>
<td>OXA-162+PER (n=4)</td>
<td>CFR (1), ECI (1), KPN (2)</td>
<td>75 25 100 100 75 75 50 50 50 25</td>
</tr>
</tbody>
</table>


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Ceftolozane/tazobactam-resistant *Pseudomonas aeruginosa* isolates in a teaching hospital in central Italy

Morroni Gianluca¹, Lucia Brescini¹,², Andrea Brenciani¹, Alberto Antonelli¹, Vincenzo Di Pilato¹, Sefora Castelletti¹,², Simona Fioriti¹, Tommaso Gian¹,², Gian M. Rossolini¹,², Andrea Giacometti¹,², Oscar Cirioni¹,²

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**Background:** Ceftolozane/tazobactam (C/T) is a novel cephalosporin/β-lactamase inhibitor combination with a potent activity against *Pseudomonas aeruginosa* isolates. Despite its recent introduction, several resistant *P. aeruginosa* isolates have been reported. We performed a survey on the activity of C/T against clinical strains of *P. aeruginosa* isolated at "Ospedali Riuniti" of Ancona, Italy, characterising the resistant isolates.

**Materials/methods:** MICs to C/T were determined with gradient test for all *P. aeruginosa* recovered at the clinical laboratory of "Ospedali Riuniti" from October 2018 to March 2019. Resistant strains were characterized and typed by SpeI-PFGE. NGS with an Illumina Miseq platform was performed on representative strains to identify the mechanisms of C/T resistance.

**Results:** Over 317 isolated and screened isolates, 15 were resistant to C/T (MIC > 8 mg/L; 4.73%). PFGE showed that 8/15 were strictly related. NGS revealed 6 different STs. The resistance mechanisms to C/T included the metallo-β-lactamase (MBL)-encoding genes *bla*<sub>VIM</sub>-2 in 8 isolates belonging to ST111, and *bla*<sub>IMP</sub> in 2 isolates (*bla*<sub>IMP</sub>-19 in ST175 and *bla*<sub>IMP</sub>-13 in ST621). Additionally, *bla*<sub>PER</sub> β-lactamase gene was detected in 2 isolates (ST235) and the *bla*<sub>GES</sub> β-lactamase gene in 1 isolate (ST175). Notably, in 2 strains (ST70 and ST3354) no acquired β-lactamase genes involved in C/T resistance has been detected but they showed alterations in *ampC*. Modifications in these genes and in *ampC* promoter (*ampR*) were also detected in all resistant strains except in ST175 isolates (possessing a wild type *ampC* and *ampR*).

**Conclusions:** Although our study confirmed a low rate of resistance to C/T, several resistance mechanisms were identified, among which production of MBLs was the most common. Moreover, we found a possible mini-outbreak of *bla*<sub>VIM</sub> positive strains, representing a concern for the clinicians and also a possible reservoir for the transmission of MBL to other species. Determination of MIC to C/T should be always performed prior administration to avoid the spread of resistant *P. aeruginosa*.

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Abstract 2577

In vitro and in vivo antimicrobial activity of cefiderocol and comparators against Stenotrophomonas maltophilia

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Background: Stenotrophomonas maltophilia is a ubiquitous multidrug-resistant (MDR) opportunistic pathogen. Regarding β-lactam resistance, the presence of at least two different types of β-lactamases – L1 metallo-type carbapenemase and L2 extended-spectrum type β-lactamase – are involved. Cefiderocol (CFDC), a novel siderophore cephalosporin, is active against carbapenem-resistant Gram-negative bacteria, including S. maltophilia. In this study, in vitro and in vivo antibacterial activity of CFDC were evaluated versus comparators including trimethoprim-sulfamethoxazole (SXT), levofloxacin (LVX) and minocycline (MIN).

Materials/methods: Minimum inhibitory concentrations (MICs) of CFDC and comparators were determined by broth microdilution method as recommended by Clinical and Laboratory Standards Institute guidelines using iron-depleted cation-adjusted Mueller–Hinton broth for CFDC. The stability against L1 and L2 β-lactamases was evaluated by their activity against Escherichia coli BL21 (DE3) expressing these enzymes. In vivo efficacy of CFDC and comparators (SXT, MIN, ciprofloxacin [CIP], LVX, ceftazidime [CAZ], cefepime [FEP], meropenem [MEM] and colistin [CST]) was evaluated using a murine lung infection model (5-week-old neutropenic ICR mice; n=5) caused by two strains, including a SXT-resistant strain. Treatment was given 2, 5 and 8 hours post-infection, and the numbers of viable cells in lungs were determined 26 hours post-infection.

Results: MIC increases for CFDC and FEP were not observed (≤2-fold) in the presence of either β-lactamase. In contrast, presence of L1 β-lactamase resulted in MIC increases for MEM and CAZ (both 16-fold), whereas presence of L2 caused the MIC to increase by 4-fold for CAZ only. In the murine lung infection model, CFDC showed >3 log10 reduction of viable bacteria in lungs at 100 mg/kg dose (%T>MIC: <50%) against both test strains (CFDC MIC: 0.5 and 0.1 mg/L). No decrease of viable cells in lungs was observed for the other comparators except that MIN, CIP, and LVX showed 2.1, 2.8, and >3 log10 reduction, respectively, at 100 mg/kg only against a low-MIC isolate.

Conclusions: CFDC is stable against both L1 and L2 β-lactamas, and showed potent in vivo efficacy in a murine lung infection model reflecting in vitro activity against S. maltophilia. These results suggest that CFDC has high potential as an effective therapeutic option for S. maltophilia infections.

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Abstract 2581

**Evaluation of Colibrí for antimicrobial susceptibility testing**

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**Background:** Colibrí™ (Copan) is a system which automatizes the picking of isolated colonies grown on petri dishes and allows the preparation of Maldi-tof targets for bacterial identification, microbial suspensions for antimicrobial susceptibility testing, and inoculation of purity plates.

**Materials/methods:** A total of 239 urine specimens were inoculated onto CHROMID®CPS elite (bioMérieux) and processed into the WASPLab® system. Isolated colonies of *E. coli* (n=165), *Enterococcus spp* (n=42) and *Staphylococcus spp* (n=32) were selected by a technician on the image. Plates were transferred to the Colibrí™ for the colony picking and the automated preparation of the bacterial suspension for the realization of the VITEK2® susceptibility cards with respectively AST-N340 card for *E. coli*, AST-P606 for *Enterococcus spp* and AST-P631 for *Staphylococcus spp*. In parallel, a microbial suspension was realized manually with the same plate using the procedure of the laboratory. Results were compared in term of Essential Agreement (EA) and Categorical Agreement (CA) globally for the card and individually per antibiotic. Acceptance criteria used for the comparison were based on ISO 20776-2.

**Results:** For the EA, a total of 2796 MIC (Minimum Inhibitory Concentration) for *E. coli*, 380 for *Enterococcus spp* and 570 for *Staphylococcus spp* were compared to the manual methodology. The global EA was respectively 99.7%, 100% and 99.3%. The individual EA varied from 93.8% to 100% for other antibiotic/species. Concerning the CA, among a total of 2781 data for *E. coli*, 376 for *Enterococcus spp* and 545 for *Staphylococcus spp*, the global CA varied from 98.4% to 99.1% with an individual CA from 95.2% to 100%.

**Conclusions:** The performance of Colibrí™ for the automated preparation of bacterial suspensions are equivalent to the manual procedure for the realization of VITEK® 2 susceptibility cards for *E. coli*, *Enterococcus spp* and *Staphylococcus spp*. Colibrí™ allows the total automation of urine specimens from the sampling to the results of VITEK®2 antimicrobial susceptibility testing. The introduction of Colibrí™ in the workflow of a laboratory allowed a consequent gain in reproducibility, productivity and traceability with a real medical added value for the patient.

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Abstract 2583

Healthcare workers in Kyrgyzstan and QuantiFERON-TB Gold Plus testing for the detection of latent tuberculosis infection

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Background: The Kyrgyz Republic has a high incidence of TB, and health care workers (HCW) are at an increased risk of infection, despite training and effective control measures being in place, due to close contact with a high density of infected individuals as well as performing high risk procedures. The aims of this study were to assess the prevalence of LTBI among HCW in major hospitals in the Kyrgyz Republic using Quantiferon-TB Gold plus (QFT), and determine if there is any difference in risk of positivity between positions, department or hospitals.

Materials/methods: Hospital employees working in the major hospitals in Karakol, Kemin, Karabalta and the National Tuberculosis Centre (NTC) in Bishkek were invited to participate in the study. Following informed consent a questionnaire was used to collect age, position, and department of employment. Blood was drawn for QFT testing for all participants. A univariate and multivariate analysis were performed using logistic regression to assess risk factors with positivity using the “Administrative” position as the base. Participants from the three hospitals were combined and compared to those working at the NTC due to differences between sites.

Results: A total of 404 HCW provided valid QFT results (NTC=220, Karabalta=98, Karakol=49, Kemin=37). Age was significantly associated with positivity (OR=1.02 per year, p-value=0.03) and therefore controlled for in all analysis. At the NTC, there was an increased odds of being QFT positive among doctors (OR=12.6, 95%, p=0.03) and lab personnel (OR=29.8, 95% p<0.001). Additionally, working in the drug resistance ward (OR=9.1, p=0.049) and smear negative ward (OR=13.2, p=0.03) had higher odds of positivity in the NTC. There was no effect of position or department on QFT positivity for the combined hospital sites.

Conclusions: Health care workers have an increased odds of being QFT positive once controlling for age differences among positions at the NTC, but the effect of position is not detected at the major hospitals combined. This study highlights the importance of monitoring LTBI in HCWs, as well as highlighting the need for increased training and protective measures against transmission of TB.

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Abstract 2585

A case of Lomentospora prolificans (LoPro) treated with the novel antifungal olorofim

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Abstract third-party references: F2G Ltd

Background: LoPro is difficult to treat with currently approved antifungals. Only voriconazole is approved for the treatment of LoPro and mortality remains high despite combination therapy and prolonged therapy is common. Olorofim is a novel antifungal agent of the orotomide class, acting via inhibition of the enzyme dihydroorotate dehydrogenase. Olorofim has shown strong in vitro and in vivo inhibition of LoPro.

Materials/methods: Case summary: Following bilateral breast enhancement in August 2018, an otherwise healthy 49-year-old woman from rural Western Australia developed infection of her right implant with L. prolificans that spread to adjacent soft tissues, rib and sternum. Implant removal (October 2018), repeated debridement, hyperbaric oxygen, voriconazole, terbinafine, miltefosine, posaconazole, and anidulafungin were employed serially, and in combination; with no control of the infection. She was transferred to Sydney and enrolled in an open-label study of the novel antifungal olorofim in November 2018 (ClinicalTrials.gov Identifier: NCT03583164), with continuing surgical debridement as needed.

Results: She was treated from 29 Nov 2018 to 16 Oct 2019 (322 days) with olorofim, initially at a dose of 60 mg twice daily. Gradual healing of the surgical site occurred with wound closure in July 2019. Wound cultures were intermittently positive for LoPro prior to wound closure, but olorofim MICs of these isolates remained at 0.25 ug/ml throughout. Because of blood trough levels at the lower end of the target range, the dose was increased to first 90 mg, and then 120 mg twice daily. Olorofim was well tolerated throughout.

Conclusions: In this case, a progressive, disfiguring, and potentially life-threatening chest wall infection due to LoPro that was unresponsive to all available therapies, however improved steadily on olorofim. In addition, olorofim was well tolerated during the extended duration required to control this complex infection.

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Abstract 2586

Genomic and phenotypic characterisation of invasive neonatal and colonising Group B Streptococcus isolates from Slovenia, 2001-2018

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Background: Group B Streptococcus (GBS) is the leading cause of invasive neonatal infection in the industrialized world. We aimed to genomically and phenotypically characterise invasive GBS isolates in Slovenia from 2001-2018 and compare them with contemporary colonising GBS isolates.

Materials/methods: One-hundred-and-fourteen invasive GBS isolates from 101 patients and 71 colonising isolates from 70 pregnant women were analysed for basic clinical characteristics, antimicrobial susceptibility and capsular serotype. Whole-genome sequencing was performed to assign multilocus sequence type (ST) and clonal complex (CC), pathogenicity/virulence factors and genome-based phylogeny. Clustered regularly interspaced short palindromic repeat (CRISPR) analysis was performed for epidemiological typing. Diagnostically important cfb region was analysed for deletions that may influence molecular diagnostic accuracy.

Results: Among invasive isolates, 41.6% and 58.4% were responsible for early-onset (EOD) and late-onset (LOD) including very late-onset disease (vLOD), respectively. All isolates were susceptible to benzylpenicillin with MIC≤0.125 mg/L. Clindamycin susceptibility was 83.6%. Overall, 7 serotypes were identified (Ia, Ib, II-V and VIII), serotype III being the predominant (59.6%). Twenty-nine MLST STs were detected that grouped into 6 CCs. The hypervirulent CC-17 was the predominant CC overall (53.2%) and within invasive (67.3%) and non-invasive (32.9%) isolates (p<0.001). It was more common among LOD (81.4%) compared to EOD (47.6%) (p<0.001). The prevalences of other CCs were 12.9% (CC-23), 11.1% (CC-12), 10.5% (CC-1), 8.2% (CC-19), 1.8% (CC-498). The remaining 2.3% of isolates were singletons. A CRISPR analysis revealed specific patterns for different CCs. CC-17 contained the shortest CRISPR loci with the lowest number of spacers. Finally, no deletions were detected in the cfb region in our study.

Conclusions: This is the first genomic characterisation of GBS isolates in Slovenia and provides a valuable background microbiological data for influencing policy changes with regards to the urgent implementation of universal screening for GBS colonisation in pregnancy. Molecular diagnostic tests based on cfb region detection can be used for this purpose. However, constant surveillance of its performance is warranted.

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Abstracts 2020

Abstract 2587

**Evaluation the impact of dengue infection in gestation and conception: an ecological study using time series analysis**

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**Background:** The World Health Organization estimates that 40% of the world’s population lives in dengue fever (DF) endemic areas, occurring about 390 million cases/year (24% symptomatic). In the last 40 years, Brazil had recurrent epidemics, approximately 1.5 million cases/year and more than 500 deaths/year were reported between 2010 and 2016. However, the consequences of infection in pregnancy and conception are still uncertain.

**Materials/methods:** In order to demonstrate the effect of DF on the pregnancy outcomes, an ecological analytical study of time series was carried out. The time series of DF incidence in women in childbearing age, incidence of prematurity, incidence of low birth weight and prevalence of congenital malformations were constructed. In order to analyze different scenarios, in addition to Brazil, eight cities with different DF transmission rates were selected. For the analysis of the time series, a Bayesian approach was used in the construction of dynamic models that describe the series and eventual association between DF and outcomes related to the newborns. The calculation of the association measure (coefficient of effect) used the Integrated Nested Laplace Approximation (INLA) method.

**Results:** In the period between January/2001-December/2013, 2,967,606 cases of DF were reported in Brazil in women aged 10-59 years (67.38/100,000) and 38,512,280 live births were registered. A significant positive association between the incidence of DF and the incidence of prematurity was detected in Brazil and four cities. The association observed suggests that epidemiological characteristics in 2010 are relevant to explain the phenomenon. It should be noted, the huge epidemic secondary to the reintroduction of DENV-4 in Brazil, from 2010. The expansion of this serotype was earlier, intense and lasting, in the capitals where the positive association was detected, whether by direct action of primary and secondary infection in pregnancy, either by the collapse of overburdened health systems or simply by the accumulation of exposed pregnancies.

**Conclusions:** The study corroborates previous findings, signals an unprecedented evidence of no proportionality, suggesting that the observed phenomenon is multifactorial, and extrapolates previous hypothesis, which attributed exclusively to the intense inflammatory state observed in the acute phase of DF the risk of prematurity.

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Abstract 2588

A novel standardised artificial sputum for external quality control of the whole TB-diagnostic workflow

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Background: Fighting tuberculosis (TB) relies on early, fast and accurate diagnosis including resistance screening. Besides a well-equipped laboratory infra structure, external quality assessment (EQA) monitoring standard diagnostic procedures is essential for guaranteeing good laboratory performance. However, till to date there is no validated, standardized test matrix that can be used for monitoring all disciplines of sputum based TB diagnostics including smear microscopy, culture, nucleic acid extraction and PCR. Since human sputum is not easily obtainable and requires extensive pre-testing for Mycobacterium tuberculosis complex (MTBC) negativity, artificial sputum (AS) would be an alternative test matrix performing such EQAs.

Materials/methods: We have developed a novel mucin-based artificial sputum (MUCAS). MUCAS was macro- and microscopically (Ziehl-Neelsen) compared to established AS based on methyl cellulose or polyacrylamide as well as to human sputum. The performance of decontaminated MUCAS samples in MGIT and Löwenstein-Jensen (LJ) cultures was also investigated. For validating MUCAS in a clinical setting, we conducted an EQA trial including five partner laboratories in Tajikistan. The laboratories received a blinded panel of 20 MUCAS samples for LJ and MGIT culture with different H37Ra concentrations and negative controls. Samples were also analyzed in the Supranational Reference Laboratory Gauting (SNRL, Germany).

Results: In contrast to other AS, MUCAS macro- and microscopically resembled human sputum. After NALC-NaOH decontamination of spiked MUCAS samples, high loads of MTB could be recovered and LJ as well as MGIT cultures could be subsequently performed. MTB survived for up to 13 days in MUCAS, which enabled shipping of viable MTB strains to Tajikistan for EQA purposes: 4 of 5 and 2 of 5 labs had false positive and negative culture results, respectively. In one lab an extremely high MGIT contamination rate was observed (14/20). No false positive results were obtained in the SNRL. 15% of MGIT cultures were contaminated and could not be analyzed. Auramine staining was only possible with high H37Ra concentrations.

Conclusions: MUCAS is a suitable matrix for EQA panels assessing Ziehl-Neelsen microscopy, mycobacterial culture and –as previously shown– molecular diagnostics.

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Multiplex detection of SNPs conferring rifampicin resistance in *Mycobacterium tuberculosis*

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**Abstract third-party references:** The research leading to these results has received funding from the Seventh Framework Programme [FP7/2007/2013] under Grant Agreement n° 604237.

**Background:** Rifampicin resistance in *Mycobacterium tuberculosis* is conferred by single nucleotide polymorphisms (SNPs). These SNPs lead to different resistance levels. The detection of *M. tuberculosis* and the identification of the SNPs conferring the rifampicin resistance is of upmost importance in the control of Multi-Drug Resistant *Mycobacterium tuberculosis* (MDR-TB) infections.

**Materials/methods:** A TB/RIF test on a cartridge was developed, fitting into the TRAPIST v6 microfluidic platform that includes a continuous-flow amplification followed by an oligochromatographic detection.

A set of three fluorescent primer pairs was selected to amplify the *Mycobacterium tuberculosis* complex and two different sequences of the *rpoB* gene covering the SNPs involved in the rifampicin resistance.

One specific probe for bacterial identification and 29 different probes, distributed on 10 *rpoB* SNP positions (430-431-432-435-441-445-448-450-452-491) to detect specifically wild type (WT) as well as mutated amino acids, were spotted on a nitrocellulose membrane.

The TB/RIF tests were performed on extracted DNA from a representative panel of characterised wild type and rifampicin resistant TB strains. The dedicated equipment measures the fluorescence intensity of each spotted probe allowing the identification of the amino acid present in the sample at each *rpoB* SNP position.

**Results:** All the DNA samples were correctly identified as *Mycobacterium tuberculosis* complex strains. All amino acids at each *rpoB* SNP position were also correctly identified and are presented in the table. The amino acid detected conferring rifampicin resistance are on the black compartments.

<table>
<thead>
<tr>
<th>Identified amino acid in rpoB positions ([<em>M. tuberculosis</em> numbering])</th>
</tr>
</thead>
<tbody>
<tr>
<td>TB strains</td>
</tr>
<tr>
<td>5671</td>
</tr>
<tr>
<td>5517</td>
</tr>
<tr>
<td>5670</td>
</tr>
<tr>
<td>5623</td>
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<tr>
<td>5700</td>
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<td>5660</td>
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<tr>
<td>5650</td>
</tr>
<tr>
<td>5850</td>
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</tbody>
</table>

**Conclusions:** The technology developed allows a specific detection, in a single assay, of each amino acid distributed on 10 mutational *rpoB* positions [wild type and mutated genotypes].

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Abstract 2590

**Impact of a training activity on collecting blood samples regarding a correct bloodstream infections diagnosis: The risks of overseeing the foundations**

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**Background:** Sepsis is one of the main causes of morbidity and mortality worldwide. Community-acquired sepsis is the most frequent source placing the Emergency Service (ES) as a crucial department to improve sepsis diagnosis. Blood cultures have high clinical relevance and early microorganisms identification involved is essential for a successful management of patients. Recommendations regarding appropriate blood culture sampling are needed being the volume inoculated in flasks and the number of sets extracted the most crucial steps.

The objective of this study was to evaluate the impact of a training activity in terms of contamination rate, number of flasks and sets received in the Microbiology Service from the ED and also the number of clinically valuable bacteremia following the ESCMID-SFM Manual of Microbiology within the pre- and post-training period.

**Materials/methods:** A prospective observational study was conducted based on the elaboration and divulgence of a blood culture extraction protocol in May-2018. Nurse training sessions were carried out monthly from June-December 2018. The number of flasks and sets received from January 2017-December 2018 were obtained from the Laboratory Information System and retrospectively analyzed. Pre-training period was considered from January 2017-April 2018, and the post-training period between May-December 2018.

**Results:** Data showed an increase in the average number of flasks received between the pre- and post-training period. Regarding the number of sets, the percentage of blood cultures collected with a double extraction improved significantly. The contamination rate (contaminated flasks/total flasks*100) decreased between both periods. The monthly average of clinical valuable bacteremia also increased (Table 1). The percentage of clinical valuable bacteremia (positive blood culture/total blood culture*100) was 10.7% in the pre-period and 15.5% in the post-period, showing a significant growth.

**Conclusions:** Nurse training sessions based on a correct blood culture extraction have high clinical impact on BSIs diagnosis. More formative initiatives should be established to guarantee a correct microbiology diagnosis in this critical situations.

**Table 1:** Results before and after training sessions.

<table>
<thead>
<tr>
<th></th>
<th>PRE-TRAINING</th>
<th>POST-TRAINING</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Flasks</strong></td>
<td>522</td>
<td>950</td>
</tr>
<tr>
<td>One-Blood Culture set [n, (%)]</td>
<td>4163 (95.7%)</td>
<td>541 (23.9%)</td>
</tr>
<tr>
<td>Two-Blood Culture set [n, (%)]</td>
<td>162 (3.7%)</td>
<td>1664 (73.5%)</td>
</tr>
<tr>
<td>Three-Blood Culture set [n, (%)]</td>
<td>26 (0.6%)</td>
<td>59 (2.6%)</td>
</tr>
<tr>
<td>Contamination Rate</td>
<td>3.3%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Bacteremias [n, (%)]</td>
<td>29.2</td>
<td>43.6</td>
</tr>
</tbody>
</table>

(□)=Monthly average; n=Total number.

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A mechanism-based pharmacokinetic/pharmacodynamic model based on pharmacokinetic and static time-kill data alone can predict the \textit{in vitro} bacterial regrowth of 3 fluoroquinolone-resistant \textit{Escherichia coli} strains after dynamic exposure

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\textbf{Background:} In order to prevent the further increase of antimicrobial resistance and improve current clinical dosing practices, a profound understanding of the underlying mechanisms of bacterial regrowth and their link to exposure and time is necessary. Rather than solely using metrics such as the minimal inhibitory concentration [MIC] [1], mechanism-based pharmacokinetic/pharmacodynamic (PK/PD) models can elucidate the link between exposure and response.

\textbf{Materials/methods:} In this work, data from static \textit{in vitro} infection models obtained from 3 fluoroquinolone resistant clinical isolates of the model pathogen \textit{E. coli} [MIC 8, 2 and 8 mg/L] under levofloxacin exposure, was combined with PK of dynamic time-kill curve experiments mimicking \textit{in vivo} antibiotic pressure at target site. This data was analysed using non-linear mixed effects modelling in NONMEM v.7.4, where sequentially the growth behaviour, PK, antibacterial effect and persister formation were characterised. Model selection was based on plausibility and accuracy of parameter estimates, goodness-of-fit and the log likelihood ratio test.

\textbf{Results:} A two-compartmental PK model with linear elimination linked to a bacterial growth model consisting of a growing and non-growing persister fraction best described the current data. Separate levofloxacin killing potencies (EC\textsubscript{50}) and maximum persister formation rates P\textsubscript{max} supported differences in underlying mechanisms of resistance and persistence between the strains. Indeed, two isolates with the same MIC, had vastly different killing and regrowth behaviour, which was represented by different EC\textsubscript{50} and P\textsubscript{max} values. Although model development was based solely on static experiments, the final model was then applied to predict time-kill curves generated under dynamic C(t) profiles mimicking clinically relevant dosing regimens and was able to predict the regrowth behaviour for all three strains, for one and two doses of levofloxacin.

\textbf{Conclusions:} In this work, we further underline the importance of alternative strategies beyond the MIC to investigate optimal dosing strategies of antibiotic drugs. We showed that the use of mechanism-based PK/PD modelling using \textit{in vitro} exposure-response data with multiple strains allows for elucidation of resistance and persistence mechanisms. It was shown that even for strains with the same MIC, these differences have a profound impact on efficacy of established dosing regimens.

\textbf{References}


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Evaluation of Colibrí for the identification of Gram-negative bacilli

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Background: Colibrí™ is a system which automatizes the picking of isolated colonies grown on petri dishes and allows the preparation of matrix-assisted laser desorption/ionization time of flight targets. Fast and reliable identification of microorganisms is a key task in microbiology to improve time to result.

Materials/methods: A total of 92 clinical urine specimens previously selected with Gram negative bacilli (Klebsiella spp n=25, Enterobacter spp n=16, Citrobacter spp n=9, Proteus spp n=19, other Proteae group n=7, Pseudomonas aeruginosa n=12, other species n=4) were inoculated onto CHROMID®CPS elite (bioMérieux) and processed into the WASPLab® system. One colony with size > 0.6mm was selected by a technician on the image and plates were transferred to Colibrí™ for the picking of the colonies, the automatic spotting and the matrix HCCA dispensing on disposable MBT Bio targets for identification with BRUKER MALDI biontyper®. In parallel, the spotting was realized manually with the same plate using the procedure of the laboratory. Identification were compared between manual and Colibrí™ spotting. In case of discrepancy spots were realized again with both methodology for confirmation.

Results: The comparison between Colibrí™ and the manual process was evaluated on a total of 114 results (including 22 re-tests). The concordance was 78.1% (n=89). The rate of discrepancies of 21.9% (n=25) concerned in majority Klebsiella species (n=9) and Proteus mirabilis (n=6) for which no peaks was observed with a Colibrí™ spotting and a score of identification > 2 with the manual methodology. Only 5 discrepancies were confirmed by the retest without any link to a specific specie. No errors of identification were observed with Colibrí™ compared to manual spotting.

Conclusions: Colibrí™ for automatic spotting of Gram negative bacilli on disposable MBT Bio targets can be implemented in microbiology laboratory for the diagnostic of urinary tract infections with a good confidence level. The use of formic acid treatment for mucous species used in the routine of the laboratory can reduce the number of unidentified isolates observed with Colibrí™

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**Whole genome sequencing for Neisseria meningitidis for health protection action**

Sharif S. M. Shaaban*, Laura Macdonald1, Heather Murdoch1, Fiona Johnston1, Roisin Ure2, Kevin Scott2, Derek Brown2, Andrew Smith2,3, Matthew Holden1,4, Claire Cameron1

1Health Protection Scotland, Glasgow, United Kingdom, 2Scottish Microbiology Reference Laboratories Glasgow, Glasgow, United Kingdom, 3University of Glasgow, Glasgow, United Kingdom, 4University of St Andrews, St Andrews, United Kingdom

**Abstract third-party references:** NHS Scotland

**Background:** Whole genome sequencing (WGS) is rapidly becoming a key component of microbial typing and outbreak tracking in public health. The highly reproducible fine discrimination offered to determine relatedness and clustering is a key advantage. However, there remain potential limitations, such as the requirement for isolates and receiving results within the time frame for health protection action. Moreover, the evidence base for what degree of genomic relatedness should trigger such action is not yet fully established.

**Materials/methods:** In Scotland, we retrospectively analysed data, from 2009-2018, to evaluate the potential impact WGS may have had for health protection purposes, had it been available real-time. This was achieved by retrospectively examining core genome MLST (cgMLST) profiles derived from WGS data for clusters that had previously been identified epidemiologically, and conversely, analysing cgMLST data to ascertain whether potentially linked cases may previously have been overlooked through traditional methods.

**Results:** Epidemiological analysis identified 10 clusters in a variety of settings. Of these, for 5, WGS could offer no further insight, as isolates were not available, or available for only one case. Four clusters were independently detected using WGS data, and one putative epidemiological cluster was dismissed using WGS data, having a difference of more than 900 alleles. In contrast, WGS detected an additional eight novel putative clusters, and an additional case for one of the existent epidemiologically defined clusters. These putative clusters have undergone further analysis to determine the likelihood of them being genuinely linked cases. However, in general, a preliminary distance threshold of ≤ 30 alleles has been deemed appropriate to initiate such further investigation.

**Conclusions:** WGS data has shown great potential in aiding public health intelligence. However, this can only be utilised when the appropriate primary samples are available. Furthermore, the thresholds at which clustering investigation is triggered, for public health purposes, and linked cases confirmed needs further definition; a challenge with an organism displaying inherent marked differences in strain variability. This analysis therefore significantly contributes to the limited evidence base, particularly the proposed analytical threshold.

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**PhenoMATRIX TAG and Colibrí for a faster workflow of the management of urine specimens**

Amandine Roché¹, Guillaume Teissier¹, Rémi Fournier¹, Thibaud Bayol¹, Pierre Mion¹, Jérémy Bayette*¹

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**Background:** LABOSUD’s department of microbiology manage more than 1000 urine samples per day. PhenoMATRIX™ (expert system of the WASPLab® solution combining plate reading algorithms and clinical information from LIS system) was installed in June 2018 for the management of clinical urine specimens. In July 2019, PhenoMATRIX™TAG and Colibrí™ were added in synergy to the initial configuration. PhenoMATRIX™TAG permits to tag isolated colonies (pick point) on the image for Colibrí™ workflow. Colibrí™ automatizes the picking of isolated colonies and allows the preparation of MALDI-TOF targets, microbial suspension for antimicrobial susceptibility testing and inoculation of purity plates.

**Materials/methods:** A qualitative study was performed on 699 clinical urine samples positive to *E. coli* to determine the capabilities of PhenoMATRIX™TAG to select available isolated colonies on CHROMID®CPSE Elite incubated 16h into the WASPLAB™. Number of plates was evaluated with 0, 1, 2 and ≥ 3 colonies tagged on the image. A quantitative study was realized on 91 positive *E. coli* plates by measuring the time spent by an user for the assignment of pick points without the implementation of PhenoMATRIX™TAG.

**Results:** Among the 699 results, 96,4% [n=674] images were marked with pick points. 91,4% [n=639] were displayed with more than 3 pick points, 2,4% [n=17] with 2 pick points and 2,6% with 1 pick point. The remaining 3,6% [n=25] not tagged plates represented high concentrated isolates without any available colonies. Regarding the quantitative study, average time for picking assignment before the implementation of PHENOMATRIX™TAG was 25,8 seconds.

**Conclusions:** The performance of PhenoMATRIX™TAG allowed to tag automatically 91,4% of the plates with more than 3 pick points, saving an average time of 1h10 min per day. In addition, the high precision of Colibrí™ for the picking of the colonies enabled the suppression of the purity plate for the Antimicrobial Susceptibility Testing. Thanks to the traceability, reproducibility, accuracy of the combined artificial intelligence and Colibrí™ system, the diagnosis of urinary tract infections to *E. coli* is completely automated with a high level of confidence.

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Abstract 2603

**ART24, a novel live biotherapeutic product, in development for the prevention of *Clostridioides difficile* infection (CDI) recurrence is effective in a mouse model of CDI infection**

Christopher Murphy¹, Tim Murphy², Ronald Farquhar¹, Laurent Chesnel*¹

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**Background:** ART24 is being investigated as a live biotherapeutic product (LBP) treatment to prevent recurrence of *Clostridioides difficile* infection (CDI) following successful antibacterial therapy. ART24 was isolated from a human fecal sample, purified and identified as a member of the *B. amyloliquefaciens/B. velezensis* group. We have determined that the strain has potent *C. difficile* killing activity *in vitro* and sought to determine if this activity translated in an *in vivo* infection model setting.

**Materials/methods:** A series of independent studies were conducted in a mouse model of *C. difficile* infection. These studies were modeled to simulate clinical conditions and determine the efficacy of orally-dosed ART24 as measured by adverse clinical signs, body weight loss, and mortality. Mice received an antibiotic cocktail for eight consecutive days in the drinking water. Five days prior to *C. difficile* infection, the antibiotic water was removed. Animals were placed in clean cages and sterile drinking water provided to the mice. Three days prior to infection with *C. difficile*, mice were dose with Clindamycin at 10 mg/kg via oral gavage in a volume of 10 mL/kg. Mice were dosed with 5x10⁸ ART24 CFU QD or TID, or saline for 10 days starting 1 day prior to infection and until study day 9. Animals were infected with *C. difficile* strain ATCC 43255 (6.3x10⁵ to 1.97x10⁶ CFU) via oral gavage. A total of 65 and 40 mice were treated with ART24 and saline respectively across the 3 studies conducted.

**Results:** Oral gavage of freshly cultured ART24 cells demonstrated protective effects in animals subsequently infected with *C. difficile* with improved survival (90% in ART24 dosed groups versus 70% in the saline control group), and a reduction in disease-related clinical observations including weight-loss, wet tail, diarrhea, hunched posture, dehydration and lethargy. ART24, washed and resuspended in sterile PBS, had equivalent efficacy in this infection model.

**Conclusions:** ART24 is efficacious in a mouse model of CDI. ART24 is a promising LBP clinical candidate being assessed for safety in a Phase 1 trial in recently cured CDI patients.

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**Abstract 2608**

**Not all candidaemias are the same: utility of a rapid identification**

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**Background:** Fungemia is a serious life-threatening illness associated with high mortality. The gold standard for the diagnosis of fungemia is blood culture. Conventional biochemical methods for species identification typically take from 24 to 72 hours and a delay of 12 to 48 hours in appropriate antifungal therapy is associated with an increased risk of mortality. Rapid identification of fungi allows a more targeted empirical therapy and a better outcome of the patient, given the different antifungal susceptibility profile of some species. For these reasons, all blood cultures positive for fungi during the period from June 2015 to October 2019 were tested by means of a multiplex Real-Time PCR for rapid identification.

**Materials/methods:** All blood cultures positive for fungi by microscopic examination after Gram staining underwent FilmArray blood culture identification panel, standard culture, identification by means of Vitek 2 and antifungal susceptibility testing by broth microdilution. Only blood cultures positive for single Candida species were included in the study. Median values of C-reactive protein and complete blood count from samples drawn concurrently with blood cultures were also evaluated.

**Results:** A total of 71 blood cultures were included in the study. The frequency of isolates was: *Candida albicans*: 34 (47.9%); *Candida glabrata*: 17 (23.9%); *Candida parapsilosis*: 16 (22.6%); *Candida tropicalis*: 4 (5.6%). The agreement between FilmArray and Vitek 2 was of 100%. Respectively for *C. albicans*, *C. glabrata*, *C. parapsilosis* and *C. tropicalis*, a significant difference was found among median values of age: 69 vs 80 vs 61 vs 61 years (*p*<0.05); C-reactive protein: 9.9 vs 21.3 vs 8.3 vs 11.9 mg/dl (*p*<0.05); neutrophils: 7840 vs 10480 vs 4920 vs 4950 cells/microliter (*p*<0.012); neutrophil/lymphocyte ratio: 6.9 vs 18.1 vs 4.3 vs 5.0 (*p*<0.02). We found a significant greater proportion of *C. glabrata* isolates resistant to fluconazole: 8/17 (47.1%; chi square: 29.6; *p*<0.0001) and of *C. parapsilosis* isolates resistant to both anidulafungin: 11/16 (68.8%; chi square: 49.7; *p*<0.0001) and micafungin: 6/16 (37.5%; chi square: 26.6; *p*<0.0001).

**Conclusions:** In this study we found a greater inflammatory state associated with *C. glabrata* fungemia, possibly due to older age and underlying disease.

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Implementing pathogen genomics effectively: a seamless service
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Abstract third-party references: NHS Scotland

Background: For whole genome sequencing (WGS) to transform pathogen typing, outbreak detection, resistance calling, and source attribution, its high-resolution discrimination must be applied appropriately to the clinical and public health questions being addressed. We have developed a fully integrated “end-to-end” process that is defined from the selection and transmission of samples to the reference laboratory, through the technical and bioinformatic pipelines, to the epidemiological actions implemented as a result of this activity. Chosen exemplars organisms include species with different molecular biology and clinical time lines, and with a diversity of clinical questions to be addressed.

Materials/methods: Pathogen sequencing is being implemented in Scotland in a collaboration between the Microbiology Reference laboratories, Health Protection Scotland (HPS), and the National Services Division (NSD). We describe the service through a total of 32 documents covering all aspects for the process including a service objective, sampling, laboratory protocols, data analysis, turnaround time, data sharing, operational capacity and quality control standards. This approach has now been applied to Neisseria meningitidis, with Mycobacteria spp. and Streptococcus pneumoniae following closely behind.

Results: The service has already yielded data used to track and trace outbreaks, as well as inform public health actions. Examples of these are common for STEC, Salmonella spp. and Shigella spp., for which the WGS service is fully established. The insights gained from working with these examples are used to supplement and improve the service for other organisms (such as current work attempting to determine the best use and results of WGS clustering for Neisseria meningitidis).

Conclusions: The ambition is to provide a seamless pathogen sequencing service from patient to clinical and public health action. We have found this approach to be effective in generating a sense of direction and focus on patient and public health deliverables. We believe this will be of value to others contemplating the introduction of pathogen sequencing service for public health benefit.

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The difference in mortality between adult patients with laboratory-confirmed influenza A and B, a single centre observational study

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Background: Seasonal influenza is an annual occurrence that leads to large community outbreaks and increased hospitalisation with significant morbidity and mortality due to complications such as secondary bacterial pneumonia. A number of studies have suggested that influenza A (IFA) is associated with increased rates of hospitalization and mortality compared to influenza B (IFB). Whipps’ Cross Hospital serves an ethnically diverse population of approximately 350,000 people in East London. During the 2017 to 2018 influenza season, moderate to high levels of influenza activity were observed in the United Kingdom with a high proportion of IFB circulating. The aim of this study was to compare demographic and clinical variables, including severity of infection and mortality, in patients diagnosed with IFA or IFB during the 2017 to 2018 UK influenza season.

Materials/methods: Patient demographic and clinical information were obtained by accessing electronic and paper medical records of patients testing IFA or IFB positive using the Cepheid GXP. We used $\chi^2$ test to compare these variables in patients with laboratory confirmed IFA and IFB.

Results: 127 adult patients had confirmed influenza, 71 (55.9%) had IFA and 56 (44.1%) IFB. 93 (73.2%) of patients diagnosed were over 60. 104 (81.9%) patients had underlying medical co-morbidities. 23 (32.4%) patients with IFA and 17 (30.4%) patients with IFB had a documented complication, most commonly bacterial pneumonia. There was no significant difference between severity at presentation, need for supplementary O2, admission to HDU/ITU or median length of stay. The overall mortality rate was 4.7% (6/127 patients) and 7.1% (9/127 patients) at 7 and 30 days respectively. There was a statistically significant difference in 7-day mortality between patients with IFA (1/71 patients, 1.4%) compared with IFB (5/56 patients, 8.9%) ($p = 0.047$) although this became non-significant at 30 days.

Conclusions: We did not observe significant differences in severity, length of stay, rates of hospitalization or rates of complication between patients with IFA and IFB. There was a statistically significant higher 7-day mortality in patients with IFB which was not apparent at 30 days.

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Evaluation of targeted antifungal prophylaxis after liver transplantation: are echinocandins the optimal choice?

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**Background:** Targeted antifungal prophylaxis (TAP) is considered the optimal strategy for prevention of invasive fungal infection (IFI) in patients undergoing liver transplant (LT). However, feasibility and efficacy of such an approach has been scarcely investigated.

**Materials/methods:** Prospective cohort study of consecutive adult patients undergoing LT at three Italian hospitals, from January 2015 to December 2018. During the study period, a common TAP protocol was followed in the participating centers. Patient were classified as having no risk (NR), low risk (LR) and high risk (HR) for IFI with indication to receive no prophylaxis, fluconazole (7-14 days) and anti-mold drug (21 days), respectively. Endpoint variable was IFI diagnosis, defined according to EORTC criteria, within 1-year after LT. IFI breakthrough (IFI-B) was defined as IFI occurring within ≤1 dosing interval after drug discontinuation.

**Results:** We included 485 LT patients: median age 56 (IQR 49.61) years, median MELD at LT 17 (IQR 12.25). IFI-risk class distribution was NR, LR and HR in 31.8%, 20.8% and 47.4% of cases, respectively. Antifungal prophylaxis was administered to 220 patients, with an overall compliance to TAP protocol of 64.1%, which raised to 71.7% among HR patients. The drugs used for TAP were echinocandins (110, 50%), liposomal amphotericin-B (88, 40%) and fluconazole (22, 10%). TAP median duration was 13 (IQR 7-20) days. IFI was diagnosed in 29 patients (6%), comprising 17 invasive candidiasis (IC) and 12 invasive aspergillosis (IA). Median time to IC and to IA was 12 (IQR 3.5-34.5) and 28.5 (IQR 12.5-81.3) days after LT, respectively. Eleven patients presented with an IFI-B, 9 of them during echinocandin TAP. Multivariate analysis adjusted for HR class, adherence to TAP, and echinocandin use, showed that only HR class was independently associated with IFI development (HR 3.02, 95%CI 1.2-7.5, p=0.017). However, there was a trend toward higher IFI risk in patients receiving echinocandins (see Figure).

**Conclusions:** We confirm TAP as a feasible and effective strategy to prevent IFI in LT recipients. Concerns about the use of echinocandins for TAP is rising due to their trend toward higher cumulative risk of IFI, mostly IFI-B.

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Head-to-head comparison of analytical sensitivities of BD MAX MDR-TB, Xpert MTB/Rif Ultra and FluoroType MTB using human and artificial sputum

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Background: A new generation of fully automated molecular tests for pulmonary tuberculosis (TB) has been recently launched with Xpert MTB/Rif Ultra [XP-Ultra] and BD-MAX MDR-TB [BD-MAX]. However, data regarding the performance of BD-MAX and the comparability of both assays based on experiments using the same defined test matrix are scarce. For the sake of comparability, it is indispensable for such studies to use the same test matrix. Since larger pools of human sputum are not easily obtainable and expensive to check for Mycobacterium tuberculosis complex (MTBC) negativity, artificial sputum highly resembling human sputum would be a valuable alternative.

Materials/methods: We have investigated the analytical sensitivities [LoD95] of BD-MAX and XP-Ultra in comparison to the well-established FluoroType MTB (FT-MTB). We have further introduced a novel, human-sputum like, mucin-based artificial sputum (MUCAS) that was used as test matrix and compared to human sputum as well as physiological saline solution each spiked with MTB in declining culture- and qPCR-controlled concentrations.

Results: With BD-MAX, XP-Ultra, and FT-MTB, we measured LoD95 values of 2.1 cfu/ml [CI95%: 0.9 – 23.3], 3.1 cfu/ml [CI95%: 1.2 – 88.9], and 52.1 cfu/ml [CI95%: 16.7 – 664.4] in human sputum; of 6.3 cfu/ml [CI95%: 2.9 – 31.8], 1.5 cfu/ml [CI95%: 0.7 – 5.0], and 30.4 cfu/ml [CI95%: 17.4 – 60.7] in MUCAS; and of 2.3 cfu/ml [CI95%: 1.1 – 12.0], 11.5 cfu/ml [CI95%: 5.6 – 47.3], and 129.1 cfu/ml [CI95%: 82.8 – 273.8] in saline solution, respectively. LoD95 of resistance markers were 9 to 48 times higher compared to LoD95 TB.

Conclusions: BD-MAX and XP-Ultra performed equally and had a significantly increased analytical sensitivity compared to the FT-MTB. MUCAS showed characteristics like human sputum while normal saline differed significantly. MUCAS would be an excellent standardized sputum-like test matrix for quality control of TB-PCR assays.

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Abstract 2614

**In vitro synergy of isavuconazole in combination with colistin against Candida auris**

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**Background:** *Candida auris* is an emerging, multidrug-resistant, pathogenic yeast, associated with invasive infections, hospital outbreaks and a high mortality rate. Colistin is a polypeptide antibiotic from the class of polymyxins with activity against gram-negative bacteria. Colistin has also shown *in vitro* activity against some fungi. The aim of the present study was to assess the *in vitro* interaction of the broad-spectrum azole isavuconazole with colistin against clinical *C. auris* isolates.

**Materials/methods:** A panel of 14 clinical *C. auris* isolates from the culture collection of the Westerdijk Fungal Biodiversity Institute were used for the experiments. Combinations of isavuconazole with colistin were tested by a broth microdilution checkerboard technique based on the EUCAST reference methodology. Plates were read spectrophotometrically, and fifty percent of inhibition was used as an endpoint for both, the drugs alone and in combination. Results were interpreted with the fractional inhibitory concentration index (FICI). Drug interactions were defined as synergistic (FICI≤0.5), indifferent (FICI>0.5≤4) or antagonistic (FICI>4). Results were also interpreted by the Bliss interaction model for visualization of the interaction. A reference surface was evaluated from the dose-response curves of each of the two agents, and eventually, the synergy levels were mapped on the experimental combination dose-response surface.

**Results:** By EUCAST methodology, isavuconazole MICs ranged from 0.004 to 1 µg/ml (geometric mean MIC of 0.21 µg/ml). When tested alone, colistin exhibited no antifungal activity with MICs of 1 28 µg/ml for all isolates. Combination of isavuconazole with colistin was synergistic for all isolates with FICIs ranging from 0.31 25 to 0.5. Interpretation by the Bliss interaction model led to synergy for 10/1 4 (7 1%) of the isolates. All other interactions were indifferent. Antagonism was never seen whatever interpretation model used.

**Conclusions:** Combination of isavuconazole with colistin interpreted by the FICI showed strong synergy against all tested isolates and for the majority of isolates interpreted by the Bliss model. Confirmation of the *in vitro* synergistic interaction of isavuconazole with colistin by another technique (e.g. gradient concentration strips) and *in vivo* is warranted.

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Abstract 2616

Challenges in investigation and control of invasive group A Streptococcus outbreaks associated with community health services delivered at home

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Abstract third-party references: Public Health England

Background: In England, a substantial proportion of healthcare, particularly wound management, is delivered by community health services delivered in the patient’s home (CHSDH). This presents unique infection control challenges. Since 2010, Public Health England has identified 16 outbreaks of invasive group A Streptococcus infection (iGAS) associated with CHSDH. This study describes these outbreaks to inform future public health actions.

Materials/methods: We included outbreaks detected between 1st January 2018 and 30th September 2019 involving ≥2 cases of iGAS infection of same emm type, linked to the same CHSDH service. We excluded outbreaks where other exposures offered a more plausible route of transmission. We interviewed the chair of each outbreak control team, with data collected through transcribed recordings using a standardized semi-structured questionnaire.

Results: We identified nine outbreaks involving 87 cases and 27 deaths (31%). Patients’ median age was 82y; 91% had received wound care. Outbreaks varied in size from 2-39 cases (median 6) and lasted from 3 to 487d (median 179d), with significant intervals between identified cases (range 0-163d). Six outbreaks identified cases through retrospective investigation (median 2.5, range 2-7). Investigations included enhanced questionnaires (7/9), network analysis (7/9), whole genome sequencing (WGS, 6/9) and screening of equipment (2/9), staff (9/9) and patients (2/9). Of 8 outbreaks with data available, 296 (median 19, 1 positive, 0.35%) staff were screened (throat and skin lesions). Specific routes of transmission were not identified.

Multiple interventions were utilised including enhanced infection control (9/9), equipment change (3/9) and penicillin V prophylaxis to HCW (7/9). Difficulties obtaining information from CHSDH services, screening and treating staff together with inadequate occupational health support, resulted in delays to investigation and implementation of control measures. Investigating teams emphasized the importance of asking about CHSDH involvement in all community iGAS cases together with role of emm type monitoring and WGS in investigation of possible outbreaks.

Conclusions: CHSDH associated iGAS outbreaks are increasingly identified in the UK with high mortality rates in vulnerable populations. Further work is needed to establish the optimal investigation and management of these outbreaks.

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Biofilm production by Gram-negative bacilli isolated from periprosthetic joint infections

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Abstract third-party references: Funded by SEIMC (Project COLBETA)

Background: Prosthetic joint infection (PJI) occurs in 1-2% of arthroplasties and is a leading cause of prosthetic failure. Most PJI are caused by staphylococci, but there is a significant increase in the proportion of PJI caused by aerobic Gram-negative bacilli (GNB) during the last years. Our aim was to determine the ability of GNB isolated from PJI to develop biofilm.

Materials/methods: Sixty-six strains isolated from consecutive patients with PJI were used. All PJI were diagnosed according to internationally accepted criteria. The samples came from hip (53.03%), knee (34.84%), shoulder (3.03%) and elbow (3.03%) infection, osteosynthesis-associated infection (4.54%) and vertebral abscess infection secondary to vertebral surgery (1.51%). The biofilm formation was evaluated using a modified method of Stepanovic et al. static biofilm assay (APMIS 2007, 115 (8): 891-9), using TSB + 1% glucose with a bacterial inoculum of 10⁶ CFU/mL at 37ºC for 24 h under static and aerobic conditions and safranin for staining. Biofilm formation of isolates was based on the optical density (OD) of each strain and the optical density control (ODc) measured at 570 nm, and classified into weak (ODc<OD<2xODc), moderate (2xODc<OD<4xODc), and strong (OD>4xODc) biofilm-former.

Results: The obtained results are shown in Table 1.

<table>
<thead>
<tr>
<th>Species</th>
<th>n</th>
<th>Median n-fold OD (Q1-Q3)</th>
<th>Median biofilm producer type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter baumanii</td>
<td>1</td>
<td>3.7 [3.0-5.7]</td>
<td>Moderate</td>
</tr>
<tr>
<td>Citrobacter freundii</td>
<td>1</td>
<td>5.5 [3.1-6.0]</td>
<td>Strong</td>
</tr>
<tr>
<td>Citrobacter koseri</td>
<td>2</td>
<td>6.5 [2.9-11.4]</td>
<td>Strong</td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td>5</td>
<td>6.9 [3.1-12.1]</td>
<td>Strong</td>
</tr>
<tr>
<td>Enterobacter hormaechei</td>
<td>2</td>
<td>3.5 [1.9-7.4]</td>
<td>Moderate</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>11</td>
<td>3.2 [2.1-4.6]</td>
<td>Moderate</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>14</td>
<td>5.3 [3.4-9.5]</td>
<td>Strong</td>
</tr>
<tr>
<td>Morganella morganii</td>
<td>5</td>
<td>7.8 [3.2-16.3]</td>
<td>Strong</td>
</tr>
<tr>
<td>Proteus mirabilis</td>
<td>10</td>
<td>5.5 [3.4-10.0]</td>
<td>Strong</td>
</tr>
<tr>
<td>Proteus vulgaris</td>
<td>1</td>
<td>2.05 [1.6-5.1]</td>
<td>Weak (Moderate)</td>
</tr>
<tr>
<td>Providencia stuarti</td>
<td>1</td>
<td>5.5 [4.5-8.7]</td>
<td>Strong</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>8</td>
<td>20.1 [11.7-40.8]</td>
<td>Strong</td>
</tr>
<tr>
<td>Raoutella ornithinolytica</td>
<td>2</td>
<td>1.7 [1.3-2.3]</td>
<td>Weak</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>3</td>
<td>5.3 [3.5-9.3]</td>
<td>Strong</td>
</tr>
</tbody>
</table>

Conclusions: All of the studied strains were biofilm producer, mostly moderate-strong ones. Noteworthy, P. aeruginosa was the strongest non-fermentating GNB biofilm producer and M. morgnii was the strongest fermentating GNB biofilm producer.

Presenter email address: macias.02@hotmail.com
Genomic characterisation of *Kerstersia gyiorum*, an isolate from a patient with acute otitis media

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**Background:** *Kerstersia gyiorum* is a Gram-negative aerobic motile bacillus of *Alcaligenaceae* family. There are about 16 reports on *K. gyiorum* isolation and most of them associated with infectious diseases in human.

**Materials/methods:** The *K. gyiorum* strain Kg_1_17 was recovered from an adult male with acute otitis media (AOM) in Moscow in 2017. Patient was successfully treated with levofloxacin and 3rd generation cephalosporin. The culture was identified with MAL-DI-TOF MS (Bruker Daltonics). MICs of antibiotics were determined by broth microdilution. MiSeq (illumina) and MinION (Oxford Nanopore) were used for complete genome sequencing. Genome was assembled using Unicycler, followed by RAST annotation.

**Results:** The isolate Kg_1_17 was identified by Biotyper software with score 2.3. The MICs of amikacin, gentamicin, ceftazidime, cefotaxime, meropenem, imipenem, doripenem, tigecycline and polymyxin B were below EUCAST epidemiological cut-off for *Pseudomonas aeruginosa*. Evaluated ciprofloxacin MIC [4 mg/L] correlated with substitutions in *gyrA* and *gyrB*. 3,574 coding sequences were annotated in genome of *K. gyiorum* (length 3,879,169 and GC% - 62.5), including nine rRNA genes, 55 tRNA, 97 1 hypothetical genes and one intact bacteriophage (76% identity with *Burkholderia* phage phi644-2). Annotated operons grouped by function and marked on legend are shown in the Figure. Extrachromosomal elements were not identified. Mobilome consisted of two transposons and 87 IS elements of 20 types. A number of potential resistance mechanisms were identified: CatB (phenicol resistance) and several efflux systems. Four putative beta-lactamases [PBL] of A- and C-like classes [two genes] and metallo-beta-lactamase were found. Analysis of protein sequence of A-like class PBL demonstrated 44-48% amino acids similarity with *Fusarium* spp. Structural comparison of all PBL show high similarities with *Methanothermobacter thermautotrophicus*, *Caulobacter crescentus*, *Veillonella parvula*, and *Burkholderia gladioli* lactamases. Putative virulence genes included: phospholipase C (*plcH*) which suppresses neutrophil respiratory burst, motility- and chemotaxis – associated genes (*cheA*, *cheB*, *cheW*, *cheY*, *flaN*). Genome comparison of isolate Kg_1_17 with public available *K. gyiorum* sequences shown high nucleotide similarity.

**Conclusions:** Identified genome markers along with previous studies allows to consider *K. gyiorum* as potential human pathogen and causative agent of AOM. Further study is needed for understanding biology and pathogenicity of this microorganism.
Ten years of antimicrobial stewardship in a tertiary care hospital in northern Italy
Richard Aschbacher\(^1\), Claudio Vedovelli\(^1\), Greta Spoladore\(^1\), Raffaella Binazzi\(^1\), Michela Falconi\(^1\), Peter Josef Santa\(^1\), Elisabetta Pagani\(^1\), Leonardo Pagani\(^1\)*

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**Background:** Antimicrobial Resistance (AMR) is a global threat, due to overuse or misuse of antibiotics, among other causes. We summarize the results of the first 10 years of the antimicrobial stewardship program (ASP) implemented in our 750-bed tertiary care hospital in Northern Italy.

**Materials/methods:** The ASP started being implemented in 2007 and from 2009 data were regularly analyzed and fed back to all stakeholders. This approach still encompasses daily ID consultation, microbiological surveillance, front- or back-end antibiotic provision by the pharmacy service, and constant activity by the Infection Control and Prevention staff. Susceptibility data are from first blood culture isolates per patient per year and results were interpreted according to CLSI until 2010 and EUCAST from 2011. Due to low numbers, isolates were pooled on a 2-year basis; statistical significance was calculated by MedCalc.

**Results:** Table shows the most relevant pathogens with respective resistance patterns in the first and last biennium. Significant decreases in resistance were observed; only resistance to cefotaxime and ciprofloxacin in *K. pneumoniae* increased significantly. These results are paralleled by the lowest antibiotic consumption over time in our Autonomous Province, compared to all other Italian regions.

<table>
<thead>
<tr>
<th>Pathogens isolated</th>
<th>% of R isolates (N. of R/N. tot.)</th>
<th>% of R isolates (N. of R/N. tot.)</th>
<th>Statistical significance (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA</td>
<td>25.0% (32/128)</td>
<td>14.8% (19/128)</td>
<td>0.04</td>
</tr>
<tr>
<td>VR-E. faecalis</td>
<td>0.0% (0/63)</td>
<td>0.0% (0/58)</td>
<td></td>
</tr>
<tr>
<td>VR-E. faecium</td>
<td>2.9% (1/35)</td>
<td>6.8% (3/44)</td>
<td>0.43</td>
</tr>
<tr>
<td>E. coli CIP-R</td>
<td>31.8% (95/299)</td>
<td>30.3% (93/307)</td>
<td>0.69</td>
</tr>
<tr>
<td>E. coli CTX-R</td>
<td>14.4% (43/298)</td>
<td>17.3% (53/307)</td>
<td>0.33</td>
</tr>
<tr>
<td><em>K. pneumoniae</em> CIP-R</td>
<td>9.8% (4/41)</td>
<td>40.8% (31/76)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><em>K. pneumoniae</em> CTX-R</td>
<td>9.8% (4/41)</td>
<td>35.5% (27/76)</td>
<td>0.003</td>
</tr>
<tr>
<td><em>K. pneumoniae</em> MEM-R</td>
<td>2.4% (1/41)</td>
<td>6.6% (5/76)</td>
<td>0.32</td>
</tr>
<tr>
<td><em>A. baumannii</em> MEM-R</td>
<td>0/0</td>
<td>0/5</td>
<td></td>
</tr>
<tr>
<td><em>P. aeruginosa</em> CIP-R</td>
<td>53.8% (28/52)</td>
<td>26.7% (12/45)</td>
<td>0.007</td>
</tr>
<tr>
<td><em>P. aeruginosa</em> CAZ-R</td>
<td>25.0% (13/52)</td>
<td>18.2% (8/45)</td>
<td>0.42</td>
</tr>
<tr>
<td><em>P. aeruginosa</em> MEM-R</td>
<td>42.0% (21/50)</td>
<td>13.3% (6/44)</td>
<td>0.002</td>
</tr>
<tr>
<td><em>P. aeruginosa</em> AMK-R</td>
<td>15.4% (8/52)</td>
<td>6.7% (3/45)</td>
<td>0.18</td>
</tr>
</tbody>
</table>

**Conclusions:** Our ASP shows sustained results in tackling AMR, even in a country with very high resistance rates. Current AMR rates allow better antimicrobial usage and resources sparing in our province.

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Abstract 2624

**Clostridioides difficile** burden of disease in adults: early experiences of a prospective population-based surveillance study of hospitalised CDI cases in the inpatient module of the City of Louisville Diarrhoea (CLOUD) study

Senen Pena-Oliva¹, Stephen Furmanek¹, Ruth Carrico¹, Joann Zamparo², Elisa Gonzalez*², Julio Ramirez¹

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Abstract third-party references: This study was sponsored by Pfizer, Inc. On behalf of the CLOUD Louisville Study Group.

**Background:** Laboratory diagnosis of **Clostridioides difficile** infection (CDI) relies on stool specimen collection from patients with diarrhea. Since many patients with diarrhea do not have a stool specimen collected, the incidence of laboratory-confirmed CDI cases may be underestimated. To understand the extent of CDI underdiagnosis among inpatients, we implemented a prospective population-based surveillance study of hospitalized patients with new-onset diarrhea in all nine adult hospitals in Louisville, Kentucky. Our objective is to present early experiences of surveillance from the inpatient module of the City of Louisville Diarrhea (CLOUD) study.

**Materials/methods:** Surveillance officers in each hospital identify all cases of new-onset diarrhea (≥3 loose stools within 24 hours, Bristol stool form scale 5-7) among eligible inpatients (Louisville resident >50 years of age) and obtain informed consent. Stool samples from consenting patients are tested at the University of Louisville reference laboratory for 1) glutamate dehydrogenase (GDH) and 2) **Clostridioides difficile** toxins A and B using C. DIFF QUIK CHEK COMPLETE®, Techlab. Here we report laboratory results from the first sixty days of surveillance.

**Results:** Surveillance for the study period was a total of 26,356 eligible patient-days (Figure 1). A total of 573 eligible patients had new-onset diarrhea, corresponding to 2.2 cases of new-onset diarrhea per 100 eligible patient-days. We enrolled 74% (425/573) of eligible patients with new-onset diarrhea and tested stool samples for **C. difficile** from 90% (382/425) of enrolled patients, for a testing density of 1.45 per 10,000 patient-days. Of the 382 tested stool specimens, 30 (8%) were GDH positive/toxin positive, 65 (17%) were GDH positive/toxin negative.

**Conclusions:** New-onset diarrhea was common among inpatients >50 years of age. Stool specimens collected from eligible inpatients with new-onset diarrhea found that 8% had CDI (GDH positive/toxin positive) and **C. difficile** was identified in the stool specimens of an additional 17% inpatients. Further analysis of these data, and the continuation of the CLOUD Study in Louisville will contribute to a better understanding of the frequency of CDI underdiagnosis and the burden of CDI in the United States.

**Figure 1. Study Flow Chart**

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**Abstract 2626**

**NDM-1 emerging on distinct plasmid backbones from the IncL/M family**

Maria Lopez*1,2, Nicholas Ellaby1, Neil Woodford1, Maria Tomas2, Matthew Ellington1

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*Background:* The global pandemic of the OXA-48 carbapenemase among genetically diverse Enterobacterales has been associated with the dispersal of IncL/M based plasmids. The emergence of other carbapenemases on IncL/M plasmids raises concerns that these plasmids could facilitate further pandemics of carbapenemases. Here we describe the emergence of NDM-1 on distinct IncL/M plasmid backbones and compare the emergent plasmids with the pandemic OXA-48 encoding plasmids.

*Materials/methods:* Reference sequences for complete IncL/M plasmids (23) from NCBI were compared against long-read sequences (11) from carbapenemase-producing Enterobacterales (CPE) isolates referred to PHE’s AMRHAI Reference Unit (2015-19). Bioinformatic tools were used to annotate resistance genes and compare plasmids.

*Results:* IncL/M plasmid and long-read sequences lengths ranged between 60,145bp and 98,533bp, there were 41 core-genes (at 95% similarity), reflecting between 50% and 34,45% of the plasmid lengths. Plasmid backbone areas were contiguous and highly conserved whilst the resistance regions were highly variable and confounded whole plasmid sequence comparisons. A widely divergent phylogenetic tree was reconstructed from the plasmid core-genes which allowed the visualization of the NDM-1 gene on plasmids from distinct clades, indicating the gene has been acquired by IncL/M plasmids more than once. Both NDM-1 IncL/M plasmid clades were distinct from the OXA-48 plasmid clade, but the NDM-1 encoding plasmids from both clades have been found isolated from clusters in diverse Enterobacterales in different locations in the UK.

Comparison of the resistance regions around the NDM-1 gene indicate that it is contained inside a Tn3-like transposon based complex class-I integron, and that variants of the same resistance integron have been acquired by the plasmids in the different branches of the IncL/M plasmid family.

*Conclusions:* The inclusion of long-read sequences in the analysis of IncL/M family has provided the data necessary to determine a constructed core genome with which to better understand the emergence of the NDM-1 gene in distinct plasmids which might otherwise have been considered related. For the IncL/M family of plasmids, separate analysis of core-genes and resistance regions enables a greater understanding about the dispersion and success of these plasmids.

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Abstract 2627

**Antimicrobial susceptibility of non-pigmented rapidly growing mycobacteria**


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**Background:** Non-pigmented rapidly-growing mycobacteria (NPRGM) can cause human infection. Susceptibility testing is recommended because patterns variability.

**Materials/methods:** Susceptibility data collected from NPRGM isolated between 2011 and 2019 were included. Isolates were recovered from different body locations. Species identification was performed using GenoType CM, AS and NTM-DR, kits (Hain Lifescience GmbH, Germany). Susceptibility testing was performed by broth microdilution method according to the CLSI standards (Sensititre microtiter trays, Thermo Scientific, USA).

**Results:** 149 strains were included: *Mycobacterium fortuitum* complex [72], *M. mucogenicum* complex [24], *M. chelonae* [22], *M. abscessus* complex [11], *M. abscessus* ssp. *abscessus* [11], *M. abscessus* ssp. *massiliense* [7], *M. peregrinum* [1] and *M. phocaicum* [1]. Results are shown in Table 1. Amikacin, tigecycline and linezolid were the most effective antimicrobial agents.

<table>
<thead>
<tr>
<th>Antibiotic (mg/L)</th>
<th><em>M. fortuitum</em> complex</th>
<th><em>M. chelonae</em></th>
<th><em>M. abscessus</em></th>
<th>Other species</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MIC90/ MIC90% susceptibility</td>
<td>MIC90/ MIC90% susceptibility</td>
<td>MIC90/ MIC90% susceptibility</td>
<td>MIC90/ MIC90% susceptibility</td>
</tr>
<tr>
<td>Amikacin</td>
<td>8 / 1 / 97.22</td>
<td>16 / 4 / 90.48</td>
<td>16 / 4 / 89.29</td>
<td>4 / &lt;1 / 96.15</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>&gt;18 / 12 / 22.64</td>
<td>1 / 0.25 / 100</td>
<td>&gt;16 / 1 / 85.71</td>
<td>8 / 0.12 / 96.15</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>&gt;8 / &gt;8 / 16.9</td>
<td>&gt;8 / 4 / 0.05</td>
<td>&gt;8 / &gt;8 / 7.15</td>
<td>&gt;8 / 2 / 65.39</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>&gt;16 / &gt;16 / 27.4</td>
<td>&gt;16 / &gt;16 / 20</td>
<td>16 / &gt;16 / 0</td>
<td>&gt;16 / 0.5 / 76.08</td>
</tr>
<tr>
<td>Imipenem</td>
<td>32 / 8 / 33.8</td>
<td>64 / 16 / 23.31</td>
<td>&gt;64 / &gt;64 / 0</td>
<td>16 / &lt;2 / 76.92</td>
</tr>
<tr>
<td>Linezolid</td>
<td>&gt;32 / 4 / 67.6</td>
<td>32 / 8 / 71.43</td>
<td>16 / 8 / 64.29</td>
<td>8 / &lt;1 / 100</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>2 / 0.25 / 91.43</td>
<td>8 / 2 / 36.09</td>
<td>&gt;8 / &gt;8 / 3.57</td>
<td>2 / 1 / 92.3</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>0.25 / 0.25 / 98.55</td>
<td>2 / 0.5 / 71.43</td>
<td>2 / &gt;4 / 75</td>
<td>&gt;4 / 0.25 / 96.15</td>
</tr>
</tbody>
</table>

**Conclusions:** Isolates of NPRGM should be tested against selected antibacterial agents, because the variability of antimicrobial susceptibility among strains.

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**Risk factors for functional decline among survivors of Gram-negative bloodstream infection**

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**Background:** Gram-negative bacteremia is associated with increased morbidity and mortality in hospitalized patients. The worldwide incidence of Gram-negative bacteremia has increased over the last decades. The main focus of current management guidelines is interventions dealing with the reduction of short term mortality. Data regarding functional capacity among survivors are limited. We aimed to determine risk factors for functional decline at 90 days among survivors of Gram-negative bacteremia and to evaluate the rate of functional decline in these patients.

**Materials/methods:** This was an observational prospective cohort study based on recently published randomized controlled trial (RCT) conducted in 3 centers in Israel and Italy between 2013 and 2017. Hospitalized patients with Gram-negative bacteremia who survived until day 90 and were not bedridden at baseline were included. The primary end point was functional decline at 90 days.

**Results:** Five hundred and nine patients were included. The median age of the cohort was 71 years [interquartile range [IQR], 60–80 years], 46.4% [236/509] were male and 352 of 509 (69%) patients were independent at baseline. Functional decline at 90 days occurred in 24.4% of patients (124/509). In multivariable analysis; older age [OR, 1.03; for an one-year increment, 95% CI 1.01-1.05], functional dependence in instrumental activities of daily living (IADL) at baseline [OR, 4.64; 95% CI 2.5-8.6], low Norton score [OR, 0.87; 95% CI 0.79-0.96] and underlying comorbidities as cancer [OR, 2.01; 95% CI 1.14-3.55], chronic pulmonary disease [OR, 2.23 95% CI 1.12-4.42] and longer length of hospital stay [OR 1.09; for one-day increment, 95% CI 1.04-1.15] were associated with functional decline. Appropriate empirical antibiotic treatment was associated with lower rates of functional decline within 90 days [OR, 0.4; 95% CI 0.21-0.78].

**Conclusions:** We have examined the degree of functional decline and its risk factors in patients surviving bloodstream infections. These patients have poor long term trajectories after clinical recovery and hospital discharge. This has vast implications for patients, their family members and health policy makers.

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Abstract 2630

**Efficacy of ceftobiprole for Pseudomonas aeruginosa hospital-acquired pneumonia in critically ill patients: a pharmacokinetic-pharmacodynamic evaluation**

Camille Mane*1, Véronique Duhalde2, Guillaume Martin-Blondel1,2,3, Didier Concordet1, Peggy Gandia1,2

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**Background:** Ceftobiprole is a new generation antibiotic indicated as a 2-hour infusion of 500 mg q8h in the treatment of community-acquired and hospital-acquired pneumonia (excluding ventilator-acquired pneumonia). This indication includes Gram-positive and Gram-negative pneumonia such as Methicillin-Resistant Staphylococcus aureus (MRSA) and *Pseudomonas aeruginosa* pneumonia. In critically ill patients, no further dose adjustment than a 4-hour infusion in patients with high glomerular filtration rate is recommended despite pharmacokinetic modification in those patients.

The objective of this study was to determine the efficacy of different ceftobiprole dosing regimens for *Pseudomonas aeruginosa* pneumonia, based on a pharmacokinetic-pharmacodynamic (PK-PD) criterion.

**Materials/methods:** Published ceftobiprole population pharmacokinetic models were screened and the most relevant model based on available construction and validation parameters selected. Simulations of kinetic profiles were performed using this model for different situations: 4 doses (500, 1 000, 1 500 and 2 000 mg), 4 infusion times (2, 4, 6 and 8h) and different renal functions (normal Glomerular Filtration Rate (GFR), high GFR (160 mL/min) and low GFR (10 mL/min).

For each situation, the percentage of simulated PK profiles meeting the PK-PD target applied in the intensive care unit was calculated (i.e. probability of target attainment). The PK-PD target is an unbound plasma concentration over 4 times the Minimal Inhibitory Concentration (MIC) of the causative bacteria for 100% of the dosing interval (100% fT> 4 MIC). In the absence of a validated ceftobiprole breakpoint for *P. aeruginosa*, the EUCAST breakpoint for non-defined species (4 mg/L) was applied.

**Results:** Simulations were performed using the Muller et al. model [AAC,2013]. With the usual dosing regimen (2-hour infusion of 500 mg q8h), 1%, 0.6% and 25% of simulated profiles reached the PK-PD target for patients with normal, high or low GFR, respectively. With a normal GFR, the PK-PD target is reached for at least 90% of simulated profiles when an 8-hour infusion (i.e. continuous infusion) of 1 500 mg q8h ceftobiprole is applied.

**Conclusions:** These results challenge the efficacy of the currently recommended dosage of ceftobiprole administered to critically ill patients treated for pneumonia.

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Validation and exploration of HldE: a promising target for antibiotic potentiation in Gram-negative bacteria

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Background: Heptose residues are the first non-essential constituents of the inner core LPS of most Gram-negative bacteria. Deep rough mutants, devoid of heptose therefore exhibiting a short LPS, were shown highly susceptible to antibiotics. HldE is a cytoplasmic enzyme participating in the biosynthesis of ADP-glycero-manno-heptose, the active form of heptose incorporated into nascent LPS. HldE inhibitors were reported. As part of our collaboration with GSK within the IMI ENABLE consortium, we have evaluated HldE as a potential target to develop antibiotic potentiators. This study presents (i) the full validation of HldE; (ii) the characterization of an optimized HldE inhibitor; (iii) investigations of tolC-hldE synthetic lethality.

Materials/methods: Lambda-red hldE-inactivated E. coli and its trans-complemented strain were generated. Genetic mutants and HldE inhibitors were characterized in standard microbiology and LPS gel assays. Spontaneous resistant mutants were studied by (q)RT-PCR and their genome sequenced. The ΔhldE mutant was inoculated to mice in a thigh infection model. Synthetic lethality was investigated using CRISPR-Cas9 system.

Results: Extended antibiotics susceptibility was confirmed in ΔhldE E. coli and by chemical HldE inhibition using a reference compound in a ΔtolC strain. Potentiation occurred at low HldE inhibition level. No resistance was selected at high concentration of the reference compound while a moderate frequency of resistance, mediated by hldE-overexpression, was observed at lower concentration. In a thigh infection model, ΔhldE displayed decreased virulence and 6-fold increased susceptibility to erythromycin.

An optimized HldE inhibitor, obtained by medicinal chemistry, exhibited increased potentiation on E. coli, although still limited to a ΔtolC background. In the latter, stand-alone antibacterial activity was observed. The inability to generate a double tolC-hldE inactivated mutant together with growth arrest when both genes were repressed suggested a synthetic lethality between tolC and hldE.

Conclusions: We have validated HldE both in vitro and in vivo as a valuable target for potentiating antibiotics and showed an intriguing synthetic lethality with tolC. In vivo decreased virulence of a ΔhldE mutant suggests that HldE inhibition could in addition reduce the bacterial virulence. Our results warrant further efforts to design HldE inhibitors.

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Abstract 2632

Rapid detection of ciprofloxacin susceptible strains of *Neisseria gonorrhoeae*; an important guide for treatment

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Background: *Neisseria gonorrhoeae* (NG) is the aetiological agent of the sexually transmitted infection, Gonorrhoea, and is associated with urethritis in males and cervicitis in females. Antimicrobial resistant (AMR) NG is a major global threat due to the emergence of multi-drug resistant strains. The World Health Organisation (WHO) proposed that molecular tests capable of detecting resistant strains could control AMR spread. In most routine laboratories, NG antibiotic sensitivities are determined by minimum inhibitory concentration (MIC) testing however, this requires growth of the organism and can take up to 72 hours for results. The *ResistancePlus*® GC kit (SpeeDx Pty Ltd) can rapidly detect *gyrA* gene mutations associated with ciprofloxacin resistance. Absence of mutations would enable precision treatment as an alternative to empirical intramuscular ceftriaxone 1g. This study compares genotypic and phenotypic data in samples from patients attending GenitourINARY Medicine clinic in Northern Ireland.

Materials/methods: Specimen extracts identified as NG positive using Cobas® CT/NG (Roche Diagnostics) and confirmed on an in-house TaqMan assay and/or Cepheid GeneXpert assay as per standard care testing, were anonymised and re-tested using *ResistancePlus*® GC kit. The rate of ciprofloxacin susceptible strains was determined. A subset of patients had a separate sample sent for MIC sensitivities, which enabled a comparison between genotypic and phenotypic results.

Results: A total of 75 NG positive samples were included in the study which tested positive on both Cobas® and *ResistancePlus*® GC test (100% agreement of NG detection between assays). Amongst 75 positive samples; 43 (57.3%) had no *gyrA* mutation; 17 (39.5%) of these were confirmed by culture, 24 (55.8%) had no additional sample sent for culture and 2 were not isolated. 26 (34.6%) positives had a *gyrA* mutation detected; 7 (26.9%) were confirmed on culture, 2 were not isolated and the remaining 17 (65.4%) had no MIC sensitivities performed.

Conclusions: *ResistancePlus*® GC can rapidly detect NG and associated ciprofloxacin resistance mutations directly from a single clinical sample, guiding treatment and preserving ceftriaxone. Here, 43 samples had no *gyrA* gene mutation detected indicating susceptibility to ciprofloxacin, yet less than half generated phenotypic data, demonstrating that *ResistancePlus* GC could facilitate individualised medicine.

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Deaths from bloodstream infections caused by antibiotic-resistant bacteria in Japan between 2015 and 2017: a population-level estimation

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Background: Bloodstream infections (BSIs) are a major cause of infectious disease-related morbidity and mortality in modern global health. However, estimating the number of deaths attributed to BSIs is challenging. The objective of this study was to understand the epidemiology of BSI-associated death caused by antibiotic-resistant bacterial species that are frequently isolated from patients in Japan.

Materials/methods: We included methicillin-resistant Staphylococcus aureus (MRSA), third-generation cephalosporin-resistant Escherichia coli (3REC), fluoroquinolone-resistant Escherichia coli (FOREC), third-generation cephalosporin-resistant Klebsiella pneumoniae (3RKP), multidrug-resistant Pseudomonas aeruginosa (MDRP), and penicillin-resistant Streptococcus pneumoniae (PRSP) in our analyses. We estimated the number of deaths from BSIs caused by these organisms in 2015, 2016, and 2017 in hospitals using the Japan Nosocomial Infection Surveillance (JANIS) database. The number of deaths was estimated using BSI mortality data obtained from previous studies. We adjusted the total number of BSIs by year and prefecture according to the proportion of the number of beds participating in JANIS. We included only beds for acute care and infectious diseases and excluded psychiatric beds and long-term care beds. We calculated 95% confidence intervals (CIs) in consideration of both bed coverage and mortality.

Results: We estimated that, on average, 5.2 (95% CI: 3.6–7.2) deaths per 100,000 population per year were attributed to BSIs caused by these major antibiotic-resistant organisms. MRSA accounted for 2.5 (95% CI: 2.0–3.1), 3REC accounted for 1.7 (95% CI: 0.9–2.7), and FOREC accounted for 2.4 (95% CI: 1.3–3.7) deaths per 100,000 population per year, respectively. MRSA and FOREC accounted for 93.3 % of the BSI deaths caused by these six major antibiotic-resistant organisms.

Conclusions: MRSA, 3REC, and FOREC account for the majority of BSI-associated deaths caused by antibiotic resistant organisms in Japan. The focus of antimicrobial resistance countermeasures should target S. aureus and E. coli as the primary organisms of concern.

BSI; bloodstream infection, MRSA; methicillin-resistant Staphylococcus aureus, 3REC, third-generation cephalosporin-resistant Escherichia coli, FOREC; fluoroquinolone-resistant Escherichia coli, 3RKP; third-generation cephalosporin-resistant Klebsiella pneumoniae, MDRP; multidrug-resistant Pseudomonas aeruginosa, PRSP; penicillin-resistant Streptococcus pneumoniae.

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Prospective genomic surveillance of multidrug-resistant organisms in Vietnamese intensive care units

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Background: Vietnam has a high burden of infectious diseases and rising rates of antimicrobial resistance (AMR). Multi-drug-resistant organisms (MDROs) are common in healthcare settings and may contribute to healthcare-associated infections. This prospective surveillance study aimed to determine the prevalence and transmission of MDRO in two hospitals in Hanoi, Vietnam, using bacterial whole-genome sequencing (WGS).

Materials/methods: All patients admitted to two ICUs at the National Hospital of Tropical Diseases (NHTD) and Bach Mai Hospital (BMH) were included. 4142 clinical and environmental samples were collected between June 2017 and January 2018, and characterised using MALDI-TOF MS, Vitek2 and WGS (HiSeq). Raw reads were de novo assembled using SPAdes. Sequencing typing (ST) and AMR gene detection was carried out using mlst and Abricate (respectively). Phylogenies of the main species were constructed using MashTree.

Results: 406 patients were included in the study (median age 53 years, 63.5% male). Three species accounted for the majority of isolates (79%): Escherichia coli (735/3890, 18.8%), Klebsiella pneumoniae (1334/3890, 34.1%) and Acinetobacter baumannii (1131/3890, 28.9%). The main STs found in A. baumannii were ST804 (17.1%) and ST195 (15.7%). The blaoxa-23 gene (83%) was the most prevalent, where 74% also carried blaoxa-66. 34 A. baumannii were identified with blondm1, of which 15 (44%) were ST355. The major K. pneumoniae STs were ST15 (32.6%) and ST16 (19.5%). 82% of all K. pneumoniae carried either KPC or NDM genes, with blapkpc (44%) and blondm1 (25%) the most common. The blonaegase gene was present in 95% of ST16 isolates and was not identified in any other ST. 202 (77%) ST16 isolates also carried a blondm4 gene. The E. coli isolates were highly variable; the main ST was ST648 (11.8%), however no other ST accounted for more than 10% of the dataset.

Conclusions: This study represents the largest prospective surveillance study of AMR in Vietnamese ICUs. The observation of similar lineages within both hospital ICUs despite no inter-hospital patient transfers could suggest community acquisition and transmission prior to hospitalisation. This presents significant challenge for AMR control in Vietnam requiring an integrated approach to antimicrobial stewardship and infection control both in hospital and community settings.

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Abstract 2635

Evolution of tuberculosis in children under five in our healthcare area
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Background: Historical series of tuberculosis (TBC) amongst children in the Basque Country showed a higher incidence of TBC-meningitis as in other regions. This was the main reason for keeping BCG-vaccine on the immunization schedule until 2013. With the withdrawal of the vaccine a rebound of the incidence of the TBC-meningitis was feared. The aim of this study was to review the TBC cases in children under 5 years at Bilbao-Basurto Health Area [2003-2019].

Materials/methods: Medical records of children under 5 years with diagnosis of tuberculosis by culture and/or molecular techniques in our area during the study period were reviewed.

Results: The pediatric population was stable around 55,000 inhabitants and there were 8 diagnosed cases of tuberculosis, with an annual incidence rate of 0.9 per 100,000 patients. The average age was 30 months. The distribution was as follows:

- In 2007, a vaccinated child of Moroccan parents with a bacilliferous uncle, with both positive culture and PCR. Treated with Rifampicin, Isoniacid and Pyrazinamide initially but replacing rifampicin with ethambutol because of an Idiopathic Thrombocytopenic Purpura.

- In 2013, three vaccinated children related to a school outbreak. The source was a bacilliferous teacher. Two of them were diagnosed in gastric aspiration by culture and the other one only by PCR. The three patients had little clinical expression and received standard treatment with good response.

- In 2014, an unvaccinated one-year-old, whose mother was bacilliferous, developed pneumonia and hiliar adenopathies. The culture and PCR were positive and was treated with standard therapy with adequate response.

- In 2019 three unvaccinated one-year-old Spanish children developed a pulmonary TBC. One of them, whose grandfather (from Cameroon) was bacilliferous, also developed tuberculous meningitis diagnosed by PCR. The molecular assay showed a mutation at the rpoB and inhA gene that confers resistance to isoniazid and rifampicin and was treated with isoniazid, pyrazinamide, ethambutol, linezolid and levofloxacin.

Conclusions: Tuberculosis in children under 5 years of age in our environment is fundamentally sporadic and outbreak related. There is only one case of multidrug-resistant M tuberculosis in relation to immigration. There was only one case of tuberculous meningitis after the vaccine withdrawal.

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Abstract 2640

Pertussis among ≤ 3 months old in Finland, 2015-2018: should we refine our adult immunisation schedule or switch to maternal immunisation?

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Background: In Finland, universal pertussis immunisation schedule consists of DTaP-IPV-Hib vaccines at 3, 5 and 12 months of age followed by 3 boosters at 4 (DTaP-IPV), 14–15 (dtap) and 25 (dtap) years. During 2015-2018, a total 45 laboratory confirmed pertussis cases ≤ 3 months of age, too young to have received effective immunisation, was notified to the National Infectious Diseases Register (NIDR). We described cases’ mothers’ age at delivery, compared it to mothers’ age at delivery for nationwide 2015-2017 birth cohorts to evaluate possible changes to the Finnish immunisation programme to maximize protection against pertussis in the very young. We aimed to study whether postponing the 25 years of age dtap booster would increase immunity in pregnant women as an alternative to maternal vaccination.

Materials/methods: We linked NIDR pertussis cases ≤ 3 months old records to births documented in the Medical Birth Register (MBR) to get information on mothers’ age at delivery. Additionally, we extracted Statistics Finland national data to assess distribution of mothers’ ages at delivery of livebirth. We then estimated at what age pertussis immunisation should be offered to still provide protection to the highest number of livebirths, assuming a protective duration of 4 years after aP containing vaccine.

Results: All 45 pertussis cases ≤ 3 months old were linked to MBR. Cases’ mothers’ age at delivery ranged from 19 to 44 years. For comparison with available nationwide data, we restricted our analysis to cases born in 2015-2017 [n=36], where 11 [31%] mothers were aged 25-29 years and 11 [31%] aged 30-34 years. In the nationwide 2015-2017 birth cohort, age distribution of delivering mothers differed with 29% [n=46542] among 25-29 years and 34% [N=53570] among 30-34 years. Finally, we calculated that dtap given at the age 25 years provides immunity to 23% [n=35760] of livebirths while postponing it to 29 years of age could provide protection to 28% [44948] of livebirths.

Conclusions: When deciding on the age of adult aP-containing dt-vaccine boosting, an additional point to consider is to maximize the protection of a newborn in absence of or as a complement to active maternal vaccination.

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Leishmania species diagnosed in European specialised treatment centres in the period 2014-2019

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Background: Leishmaniasis is endemic in the Mediterranean European countries, but is also imported in the whole of Europe from across the globe. Several specialized hospitals and medical centres diagnose and treat both visceral and cutaneous leishmaniasis caused by various species, but currently up-to-date surveillance of the species diagnosed and their presumed geographic origin is lacking.

Materials/methods: Fourteen specialized diagnostic and treatment centres from 11 European countries pooled their diagnostic data from the period 2014-2019, in order to get more insight into the presumed geographic origin of infection and species diagnosed. These 14 centres are all affiliated to the European LeishMan consortium.

Results: In total 1174 cases were diagnosed, originating from 68 different countries where leishmaniasis is endemic. Almost all species were found, both from the L. [Leishmania] and L. [Viannia] subgenus. Cutaneous leishmaniasis (n=887) was caused by all species, while mucocutaneous disease (n=37) was caused by L. braziliensis in the new world, and primarily by the L. donovani complex in the old world. Visceral leishmaniasis (n=227) was caused by either L. infantum or L. donovani, and in 1 case by the enigmatic L. enriettii complex. Almost 670 cases were imported from countries other than where they were diagnosed, either from an endemic European region, or from outside Europe (n = ca. 540). Further stratification based on year and type of traveller is ongoing, pending data collection for the entire year 2019.

Conclusions: In most European countries, notification of leishmaniasis is not mandatory. Surveillance is therefore largely dependent on initiatives from reference centres. The LeishMan network aims to further follow-up the imported and autochthonous cases in the European territory by continued data collection, for monitoring the origin of, and the diseases caused by the Leishmania parasites.

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Abstract 2642

Unexpectedly high false positive *Haemophilus influenzae* rates using a meningoencephalitis syndromic PCR panel in two tertiary centres

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**Background:** PCR panel assays are increasingly used in routine diagnostic laboratories for meningitis and (meningo-)encephalitis diagnosis. Since the implementation of the Biofire® Filmarray® Meningitis/Encephalitis (ME) panel, several cases of false-positive (FP) results for *H. influenzae* have been reported.

**Materials/methods:** Retrospective case review conducted at Geneva and Basel University Hospitals on all *H. influenzae* positive results determined by Biofire® Filmarray® ME panel on cerebrospinal fluid (CSF) samples sequentially analysed from June 2016 to October 2019. The panel was performed in strict accordance with the manufacturer’s instructions. Clinical and laboratory data were collected. Cases were defined as a true positive (TP) when confirmed by a positive *H. influenzae* specific qPCR on the same sample and/or CSF cultures, in addition to clinical manifestations and CSF analysis. Other cases were considered as a FP. Both laboratories are accredited (ISO/IEC17025) and participate in external quality control.

**Results:** A total of 3082 ME panels corresponding to 2895 patients (2252 adult, 643 paediatric) were performed: results for *H. influenzae* were negative in 99.4% (3064/3082) (95% CI 99.1–99.6%) and positive in 0.6% (18/3082) (95% CI 0.4–0.9%) CSF samples. CSF white blood cell count was determined in 1 3 samples (median 7M/L [range 1 -4031M/L]). Culture and specific qPCR were performed on 1 7/18 and 3/18 CSF samples, respectively. Among 1 7 samples sent for culture, 10 concerned patients not treated with antibiotics prior to lumbar puncture and one only was *H. influenzae*-positive. Clinical manifestations and CSF analysis were barely compatible with *H. influenzae* ME and/or an alternative diagnosis was made in 72.2% (1 3/18) cases. A total of 2 TP (one case, positive blood and CSF cultures; one case, positive blood culture), and 16 FP (three culture and qPCR negative; 1 4 culture-negative without qPCR performed) cases were retained. Nine patients received specific antibiotics for ME.

**Conclusions:** False-positive results for *H. influenzae* with the Biofire® Filmarray® ME panel were surprisingly frequent. ME panel results should always be interpreted together with clinical presentation and CSF analysis. Special caution should be paid to *H. influenzae*-positive results and a *H. influenzae* specific qPCR should be considered to mitigate the consequences of FP results.

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Pharmacodynamic analysis of meropenem in combination with a novel ß-lactamase inhibitor ANT2681 against New Delhi metallo ß-lactamase-producing *Escherichia coli*

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Background: Antabio is developing a novel metallo-ß-lactamase inhibitor with activity against NDM. ANT2681 has been shown to potentiate the MIC of meropenem against a broad range of MBL-containing clinical isolates. Preclinical pharmacokinetic and pharmacodynamic (PK-PD) studies are needed to identify the appropriate dynamically linked index.

Materials/methods: A well characterised murine neutropenic thigh infection model with a challenge strain NDM-producing *E. coli* NTBC 121 was used to perform dose range-finding and dose fractionation studies. Initial dose range-finding studies were conducted with meropenem alone to select a dose of meropenem with limited (sub-maximal) activity, to be used as a backbone in combination experiments. A dose range of 5-150 mg/kg ANT2681 q4h IV was evaluated in combination with a fixed dose of meropenem 50 mg/kg q4h SC meropenem and the EC$_{50}$ of ANT2681 was calculated. Subsequent dose fractionation experiments were performed by administering a total daily dose of 480 mg/kg ANT2681 split over q4, q8 or q12 hours and combined with a backbone of meropenem 50 mg/kg q4h SC. The plasma PK of meropenem and ANT2681 were assessed using dosages of meropenem/ANT2681 of 25/5, 100/75 and 500/240 mg/kg q24h.

Results: Linear mixed effect models were used to compare the dosing regimens. There were significant differences in log$_{-10}$CFU/g change over time [p<0.05] between meropenem alone and each MEM/ANT2681 combination regimens; however, there were no significant differences between each fractionated dose regimen of MEM/ANT2681 [i.e. 50/80 mg/kg q4h, 50/160mg/kg q8h and 50/240mg/kg q12h] demonstrating that pharmacodynamics were unlikely to be peak or time driven. Meropenem pharmacokinetics in mice were consistent with previously published estimates. ANT2681 has linear pharmacokinetics in mice.

Conclusions: Statistical analysis from dose fractionation studies demonstrate that AUC is the relevant dynamically linked index. PK-PD bridging studies to define the magnitude of the pharmacodynamic index of ANT2681 are currently being performed.

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Abstracts 2020

Abstract 2646

Compatibility of the new NTM Elite agar with MALDI-TOF for direct isolation and identification of non-tuberculous mycobacteria

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Background: Pulmonary nontuberculous mycobacteria (NTM) represent an increasing threat as NTM infection can become chronic in susceptible patients and require heavy antibiotic treatments. Their diagnosis remains difficult due to fastidious sample preparation involving prior decontamination, slow growth and pulmonary flora that can be abundant, especially in the case of cystic fibrosis (CF) patients.

RGM medium has been designed at the Freeman Hospital (Newcastle Upon Tyne, UK). This medium shows increased specificity and sensitivity compared to reference methods.

NTM Elite agar (bioMérieux) is the industrial version derived from RGM medium dedicated to the isolation of nontuberculous mycobacteria from respiratory specimen without prior decontamination.

Materials/methods: 50 well-characterized nontuberculous mycobacteria strains were subcultured on both the reference medium (Colestos) and on NTM Elite Agar. Colonies were processed in duplicate with the VITEK® MS MYCOB/NOCARDIA KIT and were analyzed by MALDI-TOF with the VITEK®MS system (KB IVD V3.2.0.). Duplicates were considered as individual tests for analysis, thus representing 100 results per tested media.

Results: The strains were identified at species or complex level at 94% on NTM Elite agar and 85% on Coletsos. The rates of no identification were 4% on NTM Elite agar and 13% on Coletsos. Duplicate spots resulted in a no identification results in only four cases for Coletso, and only one case for NTM Elite agar. This could be explained by an easier picking of the colonies on the NTM Elite agar plates compared to the Colestos tubes, especially in the case of rough colonies. The rate of misidentification was 2% for both media and concerned only one strain.

Conclusions: Isolation of nontuberculous mycobacteria from specimen without prior decontamination with NTM Elite agar, associated with a direct identification by MALDI-TOF VITEK®MS, enables a simplified streamlined screening of nontuberculous mycobacteria, thus improving patient care.

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Abstract 2647

Adherence to an admission screening for multidrug-resistant organisms in a tertiary care hospital in Switzerland

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Background: Targeted admission screening for multi-drug resistant organisms (MDRO) is a recognized measure to prevent transmission and outbreaks. The aim of this study was to evaluate adherence to our screening algorithm in patients transferred from hospitals of high prevalence areas and identify factors associated with omitted screening.

Materials/methods: We included patients transferred from abroad or from high-risk regions within Switzerland from 2013 – 2018, according to the patient administration system. These patients were cross-checked with the infection control database regarding screening for MDRO. Sex, date of birth, origin of transferal, ward at admission, date and realization of screening and screened organisms were noted. Univariable and multivariable logistic regression were performed.

Results: We included 835 patients (41.8% female). Median age was 60 years (interquartile range 45 – 71 years). Screening was done in 389 (46.6%) patients and in 333/389 (85.6%) patients all indicated organisms were screened. The following characteristics were associated with poorly performed screening in univariable analysis: female sex (40.7 vs. 50.8% in males; odds ratio [OR] 0.66 [95% confidence interval [CI] 0.50 – 0.88]), transferral from high prevalence areas in Switzerland (25.2% vs. 49.1% from abroad; OR 0.32 [CI 0.21 – 0.49]) and admission directly to the ward (12.9% vs. 56.6% in patients admitted to the emergency department; OR 0.11 [CI 0.07 – 0.17]). Adherence to the screening algorithm improved over time (28.1% in 2013 vs. 54.9% in 2018, OR 0.32 [0.19 – 0.54]). In multivariable analysis direct admission to the ward (OR 0.11 [CI 0.07 – 0.19]) and year of screening (OR 1.24 per year [1.13 – 1.35]) remained significantly associated with adherence to screening.

Conclusions: Adherence to our MDRO screening algorithm was surprisingly low but improved over time. Direct admission to the ward was a predictor of omitted screening. Strategies to evaluate and improve adherence are essential to increase detection of MDRO colonisation and to prevent their spread.

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Novel putative AHL-lactonases widely distributed across diverse carbapenemase-producing Enterobacteriaceae

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Background: Bacterial quorum signalling via acyl-homoserine lactones influences the production of virulence factors depending on bacterial population density. Quorum signal inhibition (quorum-quenching) by AHL-lactonases may provide an adjunct or alternative that could be harnessed for the treatment of bacterial infections. In Proteobacteria, AHL-lactonases are mainly classified into the metallo-β-lactamase superfamily (MBL), the phosphotriesterase family or the alpha/beta hydrolase family, each with distinct yet conserved catalytic domains. We identified multiple MBL-like proteins and alpha/beta hydrolase family lactonases in four major species of carbapenemase-producing Enterobacterales (CPE).

Materials/methods: From long-read whole genome sequences (Oxford Nanopore Technology MinIon) of eight clinical K. pneumoniae, E. coli, E. cloacae and Citrobacter freundii isolates, conserved AHL-lactonase domains were detected (Motif search, GenomeNet, Japan). Alignment of the protein sequences (Clustal) with those already described as lactonases was performed and domains confirmed via CD search (NCBI/HMMscan). BLASTp was used to assess the novelty of the detected lactonases. Sequences were uploaded to PredictProtein.org for protein structure prediction and sub-cellular localization.

Results: From a total of 18 putative AHL-lactonases from the MBL superfamily found, all possessed the characteristic Zn2+-binding motif (HXHXDH-H-D). CPE isolates from four species had a putative novel conserved Zn2+ binding motif (HGHLDH-H-D) that was not previously described as AHL-lactonase.

This highly conserved putative lactonase (87.91% amino-acid identity) had a predicted cytoplasmic location but lacked a signal peptide in all four species examined. Moreover, it was distinct to other known lactonases (~16.5% amino acid similarity), further supporting the status of this type as a novel candidate AHL-lactonase.

Alpha/beta hydrolase family proteins showed a catalytic triad associated with AHL-lactonase activity [GXSXG-E/D-H], amongst the CPE isolates, which was conserved as a GYSLG-E/D-H motif. Domains unique within each species were also found.

Conclusions: The presence and conservation of AHL lactonase domains across the four most important CPE species highlights the ubiquity of this potentially useful factor for anti-bacterial or anti-virulence strategies amongst some of the most resistant Enterobacterales we face.

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Epidemiology and management of pneumonia based on data entry in a computerised decision support system for antimicrobial prescriptions: a retrospective study

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Background: Computerized decision support systems (CDSS) are promising tools for antimicrobial stewardship (AMS). Pneumonia, one of the leading causes of antimicrobial prescriptions, is a “natural target” for AMS programs.

Materials/methods: Through the ongoing COMPASS trial [NCT03120975], we implemented a CDSS. When prescribing antimicrobials on inpatient wards, physicians must choose the indication for each antimicrobial; thereafter they are provided indication-specific treatment recommendations based on local guidelines. We extracted data for inpatients from whom the antibiotic indication contained the term “pneumonia” between January 1, 2019 and October 31, 2019. Of note, a patient could have >1 indication for the same episode. A prescription was defined as the prescription of a specific drug independent of route or dosage.

Results: Over the study period, 638 patients were treated for 669 episodes of any pneumonia diagnosis, representing 48.8% of 1371 episodes treated with antimicrobials with an indication. Median age was 77 years (IQR 65-86). Community-acquired pneumonia was the most frequent indication [413/807 indications, 51%] followed by health care associated pneumonia [179/807, 22%] (Figure 1). For 9% [53/594] of episodes with an initial pneumonia indication, the indication changed to a non-pneumonia indication during hospitalization, the inverse occurred for 10% [75/777] of episodes with an initial non-pneumonia indication. Amoxicillin-clavulanate was the most commonly prescribed antibiotic [43%, 393/906 prescriptions], followed by piperacillin-tazobactam [18%, 167/906]. Combination therapy was started for 17% [115/669] of episodes. Treatment was initiated intravenously (IV) ≥1 antibiotic IV for 64% [431/669] of episodes and oral switch (all antibiotics PO) was performed for 44% [191] after a median of 3 days (IQR 2-4). Treatment was concordant with local guidelines for 75% [672/893] of prescriptions for which recommendations were available. Median inpatient treatment duration and median length of stay for episodes for which a pneumonia indication was selected [and not changed to a non-pneumonia indication] were respectively 5 days (IQR 2-7) and 8 days (IQR 5-13).

Conclusions: A CDSS requiring physicians to provide indications for antimicrobial prescriptions enables rapid assessment of syndrome-specific indicators and thereby facilitates the development of targeted interventions promoting optimal antimicrobial therapy, such as IV PO switch, which our data show to be suboptimal.

![Figure 1. Frequency of pneumonia indications (with recommendations available) and guidelines concordance](image_url)

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Safety characterisation of ART24, a novel live bio-therapeutic product, in development for the prevention of *Clostridioides difficile* infection, by *in silico* and *in vitro* testing

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**Background:** ART24 is being investigated as a live biotherapeutic product (LBP) treatment to prevent recurrence of *Clostridioides difficile* infection (CDI) following successful antibacterial therapy. ART24 was isolated from a human fecal sample, identified, and purified. ART24 is a member of the *B. amyloliquefaciens*/*B. velezensis* group. Further, ART24 is considered a member of the “operational group *B. amyloliquefaciens*”, which consists of the soil borne *B. amyloliquefaciens*, and plant associated *B. siamensis* and *B. velezensis*, which is synonymous with *B. amyloliquefaciens* subsp. *plantarum*. The human carriage of *B. amyloliquefaciens* as well as the genome of ART24 itself were investigated as a mean to identify potential safety and toxicity concerns prior to animal and human testing.

**Materials/methods:** The whole closed, assembled and annotated ART24 genome was investigated for functional operons that contain known antimicrobial gene content, plasmid, phage content, and virulence factors using Anti-SMASH, Bagel4, plasmid-SPAdes, PHASTER, IslandViewer4 and RAST SEED viewer. In addition, standard susceptibility testing of ART24 against 16 antibiotics was determined using CLSI recommended broth microdilution and results interpreted using current CLSI and EUCAST breakpoints. Finally, available metagenomic datasets from human fecal samples were mined for the presence of *B. amyloliquefaciens* and *B. velezensis* using Kraken2, Bracken and curatedmetagenomicData to better understand the presence of the “operational group *B. amyloliquefaciens*” in the general population.

**Results:** *In silico* analysis indicates that the ART24 genome displays expected genetic properties related to *Bacillus* subspecies, and that off-target activities of virulence and antibiotic resistance mechanisms are unlikely. ART24 is susceptible to all drugs tested for which interpretative criteria are available. *In silico* analysis to identify *B. amyloliquefaciens* and *B. velezensis* gene content in metagenomic datasets showed that the operational group is present in human fecal samples analyzed at an overall low percentage relative abundance, variable between geographic regions, and was not linked with any disease state in the datasets tested.

**Conclusions:** The series of *in silico* and *in vitro* testing analyses performed on ART24 did not reveal any obvious safety concerns. ART24 is a promising LBP clinical candidate in Phase 1 clinical development for prevention of recurrent CDI.

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Use of therapeutic drug monitoring to optimise cefazolin dosing in the treatment of methicillin-susceptible Staphylococcus aureus bacteraemia

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Background: The impact of cefazolin exposure on treatment outcomes in high inoculum infections is unknown. Clinical data suggests that for β-lactams, a higher threshold of 50% ft>MIC up to 100% ft:MIC≥4 MIC is associated with positive clinical outcomes. The objectives of this study were to evaluate the achievement of cefazolin PK target attainment and to further assess clinical and microbiological outcomes in hospitalized patients with MSSA bacteremia.

Materials/methods: We conducted a single-center, retrospective review between Dec 2017 and May 2019, of adult patients receiving cefazolin for MSSA bacteremia with serum concentrations obtained at steady state. Total cefazolin plasma concentrations were adjusted for 80% protein binding to estimate unbound drug. PK targets assessed in this study were free drug concentration maintained above the MIC of the pathogen (100% ft>MIC) or 4-fold higher than the MIC of the pathogen throughout the entire dosing interval (100% ft:MIC≥4). Clinical success at the end of therapy was defined as resolution of presenting signs and symptoms of infection. Microbiological success was defined as absence of MSSA in repeat blood cultures. The MIC90 for MSSA to cefazolin is 2 mcg/ml, which was used as the MIC threshold for PK analysis.

Results: Twenty-two patients were included in the analysis. The median age was 53 (IQR, 49-65). The most common sources of the bacteremia were musculoskeletal (32%), endocarditis (18%), and SSTIs (18%). Fifty-nine percent (n=13) of patients were on continuous infusion cefazolin. The mean dose of cefazolin was 6 grams/day. The median cefazolin serum concentration was 7.1 mcg/ml (IQR, 5.6-12.3). All patients achieved 100% ft>MIC and 55% (12/22) achieved 100% ft:MIC≥4. Dose adjustments to optimize PK were performed in 27% (n=6) of patients (dose increased in 4 cases). Clinical success was achieved in all but one case (21/22). Microbiological success was achieved in all patients.

Conclusions: A PK target of 100% ft:MIC≥4 was not achieved in 45% of patients, which highlights the need for cefazolin TDM. The ability to obtain cefazolin concentrations provided the opportunity to optimize exposure in 27% of patients in this cohort. Clinical and microbiological success were achieved in the majority of patients evaluated.

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Abstract 2658

Multidrug-resistant organisms (MDRO) colonisation pattern, prevalence and acquisition in a neonatal intensive care unit, evidence for guiding active surveillance cultures: a 2-year experience active surveillance process at Saint Joseph Hospital, Jerusalem

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Background: Healthcare-associated Infections (HAIs) at neonatal intensive care units (NICU) reduce the rate of clinical and microbiological responses and increase the cost of care and hospital stays. Most HAIs are caused by 3rd generation-resistant members of the Enterobacteriaceae family (3GCREB). Proper surveillance and appropriate infection control practices can rigorously reduce the incidence of HAIs, however, overutilization of health institute resources through repetitive surveillance and microbiological investigations may not positively influence patient outcomes, but increases financial burden, and demands on staff and time. This study evaluated the value of repetitive active screening (twice weekly) for MDRO detection.

Materials/methods: The infection control committee carried out a systematic retrospective review of a 22-months experience (January 2017 to October 2018) questioning evidence for worthiness of the frequency of active screening (twice weekly) for MDROs at NICU. Overall, 740 babies screened at the NICU were included in the study, from which 2955 rectal and throat swabs’ results were reviewed, together with results of repeated active screening at the first 3, 7, 10, 20, and 30 days.

Results: Of the 2955 swabs results reviewed, 2257 swabs were negative (76.3%), while 207 (7.0%) cases had at least one colonized microorganism (negative for 3GCREB), and 45 cases (1.52%) were positive for 3GCREB. The data showed that the first 2 swabs obtained from neonates at day 3 and day 7 carried the highest number of conversions to 3GCREB compared to the 10, 20, and 30 days swabs. Only two cases of 3GCREB caused bacteremia during a 22-months period.

Conclusions: The incidence rate of total positive swabs for a single isolate was 8.52% and the 3GCREB rate was 1.52%, which is lower than rates reported by previous studies. None of the 3GCREB cases converted to CRE, likely due to appropriate infection prevention strategies, proper surveillance, and antibiotic use. Our findings showed that once weekly screening swabs is optimal and sufficient. Repetitive active screening of rectal and throat swabs twice weekly is costly and is not advisable in terms of the 3GCREB rate, rather it is preferable to repeat active screening once weekly.

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**Abstract 2659**

**Genomic analysis of VIM-2-encoding conjugative megaplasmids in Pseudomonas spp. spread interregionally in Poland**

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**Background:** Metallo-β-lactamases (MBLs) are one of the major AMR mechanisms specified by mobile genes. In *Pseudomonas* spp., MBL genes, encoding IMP and VIM types mainly, are usually located in the chromosome, and only few reports described *bla* VIM-carrying plasmids to date. Here we show complete sequences of VIM-2-encoding megaplasmids spread in pseudomonads in Poland, following our previous ECCMID presentation based on epidemiological observations.

**Materials/methods:** Over 500 non-duplicate MBL-producing *Pseudomonas* spp. isolates were submitted from all over Poland to the National Reference Centre for Susceptibility Testing in 2003-15. According to our early study, the isolates carrying In46 1 (aadB- *bla* VIM-2-aadA6) were suspected for the plasmidic location of the *bla* VIM integron, and analysed by PFGE, MLST, S1-PFGE and mating (ECCMID 2019). In this work selected strains were fully sequenced using PacBio Sequel and assembled with HGAP4, followed by manual annotation and detection of AMR and virulence genes.

**Results:** In 2003-15, 95 isolates harbored In46 1, the most common MBL-encoding integron in *Pseudomonas* spp. in Poland, having been collected in 54 hospitals in 36 cities in 10/16 administrative regions. The group comprised 33 STs of *P. aeruginosa* and four of *P. putida*, and 77 isolates had *bla* VIM-2-carrying megaplasmids (~190–~550kb) of usually high conjugative efficiency. Twenty-eight diverse isolates were selected for WGS; so far plasmids from 11 isolates from an early period (2003-2008) have been completed. All but one of the plasmids sized from 413 to 489kb, and showed remarkable identity to each other and to several other pseudomonadal plasmids, including IncP-2 VIM-2-encoding molecule from Portugal (GenBank KY494864). Interestingly, plasmid pPUV-1 (471kb) was found to be integrated into the chromosome in one of the isolates (locus PAO0069), flanked by identical clusters of recombinase/integrase genes of putative phage origin. The remaining pPUV-7 (343kb) had different backbone and belonged to another and so far unique lineage.

**Conclusions:** The WGS analysis confirmed close relatedness of VIM-2-encoding megaplasmids expanding in the Polish *Pseudomonas* population on an unprecedented scale. These seem to represent a specific variant of more broadly spread molecules, differing at least by the *bla* VIM-2 integron. Apart from functioning autonomously, the plasmids are able to integrate into the pseudomonadal chromosome.

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Metagenomics next-generation sequencing for the identification of undiagnosed DNA and RNA viruses in adult allogeneic haematopoietic cell transplant recipients with steroid refractory graft-versus-host disease

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Background: Allogeneic hematopoietic cell transplant (allo-HCT) recipients with steroid refractory/dependent graft-versus-host disease (GvHD) are highly immunosuppressed and may be more vulnerable to infections with weakly pathogenic viruses, commensal viruses, or unexpected variants overlooked by routine assays.

Materials/methods: We included 25 adult allo-HCT recipients with acute or chronic steroid refractory/dependent GvHD who were transplanted from 2016 to 2019 at Geneva University Hospitals. Plasma samples were collected throughout the period of intensive steroid treatment or second-line GvHD therapy including ruxolitinib. Metagenomics next-generation sequencing (mNGS) analysis was performed on pooled plasma samples, using a validated viral pipeline and de novo analysis. Specific real-time r(RT)-PCR was performed to confirm mNGS findings.

Results: Median duration of intensive immunosuppression was 5 months (range 1.5 to 21.6 months); 23/25 (92%) patients received ruxolitinib. GvHD-related mortality rate was 36%. In 16/25 (64%) patients, sequences of ≥3 distinct viral species were detected by mNGS; Anelloviridae and human pegivirus-1 were the most prevalent (26% and 36% patients, respectively). In 7/25 (28%) patients, all with fatal outcome, unexpected viral sequences that are not part of routine investigations were identified with mNGS. These included usutu virus (one case), rubella virus (one vaccine- and one wild-strain case), novel human astrovirus [HAstV] MLB2 (one case), classic HAstV (one case), human polyomavirus 6 and 7 (two cases), and two protoparvoviruses (one cutavirus, one bufavirus). All mNGS results were confirmed with r(RT)-PCR in unpooled plasma samples, additional available specimens and tissue biopsies over a median period of 7.1 weeks (range 0.4 to 35.4 weeks).

Conclusions: Unexpected, opportunistic and protracted viral infections were identified in 28% of highly immunocompromised allo-HCT recipients with steroid refractory/dependent GvHD. The identified viruses in the present analysis had all been previously described in humans but rarely reported as a cause of disease in allo-HCT patients or with unknown or debated pathogenicity. Rubella virus identification raises the possibility of persistence and re-emergence from past infection or vaccination. Further investigations are needed to understand the clinical significance of these viral infections.

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Baloxavir drug exposure after single-dose baloxavir marboxil is similar between children aged 1 to <12 years and adults: analysis of the miniSTONE-2 trial

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Background: miniSTONE-2 investigated the safety, pharmacokinetics (PK) and efficacy of single-dose baloxavir marboxil (BXM) in otherwise-healthy (OwH) children aged 1 to <12 years with influenza. Here, systemic exposure to BXM and its active metabolite, baloxavir, are reported.

Materials/methods: miniSTONE-2 was a global, multicenter, double-blind, active-controlled study in OwH paediatric patients with influenza, conducted during the 2018/19 season. Patients were randomised 2:1 to receive either a single oral dose of BXM (2 mg/kg for patients weighing <20 kg or 40 mg for patients ≥20 kg) or oseltamivir. Optimal paediatric doses were determined by systematic synthesis of all available PK data of baloxavir, including modelling and simulation to bridge PK in a quantitative manner between adults and paediatrics. The PK strategy for this study used a combination of sparse (107 patients) and intensive (19 patients) PK sampling. Concentrations were analysed using a non-compartmental approach.

Results: As expected, BXM (pro-drug) was rapidly hydrolysed to baloxavir, therefore systemic BXM concentrations were low or below lower limit of quantification in most patients. In the intensive PK cohort, baloxavir reached maximum concentration (Cmax) about 4 hours after administration. The observed Cmax [mean [min–max] = 73.1 [18.10–137.00] ng/mL] was in a similar range to that observed in the non-Asian adult population treated with a 40 mg dose [mean [min–max] = 63.9 [11.1–133] and 60.6 [12.2–158] ng/mL in OwH and HR patients, respectively]. In the sparse sampling cohort, the mean concentration at 24 hours (C24) was 57.1 [min–max: 0.00–217] ng/mL. The central tendency and overall range of exposure data was similar to that observed in OwH [37.2 ng/mL [7.35–81.4]] and HR non-Asian patients [35.9 ng/mL [5.77–90.2]] treated with a single 40 mg dose. Mean C24 in non-Asian adults (OwH) was 57.9 ng/mL [21.4–155], also in close agreement with C24 values observed in this study. When stratified according to body weight, plasma concentrations were similar across body weight groups.

Conclusions: When administered as a weight-based single oral dose in children, baloxavir exposure (Cmax and C24) was similar to those in adult populations receiving a single dose of 40 mg.

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**Abstract 2668**

**Frequency of Toxoplasma gondii infection in schizophrenic patients: a pilot study**

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Abstract third-party references: Supported by the Jagiellonian University Statutory Grant

**Background:** Schizophrenia is a serious mental illness characterized by many symptoms including abnormal behavior, false beliefs, decreased social interaction, strange speech and a decreased ability to understand reality. The condition may lower the life expectancy even by 20 years, occurring with a frequency of 0.5% in the general population. There have been many reports on the association of some infectious agents including parasites on the pathogenesis of mental disorders including schizophrenia with a recent review by Xiao et al. where the authors mention numerous studies linking *Toxoplasma gondii* exposure to schizophrenia. *T. gondii* general population prevalence varies globally from approximately 8% in Norway to over 60% in Africa and Latin America. Recently, France which had a high prevalence in 1965 (83%) has seen a decline to 37% in 2005. We set out to examine the frequency of *T. gondii* infection in schizophrenic patients in Southern Poland (Lesser Poland region).

**Materials/methods:** The study was performed on a schizophrenic patient group cared for by one of the largest mental health hospitals in Poland, i.e. Babiński Clinical Hospital in Cracow. The number of persons included in the study was 111 (M=39, F=72) aged 20-65. The study group included 75 patients with schizophrenia according to ICD-10 vs. 36 mentally healthy persons in the control group. Study participants' blood was tested serologically for IgM, IgG antibodies as well as *T. gondii* avidity. The studies were performed using a commercially available ELISA kit. Numerous other parameters were collected during the study, including other diseases, animal ownership, etc.

**Results:** 30 patients (40%) from the schizophrenic study group tested positive for *T. gondii* using serological methods (IgG positive). Only 10 persons (28%) from the healthy subjects control group tested positive for this parasite. More detailed analysis of the results will be shown on the poster.

**Conclusions:** The results show that patients in southern Poland (Lesser Poland region) with schizophrenia were infected with *T. gondii* in much greater number than the healthy control group. This pilot study may be a good framework for setting up a large national study in Poland.

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Abstract 2669

**Streptococcus pneumoniae** intracellular survival in THP-1 macrophages activated with different doses of lipopolysaccharide

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**Background:** *Streptococcus pneumoniae* is the leading cause of Community-Acquired Pneumonia (CAP). Excessive inflammatory response during pneumonia could lead to macrophage impaired function increasing bacterial survival. **Aim:** To develop a model of activated THP-1 macrophages derived cells infected with *S. pneumoniae*.

**Materials/methods:** Macrophages derived from THP-1 cells differentiated with phorbol 12-myristate 13-acetate (PMA), were activated for 5 hours with different doses of lipopolysaccharide (LPS) [0, 2, 5, or 10 µg/ml]. Afterwards, we analysed proinflammatory cytokines levels by RT-qPCR (IL-1β, IL-6, IL-8, IL-10, COX2, NF-KB and TNFα). In parallel, macrophages were infected with *S. pneumoniae* (Multiplicity of infection, 20:1) using different infection times: 1, 2 or 3 hours (fig. 1). Then, bacterial intracellular colonies forming units (Log10 iCFU/ml) were determined to infer macrophages’ bactericidal activity.

**Results:** The highest expression of IL-6, IL-8, IL-10, COX2, NF-KB and TNFα was with 5 µg/ml of LPS, while IL-1β and IL-10 reached it with 10 µg/ml dose. The interaction between time of infection and LPS doses gave significant differences at 2 µg/ml of LPS comparing 1 vs 3 hours of infection [3.16(2.90-3.52) vs. 2.76(2.6-2.9), p-value=0.009], and at 5 µg/ml comparing 1 vs 2 hours of infection [2.78(2.51-3.08) vs. 2.79(2.63-3.12), (p=0.030)]; in contrast, no differences were found at 10 and 0 µg/ml of LPS.

**Conclusions:** High LPS doses are associated with increased proinflammatory cytokines levels and decreased macrophages’ bactericidal activity. This model will be useful to evaluate the cellular response to immunomodulatory therapies during pneumonia or sepsis caused by *S. pneumoniae*.

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Potentiation of quinolones activity against *Escherichia coli* by suppression of SOS response and oxidative detoxification systems

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**Background:** Enhancement of *in vitro* activity of quinolones has been shown when SOS response is suppressed and reactive oxygen species (ROS) are overproduced, separately. Herein, we investigate the effect of these two processes, alone or in combination, using a genetic strategy creating doubles or triple knockouts mutants for SOS response (*recA*), detoxification effectors (*katG, katE, sodA, sodB, ahpC*), and regulator of the stress response (*oxyR and rpoS*) in an isogenic model in *Escherichia coli*.

**Materials/methods:** *E. coli* BW25113 (wild-type) single-gene deletion mutants (Δ*recA*, Δ*katG*, Δ*katE*, Δ*sodA*, Δ*sodB*, Δ*ahpC*, Δ*oxyR* and Δ*rpoS*) were selected from the KEIO collection. Double-gene deletion mutants (Δ*recA*Δ*katG*, Δ*recA*Δ*katE*, Δ*recA*Δ*sodA*, Δ*recA*Δ*sodB*, Δ*recA*Δ*ahpC*, Δ*recA*Δ*oxyR*, Δ*recA*Δ*rpoS*, Δ*katG*Δ*katE*, Δ*sodB*Δ*sodA*) and triple-gene deletion mutant (Δ*recA*Δ*katG*Δ*katE*) was generated by phage P1vir transduction. Susceptibility testing to ciprofloxacin was determined by gradient strips in aerobiosis and anaerobiosis. Antimicrobial activity was evaluated by time-kill curve assays with ciprofloxacin concentration of 1xMIC relative to Δ*recA* during 24h and spot test with different inoculum (10^2-10^7 CFU/ml) and ciprofloxacin concentration of 0.125xMIC relative to Δ*recA* (0.0005mg/L) in aerobiosis.

**Results:** Suppression of SOS response together with detoxification systems reduced ciprofloxacin MICs values up to 16-fold and 4-fold compared to wild-type strain and Δ*recA* mutant, respectively in aerobiosis. However, this effect was not observed under anaerobic conditions. Time-kill curves assays [Figure 1a] showed a significant reduction in CFU/mL of double knockout (Δ*katG*-Δ*recA*, Δ*sodA*-Δ*recA* and Δ*ahpC*-Δ*recA*) compared to Δ*recA* in short times (2h: 2-2,5Log and 4h: 2,5-4Log). Spot test [Figure 1b] showed a greater susceptibility of double (Δ*katG*Δ*recA* and Δ*katE*Δ*recA*) and triple knockout (Δ*katG*Δ*katE*Δ*recA*) respect to Δ*recA*. Also, Δ*recA* mutant increased susceptibility compared to *E. coli* BW25113 and simple (Δ*katG*, Δ*katE*) and double knockout (Δ*katG*Δ*katE*).

**Conclusions:** Suppression of SOS response and detoxification systems enhanced sensitization of *E. coli* to quinolones so that the search of inhibitors of both systems would be useful to combat resistance.

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**Figure 1.** Results of a) time-kill assays (ciprofloxacin concentration 1xMIC relative to Δ*recA*) at 2h and 4h, ***p<0.001, **p<0.005; b) spot test (ciprofloxacin concentration 0.125xMIC relative to Δ*recA*) at 24h.

a.

![Time-kill curve CIP 1xMIC (Δ*recA*)](image1)

b.

![Inoculum (CFU/mL) CIP (0.125xMIC Δ*recA*)](image2)

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**Abstract 2674**

**Antimicrobial resistance monitoring through the ATLAS global surveillance programme 2004-2018**

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**Background:** The ongoing problem of antibiotic resistance, including multidrug resistance is a global health issue. In order to determine the extent of the problem and to identify changes in the resistance patterns of global, regional and local pathogens, world-wide antibiotic surveillance programs are essential. The Antimicrobial Testing Leadership and Surveillance (ATLAS) program has provided reliable, global, regional and local in vitro susceptibility data, including mechanisms of resistance, since 2004. As it is important to monitor the emergence of new species and new resistance mechanisms over time, in this analysis we present a longitudinal analysis of resistance to commonly prescribed antimicrobials for isolates collected globally for ATLAS 2004-2018.

**Materials/methods:** A total of 284,808 non-duplicate, clinically isolated Enterobacterales were collected in 2004-2018 in the ATLAS program. Susceptibility testing was performed by broth microdilution and interpreted using 2019 EUCAST breakpoints. For tigecycline, only *Escherichia coli* and *Citrobacter koseri* are analyzed following the EUCAST 2019 guidelines. Avibactam was tested at a fixed concentration of 4 mg/L.

**Results:** The proportion of Enterobacterales isolates resistant to commonly used antimicrobials has fluctuated over the 15 years compared in this analysis, with significant increases in resistance for cefepime (9.9% to 20.1%), meropenem (1.5% to 3.0%), and piperacillin-tazobactam (12.5% to 15.4%) between 2004-2006 and 2016-2018, and ceftazidime-avibactam (0.5% to 1.6%) between 2010-2012 and 2019-2018 (p<0.05). Amikacin and tigecycline showed no significant increase in resistance over 15 years of study.

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<tbody>
<tr>
<td>Amikacin</td>
<td>2.3% (30,985)</td>
<td>4.2% (40,085)</td>
<td>3% (50,498)</td>
<td>2.5% (81,361)</td>
<td>2.5% (81,878)</td>
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<tr>
<td>Cefepime</td>
<td>9.9% (30,985)</td>
<td>15.3% (40,085)</td>
<td>16.5% (50,498)</td>
<td>17.8% (81,361)</td>
<td>20.1% (81,878)</td>
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<td>Ceftazidime-avibactam</td>
<td>NT</td>
<td>NT</td>
<td>0.5% (9,567)</td>
<td>0.6% (42,842)</td>
<td>1.6% (52,330)</td>
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<td>Meropenem</td>
<td>1.5% (5,858)</td>
<td>1.4% (39,574)</td>
<td>1.2% (50,423)</td>
<td>2% (81,361)</td>
<td>3% (81,878)</td>
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<td>Piperacillin-tazobactam</td>
<td>12.5% (30,985)</td>
<td>17.6% (40,085)</td>
<td>17.4% (50,498)</td>
<td>14.5% (81,361)</td>
<td>15.4% (81,879)</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>1.7% (9,542)</td>
<td>5.8% (12,283)</td>
<td>7% (16,311)</td>
<td>2.8% (27,511)</td>
<td>1.7% (26,846)</td>
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Percent resistant based on EUCAST 2019 breakpoint; tigecycline data includes *E. coli* and *C. koseri*, only; NT, not tested

**Conclusions:** This longitudinal analysis of a 15-year surveillance study confirms rising rates of antimicrobial resistance to commonly used antibiotics. Continued monitoring is essential to understand the scope of this global public health issue, and to aid in the development of new strategies and treatments for these key pathogens.

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Abstract 2675

**Predictors of worse outcome in patients with West Nile virus infection: a multi-centre study**

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**Background:** Although West Nile virus (WNV) infection has established itself as a real epidemiological emergency, there is still a lack of knowledge regarding its clinical connotations. The primary objective of this study is to identify negative prognostic factors (clinical, electro-encephalographic, radiological, biohumoral or microbiological) in patients with West Nile virus infection(WNI).

**Materials/methods:** This was a retrospective, observational, multicenter study conducted in five centres during the WNI outbreak occurred in Northern Italy in the 2018

All adult patients with diagnosis of West Nile infection virus were included. The diagnosis of WNI was defined by specific nucleic acid in blood, CSF, or urine, or Virus-specific IgM antibodies in CSF or serum.

The primary endpoint was worse outcome, defined by the following composite variable: 30-day mortality or presence of neurological sequelae after six months of follow-up.

**Results:** A total of 130 patients were enrolled. Median (IQR) age was 70 (49-79) years and 43% of the patients were females. The median (IQR) Charlson Index score was 4 (0.75 – 5). Patients were managed in regular wards or intensive care units in 93.1% and 6.9% of cases, respectively.

Worse outcome was observed in 33% of the cases. More specifically, we found 30-day mortality in 13.8% of cases and neurological sequelae at six months follow-up in 25% of cases. These were represented by cognitive-mnestic or motor impairment (44.8%), cranial nerve deficiency (6.8%), persistent headache (24%), neuropsychiatric disorders(17.2%).

Multivariate analysis according to logistic regression demonstrated the factors independently associated with worse outcome were: detectable viraemia at infection diagnosis [OR 2.535 [95% CI 1.00-4.437] p 0.050], leukopenia [WBC <4000/mm] [OR 3.591 [95% CI 1.147-11.240] p 0.028], fever≥38 °C [OR 3.471 [95% CI 1.165-10.347] p 0.026], diarrhea/abdominal pain [OR 3.043 [95% CI 1.106-8.374] p 0.031], onset phenotype with meningitis/encephalitis [OR 2.496 [95% CI 1.026-6.072] p 0.044].

**Conclusions:** Simple variables such as leukopenia, presence of diarrhea/abdominal pain and fever over 38 °C, together with the type of clinical onset and detectable viraemia are able to predict the outcome of WNV infection.

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**Evaluation of the RIDA QUICK Helicobacter and RIDASCREEN Helicobacter kits on stool samples for *Helicobacter pylori* diagnosis**

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¹Chu Pellegrin Bordeaux, CNR Campylobacters-Helicobacters, Bordeaux, France

**Background:** The diagnosis of *Helicobacter pylori* infection can be made by non-invasive tests. The detection of bacterial antigens in stool samples is a technique proposed by some suppliers. The objective of this study was to evaluate retrospectively the performance of the commercial RIDA®QUICK *Helicobacter* and RIDASCREEN® *Helicobacter* (r-biopharm) kits on stool samples.

**Materials/methods:** A collection of 132 stools was used in this study: 94 stools obtained from *H. pylori* negative patients (negative culture and PCR on gastric biopsy) and 38 stools from *H. pylori* positive patients (5 patients negative culture /PCR + and 33 patients culture + /PCR +). The performances (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV)) were evaluated for the RIDA®QUICK *Helicobacter* and RIDASCREEN® *Helicobacter* kits in comparison to the real-time PCR results performed on gastric biopsies (Oleastro et al., J Clin Microbiol 2003). Discordants with respect to the *H. pylori* status, were checked on the same day of the test by repeating the test. The RIDA®QUICK *Helicobacter* tests were read by the naked eye by 3 independent users. RIDASCREEN® *Helicobacter* tests were analyzed on an ELISA Etimax (Diasorin) according to the supplier’s recommendations.

**Results:** All of the readings concerning the RIDA®QUICK *Helicobacter* tests were concordant between the 3 users, ie 94/94 negative tests and 34/38 positive tests. RIDASCREEN® *Helicobacter* tests were negative in all 94 *H. pylori* negative and positive in 35/38 positive stools (see table). Reading of the RIDA®QUICK *Helicobacter* tests was not a problem in routine practice. The migration of the stool suspensions within the strip did not pose a technical problem.

**Conclusions:** The RIDA®QUICK *Helicobacter* and RIDASCREEN® *Helicobacter* kits have excellent performances and can be included in the armamentarium of diagnostic tests for *H. pylori* infection.

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<td>RIDASCREEN®</td>
<td>92.1</td>
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<td>100</td>
<td>96.9</td>
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<td>RIDA®QUICK</td>
<td>89.5</td>
<td>100</td>
<td>100</td>
<td>95.9</td>
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data in %

**Presenter email address:** philippe.lehours@u-bordeaux.fr
Abstract 2678

**Epidemiology of the Staphylococcus aureus CA-MRSA USA300 in Belgium**

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¹Laboratoire Hospitalier Universitaire de Bruxelles (LHUB-ULB), CNR Staphylocoques, Brussels, Belgium

Abstract third-party references: This study has been financed by the LHUB-ULB.

**Background:** Methicillin resistant Staphylococcus aureus (MRSA) is a major concern for public health. Since the 90s, community acquired (CA) MRSA lineages have been increasingly reported as cause of skin and soft tissue infections, necrotizing pneumonia and endocarditis. Within CA-MRSA only the USA300 North American (NA) variant has a worldwide distribution. Some studies established that its epidemiology in Europe is the result of multiple introductions with limited spread in the general population. However, data from the Belgian National Reference Center (NRC) of Staphylococci suggest that this clone is frequent (nearly endemic) in our country. Our data also suggest that the USA300 Latin American (LV) variant is emerging in Belgium. In this study, we have used whole genome sequencing (WGS) to analyze a collection of CA-MRSA USA300 and related isolates recovered in Belgium from 2005 to 2018.

**Materials/methods:** 119 isolates previously characterized by classical molecular typing methods (PCR detecting mecA, PVL and ACME; spa-typing) were selected from the NRC collection for WGS. BioNumerics v.7.6 (Applied Maths) was used for phylogenetic analysis (wgSNPs). Center for Genomic Epidemiology tools have been used to establish STs, spa-types, and SCCmec, from WGS data as well as to determine the presence/absence of ACME (related to USA300-NA), COMER (related to USA300-LV), virulence, antimicrobial, biocide and metal resistance genes.

**Results:** The wgSNPs showed the presence of three main clusters, corresponding to USA-300-NA, USA300-LV and “other” CCB CA-MRSA [Figure 1]. Some USA300-NA strains were directly related to the reference strain, suggesting multiple non-related introductions. Other strains were closely related (≤20 SNPs) implying outbreaks. In fact, two big clusters of closely related USA300-NA strains were found: (a) fluoroquinolone resistant isolates recovered between 2008 and 2017; (b) fluoroquinolone susceptible isolates recovered between 2008 and 2017; (b) fluoroquinolone susceptible isolates recovered between 2010 and 2018. Five out of 8 USA300-LV isolates were related to trips to South America. Regarding other CC8 CA-MRSA, we confirmed the introduction in Belgium of the clone ST923 previously found in Colombia and Venezuela producing pediatric infections or colonizing healthy youths and children.

**Conclusions:** In this study we elucidated the epidemiology of USA300-NA in Belgium, and confirmed the recent introduction of USA300-LV and ST923 in the country.

**Acknowledgments:** This study has been financed by the LHUB-ULB.

**Figure 1.** wgSNP minimum spanning tree of CC8 CA-MRSA isolates.

Each circle represents a strain colored on the basis of the populations found. The genome of the USA300-NA TCH1516 (accession number: NC_010070) strain (in red) was used as reference genome for mapping to determine SNP differences. Two main groups of closely related USA300 isolates were found: (a) fluoroquinolone resistant isolates recovered between 2008 and 2017 in four Belgian regions (but mainly from Brussels); (b) fluoroquinolone susceptible isolates recovered between 2010 and 2018 in four Belgian regions (but mainly from Antwerp and East Flanders). Few strains without PVL and/or ACME clustered within USA300 NA isolates, suggesting that they have lost these virulence traits. Numbers indicated n° of SNPs differences.

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ART24, a novel live biotherapeutic product, in development for the prevention of Clostridioides difficile infection spares gut commensal species in vitro and allows for expansion of beneficial bacteria

Michelle O’donnell¹, Bran Healy¹, Colin Hill², Paul Ross³, Mary Rea¹, Ronald Farquhar¹, Laurent Chesnel*³

¹Artugen therapeutics, Teagasc Food Research Centre, Fermoy, Ireland, ²University College Cork, APC Microbiome Institute, Cork, Ireland, ³Artugen therapeutics USA, Inc, Concord, United States

**Background:** ART24 is being investigated as a live biotherapeutic product (LBP) treatment to prevent recurrence of *Clostridioides difficile* infection (CDI) following successful antibacterial treatment. ART24 was isolated from a human fecal sample, purified and identified as a member of the “operational group *B. amyloliquefaciens*”. We have determined that the strain has potent *C. difficile* killing activity and sought to determine the spectrum of activity of ART24.

**Materials/methods:** To investigate the effects of ART24 on gut microbiota, three approaches were undertaken. First, ART24 cell-free pH-neutralized supernatants were prepared from 24-hour cultures and assessed for antibacterial activity using a well diffusion assay against *C. difficile* and gut commensals. Additionally, a human colonic model with frozen fecal slurry (n=6 subjects) was inoculated with 6x10⁸ CFU of vegetative ART24 and incubated for 24 hours. Lastly, minipigs were dosed with 1.06x10¹⁰ CFU/dose QD for 28 days and fecal samples were collected. DNA was extracted from the colonic model and minipig fecal samples and analyzed using qPCR and MiSeq compositional sequencing and bioinformatics along with statistical analyses.

**Results:** ART24 was found to have a relatively narrow spectrum of activity primarily against *Clostridium* and *Bacillus* species. Little to no activity against *Lactobacillus* and *Bifidobacterium* was observed indicating very weak activity against gut commensal bacteria. By qPCR and 16S analysis from the in vitro colonic model ART24 demonstrated little to no impact on other components of the gut microbiota (*Enterobacteriaceae, Firmicutes, Bacteroidetes, Verrucomicrobia, and Lactobacillus*) after 24 hours of incubation. The ART24 treated wells showed an increase in the *Bifidobacterium* genus relative to T0 where the relative abundance went from 3.95% to 16.02%. No changes in alpha and beta diversity in vitro, in the colonic model, and in the animals were observed and correlate with the qPCR and agar-based results, indicating that ART24 does not have a deleterious effect on the human colonic microbiota.

**Conclusions:** These studies suggest that ART24 has little effect on the human and minipig colonic microbiota and suggest that it supports the expansion of *Bifidobacterium*. ART24 is a promising LBP clinical candidate undergoing Phase 1 clinical development for the prevention of CDI recurrence.

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Evaluation of the expanded-coverage Staphylococcus species assays and improved methicillin resistance detection algorithms of the BioFire FilmArray Blood Culture Identification 2 (BCID2) panel

Tanner Robinson1, Jeremiah Antosch1, Kerrin Koch1, Iryna Kavetska1, Jessica Stone1, Briana Flaherty1, Maggie Buccambuso1, Kristen Holmberg1, Yang Lu1, Benedicte Pons2, Margarita Rogatcheva*1, Usha Spaulding1

BioFire Diagnostics, LLC, Salt Lake City, United States, 2BioMerieux, Grenoble, France

Background: Staphylococci are opportunistic pathogens and a major cause of both nosocomial and community-acquired bloodstream infections (BSI). Compared to the existing BioFire® FilmArray® Blood Culture Identification (BCID) Panel, the updated BioFire BCID2 Panel contains an assay with expanded coverage for Staphylococcus species. Also, alongside an updated Staphylococcus aureus assay, the BCID2 Panel includes assays for key coagulase-negative staphylococci (CoNS) like Staphylococcus epidermidis, and Staphylococcus lugdunensis. Revised algorithms, facilitated by a new assay that identifies the insertion site of the staphylococcal cassette chromosome mec in S. aureus, aid accurate reporting of methicillin-resistant S. aureus (MRSA). Here, we evaluate the coverage and performance of these assays and associated algorithms.

Materials/methods: Coverage and performance were evaluated using sequence data available for 72/77 species/subspecies, 107 Staphylococcus isolates and 107 residual positive blood cultures (PBC) collected prospectively from 9 clinical sites. For pathogen identification from residual PBC, the reference method was microbial culture performed at clinical sites. The Xpert MRSA/SA BC test (Cepheid, Inc.) and phenotypic susceptibility testing were used as reference methods for MRSA.

Results: In silico assessment predicts reactivity for 66/72 staphylococci compared to ~40 species by the BCID Panel. During analytical testing, the Staphylococcus species assay also detected 103/107 isolates. Specific assays for S. aureus, S. epidermidis, and S. lugdunensis were reactive to all relevant isolates. At least one Staphylococcus species was reported in 472/1074 (44%) samples enrolled in the prospective clinical study; the BioFire BCID2 Panel accurately identified 99.8% of these. The BioFire BCID2 Panel MRSA results were 100% concordant with phenotypic results and 95.4% concordant with Xpert MRSA/SA BC test. In addition, the algorithm accurately identified the absence of MRSA in 3/3 cases where methicillin-susceptible S. aureus was present with methicillin-resistant S. epidermidis (MRSE) in the PBC.

Conclusions: The BioFire BCID2 Panel assays for S. aureus, S. epidermidis, S. lugdunensis, and Staphylococcus spp. are highly inclusive of clinically relevant staphylococci. The high accuracy of the MRSA detection algorithms are anticipated to assist in implementation of effective treatment plans and antibiotic stewardship.

Data presented are from assays that have not been cleared or approved for diagnostic use.

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Abstract 2681

Targeting membrane transporters and energy metabolism in *Mycobacterium tuberculosis* through in silico drug repurposing

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**Background:** Energy metabolism, particularly the oxidative phosphorylation pathway, has emerged as a novel target pathway in tuberculosis (TB) drug discovery. Inhibitors of bacterial energy metabolism may interfere with several physiological processes, including the activity of efflux pumps involved in drug resistance. A way to accelerate drug discovery is to find new uses for existing approved drugs, a strategy known as drug repurposing. A repurposed drug can follow directly to preclinical testing and clinical trials, reducing time, cost and risk. We used such strategy to find drugs that target energy metabolism and membrane transporters in *Mycobacterium tuberculosis*.

**Materials/methods:** A list of *M. tuberculosis* proteins involved in energy metabolism and membrane transport was compiled using the TDR Targets and Mycobrowser databases. Each of these proteins was considered a potential drug target and its amino acid sequence used to interrogate two web-based databases [DrugBank and STITCH 5.0] that provide information on drugs and their targets. From the targets obtained from both databases only the ones predicted to interact with approved drugs were selected. The functional regions of the approved drug targets and *M. tuberculosis* targets were compared using The ConSurf Server.

**Results:** TDR Targets and Mycobrowser identified 668 genes that encode proteins involved in energy metabolism and membrane transport. Sequence similarity screenings predicted 69 targets associated with 245 approved drugs. Functional regions comparison between approved drug targets and predicted *M. tuberculosis* targets resulted in 18 potential *M. tuberculosis* targets that are expected to interact with 23 approved drugs. These drugs are predicted to target succinate dehydrogenases, sodium-potassium ATPases, NADH-dehydrogenases, among others. Some examples are thiabendazole, deslanoside and doxorubicin.

**Conclusions:** Most of the identified drugs are approved for a variety of indications, such as arrhythmia, epilepsy, chronic immune thrombocytopenia, and cancer and may serve as lead compounds for the development of new anti-TB drugs. This work has the potential to greatly benefit TB drug discovery by finding new drugs for a largely unexplored pathway and by introducing a new approach that can increase the probability of identifying effective drugs and decrease the bottlenecks of conventional drug discovery.

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Abstract 2684

(In)stability of female urinary microbiota: who’s resident and who’s passing by

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Background: The recent recognition of the female urinary microbiota (FUM) has challenged the current assumptions of the etiology, diagnosis and treatment of urinary tract diseases. Still, we have incomplete knowledge on healthy community profiles and their stability over time. Using extended culturomic approach, we aimed to evaluate FUM composition and stability of healthy women.

Materials/methods: Ten healthy reproductive-age women provided midstream urine samples (n=20) at two time points within 2,5 years interval, that were subjected to extended culturomics (100 ul urine; blood agar and supplemented chromogenic agar; 48h of incubation; different atmospheric conditions) with isolate identification to the species level by MALDI-TOF/MS and/or suitable genotypic biomarkers (16S rRNA, pheS, rpoB, recN).

Results: Over 2000 isolates (range of 17-321 isolates/sample) were assigned to 5 phyla, 45 genera and 111 species (average of 19 species/sample). The stability of phyla between 1st and 2nd sampling was observed, comprising Firmicutes (51% of species in both samples), Actinobacteria (38%, 33%), Proteobacteria (6%, 11%), Bacteroidetes (3%, 3%) and Fusobacteria (1%, 2%). A high bacterial load was observed (10^4- 10^8 CFU/ml) – in 70% samples varied up to 10^2 CFU/ml between paired samples. The Staphylococcus and Lactobacillus were the most prevalent genera present in 18 out of 20 (18/20) and 17/20 samples, respectively. The stability at species level was observed for 35 bacterial species, most being previously identified as highly prevalent e.g., Staphylococcus epidermidis (8 out of 10 individuals, 8/10) and Streptococcus anginosus (6/7) mostly in low relative abundance (RA). Notably, opportunistic pathogens associated with urogenital tract health were detected e.g., Gardnerella vaginalis (3/5), maintaining high RA at both sampling points (up to 91% RA). Additionally, one individual presented highly abundant Enterobacteriaceae member (10^7-10^8 CFU/ml) in both samples (1st sample: Citrobacter koseri [99.98% RA]; 2nd sample: Escherichia coli [90.76% RA]) together with Lactobacillus jensenii.

Conclusions: For the first time, we described that healthy FUM undergoes bacterial species shifts over time, that further complicates the establishment of a healthy FUM pattern. Despite those fluctuations, certain species are more persistent and less susceptible to changes e.g., Gardnerella vaginalis and Lactobacillus crispatus, which needs to be further explored.

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Abstract 2685

Evaluation of the Novodiag Bacterial GE+ kit for the diagnosis of intestinal bacterial infections

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Background: The bacteriological diagnosis of intestinal bacterial infections has historically been based on culture on agar plates. However, culture lacks sensitivity and some enteropathogens such as pathovars of Escherichia coli escape routine diagnosis. Our goal was to evaluate the analytical performance of the Novodiag® Bacterial GE + kit, for the detection of enteropathogenic bacteria in acute community diarrhea.

Materials/methods: 252 stools were included in this study (198 retrospective and 54 prospective). The results were compared to stool culture in first intention. In the case of negative culture, the performances were evaluated in relation to the results obtained on BD Max Enteric Bacterial Panel (retrospective stools) or by other real-time PCR formats (in-house or commercial).

Results: Of the 252 samples, 207 were positive and 45 were negative. In the prospective samples (January-March 2019), 6 stools were positive by culture (prevalence: 11.1%) and 18 with the Novodiag® Bacterial GE+ kit (prevalence: 33.3%). All enteropathogens combined, the Novodiag® Bacterial GE + kit had a sensitivity of 99.03% and a specificity of 95.65%. Only 3 discrepancies were identified: an EHEC detected by BDMax but negative by Novodiag®, culture and in-house PCR; a Campylobacter coli detected by Novodiag® but negative by PCR RidaGene Bacterial Stool Panel (r-biopharm), culture and in-house Campylobacter PCR; and 1 Campylobacter jejuni positive by PCR RidaGene and BDMax but undetected by Novodiag®. Overall sensitivities for Campylobacter, Salmonella, Shigella, Yersinia, EHEC and ETEC ranged from 99 to 100%, and specificities from 99 to 100%, PPV from 94.1 to 100% and NVP from 99 to 100%.

Conclusions: The analytical performances of the Novodiag® Bacterial GE + kit are excellent. It can be used as a routine tool in the rapid diagnosis of bacterial gastroenteritis. Despite the eNAT tube dilution of the primary sample, the detection of Salmonella sp. and EHEC was perfect. The kit has the advantage of only detecting pathogenic Yersinia sp. The performances for Campylobacters are very satisfactory.

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Abstract 2688

**Toll like receptors, IFN-lambdas and IFN-stimulated genes expression in cystic fibrosis patients with rhinovirus infection**

Federica Frasca*, Camilla Bitossi, Agnese Viscido, Giuseppe Oliveto, Mirko Scordio, Maria Trancassini, Valeria Pietropaolo, Fabio Midulla, Giuseppe Cimino, Paolo Palange, Alessandra Pierangeli, Carolina Scagnolari, Guido Antonelli

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**Background:** Since an inappropriate and sustained activation of toll like receptors (TLRs) and interferon (IFN) response may contribute to a chronic inflammatory outcome resulting in detrimental effects in CF patients, our aim is to evaluate whether human rhinovirus (HRV) infection might alter the respiratory gene expression of TLRs and type III IFN pathways compared to HRV-negative patients.

**Materials/methods:** Respiratory samples (n=515) were collected from the respiratory tract of CF patients (n=294) over a period of 12 months. HRV-RNA was tested by RT-PCR. Amplified fragments of HRV-positive samples were sequenced for HRV species characterization. Levels of TLRs (TLR2, TLR4, TLR8), type III IFNs (λ1 and λ3), IL28RA, and IFN stimulated genes (ISGs: MxA, ISG15, and ISG56)-mRNAs and HRV viral load were measured by quantitative RT/TagMan assay.

**Results:** HRV-RNA was detected in 80 out of 515 respiratory samples (15.5%) with a similar rate in all age groups (0-10 years, 11-24 years, ≥25 years). Increased transcript levels of TLRs (TLR2, TLR4, TLR8), type III IFNs (λ1 and λ3), IL28RA and ISGs (MxA, ISG15, and ISG56) were observed in HRV A-C positive patients compared to those with non-HRV infection (p<0.05 for all genes, Mann-Whitney U Test). By contrast no differences in the expression of TLRs and type III IFN pathways were found between HRV-B positive patients and those without HRV infection. Moreover, transcript levels of TLR2 (r=0.3924), TLR8 (r=0.4222), IFNA3 (r=0.4548), IL28RA (r=0.4587), MxA (r=0.4455) and ISG15 (r=0.3778) positively correlated with HRV viral load (p<0.05 for all genes, Spearman's rho coefficient).

**Conclusions:** Our results indicated that TLRs, IFNλ1/3, IL28RA and ISGs transcripts are highly expressed in the respiratory tract of HRV A-C positive CF patients and correlate with viral load.

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**Abstract 2689**

**In vitro activity of ceftolozane/tazobactam and comparators against *Pseudomonas aeruginosa* isolates collected in the United States: SMART 2018**

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**Background:** Ceftolozane is an antipseudomonal cephalosporin with improved activity compared to ceftazidime. The combination of ceftolozane and tazobactam, a β-lactamase inhibitor, is approved for treatment of complicated urinary tract and complicated intra-abdominal infections in the US and more than 60 countries, and for treatment of hospital-acquired and ventilator-associated bacterial pneumonia in the US and Europe. We evaluated the activity of ceftolozane/tazobactam (C/T) and comparators against β-lactam non-susceptible (NS) *P. aeruginosa* isolates collected in the US as part of the SMART surveillance program in 2018.

**Materials/methods:** Twenty-four medical laboratories each collected up to 250 consecutive aerobic or facultative gram-negative pathogens from various infection sources, including 895 *P. aeruginosa*. MICs were determined by CLSI broth microdilution and interpreted using CLSI 2019 breakpoints. Avibactam was obtained from BioChemPartner (www.biocompartner.com) and tested at a fixed concentration of 4 mg/L. A multidrug-resistant phenotype (MDR) was defined as non-susceptibility to three or more sentinel agents (aztreonam, cefepime, piperacillin/tazobactam, imipenem, amikacin, ciprofloxacin, colistin). Pan-β-lactam-NS was defined as non-susceptibility to all tested β-lactams (aztreonam, ceftazidime, cefepime, piperacillin/tazobactam, imipenem, meropenem).

**Results:** C/T demonstrated potent *in vitro* activity against *P. aeruginosa* collected in the US (MIC₉₀ 2 mg/L; 96.4% susceptible), with similar percentages of susceptibility observed across US census regions (Table). 30.6%, 26.8%, 23.1%, 21.6%, 25.5%, and 8.7% of collected isolates were imipenem-NS, piperacillin/tazobactam-NS, meropenem-NS, ceftazidime-NS, MDR, and pan-β-lactam-NS, respectively. Susceptibility to C/T ranged from 74.4%-92.0% among these resistant subsets of isolates, 6-19 percentage points higher than susceptibility to ceftazidime/avibactam (CZA). *In vitro* susceptibility to C/T was consistently higher among β-lactam-NS and MDR *P. aeruginosa* collected in different regions. C/T retained activity against 56.9% of all CZA-resistant *P. aeruginosa* (5.7% of collected isolates), while only 31.3% of C/T-NS isolates (3.5% of collected) were susceptible to CZA. Four metallo-β-lactamase-producing isolates were collected in 2018, in the West (n=2), Midwest (n=1) and South (n=1), and these isolates tested as resistant to both C/T and CZA.

<table>
<thead>
<tr>
<th>Organism/Phenotype</th>
<th>United States</th>
<th>West</th>
<th>Midwest</th>
<th>Northeast</th>
<th>South</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C/T CZA C/T CZA C/T CZA C/T CZA</td>
<td>C/T CZA C/T CZA C/T CZA C/T CZA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PA, All</td>
<td>895 96.4 94.3</td>
<td>214 95.8 93.0</td>
<td>428 96.3 95.6</td>
<td>103 95.2 90.3</td>
<td>150 98.7 95.3</td>
</tr>
<tr>
<td>CAZ-NS</td>
<td>193 83.9 74.6</td>
<td>48 83.3 68.8</td>
<td>80 80.0 77.5</td>
<td>31 83.9 71.0</td>
<td>34 94.1 79.4</td>
</tr>
<tr>
<td>CZA-R</td>
<td>51 56.9 0.0</td>
<td>15 66.7 0.0</td>
<td>19 42.1 0.0</td>
<td>10 60.0 0.0</td>
<td>7 71.4 0.0</td>
</tr>
<tr>
<td>C/T-NS</td>
<td>32 0.0 31.3</td>
<td>9 0.0 44.4</td>
<td>16 0.0 31.3</td>
<td>5 0.0 20.0</td>
<td>2 0.0 0.0</td>
</tr>
<tr>
<td>TZP-NS</td>
<td>240 87.9 80.4</td>
<td>56 85.7 75.0</td>
<td>108 87.0 84.3</td>
<td>40 87.5 77.5</td>
<td>36 94.4 80.6</td>
</tr>
<tr>
<td>IMI-NS</td>
<td>274 92.0 85.4</td>
<td>65 90.8 81.5</td>
<td>134 92.5 90.3</td>
<td>35 88.6 74.3</td>
<td>40 95.0 85.0</td>
</tr>
<tr>
<td>MEM-NS</td>
<td>207 87.9 78.7</td>
<td>53 86.8 75.5</td>
<td>87 86.2 82.8</td>
<td>31 87.1 71.0</td>
<td>36 94.4 80.6</td>
</tr>
<tr>
<td>pan-β-lactam-NS</td>
<td>78 74.4 55.1</td>
<td>26 76.9 53.8</td>
<td>27 70.4 63.0</td>
<td>13 69.2 46.2</td>
<td>12 83.3 50.0</td>
</tr>
<tr>
<td>MDR</td>
<td>228 86.4 78.5</td>
<td>59 86.4 76.3</td>
<td>100 84.0 81.0</td>
<td>36 86.1 75.0</td>
<td>33 93.9 78.8</td>
</tr>
</tbody>
</table>

**West:** California, Colorado, Utah; **Midwest:** Illinois, Indiana, Iowa, Michigan, Minnesota, Nebraska, Ohio, Wisconsin; **Northeast:** New York, Pennsylvania; **South:** Florida, Georgia, Kentucky, North Carolina, Texas. CAZ, ceftazidime; CZA, ceftazidime/avibactam; C/T, ceftolozane/tazobactam; TZP, piperacillin/tazobactam; IMI, imipenem; MEM, meropenem; NS, non-susceptible; R, resistant; pan-β-lactam-NS, non-susceptible to all tested β-lactams; MDR, multidrug resistant: NS to three or more sentinel agents.

**Conclusions:** C/T could provide an important treatment option for patients in the US with infections caused by drug-resistant *P. aeruginosa*, including ceftazidime/avibactam-resistant isolates and those non-susceptible to one or multiple antimicrobial agents.

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ART24, a novel live biotherapeutic product, in development for the prevention of *Clostridioides difficile* infection is bactericidal against *C. difficile* and degrades toxins A and B in vitro

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**Background:** ART24 is being investigated as a live biotherapeutic product (LBP) treatment to prevent recurrence of *Clostridioides difficile* infection (CDI) following successful antibacterial treatment. ART24 was identified from a screening effort from stool samples detecting bacteria with direct anti-*C. difficile* activity and proteolytic capability. ART24 was identified as a member of the *B. amyloliquefaciens/B. velezensis* group. We sought to determine if both of these activities translated in vitro in *C. difficile* toxin degradation and *C. difficile* killing.

**Materials/methods:** The anti-*C. difficile* activity of ART24 was investigated using a 12-well plate liquid co-culture method incubating different ratios of ART24 to *C. difficile* for 24 hours. ART24 was tested against different starting levels of *C. difficile* (10²-10⁵ CFU/ml). *C. difficile* was enumerated pre and post-incubation to assess the effect of each ratio of ART24. Extracellular protease activity from ART24 was tested for its ability to cleave purified *C. difficile* toxins A and B. Toxin cleavage experiments were run in duplicate using pH-neutralized and IPA-extracted supernatants from freshly grown ART24, prepared from 2 independent cultures. The aliquots were incubated for 2 hours at 37°C. Western blot analysis was conducted, using standardized toxin A and B antibodies. ART24 was also tested as a lyophilized powder after reconstitution and serial dilution in PBS.

**Results:** ART24 is bactericidal against *C. difficile*. The lowest ratio [ART24:*C. difficile* CFU] that supports *C. difficile* killing (>3 log reduction in 24 hours) was 300:1, with lower ratios inhibiting the growth rate of *C. difficile*. A reconstituted preparation of lyophilized ART24 caused complete cleavage of *C. difficile* toxins A and B. The amount of toxin cleavage was dependent upon the amount of lyophilized ART24 CFUs reconstituted, with lower dilutions (i.e. 10⁻² and 10⁻³ dilutions) showing more cleavage than higher dilutions (range of 10⁻⁴ to 10⁻⁷ serial dilutions).

**Conclusions:** At projected clinically-relevant concentrations, ART24 is bactericidal against *C. difficile* in liquid co-cultures and completely cleaves toxins A and B. ART24 is a promising LBP candidate in Phase 1 clinical development for the prevention of recurrent CDI.

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Background: Influenza viruses cause seasonal outbreaks and pose a continuous pandemic threat. Although vaccines are available for influenza control, their efficacy varies each season and a vaccine for a novel pandemic virus manufactured using current technology will not be available fast enough to mitigate the effect of the first pandemic wave. Antivirals can be effective against many different influenza viruses but have not been used extensively for outbreak control. Baloxavir, a new antiviral which targets the influenza virus endonuclease, has been shown to reduce virus shedding more effectively than oseltamivir, a widely used neuraminidase inhibitor drug. This raises the possibility that baloxavir could limit spread of influenza by reducing virus transmission from an infected individual to healthy contacts. To investigate this potential, we used the ferret model, which is the most widely used animal model for influenza virus transmission.

Materials/methods: We conducted studies in two different locations with different experimental setups to compare the onward transmission of A[H1N1]pdm09 virus from infected ferrets treated with baloxavir, oseltamivir or placebo, to naive sentinel ferrets exposed either indirectly in adjacent cages or directly by co-housing.

Results: Baloxavir treatment of infected ferrets significantly reduced infectious virus shedding compared to oseltamivir- or placebo-treated ferrets. The frequency of virus transmission from baloxavir-treated ferrets to untreated sentinels was reduced compared to either oseltamivir or placebo group in both experimental setups, even when treatment was delayed until 2 days post-infection. Oseltamivir had no effect on reducing transmission compared to placebo. We did not detect the emergence of drug resistant variants in baloxavir-treated animals or in untreated sentinels.

Conclusions: Using the ferret model, we showed that treatment of influenza-infected individuals with the novel antiviral baloxavir reduces the likelihood of virus transmission to untreated contacts. Our results support the concept that antiviral treatment which significantly decreases influenza virus shedding during infection can translate into reduced influenza transmission.

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**Abstract 2694**

**In vitro activity of imipenem/relebactam against *Pseudomonas aeruginosa* isolates collected from patients in Europe: SMART 2018**

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**Background:** Relebactam (REL) is an inhibitor of class A and C β-lactamases that was approved in the USA in combination with imipenem (IMI) for the treatment of complicated intraabdominal and urinary infections. We evaluated the activity of IMI/REL against recent *Pseudomonas aeruginosa* (*Psa*) isolates collected from patients in Western and Eastern Europe as part of the global Study for Monitoring Antimicrobial Resistance Trends (SMART) surveillance program.

**Materials/methods:** In 2018, 54 hospitals from 23 European countries collected up to 250 consecutive aerobic or facultative gram-negative pathogens from various infection sources. MICs were determined using CLSI broth microdilution and interpreted with EUCAST breakpoints. US FDA breakpoints were applied to IMI/REL.

**Results:** A total of 1952 *Psa* isolates were collected from patients with lower respiratory tract (64.7%), bloodstream (11.9%), urinary tract (11.8%), and intraabdominal infections (11.6%). Among the 1952 isolates, 5.7% were metallo-β-lactamase (MBL)-positive and were removed from subsequent analyses because REL is not active against class B MBLs. Among the remaining 1840 MBL-negative isolates, 90.8% were susceptible to IMI/REL (MIC₅₀, 0.5 mg/L; MIC₉₀, 2 mg/L; MIC range ≤0.12->32 mg/L), and 71.4% were susceptible to IMI (MIC₅₀, 2 mg/L; MIC₉₀, 16 mg/L; MIC range ≤0.12->32 mg/L). In the presence of REL, imipenem MICs decreased by 2 dilutions for 41.4% of MBL-negative isolates, by 3 dilutions for 21.3% of isolates, and by ≥4 dilutions for 8.9% of isolates. The in vitro susceptibility to IMI/REL and comparators of all MBL-negative *Psa* and subsets of isolates with IMI-resistant phenotypes is shown, stratified by Western and Eastern Europe and for Europe overall (Table).

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>All MBL-Psa (n=1840)</th>
<th>IMI-R MBL-Psa (n=527)</th>
<th>All MBL-Psa (n=971)</th>
<th>IMI-R MBL-Psa (n=223)</th>
<th>All MBL-Psa (n=863)</th>
<th>IMI-R MBL-Psa (n=304)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imipenem/relebactam</td>
<td>90.8</td>
<td>67.7</td>
<td>92.8</td>
<td>68.8</td>
<td>88.4</td>
<td>67.1</td>
</tr>
<tr>
<td>Imipenem</td>
<td>71.4</td>
<td>0.0</td>
<td>77.2</td>
<td>0.0</td>
<td>64.8</td>
<td>0.0</td>
</tr>
<tr>
<td>Cefepime</td>
<td>77.3</td>
<td>48.1</td>
<td>82.1</td>
<td>51.5</td>
<td>71.8</td>
<td>42.1</td>
</tr>
<tr>
<td>Cefazidime</td>
<td>73.5</td>
<td>41.2</td>
<td>76.5</td>
<td>43.0</td>
<td>70.1</td>
<td>39.8</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>77.1</td>
<td>52.0</td>
<td>78.8</td>
<td>51.0</td>
<td>75.2</td>
<td>53.3</td>
</tr>
<tr>
<td>Piperacillin/tazobactam</td>
<td>72.0</td>
<td>38.1</td>
<td>75.7</td>
<td>39.9</td>
<td>68.9</td>
<td>38.8</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>88.6</td>
<td>39.3</td>
<td>74.2</td>
<td>48.9</td>
<td>62.3</td>
<td>32.2</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>84.1</td>
<td>60.2</td>
<td>87.1</td>
<td>61.4</td>
<td>80.6</td>
<td>59.2</td>
</tr>
<tr>
<td>Colistin</td>
<td>99.7</td>
<td>99.2</td>
<td>99.5</td>
<td>98.7</td>
<td>99.9</td>
<td>99.7</td>
</tr>
</tbody>
</table>

Overall, IMI/REL was active in vitro against >90% of MBL-negative *Psa* isolates collected in 2018, 13-18 percentage points higher than the activity of the tested comparator β-lactams. IMI/REL activity for overall *Psa* and IMI-resistant *Psa* was exceeded only by colistin; IMI/REL susceptibility was slightly higher in Western than Eastern Europe. In both regions, IMI/REL maintained activity against >67% of MBL-negative *Psa* isolates that were resistant to IMI.

**Conclusions:** IMI/REL could provide an important alternative treatment option for patients in Europe with infections caused by MBL-negative isolates of *Psa*, including IMI-resistant subsets.

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Impact of a restrictive antibiotic policy on the emergence of extended-spectrum β-lactamase producing Enterobacteriaceae in the intensive care unit: a quasi-experimental observational study

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Background: Massive consumption of antibiotics in the intensive care unit (ICU) is a major determinant of extended-spectrum beta-lactamase–producing Enterobacteriaceae (ESBL-E) spreading. We evaluated whether a stewardship program including restrictive antibiotic policy in the ICU would reduce ESBL-E emergence without worsening patient’s outcomes.

Materials/methods: We conducted an observational quasi-experimental pre-post intervention study of all consecutive patients with length of stay (LOS) superior to 48h to the medical-surgical ICU of University Hospital of Guadeloupe. From Jan 1, 2014 to Dec 31, 2014, a liberal strategy was used including a broad-spectrum antibiotic as initial empirical treatment in case of sepsis or suspected infection, followed by de-escalation after 48-72h. From Jan 1, 2015 to Dec 31, 2015, a restrictive strategy was adopted which consisted of limitation of broad-spectrum antibiotics, avoidance of antibiotics targeting anaerobic microbiota and shortening of antibiotic duration. In addition, antibiotic therapy was initiated only after microbiological identification, except in cases of septic shock, acute respiratory distress syndrome and meningitis. Our primary outcome was the incidence of ICU-acquired ESBL-E and the main secondary outcome were all-cause ICU mortality and the rate of ESBL-E infections.

Results: 767 and 826 patients were respectively enrolled in the liberal and in the restrictive strategy period study. During the restrictive strategy period, less patients were treated with antibiotic therapy (41 vs 52%; p<0.001), treatment duration was shorter (5 vs 6 days; p=0.01) and antibiotics targeting anaerobic pathogens were significantly less administrated (87.1% vs 37.5%; p<0.0001). The rate of ICU-acquired ESBL-E carriage was significantly lower during the restrictive strategy period (18.9% vs 11.1%; p<0.0001). Similarly, ICU-acquired ESBL-E infection rate and ICU mortality were lower during the restrictive strategy period. In multivariate analysis, the length of stay in the ICU, the number of antibiotic administrated and the restrictive strategy period were independently associated with a lower rate of ESBL-E acquisition.

Conclusions: In a large cohort of ICU patients, a stewardship program including a restrictive antibiotic strategy showed effective in terms of reduction of antibiotic consumption, especially broad-spectrum antibiotics and antibiotics targeting anaerobic microbiota. This strategy was associated with a lower rate of ESBL-E acquisition without worsening patient’s outcomes.

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Genome-based analyses of *Klebsiella pneumoniae* to detect possible host-associations, host-adaptation and effects on virulence

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**Background:** The increase of “classical” drug-susceptible *K. pneumoniae* (cKP) with extended-spectrum-β-lactamase production (ESBL-cKP) poses a serious threat to health care. In the last 10 years a new “hypervirulent” but mainly drug-susceptible pathotype of *K. pneumoniae* (hvKP) emerged, associated with community acquired infections. Nowadays, there are more and more reports on antibiotic-resistant hvKP, affecting treatment options in ambulatory care and causing nosocomial outbreaks. Traditionally, hvKP have been defined as invasive strains of capsular serotypes K1 and K2 that are string test and rmpA/A2 positive. However, a consensus definition is still missing. Furthermore, there is less knowledge on how and why hvKP colonizes and transits to infection. We investigated genetic characteristics associated with host colonisation or invasion, in order to better understand the pathogenicity of hvKP strains.

**Materials/methods:** A collection of *K. pneumoniae* isolates from German hospitals, including susceptible cKP, ESBL-cKP and hvKP isolates were subjected to whole genome sequencing (WGS). Growth experiments and antibiotic susceptibility assays were performed and cell morphology was assessed microscopically. To analyse macrophage-mediated phagocytosis, RAW264.7 cells were infected with *K. pneumoniae* isolates and intracellular bacteria were quantified. Furthermore, the impact of hypoxia on hvKP pathogenesis was analysed.

**Results:** The majority of K1 isolates belonged to the clonal complex CC23, whereas non-K1 isolates were clonally diverse. ESBL and carbapenemases genes were present regardless of the *K. pneumoniae* multilocus sequence type and several multidrug-resistant hvKP were detected. Interestingly, microscopic analysis of cell length distribution of hvKP cultures revealed filamentous bacteria cells, whereas cKP and ESBL-cKP cultures display heterogeneous rode shaped cells. The elongation into filaments was even more pronounced under hypoxia conditions. In *vitro* phagocytosis assays revealed a lower phagocytosis rate for hvKP than for cKP and ESBL-cKP that is not altered by hypoxia.

**Conclusions:** Our analyses revealed the emergence of ESBL and carbapenemases-producing hvKP isolates in German hospitals. Furthermore, the occurrence filamentous morphotypes in hvKP cultures indicates that filamentation of hvKP bacteria cells provides a survival advantage when hvKP encounter host immune response and phagocytosis.

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Abstract 2697

**Genomic adaptation of *Staphylococcus aureus* in a diabetic foot environment**

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**Background:** *Staphylococcus aureus* is the most prevalent pathogen isolated in diabetic foot ulcers (DFU). Few publications have studied the virulence and the adaptation of this pathogen in this chronic wound conditions. The purpose of this study was to evaluate the adaptation of *S. aureus* in an *in vitro* model miming the conditions encountered in DFU.

**Materials/methods:** The *in vitro* experiments consisted to cultivate during 16 weeks four clinical *S. aureus* strains (three with infecting profiles: PVL - Edin-, PVL+ Edin-, PVL+ Edin+; and one with a colonizing profile) by successive inoculations in a specific environment based on the Lubbock biofilm model (composed by Bolton broth, human plasma, human hemolyzed blood, epithelial cells with a fixed basic pH). Before and after exposition in the medium, the four isolates were evaluated: 1) phenotypically; 2) by qRT-PCRs (to evaluate expressions of the main virulence (e.g., lukFS-PV, edinB, edinC, hla, spa, eap, fnbAB, cna) and the global regulator (agr) genes); 3) by crystal violet (to assess the biofilm formation); 4) by *Caenorhabditis elegans* model (to evaluate their virulence); and 5) by whole-genome sequencing (WGS) (to detect potential modifications of genomes).

**Results:** After 16 weeks, we observed the development of small colony variants (SCVs) and the loss of beta-hemolysin production in the 4 studied strains. qRT-PCRs showed a significant decrease of expression of the main virulence genes tested (*lukFS-PV, edinB, edinC, hla, spa*) but the increase of genes involved in adhesion and biofilm (*eap, fnb, icaA, agr*). Crystal violet confirmed the increase of biofilm formation of the isolates after exposition and a decrease of virulence was also noted (LT50: 4.2 days ±0.5 before vs 6.7 ±0.3 after exposition). WGS demonstrated a reduction (~2 Kb) of the genome of the 4 isolates after exposition and same mutations in virulence and metabolisms encoding genes (*splB, splF, sarD*) that could explain the adaptation of the bacteria.

**Conclusions:** Our *in vitro* model confirms the impact of environment on the adaptation of *S. aureus* to prolonged stress environmental conditions. These results contribute to a best comprehension of the role of *S. aureus* to limit its virulence in the chronic wounds.

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Abstract 2698

Impact of a national antimicrobial stewardship programme to switch from trimethoprim to nitrofurantoin for treatment of urinary tract infections on the incidence of Escherichia coli bloodstream infection in England, 2015–2019

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Background: Escherichia coli is the commonest cause of urinary tract infections (UTI) in England. Unsuccessful treatment of UTI may allow progression to an invasive bloodstream infection (BSI).

An increase in trimethoprim resistance detected in E. coli UTI informed the recommendation to use nitrofurantoin as first-line treatment for uncomplicated UTI in national guidelines. To encourage behavioural change consistent with this recommendation, a national antimicrobial stewardship program, Quality Premium (QP), was introduced in 2017/18 to measure trimethoprim-to-nitrofurantoin prescribing from April 2017 and trimethoprim prescribing in patients over the age of 70 years from April 2018. The QP was associated with a financial incentive for primary care coordinating bodies for meeting targets.

The aim of the study was to investigate the impact of the QP on the incidence of E. coli community-onset BSI (COBSI) and trimethoprim-resistant COBSI.

Materials/methods: The ratio of trimethoprim-to-nitrofurantoin items prescribed was calculated from dispensed public prescriptions [via National Health Service Business Services Authority].

E. coli COBSI were defined as infection episodes occurring within 48 hours of admission to a hospital in England. Data were extracted from the national mandatory surveillance system and linked to blood culture susceptibility data where available.

Interrupted time-series analysis was performed, adjusting for secular trend. The pre-intervention and post-intervention periods were defined as April 2015 to March 2017 and April 2017 to March 2019, respectively. Mean number of cases per month and associated confidence intervals (CI) were estimated using linear regression.

Results: The mean trimethoprim-to-nitrofurantoin ratio pre-intervention was 1.4, and reduced to 0.6 post-intervention. The observed number of E. coli COBSI increased by 9.0%, but the number of trimethoprim-resistant E. coli COBSI decreased by 30.1% pre- and post-intervention.

After adjustments, there were average reductions of 130 cases of E. coli COBSI (95% CI: reduction of 38 to 221, p=0.007) and 109 fewer cases of trimethoprim-resistant COBSI (95% CI: reduction of 74 to 144, p<0.001) per month.

Conclusions: The results demonstrate that the implementation of the national antimicrobial stewardship program was associated with decreased trimethoprim prescribing and increased nitrofurantoin prescribing in England. This was associated with a significant decrease in trimethoprim-resistant E. coli COBSI.

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Abstract 2700

Study of the in vitro activity of cefiderocol in comparison to other antimicrobial agents against a collection of Acinetobacter baumannii clinical isolates from different geographical locations

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**Background:** Cefiderocol, a catechol-substituted siderophore cephalosporin currently in late stage clinical development, combines rapid penetration into the periplasmic space via iron transport and increased stability to hydrolysis by all β-lactamase Ambler classes. This study provides additional data on the in vitro antimicrobial activity of cefiderocol and that of commercially available antibiotics against a defined collection of clinical multidrug and carbapenem-resistant Acinetobacter baumannii isolates.

**Materials/methods:** Antimicrobial susceptibility was tested using pre-prepared frozen 96-well microtiter plates containing twofold serial dilutions of: cefepime, ceftazidime-avibactam, imipenem-relebactam, ampicillin-sulbactam, meropenem, meropenem-vaborbactam, ciprofloxacin, minocycline, tigecycline, trimethoprim-sulfamethoxazole and colistin using standard broth microdilution procedure in cation-adjusted Mueller-Hinton broth (CAMHB). For cefiderocol iron-depleted CAMHB was used and prepared following CLSI-approved methodology. A collection of 114 clinical strains of A. baumannii from Argentina, Azerbaijan, Croatia, Greece, Italy, Morocco, Mozambique, Peru and Spain were selected.

**Results:** Minimum inhibitory concentration (MIC, mg/L) for cefiderocol and comparators against Acinetobacter baumannii are represented in this table:

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>Susceptible n=</th>
<th>Intermediate n=</th>
<th>Resistant n=</th>
<th>MIC(_{50})</th>
<th>MIC(_{90})</th>
<th>Range MIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefiderocol</td>
<td>90 (78,95%)</td>
<td>1 (0,88%)</td>
<td>23 (20,17%)</td>
<td>0,5</td>
<td>&gt;64</td>
<td>≤0,03 to &gt;64</td>
</tr>
<tr>
<td>Cefepime</td>
<td>16 (14%)</td>
<td>4 (3,5%)</td>
<td>94 (82,5%)</td>
<td>&gt;16</td>
<td>&gt;16</td>
<td>≤0,125 to &gt;16</td>
</tr>
<tr>
<td>Ceftazidime-avibactam</td>
<td>16 (14%)</td>
<td>4 (3,5%)</td>
<td>94 (82,5%)</td>
<td>&gt;16</td>
<td>&gt;16</td>
<td>≤0,125 to &gt;16</td>
</tr>
<tr>
<td>Ampicillin-sulbactam</td>
<td>25 (21,93%)</td>
<td>20 (17,54%)</td>
<td>69 (60,53%)</td>
<td>32</td>
<td>64</td>
<td>≤2 to &gt;64</td>
</tr>
<tr>
<td>Imipenem-relebactam</td>
<td>2 (1,75%)</td>
<td>2 (1,75%)</td>
<td>89 (78,07%)</td>
<td>&gt;16</td>
<td>&gt;16</td>
<td>0,125 to &gt;16</td>
</tr>
<tr>
<td>Meropenem</td>
<td>23 (20,17%)</td>
<td>2 (1,75%)</td>
<td>89 (78,07%)</td>
<td>&gt;16</td>
<td>&gt;16</td>
<td>0,125 to &gt;16</td>
</tr>
<tr>
<td>Meropenem-vaborbactam</td>
<td>23 (20,17%)</td>
<td>20 (17,54%)</td>
<td>67 (50,78%)</td>
<td>4</td>
<td>&gt;8</td>
<td>≤0,25 to &gt;8</td>
</tr>
<tr>
<td>Minocycline</td>
<td>67 (50,78%)</td>
<td>20 (17,54%)</td>
<td>27 (23,68%)</td>
<td>2</td>
<td>4</td>
<td>≤0,125 to &gt;4</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>100 (87,72%)</td>
<td>14 (12,28%)</td>
<td>14 (12,28%)</td>
<td>0,5</td>
<td>8</td>
<td>≤0,25 to &gt;8</td>
</tr>
</tbody>
</table>

\*MIC\(_{50}\) and MIC\(_{90}\): MIC to inhibit growth of 50% and 90% of isolates, respectively.

Not included: ciprofloxacin and trimethoprim-sulfamethoxazole = MIC\(_{50}\) and MIC\(_{90}\) >8.

Available CLSI breakpoints were applied to determine categories (susceptible, intermediate and resistant).
Conclusions: Almost 80% of isolates showed susceptibility to cefiderocol suggesting it as a good alternative to treat infections caused by *A. baumannii*, including carbapenem-resistant strains, as 76% of meropenem-resistant isolates were susceptible to the new drug.

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Concordance of early and late endpoints for community-acquired bacterial pneumonia (CABP) trials

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Background: While there are ongoing efforts to align regulatory requirements for antibacterial drug development, differences in recommendations for CABP trial endpoints remain. The US Food and Drug Administration recommends an early clinical endpoint (3-5 days), when historical data suggests the difference between treated and untreated subjects is greatest. The European Medicines Agency recommends assessment of overall clinical response at a test-of-cure visit after the end of therapy.

Materials/methods: We analyzed subject-level data from six recent CABP trials submitted to the FDA [n=4,645 subjects] to compare concordance between clinical outcomes at the early and late endpoints and to evaluate reasons for discordance.

Results: Clinical outcomes from early and late endpoints were concordant for 85.5% of subjects. The fraction of early responders that ultimately failed was similar to the fraction of early non-responders that ultimately succeeded (6.0% vs 8.5%, respectively). The early endpoint had a high positive predictive value (92.9%) of success at the late endpoint, with a negative predictive value of 46.2%. Multivariate logistic regression modeling found early endpoint responders/late endpoint failures were more likely to be obese, be infected with Chlamyphila pneumoniae or Staphylococcus aureus, have received antibacterial drug therapy prior to randomization, and have severe chest pain at baseline, while less likely to be North American or have sputum production at baseline. Worsening chest pain was highly associated with failure among early endpoint responders (adjusted odds ratio 22.1). Reasons for failure differed among early responders and non-responders: early responders were more likely to fail later due to non-study antibacterial drug therapy or loss to follow-up, while early non-responders had higher odds of failure due to death or discontinuation after an adverse event.

Conclusions: Overall, clinical outcomes at early and late endpoints were highly concordant. Factors associated with failure among subjects exhibiting early improvement were identified. These data will help in the continuing efforts to align CABP clinical trial requirements to better support global antibacterial drug development.

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Activity of imipenem/relebactam against non-Morganellaceae Enterobacterales and *Pseudomonas aeruginosa* isolates from 6 countries in western Europe: SMART 2016-2018

Nimmi Kothari¹, Stephen Hawser*¹, Sibylle Lob², Krystyna Kazmierczak³, Marcela González-Del Vecchio⁴, Katherine Young⁵, Mary Motyl⁴, Fakhar Siddiqui⁴, Dan Sahm⁶

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**Background:** Relebactam (REL) is an inhibitor of class A and C β-lactamas, including KPC, that was approved in the US in combination with imipenem (IMI) for treatment of complicated intraabdominal and urinary infections. We evaluated the activity of IMI/REL against non-Morganellaceae Enterobacterales (NME) and *Pseudomonas aeruginosa* (Psa) isolates collected in France, Germany, Italy, Portugal, Spain and the United Kingdom for the global SMART surveillance program.

**Materials/methods:** In 2016-2018, 36 hospitals in the indicated countries collected up to 250 consecutive gram-negative pathogens each year from various infection sources. For this analysis, only bloodstream (BSI) and respiratory tract infections (RTI) were studied. MICs were determined using CLSI broth microdilution and interpreted with EUCAST breakpoints. US FDA breakpoints were applied to IMI/REL. Multidrug-resistance (MDR) was defined as nonsusceptibility (intermediate or resistant MIC using CLSI breakpoints) to ≥3 sentinel drugs: amikacin, aztreonam, cefepime, ceftazidime (NME only), ciprofloxacin, colistin, imipenem, and piperacillin-tazobactam. Isolates testing with IMI MIC ≥2 mg/L (NME) or ≥4 mg/L (Psa) were screened for β-lactamase genes.

**Results:** Because REL is not active against class B metallo-β-lactamas (MBLs), MBL-positive isolates were removed from susceptibility analyses. These isolates made up 0.3% (3/1024) and 0.4% (19/4417) of NME and 3.6% (4/111) and 1.5% (31/2004) of Psa isolates from BSI and RTI, respectively. KPC-positive isolates were detected in 2.1% of BSI and RTI isolates, ranging from 0% of isolates collected in France and Germany to 11.1% in Italy. The in vitro susceptibility to IMI/REL and comparators of MBL-negative NME, MBL-negative Psa, and resistant subsets are shown for isolates collected from patients with BSI and RTI (Table).

<table>
<thead>
<tr>
<th>Source/Phenotype</th>
<th>IMI/REL</th>
<th>IMI</th>
<th>FEP</th>
<th>CAZ</th>
<th>TAZ</th>
<th>AMK</th>
<th>CST</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BSI (2018)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All MBL- NME</td>
<td>98.0</td>
<td>96.7</td>
<td>83.4</td>
<td>79.8</td>
<td>84.8</td>
<td>98.2</td>
<td>94.4</td>
</tr>
<tr>
<td>KPC+ MBL-NME</td>
<td>60.9</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
<td>59.1</td>
<td>77.3</td>
</tr>
<tr>
<td>All MBL- <em>Psa</em></td>
<td>96.3</td>
<td>81.3</td>
<td>87.9</td>
<td>79.4</td>
<td>81.3</td>
<td>94.4</td>
<td>100</td>
</tr>
<tr>
<td>IMI-R MBL- <em>Psa</em></td>
<td>80.0</td>
<td>0.0</td>
<td>60.0</td>
<td>40.0</td>
<td>40.0</td>
<td>80.0</td>
<td>100</td>
</tr>
<tr>
<td>MDR MBL- <em>Psa</em></td>
<td>85.7</td>
<td>33.3</td>
<td>38.1</td>
<td>9.5</td>
<td>9.5</td>
<td>85.7</td>
<td>100</td>
</tr>
<tr>
<td><strong>RTI (2016-2018)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All MBL- NME</td>
<td>96.8</td>
<td>96.7</td>
<td>83.3</td>
<td>76.1</td>
<td>77.6</td>
<td>97.7</td>
<td>85.8</td>
</tr>
<tr>
<td>KPC+ MBL-NME</td>
<td>98.9</td>
<td>3.2</td>
<td>0.0</td>
<td>0.0</td>
<td>1.1</td>
<td>46.2</td>
<td>69.9</td>
</tr>
<tr>
<td>All MBL- <em>Psa</em></td>
<td>92.7</td>
<td>72.3</td>
<td>75.7</td>
<td>75.2</td>
<td>88.4</td>
<td>87.7</td>
<td>98.9</td>
</tr>
<tr>
<td>IMI-R MBL- <em>Psa</em></td>
<td>74.0</td>
<td>0.0</td>
<td>45.4</td>
<td>41.0</td>
<td>32.8</td>
<td>67.9</td>
<td>97.3</td>
</tr>
<tr>
<td>MDR MBL- <em>Psa</em></td>
<td>76.9</td>
<td>51.9</td>
<td>21.9</td>
<td>21.2</td>
<td>8.1</td>
<td>67.9</td>
<td>95.6</td>
</tr>
</tbody>
</table>

*US FDA breakpoints for IMI/REL: ≤1/4 mg/L, susceptible; 2/4 mg/L, intermediate; ≥24/4 mg/L, resistant (Enterobacteriales); ≤2/4 mg/L, susceptible; 4/4 mg/L, intermediate; ≥28/4 mg/L, resistant (Psa). EUCAST breakpoints for IMI/REL are currently under discussion.

**Conclusions:** IMI/REL was active against >96% of MBL-negative NME and >92% of MBL-negative *Psa*. Among KPC+ NME, susceptibility to IMI increased from ≤5% to >90% upon addition of REL, and among IMI-resistant *Psa* from 0% to ≥74%. For all MBL-negative NME and *Psa*, IMI/REL activity was exceeded only by amikacin or colistin; for KPC+ NME, IMI/REL showed the highest activity.

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Abstract 2707

Biofilm formation of methicillin-resistant Staphylococcus aureus: does it vary with the type of infection?
Vanessa Silva*1, Luciana Almeida2, Sara Hermenegildo1, Nuno Cerca2, Jose Luis Capelo1, Gilberto Igrejas1, Patricia Poeta1

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Background: Methicillin-resistant S. aureus (MRSA) has been recognized as a major health problem, in particular in hospital settings. MRSA infections are often associated with the emergence of biofilms and the risk of developing chronic infections. The biofilm phenotype has been identified in up to 80% of all non-acute infections and one of their most critical features is their considerably higher resistance to environmental stress, antimicrobials, disinfectants and host immune defenses. Therefore, we aimed to characterize MRSA strains recovered from different types of human infections and to evaluate their ability to form biofilm.

Materials/methods: Eighty-three MRSA strains were recovered from bacteremia episodes (n=13), osteomyelitis (n=42) and diabetic foot ulcers (n=28). The antimicrobial susceptibility testing was performed against 14 antimicrobial agents and according to EUCAST (2018) criteria. The capacity of biofilm formation of these strains was evaluated by the microtiter dish biofilm formation assay and, according to their level of biomass, they were classified as low, moderate or high biofilm-formers.

Results: Most of the strains were classified as multidrug resistant since they were resistance to 3 or more classes of antibiotics. The isolates were categorized as low, moderate or high biofilm-formers according to the cut-off values of ≤0.6, 0.6 to 1, and >1, respectively. Strains recovered from osteomyelitis had the higher biofilm forming ability. The majority of the strains (51.8%) were classified as moderate formers, followed by low (27.7%) and high biofilm-formers (22.9%).

Conclusions: Moderate biofilm formation was observed among MRSA strains recovered from different human infections which is alarming since biofilm formation is an important cause of treatment failure. The high prevalence of high biofilm-former strains implicated in osteomyelitis is a concern since surgical interventions are the most efficient way to treat biofilm-associated infections in bone.

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Detection of Enterobacterales and associated antimicrobial resistance genes with the BIOFIRE FILMARAY Blood Culture Identification 2 (BCID2) panel

Jeremiah Antosch*1, David Judd1, Jessica Stone1, Kerrin Koch1, Tanner Robinson1, Iryna Kavetska1, Briana Flaherty1, Maggie Buccambuso1, Kristen Holmberg1, Yang Lu1, Margarita Rogatcheva1, Usha Spaulding1

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Background: Enterobacterales are a common cause of bloodstream infections (BSI), and the dissemination of extended-spectrum beta-lactamases (primarily CTX-M) and important carbapenemases (IMP, KPC, NDM, OXA-48, and VIM) among the Enterobacterales is associated with increased morbidity and mortality. The BioFire® FilmArray® Blood Culture Identification 2 (BCID2) Panel builds upon the existing BioFire® FilmArray® Blood Culture (BCID) Panel by addition/modification of assays for the rapid detection of bacteria, yeast, and select antimicrobial resistance (AMR) genes in positive blood culture (PBC). This study evaluated the expanded coverage of the updated assays for Enterobacterales (7 species-level and 2 pan-reactive) and 6 associated AMR genes.

Materials/methods: Reactivity and specificity of these assays were evaluated using in silico sequence data and pure-culture isolates. Concordance with reference methods was examined for 1,074 residual PBC samples collected from US and European clinical laboratories, with pathogen detections compared to routine culture and AMR gene detections compared to routine antimicrobial susceptibility testing (AST) in conjunction with molecular assays.

Results: The in silico assessment indicated reactivity with 207 species, representing 46 genera from 7 families of Enterobacterales as well as nearly all known alleles of AMR genes. Analytical testing confirmed reactivity with 108/108 available species, representing 31 genera from 5 families, as well as the detection of CTX-M (16 types, 12 hosts), IMP (6 types, 3 hosts) KPC (7 types, 9 hosts), NDM (4 types, 4 hosts), OXA-48 (5 types, 4 hosts), and VIM (3 types, 3 hosts) genes. Prospective testing detected 27 species of Enterobacterales in 269/1,074 PBC, with associated detections of CTX-M (46, 3 hosts), KPC (4, 1 host), NDM (1, 1 host), and VIM (4, 2 hosts) genes and demonstrated excellent concordance with reference methods. 2/2 false positive results were resolved with sequencing, and 1/1 false negative result is currently under investigation. No cross-reactivity was observed in analytical or prospective testing.

Conclusions: The BioFire BCID2 Panel will detect a wide variety of clinically relevant Enterobacterales, indicate the carriage of select AMR gene(s) when present, and is expected to aid timely and effective antimicrobial therapy.

Data presented are from assays that have not been cleared or approved for diagnostic use.

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ART24, a novel live biotherapeutic product, in development for the prevention of Clostridioides difficile infection is active against a broad range of C. difficile ribotypes in vitro

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Background: ART24 is being investigated as a live biotherapeutic product (LBP) treatment to prevent recurrence of Clostridioides difficile infection (CDI) following successful antibacterial therapy. ART24 was isolated from a human fecal sample, identified, and purified. ART24 is a member of the B. amyloliquefaciens/B. velezensis group. ART24 was found from a screening effort aimed at identifying bacteria from stool samples with direct C. difficile killing activity. The data presented here sought to investigate the broad range of activity against contemporary clinical isolates of various ribotypes.

Materials/methods: The ART24 strain was assayed for anti-C. difficile activity against a panel of 42 contemporary C. difficile isolates (25 distinct ribotypes) using an agar well diffusion method. Cell-free supernatants from fresh cultures and isopropanol extracts from lyophilized cells were tested for direct C. difficile growth inhibition. To further characterize ART24 and its anti-C. difficile activity, the effect of 20mg/ml proteinase K and gastrointestinal enzymes (chymotrypsin, trypsin) was investigated using cell-free supernatants. C. difficile agar plates were incubated in the anaerobic chamber overnight (18-24 hours) and analyzed for the presence of zones of clearing and measurement of the zones around the application of ART24 samples.

Results: Cell-free pH-neutralized supernatants from freshly grown ART24 as well as isopropanol extracts from resuspended lyophilized ART24 inhibited all 25 ribotypes of C. difficile tested. There was no difference in the zone size/activity of pH-neutralized supernatants from freshly grown ART24 and the IPA extracts from reconstituted lyophilized ART24 capsule content.

The antimicrobial activity from cell-free pH-neutralized supernatants from freshly grown ART24 was found to be resistant to the high level of gastrointestinal enzymes tested. The levels used were 20x greater than the average normal used [1mg/ml] for testing bacteriocins. Specific re-testing with proteinase K using dilutions of ART24 cell-free supernatant also showed resistance suggesting that the anti-C. difficile activity is not related to peptides.

Conclusions: In conclusion, ART24 exhibits protease-resistant anti-C. difficile activity against a broad range of contemporary C. difficile isolates including clinically relevant isolates of various and clinically relevant ribotypes. ART24 is a promising LBP candidate in Phase 1 clinical development for the prevention of CDI recurrence.

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In vitro activity of ceftolozane-tazobactam against Enterobacterales and Pseudomonas aeruginosa from patients with bloodstream infections in the Asia/Pacific region: SMART 2018

Sibylle Lob1, Krystyna Kazmierczak4*, Wei-Ting Chen2, Tsz Kin Khan3, Katherine Young4, Mary Motyl4, Dan Sahm1

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Background: Ceftolozane/tazobactam (C/T) is an antipseudomonal cephalosporin combined with a β-lactamase inhibitor. C/T has been approved by the FDA and EMA for complicated urinary tract infections, complicated intraabdominal infections, and hospital-acquired and ventilator-associated bacterial pneumonia. Using isolates collected in Asia/Pacific as part of the global SMART surveillance program, we evaluated the activity of C/T and comparators against Enterobacterales and P. aeruginosa (PA) from patients with bloodstream infections (BSI).

Materials/methods: In 2018, 42 clinical laboratories in Australia, Hong Kong, India, South Korea, Malaysia, New Zealand, Philippines, Taiwan, Thailand, and Vietnam each collected up to 50 consecutive aerobic or facultative gram-negative pathogens from BSI for a total of 1898 isolates. MICs were determined using CLSI broth microdilution and interpreted with EUCAST breakpoints. Isolates testing with C/T MIC ≥4 mg/L [Enterobacterales] or ≥8 mg/L [PA] (excluding all isolates from India and Enterobacterales from one site in Taiwan) were screened by PCR and sequencing for genes encoding β-lactamases.

Results: The 5 most common species collected were E. coli (n=880, 46.4%), K. pneumoniae (n=397, 20.9%), P. aeruginosa (n=127, 6.7%), A. baumannii (n=99, 5.2%), and E. cloacae (n=53, 2.8%). The activity of C/T and comparators against Enterobacterales and PA is shown in the table.

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>Enterobacterales (n=1571)</th>
<th>P. aeruginosa (n=127)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ceftolozane/tazobactam</td>
<td>87.6</td>
<td>89.8</td>
</tr>
<tr>
<td>Piperacillin/tazobactam</td>
<td>81.2</td>
<td>73.2</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>69.8</td>
<td>82.7</td>
</tr>
<tr>
<td>Ceftiraxone</td>
<td>64.7</td>
<td>78.0</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>64.5</td>
<td>N/A</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>94.0</td>
<td>N/A</td>
</tr>
<tr>
<td>Meropenem</td>
<td>96.1</td>
<td>78.0</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>55.2</td>
<td>75.6</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>60.9</td>
<td>74.8</td>
</tr>
<tr>
<td>Amikacin</td>
<td>95.0</td>
<td>88.2</td>
</tr>
<tr>
<td>Colistin</td>
<td>92.0</td>
<td>100</td>
</tr>
</tbody>
</table>

Among 121 molecularly characterized Enterobacterales isolates with C/T MIC ≥4 mg/L, 24.0% carried metallo-β-lactamases (MBL), 4.1% carried OXA-48-like carbapenemases, 1.7% carried KPC, and 52.9% carried only extended-spectrum β-lactamases (ESBL) and/or acquired AmpC. No acquired β-lactamases were detected in 17.4% of characterized isolates, of which 85.7% were species with intrinsic AmpC. Among 10 molecularly characterized C/T-resistant PA, 9 characterized MBL and in one no acquired β-lactamases were detected.

Conclusions: In Asia/Pacific, C/T was active against >87% of Enterobacterales from BSI (activity only exceeded by carbapenems, amikacin, and colistin) and against 99% of PA isolates [activity only exceeded by colistin]. C/T could provide an important treatment option for patients with BSI in the Asia/Pacific region.

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Abstract 2714

Crimean–Congo haemorrhagic fever in pregnancy: a systematic review and meta-analysis of clinical presentation and maternal and foetal outcomes

Nzelle Kayem*, Christina Aye‡, Charlotte Benson‡, Sarah Baker‡, Mariana Tome‡, Stephen Kennedy‡, Proochista Ariana*, Peter Horby‡

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Background: Crimean–Congo haemorrhagic fever (CCHF) is an arboviral infection with an extensive geographic distribution. It is known to cause severe and often fatal infection in man. While there are several reviews narratively summarizing evidence on CCHF in pregnancy, the evidence is often aggregated, failing to account for differences in sample sizes. Here, we critically appraise and synthesize evidence on the effects of CCHF in pregnancy.

Materials/methods: A search of clinical trial registries and bibliographic databases from their respective dates of inception to September 30, 2019, was conducted using a combination of MeSH terms and keywords. There were no language restrictions. Individual patient data were extracted to generate proportions and statistical analyses using the Freeman-Tuckey double arc-sine transformation were conducted in R.

Results: Our comprehensive review yielded 20 studies, which reported 48 pregnant women with CCHF. All of the studies were descriptive and most of these studies were methodologically robust with an overall fair or good quality rating. Key clinical features for CCHF in pregnancy were fever 98·0% (95% CI 82·2 – 100·0%, I²=0%, P=0.4) and vaginal bleeding 25·0% (95%CI 5·9-49·5%, I²=3%, P=0.36). These estimates were precise with no evidence of between-study heterogeneity. The absolute risk of foetal loss due to maternal CCHF was estimated at 47·03% (95% CI= 22·80 to 71·88%, I²= 3·81%, P=0·35, see figure) and maternal death was 16·75% (95% CI 2·00 to 44·36%, I²=30·05%, P=0·239). However, only three studies were included in the proportional meta-analysis with very small sample sizes ranging from five to eight pregnant women and the estimates are imprecise due to the wide confidence intervals.

Conclusions: While this evidence suggests that CCHF in pregnancy is characterized by vaginal bleeding and is associated with high rates of maternal and foetal death, the data is completely descriptive. Additionally, the estimates are unreliable due to the small sample sizes and may be further confounded by the inclusion of more severe cases; underscoring the need for large prospective studies to obtain a more precise estimate on the burden of CCHF in pregnancy.

PROSPERO protocol number CRD42018097022

Figure: Proportional meta-analysis forest plot for foetal loss from maternal CCHF

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Evaluation of omadacycline alone and in combination with rifampin against biofilm-producing Staphylococcus aureus and Staphylococcus epidermidis

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Background: Indwelling medical devices with associated infections represent a substantial cause of morbidity. Two common pathogens associated with these infections include Staphylococcus aureus and Staphylococcus epidermidis (common biofilm-producing bacteria). Owing to treatment failures with biofilm-associated infections, novel therapeutic approaches are urgently needed. Omadacycline (OMC), an aminomethylcycline, is highly active against S. aureus and S. epidermidis. However, there is little information on OMC activity against common biofilm-producing organisms associated with infections of implants. The objective of this study was to evaluate OMC alone and in combination with rifampin (RIF) against biofilm-producing strains of S. aureus and S. epidermidis.

Materials/methods: Eight randomly selected strains of S. aureus (five strains, three MRSA) and S. epidermidis (three strains) with variations in susceptibility to OMC and RIF were evaluated. Synergy was assessed by evaluating fold-reduction change in OMC minimum inhibitory concentration (MIC) with combination MIC and combination biofilm MIC (bMIC) testing for all strains in the presence of 0.5x MIC of RIF and 24-hour biofilm time-kill analyses (TKA) for one strain of S. aureus (N315) and S. epidermidis (NRS101) at 0.5x and 1x bMIC. In TKAs, synergy (≥ 2-log10 CFU/mL kill compared to the most effective agent alone at 24 hours) and bactericidal activity (≥ 3-log10 CFU/mL reduction at 24 hours compared to the starting inoculum) were evaluated.

Results: OMC demonstrated potent activity with low MICs against the evaluated strains (0.125-0.5 mg/L), with a slight increase of MICs in the presence of biofilm (0.25-2 mg/L). In the planktonic state, RIF reduced OMC MICs in 60% of S. aureus strains (1- to 2-fold) and 33% of S. epidermidis strains (1-fold), while RIF reduced OMC bMICs in 100% of S. aureus strains (2- to 3-fold). RIF did not impact OMC bMICs for the evaluated S. epidermidis strains. However, at 0.5x and 1x bMIC, synergy (>2.3 log10 CFU/mL reduction compared to RIF) and bactericidal activity (>4 log10 CFU/mL reduction), respectively, were observed against NRS101 with OMC and RIF combination. Furthermore, synergy was demonstrated at 1x bMIC against N315.

Conclusions: Based on these results, further research is needed to evaluate the combination of OMC and RIF for biofilm-associated infections.

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Abstract 2716

**Antibiotic prescription practices in primary care in low- and middle-income countries: a systematic review and meta-analysis**

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**Background:** Despite the well-known role of antibiotics in the development of antimicrobial resistance, important knowledge gaps still exist regarding the extent of their use in low- and middle-income countries (LMICs), particularly at the community level.

**Materials/methods:** We performed a systematic review and meta-analysis to evaluate the proportion of patients receiving antibiotics in outpatient primary care across LMICs. PubMed, Embase, Global Health and the Cochrane Library were searched for relevant publications from Jan 1, 2010 to Apr 4, 2019. Cross-sectional studies conducted in LMICs reporting data on medicine use in primary care were eligible. We used random-effects meta-analysis with Freeman-Tukey transformation to calculate pooled prevalence estimates of antibiotic prescribing and conducted several subgroup analyses. To evaluate between-study heterogeneity we calculated the I² statistic, generated prediction intervals and used random-effects meta-regression. The WHO AWaRe [Access–Watch–Reserve] framework was adopted to classify antibiotics according to their potential for selecting resistance. An existing risk-of-bias assessment tool for prevalence studies was adapted for use in our review.

**Results:** We included 41 studies conducted across 22 LMICs that reported the proportion of drug prescriptions containing antibiotics or the number of patients receiving antibiotics [the latter resulted comparable to the former as all patients received a drug prescription]. Most studies were performed in the public sector and in urban areas, and 83% used records abstraction to capture prescription details. The pooled prevalence proportion of antibiotic prescription was 51% [95% CI: 50-52], with a prediction interval ranging from 44 to 58%. Estimates were consistent across studies, and – in studies including all-comers in outpatient care - almost always exceeded the WHO recommended threshold of 30% antibiotic usage. Fourteen studies provided details on individual antibiotics: Access-group antibiotics usually represented >60% of the total, and Watch-group antibiotics [i.e. with high resistance potential] were extensively employed in Mexico [90.3%], China [78.4%] and Pakistan [47.8%].

**Conclusions:** Antibiotics are largely prescribed in outpatient primary care across LMICs. Although we would benefit from better quality data on inappropriate antibiotic use, urgent action is needed to improve prescription practices, starting from the integration of the WHO treatment recommendations and the AWaRe classification into national guidelines.

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Abstract 2717

**Diversity of methicillin-resistant staphylococci among wild Iberian hares: detection of mecA-methicillin-resistant staphylococci strains**

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**Background:** Information on the incidence of MRSA in the environment and, in particular, in wild animals, is scarce. The presence of MRSA strains in wild animals, including game species, may represent a serious threat to human and animal health. The Iberian hare is one of the most emblematic game species of Portugal and equally important in an ecological context, as they also feed various species of animal predators. In this study, we investigated the prevalence of methicillin-resistant staphylococci (MRS) in wild hares (*Lepus granatensis*), focusing particularly on MRSA strains.

**Materials/methods:** Samples from 83 wild hares were collected during the hunting season from September to December 2018. Isolation of MRS was accomplish using ORSAB medium with 2mg/L of oxacillin. The susceptibility of the isolates was tested against 14 antimicrobial agents. The presence of resistance and virulence genes was studied by PCR. *S. aureus* strains were further characterized by MLST, *agr*, *spa* and SCCmec typing.

**Results:** From the 83 wild hares analyzed, 15 MRS were isolated. More than half of the staphylococci species were identified as *S. sciuri* (*n*=8), followed by *S. aureus* (MRSA) (*n*=3), *S. vitulinus* (*n*=2), *S. lentus* (*n*=1) and *S. cohnii* subsp. *urealyticus* (*n*=1). All strains harbored the *mecA* gene responsible for the methicillin resistance. MRS isolates were coagulase negative and showed low levels of resistance. Three MRSA isolates were found, one of which had a multidrug resistance profile with resistances to β-lactams, aminoglycosides, macrolides and lincosamides. All MRSA strains were ascribed to ST2855, t1190 and SCCmec type III.

**Conclusions:** Although MRSA carriage rate was relatively low (3.6%), this frequency may be considered relevant since Iberian hares are wild free-living animals which are not treated with antibiotics and are on the bottom of the food-chain. Therefore, MRSA carriage by these animals may be explained by the uptake of these strains or resistance determinants from the natural environment. The potential of MRSA strains to survive in different ecological niches and colonize different hosts, in particular wild animals and game species, is considered an important emerging threat and ongoing MRSA surveillance in wildlife is becoming essential.

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Resolution of discrepant results observed during the clinical evaluation of investigational use only prototype of the BIOFIRE FILMARRAY Blood Culture Identification 2 (BCID2) panel

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Abstract third-party references: BioFire Diagnostics, LLC

Background: The BioFire® FilmArray® Blood Culture Identification 2 Panel is a rapid diagnostic test that provides results for 7 fungal and 26 bacterial bloodstream pathogens as well as 10 bacteria-associated antimicrobial resistance (AMR) genes from positive blood culture (PBC) samples. A multi-center prospective clinical evaluation using an investigational-use-only (IUO) version of the Panel yielded an overall sensitivity of 99.2% and specificity of 99.6% for pathogen identification. All BCID2 Panel organism assay results that were discordant with the reference method were investigated.

Materials/methods: At 7 US and 2 EU sites, 1074 residual PBC were enrolled prospectively. The reference method for evaluation of the BCID2 Panel organism assay performance was microbial culture performed at clinical sites as part of routine patient care. All false positive (FP) and false negative (FN) results were investigated using alternate PCR assays and confirmed by sequencing.

Results: Overall, 74 discordant results involving 16 bacterial and 3 fungal assays were investigated. In all 54 FP cases, 18 from polymicrobial samples, the presence of the detected analyte in the PBC was confirmed by sequencing. Of the 20 FN results, 7 were attributed to isolate misidentification by the clinical laboratory; these were resolved as true negative results by sequencing. Low analyte level (below the assay’s limit-of-detection) was determined to be the root cause of 9 FN results; 8 of which were encountered in PBC samples identified as polymicrobial by the reference method. Currently, 4 FN cases remain unresolved. Notably, 38/74 (51.3%) discrepancies needing investigation involved Staphylococcus epidermidis. In 26/29 FP cases, S. epidermidis was not recovered by culture but was sequenced from the PBC. Nine discrepancies (6 FN, 3 FP) were caused by incorrect identification of the Staphylococcus species recovered by the clinical laboratory. Low analyte titers in polymicrobial PBC was responsible for the remaining 3 FN results.

Conclusions: With 61/74 discordant results resolved favorably, the BCID2 Panel would have yielded an overall success rate of 99.8%. Therefore, the BCID2 Panel is expected to provide highly accurate identification of causative agents of bloodstream infections.

Data presented are from assays that have not been cleared or approved for diagnostic use.

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Human papilloma virus and other sexually-transmitted infection prevalence among HIV-infected and HIV-uninfected women in Sikasso, Mali

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Background: Sexually transmitted infections (STIs) in Africa remain a public health concern and little studies have been conducted to assess their prevalences in Mali. We performed a cross-sectional study including women from Sikasso, Mali, to assess viral human papillomavirus [HPV], herpes simplex virus [HSV-1 and 2], bacterial STIs [Chlamydia trachomatis [CT], Mycoplasma genitalium [MG], Neisseria gonorrhoeae [NG]] and Trichomonas vaginalis [TV] prevalences and risk factors associated with.

Materials/methods: Women HIV-infected (n=44) or HIV-uninfected (n=96) and screened for STIs in Kenedougou Solidarité community health center were included. For each one, liquid-based cytology and serum were collected. Socio-demographic data including age, marital status, marital age, education level and contraception were collected. HPV-testing was performed with the AnyplexII HPV28 (Seegene), HSV-1/2-serology and DNA genital detection with LIAISON® HSV-1 IgG/HSV-2 IgG (DiaSorin) and artus® HSV-1/2 RG PCR kit (Qiagen), respectively, and STI screening with Allplex STI Essential kit (Seegene).

Results: Median [IQR] age of women included was 37 [29-44] years and the majority (78%) was married with a marital median age of 19 [17-22] years. Forty-one (35%) were polygamous, 111 (77%) did not use contraception and 113 (78%) reached primary school or less. Overall, high-risk HPV (hrHPV) prevalence was 63%. Each woman harbored in median 1 [0-2] different hrHPV. HPV31 was the most prevalent (28%) followed by HPV56 (25%) and HPV52 (n=26, 18%). HPV16 and HPV18 prevalence was respectively 9.7% and 7.6%. Prevalence of HSV-1 and HSV-2 was respectively 92% and 46%, and of other STIs as follow: CT: 4.2%, MG: 9%, NG: 1.4% and TV: 6.9%. Among HSV-seropositive patients, 7 [15%] were positive for HSV2-DNA but none for HSV1-DNA in the genital tract. Among parameters analyzed, prevalence of hrHPV and HSV-2 infection were higher among HIV-infected women (77% versus 55%, p=0.012 and 84% versus 32%, p<0.001, respectively). HSV-2 infection was also higher among patients with hrHPV infection (56% versus 37%, p=0.05) and HIV-prevalence tended to increase with decreasing education level (p=0.055).

Conclusions: Some STIs are more prevalent in HIV-infected women, as previously reported. However, both viral and bacterial STIs were frequent and improvement of systematic screening and treatment are needed in Mali.

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Abstract 2724

Phenotypic testing of ceftriaxone susceptibility on the Pheno system in characterised Enterobacterales

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Background: Various methods to detect extended-spectrum beta-lactamase (ESBL) Enterobacterales are utilized by clinical laboratories. However, both CLSI and EUCAST support the use of current breakpoints for cephalosporins and aztreonam in lieu of ESBL testing as MIC is understood to be the in vitro predictor of clinical treatment outcomes for Enterobacterales. Despite in vitro activity, clinical data suggest the use of beta lactam/beta lactamase inhibitor combinations for bloodstream infections due to ceftriaxone (CRO) non-susceptible (NS) isolates as less favorable than definitive carbapenem therapy. Earlier detection of these organisms can help guide antibiotic therapy. The objective of this study was to compare the performance of the Accelerate PhenoTest™ (AXDX) CRO susceptibility to reference broth microdilution (BMD) for beta-lactamase producing Escherichia coli, Klebsiella pneumoniae, and Proteus mirabilis.

Materials/methods: 37 characterized E. coli, K. pneumoniae, and Proteus mirabilis isolates obtained from ARLG Virtual Biorepository, CDC Antibiotic Resistance Isolate Bank, and Accelerate Diagnostics frozen clinical isolate collection were utilized. Clinical and Laboratory Standards Institute (CLSI) broth microdilution (BMD) in triplicate was performed on each isolate as the reference method. The CLSI ESBL confirmatory disk test utilizing cefotaxime, cefotaxime plus clavulanate, ceftazidime, and ceftazidime plus clavulanate (BD Diagnostics Systems, Sparks, MD) was also performed in triplicate. Species identification and AST was also performed on the AXDX according to the manufacturer’s instructions. CLSI 2019 breakpoints were used to assess interpretation.

Results: In a collection of primarily CRO resistant isolates (29/37, 78%) overall CRO categorical agreement (CA) of AXDX was 97.3% (36/37) compared with reference BMD due to 1 minor error. The CLSI ESBL disk test resulted in 1 false negative (ESBL + AmpC) and 1 false positive (original-spectrum beta lactamase (OSBL)) (Table 1).

<table>
<thead>
<tr>
<th></th>
<th>AXDX CRO CA (%)</th>
<th>BMD CRO NS</th>
<th>ESBL Disk Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESBL±AmpC (n=23)</td>
<td>95.6%</td>
<td>23/23</td>
<td>22/23 positive</td>
</tr>
<tr>
<td>OSBL+AmpC (n=6)</td>
<td>100%</td>
<td>6/6</td>
<td>0/6 positive</td>
</tr>
<tr>
<td>OSBL (n=8)</td>
<td>100%</td>
<td>0/8</td>
<td>1/8 positive</td>
</tr>
</tbody>
</table>

Conclusions: AXDX provided accurate detection of CRO susceptibility across a collection of isolates with various genotypes. ESBL production is highly correlated to CRO non-susceptibility. Therefore, earlier phenotypic detection of CRO susceptibility may help expedite the optimization of antibiotic therapy.

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In vitro activity of lefamulin against isolates commonly causing community-acquired pneumonia collected during the SENTRY surveillance programme 2015–2019 in Europe

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Abstract third-party references: Funded by Nabriva Therapeutics

Background: Lefamulin, the first-in-class systemic pleuromutilin antibacterial, has been recently (August 2019) approved in the United States for use as an intravenous (IV), oral, or IV-to-oral switch monotherapy in adults with community-acquired bacterial pneumonia. We evaluated the in vitro activity of lefamulin and comparators against typical CAP pathogens collected in Europe in 2015–2019.

Materials/methods: Overall, 7560 clinical isolates (1/patient) were collected in Europe [41 sites, 19 countries] in 2015–2019, from patients with community-acquired respiratory tract infections or hospitalized with pneumonia (74.8%), bloodstream infections (15.1%), skin/soft tissue infections (8.5%), and other infections (1.7%). MICs were determined using reference (CLSI) broth microdilution methods; susceptibility was determined applying EUCAST (2019) breakpoints, and, for lefamulin, FDA interpretive criteria [https://www.fda.gov/drugs/development-resources/antibacterial-susceptibility-test-interpretive-criteria].

Results: Lefamulin demonstrated potent antibacterial activity against all tested pathogens and was unaffected by resistance to other antibacterial classes (Table). While 99.9% of Streptococcus pneumoniae isolates were susceptible to lefamulin (MIC50/90 of 0.06/0.12 mg/L, susceptible breakpoint of ≤0.5 mg/L), susceptibility rates of other antibacterials commonly used to treat CAP were lower (penicillin, 71.8%; azithromycin, 76.3%; tetracycline, 78.4%; and moxifloxacin, 98.4%), though rather consistent over time. Similarly, 99.5% of Staphylococcus aureus isolates were susceptible to lefamulin (MIC50/90, 0.06/0.12 mg/L, susceptible breakpoint [methicillin-susceptible S. aureus] of ≤0.25 mg/L), whereas susceptibility rates for the comparators were lower for S. aureus overall and particularly for methicillin-resistant S. aureus [% in brackets]: 73.3% [40.7%] for azithromycin, 96.9% [84.9%] for cefaroline, 82.2% [29.5%] for moxifloxacin, and 96.1% [92.7%] for doxycycline. Haemophilus influenzae (17.2% β-lactamase positive) and Haemophilus parainfluenzae isolates were largely susceptible to all comparators except trimethoprim-sulfamethoxazole (64.6% and 78.8% susceptible, respectively). Applying the susceptible breakpoint of ≤2 mg/L, 99.6% of H. influenzae isolates were susceptible to lefamulin (MIC50, 0.5/1 mg/L). Moraxella catarrhalis isolates were susceptible to all comparators and inhibited by lefamulin concentrations of ≤0.12 mg/L [MIC50/90 of 0.06/0.12 mg/L].

Conclusions: Lefamulin demonstrated potent in vitro activity against bacterial pathogens that commonly cause CAP and were isolated in Europe over the last 5 years. This activity was unaffected by resistance to other antibiotic classes and particularly those commonly used to treat CAP, including macrolides, β-lactams, fluoroquinolones, and tetracyclines.

<table>
<thead>
<tr>
<th>Organism (n)</th>
<th>MIC50/90 (mg/L)</th>
</tr>
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<tbody>
<tr>
<td>Lefamulin</td>
<td></td>
</tr>
<tr>
<td>A. pneumoniae (7965)</td>
<td>0.06/0.12</td>
</tr>
<tr>
<td>Penicillin nonsusceptible* (193)</td>
<td>&gt;0.25/1.25</td>
</tr>
<tr>
<td>Macrolide resistant* (661)</td>
<td>0.06/0.12</td>
</tr>
<tr>
<td></td>
<td>&gt;0.25/0.5</td>
</tr>
<tr>
<td>A. aerius (2293)</td>
<td>0.06/0.12</td>
</tr>
<tr>
<td>MRSA (477)</td>
<td>0.06/0.12</td>
</tr>
<tr>
<td>Multidrug resistant* (155)</td>
<td>&gt;0.25/0.25</td>
</tr>
<tr>
<td>H. influenzae (538)</td>
<td>0.01/0.5</td>
</tr>
<tr>
<td>β-lactamase-positive (185)</td>
<td>0.01/0.5</td>
</tr>
<tr>
<td>H. parainfluenzae (86)</td>
<td>0.01/0.5</td>
</tr>
<tr>
<td>M. catarrhalis (474)</td>
<td>0.06/0.12</td>
</tr>
</tbody>
</table>

MSSmethicillin-resistant S. aureus. *2019 dataset is not yet final and data as of November 11, 2019, are shown. 1Cefaroline for A. pneumoniae, H. influenzae, H. parainfluenzae, and M. catarrhalis; cefaroline for A. aerius. 2Tetracycline for S. pneumoniae, H. influenzae, H. parainfluenzae, and M. catarrhalis; doxycycline for A. aerius. 3Penicillin MIC >2 mg/L, for nonmeningitis breakpoint. Using oxacillin breakpoint. 4Multidrug resistant defined as resistant to methicillin, oxacillin, and moxifloxacin.

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Identification and clinical significance of Mycobacterium avium complex isolates in a university hospital in a 13-year period

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Background: Mycobacterium avium complex (MAC) includes a group of mycobacterial pathogens most commonly isolated from respiratory samples. MAC infection can also result in lymphadenitis and disseminated disease in both immunocompromised and immunocompetent patients. This retrospective study assessed the microbiological characteristics, the clinical relevance and the experience of molecular identification of MAC isolates recovered from patients in Attikon University Hospital, Athens Greece over the 13-year period December 2006 to November 2019.

Materials/methods: We studied 83 MAC single-patient isolates that were identified with the Genotype CM and Genotype NTM-DR assays (Hain-Lifescience). Sequencing analysis of 16S rDNA (1500-bp) and hsp65 (440-bp) genes was performed when necessary. The criteria from the American Thoracic Society/Infectious Disease Society of America (ATS/IDSA 2007) were applied to determine the clinical relevance of recovered isolates.

Results: Thirty-five strains identified as M. avium, 41 as M. intracellulare [32 as M. intracellulare subsp intracellulare and 9 as M. intracellulare subsp. chimaera], and 5 as M. marseillense. The CM and NTM-DR assays identified correctly all M. avium and M. intracellulare strains, while misidentified all M. marseillense strains as M. intracellulare. On the other hand, NTM-DR assay identified correctly all 9 M. intracellulare subsp. chimaera strains. Of the 83 MAC strains, 70 [84.3%] were recovered from respiratory specimens: 25 [71.4%] M. avium, all 41 M. intracellulare, and 4 [44.4%] M. marseillense and 13 [15.7%] MAC strains from extrapulmonary specimens: 12 M. avium and 1 M. marseillense. Of the 70 MAC strains recovered from respiratory specimens, 41 [58.6%] were considered as clinically significant according to the ATS/IDSA criteria: 17 M. avium, 3 M. marseillense, 16 M. intracellulare subsp intracellulare and 5 M. intracellulare subsp. chimaera. For 19 of them [46.3%], smears were positive for acid-fast bacilli. The remaining 29 MAC strains were not considered as clinically significant, probably representing contamination. All 13 MAC strains that were recovered from extra-pulmonary specimens were considered as clinically significant: 4 patients suffered from skin and soft tissue infection and 9 patients from AIDS and disseminated infection.

Conclusions: Of the 83 recovered MAC stains, 54 [65.1%] were linked with human disease. Our findings suggest that the combined use of molecular commercial identification tests with sequencing analysis improves the ability to correctly identify the recovered MAC strains.

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In vitro activity of imipenem/relebactam against Klebsiella pneumoniae and Pseudomonas aeruginosa isolates from patients with respiratory tract infections in the Asia/Pacific region: SMART 2015-2018

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Background: Relebactam (REL) inhibits class A and C β-lactamases and was approved in the USA in combination with imipenem (IMI) and cilastatin for treatment of complicated intraabdominal and urinary infections. We evaluated the activity of IMI/REL against isolates collected < and ≥48 hours post-admission for the SMART surveillance program in Asia/Pacific from patients with lower respiratory tract infections (LRTI).

Materials/methods: In 2015-2018, 57 clinical laboratories in Australia, Hong Kong, India, South Korea, Malaysia, New Zealand, Philippines, Taiwan, Thailand, and Vietnam each collected up to 100 consecutive gram-negative pathogens from LRTI. MICs were determined using CLSI broth microdilution and interpreted with EUCAST breakpoints, except for IMI/REL for which FDA breakpoints were used. Isolates testing with IMI MIC ≥2 mg/L (K. pneumoniae, KP) or ≥4 mg/L (P. aeruginosa, PA) were screened for β-lactamase genes.

Results: The 5 most common species collected were PA (n=3550, 29.1% of all collected), KP (n=31 20, 25.6%), A. baumannii (n=1356, 11.1%), E. coli (n=1140, 9.4%), and S. maltophilia (n=490, 4.0%). The table shows the activity of IMI/REL and comparators against KP and PA stratified by length of hospital stay at time of specimen collection.

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>K. pneumoniae</th>
<th>P. aeruginosa</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≥48 hours</td>
<td>&lt;48 hours</td>
</tr>
<tr>
<td>Imipenem/Relebactam</td>
<td>90.9</td>
<td>95.0</td>
</tr>
<tr>
<td>Imipenem</td>
<td>88.8</td>
<td>94.7</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>83.9</td>
<td>91.8</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>50.3</td>
<td>79.8</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>51.9</td>
<td>76.4</td>
</tr>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>54.6</td>
<td>76.7</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>60.5</td>
<td>80.1</td>
</tr>
<tr>
<td>Amikacin</td>
<td>51.1</td>
<td>71.5</td>
</tr>
<tr>
<td>Colistin</td>
<td>87.4</td>
<td>93.9</td>
</tr>
</tbody>
</table>

N/A, not applicable

Among IMI-resistant KP collected < and ≥48 hours post-admission (n=138), 50.7% carried metallo-β-lactamases (MBL), 39.1% KPC, 6.5% OXA-48-like carbapenemases, 2.2% AmpC extended-spectrum β-lactamases (ESBL), and in 1.4% no acquired β-lactamases were detected. 37% of IMI-resistant KP were IMI/REL-susceptible (n=52), of which 98.1% carried KPC and 1.9% only AmpC. Among all IMI-resistant PA (n=603), 13.5% carried MBL, 2.2% carried only ESBL, 0.7% GES-carbapenemases, and in 83.7% no acquired β-lactamases were detected. 64.0% of IMI-resistant PA were IMI/REL-susceptible (n=386), of which 1.0% carried only ESBL and in 99.0% no acquired β-lactamases were detected.

Conclusions: KP and PA were the two most common species in this collection of LRTI isolates from Asia/Pacific. IMI/REL maintained activity against ≥90% of isolates collected ≥48 hours post-admission, which generally showed lower susceptibility to the tested agents. Only amikacin and colistin showed comparable or higher activity. IMI/REL could provide an important treatment option for patients with LRTI in the Asia/Pacific region.

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A marked decrease in HIV-1 acquired drug resistance in Italy over the last decade

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Background: It is expected that new antiretroviral regimens reduce drug resistance in treated subjects, even if this hypothesis remains to be evaluated in recent years. Resistance and its correlates were studied in treatment failing patients in a comprehensive database over the 2009-2018 period.

Materials/methods: We analyzed 3,094 HIV-1 pol sequences and 1,058 integrase sequences from subjects enrolled in 21 Centers of the Italian ARCA database. Patients were included when they had viremia > 50 copies/mL and received a resistance genotypic test on plasma after at least 24 weeks of treatment. Mutations were identified through International AIDS Society 2019 drug resistance mutations lists and the Stanford HIVdb algorithm. Five periods of study were evaluated, one for each biennium. Trends and correlates of resistance were analyzed by Cochran-Armitage, Chi squared tests and logistic regression models.

Results: Males were 63.2%; non-B subtypes increased from 13.1% to 23.8% from the first to the last biennium (p<.001). Resistance to NRTIs, NNRTIs and PIs declined, from 61.7% to 43.5% (p<.001), from 44.7% to 40.4% (p=.024) and from 36.4% to 30% (p=.001), respectively. INSTI resistance declined from 31% to 20.8% (p=.002), when Stanford HIVdb was adopted for moderate or high grade resistance. A reduction was observed for many RT and PR mutations, such as TAMs, M184V, K103N, M46I, I47V, I54L/M, L76V, V82A/T/L, I84V and L90M, while a significant increase was found for Y181C. In the integrase region we observed the decrease of G140S, T149C, D148H and the increase of S147G and Q148R. In the multivariate analysis, the risk of resistance was not influenced by epidemiological correlates such as subtype, while it decreased significantly over time (OR per 1 biennium higher 1.13, 95% CI 1.10-1.15) and it was associated with previous antiretroviral treatments (OR per 1 more previous antiretroviral line 0.77, 95% CI 0.70-0.85).

Conclusions: A stable reduction of acquired resistance was observed over the last decade, suggesting that new antiretroviral regimens and standards provide a higher genetic barrier, with better maintenance of treatment options. Nonetheless, some concerns remain for patients who failed several previous regimens, reinforcing the need for surveillance of resistance in subjects experiencing virological failures.

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Abstract 2731

Assessment of quantitative composition of Bacteroides fragilis in children with coeliac disease at the time of diagnosis and after a six-month period of diet

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Abstract third-party references: Supported by National Science Centre in Poland grant no.2017/26/E/NZ5/00266

Background: The genetic background (DQ2 or DQ8 haplotypes encoding specific antigens in the HLA region) is necessary to induce symptoms of celiac disease (CD), however, a triggering factor is required. Recently, an important role in CD etiology has been attributed to intestinal dysbiosis. It is supposed that some microorganisms occurring in patients’ intestines, may interact with gluten, producing highly immunogenic peptides activating the immune response which triggers CD symptoms. Bacteroides fragilis belongs to the gut microbiota but in case of failure of host defense mechanism or intestinal dysbiosis this commensal microorganism may turn into pathogenic inhabitant. The potential pathogenicity of B.fragilis is related to the expression of a variety of virulence factors, including proteolytic and other hydrolytic enzymes. Perhaps, changes in number of B.fragilis and associated virulence factors may contribute to initiating CD. The aim of this study was assessment of quantitative composition of B.fragilis in children with CD at the time of diagnosis and after a six-month period of diet compared to the healthy group.

Materials/methods: The materials were stool samples taken from children hospitalized in the years 2018-2019 in University Children’s Hospital of Cracow, Poland:

I. with CD at the moment of diagnosis (n=32)
II. with CD 6 months after diagnosis (n=14)
III. healthy, being a control group (n=23)

The bacterial DNA was isolated from the samples. Amplification by the quantitative polymerase chain reaction (qPCR) was used to determine the number of B.fragilis in the group’s I-III.

Results: In group I, number of B.fragilis was significantly higher (1.77x10^9 CFU/g) compared to the control (3.64x10^8 CFU/g, p=0.014). In group II number of B.fragilis decreased (1.15x10^9) but observed changes were not statistically significant (p>0.05).

Conclusions: Obtained results showed that patients with CD at the moment of diagnosis were characterized by increased colonization of B.fragilis. Perhaps in the case of people who have genetic predisposition for the development of CD these bacteria may contribute to the induction of inflammation, which may be confirmed by reducing their number after a period of gluten-free diet.

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**Abstract 2733**

**In vitro activity of imipenem/relebactam against Gram-negative organisms collected from patients in Colombia: SMART 2015-2018**

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**Background:** Relebactam (REL) inhibits class A and C β-lactamases and was approved in the USA in combination with imipenem (IMI) and cilastatin for the treatment of complicated intraabdominal and urinary tract infections. We evaluated the activity of IMI/REL against non-Morganellaceae Enterobacterales (NME) and Pseudomonas aeruginosa isolates collected as part of the SMART surveillance program in Colombia.

**Materials/methods:** In 2015-2018, 7 clinical laboratories in Colombia each collected up to 250 consecutive aerobic or facultative gram-negative pathogens from various infection sources. MICs were determined using CLSI broth microdilution and interpreted with CLSI breakpoints. US FDA breakpoints (≤1/4 mg/L, susceptible; 2/4 mg/L, intermediate; ≥4/4 mg/L, resistant) were applied to IMI/REL. Multidrug-resistance (MDR) was defined as nonsusceptibility (intermediate or resistant MIC) to ≥3 of the following sentinel drugs: amikacin, aztreonam, cefepime, ceftazidime (NME only), ciprofloxacin, colistin, imipenem, and piperacillin-tazobactam. Isolates testing with IMI MIC ≥2 mg/L (NME) or ≥4 mg/L (P. aeruginosa) were screened for β-lactamase genes (excluding NME from one site in Colombia).

**Results:** The susceptibility to IMI/REL and comparators of all NME, all P. aeruginosa, and resistant phenotypes is shown in the table.

<table>
<thead>
<tr>
<th>Phenotype (n)</th>
<th>IMI/REL</th>
<th>IMI</th>
<th>FEP</th>
<th>CAZ</th>
<th>ATM</th>
<th>P/T</th>
<th>CIP</th>
<th>AMK</th>
<th>CST</th>
</tr>
</thead>
<tbody>
<tr>
<td>All NME (2494)</td>
<td>97.7</td>
<td>87.1</td>
<td>78.1</td>
<td>78.2</td>
<td>74.9</td>
<td>80.4</td>
<td>64.7</td>
<td>97.6</td>
<td>92.3</td>
</tr>
<tr>
<td>FEP-NS (546)</td>
<td>95.1</td>
<td>53.0</td>
<td>0.0</td>
<td>13.9</td>
<td>5.3</td>
<td>44.1</td>
<td>16.4</td>
<td>89.6</td>
<td>95.4</td>
</tr>
<tr>
<td>P/T-NS (483)</td>
<td>94.7</td>
<td>48.0</td>
<td>37.5</td>
<td>34.6</td>
<td>24.8</td>
<td>0.0</td>
<td>33.3</td>
<td>89.3</td>
<td>94.5</td>
</tr>
<tr>
<td>IMI-NS (322)</td>
<td>82.6</td>
<td>0.0</td>
<td>37.3</td>
<td>37.0</td>
<td>23.3</td>
<td>21.1</td>
<td>36.0</td>
<td>88.8</td>
<td>78.6</td>
</tr>
<tr>
<td>MDR (613)</td>
<td>95.1</td>
<td>50.1</td>
<td>15.0</td>
<td>16.0</td>
<td>4.1</td>
<td>39.5</td>
<td>17.0</td>
<td>90.4</td>
<td>94.5</td>
</tr>
<tr>
<td>All P. aeruginosa (416)</td>
<td>83.2</td>
<td>64.4</td>
<td>74.5</td>
<td>74.5</td>
<td>62.7</td>
<td>69.5</td>
<td>71.9</td>
<td>88.0</td>
<td>99.3</td>
</tr>
<tr>
<td>FEP-NS (106)</td>
<td>43.4</td>
<td>19.8</td>
<td>0.0</td>
<td>10.4</td>
<td>7.6</td>
<td>4.7</td>
<td>34.0</td>
<td>54.7</td>
<td>100.0</td>
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<tr>
<td>P/T-NS (127)</td>
<td>50.4</td>
<td>28.4</td>
<td>20.5</td>
<td>21.3</td>
<td>7.1</td>
<td>0.0</td>
<td>38.6</td>
<td>63.0</td>
<td>99.2</td>
</tr>
<tr>
<td>IMI-NS (148)</td>
<td>52.7</td>
<td>0.0</td>
<td>42.6</td>
<td>47.3</td>
<td>29.7</td>
<td>38.5</td>
<td>39.2</td>
<td>68.9</td>
<td>99.3</td>
</tr>
<tr>
<td>MDR (126)</td>
<td>46.8</td>
<td>19.8</td>
<td>18.3</td>
<td>23.0</td>
<td>5.6</td>
<td>10.3</td>
<td>28.6</td>
<td>60.3</td>
<td>98.4</td>
</tr>
</tbody>
</table>

IMI, imipenem; REL, relebactam; FEP, cefepime; CAZ, ceftazidime; ATM, aztreonam; P/T, piperacillin-tazobactam; CIP, ciprofloxacin; AMK, amikacin; CST, colistin; NS, nonsusceptible; MDR, multidrug-resistant.

Among all collected NME, 8.4% were KPC-positive and 0.6% were metallo-β-lactamase (MBL)-positive. Among 47 characterized IMI/REL-nonsusceptible NME, 27.7% carried MBL, 12.8% were KPC-positive and MBL-negative, 2.1% carried only an acquired AmpC, and in 57.4% of isolates no acquired β-lactamases were detected. Among all collected P. aeruginosa, 9.1% were KPC-positive and 4.8% were MBL-positive; among 68 characterized IMI/REL-nonsusceptible P. aeruginosa, 29.4% carried MBL, 38.2% were KPC-positive and MBL-negative, and in 32.4% no acquired β-lactamases were detected.

**Conclusions:** Among isolates collected in Colombia, IMI/REL was active against >97% of NME and >83% of P. aeruginosa, 11-23 and 9-20 percentage points, respectively, higher than tested comparator β-lactams. IMI/REL maintained activity against >82% of NME and >43% of P. aeruginosa isolates that were nonsusceptible to individual β-lactams or MDR. IMI/REL could provide an important treatment option for patients in Colombia with infections due to resistant gram-negative organisms.

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Abstract 2735

5-year Surveillance of Lefamulin against Gram-positive Cocci Collected from Acute Bacterial Skin and Skin-Structure Infections (ABSSSI) and Bloodstream Infections (BSI) in Europe (SENTRY 2015–2019)

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Abstract third-party references: Funded by Nabriva Therapeutics

Background: Lefamulin, a novel pleuromutilin antimicrobial, has been approved in the United States for the intravenous (IV) and oral treatment of community-acquired pneumonia in adults. In a phase 2 clinical trial in ABSSSI, lefamulin (150 mg IV) demonstrated clinical efficacy comparable to that of vancomycin (1000 mg IV). This study investigated the in vitro activity of lefamulin and comparators against bacterial pathogens collected from ABSSSI and BSI in Europe during 2015–2019.

Materials/methods: 2116 unique bacterial isolates were collected in Europe (19 countries, 40 sites) in 2015–2019, from patients with ABSSSI (64%) and BSI (35%). Lefamulin and comparators were susceptibility tested by reference CLSI broth microdilution, and MIC values were interpreted per EUCAST (2019) criteria.

Results: Lefamulin demonstrated potent antibacterial activity against staphylococci and β-hemolytic and viridans group streptococci (Table). Among Staphylococcus aureus isolates, 20.6% were methicillin-resistant S. aureus (MRSA), which showed particularly high resistance rates to fluoroquinolones (moxifloxacin, 68.7%) and macrolides (erythromycin, 53.2%). Lefamulin inhibited 99.5% and 98.6% of S. aureus and MRSA isolates, respectively, at 0.25 mg/L (MIC50/90 of 0.06/0.12 mg/L). Coagulase-negative staphylococci (CoNS) showed high resistance rates to macrolides (erythromycin, 55.7%), fluoroquinolones (moxifloxacin, 50.5%), aminoglycosides (gentamicin, 45.3%), and oxacillin (68.0%) but were largely susceptible (>90%) to tetracyclines, oxazolidinones, and lipo- and glycopeptides. Lefamulin displayed an MIC50/90 of 0.06/0.12 mg/L against CoNS overall and of 0.06/0.5 mg/L against S. epidermidis specifically. Lefamulin also demonstrated potent activity against β-hemolytic streptococci (MIC50/90 of 0.03/0.06 mg/L), including group A, B, C, and G isolates; β-hemolytic streptococci were largely susceptible to all tested comparators except erythromycin [21.3% resistant] and clindamycin [12.5% resistant]. Among viridans group streptococci, lefamulin showed an MIC50/90 of 0.06/0.25 mg/L, against all species except S. gallolyticus, against which lefamulin displayed an MIC50/90 of 2/4 mg/L. Overall, susceptibility/resistance rates for comparators were generally consistent over time.

Conclusions: Lefamulin demonstrated potent in vitro activity against this contemporary European collection of Gram-positive cocci gathered from ABSSSI and BSI, and lefamulin activity was unaffected by resistance to other antibiotic classes. These data support the continued development of lefamulin for the treatment of ABSSSI and further exploration of lefamulin activity in BSI.

Table. MIC50/90 of Lefamulin and Comparators (2015–2019)*

<table>
<thead>
<tr>
<th>Organisms [μg]</th>
<th>Lefamulin</th>
<th>Colistin*</th>
<th>Ceftriaxone</th>
<th>Erythromycin</th>
<th>Lincomycin</th>
<th>Tigecycline</th>
<th>Vancomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus (1380)</td>
<td>0.00/0.12</td>
<td>0.25/0.1</td>
<td>0.25/0.1</td>
<td>1/2</td>
<td>0.12/0.12</td>
<td>1/1</td>
<td></td>
</tr>
<tr>
<td>MRSA (278)</td>
<td>0.00/0.12</td>
<td>0.25/0.1</td>
<td>0.25/0.1</td>
<td>1/2</td>
<td>0.12/0.12</td>
<td>1/1</td>
<td></td>
</tr>
<tr>
<td>Coagulase-negative staphylococci (300)*</td>
<td>0.00/0.12</td>
<td>0.25/0.1</td>
<td>&gt;0.5/0.1</td>
<td>0.5/0.1</td>
<td>0.12/0.25</td>
<td>1/2</td>
<td></td>
</tr>
<tr>
<td>S. epidermidis (172)</td>
<td>0.00/0.5</td>
<td>0.25/0.5</td>
<td>&gt;0.5/0.1</td>
<td>0.5/0.1</td>
<td>0.12/0.25</td>
<td>1/2</td>
<td></td>
</tr>
<tr>
<td>Beta-hemolytic streptococci (309)*</td>
<td>0.00/0.05</td>
<td>0.03/0.05</td>
<td>0.03/0.1</td>
<td>0.5/0.1</td>
<td>0.12/0.25</td>
<td>1/2</td>
<td></td>
</tr>
<tr>
<td>S. pyogenes (153)</td>
<td>0.00/0.05</td>
<td>0.03/0.05</td>
<td>0.03/0.1</td>
<td>0.5/0.1</td>
<td>0.12/0.25</td>
<td>1/2</td>
<td></td>
</tr>
<tr>
<td>S. agalactiae (125)</td>
<td>0.00/0.05</td>
<td>0.03/0.05</td>
<td>0.03/0.1</td>
<td>0.5/0.1</td>
<td>0.12/0.25</td>
<td>1/2</td>
<td></td>
</tr>
<tr>
<td>S. dysgalactiae (62)</td>
<td>0.00/0.05</td>
<td>0.03/0.05</td>
<td>0.03/0.1</td>
<td>0.5/0.1</td>
<td>0.12/0.25</td>
<td>1/2</td>
<td></td>
</tr>
<tr>
<td>Viridans group streptococci excluding S. genticus (100)</td>
<td>0.00/0.35</td>
<td>0.12/0.35</td>
<td>0.35/0.5</td>
<td>1/1</td>
<td>0.12/0.25</td>
<td>1/2</td>
<td></td>
</tr>
<tr>
<td>S. genticus (25)</td>
<td>0.12/0.25</td>
<td>0.12/0.25</td>
<td>0.35/0.5</td>
<td>1/1</td>
<td>0.12/0.25</td>
<td>1/2</td>
<td></td>
</tr>
</tbody>
</table>


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Abstract 2736

Diagnostic utility of stool polymerase chain reaction in enteric fever: experience from a high-incidence London hospital

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Background: Enteric fever is a systemic illness that is most commonly caused by Salmonella enterica serovars Typhi and Paratyphi A. A barrier to prompt treatment is the lack of reliable diagnostic tests. Blood culture remains the most commonly utilized diagnostic modality, but only identifies 60-80% of cases. The increasing availability of stool PCR testing presents an additional technique that has potential to improve the diagnostic yield. We report on the sensitivity and utility of stool culture and PCR in a retrospective cohort of subjects with microbiologically confirmed enteric fever presenting to local healthcare services.

Materials/methods: Data were collected from electronic laboratory records to include: all positive blood and stool cultures where enteric fever-causing Salmonella species were isolated between July 2017 – September 2019; and all positive stool PCR results for Salmonella species DNA between January 2019 (when PCR was introduced) and September 2019.

Results: In total, 57 subjects met the Public Health England definition of a ‘Probable case’ of enteric fever; compatible clinical history in a returned traveller with microbiological confirmation by either blood or stool testing. Fifty-four subjects underwent blood culture testing, 23 had stool culture, and 17 had stool PCR testing. Using pooled positive results as a gold standard, the sensitivities of the individual diagnostic techniques were calculated (Table).

<table>
<thead>
<tr>
<th>No. positive/ No. tested</th>
<th>Sensitivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood culture</td>
<td>52/54</td>
<td>0.96</td>
</tr>
<tr>
<td>Stool PCR</td>
<td>15/17</td>
<td>0.88</td>
</tr>
<tr>
<td>Stool culture</td>
<td>18/23</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Table. Sensitivity of blood culture, stool PCR and stool culture in microbiologically confirmed cases of enteric fever

Only 13 (23%) of the 57 patients who met the case definition had samples taken for concomitant blood culture and stool PCR tests. Of these 13; 9 patients (69%) were positive in both blood culture and stool PCR, 2 (15%) had positive blood cultures with negative stool PCR, and 2 (15%) had positive stool PCR with negative blood cultures.

Conclusions: Results from this retrospective cohort suggest that the inclusion of stool PCR as part of routine diagnostics in those presenting with suspected enteric fever is a useful adjunct to identify cases that may be missed using blood culture alone.

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Abstract 2739

Antimicrobial susceptibility and carbapenem co-resistance among piperacillin/tazobactam-resistant Pseudomonas aeruginosa: SMART Asia/Pacific 2016-2018

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Background: Ceftolozane/tazobactam (C/T) is an antipseudomonal cephalosporin combined with a β-lactamase inhibitor. C/T has been approved by the FDA and EMA for complicated urinary tract infections, complicated intraabdominal infections, and hospital-acquired and ventilator-associated bacterial pneumonia. Using isolates collected in Asia/Pacific as part of the SMART surveillance program, we evaluated the activity of C/T and comparators against piperacillin/tazobactam-resistant (P/T-R) P. aeruginosa.

Materials/methods: In 2016-2018, 56 clinical laboratories in Australia, Hong Kong, India, South Korea, Malaysia, New Zealand, Philippines, Singapore, Taiwan, Thailand, and Vietnam each collected up to 250 consecutive aerobic or facultative gram-negative pathogens from various infection sources, for a total of 25,927 isolates including 4,362 P. aeruginosa. MICs were determined using CLSI broth microdilution and interpreted with EUCAST breakpoints. P. aeruginosa isolates (excluding those collected in India) testing with C/T MIC ≥8 mg/L or imipenem MIC ≥4 mg/L were screened by PCR and sequenced for genes encoding β-lactamases.

Results: Of the 4,362 P. aeruginosa isolates, 28.9% were P/T-R, ranging from 11.8% in New Zealand to 53.0% in India; 12.5% were resistant to both piperacillin/tazobactam and meropenem (P/T-R+MEM-R), ranging from 2.3% in New Zealand to 41.8% in Vietnam. The table shows the activity of C/T and comparators against P/T-R and P/T-R+MEM-R P. aeruginosa isolates.

The activity of C/T against P/T-R P. aeruginosa ranged from 22% observed for isolates collected in India and Vietnam to >84% in Australia, South Korea, New Zealand, and Taiwan. Against P/T-R+MEM-R P. aeruginosa, susceptibility ranged from 8% in India to 78% in New Zealand. Of the 545 P/T-R+MEM-R isolates, 392 were molecularly characterised: 36.2% carried metallo-β-lactamases (MBLs), 3.1% GES-carbapenemases, 0.3% KPCs, 3.3% only extended-spectrum β-lactamases (ESBLs), and in 57.1% no acquired β-lactamases were detected.

Conclusions: Overall, C/T maintained activity against 65% of P/T-R P. aeruginosa collected in Asia/Pacific (24% higher than meropenem) and against 34% of P/T-R+MEM-R isolates, with substantial variability observed across countries; only amikacin, and colistin showed comparable or higher activity. C/T could provide an important treatment option for patients with infections caused by antimicrobial-resistant P. aeruginosa.

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Selective decontamination of the digestive tract prevents postoperative pneumonia and anastomotic leakage after esophagectomy

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Background: Postoperative infectious complications occur frequently after esophagectomy. The use of selective decontamination of the digestive tract (SDD) might reduce postoperative infections in patients undergoing esophagectomy. The aim of this study was to evaluate the effectiveness of SDD in preventing infectious complications and anastomotic leakage after esophagectomy for cancer.

Materials/methods: A retrospective cohort study was conducted in patients undergoing elective Ivor Lewis totally minimally invasive esophagectomy in four Dutch hospitals between 2012 and 2018. Two hospitals used SDD perioperatively (start 3 days before and stop 3 days after esophagectomy) and two did not. SDD consisted of oral paste and suspension, containing amphotericin B, colistin and tobramycin. Outcomes of patients receiving SDD perioperatively were compared to those not receiving SDD. Primary outcome was 30-day postoperative infectious complication rate (more specifically; pneumonia, mediastinitis/empyema and surgical-site infections [SSI]). Secondary outcome was anastomotic leakage. Univariate and multivariate logistic regression were used to determine the effect of SDD on postoperative infectious complications and anastomotic leakage.

Results: In total, 496 patients were included (179 received SDD perioperatively). Postoperative infectious complications were observed in 214 (43.1%) patients. Pneumonia occurred in 30.2% of the patients, SSI in 5.0% and anastomotic leakage in 16.5%. One-year survival was significantly lower in patients with infectious complications compared to those without a postoperative infection (40.1% vs. 59.9%, p=0.006). Univariate analysis showed that patients who received SDD were less likely to develop postoperative infections overall (36.9% vs. 46.7%, p=0.034), pneumonia (20.1% vs. 36.0%, p<0.001) and anastomotic leakage (10.6% vs. 19.9%, p=0.008), but surgical-site infections occurred more frequently (8.9% vs. 2.8%, p=0.003) in the SDD group. In multivariate analysis, SDD showed to be an independent protective factor for postoperative pneumonia (OR 0.41, 95% CI 0.24-0.69, p=0.001) and anastomotic leakage (OR 0.46, 95% CI 0.26-0.84, p=0.011).

Conclusions: SDD seems to be an effective strategy to prevent pneumonia and anastomotic leakage after elective esophagectomy for cancer.

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Abstract 2741

**In vitro activity of imipenem/relebactam against Klebsiella pneumoniae and Pseudomonas aeruginosa isolates from Patients in intensive care unit and non-intensive care unit wards in the Philippines: SMART 2016-2018**

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**Background:** Relebactam (REL) inhibits class A and C β-lactamases and was approved in the USA in combination with imipenem (IMI) and cilastatin for the treatment of complicated intraabdominal and urinary infections. We evaluated the activity of IMI/REL against isolates collected as part of the SMART surveillance program in the Philippines from patients in ICU and non-ICU hospital wards.

**Materials/methods:** In 2016-2018, 4 clinical laboratories in the Philippines each collected up to 250 consecutive gram-negative pathogens from various infection sources. MICs were determined using CLSI broth microdilution and interpreted with EUCAST breakpoints, except IMI/REL for which FDA breakpoints were applied. Isolates testing with IMI MIC ≥2 mg/L (Enterobacterales) or ≥4 mg/L (P. aeruginosa, PA) were screened for β-lactamase genes.

**Results:** 299 K. pneumoniae (KP) and 143 PA isolates (48.5% and 65.7%, respectively, from lower respiratory tract infections; 28.1% and 19.6% from intraabdominal infections; 17.1% and 10.5% from urinary tract infections; 17.1% and 10.5% from bloodstream infections; and 1.0 and 0.7% from unspecified sources) were collected in ICU and non-ICU wards. The table shows the activity of IMI/REL and comparators against KP and PA stratified by ward type.

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>% Susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>K. pneumoniae</td>
</tr>
<tr>
<td></td>
<td>ICU (n=51)</td>
</tr>
<tr>
<td>Imipenem/Relebactam</td>
<td>94.1</td>
</tr>
<tr>
<td>Imipenem</td>
<td>88.2</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>84.3</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>70.6</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>56.9</td>
</tr>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>66.7</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>68.6</td>
</tr>
<tr>
<td>Amikacin</td>
<td>51.0</td>
</tr>
<tr>
<td>Colistin</td>
<td>92.2</td>
</tr>
<tr>
<td>N/A, not applicable</td>
<td></td>
</tr>
</tbody>
</table>

Among IMI-resistant KP (n=22), 13 isolates carried metallo-β-lactamases (MBLs), 7 KPCs, 1 AmpC, and in 1 isolate no acquired β-lactamases were detected. Seven IMI-resistant KP isolates (31.8%) were IMI/REL-susceptible and all carried KPC. Among IMI-resistant PA (n=25), 6 isolates carried MBLs, 1 carried only an extended-spectrum β-lactamase (ESBL), and in 18 isolates no acquired β-lactamases were detected. Twelve IMI-resistant PA isolates (48.0%) were IMI/REL-susceptible; of these, 1 carried only an ESBL and in 11 isolates no acquired β-lactamases were detected.

**Conclusions:** Antimicrobial susceptibility of PA was lower among isolates from ICU than non-ICU wards, while the pattern was less clear for KP. Even among ICU isolates, IMI/REL maintained activity against 94% of KP and 86% of PA, 6-37 percentage points higher than the other tested β-lactams. Only amikacin and colistin showed comparable or higher activity. IMI/REL can provide an important treatment option for patients in the Philippines, including those in ICUs.

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Abstract 2744

**Seroprevalence of anti-HCV antibodies in the Bulgarian population**

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**Background:** Hepatitis C virus (HCV) is among the leading etiological causes for the development of chronic liver disease globally. Chronic HCV infection often flows asymptomatic and is defined as a risk factor for the development of liver cirrhosis and primary hepatocellular carcinoma (HCC). Modern laboratory diagnostics of HCV is based on immunological and molecular-biological methods. The incidence of HCV, both in the overall population and among risk groups, is assessed by establishing the presence of anti-HCV antibodies. The quantification of HCV RNA is a major marker for post-therapeutic monitoring and demonstration of current infection with the virus. The purpose of the study is to provide up-to-date data on the seroprevalence of the antibodies among the Bulgarian population. There is also a high focus on the modern possibilities of diagnostics HCV infection with the application of automated serological methods (CLIA, ECLIA, ELFA), immunoassay tests (recomLine HCV IgG) and molecular analyses (RT/real-time qPCR).

**Materials/methods:** For the period from 01.01.2017 – 31.10.2019, a total of 54,185 serum / plasma samples were tested for the detection of anti HCV antibodies in individuals over a large scale of age range (4 months - 88 years). The positive and equivocal results of the screening studies were confirmed by immunoblot. HCV RNA determination by RT / real-time qPCR was performed in 119 subjects.

**Results:** A reactive (positive) results for anti HCV antibodies were obtained in 941 (1.7%) of the subjects, respectively, 53,826 (98.3%) were seronegative. The highest segment is infection in the groups 31-40 years and over 61 years. Out of the 119 subjects tested with RT / real-time qPCR, HCV RNA was demonstrated in 36 (30.2%). A higher proportion of anti HCV seropositivity was observed in hemodialysis patients who were identified as a risk contingent.

**Conclusions:** Data for Bulgaria indicate 1.7% seroprevalence of HCV. Serological screening for anti HCV antibodies among the general population and high-risk groups is important for early detection of infected asymptomatic individuals, as well as for limiting the spread of infection and preventing its adverse effects on human health.

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The accuracy of β-D-glucan and Aspergillus DNA detection by PCR in serum and bronchoalveolar lavage fluid for the diagnosis of pulmonary aspergillosis in critically ill patients with suspected ventilator associated pneumonia

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Abstract: Invasive aspergillosis is the most frequently missed infective diagnosis in critically ill patients, demonstrated by autopsy studies. Diagnosis is particularly challenging in this patient group because of limited access to validated diagnostic tests. The aim of this study was to estimate the diagnostic accuracy of three index tests: (i) β-D-glucan [BDG] in serum; Aspergillus DNA detection by PCR in (ii) bronchoalveolar lavage fluid (BALF) and; (iii) serum.

Materials/methods: Two prospective UK studies recruited 360 critically ill adults with new or worsening alveolar shadowing on chest X-ray and clinical/haematological parameters supporting suspected ventilator-associated pneumonia (VAP). All patients underwent standardised bronchoalveolar lavage and were eligible for inclusion in the present study if sufficient volumes of stored serum and BALF were available for mycological testing. Index test results were compared to a reference standard constructed for this population which defined probable Aspergillus infection using clinical, radiological and mycological criteria. Mycological criteria comprised one or more of: positive histology or microscopy; positive BALF culture; galactomannan optical index ≥1 in BALF or ≥0.5 in serum.

Results: Of 194 patients eligible for inclusion, 24 (12.4%) fulfilled the reference standard definition of Aspergillus infection. The table shows key diagnostic accuracy characteristics of the index tests. The most sensitive single test was BDG (41.7%), while the most specific was serum PCR (86.9%). For confirmation of aspergillosis, BDG plus serum PCR had highest positive predictive value (PPV) at 60% (95%CI, 20.9-89.5). For exclusion, combining negative BDG and BALF PCR, had highest negative predictive value (NPV) at 90.6% (95%CI, 85.6-94.1), providing only a small advantage over each test used alone.

Conclusions: While acknowledging limitations arising from an imperfect reference standard, our data demonstrate possible roles for BDG and BALF/serum PCR in this patient group. Serum BDG may be a favourable non-invasive test for disease exclusion.

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity% (95%CI)</th>
<th>Specificity% (95%CI)</th>
<th>PPV% (95%CI)</th>
<th>NPV% (95%CI)</th>
<th>Positive likelihood ratio (95%CI)</th>
<th>Negative likelihood ratio (95%CI)</th>
<th>Accuracy% (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BDG</td>
<td>41.7(22.1-63.4)</td>
<td>79.6(71.6-84.6)</td>
<td>21.7(13.8-32.6)</td>
<td>90.4(87.0-93.0)</td>
<td>1.94(1.1-3.4)</td>
<td>0.74(0.5-1.1)</td>
<td>74.0(67.2-80.0)</td>
</tr>
<tr>
<td>Serum PCR</td>
<td>20.8(7.1-42.2)</td>
<td>86.8(80.9-91.6)</td>
<td>18.5(8.7-35.2)</td>
<td>88.5(86.1-90.5)</td>
<td>1.6(0.7-3.8)</td>
<td>0.9(0.7-1.1)</td>
<td>78.7(72.2-84.2)</td>
</tr>
<tr>
<td>BALF PCR</td>
<td>37.5(18.8-59.4)</td>
<td>80.3(73.2-86.2)</td>
<td>22.5(13.7-34.7)</td>
<td>89.4(85.9-92.0)</td>
<td>1.9(1.0-3.5)</td>
<td>0.8(0.6-1.1)</td>
<td>74.6(67.6-80.8)</td>
</tr>
</tbody>
</table>

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Abstract 2746

A Peptoniphilus species nova closest to P. harei from human clinical materials but which was misidentified by Bruker Biotyper as P. indolicus

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Background: Clinical isolates of a strictly anaerobic Gram-positive anaerobic coccus (GPAC) referred to reference centres in Canada and the Netherlands and indistinguishable by 16S rRNA gene sequencing (16S), have been characterized and found to possibly represent a novel Peptoniphilus species, closest to P. harei. We present features of this taxon group, derived from human clinical materials.

Materials/methods: Nearly full 16S rRNA gene sequencing, MALDI-TOF MS analyses (Bruker with Biotyper ver 7854/8468) and standard phenotypic assays, including ATB 32A, were done. Some strains have also had cellular fatty acid composition (CFAs) or grew well enough for antimicrobial susceptibility testing (AST) by broth microdilution (BMD) or by Etest

Results: Eight Canadian isolates and four Dutch isolates, recovered from various human clinical materials, were found to be closest (99.3%-99.9% similarity) to each other but f98.6% to P. harei DSM10020T accession no. NR_026358. All isolates were strictly anaerobic, non-reactive to most substrates and indol positive. CFAs were consistent with the genus. AST suggested that strains were largely susceptible to common antibiotics. Interestingly, P. harei-like strains tested by MALDI-TOF Biotyper ver 7854/8468 gave rise to high scores [2.28-2.38] towards MSPs identified as P. indolicus (identifiers ENR_0001, ENR_0003, ENR_0423, ENR_0430) as well as MSPs shown as P. harei (08_570 IBS, and 06_622IBS) [scores 2.12-2.17] but scores of <1.6 towards P. harei DSM10020T. By 16S, both P. harei like and P. harei sensu stricto had <96.9% identity with P. indolicus ATCC 29427T (accession no. NR_115509).

Conclusions: These data suggest that a new Peptoniphilus species closest to P harei, recovered from human clinical specimens exists. Next steps include characterization of the isolates by whole genome sequencing, preparing a sp nov description and arrange for corrections to Bruker Biotyper ver 8468. Furthermore, the prevalence of this new species in clinical specimens will be assessed.

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Background: Rift Valley fever is an arboviral infection endemic to most of sub-Saharan Africa and the Arabian Peninsula. It is a climate-related zoonotic infection characterized by high rates of abortion and mortality in pregnant ruminants. However, there is limited data on its effects in pregnant women. Here, we summarize and critically appraise evidence on the effects of Rift Valley fever (RVF) in pregnant women.

Materials/methods: An exhaustive search of clinical trial registries and bibliographic databases from their respective dates of inception to September 30, 2019, was conducted using a combination of MeSH terms and keywords depending on the level of term indexation for the database. There were no language or study design restrictions. Individual patient data were extracted to generate odds ratios or proportions depending on available information. Statistical analyses were conducted in R and a gap analysis performed.

Results: Our comprehensive review yielded four studies reporting 51 pregnant women infected with RVF. The relative risk of foetal loss due to maternal RVF was estimated at 4.47 (95% C.I. 1.34 to 14.91, I²=76.02%, P=0.04). However, the summary estimate is not precise given the wide confidence interval and the high amount of between-study heterogeneity. Additionally, past infection is a likely confounder given that one study assessed women over a two-year period and it is unclear if all foetal losses were a result of acute infection. The formal gap analysis shows there is very little data on the maternal effects of RVF or the management of pregnant patients with RVF.

Conclusions: The currently available evidence suggests that similar to reports in ruminants, infection with RVF virus may be associated with a substantial risk of foetal loss in pregnant women. With a more than four-fold increased risk of foetal loss in positive pregnant patients, there is a need to prioritize pregnant women as a sub-group of special interest for RVF research. Well-conducted prospective studies estimating the true incidence of adverse pregnancy outcomes in pregnant women with RVF are needed.

PROSPERO protocol number CRD42018097022

Figure: Meta-analysis comparing the risk of foetal loss in RVF positive pregnant women with that in RVF negative pregnant women

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Can adjuvanted influenza vaccine given as standard of care reduce the risk for influenza outbreaks in nursing homes: evidence from a cluster-randomized trial of 823 nursing homes

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Abstract third-party references: ClinicalTrials.Gov NCT02882100, Funding via investigator-initiated grant by Seqirus.

Background: Nursing home (NH) influenza outbreaks pose a serious threat to their frail residents and occur even in vaccinated populations. More immunogenic influenza vaccines may offer an advantage to preventing outbreaks over non-adjuvanted trivalent influenza vaccines (TIV). We conducted a large pragmatic cluster randomized controlled trial to evaluate the effectiveness of an adjuvanted TIV (aTIV) vs. TIV with a secondary outcome of NH influenza outbreaks.

Materials/methods: 823 U.S. NHs with at least 50 long-stay residents aged ≥ 65 years were cluster randomized to either the aTIV or TIV for the 2016-17 influenza season (November-May). We employed a hierarchical Bayesian analysis with weakly informative priors to evaluate the impact of the intent-to-treat vaccine assignment on the number of facilities reporting outbreaks from November-March. We collected monthly outbreak data according to standard CDC definitions (2 or more cases of flu-like illness in 72 hours or 1 laboratory-confirmed influenza case and 1 other ill resident). We adjusted for facility-level vaccination rates and resident characteristics in the final model. All analyses were performed using STAN (v2.19) and R statistical software (v3.5.3).

Results: Of 823 randomized NHs, 777 [aTIV, n=387; TIV, n=390] reported on influenza outbreaks. Facilities were similar across most covariates, except race/ethnicity. TIV homes had more African-Americans (13.7 vs. 18%). Mean outbreaks/NH/month was 0.37. Of 295 outbreaks, 133 (0.34 per facility-month) vs. 162 (0.41) occurred in aTIV vs TIV facilities, respectively. The unadjusted analysis estimated relative reduction (RR) in outbreaks as 0.82, 95% credible interval: 0.65, 1.04 [Prob. RR<1, 94.6%]. Analyses adjusted for race/ethnicity, age 85 and older, staff and resident influenza and pneumococcal vaccination rate, estimated a RR 0.78, 95% CI: 0.63, 0.99 [Prob. RR<1, 97.8%].

Conclusions: Secondary findings from a cluster-randomized pragmatic nursing home trial observed ~20% fewer influenza outbreaks with aTIV vs. TIV, a finding not previously demonstrated in any experimental setting.

Figure 1. Plot of influenza outbreaks over time. % ILI - Percentage of outpatient visits with diagnosis of influenza-like illness [Centers for Disease Control and Prevention Surveillance Data]. aTIV - Adjuvanted Trivalent Influenza Vaccine [n=387]. TIV - non-adjuvanted trivalent influenza vaccine [n=390].

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Abstract 2751

**EUCIC survey on influenza vaccination among infection control team: Action speaks louder than words**
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**Abstract third-party references:** The EUCIC Influenza Survey Investigator Group, The European Committee on Infection Control (EUCIC)

**Background:** Varying rates of annual influenza vaccination of healthcare professionals (HCPs) are observed, depending on local policies, as well as HCP knowledge and perceptions. One of the tasks of the hospital infection control team (ICT) is to ensure that HCPs are vaccinated for influenza. We aimed to describe the opinions of ICT about influenza vaccine and related factors across different countries.

**Materials/methods:** A multilingual survey was performed between May 17, 2019 and July 15, 2019 targeting the opinions and practices of ICTs regarding the 2018-2019 influenza season. The participants were reached via ESCMID and EUCIC newsletters, social media, national societies’ newsletters, national scientific associations. An online survey consisting of 23 items covering potential factors that may have influenced their decision to receive or refuse the vaccine, was administered. This anonymous and voluntary survey was a collaborative study conducted by EUCIC.

**Results:** In total, 899 participants from 56 countries were enrolled. Overall reported vaccination rate was 76%, with highest rates in Finland, Portugal, Norway and Israel (100%), and lowest rates in Turkey (39%) and Italy (68%). Influenza vaccination rate was 86% among physicians and 52% among IC nurses. Personal influenza vaccine experience (49%) and scientific authorities (48%) were the most significant factors that affected participants’ vaccination decision. Regarding the 2018-19 season, self-protection (84%) and protecting patients (74%) were the most common motivators for vaccination, whereas not being in a high-risk group (32%) and inconvenience (25%) were the most common reasons for not having been vaccinated. In multivariate analysis, Turkey (OR: 0.41, 95% CI: 0.22-0.77, p=0.006) and infection control nurses (OR:0.43, 95% CI: 0.24-0.80, p=0.007) were significantly associated with not having been vaccinated, whereas vaccination of head of infection control committee (OR: 16.04, 95% CI: 8.4-30.8, p<0.001) and free vaccine (OR: 7.56, 95% CI: 2.1-27.4, p=0.02) were the strongest predictors of having been vaccinated for influenza during 2018-19.

**Conclusions:** In this multinational study, we detected that being IC nurse, leader’s vaccination status and cost of vaccine significantly affected influenza vaccination behavior of ICT. These factors should be taken into account to plan future activities aiming to increase HCPs’ influenza vaccination coverage.

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Abstract 2752

Antimicrobial activity of aztreonam-avibactam and comparator agents tested against contemporary (2019) clinical Enterobacterales isolates

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Abstract third-party references: This study was performed by JMI Laboratories and supported by Pfizer, Inc., which included funding for services preparing this abstract.

Background: Aztreonam (ATM) is a monobactam stable to hydrolysis by metallo-β-lactamases (MBL), and avibactam (AVI) is a non-β-lactam β-lactamase inhibitor that inhibits Ambler class A, C, and some class D enzymes (e.g., ESBL, KPC, and AmpC). ATM-AVI is under clinical development for treatment of serious infections caused by Gram-negative bacteria, including MBL-producers.

Materials/methods: A total of 5,671 Enterobacterales (ENT) were consecutively collected from 47 medical centres located in Western Europe (W-EU; 22 centres in 9 countries), Eastern Europe (E-EU; 10 centres in 7 countries), Asia-Pacific region (APAC; 10 centres in 6 countries), and Latin America (LATAM; 5 centres in 4 countries), and tested for susceptibility by reference broth microdilution methods in a central monitoring laboratory (JMI Laboratories). MIC results were interpreted per EUCAST criteria. Isolates were mainly from bloodstream infections (30%), urinary tract infections (24%), and pneumonia (20%).

Results: Overall, 99.8% of isolates were inhibited at ATM-AVI MIC of ≤4 mg/L (MIC50/90, ≤0.03/0.12 mg/L), including all (100.0%) carbapenem-resistant (CRE; n=133; MIC50/90, 0.25/0.5 mg/L) and 99.1% of multidrug-resistant isolates (MDR; n=1,058; MIC50/90, 0.06/0.25 mg/L). Isolates with ATM-AVI MIC >4 mg/L (n=10) were detected in only 4 countries (Australia [2], Poland [1], Thailand [2], and Turkey [5]), and included 7 E. coli, 2 E. cloacae, and 1 K. pneumoniae. Highest ATM-AVI MIC value was only 2 mg/L in W-EU and LATAM (Table). The most active comparators were meropenem (92.2-98.9% susceptible [S], 97.1% overall), tigecycline (94.9-96.4% per US-FDA criteria; 95.6% overall), and amikacin (88.1-97.7%; 95.3% overall). Susceptibility rates for ceftriaxone, levofloxacin, and gentamicin were highest in W-EU (80.5%, 79.7%, and 89.9%, respectively) and lowest in LATAM (48.8%, 52.5%, and 63.0%, respectively), whereas susceptibility rates from piperacillin-tazobactam and meropenem were highest in W-EU (85.2% and 98.9%, respectively) and lowest in E-EU (66.4% and 92.2%, respectively). CRE rates were 1.0%, 6.0%, 2.9%, and 2.0% in W-EU, E-EU, APAC, and LATAM, respectively (2.3% overall).

Conclusions: ATM-AVI demonstrated potent activity against a large collection of contemporary (2019) Enterobacterales isolates from Europe, APAC, and LATAM, including CRE and MDR isolates. Resistance rates for comparator agents were generally higher in E-EU and LATAM compared to W-EU and APAC.

<table>
<thead>
<tr>
<th>Geographic Region (no.)</th>
<th>No. of Isolates (cumulative %) Inhibited at ATM-AVI MIC (mg/L) of:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤0.03</td>
</tr>
<tr>
<td>W-EU (2,433)</td>
<td>1,847</td>
</tr>
<tr>
<td></td>
<td>(57.0)</td>
</tr>
<tr>
<td>E-EU (531)</td>
<td>414</td>
</tr>
<tr>
<td></td>
<td>(44.5)</td>
</tr>
<tr>
<td>APAC (1,005)</td>
<td>524</td>
</tr>
<tr>
<td></td>
<td>(52.1)</td>
</tr>
<tr>
<td>LATAM (492)</td>
<td>224</td>
</tr>
<tr>
<td></td>
<td>(45.5)</td>
</tr>
<tr>
<td>CRE (133)</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>(9.0)</td>
</tr>
</tbody>
</table>

* Carbapenem-resistant isolates from all regions combined. Based on EUCAST criteria.

Presenter email address: helio-sader@jmilabs.com
Background: The aim of this study was to evaluate the risk factors for candidemia in patients with liver cirrhosis

Materials/methods: This was a multicenter case-control-control (1:2:2) study performed in four Italian tertiary centres from 2006 to 2015. Cases were patients developing candidemia. For every case of candidemia, four controls divided in two groups were selected and matched according to age, sex and model for end stage liver disease (MELD) calculated at hospital admission. Controls were defined as follows: controls A were patients undergoing blood cultures for suspected infection yielding isolation of a bacterial pathogen; controls B were patients undergoing blood cultures for suspected infection yielding negative results.

Results: During the study period 90 patients with candidemia, 180 patients with bacteremia (control A) and 180 patients with culture-negative infection (control B) were included. The mean (±SD) age of 60 (±11 years) and a prevalence of 63% of male gender. Chronic viral hepatitis (59%) was the main cause of liver cirrhosis followed by alcoholic abuse (36%). The median (IQR) MELD score at hospital admission was 17 (13-23) points. Of the 90 patients with candidemia, Candida albicans was the main isolated species (64%) followed by Candida parapsilosis (14%) and Candida glabrata (9%). Septic shock was diagnosed in 24% and acute-on-chronic liver failure (ACLF) in 56% of cases.

At multivariate analysis assessed by means of multinomial conditional regression models, factors independently associated with candidemia were previous (<30 days) ACLF [OR 2.22 [95%CI 1.09-4.54]], previous (<30 days) gastrointestinal endoscopy [OR 2.22 [95%CI 1.09-4.54]], previous (<30 days) intravenous antibiotic treatment for at least 7 days [OR 3.99 [95% CI 1.28-12.44]], presence of central venous catheter (CVC) [OR 3.75 [95% CI 1.85-12.44]] and total parenteral nutrition [OR 3.79 [95% CI 1.59-8.78]] at infection onset. Conversely, rifaximin treatment was associated with lower rate of candidemia [OR 0.38 [95% CI 0.19-0.77]].

Conclusions: We identified previous antibiotic use, gastrointestinal endoscopy or ACLF and presence of CVC especially for parenteral nutrition as independent factors associated to candidemia. Surprisingly, chronic rifaximin use was a protective factor.

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Abstract 2762

CTX-M type extended-spectrum beta-lactamase in Serratia marcescens in Japan

Hiroaki Baba*1,2, Hajime Kanamori1,2, Yuki Suzuki3, Shiro Endo4, Hisakazu Yano3, Mitsuo Kaku5

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Background: Extended-spectrum β-lactamases (ESBLs) producing bacteria are increasing worldwide. Screening criteria for detection of ESBLs, however, are not standardized for AmpC-producing Enterobacteriaceae including Serratia marcescens, thereby masking the presence of ESBLs in AmpC-producing Enterobacteriaceae. We investigated the prevalence of ESBLs in clinical isolates of third-generation cephalosporin-resistant S. marcescens in Japan with phenotypic detection tests.

Materials/methods: We studied a total of 300 clinical isolates of S. marcescens that presented resistant to at least one of following 3 antimicrobial agents, cefotaxime, ceftazidime, and cefmetazole, collected throughout Japan between April and June 2017. Production of ESBL and AmpC were assessed by the Mastdiscs™ ID AmpC and ESBL ID Set and the boronic acid test. PCR screening for blaCTX-M, blaSHV, blaTEM, and blaOXA was performed on isolates that were phenotypically confirmed to be ESBL producers.

Results: Among the 300 isolates, 7 (2%) were both ESBL and AmpC-positive, 9 (3%) were ESBL-positive-AmpC-negative, 178 (59%) were ESBL-negative-AmpC-positive, 48 (16%) were both ESBL and AmpC-negative, and 58 (19%) isolates were “not applicable” by Mastdiscs™ ID (Figure). Among these 16 ESBL-positive isolates, 3, 4, 2, 9, 3, and 2 were possessed blaCTX-M-1G, blaCTX-M-2G, blaCTX-M-9G, blaSHV, blaTEM, and blaOXA respectively, and one isolate was PCR-negative. In addition to all he ESBL-positive isolates, one ESBL-negative and one “not applicable” isolates met the criteria for ESBL production in the boronic acid test. blaSHV was detected in the “not applicable” isolate.

Conclusions: Our data suggests that blaCTX-M groups of ESBLs are spreading among clinical isolates of third cephalosporin-resistant S. marcescens in Japan. Detection of ESBLs among clinical S. marcescens encourage clinicians to select more appropriate antibiotics.

Figure. Results of Mastdiscs™ ID AmpC and ESBL ID Set and PCR-screening among isolates of Serratia marcescens

Presenter email address: hbaba48@med.tohoku.ac.jp
Abstract 2766

Treatment of community-acquired bacterial brain abscess: an international multi-centre survey

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Background: Treatment of brain abscess relies primarily upon expert opinion and may differ within and between countries.

Materials/methods: Using an internet-based questionnaire, we conducted an international, multi-centre survey of real-life treatment of community-acquired BA in France, Sweden, Australia, and Denmark. Study participants were also asked to prioritise future randomised controlled trials (RCTs) on brain abscess treatment from 1 (High priority) to 6 (Low priority). Switch to oral therapy before completion of four weeks of intravenous (IV) antibiotics for brain abscess was categorised as ‘early transition to oral antibiotics’.

Results: During November 2019, 270 infectious diseases specialists (43% female) participated in the survey from France (39%), Sweden (32%), Australia (20%), and Denmark (9%). Respondents worked primarily at university hospitals (67%) with >600 beds (50%) and an on-site neurosurgical department (60%). National guidelines for treatment of BA were available in France, Sweden, and Australia.

Preferred empiric antibiotic regimen were cefotaxime (148/235, 63%) or ceftriaxone (53/235, 23%) combined with metronidazole for varying durations according to neurosurgical treatment (Figure). Routine treatment with follow-up oral antibiotics after completion of a standard IV regimen (i.e. 4-8 weeks) was used by 105/226 (46%) respondents, while early (i.e. <4 weeks) transition to oral antibiotics was used by 114/231 (49%).

Favoured oral antibiotics for brain abscess (n=143; several answers possible per respondent) included trimethoprim-sulfamethoxazole (41%), amoxicillin and metronidazole (37%), clindamycin (29%), moxifloxacin (25%), and linezolid (17%). Median prioritisation scores (n=221) with interquartile ranges for future RCTs on BA treatment were: Early transition to oral antibiotics = 1 (1-2), duration of therapy = 1 (1-2), comparison of different antibiotic regimens = 3 (2-4), use of adjunctive dexamethasone = 3 (2-4), neurological aspiration versus excision = 3 (2-4), use of prophylactic anti-epileptic drugs = 3 (2-5), and intracavitary antibiotic instillation and continuous drainage versus standard therapy = 4 (3-5). Willingness to include patients into RCTs was high for early transition to oral antibiotics 198/220 (90%) and duration of therapy 207/220 (94%).

Conclusions: Duration of intravenous antibiotic treatment and use of early transition to oral antibiotics varies substantially among specialists. RCTs are needed to better define optimal treatment of brain abscess.

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Efficacy of fosfomycin-trometamol versus fluoroquinolone single-dose as prophylaxis for trans-rectal ultrasound-guided prostate biopsy

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1Saint-Louis Hospital, AP-HP, Paris, France

Background: Antibiotic prophylaxis is essential to prevent post-TURBP urinary tract infection (UTI). Fluoroquinolones (FQ), single-dose, are the recommended prophylaxis in France. Rectal carriage of FQ-resistant bacteria is associated with an increased risk of post-TURBP UTI. We aimed to estimate if Fosfomycin-trometamol (FT) could be an alternative prophylaxis of UTI in TURBP.

Materials/methods: Preliminary report of a monocentric, prospective observational cohort study, including all consecutive patients receiving single-dose FQ (FQ-arm) or single-dose FT (FT-arm) according to physician choice for TURBP. Primary endpoint was the occurrence of post-TURBP UTI. Secondary endpoints were post-TURBP antibiotic intake and hospitalization. Relative-Risk (RR) and corresponding 95% Confidence-Intervals (95%CI) were measured using logistic regression.

Results: 222 men were enrolled from April 2017 to June 2019, 141 (64%) received FQ and 81 (36%) FT. Of which, 100 (45%) had a history of prostate biopsy. Median age was 67.6-years [IQR 61.4-66.8], Charlson score 3 [IQR 3-5], and prostate volume 45 grams [35-62]. 123 (55%) had traveled abroad within 12 months, and 69/221 (31%) had received antibiotics within 6 months. 8 (4%) reported having UTI in the past 3 months. Single-dose FQ-prophylaxis was ciprofloxacin in 128 (58%) patients, ofloxacin in 7 (3%) and levofloxacin in 6 (3%). Time between prophylaxis intake and prostate-biopsy was 2.5 hours [2.1-2.9]. Two-hundred and two (91%) had two visits, with a median time between biopsy and post-biopsy visit of 29-days [22-36]. A total of 197 (89%) patients were evaluable for primary and secondary endpoints. Overall, 24 (12%) had a post-TURBP UTI: 17/116 (15%) in FQ-arm versus 7/81 (9%) in FT-arm (p=0.295). After adjustment on Charlson' score and intake of antibiotics in the previous 6 months, no statistically significant difference was measured between FQ and FT-arms (aRR=0.55 [95%CI 0.21-1.44], p-value=0.222). For secondary endpoints, 14/116 (12%) received antibiotics after TURBP in FQ-arm versus 7/81 (9%) in FT-arm (RR=0.70 [95%CI 0.27-1.82], p-value=0.462); and 13/116 (11%) were hospitalized after TURBP in FQ-arm – 9 related to UTI – versus 3/81 (4%) in FT-arm – 1 related to UTI (RR=0.30 [95%CI 0.08-1.11], p-value=0.071). The rate of adverse events was similar between FQ and FT-arms (RR=0.3 [95%CI 0.1-1.1], p-value=0.071).

Conclusions: Rates of post-TURBP UTI were similar following FT or FQ prophylaxis. A randomized comparison of the two strategies is warranted to establish FT as a potential alternative to FQ.

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Classifying the *Mycobacterium tuberculosis* complex into the main phylogenetics lineages (Seville, Spain, 2015-2019): is something changing?

Veronica Gonzalez Galan¹, María José Torres Sanchez², Luque Rafael¹, Navarro Veronica¹, Medina Gallardo Juan Francisco¹, Raquel Valencia³, Briones Eduardo⁴, Javier Aznar*³

¹Hospital Universitario Virgen del Rocío/IBIS/CSIC/US, Sevilla, Spain, ²universidad de Sevilla, Sevilla, Spain, ¹Hospital Universitario Virgen del Rocío/IBIS/CSIC/US, Sevilla, Spain, ³Unidad de Salud Pública Sevilla, Distrito Sevilla, SAS, Sevilla, Spain


**Background:** Genotyping *Mycobacterium tuberculosis* complex (MTBC) strains plays an increasing role for understanding the epidemiology of tuberculosis. Some lineages have been associated with a wide geographic distribution, such as the MTBC lineage L4, which is the most predominant around the world. However, other lineages are restricted to certain areas. We used complementary genotyping methods to classify strains from Seville (southern Spain) into the six main human-associated lineages and sub-lineages of MTBC.

**Materials/methods:** The molecular typing was performed by applying the 43-spacer spoligotyping following standard protocols and SNP-typing was performed by a Taqman real-time PCR according to Stucki et al, 2012 protocols. All the 462 MTBC strains used in this study were from clinical samples from an ongoing molecular epidemiology study on tuberculosis in University hospital Virgen del Rocío, Seville, Spain since 2015.

**Results:** We studied 370 out of 462 strains (80.08%), classifying 91% strains into the main phylogenetic lineages. The typing results are shown in table 1. The most frequent lineage detected was L4 corresponding to 95% (n = 355) of all MTBC strains, followed by East Asian L2 with 1.62% (n = 6). L5 and L6 were the less frequent lineages with 2 and 4 cases, respectively. The most frequent sub-lineages identified were L4.1.2 (Haarlem family) with 23.24% (n = 6) and also we found 4 cases (1.08%) the emerging Uganda genotype of MTBC.

**Table 1. MTBC lineage 2015-2019.**

<table>
<thead>
<tr>
<th>MTBC lineage</th>
<th>LSP name</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Indo-OCEANIC</td>
<td>1 (0.27%)</td>
</tr>
<tr>
<td>2</td>
<td>East Asian</td>
<td>6 (1.62%)</td>
</tr>
<tr>
<td>3</td>
<td>East-African-Indian</td>
<td>2 (0.54%)</td>
</tr>
<tr>
<td>4</td>
<td>Euro-American</td>
<td>355 (95.95%)</td>
</tr>
<tr>
<td>5</td>
<td>M.Africanum West African I</td>
<td>2 (0.54%)</td>
</tr>
<tr>
<td>6</td>
<td>M.Africanum West African II</td>
<td>4 (1.08%)</td>
</tr>
<tr>
<td>total cases</td>
<td></td>
<td>370</td>
</tr>
</tbody>
</table>

**Conclusions:** This results shows the MTBC diversity circulating in Seville. Throughout the five years of study we have found strains belonging to 6 different lineages. Lineage 4 being the most prevalent (until November 2019). However, the lineages founded, that are limited to specific geographical areas such as the African continent and Asia make us aware of new patterns of tuberculosis transmission in our area.

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Ozenoxacin, a topical fluoroquinolone, demonstrates activity versus methicillin-susceptible and methicillin-resistant Staphylococcus aureus, and Streptococcus pyogenes wound isolates including fluoroquinolone-, fusidic acid- and mupirocin-resistant strains

Philippe Lagacé-Wiens*1,2, Heather Adam3, Melanie Baxter2, James Karlowsky1,2, George Zhanel2

1Saint Boniface Hospital, Shared Health, Winnipeg, Canada, 2University Of Manitoba, Winnipeg, Canada, 3Health Sciences Centre Winnipeg, Shared Health, Winnipeg, Canada

Background: Ozenoxacin (OZE) is a novel fluoroquinolone used topically for the treatment of impetigo formulated as a 1% w/w cream (10 mg/g). The purpose of the study was to assess the in-vitro activity of OZE and comparator agents against wound isolates obtained from the Canadian Antimicrobial Resistance Alliance-CARA/Health Canada partnered national surveillance study CANWARD.

Materials/methods: 751 wound isolates from CANWARD 2007-2018 were selected including 422 MSSA, 283 MRSA, and 46 Streptococcus pyogenes. Antimicrobial susceptibility testing was performed using CLSI methods (M07, 11th edition, 2018). MICs were interpreted using CLSI M100 (2018) criteria, except where indicated in the table.

Results: The activity of ozenoxacin versus various resistance phenotypes of MSSA, MRSA and S. pyogenes is depicted in the table below.

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>MSSA (MIC90/MICmax) (mg/L)</th>
<th>MRSA (MIC90/MICmax) (mg/L)</th>
<th>S. pyogenes (MIC90/MICmax) (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>N=422 0.004/0.25</td>
<td>N=293 0.12/0.12</td>
<td>N=46 0.03/0.03</td>
</tr>
<tr>
<td>Ciprofloxacin MIC ≤ 1 mg/L</td>
<td>N=281 0.004/0.004</td>
<td>N=61 0.04/0.04</td>
<td>N=41 0.03/0.03</td>
</tr>
<tr>
<td>Ciprofloxacin MIC &gt; 2 mg/L</td>
<td>N=141 0.12/1</td>
<td>N=190 0.12/0.12</td>
<td>N=4 Range 0.01-0.03</td>
</tr>
<tr>
<td>Clarithromycin-resistant</td>
<td>N=134 0.12/1</td>
<td>N=216 0.12/0.12</td>
<td>N=1 MIC = 0.33</td>
</tr>
<tr>
<td>Clarithromycin-resistant</td>
<td>N=37 0.29/1</td>
<td>N=27 0.12/0.12</td>
<td>N=1 MIC = 0.03</td>
</tr>
<tr>
<td>Fusidic acid-resistant</td>
<td>N=39 0.004/0.28</td>
<td>N=20 0.004/0.12</td>
<td>N=45 0.03/0.03</td>
</tr>
<tr>
<td>Fusidic acid MIC &gt; 206 mg/L</td>
<td>N=7 0.12*</td>
<td>N=10 0.12/0.12</td>
<td>N=1 MIC = 0.015</td>
</tr>
<tr>
<td>Mupirocin MIC &gt; 4 mg/L</td>
<td>N=13 1/1</td>
<td>N=0</td>
<td>N=1 MIC = 0.03</td>
</tr>
<tr>
<td>Mupirocin MIC &gt; 256 mg/L</td>
<td>N=6 0.12*</td>
<td>N=40 ≤ 0.02/0.12</td>
<td>N=0</td>
</tr>
</tbody>
</table>

* EUCAST breakpoint (MIC >1 mg/L)
** median MIC

Conclusions: Ozenoxacin MIC90 values are low (≤ 1 mg/L) for all species and resistant subgroups of MRSA, MSSA and S. pyogenes tested, including strains with elevated MIC to fluoroquinolones, macrolides, clarithromycin, fusidic acid and mupirocin. Ozenoxacin is very active (MIC90 ≤ 0.12 mg/L, MICmax = 0.5 mg/L) against all MRSA strains tested.

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Measles outbreak in Catania: a retrospective study and clinical revision

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1ARNAS Garibaldi Hospital, Catania, Italy, 2University of Catania, Catania, Italy

**Background:** Measles is a highly contagious air-born exanthematous disease caused by **measles morbillivirus**. Despite the introduction of recommended vaccination since the early 1990s in Italy, measles outbreaks keep occurring due to a suboptimal vaccination coverage.

**Materials/methods:** In our study we described retrospectively the latest measles outbreak in Catania occurred in 2018. First we looked to all clinical records with discharge diagnosis of measles in Garibaldi Hospital. Then we collected epidemiological and clinical characteristics of patients hospitalized in the Infectious Disease Department during the period from January to December 2018.

**Results:** 199 cases were reported in the study period. 68(34.2%) were discharged from the Emergency Department with symptomatic treatment, 18(9%) were admitted in Pneumatology department, 5(2.5%) were recovered in ICU, of whom 3(1.5%) died for severe measles pneumonia. 108(54.3%) were admitted in Infectious Disease Department: 58(53.7%) were men, median age was 27 (IQR 21-31), 106(98.1%) were not vaccinated. Median days of hospitalization were 7 (IQR 6-9), median days of fever (including days before the hospitalization) were 9 (IQR 8-12). In their clinical history 92 patients (85.1%, p<0.001) had diarrhea as a prodromal symptom. Organ impairment is summarized in Table 1, 17 patients (16%) had multi-organ impairment. Leukopenia (WBC <4000/mmc) was found in 46 patients (43%, p=0.03), and thrombocytopenia (PLT<150.000/mmc) in 68 patients (63.5%, p=0.02). Antibiotic therapy was administered to 88 patients (81.5%), 33 multi-antimicrobial therapy, 55 mono-antimicrobial therapy; amoxicillin/clavulanic acid was the most administered (77 patients). Antibiotic therapy has not reported reduction in terms of days of fever and it prolonged days of hospitalization (p=0.027). Nevertheless no fatalities occurred.

**Conclusions:** Measles still represent a pernicious condition for community. Our study demonstrates the necessity of both high level awareness in health care personnel and approved clinical management algorithms to face any possible future measles outbreaks. Last but not least, vaccination coverage must be improved to prevent future outbreaks.

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Comparison of intermittent versus continuous infusion vancomycin therapy for severe patients in intensive care unit

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¹Pontifical Catholic University of Paraná, Curitiba Campus, Laboratory of Emerging Infectious Diseases - Department of Medicine, Curitiba, Brazil, ²A.C. Camargo Cancer Center, Department of Infectious Disease, São Paulo, Brazil

Background: Patients admitted to intensive care unit (ICU) are under risk for infection by methicillin-resistant Staphylococcus aureus (MRSA). Vancomycin continues to be an important therapeutic option for MRSA treatment. Serum trough level target (15-25 μg/mL) may be achieved by continuous infusion (CI) or intermittent infusion (II), but with different delay. Aim of this study was to compare pharmacokinetic characteristics between II and CI vancomycin for critically-ill patients admitted to intensive care units.

Materials/methods: II of vancomycin was administered for 60 minutes and prescribed as a loading dose of 30 mg/kg and continued with 15mg/kg q12h. CI was prescribed as a loading dose of 30mg/kg followed by 30mg/kg on constant infusion pump. Blood samples from vancomycin II group were collected 1h before third dose, 1h, 8h and 24h after third dose infusion. Blood samples from vancomycin continuous infusion group were collected 1h after loading dose, 12h, 24h, 36h and 48h after continuous infusion initiation. Mann-Whitney or Student’s t-test and Chi-square or Fisher’s exact test were used. Statistical significance was considered if \( P < 0.05 \).

Results: Twenty-three patients were included. Eleven on CI group and twelve on II group. CI and II groups median age were 49 years. Median APACHE-II score [IQR] were 15 [14-18.5] in CI group and 17 [10-21] in II group. Site of infections were pulmonary (n=12), central nervous system (n=4), skin and soft tissue (n=3), abdominal (n=2) and catheter-related (n=2). Death rate was 36% (n=4) in CI group and 31% (n=4) in II group. Median serum concentration on CI group at H1, H12 and 24-hour were 23.9 μg/mL [9.5-38], 19.6 μg/mL [14.4-23.7] and 23.59 μg/mL [14.52-28.97], respectively. Median serum concentrations on II group at 23-hour and 25-hour were 12.30 μg/mL [7.275-18.125] and 17.58 μg/mL [12.5-22.5], respectively. Median AUC[23-48h] from II group was 357.2 mg.h/L and from CI group was 530.2 mg.h/L (p=0.559) (Figure).

Conclusions: Vancomycin CI reached steady state earlier, which guarantee therapeutic levels from the first day and makes it possible to manage therapeutic drug monitoring faster.

Figure. Serum level of vancomycin in critically-ill patients treated with continuous (n=11) and intermittent (n=12) infusion of intravenous vancomycin.

Presenter email address: jpmarochi@hotmail.com
**Abstract 2779**

**Infectious complications of patients with breast cancer treated with palbociclib: unexpected serious and opportunistic infections**

Martín Luck*, Patricia Costantini1, Gabriela Zapata2, Patricia Garcia1, Adriana Sorge1, Mara Vallejos1, Vanessa Lopez2, Andrea Aguilar2, Javier Serer1, Mariana Savignano2, Gustavo Roganovich2, Laura Albi2, Marcelo Bronzi3, Diana Bucher3, Valeria Caceres2

1Universidad de Buenos Aires, Instituto de Oncología Angel H. Roffo [Infectious Diseases Department], Buenos Aires, Argentina, 2Universidad de Buenos Aires, Instituto de Oncología Angel H. Roffo [Unit of Breast and Gynecologist Tumors Oncology Department], Buenos Aires, Argentina, 3Universidad de Buenos Aires, Instituto de Oncología Angel H. Roffo [Microbiology Department], Buenos Aires, Argentina

**Background:** An increasing number of patients with solid tumours receive target or biologic therapy due to its efficacy and safety compared with standard chemotherapy. Palbociclib is a cyclin-dependent kinase CDK4 and CDK6 inhibitor approved for the treatment of HER-2 negative metastatic breast cancer. The most common adverse event is neutropenia, but febrile neutropenia is infrequent (1,8%). In Phase II and III trials, 34 to 59% incidence of infectious complications has been reported with no mortality or opportunistic infections. The objective of this study is to describe the characteristics of infectious complications in patients receiving Palbociclib.

**Materials/methods:** Prospective, observational and descriptive study of moderate or severe infectious complications that required infectious disease consultation and/or hospital admission in women with metastatic breast cancer that received Palbociclib from March 2016 until March 2019.

**Results:** 130 patients received Palbociclib. 95/130 (73%) received Palbociclib/Letrozol and 35/130 (27%) Palbociclib/Fulvestrant. Clinical characteristics are shown in the table. 21/130 patients (16%) had 30 episodes of moderate or severe infection, 60% of them during the first 4 cycles of Palbociclib. Out of thirty episodes, two had less than 500 neutrophils/mm$^3$, and 12 less than 800 lymphocytes/mm$^3$. 13/30 episodes were microbiologically and 17 clinically documented infections. Sources of infection were skin and soft tissue (35%), respiratory (30%), Herpes simplex and Zoster (16%), urinary tract infections (5,5%) and others (13,5%). Among microbiological documented infections, 83% were bacterial and 17% fungal. Several opportunistic infections were identified: 3 Varicella zoster virus, 2 Aspergillus spp, 1 Nocardia spp, 1 Roseomania gilardii. In 14 episodes, admission was required, 4 in the ICU. Four patients died.

<table>
<thead>
<tr>
<th>Mean age (range)</th>
<th>58 years (28-91)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site of metastatic disease</td>
<td></td>
</tr>
<tr>
<td>Bone</td>
<td>86/130 (66%)</td>
</tr>
<tr>
<td>Visceral</td>
<td>58/130 (45%)</td>
</tr>
<tr>
<td>Others</td>
<td>74/130 (57%)</td>
</tr>
<tr>
<td>Previou treatment</td>
<td></td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>66/130 (51%)</td>
</tr>
<tr>
<td>Hormone therapy</td>
<td>74/130 (57%)</td>
</tr>
<tr>
<td>None</td>
<td>42/130 (32%)</td>
</tr>
</tbody>
</table>

**Conclusions:** 16% of 130 patients had at least one episode of moderate/severe infection, of which 46% required admission. Most of them in non-neutropenic patients. Four patients died.

Opportunistic infections not previously described were documented in patients that received no other immunosupression. More prospective studies are required for a proper characterization of infectious complications associated with Palbociclib.

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Amikacin probability of target attainment in critically ill oncological patients: results from a prospective observational cohort.

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Background: Aminoglycosides are major therapeutic options against resistant gram-negative bacilli (GNB). Once important variability in pharmacokinetic/pharmacodynamics parameters between populations is observed, probability of target attainment (PTA) from general populations may not be used to critically-ill oncological patients. The aim of this study was to evaluate PTA from extended interval amikacin regimen in oncological patients admitted to intensive care unit (ICU).

Materials/methods: This was an observational prospective cohort study from a brazilian cancer center. Patients with amikacin prescription, admitted to ICU, > 18 years, and diagnosed with oncological disease were included. Amikacin infusion occurred during 30 minutes and blood samples were collected until 30 minutes from infusion end (Cmax) and on day-after (Cmin) to every infused dose. According protocol, PD target was a ratio of 10 between Cmax and minimal inhibitory concentration (MIC). Clinical and laboratorial data were collected. Monte Carlo simulation was conducted to predict PTA in > 90% of patients using MICs 2, 4 and 8 mg/L. Elimination rate constants and volumes of distribution were calculated assuming a one-compartment model pharmacokinetics.

Results: Fifteen patients were included. Each patient provided between one and four pairs of concentrations (Cmax-Cmin). Ten (66%) patients were male, median age was 66 [28-74], median weight was 74.4 Kg [69-83] and septic shock was diagnosed in 7 (47%). Median albumin plasma level was 1.9g/dL [1.5-2.1] and Creatinine Clearance (ClCr) was 64 ml/min [28-150]. Median amikacin first dose and Cmax were 18mg/Kg [14-28] and 46.8 mg/L [34.9-63.8], respectively. Median elimination rate constant (kel) was 0.085 [0.05-0.10] and volume of distribution (Vd) was 0.36 L/Kg [0.30-0.44]. PTA in all included patients using MIC of 2, 4 and 8 were 8.66, 17.32 and 34.63mg/Kg, respectively (Figure). Furthermore, considering only patients with ClCr < 60ml/min, PTA using MIC of 2, 4 and 8 were 7.32, 14.65 and 29.29mg/Kg, respectively.

Conclusions: Amikacin higher doses than 15-25mg/kg on critically-ill oncological patients are needed to achieve PD considering MIC of 8mg/L regardless of ClCr. More studies are needed to understand inter-individual variability of amikacin parameters among oncological patients.

Figure. Amikacin PTA from critically-ill oncological patients using MICs of 2, 4 and 8mg/L.

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Background: Carbapenem-resistant Enterobacteriaceae (CRE) infectious disease became a notifiable disease since 2014 under the infectious diseases control law of Japan. In addition, in March 2017, a national pathogen surveillance for isolates obtained from reported CRE cases was launched to reveal the molecular epidemiology of CRE infections.

Materials/methods: Isolates, mainly from reported cases of CRE infection, were collected and sent to local public health laboratories. CRE was defined as Enterobacteriaceae resistant to meropenem (minimum inhibitory concentration [MIC] ≥ 2 µg/mL), or to both imipenem (MIC ≥ 2 µg/mL) and cefmetazole (MIC ≥ 64 µg/mL). All isolates were subjected to the disk diffusion test to screen for β-lactamase production according to the provided standardized testing protocol. All isolates were also tested for the four major carbapenemase genes (bla<sub>IMP</sub>, bla<sub>NDM</sub>, bla<sub>KPC</sub>, and bla<sub>OXA-48-like</sub>) by the PCR.

Results: Since the beginning of CRE pathogen surveillance, PCR results for 2587 isolates have been reported. The most prevalent was Klebsiella aerogenes (918, 35.5%), followed by Enterobacter cloacae (730, 28.2%), Klebsiella pneumoniae (275, 10.6%), and Escherichia coli (247, 9.5%). Among those isolates, 540 (20.9%) were carbapenemase gene-positive Enterobacteriaceae (CPE). K. aerogenes was the most prevalent species among tested CRE isolates. However, only three (0.3%) isolates were CPE compared to 537 (32.2%) for non-K. aerogenes isolates. Among CPE isolates, the most prevalent carbapenemase gene was bla<sub>IMP</sub> (488 isolates, 90.4%), which is a known domestic gene in Japan. Among the isolates harboring bla<sub>IMP</sub>, E. cloacae (157, 32.2%) was most prevalent species, followed by K. pneumoniae (123, 25.2%) and E. coli (114, 23.4%). There were 39, 13, and four isolates with bla<sub>NDM</sub>, bla<sub>KPC</sub>, and bla<sub>OXA-48-like</sub>, respectively. About 70% of these non-bla<sub>IMP</sub> CPE isolates were obtained from patients with no or an unknown linkage with travel to foreign countries. The remainder of the isolates had epidemiological linkages with mainly foreign Asian countries such as Vietnam, China, and India.

Conclusions: The national pathogen surveillance system revealed that bla<sub>IMP</sub>-positive E. cloacae was most common among CPE isolates in Japan. Increasing reports of bla<sub>NDM</sub>-positive isolates from cases without international travel may reflect sustained local transmission from imported cases.

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Abstract 2789

**Detection and quantification of hepatitis C Virus in cadaveric tissue donors’ blood using different molecular kits**

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**Background:** Tissues from cadaveric donors can be applied in several clinical condition, however, despite rigorous microbiological and viral screening of tissues donors, transmission of infectious diseases has been reported, such as hepatitis C virus (HCV). Moreover, cadaveric blood may be affected by inhibition phenomena after death. The aim of this study was to evaluate the performance, specificity, sensitivity, and accuracy of different commercial molecular tests for the detection and quantification of HCV in peripheral blood samples from cadaveric donors through artificial contamination.

**Materials/methods:** All the 20 cadaveric samples were obtained after donator or family consent term concordance. The samples were tested by spiking 1,000 IU/mL (3.00 log) of lyophilized standards of HCV 14/150 (NIBSC/WHO/2016). Samples were analyzed by XPERT HCV Viral (Cepheid), COBAS® TaqMan® HCV Test, v2.0 (Roche), and artus® HCV RG RT-PCR Kit (Qiagen). Student’s T-test and p value concordance and sensitivity, specificity and accuracy were calculated.

**Results:** Cepheid's kit could quantify all 20 cadaveric donor samples with a mean quantification of 2.50 log (SD 0.17) and 343.35 IU/ml (SD 134.36), 100% accuracy, 100% specificity and 100% sensitivity. Roche's kit showed a mean quantification of 2.62 log (SD 0.30) and 501.11 IU/ml (SD 308.96) for cadaveric donor samples, however, 2 out of 20 samples showed no detection of virus and 2 out 20 samples showed an invalid result. Moreover, 2 out 5 negative controls showed an invalid result, demonstrating 60% specificity, 80% sensitivity and 76% accuracy. For Qiagen's kit, the spiked samples showed that 8 were invalid and 12 did not have virus detected, while the negative controls showed that 4 were invalid and 1 did not have virus detected, demonstrating that the test had 0% accuracy, 20% specificity and 0% sensitivity (Figure 1).

**Conclusions:** The evaluation and comparison of different kits and brands showed a wide variability in cadaveric samples. Qiagen's kit did not present satisfactory results, while Roche and Cepheid kits can be applied for tissue donors screening for HCV with more than 1,000 IU/ml.

**Figure 1.** Boxplot indicating HCV [IU/ml] mean detection and SD among the brands for cadaveric donor samples by Student’s T-test.

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Evaluation of biofilm formation and removal efficacy of three medical-device detergents by bacterial and yeast species

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Background: Biofilm formation is a major risk upon the reuse of chronic devices and physical cleaning is essential before disinfection. This study was performed to evaluate the efficacy of enzymatic and non-enzymatic detergents against biofilms formed by various bacterial and yeast species.

Materials/methods: Biofilm removal by two enzymatic agents, Empower™ and Cidezyme™, and a non-enzymatic detergent, Matrix mint™, was tested in comparison to chlorine bleach and distilled water (DW). Staphylococcus aureus RN9120 (SA9120), Enterococcus faecalis clinical isolate (CI), Escherichia coli ATCC35218 and CI, Klebsiella pneumoniae CI, Pseudomonas aeruginosa ATCC27853, Candida albicans ATCC14053, Candida auris CI, and Trichosporon asahii CI were used for the test, with S. aureus RN6607 (SA6607) as the biofilm-negative control. After 72-hour incubation of the test organisms in tryptic soy broth (TSB) and 96-well polystyrene plates, a residual biofilm mass was measured by crystal violet staining after rinsing with the detergents with or without incubation for 30 minutes at room temperature (RT) and 37°C.

Results: All strains showed significant biofilm formation with a mean optical density at 620 nm (OD₆₂₀) ranging from 0.61 to 1.44, while SA6607 did not (OD₆₂₀: 0.10). SA9120 fully produced biofilms only when 4% NaCl was added to TSB. Compared to DW, Empower™ and Cidezyme™ significantly reduced (>50% of OD₆₂₀ at 37°C) biofilm masses for all strains except E. faecalis, T. asahii, and C. auris. Matrix mint™ did not reduce biofilms significantly at any condition.

Conclusions: Biofilm formation and detergent efficacy vary according to the bacterial and yeast species. Especially, E. faecalis, C. auris, and T. asahii biofilm were resistant to detergent treatment under all conditions.

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Abstract 2791

First epidemiological report on colistin- and carbapenem-resistant Enterobacteriaceae isolates obtained from selected tertiary hospitals in south-eastern Nigeria

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Background: Colistin is the last line of treatment reserved for Enterobacteriaceae isolates that have become resistant to drugs including the cephalosporins and carbapenems. However, there have been reports of high prevalence of carbapenem resistance in other regions of Nigeria. This study aimed at determining the occurrence of carbapenem and colistin resistant Enterobacteriaceae in clinical isolates obtained from tertiary hospitals in South-Eastern Nigeria. One tertiary hospital was selected from each of the five states that make up the region.

Materials/methods: A total of 400 Enterobacteriaceae isolates obtained from the medical microbiology laboratories were used for this study. The total number of isolates obtained from each hospital was 77, 103, 116, 52 and 52 from FMC Umuahia, AEFUTHA, ESUTH, ISUTH and COOUTH respectively. Colistin resistance was detected using broth microdilution method. Four tubes were used having concentrations of 2µg/ml, 4µg/ml, 6µg/ml and 8µg/ml of colistin sulphate (Oxoid, Batch number 2372007). Resistance to carbapenem was detected using disk diffusion method with disks containing 10µg each of ertapenem, imipenem, meropenem and doripenem. Results were interpreted based on CLSI and EUCAST version 8.1 guidelines. An isolate was recorded as being carbapenem resistant if it showed resistance to all the carbapenems tested. Data was analyzed using SPSS version 20.0

Results: Overall, colistin resistance was detected in 103 (25.75%) isolates while carbapenem resistance was observed in 117 (29.25%) isolates in tertiary hospitals in South-eastern Nigeria. From each of the states, colistin resistance was observed in 16 (20.78%), 29 (28.16%), 38 (32.76%), 11 (21.15%) and 9 (17.31%) from isolates obtained from FMC Umuahia, AEFUTHA, ESUTH, ISUTH and COOUTH respectively. Also, carbapenem resistance detected in isolates obtained from these hospitals were; 19 (24.68%), 30 (29.13%), 39 (33.62%), 15 (28.85%) and 14 (26.92%) respectively.

Conclusions: There was a high rate of colistin and carbapenem resistance in all the tertiary hospitals in South-eastern Nigeria and these calls for strict infection control measures to prevent further decline. This is because colistin resistance when fully established may result in situations worse than the era before the discovery of antibiotics.

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Abstract 2792

Empowering nurses to assess patient-reported antibiotic allergies: a pilot implementation study of a validated antibiotic allergy assessment tool

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Abstract third-party references: Austin Health

Background: Up to 23% of patients with cancer report an antibiotic allergy. A documented antibiotic allergy has significant impacts on morbidity, mortality and medication safety. However, 50% of documented penicillin allergies are low-risk and potentially amenable to direct de-labelling or removal following oral provocation. The aim of this study was to evaluate the feasibility of implementing a nurse-led antibiotic allergy assessment tool (AAAT) at point-of-care.

Materials/methods: Two weeks prior to implementation of the AAAT, an education package, comprising of two 20-minute face-face education sessions, was delivered to hematology nurses at Austin Health (Melbourne, Australia). The haematology ward implemented the AAAT on the 01/04/19 and nurses were encouraged to integrate the AAAT into their routine admission procedure. The results following this intervention were audited from 01/04/19 to 31/10/19. Completeness of antibiotic allergy documentation pre/post allergy assessment, referral of low-risk allergies to the antibiotic allergy service, and number of allergies de-labelled by the antibiotic allergy service was collected for patients (≥18 years) admitted to the ward with a reported antibiotic allergy. An independent AMS pharmacist evaluated the accuracy of the antibiotic allergy assessments by reviewing blinded nurse completed AAATs.

Results: 57 patients were included in the 6-month audit. During this period a total of 80.7% (46/57) patients had an allergy assessment undertaken by nurses using the AAAT. At the time of admission 69.6% (32/46) of patients identified had allergies with complete documentation (substance, reaction type and severity), which increased to 84.8% (39/46, p = 0.14) when the same patients were assessed by nurses using the AAAT. Of the antibiotic allergy assessments completed by nurses, 93.5% (43/46) were concordant with the assessment by the independent AMS pharmacist. 52.2% (24/46) of patients had allergies that were assessed as low-risk, of which 87.5% (21/24) were referred to the antibiotic allergy service. Of the 24 patients that were referred to the antibiotic allergy service with low-risk allergies 41.7% (10/24) had their allergy de-labelled.

Conclusions: This audit highlights the value of empowering nurses to accurately assess antibiotic allergies at point-of-care using a validated tool. The AAAT improved antibiotic allergy documentation which is central to modern AMS activity.

References:

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Abstract 2797

**Intravenous administration of personalised cocktail of bacteriophages as salvage therapy in combination with ceftazidime/avibactam in patients with relapsing *Pseudomonas aeruginosa* bacteraemia associated with intravascular implants: lesson to be learned from two cases**

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**Background:** Lytic bacteriophages trigger bacterial lysis through their multiplication in an exponential and self-sustained reaction. They have a high therapeutic potential in patients with implant-associated infection, as they have a synergistic activity with antibiotics on biofilm-embedded bacteria.

**Materials/methods:** We managed 2 patients (64, 67 yo) with relapsing *P. aeruginosa* bacteremia associated with intravascular implants (prosthetic aortic valve, coil infection following bronchial artery embolization) for whom surgery was impossible or at risk of death. Both of them experienced >6 relapses in the previous year. After discussion with the French health authority, 3 bacteriophages produced following Good Manufacturing Practice (GMP) guidelines were selected by Pherecydes based on their activity (Panel A). Hospital pharmacist mixed each phage (1 ml of 1x10\(^{10}\) PFU/ml) extemporaneously as "magistral" preparation (final dilution 1x10\(^{8}\) PFU/mL). Bacteriophages quantification before and after the mix and in the blood of the first patient were performed to determine the optimal way of preparation and administration. Phages were administered every 2 or 3 days, during 10 to 21 days in combination with cedtazidime/avibactam prescribed during 6 weeks, if possible in combination with another active drug (fosfomycin or colistin).

**Results:** Phages were administered to the first patient during a 6 hours infusion with an electronic pump. Depending on the filter used, we observed a decrease of the titer in the final solution: no bacteriophages were detected in the line, as well as in the patient’s blood. As this patient experienced a relapse, direct (5 min) intravenous injections of phages were then performed, after using the adequate filter. One bacteriophage was detected in the patient’s blood. Blood cultures became negative. A new prosthetic valve exchange was done, and postoperative cultures were now negative (panel B). The second patient also received direct IV injections following the same process, and blood cultures remained negative during the three months follow-up.

**Conclusions:** The type of filter used for the magistral preparation and the duration of the perfusion influenced the phage titer, as the titer in the patient’s blood. Personalized GMP bacteriophage therapy has the potential to be used as salvage therapy of *P. aeruginosa* intravascular implant infections.

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A Prospective randomised controlled trial comparing the effectiveness of smartphone video directly-observed therapy (VDOT) versus in-person DOT in newly-diagnosed pulmonary tuberculosis patients

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Background: In-person directly observed treatment (DOT) has been the standard of care in tuberculosis for improved drugs adherence. But it is still inconvenient for patients and service providers. Video directly observed therapy (VDOT) has been conditionally recommended as an alternative to DOT. But the evidence was graded weak due to few randomized controlled trials available and more recently, smartphone apps have been developed that enable video clips to be recorded and forwarded for later viewing smartphone (VDOT). The objective is to compare treatment successful and drugs adherence rate between smartphone VDOT versus in-person DOT

Materials/methods: A prospective randomized controlled study was conducted in newly diagnosed pulmonary tuberculosis patients in Songklanakarind Hospital. We randomly assigned participants to either smartphone VDOT (daily remote observation using LINE app) or in-person DOT until treatment completion. In VDOT group, patients were trained to record and send videos of every dose ingested 7 days per week using a smartphone app. Authorized doctor or trained treatment observer view these videos through a password-protected application. In-person DOT, we designed for use family-based DOT technique. Treatment successful and drugs adherence rate between groups were compared. Measurement of satisfaction by using patient satisfactory score.

Results: Sixty-one patients were enrolled. We randomly assigned 30 patients to smartphone VDOT and 31 patients to family-based DOT. There were no significant differences in baseline characteristics between the two groups. In the ITT analysis for the patients who already treatment completion, Anti TB drugs adherence rate was higher in VDOT group 98% compared to 78% in family-based DOT group, \( p = 0.046 \). Treatment successful rate with smartphone VDOT group was similar to family-based DOT group 100% vs. 89%, \( p = 0.089 \). And this study found, smartphone VDOT was feasible and acceptable for patients with pulmonary tuberculosis, mean satisfactory score 10 vs. 8.5 for family-based DOT \( p=0.048 \).

Conclusions: Smartphone VDOT was feasible, acceptable and enhance high treatment successful rate, with higher anti TB drugs adherence rate when compared with family-based DOT.

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Abstracts 2020

Abstract 2801

Human parechoviruses infections in northern of Spain, 2016-2019
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Background: Human parechoviruses (HPeV) are RNA viruses which belong to the family Picornaviridae and 19 genotypes are described currently. HPeV cause gastrointestinal, respiratory diseases, fever and also serious diseases such meningitis, encephalitis and sepsis-like illness. Infections are prevalent in young children, mainly in patients under three months of age. The aim of this study is to review clinical presentation, epidemiology and characteristics of HPeV cases detected from June 2016 to July 2019 in Navarra.

Materials/methods: The retrospective study included 478 clinical samples (CSF and/or blood) from 442 patients hospitalized in Navarra (650,000 citizens) from June 2016 to July 2019. HPeV were detected using a commercial PCR, Progenie Molecular). Genotyping was performed in the CNM.

Results: HPeV were detected in 8 (1.6%) samples from 5 patients: 3 were positive in CSF and blood samples and 2 only in blood. Three cases were detected in 2017 and 2 in 2019. Median age was 21 days (interquartile range IQR: 28.5-12.5 days). Three were male. Genotypes identified were HPeV3 in 4 cases and HPeV4 in one. Clinical diagnosis of the HPeV-infected patients was febrile illness or neonatal sepsis. Symptoms were: fever (5/5), irritability (4/5), rash (3/5), gastrointestinal illness (3/5), mild respiratory illness (2/5), vomiting (0/5), neurological disorders (0/5). In 4 cases, CSF biochemistry was: median white cells 2.5 leucocytes/mm3 (IQR: 0.25-4), median red blood cells 192 hematies/mm3 (IQR: 1.-1595), median glucose 51mg/dL (46.75-71.75), median protein 46.5g/L (38-50.95). There were not any neurological sequels (0/5). The study of stools was performed in 2 of the patients and in both HPeV was detected.

Conclusions: All HPeV cases were children under three months of age with febrile illness or neonatal sepsis. HPeV infections are characterized by no pleocytosis and normal glucose and proteins levels. It is important to include HPeV detection in the routine diagnosis of infections in young children with febrile illness or neonatal sepsis, being CSF or blood the most suitable samples for it. Stools are not invasive samples which could be useful

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Evaluation of the RIDA GENE CAP Bac real-time PCR assay for diagnosis of community-acquired pneumonia from human bronchoalveolar lavage (BAL)

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Background: Community acquired pneumonia (CAP) is the most frequently registered infectious disease worldwide and the most frequent fatal infectious disease in Western nations. The most common atypical CAP bacteria are Chlamydophila pneumoniae, Legionella spp. and Mycoplasma pneumoniae. This study aimed to evaluate the performance of the RIDA®GENE CAP Bac multiplex real-time PCR assay or the direct qualitative detection of Chlamydophila pneumoniae, Legionella pneumophila and Mycoplasma pneumoniae in human bronchoalveolar lavage (BAL).

Materials/methods: The RIDA®GENE CAP Bac is a qualitative multiplex real-time PCR assay targeting the 16S-rRNA for Chlamydophila pneumonia, 16s-rRNA for Legionella pneumophila and the IGS for Mycoplasma pneumoniae with fluorogenic target-specific hydrolysis probes. Evaluation of the RIDA®GENE CAP Bac assay was performed retrospectively on 282 extracted BAL leftover specimens against an routine DIN EN ISO 15189 accredited in-house real-time PCR assay on the Lightcycler 480II (Roche). DNA extraction was performed on the MagNA Pure 96 (Roche) according to laboratory SOP. In addition, also the reactivity with Legionella pneumophila (serogroup 1-14, w/o serogroup 11) from culture material was evaluated.

Results: Of the 282 samples, 17 samples were excluded as the RIDA®GENE CAP Bac assay classified them as invalid. Compared to the in-house real-time PCR as gold standard the sensitivity, specificity, PPV and NPV of the RIDA®GENE CAP Bac assay were 100%, 100%, 100% and 100 % for Chlamydophila pneumonia, 100%, 97.7%, 90.9% and 100 % for Legionella pneumophila, and 100%, 100%, 100% and 100 % for Mycoplasma pneumonia, respectively. All cultured Legionella pneumophila serogroups were detected correctly.

Conclusions: The RIDA®GENE RIDA®GENE CAP Bac multiplex real-time PCR assay showed an excellence performance in terms of sensitive and specific for the differentiation and diagnosis of Chlamydophila pneumoniae, Legionella spp. and Mycoplasma pneumoniae from human bronchoalveolar lavage (BAL).

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Abstract 2809

Nation-wide survey of catheter-related bloodstream infections in medical, surgical and intensive care settings, 2019

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Abstract third-party references: SPIADI network

Background: Prevention of intravascular catheter-related bloodstream infections (CRBSIs) is a public health issue. In this context, a nation-wide network, named SPIADI (Surveillance and Prevention of Invasive Devices Associated Infections) gathers the French infection control teams who develop in their hospitals a 3-pronged strategy combining CRBSI-monitoring, field observation, and education of the healthcare-workers responsible for insertion and use of catheters along the patient course.

Materials/methods: A nation-wide 3-month survey of CRBSIs was conducted (January-April 2019) to provide a baseline description of CRBSI events in both ICU and non-ICU French hospital settings, to identify potential interventions. We used a unit-based protocol close to ECDC-HAI-Net-ICU protocol 1.02. Briefly, for all nosocomial BSIs, the variables studied included patient age and sex, place of acquisition, portal of entry, and for CRBSI, insertion site and time between insertion and first signs of BSI.

Results:

- 1001 participating hospitals (including 64% of the 529 French tertiary-hospitals, 54% of the 570 acute-care clinics, 89% of the 18 oncology specialized-hospitals), covering 129477 beds (including 60% of the 6313 French ICU-beds), 13390393 patient-days (PD) and 701277 dialysis-sessions.
- 9381 nosocomial BSIs detected, including 3292 CRBSIs (31%); higher prevalence for dialysis-units (71%), cancerology (56%), hematology (36%) and ICUs (33%).
- CRBSI acquisition into hospitals (87%) or following home-care or inner-city-medical-care (13%); into ICUs (21%).
- CRBSI associated with implantable-venous-access-port (ivap) (33%), central-venous-catheter (cvc) (24%), peripheral-inserted-central-venous-catheter (picc) (14%) and short-peripheral-venous-catheter (PVC) (15%).
- Predominance of S.aureus (21%), CoNS (28%) and Enterobacteriaceae (19%); multidrug-resistant bacteria/fungi in 9% of CRBSI (15% in ICUs).
- 36% ivap-RBSI associated with staphylococci and arising >4 weeks after insertion, suggesting no strict asepsis during catheter use.
- 25% cvc-RBSI associated with staphylococci and arising <7 days after insertion, suggesting inadequate skin antisepsis during catheter insertion;
- time between PVC-insertion and first signs of BSI >7 days in 20% of S.aureus-pvcRBSIs, suggesting long-term use of PVCs.
- Clusters of P.aeruginosa, K.pneumoniae- and Enterobacter-CRBSI in ICU and hematology-oncology wards, suggesting environmental contamination.

Conclusions: The description of CRBSIs currently detected in intensive care, medical and surgical settings, provides multiple opportunities for improvement, and allows defining SPIADI-network priorities for 2020: [1] local observation of catheter insertion and use to detect the likely gaps between practice and guidelines, and [2] an awareness-building activity on the epidemic risk associated with sinks colonized by Enterobacteriaceae into ICUs.

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Background: Epstein–Barr virus (EBV) is a human lymphotropic herpesvirus that is carried in a latent, essentially non-pathogenic state by 80–90% of all humans. EBV is associated with a variety of lymphomas/leukemias, and other malignancies. Instead of performing a tissue biopsy of the primary tumor, EBV viral load quantification has played a more important role in the diagnosis and management of EBV-associated diseases in immunocompromised patients.

The CE-IVD marked AltoStar® Automation System AM16 [AAS] was launched by altona Diagnostics GmbH, Germany in April 2018. This flexible system automates the entire workflow from sample preparation to analysis. The purpose of this study was to evaluate the performance of the AAS relative to our current method for quantitative EBV PCR.

Materials/methods: A total of 124 samples (121 patients’ EDTA whole blood [WB] samples and 3 proficiency samples from the College of American Pathologists [CAP]) were tested in parallel using the RealStar EBV assay on the Biomerieux EasyMag/Bio-Rad CFS96 Deep Well® Real-Time System (EasyMag/CFX96) and the AltoStar EBV assay on the AM16/Bio-Rad CPX96 Deep Well® Real-Time system (AM16/CFX96). Samples with discordant results were reviewed and retested on both systems.

Results: Overall, the AM16/CFX96 system agreed well with the established EasyMag/CFX96 System.

Correlation study using EDTA WB demonstrated that the EBV viral load obtained using the AM16/CFX96 system was 0.65log10 higher than the one obtained using the EasyMag/CFX96 system.

The Limit of Detection (LoD) using the AM16/CFX96 system was 4.80E+02 IU/mL for EBV WB samples. The study of the linear range for EBV using the AM16/CFX96 system yielded a lower limit of quantification (LLoQ) of 1.5E+3 IU/mL. The coefficient of variation (%CV) of high positive control and low positive control with the AM16/CFX96 system were less than 5% and 10%, respectively.

The AM16/CFX96 significantly reduced the turn of time (TAT) for EBV WB testing by 50 per cent using AM16/CFX96.

Conclusions: With the limited number of samples we tested, the AM16/CFX96 system had a comparable lab performance to the EasyMag/CFX96 system. In addition, it improved workflow and productivity. Further evaluation using samples other than whole blood are needed.

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Abstract 2819

**Types of carbapenemases produced by Gram-negative bacteria detected isolated in cancer hospital in 2017-2019**

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**Background:** Gram-negative microorganisms producing carbapenemase are particularly dangerous in the event of infectious complications of cancer

**Materials/methods:** 161 strains of carbapenem-resistant (Car-R) gram-negative bacteria isolated from various biomaterials in 2017-2019 were studied jointly with the Research Institute of Antimicrobial Chemotherapy (Smolensk, Russia). Microorganisms were identified using MS MALDI-ToF. Carbapenem resistance was determined using Vitek 2 and WalkAway analyzers. Genes encoding carbapenemases were detected by PCR real-time. *P. aeruginosa* isolates were tested for metal-β-lactamases (MBL), including VIM, IMP and NDM. *A. baumannii* isolates were tested for the abovementioned MBLs and for OXA carbapenemases (OXA-23, -24/40, -51, -58). *K. pneumoniae* were tested for MBLs and OXA-48 and KPC - carbapenemases.

**Results:** *K. pneumoniae* accounted for 10.0% of all microorganisms isolated in 2017-2019 (2017 - 10.8%, 2018 - 9.2%, 2019 - 10.0%), *A. baumannii* accounted for 5.5% (5.1%, 5.9% and 5.0%, respectively) and *P. aeruginosa* – for 7.1% (6.7%, 7.6%, 7.1%, respectively). 161 Car-R isolates of gram-negative bacteria (123 in 2017-2018 and 38 in 2019) included 48 isolates of *A. baumannii* (29.8%), 38 isolates of *P. aeruginosa* (23.6%) and 47 isolates of *K. pneumoniae* (29.1%). The remaining Car-R isolates (17.5%) comprised single strains of various enterobacteria and were not taken into account in a further study. 94.7% of *A. baumannii* isolates were producers of OXA-23 type carbapenemases (97.1% in 2017-2018 and 92.3% in 2019), 88.2% of *K. pneumoniae* isolates produced OXA-48 type carbapenemases (86.5% in 2017-2018 and 90.0% in 2019), KPC-carbapenemases (2.1%) and metal-β-lactamases NDM-type (2.1%). 44.2% of *P. aeruginosa* isolates produced VIM-type MBL (46.7% in 2017-2018 and 41.7% in 2019) (p> 0.05).

**Conclusions:** no significant difference in species composition and types of carbapenemases, produced by *A. baumannii, K. pneumoniae* and *P. aeruginosa* in 2017-2019, was seen. Car-R *K. pneumoniae* mostly (88.2%) produced OXA-48 carbapenemases. *A. baumannii* mostly (94.7%) produced OXA-23. *P. aeruginosa* frequently produced MBL (44.2%, type VIM). Production of MBL (NDM type) by *K. pneumoniae* was low (2.1%). The determination of the types of carbapenemases in cancer patients with nosocomial infections is extremely valuable, as it allows to determine strategy and tactics of antibiotic therapy in a particular hospital.

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Molecular epidemiology of vancomycin-resistant enterococcus in parts of China
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Background: Enterococcus is conditional pathogens that are associated with nosocomial infections, often causing bloodstream and urinary tract infections. Vancomycin-resistant Enterococci (VRE) mostly is Enterococcus faecium carrying vanA type in China, but vanM type was reported in several hospitals in Shanghai, China. Most VRE strains in hospitals are clonal complex 17 (CC17). This study retrospectively studied the molecular epidemiology of VRE in multiple centers in China from 2006 to Oct 2019 to understand the epidemiological characteristics.

Materials/methods: A collection of 245 VRE (240 VREfm and 5 VREFs strains) strains from 16 hospitals of China were selected in this study. MICs of antibiotics were determined by using a microdilution broth method. Vancomycin resistance and virulence genes were detected by PCR. The clonal dissemination and genetic relationship of strains were analyzed by PFGE and MLST. 25 VREfm isolates from blood were analyzed by WGS, and vancomycin resistance and virulence genes were further identified. The phylogenetic tree conducted by wgSNP and cgMLST was used to presume the genetic relationship of Enterococcus faecium.

Results: No tetracycline, daptomycin and linezolid non-sensitive VRE isolates were found, but the increased trends for daptomycin MICs were observed. 93.3% (224/240) of the strains carried vanA, while the strains carrying vanA and vanM accounted for 6.3% (15/240), which were all from Beijing. Up to 82.9% (199/240) and 55.4% (133/240) of the strains carried esp and hyl, respectively. The majority of ST types of VREfm strains belonged to ST78 (45.8%, 110/240), which grouped into CC17. The results of PFGE showed a highly diverse genetic background. The results of cgMLST and wgSNP were more consistent.

Conclusions: VRE in China is still dominated by vanA-VanA type. Daptomycin and linezolid still have good activities for VRE in vitro, but the increased trends for MICs for daptomycin were observed. The dominant clone of VRE in China was ST78-CC17. Based on wgSNP typing, a few VREfm strains were epidemic in the same ward or among different wards in the same hospital, and even in different hospitals and cities, sometimes caused outbreaks.

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No negative conversion at follow-up blood culture (FUBC) is significant predictors of early [1-week] mortality in carbapenem-resistant Enterobacteriaceae or vancomycin-resistant enterococci bacteraemia patient: univariate and multivariate analysis

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1Gil Hospital, division of infectious disease, internal medicine department, incheon, South Korea

Background: In bacteremia patients, initial mortality is important. The aim of this study is to find some initial parameters that can predict early [1 week] mortality in carbapenem-resistant Enterobacteriaceae (CRE) or vancomycin-resistant Enterococci (VRE) bacteremia patients.

Materials/methods: From January 1, 2015 through June 30, 2019, we collected CRE and VRE true bacteremia patient in a tertiary hospital, South Korea. Baseline characteristics, initial laboratory data, vital signs, PITT bacteremia score, and early [1 week] mortality were collected. Patients were divided into alive or death group by their survival or death 1 week after initial bacteremia onset. Univariate and multivariate analysis was done.

Results: Total 171 patients was included, 121 were survived and 50 were dead at 1 week after bacteremia onset. There were no differences in baseline characteristics between two groups. In univariate analysis, respiratory-derived, Central line associated blood stream infection, whether follow-up blood culture (FUBC) negative conversion, initial hypotension, and initial C-reactive protein ≥15 mg/dL were related with early mortality of CRE or VRE bacteremia. In multivariate analysis, only no negative conversion in FUBC had statistically significant association with early mortality (OR 1.762, 95% CI=5.726-54.244)

Conclusions: There were several indicators that predicts early mortality in CRE or VRE bacteremia. Only negative conversion of FUBC were statistically significant predictors of early mortality in multivariate analysis.

Table 1. Factors associated with early (1 weeks) mortality of CRE1 or VRE2 bacteremia; Univariate and multivariate analysis.

<table>
<thead>
<tr>
<th>Severity score</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alive (N=121)</td>
<td>Death (N=50)</td>
</tr>
<tr>
<td>Hospitalized over 90 Days</td>
<td>25(20.7%)</td>
<td>4(8.0%)</td>
</tr>
<tr>
<td>Respiratory-origin</td>
<td>28(23.1%)</td>
<td>22(44.0%)</td>
</tr>
<tr>
<td>CLABSI</td>
<td>65(53.7%)</td>
<td>16(32.0%)</td>
</tr>
<tr>
<td>No negative conversion of FUBC</td>
<td>104(86.0%)</td>
<td>10(20.4%)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>30(25.0%)</td>
<td>32(64.0%)</td>
</tr>
<tr>
<td>CRP≥15</td>
<td>38(32.5%)</td>
<td>28(58.3%)</td>
</tr>
<tr>
<td>PBS (Mean± SD)</td>
<td>1.88±2.67</td>
<td>5.58±4.07</td>
</tr>
<tr>
<td>APACHE IV score (Mean± SD)</td>
<td>74.63±21.04</td>
<td>106.18±29.85</td>
</tr>
</tbody>
</table>

carbapenem-resistant Enterobacteriaceae, 2 vancomycin-resistant Enterococci

* OR=odds ratio; CI=confidence interval; CLABSI= Central line associated blood stream infection; FUBC= Follow-up blood culture; CRP=C-reactive protein; APACHE= acute physiology and chronic health evaluation; SD=standard deviation; PBS= PITT Bacteraemia Score.

Presenter email address: blackshj@naver.com
Abstract 2828

**Accuracy of predicting early mortality of severity indicators among carbapenem-resistant Enterobacteriaceae or vancomycin-resistant enterococci bacteraemia patient: univariate and multivariate analysis**

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**Background:** The desire to predict patient outcome is existed traditionally. It’s more concerning among the severe cases like carbapenem-resistant Enterobacteriaceae (CRE) and vancomycin-resistant Enterococci (VRE) bacteremia. The aim of this study is to evaluate specific severity index that correlates with early mortality in CRE and VRE bacteremia patients.

**Materials/methods:** From January 1, 2015 through June 30, 2019, we collected CRE and VRE true bacteremia patient in gil medical center, single tertiary hospital in incheon, South korea. Patients were divided into alive group versus death group, by their survival or death after 1weeks of initial bacteremia onset. To evaluate severity, acute physiology and chronic health evaluation [APACHE]-IV score, APACHE-mortality rate, sequential organ failure assessment (SOFA) score, PITT bacteremia score, systemic inflammatory response syndrome (SIRS) score, and Charlson-comorbidity index was calculated for each of the patient. Univariate and multivariate analysis was done by SPSS 24.

**Results:** Total 171 patients was included. 100 of the patient had CRE bacteremia and 71 of the patients had VRE bacteremia. 73 patients are alive (alive group) and 98 patients were dead (death group). At univariate analysis, all index except Charlson-comorbidity index had statistically significant association with early-mortality of CRE and VRE bacteremic patients. In multivariate analysis, only PITT bacteremia score was statistically significant to early mortality of CRE and VRE bacteremia patient. The odds ratio was 1.329 (95% CI 1.049-1.684).

**Conclusions:** Among severity indexes, only PITT bacteremia score has statistically significant relationships with early mortality of CRE and VRE bacteremia.

<table>
<thead>
<tr>
<th>Severity score</th>
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<tr>
<td></td>
<td>Alive group (Mean±SD)</td>
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</tr>
<tr>
<td>APACHE IV score</td>
<td>74.63±21.04</td>
<td>106.18±29.85</td>
</tr>
<tr>
<td>APACHE mortality rate</td>
<td>44.30±26.25</td>
<td>71.39±18.10</td>
</tr>
<tr>
<td>SOFA* score</td>
<td>7.38±4.16</td>
<td>11.92±3.59</td>
</tr>
<tr>
<td>PITT bacteremia score</td>
<td>1.88±2.67</td>
<td>5.58±4.07</td>
</tr>
<tr>
<td>SIRS*</td>
<td>2.09±1.20</td>
<td>2.76±1.10</td>
</tr>
<tr>
<td>Charlson-comorbidity index</td>
<td>6.52±3.06</td>
<td>7.02±3.07</td>
</tr>
</tbody>
</table>

* SD=standard deviation; CI=confidence interval; SOFA=sequential organ failure assessment; SIRS=systemic inflammatory response syndrome

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Factors associated with the recurrence of Clostridiodes difficile infection in a university hospital

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Background: Around 25% of patients with Clostridium difficile infection (CDI) suffer a recurrence of the disease after finishing the treatment. We describe the factors associated with the recurrence of CDI in a university hospital.

Materials/methods: We performed a retrospective study of all patients older than 18 years with CDI between 2017-2018 in University Hospital of Cabueñes, Spain. C. difficile was detected in stool samples by detection of GDH antigen and toxins A and B using an immunoassay (C. Diff Quick Check Complete, Alere). Those samples with GDH (+)/Toxins (-) were analyzed with the PCR-based assay GenomEra CDX System (ABACUS Diagnostica) to detect gen tcdB. Qualitative variables were compared using the Chi2 test or the Fisher exact test. For quantitative variables, the Student t test or the Mann-Whitney U test were used. Significance was designated at p<0.05.

Results: 60 patients (52.5% females, mean age: 71 years, mean stay before the infection: 6 days) were included. The most frequent underlying diseases were diabetes (23.7%), respiratory diseases (18.6%), inflammatory bowel diseases (12%), neoplasms (13.6%), and hematologic disease (12%). 90% of patients received omeprazole and 91.5% antibiotics. Sixteen (26.7%) patients had a recurrence in five for one second time, seven had three episodes, one four episodes and two five episodes. The first line treatment was metronidazole in 49 patients and vancomycin in the rest. Recurrences were treated first with vancomycin and the rest with fidaxomicin (three cases). Two cases treated with fidaxomicin didn't cure and the patients went under fecal transplant. Omeprazole was retired in 35.4% of patients and antibiotherapy in 81.6% without relation with the apparition of relapses. Six patients died due to the infection. There is not significantly differences in sex, age, or underlying diseases between relapses or not. Toxin was negative more frequent in relapses group (58.3% p=0.055) but multivariable not confirmed this association.

Conclusions: Relapses are frequent in Clostridium difficile infection without relation with sex, age or underlying disease. It is necessary more studied about the virulence factors of the CD and his relationship with human gut microbiota.

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Abstract 2841

**Bacterial contamination of collagen membranes in dental surgery**

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**Background:** Wide using of barrier membranes in dental and maxillofacial surgery is due to the predictability of treatment and the simplicity of the protocol. Resorption of collagen membranes occurs primarily under the action of collagenases and proteases. These enzymes are produced, including parodontopathogenic bacteria, for example, Porphyromonas gingivalis, Actinobacillus actinomycetemcomitans and Treponema denticola. Inflammation and contamination by microorganisms accelerate the splitting of membranes and can lead to the development of postoperative complications, up to the loss of bone tissue volume and the need for repeated operations.

**Materials/methods:** Twenty patients underwent surgery for chronic apical periodontitis (10 patients), radicular cysts (6 patients), third molar retention (4 patients). During the operation from the biotopes of the surgical intervention area, smears were taken for subsequent polymerase chain reaction diagnostics. Determination of DNA of parodontopathogenic and conditionally pathogenic microflora was carried out to 14 species of microorganisms. After filling with a blood clot sockets of extracted teeth and bone cavities after cystectomy, they were covered with barrier membranes made of type II collagen. Re-sampling of material for polymerase chain reaction diagnostics was carried out on the 7th day using a mandrel needle. The needle was inserted under the barrier membrane and the contents of the wound were aspirated with a syringe.

**Results:** The biotopes composition of surgical area in day of surgery is represented by the following species: Porphyromonas gingivalis (6 patients), Streptococcus spp. (5 patients), Bacteroides forsythus (2 patients), Klebsiella spp. (4 patients), Helicobacter pylori (2 patients), Treponema denticola (2 patients), Actinobacillus actinomycetemcomitans (3 patients). On day 7 only 3 microorganism’s DNA was determined: Streptococcus spp. (5 patients), Treponema denticola (2 patients), Actinobacillus actinomycetemcomitans (3 patients) in patients who were carriers before the operation. These bacteria have sizes from 0.4 to 1.5 μm, while others, not detected after surgical accommodation, are 3 to 6 μm.

**Conclusions:** Investigation of barrier membranes microstructure is of clinical importance and requires further analysis, data on microbial contamination of membranes and their permeability by microorganisms will help prevent wound infection.

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Cerebrospinal fluid metabolomics profile in herpes virus type 1 encephalitis

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Background: Metabolomics may identify disease-specific variations in small molecules (metabolites), thus enabling pathogenesis insights and providing new potential biomarkers. We exploited this technique to detect differences in cerebrospinal fluid (CSF) metabolomic spectra in patients with acute Herpes Virus type-1 (HSV-1) encephalitis.

Materials/methods: We analyzed CSF samples from 11 patients with HSV-E and, as controls, from 9 HIV-negative patients with progressive multifocal leukoencephalopathy (PML), 17 patients with inflammatory or non-inflammatory non-infectious neurological diseases (NID) and 20 healthy subjects (HC). Analysis was performed at Metabolon (Durham, NC) using both liquid and gas chromatography/mass spectrometry. Molecules were identified by comparison to library entries or purified standards, and peak areas values were log-transformed and normalized by median. Metabolites associated with p<0.05 and q<0.1 in the ANOVA model were considered significant. Tukey’s test was run to identify differences in groups pairwise comparisons. Unsupervised hierarchical cluster analysis (HCA) based on significant metabolites by ANOVA was used to inspect the natural structure of correlation between samples and normalized metabolite concentrations were represented in a heat-map. HSV-1 viral load was quantified by real-time PCR and correlated with peak area values using Spearman’s test.

Results: HSV-E, PML and NID were comparable for age and gender (median age 61 years, 40% males); HC were younger (median age 46) and predominantly men (90%). 25 metabolites were differentially expressed among the four groups, and the majority belonged to kynurenine/tryptophan, mitochondrial function and oxidative stress pathways. HSV-E clustered separately from NID, HC and PML, which in turn tended to cluster together, as shown in Figure 1 (where each column identifies a patient: above by HCA and below by heat map). Kynurenine, 2-hydroxybuthyrate, cytidine and 3-dehydrocarnitine distinguished HSV-E from all the other groups, whereas kynurenine, isocitrate and ascorbate differentiated either HSV-E or PML from NID. Among these molecules, kynurenine correlated with CSF HSV-1 viral load (Spearman r= 0.67, p 0.02).

Conclusions: Our study shows specific metabolic CSF alterations in HSV-E, when compared to PML, NID and HC, and found kynurenine to be significantly associated with HSV-1 viral load. This approach seems promising for the identification of biomarkers and therapeutic targets for HSV-E.
**Abstracts 2020**

*Main D: Neurodegenerative diseases (n=4); inflammatory diseases of the central nervous system (n=5); inflammatory diseases of the peripheral nervous system (n=3); non-inflammatory neurological diseases (n=5)*

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Abstract 2847

Can we use sepsis scores to predict bacteraemia in the elderly?
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Background: Community-acquired Escherichia coli and Klebsiella sp. bacteraemia are associated with high mortality rates in the elderly. Sepsis scoring systems may be useful tools to predict bacteraemic cases and facilitate early broad-spectrum antibiotic therapy but need validation in this population. Unnecessary broad-spectrum antibiotic therapy in this age-group can have significant adverse effects including emergence of resistance. This study aimed to test a range of scoring systems and their ability to predict Gram-negative bacteraemia in elderly patients presenting to the emergency department.

Materials/methods: Blood cultures of patients over 65 years admitted to a London hospital between September 2017 and January 2019 were retrospectively reviewed (n=2588). We selected E. coli or Klebsiella sp. Bacteraemia (“GNR”, n=185) and negative cultures (n=2403). A comparison of Systemic Inflammatory Response Syndrome (SIRS), qSOFA, National Early Warning Score (NEWS), National Early Warning Score 2 (NEWS2) and modified Pitt score was carried out on a random selection of 51 cases from each group. “R” was used for statistical analysis.

Results: T-tests demonstrated differences in scores between GNR and negative cultures among all systems: Pitt (p=0.0026), NEWS (p=0.033), NEWS2 (p=0.0076), qSOFA (p=0.033) and SIRS (p=0.043). Based on these results we analysed the conditional probabilities of bacteraemia given the grouped NEWS2 scores (table 1) and compared them to the baseline probability (0.062). We observe a far greater incidence rate of bacteraemia amongst patients with NEWS2 > 9 (100%) scores compared to the baseline probability (6.2%), suggesting that patients with NEWS2 scores > 9 have a high positive predictive value for bacteraemia.

Table 1. Probability of bacteraemia for NEWS2 score range.

![Table 1](image)

Conclusions: All scoring systems showed significant differences for GNR bacteraemia and negative patients. The greatest difference was seen with NEWS2, suggesting this could be used as a more accurate predictor of Gram-negative bacteraemia and support use of broad-spectrum antibiotic therapy in this group. Further validation is being carried out on a larger dataset to determine the optimal cut-off score with greatest sensitivity and specificity. Despite current literature demonstrating that the sensitivity of established scoring systems is sub-optimal in the elderly, we have encouraging data suggesting a role for using NEWS2 as a predictor of bacteraemia in elderly patients.

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Improvement of infection rates and hand hygiene adherence in pre-post comparison after introduction of an infection-prevention-measures-bundle implemented by an infection prevention link physician

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Abstract third-party references: German Federal Ministry of Health

Background: In the project "HygArzt", the effects of an infection-prevention-measures-bundle (IPM) implemented by an infection prevention link physician (PLP), who mediates between infection control- and clinical departments in Germany, in trauma surgery/orthopedics on the nosocomial infections (NI) rates (NIR) and epically on surgical site infections (SSI), were investigated.

Materials/methods: A pre-/post- intervention study design was used. Trauma surgery and orthopedic patients on normal wards were included. As intervention a bundle was implemented, which consisted of: decolonization of patients before surgery, standardized wound care, usage of remanent disinfectants for skin preparation in the operating theatre and prophylactic closed incision negative pressure wound therapy for high-risk wounds. To identify NI, clinical signs of infection were recorded according to KISS and CDC definitions. Additionally, an active surveillance, including attendance to morning rounds was performed. In addition to the NI, process parameters such as general hand hygiene adherence (HHA) and dressing change HHA were investigated.

Results: During the pre-phase (1141 surgeries) 61 NIs were recorded (NIR 5.3% [CI 95% 4.0; 6.6]) including 44 SSIs [rate 3.1% [CI 95% 1.5; 3.2]]. In the post-phase (1546 surgeries) 35 NIs were recorded (NIR 2.3% [CI 95% 1.1; 2.7]) including 26 SSIs [rate 1.7% [CI 95% 1.1; 2.3]]. The post-phase showed significant lower relative risks for NIs (RR=0.43 [CI 95% 0.28; 0.64], p<0.001) and SSIs (RR=0.44 [CI 95% 0.27; 0.70], p<0.001) compared to the pre-phase. The general HHA was significantly increased (3453 observations in pre- and 3686 observations in post-phase). The most significantly increase in adherence was observed “before aseptic procedure” (pre: 34%, post: 79%; p<0.001) and “before touching a patient” (pre: 37%, post: 77%; p<0.001) in all type of indications (“after body fluid exposure risk” (pre: 79%, post: 95%; p<0.001), “after touching a patient” (pre: 66%, post: 99%; p<0.001), “after touching patient surrounding” (pre: 71%, post: 90%; p<0.001)) was a significant HHA increase in the post-phase. HHA during dressing change was also significantly increased.

Conclusions: NI and SSI rates could be reduced by an infection control-bundle in orthopedic/trauma patients implemented by a PLP. The trainings of the PLP improved the HHA.

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Optimal treatment duration of *Pseudomonas aeruginosa* Infections in allogeneic haematopoietic cell transplant recipients

Flaminia Olearo*, Ilona Kronig1, Nicolas Mueller1, Urs Schanz1, Nina Khanna1, Jakob Passweg2, Michael Medinger1, Stavroula Masoundi Levrat1, Yves Chalandon1, Christian Van Delden1, Dionysios Neofytos1

1University Hospital of Geneva, Geneva, Switzerland, 2University Hospital of Zurich, Zurich, Switzerland, 3University Hospital of Basel, Basel, Switzerland

**Background:** There are limited data on appropriate treatment durations of *Pseudomonas aeruginosa* (PA) infections, including PA-bloodstream infections (PA-BSI) and pneumonia (PA-PNA), in allogeneic hematopoietic cell transplant recipients (allo-HCTr).

**Materials/methods:** We conducted a retrospective study using the Swiss Transplant Cohort Study from 2011 to 2018. Allo-HCTr with PA-BSI and PA-PNA, and available follow-up data for ≥365-days post-infection were included. The objectives were to describe incidences and treatments of primary and recurrent PA-infections.

**Results:** Fifty-four patients with primary PA-infection were identified among 1299 allo-HCTr, with a cumulative incidence of 3.8% (incidence rate 0.025/1000-person-years; Figure 1a). Twenty-two (40.7%), 23/54 (42.6%), and 9/54 (16.7%) patients were diagnosed with PA-BSI, PA-PNA and concomitant PA-BSI+PNA, respectively. Median time to primary PA-infection was 274.5 (interquartile ratio, IQR: 105-707) days post-HCT. Most of available PA-isolates (30/48, 62.6%) were susceptible to all antibiotic-classes tested. 81.5% (44/54) of patients received a monotherapy during the course of treatment. Median duration of antibiotic treatment for primary PA-infection was 16.5 (IQR: 13-29) days. Seventeen of 46 (36.9%) patients with available data developed a recurrent PA-infection (cumulative incidence: 35.1%; Figure 1b) at a median of 28 days (IQR: 13-38) after primary PA-infection. Recurrent PA-infections were observed equally among patients with primary PA-BSI (6/22, 30%), PA-PNA (9/23, 47.4%) and PA-BSI+PNA (2/9, 22.2%; P-value: 0.48; Figure 1c). Fourteen of 17 (82.4%) patients had one and 3/17 (17.6%) patients had >1 recurrent PA-infections. Patients with recurrent PA-infection were more likely to have received shorter treatment courses for their primary infection (median: 13 days, IQR: 11-16) compared to those without recurrence (median: 25, IQR: 14-31; P-value: 0.005). Recurrent infection was observed in 8/31 (25.1%) and 9/15 (60%) patients who received treatment for ≥14 and <14 days, respectively (P-value: 0.02). Similarly, recurrent infection was observed in 3/20 (15%) and in 14/26 (53.8%) patients who received treatment for ≥21 and <21 days, respectively (P-value: 0.007). Treatment of the primary PA-infection for ≥21 days (OR: 0.15, 95%CI 0.03-0.64, P-value: 0.005) was the only protective factor identified against recurrent PA-infection.

**Conclusions:** Incidence of primary PA-infection was low in allo-HCTr. However, we report a high rate of recurrent PA-infections with almost 1 in 3 allo-HCTr developing a recurrence after prior PA-infection. Longer treatment courses appeared to be protective for PA-infection recurrence.
Abstracts 2020

Figure 1. In this figure the incidence rates of primary PA infections (1a), recurrent PA infections overall (1b) and by type of recurrent PA infections (1c) are presented.

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Abstract 2858

Global prevalence estimates of syphilis among men who have sex with men: a systematic review and meta-analysis

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Background: Men who have sex with men (MSM) represent an important population at high-risk of syphilis. Recent resurgence of syphilis in some countries has been observed exclusively in this population. Despite the importance of MSM to syphilis control and elimination efforts, there have been no systematic reviews and meta-analyses to produce pooled prevalence estimates at the global level.

Materials/methods: We searched MEDLINE, EMBASE, LILACS, and AIM databases for studies reporting syphilis prevalence among MSM that were conducted between January 2000 and April 2019. Studies included had reported syphilis as diagnosed by at least one biological assay. Point prevalence estimates were corrected using the sensitivity and specificity of diagnostic assays. We adopted random effects models to produce pooled prevalence estimates by the eight regions of the Sustainable Development Goals (SDG). We also conducted sensitivity analyses based on quality assessments of included studies.

Results: Of 3,995 records screened, we identified 177 eligible studies from 46 countries (Figure). Overall, the pooled prevalence estimate of syphilis in MSM was 8.6% [95%CI 8.1-9.2] based on 47,256 positive tests among 547,112 individuals. Pooled prevalence was 9.6% [95%CI: 8.6-10.6] (N=84 studies) across studies from 2000 to 2009, and 7.8% [95%CI: 7.2-8.5] among studies between 2010 and 2019 (N=93 studies). The lowest regional prevalence estimate was 1.2% in both Australia and New Zealand and sub-Saharan Africa [95%CI: 0.3-2.7 and 0.4-2.3, respectively], whereas the highest was 11.0% in Northern Africa and Western Asia [95%CI: 8.9-13.6]. Subgroup analyses revealed some evidence of differences among SDG regions, study periods, income levels, legality of same-sex acts, sub-population groups of MSM, and sampling methods. Sensitivity analyses detected no apparent difference between overall pooled prevalence estimates calculated with or without studies that were at high-risk of bias [8.6% [95%CI 8.1-9.2] vs. 8.7 [95%CI: 8.1-9.3], respectively].

Conclusions: The global syphilis prevalence estimate among MSM is substantially higher than that of the general population. To achieve the targets for the 2030 set in the World Health Organization Global Health Sector Strategy for reduction of syphilis among the general population, rapid scale-up of evidence-based interventions is needed to interrupt the recent resurgence of syphilis among MSM.
**Abstract 2861**

**MERS-related Coronavirus screening and trends in returning travellers**  
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**Background:** Middle East respiratory syndrome coronavirus (MERS-CoV) is an imported zoonotic infection of camels that causes respiratory illness, with a substantial mortality rate and a high economic impact in healthcare-related transmissions. Public Health England (PHE) Birmingham Laboratory is one of only two UK centres that provide screening for MERS-CoV. Respiratory samples were audited from travellers returning 2016-2019.

**Materials/methods:** Respiratory specimens from patients fulfilling the PHE screening criteria (www.gov.uk) were tested for MERS-CoV and a panel of respiratory viruses, and correlated with sample type, geographical risk, and symptoms.

**Results:** 601 patient samples were received over 46 months. Camel exposure was documented in 24 patients. MERS-CoV was identified in a single patient with geographical risk factors, not associated with pilgrimage. This patient was simultaneously infected with rhinovirus and adenovirus at presentation. Referrals for testing doubled in the months following this case, indicating a heightened awareness of the virus.

Other viral causes were identified in 237 patients (39.6%). Of these, rhinoviruses were the greatest cause of infection, detected in 67 patients (28.2%), followed by influenza viruses (Influenza A H1pdm09 in 35 (14.8%), A H3 in 51 (21.5%) and Influenza B in 14 (5.9%)). 37 patients had more than one virus detected. A bacterial cause was reported in 11 patients. The advance of the Hajj through the solar year (from mid-September 2016 to mid-August 2019) revealed a decline in influenza (25% in 2016 to 19.3% in 2019) and an increase in rhinovirus (17.9% in 2016 to 31.6% in 2019).

Among 160 patients from whom both upper (URT) and lower respiratory tract (LRT) samples were received, 58 (36%) were discordant. Rhinovirus and influenza were more likely detected in LRT samples.

**Conclusions:** Despite a large number of patients having a clinical picture consistent with MERS-CoV and epidemiological risk factors, MERS-CoV was only identified in one patient, with rapid infection control procedures preventing spread. Whilst MERS-CoV remains a substantial public health risk, clinicians in Europe managing suspected cases are more likely to encounter patients with rhinovirus or influenza virus and should initiate early appropriate management, including good infection control. The advisability of providing LRT samples is emphasised.

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Identification, genotyping and antimicrobial susceptibility testing of Brucella spp. isolated from livestock in Egypt

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Background: Brucellosis is a highly contagious zoonosis worldwide with economic and public health impacts. The aim of the present study was to identify Brucella (B.) spp. isolated from animal populations located in different districts of Egypt and to determine their antimicrobial resistance.

Materials/methods: In total, 34 suspected Brucella isolates were recovered from lymph nodes, milk, and fetal abomasal contents of infected cattle, buffaloes, sheep, and goats from nine districts in Egypt. The isolates were identified by microbiological methods and matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS). Differentiation and genotyping were confirmed using multiplex PCR for B. abortus, Brucella melitensis, Brucella ovis, and Brucella suis (AMOS) and Bruce-ladder PCR. Antimicrobial susceptibility testing against clinically used antimicrobial agents (chloramphenicol, ciprofloxacin, erythromycin, gentamicin, imipenem, rifampicin, streptomycin, and tetracycline) was performed using E-Test. The antimicrobial resistance-associated genes and mutations in Brucella isolates were confirmed using molecular tools.

Results: In total, 29 Brucella isolates (eight B. abortus biovar 1 and 2 B. melitensis biovar 3) were identified and typed. The resistance of B. melitensis to ciprofloxacin, erythromycin, imipenem, rifampicin, and streptomycin were 76.2%, 19.0%, 76.2%, 66.7%, and 4.8%, respectively. Whereas, 25.0%, 87.5%, 25.0%, and 37.5% of B. abortus were resistant to ciprofloxacin, erythromycin, imipenem, and rifampicin, respectively. Mutations in the rpoB gene associated with rifampicin resistance were identified in all phenotypically resistant isolates. Mutations in gyrA and gyrB genes associated with ciprofloxacin resistance were identified in four phenotypically resistant isolates of B. melitensis.

Conclusions: This is the first study highlighting the antimicrobial resistance in Brucella isolated from different animal species in Egypt. Mutations detected in genes associated with antimicrobial resistance unravel the molecular mechanisms of resistance in Brucella isolates from Egypt. The mutations in the rpoB gene in phenotypically resistant B. abortus isolates in this study were reported for the first time in Egypt.

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Abstract 2863

Clinical efficiency of anti-\textit{Blastocystis} therapy in ulcerative colitis patients
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\textbf{Background:} Ulcerative colitis (UC) is an inflammatory bowel disease with chronic and recurrent course. High prevalence of \textit{Blastocystis} sp. was revealed in the structure of intestinal protists in UC patients, and protozoa could be a contributing cause of UC. The aim of the study is to estimate the influence of \textit{Blastocystis} sp. on the course of UC.

\textbf{Materials/methods:} The prospective, interventional, randomized, double-blinded clinical study was performed. UC patients with severe form were selected according to Mayo Clinic score consisting of 4 items: stool frequency, rectal bleeding, findings of flexible proctosigmoidoscopy and patient’s functional assessment. 20 (1\textsuperscript{st} group), 25 (2\textsuperscript{nd} group) and 22 (3\textsuperscript{rd} group) UC patients with \textit{Blastocystis} infection were treated with nitazoxanide (1.0 g/day), mesalazine (1.5-2 g/day) and combination of nitazoxanide (1.0 g/day) and mesalazine (≥1.5-2 g/day) for 14 consecutive days, respectively. Parasitological (triple coprocscopy), clinical and endoscopic examination was conducted before therapy, immediately and in 6 and 12 weeks after therapy completing.

\textbf{Results:} After completion of the therapy with nitazoxanide and combination of nitazoxanide with mesalazine elimination of \textit{Blastocystis} sp. among UC patients was observed in 100% cases. However, in 6 weeks after the course of therapy with nitazoxanide low intensity of \textit{Blastocystis} sp. was detected in 5.0±4.8% of UC patients. In 12 weeks after the course of therapy low intensity of \textit{Blastocystis} sp. was detected in 10±6.7% and 18.2±8.2% of UC patients obtained nitazoxanide and combination of nitazoxanide and mesalazine, respectively. Any significant changes in prevalence and intensity of \textit{Blastocystis} sp. were not found in UC patients of the 2\textsuperscript{nd} group after therapy completing and in 6 and 12 weeks after the course of therapy. Despite a limited amount of participants under study after therapy a positive clinical response, clinical remission and mucosal healing were revealed in all groups. During all period of follow-up the best response to the therapy, especially mucosal healing was detected among UC patients obtained combination of nitazoxanide with mesalazine.

\textbf{Conclusions:} Diagnosis of \textit{Blastocystis} sp. and anti-\textit{Blastocystis} therapy should be introduced in the complex examination and therapy of UC.

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A machine learning model for evaluating Chagas disease screening in immigrant populations

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Background: The migration of people from endemic areas for Chagas disease is a growing reality in Europe making. This study presents a mathematical model based on machine learning methodologies to evaluate the burden of Chagas disease and contribute to the design of screening programs in this population.

Materials/methods: A retrospective cross-sectional screening program of Chagas disease was conducted in all immigrant patients from endemic areas attended the Tropical Medicine Unit of the Hospital Universitario Central de Asturias. The ID-Chagas antibody test [particle gel immunoassay (]) was used as a screening assay. All positive samples were confirmed by determination of anti-T. cruzi antibodies by indirect immunofluorescent antibody test and by polymerase chain reaction (PCR). A mathematical model based on machine learning methodologies was designed to establish the set of most discriminatory prognostic variables to predict the appearance of the Chagas disease in the immigrant population.

Results: We analyzed 346 patients (66.2% female, mean age: 36 years; Time in Spain: 5.5 years). The screening was positive in 39 patients (11.2%); 78.4% of them female; mean age: 40 years; Time in Spain: 4.7 years. No patients were diagnosed during the first year in Spain. The countries of origin were Bolivia (82%), Brazil (8%), Paraguay and Argentina (5.5% each). In univariable an multivariable analysis a positive screening was significantly associated with coming from Bolivia [P < 0.0001; OR 29.7600; [11.088-79.870]. The estimated probability of having Chagas disease is 0.0388, and therefore an average of 26 screenings is needed to detect the first Chagas case. Chagas is predicted with an accuracy of 92.88%. Taking as reference the population from the endemic zone resident in Spain as of January 1, 2019, according to the mathematical model, it is expected that they reside in the country 42,904 persons with Chagas disease.

Conclusions: Our estimates of the population at risk show the existence of 42,904 probable infected by T. cruzi, with only 26 screens needed to find a positive patient. Current screening based on screening in pregnant women and their children should become universal for all immigrants from the endemic area.

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Abstract 2867

**Evaluation of endoperoxides and tetrahydropyrans as potential anti-leishmanial drugs**

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**Background:** Human leishmaniasis is a neglected disease, for which the drug arsenal is limited. Thus, the development of new molecules against leishmaniasis is a priority. In this context, natural products may serve as structural template for drug discovery, for example, natural endoperoxides, including artemisinin and its semi-synthetic derivatives, have shown anti-leishmanial activity. In the present study, a series of endoperoxides were synthesized together with their corresponding tetrahydropyrans, which bear the same substitution pattern of endoperoxides, but lack the peroxide bridge. These new compounds were tested to assess their in vitro anti-leishmanial potential and the mechanism of action of the most effective ones was investigated.

**Materials/methods:** Synthesis of endoperoxides and tetrahydropyrans was achieved through an efficient and low cost approach. Drug susceptibility assays were performed on promastigotes and amastigotes of *Leishmania donovani*, while cytotoxicity of the compounds was analyzed on mammalian cells. The role of iron in the anti-leishmanial bioactivity of the compounds was tested as well as generation of reactive oxygen species (ROS) in untreated and treated promastigotes. Distribution of the compounds within the parasite was analyzed by confocal microscopy.

**Results:** Screening on *L. donovani* promastigotes and amastigotes revealed that 3 endoperoxides and 3 corresponding tetrahydropyrans exhibited good inhibitory activity. These promising compounds were further investigated for their mechanism of action against *L. donovani*: the presence of iron chelator desferrioxamine did not affect the anti-leishmanial bioactivity of the compounds, suggesting that iron does not play a crucial role in the activation of the selected molecules. Compound-treated parasites showed an increase in the intracellular ROS levels, indicating the development of a moderate oxidative stress upon treatment. Further, studies on confocal microscopy were performed on fluorescent–labeled compounds: tetrahydropyrans mainly accumulated in the parasite cytoplasm, while endoperoxides also localized in the nucleus.

**Conclusions:** Six compounds proved to be significantly active against *L. donovani* promastigotes and amastigotes, with low cytotoxic effects towards mammalian cells. The preliminary data about the mechanism of action of these molecules suggest that peroxide function is not a crucial pharmacophoric requirement for the anti-leishmanial bioactivity.

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**Difficult-to-treat mucocutaneous leishmaniasis in an elderly Italian traveller returning from Argentina resolved with combination treatment**

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**Background:** Mucocutaneous leishmaniasis (MCL) is a complication of tegumentary leishmaniasis causing potentially life-threatening lesions in the ear, nose and throat [ENT] district, most commonly due to *Leishmania (Viannia) braziliensis*. We report a case of relapsing MCL in an elderly Italian traveler returning from Argentina.

**Materials/methods:** Case-report of relapsing mucocutaneous leishmaniasis.

**Results:** A 65-year-old Italian male patient with chronic kidney disease (CKD) (eGFR 33.3 mL/min), arterial hypertension, prostatic hypertrophy, diabetes mellitus was referred from another center for relapsing MCL causing severe dyspnea, dysphonia, and nasal ulceration. Three years earlier, after a travel to Argentina, he developed a chronic cutaneous ulcer in the right leg which healed slowly and was followed by the appearance of nose ulceration and ENT symptoms. By that time the patient underwent ENT examination revealing severe edema and erythema of nasopharynx and larynx (Figure). A nasopharyngeal biopsy revealed a lymphoplasmacytic inflammation and presence of *Leishmania* amastigotes, subsequently identified as *L. (V.) braziliensis*. Despite receiving 4 courses of liposomal amphotericine B (L-AmB) (3mg/kg day 1-5, 10) and two courses of miltefosine (50mg tid for 28 days) in a two-years period, the symptoms relapsed few months after the end of each course. We decided to start treatment with intravenous pentamidine 4mg/kg on alternate days for 10 doses followed by one dose per week for additional 7 doses, intralosomal meglumine antimoniate on the nasal lesion once per week for 6 doses, oral azoles for three months, and aerosolized L-AmB on alternate days for three months. Few reversible side effects were observed and the treatment led to regression of mucosal lesions (Figure) and respiratory symptoms.

**Conclusions:** This case highlights the difficulties in managing a life-threatening refractory case of MCL in a patient with multiple comorbidities. Even though parenteral antimonial derivatives are traditionally considered the first choice for treatment of MCL, they are relatively contraindicated in case of CKD, as dose adjustment in case of impaired renal function is unknown, and the use of alternative drugs is recommended. This case was resolved with a combination treatment, including aerosolized L-AmB that, to the best of our knowledge, was never used before for MCL.

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Abstract 2875

**Quinacrine is effective for treatment of resistant giardiasis**

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**Background:** Nitroimidazole-refractory (i.e. metronidazole, tinidazole) giardiasis is an increasing problem worldwide, especially on the Indian subcontinent. There is limited evidence for alternative treatment. The old drug quinacrine has been increasingly used with promising results. The aim of this study was to assess the efficacy of quinacrine in a larger patient material.

**Materials/methods:** All verified cases of giardiasis at the Department of Infectious Diseases, Karolinska University Hospital, Sweden, during 2008-2017, were retrospectively identified. Nitroimidazole-refractory giardiasis was defined as parasitologically confirmed treatment failure (positive stool microscopy or PCR [BD MAXTM Enteric Parasite Panel; Franklin Lakes, NJ, USA]) after at least two treatment courses with nitroimidazoles. Information on patients’ demographics, travel/migration history, diagnostics, treatment and outcome were collected from medical records.

**Results:** Of 159 patients with intestinal giardiasis 67 (42%) cases of nitroimidazole-refractory giardiasis were identified. Forty-eight (72%) had acquired the infection on the Indian subcontinent, and the most common reason for travel was tourism (80%). The median age was 35 years (3-73) and 29 (43%) were females. No cases of HIV or IgA deficiency were identified. Of the 67 nitroimidazole-refractory cases 33 were treated with quinacrine as monotherapy (100mg t.i.d. for 5-7 days) while three patients received combination treatment with quinacrine and metronidazole. Other drugs used were albendazole, paromomycin, nitazoxanide, or combinations of these medications. Of 36 quinacrine treated cases 33 had follow-up stool samples (31 had two or more samples, two had a single sample). In all but one (32/33) all follow-up samples were negative (97% parasite efficacy). One patient was PCR positive and symptomatic after treatment (but microscopy negative), but was finally cured after receiving quinacrine in combination with paromomycin. The overall parasite efficacy in those not treated with quinacrine was 59%. One patient reported possible side effects to quinacrine (headache, nausea, dizziness), but all patients completed the full treatment course.

**Conclusions:** Quinacrine is an effective alternative for nitroimidazole-refractory giardiasis with a good tolerability.

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Characterisation of methicillin-resistant Staphylococcus aureus strains isolated from purulent subcutaneous lesions of food-producing rabbits

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Background: Rabbit meat is highly consumed in Portugal. Lesions detected during the post-mortem examination, in particular purulent infections such as abscesses, may lead to rejection of the carcass resulting in high economic losses. Furthermore, cross-contamination may occur leading to the dissemination of the pathogen. Staphylococcus aureus are mostly associated with this type of infections and are considered one of the main pathogens causing food poisoning worldwide due to its ubiquity and its ability to form enterotoxins in food, responsible for causing human disease. Therefore, we aimed to investigate the prevalence and antibiotic resistance profiles of MRSA strains isolated from purulent lesions of food-producing rabbits.

Materials/methods: Samples from purulent lesions of 66 rabbits (Oryctolagus cuniculus) were collected during a period of 4 months in a slaughterhouse in Portugal. Samples were seeded onto ORSAB plates with 2mg/L of oxacillin for MRSA isolation. Susceptibility to antibiotics was tested by the Kirby-Bauer disk diffusion method against 14 antimicrobial agents. The presence of resistance genes, virulence factors and the immune evasion cluster system were studied by PCR. All isolates were characterized by agr and spa typing.

Results: The presence of mecA-positive MRSA was detected in 16 (24.2%) animals of the 66 analyzed. All strains displayed a multidrug-resistant phenotype and all presented resistance to penicillin, erythromycin and clindamycin. Ten isolates showed resistance to tetracycline and harbored the tet(K) gene. Resistance to aminoglycosides was also detected, being 7 isolates resistant to gentamycin, tobramycin and kanamycin, and all harbored the aac(6')-Ie-aph(2'')-Ia gene. The IEC genes were detected in 3 isolates. All strains were positive for agr type III. Isolates were assigned to 7 different spa types (t1190, t2802, t002, t1094, t084, t032 and t1491) which were grouped into 5 clonal complexes, of which CC97 was the most prevalent.

Conclusions: This study revealed the presence of MRSA strains in food-producing rabbits at slaughterhouse level with multidrug resistance phenotypes. This may represent serious food safety and public health concerns since cross-contamination may occur leading to the spread of MRSA and, eventually, the possibility of ingestion of contaminated meat.

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Abstract 2879

**Rapid antiretroviral therapy initiation in the era before universal treatment, Croatia, 2005 to 2014**

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**Background:** Croatia has a centralized system of HIV care and all patients are treated at the University Hospital for Infectious Diseases (UHID) in Zagreb. The aim of our study was to examine factors related to rapid ART initiation among persons who entered HIV care in Croatia from 2005 to 2014.

**Materials/methods:** Included into the study were Croatian citizens/residents ≥18 years who entered HIV care and started ART at UHID. Excluded were pregnant women and those who were in care elsewhere before entering care at UHID. The follow-up ended on Dec/31/2017 (earlier if died, moved or lost to follow-up). The time from HIV diagnosis to ART initiation was categorized: up to 30 days (“rapid”), from 31 days to one year (“intermediate”), and more than one year (“delayed”). We conducted quantile regression analysis to study factors related to the time from confirmed HIV-diagnosis to ART initiation with gap in care (>1 year without follow-up) considered the major predictor variable.

**Results:** 628 patients were included into the study with a total of 4333.0 (median per-person, 6.7 [Q1 -Q3: 4.3-9.5]) years of follow-up. 91.9% (577/628) were men; median age was 36.1 (Q1 -Q3: 29.6-43.8) years. The median time from HIV-diagnosis to ART initiation was 31 days (Q1 -Q3: 0.3-17.7 months). Rapid ART initiation was observed in 49.8% (313/628) patients, 21.7% (136/628) and 28.5% (179/628) had intermediate and delayed initiation, respectively. On regression analysis, calendar year of entry into care, and markers of more advanced HIV disease (higher viral load, lower CD4 cell count and clinical AIDS) were significantly associated with earlier ART initiation. A gap in care before ART initiation was significantly associated with later ART initiation at all quantiles. Gap after ART, gender, transmission risk [MSM vs not MSM], age and place of residence [Zagreb vs outside Zagreb] did not have a significant impact on time to ART initiation.

**Conclusions:** A significant proportion of patients started ART early in Croatia in the period 2005–2014. Early ART initiation was not associated with a subsequent gap in care whereas longer waiting for ART initiation was associated with a gap in care before ART initiation.

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Nonsteroidal anti-inflammatory drugs as a promising alternative to antibiotics to combat methicillin-resistant Staphylococcus aureus biofilms

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Background: Nonsteroidal anti-inflammatory drugs (NSAIDs) are a diverse group of drugs that have anti-inflammatory, antipyretic and analgesic effects which are frequently associated with bacterial infections. Nevertheless, available information on the antibacterial action of NSAIDs are scarce. Currently, few antibiotics are available to treat infections caused by multidrug-resistant bacteria, in particular, methicillin-resistant Staphylococcus aureus (MRSA), thus, alternative approaches to controlling bacterial infections are urgently required. The main goals of this study were to determine the minimum inhibitory concentration (MIC) and the activity of NSAIDs on the control of biofilms of MRSA strains.

Materials/methods: MICs were determined by the broth microdilution method using 2 NSAIDs used in human medicine, namely naproxen and diclofenac, against 8 multidrug-resistant MRSA strains isolated from infected diabetic foot ulcers. The antibiofilm activities were determined by the microtiter biofilm assay. In order to assess the NSAIDs ability to control adhered cells and 24h old biofilms, bacterial suspension was added to 96-well microtiter plates and incubated for 2h and 24h, respectively. After the incubation period, the plates were washed, each NSAIDs solution to a final concentration at MIC and 5xMIC and fresh medium were added. The plates were incubated for 24h after which the biofilm biomass was measured.

Results: MICs of naproxen and diclofenac ranged from 1000 to 2000 µg/ml and 500 to 1500 µg/ml, respectively. Diclofenac showed a higher potential to remove adhered cells than naproxen (41.9% and 37.7%, respectively). Naproxen showed moderate ability to remove adhered cells at MIC; nevertheless, 5xMIC showed inferior values of adhered cells removal. On the opposite, a higher biomass removal was detected at 5xMIC of diclofenac than at the MIC values. Regarding the biomass removal of 24h old biofilms, naproxen showed better results with biomass elimination reaching 22% in comparison to diclofenac with a maximum removal of 17%.

Conclusions: Both naproxen and diclofenac showed efficacy against MRSA strains. Diclofenac showed a higher potential to remove adhered cells whereas naproxen had better efficacy in biomass removal of 24h old biofilms. Therefore, these non-antibiotic drugs may be used as an alternative to antibiotics since they may act through different mechanisms from those of antibiotics.

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Background: Respiratory syncytial virus (RSV) is a well-known pediatric pathogen, but lately it has been increasingly recognized as a prominent pathogen in adults. However, the role of RSV in the elderly population (>65 years) during the influenza season has not been sufficiently assessed.

Materials/methods: This study was performed during the influenza season, from September 2017 to April 2018 in a tertiary Spanish hospital. The study population included only patients older than 65 years with either community-acquired or hospital/healthcare-associated influenza-like illness, according to the European Centre for Disease Prevention and Control criteria. Samples were analyzed using a rapid molecular assay (Xpert® Flu/RSV). RSV-positive patients were compared with a randomly age-stratified influenza positive control group. We compared Influenza and RSV infected populations regarding outcome, days of antibiotic use, length of stay, ICU admission and use of specific antiviral treatment.

Results: Of the 4009 samples processed during the study period, 2441 (60.9%) of the samples corresponded to adults > 65 years old and 842 (34.5%) had a positive result as follows: 394 (16%) Flu A; 289 (12%) Flu B and 159 (6.5%) RSV. When RSV-positive and influenza-positive patients were compared, RSV-positive patients presented with more comorbidities as expressed by Charlson index (6.08 vs 5.40; p = 0.005), and their disease was more frequently healthcare-related (44/159, 27.7% vs 23/159, 14.5%; p =0.006). They also had significantly less antivirals prescribed (2/159, 1.25% vs 119/159, 75%; P < 0.001). Admission rates were similar among RSV and influenza patients (128/159; 80.5% for RSV and 129/159, 81.1% for influenza), but median length of stay was slightly higher among influenza patients (11.2 days vs 8.6 p=0.1). Admission to ICU was required only in 3 RSV patients and 5 flu patients. Mortality was also higher in RSV-positive patients (20/159, 12.5% vs 12/59, 7.5%; P = 0.5).

Conclusions: RSV is a major cause of moderate-to-severe influenza-like illness, with a high mortality, probably related to the lack of specific treatment for this population. More studies regarding efficacy of oral antiviral agents for elderly RSV infected patients must be developed.

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Abstract 2888

Interest of rapid detection of emerging extensively drug-resistant bacteria by PCR associated with temporary dedicated team for high-risk patients

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Background: Management of "high-risk patients" for carbapenemase-producing Enterobacteriaceae (CPE) or vancomycin-resistant enterococci (VRE) is based on a rapid search and isolate strategy. In order to avoid contact cases, French recommendation suggests a dedicated team at hospital admission. This recommendation is difficult to apply and maintain until the results of the cultures (48h). Here, we report the results of a new management strategy combining early detection with PCR and dedicated team during few hours.

Materials/methods: Repatriated patients, contact patients or previously known CPE/VRE carriers were targeted as being "high-risk" patients for CPE/VRE carriage.

In order to control the spread of CPE/VRE and facilitate the implementation of control measures for these patients, we proposed to medical wards a strategy combining :
- isolation in a single room, contact precautions and dedicated team at admission
- patient rectal screening with culture and Xpert® Carba-R v2 and Xpert® VanA/VanB 24H a day.

In case of PCR negativity, dedicated team was stopped and standard contact precautions maintained until culture results. If PCR was positive, the dedicated team was maintained or a high level of contact precautions implemented in case of understaffed.

Results: Between july 2018 and august 2019, 189 rectal screening were performed. Among them, 26 PCR were prescribed at admission.

Nine of the 26 PCR were positive [34,6%] with 5 OXA-48, 1 NDM, 2 OXA-48+NDM, 1 false positive with VanB. Four patients benefited of dedicated team during hospitalization [no contact case] and 4 patients of high contact precautions level without dedicated team, generating 108 contact cases and no secondary case.

Analysis of the 189 prescriptions reveals that 15 other patients could have benefited from a PCR. Six CPE [40%] were isolated in culture generating 131 contact cases and 2 secondary cases.

Conclusions: Combination of rapid molecular screening of CPE/VRE 24 h a day and dedicated team pending PCR's results allows adhesion of the caregivers to heavy complementary measures. This strategy avoids late discoveries of CPE/VRE, limits the number of secondary cases [0/108 vs 2/131 contacts] and reduces costs related to the dedicated teams [4 hours vs 48 hours for 17 negative patients].

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Abstract 2889

Antimicrobial therapy with aminoglycoside or meropenem in the intensive care unit for hospital-associated infections and risk factors for acute kidney injury

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Background: Aminoglycosides were discovered more than 75 years ago and remain an interesting and effective class of antibiotics used in the context of multidrug resistance. Nevertheless, there have historically been concerns of acute kidney injury (AKI) with the use of aminoglycosides. The present study aimed to compare the AKI incidence and mortality rate between critically-ill patients treated with aminoglycoside or meropenem in the intensive care unit setting using a propensity score matching approach.

Materials/methods: This cross-sectional study was conducted at two university hospitals from January 2011 to October 2017. At both centers, amikacin was prescribed at 15 mg/kg daily infused over 30 minutes, while gentamycin was prescribed at 3 mg/kg daily and meropenem with a minimum dose of 1,000 mg q8h infused over 3 hours after the loading dose regimen. Clinical and laboratorial data were evaluated to exclude potential confounders and to calculate the Charlson index. AKI was classified according to the Acute Kidney Injury Network criteria. All tests were two-tailed, and a p value ≤0.05 was considered significant in the univariate and multivariate analyses.

Results: We included 494 patients, 95 and 399 of whom used meropenem or aminoglycoside, respectively. Patients in the subgroup that used meropenem were matched with controls (aminoglycoside). Among the 494 patients, 120 developed any grade of AKI (24.2%). After propensity score matching, there were no significant differences in AKI incidence and mortality rate between the aminoglycoside and meropenem groups (p=0.324 and 0.464, respectively). Association between use of nephrotoxic drugs and AKI development demonstrated statistical significance only for vancomycin (p=0.002) and loop diuretics (p=0.033).

Conclusions: Patients on the aminoglycoside regimen neither presented a higher AKI incidence nor mortality rate when compared with those on the meropenem regimen. Aminoglycosides may be a safe option for the treatment of critically-ill patients on carbapenem sparing antimicrobial stewardship programs.

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**Abstract 2892**

**Debridement And Implant Retention (DAIR) with local administration of personalised cocktail of bacteriophages (PhagoDAIR) followed by suppressive antibiotic therapy as salvage therapy in patients with relapsing prosthetic knee infection (PKI)**

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**Abstract third-party references:** Lyon BJI study group

**Background:** Lytic bacteriophages trigger bacterial lysis through their multiplication in an exponential and self-sustained reaction. They have a high potential in patients with prosthetic joint infection, as they have a synergistic anti-biofilm activity with antibiotics. In elderly patients with chronic PKI, suppressive antibiotic therapy is sometimes used after performing an open “DAIR” procedure, but the rate of success is only approximately 60%. Arthroscopic DAIR is considered to be not appropriated, as this procedure is associated with a higher failure rate.

**Materials/methods:** We proposed in “CRIOAc Lyon” to perform DAIR with local administration of a personalized cocktail of anti-*S. aureus* or anti-*P. aeruginosa* bacteriophages [PhagoDAIR] followed by suppressive antibiotic therapy in patients with relapsing PKI in therapeutic dead-end (for whom revision or transfemoral amputation was not feasible) (panel A). Each case was discussed with ANSM, the French health authority. Bacteriophages, produced according Good Manufacturing Practice (GMP) guidelines, were finally selected from the Pherecydes library depending on the phagogram (panel B). Hospital pharmacist mixed each phage (1 ml of 1x10\(^{10}\) PFU/ml) extemporaneously as “magistral” preparation (final dilution 1x10\(^{8}\) PFU/mL).

**Results:** Four patients (64, 81, 84, 89 yo) were treated with the PhagoDAIR procedure. All of them had relapsing PKI due to methicillin-susceptible *S. aureus* (2 patients), *S. lugdunensis* (1 patient) and *P. aeruginosa* (1 patient). Arthroscopic DAIR was performed in 2 patients (arthrotomy not feasible) (panel C), open DAIR was performed in the 2 others, with soft tissue flap in one of them. Patients were initially treated with antibiotics in combination during 6 to 12 weeks, followed by suppressive anti-biotherapy (cephalexin for staphylococci PKI, ciprofloxacin for *P. aeruginosa* PKI). During a follow-up of 6, 7, 12 and 24 months, respectively, the outcome was favorable with considerable improvement of the function for all patients and disappearance of signs of infection (panel D) [video available].

**Conclusions:** Personalized GMP bacteriophage therapy has the potential to be used as salvage therapy during DAIR in patients with relapsing *S. aureus*, *S. lugdunensis* and *P. aeruginosa* PKI, to improve the efficacy of suppressive antibiotics, and to avoid considerable loss of function.
Detection of microorganisms in sonicated titanium screw model after in vitro biofilm production using culture, MALDI-TOF MS and qPCR

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Background: Sonication can increase the sensitivity of prosthetic device cultures, since it can disrupt the bacterial biofilm associated with infections. Molecular investigation of sonicated fluid has been described, aiming to improve the sensitivity of the diagnosis. The aim of this study was to evaluate the sonication technique with a plastic bag and the effect of refrigeration on microorganism detection with conventional culturing, MALDI-TOF MS (mass spectrometry) and qPCR (real-time PCR) assay on an orthopedic screw model.

Materials/methods: Biofilms of Staphylococcus aureus, Pseudomonas aeruginosa, and Candida albicans were produced on orthopedic screws, which were stored under different conditions and temperatures before sonication. After sonication, MALDI-TOF MS, qPCR and culture protocols were performed using the sonicated fluid for detecting the microorganisms involved in the biofilm. The results were analyzed by non-parametric Mann Whitney test and difference was significant when p <0.05.

Results: The bacterial bioburden decreased by approximately 1log after the refrigeration period, in the screws containing P. aeruginosa and S. aureus biofilms. All the microorganisms involved in the screw biofilms were detected with MALDI-TOF and qPCR. In culture, reduction was significant in the groups with P. aeruginosa stored in plastic bags, where the count in the immediate group was 9x10⁷ CFU/mL and the count in the post-refrigeration group was 2x10⁶ CFU/mL (p <0.05). S. aureus colony counts reduced from 4x10⁸ CFU/mL in the immediate SP to 1x10⁷ CFU/mL in post-refrigeration SP (p <0.05) (Figure 1).

Conclusions: Significant reductions in CFU counts occurred only in groups stored in the plastic bag, indicating that changes in temperature and humidity may favor cell death. Microbial identification by MALDI-TOF in sonicated fluid is feasible, provided that the sample has enough bioburden. With qPCR, there were no differences between the detection in the screws processed immediately or after refrigeration. It is necessary to consider whether the refrigeration period would affect microbial recovery in an explanted prosthesis.

Figure 1. (A) Distribution of S. aureus samples after different processing conditions; (B) Distribution of P. aeruginosa samples after different processing conditions; (C) Distribution of C. albicans samples after different processing conditions. RC: Rigid recipient, PB: Plastic bag.

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Abstract 2897

**Changes in the characteristic of the population with chronic hepatitis C receiving treatment with direct acting antivirals in a referral centre during the post-interferon era**

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**Background:** Treatment of chronic hepatitis C (CHC) has been revolutionized since the widespread availability of direct acting antivirals (DAAs) in 2015. These regimens allow now the eradication of hepatitis C virus (HCV) in the majority of those treated. However, the characteristics of treated patients are changing, and it is difficult to forecast the future needs in term of treatment number and characteristics.

**Materials/methods:** We retrospectively collected the demographic and clinical characteristic of all those treated with DAAs from 01/01/2015 to 30/10/2019 in a referral centre in Northern Italy and we stratified these characteristics according to the year of treatment.

**Results:** Overall, 2569 patients were treated: 230 (9%) in 2015, 261 (10.2%) in 2016, 660 (25.7%) in 2017, 988 (38.5%) in 2018 and 430 (16.7%) in 2019. Male were the majority until 2018 when female surpassed them (P=0.01). Cirrhotics were the majority until 2017, when DAAs treatment was granted to all those infected, then non-cirrhotic largely exceeded them (P=0.01). The fraction of foreigners almost doubled from 2015 to 2019 (4.3% vs 8.1%, P=0.04). The sustained virologic response rates steadily increased during the study period, from 93% in 2015 to 96.9% in 2018 (P=0.01). Interestingly, also the median age at treatment progressively increased during the study period, from 59.8 in 2015 to 62.2 in 2019 (P=0.04). Finally, the prevalence of HIV-infected patients reached the top in 2016 (16.9%) and the steadily decreased to 10.2% in 2019 (P=0.01).

**Conclusions:** The population of patients receiving antiviral treatment with DAAs is becoming older, it is composed by a thin majority of female and overall has a low-grade of liver fibrosis. Rates of successful treatment are moving toward 100%.

**Figure 1.** Trend in sex distribution, presence of cirrhosis, coinfection with HIV and SVR rates in the Pavia HCV-cohort according to year of treatment.

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**Abstract 2898**

**One-stage extraction and replacement of infected cardiac implantable electronic devices**

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**Background:** Infective complications of CIED such as endocarditis and/or infections of the pocket had a constantly growing incidence in last years. International guidelines state that devices’ removal is mandatory to eradicate the infection and recommend a transvenous extraction. However, there is no evidence about the timing of reimplantation. Usually a new CIED is reimplemented 7-10 days after the extraction and during this period in CIED-dependent patients a temporary CIED is used.

The aim of this study is to evaluate the possibility of a one-stage strategy of transvenous extraction and replacement of CIED in CIED-dependent patients with a CIED-related infection.

**Materials/methods:** All patients with a CIED-related infection from March to September, 2019 were enrolled. All patients underwent one-stage CIED removal and reimplantation. Blood and lead culture were performed. Biofilm production was established by culture on Congo Red agar.

**Results:** Eighteen patients were enrolled (12/18 with a CIED-related endocarditis, 6/18 with infection of the pocket). Blood cultures resulted positive in 33% of patients at admission. In 17 patients Gram positive cocci were isolated (7 S. epidermidis [5/7 methicillin-resistant], 3 S. aureus [2/3 methicillin-resistant], 3 S. lugdunensis, 1 S. haemolyticus, 1 S. caprae, 1 S. schleiferi, 1 S. warneri) while in the remaining patient infection was due to Pseudomonas aeruginosa. A combination therapy with activity against (daptomycin plus ceftobiprole or cefazolin) biofilm was administered to the first 17 patients. In the case with P. aeruginosa isolation, a combination of cefiderocol and imipenem was given. All patients were cured with no complications nor infection recurrences [median follow-up 80 days]. Two S. epidermidis strains were tested for biofilm production and both resulted positive (black colonies growth on Congo Red agar).

**Conclusions:** One-stage extraction and reimplantation could be a promising strategy to treat CIED-related infection if associated with anti-biofilm antibiotic treatment [es: daptomycin] even in case of highly biofilm-producing S. epidermidis.

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Abstract 2900

**Can a combination of several biological markers help to diagnose influenza co-infections?**

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**Background:** Diagnosis of bacterial coinfection during an episode of community influenza is difficult to achieve in practice. The diagnosis is based on compatible clinical examination with aggravation of symptoms following an improvement, usually around the fifth day, associated with an increase in leukocyte count and CRP. The aim of this study was to propose a composite score based on biological exam able to differentiate patients with influenza with and without bacterial coinfection.

**Materials/methods:** In this retrospective cohort study, 47 consecutive patients who were admitted to the emergency department with positive influenza PCR and who had a blood count and CRP assay from 2018-12-26 to 2019-02-02 were included.

Patients were classified as coinfected or not based on their progress and the conclusion of the hospitalization report. Patients who returned home without antibiotic from the emergency department were classified as not coinfected. We created a composite score including leukocyte count and CRP assay by multiple linear regression. The score results for each patient were included in an ROC curve.

**Results:** Of these 47 patients, 18 were classified as coinfected and 29 as not coinfected. Using the CRP with a threshold at 77.5 mg/L, we obtain a sensitivity of 61%, a specificity of 93% and a likelihood ratio of 8.86. Using leukocytes, we obtain a sensitivity of 61%, a specificity of 90% and a positive likelihood ratio of 5.91.

Composite score determined by the multiple linear regression is calculated as:

Score = 0.00436 × (CRP) + 0.0282 × (Leucocyte count) - 0.1349.

The score results were represented in an ROC curve (Graph 1). With a cut off score at 0.41, we obtain a sensitivity of 83%, a specificity of 90% and a positive likelihood ratio of 8.61.

**Efficacy of a leukocyte count and CRP combination to diagnose a superinfected flu**

**Conclusions:** We have shown that a score combining two biological markers having low diagnostic values can obtain a score with a higher diagnostic value.

The categorization of patients based on hospitalization reports without objective clinical criteria, generally based on CRP and leucocytes that have been evaluated, and the small size of our cohort limit the impact of our study. Our study is preliminary to work combining other biomarkers to create a more effective score.

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Abstract 2907

The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS): roll-out of a successful antimicrobial stewardship programme in Nigeria using the global-PPS tool

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Background: There are no formal stewardship programs in Nigeria. We aimed to assess the effect of antimicrobial stewardship actions in the “Lagos University Teaching Hospital” in Nigeria using the standardized Global-PPS (www.global-pps.com).

Materials/methods: The Global-PPS was conducted in April 2015, August 2017 and December 2018. Detailed data was collected for all in-patients receiving an antimicrobial on the day of PPS. Data collected details on antimicrobial agents, indications for antibiotics and a set of quality indicators. From 2016, survey data were periodically disseminated at hospital grand rounds and clinical meetings to educate prescribers and inform all paramedical staff. An antibiotic policy was also formulated, and disseminated to all clinical departments. Surgeons were counselled on surgical prophylaxis at a clinical meeting. In the paediatric department, antibiotic guidelines were developed in December 2017 and a prospective audit with intervention and feedback was initiated a month before the 2018 Global-PPS.

Results: Out of 183, 258 and 305 admitted patients, 82.5%, 65.5% and 51.1% were on antibiotics in 2015, 2017 and 2018 respectively (table). All quality indicators, except for missing guidelines in adult wards, improved in 2018 as compared to 2015 and 2017. Prospective audit over 6 months in 2019 revealed 59.3% compliance with guidelines. Out of 360 interventions, compliance was 51.1%. Inappropriate antibiotic prescribing was mainly related to unnecessary and wrong type of antibiotic while de-escalation was the intervention most commonly complied with.

Conclusions: The gradual initiation of several antimicrobial stewardship interventions since 2016 enhanced substantial improvements of appropriate antibiotic prescribing as measured by three Global-PPS. The follow up Global-PPS in 2018 revealed satisfying results. Repeated measurements are needed to enhance sustainable improvements.

Table. Quality indicators for antibiotic prescribing following three Global-PPS

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Impact of early appropriate antimicrobial therapy on a new hierarchical endpoint for ventilator-associated bacterial pneumonia

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Background: Recently, a multinational expert consensus was obtained on a definition of clinical cure and on a composite endpoint (including survival, mechanical ventilation (MV)–free days though day 28, and clinical cure at day 8-10 after treatment initiation) that could be used in ventilator-associated pneumonia (VAP) trials (1). The aims of this work were to evaluate the impact of early adequate antimicrobial treatment (EAT) on VAP outcome using these clinical cure definition and consensus composite endpoint.

Materials/methods: Retrospective analysis of French database OutcomeRea (1997 -2016) including patients with VAP. Adequate treatment was considered early if administered within the 24h after pneumonia. Clinical cure was defined as the resolution of signs present at enrolment i.e. hypoxemia, vasopressor, fever/hypothermia, purulent tracheal secretions and leucocytosis/leukopenia. A variable was computed to assess the three elements of the composite endpoint successively; its rank ranged from 1 (patient alive, never required mechanical ventilation and cured) to 709 (patient died).

Results: 1181 VAP episodes were included. Antimicrobial treatment was adequate early in 599 episodes (51%); The median [IQR] delay before adequate treatment was 3 [2 ; 4] days in the other patients (p<0.01). Mortality rates were 200/599 (33.4%) and 192/582 (33.0%) in the EAT and the no-EAT groups respectively (p=0.88). Among the survivors at day 28, MV duration was long (12 in EAT vs 11 days in no-EAT, p=0.94) and clinical cure rate was high (84.0 vs 87.7%, p=0.13). Resolution rates of signs of pneumonia were variable ranging from more than 80% (fever and tracheal secretions) to less than 50% (hypoxemia). The composite outcome did neither differ according to EAT (median rank 370 vs 359, p=0.69). This lack of difference persisted regardless of the pathogen involved.

Conclusions: A composite outcome validated by a Delphi process, involving international expert panel, is able to better classify VAP patients. We did not find any impact of EAT on mortality, clinical cure rate and duration of MV in survivors or this new hierarchical composite endpoint. This result suggests a minimal impact of early appropriate therapy of VAP on patients’ outcome.


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**Abstract 2912**

**esp17 and its importance in dry stress resistance**

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**Background:** *Staphylococcus aureus* has been documented to have resistance in various stressful conditions outside of the host. One prominent characteristics of *Staphylococcus aureus* is desiccation tolerance. My project focuses on one of the genes found in our group as ones expressing in subpopulation termed esp. (expression in subpopulation). The esp17 gene is predicted to be a transcription factor [arsR homologue] and a part of a three- gene operon [esp17-arsB-arsC]. Our group had previously documented high desiccation tolerance in an esp17-overexpressed strain compared to Wild type RN4200. Our group also found an esp17 operon deletion mutant has increased susceptibility to desiccation. I aimed to show further importance of esp17 in desiccation resistance by generating an esp17 single gene deletion mutant and testing its effect in desiccation related experiments.

**Materials/methods:** RN4220, overexpression and esp17 were cultures for 16 hours in 5mL TSB medium. Due to the overexpression strain esp17 being in Trans with pRIT plasmid it was exclusively supplemented with chloramphenicol. Optical density was measured, and cultures were adjusted to an OD600. Serial dilutions of the adjusted cultures were plated on TSA to enumerate CFU at T=0. 10 µL of the adjusted cultures were placed into 96 well plates in triplicate after which they were dried under airflow at room temperature. The 96 well plates were incubated in an ADVANTEC™ humidity-controlled incubator and bacteria were collected in 200uL TSB by vigorous scraping and mixing with a pipette at 2- and 5-days post inoculation. Survival under dry stress was calculated as the fraction of CFU at each time point relative to at T=0.

**Results:** The results show clear survivability advantage in both strains, RN4220 and overexpression whilst esp17 and esp17-operon survival is greatly diminished in dry stress conditions. These results are significant in day 2 comparing RN4220 with esp17. Notably there is high number of CFU in day 2 results compared to day 0 results.

**Conclusions:** The experiments carried out shows the importance of esp17 in desiccation resistance.

![Desiccation assay](image-url)

**Figure 3.** Desiccation assay. Filled black: RN4220, open: Δesp17, filled gray: overexpression.

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Prevalence of different resistance mechanisms in carbapenemase-producing organisms in Kenya: a phenotypic study

Anne Amulele*, Joseph Waichungo1, Alfred Mwanzu1, Edwin Machanja1, David Wareham2, James A Berkley1, Nicola Claire Gordon3

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Background: Antimicrobial resistance is currently one of the leading threats to human health globally. Carbapenem resistant organisms (CROs) are a top priority, however, knowledge on these organisms in Africa is limited. The aim of this study is to determine the resistance mechanisms in CROs from Kenya.

Materials/methods: We identified imipenem non-susceptible Enterobacterales, Acinetobacter spp and Pseudomonas aeruginosa isolated from clinical samples from patients admitted to Kilifi County Hospital (KCH) from 2005 to 2019. Additionally, rectal swabs were obtained from malnourished children admitted to KCH, Coast General Hospital, Mombasa and Mbagathi Hospital, Nairobi and screened for carbapenem resistance. Antibiotic susceptibility was determined using the disc diffusion method and carbapenem resistance confirmed using imipenem, meropenem and ertapenem discs. We detected carbapenemases using the modified carbapenem inactivation method (mCIM) and Triton Hodge test (THT), metallo-β-lactamases (MBLs) using EDTA-mCIM (eCIM) and AmpC cephalosporinase using MAST-AmpC detection set.

Results: We identified 104 imipenem non-susceptible bacteria from historic samples; 86 were confirmed to be carbapenem resistant on repeat testing. Of these, 32 were from blood, 30 from rectal swabs, urine (11), pus (9), aspirate (2), cerebrospinal fluid (1) and sputum (1). There were 36 Acinetobacter spp (18 A. baumannii), 9 P. aeruginosa and 41 Enterobacterales namely: 25 E. coli, 11 K. pneumoniae, 3 E. cloacae, 1 M. morganii and 1 C. freundii. Carbapenemases were detected in 28/34 (82%) and 25/34 (74%) of Enterobacterales by mCIM and THT respectively of which 22/28 (79%) were MBLs and 6/28 were serine-based carbapenemases. We did not detect carbapenemases in P. aeruginosa by either method while 33/35 Acinetobacter spp were positive by THT. AmpC activity was detected in only 3/17 non-producers and were E. cloacae, K. pneumoniae and M. morganii.

Conclusions: Metallo-β-lactamases were the main carbapenem resistance mechanism in Enterobacterales isolates tested, while resistance in P. aeruginosa was likely to be due to non-enzymatic methods. Given that carbapenems are rarely available in public hospitals in Kenya, the range of species and mechanisms identified in this study is concerning and demonstrates that the emergence and spread of CROs in this region is multifactorial rather than due to establishment of a successful clone.

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Salvage treatment of invasive pulmonary aspergillosis with isavuconazole and caspofungin combination in a lung transplant recipient

Paolo Pavone*, Carolina Carillo1, Ylenia Pecoraro1, Federico Venuta1, Claudio M. Mastroianni1, Gianluca Russo1

1Sapienza University, Rome, Italy

**Background:** Isavuconazole (ISA) has recently been approved as a first line treatment for invasive pulmonary aspergillosis (IPA). Anyway clinical data in lung transplant recipients and/or patients failing voriconazole are lacking.

**Case Report:** A 50 years-old man underwent bilateral lung transplant in April 2019 and was started on tacrolimus and azathio- prine. During the hospital stay he received antifungal prophylaxis with inhaled liposomal amphotericin B (AMPHO) at the dose of 25 mg/day. In July 2019 he came back to emergency reporting shortness of breath and a CT scan of the chest showed diffuse peri-bronchial ground glass opacities, galactomannan was strongly positive in the BAL (7.3 index), fungal culture growed *Aspergillus flavus* so that a diagnosis of IPA with radiological airway invasive pattern was made. The patient was consequently started on iv AMPHO 3 mg/kg but after two weeks he was switched to voriconazole (VORI) (6 mg/kg loading dose and then 4 mg/kg q 12 hours) because of kidney toxicity. Given the wide fluctuations of VORI plasma levels (last value: 0.6 μg/ml despite TDM-guided dose adjustment), the lack of clinical response (persistently positive galactomannan in BAL and positive fungal culture, respiratory insufficiency, no significant change in the CT chest) and the development of liver toxicity the treatment was switched to iv ISA (200 mg q 8 hours loading dose for 2 days and then q24 hours) combined with caspofungin (70 mg loading dose and then 50 mg/day). After 14 days of treatment ISA plasma value was 2.66 μg/ml. *Aspergillus flavus* susceptibilities excluded azole-resistance: VORI MIC 0.125, ISA MIC 0.125, caspofungin MIC 0.016, AMPHO MIC 2. After 8 weeks lung function and CT chest had mild improvement while BAL galactomannan was reduced but still positive (2.92 index). Lung biopsy after treatment showed chronic lung inflammation but no hyphae and other signs of fungal invasive disease. Class I and II-HLA antibodies were negative in the blood.

Conclusions: ISA and caspofungin combination was well tolerated and associated with normal ISA plasma levels but treatment didn’t lead to microbiological cure in a lung transplant recipient with invasive pulmonary aspergillosis by *A. flavus* and possible chronic lung rejection.

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Abstract 2921

**Bacteraemia with ESBL-producing Enterobacteriaceae is associated with increased levels of IgG antibodies specific to CTX-M-15 and/or CTX-M-27**

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**Background:** Infections with extended spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae (EPE) are increasing worldwide. Molecular methods such as whole genome sequencing have been used successfully to reveal antimicrobial resistance and virulence genes of pathogenic EPE, but considerably less is known about the adaptive immune response to such infections.

**Materials/methods:** Patients with previous bacteraemia with EPE (n=59) or non-ESBL-producing Enterobacteriaceae (n=42) were recruited in this prospective observational study in Skåne, the south of Sweden. Sera were collected from 9 up to 21 months after bacteraemia. Enzyme-linked immunosorbent assay (ELISA) was used for detection of specific IgG antibodies directed against His-tagged recombinant beta-lactamases CTX-M-15 and CTX-M-27 that were expressed in *Escherichia coli* BL21 (DE3). Recombinant BRO-1 and TEM-1 were included as controls. The beta-lactamase resistance genes of EPE blood isolates were amplified by colony PCR with CTX-specific primers and typed by DNA sequencing.

**Results:** Out of 59 patients with EPE bacteraemia, 18 (30.5%) had detectable IgG specific to CTX-M-15 and/or CTX-M-27. In the control group with non-ESBL-producing *E. coli* bacteraemia, only 4 (9.5%) out of 42 patients carried detectable IgG against CTX-M-15/CTX-M-27 (p<0.01). Our preliminary data revealed that the majority (94%) of the EPE blood isolates from patients with detectable anti-CTX antibodies indeed carry the *blaCTX-M-15* or *blaCTX-M-27* genes. The patients of the EPE group had a significantly higher median Charlson comorbidity index and greater portion of renal disease, compared to the control group.

**Conclusions:** This study implies that bacteraemia during EPE infection has triggered a substantial adaptive immune response resulting in production of antibodies targeting one of the EPE virulence factors, the CTX enzyme. It is interesting to further investigate the importance or protective role of the humoral immune responses against EPE infections. In addition, our finding sheds new light upon the potential of the host immune response as a prognosis/diagnostic tool for detection of EPE-related infections.

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Abstract 2923

Analysis of adherence to treatment among rural patients with various behaviour and social characteristics
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Background: Non-adherence to tuberculosis (TB) treatment remains one of the main obstacles that need to be overcome by multi-drug resistant (MDR) TB control programmes especially in the remote rural areas. The present study attempted to identify various factors accounting for non-adherence that could help to achieve better treatment outcomes among rural patients.

Aim: To analyse the correlation between both social and behaviour characteristics and adherence to MDR TB treatment among rural patients.

Materials/methods: A cohort of 210 rural patients of older than 18 years with newly diagnosed sputum smear-positive pulmonary MDR TB and admitted to the principal Saratov regional tuberculosis hospital were enrolled in the case-control study divided between 70 non-adherent (with 2 and more violations of the regimen - NA) and 140 adherent (A) patients. Each participant was interviewed using a structured questionnaire after first 6 months of direct observation treatment at the hospital.

Univariate logistic regression analysis was performed to identify significant factors associated with treatment default. Statistical significance was taken as P < 0.05.

Results: The main factors associated with MDR TB treatment non-adherence were social, family and personal factors. Missing treatment was significantly associated with the patient’s income (OR: 5.6, 95% CI: 4.4-6.8), unsolved medical and social problems in the family (OR: 2.7, 95% CI: 2.4-3.1), concern to lose a job (OR: 2.2, 95% CI: 2.0-2.4) and problems while interacting with others (OR: 2.2, 95% CI: 1.9-2.5). Unemployment, alcoholism, previous imprisonment and homelessness as a cause of MDR TB treatment default were associated with rural marginal population. Factors significant in the bivariate analyses—literacy and low status occupation—were not found to be significantly associated with non-adherence.

Conclusions: Low socio-economic status and marginal features are important risk factors for non-adherence to TB treatment of rural TB patients. Social support and adequate psychological supplies for treatment can help patients overcome structural and personal barriers.

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Decrease in antibiotic days of therapy after notification of *Clostridioides difficile* carriage status: an interventional study

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**Background:** *Clostridioides difficile* (CD) is a leading cause of healthcare-associated infections. Screening asymptomatic patients for CD carriage is controversial. We assessed changes in antibiotic prescription practices after notification of carriage status and its effect on the incidence of CDI among carriers.

**Materials/methods:** Since June 2017 patients admitted to internal medicine wards were screened for CD carriage by CD toxin-B PCR using rectal swabs. During phase I, June-August 2017, we screened all patients but clinicians were blinded to carriage status. During phase II (2018), only high-risk patients (elderly & those recently hospitalized) were screened and clinicians were notified about carriage status. Additionally, antibiotic stewardship meetings were held with an infectious disease specialist. CDI diagnosis protocol in both study phases included a stool sample for 2-step EIA/PCR in any patient with >3 unformed stools/24h.

**Results:** During phase I, 92 carriers were detected, of these 69 had high risk and fulfilled the screening criteria implemented in phase II. During phase II, 421 carriers were detected. Despite no change in CDI diagnosis protocol, the proportion of stool samples sent for CDI diagnosis among carriers increased, when CD carriage was notified (Phase II); from 16.0% of carriers having an unformed stool sent, to 28.4% in the first quartile of phase II (p=0.0038).

Despite this, a significant decrease in CDI among carriers was observed; from 16.0% of carriers developing CDI during hospitalization to 7.5% in phase II (p=0.006), a 51% reduction in the incidence rate of CDI among carriers (12.23/1000 HD to 6.24/1000 HD).

Concurrently, a significant reduction in antibiotic treatment (days of therapy (DOT)/hospital days; %DOT) of carriers was observed; from 57.1% in phase I, to 41.5% in phase II, p=0.009. An even greater reduction (of 32%) was observed when the same time periods in the subsequent years were compared (from 57.1% to 38.9%, p=0.009).

**Conclusions:** Screening for CD carriage on admission and notifying clinicians increased the index of suspicion of active CDI, yet resulted in reduced rates of CDI among carriers. This is probably due to a significant reduction in the percentage of antibiotic DOT during hospital stay.

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Abstract 2927

**Effect of augmented renal clearance on the extended-interval dosing of aminoglycosides in critically ill pediatric patients**

Nathaniel J. Rhodes*1,2; Sean Avedissian3,4; Alla Hadid1; John Bradley5,6; Jennifer Le7

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**Background:** Augmented renal clearance (ARC) has been documented among critically-ill pediatric patients treated with aminoglycosides. However, the effect of ARC on aminoglycoside PK/PD attainment with extended-interval dosing is unknown. We evaluated the effect of ARC on the probability of achieving efficacious or potentially nephrotoxic aminoglycoside exposures in pediatric patients.

**Materials/methods:** We fit a population model of gentamicin and tobramycin PK from pediatric patients with normal to high renal function using Pmetrics. Total clearance was scaled to total body weight \((CL0 \times TBW/70)^{0.75}\), age \((age/TM+ageH)\), and serum creatinine \((CL1 \times Scr/0.5)\). An additive categorical variable \((CL2)\) was integrated for ARC severity (i.e., none, moderate, or severe). Monte Carlo simulations were conducted based on age (fixed at 1, 4 and 12yrs) and TBW (fixed at 8.5, 15, and 50kg). Scr was fixed at 0.5mg/dL. Extended-interval dosing regimens of 5-12 mg/kg/day were compared against MICs from 0.25-1mg/L. In the PTA, an AUC\(_{0-24hr}\)/MIC ratio of 70 was considered for efficacy. The probability of nephrotoxic exposures \(P_{toxicity}\) was defined as the projected incidence of \(C_{min0-24hr}\) of >2mg/L.

**Results:** A total of 85 pediatric patients (range 1.25-21yrs, 54% female) contributed 175 concentrations [median (IQR) 2 [1-2] concentrations/patient]. A two-compartment covariate-adjusted model was best and most parsimonious [population \(R^2=0.872\), individual \(R^2=0.981\), AIC=227]. The mean value of the model parameters \(CL0, CL1, CL2, Q, Vc, Vp, TM, and H\) were 9.2L/hr, 0.41L/hr, 0.4L/hr, 1.03L/hr, 18.1L, 67.6L, 10yrs, and 2 respectively. The simulation analyses are summarized in the Table below. Above an MIC of 1mg/L, all regimens had <90% PTA.

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>MIC [mg/dL]</th>
<th>Dose (mg/kg/day) yielding PTA&gt;90% and (P_{toxicity}&lt;5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>0.25</td>
<td>None</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>5-12</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>7-12</td>
</tr>
<tr>
<td>0.5</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>10-12</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>None</td>
</tr>
</tbody>
</table>

**Conclusions:** ARC and elevated MICs were associated with lower PTA using standard extended-interval dosing regimens. More intense regimens may be required for moderate to severe ARC, but a careful assessment of toxicity risk and post-antibiotic effect is needed. Empirical combination with non-aminoglycosides in critically-ill patients appears prudent.

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Abstract 2929

Serum \((1 \rightarrow 3)\-\beta\-D\-glucan\) has suboptimal performance for the diagnosis of \textit{Pneumocystis jirovecii} pneumonia and correlates poorly with respiratory burden measured by quantitative PCR in patients with cancer

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\textbf{Background:} \textit{Pneumocystis jirovecii} pneumonia (PCP) is a common opportunistic infection. Serum \((1 \rightarrow 3)\-\beta\-D\-glucan\) (BDG) has shown both excellent correlation with high fungal burden and clinical performance as a surrogate diagnostic marker for PCP in HIV/AIDS patients. Non-HIV immunocompromised patients are characterized by lower fungal burden. We evaluated the test performance of BDG and its correlation with quantitative PJP PCR in non-HIV cancer patients.

\textbf{Materials/methods:} The study extended from 04/2014 to 02/2019. Definite PCP was defined as presence of clinical-radiological features suggestive of PCP plus both PCR(+)\_microscopy(+) in BAL samples, while probable PCP shared the same features but with PCR(+)\_microscopy(-). PCR(-) patients were used as non-PCP controls. Patients had concomitant serum BDG. After excluding those with another fungal pneumonia or recent IVIG (\(\leq 60\) days), we performed a correlation analysis between PCR and BDG, and assessed BDG clinical performance.

\textbf{Results:} Among 2972 patients, we identified 101 PCR(+) patients (73 definite/probable, 28 possible) and 76 non-PCP controls. Data analysis showed low positive BDG/PCR correlation among 101 PCR(+) cases (Spearman's coefficient= 0.48; \(p<0.001\)). The analysis was performed on definite/probable cases, and also showed low positive correlation (0.31; \(p=0.02\)). BDG performance on PCR(+) cases at different BDG cutoffs (\(\geq 80\); \(\geq 200\) and \(\geq 400\) pg/mL), demonstrated poor sensitivity, while at BDG cutoff \(\geq 400\), specificity increased (93%) and NPV decreased (47%). The analysis was repeated on definite/probable cases using different PCR levels as method of reference, at different BDG cutoffs (\(\geq 80\); \(\geq 200\) and \(\geq 400\)). At PCR \(\geq 84\) and BDG \(\geq 80\), the test showed sensitivity=67%; specificity=85%; PPV=85% and NPV=72%. Performance improved at increasing PCR levels, achieving sensitivity=65%; specificity=93%; PPV=81% and NPV=85%, when both PCR \(\geq 2000\) and BDG \(\geq 400\) were used.

\textbf{Conclusions:} BDG and PCR levels do not correlate well in non-HIV cancer patients, and their combined test performance to rule out PCP suffers from suboptimal sensitivity and NPV. Only at high values of both tests, the NPV was acceptable, but this was seen only in patients with definite/probable PCP. A negative BDG test should not be used to rule out PCP in non-HIV cancer patients. BDG appears to be a suboptimal surrogate marker for diagnosis of PCP in this population.

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**Abstract 2930**

**Two-photon microscopy contribution for exploration of innate immunity pulmonary mechanism after influenza virus infection of mice model**

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¹IRBA, Bretigny sur orge, France

**Background:** flu is important public health threat, very contagious and causing morbimortality. anti-viral treatments are not totally effective in severe cases and recent studies showed that adding anti-inflammatory treatment could reduce mortality. the precise knowledge of pulmonary innate immune mechanism appears to be essential, the role of innate immunity has already been studied after influenza virus infection but exclusively by indirect techniques. the emergence of high-resolution imaging tools can now allow precise exploration of cellular interactions. intravital microscopy has previously, but rarely, been used in respiratory infectious diseases only with bacillus anthracis. it should be evaluated for more conventional and usual pathogens. the objective of this work is to investigate the immune mechanisms and cellular interactions linked to influenza virus infection with two-photon microscopy in murine model.

**Materials/methods:** infection by nasal inhalation of transgenic mice (c57bl6/J whose cd11c+ cell was coupled with yellow fluorescent protein) with influenza virus strains adapted to mice: pr8 (h1n1, a/pr/8/34) and wsn (h1n1, a/wsn/33) whose ns1 protein was coupled with red fluorescent protein. after euthanasia, lungs are explanted and studied with different techniques: flow cytometry, two-photon microscopy. different cell types have been analyzed: macrophage, neutrophil polynuclear, nk cell, dendritic cell. this exploration has been done at day 1, 2, 3, 4 post-infection.

**Results:** our data in flow cytometry confirmed important macrophage and neutrophil polynuclear recruitment. two-photon microscopy showed temporal evolution of bronchial epithelium infection, epithelial damages and massive local macrophages influx [figure below]. the two viral strains seemed to have same immune recruitment but different in importance and kinetics. we have also developed technique for in vivo analysis of dendritic cells and macrophages trafficking and interactions after influenza virus infection.

**Conclusions:** two-photon microscopy, allowed us to visualize infection, location and kinetics of immune recruitment, pulmonary damages and evaluation of cells trafficking. this microscopy seems to be an excellent tool for in vivo exploration of immune mechanisms after influenza virus infection. our results are importants for design of future in vivo pre-clinical studies of vaccines trial or development of new therapeutic strategies.

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Methicillin-susceptible Staphylococcus aureus in community-acquired pneumonia: risk factors and outcomes

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Abstract third-party references: Dr Cillóniz is the recipient of a postdoctoral grant (Strategic plan for research and innovation in health; ERIS 2016–2020), the SEPAR fellowship 2018, and a grant from the Fondo de Investigación Sanitaria (PI19/00207).

Background: The epidemiology of Staphylococcus aureus is changing, with several studies reporting a decline in methicillin-resistant S. aureus (MRSA) infection and an increase in methicillin-susceptible S. aureus (MSSA) infection. We aimed to describe and compare the prevalence, clinical features, and risk factors of community-acquired pneumonia (CAP) caused by MSSA with that caused by Streptococcus pneumoniae.

Materials/methods: This was a prospective observational cohort study of consecutive adults with CAP and a definitive etiology that were enrolled between January 2004 and December 2018. Patients were divided into groups with MSSA CAP and pneumococcal CAP for analysis.

Results: A microbial etiology was established in 1,548 patients with CAP, of which 52 cases were caused by MSSA and 734 were caused by S. pneumoniae. MSSA affected 1% of all patients hospitalized with CAP, and 3% when a microbiological diagnosis was obtained. The presence of fever was independently associated with a lower risk of MSSA CAP. Patients with CAP due to MSSA had higher 30-day mortality than patients with pneumococcal CAP, both before and after adjustment for potential confounders. MSSA infection, older age, inhaled corticosteroid use, lymphopenia, acute renal failure, acute respiratory distress syndrome, and septic shock were associated with 30-day mortality (table 1).

Conclusions: MSSA CAP was associated with worse outcomes compared with pneumococcal CAP in our cohort. The absence of fever was associated with an increased risk of MSSA CAP. Methicillin-susceptibility in S. aureus strains causing CAP should not be regarded as a marker of lesser severity.

Table 1. Significant risk factors for 30-day mortality in all study population in Cox regression analyses (N = 786)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate a</th>
<th>Multivariable b</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR 95% CI</td>
<td>P-value</td>
</tr>
<tr>
<td>MSSA CAP</td>
<td>3.12 1.63 to 5.97</td>
<td>0.001</td>
</tr>
<tr>
<td>Age ≥ 65 years</td>
<td>2.92 1.56 to 5.47</td>
<td>0.001</td>
</tr>
<tr>
<td>Inhaled corticosteroids</td>
<td>1.60 0.94 to 2.74</td>
<td>0.085</td>
</tr>
<tr>
<td>Chronic renal disease</td>
<td>2.56 1.36 to 4.99</td>
<td>0.004</td>
</tr>
<tr>
<td>Neurologic chronic disease</td>
<td>2.18 1.37 to 3.94</td>
<td>0.002</td>
</tr>
<tr>
<td>Nursing home</td>
<td>2.70 1.34 to 5.18</td>
<td>0.005</td>
</tr>
<tr>
<td>Pleuritic pain</td>
<td>0.53 0.36 to 1.00</td>
<td>0.050</td>
</tr>
<tr>
<td>Fever</td>
<td>0.46 0.27 to 0.76</td>
<td>0.003</td>
</tr>
<tr>
<td>Lymphocytes &lt;431 cell/mm³</td>
<td>2.69 1.66 to 4.47</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ARDS</td>
<td>4.64 2.53 to 7.84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pneumococcal bacteremia</td>
<td>1.29 0.72 to 2.32</td>
<td>0.39</td>
</tr>
<tr>
<td>MSSA bacteremia</td>
<td>8.00 3.28 to 19.51</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>3.98 2.36 to 6.71</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septic shock</td>
<td>4.06 2.45 to 6.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ICU admission</td>
<td>2.16 1.32 to 3.52</td>
<td>0.002</td>
</tr>
</tbody>
</table>

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Abstract 2934

**Sepsis due to Gram-positive bloodstream infections in critically ill patients during a five-year period (2012-16): dissemination of linezolid-resistant *Staphylococcus epidermidis* ST22 and predictors of fatality**

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**Background:** Even though Gram-negative bacteria predominate among Greek critically ill patients, Gram-positive cocci provoke a considerable proportion of bloodstream infections especially catheter-related (CR-BSIs). The aim of the present study was to identify the molecular characteristics of Gram-positive cocci isolated from blood cultures and clinical outcome among critically ill patients.

**Materials/methods:** This retrospective study was conducted in the general Intensive Care Unit of the University General Hospital of Patras, Greece, during a five-year period (2012-16). All adult patients with a Gram-positive BSI were included. PCR was applied to identify mecA gene (staphylococci); vanA, vanB and vanC genes (enterococci). Linezolid-resistant *S. epidermidis* were further typed by multilocus sequence typing. Mutations in region V of 23S rDNA and ribosomal protein L4 were investigated by PCR and sequencing analysis. The presence of cfr gene was tested by PCR.

**Results:** In total, 141 Gram-positive BSIs were included. Coagulase negative staphylococci predominated (n=69; 65 methicillin-resistant, 23 linezolid-resistant carrying both C2534T and T2504A mutations and belonging to ST22 clone), followed by enterococci (n=46; 11 vancomycin-resistant carrying vanA gene), *S. aureus* (n=22; 10 methicillin-resistant) and streptococci (n=4; two *S. agalactiae*, one *S. galolyticus*, one *S. mitis*). The most common type of infection was catheter-related (66; 46.8%), followed by primary BSI (28; 19.9%). Septic shock was observed among 57 patients (40.4%). Overall 14-day fatality was 24.8% (35 patients). Multivariate analysis revealed septic shock (P=0.039; OR 4.0, CI 1.1-10.9) as independent predictor of fatality, while appropriate empiric antimicrobial treatment (P=0.011; OR 0.20, CI 0.06-0.69) and catheter-related BSI (P=0.024; OR 0.28, CI 0.09-0.85) were identified as a predictor of good prognosis. In order to investigate risk factors for development BSI due to linezolid-resistant *S. epidermidis*, a multivariate analysis was performed and revealed administration of linezolid (P=0.015; OR 4.9, CI 1.4-18.1) as the only independent risk factor.

**Conclusions:** Even though most Gram-positive cocci were multidrug-resistant, fatality rate was low since most BSIs were catheter-related. Among CNS, linezolid-resistant isolates represented one third of BSIs due to the dissemination of ST22 *S. epidermidis* propagated by utilization of linezolid.

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Combination empiric treatment is equivalent to monotherapy in 317 sepsis episodes due to carbapenemase-producing Klebsiella pneumoniae in critically ill patients

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Background: Combination treatment was found to be superior to monotherapy in the treatment of carbapenemase-producing Klebsiella pneumoniae (CP-Kp). The objective was to study the epidemiology, and outcome of CP-Kp bacteremia among critically ill patients.

Materials/methods: During a 9-year period (2010-18), CP-Kp isolates, from bacteremic Intensive Care Unit (ICU) patients, at a University Hospital, were studied. Antibiotic susceptibility testing was performed by the agar disk diffusion method according to EUCAST guidelines. MICs of meropenem, tigecycline and ceftazidime/avibactam were determined by Etest (bioMerieux), whereas for colistin, the broth microdilution method was applied. All isolates were tested by PCR for the presence of $bla_{KPC}$, $bla_{VIM}$, $bla_{NDM}$ and $bla_{OXA-48}$ genes.

Results: Among 2780 ICU hospitalized patients, 317 (11.7%) CP-Kp bloodstream infections were observed (284 patients). Resistance to gentamicin was found in 207 isolates (65.3%); colistin in 146 (46.1%); tigecycline in 89 (28.1%). The majority of infections were caused by KPC-producing isolates (260 episodes; 82%), followed by VIM-producing (28 episodes; 8.8%), NDM-producing (16 episodes; 5.0%) and KPC and VIM co-producing isolates (13 episodes; 4.1%). 14-day mortality was 25.5% (81 patients). Multivariate analysis identified septic shock ($P<0.001$; OR 5.1, CI 2.4-10.8), SOFA score upon BSI onset ($P<0.001$; OR 1.3, CI 1.1-1.4), corticosteroid co-administration ($P<0.001$; OR 2.6, CI 1.3-5.0) and infection by $bla_{VIM}$-carrying isolate ($P=0.006$; OR 4.6, CI 1.6-13.6) as independent predictors of mortality, whereas treatment with at least one appropriate antibiotic was a predictor of survival ($P=0.027$; OR 0.463, CI 0.233-0.916). Among septic shock patients (151; 47.6%), multivariate analysis revealed SOFA score upon BSI onset ($P=0.001$; OR 1.3, CI 1.1-1.4) and corticosteroid co-administration ($P=0.016$; OR 2.5, CI 1.2-5.2) as independent predictors of mortality, whereas treatment with at least one appropriate antibiotic was a predictor of survival ($P=0.022$; OR 0.407, CI 0.188-0.877). No difference on mortality was observed among monotherapy or combination treatment, even in patients with septic shock (Figure 1).

Conclusions: KPC-producing isolates remain the most prominent among CP-Kp. Septic shock and corticosteroid administration were associated with increased mortality. Better outcome was observed in patients who received empirically at least one appropriate antibiotic, while combination treatment did not offer any additional effect.

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Dihydropyridine-class antihypertensive drugs exhibit strong bactericidal activities against *Helicobacter pylori* and significantly reduce gastric colonisation in mice.

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**Background:** *Helicobacter pylori* is the most prevalent human pathogen worldwide and a major cause of gastritis, peptic ulcer disease and gastric cancer. In previous works, we validated a new effective anti-*H. pylori* therapeutic target, the essential response regulator HsrA. A high-throughput screening of a repurposing collection of 1120 FDA-approved, off-patent small drugs using a fluorescence-based thermal shift assay led to identifying several non-antibiotic drugs that specifically bound to HsrA and notably increased the protein conformational stability, causing a shift of the protein unfolding curve to higher temperatures due to the increased melting temperature. One of these HsrA ligands was the dihydropyridine (DHP)-class of calcium channel blocker Nicardipine. In the present study, we investigated the effect of Nicardipine and other highly prescribed commercially available DHP-class antihypertensive drugs on the biological activity of the *H. pylori* essential response regulator HsrA. The *in vitro* and *in vivo* antimicrobial activities of DHP-class inhibitors of HsrA against *H. pylori* were also evaluated.

**Materials/methods:** The ability of different DHP-class drugs to inhibit the HsrA function was determined by electrophoretic mobility shift assays. The antibacterial activity of HsrA inhibitors was tested against three different strains of *H. pylori* by determining their minimal inhibitory/bactericidal concentrations [MIC/MBC]. The efficacy of two representative DHP drugs in eradicating the *H. pylori* gastric mucosal colonization was assessed in a mouse model.

**Results:** Six different DHP-class drugs, including Nifedipine, Nicardipine, Nisoldipine, Nimodipine, Nitrendipine and Lercanidipine, noticeably inhibited the DNA binding activity of HsrA and showed potent bactericidal activities against *H. pylori*, with MIC values in the range of 4 to 32 mg/L. Oral treatments with 100 mg/kg/day of marketed formulations of Nimodipine or Nitrendipine in combination with omeprazole significantly reduced the *H. pylori* gastric colonization in mice.

**Conclusions:** The results support the use of DHP-class antihypertensive drugs in novel antimicrobial strategies against *H. pylori* infections. Currently prescribed DHP-class drugs could be also employed as “lead compounds” to synthesize more efficacious antimicrobials against *H. pylori*, even when the antihypertensive effects of these molecules result mitigated.

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Abstract 2939

Emergence of mobile mcr-8 colistin resistance in Klebsiella pneumoniae from clinical infections of hospitalised patients in Bangladesh

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1Cardiff University, Cardiff, United Kingdom, 2Public Health Wales, Cardiff, United Kingdom, 3Dhaka Medical College, Dhaka, Bangladesh

Background: Emergence of colistin resistance in Klebsiella pneumoniae has become a serious concern in clinical practice, compromising treatment options for life-threatening infections.

Materials/methods: Bacterial strains were characterized by phenotypic and genomic analysis in both Illumina MiSeq and Oxford Nanopore minION sequencing. Plasmid profile was further evaluated by PFGE followed by probing with gene of interest and conjugation assay. Stability of colistin resistance in plasmid was assessed by serial passaging up to 12 days without selection and DNA quantification by QPCR.

Results: Colistin resistant K. pneumoniae were recovered from 3 patients admitted in urology and NICU from 3.4.17 to 13.07.17, belonged to ST15. The first strain was isolated from urine of a patient with benign prostate enlargement with diabetes mellitus and the second from urine of a patient with renal carcinoma. Both patients were catheterized and were discharged at 20 and 35 days of hospital stay, respectively. The third case was a pre-term, low-birth weight neonate who died on the 18th day of hospitalization and colistin resistant K. pneumoniae was identified from blood. There was no overlapping of hospital stay among the cases. All 3 strains had common resistance profile: resistant to amoxicillin-clavulanate, piperacillin-tazobactam, cephalexins, ciprofloxacin, levofloxacin, gentamicin, trimethoprim-sulfamethoxazole and colistin and susceptible to carbapenems, amikacin and fosfomycin. Whole genome sequencing and S1 PFGE confirmed that colistin resistance of all 3 isolates was linked to mcr-8.1, found in an identical IncFIB(pQil) plasmid of 113,102 kb. Genetic environment analysis showed that two genes upstream of mcr-8.1 (Δgtf-ΔNAT-mcr-8.1) were flanked by IS5 and the downstream (mcr-8.1-ΔcapR-ΔbaeS-ΔgksA-Δgtf-ΔHTH-ΔHP-De-ΔgkA-MipA-sbmC-ΔHP-bla) by ISKpn21. Additional resistance profiles was found: sul2-1d-APH(6′)-APH(3′)-Ib; flanked by IS101 at the downstream and blaCTX-M-15 and blaTEM-1b within a composite transposon. Conjugation assay demonstrated that mcr-8.1 can be transferred to E. coli J53 with a frequency range of 3.1 x 10-2 to 8 x 10-2. MCR-8 in the plasmid was found to be highly stable without antibiotic selection in K. pneumoniae.

Conclusions: Report of mcr in clinical infections from Bangladeshi hospital highlights the urgent need for rational usage of antimicrobials in the country.

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Abstract 2940

**What is the optimal timing and technique for the source control in the subgroup of septic shock patients with intra-abdominal infections?**

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¹Kastamonu State Hospital, Kastamonu, Turkey, ²Ege University Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Izmir, Turkey

**Background:** In this study it was aimed to evaluate the efficacy and optimal timing with technique of the source control for the subgroup of septic shock (SS) patients with intraabdominal infections (IAI) in a tertiary-care educational hospital.

**Materials/methods:** Patients who had SS (sepsis+hypotension+adrenergic agent; after the date of 28th Feb 2016, arterial lactate level of >2mg/dl criterion was also added) with IAI and consulted by Infectious Diseases consultants between December 2013 and October 2019 in our centre were recorded prospectively. Statistical analysis was performed via Chi square test and Student T test while a p value less than 0.05 was considered significant.

**Results:** There were a total of 143 patients (mean age 67.2±1.22 years and 42.7% female). Microbiological etiology was elucidated in 69 (48.2%) of 143 IAI cases (Table 1). The most common pathogen was *E.coli* (29/69, 42%) and multiple pathogens were recorded in 25 of 69 culture positive cases (Table 1). Overall mortality was 46.1% at the 72nd h visit while day 14 and 30 mortality rates were 69.2% and 73.4%, respectively. Source control by surgical or percutaneous operation was performed in 48 of 143 cases (33.5%) and mortality rate was significantly lower in cases that were performed source control at anytime during SS (24/48 vs 81/95, p=0.000007). In 18 of 48 cases (37.5%) source control was performed during the first 12 hours (as suggested by guidelines) and mortality was significantly lower in this group versus others (6/18-33.3% vs 99/125-79.2%, p=0.000038). In 31 of 48 cases invasive surgical operation was performed while percutaneous source control was performed in 17 cases and mortality rates among invasive operation group was statistically higher than the percutaneous group (20/31 vs 4/17, p=0.015) while the mean SOFA scores were recorded as 9.58±1.08 for invasive source controlled group and 12.75±1.31 for percutaneous source controlled group (p=0.195).

**Conclusions:** Source control has major and vital importance in terms of mortality rates for IAI related septic shock patients especially during the first 12 h of identification. The more favourable outcomes observed during the source control via percutaneous procedures in our cohort needs to be confirmed in larger studies.

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Number</th>
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</thead>
<tbody>
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<td>29</td>
</tr>
<tr>
<td><em>Enterococcus</em> spp.</td>
<td>18</td>
</tr>
<tr>
<td>Yeasts</td>
<td>15</td>
</tr>
<tr>
<td><em>Klebsiella</em> spp.</td>
<td>13</td>
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<tr>
<td><em>Pseudomonas</em> spp.</td>
<td>6</td>
</tr>
<tr>
<td><em>Staphylococcus</em> spp.</td>
<td>6</td>
</tr>
<tr>
<td><em>Acinetobacter</em> spp.</td>
<td>5</td>
</tr>
<tr>
<td>Others*</td>
<td>13</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>103</td>
</tr>
</tbody>
</table>

*Proteus spp.–2, Enterobacter spp.–3, C.straturn–3, Morganella spp.–2, S.aureus–1, S.cassie–1, S.enterohammonas spp.–1*

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Abstract 2942

**Carbapenemase-producing and colistin-resistant Enterobacteriaceae in intensive care unit patients from Mediterranean countries, 2019**

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**Background:** Carbapenemase-producing (CPE) and colistin-resistant (colRE) Enterobacteriaceae are associated with an increased mortality in ICUs. Routine monitoring of antimicrobial resistance in acute care hospitals from Mediterranean countries remains uncommon. Data regarding CPE and colRE-carriage in ICU patients are scarce.

**Materials/methods:** We conducted a 1-day prevalence study in 9 ICUs from Morocco, Tunisia, Egypt and Lebanon (in January 2019). In each center, 30 consecutive patients were consented for medical records accession and sampled for fecal/rectal swab culture. Clinical data were collected (morbidities, duration of hospitalization before screening, previous hospitalization and antibiotic use). Swabs were streaked on CHROMagar-mSuperCARBA agar plates. Enterobacteriaceae isolates were sent to a central laboratory for antibiotic susceptibility testing, molecular characterization of the mechanisms involved with resistance against β-lactams, carbapenems and colistin, and 50 representative CPE were subjected to WGS.

**Results:**
- 256 patients (neonates and adults, mean age 57y) were enrolled and screened for CPE carriage; 44 and 48% with previous hospitalization or antibiotics, respectively.
- 110 Enterobacteriaceae on mSuperCarba plates were detected, including 102 CPE (61 K.pneumoniae, 30 E.coli, 11 others). CPE carriage rate of 28% (figure 1). 29 CPE only susceptible to tigecycline (100%) and colistin (81%). High diversity of carbapenemase determinants: 52% **bla**\_OXA48, 6% **bla**\_OXA244, 4% **bla**\_OXA181, 3% **bla**\_OXA232, 23% **bla**\_NDM1, 22% **bla**\_NDM5, 1% **bla**\_NDM-7 and 1% **bla**\_NDM-19; 14 CPE with 2 determinants.
- 14 ColRE detected (4 E.coli, 10 K.pneumoniae; MIC 4-16 mg/L), susceptible to tigecycline. ColRE carriage rate of 5%.
  - **mcr**\_1 in 1 ESBL-ST359-E.coli, 3 **bla**\_OXA48-ST1196-E.coli
  - **mcr**-like genes sharing 43% identity with **mcr**-7 or -10 in 10 K.pneumoniae.
  - mutations in **pmr**A and **pmr**B: 2 **bla**\_NDM-ST1162-K.pneumoniae (**pmr**A-A44T,**pmr**B-T246A/L213M/T157P); 1 **bla**\_NDM-ST383-K.pneumoniae carrying various carbapenemase genes (**pmr**A-G144D/D149E/N219H,**pmr**B-T246A/A228T/M175V/N105S/ASV);
- CPE carriage was associated with neonatal status and prolonged hospitalization (p<0.001).

**Conclusions:** We documented the worldwide spreading of conjugative plasmids and the establishment of CPE and colRE in Mediterranean ICUs. While colonization increases the risk of infection, and given the high mortality rate observed with CPE infection, our findings underline a crucial need to intervene forcefully and control the spread of CPE/ColRE into neonatal and adult ICUs.

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Clinical effectiveness of 13-valent and 23-valent pneumococcal vaccination among middle-aged and older adults with immunocompromising conditions

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Abstract third-party references: Funding by PERIS SL T002/16/00063

Background: Clinical benefits using the 13-valent pneumococcal conjugate vaccine (PCV13) and/or the 23-valent pneumococcal polysaccharide vaccine (PPsV23) are controversial. This study investigated clinical effectiveness for both PPsV23 and PCV13 in preventing pneumonia among immunocompromised adults.

Materials/methods: Population-based cohort study involving 203,447 Catalan adults (aged ≥50 years) with potential immunocompromising conditions (i.e., asplenia, immunodeficiency/HIV infection, severe renal disease, solid or haematological neoplasia and/or immunosuppressive treatment), who were prospectively followed between 01/01/2017 - 31/12/2017 (Funding: PERIS SL T002/16/00063). Primary outcomes were hospitalisation from pneumococcal or all-cause pneumonia and main explanatory variable was PCV13/PPsV23 vaccination status. Cox regression was used to estimate vaccination effectiveness adjusted for age, sex and presence of other baseline-risk conditions.

Results: Cohort members were followed for a total of 192,716 person-years (7248 PCV13 vaccinated and 115,574 PPsV23 vaccinated), observing 480 pneumococcal pneumonias (36 in PCV13 vaccinated, 364 in PPsV23 vaccinated) and 3622 all-cause pneumonias (264 in PCV13 vaccinated, 2817 in PPsV23 vaccinated). Global incidence rates (per 100,000 person-years) were 249.1 for pneumococcal pneumonia (496.7 in PCV13 vaccinated, 314.9 in PPsV23 vaccinated) and 1879.4 for all-cause pneumonia (3642.4 in PCV13 vaccinated, 1810.6 in PPsV23 vaccinated). Pneumococcal vaccination did not significantly alter the risk of pneumococcal pneumonia [multivariable hazard ratio [HR] for PCV13: 1.43, 95% confidence interval [CI]: 0.99-2.06, p=0.057; HR for PPsV23: 1.27, 95% CI: 0.99-1.64, p=0.065] but it appeared significantly associated with an increasing risk of all-cause pneumonia among vaccinated subjects [HR for PCV13: 1.34, 95% CI: 1.17-1.54, p=0.001; HR for PPsV23: 1.15, 95% CI: 1.05-1.27, p=0.004]. The PCV13 did not significantly alter the risk of death from pneumococcal pneumonia [HR: 2.02; 95% CI: 0.58-7.07, p=0.270] or death from all-cause pneumonia [HR: 0.88; 95% CI: 0.56-1.38, p=0.581], whereas the PPsV23 did not alter the risk of death from pneumococcal pneumonia [HR: 2.77; 95% CI: 0.94-8.13; p=0.064] and was associated with a marginally significant reduction in the risk of death from all-cause pneumonia [HR: 0.75; 95% CI: 0.56-1.00; p=0.046].

Conclusions: Data does not support clinical benefits from adults pneumococcal vaccination (nor PCV13 neither PPsV23) in preventing pneumonia among immunocompromised subjects.

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A study of Bartonella bacilliformis bacteraemia in asymptomatic individuals during an inter-outbreak period in an endemic region

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Background: Carrion’s disease is a bacterial disease that affects remote Andean communities, principally in Peru, Colombia and Ecuador. It is caused by bacteria Bartonella bacilliformis, and it is believed to be transmitted from human to human by sand fly vector of the genus Lutzomyia. There are two distinct clinical forms of the disease: acute form, also known as Droya fever and chronic form or Verruga peruana. The disease tends to occur in outbreaks, usually during the rainy season. Many candidates for reservoir have been proposed until now such as Euphorbia plants and various domestic and wild animals. No animal reservoir has been found, but individuals with asymptomatic infection have been identified, raising the possibility that human asymptomatic B. bacilliformis carriers act as reservoirs for the infection between the outbreaks. The aim of this study was to investigate the prevalence of asymptomatic B. bacilliformis bacteraemia in individuals living in endemic Andean communities during a non-outbreak period.

Materials/methods: A cross-sectional field study was done in July 2019 in Ancash, Peru in two different communities which had previously experienced outbreaks of B. bacilliformis. Community members older than one year were invited to participate: eligible were those who were without any clinical signs or symptoms of acute or chronic B. bacilliformis infection. Demographic data and medical history were collected by questionnaire. B. bacilliformis bacteraemia was determined using blood culture.

Results: 177 people were included in the study from two different communities in endemic region. 64.4% were females and the median age of the participants was 34 years (interquartile range 25-49 years). More than half of them were farmers or house workers (83.6%). 11 participants out of 177 reported having experienced the acute form of the disease in the past, whereas 50 of them reported having experienced the chronic form of the disease. None of the blood cultures was positive after 56 days of incubation. Thus, the prevalence of B. bacilliformis bacteraemia in the communities was 0%.

Conclusions: Our data do not support the hypothesis that asymptomatic humans represent a significant reservoir of infection between outbreaks. Further investigation on alternative reservoir species is now warranted.

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Optimal PK/PD target and high efficacy rates of ceftolozane-tazobactam in patients with infections caused by extensively drug-resistant Pseudomonas aeruginosa

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1Parc de Salut Mar, Barcelona, Spain, 2Hospital La Paz, Madrid, Spain

Background: Ceftolozane/tazobactam is a new drug active against extensively drug-resistant Pseudomonas aeruginosa (XDR-PA). The aim was to describe the PK/PD target of ceftolozane in patients with XDR-PA infections and its association with clinical outcomes.

Materials/methods: Retrospective observational study conducted from February 2018-October 2019. Demographic, clinical, microbiological and pharmacokinetic variables were collected. Ceftolozane plasma concentrations were obtained pre-dose at steady state (Cmin in intermittent/extended infusion) or Css in continuous infusion and analysed by HPLC. Free concentrations were calculated assuming a ceftolozane plasma protein binding of 21%. A 100% freeT>MIC was considered as optimal PK/PD target and 100% freeT>10MIC as supratherapeutic. Ceftolozane MIC was determined by broth microdilution.

Results: Thirty patients included (23.3% critically ill). Most common infections were urinary tract infections (23.3%), osteomyelitis (16.7%) and pneumonia (13.1%).

Table 1. Patients’ characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male,n(%)</td>
<td>19 [63.3]</td>
</tr>
<tr>
<td>Ceftolozane dose/day:</td>
<td></td>
</tr>
<tr>
<td>- ≤ 1 g</td>
<td>7 [23.3]</td>
</tr>
<tr>
<td>- ≥ 2 ≤ 3 g</td>
<td>12 [40]</td>
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<tr>
<td>- &gt; 3 g</td>
<td>11 [36.7]</td>
</tr>
<tr>
<td>Age (years)</td>
<td>67.0 [90.0-36.0]</td>
</tr>
<tr>
<td>Administration:</td>
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<tr>
<td>- Continuous infusion,n(%)</td>
<td>22 [73.3]</td>
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<td>- Intermittent infusion,n(%)</td>
<td>5 [16.7]</td>
</tr>
<tr>
<td>- Extended infusion,n(%)</td>
<td>3 [10.0]</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
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<tr>
<td>Plasma concentration (mg/L):</td>
<td></td>
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<tr>
<td>- freeCmin</td>
<td>29.3 [44.0-7.3]</td>
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<tr>
<td>- freeCss</td>
<td>28.6 [8.1-67.0]</td>
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<td>Renal replacement therapy,n(%)</td>
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<tr>
<td>MIC₅₀/MIC₉₀ (mg/L)</td>
<td>2/4</td>
</tr>
<tr>
<td>SOFA score</td>
<td>2 [0-10]</td>
</tr>
<tr>
<td>PK/PD target:</td>
<td></td>
</tr>
<tr>
<td>- Optimal,n(%)</td>
<td>30 [100.0]</td>
</tr>
<tr>
<td>- Supratherapeutic,n(%)</td>
<td>20 [66.7]</td>
</tr>
<tr>
<td>Baseline GFR &lt;50ml/min,n(%)</td>
<td>10 [33.3]</td>
</tr>
<tr>
<td>Mechanical ventilation,n(%)</td>
<td>5 [16.7]</td>
</tr>
<tr>
<td>Fluid overload,n(%)</td>
<td>8 [26.7]</td>
</tr>
</tbody>
</table>

Clinical cure was achieved in 27 (90%) patients and microbiological eradication in 21 (70%). No differences were observed in the free ceftolozane concentrations between patients with and without clinical cure [34(26.5-46.4) vs 36.7(10.2-84.8) mg/L] (p=0.384). A supratherapeutic PK/PD ratio was not related to better clinical outcomes (p>0.53).

Conclusions: Ceftolozane/tazobactam showed a high rate of clinical and microbiological cure regardless of the strategy of administration. All patients achieved an optimal PK/PD target being this index supratherapeutic in 66.7 of the patients. Therapeutic drug monitoring may be useful to optimize the PK/PD of ceftolozane/tazobactam, especially in patients with overexposure in which a dosage reduction may reduce potential adverse events and treatment costs.

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Abstract 2949

**Evaluation of effect of combination chemotherapy with tetracycline and fluoroquinolone for Japanese spotted fever**

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**Background:** Japanese spotted fever (JSF) is an emerging infectious disease caused by *Rickettsia japonica* and is endemic in Japan and Korea. JSF is a nationally notifiable disease in Japan, and recently 200 to 350 cases occur annually. The precise mortality is unclear, but at least 11 deaths in 278 cases were confirmed by October from January in 2019 and its mortality was estimated approximately 4% under standard medical care. For JSF, the chemotherapy with tetracycline is recommended like other rickettsial diseases, because of lack of evidence for JSF treatment. However, several cases reported that tetracycline is ineffective, but fluoroquinolone is effective. Hence, the combination chemotherapy with tetracycline and fluoroquinolone begun from initial treatment in some medical institutions. The aim of this study is to evaluate the combination therapy with tetracycline and fluoroquinolone for JSF.

**Materials/methods:** We retrospectively reviewed the medical records of JSF cases from 2012 to 2019 in Ise Red Cross Hospital and Minami-ise Municipal Hospital, that initiated the combination therapy immediately after diagnosis. Diagnostic criteria were positive results in molecular-based tests at the acute phase and/or increased serum antibody titers.

**Results:** A total of 196 cases (male; 45%, age; 70.5 ± 14 years) was investigated. Of those, 189 cases were hospitalized. The 194 cases were treated with the combination therapy: 192 cases of minocycline (200 mg/day) and levofloxacin (250-500 mg/ day); and 2 cases of minocycline (200 mg/day) and ciprofloxacin (300 mg/day). The time from onset to administration was 3.8 ± 2.4 days and the administration period was 3-14 days. Two cases died within a week. The first case was an 88-year-old woman who treated from the second day of onset but died on the third day with multiple organ failure. Another case was a 74-year-old woman who died suddenly due to gastrointestinal bleeding during the recovery. The average period of stay was 9.4 ± 7.3 days. Forty-seven percent of the patients were discharged within 7 days, while 4 cases were weakened and hospitalized for more than 30 days.

**Conclusions:** Although there are some fulminant cases, early combination therapy with tetracycline and fluoroquinolone improves JSF mortality to approximately 1%.

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Clinical outcomes of 3-day course of adjunctive oral ivermectin for the patients with chikungunya viral infection: a preliminary study

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Background: Chikungunya (CHIK) fever is characterized by abrupt onset of high grade fever, rash and debilitating joint pain. Ivermectin has in vitro efficacy to inhibit replication of chikungunya virus (CHIKV), then clinical trial of this drug is needed.

Materials/methods: Forty patients with symptoms of CHIK fever with virological confirmation of CHIKV infection were enrolled and randomized (1:1) to receive 200 mcg/kg/day of oral ivermectin for 3 days as the adjunctive therapy to standard treatment. Physical examinations and blood tests including basic laboratories, polymerase chain reaction (PCR) for CHIKV, c-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were performed in first weeks and every week for 12 weeks.

Results: Clinical characteristics and basic laboratories of these 2 groups was indifferent. Time to disappearance of fever and joint pain among the patients receiving adjunctive ivermectin were significantly shorter than those receiving only supportive treatment [1.3 days VS. 2.2 days, P = 0.002 and 1.9 days VS. 2.8 days, P < 0.001, respectively]. Pain score in first 7 days and among those receiving adjunctive ivermectin was significantly lower than those receiving only supportive treatment [P < 0.001]. Persistent joint pain was observed in 2 patients receiving adjunctive ivermectin and 9 patients receiving only supportive treatment accounting to relative risk of 0.22 (0.05-0.90), P = 0.04. Time to disappearance of CHIKV among the patients receiving adjunctive ivermectin were significantly shorter than those receiving only supportive treatment [1.9 days VS. 5.1 days, P < 0.001]. The level of CRP and ESR in first 7 days among those receiving adjunctive ivermectin was significantly lower than those receiving only supportive treatment [P < 0.001]. Adverse drug reactions were not different between these 2 groups.

Conclusions: Favorable outcomes of 3-day course of adjunctive oral ivermectin for the patients with CHIKV infection was demonstrated

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Abstract 2951

Incidence and risk of hospitalised pneumococcal pneumonia among Catalonian adults with distinct underlying medical conditions

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Abstract third-party references: Supported by grant (FIS-P15/01230)

Background: This study investigated the incidence of pneumococcal pneumonia requiring hospitalisation among middle-aged and older adults with and without specific underlying medical conditions, evaluating the influence of these conditions in the risk of developing pneumonia.

Materials/methods: Population-based prospective cohort study that included 2,025,730 individuals ≥50 years around Catalonia, Spain. The information system for the development of research in primary care of Catalonia (SIDIAP Research Database) was used to establish baseline characteristics of the cohort (vaccination status [PCV13 and/or PPV23], comorbidities and underlying medical conditions). Hospitalisations from pneumococcal pneumonia occurred among cohort members between 01/01/2015-31/12/2016 were collected from hospital discharge codes of 68 reference Catalonian hospitals (FIS-P15/01230). Cox regression was used to estimate the association between baseline conditions and the risk of developing pneumonia.

Results: Cohort members were followed for a total of 3,897,151 person-years, observing 3259 first episodes of hospitalised pneumococcal pneumonia across study period. Incidence rate (per 100,000 person-years) was 83.6 globally (106.1 in men vs 64.7 in women; 34.4 in 50-64 years vs 90.9 in 65-79 years vs 239.8 in aged 80 years or older). Greatest incidence emerged among persons with haematological neoplasia (729.5) followed by immunodeficiency (539.1), severe renal disease (377.1), HIV infection (325.2), chronic pulmonary disease (300.4), immunosuppressive treatment (245.4), chronic heart disease (206.1), chronic liver disease (195.3), solid neoplasia (176.4), alcoholism (165.1) and diabetes mellitus (148.3). In multivariable analyses, apart from increasing age, haematological neoplasia (Hazard Ratio [HR]: 5.65), HIV infection (HR: 4.32), immunodeficiency (HR: 3.48) and chronic pulmonary disease (HR: 2.86) were the conditions most strongly associated with an increasing risk. Pneumococcal vaccination (nor PCV13 neither PPVs23) did not emerge associated with reduced risks.

Conclusions: Old age, immunocompromising conditions and chronic pulmonary diseases are major risk factors for pneumococcal pneumonia in adults. Our data underlines the need for better prevention strategies in these persons.

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Abstract 2952

The genetic architecture of tuberculosis susceptibility: comprehensive research synopsis, meta-analysis, and epidemiological evidence

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Background: Hundreds of studies have been conducted to investigate associations between variants and tuberculosis risk so far. But results have been inconclusive. Here we systematically provide a summary of the understanding of the genetic architecture of tuberculosis susceptibility.

Materials/methods: We searched PubMed, Embase and Web of Science to identify genetic association studies of tuberculosis published through July 22, 2019. We conducted meta-analyses for the genetic association on tuberculosis risk. We graded levels of cumulative epidemiological evidence of significant genetic associations using the guidelines proposed by the Human Genome Epidemiology Network and false-positive report probability tests. We performed functional annotations for these variants using data from the Encyclopedia of DNA Elements (ENCODE) Project and other databases.

Results: We identified 634 eligible articles comprising 268737 cases and 841031 controls through screening a total of 22041 citations. Meta-analyses were conducted for 591 genetic variants in 309 genes. We found 37 variants were nominally significantly associated with tuberculosis risk. Cumulative epidemiological evidence for a significant association was graded strong for 10 variants in or near 10 genes which together explained approximately 9.59% of familial relative risk of tuberculosis. Data from the ENCODE and other databases suggested that 8 of these 10 genetic variants with strong evidence might fall within putative functional regions.

Conclusions: Our study summarizes current literature on the genetic architecture of tuberculosis susceptibility and provides useful data for designing future studies to investigate genetic association for tuberculosis risk.

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Abstract 2953

Posaconazole dosing and association with therapeutic drug levels in allogeneic cell transplant recipients

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Background: Real-life data on posaconazole (POS) therapeutic drug monitoring (TDM) in allogeneic hematopoietic cell transplant recipients (allo-HCTr) are limited.

Materials/methods: All allo-HCTr participating in the Swiss Transplant Cohort Study (STCS) who received POS as prophylaxis and/or treatment between 1.1.2016 and 31.12.2018 were identified through hospital-pharmacy and the STCS databases at the three allo-HCT-centers in Switzerland. Allo-HCT, POS-administration, POS-TDM, and other laboratory variables were recorded. Herein, we present preliminary data on POS-TDM distribution from 2 allo-HCT-centers.

Results: A total of 1554 POS-TDM-levels were recorded in 230 patients in 2 allo-HCT-centers: 1066 and 488 POS-TDM-levels were performed in 157 and 73 patients, who received POS-prophylaxis and POS-treatment, respectively (Figure 1a-b). POS was administered for 120 days [mean, range: 2-1218]; 117 and 137 days in the POS-prophylaxis and POS-treatment groups, respectively. The mean POS-TDM-level was 1.47mg/L [range: 0-8.28]: 1.4 and 1.65mg/L in the POS-prophylaxis and POS-treatment groups, respectively (P-value<0.001; Figure 1c). POS-TDM-levels on day(D)7±3, 14±3, 28±3, 42±3, and 84±3 were available for 170, 131, 111, 82, and 40 patients, respectively. The mean POS-TDM-levels by D7±3, 14±3, 28±3, 42±3, and 84±3 were 1.03, 1.3, 1.55, 1.64, and 1.76mg/L, respectively (Figure 1d). Amongst 157 patients who received POS-prophylaxis, 214/1066 (20.1%) of POS-TDM-levels were <0.7mg/L. The mean POS-TDM-levels on D7±3, 14±3, 28±3, 42±3, and 84±3 were 1.02, 1.18, 1.57, 1.62, and 1.76mg/L, respectively (Figure 1e). A total of 43/118 (36.4%) and 11/74 (14.5%) patients with POS-TDM-levels available by D7±3 and D28±3, respectively, had POS-TDM-level<0.7mg/L. In multivariable analyses, allo-HCT at center-A was protective of POS-TDM-level <0.7mg/L by D7±3 (odds ratio, OR:0.19, P-value:0.001). Amongst 73 patients who received POS-treatment, 149/488 (30.5%) of POS-TDM-levels were <1.0mg/L. The mean POS-TDM-levels on D7±3, 14±3, 28±3, 42±3, and 84±3 were 1.06, 1.45, 1.51, 1.69, and 1.74mg/L, respectively (Figure 1f). A total of 20/46 (43.5%) and 11/35 (31.4%) patients with POS-TDM-levels available by D7±3 and D28±3, respectively, had a POS-TDM-level<1.0mg/L. There were no variables associated with POS-TDM-level<1.0mg/L by D7±3.

Conclusions: Large variability in POS-TDM-levels is observed in allo-HCTr, with subtherapeutic POS-TDM-levels observed in up to 1/3 of patients and incremental changes attained with longer administration courses. Local practices are important determinants of POS-TDM-levels.

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**Abstract 2956**

*Clostridium butyricum* S88 modifies lipid metabolism in gut microbiome and colon tissue to protect antibiotic-induced colon epithelial damages

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**Background:** *Clostridium butyricum* MIYAIRI S88 (CBM 588) is a life biotherapeutic product that has been used for anti-diarrheal medicine in Japan. In our previous study, we admitted that antibiotics caused gut dysbiosis and colon epithelial damage. Then, CBM 588 showed the contribution to modify the gut microbiome and reduce the colon epithelial damage. However, the mechanisms of CBM 588 on the protection from the gut epithelial damage has not been cleared.

**Materials/methods:** In vivo study, mice were divided into four groups and CBM 588, clindamycin (CLDM), and normal saline (control) was orally administered for 4 days (only CLDM, only CBM 588, CBM 588 + CLDM, water). After 4 days administration, colon tissues were removed for analysis lipid metabolites and metabolic enzyme expressions. Lipid metabolites were measured with LC-MS/MS.

**Results:** In lipid metabolome analysis, eicosanoids (EPA, stearic acid, linoleic acid) and some fatty acids (oleic acid, palmitoleic acid) were enhanced in only CLDM administration group, compared with other groups. On the other hand, in CBM 588 + CLDM administration group showed the up-regulation of flavonoids (genistein, daidzein) than that of CLDM group (Figure).

**Conclusions:** CLDM administration increased some eicosanoids and fatty acids productions related to inflammation. However, CBM 588 protected from the up-regulation of these lipid metabolites. Additionally, CBM 588 increased flavonoids (genistein, daidzein) have anti-oxidant stress effects. Therefore, our results suggest that CBM 588 has impacts to reduce oxidative stress and anti-inflammation in gut epithelial cells. These results support the facts that CBM 588 has protective effects from colon gut epithelial damage due to antibiotics.

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Abstract 2958

Use and impact of aminoglycoside empirical combination therapy in intensive care unit patients with ESBL-producing Enterobacteriaceae bloodstream infections: a multi-centre retrospective observational cohort

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Background: Empirical prescription of aminoglycoside (AG) combination therapy may be of particular interest in case of septic shock due to extended-spectrum beta-lactamase producing enterobacteriaceae (ESBL-E) bloodstream infections (BSI), because of synergistic bactericidal activity, and antimicrobial spectrum broadening. We conducted a retrospective study to evaluate use and impact of initial prescription of AG in ICU patients with ESBL-E BSI.

Materials/methods: Between January 2011 and September 2017, patients treated for ESBL-E BSI in the ICU of 6 French hospitals were included in a retrospective observational cohort study. The primary endpoint was mortality at day 30. Secondary endpoints were empirical antibiotic therapy adequacy and renal failure occurrence.

Results: Three hundred and seven patients were included. Among them, 169 (55%) received an AG as initial treatment. Patients who were treated with AG were more likely to receive immunosuppressive therapy (15% vs 5%, p=0.01) and to show septic shock (57% vs 43%, p=0.02) at BSI onset. ESBL-E isolates were sensitive to at least one AG in 55% of cases. Death rate at day 30 was 40% (43% with AG vs 39% without AG, p=0.55). By multivariate analysis, factors independently associated with death were age≥70 years (OR: 2.67; 95%CI: 1.09-6.54, p=0.03), history of transplantation (OR 5.2; 95% CI: 1.4-19.35, p=0.01), hospital acquired infection (OR 8.67; 95% CI: 1.74-43.08, p=0.008), need for vasoactive drugs >48h after BSI onset (OR 3.61; 95% CI: 1.62-8.02, p = 0.001), occurrence of acute respiratory distress syndrome (OR 2.42; 95% CI: 1.14-5.16, p=0.02) or acute renal failure (OR 2.49; 95%CI: 1.14-5.47, p = 0.02). Rate of renal impairment occurrence was similar in patients treated with or without AG (21% vs 24%, p=0.59). The adequacy rate of empirical antibiotic therapy was higher in the AG group (91.7% vs 77%, p = 0.001).

Conclusions: In our cohort of ICU patients with ESBL-PE BSI, prescriptions of AG as empirical combination therapy represented more than one half of antibiotic therapies. Our study showed no impact of AG prescription on 30 days mortality rate, even if appropriateness of initial antibiotherapy increased in case of AG prescription.

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Triangulating the molecular epidemiology of carbapenem-resistant Enterobacteriales in humans, food-producing animals and the environment in a One Health context

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Background: Antimicrobial resistance (AMR) is a consequence of selection pressure from indiscriminate antibiotic use in humans, animals and the environmental, requiring a One Health approach towards its understanding and containment. This study aims: 1) to determine carriage and colonization of carbapenem resistance Enterobacteriaceae (CRE) in humans, livestock animals (pigs), and environmental sources within the same geographical area of UMgungundlovu district, KwaZulu-Natal, South Africa. 2) to comprehensively delineate the molecular epidemiology, nature and extent of AMR specifically in CRE in the “One Health” context to inform evidence-based strategies for its monitoring, prevention and containment.

Materials/methods: This study was approved by the Biomedical Research Ethics Committee[BE599/16], the Animal Research Ethics Committee[AREC/P9/018D] University of KwaZulu-Natal and Department of Agriculture, Forestry and Fisheries, Republic of South Africa[Ref12/11/15]. Screening rectal swabs were obtained from pigs and humans with water samples collected from a wastewater treatment plant. ChromID CARBA chromogenic agar [bioMerieux] was used to isolate CRE from all samples. Following microbial identification and antibiotic susceptibility tests, isolates were subjected to whole genome sequencing (WGS).

Results: Of 587 rectal swab samples screened for CRE, 230 (39.1%) were from humans, 345 (58.7%) were from pigs with 12 (2%) water samples. A total of 19/587 (3.2%) samples i.e. 15 from humans and 4 from the environment yielded CRE. No CRE were isolated from the pig samples. The commonest CRE identified was K. pneumoniae 9/19 (47%), followed by Enterobacter hormaechei 6/19 (32%), K. quasi-pneumoniae 2/19 (11%), a novel ST498 Citrobacter freundii 1/19 (5%) and Serratia marcescens 1/19 (5%). Eighteen of the 19 isolates were extensively drug resistant (XDR). K. pneumoniae (ST17) and Enterobacter hormaechei (ST90) were the predominant CRE strains isolated from both humans and the environment. The blaOXA 48, blaNDM-1 and blaGES-5 bearing plasmids mediating carbapenem resistance were found in multiple species/clones from both sectors. The isolates also harboured other mobile genetic elements [insertion sequences, integrons and transposons] propagating the spread of AMR across sectors.

Conclusions: This One Health Study highlights common CRE with associated resistome isolated from humans and the environment, highlighting the potential fluidity of resistome and mobilome propagation.

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Abstract 2960

The comparison of the rapid blood identification results within/after 8 hours from positive signal of blood culture bottle

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Background: The BioFire Filmarray Blood Culture Identification Panel (BCID) is a test for the rapid identification of major pathogen/organism groups that are main causes of sepsis and for detection of three antibiotic resistance genes by using a multiplexed PCR assay. The accuracy for the BCID panel is assessed only for tests within 8 hours of positive blood cultures. However, in practical situations, it is often necessary to perform BCID tests after 8 hours of positive blood culture. Therefore, we conducted the evaluation of the BCID after 8 hours of positive blood culture, as compared to the tests within 8 hours of positive blood culture.

Materials/methods: We tested BCID panel on 141 samples (67 within 8 hours, 74 after 8 hours from positive signal of blood culture bottle) from patients hospitalized in a tertiary hospital in Korea. The bacterial identification and antimicrobial sensitivity of all samples were confirmed by VITEK2 as reference method.

Results: Fifty-eight (within 8 hours) and 63 (after 8 hours) samples were analyzed, except for samples with bacteria which were not in BCID panel. The agreement of results of BCID with VITEK2; within 8 hours was 94.8% (55/58), after 8 hours was 92.1% (58/63), respectively. The discrepancies within 8 hours were 2 misidentification and 1 false negative for mecA gene. On the other hands, the discrepancies after 8 hours were 3 false negative for bacteria, 1 misidentification, and 1 false positive for mecA gene.

Conclusions: In this study, the BioFire Filmarray BCID test results performed after 8 hours of positive blood culture showed good performance compared to those performed within 8 hours. If necessary, BCID test after 8 hours may be helpful in the diagnosis and treatment of bacteremia patient.

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Abstract 2961

Serum IFI27 mRNA as a novel host response biomarker of monitoring the influenza A virus infection
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Background: Biomarkers for detection of influenza A virus (IAV) infection are limited and can hardly monitor the activity for IAV infection. Previous research had found that the IFI27 mRNA in the whole blood samples could be regarded as a single-gene biomarker discriminating IAV and bacterial infection. This study aims to further investigate serum IFI27 mRNA as a novel host response biomarker for monitoring the severity of IAV infection and the efficacy of therapy.

Materials/methods: 261 patients were included with well-defined phenotypes (influenza infection, bacterial infection and respiratory virus infection without IAV) and 100 healthy controls. Serum IFI27 mRNA was analyzed in all participants and in vitro and in vivo experiments were performed to validate this biomarker.

Results: Serum IFI27 mRNA expression in influenza infection patients was significantly higher than other infected patients and controls. It displayed 81.8% and 77% diagnostic accuracy (AUC) in discriminating influenza infections from bacterial infections and other respiratory virus infections without IAV. Among the IAV infected patients, the serum IFI27 mRNA peak levels of severe IAV infections were significantly higher than mild and moderate infections. Blood samples were collected at five time-points from 91 IAV infected patients after being hospitalized (D1, D3, D5, D7 and Discharged) to observe IFI27 mRNA expression trend during IAV infection treatment. Serum IFI27 mRNA expression was consistent with the temperature and CRP trend, and for most patients it had returned to a very low level when they recovered. The analysis for serum extracellular vesicles showed that most serum IFI27 mRNA might exist in serum exosomes. In vitro studies confirmed that both endocellular and extracellular IFI27 mRNA in A549 cells were up-regulated and consistent with the increase of influenza virus RNA. In mice infection model, IFI27 mRNA in serum and lung was up-regulated according with influenza virus in lung tissues and the serum IFI27 mRNA declined significantly when the influenza RNA replication was ceased.

Conclusions: Serum IFI27 mRNA may be a novel potential host response biomarker which could not only distinguish the influenza infection from bacterial or other respiratory virus but also facilitate the monitoring of IAV infection and the therapeutic efficacy.

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Comparison of clinical manifestations, antimicrobial susceptibility patterns, and carbapenem resistance determinants between *Acinetobacter seifertii* and *Acinetobacter nosocomialis* isolated in Taiwan

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**Background:** *Acinetobacter seifertii*, a new member of the *Acinetobacter calcoaceticus-Acinetobacter baumannii* (Acb) complex, has emerged as a cause of severe infections in humans. Using reference molecular methods, *A. seifertii* is most closely related to *Acinetobacter nosocomialis*, which is the major pathogen of Acb complex. We aimed to explore the clinical and molecular differences between these two species.

**Materials/methods:** This retrospective study enrolled 83 adults with *A. seifertii* bloodstream infection (BSI) and 402 with *A. nosocomialis* BSI at 4 medical centers over a 9-year period. The species identification was confirmed by MALDI-TOF MS and rpoB sequencing. Clinical information, antimicrobial susceptibility, and carbapenem resistance determinants were analyzed.

**Results:** There were no significant differences in underlying diseases and mortality between patients with *A. seifertii* BSI and those with *A. nosocomialis* BSI. Compared to patients with *A. nosocomialis* BSI, those with *A. seifertii* BSI were more likely to have acquired the isolate in the intensive care unit (ICU), and have recent ICU stay, central venous catheter and ventilator use at the onset of bacteremia, and pneumonia as the source of BSI. Compared with *A. nosocomialis*, *A. seifertii* was significantly less susceptible to colistin, amikacin, gentamicin, ceftazidime, cefepime and piperacillin/tazobactam, and more susceptible to imipenem, meropenem, ciprofloxacin and tigecycline. Carbepenem non-susceptibility was observed in 16.3% *A. seifertii* isolates and 34.6% *A. nosocomialis* isolates. Plasmid-borne ISAba1-bla<sub>OXA-51</sub>-like and IS1006-ΔISAba3-bla<sub>OXA-58</sub>-like contributed to carbapenem resistance in most *A. seifertii* and *A. nosocomialis* isolates, respectively.

**Conclusions:** Patients with *A. seifertii* BSI and those with *A. nosocomialis* BSI had similar underlying diseases and mortality rates. *A. seifertii* was significantly less susceptible to colistin, amikacin, gentamicin, ceftazidime, cefepime and piperacillin/tazobactam, and more susceptible to imipenem, meropenem, ciprofloxacin and tigecycline than *A. nosocomialis*. The major carbapenem resistance determinants of *A. seifertii* and *A. nosocomialis* were plasmid-borne ISAba1-bla<sub>OXA-51</sub>-like and IS1006-ΔISAba3-bla<sub>OXA-58</sub>-like, respectively.

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Abstract 2965

**Endemicity of carbapenemase-producing Enterobacteriaceae in Hong Kong**

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**Background:** To study the epidemiology of carbapenemase-producing Enterobacteriaceae (CPE) in a healthcare region in Hong Kong.

**Materials/methods:** We adopted multi-pronged screening strategy for early recognition of gastrointestinal colonization of CPE in our healthcare region with 3,200 beds. Patients were prospectively screened by collection of fecal specimens upon admission (targeted screening) and during hospitalization (opportunistic screening, safety net screening, and extensive contact tracing). Newly diagnosed CPE patients were put on contact precautions with cohort nursing. Specimens were collected and subjected to broth enrichment culture and multiplex polymerase chain reaction. Newly acquisition of nosocomial CPE was assessed per 1,000 CPE colonization-days.

**Results:** From July 1, 2011 through June 30, 2019, 193,703 fecal specimens collected from 77,195 patients, 3,287 specimens (1.70%) from 1,501 patients (1.36%) had CPE. The number and prevalence (per 100,000 patient-days) of CPE increased from 1 (0.13) in 2011 to 315 (75.22) in the first 6 months of 2019 (P<.001). In the acute care setting, nosocomial CPE cases were first observed in 2014. With an increasing trend of CPE colonization day from 878 days (2014) to 8215 (January to June 2019), total number of nosocomial acquisition of CPE per 100,000 CPE colonization day reduced from 1253 (2014) to 621 (January to June 2019) with enforcement of staff and patients' hand hygiene, and environment disinfection. Community acquired CPE in patients without prior hospitalization in the past 2 years increased from 0.67 (2014) to 22.73 (January to June 2019) per 100,000 admission (P<0.01), which constituted 3.3% (35/1051) of newly diagnosed CPE case. New Delhi metallobeta-lactamase (NDM) constituted 73.2% (769/1051) carbapenemase, followed by OXA (20.6%), KPC (5.2%), and others (1.1%).

**Conclusions:** Although proactive infection control measures mitigated the risk of nosocomial transmission of CPE in the hospitals, community acquisition of CPE is increasingly reported. Epidemiological analysis to understand risk factors for community acquisition of CPE is urgently warranted.

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Abstract 2972

Performance evaluation of the STANDARD F Influenza A/B FIA for detection of influenza A/B virus infection

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Background: Rapid diagnosis of influenza is important for early treatment and infection control. PCR test, currently used as a confirmatory test for influenza infection, has a disadvantage in that the method is complicated and it takes long time to report the results. In the case of conventional rapid antigen test, the result can be confirmed in a short time, but the sensitivity is low. We evaluated the performance of STANDARD F Influenza A/B FIA test, which uses fluorescence immunochromatography for improving sensitivity.

Materials/methods: The evaluation was performed using 269 patient samples that were referred for examination due to suspicion of influenza infection. Performance of the STANDARD F Influenza A/B FIA was compared to that of the SD BIOLINE Influenza Ag test. A real-time reverse transcriptase-polymerase chain reaction assay (Allplex Respiratory Panel 1) was used as reference standards.

Results: In detecting influenza A virus, STANDARD F Influenza A/B FIA showed sensitivity of 73.3% and specificity of 96%. SD BIOLINE Influenza Ag test showed 56.7% sensitivity and 100% specificity. In detection of influenza B virus, STANDARD F Influenza A/B FIA and SD BIOLINE Influenza Ag test showed 100% and 93.3% sensitivity, respectively. Specificity for influenza B virus was 100% in both tests.

Conclusions: The STANDARD F Influenza A/B FIA test was more sensitive than conventional rapid antigen test to detect influenza A and B viruses. It might be useful for rapid diagnosis of influenza.

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Genetic characterisation of co-produced KPC-3, CTX-M-15 and SHV-1 β-lactamases in carbapenem-resistant Klebsiella pneumonia ST512 causing bloodstream infections in an endemic tertiary hospital

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Background: Carbapenem-resistant (CR) Klebsiella pneumoniae (KPN) is designated by the CDC (Centers for Disease Control and Prevention) as one of the microorganisms that poses an urgent threat to public health worldwide. As an opportunistic pathogen, KPN is responsible of urinary, respiratory and bloodstream infections (BSI) in nosocomial settings and community. The most common carbapenemase found in KPN is KPC enzyme but KPN is also considered a reservoir of classes B and D carbapenemases and extended-spectrum β-lactamases (ESBLs) such as CTX-M-enzymes. Aim of the study was to investigate the genetic variants and genetic context of ESBLs and carbapenemases in KPN isolates causing BSI in an endemic tertiary hospital.

Materials/methods: Thirty-three KPN were isolated from blood culture samples of hospitalized patients in a tertiary hospital. Antimicrobial susceptibilities of these strains were evaluated towards clinically relevant β-lactams and other antibiotics using Vitek2 instrument (bioMérieux, Marcyl-Etoile, France) and confirmed with Etest (bioMérieux). The results were interpreted according to the EUCAST breakpoints as updated in 2016 and later version (http://www.eucast.org). Genotyping was performed by Multilocus Sequence Typing (MLST). Identification of β-lactamase genes and mobile genetic elements were performed by PCR and sequencing.

Results: All KPN strains were showed MIC values for meropenem, ertapenem and imipenem higher than 64 μg/mL. MLST analysis ascertained that the K. pneumoniae isolates could be included in sequence type ST512. The blaKPC-3 and blaCTX-M-15 were found in a large plasmid of more than 100 Kb. The analysis of genetic context of these bla genes demonstrated that the blaKPC-3 gene was found in Tn4401a transposon with the trpR, trpA, ISKpn6 and ISKpn7 mobile elements and blaCTX-M-15 was found downstream the insertion sequence ISEcp1. A class 1 integron carrying aadA2 gene cassette that encode for an aminoglycoside adenyltransferase was identified.

Conclusions: Bloodstream infection causes significant patient morbidity and mortality and KPN is the second Gram-negative bacteria, after E. coli, involved in BSI worldwide. Carbapenem resistant KPN are endemic in many tertiary hospitals. Genetic characterization of carbapenemases permit to monitor also other molecular antibiotic resistance gene responsible of the extensively drug resistance of this dangerous epidemic hospital plague.

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Molecular epidemiology and spatiotemporal analysis of carbapenem-resistant Acinetobacter baumannii in networks hospital in southern Thailand

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Background: Carbapenem-resistant Acinetobacter baumannii (CRAB) is a major hospital-acquired pathogen in Thailand. The nature of its transmission is poorly understood. Here, we investigated the genotypic and spatiotemporal pattern of CRAB infection at network hospitals in southern Thailand.

Materials/methods: We prospectively collected clinical data and clinical specimens of patients infected with CRAB at 9 networks hospitals (one university hospital, 3 tertiary care hospitals and 5 provincial hospitals) in southern Thailand between October 2018 and September 2019. We also did active systematic surveillance of CRAB from throat swab, rectal swab, endotracheal tube aspiration and gastric content. In addition, we collected environmental cultures in each hospital. Each CRAB was identified at the genomospecies level including carbapenemase genes. A spatiotemporal analysis was performed by admission wards, hospitals, time of infection and pulsed-field gel electrophoresis (PFGE) groups of CRAB.

Results: Fifty PFGE groups were identified among the 1,205 CRAB infections. All CRAB isolates were assigned to International Clonal Lineage II. Gene blaOXA-23 was the most prevalent carbapenemase gene. Outbreaks were observed mainly in university and 3 tertiary hospitals. The association between PFGE group and hospitals was significant. Spatiotemporal analysis identified 38 clusters of single PFGE group infections. Twenty clusters involved multiple hospitals simultaneously. Fifteen clusters involved only isolates from patients with CRAB infection while up to twenty-five cluster involved isolates from surveillance (colonization). Ten clusters involved isolates collected from hospital environment. Previous use of carbapenems is strongly associated with CRAB infection and colonization.

Conclusions: CRAB transmitted both within hospitals and between network hospitals. Better understanding and control of the transmission of CRAB are needed.

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Abstract 2981

Ultrasound-guided local administration of personalised cocktail of bacteriophages followed by suppressive antibiotherapy as salvage therapy in patients with relapsing total femur prosthetic joint infection (PJI)

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Abstract third-party references: Lyon BJI study group

Background: Lytic bacteriophages are of interest to treat patients with PJI based on their synergistic activity with antibiotics on bacteria in biofilm. In patients with relapsing total femur PJI, disarticulation is often unfortunately the only final option. In such a population, suppressive antimicrobial therapy is sometimes used after performing an open “DAIR” procedure, but the skin closure may be not possible and the success rate of this conservative approach is so low in such patients.

Materials/methods: In our reference regional center “CRIOAc Lyon” ultrasound-guided (panel A) local administration of personalized cocktail of bacteriophages of anti-S. aureus or anti-P. aeruginosa bacteriophages followed by suppressive antibiotherapy is proposed for relapsing total femur PJI with no therapeutic option or therapeutic dead-end (panel B, C). Each case was discussed with the French health authority. Bacteriophages were produced following the Good Manufacturing Practice (GMP) guidelines and were selected by Pherecydes, according to their activity (panel D). Hospital pharmacist mixed each phage (1 ml of 1x10^10 PFU/ml) extemporaneously as “magistral” preparation (final dilution 1x10^8 PFU/mL).

Results: Two patients (55 and 84 yo) experiencing a relapsing S. aureus or P. aeruginosa total femur PJI following previous debridement and implant retention procedure, were treated with personalized cocktails. One patient had soft-tissue defect with suppurative discharge (panel C). At the time of injection, both patients had already received targeted antibiotics, cefoxitin (for S. aureus) and ceftazidime (for P. aeruginosa), respectively. After the phage injection, antibiotics were switched to daptomycin-levofloxacin followed by doxycycline for the first one, and ceftazidime was maintained for the second. After a follow-up of 8 months, clinical signs of infection were improved, as systemic biologic markers of infection, in the first patient (panel E). Superinfection with C. albicans was unfortunately discovered at the time of phage injection, with C. albicans persistence and unfavorable outcome in the second one.

Conclusions: Ultrasound-guided local administration of personalized cocktail of GMP bacteriophages followed by suppressive antibiotherapy in patients with relapsing total femur PJI has the potential to be used as salvage therapy to control the infection and avoid disarticulation. Dramatic superinfection could be diagnosed at the time of phage administration.

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Severe candidaemia in a tertiary care hospital

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Background: We describe the main epidemiologic, clinical, microbiological characteristics and mortality of a cohort of severe candidaemia (SC) in University Hospital of Salamanca.

Materials/methods: All cases of candidemia in adults detected at our Hospital were prospectively registered from 2010 to 2016. We analyzed the differential characteristics according to the severity of presentation. SC was defined as cardiovascular, respiratory, renal, neurologic or hematological failure. Continuous variables were compared using the Student’s T test. Categorical variables were compared using X^2-test or Fisher’s test.

Results: Among the 233 episodes of candidemia included, 98 were SC. The group of patients with SC was significantly older (72 vs 68, P<0.01), had more alcohol abuse related disorder (8.2% vs 1.5%, P=0.02) and chronic kidney disease (10.2% vs 3.0%, P=0.02). Patients with SC had significantly less hematologic neoplasm (12.2% vs 26.7%, P<0.01), bone marrow transplantation (4.1% vs 14.1%, P=0.01), solid organ neoplasm (35.7% vs 52.6%, P=0.01) and chemotherapy (12.2% vs 29.6%, P=0.01). Patients with hematologic neoplasm had more frequently a vascular catheter focus (39.6% vs 31.6%, P=0.29) and C. parapsilosis infection (52.1% vs 39.0%, P=0.10). Patients with SC had more previous intensive care unit stay (31.6% vs 8.9%, P<0.01), blood products transfusion (53.6% vs 39.3%, P=0.03) and presence of urinary catheter (67.3% vs 34.1%, P=0.01). C. albicans was more frequent in the SC group (46.9% vs 32.6%, P=0.03) and C. parapsilosis was less frequent (31.6% vs 49.6%, P=0.01). Urinary tract focus was more frequent in SC patients (11.2% vs 3.7%, P=0.03) and vascular catheter focus was less frequent (28.6% vs 37.0, P=0.18). Patients with SC receipt more appropriate empirical antifungal treatment (30.6% vs 19.3%, P=0.04). Candidemia-related mortality at 30 days was more frequent in patients with SC (37.8% vs 9.6%, P<0.01). C. albicans and C. parapsilosis related mortality was 46.0% and 28%, respectively.

Conclusions: Remarkably, we found that patients with SC had less frequently hematologic neoplasm, chemotherapy and bone marrow transplantation. This could be explained because of a higher frequency of catheter associated candidemia and C. parapsilosis infection in patients with these conditions both factors widely known to be related with less severe disease and mortality.

<table>
<thead>
<tr>
<th>Table 1. Characteristics of patients with severe candidaemia</th>
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<tbody>
<tr>
<td>Total</td>
</tr>
<tr>
<td>N=233</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>Alcohol abuse related disorder</td>
</tr>
<tr>
<td>Hematologic neoplasm</td>
</tr>
<tr>
<td>Bone marrow transplantation</td>
</tr>
<tr>
<td>Solid organ neoplasm</td>
</tr>
<tr>
<td>Chemotherapy</td>
</tr>
<tr>
<td>Previous blood products transfusion</td>
</tr>
<tr>
<td>Previous urinary catheter</td>
</tr>
<tr>
<td>Candida albicans</td>
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<tr>
<td>Candida parapsilosis</td>
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<tr>
<td>Related mortality</td>
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Abstract 2985

**Short-term peripheral venous catheter-related bloodstream infections in French healthcare settings, 2019**

Marie Decalonne¹, Rémi Gimenes¹, Florent Goube¹, Agnès Petiteau¹, Anne Berger-Carbonne², Stéphane Le Vu², Nathalie Laure Van Der Mee-Marquet*¹

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Abstract third-party references: SPIADI network

**Background:** Widely used in healthcare settings, short-term peripheral venous catheters (PVCs) can be responsible for potentially severe bloodstream infections (pvcRBSI), especially when caused by *S.aureus*, in relation to the possible severe complications associated with *S.aureus*-BSIs. pvcRBSI- and *S.aureus*-pvcRBSI-incidence rates are scarce. Through a large French hospital network we aimed at quantifying pvcRBSI incidence and associated factors.

**Materials/methods:** A nation-wide 3-month survey of central and peripheral venous catheter RBSIs [January-April 2019] in ICU and non-ICU settings was conducted by the SPIADI [Surveillance and Prevention of Invasive Devices Associated Infections] network, using a unit-based protocol close to ECDC-HAI-Net-ICU protocol 1.02. For all nosocomial BSIs in SPIADI network, patient age and sex, place of acquisition, portal of entry, and for catheter RBSI, insertion site and time between insertion and first signs of BSI were collected. BSI-incidence rates are provided per 1000 patient-days (PD).

**Results:**

- 1001 participating hospitals (including 64% of the 529 French tertiary-hospitals, 54% of the 570 acute-care clinics, 89% of the 18 oncology specialized-hospitals), covering 179477 beds (including 60% of the 6313 French ICU-beds), 13390393 patient-days (PD) and 701277 dialysis-sessions.
- Of 9381 nosocomial BSIs, 31% were Catheter_RBSIs, and of these 13% were pvcRBSIs recorded in medical wards (73%), surgical wards (17%), ICUs (4%), and other wards (6%).
- pvcRBSI incidence ranged between 0 and 1.11/1000PD, according to hospital-type and patient-category.
- pvcRBSIs were mostly associated with *S.aureus* (52%) of which 11% were MRSA, *Enterobacteriaceae* (21%) and CoNS (15%);
- the time between PVC-insertion and the first signs of BSI was >7 days in 22% of the pvcRBSIs, and 20% of the *S.aureus*-pvcRBSIs.

**Conclusions:** The pvcRBSIs remain scarce events. However, as *S.aureus*-BSI is associated with possible severe complications, the preponderance of *S.aureus* responsible for pvcRBSI is worrying. The frequent >7 days-lapse of time between PVC insertion and first signs of pvcRBSIs suggests substantial long-term use of PVCs. In line with the current guidelines, the local infection control teams should promote an appropriate length of PVC use: PVC should be removed as soon as it is no longer required. Our findings provide multiple opportunities for improvement, and allows defining local observation of catheter insertion and use as a SPIADI-network priority for 2020.

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Detection and antibiogram of *Escherichia coli* O157 from *Oreochromis niloticus* (Tilapia) Sold in Ibadan, Nigeria

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**Background:** *Escherichia coli* - (*E. coli*) are classified as part of non-indigenous bacteria of fish. Most *E. coli* strains are non-pathogenic, however few pathogenic *E. coli* varieties that produce toxins and other virulence factors that enable them to invade and damage host cells are known. They play roles in fish spoilage and causing humans' diseases - (food poisoning, gastroenteritis, septic shock, meningitis, and urinary tract infections). *E. coli-O157* is a pathogenic strain attributed to estimate of 3,600 human hospitalization the in US. Presence of *E. coli-O157* in food products especially, fish and fish products indicates unhygienic aquatic environment and/or post-harvest handling procedures. *E. coli-O157* isolation from food materials, antimicrobial resistance and Multi-Drug Resistance -(MDR) patterns are of global-public-health concerns. This study, therefore, investigated prevalence and antibiogram of *E. coli-O157* from *Oreochromis niloticus*-(O. niloticus) sold in Ibadan.

**Materials/methods:** A total number of 156 samples consisting of gills-(n=52), intestines-(n=52) and skins-(n=52) were collected from 52 *O. niloticus* from Egbeda, Ido, Ibadan North-East and Ibadan North-West for bacteriological analysis. *E. coli-O157* isolation and identification were performed according to the European Union Reference Laboratory standards (EU, 2017). Antibiogram was performed with agar disk diffusion method and interpreted with Clinical and Laboratory Standards Institute-(CLSI) 2017 standard.

**Results:** Overall *E. coli-O157* prevalence of 62.5% was obtained from *O. niloticus* in this study. The prevalence comprises of 62.5%, 37.5% and 87.5% for Gill, Intestine, and Skin, respectively. Isolates exhibited resistance patterns comprising:- 100.0%-(Ceftazidime-CPZ, Cefuroxime-CRX and Meropenem-MEM), 91.7%-(Cefotaxime-CTX), 83.3%-(Tetracycline-TET), 41.5%-(Cotrimoxazole-COT), 75%-(Ceftriaxone-CTR), 16.7%-(Gentamycin-GEN), 0%-(Amikacin-AMK), 8.3%-(Ciprofloxacin-CIP) and 0.0%-(Chloramphenicol-CHL). A multi-drug resistance pattern: CRX-CFZ-MEM-(100%), CRX-CTR-CFZ-MEM-(83.3%), CRX-CTR-CTX-CFZ-MEM-TET-(66.7%), CRX-CTR-CTX-CFZ-MEM-TET-COT-(58.3%) and CRX-CTR-CTX-CFZ-MEM-TET-COT-GEN-(8.3%) were observed.

**Conclusions:** Prevalence of *E. coli-O157* in *O. niloticus* sold in Ibadan is indicative of high aquatic contaminations and portends public health risks. High resistances and MDR patterns of isolates to antibiotics signifies misuse and/or indiscriminate disposal of antibiotics and risks of possible transmission of resistant/MDR genes to fish consumers.

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**Abstract 2993**

**Genetic relatedness of ceftriaxone-resistant multidrug-resistant Neisseria gonorrhoeae isolates in Singapore**

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**Background:** Multidrug-resistant Neisseria gonorrhoeae is a significant public health threat. We recently reported the first case of ceftriaxone-resistant multidrug-resistant N. gonorrhoeae in Singapore (2018). Since then, we have encountered two further cases of ceftriaxone-resistant N. gonorrhoeae. We report here the phenotypic characteristics and genetic relatedness of these local ceftriaxone-resistant N. gonorrhoeae strains.

**Materials/methods:** Urethral swabs were inoculated onto GC-LectTM Agar and colonies were identified using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and API NH. Minimum inhibitory concentration values for ceftriaxone and 13 other antimicrobials were determined using Etests. Ceftriaxone-resistant isolates 19DG543 and 19DG787 were whole genome-sequenced with Illumina MiniSeq platform. Core genome single nucleotide variation (SNV) analysis was used to determine genetic relatedness of the ceftriaxone-resistant isolates.

**Results:** Both 19DG543 and 19DG787 were phenotypically similar to the 2018 ceftriaxone-resistant N. gonorrhoeae isolate (18DG342). All three isolates were non-susceptible to ceftriaxone; resistant to cefixime, penicillin and ciprofloxacin; and of intermediate resistance to tetracycline. They remained susceptible to azithromycin and spectinomycin. All three cases were treated with intramuscular Ceftriaxone 500g with clinical cure.

*In silico* molecular typing showed that 19DG787 was genetically similar to 18DG342. They both belong to the novel Neisseria Multi Locus Sequence Typing (MLST) ST 13871, which so far has only been reported by our group. 19DG787 and 18DG342 were of the same N. gonorrhoeae multiantigen sequence type (NG-MAST) ST1086 and had the same N. gonorrhoeae sequence typing for antimicrobial resistance (NG-STAR) profile 233. 19DG543 was distinct from 19DG787 and 18DG342. 19DG543 belonged to MLST ST1903, which is the global circulating ceftriaxone-resistant N. gonorrhoeae MLST type reported in Japan, Australia and Canada.

Core genome SNV analysis showed that 19DG787 is closely related to 18DG342; with a difference of 4 SNVs between the core genomes. 19DG543 clustered most closely with the ceftriaxone-resistant strain reported in Australia (47707).

**Conclusions:** This study confirms that both the importation of global circulating ceftriaxone-resistant strain(s) and the dissemination of a local ceftriaxone-resistant ST13871 strain are threatening the efficacy of the current mainstay ceftriaxone and azithromycin dual therapy. Continued surveillance will determine the extent of ceftriaxone-resistant N. gonorrhoeae dissemination to inform local therapeutic and surveillance practices.

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In the absence of pressure, physical interaction within nasopharyngeal pneumococcal biofilms leads to acquisition of cephalosporin resistance but not to capsule switch events

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Background: Streptococcus pneumoniae (Spn) acquires genes for antibiotic resistance, for example cephalosporin resistance via PBP mutations and undergoes capsular switch events while residing in the nasopharynx. We simulated nasopharyngeal pneumococcal colonization to study population dynamics, acquisition of resistance, and capsule switch events.

Materials/methods: Nasopharyngeal biofilm consortia made by two Spn strains belonging to non-vaccine serotype (S) 2, and vaccine types S4, S6B, S19A, or S19F was investigated. The relative density of each strain within the biofilm consortia was obtained and the ultrastructure of biofilms was analyzed by super-resolution, confocal laser scanning, and electron microscopy. Transference of cephalosporin resistance from strains isolated from pneumococcal disease was investigated. To investigate capsule switch events, we engineered a donor vaccine strain carrying resistance to erythromycin near the capsule locus. This strain transferred the resistance marker to a recipient Spn strain when incubated in the simulated nasopharyngeal environment. The recombination frequency (rF) was obtained and capsule switch events of the recombinants was investigated by Quellung reactions and Sanger sequencing of a ~30 kb region surrounding the capsule locus for 10 recombinants.

Results: Mixtures of any two Spn strains formed a nasopharyngeal biofilm consortium. Microscopy studies demonstrated spatial localization of Spn strains within these consortia characterized by a fused structure. Formation of this structure preceded a rapid acquisition of cephalosporin resistance from donor vaccine strains to a non-vaccine recipient. Acquisition of resistance located upstream the capsule locus did not lead to capsule switch events in the recombinants.

Conclusions: In the absence of antibiotic pressure, or antibodies against the capsule, physical interaction within pneumococcal nasopharyngeal biofilm consortia allows passive acquisition of cephalosporin resistance without affecting the capsule expression of recipients.

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Genetic polymorphism of metabolic enzymes of Leishmania spp. parasites isolated from different clinical types of cutaneous leishmaniasis patients

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Background: Cutaneous leishmaniasis (CL), mainly caused by Leishmania major and L. tropica species, is a geographically extensive disease with diverse clinical manifestations. The most common CL lesion is a self-healing typical ulcer, leaving a scar, however, lesions can be highly polymorphic, and frequently appear as atypical lesions described as ‘eczematoid’, ‘chancriform’, ‘erysipeloid’, ‘zosteriform’, ‘lupoid’, ‘sprotrichoid’, etc. Parasite genetic diversity is proposed to be one of the factors affecting the characteristics of clinical lesions in CL. This study aim to explore potential association of genetic diversity of enzymatic markers with clinical type of CL.

Materials/methods: Totally 38 CL patients including 18 atypical CL due to L. major/L. tropica, 10 typical CL due to L. major and 10 typical CL due to L. tropica were included in the study. Specific PCRs were used for amplification of 6 genes encoding metabolic enzymes, mainly used for MLEE, including isocitrate dehydrogenase (icd), mannose phosphate isomerase (mpi), glucose-6-phosphate dehydrogenase (g6pd), fumarate hydratase (fh), 6-phosphogluconate dehydrogenase (6pgd) and aspartate aminotransferase (asat). Alignment, phylogenetic analysis and genetic diversity analyses were performed using BioEdit, Mega7, DnaSP and MLSTest softwares.

Results: The comparison of partial sequences of enzyme genes with reference sequences allowed for the identification of a few polymorphisms in particular in 6pgd gene in L. major (Eta index=24) and icd gene in L. tropica (Eta index=30). Highest rate of haplotype diversity (Hd) in L. major was for 6pgd gene (0.377) and in L. tropica was for icd gene (0.659). Totally, 12 distinct Diploid Sequence Type (DST) in L. major and 8 distinct DST in L. tropica strains were recognized. Neucleotide diversity (π) and Hd indices of sequenced genes were not significantly different between atypical and typical CL patients.

Conclusions: The sequence analysis of six metabolic enzyme genes suggests genetic variability in L. major and L. tropica strains causing CL. A high number of new DSTs has been found among the isolates showing a significant variations in the sequences of these enzyme genes. However, no correlation between polymorphism of these genes and clinical type of CL has been detected.

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Abstract 3004

A second surgical debridement for acute periprosthetic joint infections should not be discarded
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1University of Groningen, University Medical Center Groningen, Groningen, Netherlands, 2Martini Hospital, Groningen, Netherlands, 3Medical Center Leeuwarden, Leeuwarden, Netherlands, 4Martini Hospital, Certe, Groningen, Netherlands, 5University of Groningen, University Medical Center Groningen, Groningen, Groningen, Netherlands

Background: In acute periprosthetic joint infections (PJI), a second surgical debridement (DAIR) after a failed first one is disadvised in current international recommendations. We identified the failure rate of a second DAIR and aimed to identify patients in whom an additional debridement might still be beneficial.

Materials/methods: Patients with acute PJI of hip or knee and treated with DAIR between 2006 and 2016 were retrospectively evaluated. Failure of a second DAIR was described as: i) the need for additional surgical intervention to achieve infection control, ii) the need for antibiotic suppressive therapy due to persistent clinical and/or biochemical signs of infection or iii) PJI related death.

Results: From the 455 cases treated with DAIR, 144 cases underwent a second debridement (34.6%). Thirty-seven cases failed (37/144, 25.7%). The implant needed to be removed in 23 cases (23/144, 16%). Positive cultures during the second DAIR (OR 3.16 [95% CI 1.29–7.74]) and chronic renal insufficiency (OR 3.6 [95% CI 2.03–91.33]) were independent predictors for failure in the multivariate analysis. No difference in failure was observed between persistent infection with the same microorganism and reinfection with a new microorganism (failure rate 31.6% versus 34.6% resp., p 0.83). A BMI > 30 kg/m² was an independent predictor for treatment success (OR 0.26 [95% CI 0.09–0.72]).

Conclusions: A second DAIR had a low failure rate in our cohort of patients and the implant could be retained in the majority of them. A second DAIR should not be discarded in acute PJIs, especially not in obese patients and those without chronic renal insufficiency.

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Antimicrobial susceptibility and clinical characteristics of severe pneumonia due to Haemophilus influenzae: an observational study

Pierre Danneels1, Maria Concetta Postorino1, Alessio Strazzulla*1, Aurelia Pitsch2, Sebastien Jochmans3, Mehran Monchi3, Vincent Dubee4, Sylvain Diamantis1

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Background: Treatment of Haemophilus influenzae (Hi) pneumonia is of concern because resistance to amoxicillin enhances prescription of third generation cephalosporins (C3G). However, this practice should be discouraged to minimize the impact on microbiota and selection of extended-spectrum β-lactamases (ESBL). Aim of this study was to describe the evolution of resistance patterns and clinical characteristics of patients hospitalized in intensive care unit with Hi associated pneumonia.

Materials/methods: We conducted a retrospective observational study including patients from 2008 to 2017 with diagnosis of pneumonia hospitalised in ICU. As comparator, we confronted characteristics of Hi pneumonia with Streptococcus pneumoniae (Sp) pneumonia. General characteristics, medical history, risk factors for pneumonia, co-morbidities and critical illness criteria were collected. Data about antimicrobial resistance were interpreted according to 2005-2013 EUCAST guidelines.

Results: Overall, 113 patients with Hi and 132 with Sp pneumonia were included in the study. Percentages of amoxicillin/clavulanic acid (AMC) resistance among Hi strains decreased over years (from 10% in 2008-2009 to 0% in 2016-2017, p=0.15). Also, percentages of Sp resistant strains for amoxicillin and moxifloxacin decreased over years (respectively from 25% to 0%, p<0.001, and from 21% to 0%, p<0.001) as shown in Figure 1. Patients with Hi experienced higher prevalence of bronchitis (18% vs. 8%, p=0.02), chronic obstructive pulmonary disease (43% vs. 30%, p=0.03), hospital-acquired pneumonia (HAP) (18% vs. 7%, p=0.01), ventilator associated pneumonia (13% vs. 5%, p=0.02) and longer duration of mechanical ventilation (8 days vs. 6 days, p=0.04) than patients with Sp pneumonia. On the contrary, patients with Sp pneumonia had more frequently local complications (17% vs. 7%, p=0.03). De-escalation of antibiotics was more frequent in patients with Sp than in patients with Hi (67% vs. 53%, p=0.03).

Conclusions: Patients with Hi pneumonia had higher risk of clinical complications than Sp pneumonia. Our data suggest that mono-therapy with AMC was effective on both Hi and Sp and could be considered as empirical treatment in patients with community-acquired pneumonia and HAP, permitting to spare C3G and, therefore, to reduce the impact on microbiota and the selection of ESBL bacteria.

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Abstract 3009

Activities of eight antifungal agents against Candida auris biofilms
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Background: Candida auris (CAU) has emerged rapidly as a prolific nosocomial pathogen, causing infections worldwide, surviving and persisting in the hospital environment and most of the times developing multi-drug resistance (MDR). CAU forms biofilms (BF) on biological and inert surfaces, such as intravascular catheters. Polyene, triazoles and echinocandins, three classes of antifungal agents with distinct mechanisms of action, are used as standard therapy for Candida infections.

Materials/methods: Five CAU isolates, each belonging to a different clade, were grown in RPMI-1640/2% glucose in 96-well plates under constant shaking for 48h/37°C in order to form BF. BFs were then incubated with no-drug (controls) or with two-fold dilutions of amphotericin B, posaconazole, voriconazole, fluconazole, itraconazole, caspofungin, anidulafungin and micafungin ranging from 2-2048 mg/L for further 24h. Percent BF damage was assessed colorimetrically by XTT assay. BF-MIC was defined as the minimal drug concentration causing ≥50% reduction in metabolic BF activity vs. controls. Susceptibility of PL cells was tested using EUCAST method (n=6).

Results:

<table>
<thead>
<tr>
<th></th>
<th>PSC PLK/BF</th>
<th>VRC PLK/BF</th>
<th>ITR PLK/BF</th>
<th>FLU PLK/BF</th>
<th>CAS PLK/BF</th>
<th>AND PLK/BF</th>
<th>MICA PLK/BF</th>
<th>AMB PLK/BF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>0.016/256</td>
<td>0.06/256</td>
<td>0.03/256</td>
<td>32/1024</td>
<td>0.25/128</td>
<td>0.25/32</td>
<td>0.125/128</td>
<td>0.25/2</td>
</tr>
<tr>
<td>S. America</td>
<td>0.25/16</td>
<td>0.25/16</td>
<td>1/16</td>
<td>128/128</td>
<td>0.125/128</td>
<td>0.125/4</td>
<td>0.125/1024</td>
<td>0.5/2</td>
</tr>
<tr>
<td>Korea</td>
<td>0.5/256</td>
<td>0.25/1024</td>
<td>0.25/1024</td>
<td>32/1024</td>
<td>0.125/128</td>
<td>0.06/512</td>
<td>0.125/2048</td>
<td>0.5/4</td>
</tr>
<tr>
<td>India</td>
<td>0.25/32</td>
<td>0.5/128</td>
<td>1/64</td>
<td>128/128</td>
<td>4/256</td>
<td>0.5/256</td>
<td>1/2048</td>
<td>2/2</td>
</tr>
<tr>
<td>Iran</td>
<td>0.03/4</td>
<td>0.016/16</td>
<td>2/4</td>
<td>0.5/16</td>
<td>0.025/2</td>
<td>0.06/2</td>
<td>0.25/2</td>
<td>1/2</td>
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<tr>
<td>CA-M61</td>
<td>0.01/128</td>
<td>0.5/512</td>
<td>0.03/128</td>
<td>1/1</td>
<td>0.06/1</td>
<td>0.03/1</td>
<td>0.125/1</td>
<td>0.5/1</td>
</tr>
<tr>
<td>CP-A71</td>
<td>0.01/256</td>
<td>0.125/512</td>
<td>0.03/128</td>
<td>8/8</td>
<td>0.03/1</td>
<td>0.03/1</td>
<td>0.125/1</td>
<td>0.25/1</td>
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</tbody>
</table>

All CAU isolates except one were FLU-R for PLK. South american, korean and indian isolates had high PLK-MIC to all antifungals compared to standard C. albicans and C. parapsilosis (CA-M61 and CP-A71). All isolates had much higher BF-MIC ranging from 16-2048mg/L compared to PLK except for Iran isolate. AMB exhibited BF-MICs that were low and close to PLK-MIC.

Conclusions: While CAU BFs have MICs of azoles and echinocandins much higher than PLKs, AMB exhibits much lower BF-MICs that are comparable to those of corresponding PLK.

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In vitro activity of omadacycline against pathogens isolated from mainland China during 2017-2018

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Background: Antibiotic resistance of bacterial pathogens isolated in China is a major concern, and new antibacterial agents are needed in this country. Omadacycline is a novel tetracycline derivative and was developed to address such resistance. The efficacy of Omadacycline has been demonstrated in clinical trials for acute bacterial skin and skin structure infections (ABSSSI) and community acquired bacterial pneumonia (CABP). However, susceptibility data has largely been limited to Western countries. This study was conducted to determine the in vitro activity of Omadacycline against a large collection of patient isolates from a geographically diverse group of medical centers in Mainland China.

Materials/methods: 1,041 recent clinical isolates obtained from patients hospitalized in 29 provinces and municipalities across China. The in vitro activity of Omadacycline and comparator agents was assessed using microbroth dilution according to CLSI methodology.

Results: Omadacycline was very active against methicillin-susceptible and -resistant Staphylococcus aureus with MIC90 values of 0.25 and 1 mg/L, respectively. All isolates of Enterococcus faecalis and E. faecium, including vancomycin-resistant isolates, were inhibited by ≤0.25 mg/L of Omadacycline. It was highly active against Streptococcus pneumoniae irrespective of susceptibility to penicillin or macrolides (MIC90 values 0.06-0.12 mg/L). It was also active against β-hemolytic and viridans group streptococci (MIC90 values 0.06-0.12 mg/L). The MIC distribution of Omadacycline was nearly identical against ESBL-positive and ESBL-negative E. coli. In addition, 95% of carbapenem-resistant E. coli (KPC or NDM producers) isolates were susceptible to Omadacycline (MIC90 = 4 mg/L). Omadacycline was as potent as tigecycline against Enterobacter cloacae and Citrobacter freundii. Omadacycline also showed good activity against Acinetobacter baumannii, inhibiting all isolates (including carbapenem-resistant) at ≤8 mg/L. Against Hemophilus influenzae and Moraxella catarrhalis, the MICs of omadacycline were low and not influenced by the presence of β-lactamase (100% susceptible).

Conclusions: Overall, the activity of Omadacycline was very good against isolates commonly associated with ABSSSI or CABP, and the susceptibility of Chinese isolates was similar to that reported for these pathogens from large surveillance studies outside China. This, coupled with the oral dosing option, makes omadacycline an attractive option for treatment of these infections in Chinese patients.

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Abstract 3014

Quantitative PCR detection of circulating DNA for the diagnosis of mucormycosis: prospective evaluation in the ModiMucor study

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1Parasitology-Mycology department, University Hospital of Besançon, Besançon, France, 2University Hospital of Dijon, Dijon, France, 3University Hospital of Besançon, Besançon, France, 4University Hospital of Strasbourg, Strasbourg, France, 5APHP Saint Louis Hospital, Paris, France, 6University Hospital of Nantes, Nantes, France, 7APHP Necker Hospital, Paris, France, 8University Hospital of Creteil, Creteil, France, 9University Hospital of Amiens, Amiens, France, 10University Hospital of Lyon, Lyon, France

Background: Modimucor is a French prospective multicentre study that aims to assess the performance of Mucorales PCR on blood samples for the diagnosis of mucormycosis.

Materials/methods: Patients with risk factors for invasive mold infection (hematological diseases, burns diabetes, solid organ transplantation, trauma, or diabetes) and patients diagnosed with mucormycosis were enrolled prospectively. Serum samples were collected twice-a-week, and Mucorales PCR were performed at the time of serum sampling, in each center, as previously described [Millon, Clin Microbiol Infect 2016]. Clinical data and biological data were collected up to 6 months after enrollment. Data analysis was performed using STATA 14 software.

Results: 249 patients from 9 University Hospital in France were enrolled from January 2015 to June 2017.

Forty-two patients were diagnosed with probable (n=11) or proven (n=31) mucormycosis according to EORTC/MSG criteria (including 12 mixed Aspergillus-Mucorales infections). Sensitivity and specificity of Mucorales PCR for diagnosis of probable or proven mucormycosis were 88.1% (37/42), and 89.7% (183/204), respectively. The first PCR-positive sample was observed in an average of 3.3 days before the first imaging criteria. Liposomal Amphotericin B was initiated in an average of 4.7 days after the first PCR-positive sample. Survival at 6 months was 53.9% (14/26) in patients with PCR becoming negative within 7 days after treatment initiation, and 0% (0/11) in patients with PCR remaining positive (Fisher’s exact test p = 0.002).

Eighteen patients with host factor and radiological signs for possible IMI had positive Mucorales PCR, including 11 patients with at least 2 consecutive positive samples. All of them were given liposomal Amphotericin B, in an average of 1.8 days after the first PCR-positive sample. In this subgroup, survival at 6 months was 80% (12/15) in patients with PCR becoming negative within 7 days after treatment initiation, and 0% (0/3) in patients with PCR remaining positive (Fisher’s exact test 0.025).

Conclusions: Mucorales PCR is a sensitive tool that helps to anticipate the diagnosis of mucormycosis. Decrease in DNA load after treatment was associated with a better outcome. This new tool is becoming essential in the clinical management of mucormycosis.

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**Abstract 3020**

**β-lactam allergy and risk of multidrug-resistant bacteria acquisition in an intensive care unit: a cohort study**

Alessio Strazzulla*, Laura Iordache, Astrid De Pontfarcy, Aurelia Pitsch, Nabil Belfeki, Sebastien Jochmans, Guillaume Lezmi, Mehran Monchi, Sylvain Diamantis

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**Background:** Patients with β-lactam allergy are frequently exposed to treatments by broad spectrum antibiotics. However, the risk of extended spectrum β-lactamase (ESBL) carriage in this population has been poorly investigated. Aim of this study was to evaluate characteristics and clinical outcomes of patients admitted in intensive care unit (ICU) with and without declared β-lactam allergy at admission.

**Materials/methods:** The study included patients admitted in ICU from 2007 to 2012. The presence of multidrug resistant bacteria was documented in rectal and nasal swab at admission and discharge. Clinical characteristics and outcomes of patients labelled allergic to β-lactams and unlabelled patients were compared.

**Results:** Patients labelled allergic had significantly higher rates of ESBL at admission (13.3 % vs 4.3%, p=0.0220) and at discharge (20% vs 8.9%, p=0.0460) than unlabelled patients but no significant difference in rates of ESBL acquisition was detected. No differences in mortality, duration of hospitalisation and typical risk factors of ESBL acquisition (intubation, CVC and duration of hospitalization) were reported. No differences in carriage of methicillin resistant *Staphylococcus aureus* were detected (Table 1).

**Conclusions:** This study showed that patients with declared β-lactam allergy had a higher risk of ESBL carriage at admission and at discharge.

<table>
<thead>
<tr>
<th>CHARACTERISTIC</th>
<th>OVERALL</th>
<th>PREVALENCE ALLERGY (%)</th>
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<th>P-value</th>
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<td>62 (17.3)</td>
<td>62 (17.4)</td>
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<td>15 (40.9)</td>
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<td></td>
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<td>27 (59.1)</td>
<td>836 (62.6)</td>
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<td>SIRS [mean (SD)]</td>
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<td>Mortality ventilation [n (%)]</td>
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<td>71 (46.6)</td>
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<td>MDR strains at discharge [n (%)]</td>
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<td>MRSA at discharge [n (%)]</td>
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<td>MRSA at discharge [n (%)]</td>
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</tbody>
</table>

**Presenter email address:** alessiostrazzulla@yahoo.it
Effectiveness of trimetoprim-sulfametoxazole for treatment of ventilator-associated pneumonia: a cohort study

Alessio Strazzulla*1, Maria Concetta Postorino1, Anastasia Purcardea1, Catherine Chakvetadze1, Astrid De Pontfarcy1, Gianpiero Tebano1, Aurelia Pitsch1, Lyvan Yong2, Sebastien Jochmans2, Christophe Vinsonneau2, Mehran Monchi2, Sylvain Diamantis1

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Background: Trimetoprim-sulfametoxazole or co-trimoxazole (TMP-SMX) is naturally active against a broad spectrum of microorganisms, including the most frequent agents of ventilator associated pneumonia (VAP), except for Pseudomonas aeruginosa. It is currently approved for pneumonia (notably Pneumocystis jirovecii pneumonia and community acquired pneumonia) but it is neither recommended nor formally contraindicated for the empiric treatment of VAP. Aim of this study is to evaluate the effectiveness of trimetoprim-sulfametoxazole (TMP-SMX) for treatment of ventilator associated pneumonia (VAP).

Materials/methods: Retrospective cohort study including patients with VAP from 2011 to 2017. Two groups were analysed: TMP-SMX group, including patients who had received TMP-SMX (as first line and as de-escalation), and No-TMP-SMX group, including patients who had not received TMP-SMX treatment. Primary clinical outcome was mortality at 30 days from starting the antibiotic treatment (T30). Secondary outcomes were: mortality at end of treatment (EoT), day survival at T30, acquisition of multidrug resistant bacteria during hospitalization in intensive care unit.

Results: Eighty cases of VAP were included and distributed into two groups: No-TMP-SMX (31/80; 39%) and TMP-SMX (49/80; 61%). Univariate analysis reported no significant differences when the TMP-SMX group was compared to No-TMP-SMX group, except for frequency of male gender (p=0.025), as shown in Table 1. No significant statistical correlations between mortality at T30 and individual factors were detected by the multivariate model. No cases of either severe allergy or Clostridium difficile disease were reported in TMP-SMX and No-TMP-SMX group.

Conclusions: TMP-SMX treatment was not associated with higher mortality at EoT and T30 in comparison to the No-TMP-SMX group. TMP-SMX had a good safety profile, in terms of ecology (acquisition of MDR bacteria and Clostridium difficile disease) and clinical management (no allergy events).

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>STANDARD TREATMENT (N=31)</th>
<th>TMP-SMX (N=49)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biological parameters</td>
<td>65.4 (15.3)</td>
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<td>Male gender (%)</td>
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<td>Clinical parameters</td>
<td>55.7 (19.9)</td>
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<td>SAPS-II (SD)</td>
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<td>37 (7.3)</td>
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<td>Antibiotic treatment before VAP (%)</td>
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<td>18 (36.7)</td>
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<td>Early VAP (%)</td>
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<td>18 (36.7)</td>
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<td>Shock (%)</td>
<td>21 (67.6)</td>
<td>32 (65.3)</td>
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<td>Bacterial isolates from lower respiratory tract samples</td>
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<td>7 (14.3)</td>
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<td>Staphylococcus aureus (%)</td>
<td>8 (25.8)</td>
<td>10 (20.4)</td>
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<td>Mixed cultures and/or other bacteria (%)</td>
<td>5 (16.2)</td>
<td>6 (12.3)</td>
<td>0.874</td>
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<td>Clinical outcomes</td>
<td>30 mortality ( %)</td>
<td>30 (6)</td>
<td>16 (32.7)</td>
</tr>
<tr>
<td>T30 mortality ( %)</td>
<td>24.3 (10)</td>
<td>24.8 (6.4)</td>
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<td>MDR bacteria acquisition during hospitalization ( %)</td>
<td>9 (29)</td>
<td>7 (14)</td>
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Presenter email address: alessiostrazzulla@yahoo.it
Capillary micro-sampling versus conventional sampling to conduct a clinical pharmacokinetic study for meropenem in critically ill patients

Yarmary C. Guerra Valero*, Jason Roberts1,2,3,4, Jeffrey Lipman1,4,5, Cheryl Fourie1, Therese Starr4, Steven Wallis1, Suzanne Parker1

1The University of Queensland, UQ Centre For Clinical Research, Herston, Australia, 2Royal Brisbane and Women’s Hospital, Department of Pharmacy, Herston, Australia, 3The University Of Queensland. School of Pharmacy, Centre of Translational Pharmacodynamics, Woolloongabba, Australia, 4Royal Brisbane and Women’s Hospital, Intensive Care Services, Herston, Australia, 5Queensland University of Technology, Faculty of Health, Brisbane City, Australia

Background: Critical illness has been shown to affect the pharmacokinetics of antibiotics, which can lead to ineffective antimicrobial exposure and the potential emergence of antimicrobial-resistant bacteria. The lack of studies describing antimicrobial pharmacokinetics in critically ill patients has led to significant off-label dosing. Conventional sampling to conduct clinical pharmacokinetic studies usually involve sampling of frequent and large volumes of blood (>2 mL) obtained using arterial or venous cannula. This can impact on the pathophysiology and/or the well-being of a patient, particularly a neonate or pediatric patient. Capillary microsampling (CMS) facilitates the collection of small volumes (<0.05 mL) by using minimally invasive procedures, such as finger prick. Implementation of CMS into clinical studies requires a two-stage assessment: a bioanalytical validation and clinical bridging study.

Materials/methods: Twenty-four paired plasma samples from critically-ill adults receiving intravenous meropenem were collected as both CMS from a finger-prick and as conventional sampling from an arteriovenous cannula. A 2.5 µL plasma sample was mixed with internal standard, [2H6]−meropenem and treated with acetonitrile and analyzed using HILIC LC-MSMS.

Results: Bioanalytical validation testing across the range of 0.2 to 100 µg/mL met acceptance criteria. Figure 1 illustrates a mean pharmacokinetic profile of six critically ill patients receiving meropenem. The maximum concentration and the minimum concentration measured were 32.1 mg/L and 6.33 mg/L for CMS and 36.2 mg/L and 6.40 mg/L for conventional sampling, respectively. The area under the concentration-time curve from 0 to 6 hours (AUC0–6h) ranged between 8.06 and 260 mg/L.h for CMS and from 8.08 and 270 mg/L.h for conventional sampling. Peripheral CMS results showed a mean bias of 1.5 (limits of agreement: -7.3 to 10.3) µg/mL compared to conventional sampling; the difference in concentration between the paired plasma samples was within 20% of the mean of the paired samples for 88% of the 24 samples tested.

Conclusions: Laboratory-based bioanalytical validation found the method was suitable for measuring meropenem in plasma. The clinical bridging study revealed no significant bias and a strong correlation between both sampling methods demonstrating that plasma samples collected as CMS from finger prick were a valid alternative to conventional plasma sampling.

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Abstracts 2020

Abstract 3029

A nation-wide parent survey of antibiotic use in Australian children

Rebecca Anderson1, Anthea Rhodes1,2, Noel Cranswick1,2,3, Marnie Downes2,3, Jonathan O’hara1, Mary-Anne Measey1,3, Amanda Gwee*1,2,3

1The Royal Children’s Hospital, Melbourne, Melbourne, Australia, 2University of Melbourne, Melbourne, Australia, 3Murdoch Children’s Research Institute, Melbourne, Australia

Background: Antimicrobial resistance is increasing globally, largely due to high rates of antibiotic use and misuse. Factors that influence frequent antibiotic use in children are poorly understood. This study describes rates of antibiotic use in Australian children and investigates parental factors including knowledge, attitudes and behaviours that influence antibiotic use.

Materials/methods: An online questionnaire relating to antibiotic use was administered as part of the Royal Children’s Hospital National Child Health Poll to a randomly-recruited nationwide sample of parents or guardians of children aged 0–17 years in Australia. Data on antibiotic use in children, and parental knowledge of appropriate indications for antibiotics and behaviours were collected. Standard binary logistic regression was used to assess associations between parent demographics and behaviour with antibiotic administration.

Results: The survey was completed by 2157 parents (64% completion rate), of which 1131 (52%) reported having given oral antibiotics to one or more of their children in the preceding 12 months. Of the 3971 children represented overall, 1719 (43%) had received at least one course of antibiotics. The average number of courses per child was 0.86 overall and 1.96 courses per child among those with reported antibiotic use. Notably, 194/1131 (17%) parents reported giving antibiotics to their child without a prescription, accessing the medication from leftover courses, family or friends, pharmacies or purchasing the medication online. Poor parental knowledge of antibiotic indications was associated with antibiotic use.

Conclusions: Reducing excessive use of antibiotics in children is necessary in the global strategy for preventing antimicrobial resistance. To the best of our knowledge, this is the first nationwide study of parent-reported antibiotic use in children that also accounts for non-prescription antibiotic use. We have demonstrated high community rates of antibiotic use in children and highlighted an urgent need to improve prescribing practices, increase governance over access to antibiotics and provide routine educational interventions at a primary care level.

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Abstract 3030

Acceptability and usefulness of self-collected mid-turbinate swabs to diagnose and measure viral shedding in a pilot randomised controlled trial of hypertonic saline nasal irrigation and gargling in adults with a common cold

Sandeep Ramalingam*1, Cat Graham2, Jenny Dove1, Lynn Morrice1, Aziz Sheikh2

1Royal Infirmary of Edinburgh, Edinburgh, United Kingdom, 2University of Edinburgh, Edinburgh, United Kingdom

Abstract third-party references: NHS Lothian, University of Edinburgh, Cornish Sea Salt, Copan, Edinburgh And Lothians Health Foundation

Background: There are no effective interventions for a viral upper respiratory tract infection (URTl). We conducted a pilot randomised controlled trial of hypertonic nasal irrigation and gargling (HSNIG) vs standard care in adults with URTI to confirm laboratory evidence that epithelial cells utilise chloride ions to fight viral infections. As saline could not be a placebo, we used viral shedding as an independent marker of viral inhibition (www.clinicaltrials.gov:NCT02438579).

Materials/methods: Adults within 48 hours of URTI were minimised by sex/smoking status. The intervention arm were taught to prepare hypertonic saline with Cornish sea-salt and perform HSNIG. The control arm received usual care. All were taught to collect a mid-turbinate (MT) swab in eNAT transport medium (Copan) and baseline samples collected. Sequential MT swabs were self-collected first thing in the morning on 4 consecutive days and returned by post for testing. A validated symptom diary (WURSS-21) was maintained (until well for two days, ≤14 days). Day 0 samples were tested by the respiratory panel. If a virus was identified, all 5 samples were tested in parallel. The cycle threshold value was converted to log10 values to determine change in viral shedding.

Results: Of 68 participants recruited, follow up data was available from 61 (Intervention:30, Control:31). Both arms found collecting swabs easy (93% Vs 72%; p=0.08) and returning swabs easy (100% Vs 97%). Viral aetiology was identified in 74% of baseline swabs (49/66). In the intervention arm, 87% found HSNIG acceptable, 93% thought HSNIG made a difference to their symptoms, duration of illness was lower by 1.9 days (p=0.01), over-the-counter medication use was lower by 36% (p=0.004), transmission within household contacts was lower by 35% (p=0.006). A higher proportion in the intervention arm had a fall in viral shedding by ≥0.5log10/day compared to controls (p=0.04).

Conclusions: HSNIG is an acceptable intervention. The reduction in duration of symptoms, over-the-counter medication use, illness within households and viral shedding point to its effectiveness against the common cold. The ease of collection and return of swabs, and virus detection in a large proportion of samples will help design the definitive trial.

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Rising incidence and mortality of bloodstream infections in Finland: a nation-wide population-based study during 2004–2018

Keiju Kontula*, Kirsi Skogberg1, Jukka Ollgren3, Outi Lyytikainen3, Asko Järvinen2

1Helsinki University Hospital, Division of Infectious Diseases, Inflammation Center, Helsinki, Finland, 2Helsinki University Hospital, Division of Infectious Diseases, Inflammation Center, Helsinki, Finland, 3National Institute for Health and Welfare, Department of Health Security, Helsinki, Finland

Background: Bloodstream infections (BSI) are related to significant morbidity and mortality. Our aim was to explore temporal changes in the incidence, outcome and causative agents of BSIs in Finland.

Materials/methods: We used data from the nationwide laboratory-based surveillance to analyze all BSIs in Finland during 2004–2018. Data on the date of death was retrieved from the Population Information System. Age- and gender-specific incidence and mortality rates were calculated by using population data from Statistics Finland.

Results: During 2004–2018, a total of 173,715 BSIs among 147,953 patients were identified (average annual incidence, 2.16 BSIs/100,000 population). The annual incidence increased from 150 to 309/100,000 population during 2004–2018; average annual increase was 5.2%. The increasing trend was sharpest among elderly, whereas among children there was a decreasing trend. Of all BSIs, 22,474 (1.3%) were fatal within 30 days; case fatality was highest (1.3.5%) in 2011 and lowest (1.2.1%) in 2017. The all-cause mortality within 30 days increased from 20 to 39/100,000 population during 2004–2018. The average annual increase was 4.8%; it was most notable among elderly. The proportion of gram-negative bacteria as causative agents increased from 42% to 48%, whereas BSIs caused by gram-positive bacteria decreased from 50% to 43%. No changes were observed in fungal or polymicrobial BSIs (from 1.7% to 1.1% and 6.5% to 7.1%, respectively). The incidence of Escherichia coli increased from 39 to 91/100,000 and Staphylococcus aureus from 19 to 39/100,000. Altogether, 3150 (1.8%) BSIs were caused by multi-drug-resistant microbes, and their proportion increased from 0.4% in 2004 to 2.8% in 2018, mostly due to extended-spectrum β-lactamase-producing E. coli and Klebsiella pneumoniae.

Conclusions: A twofold increase was noted in the incidence and mortality of BSIs in Finland during 2004–2018, and most of it occurred among elderly persons. However, case fatality remained unchanged, maybe related to improved diagnostics and treatment. The proportion of gram-negative bacteria as causative agents increased, and a rising trend in resistance was observed, which may cause problems in the future regarding of antimicrobial therapy. Our findings highlight the need for continuous surveillance of BSIs and active implementation of preventive measures.

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Synthesis of nano-capsulated caprylic acid: evaluation of antifungal activity and its effect on EFG1 gene expression in Candida albicans

Maryam Roudbary1, Shahla Roudbarmohammadi2, Reyhaneh Zarimeidani3, Sara Mardani2

1Iran University of Medical Sciences, School of Medicine, Department of medical mycology and parasitology, Tehran, Iran, 2Tarbiat Modares University, Faculty of Medical sciences, Department of Medical Mycology, Tehran, Iran, 3Tarbiat Modares University, Faculty of Medical Sciences, Department of Medical Mycology, Tehran, Iran

Background: Increasing reports of resistant Candida species in clinical settings, discovering new antifungal agents with minimum side effects are highly deliberated worldwide. Nowadays, the nanotechnology approach can be used as an alternative option in drug delivery system. Recently, the antifungal properties of the medium chain fatty acid include Caprylic acid have been presented. This study aimed to investigate the antifungal activity of Caprylic acid and nano-encapsulated Caprylic acid on Candida albicans (C. albicans) and its effect on the expression of EFG1 gene was assessed.

Materials/methods: Minimum inhibitory concentration (MICs) of the Caprylic acid and nano-encapsulated Caprylic acid on C. albicans was evaluated according to CLSI method (M27-S3) compared to fluconazole. For this, serial dilution of Caprylic acid and nano-encapsulated Caprylic acid was prepared in concentration of 400, 450, 500, 550, 600, 625 µl/ml and 50, 25, 12.5, 6.25, 3.125, 1.5625 µl/ml respectively. RNA extracted from C. albicans before and after exposure to Caprylic acid and nano-encapsulated Caprylic acid, then cDNA synthesized and the mRNA expression of EFG1 gene of each group was evaluated using Real-time PCR assay. Cellular viability of epithelial cell line against Caprylic acid and nano-encapsulated Caprylic acid was examined using MTT assay.

Results: According the findings, MIC90 of Caprylic acid was 500µg/ml and MIC50 was 450µg/ml, whereas MIC90 for nano-encapsulated Caprylic acid indicated 6.2µg/ml and MIC50 showed 3.1µg/ml. The MFC of Caprylic acid and encapsulation Caprylic acid determined as 600µg/ml and 12.5µg/ml respectively. mRNA level of EFG1 gene significantly decreased in C. albicans treated with Caprylic acid and nano-encapsulated Caprylic acid compared to control group. Moreover, the EFG1 expression after exposure to Caprylic acid nanocapsulated was 4-fold lower than Caprylic acid treatment (p=0.002). The MTT results showed, Caprylic acid indicated higher cell viability than nano encapsulated caprylic acid.

Conclusions: Design of drug delivery systems based on nanotechnology could be overcome the defects of available common drugs. According the obtained results, nanoencapsulated Caprylic acid successfully inhibited the C. albicans growth with the low MIC compared to Caprylic acid. Taken together, it is suggested Caprylic acid nano-encapsulated may be used as a safe and suitable agent against Candida species, however more studies are required in the future.

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Abstract 3035

Impact of an antimicrobial stewardship programme on antibiotic resistance profile of urinary Enterobacteriaceae isolated from nursing home residents: a retrospective cohort study

Alessio Strazzulla1, Samuel Bokobza2, Edgar Ombandza1, Khadjah Kherallah1, Stéphane Hommel1, Raouf Draidi1, Cédric Bonutto2, Dominique Bonnet Zamponi1, Rémy Gauzit1, Sylvain Diamantis1

1Centre Hospitalier de Melun, Infectious Diseases Unit, Melun, France, 2Centre Hospitalier de Provins, Provins, France, 3Sorbonne University, Paris, France, 4Centre Hospitalier Universitaire de Cochin, Paris, France

Background: Antibiotic resistance is common in isolates from nursing home residents, affecting in particular urinary isolates. This study investigates the impact of an antimicrobial stewardship program on fluoroquinolone (FLQ) resistance in urinary Enterobacteriaceae isolated from residents of three French nursing homes.

Materials/methods: A multicentric retrospective before-and-after study was conducted. All the first urinary Enterobacteriaceae isolates obtained from nursing home residents were included. Two time frames were analysed: 2013-2015 and 2016-2017. The antimicrobial stewardship program started in 2015 and was based on: i) a single training day for use of an "antimicrobial stewardship kit for nursing homes"; ii) daily support and training of the coordinating-physician by an antibiotic mobile team (AMT) in two out of three nursing homes.

Results: Overall, 338 urinary isolates were analysed. Escherichia coli was the most frequent species (212/338, 63%). A significant reduction of resistance to ofloxacin was observed between 2013-2015 and 2016-2017 in the whole set of isolates (p=0.004), among isolates obtained from patients hospitalised in the county nursing home with AMT support (p<0.01) and among Enterobacteriaceae isolates other than E. coli (p=0.006).

Conclusions: Our antimicrobial stewardship program allowed to reduce the rate of resistance to FLQ among urinary Enterobacteriaceae isolated from nursing home residents. A support of the AMT and a continuous training of the coordinating-physician seemed to be an important component to ensure the efficacy of the intervention.

<table>
<thead>
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<td>76 (67)</td>
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</tr>
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<td>116 (52)</td>
<td>29 (26)</td>
<td>&lt;0.001*</td>
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<td>24 (11)</td>
<td>9 (8)</td>
<td>0.5</td>
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<td>TMP/SMX</td>
<td>52 (23)</td>
<td>19 (17)</td>
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A. Overall

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<tr>
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<tr>
<td>Ofloxacin</td>
<td>1 (3)</td>
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<td>0.4</td>
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<tr>
<td>TMP/SMX</td>
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B. County Nursing Home without Antibiotic Management Team Support

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<td>21 (14)</td>
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C. Hospital Nursing Home with Antibiotic Management Team Support

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<td>0.2</td>
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<tr>
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<td>11 (25)</td>
<td>11 (25)</td>
<td>0.4</td>
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</table>

D. County Nursing Home with Antibiotic Management Team Support

|---------------------|-----------|-----------|------|
| Presenter email address: alessiostrazzulla@yahoo.it
Abstract 3036

Characterisation of ceftolozane/tazobactam resistance amongEnterobacterales andPseudomonas aeruginosaisolates recovered during the SUPERIOR study using whole genome sequencing.

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Background: Ceftolozane/tazobactam (C/T) is a novel β-lactam/β-lactamase inhibitor combination used for infections caused by multidrug-resistant (MDR) gram-negative bacteria. We studied the population structure and resistome of MDR Enterobacterales and Pseudomonas aeruginosaisolates, either C/T-susceptible or -resistant, recovered from intraabdominal and urinary tract infections in 8 Spanish Hospitals (SUPERIOR Study, 2016-2017).

Materials/methods: MICs were determined (ISO-broth microdilution, EUCAST criteria). Forty-fiveEscherichia coli, 43Klebsiella spp. and 13P. aeruginosaisolates were selected for whole genome sequencing (WGS) regarding C/T susceptibility. DNA extraction (Chemagic-DNA Bacterial External Lysis Kit, PerkinElmer, USA) and WGS (Illumina-NovaSeq 6000 platform, OGC, UK) were performed. SPAdes and Prokka were used for de novo assembling and annotation, respectively. In silico MLST assignment was performed. Resistance genes were identified using Abricate with ARG-ANNOT database (95% identity/90% coverage).E. coli phylogroups (ClermonTyping), serotypes (SerotypeFinder) and fimH-types (FimTyper) were determined. Kleborate software was used for capsule (K) and LPS (O) serotype prediction in Klebsiella spp. P. aeruginosao-specific antigen was identified (Blastn, OSA database).

Results: Overall C/T susceptibility was: 96.2%E. coli, 72.9%K. pneumoniaeand 91.3%P. aeruginosais. AmongE. coli, two carbapenemase producers [VIM-2+SHV-12-STnew-O:9:H12-H35 and OXA-48-ST38-O:0?H15-H65] but C/T-susceptible [MIC=0.5/4 mg/L] were detected. The most prevalent clone was the ST131-B2-O25:H4-H30 [n=16] associated with CTX-M-15 [11/16] and C/T-susceptibility [14/16] [MIC range=0.25/2-1/4 mg/L]. Among C/T-resistant isolates [n=8] [2/4->64/4 mg/L], a high diversity was found in ESBL [4/8] and non-ESBL [4/8] producers. AmongKlebsiella spp., 16 OXA-48+CTX-M-15 producers were detected [ST11-KL24-O2v1 (12/16), ST392-KL27-O4 (2/16), ST15-KL112-O1v1 (2/16)], all of them C/T-resistant [4/4->64/4 mg/L]. Moreover, ST101-NDM-1+CTX-M-15-KL17-O1v1 [->64/4 mg/L] and ST15-OXA-48+VIM-2+CTX-M-1-KL112-O1v1 [64/4 mg/L] were identified. A higher diversity of high-risk clones [ST11, ST15, ST30P] was also detected among ESBL/non-ESBL producers irrespective of C/T susceptibility. InP. aeruginosais, 6 carbapenemase producers C/T-resistant [16/4->64/4 mg/L] were detected: VIM-20-ST175-04 [3/6], VIM-1-ST309-011 [2/6] and VIM-2-ST175-04/011 [1/6]. Moreover, a C/T-susceptible VIM-36-ST175-04 isolate [2/4 mg/L] was identified.

Conclusions:K. pneumoniae-ST11-OXA-48+CTX-M-15 C/T-resistant andE. coli-ST131-CTX-M-15-OXA-48:H4-H30 C/T-susceptible are the most frequent clones in Spanish Hospitals. InP. aeruginosais, C/T-resistance is mainly related to VIM enzymes and the ST175 clone. Carbapenemase genes do not always correlate to C/T resistance, but other mechanisms might be involved.

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The rapid method for detecting Neisseria gonorrhoeae and antimicrobial susceptibility

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**Background:** Neisseria gonorrhoeae is known as a microorganism that transfers from infected genitalia and causes urinary tract infection. The diagnosis of N. gonorrhoeae infection has been used polymerase chain reaction (PCR). However, these diagnostic kits and methods could not analyze antimicrobial susceptibility. Therefore, we tend to use broad spectrum antimicrobial agents and make multiple resistance N. gonorrhoeae. We created a new rapid method that detects mutation of penA (penicillin resistance associated gene) and gyrA (quinolone resistance associated gene) at the same time as diagnosis of N. gonorrhoeae.

**Materials/methods:** The N. gonorrhoeae were extracted directly from urine sample. Secondary, we extracted and purified DNA of N. gonorrhoeae. Thirdly, we made the specified primers with locked nucleic acid (LNA) and probes for the purpose of detecting SNP mutations on penA and gyrA genes, and amplified via real time PCR. These primers were designed only to amplify against wild types. The real time PCR were finished 15 minutes.

**Results:** Total 38 N. gonorrhoeae samples were amplified by real time PCR using N. gonorrhoeae specific primers and probes. No other species causing urinary infections were not increased. All wild type of penA and gyrA were amplified by penA and wild type gyrA specific primers and probes. On the other hand, all mutant type of penA and gyrA were not detected. These reactions were detected 15 mins from PCR starting.

**Conclusions:** We presented that N. gonorrhoeae infections could not been only detected quickly but also detected antibiotics resistance in same time via this study. We have been trying to develop next generation methods that detecting N. gonorrhoeae infection and antimicrobial susceptibility easily and quickly.

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Abstract 3040

An emerging methicillin resistance mechanism due to loss-of-function of the GdpP protein in mec gene-negative staphylococci undetected by reference methods

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Background: B-lactam resistance in Staphylococci is mediated by mec genes and usually diagnosed by Cefoxitin disk diffusion and PCR testing. Here, we report methicillin-resistant Staphylococcus lugdunensis and Staphylococcus aureus strains lacking mec gene misdiagnosed by reference methods. Since the strains are not B-lactamase hyperproducers we investigated the molecular basis of their methicillin resistance.

Materials/methods: We tested 2 Staphylococcus lugdunensis (SL1, SL2) and 4 Staphylococcus aureus isolates (SA1, SA2, SA3, SA4): (i) by Cefoxitin disk diffusion (DDFOX), (ii) for agar dilution Oxacillin MIC (AD), (iii) by VITEK®2 (bioMérieux) for antimicrobial susceptibility testing containing Oxacillin MIC (V2OXA) and Cefoxitin Screen Test (V2OXSF), (iv) for mec genes (meca, B, C) and (v) by whole genome sequencing (WGS).

Results: The 6 isolates were detected as methicillin susceptible by DDFOX and were mec negative. However all isolates displayed variable results for V2OXA MIC (0.5 to >=4mg/L) and V2OXSF [POSITIVE or NEGATIVE]. For S. lugdunensis isolates the V2OXSF growth curve atypical pattern has led to investigate the OXSF wells. The plates inoculated with the broth extracted from the OXSF well showed two colony morphotypes (small “P” and regular “G”) for both isolates. The small colonies (SL1P, SL2P) were Oxacillin resistant (V2OXA MIC≥4; AD MIC=4) and V2OXSF POSITIVE whereas the regular colonies (SL1G, SL2G) were Oxacillin susceptible (V2OXA MIC<2; AD MIC=0,5) and V2OXSF NEGATIVE. The 4 morphotypes were confirmed as Cefoxitin susceptible by DDFOX and mec negative. Interestingly, WGS revealed, in phenotypically Oxacillin resistant isolates, a GdpP truncation in the N-terminal domain containing a diguanylate cyclase (GGDEF) motif for the subpopulation of small colonies of S. lugdunensis (SL1P, SL2P) and also for S. aureus isolates SA1 and SA3. However, GdpP non synonymous mutations were detected in SA2 and SA4 isolates. GdpP is a cyclic diadenosine monophosphate phosphodiesterase enzyme which function is the hydrolysis of a signaling nucleotide (c-di-AMP).

Conclusions: We described mec negative S. lugdunensis and S. aureus strains detected by VITEK2 OXSF test expressing heterogeneous methicillin resistance due to a loss of function of GdpP previously described as associated with reduced growth which may arise as a result of the selective pressure of exposure to B-lactams.

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Abstract 3047

**Prognostic factors in HIV-infected patients with lymphoma: a single-centre experience**
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**Background:** with the present study we aimed to evaluate prognostic factors in HIV patients with non-AIDS and AIDS-related lymphoma.

**Materials/methods:** This was a retrospective cohort study of patients with lymphoproliferative disorders and HIV infection, enrolled from January 2000 to July 2019 and followed up for at least 2 years.

**Results:** Overall, 94 patients were included. Of these, 73/94 (77.6%) were male and the median (IQR) age was 46 (13-79). At lymphoma diagnosis the median CD4+ cell count was 228 cell/mmc (11-1377) and 34/94 (36.6%) of patients had undetectable HIV-RNA, 21/94 (20%) patients had a prior AIDS-defining condition. Histologic subtypes were diffuse large B-cell lymphoma (DLBCL; n=44, 51%), plasmablastic lymphoma (PBL; n=4, 4.9%), Burkitt lymphoma (BL; n=27, 29%), T-cell lymphoma (n=3, 3.2%), Hodgkin lymphoma (n=21, 19%). Chemotherapy was administered to 79/94 (84%) pts. The most frequently used chemotherapy regimen was CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone), administered in 42% of the patients with DLBCL, followed by BFM (Berlin-Frankfurt-Munster). Rituximab was administered to 27% of the patients and autologous stem cell transplantation was performed in 7 (8.5%) cases. Forty (51.3%) patients achieved complete remission. At the end of 2-year follow-up 82 (87%) cases were evaluable, after excluding lost to follow-up, 2-year mortality rate was 42% (35 fatal cases). Variables associated with survival at univariate analysis were prior AIDS (p=0.046), CD4+ <15% at the diagnosis of lymphoma (p=0.041), histologic subtype (p<0.001), Ann Arbor III-IV stage (p=0.033), B symptoms (p=0.009), extranodal disease (p=0.022), IPI score >2 (p=0.003) and complete remission at first line chemotherapy (p=0.0001). At multivariable analysis performed with a Cox regression model, IPI score > 2 [HR 3.18 (95% CI 1.20-8.42)], Burkitt subtype [HR 2.60 (95% CI 1.32-5.14)] were associate with mortality whereas receiving cART was associated with survival [HR 0.38 (95% CI 0.17-8.56)].

**Conclusions:** cART introduction had entailed a significant improvement in complete response rate and overall survival. Tumor-related factors became the most consistent prognostic factors of survival. In our study IPI score > 2, extra-nodal disease predicte significantly worse final outcome. These findings suggest that aggressive chemotherapy for patients with HIV-related lymphoma, must be adopted, regardless of their HIV status.

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Characterisation of carbapenemase-producing Serratia marcescens clinical isolates recovered in a hospital in Madrid (Spain) using whole genome sequencing

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Background: The prevalence of carbapenemase-producing Serratia marcescens (CPSm) causing infection is increasing in hospital settings. We study the population structure and plasmid content of CPSm isolates recovered from infected patients admitted at the Ramón y Cajal University Hospital using whole genome sequencing.

Materials/methods: Between March-2016 and December-2018, 50 CPSm isolates (42 VIM-1-CPSm and 8 OXA-48-CPSm) from 34 infected patients were recovered in our Hospital. Carbapenemase genes identification (PCR and sanger sequencing) and Pulse-field gel electrophoresis (PFGE) were performed. DNA extraction (Chemagic DNA Bacterial External Lysis Kit, PerkinElmer, USA) and Whole Genome Sequencing (Illumina-NovaSeq 6000 platform, OGC, UK) were carried out on one representative CPSm isolate of each PFGE-clone (n=5). SPAdes and Prokka were used for de novo assembling and annotation, respectively. Bacterial identification was confirmed using Kraken. Resistance and virulence genes were identified by Abricate (ARG-ANNOT and vfdb databases) (95% identity-90% coverage). MASH and iTOL application were used to generate and trace a similarity tree. Plasmid characterization and reconstruction were performed using PlasmidFinder and PLACNETw tools, respectively.

Results: Carbapenemase production was confirmed in the 5 CPSm isolates [VIM-1 (n=3) and OXA-48 (n=2)]. Similarity tree construction revealed a MASH-distance ≤0.03 among VIM-1-CPSm isolates and 0.00007 between OXA-48-CPSm isolates. Genome analysis confirmed the presence of genes conferring co-resistance to other antimicrobial groups in both VIM-1-CPSm (aacA4, blaSR T-1, dfrB1, sul1, catB2, catA1, msrE, mphE and aadA1) and OXA-48-CPSm (aacA4, blaSR T-1) isolates. The virulence factor daaF was identified in one VIM-1-CPSm isolate. Plasmid reconstruction shown that OXA-48- and VIM-1-CPSm isolates harboured an IncL-pOXA-48 (62038 pb) and an IncL-pVIM-1 (65114 pb) plasmid, respectively, with a 91% of coverage (~57 Kb) and 99,98% of identity. blaOXA-48 was located as part of the Tn1999 composite transposon in a ~5 Kb specific region without any other antibiotic resistance gene. pVIM-1 plasmid harboured a class 1 integron (~8 Kb) containing 'blaVIM-1+aacA4+dfrB1+aadA1+catB2+qacEDelta1+sul1'.

Conclusions: S. marcescens plays an important role in the spread of VIM-1 and OXA-48 carbapenemases in our Hospital. An ~62kb IncL-pOXA-48 plasmid widely disseminated in other Enterobacterales spp. (Klebsiella pneumoniae and Escherichia coli) and a closely related ~65kb IncL-pVIM-1 were detected in CPSm isolates.

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Abstract 3049

Does early de-escalation to anti-staphylococcal beta-lactams impact the duration of bacteraemia in patients with methicillin-susceptible Staphylococcus aureus endocarditis?

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Background: Anti-staphylococcal beta-lactam (ASBL) antibiotics are widely accepted as superior agents over vancomycin for the treatment of methicillin-susceptible Staphylococcus aureus (MSSA). Mortality risk increases by 16% for each day of Staphylococcus aureus bacteremia. Current standard for identification and susceptibility testing of blood cultures requires 36-48 hours from the time of positivity. Rapid diagnostic tests (RDT) have significantly reduced this time. We aimed to study the impact of Verigene® Nanosphere on the duration of bacteremia in patients with MSSA bacteremia due to infective endocarditis.

Materials/methods: Retrospective, quasi-experimental, single center, cohort study that included adult patients with a diagnosis of MSSA endocarditis from January 2013 to June 2018. Enrolled patients must have reviewable dates and times of the following: initial culture collection, initial culture positivity, RDT results, empiric antibiotic initiation, and first doses of ASBLs. Patients were divided into two cohorts based on the implementation of Verigene® RDT in September 2015. Patients post-implementation were compared to patients pre-RDT. Primary outcome was defined as time to clearance of blood cultures.

Results: Total of 105 patients were included. Nanosphere test was performed in 54/105 patients (51.4%). Median time to positivity in the pre-RDT and RDT was 14.1 and 14.5 hours, respectively [p = 0.166]. Median time to ASBL in the pre-RDT and RDT was 63.5 and 37 hours, respectively [p < 0.01]. Five patients (4.8%) did not clear their MSSA bacteremia. The median time to culture clearance in the pre-RDT patients was 96.8 hours (IQR 64.8-120.6) compared to RDT cohort was 94.6 hours (IQR 67.2-142.8); p = 0.807.

Conclusions: Time to definitive beta-lactam therapy was statistically shorter with Verigene® while time to positivity was similar in both cohorts. However, a difference in time to bacteremia clearance was not observed between MSSA endocarditis patients who had RDT performed on their blood cultures and those who were managed traditionally. Further evaluation of factors such as early vancomycin exposure and source control is necessary to assess the impact of RDT coupled with early de-escalation on the duration of MSSA bacteremia in infective endocarditis patients.

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Monitoring and drug resistance analysis of isolated bacteria from tuberculosis patients in west China hospital of Sichuan University from 2010 to 2019

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Background: Anti - tuberculosis treatment using multiple antibiotics, drug use and treatment for a long time. It is not known whether bacteria isolated from TB patients who have been treated with antibiotics for a long time have higher drug resistance. Therefore, we intend to investigate the distribution of bacteria isolated from TB patients and the characteristics of drug resistance.

Materials/methods: By retrospective method, bacteria isolated from tuberculosis patients in west China hospital of sichuan university from January 2010 to July 2019 were statistically analyzed. VITEK2 compact automatic microbiological analyzer was used for bacterial strain identification and drug susceptibility test, and WHONET5.6 software was used for statistical analysis of drug sensitivity results. SPSS19.0 statistical analysis software was used to compare the bacterial culture results of isolated bacteria in tuberculosis patients with 101,415 hospitalized patients in the same period.

Results: Among 1808 patients with positive mycobacterium tuberculosis culture, 444 strains of effective bacterial strains were isolated after eliminating the duplicate strains of the same patients. The top five bacteria were klebsiella pneumoniae (16.2%), acinetobacter baumanni (14.2%), pseudomonas aeruginosa (9.7%), escherichia coli (9.0%).

The antimicrobial resistance rate of bacteria isolated from tuberculosis patients was generally higher than that of hospitalized patients during the same period. Among them, the drug resistance rates of escherichia coli to ciprofloxacin, tetracycline, ceftriaxone, ampicillin/sulbactam, cefotaxime, compound xinnoxacin, levofloxacin, amtronan and gentamycin were statistically different between the two groups (P < 0.05). The resistance rate of klebsiella pneumoniae to antibiotics other than gentamicin, cefuroxime and cefutetan was statistically significant between the two groups (P < 0.05). The drug resistance rate of other antibiotics except piperacillin/tazobatam, tetracycline and donipenem showed statistical difference between the two groups (P < 0.05). Rifampin had a statistically significant difference in staphylococcal resistance between TB patients and hospitalized patients. The drug resistance rate of enterococci isolated from tuberculosis patients was generally higher than that of hospitalized patients, and there were significant differences between penicillin G, vancomycin, ampicillin and levofloxacin (P < 0.05).

Conclusions: Because anti-tb treatment requires long-term multi-drug combination therapy, bacteria isolated from tuberculosis patients treated with long-term antibiotics have higher resistance to most antimicrobial agents than common bacterial infections in hospitalized patients.

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Confronting ceftolozane/tazobactam susceptibility in multidrug-resistant Enterobacterales isolates and whole genome sequencing results [STEP study]

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Background: Ceftolozane/tazobactam (C/T) is frequently used for infections caused by multidrug-resistant (MDR) gram-negative bacteria. We study the population structure and the resistome of MDR-Enterobacterales isolates, C/T-susceptible and -resistant, recovered from low respiratory, intraabdominal and urinary tract infections of ICU patients from 11 Portuguese Hospitals (STEP study, 2016-2017).

Materials/methods: MICs were determined (ISO-broth microdilution, EUCAST criteria). Thirty E. coli and 79 Klebsiella spp. isolates were selected. DNA extraction (Chemagic DNA Bacterial External Lysis Kit, PerkinElmer, USA) and whole genome sequencing (Illumina-NovaSeq 6000 platform; OGC, Oxford, UK) were performed. SPAdes and Prokka were used for de novo assembling and annotation, respectively. Bacterial identification was confirmed using Kraken. In silico MLST assignment was performed. Resistance genes were identified using Abricate with ARG-ANNOT database (95% identity/90% coverage). Among E. coli isolates, phylgroups [Clermontyping], serotypes [SerotypeFinder] and fimH types [FimTyper] were determined. Capsule (K) and LPS (O) serotype prediction was performed in Klebsiella spp. isolates by Kleborate software.

Results: Among E. coli, two VIM-2 producers susceptible to C/T (0.5/4-1/4 mg/L) were detected [ST131-B2-H30-025:H4-CTX-M-15 and ST188-C-H39-022:H4]. A C/T-resistant (16/4 mg/L) KPC-3-producing-ST5463-cladeV-H160-0164:H55 isolate was also identified. Among ESBL producers (n=39), the most frequent clone was ST131-B2-H30-025:H4 (n=14) associated with CTX-M-15 [10/14] or CTX-M-27 [4/14] production, all of them C/T-susceptible [MIC range: 0.25/4-1/4 mg/L] except one [2/4 mg/L]. In non-ESBL producers (n=8) [0.25/4-1/4 mg/L], a high clonal diversity was found. Among Klebsiella spp. isolates, K. pneumoniae was the most frequent species (n=68), followed by K. aerogenes (n=7), K. variicola (n=2) and K. oxytoca (n=2). All carbapenemase producers (n=21) were C/T-resistant [2/4-64/4 mg/L], except one (OXA-48-ST215-KL16-01v1) [1/4 mg/L]. The most frequent K. pneumoniae clones were: KPC-3-ST13-KL3-01v2 (n=5), KPC-3-ST5-KL112-01v1 (n=2), KPC3-ST231-KL51-01v2 (n=2), OXA181-ST17-KL25-05 (n=2) and OXA-48-ST215-KL16-01v1 (n=2). KPC-3+VIM-2 co-production was identified in a ST405-KL151-04 isolate. A high diversity [ST15, ST307, ST405], mainly C/T-resistant [2/4-64/4 mg/L], was also detected among ESBL (n=41) and non-ESBL (n=17) producers.

Conclusions: E. coli-ST131-CTX-M-15-B2-025:H4-H30 C/T-susceptible is the most frequent clone in ICU Portuguese Hospitals. A high diversity of K. pneumoniae clones was also found mainly associated with KPC-3 and C/T-resistance. Carbapenemase genes are not always correlated to C/T resistance, but other mechanisms might be involved.

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Abstract 3053

**Analysis of resistance mechanism affecting ceftolozane/tazobactam in *Pseudomonas aeruginosa* isolates using whole genome sequencing (STEP Study)**

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**Background:** Ceftolozane/tazobactam (C/T) is frequently used for the treatment of infections by multidrug-resistant (MDR) *Pseudomonas aeruginosa* isolates. We characterized the population structure and the resistome of *P. aeruginosa* isolates with a phenotype compatible with carbapenemase production, susceptible or resistant to C/T, collected between 2016 and 2017 from low respiratory, intraabdominal and urinary tract infections of ICU patients from 11 Portuguese Hospitals (STEP study).

**Materials/methods:** MICs were determined (ISO-broth microdilution) and interpreted according to EUCAST criteria. A total of 21 C/T-resistant *P. aeruginosa* isolates recovered during the STEP surveillance study were analyzed and compared with 21 C/T-susceptible *P. aeruginosa* from the same study. DNA extraction from exponential growth cultures was carried out (Chemagic DNA Bacterial External Lysis Kit, PerkinElmer, USA). Whole genome sequencing was performed by the Illumina-NovaSeq 6000 platform (OGC, Oxford, UK). SPAdes was used for de novo assembling and assembly evaluation was performed by QUAST. Draft genomes were annotated by Prokka. In silico MLST assignment was performed. Antimicrobial resistance genes were identified using Abricate and ARG-ANNOT database (threshold, 95% identity; 90% coverage). O-specific antigen was identified using Blastn with OSA database.

**Results:** Among C/T-resistant *P. aeruginosa* (MIC range: 8/4->64/4 mg/L), carbapenemase production was detected in 16 isolates (61.5%). The most frequent carbapenemase was GES-13 (n=13) associated with the clone ST235-O11 [32/4->64/4 mg/L]. VIM-2 production was also detected in ST244-05 (n=2) and ST179-06 (n=1) clones (>64/4 mg/L). Among non-carbapenemase producers, the most frequent clone was the ST348-O12 (n=3) (8/4 mg/L), followed by ST554-02/05 (n=1) (>64/4 mg/L) and ST313-01 (n=1) (16/4 mg/L). In C/T susceptible isolates (0.5/4-4/4 mg/L), a higher clonal diversity was found (ST235-011, ST253-010/012, ST179-06, ST244-05/06/012, ST2959-011, ST308-011, ST309-011, ST3292-06, ST446-011, ST499-01 and ST971-01). Moreover, KPC-3 production was detected in two isolates (ST499-01 and ST253-012) (1/4 mg/L).

**Conclusions:** Production of GES-13 and VIM-2 is associated with C/T resistance in certain *P. aeruginosa* clones (ST235-011 and ST244-05) in ICU Portuguese Hospitals. Interestingly, *blaKPC-3* gene was also identified in two C/T-susceptible *P. aeruginosa* isolates. C/T resistance is not always due to the presence of carbapenemase genes and other mechanisms might be involved.

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Abstract 3058

Validation of serum procalcitonin measurement for the diagnosis of rickettsial infections disease
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Background: Rickettsiosis presents systemic inflammation without organ specificity disorders and requires differential diagnosis of viral infections, vasculitis and autoimmune diseases, etc. Rickettsiosis is known to increase serum C-reactive protein (CRP) level. CRP is a useful biomarker for differentiation from viral infections but is not a sufficient marker due to its low specificity for bacterial infections. Procalcitonin (PCT), on the other hand, has been reported to be highly specific for bacterial infections, but there is no evidence for rickettsial disease diagnosis.

Materials/methods: The purpose of this study is to investigate whether serum PCT level is elevated during the acute phase of Japanese spotted fever (JSF), a rickettsial disease caused by Rickettsia japonica in eastern Asia. The subjects were JSF patients who were hospitalized at the Ise Red Cross Hospital between 2013 and 2018. Serum PCT and CRP concentrations were measured within one day after the patient visited. Measurements were evaluated at multiple cut-off points to determine sensitivity. Diagnostic criteria were positive results in molecular-based tests at the acute phase and/or increased serum antibody titers.

Results: A total of 104 cases (male: 45%, age: 69.7 ± 13.1 years), diagnosed with JSF and were cured with tetracycline and fluoroquinolone. The time from onset to arrival was 3.8 ± 3.1 days. The average serum PCT concentration was 1.8 ± 5.1 ng/mL. As determined by PCT levels, 57% were positive at the facility’s normal upper limit of 0.5 ng/mL and 11% were positive at the sepsis cut-off point of 4.0 ng/mL used in the literature. The average serum CRP level was 11.5 ± 6.8, 100% positive for the upper limit of normal 0.1 mg/dL of the facility and 85% positive for the acute inflammation cut-off point of 5 mg/dL. Serum PCT levels did not correlate with CRP levels (R=0.146, ns).

Conclusions: Among JSF cases with elevated CRP levels, the sensitivity of PCT is low, but some cases show high PCT concentrations. Serum PCT measurement is unlikely to be a reliable biomarker in the diagnosis of rickettsiosis.

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Non-invasive ventilation in patients with acute respiratory failure secondary to viral respiratory infection: a nested case-control study

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Background: While non-invasive ventilation (NIV) can often be an effective strategy to tackle acute respiratory failure (ARF) on exacerbations of chronic respiratory disease and decompensation of heart failure, its role on viral and bacterial pneumonia remains controversial. We aimed to study possible predictors of NIV failure in a cohort of patients admitted for acute viral respiratory infections.

Materials/methods: We recruited our study subjects from a multi-center southern European cohort of patients admitted with lower respiratory viral infections over the 2017-2018 and 2018-2019 winter seasons. Cases were defined as patients who either died in the course of admission and/or required invasive mechanical ventilation (IMV), after being submitted to NIV. Controls were patients who were submitted to NIV and survived admission without the need for IMV. Predictive variables with p values <0.25 on univariate analysis were included in the multivariate logistic regression model.

Results: There were a total of 150 patients included in this study. Mean age was 68.9 years. Concerning the most relevant comorbidities, 19% (n=28) had a history of smoking, 31% (n=46) diabetes, 43% (n=65) heart failure, 33% (n=65) either chronic obstructive lung disease or asthma and 17% (n=25) active malignancy (11% haematological, 6% solid). The majority of infections (55% n=83) were caused by Influenza A, of which 41 (27%) were sub-typed as H1N1; RSV was isolated in 40 patients (27%). There were 47 patients who were ultimately submitted to IMV, 43 deaths and a total of 64 (43%) meeting study criteria for failure (cases). On univariate analysis lower age, absence of heart failure, infection by H1N1 strains and the presence of a radiological infiltrate were associated with NIV failure (p<0.05), while on multivariate analysis the variables which were found to be significant predictors were the presence of a solid malignancy (adjusted odds ratio [aOR] 4.8 CI95%[1.0-24.5]) and H1N1 (aOR 4.2 CI95%[1.7-10.7]).

Conclusions: Almost half of all patients in our study had a failure of NIV. Particular Influenza strains might be predictive of NIV failure. Even though NIV has a role in managing patients with ARF, its use in cases related with respiratory viral infection should be considered judiciously.

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Abstract 3061

Comparison of *Escherichia coli* multilocus sequence typing from the UK, Saudi Arabia and Kazakhstan indicates that UK sepsis rates are directly related to carriage of pathogenic *E. coli* strains in the community

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**Background:** *E. coli* consists of commensal and pathogenic strains. We sought to understand the increasing *E. coli* sepsis rates in the UK by identifying the prevalence of pathogenic phylogroup B2 *E. coli* strains in the community. We did this by randomly selecting *E. coli* isolates from sewage and comparing prevalence between countries with high and low sepsis rates.

**Materials/methods:** Sewage samples were collected April-June 2019 from Kazakhstan, Saudi Arabia and the UK. Each 30ml sample was collected on entry to a single sewage works that served populations of 200-500 thousand people. Circa 50-100 *E. coli* isolates were randomly picked from well-spaced colonies on UTI brilliance agar plates. A further c. 50 ciprofloxacin resistant and 50 cefotaxime resistant isolates were randomly selected from UTI brilliance plates containing 1mg/L ciprofloxacin and 10mg/L cefotaxime, respectively. Species ID was confirmed by MALDI-TOF-MS. Each isolate was tested for phylogroup by multiplex PCR (Doumith method). Isolates belonging to the pathogenic B2 phylogroup were further identified by a multiplex PCR designed to detect known pathogenic *E. coli* MLST groups.

**Results:** The prevalence of B2 phylogroup *E. coli* strains varied considerably between different countries. Sewage collected from the Qassim region of S. Arabia had the lowest prevalence of B2 strains (2%) as compared to Karaganda, Kazakhstan (13%) and Ponthir, South Wales (43%). This same trend was found with resistant isolates with 66% of ciprofloxacin resistant isolates and 52% of cefotaxime resistant isolates were randomly selected from UTI brilliance plates containing 1mg/L ciprofloxacin and 10mg/L cefotaxime, respectively. Species ID was confirmed by MALDI-TOF-MS. Each isolate was tested for phylogroup by multiplex PCR (Doumith method). Isolates belonging to the pathogenic B2 phylogroup were further identified by a multiplex PCR designed to detect known pathogenic *E. coli* MLST groups. Specific multiplex PCR for known sepsis causing *E. coli* sequence types (ST) identified ST73, ST95 and ST131 isolates from the UK and Kazakhstan but not from Saudi Arabia. These three pathogenic *E. coli* ST accounted for 35% and 9% of all *E. coli* strains carried in the community (80% and 66% of B2 strains) in S. Wales and Karaganda, respectively.

**Conclusions:** The UK *E. coli* sepsis rate is closely related to high carriage rates of pathogenic *E. coli* ST in the community. The rising rate over the last 20 years is most likely explained by increasing prevalence of these strains through time.

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Syndromic tests for meningitis: patient screening before testing allows a high efficient medical value

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"Hospices Civils De Lyon - HcI, Plateau de Microbiologie 24/24 - Centre de Biologie et Pathologie Nord, Lyon, France, 2Hospices Civils De Lyon - HcI, Plateau de Microbiologie Moléculaire - Centre de Biologie et Pathologie Nord, Lyon, France, "Bichat-Claude Bernard Hospital, Laboratoire de Virologie, Paris, France"

Background: Evaluation of the impact of the syndromic molecular test Biofire Meningitis / Meningoencephalitis (FAME, bioMérieux) on the diagnosis, the anti-infectious therapy, the para-clinical examinations, the isolation and the project of care of the patient.

Materials/methods: Prospective single-center study (2017-2019) on 149 patients (86♂, 63♀ - mean age 29 years) admitted to the emergency room or intensive care units (pediatric and adult) or in infectious clinical ward for a suspected community-acquired meningitis / meningoencephalitis (MME) and with CSF with more than 9 leukocytes/μL. The FAME was produced 24 hours on 7 and a standardized survey of 44 questions was filled during the telephone communication of the FAME results to the clinicians by the medical biology student (MS Form).

Results: Of 149 patients, 57 and 65 were suspected of bacterial and viral meningitis respectively, and 68 patients had a positive FAME (45%): enterovirus (36), VZV (10), HSV (8), N. meningitidis (3), Streptococcus pneumoniae (3), S. agalactiae (3), Listeria (2), H. influenzae (2). FAME was delivered in 57% and 32% of cases in less than 4 and 8 hours after CSF sampling respectively. 47 and 97 patients were on anti-infectious drugs respectively before and after CSF puncture. In 43%, the FAME help to establish the final diagnosis of meningitis/encephalitis and in 27% to exclude it. FAME modify isolation status for 19% of patients and the care project in 63% of cases with only 7% of "go back home". Antibiotic therapy was affected (addition, dis-continuation, modification) by the FAME in 34% of patients against 23% for antivirals. Finally, in 12 and 8% of cases, the FAME helped to cancel or add additional exams.

Conclusions: Screened according to clinic and biological restrictive criteria, carried out 24 hours a day according to an "emergency" pre-analytical workflow and systematically associated with stewardship, the FAME shows a high positivity rate associated with therapeutic, para-clinical and multiple organizational impacts demonstrating the high medical value of this syndromic molecular test in an emergency context.

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Abstract 3070

Exploring the utility of optimised meropenem exposures against carbapenem-resistant Escherichia coli with and without KPC

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Background: The complexity of treating carbapenem-resistant Enterobacteriaceae (CRE) is growing as carbapenemase- and non-carbapenemase-producing isolates are encountered across diverse species. Rates of carbapenem-resistance among Escherichia coli (CREc) are low, but increasing. CREc typically demonstrate meropenem minimum inhibitory concentrations (MICs) ≤8µg/mL suggesting treatment with meropenem may be viable.

Materials/methods: We investigated the killing effects of standard [1g q8h over 30 minutes] and optimized [2g q8h over 3 hours] meropenem regimens in 1-compartment and hollow-fiber (HFIM) infection models using a starting inoculum of 1x10⁶ and 1x10⁸ CFU/mL, respectively. Meropenem exposures were confirmed by LC-MS/MS. Subpopulations were selected by agar plates containing meropenem 4x baseline MIC. Isolates were characterized by whole-genome sequencing.

Results: 29 CREc were screened. Meropenem MICs ranged from 0.12–16µg/mL. 38% produced KPC. 8 isolates were selected for testing (Table). In 1-compartment model, standard dosing resulted in bactericidal killing (>3-log₁₀ CFU/mL) at 72 hours in one isolate [meropenem MIC=1µg/mL, KPC-negative]; regrowth occurred in the remaining 7 isolates. Optimized dosing resulted in bactericidal activity against 3 isolates [all KPC-negative]. Mean log-kills were significantly greater against non-KPC compared to KPC-producing isolates [-3.23 vs. 0.91; P=0.01]. Subpopulations were selected against isolates that produced KPC and demonstrated meropenem MICs ≥2µg/mL; mutant colonies demonstrated 8–64-fold increased MICs. For validation, we tested two isolates (one w/ one w/o KPC; meropenem MIC=4µg/mL for both) over 10 days. Against the non-KPC-producing isolate, regimen was bactericidal. Standard and optimized exposures selected for higher-level resistance at 72 and 96 hours, respectively, meropenem MICs increased 2–4-fold. Against the KPC-producing isolate, higher-level resistance was selected within 12 hours by both regimens; MICs increased 4–16-fold. Interestingly, meropenem-vaborbactam 4g q8h demonstrated rapid bactericidal killing and suppression of resistance against both isolates.

Conclusions: Against CREc, both meropenem MIC and presence of KPC predict in vitro responses to meropenem. For KPC-producing CREc, meropenem was not bactericidal and selected for further resistance despite optimized exposures. For non-KPC-producing CREc, bactericidal killing occurred over 72 hours against isolates with MICs ≤4µg/mL, but resistance emerged after 72 hours in HFIM. These data underscore the role of novel β-lactam/β-lactamase inhibitor combinations for treatment of CREc despite lower meropenem MICs.

Table. Characteristics of CR E. coli isolates tested in this study

<table>
<thead>
<tr>
<th>Isolate</th>
<th>ST</th>
<th>Meropenem MIC (µg/mL)</th>
<th>β-lactamases</th>
<th>ompC*</th>
<th>ompF</th>
<th>Log-kill with meropenem 1g IV q 8h (Effect)</th>
<th>Log-kill with meropenem 2g IV q 8h (Effect)</th>
</tr>
</thead>
<tbody>
<tr>
<td>493</td>
<td>131</td>
<td>1</td>
<td>CTX-M-15, OXA-1</td>
<td>9bp ins, 33bp del at 177, 13bp del at 238, 8bp del at 239</td>
<td>334stop</td>
<td>-4.19 (Bactericidal)</td>
<td>-3.66 (Bactericidal)</td>
</tr>
<tr>
<td>477</td>
<td>2541</td>
<td>2</td>
<td>CMY-2, OXA-1</td>
<td>24bp del at 181</td>
<td>IS91 ins</td>
<td>1.71 (Regrowth)</td>
<td>-3.70 (Bactericidal)</td>
</tr>
<tr>
<td>174</td>
<td>405</td>
<td>4</td>
<td>CTX-M-15, OXA-1</td>
<td>61bp ins, 82 bp del at 172</td>
<td>83stop</td>
<td>1.13 (Regrowth)</td>
<td>-3.34 (Bactericidal)</td>
</tr>
<tr>
<td>482</td>
<td>127</td>
<td>1</td>
<td>KPC-3, TEM-1A</td>
<td>24bp del at 181</td>
<td>WT</td>
<td>0.77 (Regrowth)</td>
<td>-2.33 (Indifferent)</td>
</tr>
<tr>
<td>468</td>
<td>131</td>
<td>2</td>
<td>KPC-3, TEM-1B</td>
<td>82stop</td>
<td>N52D, S226P, E306D</td>
<td>2.89 (Regrowth)</td>
<td>2.47 (Regrowth; ↑ MICs)</td>
</tr>
<tr>
<td>432</td>
<td>131</td>
<td>4</td>
<td>KPC-3, OXA-9, SHV-11, TEM-1A</td>
<td>9bp ins, 33bp del at 177, 13bp del at 238, 8bp del at 239</td>
<td>N52D, S226P, E306D</td>
<td>2.70 (Regrowth)</td>
<td>1.91 (Regrowth; ↑ MICs)</td>
</tr>
<tr>
<td>369</td>
<td>131</td>
<td>8</td>
<td>KPC-2, OXA-9, TEM-1B</td>
<td>9bp ins, 33bp del at 177, 13bp del at 238, 8bp del at 239</td>
<td>N52D, S226P, E306D</td>
<td>1.99 (Regrowth)</td>
<td>2.49 (Regrowth; ↑ MICs)</td>
</tr>
</tbody>
</table>

*Various other non-synonymous amino acid substitutions were noted

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Abstract 3077

**Benzofuroxans: discovering new compounds to fight tuberculosis**

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**Abstract third-party references:** Supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP 2018/21778-3 and 2018/00163-0)

**Background:** Tuberculosis (TB), an infectious disease caused by *Mycobacterium tuberculosis*, remains as the world’s leading cause of death from a single infectious pathogen. In 2017, the number of deaths was estimated in 1.3 million. The recommended treatment is becoming increasingly ineffective against the resistant strains. Thus, there is an urgent need to new antimicrobials for TB, that could reduce the duration of treatment, lowering adverse effects and providing a more effective therapy for multidrug-resistant TB.

**Materials/methods:** New benzofuroxan (BZ) compounds were synthesized employing molecular hybridization techniques, using as the base the chemical structure of linezolid and the BZ 8 (C13H9O3N5). The primary analysis was the determination of minimal inhibitory concentration (MIC90), by Resazurin Microtiter Assay (REMA) method using the standard strain H37Rv and clinical isolates. This assay is based on micro dilution in 96-well microplates, ranging the concentration compounds from 0.1 to 25 mg/mL, using a bacterial inoculum concentration of 10⁵ CFU/mL. The microplates are incubated during 7 days and, after that, a solution of resazurin is applied and the fluorescence was read after 24-48 h. The MIC90 is considered the minimal concentration that inhibit 90% of the bacterial inoculum. The cytotoxicity was assessed using lung fibroblasts (MRC-5) and macrophages (J774A.1) seeded in a 96-well cell culture plate. After 24 h the substances were added in concentrations ranging from 0.4 to 100 µg/mL. After 24 h of incubation, resazurin solution was added and the fluorescence measured and determined the half inhibitory concentration (IC50).

**Results:** The results obtained against the standard strain demonstrated the large potential of these compounds, presenting MIC90 values from 0.1 to 3.8 µM. Against clinical strains, the compounds presented MIC90 values ranging from 0.2 to 9.3 µM, an inhibitory potential comparable to standard strain. Cytotoxic effects were observed in MRC-5 above 28.0 µM and in J774A.1 only above 40.8 µM, with selectivity index (SI) (SI=IC50/MIC90) higher than 50 in all cellular types.

**Conclusions:** These results evidenced that the BZ compounds can be considered as promising anti- *M. tuberculosis* agents that, comparing to BZ 8, presented better potential against resistant strains.

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**Abstract 3079**

**Bacillus subtilis as a causative of true bacteremia in patients with peritonitis**

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**Background:** Bacillus subtilis is a spore-forming gram-positive rod and found ubiquitously in soil, in air, in human gastrointestinal tracts and others. Because of its high ubiquity and low pathogenicity, *B. subtilis* has been regarded as a culture contaminant and little is known about its bacteremia. Recently, we isolated *B. subtilis* from two of two blood-culture sets and ascites from patient with secondary bacterial peritonitis due to bowel obstruction and perforation. This suggests the possibility of true *B. subtilis* bacteremia.

Therefore, we supposed that true *B. subtilis* bacteremia may be related to intra-abdominal infections and that the number of bacteremia caused by the organism has been underestimated. The aim of this study is to clarify the clinical picture of *B. subtilis* bacteremia and define the significance of *B. subtilis* isolated from blood cultures.

**Materials/methods:** This study was performed at a 750-bed University Hospital in Tokyo, Japan. To compare isolates from blood and ascites of a single patient, we performed multilocus sequence typing (MLST). We analyzed data obtained in our hospital from January 2010 through October 2019 to compare the difference in risk for *B. subtilis* bacteremia between peritonitis and pneumonia patients. We also constructed antibiogram of *B. subtilis* isolated from stool samples. Antimicrobial susceptibility was determined using a fully automated identification/susceptibility test system RAISUS ANY.

**Results:** The strains isolated from different specimens from a patient showed the same MLST sequence type. *B. subtilis* was isolated from multiple sets from 7 out of 831 peritonitis and 6 out of 7612 pneumonia patients, which means the risk for *B. subtilis* bacteremia was about 11 times higher in peritonitis patients. In addition, the organism was isolated from single sets from 12 out of 831 peritonitis and 35 out of 7612 pneumonia patients, which indicates even single positive culture could represent true *B. subtilis* bacteremia in patients with peritonitis. The antibiogram indicates most of the strains were susceptible to major antibiotics.

**Conclusions:** We suggest to consider *B. subtilis* as a causative of true bacteremia when it is isolated from peritonitis patients. *B. subtilis* may therefore be a more important human pathogen than previously thought.

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Abstract 3080

Validity of International Classification of Diseases (ICD) for the identification of herpes zoster virus infection requiring hospitalisation
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Background: In Quebec, the provincial administrative database MED-ECHO (Maintenance et exploitation des données pour l’étude de la clientèle hospitalière) is used to assess the burden of hospitalizations related to herpes zoster (HZ) disease. This study aims at determining the positive predictive value (PPV) of primary and secondary HZ diagnosis, as established by MED-ECHO.

Materials/methods: We performed a validity study as part of a retrospective cohort study of all adult (≥ 18 years old) HZ cases hospitalized at the Centre Hospitalier Universitaire de Sherbrooke between 2000 and 2015. The cases were identified using ICD codes from MED-ECHO. The ICD-9 (053.xx) and ICD-10 (B02.x) codes were used to search for hospitalizations due to HZ with or without complications. Potential cases were reviewed to confirm the management of a problem related to HZ during hospitalization.

Results: A total of 1238 hospitalizations (310 as primary diagnosis and 928 as secondary diagnosis) due to HZ with or without complications were identified in MED-ECHO during 2000-2015. Among these, 530 hospitalizations (43%) were due to active disease or a complication related to a recent or previous HZ episode. These hospitalizations were due to active disease at the time of admission (333/530, 63%), HZ that developed during hospitalization (126/530, 24%), or a complication related to a recent or previous HZ episode (e.g., post-herpetic neuralgia; 71/530, 13%). The PPV was significantly higher when HZ was the primary diagnosis (276/310, 89%, 95% CI: 85%-92%) than when HZ was a secondary diagnosis (254/928, 27%, 95% CI: 25%-30%) (p <0.0001). Primary diagnoses were represented mainly by active disease upon admission (231/276, 84%) and complications related to a recent or previous HZ episode (40/276, 15%), and secondary diagnoses by HZ that developed during hospitalization (122/254, 48%) and active disease upon admission (102/254, 40%).

Conclusions: The PPV of ICD codes for HZ disease is high when HZ is the primary diagnosis in the MED-ECHO administrative database. Although its predictive value is lower, it is essential to consider HZ-related ICD codes identified as secondary diagnoses, which accounts for one-third of all active infections, and to adequately assess the burden of hospitalization related to HZ.

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Abstracts 2020

Abstract 3083

Usefulness of anaerobic blood culture vials for the microbiological diagnosis of candidaemia
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Abstract third-party references: On behalf of the GMC study group

Background: Despite Candida spp growth in aerobic atmosphere, some clinical strains have been isolated from anaerobic blood culture (BC) vials. We aimed to assess the usefulness of these vials for the diagnosis of Candidemia.

Materials/methods: This retrospective multicentric study was performed by 4 centers between September 1, 2016, and August 31, 2019. A single episode of monomicrobial candidemia per patient and Candida species was included. For each episode, microbiological data of all BC vials sampled within 2 hours before and after the first positive BC vials were recorded, including: i) type of vials; ii) the origin of the sample; iii) result and, for positive vials, iv) Candida species and time-to-positivity (TTP).

The Becton Dickinson and the bioMérieux systems were used by 2 centers each.

Results: 297 episodes of candidemia were included involving 173 (58.2%) C. albicans, 58 (19.5%) C. glabrata, 24 (8.1%), C. parapsilosis, 14 (4.7%) C. tropicalis, 11 (3.7%) C. krusei and 17 (5.8%) others Candida species.

Both aerobic and anaerobic vials were positives in 36 (14.7%) episodes, while only the aerobic or the anaerobic vials were positives in 244 (82.2%) and 17 (5.7%) episodes respectively. All episode with only anaerobic vials positives involved C. glabrata and represents 29.3% of all C. glabrata episodes. This rate was significantly higher for the BD than the bioMérieux systems (39.5% vs 10.0%; P<0.01).

The median TTP was significantly shorter for C. albicans than C. glabrata in aerobic vials (34.0 vs. 67.0; P<0.01). Considering C. glabrata, the median TTP was significantly shorter for anaerobic than aerobic vials (41.0 vs. 67.0; P<0.01). Despite, both devices display similar TTP for C. albicans, median TTP for C. glabrata was shorter using the bioMérieux system for both aerobic (31.2 vs 68.5; P<0.01) and anaerobic vials (17.8 vs 43.0; P<0.01).

Conclusions: The anaerobic vial is essential for the microbiological diagnostic of C. glabrata fungemia mainly when using the BD system. Furthermore, the BioMérieux system seems more accurate for C. glabrata.

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Development of a biosensor for the detection of Campylobacter jejuni
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Abstract third-party references: This project is supported by Tarbiat Modares University, Tehran, Iran.

Background: C. jejuni is an important human pathogen and causing campylobacteriosis which is known as diarrheal disease worldwide. Due to fastidious growth requirements, the isolation of the bacterium is not routinely done in many clinical laboratories. Most methods including culture, biochemical tests, serological and molecular assays are time-consuming, high costs and variable sensitivity in results. The aim of this study was to design a biosensor using the plasmonic properties of gold nanorods in the detection of campylobacteriosis.

Materials/methods: By evaluating different studies, cadF gene was selected as the target gene. Using bioinformatics tools such as CLC Sequence Viewer 7.6 software, GeneRunner, NCBI, etc, a C. jejuni-specific part of the cadF gene (44 bp) was specified and two probes were designed on this fragment. Gold nanoparticles were synthesis according to seed-mediated growth protocol and then characterized using UV-vis, zeta potential, FT-IR, and transmission electron microscopy. Then, probes were conjugated with nanoparticles to produce nanoprobes. To confirm nanoprobes, all the above-mentioned assays were performed again. The system was evaluated on 50 fecal specimens previously tested as positive for C. jejuni DNA by real-time PCR. Finally, limits of detection (LOD), sensitivity, specificity, and turnaround time of the assay were done using the standard strains of Campylobacter spp. and other intestinal bacteria.

Results: The theoretical assessments of the selected fragment showed that it was highly conserved among C. jejuni. In addition, probes were completely specific and no significant matches to other bacteria genome sequences were seen. The plasmonic evaluation of the nanoparticles and nanoprobes using UV-vis and other methods showed that they were synthesized as rod-shaped nanostructures (~32×~11 nm) and were correctly conjugated with probes. Comparison with real-time PCR results on clinical samples, the sensitivity of the biosensor was 88% (44/50 cases). The specificity of the assay was 100% and plasmonic changes were detected only for C. jejuni. The limit of detection biosensor (10^2 copies) was identified. The result was obtained about 5 min for each test.

Conclusions: Due to acceptable specificity and sensitivity, speed, and simplicity, the biosensor could be applied as a new diagnostic tool in the clinical diagnostics.

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Background: Thailand is classified as a high tuberculosis-burden country with 156 cases per 100,000 population in 2018. Reported cases of tuberculosis among prisoners may account for 30% of tuberculosis with an incidence of 880-5,803 cases per 100,000 inmates in low- to middle-income countries. Beginning in 2017, an active case–finding strategy for tuberculosis was implemented in all prisons in Thailand. Mass chest radiograph screening is performed in all prisoners to identify and bring into treatment tuberculosis cases as soon as possible.

Materials/methods: A retrospective descriptive study was conducted at Songkhla provincial hospital between 2016 and 2019. Inmates of four prisons in Songkhla Province were assessed by tuberculosis screening using mass chest radiographs from 2017. If abnormal chest radiography revealed compatibility with tuberculosis, sputum microscopy and sputum GeneXpert were performed. Data were analyzed using descriptive statistics.

Results: After implementing the active case-finding strategy in 2017, the incidence of tuberculosis in prisons rose from 739 cases per 100,000 inmates in 2016 to 1,548 in 2017, 1,882 in 2018, and 3,694 per 100,000 inmates in 2019. The tuberculosis cases in the prisons accounted for 5% in 2016 and continued to rise to 20% in 2019 of all tuberculosis cases in Songkhla Province. Furthermore, sputum microscopy or GeneXpert detected tuberculosis positive between 10% and 16% of all tuberculosis cases in the four prisons. The rates of treatment success were 90%-94% and the case fatality rates were 11-58 cases per 100,000 inmates at the four prisons.

Conclusions: The active case-finding strategy using mass chest radiography increases the early detection of tuberculosis cases in prisons. Prisoners are at a high risk for tuberculosis infection due to multiple factors such as overcrowding, poor ventilation, poor nourishment, and repeated prison transfers that encourage the transmission of tuberculosis infection. A recent TB infection can cause active disease in two years. Thus, early recognition of active tuberculosis using mass chest radiography can reduce further transmission of infection.

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Treatment of hepatitis C with direct-acting antiviral (DAA) agents: sustained virological response rate in a real care setting in the state of Ceará, north-eastern Brazil

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Background: Hepatitis C affects 0.8% of the Brazilian population and is the leading cause of liver transplantation and hepatocarcinoma. The Brazilian public health system has provided treatment with direct-acting antiviral (DAA) agents since October 2015. This study aims to analyze sustained virological response (SVR) in patients with chronic hepatitis C treated with DAA in the state of Ceará, northeast of Brazil.

Materials/methods: Medical records of hepatitis C patients treated with DAA from October 2015 to March 2019 were reviewed. Only patients with chronic hepatitis C over 18 years old, and without previous treatment with DAA were analyzed. The treatments were prescribed according to the recommendations of the Brazilian Ministry of Health. SVR was defined as undetectable hepatitis C virus viral load after three months of treatment completion.

Results: A total of 654 patients with a mean age of 57.4 years (SD ± 3.5) were included, 403 (61.6%) men, and 303 (46.3%) cirrhotics. Overall, 625 (95.5%) achieved SVR. When analyzing SVR for different treatments, SVR was achieved in 92.8% of patients treated with sofosbuvir + daclatasvir (n = 197), 95.5% with sofosbuvir + daclatasvir + ribavirin (n = 290), 99% with sofosbuvir + simeprevir (n = 107), 96.1% with sofosbuvir + simeprevir + ribavirin (n = 25), 100% with ombitasvir + paritaprevir + dasabuvir + ritonavir with or without ribavirin (n = 21). SVR was achieved in more than 95% of patients with genotypes 1A, 1B, and 3. SVR was achieved in over 95% of patients in special situations such as cirrhosis, HBV coinfection, HIV coinfection and liver transplantation.

Conclusions: SVR was obtained in more than 95% of patients with hepatitis C treated with DAA in a setting of real care practice in the state of Ceará, northeast Brazil. SVR rates were high even among patients with cirrhosis, HBV coinfection, HIV coinfection and liver transplantation.

<table>
<thead>
<tr>
<th>Genotypes and special situations</th>
<th>RVS(%)</th>
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</thead>
<tbody>
<tr>
<td>Genotype 1A (n=171)</td>
<td>96.7</td>
</tr>
<tr>
<td>Genotype 1B (n=295)</td>
<td>96.9</td>
</tr>
<tr>
<td>Genotype 2 (n=13)</td>
<td>84.6</td>
</tr>
<tr>
<td>Genotype 3 (n=143)</td>
<td>95.9</td>
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<tr>
<td>Cirrhotic (n=303)</td>
<td>92.7</td>
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<tr>
<td>Non cirrhotic (n=273)</td>
<td>97.1</td>
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<tr>
<td>HBV coinfection (n=11)</td>
<td>100</td>
</tr>
<tr>
<td>HIV coinfection (n=37)</td>
<td>97.3</td>
</tr>
<tr>
<td>Liver transplantation (n=134)</td>
<td>94.7</td>
</tr>
</tbody>
</table>

Presenter email address: robertojusta@gmail.com
Abstract 3088

**SUSANA project: real-world data coming from the use of new antimicrobial drugs**

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**Background:** Although randomized clinical trials are considered the standard criterion for generating clinical evidence, real-world evidence evaluating efficacy and safety of new drugs is essential to improve their use. We present the preliminary data from the SUSANA Project, a study designed to evaluate the safety of new antibiotics in the real life.

**Materials/methods:** This observational retrospective study started on April 2019 in a network of Italian Infectious Diseases Units. Patients treated with ceftazidime/avibactam, ceftolozane/tazobactam, dalbavancin, and fosfomycin e.v. were included. Primary objective was the surveillance of adverse events (AE), to evaluate their frequency, type and severity. Secondarily, we aimed at investigating factors associated with AE onset. Causality was evaluated according to Jones’ algorithm.

**Results:** The study started on April 2019. To date, 40 patients entered the study (33% women). Mean age was 64.1 (range 18-89). Infection site was skin (14), breathing apparatus (7), genitourinary tract (7), osteoarticular tissue (6), abdomen (5), cardiovascular system (5), CNS (1), other or unidentified (5). Infection was at multiple sites in 7 cases. Antibiotic treatment was empirical in 13 (32.5%) patients. Fifteen subjects received ceftazidime/avibactam (6 with fosfomycin), 7 ceftolozane/tazobactam (1+fosfomycin, 12 dalbavancin (1+fosfomycin, 1+ceftolozane/tazobactam) and 6 fosfomycin. Ten patients (25%) suffered from at least 1 AE: 3 patients on ceftazidime/avibactam + fosfomycin had multi-organ failure (remote causality); 1 subject on ceftazidime/avibactam presented a skin rash (probable causality) and 1 had vomiting and peripheral ischemia (both remote causality); among 10 on dalbavancin alone, 1 had diarrhea and 1 limbs edema (both possible causality); 1 patient on fosfomycin alone had hyponatremia (remote causality). One patient on ceftolozane/tazobactam + fosfomycin presented hypernatremia (highly probable causality), atrial fibrillation, myocardial infarction, and intestinal stoma obstruction (all remote causality). Outcome was known for 32 patients: infection relapsed in 5 of them, 23 recovered, 1 interrupted an empiric treatment, 3 died because of multiorgan failure.

**Conclusions:** Preliminary results of the SUSANA project show a high prevalence of AE in patients treated with the antimicrobials evaluated. However, most of them had low relationship of causality with the drugs and were probably related to the clinical evolution of the primary conditions.

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How to screen OXA-244, a difficult to detect emerging OXA-48 variant?

**Background:** OXA-244, a single-point mutation variant of OXA-48, possesses a weaker hydrolytic activity towards carbapenems and temocillin compared with OXA-48. Of note, these molecules are present at high concentrations in several screening culture media used for the detection of carbapenemase-producing Enterobacteriaceae (CPEs). Thus, it has been reported that OXA-244-producers often do not grow on screening media. Unfortunately, the prevalence of OXA-244-producers is constantly increasing in France. Indeed, the number of OXA-244-producers received at the French National Reference Center (F-NRC) for CPEs rose from 7 (0.6% of all CPE) in 2015 to 44 (3.2%) in 2019, with a majority of *E. coli* (96%). Therefore, it is crucial to detect them accurately in order to avoid their massive dissemination.

**Materials/methods:** Here, we evaluate the performances of 3 commercially available CPE screening media for their ability to detect OXA-244-producers: chromiD CARBA SMART (bioMérieux), Brilliance CRE (Thermofisher), and mSuperCARBA (MAST Diagnostic). Since most OXA-244-producers expressed an ESBL, two additional ESBL screening media were also tested: Brilliance BLSE and ChromiD ESBL. MICs of temocillin and imipenem were performed by broth microdilution. The clonality of OXA-244-producing *E. coli* (*n* = 42) was assessed by MLST (S, 32 and 5 in 2017, 2018 and 2019, respectively).

**Results:** Overall, the sensitivity of the ChromiD CARBA SMART, Brilliance CRE and mSuperCARBA media were respectively 13% (IC95=7.4-21.2%), 53% (IC95=42.8-62.9%) and 99% (IC95=93.4-100%) for the detection of OXA-244-producers. Among the 100 OXA-244-producing strains, 76% grew on ESBL screening medium. MLST analysis identified two major STs in OXA-244-producing *E. coli* (*n* = 42) as ST-38 (n = 13) and ST-361 (n = 9).

**Conclusions:** Our results confirmed that ChromiD CARBA SMART medium is inefficient to detect OXA-244-producers. At the opposite, OXA-244-producers perfectly grow on the mSuperCARBA medium. The huge prevalence of ESBL in OXA-244-producer allow to detect 76% of them on ESBL screening media.

Accordingly, a positive signal for *bla*OXA-48 using molecular method directly from rectal swab sample but with no growth on ChromiD CARBA SMART or Brilliance CRE might be an OXA-244 producer. Therefore, inoculation of mSuperCARBA medium might be of interest to cultivate this CPE.

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Darunavir/cobicistat monotherapy as simplification strategy for HIV patients: a retrospective Multi-centre Spanish Study (DRV-simply)

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Background: Darunavir 800mg plus ritonavir 100mg (DRV/r) monotherapy has been a has proved to be an interesting reverse transcriptase inhibitor (NRTI)-sparing simplification strategy recommended in selected patients in some European guidelines in the past and still used in some patients. Darunavir/cobicistat 800/150mg (DRV/c) is bioequivalent to and simpler than DRV/r as it is co-formulated. For these reasons, DRV/c has widely replaced DRV/r in Spain. Because DRV/c has a 25% lower trough levels than DRV/r, the efficacy and safety of switching to DRV/c monotherapy is unclear.

Materials/methods: A multicenter retrospective-longitudinal study was performed from September 2015 to December 2017 in all HIV-adult participants with at least prior 24 weeks of HIV-1 RNA<50 copies/ml who switched to DRV/c. Primary end-point was the percentage of patients with ≥ 50 copies/mL at 48 weeks. Secondary endpoints were virological success, side-effects and CD4, lipid, and creatinine changes.

Results: 530 patients were included in this study. Median (IQR) age, treatment duration and previous treatments were: 50 years (47–55), 12 months (9–15), and 6 (4-9), respectively. Median nadir and baseline CD4+ T-cell counts were 216 (126–343) and 695 (538–866) cells/mm3, respectively. Previous treatments were PI monotherapy 91% (71% of them DRV/r) and 9% dual or triple therapy. At 48 weeks, percentage of patients with ≥ 50 copies/mL was 78 (14.7%): 61 (11.5%) discontinued treatment for non-virological reasons, 7 (1.3%) developed VF (none of them selected any DRV-resistance associated mutations (RAM) and all were re-suppressed with a dual-triple DRV/c-containing regimen) and 10 (1.9) had blip. Median CD4/CD8 ratio was 1.01 at baseline and 1.00 at week 48 (p=0.450). Median triglycerides levels decreased from 167 mg/dL to 151 mg/dL (p =0.0001) and HDL increased 1.5 mg/dl from baseline to 48 weeks. Creatinine plasma levels increased from 0,79 mg/dL at baseline to 0,86 mg/dL at 48 weeks (p =0.001). No significant differences in LDL and total Cholesterol levels.

Conclusions: Switching to DRV/c monotherapy from DRV/r was safe and effective in virologically suppressed HIV-infected patients.

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**Abstract 3096**

**Clinical characteristics and outcome of bloodstream infections in HIV-infected patients with febrile neutropenia: A case-control study.**

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**Background:** We aimed to compare the clinical characteristics and outcomes of bloodstream infections (BSI) in febrile neutropenic patients (FNP) with and without HIV infection, and to analyze the prognostic factors for mortality.

**Materials/methods:** All episodes of BSI in FNP were prospectively collected (1997-2018). A case (HIV-infected) – control (non-HIV-infected) sub-analysis was performed with a ratio of 1:2, matching the patients for age, gender, baseline disease and etiological microorganism. Factors associated with 30-day mortality in the overall and case-control cohorts were assessed using logistic regression models.

**Results:** Among 1,756 BSI episodes in FNP, 60 (3.4%) occurred in HIV-infected patients. In those, most prevalent risk behavior was that of men who had sex with men (51.7%); 58.3% had CD4 <200 cells/mm3; 51.7% had a positive HIV-1 RNA viral load before the episode; and 70% met AIDS-defining criteria. Most patients (93.3%) were taking antiretroviral therapy (ART) at the time of the BSI, with a protease inhibitor-based ART being the most common regimen (53%). Overall, HIV-infected patients were younger, more frequently male and more commonly presenting chronic liver disease (p<0.001 for all). Conversely, HIV-infected patients received significantly less hematopoietic stem cell transplantation (HSCT) (p<0.001). No differences in the source of infection or proportion of patients with severe neutropenia (<100 cells/mm3) were detected. BSI due to Enterococcus spp. was significantly more frequent among HIV-infected patients (p=0.017) with no differences in other pathogens. Finally, HIV-infected patients presented with shock more frequently (p=0.014) and experienced higher mortality (31.7% vs. 18.1%, p=0.008). However, in multivariate analysis, HIV infection was not an independent risk factor for mortality. When comparing the case-control cohort, cases (HIV-infected) had chronic liver disease (p=0.003) more frequently, while acute leukemia (p=0.13) and HSCT (p=0.23) were more frequent among controls (non-HIV). Cases had a non-significant trend towards receiving inappropriate empirical antibiotic treatment (p=0.206), presenting with shock (p=0.105) and having higher mortality (p=0.084). However, in multivariate analysis, HIV infection was not associated to mortality.

**Conclusions:** FNP with HIV infection presenting BSI have different epidemiological and clinical profile and had higher mortality. However, HIV infection by itself was not associated with mortality, neither overall nor within the case-control cohorts.

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Abstracts 2020

Abstract 3097

**Laboratory productivity index and efficiency gains at 3 benchmark BD Kiestra TLA sites**

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Abstract third-party references: On behalf of Krešimir Renić, P.Eng. Lean Healthcare Consultant, Supported by Becton Dickinson

Background: Microbiology labs face many challenges including increasing sample volumes, cost containment pressures and staff shortages. Institutions respond by consolidating and automating processes to improve efficiency, quality and cost-effectiveness. This abstract describes a summary of efficiency gains realized through the combination of BD Kiestra™ Total Lab Automation (TLA) technology and Lean process improvements at three benchmark sites.

Materials/methods: A metric known as Laboratory Productivity Index (LPI) was used to measure the capacity of laboratory staff to process microbiological specimens. LPI is the ratio of specimens processed per day divided by the combined fulltime equivalent (FTE) of in-scope staff. In-scope labor is the proportion of FTE involved in the processing of specimens prior to and after incubation. Average daily specimen volumes for each of the benchmark sites were respectively calculated using LIS data from two-week periods with high specimen volumes relative to other periods throughout the year. In-scope FTE was established based on in-lab workflow observation prior to and following lab training and TLA go-live.

The average weekday specimen volume (\(Vol_{avg}\)) and the in-scope FTE were used as the numerator and denominator respectively to calculate the pre-and-post automation LPI. Post-automation LPI was validated using anonymized instrument data.

Results: In a non-automated lab, an LPI under 20 is typical. Pre-automation LPI values were captured at each benchmark site through MPD™ Lean & Automation Impact Assessment (AIA) engagements. Post-automation LPI values were calculated through BD Kiestra System Performance data in June 2019.

The three benchmark BD Kiestra TLA labs improved LPI by 2.9 – 4.2× compared to pre-automation; LPI increased from:

- 16.7 to 48.8 – benchmark site 1
- 14.8 to 63.5 – benchmark site 2
- 19 to 65.6 – benchmark site 3

Conclusions: The combination of BD Kiestra technology and Lean process improvement consulting can significantly improve lab productivity while reducing turn-around time in a consolidated testing environment.

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Abstract 3099

Discordant *Clostridioides difficile* diagnostic assay and treatment practice: a retrospective observational study

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**Background:** *Clostridioides difficile* infection (CDI) diagnosis relies on multiple-step algorithms and the decision to treat patients with discordant results is determined by individual clinical evaluation. We aim to determine the proportion of patients with discordant test results who received a treatment for *Clostridioides difficile* infection (CDI) and to identify patient characteristics associated with the decision to treat CDI.

**Materials/methods:** Retrospective and observational study of all adult patients with *C. difficile* discordant test results (positive nucleic acid amplification test [NAAT+]/negative enzyme immunoassay [EIA-]) between March 2017 and March 2019. A multiple, stepwise, backward logistic regression model was used to determine the association of nine patient characteristics with treatment introduction, including risk factors for CDI.

**Results:** Among 4562 adult patients tested for *C. difficile* between March 2017 and March 2019, 239 patients with discordant test results (positive nucleic acid amplification test [NAAT+]/negative enzyme immunoassay [EIA-]) were included. CDI treatment was administered in 147/208 (71%) cases. In multivariate analysis, the presence an abdominal computed tomography (CT) scan with signs of colitis (OR 14.7; 95% CI 1.96 to 110.8) was independently associated with CDI treatment.

**Conclusions:** The proportion of NAAT+/EIA- patients who received treatment questions the contribution of the EIA for the detection of toxin A/B after NAAT to limit overtreatment. Additional studies are needed to investigate if other factors are associated with the decision to treat.

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Abstract 3101

Identified beta-lactamase genes in *Aeromonas* species: an experience from Qatar

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**Background:** *Aeromonas spp.* are ubiquitous aquatic organisms, associated with multitude of diseases in several species of animals, including fishes and human. They were resistant to frequently used antibiotics for human infections. We aim to explore the genes responsible for β-lactamase enzymes in *Aeromonas*.

**Materials/methods:** Thirty-five preserved *Aeromonas* positive blood cultures between 2012 and 2016 were identified at Hamad General hospital laboratory department (State of Qatar). *Aeromonas* species and sensitivity were identified by BD Phoenix. Sixteen isolates were revived successfully, out of which 10 isolates underwent whole-genome sequencing. Two separate databases were used for antibiotic resistance gene finding: CARB and Resfinder.

**Results:** *Aeromonas hydrophila* was the most identified species (4/10). Followed by *Aeromonas veronii* and *Aeromonas sobria*, (3/10) and (2/10) respectively. *Aeromonas caviae* was found in one isolate.

All isolates were resistant to Ampicillin but susceptible to Ceftazidime, Cefepime, and Meropenem. 90% of isolates remain susceptible to Amoxicillin-clavulanate. Cefuroxime was sensitive in 50% of isolates while ceftriaxone was sensitive in 90% of the isolates.

The majority of isolates possess OXA-12 [9/10]. CphA7 gene was found in six isolates. Other identified genes are cphA3 (3/10), AOU-3 [2/10], DHA-17 [2/10], Escherichia coli ampH beta-lactamase [1/10], and ACT-2 [1/10] (Figure 1).

**Conclusions:** *Aeromonas* species possess different β-Lactamase genes. The most common genes are OXA-12 and CphA7. Cefazidime, fourth-generation cephalosporins and carbapenems (Meropenem) remain reasonable options for empiric therapy in bacteremic patients till final culture susceptibility result for other antibiotics is identified.

**Figure 1. Resistance genes distribution**

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Abstract 3103

High-resolution mapping reveals emergence and autochthonous transmission of dengue fever outbreak in a previously low-epidemic region in south-east China, 2019

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Background: Dengue fever is a mosquito-borne febrile illness affecting more than 100 countries in tropical and subtropical areas. South-east Asia is facing horrible dengue outbreak this year and over 1000 cases have been reported in Jiangxi, a low-epidemic region in China. We performed this study to investigate the origin and driving force of Jiangxi dengue outbreak.

Materials/methods: We recruited clinically or laboratory diagnosed dengue infections from Nanchang ninth Hospital, Zhangshu People’s Hospital, Fengcheng People’s Hospital and Nanchang Xian People’s Hospital in Jiangxi Province, China, from April 2019 to September 2019. Blood samples were collected from those who gave consents. We performed real-time PCR with specific probe and calculated relative quantification copies. 14 samples from Jiangxi with relatively higher viral copies and 2 samples retrieved from Huashan Hospital were prepared for high-throughput sequencing. A total of 61 complete dengue virus genomes including nucleotide and accordingly amino acid sequences were downloaded from NCBI database to analyze.

Results: A total of 154 patients were enrolled in the study and 113 blood samples from 91 patients received real-time PCR test. Among enrolled patients, 42 cases were identified as overseas inputs and the majority of which came from Cambodia. No severe cases were reported. In 113 samples, 106 were classified as DENV-1, 2 were identified DENV-2 and 5 were negative. 16 DENV-1 genomes sequenced in this study were in high similarity with Cambodia stains and other south-east Asia strains. 114 SNPs were detected among 16 strains, revealing genome changes of strains among Nanchang, Zhangshu and Fengcheng. A total of 20 non-synonymous mutations were detected in 16 strains, indicating fast variation throughout transmission. Geographic and temporal analysis based on sequenced data identified transmission events of DENV-1 resulting long-term establishment of epidemic situation in south-east Asia and southern China.

Conclusions: This epidemiologic study demonstrated this dengue fever outbreak in Jiangxi originated from input cases from Cambodia. New air line from Nanchang to Cambodia brought dengue emergence and autochthons transmission to different cities in Jiangxi. Not only epidemic places, any place with travelers from epidemic areas should emphasize the prevention and control of dengue fever in the future.

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Abstract 3104

**Should Chlamydia trachomatis be part of migrant screening?**

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**Background:** With 22.3 billion migrants living in Europe in 2018, migrant’s health is becoming a major public health issue. Europe is presently reflecting upon the best strategy for sexually transmitted infections (STI) screening in migrants. Yet, there are few data about *Chlamydia trachomatis (CT)* prevalence among this population. The main objective of our study is to evaluate *CT* prevalence in asymptomatic migrants consulting in STIs clinics then to identify risks factors associated to *CT* infections.

**Materials/methods:** All asymptomatic individuals over 18 years of age attending a STIs free clinic in Paris from 01/2017-12/2018 were eligible. They were screened for *CT* in urinary, vaginal, oral, rectal samples according to gender and sexual behaviors. Non-migrants were individuals born in France, newly arrived migrants had migrated to France within the past year, and long-term migrants had migrated more than a year ago. Prevalence were estimated and adjusted OR (aOR) were calculated using logistic regression.

**Results:** During the study period 5959 individuals attended the STIs free clinic. A total of 4948 were retained in the analysis, including 771 (16%) migrants. *CT* prevalences were: 7.7% (n=41) in long term migrants, 5.9% (n=14) in newly arrived migrants and 5.1% (n=212) in non-migrants. Compared with non-migrants, the risk of *CT* infections in migrants was higher in newly arrived and long-term migrants, aOR=2.50 [95% CI 1.19-5.24] and aOR=2.04 [95% CI 1.43-2.93]. Other factors associated with *CT* infections were: number of sexual partners in the last year [aOR=1.51 [95% IC 1.06-2.17] for 6-10 and aOR=2.47 [95% IC 1.44-4.23] for >10 partners], sexual orientation [aOR=0.26 [95% IC 0.14-0.48] for men having sex with men], age [aOR=4.48 [95% IC 2.35-8.56] for <35 years of age] and gender [aOR=1.72 [95% IC 1.32-2.22] for women].

**Conclusions:** Our study suggests that *CT* screening should be recommended in all migrants. Yet, *CT* screening is currently not recommended in migrants neither in the French guidelines nor in the European Center for Disease Prevention and Control (ECDC) guidelines on newly arrived migrants.

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Abstract 3106

 Artificial intelligence and automation of microbiology: the urinalysis 3.0

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Background: Design, evaluation and implementation of an artificial intelligence (AI) system PhenoMATRIX ™ (PNMX) for the automated interpretation of urine analysis (UA).

Materials/methods: The interpretation of UA needs i) clinical signs (fever, clinical signs of urinary tract infection, pregnancy) collected since the connected prescription (Easily, HCL); ii) population and hospitalization data from the laboratory informatics system (LIS, GLIMS, MIPS); (iii) cytology derived from urinary cytology machines (UF1000i®, Sysmex) or manually entered in the LIS; and iv) prior anteriories (antibiotic susceptibility testing (AST) <7 days). Based on the chromogenic medium (CHROMID®CPSE, bioMérieux), the PNMX IA integrates algorithms applied to images produced by WASPLab® systems (Copan) and synthesizes with the data from the third party systems [see above]. During the design, 3 decision trees (mid-jet ECBU, catheter, stoma) were constructed by the laboratory team to describe the reading and interpretative workflow (MS Visio). The PNMX IA was then coded in the system and evaluated using a previously obtained collection of 4802, 957 and 97 images of UA mid-jet, by catheter and stoma respectively. The PNMX IA data was compared to the manual-acquired Data (MAD) by laboratory technicians. For the mid jet UA, a second version of the decisional tree was carried out then evaluated on an additional collection of 2131 images. In case of discrepancy between the two methods, the images were reviewed by 4 TLBMs and 1 medical microbiologist and reclassified on the basis of previously established standard operative procedures (SOP) and decision trees.

Results: The performance data are presented in Table 1. The categorization errors between identification (ID) versus ID + AST are defined as minor. Are defined as major, the categorization errors between contaminated UA/non-significant culture urine versus ID or ID/AST.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>decisional tree version</th>
<th>Results in agreement</th>
<th>Minor errors</th>
<th>Major errors</th>
<th>Errors caused by laboratory technicians</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stoma</td>
<td>1</td>
<td>83%</td>
<td>17%</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Catheter</td>
<td>1</td>
<td>71%</td>
<td>3%</td>
<td>22%</td>
<td>4%</td>
</tr>
<tr>
<td>Mid jet</td>
<td>1</td>
<td>84%</td>
<td>7%</td>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Mid jet</td>
<td>2</td>
<td>91%</td>
<td>2%</td>
<td>4%</td>
<td>3%</td>
</tr>
</tbody>
</table>

Conclusions: The PNMX IA applied to UA has a high performance level (=91%). In just a few clicks, a large number of urines are quickly, securely, reproducibly and faithful to the laboratory interpretation thanks to the large number of data collected, including clinic signs provided by the connected prescription.

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Adherence to antibiotic guidelines at a Danish university hospital, a quantitative and qualitative prospective study
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Background: Both government and local committees publish antibiotic guidelines, but less is known about adherence. This study aims to examine guideline adherence in a low resistance area as Denmark and factors influencing doctors’ antibiotic prescriptions.

Materials/methods: The study was conducted at the inpatient emergency medical department of Aalborg University Hospital. All patients 18 years or older, who had systemic antibiotics prescribed within their 24 hours of admission, from 1 September through 31 December 2018 were included. Age, gender, allergy, nursing home, reduced kidney function, chronic obstructive pulmonary disease (COPD), blood culture, tentative diagnosis, prescription was done by doctor from department of infectious diseases (ID) or clinical microbiology (CM). Interviews using semi-open and rubricated questions were conducted with both junior and special doctors.

Results: 952 were included (median 70 years, 28.9% had COPD, 17.5% prescriptions by ID/CM doctor). 80.2% of the patients received tentative diagnoses: most often acute exacerbation of COPD 21.2%, pneumonia 20.6% and urinary tract infection 12.5%. The most prescribed antibiotic was piperacillin/tazobactam 16.9%, amoxicillin/clavulanic 16.4%, penicillin 14.8%, gentamicin 13.1% and ampicillin 9.6%. Blood culture was taken on 70.7% of patients.

Overall guideline adherence therapy was 59.8%. 763 patients were treated under a diagnosis and 70.3% of them received guideline adherent therapy. Significant higher guideline adherence was also found among patients with acute exacerbation of COPD (p-value 0.000), erysipelas (p-value 0.000), febrile neutropenia (p-value 0.016), reduced kidney function (p-value 0.003) and the prescriptions were made by ID/CM doctor (p-value 0.000).

24 interviews were conducted with: 1 medical student, 20 junior doctors, 3 special doctors. 75.0% stated they had problems finding the desired guideline. 62.5% stated education to increase adherence. 33.3% wanted to change electronic to printed guideline.

Conclusions: We report guideline adherence in 59.8% of the antimicrobial prescriptions at the inpatient emergency medical department of Aalborg University Hospital. A tentative diagnosis showed a higher adherence on 70.3%. 62.5% of the doctors stated education, on both junior and senior doctors, as most important focus area as the doctors answered, that if they experience discrepancy between a guideline and advice from a senior, they follow their senior doctor.

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Delayed diagnosis of infectious endocarditis: retrospective analysis conducted at an university hospital in the south of Italy

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Background: Infectious Endocarditis (IE) is a potential life threatening disease with variable clinical onset and course. Despite the improvement of diagnostic techniques, a high percentage of delay in diagnosis persists, with related morbidity and mortality. The aim of the study is to evaluate the presence of delayed diagnosis and its supportive factors at the University Hospital in Salerno.

Materials/methods: observational retrospective study conducted from January 1st 2013 to May 30th 2019. A total of 111 patients with IE (according to modified Duke criteria) enrolled. Statistical analysis done with SPSS software for Macintosh.

Results: 111 patients (68 males, 61.3% of total) were enrolled. The mean age was 64. 61 patients (55% of the total) received inappropriate antibiotic therapy before diagnosis. The most isolated microorganism was Coagulase Negative Staphylococcus (17.1% of total). 35 patients (31.5% of total) developed IE on prosthetic valve. The lag time symptoms onset - diagnosis of IE was 20 days (OR 10-40); the lag time hospitalization - diagnosis of IE was 4 days (OR 2-8). Linear regression analysis showed a statistically significant correlation between lag time symptoms onset/diagnosis (independent variable) and diagnosis of Staphilococcus Aureus IE (non standardized coefficient of linear correlation B 23.71, R2 0.037, P < 0.05). Moreover, this study shows that a delay of > 15 days in the diagnosis of IE, increases of 3.7 times the risk of death (OR 3.75; IC95% 1.29-10.93; P < 0.05). IE on prosthetic valve is a RF for worst outcomes because it increases the death risk of 3.4 times (OR 3.4; IC95% 1.21-9.59; P < 0.05). Multivariate analysis confirmed the significance between independent RF for statistical analysis such as diagnostic delay of more than 15 days, infection of prosthetic valve and unfavorable outcome (diagnostic delay >15 days OR 5.2, IC 95% 1.62-16.7, P 0.01; prosthetic valve OR 4.8, IC 95% 1.52-15.7, P <0.01)

Conclusions: Diagnostic delay of IE is significantly related to S. aureus etiology and it correlates with unfavorable outcomes. Delayed diagnosis of IE represents a big challenge in the management of this disease requiring an “Endocarditis Team” able to guarantee a multidisciplinary approach of IE.

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Inflammatory changes on routinely-performed Papanicolaou smear are more frequently associated with bacterial vaginosis

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Background: The results of cervical Papanicolaou (Pap) smears tests frequently include comments on the possible presence of infection based on cytological criteria. However, the clinical importance of these findings is unknown. This study assessed the possible association, if any, between inflammatory changes reported on Pap smears with the isolation of pathogens in the genital tract of asymptomatic women.

Materials/methods: Reproductive age nonpregnant women and menopausal women with inflammatory changes on routinely performed Pap smear in the last five years were included in the study. Genital tract samples were inoculated onto appropriate plates for standard cultures and incubated at 37°C. A wet mount and a gram-stained smear were examined to obtain valuable information about the microorganisms present and to apply Nugent criteria for the diagnosis of bacterial vaginosis. The identification of the isolated pathogens was performed with the automated system VITEK 2 (BioMerieux, Marcy l’Etoile, France). Statistical analysis was performed using chi square test and values ≤ 0.05 were considered statistical significant.

Results: A total of 2939 women (1708 of reproductive age and 1231 menopausal) with inflammation on the Pap smear, participated in the study. Negative cultures were detected in 40% and 64% of the reproductive age and menopausal women, respectively. Bacterial vaginosis was diagnosed more frequently, specifically 70.3% in reproductive age women and 79.7% in menopausal women. Candida species were isolated in 17.3% of reproductive age women and in 7.7% of menopausal women. In contrast, aerobic vaginitis was diagnosed in similar percentages in the two groups of women studied, 12.3% and 12.6% in reproductive age and menopausal women, respectively.

Conclusions: Our results suggest that a report of inflammatory changes on the cervical Pap smear cannot be used to reliably predict the presence of a genital tract infection since, in a significant proportion of our subjects, cultures were negative. However, the isolation of different genital tract pathogens in 60% and 36% of reproductive age and menopausal women with inflammation on Pap smears, respectively, cannot be overlooked and must be regarded with concern. Interestingly, in these women, bacterial vaginosis was diagnosed more often than other clinical entities.

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Abstract 3111

Contaminating microflora during examination for tuberculosis: saprophytes or potential pathogens?

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Background: Various representatives of the order Actinomycetales may exhibit an acid resistance property. Acid-fast bacteria can be a true contaminating microflora, and can be associated with a clinical picture similar to tuberculosis.

Materials/methods: The study included 1024 clinical samples that were inoculate in the Mycobacteria Growth Indicator Tube (MGIT) for the diagnosis of tuberculosis and were identified by the BACTEC system as contaminated by extraneous microflora. Mycobacterium tuberculosis complex DNA was not detected in all samples. Then, of all the selected MGITs, reseeding was culture on blood agar in order to isolate and identify microorganisms that caused the contamination. The cultivation was carried out for 21 days at a temperature of 28 and 37 °C. Grown microorganisms were identified using a MALDI-ToF mass spectrometer (Bruker ™, Germany). Only acid-fast microorganisms were included in the analysis.

Results: The total number of microorganisms isolated from clinical samples was 933 strains. Of these, 80 strains (8.6%) belonging to 6 genera were acid-fast. The most numerous was the group of bacteria from the genus Streptomyces - 37 strains: S.violaceoruber - 12, S.phaeochromogenes - 11, S.badius - 2, S.chartreusis - 2, one strain each - S.albus, S.hirsutus, S.lavendulae, S.avidinii; 6 strains could only be identified before the genus. All bacteria belonging to the genus Nocardiа - 13 strains were identified to the species: N.farcinica - 6, N.cyriacigeorgica - 3, N.brevicatena - 2, N.nova - 1, N.carnea - 1. Out of 13 strains of Gordonia spp. 12 strains were identified to the species: G.sputi - 7, G.rubripertictata - 4, G.bronchialis - 1. In 8 cases, bacteria of the genus Brevibacterium were isolated: B.casei - 6, B.celere - 1, B.barstelensis - 1. Tsukamurella paurometabola 4 strains were isolated, one strain was identified before the genus Tsukamurella. Four strains of Cellulosimicrobium cellulans were also isolated.

Conclusions: The identification of microorganisms isolated from clinical specimens during screening for tuberculosis is an important criterion, which allows differentiating contaminating microflora from bacteria of clinical significance. Using MALDI-ToF mass spectrometry, it was possible to identify 91.3% of acid-fast bacteria isolated from clinical specimens during examination for tuberculosis.

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Abstract 3112

Diagnostic value of the molecular detection of Sarcoptes scabiei from a skin scraping in patients with suspected scabies

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Background: Scabies is a highly contagious parasitic disease associated with long-term residence in nursing homes, and it is a public health burden worldwide. However, atypical skin manifestations are frequent and the widely used diagnostic test based on microscopic examinations have limited sensitivity. We evaluated the diagnostic value of polymerase chain reaction (PCR) from skin scraping in patients with suspected scabies

Materials/methods: Adult patients with suspected scabies, unrelated diseases or healthy volunteers were enrolled at a tertiary hospital, in Seoul, South Korea, from December 2017 through October 2018. We classified participants based on the consensus criteria established by the International Alliance for the Control of Scabies in 2018; confirmed (microscopic mite detection), clinical (scabies burrow or typical lesions with two history features including itch and close contact with scabies patients), suspected scabies (typical lesion with one history feature or atypical lesion with two history features), or no scabies. PCR was performed on the skin scrapings to target the cytochrome c oxidase subunit 1 (cox1) gene of Sarcoptes scabiei.

Results: A total of 57 participants, 43 with suspected scabies, 14 with unrelated diseases, and 4 healthy volunteers were enrolled. Of the 43 patients, 22 were classified as confirmed scabies, 2 as clinical scabies, 6 as suspected scabies, and 3 as no scabies (Table 1). The sensitivities of the microscopic examination were 100%, 92%, and 73% in confirmed scabies; confirmed and clinical scabies; and confirmed, clinical, and suspected scabies, respectively (p=0.006). The sensitivities of PCR were 86%, 83%, and 80% in confirmed scabies; confirmed and clinical scabies; and confirmed, clinical, and suspected scabies, respectively (p=0.59). The specificity of the scabies PCR in the no scabies control was 100% (95% CI=80–100).

Conclusions: PCR testing for scabies may be helpful in the improvement of sensitivity for the diagnosis of scabies by clinical criteria.

Table 1. Comparison of diagnostic performance of the scabies PCR and microscopy in confirmed, clinical, and suspected scabies patients.

<table>
<thead>
<tr>
<th></th>
<th>Confirmed scabies (n=22)</th>
<th>Confirmed + clinical scabies (n=24)</th>
<th>Confirmed + clinical + suspected scabies (n=30)</th>
<th>No scabies (n=17)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive (n)</td>
<td>19</td>
<td>20</td>
<td>24</td>
<td>0</td>
</tr>
<tr>
<td>Negative (n)</td>
<td>3</td>
<td>4</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Sensitivity (% 95% CI)</td>
<td>86 (65–97)</td>
<td>83 (63–95)</td>
<td>80 (61–92)</td>
<td></td>
</tr>
<tr>
<td>Specificity (% 95% CI)</td>
<td>100 (80–100)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microscopy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive (n)</td>
<td>22</td>
<td>22</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>Negative (n)</td>
<td>0</td>
<td>2</td>
<td>8</td>
<td>17</td>
</tr>
<tr>
<td>Sensitivity (% 95% CI)</td>
<td>100 (85–100)</td>
<td>92 (73–99)</td>
<td>73 (54–88)</td>
<td></td>
</tr>
<tr>
<td>Specificity (% 95% CI)</td>
<td>100 (80–100)</td>
<td></td>
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</tbody>
</table>

*No scabies* included thirteen skin scrap specimens from patients with alternative diagnosis and four skin scrap specimens from healthy volunteers.

*Difference in the sensitivity of the PCR test between the three groups was not statistically significant (p=0.59).

*Difference in the sensitivity of the microscopic examination between the three groups was statistically significant (p=0.006).

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Abstract 3113

Application of peptides as a novel method to enrich and identify of Candida species

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Background: Among invasive fungal infections, Candida species are responsible for more than 50% of all cases worldwide. Invasive candidiasis causes a high range of morbidity and mortality, and therefore the pathogens need to be rapidly identified. In this study, we set up a novel method to detect Candida species using a synthetic antimicrobial peptide. The peptide was modified by labelling with a fluorescent probe. Adherence of this peptide to the fungal cell wall was tested by immunofluorescence microscopy, and its identification was performed by MALDI-TOF MS.

Materials/methods: Different strains of Candida species, including C. albicans, C. glabrata, C. tropicalis, and C. parapsilosis were tested. Escherichia coli (NCCB 100297) and Staphylococcus aureus (NCCB 100294) were used as control. Cells were suspended and further diluted in 1 ml RPMI1640 and incubated at room temperature for 15 min with fluorescently-labelled peptides. Thereafter, it was washed with PBS and coverslips were mounted. Fluorescent images were obtained with an immunofluorescence microscope (Zeiss, Axioplan) adjusted with a wavelength in the range of 488 nm (green). Identification by MALDI-TOF MS was done by lysing the cells and spotting in duplicate. Dried spots were firstly overlaid with the peptide and then with 1 µl of MALDI matrix. Spectra were acquired in the mass range between 2 and 20 kDa and analyzed by FlexAnalysis 3.3 software (Brüker Daltonics).

Results: The cell wall of the tested Candida species was clearly stained with the fluorescent-labeled peptide. E. coli cells did not stain while those of S. aureus were intracellularly labeled. By MALDI-TOF MS, each microorganism was correctly identified. The peptide peak was obviously distinguished in the mass range between 2 and 20 kDa. Peak-shifting of labeled peptide combined with each of the microorganisms supported the identification and confirmed peptide binding.

Conclusions: This study showed that there is a significant binding of fluorescently-labeled peptide to the cell wall of Candida species. This method may help us to detect and identify the yeasts from sepsis in seriously ill patients in the future.

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**Abstract 3114**

**French general practitioner attitude regarding human papilloma virus vaccine in females and males: positive perceptions but missed opportunities**

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**Background:** In France, HPV vaccination is recommended for all females up to 19 years, and for two male categories: men who have sex with men (MSM) up to 27 years (since 2016), and immunocompromised males up to 19 years (since 2014). However, vaccine coverage in France is below 20% for females, and probably even lower for MSM. We aimed to evaluate the attitude of general practitioners (GP) regarding this vaccine in these two populations.

**Materials/methods:** We elaborated an anonymous, online questionnaire exploring GP perceptions and practices related to this vaccine through scores ranging from 0 to 100. The questionnaire was diffused between June 2018 and January 2019.

**Results:** A total of 337 GP participated (age 44.4±12, females 58.8%); 84.3% declared they generally knew their patient sexual orientation.

When asked whether they were in favor of HPV vaccine in girls and MSM, on a 0-100 scale, the medians/IQT answers were 99[80-100] and 10 [71-100], respectively. They were concerned by HPV vaccine potential adverse effects at a median of 10[0-30]. They declared, on a 0-100 scale, that they took the opportunity of a contraceptive prescription in females to check HPV vaccination status at a median of 60 [20-90]; answers regarding this behavior were higher in the participants above 44 years (median 80[30-100] vs 50[20-80], p=0,001). 59.1% proposed the HPV vaccine to females with the DTPP booster at the age of 11. They evaluated that 43.6±22% of their females patients under the age of 20 were vaccinated.

Among the participants, 62.8% were aware of the 2016 recommendations regarding MSM vaccination; they were younger than the others (42.9±11 vs 46.6±11 years, p=0.037). Only 15.7% had already offered this vaccine to males. On a 0-100 scale, they declared that they had in mind the HPV vaccine when seeing a male of 27 or younger at a median of 0[0-10]. They supported an equal vaccination of both genders at a median of 100[50-100].

**Conclusions:** Adherence to HPV vaccination among GP in this study is strong, but missed opportunities remain regarding females and males. This would probably be improved by undifferentiated vaccination of both genders.

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Impact of a dedicated Clostridiodes difficile infection isolation ward on clinical outcomes

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Background: Clostridium difficile infection (CDI) remains a globally important adverse event of antibiotics. In the UK, CDI accounts for an additional £4,000 per patient. In 2012, a dedicated CDI ward at Hull University Teaching Hospitals (HUTS) was opened; it closed in 2016 following a sustained reduction in incidence. This analysis aimed to assess the impact of the CDI ward on readmission, recurrence and 30-day, 90-day and 1-year mortality.

Materials/methods: From all CDI patients treated at HUTS during the periods before (N = 148, 04/10-12/11), during (N = 332, 04/12-05/16) and after (N = 89, 09/16-12/18) the CDI ward was open, a random sample of N = 75 patients was selected for each period (N = 223). Data including comorbidities, clinical data, treatment and outcomes was collected from discharge letters and hospital systems. Data was analysed using STATA. Predictor variables with p<=0.1 by univariate analyses were included in multivariate logistic regression analyses.

Results: The median age of patients was 76, 80 and 78 years in the before, during and after periods. The commonest ribotypes were 001 (13%) and 078 (13%). 28%, 16% and 23% of patients died within 30-days in the before, during and after periods. Admission to the CDI ward was not significantly associated with outcomes.

<table>
<thead>
<tr>
<th>Predictive variable</th>
<th>Clinical outcomes</th>
<th>Statistically significant adjusted odds ratios (95% CI), p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>30-day mortality</td>
<td>90-day mortality</td>
</tr>
<tr>
<td>ICU admission</td>
<td>0.13</td>
<td>0.19 (0.07-0.57), 0.003</td>
</tr>
<tr>
<td>Age</td>
<td>1.05 (1.02-1.09), 0.004</td>
<td>1.05 (1.02-1.08), 0.001</td>
</tr>
<tr>
<td>Co-morbidities</td>
<td>1.29 (1.12-1.48), 0.000</td>
<td>1.20 (1.05-1.38), 0.008</td>
</tr>
<tr>
<td>Neutrophils on onset</td>
<td>1.07 (1.02-1.13), 0.011</td>
<td>1.06 (1.01-1.11), 0.023</td>
</tr>
<tr>
<td>Albumin on onset</td>
<td>1.06 (1.01-1.12), 0.03</td>
<td>3.69 (1.02-13.3), 0.046</td>
</tr>
<tr>
<td>Radiological changes</td>
<td>1.06 (1.01-1.12), 0.03</td>
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</table>

Conclusions: The dedicated CDI ward had no identifiable impact on outcomes. However, variables associated with the nature of the patient and severity of infection at onset were independent predictors of negative outcomes; suggesting that these are more important in determining CDI outcomes.

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Identification of clinical isolates of Tannerella forsythia by MALDI-TOF mass spectrometry

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**Background:** Tannerella forsythia (Tf) is an anaerobic, nutritionally fastidious gram-negative bacterium, regularly regarded as periodontal pathogen. Isolation of Tf from clinical samples and cultivation are used for research and diagnostic purposes. Identification of Tf grown in culture is time-consuming and is based either on colony morphology and biochemical characteristics (API, BANA) or DNA-based assays (DNA-DNA hybridization, 16S rRNA sequencing). Recently, matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF) has become a widespread routine rapid and reliable method for identification of bacterial and fungal pathogens. Bruker’s commercially available MBT MSP Library includes mass spectra of all clinically relevant periodontal pathogens (Prevotella nigrescens/intermedia, Fusobacterium nucleatum, Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans) except Tf. The aim of our study was thus to create a custom MALDI-TOF library for fast and simple identification of Tf.

**Materials/methods:** Pure cultures of Tf were cultivated on Tryptic soy agar with N-acetylmuramic acid in anaerobic conditions for 7 days. MALDI-TOF library was constructed using spectra generated from DSM 1028359 reference strain and 14 clinical isolates which were identified by sequencing the 16S rRNA gene. Mass spectra for library creation were acquired with Microflex LT (Bruker Daltonics, Germany). Spectra were analysed using FlexControl software; a minimum of 20 good quality spectra with minimum peak shift of individual masses (500 ppm) per isolate were used to create main spectrum profiles using Compass Explorer software. The custom library was then challenged with 13 routine isolates.

**Results:** A total of 28 periodontal Tf isolates were included. MALDI-TOF identification for all tested isolates matched the results of identification based on morphological characteristics and 16S rRNA sequencing with highly probable species identification (LogScore >2.0). Protein profiles did not match existing profiles in the database containing 7595 bacterial species (Vdb-8468), dendrogram showed Tf clustering in a branch separate from the genus Bacteroides.

**Conclusions:** Mass spectra of our isolates identified as Tf by 16S rRNA sequencing were found to significantly differ from other mass spectra included in the Bruker’s commercially available MBT MSP Library. We have created a custom MALDI-TOF library, which allows fast and simple identification of Tf grown in culture.

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Abstract 3121

National survey of carbapenemase-producing Klebsiella pneumoniae and Escherichia coli in Belgium in 2019

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Background: Carbapenemase-producing Enterobacteriaceae (CPE) isolates are spreading and represent a serious threat for global public health. We conducted a nationwide survey to monitor the evolution of the epidemiology of carbapenemase-producing K. pneumoniae (CPKP) and E. coli (CPEC) in Belgium.

Materials/methods: The survey includes 75 (63 hospital-based and 12 community-serving) laboratories requested to refer non-duplicate consecutive K. pneumoniae and E. coli isolates collected from clinical specimens (fecal samples excluded) between May and October 2019 to the National Reference Center for decreased carbapenem susceptibility or suspicion of CPE. Isolates were tested for susceptibility phenotype by disk diffusion and for carbapenemase production by Beta-Carba test (BioRad) and by immunochromatographic lateral flow assay (LFA) RESIST-4 OKVN (Coris BioConcept). Other carbapenemases were sought by molecular methods in case of suggestive phenotype with negative result by LFA.

Results: Of the 235 referred isolates, 175 (74%) including 144 K. pneumoniae and 31 E. coli, collected from 48 laboratories were confirmed as CPE. Distribution of the different carbapenemase types by decreasing frequency was: OXA-48 (n=136; 78%), KPC (n=18; 10%), NDM (n=14; 8%), VIM (n=3; 2%) and IMP (n=1; 1%); 3 K. pneumoniae coproduced two different types (2 OXA-48+NDM and 1 KPC+NDM). Compared to a previous survey including the same laboratories in 2015, the number (proportion) of laboratories reporting CPKP/CPEC increased from 35 (47%) in 2015 to 46 (61%) in 2019 (p=0.07). The number of local CPKP/CPEC grouped cases (>1 case of the same CPE type) increased significantly from 24 in 2015 to 37 in 2019 (p=0.027) as did the number of laboratories reporting two or more different carbapenemase types (n=8 in 2015 and n=13 in 2019; p=0.21).

Conclusions: Our data confirm the worsening epidemiological status of CPKP/CPEC in Belgium in 2019. Overall, OXA-48 remained by far the predominant carbapenemase, but the increasing number and proportion of laboratories having more than one carbapenemase type detected from clinical specimens strongly suggests their spread and diversification both in hospital and community settings.

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Heat wave-associated Vibrio infections in Germany 2018 and 2019

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Background: Climate change already has enormous implications for human health, especially for the burden of vector- and waterborne infectious diseases. Vibrio spp. are gram-negative bacteria with a worldwide distribution in marine ecosystems that are regarded as emerging human pathogens due to a rapidly warming ocean environment. Unprecedented heat waves in summers of 2018 and 2019 have led to high sea surface temperatures in Europe. Such heat waves have previously been linked to Vibrio outbreaks in other countries. In Germany, reporting of Vibrio infections is not mandatory, so high numbers of unreported infections must be assumed.

Materials/methods: We are conducting a retrospective multi-center analysis of patients that were diagnosed with autochthonous infections with Vibrio spp. in the summers of 2018 and 2019 in German hospitals and outpatient clinics.

Results: At the time of this preliminary analysis, a total of 32 patients diagnosed with autochthonous infections with V. vulnificus, V. parahaemolyticus, V. cholerae (non-O1/O139), V. alginolyticus and V. fluvialis respectively could be included in our study (Table 1). Seventeen patients acquired wound infections, 10 patients suffered from ear infections, 5 patients presented with gastroenteritis. All Vibrio infections have been acquired in the Baltic Sea during the months July and September.

Conclusions: The heat waves in 2018 and 2019 respectively caused unprecedented numbers of human infections with Vibrio spp. acquired in the German Baltic Sea. Ongoing global warming will likely lead to a worldwide increase of these emerging waterborne pathogens warranting awareness among physicians, microbiologists and health care authorities.

<table>
<thead>
<tr>
<th>V. vulnificus</th>
<th>V. parahaemolyticus</th>
<th>V. cholerae</th>
<th>V. alginolyticus</th>
<th>V. fluvialis</th>
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<tbody>
<tr>
<td>Wound infections</td>
<td>6</td>
<td>2</td>
<td>?</td>
<td>1</td>
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</tbody>
</table>

Table 1: Autochthonous Vibrio infections in Germany 2018 and 2019

Presenter email address: thomastheobrehm@gmail.com
Abstract 3127

Carriage of ESBL-producing Gram-negative bacteria by houseflies captured in hospital and suburban surroundings in Ethiopia differs greatly

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Background: Local data from the Asella Referral and Teaching Hospital (ARTH) reveal a high prevalence of extended-spectrum β-lactamase- (ESBLs) producing Gram-negative bacteria in clinical isolates. To investigate possible routes of transmission, we determined the colonization of houseflies with ESBL-producing Gram-negative bacteria at the ARTH compound and in Asella town.

Materials/methods: In August 2019, we collected a total of 85 houseflies; 20 from the neonatal intensive care unit (NICU), 12 from the orthopedic ward, 26 from the hospital’s waste disposal area and 27 from a butchery 1.4 km from the hospital. The flies were trapped with retail flycatchers and stored in sterile normal saline. After maceration in sterile saline suspensions were inoculated on MacConkey-Agar and incubated at 37°C. Identification and antimicrobial susceptibility testing were performed using MALDI-TOF-MS and VITEK2.

Results: A total of 103 isolates were obtained from 85 flies (NICU: 11, orthopedic ward: 10, waste disposal area: 37, butchery: 45). The prevalence of ESBL was 2.2 % (1/45) in the butchery and 69 % (40/58) in the hospital compound (orthopedic ward: 90 %, NICU: 82 %, waste disposal area: 58 %), with the difference between hospital and surroundings was statically significant (p ≤0.001). The frequency of ESBL was 75 % (6/8) in Enterobacter spp., 75 % (6/8) in Raoultella spp., 67 % (6/9) in Citrobacter spp, 64 % (7/11) in Klebsiella pneumoniae and 56 % (5/9) in Escherichia coli isolates, respectively. Of the 41 confirmed ESBL genes detected, 83 % were CTX-M-like, 80 % TEM-like, 22 % SHV-like and 2 % CTX-M-2-like. CTX-M-9 and CTX-M-8/25-like genes were not detected. All ESBL positive Klebsiella pneumoniae possessed both CTX-M-1 and SHV genes.

Conclusions: A high proportion of houseflies trapped within the hospital compound were colonized with ESBL-producing bacteria, whereas houseflies collected in a butchery 1.4 km from hospital were colonized at a much lower rate. Houseflies may be a factor in the spread of multidrug-resistant (MDR) microbes in hospitals. Further studies are needed to determine the possible source of MDR in houseflies and the impact on the high rate of MDR nosocomial infections.

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Piperacillin-tazobactam versus carbapenem for the treatment of bloodstream infection caused by CTX-M-type ESBL-producing Enterobacteriaceae

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Background: In the MERINO trial, piperacillin/tazobactam [PTZ] failed the non-inferiority challenge with meropenem as target-ed therapy for bloodstream infection [BSI] due to E.coli or K.pneumoniae ceftriaxone-resistant. Microbiological methods were criticized due to AmpC enzymes inclusion, predicting no response to PTZ, and a non-reference method use rather than broth microdiluition, as susceptibility test for PTZ.

Materials/methods: Retrospective study of adult patients with E.coli or K.pneumoniae ceftriaxone-resistant positive BC admitted to five medicine wards, at Careggi Hospital (Firenze-Italy), between 2014 and 2018 with availability of bacterial strains [CARESBLI Study, Ethical Approval 07/05/2019, code 14445/OSS]. Molecular screening for blaCTX-M genes and others ESBLs as well antimicrobial susceptibility testing with broth microdiluition were performed. E. coli ATCC 25922 and ATCC 35218 were used as control strains. Patients were grouped according to whether they were treated entirely with carbapenem or with PTZ or empirically with PTZ and then escalated to carbapenem [figure 1]. Aim was to determine whether PTZ was efficacious as carbapenems, empirically or targeting therapy, focusing on clinical improvement within 48-72 hours of starting empirical therapy (decreasing SOFA score) and on 30-day mortality since BC withdrawal.

Results: Eighty patients were included with a median age of 79 years whom 36 (45%) women. E.coli isolates were prevalent [93.8%] and the most frequent ESBL was CTX-M [95%]. 58 strains [72.5%] had MICs <=8 µg/ml to PTZ. Urinary source was predominant [80%] with non-severe presentation for the majority of cases [62.5%]. Median Charlson Comorbidity Index was 6. Overall 30-day mortality was 13.8%. No significant differences, regarding demographic, microbiological, clinical presentation and outcomes characteristics, were found between the treatment groups. In logistic-regression, an inappropriate empirical therapy resulted associated [OR 0.13,CI 95%0.02-0.06,p=0.001] against clinical improvement. Neither empirical nor targeted treatment, with PTZ or carbapenem, included escalation regimen, were associated with 30-day mortality.

Conclusions: The study did not reveal any significant difference, regarding clinical improvement and mortality, between PTZ and carbapenem, treating BSI due to CTX-M-type ESBL-producing Enterobacteriaceae, mainly from urinary and abdominal sources, in a real-life elderly population with a high comorbidity burden. Therefore it confirms the relevance of appropriate empirical therapy on outcome in these difficult-to-treat infections.
Clonal characterisation of Acinetobacter baumannii strains in a public hospital in Brazil

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Abstract 3133

Background: The survival and spread of CRAB (Carbapenem-resistant Acinetobacter baumannii) in the hospital environment is a constant concern. Identification of strains in molecular aspects can be used to identify outbreaks of infection and to monitor inter-institutional, regional and international CRAB transmission, and are extremely useful for rapidly identifying the emergence and spread of multiresistant clones. The aim of this study was to verify the genetic similarity of the isolates found from A. baumannii by MALDI-TOF and automated rep-PCR.

Materials/methods: The strains were subjected to a protein extraction process. One microliter of the extracted slide solution was added after drying at room temperature 1µL of the matrix (α-cyano-4-hydroxy-cinnamic acid solution) was added. Then, direct detection of the microorganism was performed by MALDI-TOF mass spectrometry on Vitek® MS equipment, where clones were considered when similarities were greater than 75%. The different clones identified were confirmed by Diversilab® automated rep-PCR system, and isolates with similarity greater than 95% were considered rep-PCR clones.

Results: Fifty bacterial CRAB isolates were analyzed. Through direct identification by MALDI-TOF, the isolates were verified for similarity using the taxonomy tool of the Saramis software, where three clusters were observed. The first cluster had a similarity in 94% of the samples (n = 47). Two more clusters were observed, where one was contemplated only by one bacterial isolate, and the other cluster was contemplated by two bacterial isolates. Ten bacterial isolates were selected from the total of samples, and evaluated for similarity by automated rep-PCR, which demonstrated the presence of the same three clusters among the CRAB isolates, corroborating the similarity data obtained by the Saramis software.

Conclusions: Clonal similarity of bacterial isolates of A. baumannii can be evaluated and studied using Saramis software. The presence of a large clonal group showed that there is only one widespread strain in the hospital setting, which may be caused by its easy spread due to its survival in inanimate environments and cross-resistance between objects, surfaces and health professionals.

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Abstract 3134

**Anti-biofilm and antibacterial properties of cationic amphipatic AMP mimics**

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**Background:** The development of antibiotic resistances by microorganisms has led to a need to find novel antibacterial agents or combinations of agents as the first line of treatment for various infections. Peptoids, oligomers of N-substituted glycines, are attracting due to their advantageous properties as peptidomimetics, including designable well-defined three-dimensional structures and stability toward proteolysis. This study aimed to investigate the anti-biofilm and antimicrobial properties as well as their potential synergy with antibiotics of a set of peptoids mimicking helical antimicrobial peptides (AMPs) using Gram-positive and Gram-negative bacteria.

**Materials/methods:** Antibiofilm activity was determined by measuring the biofilm biomass (viable bacteria) after 3h of cocultivation and after treatment of formed biofilms with the peptoid molecules to be tested. Antibacterial activity was measured by determining the minimum inhibitory concentration (MIC) by a microtiter broth dilution in Müller-Hinton and mammalian cells culture media. Based on the MIC of each antimicrobial agent, a checkerboard assay was performed to investigate the synergy between them, which was expressed as the fractional inhibitory concentration (FIC).

**Results:** Several cationic amphipatic peptoids displayed antibiofilm and antibacterial activity, the latter being enhanced in mammalian culture cells medium compared to MH medium, with low hemolytic activity and cytotoxicity. The combination of a selected peptoid and the antibiotic erythromycin showed synergistic activity against Gram-negative bacteria, and this activity was retained and even enhanced when incubated in mammalian cells culture medium compared to standard bacteriologic media.

**Conclusions:** Peptoid-type AMP mimics alone and in combinations with antibiotic are promising strategies to fight biofilm formation and antibiotic resistant bacteria

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Should serum D-dimer be added as a first-line screening test for prosthetic joint infection?

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**Background:** Although the updated definition of prosthetic joint infection (PJI) introduced serum D-Dimer in the preoperative score in evaluating, this new biomarker has not yet been validated between the different workgroups. We investigate the value of serum D-dimer prior to revision arthroplasty and compare with the measurements of serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels for the diagnostic of PJI.

**Materials/methods:** This prospective study enrolled patients undergoing revision arthroplasty from February 2012 to February 2014. PJI was defined according to Infectious Diseases Society of America (IDSA) criteria. The four types of PJI were classified according to the Tsukayama et al. criteria. In all patients, serum D-dimer, ESR and CRP level were measured preoperatively. The diagnosis accuracy of different tests was evaluated constructing receiver-operating-characteristic (ROC) curve areas.

**Results:** Of the 185 patients studied, 145 had aseptic failure (AF) and 40 PJI. There were 5 (12.5%) type I infections, 26 (65%) type II, 4 (10%) type III and 5 (12.5%) type IV according to the Tsukayama et al. classification. The median of D-Dimer levels was higher in PJI 1727 (185-6681) than in AF patients 640 (67-5958) (p=0.032). The areas under the ROC curve for D Dimer, PCR and ESR were 0.763 (95% confidence interval 0.683-0.844), 0.790 (0.712-0.868) and 0.733 (0.636-0.830), respectively. Based on the Youden’s index, 950 ng/ml was the optimal threshold value for serum D-dimer for diagnosing PJI. D-dimer showed a sensitivity and specificity of 77% and 66%, respectively, while serum CRP (>0.5mg/dl) and ESR (>12mm/h) demonstrated a sensitivity of 82% and 80% and specificity of 61.4% and 64%, respectively. Serum D-dimer diagnosed 73% of type II infections, 60% of type IV and all the cases of Types I and III.

**Conclusions:** Serum D-dimer levels are higher in patients with PJI than those with AF. However, the value of D-Dimer compared to traditional inflammatory parameters is limited. Due to factors that influences serum biomarkers, diagnostic strategies as the first-line approach should be individualized according to the patients’ age, comorbidity, clinical presentation or implant-related factors.

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Contaminating microflora at a tuberculosis test: dependence on medium for primary inoculation

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Background: A microbiological study of tuberculosis involves the use of certain artificial nutrient media and a decontamination process aimed at suppressing the growth of concomitant bacterial flora.

Materials/methods: The study analyzed the culture of the following types of clinical material: bronchial washings, sputum, urine, separated from fistulas, gastric lavage, pleural fluid. We used dense Levenshtein-Jensen media and Finn II, as well as Middlebrook 7H9 liquid medium. The material was represented by 865 samples with contaminating flora, which were scattered on solid nutrient media: 5% blood agar (Bio-Rad), universal chromogenic medium (Bio-Rad), Saburo agar (HiMedia). After incubation and cultivation in the case of growth detection, the cultures were identified using a MALDI-ToF mass spectrometer (Microflex LT, Bruker). A total of 1093 microorganism strains were isolated and identified.

Results: As a result, in 457 samples (52.8%), growth was detected on Levenshtein-Jensen medium, in 322 samples (37.2%), growth was detected on Finn II medium, in 214 cases (24.7%), growth was detected on Middlebrook 7H9 medium. In 168 cases (19.4%), growth was detected immediately on two solid media. The increase in the probability of seeding from clinical material when using Middlebrook 7H9 medium of microorganisms of the genera Arthrobacter spp., Brevibacterium spp., Cellulosimicrobium spp., Gordonia spp., Lysinibacillus spp., Microbacterium spp., Sporothrix spp. Was statistically significant. (from 1 to 3.9% of the total number of crops in comparison with dense nutrient media). However, these bacteria and micromycetes were not detected when sowing on solid nutrient media. Also, Nocardia spp., Paenibacillus spp., Ralstonia spp., Streptomyces spp. Were more often detected on Middlebrook 7H9 liquid medium. (2.6-14.9% of the total number of crops compared with solid nutrient media). In turn, Aspergillus spp., Candida spp., Pseudomonas spp., Corynebacterium spp., Escherichia spp., Klebsiella spp., Staphylococcus spp., Were detected much more often on dense nutrient media of Levenshtein-Jensen and Finn II.

Conclusions: Thus, the use of Middlebrook 7H9 liquid medium increases the likelihood of identifying some acid-resistant actinomycetes (Gordonia spp., Nocardia spp.) That have a clinical and radiological picture similar to tuberculosis. This reduces the likelihood of seeding bacteria from the order Enterobacteriales, some micromycetes and non-fermenting gram-negative bacteria.

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Abstract 3138

**Presence and persistence of hepatitis E virus PCR in patients with specific IgM positivity**

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**Background:** Diagnosis of Hepatitis E virus (HEV) infection is based on specific IgM and/or RNA, besides, PCR is not always available so IgM, IgG follow-up sample and avidity could be essential for diagnosis of the HEV acute infection.

Analyse the presence and persistance of HEV-RNA in patients with specific IgM, evaluated with four comercial assays, to know the IgM utility as viremia predictor.

**Materials/methods:** From 2011 to 2018, 131 patients were HEV positive with indirect EIA IgM (HEV IgM Dia.Pro, Italy), being also analyzed 106 with an in-house PCR (with the WHO Standard HEV strain as positive control) and with: Capture IgM EIA (Wantai Diagnostic, China), indirect IgM EIA (Mikrogen, Germany), CLIA IgM and IgG (Vircell, Spain). In 38 patients follow-up samples were obtained.

**Results:** RNA-HEV was positive in 39 patients. Samples were obtained between 2-26 days after symptoms onset (DAO) (mean 11.1±6.28) for positive PCR and between 1-120 DAO (mean 27.8±30.17) for negative PCR.

Following-up samples in 38 patients were collected after 33 DAO. Only one, with normal ALT, continued being repeatedly positive at 77 DAO.

**Conclusions:** All analyzed IgM kits detect practically 100% of the positive PCR cases in samples less than 30 DAO, but the persistence of IgM could be prolonged in negative PCR patients. Viremia may be negative in a few patients less than 30 DAO. The high IgM-index could help to predict the PCR positivity. Vircell IgM detects less positive cases in patients with negative HEV-RNA.

<table>
<thead>
<tr>
<th>Serology</th>
<th>PCR positive</th>
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<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>Mean Index (Range)</td>
</tr>
<tr>
<td>Dia.Pro IgM+</td>
<td>39 (100%)</td>
<td>11.8 (2.1-15.0)</td>
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<tr>
<td>Vircell IgM+</td>
<td>37 (94.87%)</td>
<td>6.5 (0.6-13.5)</td>
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<tr>
<td>Vircell IgG+</td>
<td>39 (100%)</td>
<td>8.7 (1.5-28.2)</td>
</tr>
<tr>
<td>Wantai IgM+</td>
<td>36 (97.43%)</td>
<td>12.2 (1.1-18.4)</td>
</tr>
<tr>
<td>Mikrogen IgM+</td>
<td>39 (100%)</td>
<td>103.7 (30.4-149.4)</td>
</tr>
<tr>
<td>Low avidity IgG</td>
<td>36 (92.30%)</td>
<td>21.0 (2.0-41.0)</td>
</tr>
</tbody>
</table>

Dia.Pro Positive IgM S/CO >1.2; Vircell Positive IgM S/CO > 0.5; Vircell Positive IgG S/CO > 1.1; Mikrogen Positive IgM >24 U/ml; Wantai Positive IgM ≥1 U/ml; Low avidity ≤ 45.

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Abstract 3141

The predictive value of disc diffusion assay results for resistance in Gram-negative bacteraemia: a UK district general hospital experience

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Abstract third-party references: Barts Health NHS Trust

Background: Gram negative bacteremia poses both significant clinical and antimicrobial stewardship concerns for clinicians. Direct sensitivity testing through antimicrobial disc diffusion (DD) assays can provide a rapid guide to resistance patterns, potentially allowing the avoidance of unnecessary escalation and even safe de-escalation in blood stream infections. However, DD assays are only cautiously recommended by the British Society for Antimicrobial Chemotherapy due to concerns over disparity with automated methods, reflecting a dearth of experience and data with their use. The data presented here aims to further inform this evolving practice.

Materials/methods: 710 Gram negative blood culture isolates identified over 2 years at Newham University Hospital in East London were analyzed. 650 samples were then identified that had undergone resistance and susceptibility testing with DD and microbroth dilution assays, with 583 samples returning comparable paired results for commonly used antimicrobials. These samples were then analyzed to calculate predictive values for DD results, with further sub-analysis performed on a species level for common pathogens.

Results: In sample sizes ranging from 472 to 574 isolates, DD assays accurately predicted sensitivity to amikacin (negative predictive value = 95.59%), ampicillin (97.09%), co-amoxiclav (95.37%), cefuroxime (97.10%), ciprofloxacin (96.61%), ertapenem (98.81%), gentamicin (98.25%), and piperacillin/tazobactam (96.83%). However, a resistant DD result was less predictive of true resistance, which was particularly apparent for beta-lactam agents (co-amoxiclav positive predictive value = 60.37%; ertapenem = 61.90%; piperacillin/tazobactam = 42.86%).

Conclusions: DD assays consistently overcall resistance for certain beta-lactam antimicrobials in Gram negative blood stream infections, particularly beta-lactam/beta-lactamase inhibitor combinations; however, they can confidently predict sensitivity for a range of commonly used antimicrobial agents. This suggests that infection specialists can use these results to narrow antimicrobial therapy with a good degree of certainty, improving not only patient care but also antimicrobial stewardship.

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Abstract 3145

**Antimicrobial resistance surveillance data of Helicobacter pylori in Belgium (2016-2019)**

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**Background:** Resistance to antibiotics is the major cause of treatment failure of Helicobacter pylori (HP) infection and recommendations of HP eradication therapy schemes are based on the resistance levels among the treatment-naive population. This study aimed to monitor primary antimicrobial resistance rates of HP in Belgium.

**Materials/methods:** Between Jan. 2016 and Oct. 2019, more than 16000 gastric biopsy specimens of patients attending upper gastrointestinal endoscopy (around 85 % originated from five large endoscopy clinics located in three different cities) were referred to the national reference laboratory for HP detection either by culture and/or by PCR (Amplidiag® H. pylori +ClariR PCR assay, Mobidiag). In vitro susceptibility testing to clarithromycin (CLA), metronidazole (MTZ), levofloxacin (LVX), amoxicillin (AMX) and tetracycline (TET) was performed using gradient strip (Etest, bioMérieux) diffusion method and interpreted according to EUCAST clinical breakpoints. Isolates from patients known to have received previous eradication therapy were excluded from the analysis.

**Results:** In total, 3310 samples were positive for HP by culture and/or by PCR. The HP positive rate was significantly higher in period where first-line PCR was performed compared to first-line culture (19.3% vs 17.7%; p=0.01). The mean primary resistance proportions in 2019 were of 20.6% for CLA, 39.7% for MTZ and 24.5% for LVX, while resistance rates to AMX and TET remained constantly less than 1%. Double drug resistance (CLA/MTZ) rate significantly increased yearly from 2016 to 2019 (8.0% to 12.0%; p=0.04), while the triple resistance (CLA/MTZ/LVX) rate was also higher in 2019 compared to 2016 (5.4% vs 4.1%). The primary resistance to MTZ was significantly higher in females while higher resistance rates to CLA and to LVX were found in subjects aged > 40 years.

**Conclusions:** High resistance rates to CLA, MTZ and LVX together with the significant trend of increase in double drug resistance [CLA/MTZ] rate observed in Belgium support documented susceptibility guided therapy of H. pylori infection instead of empirical treatment. Resistance surveillance data of H. pylori are important to optimize the therapeutic strategies.

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Extracorporeal membrane oxygenation does not impact the pharmacokinetics of liposomal amphotericin B

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Background: Extracorporeal membrane oxygenation (ECMO) is a temporary life support technique which is increasingly used for cardiac and/or respiratory failure. Amphotericin B is a major antifungal drug with a broad-spectrum activity. To circumvent its renal toxicity, a liposomal formulation (L-AmB) was developed which is extensively used in the Intensive Care Unit (ICU). Even though the influence of ECMO on pharmacokinetics (PK) has been demonstrated for many drugs very little data relating to the effect of ECMO on L-AmB pharmacokinetics has been reported to date.

Materials/methods: Six-point PK profiles of L-AmB were analysed to monitor the efficacy of treatment in three patients undergoing ECMO. Monte Carlo simulations were performed, in parallel for each patient, based on the L-AmB population pharmacokinetic model published by Würthwein et al. for hematopoietic stem cell recipients. The Empirical Bayes Estimates of PK parameters were subsequently computed, and the most likely kinetic profile of the patient deduced. This profile was used to estimate the Area Under the Curve (AUC) and the through concentration (Cmin) for each individual patient.

Results: Estimated AUCs were 176.6, 113.0 and 92.7 mg.h/L and estimated Cmin were 4.0, 1.9 and 2.4 mg/L for the three patients, respectively. PK profiles of Patients 2 and 3 were determined before steady state was reached, leading to lower AUCs and through concentrations compared with Patient 1. However, estimated profiles were consistent with observed concentrations in all three patients.

Conclusions: Estimated Cmin at T24 after the start of infusion and estimated AUCs were similar to those reported in ICU patients with or without ECMO. Moreover, our study does not appear to highlight any difference in L-AmB pharmacokinetics between ICU patients undergoing ECMO and hematopoietic stem cell recipients, even before reaching steady state. Based on these preliminary results, no L-AmB dose adjustment seems necessary for patients undergoing ECMO. These results need to be confirmed in a larger cohort.

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Clinical and epidemiological characteristics of infective endocarditis with negative blood cultures: a multi-centre case-series in the south of Spain

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Background: Negative blood-cultures infective endocarditis (NBC-IE) account for 3-31% of all infective endocarditis (IE) and, historically, these patients suffers of worse outcome due to delay in diagnosis, inappropriate antimicrobial therapy and frequent need for surgery.

Materials/methods: The study included all adult patients, prospectively recruited from eight hospitals in Andalusia region (Spain), with definite IE diagnosis, according to modified Duke criteria, with at least two sets of blood-cultures drawn and with hospital admission between 2008 and 2018. In the case of NBC-IE, systematic serological assessment for C.burnetii, Bartonella spp, M.pneumoniae and L.pneumophila was provided as well as polymerase chain reaction (PCR) analysis and culture on valvular surgical specimens. Exclusion criteria: concomitant infected intracardiac-device and life expectancy less than 48 hours since admission. Positive blood-cultures infective endocarditis (PBC-IE) refers to consistent with IE microorganism recovery from blood-cultures according to modified Duke criteria. Main aims were to investigate NBC-IE group features comparing to PBC-IE counterpart and to describe non-blood-cultures-made etiologies.

Results: One-thousand-and-nine patients were included whom 921 (91.2%) had PBC-IE while 88 (8.8%) with NBC-IE. Six-hundred-seventy-one (66.5%) were male and median age was 67 years (IQR 55-75). Previous antibiotic (OR 5.3, CI95% 3.3-8.3) and community-acquired onset (OR 2.3, CI95% 1.4-3.9) were more frequent in the NBC-IE. Previous vascular manipulation (OR 2.2, CI95% 1.3-3.2) was significantly associated with PBC-IE. A significant proportion of patients with NBC-IE required cardiac-surgery (57% vs 37%, p=0.001) while no statistical difference regarding in-hospital/30-days mortality and length of in-hospital were found. Non-bloodculture-made diagnosis was achieved for 34 patients, of whom 26 (76.5%) with PCR or culture on surgical specimen (figure 1).

Conclusions: This case-series revealed no difference, regarding clinical complications and mortality, between PBC-IE and NBC-IE despite a significant higher cardiac-surgery requirement in the latter. C. burnetii and T. whipplei were confirmed as fastidious pathogens with a remarkable amount of surgical diagnosis through valvular PCR analysis or culture. Therefore, several traditional bacterial etiologies could have been missed because of prompt antibiotic courses. To maximize the chances to reach a microbiological diagnosis, is strongly recommended to delay any antimicrobial treatment, according to patient’s clinical stability, after correct blood samples withdrawal.
Clinical experience of dalbavancin in infectious endocarditis: stratifying its impact on treatment

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Background: Dalbavancin (DAL) is approved for SSTI treatment caused by Gram-positive cocci (GPC). Recently, it has been used, off-label, as part of Infectious Endocarditis (IE) treatment, although evidence is low.

There is little experience with prolonged IE treatment with DAL, as it is generally indicated as consolidation therapy. Assessing the impact of DAL in IE treatment is challenging.

Objective: To describe our experience on IE cases treated with DAL, its efficacy, safety profile and the impact on their treatment.

Materials/methods: Retrospective, observational study of IE adult-patients treated with DAL, during 2016-2018. The impact of DAL on the IE treatment was classified as:

- Medium: when DAL was given for ≥7 days, but it was <50% of total treatment.
- High: when DAL was given for ≥7 days and represent ≥50% of total treatment.

We analyzed clinical characteristics, outcome, adverse effects, economic impact of savings in hospitalization days.

Results: Overall, of the 150 IE cases treated during the study period, 119 were caused by GPC. 14 patients (9.3%) of the total and 11.8% of the GPC IE cases received DAL as part of their treatment; 85.7% were males, median age was 61y. The majority were patients with aortic IE (8 cases, 57.1%), prosthetic IE (8, 57.1%), 5 (35.7%) were due to S. aureus and 7 (50%) underwent surgery.

According to our classification, in 4 cases DAL had a HIGH impact on treatment and in 10 a MEDIUM impact.

Median treatment days was 14 (range:19-98) and 85.7% were treated with 1,500mg every two weeks.

Treatment tolerance was good, two patients had a mild adverse event. After six months follow-up, all cases were cured without recurrences. Moreover, 12 patients (85.7%) could be treated as outpatients. After considering DAL and hospitalization-days cost, we calculated an average saving of 7,119 euros per-patient.

Conclusions: Dalbavancin has been used mostly as a sequential IE treatment, only in four patients DAL had a high impact on treatment. Dalbavancin is safe and well-tolerated, even in larger treatments and allows the outpatient management, reducing hospital stay cost. Future IE series treated with dalbavancin must assess its impact on treatment.

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Abstract 3160

Implementing antibiotic stewardship in humanitarian contexts: MSF’s experience
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Background: Antibiotic resistance (ABR) is a significant threat to human health worldwide. MSF has implemented 11 antibiotic stewardship (ABS) programmes, aiming to be effective, sustainable and context-adapted. Inpatient surgery, neonatal and burns units, and services managing immunocompromised patients (e.g. malnourished children) were prioritized for implementation.

Materials/methods: ABS programmes are led by non-specialised doctors, trained by infectious disease physicians. Tools developed to standardise implementation include context-adapted guidelines (given heterogeneity in ABR) and surveillance systems to facilitate local cumulative antibiograms.

Results: Median implementation time was six months. Resistance rates in clinically significant isolates were higher in the Middle East. In 2018, 59% of samples from Aden had at least one multi-resistant organism (MRO), with 70% extended spectrum beta-lactamase (ESBL)-producing enterobacteriaceae; in Amman, 51% of samples had at least one MRO. Carbapenem-resistant enterobacteriaceae were identified in five of six projects in the Middle East. By comparison, 24% of the enterobacteriaceae in Mali were ESBL-producers. Higher rates of resistance (such as those in the Middle East) tend to be associated with more restrictive ABS programmes. Lessons learned include the need to strengthen infection prevention and control alongside, or before, ABS programme implementation. Access to microbiology should be implemented after strengthening stewardship.

Conclusions: Implementing successful stewardship programs in humanitarian contexts is feasible. A restrictive model of stewardship appears to be easier to implement. Antibiotic costs and human resource constraints limit duplication of the ABS model in public hospitals in contexts where MSF works.

Table 1 MSF Antibiotic Stewardship Programmes

<table>
<thead>
<tr>
<th>Location</th>
<th>Year of implementation</th>
<th>Diagnostic provider</th>
<th>Unit type</th>
<th>Stewardship FTE*</th>
<th>No. of beds</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amman, Jordan</td>
<td>2013</td>
<td>MSF</td>
<td>Trauma/osteomyelitis</td>
<td>1FTE</td>
<td>148</td>
</tr>
<tr>
<td>Koutiala, Mali</td>
<td>2013</td>
<td>MSF</td>
<td>Paediatrics/malnutrition</td>
<td>1FTE</td>
<td>185</td>
</tr>
<tr>
<td>Port au Prince, Haiti</td>
<td>2017</td>
<td>External</td>
<td>Burns</td>
<td>1FTE</td>
<td>40</td>
</tr>
<tr>
<td>Zahle, Lebanon</td>
<td>2017</td>
<td>External</td>
<td>Paediatric intensive care</td>
<td>0.5FTE</td>
<td>24</td>
</tr>
<tr>
<td>Aden, Yemen</td>
<td>2017</td>
<td>MSF</td>
<td>Trauma</td>
<td>1FTE</td>
<td>105</td>
</tr>
<tr>
<td>Madarounfa, Niger</td>
<td>2018</td>
<td>Epicentre</td>
<td>Paediatrics/malnutrition</td>
<td>1FTE</td>
<td>115-200</td>
</tr>
<tr>
<td>Baghdad, Iraq</td>
<td>2018</td>
<td>External</td>
<td>Trauma/osteomyelitis</td>
<td>0.5 FTE</td>
<td>20</td>
</tr>
<tr>
<td>Gaza, Palestine</td>
<td>2018</td>
<td>External</td>
<td>Trauma/osteomyelitis</td>
<td>1FTE</td>
<td>27</td>
</tr>
<tr>
<td>Bangui, CAR</td>
<td>2018</td>
<td>MSF [since 2019]</td>
<td>Trauma</td>
<td>1.5 FTE</td>
<td>80</td>
</tr>
<tr>
<td>Monrovia, Liberia</td>
<td>2019</td>
<td>MSF [since 2019]</td>
<td>Paediatrics</td>
<td>0.5FTE</td>
<td>92</td>
</tr>
<tr>
<td>Qayarrah, Iraq</td>
<td>2019</td>
<td>External</td>
<td>General hospital/burns</td>
<td>0.5FTE</td>
<td>62</td>
</tr>
</tbody>
</table>

*FTE: full time equivalent staff

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Abstract 3161

Infectious complications in kidney transplant recipients: a prospective cohort study

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Background: Although Infectious complications are a major cause of morbidity and mortality in kidney transplant (KT) recipients, little is known about their natural history and determinants at a population level in the recent era.

Materials/methods: Nationwide cohort including all consecutive patients from 6 french centers, receiving a kidney transplantation from 2000 to 2015 with prospective uniform and quality-checked extensive data collection including a systematic record of post-transplant infectious complications (site and pathogen involved).

Results: 9,563 KT recipients were included with a median follow-up time post-transplant of 7 years (IQR 4-10). During the follow-up, 11,173 infectious complications were diagnosed in 4,482 patients. The first infectious episode occurred after a median 192 days (IQR 23–852) after KT. Infections were bacterial (n=6,119, 54.7%), viral (n=1,912, 17.1%), fungal (n=462, 4.1%) or parasitic (92, 0.9%), and 2,583 (23.1%) where from unknown pathogen. Main sites were upper urinary tract (n=4,636, 41.5%), followed by lower respiratory tract (2,546, 22.8%), GI tract (n=1051, 9.4%), and skin (977, 8.7%). Main pathogens were bacterial: Enterobacteriaceae (3,522, 31.5%), staphylococci (627, 5.6%), enterococci (545, 4.9%), pseudomonas (446, 4%), Clostridium difficile (189, 1.7%), tuberculous and non tuberculous mycobacteria (105, 0.9%) and Streptococcus pneumoniae (103, 0.9%); viral: Cytomegalovirus (626, 5.6%), Varicello-zoster virus (582, 5.2%), BK virus (231, 2.1%), Norovirus (129, 1.6%), Hepatitis E virus (82, 0.7%); fungal: Pneumocystis jiroveci (138, 1.2%), candida (129, 1.2%) and aspergillus (108, 1%). Infectious episodes were associated with an increased risk of death (p<0.001). The main independent determinants for infection were: recipient age, female gender, history of diabetes, hypertension, major cardiovascular events, induction treatment, eGFR at 1-year post KT, acute rejection, donor age and graft rank (p<0.001 for all comparisons).

Conclusions: In this first population-based assessment of infections after KT, upper urinary tract and lower respiratory tract infections were the most frequent infections. Improvement of prevention measures would prevent many of them. These results suggest the potential for a data driven approach of infectious disease to improve patients risk stratification and help clinicians in the clinical management and immunosuppressive regimens adaptation.

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An unusual case of a Spanish traveller patient with chyluria and molecular diagnosis of schistosomiasis

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Background: Schistosomiasis is a Neglected Tropical Diseases that affects about 250 million of people in tropical and subtropical areas and also in travelers. The infection occurs after a contact with cercariae contaminated water, often clinically silent and after a long-term of time presenting serious damage in organs. Schistosoma mansoni adult worms reside in mesenteric veins causing intestinal and hepatosplenic schistosomiasis. Sporadically, eggs and worms are found outside the portal system, causing ectopic schistosomiasis.

The recommended treatment with praziquantel (40 mg/Kg) achieve a cure rate of 77%, and repeated treatment is often needed for a complete cure. In infected travelers, the diagnosis and treatment of schistosomiasis is a challenge because the elimination of eggs is very scarce compared to infected people in endemic areas of schistosomiasis.

Materials/methods: We present a rare case of schistosomiasis in a Spanish teenager who, after 10 months of a travel to Puerto Rico, presented an intense chyluria and eosinophilia (>900/mm3), without other symptoms. Tests to rule out microfilariae, including Knott’s test, thick drop, serology with filarial recombinant antigens (Loa loa, Onchocerca, Wuchereria) and PCR for filaria were negative. Strongiloides stercoralis [PCR and serology] and Toxocara [serology] were discarded.

Schistosomiasis mansoni was diagnosed through serology tests and specific S. mansoni DNA detection by LAMP [Loop-mediated isothermal amplification] in feces, serum and urine. No Schistosoma eggs were observed in urine or feces by Kato-Katz slides and concentration. One month before treatment, the chyluria disappears and a normal isotopic lymphography rule out another cause of chyluria.

Results: Initial treatment was carried out in December 2018 with a single dose of praziquantel [40 mg/Kg]. Four months after treatment, the eosinophilia and LAMP assay remained positive. A second dose of praziquantel was administered in April 2019 but eosinophilia and LAMP remain positive after 12 months. Actually, a new treatment with praziquantel [40 mg/Kg, 3 doses/day] is being considered.

Conclusions: To our knowledge this is the first case of chyluric Schistosomiasis caused by S. mansoni.

New specific and sensitive molecular techniques as LAMP can help diagnosis and monitoring treatment of schistosomiasis, especially in patients with low parasitic load, as often occurs in travelers.

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Abstract 3163

Short-term peripheral venous catheter-related bloodstream infections
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Background: In the United States, nosocomial bloodstream infections (BSIs) are the eighth-leading cause of mortality, with approximately 31,000 deaths per year. Most nosocomial BSIs are associated with intravascular catheter use. Almost 80% of hospital admissions involve an average of two peripheral intravenous catheters (PIVC) per patient, and PIVC-related BSI rates range from 0.1 to 0.18 per 1000-patient days. To improve nursing satisfaction, a new institutional policy change was implemented to extend duration between required PIVC change in our local hospital. We aimed to evaluate if this change was associated with higher rate of BSI.

Materials/methods: The Audie L Murphy South Texas Veterans Health Care system, a 268-bed tertiary care center, implemented a policy whereby PIVC was changed every 3 days to every 7 days or as needed (whichever was shorter). We performed a retrospective chart review of pre- and post-intervention BSI rates. Patients admitted to acute care units – surgical ICU, surgical ward, medical ward, medical ICU, cardiac ICU, and intermediate care unit – were included for analysis. May to October 2016 was defined as the pre-intervention period, and September 2017 to February 2018 as post-intervention. PIVC-related BSI was defined as BSI with a recognized non-commensal pathogen on or after the 4th day of those patients with PIVC present for 3 or more consecutive days. We excluded those with concomitant central venous catheter, or BSI secondary to another site. BSI rates were compared between the pre- and post-intervention period using the chi-square test.

Results: A total of 102 BSI cases in 14553 bed-days occurred during the pre-intervention period; 8 of the 102 cases had no identifiable source, and 2 of those met the definition of PIVC-related BSI. Similarly, 61 BSI cases in 14108 bed-days occurred during the post-intervention period; 14 cases had no identifiable source, and 3 of those were PIVC-related BSI. PIVC-related BSI rate pre-intervention was 0.14 per 1000 bed-days, compared to post-intervention rate of 0.21 per 1000 bed-days (p=0.6298).

Conclusions: Decreasing the frequency of scheduled PIVC changes from every 3 to every 7 days (or as needed) did not appear to increase the rate of PIVC-related BSI in our institution.

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**Abstract 3164**

**Daptomycin plus fosfomycin or ceftaroline is active in vitro against high-level aminoglycoside-resistant and vancomycin-resistant or vancomycin-susceptible Enterococcus spp. strains**

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**Background:** Together Enterococcus faecalis (EFS) and Enterococcus faecium (EFM) account for up to 15% of infectious endocarditis. Multidrug resistance to aminoglycosides (HLAR), beta-lactams and vancomycin often occur and therefore synergistic bactericidal combinations of two antibiotics are recommended. This *in vitro* synergy study evaluates the activity of DAP+FOM or CTL against eight HLAR Enterococcus strains.

**Materials/methods:** Four VRE EFM and four EFS [two VRE and two VSE] strains were tested. DAP, CFT, FOM MICs/MBCs were determined by the microdilution broth method. *In vitro* synergy was performed by time-kill studies (TKC). TKC antibiotic concentrations ranged from ¼xMIC to 1xMIC and two inocula were tested: a standard inoculum (SI) equal to 10^5-6 cfu/ml and a high inoculum (HI) equal to 10^8 cfu/ml mimicking the cfu density in mature infected vegetations. The results of the combination at 24h were compared with those of the most active single drug; synergy was defined as a ≥2-log increase in killing. Bactericidal activity (BA) was defined as a ≥3-log_10 decrease in cfu/ml of the initial inoculum at 24h.

**Results:** EFM strains were ampicillin and ceftaroline resistant (MIC/MBC ≥ 32 µg/mL). EFS strains were ampicillin (MIC/MBC ≤ 2/2 µg/mL) and ceftaroline (MIC/MBC ≤ 4/16 µg/mL) susceptible. All the strains were FOM resistant (MIC/MBC ≥ 64 µg/mL). VRE-1 was DAP resistant (MIC/MBC = 4/8 µg/mL) and VSE-188 showed daptomycin non-susceptibility when grown under sub inhibitory daptomycin conditions (MIC/MBC = 8/16 µg/mL). TKC results are displayed in the table below.

<table>
<thead>
<tr>
<th>STRAIN</th>
<th>DAP+FOM (Inoculum)</th>
<th>DAP+FOM (High)</th>
<th>DAP+CTL (Standard)</th>
<th>DAP+CTL (High)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VSE-188 (EFS)</td>
<td>Synergy</td>
<td>Indifference</td>
<td>Synergy</td>
<td>Indifference</td>
</tr>
<tr>
<td>VSE-324 (EFS)</td>
<td>Synergy</td>
<td>Indifference</td>
<td>Synergy</td>
<td>Synergy + BA</td>
</tr>
<tr>
<td>VRE-31 (EFS)</td>
<td>Synergy</td>
<td>Indifference</td>
<td>Synergy</td>
<td>Indifference</td>
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<tr>
<td>VRE-32 (EFS)</td>
<td>Synergy</td>
<td>Indifference</td>
<td>Synergy</td>
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</tr>
<tr>
<td>VRE-1 (EFM)</td>
<td>Synergy</td>
<td>Indifference</td>
<td>Synergy</td>
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<tr>
<td>VRE-35 (EFM)</td>
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<td>VRE-98 (EFM)</td>
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<td>VRE-99 (EFM)</td>
<td>Synergy</td>
<td>Indifference</td>
<td>Synergy</td>
<td>Indifference</td>
</tr>
</tbody>
</table>

Both combinations were effective in preventing the development of DAP-resistance in the VRE-1 and VSE-188 strains.

**Conclusions:** *In vitro* DAP+FOM was as active as DAP+CTL, suggesting that these combinations could be effective in treating Enterococcus infections and thus worthy of further studies in the *in vivo* experimental model.

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Tolerance of pyrazinamide for the treatment of tuberculosis in elderly patients over 75 years

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Background: Pyrazinamide for the treatment of tuberculosis in patients over 75 years old has a controversial tolerance profile. Our aim was to assess frequency, severity and risk factors of adverse events (AEs) in elderly subjects treated for tuberculosis with or without pyrazinamide.

Materials/methods: Retrospective monocentric study at Toulouse University Hospital (France) including patients over 75 years treated for active tuberculosis between 2008 and 2018. The frequency, type, severity, accountability of AEs of anti-tuberculosis treatment were compared between patients receiving or not pyrazinamide. The risk factors for AEs were investigated by univariate and multivariate analyses by binary logistic regression.

Results: Among the 110 patients included, 54 (49.1%) received pyrazinamide (group 1) and 56 (50.9%) received pyrazinamide free-regimens (group 2). Groups were comparable regarding the severity and locations of tuberculosis. Compared to group 1, patients in group 2 were older (aged over 85: 46.4% versus 24%, p=0.025), less autonomous (median Katz ADL: 5.0 versus 6.0, p=0.049), had higher levels of transaminases (median SGOT: 29 versus 23 IU.L⁻¹, p=0.028) and received more often empirical tuberculosis treatments (66.1% versus 42.6%, p=0.013). AEs related to anti-tuberculosis treatment occurred in 31/54 (57.4%) in group 1 and 14/56 (25%) in group 2 (p=0.0017), with a trend for higher rates of allergy and digestive disorders, but not hepatotoxicity, in group 1. Pyrazinamide-related AEs occurred in 22/54 (40.7%) of exposed subjects, leading to stop pyrazinamide in 14/22 (63.6%). AEs definitely or potentially related to ethambutol occurred in 13/44 (31.7%) of exposed subjects in group 1, and 3/52 (5.4%) in group 2 (p=0.0025). Serious AEs occurred in 13/31 (41.9%) in group 1, and 5/14 (35.7%) in group 2 (p=0.69). Three deaths potentially related to AE occurred in group 1 and none in group 2. Independent risk factors for AEs of anti-tuberculosis treatment were the use of pyrazinamide [odds ratio 4.5, CI95 1.7-12, p=0.003] and diabetes [odds ratio 3.5, CI95 1.06-11.6, p=0.04]. No predictive factors of pyrazinamide-related AEs were identified.

Conclusions: In elderly French subjects, use of pyrazinamide was associated with more frequent AEs of anti-tuberculosis treatment and of ethambutol, and its toxicity was not predictable.

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Abstract 3168

Impact of beta-lactam allergy label on preoperative antibiotic prophylaxis
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Background: Surgical site infection (SSI) is a common post-procedure complication which may be prevented by adhering to established recommendations, including the administration of preoperative antibiotic prophylaxis. Patients with a beta-lactam allergy (BLA) have an increased risk of SSI, which has been attributed to the lack of optimal preoperative antibiotic administration.

Materials/methods: This was a single-center, retrospective, matched cohort study of adult patients who underwent a clean or clean-contaminated abdominal hysterectomy, coronary artery bypass graft (CABG), colon surgery, or knee replacement between July 1, 2018 and June 30, 2019. Patients with a BLA label were matched to patients without a BLA label based on procedure, age, and BMI. The primary outcome was the rate of appropriate preoperative antibiotic prophylaxis, defined as concordance with the institution’s guideline. The guideline includes recommendations for appropriate antibiotic selection based on the presence or absence of a severe BLA and MRSA risk factors as well as appropriate antibiotic dose timing prior to incision. Secondary endpoints included surgical site infection (SSI), length of stay (LOS), mortality, and colonization or infection with a multidrug resistant organism (MDRO).

Results: Among the 867 procedures identified, 160 patients had a BLA at the time of the procedure and 130 matches were identified. Consequently, a total of 260 patients were included. Knee replacement (38%) was the most common procedure type, followed by hysterectomy (25%), colorectal (18%), and CABG (18%). Among patients with a BLA label, severe IgE-mediated reaction (44%) was most the common reaction type, followed by mild-moderate (32%), unknown (13%), and intolerance (10%). Appropriate preoperative antibiotic prophylaxis was significantly higher among patients without a BLA (76% versus 37%, p<0.001). This difference remained when removing the requirement to assess for patient-specific MRSA risk factors (80% versus 39%, p<0.001). Among the 54 patients with a mild-moderate reaction or intolerance, 29 (54%) patients received antibiotics that would have been appropriate only if the patient had a severe BLA. No differences in SSI, LOS, mortality, and MDROs were observed.

Conclusions: Patients with a BLA were more likely to receive inappropriate preoperative antibiotic prophylaxis compared to patients without a BLA.

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Efficacy of temocillin versus carbapenems for the treatment of extended spectrum beta-lactamase-producing Enterobacteriaceae urinary tract infections: a case control study

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Background: Temocillin may represent an alternative to carbapenems for the management of ESBL-E UTI. However, clinical data regarding its efficacy are scarce.

Materials/methods: Multicenter retrospective case-control study (6 French tertiary-care hospitals), to assess the efficacy of definitive therapy with temocillin or carbapenems in patients with ESBL-E UTI. Cases and controls were adults with definite diagnosis of ESBL-E UTI between January-2015 and October-2019. Cases were treated with temocillin for ≥50% of the effective antibiotic therapy duration [TEMO-arm]. Control exclusively received carbapenem over the effective antibiotic therapy duration [CP-arm]. They were statistically matched (1:1 ratio) on sex and age. Primary endpoint was clinical response at the End-of-Treatment [EOT]. Secondary endpoint was mortality within 3-months after the start of effective antibiotic therapy. Analysis using descriptive statistics and logistic regression.

Results: A total of 178 patients were screened for eligibility and 142 (80%) retained in analysis after statistical matching [71 cases, 71 controls]. Median age was 69.7-years [IQR,58.3-68.3] and 94(66%) were male. There was no difference between TEMO-arm and CP-arm for Charlson’ score [4 [IQR,2-6] vs. 3 [IQR,2-5], p=0.362] and immunocompromised status [53/71(56%) vs. 48/71(53%), p=0.611]. A total of 49(34%) patients were renal-transplant recipients [SOT-status, p=0.717], 47(33%) had bacteremia [p=1.000] and 18(13%) had sepsis [p=0.382]. Microorganisms involved were similar between arms [p=0.994]: K.pneumoniae in 59/142(42%), E.coli in 55/142(39%), Enterobacter spp. in 24/142(17%), others in 4/142(2%). Overall, time to effective antibiotic therapy was 0-days [IQR,0-2], 29/71(41%) patients received carbapenems as empirical therapy in TEMO-arm and 32/71(45%) in CP-arm. Empirical antibiotic therapy was significantly more often effective in TEMO-arm [OR=2.71 [95%CI,1.33-5.50], p-value=0.006]. In TEMO-arm, 6/71(8%) patients received temocillin in first line, for others temocillin was initiated after 3-days of effective therapy [IQR,1-4]. Temocillin was given at 2g-b.i.d [IQR,1-2] for 11-days [IQR,8-14], sparing 832-days of carbapenems. Overall, effective antibiotic duration was significantly shorter in TEMO-arm [14-days [IQR,12-16] vs. 16-days [14-21], OR=0.93 [95%CI,0.88-0.99], p=0.017]. Clinical response rate at EOT was 68/71(96%) in TEMO-arm vs. 70/71(95%) in CP-arm, without difference after adjustment on SOT-status [aOR=0.33, [95%CI,0.03-3.22], p=0.337]. There was no difference in mortality [10/142(7%), p=0.981].

Conclusions: Temocillin efficacy seems comparable to carbapenems in the treatment of ESBL-E UTI.

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Prevalence of antibiotic resistance among Enterobacterales isolates recovered from urinary samples in France


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Abstract third-party references: On behalf of the GMC study group

Background: Antibiotic resistance in Enterobacterales is a major public health issue and community-acquired urinary tract infections (cUTIs) are the most frequent infections due to Enterobacterales in the community. The worldwide spread of ESBL-producing isolates (ESBL-E), especially Escherichia coli, is of particular concern because of its spread in the community. In France, 3.6% of cUTI are due to ESBL-E. Their management was recently updated in France. The aim of the study was to assess the prevalence of resistance to antibiotics recommended for the treatment of UTI in France.

Materials/methods: Twenty-seven French clinical laboratories participated in the study. All Enterobacterales isolates collected from urinary samples between September 2017 and August 2018 were retrospectively included. Duplicates were excluded. Antimicrobial susceptibility testing and interpretation were performed according to EUCAST guidelines 2017.

Results: A total of 135,065 clinical isolates were included among which 72.1% E. coli, 9.4% Klebsiella pneumonia, and 5.8% Proteus mirabilis. ESBL-E accounted for 6.7%, while ESBL-E prevalence was significantly different among French regions, ranging from 3.9% in Centre to 11.7% in Ile-de-France (P<0.01). ESBL-E rate ranged from 3.4% [outpatients] to 15.9% [geriatric wards]. The rate of ESBL-E was significantly lower among E. coli than among K. pneumoniae isolates (5.6% vs 19.5% respectively, P<0.01).

Overall, the rates of resistance were lower for fosfomycin (4.6%), mecillinam (11.8%) and nitrofurantoin (15.2%), than for ciprofloxacin (16.7%), cotrimoxazole (30.4%) and amoxicillin-clavulanate (40.7%). In E. coli, the prevalence of fosfomycin and nitrofurantoin resistance and was both 1.1%.

The 3 main species displayed specific profiles of resistance, P mirabilis being significantly more susceptible to amoxicillin-clavulanate (11.8%) and cefotaxime (1.5%) but more resistant to cotrimoxazole (39.7%) and mecillinam (36.6%). K. pneumoniae was more resistant to fosfomycin (22.1%), cefotaxime (30.1%), nitrofurantoin (40.6%) and ciprofloxacin (32.0%). E. coli was significantly less resistant to nitrofurantoin (1.1%) and fosfomycin (1.1%).

Conclusions: Our results show heterogeneous rates of ESBL-E in France depending on the French region, the clinical context, and the bacterial species. Consequently, probabilistic treatment should be adapted to the clinical, microbiological and local context. Longitudinal studies are needed to assess the evolution of the prevalence of antibiotic resistance prevalence in urinary tract isolates.

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Abstract 3174

Clinical and economic outcome evaluation of cefepime 4 grams/day extended infusion in pneumonia and sepsis

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Background: Cefepime displays time-dependent bactericidal activity, and its efficacy is optimized when free drug concentrations exceed the minimum inhibitory concentration (MIC) for at least 60-70% of the dosing interval. Cefepime regimens utilizing 1 gram infused over 3 hours every 6 hours are able to achieve pharmacodynamic efficacy against bacteria with an MIC of ≤8 mcg/mL in Monte Carlo simulations. This regimen’s impact has not been evaluated in clinical practice. UMass Memorial Medical Center in Massachusetts, USA changed its cefepime intermittent infusion (II) protocol, 2 grams infused over 30 minutes every 8 hours to an extended infusion protocol (EI), 1 gram infused over 3 hours every 6 hours. Dosing was adjusted for renal function. The objective of this study was to compare clinical and economic outcomes between II and EI.

Materials/methods: A retrospective cohort study was conducted on inpatients who received EI or II between 2016 and 2018. Inclusion criteria were: age > 18 years, diagnosis of sepsis or pneumonia and prescribed cefepime. Exclusion criteria included: receipt of an additional beta-lactam with activity against Pseudomonas aeruginosa, receipt of both EI and II, comfort measures only, febrile neutropenia with unknown source or organism resistant to cefepime.

Results: The study included 111 patients who received II and 93 who received EI. Baseline characteristics were similar between the two groups. Hospital and intensive care unit (ICU) length of stay was not different between groups (hospital days: II: 7.67 vs EI: 8.07, p=0.67; ICU days: II: 2.6 vs EI: 2.2, p=0.15). Mortality was infrequent in both groups, though deaths were numerically fewer in EI (II: 5.4% vs EI: 3.2%, p=0.45). 90-day readmission rates were similar between groups (II 61.3% vs EI 67.7%, p=0.34). Cefepime cost per patient was lower in EI (average cost II:$86.06 vs EI $43.39).

Conclusions: EI is feasible to administer in the inpatient setting, optimizes pharmacodynamics and did not result in different clinical outcomes in this study. Costs may be reduced by utilizing a prolonged infusion dosing regimen with 4 grams/day vs 6 grams/day. Larger studies should be conducted to evaluate the impact of cefepime prolonged infusion on inpatient mortality.

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Abstract 3175

**Infective endocarditis in older adults: distinguishing features**

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**Abstract third-party references:** FAPERJ/Brazil

**Background:** Infective endocarditis (IE) is a severe disease, especially in older adults.

**Materials/methods:** This is a cohort of adults with definite IE enrolled January 2006 - September 2019. The International Collaboration on Endocarditis case report form was used to collect data. Patients older than 60 years were compared to the remaining cohort in order to identify distinguishing characteristics of IE in older adults. Jamovi 1.0.7 software was used for statistical analysis.

**Results:** Older adults corresponded to 93/359 (25.9%) episodes of IE; they were more often male (72% vs 60.2%, p=0.04) and had significantly more associated conditions: heart failure (53.3% vs 35.7%, p=0.003), COPD (10.9% vs 2.7%, p=0.002), coronary artery disease (31.5% vs 61.1%, p<0.001), cerebrovascular disease (10.8% vs 4.9%, p=0.047), pacemakers (20.4% vs 8.3%, p=0.002), chronic renal failure (27.5% vs 17.2%, p=0.044), and neoplasia (12.9% vs 3.9%, p=0.002). Regarding previous procedures, they significantly more often had previous heart surgery (52.7% vs 32.2%, p<0.001), percutaneous cardiac interventions (10.9% vs 3.4%, p=0.006) and CABG (16.2% vs 2.3%, p<0.001). Older patients less often had rheumatic valvulopathy (20.2% vs 37.7%, p=0.002), but more often presented late prosthetic valve IE (25.7% vs 11.8%, p=0.006) and hospital-acquired IE (39.8% vs 24.5%, p=0.005). Differences regarding clinical features were that older patients less often had fever (88.2% vs 94.7%, p=0.034), embolism (35.2% vs 56.9%, p<0.001), including central nervous system events (12.2% vs 29.1%, p=0.025) and splenomegaly (10.5% vs 26.5%, p=0.002). Regarding etiology, older patients more often had enterococci (20.4% vs 7.5%, p<0.001) and less often had *viridans* group streptococci (16% vs 26%, p=0.047). They more often needed to be mechanically ventilated before surgery (30.3% vs 18%, p=0.015) and to have inotropes (33.7% vs 21.8%, p=0.028). Although older patients had surgical indication in 81.7%, only 66.3% were operated on; in comparison, of the 88.7% of younger patients for whom surgery was indicated, 94% were operated on. Mortality was significantly higher for older patients (43.0 vs 18.1%, p<0.001).

**Conclusions:** Older patients more often had associated comorbidities, late prosthetic IE, hospital-acquired infection and high mortality.

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Abstract 3176

**Retrospective study of nosocomial infections in patients with extracorporeal membrane oxygenation therapy in a coronary unit**

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**Background:** The use of extracorporeal membrane oxygenation therapy (ECMO) in the treatment of patients admitted to coronary units has increased. Data regarding infections in this population is scarce.

**Objective:** To describe the epidemiology of infections in patients with ECMO at a coronary unit, risk factors, outcome and factors associated with mortality.

**Materials/methods:** Retrospective study including all adult-patients admitted to the coronary unit between July 2013 and March 2019, with ECMO implanted for >48 hours.

Demographics, comorbidities, duration of ECMO, number and type of infections, other complications and outcome were collected. Risk factors related to infection and mortality were analyzed.

**Results:** Overall, 69 patients were admitted to the coronary unit and had an ECMO >48 hours. 82.5% were men, median age of 58 years, 75.4% had previous cardiac disease and cardiogenic shock was the main indication for ECMO (55.1%).

30.4% of patients were previously colonized and 14.5% had an infection prior to ECMO placement.

A total of 29 patients (42%) presented infection while on ECMO. Thirty-three episodes of infection were diagnosed, the most frequent were: VAP (19 cases, 57.6%), tracheobronchitis (3 cases, 9.1%), bacteremia (3 cases, 9.1%), SSTIs (3 cases, 9.1%) and CMV reactivation (3 cases, 9.1%). There were no ECMO-related infections. Most frequent non-infectious complications were: thrombopenia (50.7%), hypoxemia (47.8%), hemorrhage (29.9%) and acute renal failure (29.4%).

Mortality during ECMO was 39.1%, hospital mortality 46.4% and infection-related mortality 5.8%.

Patients who developed infection had lower survival, although the difference was not significant. The only variable related to infection development was: days on ECMO [OR 1.14, 95% CI 1.01-1.30, p=0.029] and the only variables related to mortality were lactic acidosis after ECMO [OR 2.08, 95% CI 1.19-3.62, p=0.009] and higher Cr after ECMO [OR 13.35, 95% CI 1.43-124.8, p=0.023].

**Conclusions:** Overall, 42% of patients in a coronary unit in ECMO >48h develop an infection, mostly VAP (57.6%) followed by tracheobronchitis (9.1%), bacteremias, CMV reactivation and SSTIs (9.1%) each.

Mortality in patients with ECMO was 46.4%, and infection-related mortality was 5.8%. The survival of patients who develop an infection is lower. The risk factor related to developing an infection is the ECMO duration.

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Prevalence of high- and low-risk human papilloma virus in the anus and rectum, vagina and pharynx of asymptomatic men and women attending a sexually-transmitted diseases clinic

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**Background:** There are gaps in knowledge regarding the epidemiology of high and low risk human papilloma virus [HPV] in people with risk factors for sexually transmitted diseases [STDs].

**Materials/methods:** A random sample of people attending an STD clinic in Tel Aviv were tested for the presence of HPV genotypes by rectal vaginal and throat swabs using the Anyplex\(^{TM}\) II (Seegene) kit which detects 19 high risk and 9 low-risk HPV genotypes. Data regarding sexual habits and medical history was obtained.

**Results:** Of 99 people included 77 (77.8%) were males. Mean age was 30.5 years. 52 (52.5%) were heterosexuals, 51 (51.5%) were men who have sex with men, 5 were sex workers, and 3 were HIV positive. 85 (85.9%) had a recent new sexual partner and 73 (73.7%) had >20 sexual partners. 66 (66.7%) reported anal intercourse and 91 (91.9%) oral intercourse. Only 25 (25.3%) used condoms regularly. 39 (39.4%) had an STD in their past. Only 16 people (16.2%) received HPV vaccine. 18 (18.2%) reported known HPV lesions in the past. 52 (52.5%) people were positive for HPV in at least one site, of these 42 (80.7%) had ≥1 high risk HPV genotype. HPV was most common in the vagina (12/21, 57.1%) and 8 (66.7%) had high risk HPV genotypes. 47 (51.1%) had positive HPV from the anus, of these 33 (70.2%) had high risk HPV. 7 (11.5%) had a positive HPV from the throat, of these in 5 (71.4%) HPV were high risk. The median number of HPV genotypes/person in HPV positive people was one (1-8). The most common HPV genotypes were HPV6, HPV42, HPV53 and HPV68. Of infected people 41 (78.8%) were HPV positive in only one body site, 9 (17.3%) in two sites and 2 women were infected in 3 sites. In 10 (90.9%) there was concordance in ≥1 genotype between ≥2 body sites.

**Conclusions:** In high-risk patients, carriage of HPV was common regardless of the presence of warts. Most of the prevalent HPV genotypes were carcinogenic. Most people were infected only in one body site but concordance between genotypes was high when multiple body sites were involved.

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Aims and challenges of founding a national network of young clinical microbiologists: a French experience

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Abstract third-party references: On the behalf of the RéJMiC [study group of French Microbiology Society]

Background: Residents and young clinical microbiologists (CM) sometimes experience difficulties in reaching their elders, connecting with their peers and accessing relevant information to build their career. Creating a network where specialty knowledge is shared, and professional issues discussed, can help and result in sustainable partnerships among the youngest. However, development of such networks is challenging and may face obstacles. The aim of the study was to share our one-year experience in France to promote the importance of young professional network creation.

Materials/methods: One-year post creation, founding members of RéJMiC [Réseau des Jeunes Microbiologistes Cliniques] [n=16] were consulted to assess the five biggest challenges faced in the network creation. To assess the extent of our network, data were extracted from RéJMiC Facebook group from 18 November 2018 to 18 November 2019.

Results: The following were found to be the most important steps toward the creation of the network:

1. Defining young microbiologists status and writing purposes of the network: promote knowledge sharing, bring together microbiologists from different backgrounds (bacteriology, virology, parasitology, mycology and infection control), ease access to information [up-to-date literature, available grants, ESCMID activities], collaborate with existing networks and societies (i.e. Réseau des Jeunes Infectiologues Français) through common projects

2. Reaching the national society for CM in France [Société Française de Microbiologie, SFM] by the written proposition of creating a network (cf. 1.)

3. Meeting on a regular basis (every 6 weeks) through conference calls with founding members

4. Building a local network with regional representatives in each university hospital in France

5. Communicating regularly through social media and SFM website

One year from creation, we reached 13/30 university hospitals in France, with presently a regional representative in each. A total of 269 members requested to join our closed Facebook groups from 53/101 counties in France [Fig.1]. Fifty percent of memberships were reached in one month, following a logarithm curve.

Conclusions: This one-year experience can be helpful for young CM willing to create their own national network. Future aims are to improve our communication skills through other social medias [Twitter, Instagram], further develop our network and strengthen ongoing collaborations.
Figure 1. Distribution of Facebook RéJMiC members in French countries

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Abstracts 2020

Abstract 3183

Neuroparacoccidioidomycosis: analysis of 10 cases observed in an endemic area in Argentina
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Background: To describe the epidemiological, clinical, imaging and evolutionary characteristics of patients diagnosed with paracoccidioidomycosis associated with the involvement of the central nervous system in the Hospital Escuela de Agudos Dr. Ramón Madariaga from 2012 to 2019.

Materials/methods: All cases with a diagnosis of paracoccidioidomycosis were reviewed. Those with neuroparacoccidioidomycosis were analyzed and studied prospectively from 2012 to 2019. Nuclear magnetic resonance imaging was reassessed by personnel specialized in diagnostic imaging.

Results: From 52 cases of paracoccidioidomycosis (PCM) who were assisted in our center in the period evaluated 10 (19.2%) of them were diagnosed as neuroparacoccidioidomycosis (NPCM). All were men, residents of the endemic zone, 100% smokers. Mean age of 52.5 (40-67 years). Concomitantly 1 patient had a diagnosis of stomach cancer and 1 patient with Hansen disease. 70% of the patients presented neurological symptoms at diagnosis. Of the 7 patients who neurological clinic, the most frequent symptoms were headache and weakness (57.1%), paresthesias and gait disorders (42.9%), vomiting, dizziness and paresis (28.6%), blurred vision (10%), involuntary movements (10%), seizures (10%) and dysarthria (10%). All patients presented respiratory compromise due to positive cultures (20%) or presence of concomitant infiltrate in patients with mucous involvement (30%) and nodal involvement (20%). Two patients had brain biopsy with pathology and positive culture. The presence of the fungus were by pathological anatomy in 70% and by culture in 60%. In the imaging assessment, the patients presented a unique brain lesion (60%), post contrast enhancement (90%), being peripheral in 66%, annular in 22% and nodular in 11%. Restricted diffusion was evident in 90% of the patients, and in 33% the restriction was slight. All patients began antifungal treatment. During hospitalization, 2 patients died due to complications secondary to hospitalization. Outpatient follow-up was abandoned by patients in most cases.

Conclusions: The presence of Paracoccidiodes spp by direct observation, culture or histopathology outside the CNS should make us extend the search towards cerebral compromise, which is why we consider it essential to request a nuclear magnetic resonance with gadolinium and an open communication with the image specialists about what we are looking for.

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Abstract 3184

**Lyme neuroborreliosis epidemiology in Denmark, 1996 to 2015**

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**Background:** Lyme's neuroborreliosis (LNB), a neuroinfection caused by *Borrelia burgdorferi sensu lato*, has recently been added to the list of notifiable diseases under European Union epidemiological surveillance aiming to achieve reliable information on the incidence of the disease and to assess the trend over time of LNB. We aimed to describe the seasonal effect on LNB incidence and to identify risk groups and high incidence regions as well as describe changes in yearly LNB incidence in Denmark.

**Materials/methods:** From all Danish Departments of Microbiology we identified all patients who performed a positive *B. burgdorferi* intrathecal antibody index between 1996 to 2015 (n= 2,791). From the Danish National Registries, we obtained data on gender, age, yearly income, highest educational attainment and county of residence for each year between 1996 to 2015 on all Danish residents. We calculated the number of LNB cases per month, and incidence and incidence ratios of LNB by comparing gender and categories of age, income, education, county of residency and calendar year.

**Results:** The average yearly incidence of LNB for the entire study period was 2.6 per 100.000 individuals. The number of LNB cases was highest in the months from July to November (p-value < 0.000001) with the number of new cases per month being lowest in March (2.8 cases of LNB/month) and highest in August (26.6 cases of LNB/month). The incidence per year was highest among men (3.0 LNB cases per 100.000 individuals), individuals aged 0-15 (4.2 LNB cases per 100.000 individuals), individuals with a yearly income of >449.000 DKK (3.6 LNB cases 100.000 individuals) and individuals with a master’s degree or higher (3.3 cases per 100.000 individuals). We observed the highest incidence per year in eastern Denmark. The incidence per year was 2.2 per 100.000 individuals in 1996-1999, rose to 2.7 in 2004-2007 and then declined again to 1.1 per 100.000 individuals in 2012-2015.

**Conclusions:** The monthly incidence of LNB was highest in late summer and early fall. The yearly incidence of LNB was increasing from 1996 to 2007 but thereafter declined to 2015, irrespective of gender, age, income, education or county of residency.

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Risk of mood-affective disorders and use of psychoanaleptics in Lyme Neuroborreliosis patients

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Background: We performed a population-based, nationwide cohort study to examine the association between LNB and mood affective disorders.

Materials/methods: We identified all Danish residents with a positive *Borrelia burgdorferi* intrathecal antibody index between 1995 and 2015 (n=2,898). From national registries, we identified a comparison cohort from the general population matched on gender and date of birth (n=28,980) and extracted data ICD-10 diagnoses and hospital contact due to psychiatric diseases as well as on type and dosage of prescribed medicine. We examined the short-term (<1 year) and long-term (>1 year) risk of all mood affective disorders (F30-F39), manic disorders (F30-F31), episodic depression (F32), periodic depression (F33) and persistent mood affective disorders (F34) by calculating hazard ratios (HR). We also compared the difference in the proportion of individuals with a hospital contact due to these diseases and a prescription for psychoanaleptics (N06) and antidepressants (N06A) between LNB patients and the comparison cohort. All analyses were performed with 95% confidence intervals (95% CI) and stratified according to gender and age (< versus >= 50 years of age).

Results: LNB patients were at increased long-term risk of mood affective disorders (HR 1.4, 95% CI: 1.1 to 1.8) and periodic depression (HR 1.7, 95% CI: 1.2 to 2.5) but not of any other diagnoses compared with the comparison cohort. LNB patients seemed to have more hospital contacts due to mood affective disorders, although the difference was not statistically significant. There was no difference in the proportion of individuals with a hospital contact due to any of the other psychiatric diseases examined. LNB patients were prescribed more psychoanaleptics [1 year after and 16-18 years after LNB diagnosis] and antidepressants [1-2 years and 8-18 years after LNB diagnosis]. In the stratified analyses, the increased risk of diagnosis, hospitalization and medicine prescription applied only for women aged >= 50 years.

Conclusions: Our data indicate that LNB patients are at increased risk of- and burden from mood affective disorders/depression and warrant an individualized follow-up after LNB with special emphasis on depression risk among women aged more than 50 years.

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Abstract 3186

A computerised decision support system (CDSS) for antibiotic prescribing in primary care: Antibioclic: implementation, adoption and sustainable use in the era of extended antimicrobial resistance.

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Background: Computerized decision support systems (CDSS) for antimicrobial prescribing could be effective and induce prolonged impact on practices. CDSS development for primary care and data regarding their implementation, use and adoption are scare.

Materials/methods: To describe the development, implementation, adoption and sustainable use of a French CDSS for antibiotic prescribing in primary care (Antibioclic), which targets 37 infectious diseases, is freely available 24/24-7/7 on a website since 2011, and as a smartphone application since 2017. Analysis of the requests performed between 2012 and 2018, and the results of 2 web-based cross-sectional studies conducted over 2-months in 2014 and 2019.

Results: The number of requests increased from a median of 796/day [IQR,578–989] in 2012 to 11,125/day [5,592–12,505] in 2018. Unique users increased from 414/day [245–494] in 2012 to 5,365/day [2,891–5,769] in 2018. The smartphone application was downloaded 22,970 times on Android and 15,200 times on iOS. Time to perform a request was 2 minutes [1·9–2·1]. Among 3,542,347 requests in 2018, 78% were for adults and an antibiotic was recommended systematically in 2,254,866 (63·7%), not systematically in 1,223,013 (34·5%), and not recommended in 64,468 (1·8%). Six situations accounted for ≥50% of requests: cystitis 504,428 (1·4·2%); acute otitis media 410,219 (11·6%); acute sinusitis 340,128 (9·6%); community-acquired pneumoniae 327,669 (9·3%), sore throat 210,954 (6·0%), and pyelonephritis 210,847 (6·0%). Of 4,959 users surveyed, 4,016 (81%) were GPs, 2,314 (58%) women, median age 38-years [31–52]. Using cross-sectional responses and number of requests over time, we estimated that approximately 5,743 GPs are using Antibioclic daily, corresponding to a 9·9% coverage rate of the 58,140 GPs registered in primary care in France. Among users, 972 (24%) reported systematically using Antibioclic when initiating an antibiotic course and 3,743 (93%) strictly followed Antibioclic recommendation for the latest antibiotic prescription. Median level of satisfaction for CDSS use and CDSS ergonomics were 5/5 [4 – 5].

Conclusions: Antibioclic has been adopted and is widely used in primary care in France. Its interoperability could allow an adaptation and implementation in other countries as part of national antimicrobial resistance action plans.

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Abstract 3187

**Efficiency of antibiotic prophylaxis in recurrence of UTI among kidney transplant recipients**

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**Background:** Upper urinary tract infections (UUTI) are the most frequent of severe infections in kidney transplant recipients (KTR). Recurrences of UUTI are also associated with hospitalization, graft dysfunction and loss. Antibiotic prophylaxis (ABP) might be useful to prevent recurrence, but its efficiency has never been demonstrated in KTR.

**Materials/methods:** We conducted a monocentric retrospective study in our kidney transplant unit from 2004 to 2018. We included all KTR with recurrent UUTI who received ABP for at least 3 months. Recurrent UUTI were defined as follows: 3 pyelonephritis in 12 months or 2 pyelonephritis in 6 months. We excluded patients with ureteral or bladder catheter.

**Results:** We included 18 KTR (11 female). Mean age was 55y (±16.8). Post-transplant diabetes was observed in 11, rejection in 8 cases. Causes of transplantation were chronic abnormalities of kidney urinary tract (n=5), chronic glomerulonephritis (n=4), polycystic kidney disease (n=3) and others (n=6). Before ABP initiation, patients experienced a mean of 4.4 (±2.1) recurrence UUTI during a mean time-interval of 33.6 (±42.5) months. Recurrent UUTI were explored by bladder/graft ultrasound (n=10/18), cystourethrography (n=12/18) and gynecological consultation (n=7/11 women).

Pathogens involved in UUTI (n=79) before ABP were mainly Escherichia coli (n=40, 50%), Klebsiella pneumoniae (n=10, 12%). Ten patients were reported ≥1 Extended spectrum beta-lactamase producing enterobacteria (ESBL-E) UUTI.

ABP consisted in 1 antibiotic (n=5), or a combination of 2 (n=6), 3 (n=6), or 4 (n=1) antibiotics. Main antibiotics were fosfomycin-trometamol (n=16), cefixime and pivmecillinam (n=7, each), amoxicillin-clavulanate (n=4). No severe adverse event was observed. Mean ABP exposure was 35.4 months (±17.2). Under ABP, 9/18 reported a complete resolution of symptoms without any recurrent of UUTI over 39 months, 8 reported an improvement with an average decrease of 70% of their recurrences over 32 months and 1 reported no benefit (no side effect).

11/23 recurrences of UUTI were caused by pathogens resistant to at least one molecule of the antibiotic prophylaxis combination, including 5-ESBL-E.

No graft loss or death was observed under ABP.

**Conclusions:** In KTR experiencing recurrent UUTI, continuous prophylaxis may be safe and efficient to reduce recurrences.

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Abstract 3189

**Caspofungin weight-based dosing supported by a population pharmacokinetic model**

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**Abstract third-party references:** Anne-Grete Martson was supported for this project by the Foundation “De Drie Lichten” in The Netherlands. Anne-Grete Martson was funded by Marie Skłodowska-Curie Actions [grant agreement no. 713660—PRONK-JEWAIL—H2020-MSCA-COFUND-2015].

**Background:** Caspofungin exposure varies in critically ill patients with invasive *Candida* infections. The objective of this study was to determine a dosing regimen of caspofungin using population pharmacokinetic modelling.

**Materials/methods:** This study included data from a prospective study in 20 critically ill patients. The sampling was performed before the dose and after 1, 2, 3, 4, 6, 8, 12 and 24 h of the dose (on days 2-4). Non-parametric population pharmacokinetic modelling, probability of target attainment (PTA), and internal validation was performed using Pmetrics. For the PTA a target 24-hour steady-state AUC value of 98 mg*h/L was used as an efficacy threshold and 200 mg*h/L as an arbitrary maximum.

**Results:** The median age was 56 (range 25-83) years, and the median weight was 78 (range 48-139) kg. The final model was a 2-compartment model which included normalized weight as a covariate on volume of distribution (Vd). The mean Vd of the central compartment was 7.89 (SD 3.12) L/kg, the mean elimination rate constant Ke was 0.09 (SD 0.04) h⁻¹, the rate constant for the caspofungin distribution from the central to the peripheral compartment was 0.42 (SD 0.39) h⁻¹, and the rate constant for the caspofungin distribution from the peripheral to the central compartment was 0.60 (SD 1.04) h⁻¹. The visual predictive check showed good performance of the model.

A loading dose of 1.5 mg/kg on the first day, followed by a maintenance dose of 1.25 mg/kg resulted in target AUC (≥ 98*h/L) on day 1 and day 3 in 80% and 95% of the patients respectively. Moreover, this dosing schedule results in only 12% of patients with an AUC ≥ 200mg*h/L.

We also simulated the currently registered fixed dose of caspofungin [70 mg daily dose] in 80 and 120 kg patients and observed that only 48% and 8% would reach the target AUC on day 3 respectively.

**Conclusions:** This study suggests that the standard caspofungin dose might not be suitable for critically ill patients. A weight-based dose regimen might be appropriate to achieve adequate exposure and the PTA should be prospectively evaluated.

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Variable number tandem repeat analysis on patient Pseudomonas aeruginosa (PsA) bacteraemia isolates and hospital shower water PsA strains to determine their links

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Background: PsA is a major cause of hospital acquired infections and genomic typing has being performed in recent years. VNTR sequencing allows rapid and straightforward comparative analysis in epidemiological investigations. PsA’s genome is relatively rich in tandem repeats, enabling Multiple loci VNTR analysis (MLVA) to find the relatedness of strains by comparing their VNTR profiles.

Materials/methods: VNTR profiles of strains from nine clinical (hospital-acquired bacteraemia from five wards A-E) and nineteen environmental (shower water from six wards B-G) isolates collected between November 2018 and January 2019 from a multi-disciplinary London teaching hospital were compared. MLVA targeted nine loci: ms172, ms211, ms213, ms214, ms217, ms222, ms2017, ms209 and ms61. Patient and environmental VNTR profiles were matched by time and location to determine potential transmission routes.

Results: One shower water isolate from a single-isolation-room in augmented-care-ward (B) was taken three days before the occupying patient (same room) developed bacteraemia; isolates showing indistinguishable VNTR profiles (1, 2, 3, 5, 5, 2, 3, 7, 2, 14). This profile was found in another shower water isolate (ward B). A similar VNTR profile (1, 2, 3, - , 4, 1, 9, 2, 11) caused bacteraemia on ward A during the same week.

On ward C, the same VNTR profile (1, 2, 4, 1, 9, 2, 11) was detected in a shower three days after isolation from a patient who probably had used the shower.

Two similar VNTR profiles (1, 2, 3, 6, 6, 3, 8, 2, 9 and 1, 2, 3, 6, 6, 3, 8, 2, 9) were isolated from two showers (ward B) on the same day with a third related profile (1, 2, 3, 6, 6, 3, 8, 2, 9) causing bacteraemia in a different room (same ward). Their single-locus-variant (1, 2, 3, 6, 6, 3, 8, 2) was seen in two different shower water isolates (wards D&F).

A further strain (VNTR: 1, 2, 3, 6, 3, 2, 13, 5, 7) was isolated in two different showers (wards E,F).

The most prevalent environmental strain (VNTR: 1, 2, 5, 3, 2, 6, 1, 6, 4, 13) was isolated on (3/19) occasions (16%). More than half of patient (5/9) and 21% of environmental (4/19) strains showed unique VNTR profiles within this cohort.

Conclusions: MLVA demonstrated that VNTR profiles among patient and shower water PsA isolates of this hospital are quite diverse. However, there were a few indistinguishable VNTR profiles observed in bacteraemia isolates and shower water strains from the same locations (rooms and wards) suggesting that the shower environment should be considered as a source of transmission of PsA.

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Urinary tract infections in nursing homes in the era of multidrug resistance: a 4-year study

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Background: Urinary tract infections [UTIs] are very common in residents of nursing homes, related to their own comorbidities and the risk of spreading microorganisms from direct contact between patients. Also, the spread of antimicrobial resistance is an important health concern.

Our aim was to study UTIs in nursing homes in the province of Albacete [Spain], and define their etiology and multidrug-resistance [MDR] profile compared to those found in the general population: primary care [PC] and specialised care [SC].

Materials/methods: A retrospective study of the urine samples from 11 nursing homes in our health area during the last 4 years [2015-2018]. Identification and bacterial susceptibility testing were performed using chromogenic medium [CPSE bioMérieux] and MaLDI-ToF [bioMérieux], and microdilution-based methods [VITEK® and MicroScan] respectively.

Results: We received 5212 urine samples from nursing homes: 4534 (86.9%) mid-stream urines, and 678 (13%) catheter specimen urines. Of these, 61.2% were positive samples, while in PC and SC the percentage decreased to 21.1% and 24% respectively \( (p<0.05) \). We found that 22.9% of the pathogens isolated in samples from nursing homes were MDR, compared to 6.1% in PC and 8.1% in SC \( (p<0.05) \). The frequency of MDR in nursing homes was higher in catheter specimen urines [32.1%] than in mid-stream urines [20.8%] \( (p<0.05) \).

The percentages of MDR found in samples of nursing homes, and the statistical significance of their difference with respect to those isolated in PC and SC, are shown in the table below

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Nursing Homes (IC 95%)</th>
<th>PC</th>
<th>( p )</th>
<th>SC</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Escherichia coli</em> ESBL</td>
<td>26.5 (24.4-28.8%)</td>
<td>6.7</td>
<td>&lt;0.05</td>
<td>8.4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td><em>Klebsiella pneumoniae</em> ESBL</td>
<td>45 (40.6-49.5%)</td>
<td>10.1</td>
<td>&lt;0.05</td>
<td>23</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>MDR-<em>Acinetobacter baumannii</em></td>
<td>87.5 (47.4-99.7%)</td>
<td>33.3</td>
<td>&lt;0.05</td>
<td>65.5</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>(MDR-AB)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRSA</td>
<td>81.8 (69.7-89.8%)</td>
<td>39.7</td>
<td>&lt;0.05</td>
<td>43.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>MDR-<em>Pseudomonas aeruginosa</em></td>
<td>15.6 (11.5-20.8%)</td>
<td>1</td>
<td>&lt;0.05</td>
<td>5.9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>(MDR-PA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbapenemase-producing</td>
<td>0.1 (0.03-0.4%)</td>
<td>0.2</td>
<td>&gt;0.05</td>
<td>0.1</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Enterobacteriaceae (CPE)</td>
<td></td>
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</tr>
</tbody>
</table>

Conclusions: Overall, the percentage of positives and MDR isolates were significantly higher in urine samples from geriatric patients compared to PC and SC. In those patients, almost one-quarter of the microorganisms were MDR. ESBL-Enterobacteriaceae were the most frequent, with *K. pneumoniae* prevailing over *E. coli*. The percentages of MRSA and MDR-PA were also significantly higher. Instead, there weren't significant isolates of CPE.

Overdiagnosis of UTIs in nursing homes may cause inappropriate use of antibiotics, acting as a reservoir of MDR microorganisms, as seen in other studies. Our results suggest the need to extend the specific strategies and programs to nursing homes, and ensuring a sufficient number of specialized staff in infection control.

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Abstract 3192

Hemagglutinin sequence-derived phylogenetic and genetic characterisation of A(H3N2) influenza viruses circulating during 2013-2019 winter seasons in Southern Greece

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Background: Seasonal genetic characterization of influenza viral haemagglutinin (HA), monitors amino acid substitutions within the antigenic (A-E) receptor binding sites and substitutions associated with potential glycosylation gain/loss (potential effects in masking/uncovering antibody epitopes). We aim to compare genetic and phylogenetic characteristics of the circulating viruses to the seasonal vaccine viruses during peak influenza activity in Southern Greece for surveillance purposes.

Materials/methods: During 2013-2019 winter seasons, 1,315 respiratory samples were tested positive for H3N2 virus by RT-PCR (120-2013/14, 352-2014/15, 7-2015/16, 691-2016/17, 11-2017/18 and 134-2018/19). Sanger sequencing of the complete viral HA gene was attempted directly on the 10% percentage of representative original samples (N=131).

Results: Comparative mutation analysis to seasonal vaccine viruses, Greek viruses circulating in 2013-14 and 2015-2016 seasons exhibited substitutions only in A and B sites, whereas during 2016-2017, seasonal viruses revealed amino acid substitutions in all antigenic sites. F159Y amino acid substitution within the immunodominant antigenic site B in 2014-2015 and 2015-2016 viral HA was associated with vaccine mismatches. The aa alteration K160T (site B) associated with gain of a glycosylation site, was observed in all viruses circulating since 2014.

Conclusions: Our genetic characterization data are in line with evidence from 1968-2013 seasonal surveillance studies, that most H3N2 vaccine mismatches attributed to HA antigenic site B mutations. The 2014-2015 3C.2a-clade emergence was associated with an increased level of genetic diversification among circulating Greek viruses. In line, during 2014-2016 A[H3N2] epidemics included in our study, WHO recommended twice a vaccine virus change need. In addition, seasonal vaccine escape viruses circulated in 2015-2016 season exhibited diversity in phylogenetic grouping and mutations only in A and B antigenic sites. Phylogenetic clustering patterns not only update on the virus evolution but heavily influence vaccine decisions.

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**Abstract 3194**

*Clostridioides difficile* NAAT-positive with toxin-negative test results: impact of antibiotic treatment on clinical outcomes

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**Background:** In our study, we aimed to characterize the clinical outcomes among *C. difficile* (Cdiff) NAAT+ patients with either toxin+ or toxin- results and the effect of antibiotic treatment.

**Materials/methods:** This retrospective cohort of consecutive adult inpatients with diarrhea and Cdiff NAAT+ results was performed at a 604 bed academic medical center in Milwaukee, Wisconsin. Cdiff tests consist of a two-step process: NAAT (Xpert® *C. difficile*; Cepheid) and if positive a toxin assay (C. diff Quik Check Complete; Alere, Waltham, MA). Only the first positive Cdiff NAAT test per patient was included. Antibiotic treatment against Cdiff was captured if received within 3 days of NAAT+ result. Outcome variables included length of stay (LOS) from NAAT+ to discharge, 30-day mortality, colectomy, and CDI recurrence within 30-90 days. Analyses included generalized linear models and COX-proportional hazards models. Backward stepwise selection logistic regression model with a p-value threshold of 0.1 was used to analyze for Cdiff recurrence.

**Results:**

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Toxin status (n=755)</th>
<th>Treatment status NAAT+/toxin- (n=491)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NAAT+/toxin+ (n=264)</td>
<td>NAAT+/toxin- (n=491)</td>
</tr>
<tr>
<td>Age &gt; 65 yrs</td>
<td>57.6%</td>
<td>44.8%</td>
</tr>
<tr>
<td>Antibiotic exposure (&lt;3 months)</td>
<td>97.4%</td>
<td>88.4%</td>
</tr>
<tr>
<td>Immune-modulators (&lt;3 months)</td>
<td>53.8%</td>
<td>55.6%</td>
</tr>
<tr>
<td>Hematological/Oncological condition</td>
<td>38.6%</td>
<td>39.7%</td>
</tr>
<tr>
<td>Transplant History</td>
<td>10.2%</td>
<td>12.8%</td>
</tr>
<tr>
<td>Inflammatory Bowel Disease</td>
<td>7.6%</td>
<td>11.8%</td>
</tr>
<tr>
<td>Comorbidity score</td>
<td>5.2 ± 2.6</td>
<td>5.5 ± 2.7</td>
</tr>
<tr>
<td>White Blood Cells (WBC)</td>
<td>12.7 ± 8.6</td>
<td>9.9 ± 7.3</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.5 ± 1.7</td>
<td>1.7 ± 2.1</td>
</tr>
</tbody>
</table>

**Results:**

From January 2017 to June 2019, 755 NAAT+ patients were identified: 264 [35%] toxin+ and 491 [65%] toxin-. Out of NAAT+/toxin- patients 256 [52%] were treated. NAAT+/toxin+ patients had higher WBC counts [12.7 vs. 9.9, p=0.001] and higher antibiotic exposure in the preceding 3 months of NAAT+ result [97.4% vs. 88.4%, p=0.001]. Among NAAT+/toxin- patients, patients who received treatment had higher WBC counts [11.3 vs. 8.4, p=0.001] and more antibiotic exposure [95.3% vs. 80.9%, p=0.001]. There was no statistical difference in outcome variables between NAAT+/toxin+ and NAAT+/toxin- groups. Antibiotic treatment for NAAT+/toxin- patients increased the odds of CDI recurrence [OR:3.27, 95%CI 1.19-9.01, p=0.02]; however, this effect dissipated in the adjusted model. CDI recurrence was associated with immune-modulators exposure [OR:2.93, 95%CI 1.05-8.21, p=0.04] and a higher Elix-Hauser Comorbidity score [OR:1.21, 95%CI 1.03-1.43, p=0.02] in treated vs. untreated NAAT+/toxin- patients.

**Conclusions:** There was no difference in outcomes based on toxin results or treatment among NAAT+/EIA- patients. CDI recurrences were greater in patients with higher comorbidity scores or receiving immune-modulators.

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Abstract 3196

**Bacteriophage control the prevalence of *Escherichia coli* ST131 in different countries**

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**Background:** *Escherichia coli* is the most important bacterial species in Europe, being the main cause of both urinary tract and blood infections. The *E. coli* species consists of at least 10,000 sequence types (ST) with ST131 being the dominant cause of quinolone and β-lactam resistant infections throughout Europe.

**Materials/methods:** We collected 193 ST131 isolates from human bacteraemia, faeces and sewage in the UK in 2014 and performed whole genome sequencing of these by Miseq technology. Core genome (CG) comparison of the ST131 isolates was achieved using blast 2.7.1 on 2513 CG targets and CG tree generated using Ridom seqsphere. Each ST131 isolate was tested for susceptibility to bacteriophage. Bacteriophages were isolated from human sewage collected from four countries in April-June 2019: The UK, Kazakhstan, Saudi Arabia and Bangladesh. Bacteriophage were tested for activity by plaque assays on each ST131 isolate and characterized by electron microscopy and sequencing. The *E. coli* ST131 prevalence was also assessed in each country by random selection of 100 *E. coli* from the sewage samples and confirmation of the number of ST131 isolates by specific PCR.

**Results:** The 193 *E. coli* ST131 isolates represented a broad range of cgMLST types and were spread throughout the ST131 cgMLST tree. We found that *E. coli* ST131 prevalence was dramatically different in the four countries: 11% in the UK, <1% in S. Arabia, 4% in Kazakhstan and undetectable in Bangladesh. However, ST131 specific bacteriophages were highly prevalent in Bangladesh and Saudi Arabia (able to kill 70% and 72% of UK ST131 isolates, respectively) yet much less common in the UK (32%) and rare in Kazakhstan (5.8%). Electron microscopy revealed that ST131 bacteriophage belonged to several different families including the siphoviridae, podoviridae and myoviridae.

**Conclusions:** We found that the UK had the highest and Bangladesh the lowest carriage rates of *E. coli* ST131. Thus ST131 prevalence varies greatly by geographical location. Conversely, sewage from Bangladesh contained bacteriophage that could kill 72% of UK ST131 whereas sewage from the UK could only kill 32% of strains. This strongly suggests that prevalence of ST131 in different countries is controlled by bacteriophage.

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Non-beta-lactam antibiotic hypersensitivity reactions in children

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Background: Antibiotics are among the most common prescriptions in children and non-β-lactam antibiotics (NBLA) account for almost half of those prescribed in Australian paediatric hospitals.1) Despite this, there is a current paucity of data on the clinical presentation and frequency of true NBLA allergies in children. NBLA allergies were reported in 4.7% of children in a previous paediatric study, with macrolides and sulfonamides the most frequently implicated.1) This study describes reported hypersensitivity reactions to NBLAs in children and the results of allergy evaluation.

Materials/methods: A total of 141 children, aged between 0 and 18 years, with a suspected NBLA allergy who had skin testing and/or an intravenous or oral challenge test (OCT) between May 2011 and June 2018 were included. Patients were excluded if they were older than 18 years or did not complete the OCT for reasons other than allergic reaction. Patients records were retrospectively reviewed and data on the clinical history of the NBLA reaction was entered into a REDCAP® database. Patients were classified as having an immediate or non-immediate reaction based on timing of symptoms and further classified as severe or non-severe. Data was then critically analysed and evaluated.

Results: Over the 7-year study period, 141 children had 150 allergy evaluations to 15 different NBLAs. The median time from the initial reported reaction to allergy evaluation was 1.9 (range 0.1 to 14.9) years. Overall, 27/150 (18.0%) challenge tests to a NBLA were positive with the rate of positive OCTs highest for trimethoprim-sulfamethoxazole [15/46, 32.6%] and macrolides [8/77, 10.4%]. Although 4 children reported initial anaphylactic reactions, no patients had severe symptoms on rechallenge or required adrenaline. Of the challenges that were positive, the majority of children [23/27, 85.2%] had similar symptoms on repeat challenge to those that were initially reported.

Conclusions: Overall, almost one-fifth of reported NBLA allergies were confirmed by allergy evaluation. Timely access to allergy evaluation on to de-label these patients is needed to preserve first line antibiotics.

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Are neurological co-infections common in AIDS-related cerebral toxoplasmosis?: a prospective cohort study on late cART era in São Paulo, Brazil

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Background: Cerebral toxoplasmosis continues to be the most frequently neurological cause of hospital admission in people living with HIV/AIDS (PLWHA) from resource-limited settings. Concomitant neurological diseases in PLWHA is a challenging subject that has not been sufficiently evaluated in prospective clinical studies. The aim of this study was to identify the frequency, main features, and outcome of cerebral toxoplasmosis with neurological co-infections in PLWHA.

Materials/methods: We conducted a prospective observational cohort study at a tertiary teaching center in São Paulo, Brazil, between January-July 2017. PLWHA with age ≥ 18 years old and cerebral toxoplasmosis were consecutively included. Standardized neurological exam was performed at admission and weekly up to discharge or death. Diagnosis and treatment followed institutional routine; neuroradiology, molecular diagnosis on cerebrospinal fluid (CSF), neurosurgery, and Intensive Care Unit (ICU) were available. Main outcomes were frequency and in-hospital mortality of related cerebral toxoplasmosis with neurological co-infections in PLWHA. \(P\leq0.05\) was considered significant in univariate analysis.

Results: Were included 44 (4.3\%) cases among 1,032 hospitalized patients in the study period. Cerebral toxoplasmosis was the more frequent diagnosis among all patients with neurological diseases [44/105, 42\%]. Median age was 44 years-old (interquartile range, IQR: 35-50) and 50\% were male. Median CD4 lymphocytes cell count was 50 cells/mm\(^3\) (IQR 15-94). Multiple lesions on computed tomography were present on 59\% of cases. Neurological co-infections were diagnosed in 20\% (\(n=9\)) of cases and \textit{Cytomegalovirus} (CMV) was the most common etiology (\(n=5\); encephalitis, \(n=3\); polyradiculopathy, \(n=2\)). PLWHA with neurological co-infections presented higher length of hospitalization [30 vs. 62 days (\(P=0.021\))] and more frequent ICU admission [14 vs. 44 (\(P=0.045\))]. Trimethoprim-sulfamethoxazole was used in all but 2 patients. Global mortality rate was 13.6\% (\(n=6\)) (co-infections, 33\% vs. no co-infection, 8.6\%, \(P=0.054\)).

Conclusions: Neurological co-infections were common in PLWHA with cerebral toxoplasmosis and CMV was the main concomitant infection. PLWHA with neurological co-infections showed higher length of hospitalization and more frequent ICU admission. Co-infection is probably associated with increased mortality but further investigation is necessary. These findings highlight the impact of neurological co-infections and its potential implications in the management and outcome of cerebral toxoplasmosis in PLWHA.

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Abstract 3199

From OPAT to COpAT in a regional New Zealand hospital

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Background: Rotorua Hospital is a 180-bed general regional hospital serving Rotorua (a 59,500-inhabitants’ town in the upper North Island of New Zealand/Aotearoa). The Antimicrobial Stewardship Service is run by the Hospital Pharmacy with the support of the Infectious Disease (ID) Physician and the Clinical Microbiologists (CM) from the local laboratory. Historically, the Hospital had a busy Outpatient Parenteral Antibiotic Therapy (OPAT) service, using 24-hour infusers and PICC lines to deliver long (4 to 6 weeks) antibiotic treatments at the patients’ homes; in the peak month (July 2018) 208 infusers were utilised. Following the publication of large trials (eg OVIVA and POET) supporting the switch to oral antibiotics, the AMS service initiated in February 2019 a systematic review of all antibiotic treatment plans before discharge, implementing mandatory ID or CM approval and offering instead advice about optimising oral antibiotics as COpAT (Complex Outpatient Antibiotic Therapy). A large proportion of infusers were loaded with beta-lactams (penicillin, flucloxacillin, and cefazolin) that were replaced with the oral equivalents boosted with probenecid. A smaller proportion was loaded with piperacillin/tazobactam or vancomycin, which largely account for the remaining OPAT after the policy change. For orthopedic or other bioprosthetic infections, combinations of biofilm-active antibiotics (rifampicin plus either cotrimoxazole or ciprofloxacin) were also used.

Materials/methods: The Rotorua Hospital Pharmacy extracted from their electronic dispensing records the numbers and costs of the antibiotic infusers in 6 months before the new policy was implemented (Feb to Aug 2018) and in the same 6 months after the implementation (Feb to Aug 2019).

Results: From Feb to Aug 2018, 1,005 antibiotic infusers were dispensed; this fell to 472 (a 53.1% decline) from Feb to Aug 2019. The cost fell from NZD11,422 before implementation to NZD51,591 after implementation (a 54.9% decline).

Conclusions: Our policy change lead to a significant reduction of the use of antibiotic infusers, with savings that go beyond the pure pharmaceutical cost and also involve avoiding the necessity of a PICC-line and the need for a visiting Nurse at home to change the infusers daily. The PICC line-related complications (thrombosis and infections) were also avoided.

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Ceftolozane-tazobactam for treatment of severe ESBL-producing Enterobacteriaceae infections: a multi-centre nationwide clinical experience (Ceftabuse II Study)

Matteo Bassetti1, Antonio Vena1, Daniele Roberto Giacobbe1, Marco Falcone2, Giusy Tiseo2, Maddalena Giannella2, Renato Pascale1, Marianna Meschian1, Margherita Digaetano2, Alessandra Oliva3, Cristina Rovelli4, Novella Carannante5, Angela Raffaella Losito4, Sergio Carbonara4, Michele Fabiano Marian4, Antonio Mastroianni5, Gioacchino Angarano5, Mario Tumbarello5, Carlo Tascini7, Paolo A. Grossi5, Claudio M. Mastroianni5, Cristina Mussini4, Pierluigi Viale1, Francesco Menichetti5, Claudio Viscoli5, Alessandro Russo*5

1Genoa, Italy, 2Pisa, Italy, 3Bologna, Italy, 4Modena, Italy, 5Rome, Italy, 6Varese, Italy, 7Naples, Italy, 8Bari, Italy, 9Cosenza, Italy

Background: few data are reported in literature about outcome of patients with severe ESBL-producing enterobacteriaceae infections treated with ceftolozane/tazobactam (C/T), in empiric or definitive therapy.

Materials/methods: a retrospective study was performed at 24 hospitals in Italy (June 2016-June 2019). All adult patients treated with ≥4 days of C/T were enrolled. Successful clinical outcome was defined as complete resolution of clinical signs/symptoms related to ESBL-producing enterobacteriaceae infection and lack of microbiological evidence of infection. Primary endpoint was to identify predictors of clinical failure of C/T therapy.

Results: C/T treatment was documented in 153 patients: pneumonia was the most common diagnosis (n= 46, 30%) followed by 34 cases of complicated urinary-tract infections (22.2%), 25 cases of acute bacterial skin and skin-structure infections (16.3%), and 25 cases of complicated intra-abdominal infections (16.3%). Septic shock was observed in 36 (23.5%) patients. C/T was used as empiric, then confirmed therapy, in 46 (30%) patients; as monotherapy in 127 (83%) patients. C/T doses were 1.5 g q8h in 115 patients (75%) and 3 g q8h in 38 patients (25%). When used as second-line or later, the most common reasons for discontinuation of previous antibiotics were in vitro resistance of strains and clinical failure of previous therapy. Favorable clinical outcome was observed in 128 (83.7%) patients; 25 patients considered to have failed C/T therapy. Overall, 30-day mortality was reported for 15 (9.8%) patients. At multivariate analysis, Charlson Comorbidity Index >4 (OR 3.3, CI95% 2.1-4.2, p=0.01), septic shock (OR 5.2, CI95% 3.2-7.4, p=0.001), continuous renal replacement therapy (OR 2.3, CI95% 1.87-4.3, p=0.02) were independently associated with clinical failure, while C/T in empiric therapy (OR 0.22, CI95% 0.11-0.67, p<0.001), and adequate source control of infection (OR 0.32, CI95% 0.24-0.77, p=0.001) with clinical success.

Conclusions: data showed that C/T could be a valid option in empiric and/or targeted therapy also in patients with severe infections caused by ESBL-producing enterobacteriaceae. Clinicians should be aware of the risk of clinical failure with C/T therapy in septic patients receiving CRRT.

Figure 1. Successful clinical outcome and clinical failure in patients receiving C/T as empiric therapy, targeted or rescue therapy

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**Bacteriophage-controlling dominant sequence types of carbapenem-resistant Escherichia coli in Bangladesh**

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**Abstract 3202**

**Background:** E. coli is universally carried in the human gut and the main cause of urinary tract and blood infections. Previously, we have noted that carbapenem resistance (NDM) is restricted to a small number of prevalent E. coli sequence types (ST).

**Materials/methods:** Sewage was collected from 58 sites across Dhaka, Bangladesh in 2012, 2018 and 2019. E. coli were isolated by plating on meropenem (0.5mg/L) with species confirmation by MALDI-TOF-MS. At the same time bacteriophage were isolated by centrifugation and filtration and pooled for each time point. E. coli ST were identified using a combination of CH typing and whole genome sequencing using Miseq technology. Fifty-three carbapenem resistant isolates of E. coli collected in 2012 were individually tested for susceptibility to bacteriophage pools isolated in 2012, 2018 and 2019 by bacteriophage plaque assays. Bacteriophage titre and plaque size were recorded. Bacteriophage were also characterized by electron microscopy and sequenced using Miseq technology.

**Results:** From 2012 sewage we recovered 53 carbapenem resistant E. coli isolates that belonged to only three different ST: ST101, ST648 and ST405. E. coli ST101 isolates were commonly found at numerous locations but E. coli ST405 was found only at a single location. ST648 isolates were found at an intermediate prevalence. The prevalence of bacteriophage, able to kill each E. coli ST group was directly yet inversely related to the prevalence of each E. coli ST. Bacteriophages were found in 2012 (at high titre 10⁶-10⁸ pfu/ml) that were able to kill all ST405 isolates (5/5). However, the bacteriophage pool from 2012 sewage was only able to kill a single ST101 E. coli isolate (1/20). The 2018/2019 samples contained a similarly high abundance of bacteriophages against ST405 and ST648 (similar to that seen in 2012). However, the 2019 sewage sample contained bacteriophage capable of killing 5 different ST101 E.coli- a 5-fold increase compared to 2012.

**Conclusions:** These results give evidence that bacteriophages play a key role in modulating dominant resistant E. coli populations. They also suggest that these natural processes could be artificially manipulated to favour non-resistant E. coli types and control resistant E. coli populations.

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Successful use of the novel antifungal olorofim in the treatment of disseminated coccidioidomycosis

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Background: Infection due to Coccidioides spp. ranges from asymptomatic acquisition with resultant immunity, to severe, multifocal, life-threatening disease. There is a high failure rate with currently approved antifungals and new therapeutic options are needed. Olorofim, a novel antifungal, has potent anti-Coccidioides activity in a murine model of infection.

Materials/methods: An open-label Phase 2 study of olorofim in patients with Invasive Fungal Disease lacking alternative treatment options is ongoing.

Results: A 45 y/o African-American man with insulin-dependent diabetes mellitus developed disseminated coccidioidomycosis with severe lung disease and concurrent meningitis. He was treated with fluconazole 800 mg daily, however four weeks later exhibited continued progression of disease and changed to voriconazole 200 mg twice daily. His pulmonary disease continued to worsen and therapy changed to itraconazole 200 mg twice daily due to voriconazole intolerance.

The patient continued to deteriorate and therapy was changed to liposomal amphotericin B (L-AMB) (5 mg/kg/day) and posaconazole 300 mg daily (tablet). His serum Coccidioides complement fixation titer (CF) was 1:128. One month later he was significantly hypokalemic, L-AMB was stopped, and salvage posaconazole and micafungin 150 mg IV initiated. He continued to deteriorate, was unable to work, was dependent on supplementary oxygen, and required a walking frame.

Eight months after his initial infection therapy was changed to posaconazole 300 mg daily plus olorofim 120 mg twice daily. The patient noted rapid improvement of his cough and malaise within a week with resolution of all other symptoms in this time frame.

After three months of posaconazole plus olorofim he returned to his normal activity level without use of oxygen or a walking frame. CSF examination showed complete normalization of his CSF indices and negative coccidioidomycosis serology from spinal fluid. The serum Coccidioides CF titer declined to 1:64. Repeat pulmonary CT scan showed improvement in multifocal infiltrates.

After 5 months of therapy he returned to work and the Coccidioides CF titer had declined to 1:32. He has tolerated all medications.

Conclusions: Adding olorofim to a failing regimen for severe, disseminated coccidioidomycosis resulted in significant clinical, serologic, and radiologic improvement. Olorofim should be further evaluated in coccidioidomycosis.

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Abstract 3205

Haemodialysis-associated infective endocarditis

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Abstract third-party references: FAPERJ, Rio de Janeiro, Brazil

Background: Patients with chronic renal failure (CRF) undergoing haemodialysis (HD) are at increased risk of infective endocarditis (IE) due to vascular access-related bacteraemia, accelerated degeneration and calcification of heart valves, and immune dysfunction.

Materials/methods: We compared cases of HD-associated IE in adults with other IE cases from a prospective cohort in a cardiac surgery hospital from 2006 to 2019. All IE was definite by Duke’s modified criteria. Jamovi 1.0.7 software was used for statistical analysis.

Results: We identified 26 patients on HD out of 359 with IE (7.2% of the cohort). They were male 19/26 (73%), aged 47.3 ±16.2 years; 88.5% vs 51.2% were transferred from other sites (p <0.001). Half came from HD clinics and half from other hospitals, while in the rest of the cohort this represented 26.8% and 4.8%, respectively (p <0.001). Accesses were femoral in 9 (34%); 5 had arteriovenous fistula (AVF), the median time from HD to diagnosis of IE was 85 days. There were no differences regarding comorbidities, except for diabetes (30.8% vs 10.2%, p = 0.002). Only 8.5% of HD IE patients had rheumatic valvulopathy vs 35.1% (p = 0.006). There was no difference between valve types (native or prosthetic), blood culture positivity (73.1% vs 67.8%), presence of fever (96.2% vs 92.7%), splenomegaly (15.4% vs 23%) and embolic vascular events (57.7% vs 50.8%). Enterococci were the most common microorganisms (34.6% vs 9.0%), there were fewer viridans group streptococci (3.8% vs 25.2%, p < 0.014), more coagulase-negative staphylococci (19.2% vs 8.1%, p = 0.069) and no difference for Staphylococcus aureus and Gram negative bacilli. There was no difference regarding surgical indication (30.8% vs 24.1%) and actual surgical rates (73.1% vs 80.1%). Moreover, no difference in mortality (30.8% vs 24.1%) was seen.

Conclusions: HD-associated IE occurred shortly after the procedure (median 3 months). Enterococci were the most common pathogens, probably due to the insertion of femoral catheters. Fever, complications, and mortality were similar to patients with IE in general. The high frequency of HD-associated IE from other hospitals suggests that infection control practices should be improved in those institutions, as well as in dialysis clinics.

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Abstract 3210

Clinical evaluation of the mosquito-borne virus panels of Genematrix based on multiplex real-time PCR

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Background: Fast and accurate early diagnosis of mosquito-borne viral infection diseases is crucial for its prevention of transmission. NeoPlex™ ARV-6 and NeoPlex™ ZDC Detection Kits are single-tube multiplex real-time RT-PCR assays based on Genematrix proprietary C-Tag™ technology, simultaneously detecting Zika, Dengue, Chikungunya, YellowFever, WestNile and RossRiver (ARV-6), and Zika, Dengue and Chikungunya virus (ZDC), respectively. Here we report the clinical evaluation of NeoPlex™ ARV-6 and ZDC Detection Kits.

Materials/methods: To evaluate NeoPlex™ ARV-6, total 629 plasma and serum specimens (Beir resources, VA; Cerba Xpert, France; ABO Pharmaceuticals, CA) including 393 spiked serum specimens were prepared. To evaluate the clinical performance of NeoPlex™ ZDC, 372 human serum and 364 plasma specimens were retrospectively collected in Philippines. The samples were cross-examinationally tested with type-specific sequencing for NeoPlex™ ARV-6 and RealStar Zika, DENV and CHIKV RT-PCR Kits (Altona diagnostics, Germany) for NeoPlex™ ZDC, following manufacturer’s instructions. The sensitivity and specificity (with 95% CI) were calculated by the comparators and type-specific sequencing as a gold standard. The correlations between NeoPlex™ ZDC and comparators were measured by positive, negative and overall percent agreements.

Results: The clinical sensitivity for NeoPlex™ ARV-6 was as following respectively: Zika 98.1% (0.93-0.99), Dengue 100% (0.97-1.00), Chikungunya 96.6% (0.91-0.98), WestNile 100% (0.92-1.00), YellowFever 100% (0.93-0.99), RossRiver 95.0 (0.83-0.98). The clinical specificity for NeoPlex™ ARV-6 was as following respectively: Zika 98.5% (0.97-0.99), Dengue 100% (0.99-1.00), Chikungunya 99.3% (0.99-1.00), WestNile 99.7% (0.98-0.99), YellowFever 100% (0.99-1.00), RossRiver 99.8% (0.99-0.99). The clinical sensitivity for NeoPlex™ ZDC in human plasma and serum were as following respectively: Zika 100% and 98.48% (94.34-100, 91.90-99.73), Dengue 99.10% and 99.12% (95.07-99.84, 95.20-99.84), and Chikungunya both 100% (91.43-100, 91.80-100), while the clinical specificity for those were as following respectively: Zika both 100% (98.74-100, 98.76-100), Dengue 99.60% and 99.61% (97.80-99.93, 97.84-99.93), and Chikungunya both 100% (99.82-100, 98.85-100). Positive, negative and overall percent agreements were over 98.66%, showing Cohen’s kappa between 0.9866-1.

Conclusions: Compared with commercial diagnostics, Neoplex™ ARV-6 and ZDC, based on C-Tag™ multiplex real-time PCR technology, have proved their usefulness on clinical and diagnostic uses for detecting mosquito-borne viruses in a single-tube PCR reaction with high clinical sensitivity and specificity.

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Abstract 3212

In vitro activity of eravacycline and comparators against 931 non-fastidious and 323 fastidious clinical isolates from China

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Background: Eravacycline (ERV), a novel fluorocycline antimicrobial agent approved for the treatment of complicated intra-abdominal infections (cIAI) in the USA and EU in 2018, has demonstrated in vitro activity against multi-drug-resistant (MDR) strains. We evaluated the activity of ERV against clinical isolates of Enterobacteriaceae, A. baumannii, Staphylococcus spp, Enterococcus spp, S. pneumoniae, H. influenzae and M. catarrhalis including those that are MDR, from hospitals in China.

Materials/methods: A total of 1254 organisms collected from intra-abdominal and respiratory infections during the China Antimicrobial Surveillance Network (CHINET) 2017-2018 were included. Isolates were identified by standard biochemical algorithms and MALDI-TOF-MS. Antimicrobial susceptibility testing was performed by the broth microdilution reference methods, and MICs were interpreted per EUCAST criteria.

Results: ERV inhibited 98.3% E. coli isolates at 0.5 µg/ml. ERV had similar MIC90 values (2 µg/mL) against Klebsiella spp, Enterobacter spp and Citrobacter spp to tigecycline. ERV and tigecycline showed decreased activity against Proteus spp and Morganii spp with MIC50 values (1-2 µg/mL). The MIC50 and MIC90 values against A. baumannii were 0.5 and 1 µg/ml, respectively, two-fold lower than that of tigecycline. MIC90 values of ERV against S. aureus, CoNS, E. faecalis (including 8 linezolid-nonsusceptible strains) and E. faecium (including 21 vancomycin-resistant strains) were 0.125, 0.5, 0.125 and 0.06 µg/ml, two/four-fold lower than that of tigecycline. The modal MIC of ERV against S. pneumoniae, H. influenzae and M. catarrhalis were 0.008, 0.125 and 0.06 µg/ml respectively.

Conclusions: ERV possessed significant in vitro activity against contemporary clinical isolates of Enterobacteriaceae and A. baumannii from China, including carbapenem-resistant strains. ERV demonstrated lower MIC90 values than tigecycline against Staphylococcus spp, Enterococcus spp, S. pneumoniae, H. influenzae and M. catarrhalis.

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Abstract 3215

Development of new bicyclic nitroimidazoles as antitubercular and antiparasitic agents
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Background: Infectious diseases are a major global health threat requiring new treatment options. The nitroimidazoles are an old class of antibiotics that have been widely used to treat parasites, mycobacteria, and both Gram-positive/Gram-negative bacteria [1]. Delamanid and pretomanid, nitroimidazoles with bicyclic cores, are new candidates for the treatment of tuberculosis [2,3]. They also show repurposing potential against Leishmania donovani, the causative agent of visceral leishmaniasis [4]. Another bicyclic nitroimidazole, fexinidazole, was recently approved as the first oral treatment for Human African Trypanosomiasis. Inspired by the dual antitubercular and antiparasitic activities of these compounds, we have developed a new bicyclic subclass, 2-nitroimidazo-pyrazinones, with activity against Mycobacterium tuberculosis, intestinal parasites (Giardia lamblia) and kinetoplastids (Trypanosoma brucei brucei and Trypanosoma cruzi) [5]. Similar to other bicyclic nitroimidazoles, our compounds have limited aqueous solubility and therefore require further optimization, as well as assessment in vivo.

Materials/methods: New analogs, designed to improve solubility, were synthesized using modifications of previous synthetic routes. They were assessed in biological assays for antimicrobial activity against a range of organisms, along with measurements of aqueous solubility. Promising compounds were tested for protein binding and plasma/microsomal stability, and advanced into mouse pharmacokinetic and efficacy testing. We also investigated the potential of nanoparticle formulations to improve solubility for oral delivery.

Results: We describe three new series of pyrazinones with improved solubility. The structure-activity relationship (SAR) study showed distinct trends across tested organisms, suggesting their selectivity for different pathogens. Selected potent analogues had low cytotoxicity against human cell lines, good oral availability in mice with favourable pharmacokinetic profiles, and were efficacious in in vivo models. Nanoparticle formulation with lactoferrin, an iron-binding glycoprotein, enhanced solubility by over 3-fold.

Conclusions: This work has highlighted the potential of different subclasses of nitroimidazoles to be developed as therapeutics to address the unmet medical needs caused by bacterial and parasitic infections. We have been able to improve both solubility and potency of our novel 2-nitroimidazo-pyrazinones, and demonstrate in vivo efficacy.


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Abstract 3216

**Antibiotic utilisation and Clostridoides difficile rate: a 12-year time series and cross-correlation analysis**

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**Background:** Clostridoides difficile infection was independently associated with extended-spectrum cephalosporins, fluoroquinolones, carbapenems and clindamycin. We observed declining rate of *C. difficile* after 10 years of antimicrobial stewardship programme in a university teaching hospital in Singapore. We aimed to investigate the temporal relationship between antibiotic usage and *C. difficile* rate.

**Materials/methods:** Monthly utilisation of antibiotics in defined daily doses (DDD) and incidence of *C. difficile* per 1,000 patient-days from January 2007 to December 2018 were obtained from the hospital’s database. Each time-series was pre-whitened to account for autocorrelation. An autoregressive integrated moving average (ARIMA) model was fitted to an antibiotic utilisation time-series filtered to obtain white noise residuals. The *C. difficile* incidence time series was filtered with the same model. The cross-correlation function (CCF) was computed between the filtered time-series for each antibiotic use and *C. difficile* incidence at lags up to 12 months. We investigated the lag in the CCF at which the peak correlation of statistical significance (p<0.05) occurred, to determine the lead time of antibiotic utilisation relative to *C. difficile* incidence.

**Results:** The incidence rate of *C. difficile* showed downward trend from monthly average of 0.60/1000 patient-days in 2007 to 0.46/1000 patient-days in 2018. *C. difficile* rate was correlated with overall broad-spectrum antibiotic utilisation (0.22, p=0.01). Utilisation of beta-lactams with beta-lactamase inhibitors (BLBLI) (0.20, p=0.01) and carbapenems (0.20, p=0.02) was correlated with *C. difficile* incidence. No significant correlation was found with fluoroquinolones (0.12, p=0.16) and 3rd generation cephalosporins (0.11, p=0.18). Utilisation of individual antibiotics; co-amoxiclav (0.20, p=0.02), imipenem (0.27, p=0.01), ertapenem (-0.19, p=0.02) and clindamycin (-0.17, p=0.047) was correlated with *C. difficile* rate. The lead time at which peak correlation occurred was 0 month for overall broad-spectrum antibiotics, BLBLIs and co-amoxiclav, 1 month for ertapenem, 2 months for imipenem, 3 months for the carbapenem group and 7 months for clindamycin.

**Conclusions:** Utilisation of overall broad-spectrum antibiotics, carbapenems and BLBLI significantly correlated with *C. difficile* incidence rate. Focusing on individual antibiotics may not be effective in controlling *C. difficile*.

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In vitro activity of ibrexafungerp in pH 7.0 and pH 4.5 testing environments against 187 fluconazole-susceptible and -resistant Candida species from vulvovaginal candidiasis patients

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Abstract

Background: Recent studies report a rapidly growing incidence of resistance to the azole drug class in Candida species, notably C. glabrata, C. parapsilosis, and C. krusei. Among patients with vulvovaginal candidiasis (VVC), C. albicans is the most frequently observed Candida species. What is extremely worrisome is the increase in fluconazole (FLU) resistance observed in C. albicans vaginal isolates. Previous in vitro studies have shown that fluconazole in low pH testing environments, pH 4.5, has a negative effect on the activity of fluconazole. Ibrexafungerp is an oral anti-fungal agent belonging to a novel class of glucan synthase inhibitors, triterpenoids, and has shown activity against azole-resistant Candida species.

Materials/methods: Ibrexafungerp was evaluated in vitro against 187 vaginal Candida isolates: 52 FLU–resistant C. albicans (FLU MIC > 2 ug/mL), 30 FLU–sensitive C. albicans (FLU MIC < 2 ug/mL), 30 randomly selected C. glabrata isolates and 25 each randomly selected isolates of C. krusei, C. parapsilosis, and C. tropicalis. Susceptibility tests were performed according to CLSI M27-A4 guidelines with the media adjusted to pH 7.0 and pH 4.5; ibrexafungerp MIC readings were conducted at 24 and 48 hrs.

Results: Ibrexafungerp demonstrated in vitro activity against all the VVC clinical isolates tested. No differences were observed in ibrexafungerp's MIC90 values (24 hr endpoint at pH7) between the FLU-resistant and FLU-sensitive C. albicans isolates (MIC90 = 0.03 µg/mL). Against the C. glabrata, C. krusei, C. parapsilosis, and C. tropicalis isolates, ibrexafungerp MIC90 values were 0.125, 0.5, 0.25, and 0.125 µg/mL, respectively. Ibrexafungerp's MIC values were not adversely affected when tested at lower pH (4.5). These values are similar to those observed in earlier epidemiologic studies of ibrexafungerp.

Conclusions: Ibrexafungerp exhibited significant in vitro activity against FLU-resistant and FLU-sensitive, vaginal, Candida spp isolates. The potent in vitro activity of ibrexafungerp was retained at lower pH (4.5), relevant for the vaginal milieu. These results suggest that ibrexafungerp is a highly-promising, orally bioavailable antifungal agent for the treatment of VVC and prevention of recurrence.

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**Abstract 3221**

**Using saliva for precision dosing of antifungal drugs: saliva population pharmacokinetic model**

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**Background:** Evidence supporting precision dosing has grown stronger for many antifungal drugs. Prompt action on sub- or supra-therapeutic drug exposure will likely optimize treatment outcomes for invasive fungal infections. Saliva sampling is being considered as a non-invasive, more feasible alternative to plasma sampling for therapeutic drug monitoring (TDM). However, very limited studies have explored the saliva-based TDM, with currently no clinically-validated saliva models.

**Materials/methods:** We conducted a systematic review using database search of up to July 2019 on PubMed® and Embase® to evaluate the evidence supporting saliva-based TDM for azoles, echinocandins, amphotericin B and fluocytosine. For eligible drugs, a saliva population pharmacokinetic analysis was performed using Nonlinear Mixed Effects Modelling in NONMEM 7.4.

**Results:** From the systematic review of 14 included studies, fluconazole and voriconazole demonstrated a good saliva penetration with an average saliva-plasma ratio of 1.21 (±0.31) for fluconazole and 0.56 (±0.18) for voriconazole, and strong correlation [r=0.89-0.98] between saliva and plasma total drug concentrations. Based on the evidence for TDM, and available data, a population pharmacokinetic analysis was performed for voriconazole. 137 voriconazole plasma and saliva concentrations from 11 patients (10 adults, 1 child) were available from the included studies. Voriconazole pharmacokinetics was best described by a 1-compartment model with first order absorption, parameterized by clearance of 4.56 L/h (36.9% CV), volume of distribution of 60.7 L, absorption rate constant of 0.858 (fixed), and bioavailability of 0.849. Distribution from plasma to saliva was kinetically identical to the plasma kinetics, but the extent of distribution was lower, which was modelled by a scale factor of 0.5 (4% CV) to describe distribution from the plasma compartment to saliva [Figure 1]. This value is also consistent with the free fraction of voriconazole (42%), which penetrates saliva. A proportional error model best accounted for the residual variability.

**Conclusions:** The developed saliva model provides a promising framework for facilitation of saliva-based precision dosing of voriconazole. Development of saliva assays, prospective pilot studies on saliva-based TDM, and salivary pharmacokinetic studies on newer antifungal drugs, will help to implement this innovative precision dosing framework in clinical practice.

**Figure 1.** Saliva population pharmacokinetic model of voriconazole.

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Abstract 3224

Risk factors for treatment failure of prosthetic joint infections: a multi-centre prospective cohort study

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Background: According to current guidelines, two-stage exchange revision remains the gold standard for the treatment late prosthetic joint infections (PJIs), whereas debridement, antibiotics, and implant retention (DAIR) has been widely accepted for acute infections. While the rates of success following prosthesis removal reaches up to 80-90%, unacceptable higher rates of failures after DAIR have been frequently described. We aimed at evaluating the epidemiology and the outcome of patients treated for PJIs and identify factors predictive of failure.

Materials/methods: From July 2013 to December 2015, patients with PJIs were prospectively enrolled in a national cohort study among 12 hospitals to describe pathogens, diagnosis, surgical strategies adopted, and factors associated with failure after 2-years follow-up. PJIs was defined using the IDSA criteria. Treatment failure was defined as recurrent PJIs, amputation, death, or chronic antibiotic suppression. Potential risk factors for treatment failure were assessed using a Cox regression model.

Results: A total of 199 patients undergoing hip, knee and shoulder (n=3) arthroplasty were available for analysis. Twenty-two (11%) patients died during the follow-up. In the two-year post-diagnosis analysis, overall treatment failure occurred in 17% (n=34/199). Knee and hip rate failure in the 2-year follow up were 16.2% (n=11/68), 18.2% (n=14/77), respectively. DAIR, one-stage exchange, two-stage exchange, and arthrodesis was performed in 44.7%, 25.4%, 22.3%, 7.6% respectively. Failure rates for DAIR, one-stage exchange, two-stage exchange, and arthrodesis after 2-year follow-up were 28.6% (n=16/56), 4.8% (n=2/42), 15.8% (n=6/38), 0% (n=0/15), respectively. Factors independently associated with PJIs failure were older age (adjusted hazard ratio [aHR], 1.03; 95% confidence interval [CI], 1.00–1.07; p =0.017), DAIR strategy (aHR, 3.21; 95% CI, 1.56–6.57; p <0.001), and infection due to Acinetobacter sp. (aHR, 3.38; 95% CI, 1.03–11.04; p =0.044). Microbial diagnosis yielded positive culture in 71.7%. Staphylococcus aureus (34%), coagulase-negative staphylococci (28%), Pseudomonas aeruginosa (17%) were more prevalent. Polymicrobial PJIs were diagnosed in 32.8%.

Conclusions: In this cohort of patients with PJIs an overall 2-years failure-free survival rate was 83%, in which patients undergoing DAIR for PJIs eradication and Acinetobacter sp. infection was independently associated with failure.

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Abstract 3225

**Efflux pumps contribute to intrinsic clarithromycin resistance in clinical *Mycobacterium abscessus* isolates**

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**Background:** The emergence of clarithromycin resistance is a challenge in treating *Mycobacterium abscessus* infections. Known mechanisms that contribute to intrinsic clarithromycin resistance focus on *rrl* gene-related mutations, but resistant clinical isolates often exhibit an inconsistent *rrl* genotype.

**Materials/methods:** In this study, 194 clinical *Mycobacterium abscessus* isolates were collected from patients with lung infections and the whole-genome of each isolate was sequenced. A comprehensive examination of the molecular mechanisms underlying intrinsic clarithromycin resistance was performed, combining MIC determination, comparative genome sequence analysis and qRT-PCR.

**Results:** Of the 194 isolates, 13 (6.7%) were clarithromycin resistant; only seven of these harbored a *rrl* 2270/2271 mutation. The remaining 6 resistant isolates did not exhibit a specific resistance-associated mutation in the clarithromycin target-site genes, *rrl, rplC, rplD and rplV*, or in the *rrl* modification gene *erm* [41]. qRT-PCR analysis showed that the increased expression of the efflux pump genes, MAB_2355c, MAB_1409c and MAB_1846, as well as their positive regulatory gene *whiB7*, consistently correlated with increased clarithromycin resistance. The presence of efflux pump inhibitors significantly decreased the MIC of clarithromycin for nonsusceptible isolates, especially the intrinsic resistant isolates that exhibited no *rrl* 2270/2271 mutation.

**Conclusions:** These findings indicate that efflux pumps play a prominent role in the intrinsic resistance of *M. abscessus* to clarithromycin, complementing other known resistance mechanisms.

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Clinical impact of metagenomic next-generation sequencing of plasma cell-free DNA for the diagnosis of infectious diseases: a multi-centre retrospective cohort study

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Background: Metagenomic next-generation sequencing (mNGS) of plasma cell-free DNA has emerged as an attractive diagnostic modality allowing broad-range pathogen detection, noninvasive sampling, and earlier diagnosis. However, little is known about its real-world clinical impact as used in routine practice.

Materials/methods: We performed a retrospective cohort study of all patients for whom plasma mNGS (Karius test) was performed for all indications at 5 U.S. institutions over 1.5 years. Comprehensive chart review was performed, and standardized assessment of clinical impact of the mNGS based on the treating team’s interpretation of Karius results and patient management was established.

Results: A total of 82 Karius tests were evaluated, from 39 (47.6%) adults and 43 (52.4%) children and a total of 53 (64.6%) immunocompromised patients. Karius positivity rate was 50/82 [61.0%], with 25 [50.0%] showing two or more organisms (range, 2-8). The Karius test results led to positive impact in 6 [7.3%], negative impact in 3 [3.7%], no impact in 71 [86.6%], and was indeterminate in 2 [2.4%]. Cases with positive Karius result and clinical impact involved bacteria and/or fungi but not DNA viruses or parasites. In 10 patients who underwent 16 additional repeated tests, only one was associated with clinical impact.

Conclusions: The real-world impact of the Karius test as currently used in routine clinical practice is limited. Further studies are needed to identify high-yield patient populations, define the complementary role of mNGS to conventional microbiological methods, and how best to integrate mNGS into current testing algorithms.

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Abstract 3227

**Applicability of dried blood spot for molecular epidemiology of HCV in coagulopathy patients**

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**Abstract third-party references:** Supported by FAPERJ, CNPQ, FIOCRUZ

**Background:** Hepatitis C virus (HCV) can be transmitted by contact with blood and biological fluids. HCV infection is highly prevalent in certain groups, including individuals with coagulopathy who are frequently exposed to blood. The objective of this study is to evaluate the genetic variability of HCV using serum and dried blood spot (DBS) samples in patients with coagulopathy.

**Materials/methods:** A total of 40 patients with chronic hepatitis C were recruited, 18 of whom had hereditary coagulopathy and 22 had no coagulopathy. Serum and DBS samples were collected from each patient and submitted to qualitative PCR for amplification of NS5B regions. Samples with detected RNA were then submitted to Sanger nucleotide sequencing for genotype determination, phylogenetic analysis and determination of resistance mutations.

**Results:** Mean age of the studied population was 44.6 ± 10.7 and the majority of the individuals were male (80%). HCV RNA was detected in 31 (77%) serum and 32 DBS (80%) where 28 individuals had HCV RNA in serum and DBS simultaneously. NS5B detection was associated to serum viral load and was more frequent in patients without coagulopathy. Regarding the HCV genotypes in serum, most of them belongs to genotype 1 (n = 14), where 5 of them had coagulopathy. Other genotypes were observed only in control group: genotype 2 (n = 1), genotype 3a (n = 7) and genotype 4 (n = 1). The same genotypes were observed in serum and DBS from the same individual and high homology between these isolates.

**Conclusions:** In this study, high prevalence of genotype 1, high concordance of genotypes obtained in serum and DBS and similarity between these isolates were observed, showing the applicability of DBS to molecular epidemiological studies of HCV.

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A phase II open-label clinical trial of investigational microbiota-based drug RBX2660 for prevention of recurrent *Clostridioides difficile* infection: two-years evaluation of efficacy, durability, microbiome changes and participant demographics

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Abstract third-party references: This analysis was funded by Rebiotix Inc., Roseville, MN

**Background:** Recurrent *Clostridioides difficile* infection (rCDI) is associated with mortality, compromised quality of life, and substantial medical cost worldwide. Disruption of the intestinal microbiome contributes to rCDI and microbiota therapy is gaining acceptance to prevent rCDI in multi-recurrent individuals. We present the 24-month analysis of safety, efficacy, and microbiome restoration from a Phase 2 open-label trial of the investigational microbiota-based drug RBX2660 for prevention of CDI recurrence. In addition, we report a subpopulation analysis to address potential demographic differences on treatment outcome and durability.

**Materials/methods:** This multicenter, open-label Phase 2 study included participants with multi-recurrent CDI who received ≤2 doses of RBX2660 delivered via enema 7 days apart. Efficacy was defined as absence of CDI recurrence through 8 weeks after the last dose. Durability was defined as continued CDI absence beyond 8 weeks. Safety and durability assessments occurred at 3, 6, 12, and 24 months. A general linear model was performed to assess the influence of age (≥65 years, <65 years), sex (female, male), and their interaction on clinical outcome. Participant stool samples were collected prior to and for up to 720 days after treatment, and microbiome changes were assessed by shallow shotgun sequencing.

**Results:** The RBX2660 efficacy to prevent rCDI at 8 weeks (79%;112/142) was higher than the CDI-free rate in the historical control group (31%, 23/75; p<.0001). The safety profile was consistent with previous reports for RBX2660. Among 97 participants who achieved treatment success at 8 weeks and were evaluable for long-term durability, 8 experienced a new CDI episode by the 24-month follow-up for an overall durability of 92%. Microbiome analysis of 503 stool samples from 110 treatment responders showed that the relative abundance of Bacteroidia and Clostridia shifted significantly higher within 7 days of treatment relative to baseline while Gammaproteobacteria and Bacilli declined sharply, and these changes persisted to at least 24 months. Age and sex did not have a statistically significant impact on efficacy or durability.

**Conclusions:** RBX2660 was efficacious for preventing rCDI, with clinical durability and maintained shifts in microbiome composition to 24-months after treatment. Importantly, neither efficacy nor durability was dependent on age or sex.

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Abstract 3238

**Amikacin resistance due to the aphA6 gene in multiply antibiotic-resistant Acinetobacter baumannii isolates belonging to global clone 1 from Iran**

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**Background:** TnaphA6-carrying repAci6 plasmids have been detected in Acinetobacter baumannii isolates belonging to global clones, GC1 and GC2, worldwide. Here, we examined whether RepAci6 plasmids family play a role in the dissemination of the aphA6 in GC1 A. baumannii isolates from Iran.

**Materials/methods:** A set of 55 multiply antibiotic-resistant A. baumannii isolates belonging to GC1 were included in this study. The susceptibility testing to amikacin (30 μg), kanamycin (30 μg), and neomycin (30 μg) was performed. PCR was used to examine the presence of the aphA6 gene and also to determine if it is located in TnaphA6. PCR was also used to examine whether TnaphA6 is present in a context similar to the backbone of plasmids encoding RepAci6. Unique sequences on either side of the repeated sequence 1, 2 and 3 (often found in repAci6 plasmids) were joined using previously designed PCRs, in cases that TnaphA6 was found in a context similar to the backbone of plasmids that carry the repAci6 gene.

**Results:** We found that 22 isolates carried the repAci6 gene, suggesting that they contain a RepAci6 plasmid family. Using primers linking the aphA6 gene to the backbone of repAci6 plasmid, it was revealed that 16 isolates from different hospitals harbored TnaphA6 on a repAci6 plasmid.

**Conclusions:** This study provides evidence for the dissemination of TnaphA6 on the plasmids encoding RepAci6 in Iranian A. baumannii isolates. Furthermore, it seems that TnaphA6 might be acquired by distinct plasmids separately as it was found to be located on the variants of repAci6 plasmids.

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Abstract 3242

Effective utilisation of limited isolation rooms to provide safe patient care and staff safety in lower/middle-income country

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**Background:** A tertiary care hospital is a 750 bedded hospital with only 17 airborne infection isolation room (AIIR)/negative pressure rooms to isolate patients who have been diagnosed or are suspected with prevalent diseases like tuberculosis, measles, and chickenpox. On the other hand, only 14 single room isolation are available to isolate multi drug resistant organisms (MDRO) like CRE (Carbapenem Resistant Enterobacter) or Colistin Resistant MDRO. Due to limited number of isolation rooms average number of hours to isolate infected patients took around 20 hours which ultimately places direct health care staff at risk of exposure to infected patients.

**Materials/methods:** Plan-Do-Study-Act (PDSA) quality improvement methodology was utilized to decrease the average number of hours to isolate infected patients and to reduce the exposure of health care workers to communicable diseases. Detailed analysis were done to identify root cause and its effect at multiple levels to ascertain reasons. Multiple strategies were done with multidisciplinary team which include but are not limited to coordination with IT team to place isolation alerts in system, screening flyers and questions at ED triage, close coordination with admission and bed management office (BMO), daily morning and evening rounds by IPs in ED, daily morning meeting with microbiology and BMO to intervene immediately to isolate patient timely, introduction of IPs 24/7 on-call system to facilitate units, ED, BMO and admission office immediately to provide recommendations for patient placement and cohorting same infection patients wherever possible.

**Results:** Results showed significant reduction in the number of hours to isolate infected patients from 20 hours to 4 hours in one year. As a result, rate of Health Care Worker’s exposures to communicable diseases also decreased from 6.7 to 1.5. TB exposure decreased from 6.0 to 1.9, Measles 4.75 to 1.5 and Chickenpox 7.3 to 1.0. Significant reduction on cost incurred by organization for the employees who were exposed to these diseases for post exposure prophylaxis also decreased i.e. from around Rs. 290000 ($3000) to Rs. 59520 ($600).

**Conclusions:** Multidisciplinary approach provides a proven strategy to bring improvement and enhance patient and staff safety in limited resource settings.

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**Efficacy of cefiderocol against carbapenem-resistant Acinetobacter baumannii in ventilator-associated pneumonia mouse model**

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**Background:** Cefiderocol (CFDC) is a novel siderophore cephalosporin with potent activity against carbapenem-resistant Gram-negative bacilli and stability against carbapenemase. We evaluated the efficacy of cefiderocol against carbapenem-resistant A. baumannii in ventilator-associated pneumonia (VAP) mouse model.

**Materials/methods:** Carbapenem-resistant A. baumannii (blaOXA-51-like) was used in this study. MICs of CFDC and meropenem (MEPM) were measured by micro dilution assay. In VAP model, 5mm length tube was inserted through a vocal code of cyclophosphamide-induced immunocompromised ddY mouse (6 weeks old, male), followed by bacterial inoculation (5x10^5 cell/mouse). Antibiotics were administered intraperitoneally three hours post infection. Drug administration doses and intervals were determined based on plasma drug concentrations of infected mouse. In treatment study, survival rates for 120 hours and number of bacterial loads of the lungs and blood were counted and histopathological examination of the lungs at 48 hours post infection were evaluated.

**Results:** MICs were 0.5 mg/L for CFDC and 128 mg/L for MEPM. According to PK analysis, 55 mg/kg of CFDC and 1,100 mg/kg of MEPM (combined with same dose of cilastatin) was administered every six hours, in order to achieve time above MIC >70% for CFDC and >30% for MEPM, respectively. These exposures could be achieved in human for CFDC, but could not be achieved for MEPM due to high MEPM MIC of the test strain. In treatment study, all the mice in both treatment groups survived and survival rate was statistically significantly improved, compared to 28.6% (2/7) survival rate in control group. The number of bacterial load of the lungs (n=6-7, log10 CFU/lung±SEM) was significantly reduced in CFDC group (4.64±0.29, \(P<0.0001\)) and MEPM group (3.19±0.11, \(P<0.0001\)), compared to 7.99±0.44 in control group. Bacteremia was observed in 33.3% (2/6) of mice in control group, while no mouse in treatment groups. In lung histopathological examination, infiltration of inflammatory cells and hemorrhage in alveoli were observed in control group, which were limited in treatment groups.

**Conclusions:** In this study, we showed the efficacy of CFDC against carbapenem-resistant A. baumannii in VAP mouse model. CFDC can be a potent treatment option against VAP caused by carbapenem-resistant A. baumannii.

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**Intracellular drug targets in Mycobacterium tuberculosis revealed by a chemogenetic approach**

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**Background:** Mycobacterium tuberculosis (Mtbg), the etiological agent of tuberculosis, causes chronic lung diseases to one third of the global population. Due to increasing prevalence of multi-drug-resistant tuberculosis with limited alternatives to first-line antituberculosis drugs, there is an urgent need to combat these resistant Mtb by novel drug discovery approach. We develop an advanced intracellular drug-screening assay to screen compounds in Mtb infected macrophages. The objective of this investigation is to identify hit compounds mode of action or drug targets from this drug discovery approach using WGS and bioinformatics analysis.

**Materials/methods:** 80 hit compounds were subject to in vitro MICs in different carbon sources. High-throughput phenotypic screening were performed and 1-6 resistant mutants were obtained from each hit compound. The genomes of parental strain and the mutants were sequenced using Illumina MiSeq. The reads were mapped to the standard reference genome H37Rv using BWA, and the variants were identified and annotated by GATK and snpEff.

**Results:** The genomes of 53 Mycobacterium tuberculosis mutants, screened from 15 different hit compounds, were sequenced. We found 90 mutations in at least 25 different genes that was associated with potential drug resistance acquisitions. Independent mutations were reported in ethA, which is a mycobacterial enzyme responsible for the drug ethionamide bio-activation to treating tuberculosis. A mutation was found in rpoB, which is a known drug target, encoding the beta subunit of RNA polymerase. Apart from known drug targets, multiple mutations were discovered in novel antimycobacterial drugs such as mmpL3, which is a membrane transporter in the resistance-nodulation-cell division family. Mutations were also reported in candidate drug targets such as prrB, which belongs to a two-component regulatory system composed of PrrB histidine kinase, and other genes.

**Conclusions:** Bioinformatics analysis of WGS of mutants screened against various compounds identified several promising genes that confer resistance to given chemical entity and as such may provide insight into their mode of action or drug targets. Some targets of these chemical libraries are consistent with those that are tied to the proposed mechanism of action or resistance. The investigation has extended our understanding of the biological basis for the antituberculous actions.

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Tetanus prophylaxis in wound management of patients with rheumatoid arthritis

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1National Coordination Centre for Communicable Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands, 2Leiden University Medical Center, Leiden, Netherlands, 3Centro Hospitalar do Porto, Porto, Portugal, 4Oxford University Hospitals, Oxford, United Kingdom, 5Centro Hospitalar Universitário São João, Porto, Portugal, 6Lausanne University Hospital, Lausanne, Switzerland

Background: Adults with wounds who have received primary tetanus toxoid (TT) vaccines are given a booster if the last TT-dose was ≥ 5-10 years. Immunocompromised patients frequently receive a booster regardless of a recent dose plus additional tetanus immunoglobulin (TIG). We aimed to evaluate this strategy for patients with rheumatoid arthritis (RA).

Materials/methods: Studies were searched in PubMed that examined immunogenicity of a TT 20 IU booster in adult RA patients. Protection was defined as anti-TT IgG > 0.1 IU/ml.

Results: In 5 studies antibody response was measured 4-5 weeks after TT vaccination in 347 patients, age 18-81 years. No healthy controls were examined for comparison. Treatment consisted of DMARDs and/or biologicals with or without corticosteroids.

At baseline 15/269 (5.6%) patients were not protected. It was unclear if this was due to old age, missing primary vaccinations or a very long period since the last dose. In one study (n=68) the lower bound of the 95% CI of the geometric mean titer was > 0.1 IU/ml. One study (n=10) did not provide baseline titers, but only post-vaccination titers: all > 1.0 IU/ml.

After vaccination 5/269 patients (1.9%) were not protected: they used MTX alone (n=3), or rituximab/MTX or tocilizumab/MTX (1 each). A ≥2-fold increase was demonstrated in 57-74% and ≥4-fold increase in 40-59% of patients. Responses in patients with rituximab/MTX (n=64), tocilizumab/MTX (n=50) or tabalumab/MTX (n=51) were similar to those with MTX alone. Use of baricitinib with or without MTX gave similar ≥2- or ≥4-fold changes as other immunosuppressants.

Conclusions: The booster response in case of a TT-dose < 5 years has not been evaluated in RA patients. Most patients (94%) are protected before vaccination if the last dose was ≥ 5 years ago. A single booster raises this to 98%. Unclear is if age, insufficient number of childhood vaccines, long interval since last dose, or immunosuppressive therapy limits antibody response. Recall response is not affected by treatment combinations compared to methotrexate alone. Consequently, additional TIG next to TT-vaccination should be considered in tetanus prophylaxis in case of a TT-dose > 5 year since last dose or incomplete childhood vaccinations.

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Relevance of EORTC-MSG criteria in invasive fungal infections in lung transplant recipients

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1Université Bordeaux, Bordeaux, France, 2Hôpital Pellegrin, CHU Bordeaux, Service des Maladies Infectieuses et Tropicales, Bordeaux, France, 3Hôpital Haut-Lévêque, CHU Bordeaux, Service des Maladies Respiratoires, Pessac, France, 4Hôpital Haut Lévêque, CHU Bordeaux, Service d’Anesthésie-Réanimation II, Unité de Réanimation polyvalente de la Maison du Haut-Lévêque, Pessac, France, 5Université Bordeaux, UMR CNRS 5234, Bordeaux, France, 6CHU Bordeaux, Laboratoire de Parasitologie-Mycologie, Bordeaux, France, 7Hôpital Pellegrin, CHU Bordeaux, Pharmacie, Bordeaux, France, 8Hôpital Haut-Lévêque, CHU Bordeaux, Service d’Imagerie Thoracique et Cardiovasculaire, Pessac, France, 9Hôpital Haut-Lévêque, CHU Bordeaux, Service de Chirurgie Thoracique, Pessac, France

Background: Invasive fungal infections (IFI) are a major cause of mortality in lung transplant recipients (LTRs). The earlier the diagnosis is made, the sooner appropriate treatment can be initiated and better would be the prognosis. Unfortunately, diagnostic tools’ performance varies according type of immunodepression. EORTC-MSG criteria are used in clinical trials to classify IFI in proven, probable or possible form. In critically ill patients, clinical algorithm was proposed to diagnose putative aspergillosis. We assessed if these criteria are relevant in LTRs population.

Materials/methods: A retrospective study of IFI occurring in LTRs followed in Bordeaux University Hospital, France, from 2011 to 2017 was conducted. All episodes considered by clinicians as IFI in LTRs were analyzed. Proven and probable IFI fulfilling EORTC-MSG criteria were compared to probable IFI treated but not fulfilling all EORTC-MSG criteria. We described IFI and compared 6-months survival.

Results: During the 7-years study period, 36 IFI were diagnosed, among them 28 pulmonary IFI were selected for comparative analysis. Twenty-five episodes were considered as invasive pulmonary aspergillosis (IPA). IFI occurred at a median time of 436 days post-transplantation (2-9031 days). Twenty-four (67%) occurred in patients who had fungal colonization before IFI. Seven (19%) occurred despite specific antifungal prophylaxis and 15 (42%) patients had bacterial co-pathogens with Pseudomonas spp in 9 cases (60%). Aspergillus fumigatus was found in 53% and galactomannan in bronchoalveolar lavage was positive in 75% but realized only for 16/25 (64%) IPA. Main radiologic abnormalities were nodules (n=23, 69%), with halo sign (n=11, 48%), cavity (n=8, 24%), consolidation (n=7, 21%) and air-crescent sign (n=4, 12%). Twelve patients (63%) had specific radiologic signs defined in EORTC-MSG criteria. There were no statistically differences between EORTC group and non-EORTC group in term of 6-months survival (55% vs 75%, p=0.32), as well as in clinical, radiological and mycological data. Twenty-two (88%) IPA fulfilled putative invasive aspergillosis criteria. Cumulative incidence over the study period reached 20,2%.

Conclusions: Survival was not statistically different between LTRs who developed IFI fulfilling EORTC-MSG criteria and those not. Radiological criteria should be improved and other lesions as tree-in-bud micronodules, ground-glass opacities and consolidation have to be considered.

Aeromonas Presenter email address: lisa.martin.2802@gmail.com
**Abstract 3257**

**Rapid, direct antimicrobial susceptibility testing of positive blood cultures within 4 hours using ATP bioluminescence detection and machine learning method**

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**Background:** To prevent the spread of drug-resistant bacteria, a rapid and accurate antimicrobial susceptibility test (AST) is required. Since the amount of adenosine triphosphate (ATP) increases prior to bacterial division, ATP bioluminescence-based detection can serve as an AST method that can rapidly detect bacterial growth. We performed rapid AST by the ATP bioluminescence method using clinical samples of positive blood cultures (PBCs). A minimum inhibitory concentration (MIC) that was determined by a machine learning-based algorithm within 4 h was compared to the conventional MIC results obtained by the turbidity method at 24 h.

**Materials/methods:** We prepared two kinds of AST panels, one each for a gram-negative rod (GNR) and a gram-positive coccus (GPC). The GNR panel contained 12 antimicrobials and the GPC panel contained 10 antimicrobials; a set of 7 or 8 two-fold serial dilutions were prepared for each antimicrobial. At first, we developed the dataset by measuring the ATP bioluminescence for 4 h and conventional turbidity at 24 h, using pure colonies of *Escherichia coli* (77 strains) and *Staphylococcus aureus* (94 strains). The MIC determination algorithms for GNR and GPC were created using a machine learning method based on the dataset, and were validated by evaluating the essential agreement (EA) rates. These algorithms were then applied to the ATP bioluminescence data obtained from 14 clinical samples of PBCs at the Toyama University Hospital. The determined MICs were compared with the conventional MICs obtained by the turbidity method to evaluate the EAs and the categorical agreements (CAs).

**Results:** The EAs of *E. coli* and *S. aureus* from pure colonies at 4 h were 97.3% and 96.3%, respectively. These data indicated that the algorithm can accurately determine the MIC for pure colonies. The EAs and CAs for the PBCs are shown in Table 1. The EAs and the CAs in average for 14 clinical samples were 89.2% and 89.9%, respectively.

**Conclusions:** The rapid AST method using ATP bioluminescence detection could successfully determine MICs directly from PBCs within 4 h. Thus, this method is promising as it can facilitate appropriate antimicrobial treatment, and reduction in medication and hospital admission charges.

**Table 1. EAs and CAs of positive blood culture samples determined after 4 h of culture using ATP bioluminescence detection and machine learning method.**

<table>
<thead>
<tr>
<th>Strain number</th>
<th>#1</th>
<th>#2</th>
<th>#3</th>
<th>#4</th>
<th>#5</th>
<th>#6</th>
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<tr>
<td>Species</td>
<td>E. coli</td>
<td>E. coli</td>
<td>K. pneumoniae</td>
<td>K. pneumoniae</td>
<td><em>P. aeruginosa</em></td>
<td><em>P. aeruginosa</em></td>
</tr>
<tr>
<td>EA</td>
<td>12/12</td>
<td>10/12</td>
<td>12/12</td>
<td>12/12</td>
<td>10/10</td>
<td>10/10</td>
</tr>
<tr>
<td>CA</td>
<td>12/12</td>
<td>10/12</td>
<td>12/12</td>
<td>11/12</td>
<td>8/10</td>
<td>10/10</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Strain number</th>
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<th>#8</th>
<th>#9</th>
<th>#10</th>
<th>#11</th>
<th>#12</th>
<th>#13</th>
<th>#14</th>
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<tbody>
<tr>
<td>Species</td>
<td><em>S. aureus</em></td>
<td><em>S. aureus</em></td>
<td><em>S. epidermidis</em></td>
<td><em>S. epidermidis</em></td>
<td><em>S. epidermidis</em></td>
<td><em>S. epidermidis</em></td>
<td><em>S. caprae</em></td>
<td><em>S. capitis</em></td>
</tr>
<tr>
<td>EA</td>
<td>9/10</td>
<td>8/10</td>
<td>9/10</td>
<td>7/10</td>
<td>9/10</td>
<td>9/10</td>
<td>10/10</td>
<td>8/10</td>
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<tr>
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<td>8/10</td>
<td>9/10</td>
<td>8/10</td>
<td>9/10</td>
<td>10/10</td>
<td>9/10</td>
<td>7/10</td>
</tr>
</tbody>
</table>

**Avg.**

Note: The denominator shows the total number of tested antimicrobials and the numerator shows the number of antimicrobials of agreement. In case of *P. aeruginosa*, two antimicrobials were excluded from the evaluation because no breakpoint was provided in the CLSI guideline. The EA is of agreement within ±1 two-fold dilution of the conventional MIC and the CA is in the same category of results (SIR) as the conventional results.

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Abstract 3259

Serum levels of neutrophil elastinase-associated lipocalin in acute brucellosis and brucellar spondylodiscitis
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Abstract third-party references: This study was supported by the Scientific Research Projects Coordination Unit of Selcuk University with project number 18401011.

Background: Brucellosis is a zoonotic infectious disease caused by Brucella spp., an intracellular bacterium. Its most common complication is musculoskeletal system involvement. The neutrophil gelatinase-associated lipocalin (NGAL) molecule is a major component of the natural antimicrobial immune system. It appears early in granulocyte differentiation and is, therefore, a marker of neutrophil formation. NGAL acts as a siderophore-binding protein to prevent bacterial iron uptake. The objective of this study is to measure the serum levels of NGAL in patients with acute brucellosis and brucellar spondylodiscitis, and to determine whether there is a correlation between serum NGAL levels and the progression and complications of the disease.

Materials/methods: This study was conducted with 240 patients and 120 healthy controls. Acute brucellosis was diagnosed with standard tube agglutination test (≥ 1/160), and/or there was Brucella spp. growth in the blood culture. NGAL levels were determined with ELISA assay.

Results: The median NGAL value was 456.67 ng/L in patients with acute brucellosis and 113.84 ng/L in the control group. The median NGAL value was statistically higher in the patient group (p=0.001). The median NGAL value was 1885.62 ng/L in patients found to have brucellar spondylodiscitis and 356.87 ng/L in those who had no brucellar spondylodiscitis. This difference was statistically significant (p=0.001) (Figure 1). The erythrocyte sedimentation rate (ESR) and C-reactive protein values were found higher in patients who had brucellar spondylodiscitis than in those who did not. The blood culture positivity rate was 36.02%. Patients whose blood cultures were positive had higher NGAL levels (p=0.001). The blood culture positivity rate was higher in patients who were diagnosed with brucellar spondylodiscitis than in those who had no brucellar spondylodiscitis (p=0.001). A regression analysis showed that female gender and high levels of NGAL, ESR, and alanine aminotransferase could be used as predictors of brucellar spondylodiscitis. The explanatoriness of the model was 82.3%.

Conclusions: NGAL seems to be a useful marker for the diagnosis of acute brucellosis and to predict the presence of brucellar spondylodiscitis.

Figure 1: NGAL levels of acute brucellosis patients with and without brucellar spondylodiscitis.

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**Clinical evaluation of a multiplex real-time PCR-based Neoplex RV-Panel A kit for the simultaneous detection of respiratory viral pathogens**

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**Background:** Nucleic acid amplification assay, in particular, multiplex real-time PCR has become one of the routine clinical diagnostic tools for the detection of respiratory infectious agents, because it is faster, more accurate and convenient than traditional methods. Neoplex™ RV-Panel A detection kit (Genematrix, Seongnam, Korea) applies single-tube multiplex real-time RT-PCR based on Genematrix’s proprietary C-Tag™ technology. High multiplexing based on C-Tag™ technology allows simultaneous detection of 10 respiratory viral pathogens in a single tube. This study aims to evaluate the clinical performance of Neoplex™ RV-Panel A detection kit compared with Allplex™ Respiratory Panel 1 and 2 (Seegene, Seoul, Korea) in nasopharyngeal swab.

**Materials/methods:** A total of 439 samples were retrospectively collected from residual nasopharyngeal swab samples. Nucleic acid eluted to a final volume of 50 ul was extracted using QIAamp® DSP Viral RNA Mini kit (Qiagen, Hilden, Germany). Using the comparators with Neoplex™ RV-Panel A, the cross-examination was performed on Influenza virus A(Flu A), Flu A/H1N1pdm09, Flu A/H3N2, Influenza B(Flu B), Respiratory syncytial virus(RSV) A, B, Parainfluenza virus(PIV) 1,2,3, and Adenovirus(AdV) by randomized single-blind method. The clinical sensitivity and specificity of Neoplex™ RV-Panel A were calculated by comparing the true positive and negative results confirmed by the comparators and reference method (sequencing assay). The correlation was measured by positive, negative percent agreement (PPA, NPA), overall percent agreement and Cohen's kappa. The estimates were given along with 95% CI.

**Results:** A total of 439 samples were identified without screening failure. The clinical sensitivity of Neoplex™ RV-Panel A was respectively calculated as followed: 100% for Flu A(96.87-100), A/H1N1pdm09(94.34-100), A/H3N2(93.47-100), RSV A(91.43-100), RSV B(94.08-100), PIV 1(92.73-100), PIV 2(91.43-100) and PIV 3(91.80-100), 98.25% for Flu B(90.71-99.69) and 97.50% for AdV(91.34-99.31). The clinical specificity was 100% (98.81-100) for all targets. The PPA, NPA and overall percent agreement were over 96.51% (94.11-97.95), and Cohen's kappa values were measured 0.9528-1.0.

**Conclusions:** Neoplex™ RV-Panel A detection kit is a sensitive and specific multiplex assay that is highly comparable to the commercial diagnostic kits. By detecting 10 respiratory viral pathogens simultaneously in a single test, Neoplex™ RV-Panel A detection kit could be a convenient tool for clinical and diagnostic facilities.

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Abstract 3265

First-described human fatal encephalitis caused by avian paramyxovirus serotype 1: agent of Newcastle disease
Sarah Winter1, Emmanuèle Lechapt2, Guillaume Gricourt3, Melissa Ndebi1, Nathalie Boddart1, Manoelle Kossorotoff4, Thomas Blauwblomme4, Demontant Vanessa1, Paul-Louis Woerther1, Jean-Michel Pawlotsky1, Stéphane Blanche4, Benedicte Neven4, Christophe Rodriguez*3


Background: Emerging diseases pose a significant risk to human health and are largely zoonotic. Accurately and early estimating the burden of these diseases is critical to identify public health policy and assessing its impact on control of them. One aspect of surveillance involves diagnosing the first human cases of transmitted pathologies including new pathogens. In this case, the broad spectrum of clinical metagenomics (CMg) is an unprecedented tool to achieve this goal. We report here a case of fatal zoonotic encephalitis by an avian virus described for the first time in human.

Materials/methods: A Turkish patient, diagnosed with ARPC1B deficiency was treated with bone marrow transplantation at the age of 12. Four months later, after a 3-day trip to Dubai, she presented with partial and then generalized seizures leading to the diagnosis of meningo-encephalitis confirmed by MRI. The exploration of different CSFs, negative by conventional microbiological techniques and the deterioration of clinical and radiological signs, led to a cerebral biopsy that establish the diagnosis by CMg but without saving the patient who died 2 months after the beginning of the symptoms. An 15189 accredited CMg technics was routinely performed with specific pan-pathogen extraction, DNA/RNA library prep followed by sequencing with NextSeq500 (Illumina) and analyzed with MetaMIC software.

Results: CMg have identified an Avian Paramyxovirus type 1 [APMV-1] responsible of New Castle Disease Virus (NDV) with a viral load of 3.7 log copies of genome/mg of biopsy. This result was confirmed retrospectively by qPCR [2.7-3.3] log copies of genome/mg of biopsy. Genome reconstruction of the virus yielded a sequence covering 99.8% and its analysis show (i) a closeness with pigeons from the Middle Eastern Region, (ii) the presence of avian most neuro-virulent described mutations in fusion protein [F].

Conclusions: Clinical metagenomics is the only microbiology technique that has made it possible to establish the diagnosis, quantification and characterization of the virus without a priori. To date it has not been established whether the virus came from Dubai or Turkey. However, the neurovirulence of the virus associated with the patient’s immune deficiency probably explains the severity of the infection.

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Abstract 3274

**Normocellular bacterial meningitis in adults: a prospective nationwide cohort study**

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**Background:** Normocellular community-acquired bacterial meningitis (CABM) is rare and likely underdiagnosed. The risk factors and outcome for this condition are poorly known. We aimed to examine the incidence, predisposing factors and outcome of patients with normocellular CABM.

**Materials/methods:** We accessed the nationwide and prospective database of the Danish Study Group of Infections of the Brain (DASGIB) to identify all adults with normocellular CABM treated at departments of infectious diseases in Denmark from year 2015 through 2018. Normocellular CABM was defined as a clinical presentation consistent with CABM combined with isolation of a pathogen in the cerebrospinal fluid (CSF) and a CSF leukocyte count ≤10 x 10^6/L. Outcome was categorised according to the Glasgow Outcome Scale (GOS) at discharge.

**Results:** Normocellular CSF was found in 12/696 (1.7%) CABM patients [Table 1]. The median age was 69.5 years [range 17-92] and 8/12 were male. Causative pathogens included *Streptococcus pneumoniae* in 10 patients [CSF cultures], *Staphylococcus aureus* in one [CSF culture], and *Neisseria meningitidis* in one [PCR of the CSF]. Eight patients had immuno-compromising conditions or were treated with potential immunomodulating drugs. In 4/11 patients, empirical treatment for CABM was interrupted due to low CSF cell count. Fatal outcome occurred in 3/12 patients and 8/12 had a Glasgow Outcome Scale (GOS) score of 1-4 at discharge.

**Conclusions:** Although infrequent, normocellular CABM should be considered in immuno-compromised patients and antimicrobial therapy for CABM continued until CSF microbiology examinations prove negative.

<table>
<thead>
<tr>
<th>Median age (range)</th>
<th>Male</th>
<th>Predisposing condition (7/12)*</th>
<th>Immunosuppressive therapy (3/11)</th>
<th>Septic shock</th>
<th>Causative pathogen</th>
<th>Detection method</th>
<th>Meningitis treatment interrupted</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>69.5 years (17-92)</td>
<td>8/12</td>
<td>Epidural catheter 1</td>
<td>Anagrelid 1</td>
<td>3/12</td>
<td><em>Streptococcus pneumoniae</em> 10</td>
<td>Culture: 11/12</td>
<td>Yes: 4/11</td>
<td>Died: 3/12</td>
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<tr>
<td></td>
<td></td>
<td>Alcohol abuse: 2</td>
<td>Interferon β-1a: 1</td>
<td></td>
<td><em>Neisseria meningitidis</em> 1</td>
<td>PCR: 1/12</td>
<td>No: 7/11</td>
<td>GOS 1-4: 8/12</td>
</tr>
<tr>
<td></td>
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<td>Thiamazol: 1</td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>MGUS (diagnosed during admission): 1</td>
<td></td>
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</tbody>
</table>

GOS: Glasgow Outcome Scale. MGUS: Monoclonal gammopathy of undetermined significance. *Some patients had more than one predisposing condition. #Defined by systolic blood pressure < 90

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Abstract 3275

Comparison of pneumonia and bacteraemia Caused by Stenotrophomonas maltophilia: analysis of risk factors, clinical outcomes and impact on antibiotic resistance

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Abstract third-party references: On behalf of Taipei Medical University

Background: Stenotrophomonas maltophilia (S. maltophilia) infections has increasingly emerged as a nosocomial pathogen in healthcare setting, especially in pneumonia and bacteraemia patients associated with high morbidity and mortality. The objective of this study was to compare clinical feature, risk factors, treatment outcome, and antibiotic resistance in patients with pneumonia and bacteraemia caused by S. maltophilia infections.

Materials/methods: We conducted a retrospective study in a tertiary teaching hospital in northern Taiwan. The medical records of the 319 patients of hospital-acquired S. maltophilia infections between July 1, 2016 and June 30, 2019 were reviewed, and sorted into groups of S. maltophilia bacteraemia (n = 56) and pneumonia (n = 263).

Results: The hospital-acquired S. maltophilia bacteraemia group was found to be significantly has higher 30-day mortality, more frequently central venous catheter use, respiratory failure with ventilator, Thrombocytopenia, solid organ malignancy, heart failure, and renal failure with hemodialysis than pneumonia group. The old aged patients were found to be more frequently in pneumonia group. The antibiotic susceptibility test of S. maltophilia revealed that the most susceptible agent of bacteraemic and pneumonic group was Tigecycline, followed by TMP/SMZ, levofloxacin and moxifloxacin respectively.

Conclusions: In this study, we found significantly higher mortality rate in the S. maltophilia bacteraemic group. The susceptibility test of tigecycline revealed better susceptible rate than TMP/SMZ (91.3% in pneumonic group and 85.7% in bacteraemic group respectively), and the levofloxacin had better susceptible rate in the pneumonic group than in the bacteraemic group. This result impact the empiric therapy of S. maltophilia infections in both pneumonic and bacteraemic patients, and the combination therapy of tigecycline + fluoroquinolones may be consider for severe sepsis or multidrug drug resistant of S. maltophilia infections.

Table 1

Antimicrobial susceptibility test (%) of bacteraemia and pneumonia group caused by S. maltophilia infections.

<table>
<thead>
<tr>
<th></th>
<th>Bacteraemia, n=56</th>
<th>Pneumonia, n=263</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMP/SMZ</td>
<td>46(82.1)</td>
<td>226(85.9)</td>
<td>0.567</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>48(85.7)</td>
<td>240(91.3)</td>
<td>0.446</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>35(62.5)</td>
<td>209(79.5)</td>
<td>0.025</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>34(60.7)</td>
<td>176(66.9)</td>
<td>0.674</td>
</tr>
<tr>
<td>Cefoperazone/Sulbactm</td>
<td>21(37.5)</td>
<td>107(40.7)</td>
<td>0.907</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>6(10.7)</td>
<td>34(20.5)</td>
<td>0.232</td>
</tr>
<tr>
<td>Ceftazidine</td>
<td>11(19.6)</td>
<td>29(11.0)</td>
<td>0.210</td>
</tr>
<tr>
<td>Minocycline</td>
<td>8(14.3)</td>
<td>8(3.0)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

# Data are expressed as case numbers (%) or mean ± standard deviations.

# TMP/SMZ: Trimethoprim/Sulfmethoxazole

Presenter email address: 89425@w.tmu.edu.tw
Characterisation of prevalence and resistance of *Aeromonas* isolated from patients with acute diarrhoea in Zhejiang province from 2010 to 2017

Xiao Chen*1, Wang Ruonan*2, Zhu Qiaoyun*2

*1 the First Affiliated Hospital, College of Medicine, Zhejiang University, hangzhou, China; *2 the First Affiliated Hospital, College of Medicine, Zhejiang University, hangzhou, China

**Background:** To learn the distribution and antimicrobial susceptibility of *Aeromonas* isolated from Patients with Acute Diarrhea in Zhejiang Province, and to provide basis for prevention and treatment.

**Materials/methods:** The fecal specimens of patients with acute diarrhea in 5 hospitals of Zhejiang Province from January 2010 to December 2017 were collected. The routine microbiological test procedure combining with MALDI-TOF mass spectrometry was carried out to identify the common intestinal pathogenic bacteria. The *Aeromonas* isolated were subjected to antimicrobial susceptibility test by Kirby-Baur method.

**Results:** A total of 12509 patients with acute diarrhea were enrolled in the study. 636 (5.1%, 636/12509) specimens were positive for *Aeromonas* strains and this pathogen was the third most prevalent bacterial pathogen after *DEC* and *Vibrio parahaemolyticus*. The *Aeromonas* could be isolated among different age groups, and the highest among the elderly was over 60 years old. *Aeromonas* was isolated whole year round and the peak season was summer (June to August). There was no significant difference in the detection rate between male and female.

A total of 688 strains of *Aeromonas* were isolated from 636 patients, among which only one *Aeromonas* species was isolated from 587 specimens, two *Aeromonas* species were isolated from 46 specimens, and three *Aeromonas* species were isolated from 3 specimens. As the sole pathogen, 587 strains were mainly composed of *Aeromonas veronii* (194, 28.20%) and *Aeromonas caviae* (182, 26.45%), followed by *Aeromonas hydrophila* (97, 14.10%).

Nearly half of *Aeromonas* is relatively less sensitive to cefoxitin (63.37%), tetracycline (61.63%) and imipenem (60.47%), and >85% isolates were sensitivity to quinolones. The resistance of *Aeromonas* to most antibiotics was significantly different among the three strains of *A. hydrophila*, *A. caviae* and *A. veronii* (P<0.05). The resistance rate of cefoxitin is higher than that of *A. caviae* and *A. veronii*.

**Conclusions:** *Aeromonas* is one of common pathogenic bacteria causing diarrhea in summer and autumn in coastal areas. The resistance of *Aeromonas* to most antibiotics was significantly different among different species.

**Presenter email address:** zsfchx80@163.com
Abstract 3280

Malaria outbreak investigations reveal high seroprevalence of arbovirus infections among febrile cases in Baringo County, Kenya

Timothy Nzomo*1, Roba Abdi1

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Background: Clinical symptoms of malaria remain virtually indistinguishable to those of arbovirus infections, including Dengue and Chikungunya viruses, leading to misdiagnoses in a significant number of individuals. Baringo County in Kenya recently experienced an upsurge of malaria cases. We aimed at providing differential diagnoses to support outbreak investigation, and hereby describe arbovirus co-infections among 63 febrile, clinically suspected cases in Baringo County, Kenya

Materials/methods: Sixty three matched samples of plasma, whole blood and Giemsa-stained blood smears were collected from febrile cases clinically suspected of malaria in the field and shipped to the national reference laboratory. Samples were tested using enzyme-linked immunosorbent assay (ELISA) for Dengue virus (DENV) and Chikungunya virus (CHIKV) IgM antibodies. Blood smear slides were examined by microscopy for malaria. Additionally, real-time PCR was performed for DENV, CHIKV and malaria.

Results: Out of the 63 matched blood smear that were received at the central lab for verification of field investigations, malaria was detected in 30 (47.6%) by microscopy. By PCR, malaria was detected in 17 (53.1%) of the 31 samples that passed the specimen quality assurance criteria for the test. All malaria parasites belonged to the *P. falciparum* species. Anti-DENV and anti-CHIKV IgM was detected in 28% and 53% respectively of the 63 samples tested, with 17% co-infected with both viruses. PCR results were negative for the two viruses. Malaria and arbovirus co-infection was found in 22.2% of the cases.

Conclusions: The results indicate co-circulation of malaria parasites with arboviruses and underscore the need for heightened surveillance for the viruses in the region. Further, there is need to increase clinician suspicion index for arbovirus infections in individuals presenting with acute febrile illness.

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Abstract 3282

**Plasmid diversity among genetically related *Klebsiella pneumoniae* blaKPC-2 and blaKPC-3 isolates collected in the Dutch national surveillance**

Antoni P.A. Hendrickx1, Fabian Landman1, Angela De Haan1, Dyogo Borst1, Sandra Witteveen1, Marga Van Santen1, Han Van Der Heide1, Leo Schouls1

1National Institute for Public Health and the Environment, Center for Infectious Disease Control (CIb), Bilthoven, Netherlands

**Background:** Carbapenemase-producing *Klebsiella pneumoniae* emerged worldwide the past three decades as an important pathogen causing high morbidity and mortality in hospitalized patients. For genomic pathogen surveillance, it is important to track the spread of bacterial strains including the plasmids they contain. However, little is known concerning the plasmid repertoire among *K. pneumoniae* strains. Therefore, the aim was to recapitulate the size, contents and diversity of the plasmids of genetically related *K. pneumoniae* strains. Hence, the aim was to recapitulate the size, contents and diversity of the plasmids of genetically related *K. pneumoniae* strains harboring the beta-lactamase gene *blaKPC-2* or *blaKPC-3* to determine their dissemination in The Kingdom of the Netherlands.

**Materials/methods:** Illumina next-generation genome sequencing was combined with Nanopore long-read sequencing to reconstitute complete plasmids (plasmidome) of *K. pneumoniae* isolates. wgMLST, UPGMA clustering, PHASTER and automated resistome (ResFinder) and replicome (PlasmidFinder) analyses were performed to determine the genetic relatedness and diversity of the contents of plasmids among *K. pneumoniae* cluster isolates.

**Results:** wgMLST revealed five genetic clusters (termed KpnClusters) comprised of *K. pneumoniae* blaKPC-2 isolates and four clusters consisted of *blaKPC-3* isolates. Each cluster had a distinct resistome and plasmidome, while isolates within clusters were highly similar. Only KpnCluster-019 blaKPC-2 isolates were found both in the Netherlands and the Caribbean islands. *K. pneumoniae* blaKPC-3 isolates were found predominantly in the collection from the Netherlands. Eighteen plasmids were identified and UPGMA analysis revealed that the plasmids were unrelated. However, the large [150-250 kb] and medium [50-150 kb] sized plasmids contained one or two replicons from the incompatibility group IncFIB(K) and IncFII(K), IncHI2 and IncHI2a, or IncFIB[pQil] and IncFII(K). These plasmids carried multiple different antibiotic resistance genes, but shared a variety of transposons, insertion sequence elements, conjugal transfer systems, cation transport systems, toxin/antitoxin systems, and RCS47 P1-prophage-related sequence elements. The small plasmids (<50 kb) with ColRNAI or IncY/IncX3/IncP6 type of replicons carried genes implicated in virulence, including a Type IV secretion system, colicin, and a biofilm dispersion protein.

**Conclusions:** A *K. pneumoniae* blaKPC-2 strain from KpnCluster-019 with unique resistome and plasmidome was transmitted between The Netherlands and the Caribbean. Implementing long-read sequencing in the Dutch surveillance provides important new insights in the success of transmission of *K. pneumoniae* strains and plasmids.

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**Abstract 3290**

**In vitro activity of cefiderocol against Gram-negative pathogens from different infection types**

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**Background:** Cefiderocol (CFDC) is a novel siderophore cephalosporin that has demonstrated potent activity against Gram-negative pathogens including carbapenem non-susceptible (NS) strains. We conducted a series of surveillance studies (SIDERO-WT) to evaluate *in vitro* activity of CFDC against clinical isolates collected in 2014-2018 mainly from Europe and North America. In this study, we compared *in vitro* activity of CFDC and comparator agents against Gram-negative pathogens from different infection types.

**Materials/methods:** A total of 38288 Gram-negative pathogens were included in the study (including 17234 from North America and 20911 from Europe). Minimum inhibition concentrations (MICs) were determined for CFDC, cefepime (FEP), cef-tazidime-avibactam (CZA), ceftolozane-tazobactam (C/T), ciprofloxacin (CIP), colistin (CST) and meropenem (MEM) by broth microdilution according to Clinical and Laboratory Standards Institute (CLSI) guidelines. CFDC was tested in iron-depleted cation-adjusted Mueller–Hinton broth according to CLSI guidelines. The CFDC susceptibility rate was estimated based on CLSI provisional susceptible breakpoint (4 mg/L) while for the comparators EUCAST breakpoints were applied.

**Results:** Pathogens isolated from respiratory samples represented 34% of the strains while pathogens from cUTI samples represented 22% and from bloodstream infections 14.9%. The distribution of pathogens varied with the site of infection with *Pseudomonas aeruginosa* being mostly present in respiratory samples and *Escherichia coli* in the samples from urinary tract and from blood stream infections. Meropenem non-susceptible isolates [MIC>2 mg/L] were mostly present in respiratory samples [26.3%], followed by bloodstream infections [12.8%] and samples from urinary tract [7.7%]. Susceptibility to cefiderocol varied between 98.7% and 99.6% depending on the source of infection.

**Conclusions:** CFDC maintained potent antibacterial activity against Gram-negative pathogens regardless of the site of infection.

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Abstract 3291

**Mother-to-child transmission of curable sexually-transmitted infections in HIV-infected women in South Africa**

Remco Peters*, Ute Feucht, Dawie Olivier, Lindsey De Vos, Phuti Ngwepe, Jeffrey Klausner, Andrew Medina-Marino

1Foundation for Professional Development, Pretoria, South Africa, 2University of Pretoria, Pretoria, South Africa, 3University of California, Los Angeles, Los Angeles, United States

**Background:** South Africa has a very large burden of sexually transmitted infections (STIs). STIs can be transmitted from mother to child during pregnancy or delivery. Newborn infections have been associated with morbidity and mortality. We report on the frequency and characteristics of mother-to-child transmission of three curable STIs: *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG) and *Trichomonas vaginalis* (TV).

**Materials/methods:** Nasopharyngeal swabs were obtained from newborns of HIV-infected mothers diagnosed with CT, NG or TV at their postnatal visit at three primary healthcare facilities in Tshwane District, South Africa. Swabs were tested using the Xpert® CT/NG and TV assays. Targeted treatment was provided to newborns with a positive Xpert® result and test-of-cure was done after three weeks.

**Results:** Eighty-five mother-newborn pairs were enrolled within 60 days of delivery (Median= 6 days; IQR= 4 days). The frequency of mother-to-child transmission was highest for CT followed by NG and TV (Table 1); these frequencies were 43%, 29% and 24% if analysis was limited to visits within two weeks from delivery. Positive Xpert results were recorded in asymptomatic newborns for CT at up to 45 days post-delivery and for TV up to 44 days.

**Table 1. Frequency of Mother-to-child STI transmission**

<table>
<thead>
<tr>
<th></th>
<th>Number of mothers with positive test</th>
<th>Proportion of neonates with positive test</th>
<th>Transmission rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Chlamydia trachomatis</em></td>
<td>63</td>
<td>25/62</td>
<td>42%</td>
</tr>
<tr>
<td><em>Neisseria gonorrhoeae</em></td>
<td>7</td>
<td>2/7</td>
<td>29%</td>
</tr>
<tr>
<td><em>Trichomonas vaginalis</em></td>
<td>28</td>
<td>8/28</td>
<td>29%</td>
</tr>
</tbody>
</table>

Lower maternal CD4 count (p=0.020) and emergency caesarean section (p=0.095 vs. normal vaginal delivery and p=0.043 vs. elective caesarean) were associated with CT transmission to the newborn, but not with TV transmission. Maternal age, gestational age at delivery, (un)suppressed viral load and breastfeeding were not associated with a positive Xpert® result. Newborn test-of-cure showed that STIs had been cleared following treatment.

**Conclusions:** Mother-to-child transmission of curable STIs is common amongst STI-HIV co-infected women in South Africa. These STIs may be present in the airways of exposed newborns for considerable time after delivery, result in infection or colonization and may increase their risk for other infectious or chronic health conditions. Screening for STIs during pregnancy is warranted in high prevalence settings to prevent mother-to-child transmission.

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Six versus four weeks of intravenous antibiotic treatment for Staphylococcus aureus endocarditis

Sabrine Douiyeb*1, Anda Samson2, Nienke Roescher3, Thomas Van Der Vaart4, Jan Van Der Meer4, Wazir Baig5, Jianhua Wu5, Anna Collell Prats1, David Harvey6, Richard Gillott1, Kim Sigaloff1, Jonathan Sandoe1

1Amsterdam UMC, locatie VUmc, Amsterdam, Netherlands, 2Hull University Teaching Hospitals NHS Trust, Hull, United Kingdom, 3St. Antonius Hospital, Nieuwegein, Netherlands, 4Academic Medical Centre, Amsterdam, Netherlands, 5Leeds General Infirmary, Leeds, United Kingdom, 6Wirral University Teaching Hospital NHS Foundation Trust (WUTH), Birkenhead, United Kingdom, 7University Hospitals Plymouth NHS Trust, Plymouth, United Kingdom

Background: There is limited evidence to guide the duration of treatment of left sided Staphylococcus aureus native valve (SA-NVE) which is reflected in different guideline recommendations; European Society guidelines (ESC) advise 4-6 weeks, while the British guidelines recommend 4 weeks. We compared outcome and characteristics of patients treated with 4 vs 6 weeks antibiotics.

Materials/methods: A multi-center retrospective study in 7 hospitals in England (Leeds, Wirral, Hull and Plymouth) and the Netherlands (Amsterdam, Nieuwegein). Eligible were patients admitted between 2011 and 2018 with definite methicillin-sensitive SA-NVE (modified Duke criteria). Exclusion criteria were: <18 years, prosthetic valve or device, right sided endocarditis, MRSA or complications requiring extension of antimicrobial treatment, such as vertebral osteomyelitis, abscess (spleenic, cerebral, intracardiac) or death during therapy. Demographics, treatment and outcome variables were collected. Clinical cure was defined as the absence of relapse or death within 6 months following completion of antibiotic therapy.

Results: Sixty-two patients met the inclusion criteria; 17 were treated for 4 weeks; 28 days (IQR 26 to 30) and 43 patients for 6 weeks; 43 days (IQR 42 to 48). Selected complications (septic arthritis, embolic event, lung empyema and endophthalmitis) were more prevalent in the 6 week group (24% vs 60%). Fifty-one percent of the 6 week group required surgery versus 27% in the 4 week group. Sixteen patients (94%) achieved clinical cure in the 4 week group versus 32 (71%) patients in the 6 week group.

Conclusions: 4 weeks treatment was effective for some patients with SA-NVE. Patients treated with 6 weeks had more complications, suggesting our patients groups were not equivalent. A prospective randomized controlled trial may be justified to evaluate the optimal treatment duration for SA-NVE. If the duration of treatment can be shortened safely, patients well-being, adverse drug events and healthcare costs could be positively impacted.

<table>
<thead>
<tr>
<th></th>
<th>4 week group</th>
<th>6 week group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, male</td>
<td>9 (53%)</td>
<td>34 (76%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>61 (43-75)</td>
<td>58 (43-73)</td>
</tr>
<tr>
<td>Charlson comorbidity score</td>
<td>4 (3-6)</td>
<td>3 (1-4)</td>
</tr>
<tr>
<td>Complications</td>
<td>4 (24%)</td>
<td>27 (60%)</td>
</tr>
<tr>
<td>Surgery</td>
<td>4 (24%)</td>
<td>23 (51%)</td>
</tr>
<tr>
<td>Clinical cure</td>
<td>16 (94%)</td>
<td>32 (71%)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>7 (16%)</td>
</tr>
<tr>
<td>Relapse</td>
<td>1 (6%)</td>
<td>3 (7%)</td>
</tr>
</tbody>
</table>

Presenter email address: sabrine.douiyeb@live.com
Abstract 3294

Safe and high-throughput screening of natural compounds using pseudo-virus expressing SFTSV glycoprotein

Hye Hee Cha*1, Ji Yeun Kim1, So Jung Park2, In Ki Kim2, Sung-Han Kim1

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Background: Severe fever thrombocytopenia syndrome (SFTS) is an emerging tick borne infectious disease, which is prevalent in Korea, China, and Japan. The mortality rate of SFTS has been high as ever, that was 20.0% (173/866) in Korea through 2013 to 2018. However, any antiviral therapies for the SFTS were not developed yet.

Materials/methods: We generated pseudotype vesicular stomatitis viruses (VSV) expressing SFTS virus (SFTSV) glycoprotein (SFTS-PV) and developed a safe high-throughput inhibition assay using the SFTS-PV. We screened 502 natural compounds as entry inhibitors of SFTS-PV. The dose dependence of inhibition by hit compounds against SFTS-PV and VSV-PV was measured, and the dose-dependent cytotoxicity of hit compounds was also evaluated. The entry blocking effects of hit compounds were determined by comparing the infectivity between the compounds treatment before and after SFTS-PV attachment.

Results: Chelerythrine, Dihydrotanshinone, and β-Zearalanol treatment at low concentrations (1 μg/ml) resulted in >50% inhibition of SFTS-PV infectivity without significant cytotoxicity (Fig. 1). The compounds showed reduced inhibition activity after SFTS-PV had already been entered into cells, signifying their role as SFTS-PV entry inhibitors.

Conclusions: The results of this study suggest that a high-throughput assay using SFTS-PV is useful for massive screening antiviral compounds against SFTSV. Further studies using authentic SFTSV and animal challenge study are warranted to evaluate antiviral effects of these three hit compounds, Chelerythrine, Dihydrotanshinone, and β-Zearalanol.
Relative infectivities of the three hit compounds [A] Chelerythrine, [B] Dihydrotanshinone, [C] β-Zearalanol were dose-dependently evaluated against SFTS-PV (red bar) and VSV-PV (blue bar) from 0.25 to 4 μg/ml. At the same dose, cell viabilities (green bar) of hit compounds were also determined. The experiment was repeated three times and the data are presented as mean percentages and standard deviations.

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A highly sensitive, non-amplification detection method of nucleic acids in bacilli and viruses

Etsuro Ito*, Naoki Kawada1, Yuta Kyose1, Masatoshi Okamatsu2, Yoshihiro Sakoda1, Teruki Yoshimura1, Rikiya Takeuchi4, Yoshiya Ohta4, Kazunari Nakaishi4, Satoshi Watabe4

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Background: Even though the definite diagnoses for infectious diseases have been long believed to be performed with PCR, there are many issues in PCR. For example, they are non-specific or false positive amplifications; volume limit for a target sample; deactivation of enzymes used; complicated techniques, and so forth. To overcome these, we propose a de novo detection method for nucleic acids without any amplification, and show the results for DNA of MPB 64, a specific protein in Mycobacterium tuberculosis [1B] and those for RNA of an avian influenza A virus HA gene.

Materials/methods: We combined nucleic acid hybridization and thio-NAD cycling. The nucleic acid probes, linked with ALP, were hybridized to the target sequences. A cycling reaction was conducted by a dehydrogenase [3α-hydroxysteroid dehydrogenase] with co-factors [NADH and thio-NAD] and substrates [androsterone phosphate]. We then measured accumulated thio-NADH at the absorbance of 405 nm. That is, our new method does not amplify the target nucleic acids.

Results: We obtained that the limit of detection (LOD) was $4.2 \times 10^3$ copies/μL, and that the limit of quantification (LOQ) was $1.4 \times 10^4$ copies/μL for the single strand of MPB64. Using the double strand, the LOD was $1.4 \times 10^4$ copies/μL, and the LOQ was $4.7 \times 10^4$ copies/μL. Furthermore, the LOD and LOQ of the synthesized RNA for an avian influenza A virus HA gene were $2.3 \times 10^4$ copies/μL and $7.7 \times 10^4$ copies/μL, respectively.

Conclusions: Because the protocol of washout is included in our method and the measurement volume is larger than PCR, the possibility of false positive or negative results is decreased. The deactivation of enzymes can be avoided because the thermal cycle is not performed. Our method does not need DNA amplification, and thus designing probe sequences is not restricted by amplification products. Therefore, we deal with high mutation rates of RNA viruses. In addition, we can detect samples by only using a small microplate reader, so that we do not need to use the expensive device for PCR. Therefore, our new method overcomes every difficulty of PCR.

Presenter email address: eito@waseda.jp
Abstract 3306

Antibiotic treatment for paediatric outpatients with community-acquired pneumonia: findings from 10 years of prescribing habits in Italy

Paola Costenaro*, Anna Cantarutti1, Elisa Barbieri1, Antonio Scamarcia2, Andrea Oletto3, Paolo Sacerdoti4, Rebecca Lundin4, Luigi Cantarutti2, Carlo Giaquinto1,3,4, Daniele Donà1

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Abstract third-party references: University of Padua

Background: Despite national and international efforts to promote appropriate antibiotic prescribing, Italian paediatric antimicrobial prescription rates are among the highest in Europe, with an overuse of broad-spectrum antibiotics. Community-acquired pneumonia (CAP) is one of the most common infections in pediatrics, and a main cause of antibiotic prescriptions. Aim of this study is to describe the first-line treatment approach for CAP at primary care level in Italian children.

Materials/methods: Retrospective observational study conducted among children with CAP enrolled in Pedianet, a network of community-based paediatricians from 12 Italian regions (http://www.pedianet.it). Children (3 months-14 years of age) with at least one reported CAP from 01/01/2009 to 31/12/2018 were included, if treated with antibiotics (ABT). CAP was defined according to ICD-9-CM (codes 485, 486, 482.9, 481), a new episode was recorded if occurring >=30 days after previous CAP. We defined “narrow-spectrum” (NS) ABT if treatment was amoxicillin and “broad-spectrum” (BS) if amoxicillin/clavulanic acid, cephalosporins or any combination ABT. Chi-squared and Fisher’s test were used for categorical or continuous variables. Crude and adjusted logistic regression for the ODDS of receiving a NS-ABT were conducted (all episodes of CAP and per patient). A p-value <0.05 was considered statistically significant.

Results: Among 9691 CAP, 7260 episodes from 6409 children followed by 147 pediatricians were included. The 16.7% of CAP (95% C.I.15.9%-17.6%) received a narrow-spectrum ABT while 53.3% (95% C.I.52%-54.4%) received a broad-spectrum ABT and 30% (95% C.I. 28.9%-31.1%) a macrolide. Within 10 years, an increasing trend of NS-ABT prescription was observed [p<0.001, Chi-square test for linear trend]. Factors independently associated with reduced ODDS of receiving a NS-ABT compared to BS-ABT including macrolides were being older than 5 years (OR 0.45, 95% C.I.0.39 - 0.52), living in Center/South of Italy (OR 0.13, 95% C.I.0.10 - 0.16) and being exposed to ABT 3 months before (OR 0.61, 95% C.I. 0.53 - 0.70). These findings were confirmed comparing NS-ABT versus BS-ABT excluding macrolides (n=5079) and when adjusted analysis was limited to index CAP.

Conclusions: Our findings provide an alarming overview of the Italian prescribing habits, reporting a very limited use of NS-ABT for children with CAP.

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Abstract 3311

Utility of central venous catheter cultures in predicting blood culture susceptibilities in catheter-related bloodstream infections due to *Staphylococcus* spp.

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**Background:** Central venous catheter (CVC) and blood cultures are frequently collected from patients undergoing evaluation for catheter-related bloodstream infection (CRBSI). However, whether CVC culture susceptibility results predict blood culture results in patients diagnosed with CRBSI remains unknown.

**Materials/methods:** We conducted this retrospective observational study of all CRBSI cases at the National Center for Global Health and Medicine, Japan between April 2012 and September 2019. CRBSI was defined as positive if microbiology culture results from both CVC and blood were the same. CVC culture susceptibility results (consistent completely and not consistent) were compared with corresponding blood culture results for antimicrobials against *Staphylococcus* spp., Enterobacteriaceae, and non-fermenting bacteria (NFB).

**Results:** Of 275 patients with CRBSI, 139 (50.5%), 77 (28.0%), 23 (8.4%), 16 (5.8%), and 20 (7.3%) patients were infected with *Staphylococcus* spp., *Candida* spp., *Enterobacteriaceae*, NFB, and other organisms, respectively. The proportions of completely consistent antimicrobial susceptibility between CVC and blood among *Staphylococcus* spp., *Enterobacteriaceae*, and NFB were 92.1%, 60.9%, and 56.3%, respectively. Antimicrobial susceptibilities of *Staphylococcus* spp. were more statistically consistent than those of *Enterobacteriaceae* (Odds Ratio [OR] = 7.5, 95% Confidence Interval [CI] 2.6-21.2, p<0.001) or NFB (OR=9.1, 95% CI 2.8-30.0, p=0.001) (Table 1).

**Conclusions:** Early targeted therapy using CVC culture results may lead antimicrobial stewardship among CRBSI due to *Staphylococcus* spp. However, the results of both CVC and blood cultures are needed for de-escalation in CRBSI due to *Enterobacteriaceae* and NFB.

### Table 1. Comparison of antimicrobial susceptibilities among CVC and blood cultures of CRBSI

<table>
<thead>
<tr>
<th></th>
<th><em>Staphylococcus</em> spp.</th>
<th><em>Enterobacteriaceae</em></th>
<th>Non-fermenting bacteria</th>
<th><em>Staphylococcus</em> spp. vs <em>Enterobacteriaceae</em></th>
<th><em>Staphylococcus</em> spp. vs Non-fermenting bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>P value</td>
<td>OR (95% CI)</td>
<td>P value</td>
<td></td>
</tr>
<tr>
<td>Consistent</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>completely</td>
<td>126 (92.1)</td>
<td>14 (60.9)</td>
<td>9 (56.3)</td>
<td>7.5 (2.6-21.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Not consistent</td>
<td>11 (7.9)</td>
<td>9 (39.1)</td>
<td>7 (43.8)</td>
<td>9.1 (2.8-30.0)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Unless otherwise stated, data are presented as n (%).

* Coagulase-Negative *Staphylococcus* [n=90], Methicillin-Susceptible *Staphylococcus aureus* [n=27], and Methicillin-Resistant *Staphylococcus aureus* [n=22]

†*Klebsiella* spp. [n=11], *Enterobacter* spp. [n=6], *Serratia marcescens* [n=4], and *Escherichia coli* [n=2]

‡*Pseudomonas aeruginosa* [n=14] and *Stenotrophomonas maltophilia* [n=2]

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Abstract 3312

**Exploration of the added value of rifampicin to antibiotic regimens for the management of *Cutibacterium* periprosthetic joint infection**


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**Background:** Despite considerable advances in prevention strategies, periprosthetic joint infection (PJI) remains a feared complication of joint replacement. *Cutibacterium* species are common pathogens in PJI. These infections are treated with β-lactams or clindamycin as monotherapy, or in combination with rifampicin. Clinical evidence supporting the value of adding rifampicin for treatment of *Cutibacterium* PJI is lacking.

**Materials/methods:** In this multicenter retrospective study, including centers in Europe and the USA, we evaluated patients with *Cutibacterium* PJI, defined by growth from at least two cultures from two different diagnostic samples. A minimum of 12 months of follow-up alongside availability of information about clinical presentation, antibiotic and surgical treatment, and infection outcome was required. The primary endpoint was infection relapse, defined as persisting signs or symptoms of infection or microbiologically proven infection with the same *Cutibacterium* species. We used Fisher exact tests to analyze whether rifampicin had an added value to an antibiotic regimen for cure of *Cutibacterium* PJI, for different surgical strategies.

**Results:** In this ongoing study, 137 patients (68.6% male, median age 67 years) were analyzed to date, including 68 (49.6%) hip, 56 (40.9%) shoulder, 12 (8.8%) knee, and 1 (0.7%) elbow prostheses. Most infections presented more than one month after the last surgical intervention (median 1.4 years, range 0.3-25.5 years). The most frequent surgical intervention was two-stage exchange (75, 54.7%), followed by one-stage exchange (29, 21.2%), and debridement and implant retention (DAIR, 29, 21.2%). Rifampicin was included in the antibiotic regimen in 49 (35.8%) cases. Infection relapse occurred in 23 (16.8%), and new infection with another microorganism in 11 (8.0%) cases. The use of rifampicin had no obvious association with relapse for all cases (p = 1), or when the different surgical strategies were separately analyzed (Figure).

**Conclusions:** In this observational, retrospective study, there was no apparent benefit of the use of rifampicin combination therapy in *Cutibacterium* PJI, independent of surgical strategy.

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Leishmaniasis in Turkey: assessment of the efficacy of antimicrobial peptides against *Leishmania tropica* in vitro

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**Background:** Emerging worldwide resistance of *Leishmania* isolates to antimonial compounds indicates the urgent need for novel therapeutic agents in leishmaniasis treatment. Various natural or synthetic compounds are assessed in laboratories for their efficacy against *Leishmania* isolates to develop a non-toxic, relatively inexpensive and highly effective new drugs. Antimicrobial peptides (AMPs) are involved in the development of natural immunity in humans and are promising candidates due to their large efficacy spectrum, fast-activity and low resistance risk. Among them, cathelicidins are positively charged peptides that interact with negatively charged membranes of bacteria, fungi and protozoa and kill directly or through formation of pores on the membranes. The aim of this study is to design cathelicidin-like helical peptides (CLHP) by mimicking phylogenetically protected general sequences and structures of cathelicidins and compare their in vitro anti-parasitic activities with an antimonial compound, meglumine antimoniate (MA) on *Leishmania tropica* isolate of a native cutaneous leishmaniasis (CL) patient.

**Materials/methods:** Five study (TN1 -5) and two control groups (MA and Drug-Free Control [DFC]) were developed initially. MA-susceptible *L. tropica* isolate kept at liquid nitrogen were thawed and inoculated first in NNN, and then in RPMI-1640 medium with 10% FBS (fetal bovine serum), 1% Penicillin-Streptomycin and 0.2% Gentamicin. Five CLHPs (TN1 -5), initially designed in our lab and received lyophilized from the producing company, were diluted in dimethyl sulphoxide before use. One hundred microliters of each CLHP and MA were added in the first wells of the test plate and serial dilutions were made to obtain doses within 512 and 4 ug/ml. One hundred microliters of culture having 1x10⁸*L. tropica* promastigotes was added in all wells, except DFCs. Counts and viability of parasites were tested with XTT method after 24 and 48 hours.

**Results:** Our findings indicated that TN-3 maintained its efficacy against *L. tropica* at lower dose (32 ug/ml) until the end of 48th hours. Only TN-5 showed no anti-*Leishmania* activity, even at its highest dose tested (Table 1).

**Conclusions:** This preliminary study showed that, owing to its long-lasting anti-parasitic activity at a lower dose, TN-3 deserves further assessments against different *Leishmania* species, along with in vivo toxicity tests.

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Abstract 3318

Predicting antistaphylococcal effects of daptomycin and gentamicin combinations in an in vitro dynamic model using MICs determined at pharmacokinetically-derived concentration ratios

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Background: The checkerboard technique is widely used to determine the activity of antibiotic combinations. However, ratios of antibiotic concentrations utilized in this method do not always relate to concentration ratios that mimic antibiotic pharmacokinetics in humans. To explore whether susceptibility testing with daptomycin (DAP) + gentamicin (GEN) at concentration ratios that correspond to the ratios of 24-hour area under the concentration – time curve (AUC24) is a better predictor of the antibiotic combinations, *Staphylococcus aureus* was exposed to daptomycin and gentamicin in an in vitro dynamic model that simulates single and combined treatments with the therapeutic AUC of GEN (AUCGEN) and sub-therapeutic AUCs of DAP (AUCDAP).

Materials/methods: Susceptibility of *S. aureus* ATCC 25923 to DAP (MICDAP) and GEN (MICGEN) was tested for single and combined agents at DAP-to-GEN concentration ratios that correspond to their AUC ratios in five-day treatment simulations: 1:2 [AUCDAP 30 μg×h/ml to AUCGEN 65 μg×h/ml], 1.5:1 [AUCDAP 100 μg×h/ml to AUCGEN 65 μg×h/ml]. Based on time-kill data, the area under time-kill curve (AUBC) was determined from the beginning of treatment to 120 h.

Results: The anti-staphylococcal activity of DAP and GEN in combination was greater than with single agents. The results of susceptibility testing were interpreted as additive according to FICs (0.64 (1:2 ratio) and 1.18 (1.5:1 ratio)). In combined DAP plus GEN multiple-dose simulations, *S. aureus* killing was more pronounced at each time point compared to single treatments, possibly as a result of lowering the MIC of both antimicrobial agents and thereby increasing the actual AUC/MIC ratios. AUBCs for both combined treatments were similar and 1.3-fold lower than in mono-treatment with GEN (as a more active single agent) indicating that the effect of DAP plus GEN combination can be considered as additive.

Conclusions: These findings suggest that the combination of DAP with GEN against *S. aureus* is additive given the results of both susceptibility testing and pharmacodynamic experiments; antibacterial effects of DAP plus GEN combinations can be predicted by AUC/MICs of antibiotics using their MICs determined at pharmacokinetically-derived DAP-to-GEN concentration ratios.

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Abstract 3319

**Antimicrobial resistance in urinary tract infection cases submitted to a computerised decision support system for antibiotic prescribing in primary care in France**

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**Background:** Global surveillance of antimicrobial resistance (AMR), including the European Antimicrobial Resistance Surveillance Network (EARS-NET), report aggregated data, making impossible to characterize AMR by infection type and patient characteristics. Furthermore, the reports are available after ≥1-year due to the collection process, delaying measurement of benchmarks for Health Policy impact. General practitioners (GPs) using online CDSS for antimicrobial prescribing in UTI could provide more detailed and timely data on AMR in primary care.

**Materials/methods:** We used data collected daily between November-1, 2017 and August-19, 2019 in the web-based CDSS "Antibiotic+" to describe resistance rates in UTI seen in Paris area. We compared, using Chi-squared test, AMR frequencies to the data last transmitted to EARS-NET (year-2017) for France.

**Results:** Over study period, 1741 GPs registered to the CDSS. Median age was 50-years [IQR, 38-60] and 1131 [65%] were female. Overall, they used the CDSS for prescription in UTI in 27,813 cases, including 25,613 [92%] adults. Most cases concerned treatment of cystitis [13,619 [49%]], masculine-UTI [7,382 [27%]] and pyelonephritis [6,746 [24%]]. Few concerned asymptomatic bacteriuria in pregnant women [66 (<1%)]. In the previous 6 months, fluoroquinolones [FQ] had been used in 19% [n=5,318] of the cases, and 4% [n=1,143] had been hospitalized. In approximately 4 cases out of 10 [n=10,757], urine cultures were available at the time of consultation. Reported microorganisms included *E.coli* [7,078 [66%]], *K.pneumoniae* (1,039 [10%]), *P.mirabilis* (626 [6%]), and others [2,014 [19%]]. Resistance to C3G and FQ were respectively 6% and 16% in *E.coli*, 8% and 11% in *K.pneumoniae*, 3% and 13% in *P.mirabilis*. ESBL-production rates [ff2%] were similar in all species. FQ-resistance rate was higher in upper-UTI than in lower-UTI [958/5,482 (17%) vs. 680/5,215 (13%), p-value<0.001]. It was similar for C3G-resistance [479/5,482(9%) vs. 473/5,212(9%), and ESBL-production [86/5,275 (2%) vs. 93/5,482 (2%)]. Overall, FQ-resistance rate in *E.coli* was higher in patients seen by "Antibioclic" users than reported to EARS-NET for France [1,167/7,078 (16%) vs. 3,451/42,630 (8%), p-value<0.001]; but did not statistically differ from *E.coli* invasive strains issued from blood-cultures in EARS-NET [2,003/13,352,15%, p=0.087].

**Conclusions:** The use of CDSS data allows monitoring AMR in primary care by infection type in real-time. AMR rates may be more informative than in EARS-NET since only clinically relevant urine cultures were considered.

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Abstract 3322

Implementation of EUCAST rapid antimicrobial susceptibility testing combined with routine infectious disease bedside consultation

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Background: Recently, EUCAST methodology for rapid antimicrobial susceptibility testing (RAST) directly from positive blood cultures was released. The aim of our prospective single-center clinical study was to assess the proportion of readable and discrepant results compared to routine antimicrobial susceptibility testing, and the clinical consequences drawn by infectious disease (ID) physicians from RAST results during same-day bedside consultation.

Materials/methods: All positive blood cultures suitable for RAST from January to November 2019 were included and RAST results at 4 and 6 hours compared to standard disk diffusion. The real-life impact of RAST on clinical decisions was assessed during same-day infectious disease bedside consultation based on 6-hour-RAST-results.

Results: RAST was performed in 131 bacterial isolates. The proportion of readable results was higher after 6 hours of incubation than after 4 hours (751/815 versus 569/751, p<0.0001). Major discrepancies (“S to R” or “R to S”) were observed less often after 6 hours than after 4 hours (7/751 vs 15/569, p=0.029). ID consultation was performed in 113 patients after RAST results. Following RAST results, antimicrobial treatment was changed in 68/113 patients, empiric treatment left unchanged because of the RAST result in 13/113 patients, and RAST results had no effect on antimicrobial treatment in 23/113 patients. Change of antimicrobial treatment was most often observed in patients with bacteraemia due to S.aureus (38/42) and E.faecium (6/7), less commonly in E.coli (11/41), K.pneumoniae (3/9), P.aeruginosa (3/8) and E.faecalis (1/2) and never in S.pneumoniae (0/4).

Additional measures such as contact isolation, additional resistance testing or radiologic tests were ordered in 49/113 (43.4%) of cases (S.aureus (35/42), E.faecium (3/7), E.coli (8/41), and K.pneumoniae (1/9), but not in E.faecalis or S.pneumoniae). There was only one therapeutically misleading RAST result (cefoxitin “R” after 4 hours and “ATU” after 6 hours in S.aureus leading to daptomycin treatment for one day).

Conclusions: RAST results after 4 hours were significantly less often readable than at 6 hours and more often discrepant and should thus be interpreted with caution. Misleading results were rare. RAST results led to a clinical consequence in 71% of same-day infectious disease bedside consultations.

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Pneumococcal serotypes distribution in older adults hospitalised with CAP using the UAD Test (The CAPA study)

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Background: Age is a clear risk factor for Community Acquired Pneumonia (CAP) and for pneumococcal disease. Hospitalisation due to pneumococcal-CAP is associated with cardiac complications, worsening of quality of life and decrease in life expectancy. Pneumococcal vaccination of adults aged 60/65 is recommended. PCV13 has demonstrated efficacy and effectiveness against vaccine type CAP in the elderly. The burden of disease due to PCV13 serotypes in the context of childhood immunization is a key factor for the evaluation of the value of PCV13 for the elderly. This study aimed to determine the evolution of PCV13 serotypes causing CAP and pneumococcal-CAP in elderly adults in Spain from 2011 to 2016.

Materials/methods: A prospective, observational, hospital-based study of chest X-ray confirmed CAP in immunocompetent adults (≥18years) performed in 4 Spanish hospitals from November 2011 to November 2016. Microbiological confirmation was obtained by the novel UAD (Pfizer’ PCV13 serotype specific urinary antigen detection) test, BinaxNow® and conventional cultures. Serotyping of pneumococcal isolates was accomplished in a central laboratory by multiplex-PCR and confirmed by the Quellung reaction.

Results: For this analysis we included 1,323 adults aged ≥65 hospitalised with confirmed CAP during the 5-year period. Mean age was 78. S. pneumoniae was confirmed by any microbiological test in 363 (27.4%) of the cases. At least 1 underlying condition was present in 94.9% and 93.4% of the adults with CAP and pneumococcal-CAP cases. 91.7% of CAP cases had a PSI ≥III. The most frequent conditions in pneumococcal-CAP cases were, COPD (94,25.9%), diabetes (92,25.3%) and previous pneumonia (73,20.1%). Nearly 66% (239) had received flu vaccine in the previous year, and 13.2% (48) had received a pneumococcal vaccine. Fatality rate at 30 days was 5.2% for pneumococcal cases. Table shows distribution of PCV13 serotypes causing CAP and both invasive1 and non-invasive2 pneumococcal-CAP by study period. By region, in 2015-2016, PCV13-type CAP was 19.2% in Catalonia, 11.3% in Vizcaya, 9.1% in Valencia, and 7.7% in Galicia.

Conclusions: In Spain a significant burden of PCV13-type serotypes continued to cause CAP in older adults in a context of PCV13 immunization of children and PPV23 immunization of older adults.

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*Only serotypes with at least 1% of cases have been included. 1Isolates of S. pneumoniae in blood and or pleural fluid. Among 50 cases identified, 3 isolates not serotyped. 2Confirmed pneumococcal CAP (by UAD or BinaxNow®) for which blood or pleural fluid culture result was negative.

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Abstract 3328


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Background: The introduction of pneumococcal conjugate vaccines (PCVs) has led not only to a reduction in the incidence of invasive pneumococcal disease (IPD) but also to a change in its epidemiology. In Spain, PCV7 and PCV13 conjugate vaccines were introduced in 2001 and 2010, respectively. The objective of this study was to analyze the effect of the introduction of PCVs in children in adult IPD caused by antibiotic-resistant pneumococci.

Materials/methods: All confirmed IPD episodes (CDC criteria) of adults admitted to Hospital Universitari de Bellvitge (Barcelona, Spain) are prospectively collected. Isolates are routinely identified, serotyped, tested for antimicrobial susceptibility (CLSI) and genotyped (PFGE/MLST). Clinical data are prospectively recorded. This study includes a 25-year period which, for analysis purposes, was divided as follows: pre-PCV(1994-2001), early-PCV7(2002-2005), late-PCV7(2006-2010), early-PCV13(2011-2015) and late-PCV13(2016-2018). Isolates were classified according to their resistance phenotype: penicillin susceptible (PS; MIC<0.12mg/L), penicillin non-susceptible (PNS; penicillin MIC≥0.12mg/L) or multidrug-resistant (MDR; PNS plus resistant to other 2 groups). Differences in the incidence of IPD, rates of resistance and clinical characteristics were assessed using the Chi-square test.

Results: 2095 episodes of adult IPD were analyzed. The overall IPD incidence showed a non-significant decrease from 13.9 to 12.1 episodes/100000 population (-13.1%; 95%CI, -25.7% to 1.6%; pre-PCV vs late-PCV13). The incidence of PS remained stable (9.1 to 8.7; -4.0%, -20.4% to 15.7%), whereas that caused by MDR/PNS significantly decreased (4.9 to 3.4; -30.1%, -6.8% to -47.5%). Reductions in rates of resistance were observed for: penicillin (34.8% to 28.0%), cefotaxime (18.5% to 10.3%), chloramphenicol (15.5% to 5.1%) and co-trimoxazole (42.8% to 25.7%). Resistance to erythromycin increased (18.7% to 24.8%). IPD caused by MDR/PNS pneumococci was statistically associated to older patients, higher McCabe score, nosocomial acquisition, existence of comorbidities and prior antibiotic therapy. 30-day mortality was significantly higher for MDR/PNS episodes (24.1% vs 16.6%). Currently, two PMEN clones are responsible for 50% of the IPD caused by MDR/PNS pneumococci: Spain9V-3(ST156) and Denmark14-32(ST230).

Conclusions: The introduction of PCVs in children has had a limited impact on the adult IPD in our geographical area. Nevertheless, a beneficial effect on the rates of resistance was observed for most antimicrobials.

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Clinical evaluation of the ID-fungi plates for direct identification of dermatophytes on nail, hair and skin samples by MALDI-TOF MS

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Background: The identification of filamentous fungi (FF) by Maldi-Tof MS is still not optimal. One of the main pitfalls is the colony harvesting for deposit on the Maldi plate which is often difficult due to fungal adherence to the medium. To improve this limiting factor, a new ID-fungi® plate medium (Conidia, France) has been recently developed. This medium allows the growth and easy sampling without the need for subculture. This study presents the preliminary results of the detection and identification of FF by Maldi-Tof from colonies directly harvested from ID-fungi® plates. The results have been compared with traditional diagnostic methods.

Materials/methods: A total of 86 Conidia® plates have been inoculated with nails, skin and hair from patients presenting to the dermatology unit of the University Hospital of Liège. In parallel, Sabouraud medium with antibiotics and cycloheximide (bioMérieux, France) have been inoculated. From Conidia® plates, each positive culture has been analysed by Maldi-Tof-MS using the extended direct deposit with formic acid or complete formic acid/acetonitrile extraction. From Sabouraud medium, the identification was done by microscopy. ITS sequencing was run on every colony as gold standard for identification.

Results: Among the 86 Conidia® plates, 19 (22%) were positive for dermatophytes. The Maldi-Tof identification rate by extended direct deposit was 16/19 (84,7%) considering that the three misidentified dermatophytes were T. interdigitale strains identified as T. tonsurans, a cross-reaction already seen in our previous study and well described in the literature. In comparison with the Sabouraud agars, Conidia® let grow 6 additional dermatophytes. However, 7 other dermatophytes growing on Sabouraud were not present on Conidia®. These discordances are possibly due to insufficient sample volume inoculated on each medium. On Conidia® plates, we also perfectly identified 6/9 (66,6%) other non-dermatophytes molds. The three missing species are not represented in the Bruker Filamentous fungi 2.0 database.

Conclusions: The Conidia plates are a promising tool to reduce the TAT for filamentous fungi identification. A fast and accurate identification can be obtained for the main fungal species by Maldi-Tof MS. However the Bruker database has to be improved because it is still incomplete.

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Abstract 3334

**Evolution of pneumococcal serotypes causing CAP in adults by co-morbidities in Spain using the UAD test (the CAPA study)**

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**Abstract third-party references:** This is a Pfizer sponsored study

**Background:** Introduction of PCV7 and PCV13 for children in national immunization programs (NIP) has reduced incidence of Invasive Pneumococcal Disease (IPD) and pneumococcal Community Acquired Pneumonia (CAP) in adults with and without underlying conditions. Nevertheless, reductions in overall IPD and PCV13-type IPD incidence differ by age and comorbidities, suggesting that not every adult is equally protected by the indirect effect. In Spain, PCV13 was introduced in the childhood NIP in 2015-2016. PCV7 and PCV13 were available but afforded by parents (estimated uptake 61%) from 2000 and 2010 respectively. PPV23 was recommended for at risk subjects since 2001 and for adults aged 60/65 since 2004 with moderate uptake. PCV13 was recommended for at high risk adults since 2012 with low uptake. This study aimed to evaluate indirect effects on CAP and pneumococcal-CAP caused by PCV13 serotypes from 2011-2012 to 2015-2016 among adults with and without comorbidities.

**Materials/methods:** Prospective, observational study of immunocompetent adults (≥18y) admitted to 4 Spanish hospitals with chest X-ray confirmed CAP between November 2011 and November 2016. Microbiological confirmation was obtained using the Pfizer PCV13 serotype specific urinary antigen detection (UAD) test, BinaxNow® and conventional cultures. Serotyping of isolates was accomplished in a central laboratory by multiplex-PCR and confirmed by the Quellung reaction.

**Results:** Of the 2,086 adults hospitalized with CAP included in the study, 548 (26.3%) had pneumococcal-CAP. Mean age 67. Patients with ≥1 comorbidity accounted for 88.2% and 87% of CAP and pneumococcal-CAP cases respectively. Most frequent conditions in adults with CAP: diabetes (488; 23.4%), COPD (384; 18.3%), previous pneumonia (373; 17.9%) and smoking (354; 17%). Table shows evolution of PCV13 serotypes causing CAP and non-invasive1 and invasive2 pneumococcal-CAP, between 2011-2012 and 2015-2016 by presence of most frequent underlying conditions.

**Conclusions:** In Spain, PCV13-type CAP and pneumococcal-CAP decreased in adults possibly due to the indirect effect of childhood immunization. Nevertheless, no significant decrease was observed in adults with chronic respiratory disease, heart failure and in adults without underlying conditions. PCV13 serotypes accounted for up to 50% of pneumococcal-CAP cases in adults with comorbidities 6 years after PCV13 use in children and more than a decade of PPV23 recommended for people at risk.

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Abstract 3335

Clinical evaluation of a cartridge-based DNA extraction method for the whole molecular TB-diagnostic workflow
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Background: Accurate tuberculosis (TB)-diagnostic is imperative to initiate an effective treatment. In parallel to low sensitive smear microscopy and time-intense culture, nucleic acid amplification tests (NAATs) detecting Mycobacterium tuberculosis complex (MTBC) and important antibiotic resistances have become available in the past years. Besides fully automated and cartridge based test, NAATs such as FluoroType MTB (FT-MTB), GenoType MTBDRplus (GT-plus) and GenoType MTBDRsl (GT-sl) of Hain Lifescience need external DNA preparation of decontaminated sputum prior to testing. This requires a well-equipped and expensive laboratory infrastructure, which might not be affordable in high incidence countries. We have developed a low-cost DNA extraction cartridge that is run in a programmable centrifuge. In this study we evaluated whether cartridge-extracted DNA (Crt.-DNA) is suitable for MTBC, rifampicin (rif), isoniazid (inh) and second line antibiotic resistance testing using FT-MTB, GT-plus, GT-sl and pre-characterized sputum samples from TB-patients.

Materials/methods: GeneXpert MTB/RIF (Xpert, Cepheid) confirmed MTBC-positive sputum samples were obtained from the German-Nepal tuberculosis project (Genetup, Nepal) and the National Reference Laboratory Tashkent (Uzbekistan). After liquefaction, sputum was loaded in extraction cartridges that were processed in a programmable centrifuge harboring a special rotor. The extracted DNA was subject to FT-MTB. All MTBC-positives were further screened for rif and inh resistance by GT-plus. Rif and multidrug resistant (MDR) samples were additionally tested for resistance against second line antibiotics using GT-sl.

Results: 86% (36/41) of Xpert positive samples were identified as MTBC-positive by FT-MTB after cartridge-based DNA extraction (Crt.-DNA). While 100% of Xpert high and medium positives were positive, FT-MTB only detected around 75% of Xpert low/very low positives. 82% (31/38) of subsequently GT-plus tested samples yielded a valid result. Again, Xpert low/very low positives performed less well with only around 50% being analysable. 6 MDR samples were identified and further screened for resistance against second line antibiotics by GT-sl. 100% (6/6) of test results were valid and resistances against fluoroquinolones, kanamycin, amikacin and capreomycin were detected. 100% specificity was obtained.

Conclusions: We could show that cartridge-extracted DNA is suitable for molecular diagnostics including MTBC-screening as well as rif, inh and second line antibiotic resistance testing using Hain technology.

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Abstract 3336

Outbreak of an uncommon rifampicin-resistant blaNDM-1 *Citrobacter amalonaticus* strain in a digestive rehabilitation centre: the putative role of rifaximin

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**Background:** We report a sudden emergence and spread of an uncommon carbapenemase-producing Enterobacteriaceae (CPE) strain in a digestive rehabilitation center that exhibited phenotypic and genotypic resistance to rifamycins.

**Materials/methods:** Due to a history of CPE exposure in another healthcare facility, a cirrhotic patient was screened one month after his admission to a 22-bed digestive rehabilitation center that is east of a Parisian suburb. A rectal swab yielded a *Citrobacter amalonaticus* harboring a NDM carbapenemase. Three successive weekly screening campaigns of the hospitalized patients identified four additional carriers. An outbreak investigation was performed by the local infection control team. Antimicrobial consumption was obtained from the Pharmacy Department. Antimicrobial susceptibility was tested [MIC - microdilution method]. All five epidemic strains were whole genome-sequenced, allowing their resistome identification, their comparison through the core genome MLST approach and a phylogenetic analysis through single nucleotide polymorphisms (SNP).

**Results:** This digestive rehabilitation unit mainly hosted patients suffering from cirrhosis, and some of them were at the stage of hepatic encephalopathy. Some patients suffering from alcoholic addiction were disoriented, and were not compliant with basic hygiene recommendations. Regarding antimicrobial selection pressure, three out of the five carriers were under long-term rifaximin treatment to prevent recurrent overt hepatic encephalopathy. All five strains were identical (0 to 1 different alleles among the 2706 genes of the cgMLST scheme). Only meropenem (MIC = 2 mg/L), amikacin (4 mg/L), tigecyclin (0.5 mg/L) and colistin (0.5 mg/L) presented in vitro activity. Regarding rifaximin, the epidemic strain MIC was 512 mg/L, far above the reported breakpoint of 32 mg/L. The in silico analysis identified bla NDM-1, mcr-9 and arr-3 that encodes a rifampin ADP-ribosyl transferase conferring a high level of rifampin resistance. The phylogenetic analysis confirmed the inclusion of the epidemic strain in the C. amalonaticus clade and its distance from the other published strain harboring a bla NDM-1 gene. In this ward in 2018 the rifaximin consumption was 162 DD per 1000 patient days.

**Conclusions:** We support the prudent use of long-term rifaximin therapy in wards where infection control measures are not strictly respected and recommend the thorough monitoring of emerging rifampicin-resistant MDR strains.

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Predominant mechanisms of carbapenem resistance in *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* and tools for their detection

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**Background:** The aim was to determine predominant mechanisms of carbapenem resistance in *Pseudomonas aeruginosa* and *Klebsiella pneumoniae*.

**Materials/methods:** 85 isolates of *P. aeruginosa* and 113 isolates of *K. pneumoniae*, isolated in January-September 2019, were analyzed. Identification was performed using MS Maldi-ToF (Bruker, Germany), antibiotic susceptibility - Vitek-2 (BioMerrieux, France). The Advanced Expert System with a set of Global European-based plus Phenotypic parameters was used. Susceptibility to carbapenems was manually adjusted to EUCAST breakpoints, v. 9.0 (2019). Analysis of carbapenem resistance was performed automatically by VITEK-2. The obtained results were compared with the data of molecular genotyping, performed jointly with the Institute of antimicrobial chemotherapy (Smolensk, Russia).

**Results:** 34/85 (40.0%) isolates of *P. aeruginosa* and 35/113 (31.0%) isolates of *K. pneumoniae* were carbapenem-resistant (Car-R). MICs of imipenem or meropenem for Car-R *P. aeruginosa*, were 8 µg/ml (6/34, 17.6%) and ≥16 µg/ml (28/34, 82.4%). Carbapenemase production was observed in 24/34 (70.6%) cases (not otherwise specified [NOS], VITEK-2) and in all cases, it was accompanied with carbapenem impermeability. Only carbapenem impermeability was observed in additional 10 cases, totally accounting for 100% of Car-R *P. aeruginosa* isolates. Among 35 Car-R *K. pneumoniae*, MICs of imipenem or meropenem were 8 µg/ml in 13/35 (37.1%), ≥16 µg/ml in 22/35 (62.9%) cases. Carbapenemase production was observed in 35 (100%) isolates (NOS, VITEK-2). In 32/35 (91.4%) isolates carbapenemase production was accompanied by carbapenem impermeability. Appropriate genotyping results were obtained for 11 *P. aeruginosa* and 10 *K. pneumoniae* isolates. 5/11 (45.5%) *P. aeruginosa* isolates were producers of VIM metal-beta-lactamases, and all *K. pneumoniae* isolates produced serine carbapenemases, including 9 (90.0%) OXA-48 and 1 (10.0%) KPC.

**Conclusions:** A 9-month analysis (2019) showed that carbapenemase production by *P. aeruginosa* and *K. pneumoniae* isolates was noted in 70.6% and 100% of cases, respectively. Moreover, carbapenem impermeability in *P. aeruginosa* [100%] and *K. pneumoniae* [91.4%] in parallel with carbapenemase production was seen. The combination of these 2 mechanisms makes it impractical to use high doses and prolonged infusions of carbapenems, and requires treatment based on modern inhibitor-protected cephalosporins.

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Abstract 3339

**A common protocol for the simultaneous processing of multiple bacterial species for whole genome sequencing**

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**Background:** Bacterial whole genome sequencing (WGS) will become increasingly used by local microbiology laboratories where test volume is low compared with national capabilities. The need for rapid turnaround (frequent sequencing runs) of relatively low isolate numbers must be balanced with cost-effectiveness achieved by maximizing the number of multiplexed isolates in any given run. Here, we describe a single universal protocol for simultaneous DNA extraction and sequencing of numerous different common bacterial species, allowing the sequencing of mixed isolate runs to meet variable needs.

**Materials/methods:** We assembled test panels comprising 71 isolates representing 20 clinically important bacterial species. Panels 1 and 2 were selected from clinical isolates to represent leading causes of outbreaks and infection. Panels 3 and 4 were selected from previous studies used to demonstrate the utility of WGS in the clinical setting. The basis for the DNA extraction process was the QIAgen mini DNA kit, to which different combinations of reagents that are commonly used for specific pathogens were added to optimize DNA recovery from each test panel. DNA recovery was quantified using a Qubit fluorometer, with >3.3ng/ul required for library preparation. Thereafter, a common processing pathway was used to prepare the sequencing libraries using the Illumina Nextera Flex kit, which were sequenced overnight on an Illumina MiniSeq.

**Results:** The addition of lysostaphin, lysozyme or buffer ATL (a tissue lysis buffer) alone did not produce sufficient DNA for library preparation (<3.3ng/ul) across the species panels tested. By contrast, lysozyme plus lysostaphin produced sufficient DNA across all 20 species. 15/20 species could be extracted from a 24 hour culture plate, while the remainder ([Campylobacter jejuni, Haemophilus influenzae, Legionella pneumophila, Neisseria meningitidis, and Streptococcus pneumoniae]) required 48-72 hours incubation for sufficient growth. Tests performed by different people on different days demonstrated 100% reproducibility. Sequencing of the resulting DNA was used to recapitulate previous findings for species, relatedness and outbreak detection, antimicrobial resistance gene detection and capsular type.

**Conclusions:** This single protocol for simultaneous processing and sequencing of multiple bacterial species supports low volume rapid turnaround time sequencing of multiple species of clinical importance by local clinical microbiology laboratories.

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Identification of anti-TPI H8 antibody-epitope analogues as putative active vaccine against *Staphylococcus aureus*

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**Background:** *Staphylococcus aureus* (*S. aureus*) is a major human pathogen that can cause clinical infections like bactereemia and endocarditis. The morbidity and socioeconomic burden associated with infections with methicillin-resistant *S. aureus* (MRSA) combined with a lack of new antibiotics define a clear unmet medical need for novel approaches, including vaccination. Currently, there is no vaccine available. By proteomic approach, we identified vaccine candidates involved in essential metabolic pathways also displayed on the surface of *S. aureus*. Vaccination with triose-phosphate isomerase (TPI), a highly conserved glycolytic enzyme, showed significant protection in our murine sepsis model. Subsequently, anti-TPI monoclonal antibodies (moAbs) were generated for passive immunization of mice. One anti-TPI moAb (H8) provided significant higher survival rates compared to others after *S. aureus* challenge. Obviously, protection is epitope specific. By using this reverse immunology approach we identified the H8-TPI-epitope which could serve as protective active vaccine. However, moAb H8 recognizes a discontinuous epitope contained in a stretch of 100 amino acids. For cost-effective production of an epitope vaccine, the moAb H8 epitope sequence needs to be shortened without losing its ability to generate anti-TPI H8-like antibodies. In this study, we used different approaches to identify H8 epitope analogues.

**Materials/methods:** Using the NEB 12-mer peptide-phage display library H8-mimotopes, structurally mimicking the H8-TPI-epitope, were selected. After three rounds of biopanning against immobilized H8 antibody, three mimotopes were enriched and analyzed for specific binding to moAb H8. Additionally, based on antigen fragment cloning and binding assay results we generated a peptide assumed to contain the discontinuous H8 epitope, called H8-Disco. After immunization of mice with KLH-conjugated mimotopes and H8-Disco, serum was analyzed for the presence of TPI-specific antibodies by ELISA.

**Results:** Three mimotopes bind specifically to moAb H8 in phage ELISA binding assays, while they do not bind an isotype matched IgG1 control antibody or BSA. However, the mimotopes did not induce TPI-specific antibodies in mice. In contrast, H8-Disco does induce a humoral TPI-specific immune response after active vaccination.

**Conclusions:** H8-Disco could serve as epitope vaccine against *S. aureus*. The protection potential needs to be evaluated in our *S. aureus* mouse infection model.

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Abstract 3341

**Miconazole/domiphen bromide: a fungicidal combination treatment against biofilms of various azole-sensitive and azole-resistant Candida spp.**

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**Background:** Mucosal biofilm-related Candida infections are very common and can occur for example on genital organs. Such infections are difficult to treat, since miconazole (MCZ), the preferred topical treatment, is only moderately active against biofilms. We discovered a fungicidal combination consisting of MCZ and a quaternary ammonium compound, domiphen bromide (DB), that is active against biofilms of *Candida albicans* and *Candida glabrata*. Here we investigated the activity spectrum of MCZ-DB, the combination’s effect *in vivo* and its mode of action.

**Materials/methods:** Activity against *Candida albicans*, *Candida auris* and *Candida glabrata* biofilm and planktonic stationary cultures was assessed by treating cultures with MCZ, DB or a combination and performing CFU determination after 24h (biofilms) or 2,5h (planktonic cultures) treatment. The *in vivo* activity of the MCZ-DB combination was examined in a *Candida* vaginitis rat model during 14 days. The combination treatment’s mode of action was studied in planktonic *C. glabrata* cultures, using a fluorescently labeled ketoconazole derivative (FKD) (1) to investigate the effect of DB on azole uptake and its subcellular localization, via FACS analysis and confocal microscopy, respectively. BCECF-AM staining was used to study DB’s effects on *C. glabrata* vacuolar pH.

**Results:** MCZ-DB leads to a significant CFU reduction as compared to single compound treatments in biofilms of azole-resistant *C. albicans* isolates, *C. auris* biofilms and planktonic cultures of *C. albicans* and *C. glabrata* in stationary phase. Moreover, the combination treatment significantly reduces the infection burden as compared to single compound treatment in an in vivo vaginitis rat model. Apparently DB (i) enables increased FKD uptake in *C. glabrata* cells at low doses, (ii) alters cytoplasmic distribution of high FKD doses and (iii) negatively affects vacuolar integrity.

**Conclusions:** Our data reveal that MCZ-DB combination treatment has fungicidal antibiofilm activity against various azole-resistant and azole-sensitive Candida spp., probably because DB increases intracellular MCZ availability.


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Abstract 3342

Amikacin initial dosing in emergency surgery: pharmacokinetics and determinants of optimal dose

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Background: Amikacin usual dose (15-30 mg/kg) may not be optimal in emergency surgery. The objectives of this study were to describe the pharmacokinetics (PK) of amikacin in emergency surgery patients and to evaluate optimal initial dosage.

Materials/methods: This was a retrospective analysis of data from patients who underwent emergency surgery, over 3.5 years in Centre Hospitalier Lyon Sud, Lyon, France. We performed Bayesian estimation (BestDose software) of patients’ individual PK parameters based on peak (Cmax) and trough concentration (C24h) after the first dose. We calculated the optimal dose that would have been necessary to achieve the target Cmax of 64 mg/L in each patient. We also simulated the target attainment (TA) for various alternative doses. Determinants of optimal dose were investigated by using regression tree analysis.

Results: Data from 84 patients (36 women and 48 men) were available. The population characteristics (mean ± SD) were as follows: creatinine clearance, 85 ± 45 mL/min; age, 63 ± 16 years; body weight, 71 ± 18 kg. The mean first amikacin dose was 1753 ± 548 mg. The mean Cmax and C24h were 78 ± 28 mg/L and 7 ± 9 mg/L, respectively, with 32% of patients having Cmax < 64 mg/L. Median (min-max) values of amikacin volume of distribution, plasma clearance and half-life, were as follows: 0.24 (0.13-0.66) L/kg, 46 (5-367) ml/min and 2.5 (1.7 – 10.3) h, respectively. Optimal doses estimated by the model ranged from 773 mg to 4803 mg (median = 1449 mg). The simulated TA for doses of 20, 25 and 30 mg of TBW were 36%, 79%, and 94%, respectively. A fixed dose of 2500 mg was associated with TA of 95%. Ideal body weight (IBW) was the primary predictor of optimal dose, with a dose of 2180 mg in patients with IBW > 71.2 kg versus 1414 mg in patients with IBW ≤ 71.2 kg.

Conclusions:Considerable variability in amikacin PK and dosage requirements was observed in emergency surgery patients. A dose of 30 mg/kg of TBW or a fixed dose of 2500 mg appear to be the best dosing strategies.

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Abstract 3344

Clinical characteristics, disease management and treatment outcome of paediatric tuberculosis in Denmark

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Background: In Western Europe, pediatric tuberculosis (TB) is rare and clinical characteristics often unspecific potentially causing diagnostic delay and poor treatment outcome.

Materials/methods: Nationwide study of children ≤ 18 years with TB from 2009 through 2014 in Denmark. Demographic-, clinical- and microbiological data and treatment outcome results were obtained from registers and medical records.

Results: In total, 168 pediatric TB cases were identified; the majority were immigrants (71%), primarily from Africa (40%) and Asia (38%). Co-morbidities were rare (4.8%) of which asthma was the most common (63%). Danish children were more likely to be diagnosed as part of contact tracing (69%) whereas the majority of immigrants (66%) were diagnosed due to symptoms (p<0.0001). Mean health system delay was longest for immigrants with extra pulmonary TB (39 days). The most common symptoms were fever, night sweat, cough, enlarged lymph nodes and pain. C-reactive protein and erythrocyte sedimentation rate were often elevated, however, 1/3 of the children had normal blood tests at the time of diagnosis. The treatment success rate was 93%, slightly higher in Danish children (98%) compared to immigrants (92%) and cases of treatment failure were restricted to adolescents of which 88% (7/8) were among immigrants.

Conclusions: The majority of pediatric TB in Denmark occurs among otherwise healthy immigrant children with symptomatic TB and a health system delay of just over one month. The treatment success rate was 93%, and possible improvements should be targeted enhanced case detection and treatment adherence of immigrant adolescents.

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Abstract 3345

Antimicrobial-resistant Bacteroides fragilis detected from blood culture in 2 tertiary hospitals
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Background: The presence of drug-resistant Bacteroides fragilis is a major problem in the selection of empirical treatments for intraabdominal infections. In particular, chromosome-located β-lactamase cfiA is associated with resistance to carbapenems, and as the frequency of clinical use of carbapenem increases, there is a concern about the increase in the frequency of colonization and infection of the isolates. In this study, we examined the drug susceptibility of B. fragilis strains isolated from blood culture in clinical settings and the possession of each drug resistance gene.

Materials/methods: 43 strain of B. fragilis were isolated from blood culture at the 2 tertiary referral hospitals from January 2014 to December 2018 and identified in MALDI Biotyper (Bruker). DNA was extracted from each strain, and the presence or absence of the nine genes (cepA, cfxA, cfiA, IS, ermA, ermB, mefA, tetQ, nimB) elated to the antimicrobial agent was confirmed using PCR.

Results: As a result of drug susceptibility test, resistance rate to carbapen (doripenem and meropenem) showed 9.3% [4/43]. The resistance rates to sulbactam/ampicillin and cefmetazole recommended for the treatment of anaerobic bacteria were as low as 14.0% and 7.0%. The resistance rate of clindamicin is over 30%. Also, no resistant strain of metronidazole was found. In the result of PCR, cepA gene of β-lactamase was detected at a high rate of 86% [37/43], followed by 72.1% [31/43] of tetQ gene involved in tetracycline resistance. All two carbapen-resistant strains carried the cfiA gene, but only one had an Insertion Sequence (IS).

Conclusions: The expression of cfiA gene involves IS element as a promoter, but some strains of IS element was not detected. Involvement of penicillin binding protein, increase of efflux pump, and mutation of outer membrane porin protein was also considered as the cause of carbapenem resistance. In addition, in this study, sensitivity to metronidazole was maintained in all strains and was considered to be one of the excellent treatment options for cases suspected of having B. fragilis involvement.

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Insight into Chlamydia trachomatis persistence

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Background: Chlamydia trachomatis is the agent of the most common bacterial sexually transmitted infection. Under stressful conditions, Chlamydia fails to successfully replicate inside the epithelial cells and switches to a persistence state. In vitro, this condition can be induced by beta-lactam antibiotics, as penicillin, and reversion to productive infectious elementary bodies can be obtained upon removal of the drug.

The aim of this study was to get new insights into the interactions between C. trachomatis and the epithelial host cells during persistence condition.

Materials/methods: The normal chlamydial development cycle was compared with penicillin-induced persistence and the following aspects were investigated: (i) cell survival/death, (ii) externalization of phosphatidylserine, (iii) caspase 1 and caspase 3/7 activation, and (iv) reactive oxygen species (ROS) production. Experiments were conducted using HeLa cells and two different serovars (D and L2) at three different levels of multiplicity of infection (MOI 0.3, 1, 3). In particular, the exposure of phosphatidylserine in Chlamydia-infected cells was evaluated at three different time points (8, 24, 48 h post-infection) by flow cytometry analysis, whereas the determination of caspases activation was carried out by a biochemical approach. Finally, ROS production was assessed on HeLa cells at 48 hours post infection by means of a fluorescent probe.

Results: At 72 hours post-infection, the cytotoxic effect displayed by Chlamydia was completely abolished for both serovars and for all levels of multiplicity of infection only in the cells with aberrant inclusions. At the same time, C. trachomatis was able to switch off the exposure of the lipid phosphatidylserine on the surface of epithelial cells and to strongly inhibit the activation of caspase 1 and caspase 3/7 only in penicillin-treated cells. Forty-eight hours post-infection, C. trachomatis elicited a significant ROS expression both in case of a normal cycle and in case of persistence. However, serovar L and penicillin-free infection activated a higher ROS production compared to serovar D and to penicillin-induced persistence, respectively.

Conclusions: In conclusion, we added knowledge to the cellular dynamics taking place during chlamydial persistence, demonstrating that C. trachomatis creates a suitable niche to survive, switching off signals able to activate phagocytes/leukocytes recruitment.

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Optimal antimicrobial therapy duration for patients with acute cholangitis after successful drainage by Endoscopic retrograde cholangiopancreatography (ERCP)

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**Background:** Recommendations regarding the duration of antimicrobial therapy in cholangitis after successful endoscopic biliary drainage vary. Aim of this study was to compare the occurrence of local infectious complications in patients with acute cholangitis treated with antibiotics for three days or less compared to four days or more.

**Materials/methods:** We performed a retrospective multicenter study in seven hospitals in the Netherlands. Patients who received a successful biliary drainage by endoscopic retrograde cholangio-pancreatography (ERCP) because of cholangitis due to common bile duct stones between 2012-2017 were included. The primary outcome was the occurrence of a local infectious complication within three months after ERCP. Secondary outcomes included *Clostridioides difficile* infection, total length of stay and all-cause mortality.

**Results:** A total of 426 patients with cholangitis were identified and 296 patients met all inclusion criteria. Therapy duration was ≤ 3 days in 137 patients (46.3%). During follow-up 41 patients (13.9%) developed a local infectious complication. Occurrence of infectious complications did not differ between the two groups \(P=0.32\). No patient developed *Clostridioides difficile* infection. Median hospital stay was six days [IQR 4-8 days] in the short antibiotic group compared to seven days [IQR 5-9 days] in the long group \(P=0.03\). Four (1.4%) patients died during follow-up, all were treated for ≥ 4 days \(P=0.13\).

**Conclusions:** Antimicrobial therapy of three days or less seems to be sufficient after successful biliary drainage in patients with acute cholangitis. Randomized trials should confirm our findings.

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Abstract 3356

**Differential resistance of Candida auris biofilms against surface disinfectants commonly used in the hospital**

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**Background:** Candida auris is an emerging fungal pathogen causing hospital outbreaks. The aim of our study was to test Candida auris for susceptibility to surface disinfectants commonly used in hospitals.

**Materials/methods:** The efficacy of seven disinfectants was tested in a static biofilm microtiter plate model using tetrazolium salt reduction (XTT) assay and a modified crystal violet staining. The log10 reduction assay was used to quantify the viable cells after exposure to the disinfectants. Four biofilm forming reference strains of C. auris (the non-aggregating NCPF 8971, aggregating NCPF8977, NCPF8984, DSM 21092) and a C. albicans ATCC10231 strain were tested against: A: an ethanol based disinfectant, B: a quaternary ammonium based disinfectant, C: a disinfectant based on a mix of glutaraldehyde, quaternary ammonium and surfactant, D: and E: 3.4% and 4.25% hydrogen peroxide alone respectively, F: a potassium peroxymonosulfate based disinfectant and, G: a micelic formulation containing 12% v/v hydrogen peroxide. All tests were done in quadruplicate.

**Results:** In the XTT assay disinfectants A, B, and C achieved more than 80% reduction of biofilms metabolic activity and more than 5 log10 reductions of viable cells in all strains tested. The non-aggregating C. auris 8971 was resistant to H2O2 alone (D, E) and to the H2O2 micelic biocide (G), but susceptible to the potassium peroxymonosulfate based disinfectant [F] showing more than 5log10 viability reduction. The aggregating NCPF8977 and DSM21092 showed equally a resistance to D and G but not to E and F. C. auris NCPF8984 was resistant to F but sensitive to H2O2 (D and E). C. albicans ATCC10231 biofilms were resistant to disinfectants D, E, F and G.

**Conclusions:** The susceptibility of Candida auris to surface disinfectants is highly differential. Levurocidal activity of tested surface disinfectant is highly depending on the Candida species and its phenotypical growth pattern.

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MPC-based prediction of anti-mutant effects of linezolid/daptomycin combinations against Staphylococcus aureus: a study in an in vitro dynamic model

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Background: In our studies with linezolid (L) + rifampicin- and L + gentamicin-exposed Staphylococcus aureus, the enhancement of anti-mutant effects of the antibiotic combinations was attributed to lengthening times above the mutant prevention concentration (MPC; T>MPC) caused by lowering the MPCs. To explore if this is applicable to combinations of L with daptomycin (D), the enrichment of L- and D-resistant mutants of S. aureus was studied by simulating single (L or D) and combined (L+D) treatments.

Materials/methods: The MPCs of L and D alone and in combination at a pharmacokinetically derived L-to-D concentration ratio (1:2) that corresponds to the simulated ratio of the areas under the concentration-time curve (AUCs) were determined for S. aureus ATCC 700699 and S. aureus 2061. Five-day treatments with twice-daily L and once-daily D were simulated at two therapeutic (240 and 480 μg×h/ml – regimens L240 and D480, respectively) and two sub-therapeutic AUC (120 and 240 μg×h/ml – regimens L120 and D240, respectively). Simulated combined treatments were L240+D480 and L120+D240. Areas under the bacterial mutant concentration–time curve were calculated for mutants resistant to L (AUBC_M(L)) or D (AUBC_M(D)).

Results: Under the influence of D the MPCs of decreased from 10 to 3 (S aureus ATCC 700699) and to 4 μg/ml (S. aureus 2061). Under the influence of L the MPCs of D decreased from 14 to 6 and from 10 to 8 μg/ml, respectively. Lowering the MPC led to an increase in T>MPC that resulted in lower AUBC_M(L) and AUBC_M(D) in combined treatments compared to single drug treatments. A strain-independent relationship was established between AUBC_M(L) and T>MPC (sigmoid, r² 0.97) and between AUBC_M(D) and T>MPC (monoexponential decay, r² 0.90).

Conclusions: These findings suggests that [1] suppression of L- and D-resistant S. aureus exposed to L+D combinations is consistent with an increase in T>MPC caused by lowering the MPCs of antibiotics in combination, and [2] T>MPC could be used as a predictor of staphylococcal resistance to the L+D combination.

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Abstract 3358

EUCAST improved screening algorithm for beta-lactam resistance in Haemophilus influenzae

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Background: EUCAST recommends screening for beta-lactam resistance in Haemophilus influenzae with the benzylpenicillin (PCG) 1 unit disk. The PCG screening test is a sensitive test to detect all known beta-lactam resistance mechanisms, but it cannot differentiate between beta-lactamase production and PBP3 mutations. The aim of this study was to evaluate if the amoxicillin-clavulanic acid (AMC) 2.1 µg disk can be used as an additional test to identify beta-lactam resistant H influenzae with beta-lactamase only.

Materials/methods: Disk diffusion was performed according to EUCAST on MH-F agar from BD (BBL) and Thermo Fisher Scientific (Oxoid) on an international collection of H.influenzae (n=144). All isolates were beta-lactamase positive. PBP3 mutations were identified by PCR (mutations at AA 517, 526 or 528) in 57 isolates (40%). Broth microdilution (BMD) for beta-lactam agents was performed according to ISO 20776-1 on custom Sensititre panels (Thermo Scientific) using MH-F broth as recommended by EUCAST. EUCAST Breakpoints v. 9.0 were used to interpret the results.

Results: All isolates were correctly detected as beta-lactam resistant with the PCG disk (<12 mm). Isolates with beta-lactamase only were susceptible with BMD for amoxicillin-clavulanic acid and all cephalosporins and carbapenems tested. Seventy-eight isolates were susceptible with the EUCAST standard breakpoint for AMC 2.1 µg (≥15 mm), and 75 of these had beta-lactamase only [Figure 1]. Three isolates with PBP3 mutations were also categorised as susceptible with the AMC disk. Two of these were susceptible for all beta-lactamase stable agents tested. The third isolate had an elevated MIC for cefuroxime only (4 mg/L). Isolates with AMC <15 mm and PBP3 mutations had various susceptibility patterns for the beta-lactam agents tested.

Conclusions: The amoxicillin-clavulanic acid 2.1 µg disk can be used with the EUCAST disk diffusion test to identify beta-lactam resistant H.influenzae with beta-lactamase only. Beta-lactamase positive isolates with AMC 2.1 µg ≥15 mm can be reported susceptible for penicillins with beta-lactamase inhibitors, cephalosporins and carbapenems for which EUCAST breakpoints are available. We propose to include AMC 2.1 µg to be used together with the PCG 1 unit disk and a beta-lactamase test in the EUCAST screening algorithm for beta-lactam resistance in H.influenzae.

![Figure 1. Inhibition zones for H. influenzae (144 beta-lactamase positive isolates) and amoxicillin-clavulanic acid 2.1 µg.](image-url)

Black bars correspond to isolates with beta-lactamase only (n=87) and red bars to isolates with beta-lactamase and PBP3 mutations (n=57). The EUCAST zone diameter breakpoint for amoxicillin-clavulanic acid is shown as a dotted line.

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**Abstract 3359**

**Invasive *Haemophilus influenzae* type b (Hib) disease in children in Italy, after 20 years of routine use of conjugate Hib vaccines**

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**Background:** *Haemophilus influenzae* serotype b (Hib) was the leading cause of bacterial meningitis in children before the implementation of infant immunization with conjugate Hib vaccines. In Italy, children are scheduled for Hib vaccination at 3, 5 and 11 months. Despite the effectiveness of the vaccine, invasive Hib disease cases are reported in children either because of incomplete vaccination status (failure to vaccinate) or through true vaccine failure (TVF).

**Materials/methods:** Data on invasive *H. influenzae* cases were detected through the National Surveillance of Invasive Bacterial Disease. All invasive Hib disease cases in children <18 years reported during 2012-2018 were included in the study. Hib isolates were subjected to MLST and PFGE analysis. The number of copies of the *capb*-locus was determined by Southern blot analysis.

**Results:** Overall, 31 cases of invasive Hib disease in children were reported. The median age of children was 12 months (range 3 months-15 years). A decrease in coverage (by 36 months of age) was observed in 2014-2016, corresponding to a clear rise in incidence starting from 2016 until 2018, especially in children <5 years. Fourteen children were fully vaccinated (TVFs), 14 were unvaccinated and 2 partially vaccinated. Most cases in children ≤2 years occurred in unvaccinated subjects. Meningitis was more frequent among unvaccinated children (71.4%) than among TVFs (42.8%), although this data was not statistically significant, p=0.12. No significant association was found between characteristics of children and TVF. Out of 31 cases of invasive Hib disease, 24 isolates were available. The predominant ST was ST6 (17/24, 71%) followed by ST95 (n=2). Cluster analysis of ST6 isolates by PFGE identified five variants. Six isolates (25%) contained multiple copies of the *capb*-locus distributed among TVFs (30%) and unvaccinated children (16.7%).

**Conclusions:** Our data show that both failure to vaccinate and TVFs are associated with the occurrence of invasive Hib disease in children in Italy, during the present vaccination era. Most cases in children ≤2 years were vaccine-preventable. No host predisposing factors for TVF were recognized. TVF were not significantly associated with either specific genotypes or amplification status of the *capb* locus.

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Abstract 3364

Incidence of venous thromboembolism among patients receiving outpatient parenteral antimicrobial therapy at Sheffield Teaching Hospitals NHS Foundation Trust, UK: an observational study

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Background: Outpatient parenteral antimicrobial therapy (OPAT) is increasingly used to facilitate early discharge from hospital and prevent hospital admission, for patients with infections requiring intravenous antibiotics. It is routine, evidence-based practice to prescribe venous thromboembolism (VTE) prophylaxis for medical and surgical inpatients. However, optimal practice for patients receiving OPAT is not known. The aim of our study was to describe current clinical practice in relation to VTE risk assessment and prophylaxis, and determine the 90-day incidence of VTE events in our cohort of OPAT patients.

Materials/methods: Electronic records were used to retrospectively review OPAT episodes at Sheffield Teaching Hospitals between September 2018 and March 2019. Region-wide electronic results systems were used to determine if any VTE episodes occurred within 90 days of an OPAT episode.

Results: 261 OPAT patient episodes were included. The median age was 59 years (range 16-94). 163 (62%) were inpatients prior to OPAT, with 138 (85%) receiving either prophylaxis or full anticoagulation at the time of transfer to OPAT. The most common conditions treated were skin and soft tissue infection n=128 (49%), bone and joint infection n=48 (18%), abdominal/urogenital infection n=21 (8%), endocarditis/endovascular infection n=20 (7%). 46 patients (16%) were assessed for VTE at the onset of the illness requiring OPAT, with 9 (3%) new VTE diagnoses.

201 (77%) episodes had a VTE risk assessment upon commencing OPAT, using the standard hospital-wide VTE risk assessment tool. Median number of VTE risk factors was 2 (range 0-5). 10 patients (4%) were prescribed VTE prophylaxis while receiving OPAT and 37 (14%) were fully anticoagulated for other reasons. The reason for not prescribing VTE prophylaxis was documented in 188 (75%) of 251 episodes: ambulatory n=144 (77%), already anticoagulated n=34 (18%), resolving infection n=5 (3%).

No new episodes of VTE occurred in the 90 days following OPAT therapy.

Conclusions: In this cohort, the incidence of VTE following OPAT was zero. The main limitations of the study were its small size and retrospective nature. Larger prospective studies are required to evaluate the risk of VTE in OPAT patients, in order to develop risk assessment tools appropriate to OPAT.

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Importance: The incidence of acute viral and bacterial infections in children are often presented separately for different pathogens in epidemiological studies making direct comparisons of morbidity burden between pathogens difficult. Despite the modern immunisation program, pediatric emergency departments [ED] still have numerous annual visits. We aimed to demonstrate the current morbidity burden of microbes leading to ED visits in acutely ill children, using enhanced microbiological diagnostics.

Materials/methods: This population-based registry study used a cohort of all infants and children that visited Oulu University Paediatric ED, Finland, during one epidemiological year. We actively used multiplex respiratory viral and bacterial PCR (Allplex respiratory panel 4, Seegene Inc, detecting Chlamydia pneumoniae, Mycoplasma pneumoniae, Legionella pneumophila, Bordetella pertussis, Bordetella parapertussis, and an Anyplex II RV16 kit for 16 respiratory viruses) in all children with respiratory symptoms or fever of unknown origin. We reviewed all medical records and systematically collected data on bacterial samples, including urine, CSF, and blood culture samples, specific viral or bacterial PCR samples, such as HSV, VZV, enterovirus, Chlamydia pneumoniae and Bordetella pertussis. Serological data were collected for several pathogens including EBV, Mycoplasma pneumoniae and pathogens typical for Finland, Puumala hantavirus infection and tularemia. Specific clinical diagnoses for infectious diseases were recorded.

Results: In 4639 acutely ill children, infection diagnoses covered 55% of all ED diagnoses. The most common viral pathogens leading to ED visits were rhinovirus, accounting for 26% of visits due to respiratory symptoms, followed by adenovirus [10%), and RSV [7%]. Mycoplasma comparisons and Chlamydia pneumoniae caused 4% of respiratory infections. The most common bacterial pathogen was Escherichia coli, accounting for 4% for all ED visit due to any infection. Vaccine-preventable diseases, including rotavirus and pneumococcal sepsis, were rare findings during the study period. Full list of pathogens and their morbidity burden at pediatric ED will be presented.

Conclusions: Currently, rhinovirus and Escherichia coli account for the largest morbidity burden of infections leading to ED visits at a pediatric hospital. To reduce pediatric ED visits, future research should aim for preventing the most prevalent infections leading to ED visits in acutely ill children.

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Global increase in antibiotic-resistant *Escherichia coli* in food-animals: a genomic public data approach

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**Background:** The use of genomic technologies in antibiotic-resistance epidemiology is increasing the number of deposited genomes in public repositories. Globally, this data is largely unexplored due to its heterogeneous nature. This is especially problematic in food-animal data, where isolation sources and hosts are very diverse. We aim to query *Escherichia coli* genomes of food-animal origin in public repositories to perceive global resistance trends.

**Materials/methods:** A systematic search for *E. coli* genomes was performed in NCBI, PATRIC and EnteroBase. Metadata was standardized by assigning a food-animal host, an isolation location and date. Assemblies were downloaded and duplicates removed. Assemblies were screened for acquired resistance genes (ARG) with ResFinder and population structure was analyzed using cgMLST and ClermonTyping. The number of affected classes were calculated based on ARG's predicted phenotypes and modeled with a Poisson regression to understand resistance evolution overtime.

**Results:** A total of 7635 *E. coli* genomes had an identifiable food-animal host. Most genomes were recovered from cattle (51.8%), followed by poultry (26.4%) and swine (16.4%). The majority originated from USA (59.7%), and to lesser extent China (13.9%) and UK (11.6%). *E. coli* belonged mostly to B1 (43.4%) and A (22.9%) phylogenetic groups which have been widely associated with animals. Identified clonal complexes (CCs) were also consistent with previous reports: CC11 (14.7%), CC10 (10.5%) and CC155 (8.4%). 4496 genomes (59%) contained ARG, being the most frequent those conferring resistance to aminoglycosides (*aph(6)-Id*, 56.5%), sulphonamides (*sul2*, 53.8%), tetracyclines (*tet(A)*, 52.7%) and narrow-spectrum β-lactams (*bla*<sub>TEM-1</sub>, 34.4%). Extended-spectrum β-lactamases were identified in 18% genomes containing ARGs. Poisson regression indicated that the number of affected antibiotic categories increased between 1970 and 2018. This increase was more pronounced in poultry isolates (from 1 antibiotic to 5), than in swine (from 2 to 4) or cattle (from 1 to 2) isolates.

**Conclusions:** Our analysis yielded information consistent with reports on antibiotic-resistant *E. coli* from food-animals, highlighting the reliability of using public genomes in global surveillance. Moreover, our data suggests that resistance is increasing at different rates in the different animal hosts, indicating that measures to contain resistance spread need to be adapted to each food-animal species.

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Abstract 3372

Effectiveness of the 23-valent pneumococcal polysaccharide vaccine against vaccine serotype pneumococcal pneumonia in adults

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Background: Vaccination with the 23-valent pneumococcal polysaccharide vaccine (PPV23) is available in the UK to adults aged 65 or over and those in a clinical risk group. We evaluated the vaccine effectiveness (VE) of PPV23 against vaccine-type pneumococcal pneumonia in a cohort of adults hospitalised with community-acquired pneumonia (CAP).

Materials/methods: This was a secondary analysis of data collected from a prospective cohort study of adults hospitalised with CAP from September 2013 to August 2018. A modified case-control test negative design was used. Pneumococcal serotypes were identified from urine samples using a multiplex immunoassay (Bio-plex24) or from blood cultures positive for Streptococcus pneumoniae. The exposure of interest was PPV23 vaccination at any time point prior to the index admission. The primary outcome was PPV23 serotype-specific pneumococcal pneumonia. A case was defined as pneumococcal pneumonia where a PPV23 vaccine serotype was detected; a control as non-PPV23 serotype pneumococcal pneumonia or non-pneumococcal pneumonia. Logistic regression was used to derive adjusted odds of vaccination in cases compared to controls; VE estimates were calculated as (1-odds ratio) x100%.

Results: Of 2357 patients, vaccine status was obtained from primary care records in 77.2% and self-reported in 32.8%. There were 717 PPV23 cases (48% vaccinated) and 1640 controls (54.5% vaccinated). Compared to controls, cases were a similar age (65.4 vs 66.5 years) with a better baseline performance status (p-trend=0.01), had higher severity disease on admission (26.2% vs 21.5% high severity by CURB65; p-trend=0.01), were less likely to have malignancy (7.3% vs 10.3%; OR 0.68 95%CI 0.49-0.95, p=0.02) or cardiac disease (12% vs 16.9%; OR 0.67 95%CI 0.52-0.87, p=0.003) but more likely to be alcohol dependent (3.6% vs 2.1%; OR 1.78 95%CI 1.06-2.99, p=0.03). The adjusted VE estimate against PPV23 serotype disease was 24% (95%CI 7 to 38%, p=0.01). When cases were restricted to serotypes in PPV23 but not in the 13-valent pneumococcal conjugate vaccine (PPV23/non-PCV13), the adjusted VE estimate was 29% (95%CI 4 to 45%, p=0.01).

Conclusions: PPV23 vaccination in line with current UK vaccine policy appears modestly effective against PPV23 serotype pneumococcal pneumonia. The estimated VE against PPV23/non-PCV13 serotypes was similar.

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Abstract 3373

High-dimensional single cell analysis identifies unexpected distribution of T cell populations in liver transplanted HIV-positive patients

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Background: In patients undergoing orthotopic liver transplant (OLT), immunosuppressive (IS) treatment is mandatory and infections are the leading cause of morbidity/mortality. Thus, it is essential to understand the functionality of cell-mediated immunity after OLT and which alterations can increase the infection risk. For this reason, we studied T cell subsets and functionality in these patients, comparing HIV positive and HIV negative patients.

Materials/methods: In each of these groups we enrolled 27 patients (total 108): HIV+ transplanted patients; HIV- transplanted patients; HIV+ non-transplanted patients; healthy subjects (CTR). Activation and differentiation of T cells were analyzed by 18-parameter polychromatic flow cytometry; cytokine production was assessed by intracellular staining after PBMC in vitro stimulation.

Results: Median age was 55 years (52-59), median CD4 count in HIV+ patients was 567/mcl (342-744), all had undetectable viral load. The majority of transplanted patients had tacrolimus as immunosuppressor (72%) with no differences between HIV+ and HIV- patients. No differences in tacrolimus plasma levels were observed between HIV+ and HIV- patients. Different distributions of CD4+ and CD8+ T cell subtypes were found among liver transplanted patients with or without HIV (figure 1). In particular, a cluster representing effector memory (EM) cells expressing PD1 was mostly abundant in non-HIV transplanted patients if compared to HIV positive transplanted patients. Regarding polyfunctionality, HIV negative transplanted patients were characterized by higher levels of CD4+ T cells able to produce at the same time IFN-g and TNF-a, showing a marked Th1-skewed phenotype.

Conclusions: HIV negative transplanted patients have more exhausted/immunosenescent T cells compared to HIV positive transplanted patients. This seems to indicate that patients who already experienced a form of immunosuppression due to HIV infection respond differently to anti-rejection therapy.

Figure 1

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Abstract 3377

Distribution of capsular types among multi-resistant Klebsiella pneumoniae in the south of Spain by using a whole genome sequence-based solution

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Background: Polysaccharide capsule or K-antigen, a major virulence factor of K. pneumoniae, has long been used as the main method for typing and is the most promising antigen for a vaccine candidate for humans. Traditional serotyping could be inconsistent due to cross-reactivity. PCR-based genotyping using the wzy and wzc capsular genes yielded limited results due to modifications of the cps region in specific strains. A new whole genome sequencing (WGS) based tool, Kaptive web, has been recently developed for serotype prediction. The aim was to study the prevalence of K and O loci among multi-resistant isolates in our region with this typing method.

Materials/methods: After routine PFGE analysis of the strains remitted to the Regional Reference Laboratory of Andalucía [PIRASOA] (South of Spain) from 24 hospitals, 134 isolates as representative of every pulsotype were selected. Genomic DNA was extracted and sequenced via Illumina MiSeq and reads were de novo assembled using CLC genomics. Genome assemblies were uploaded to CARD and ResFinder for resistance determinants, and to MLSTFinder and Kaptive web for typing.

Results: At least one carbapenemase was identified in 81 (61%) isolates. The main carbapenemases were OXA-48 (28 isolates, 35%) and KPC-3 (27 isolates, 33%), followed by VIM-1 (10 isolates, 12%). Thirty-eight clones were identified in total and 5 STs were predominant (74%) among carbapenemase producers [ST512/KPC-3, ST307/OXA-48, ST307/KPC-2, ST15/OXA-48, ST15/VIM-1, ST11/NDM-7]. Good confidence level or better with K locus were obtained with 114 (86%) assemblies yielding 30 K and 9 O loci among carbapenemases producers. The predominant clones showed 10 K types and 5 O types: all ST512 and ST258 genomes were KL107/O2v2; ST307 genomes were KL102/O2v2 and KL10/O3/O3a; ST11 genomes were KL25/O5, KL24/O2v1 and KL27/O2v2; ST15 were KL64/O1v1, KL48/O1v1, KL28/O1v1 and KL112/O1v1.

Conclusions: 1) Kaptive web is an easy-to-use tool which simplifies the study of K-locus-related genes; 2) a reduced number of K-antigens were identified among the predominant carbapenemases producers in our region; 3) ST15 and ST11 harbored a higher diversity of K-loci than other carbapenemases-producing clones, reflecting the existence of multiple sub lineages dissemination.

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Local signs at insertion site and prediction of catheter-related infections in short-term central venous and arterial catheters in the intensive care unit: individual findings from four multi-centre randomised controlled trials

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Abstract 3378

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Background: Little is known on the role of exit-site signs in predicting intravascular catheter infections. This study aimed to describe the association between local signs at the exit-site and catheter-related bloodstream infections (CRBSI) and which clinical conditions may predict CRBSIs if inflammation at insertion site is present.

Materials/methods: We used individual data from four multicenter randomized-controlled trials in intensive care units (ICUs) that evaluated various prevention strategies regarding colonization and CRBSI in arterial and central venous catheters. We used univariate and multivariate logistic models stratifying by center in order to identify variables associated with redness, pain, non-purulent discharge, purulent discharge and ≥1 local sign and subsequently evaluate the association between CRBSI and local signs. Moreover, we evaluated the role of the different local signs for developing CRBSI in subgroups of clinically relevant conditions.

Results: A total of 6,976 patients and 14,590 catheters (101,182 catheter-days) and 114 CRBSI (0.8%) from 25 ICUs with described local signs were included. Redness, pain, non-purulent discharge, purulent discharge and ≥1 local signs at removal were observed in 1,633 (11.2%), 59 (0.4%), 251 (1.7%), 102 (0.7%) and 1,938 (13.3%) episodes, respectively. The sensitivity of ≥1 local sign for CRBSI was by 40.4%. Positive predictive value (PPV) was low for redness (2%), pain (3%), non-purulent discharge (3%) and ≥1 local sign (2%), but increased for purulent discharge (12.7%). After adjusting on confounders, CRBSI was associated with redness, non-purulent discharge, purulent discharge and ≥1 local sign (Figure). The presence of ≥1 local sign was more predictive for CRBSI in the first 7 days of catheter maintenance (OR 6.30 vs. OR 2.61 for >7 catheter-days, p = 0.02).

Conclusions: This post-hoc analysis showed that local signs were significantly related to CRBSI in the ICU. In the first 7 days of catheter maintenance local signs were highly predictive for CRBSI.
Figure: Unadjusted and adjusted CRBSI-risk for the different local signs.

Legend. *For redness we adjusted for the following confounding factors: Age, SOFA score, duration of catheter maintenance, immunosuppression, insertion site. **For pain we adjusted for the following confounding factors: mechanical ventilation at insertion and vasopressor at insertion. ***For non-purulent discharge we adjusted for the following confounding factors: Age, duration of catheter maintenance, insertion site and mechanical ventilation at insertion. ****For purulent discharge we adjusted for the following confounding factors: duration of catheter maintenance and catheter type. *****For ≥1 local sign we adjusted for the following confounding factors: Age; SOFA score, immunosuppression, duration of catheter maintenance and insertion site. CRBSI: Catheter-related bloodstream infection.

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**Abstract 3381**

**DNA thermo-protection facilitates whole genome sequencing of mycobacteria direct from clinical samples by ONT MinION**

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**Background:** Mycobacteria tuberculosis (MTB) is the leading cause of death from infection. Improved access to rapid diagnosis and antimicrobial resistance determination, such as by whole genome sequencing, is required in regions with the highest incidence. Our aim was to develop a simple, low-cost method of preparing DNA for MinION (Oxford Nanopore Technologies) sequencing direct from MTB positive clinical samples without culture. Commercial kits which increase cost, shipping, storage requirements, and protocol complexity were avoided.

**Materials/methods:** Simultaneous sputum liquefaction, heat-inactivation and sample enrichment for target DNA was performed in a novel thermo-protection buffer. The buffer was designed to protect DNA from thermo-degradation, by emulating intracellular conditions of hyperthermophiles. An equal volume of buffer (4M KCl, 0.05M HEPES buffer pH7.5, and 0.1% DTT) was added to sputum. Following liquefaction, samples were heated at 99°C for 30 minutes. Two wash/centrifugation steps were followed by DNA extraction, sequencing (one MinION R9.4.1 flow cell/sample) and assembly against a reference. GeneXpert (Cepheid) and Microscopy (ZN/auramine stain) data were collected.

**Results:** Initial experiments confirmed that KCl buffer protected Mycobacteria DNA (extracted and intracellular) during heating at 99°C for 30 minutes. Human DNA degraded faster than Mycobacteria DNA, therefore target DNA content was improved. Standardised, mock clinical samples comprising infection-negative sputum spiked with BCG at 0-10⁷/ml, underwent direct-from-sample sequencing in four replicate experiments. The limit of detection (LOD) was 10⁵ BCG cells/ml, with 31, 49, 51, and 59 MTB complex reads (Figure). The GeneXpert LOD for the same samples was 10² and Microscopy 10³. Maximal genome coverage (>97% at 5x depth) was achieved at 10⁴ BCG cells/ml; >91% coverage (1x depth) at 10³ BCG cells/ml.

Ten MTB positive clinical samples were sequenced. Initial sample volumes ≥1ml yielded higher average depth of coverage (range 5.89-45.01); ≤0.5ml less (0.55-4.75). All six samples ≥1ml yielded >99% 1-fold genome coverage and 5/6 yielded >98.7% 5-fold genome coverage. Four of these were high titre by GeneXpert/microscopy, two low. The depth across 22 antimicrobial susceptibility genes mirrored the average, confirming potential for resistance prediction.

**Conclusions:** Direct-from-sample MinION sequencing of MTB genomes can be achieved from 1ml positive sputum, using a low cost thermo-protection buffer.

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**Invasive aspergillosis by cryptic Aspergillus species in a 700-bed third level hospital**

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**Background:** Aspergillus species are the moulds most commonly involved in invasive fungal infection. These infections are usually severe and have emerged as a significant cause of morbidity and mortality. Cryptic species retrieved from clinical samples ranged from 12 to 14% according to two multicenter studies of filamentous fungi and antifungal resistance in Spain (FILPOP), and were generally more resistant to commonly used antifungal agents. The objective of this study was to describe the frequency, clinical and microbiological characteristics and outcomes of invasive aspergillosis caused by cryptic species in our center.

**Materials/methods:** We retrospectively identified all microbiologically documented cases of aspergillosis in our center from January 2013 to December 2018. Information about the patient's demographics, clinical data and received treatment was obtained from their medical records. The definitive species identification of the clinically significant isolates was achieved by sequencing methods (ITS region and β-tubulin).

**Results:** A total of 629 Aspergillus spp were recovered, from 489 patients. One hundred-nine of these episodes were clinically relevant, whereas 321 were considered as colonizations/contaminations. We identified 10 cryptic species, representing 9.17% of all the clinically relevant isolates, namely: Aspergillus arcoverdensis [2], Aspergillus lentulus [2], Aspergillus ellipticus [2], Aspergillus alliaceus [1], Aspergillus nomius [1], Aspergillus tubingensis [1] and Aspergillus amstelodami [1]. All patients were males, three patients presented HIV infection, two malignant tumors, one solid organ transplantation, one previous pulmonary cavity, one hematologic disease and one local corticoid injection. 40% of patients died from the fungal infection.

**Conclusions:** The frequency of cryptic species in our center was 9.17%. Most patients had some type of immunosuppression and the mortality rate was 40%. The identification of cryptic species is important, not only to improve the appropriateness of antifungal treatment but also to increase the knowledge about these new species.

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Abstract 3384

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Background: With publication of the ‘value assessment frameworks for antibiotics’ by the Office for Health Economics (OHE) and others, it has become widely accepted that antibiotics are undervalued when assessed through existing health technology appraisal processes. Therefore, the inclusion of a more complete set of value elements is required when valuing an antibiotic to ensure the wider societal value of an antibiotic is captured.

Materials/methods: The value elements considered within this analysis are enablement-, insurance-, and productivity-value;

1) Insurance value - withholding wider use of an antibiotic, and reserving it for tackling resistant infections, thus providing insurance against possible future outbreaks of infections with resistant pathogens.

2) Enablement value - benefits associated with enabling other treatments or procedures to take place, e.g., surgical and medical procedures that may not be possible if antimicrobials were not available to prevent or treat surgical site or post-procedure infections.

3) Productivity benefits associated with having a larger, more active workforce, due to the changes in the mortality and in-hospital morbidity associated with infections.

Novel methodical approaches have been explored for each value element with methods proposed created through collaboration and expert elicitation from several stakeholder groups, including; microbiologists, actuaries, economists, life science experts and medical doctors across various specialty areas including; oncologists, neurologists, generalist-, cardiac- and orthopaedic-surgeons.

Results: The outlined methods build on the work from OHE and others, demonstrating a quantifiable output can be determined and associated to the antibiotic included within the modelling. Through these methods we begin to capture the additional benefits that a new antibiotic can bring to the healthcare system and patients. Work is to be continued on both insurance value, whereby a stochastic modelling approach will be taken, and enablement value, as we build this into a dynamic transmission model.

Conclusions: Value alone will not tackle the wide-reaching concerns of antimicrobial resistance, continued efforts on stewardship and building of R&D initiatives need to be increased. However, these methods proposed aim to accelerate the development of quantifying these value elements, building a more comprehensive picture of the value antibiotics bring to society.

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MBT STAR-Carba assay: going beyond the routine protocol
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Abstract third-party references: Supported by SONATINA 2 project No. 2018/28/C/ST4/00434 from National Science Centre, Poland.

Background: The increasing frequency of resistance against carbapenems represents a serious threat to public health. Therefore, the development of new techniques for rapid detection of carbapenemase-producing bacteria is globally of great importance. A promising tool could be the monitoring of carbapenemase hydrolytic activity by MALDI-TOF/MS. The main goal of our study was to evaluate the effect of bacterial suspension density and incubation time on the sensitivity of the MBT STAR®-Carba kit (Bruker Daltonics) for the detection of hydrolytic activity of bacteria possessing different classes of carbapenemases.

Materials/methods: Hydrolytic activity was investigated in 12 Enterobacteriaceae and 3 Pseudomonadaceae strains expressing various carbapenemases (e.g. KPC, NDM-1, OXA-type) using in parallel the MBT STAR®-Carba kit according to the manufacturer’s protocol with 1 µl loop of material as well as applying an in-house method with different bacterial suspension concentrations (1–7 McFarland) and incubation times (1–30 minutes). Samples were analyzed via microflex LT/SH instrument (Bruker Daltonics) and MBT Compass platform with MBT STAR-BL Module (Bruker Daltonics). Results were analyzed based on the level of antibiotic hydrolysis (normalized logRQ value) dependent on the density of the bacterial suspension, kinetic curves as well as on grouping of the strains in principal component analysis (PCA).

Results: Analysis revealed a class dependent effect of bacterial density on the normalized logRQ values. In general, Pseudomonadaceae strains demonstrated relatively lower hydrolytic activity and distinct normalized logRQ/suspension density correlations compared to the Enterobacteriaceae members. Moreover, a significant variation in incubation time needed to detect hydrolytic activity was noted. PCA analysis also revealed a carbapenemase class dependent effect, grouping strains mostly into class D and class A harboring strains. Nevertheless, in almost all cases a present hydrolytic activity was obtained after less than 30 minutes of incubation.

Conclusions: The MBT STAR®-Carba assay represents a very rapid and highly sensitive but also robust tool for detection of a broad spectrum of carbapenemase-producing bacteria. Moreover, besides the standard workflow, the application of a defined suspension density can increase knowledge about differences in the antibiotic hydrolysis level of an investigated strain. Further, it might enable to shorten individual incubation times and thus the whole analysis.

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Abstract 3386

The antimicrobial susceptibility profile and prevalence of known anaerobic resistance genes in less common anaerobic Gram-negative bacteria, isolated in the Netherlands

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Background: In the past years antimicrobial resistance among anaerobes, as in aerobes, is increasing. Well studied is the increase of resistance in the Bacteroides group, Clostridium spp. and Prevotella spp. Studies focusing on the antimicrobial resistance in less common gram-negative anaerobes, e.g. Fusobacterium and Bilophila, are scarce. In this study we assessed the antimicrobial susceptibility profile and the prevalence of antimicrobial resistance genes among less common gram-negative anaerobes.

Materials/methods: In this study, a total of 163 anaerobic gram-negative anaerobes were included, covering the genera Alistipes spp. (n=7), Bilophila spp. (n=41), Dialister spp. (n=10), Fusobacterium spp. (n=101) and Sutterella spp. (n=4). All isolates were consecutively isolated in the years 2015-2018 from a variety of human clinical samples. Isolates were identified using MALDI-TOF MS. MIC values for different antibiotics were determined using E-test and interpreted according EUCAST guidelines. Nitrocefinase discs were used to detect the production of beta-lactamases. A targeted PCR, using specific primers, was used to detect the presence of resistance genes (cfxA, ermF, nim and tetQ).

Results: Resistance to amoxicillin was detected in 58 of the 163 (36%) tested isolates, ranging from >90% in Bilophila isolates to 0% in Dialister isolates, while 10 of the 163 (6%) isolates were shown to produce beta-lactamase. All Sutterella isolates (n=4) were resistant to clindamycin and 3 were resistant to metronidazole. The tetQ gene was detected in 2 of the 7 (29%) Alistipes isolates. However, resistance to tetracycline was not detected. No cfxA, ermF or nim genes were detected in all tested isolates.

Conclusions: No correlation was observed between phenotypic resistance and the presence of a known antimicrobial resistance gene nor between amoxicillin resistance and the production of beta-lactamase. This might suggest that novel antimicrobial resistance mechanisms or other unknown resistance mechanisms are present in the tested isolates. Whether the observed resistance is intrinsic needs to be assessed. Whole genome sequencing might help understanding the origin of the detected antimicrobial resistance.

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Minimum Inhibitory Concentration distributions and putative new resistance mechanisms for mecillinam and trimethoprim in *Staphylococcus saprophyticus*

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**Background:** *Staphylococcus saprophyticus* is the second most common bacteria causing uncomplicated urinary tract infections (UTI). As a Gram-positive coccus it is considered non-susceptible to the beta-lactam mecillinam, with no defined breakpoint and minimum inhibitory concentration (MIC) distribution from 8-256 mg/L. However, this consideration does not correlate with clinical outcome, as cure rates with pivmecillinam are high. With this study we wanted to provide a more comprehensive MIC distribution analysis of mecillinam for *S. saprophyticus* and investigate any potential resistance mechanisms. The MIC distribution for trimethoprim was also investigated, as no data were available at the time.

**Materials/methods:** 117 isolates representative of *S. saprophyticus* population structure described in a previous study were included: 113 isolates were from human UTI (Denmark, 90; Poland, 1; Spain, 9; Portugal, 13) and four from veterinary sources (Portugal). E-tests were used to determine MICs. All isolates had been whole-genome sequenced and a machine-learning approach was used to identify 198 genetic features that distinguish mecillinam resistant isolates with MIC≥256 from isolates with MIC<256.

**Results:** For mecillinam, MICs ranged from 4 to ≥ 256, with a binary clustering around 32 and ≥256, respectively (figure 1). Only one isolate was below the currently considered breakpoint (8 mg/L) of mecillinam for Enterobacterales. Some top genetic features for isolates with MIC≥256 include mutations in coding regions for proteins involved in cysteine metabolism, mecA presence (n=3), regulatory regions for glutamine transporters, and the multidrug resistance protein Ykkc. For trimethoprim, the MICs clustered around 0.5 and only six isolates had a MIC above the currently considered breakpoint (2 mg/L) for Enterobacterales. Of these, three had the previously described trimethoprim resistance gene *dfrG*.

**Conclusions:** All but six investigated isolates could be considered susceptible to trimethoprim. The clinical success often seen after pivmecillinam treatment of uncomplicated UTI caused by *S. saprophyticus* infections could be explained by the binary clustering of MICs found here, as the mecillinam urine concentration (about 200 mg/L) surpasses the former clustering group but not the latter, during conventional pivmecillinam therapy.

Figure 1. MIC distribution of mecillinam and trimethoprim in 117 *S. saprophyticus* isolates
Abstract 3389

**Optimising the treatment of upper respiratory tract infections and tackling antibiotic resistance: effect of online education on physician knowledge and confidence**

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Abstract third-party references: Medscape Education

**Background:** Macrolides are established and widely used for treating a range of upper respiratory tract infections (URTIs). We assessed if online medical education for pulmonologists, paediatricians and primary care physicians could improve knowledge regarding optimal use and effectiveness of macrolides in the treatment of URTIs [including otitis media and bacterial rhinosinusitis] and best practice in antibiotic stewardship. We also assessed physician confidence in their ability to optimally select the appropriate macrolide for URTIs.

**Materials/methods:** Online independent CPD program featuring 4 short sequential expert video commentaries. Repeated pairs of pre- and post-assessment questions with data assessed by Pearson's Chi-Square ($P<0.05$ statistically significant) and Cramer's V [modest impact 0.1; extensive impact $>0.26$]. Data collected 6th June to 29th October 2019.

**Results:** 5,567 physicians participated from Asia, Latin America, Middle East/North Africa and Australia/New Zealand. Overall, there was a 100% relative increase ($P<0.001$) with extensive impact in physician knowledge gains. The activity significantly improved knowledge in all aspects of macrolide use and resistance in URTIs (Table). Significant differences were also reported in the average confidence shift ($P<0.001$) and the shift to mostly or very confident ($P<0.01$) in the physician's ability to select the optimal and appropriate antibiotic for URTIs.

<table>
<thead>
<tr>
<th>Question</th>
<th>Proportion of participants with the correct Pre-test answer</th>
<th>Proportion of participants with the correct post-test answer</th>
<th>Positive % change</th>
<th>P value</th>
<th>Cramer's V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Which class of antibiotics is not associated with colonization resistance and has the appropriate spectrum of activity against pathogens that typically cause community-acquired respiratory tract infections?</td>
<td>61%</td>
<td>84%</td>
<td>38%</td>
<td>0.0001</td>
<td>0.18</td>
</tr>
<tr>
<td>Which macrolide antibiotic has the following advantages: activity against common pathogens in URTIs, convenient dosing, half-life of 2 to 3 hours for 500 mg, and high epithelial lining fluid concentration?</td>
<td>33%</td>
<td>87%</td>
<td>165%</td>
<td>0.0001</td>
<td>0.29</td>
</tr>
<tr>
<td>Antibiotics with a prolonged half-life are known to increase one of the following bacterial resistance, elevated macrophage concentration, gastric instability or immunomodulation</td>
<td>30%</td>
<td>74%</td>
<td>147%</td>
<td>0.0001</td>
<td>0.34</td>
</tr>
</tbody>
</table>

**Conclusions:** Despite macrolide antibiotics being widely available for a considerable length of time, online medical education significantly improves physician's knowledge and confidence in correct and prudent use for the treatment of URTIs.

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Abstract 3397

**Qualitative detection of OXA-23-like, OXA-24-like and OXA-58-like carbapenemases from Acinetobacter species by real-time PCR**

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**Background:** Carbapenemase producing Acinetobacter species, especially Acinetobacter baumannii, are often associated with treatment failures and hospital outbreaks, consequently rapid and reliable detection of specific resistance markers is paramount. The most common carbapenemase found in A. baumannii, namely OXA-23-like, OXA-24-like and OXA-58-like, belong to the Oxacillinase group (Class D β-lactamases) which is notoriously difficult to identify phenotypically due to the lack of specific inhibitors, therefore a multiplex real-time PCR assay was designed and validated.

**Materials/methods:** All available variants of the above three carbapenemases were downloaded [as of November 2019] from the Beta-Lactamase DataBase (http://bldb.eu/) aligned with Clustal Omega and oligonucleotides designed using Primer-BLAST. Monoplex assays were optimized on the Rotor-Gene Q (Qiagen) using the Rotor-Gene Multiplex PCR Kit (Qiagen) and then combined into a 4-plex assay that included an internal control to discount inhibition. A panel of 120 previously characterised strains (18 different species in total) carrying a total of 20 OXA-23-like, 17 OXA-24-like and 20 OXA-58-like markers plus a wide range of different β-lactamases, often in combination, was tested to determine assay sensitivity and specificity. DNA was extracted by heat treatment (10min at 100°C) and extracts diluted 1:20 in nuclease-free water to avoid PCR inhibition.

**Results:** The in silico approach allowed to design oligonucleotides in conserved regions of the OXA-24-like and OXA-58-like alignments. Among the 42 OXA-23-like variants, a SNP was identified in OXA-27, OXA-166, OXA-811, OXA-812 and OXA-816 (five different SNPs in total); none among these variants was available for in vitro analysis, however given the SNPs location (i.e. non-3’ end of binding sites) they should still be detected. Expected results were obtained for all 120 strains (100% sensitivity and specificity) and for all possible target combinations using A. baumannii NCTC 13301 (OXA-23), A. baumannii NCTC 13302 (OXA-24) and A. baumannii NCTC 13305 (OXA-58). Cross-reaction with other resistance markers, including Oxacillinases, was not observed. Inhibition was also not observed.

**Conclusions:** The assay is easy to perform with results available in ca. 70 minutes (plus the heat-inactivation time). It enables unequivocal detection and differentiation of OXA-23-like, OXA-24-like and OXA-58-like carbapenemases even when more than one resistance marker is simultaneously present.

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**Abstract 3398**

**Comparison of environmental Legionella pneumophila and Legionella spp. detection from water and swab samples by culture and qPCR**

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**Background:** Water is the recommended sample for environmental Legionella spp. detection by culture and molecular tests. Copan SRK™ environmental collection kit, a FLOQSwabs® and a medium tube, has been previously validated for Legionella pneumophila viability at room temperature (RT) for 48hrs and at 2-8°C for 72hrs by culture and different molecular assays. The objective of this study was to compare water to swabs collected at the water source using SRK™ environmental collection kit, for the detection of Legionella spp. (LS) and Legionella pneumophila (LP) by culture and qPCR.

**Materials/methods:** Paired water and SRK™ swabs samples (N= 361) were collected in duplicate from wells (n=85), house water (n=268), and cooling towers (n=8). Two liters of water were collected and SRK™ sampling was performed by swabbing the water source and storing the FLOQSwab® in the SRK™ medium tube (Copan). One liter of water was processed for culture following SOP. The other liter was filtered, nucleic acids extracted using the DNA Extraction Kit I (Bioside) and analyzed with the qualyfast® Legionella qPCR (Bioside) for simultaneous detection of LS and LP. Swab samples were vortexed and 200μl of SRK™ medium were plated on BCYE agar and incubated at 32°C for 10 days. Nucleic acids were extracted from 200μl of SRK™ medium and 5μl of extract analyzed using qualyfast® Legionella qPCR (Bioside).

**Results:** Concordant results were obtained from 98.9% (357/361) of paired swab and water samples using culture. 81 resulted positive (41 LS and 40 LP) and 276 were negative. Contrarily, 4 swabs resulted positive (3 LS, 1 LP) with paired negative water. qPCR detected 136 positives in both sample types (93 LS, 43 LP) and 219 negatives. Six SRK™ swabs resulted positive (4 LS, 2 LP) with corresponding negative water.

**Conclusions:** Data obtained in this study demonstrates that swabs samples collected with the SRK™ environmental kit detected the same number of positive Legionella spp and Legionella pneumophila as in paired water samples by both culture and qPCR using qualyfast® Legionella assay. SRK™ environmental kit collected samples are easier to process compared to water and can be stored for up to 72 hrs. before testing.

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Abstract 3402

Evaluation of CARBA PAcE, a novel rapid test for detection of carbapenemase-producing Enterobacterales
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Background: Rapid detection of carbapenemase producing Enterobacterales (CPE) is indispensable for patient management and infection control. Today, there is an increasing number of commercially available tests kits, which differ strongly in accuracy and turnaround time. Recently, MAST CARBA PAcE was released, a new colorimetric test for rapid detection of CPE with a turnaround time of only 10 minutes. This study evaluates the performance of this test against the well-established zinc supplemented carbapenemase inactivation method (zCIM).

Materials/methods: CARBA PAcE (Mast Diagnostica, Reinfeld, Germany) and zCIM (in-house) were challenged with 108 molecularly characterized CPE and 46 non-CPE controls. CARBA PAcE was performed according to manufacturer’s recommendations. zCIM was performed as previously described using tryptic soy broth, but with a higher zinc concentration (1.5 mM ZnSO4).

Results: CARBA PAcE correctly detected 76 (70%) CPE when isolates were grown on Mueller-Hinton agar (MHA). Forty-two (91%) non-CPE were tested correctly negative. False negative samples were additionally tested after cultivation on Columbia blood agar, which improved the overall sensitivity to 87% and the sensitivity for class B carbapenemases from 66% to 92%. Using zCIM 104 (96%) CPE and 46 (100%) non-CPE were correctly classified (Table 1).

<table>
<thead>
<tr>
<th>Class</th>
<th>CARBA PAcE</th>
<th>zCIM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class A</td>
<td>GES (n=2)</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>IMI (n=9)</td>
<td>11%</td>
</tr>
<tr>
<td></td>
<td>KPC (n=21)</td>
<td>100%</td>
</tr>
<tr>
<td>Class B</td>
<td>IMP (n=4)</td>
<td>100%</td>
</tr>
<tr>
<td></td>
<td>NDM (n=29)</td>
<td>62%</td>
</tr>
<tr>
<td></td>
<td>VIM (n=20)</td>
<td>65%</td>
</tr>
<tr>
<td>Class D</td>
<td>OXA-48 (n=8)</td>
<td>88%</td>
</tr>
<tr>
<td></td>
<td>OXA-48-like (n=18)</td>
<td>78%</td>
</tr>
<tr>
<td></td>
<td>OXA-58 (n=2)</td>
<td>50%</td>
</tr>
</tbody>
</table>

Table 1: Test sensitivity of CARBA PAcE with isolates from Mueller-Hinton agar and zCIM according to carbapenemase type

Conclusions: To the best of our knowledge, this is the first systematic evaluation of the CARBA PAcE assay. A big advantage is the low turnaround time of 10 minutes, making it the most rapid colorimetric test available. We strongly recommend to perform this test on isolates cultured on blood agar, as the sensitivity is insufficient when MHA was used, especially for metallo-beta-lactamase producing isolates. GES and IMI were only insufficiently detected by CARBA PAcE. The zCIM showed an excellent sensitivity and specificity, but at the cost of a rather long turnaround time of about 20 hours.

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Detection of transferable CTX-M-producing multidrug-resistant Enterobacteriaceae from public transportation in China

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Abstract third-party references: Department of Microbiology, Zhongshan School of Medicine, Sun Yat-sen University

Background: Multidrug resistance (MDR) in bacteria is a serious public health problem. In China, ∼248 million people are in daily direct contact with public transportation. However, no focus has been given to transportation as a source of acquisition of bacteria encoding Extended-Spectrum β-Lactamases (ESBLs). Herein, for the assessment of the blaCTX-M transmission, we investigated CTX-M-producing MDR Enterobacteriaceae from public transportation and explored their genomic characteristics.

Materials/methods: A total of 800 non-duplicated surface samples were collected from public transportation in Guangzhou, China, from October 2016 to April 2017. Polymerase chain reaction (PCR) assays were performed to detect blaCTX-M genes. Minimum inhibitory concentrations were determined by broth microdilution method. Liquid mating was performed to check the transferability of blaCTX-M genes. S1-nuclease digestion and pulsed-field gel electrophoresis (S1-PFGE) and Southern blotting were performed with blaCTX-M carrying plasmids. Whole-genome sequencing (WGS) was performed.

Results: Out of 800 surface samples, 737 (92.13%) were successfully cultured and screened for the different blaCTX-M variants using PCR and Sanger sequencing. Out of 737 samples, 30 (4.07%) were confirmed as CTX-M positive isolates. MALDI-TOF identification and 16S rDNA sequencing revealed that 22/30 (73.33%) isolates were Escherichia coli, 6/30 (20%) were Klebsiella pneumoniae, and 2/30 (6.67%) were Leclercia adecarboxylata. WGS analysis identified four subtypes of CTX-M including; CTX-M-55 (7/22 E. coli isolates), CTX-M-65 (7/22 E. coli isolates), CTX-M-190 (4/22 E. coli isolates), and CTX-M-14 (4/22 E. coli and 2 Leclercia adecarboxylata isolates), and CTX-M-3 (6 K. pneumoniae isolates). In silico MLST analysis identified nine sequence types (STs), out of them, one is a novel ST related to the K. pneumoniae isolates. Antibiotic resistance genes were identified using ResFinder3.2, where 27 resistant genes were detected. S1-PFGE, Southern blotting, and WGS revealed a ~220kb IncHI2 plasmid carrying CTX-M-65 (7/22 E. coli isolates) and a ~65kb IncI2 plasmid carrying CTX-M-190 (4/22 E. coli isolates), where both were transferable.

Conclusions: These results suggest that CTX-M-producing bacteria are circulating within the public transportation system during the time of our analysis, indicating that these bacteria are likely to transfer to humans through public transportsations that may act as a potential reservoir for the transferable ESBLs genes.

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Evaluation of neuro-filament light chain as a biomarker for neuronal damage in experimental pneumococcal meningitis

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Background: Pneumococcal meningitis (PM) is associated with an excessive neuroinflammation causing injury to the brain and the inner ear, leading to neurological sequelae. Neurofilaments are intermediate filaments, which provide structural support for the neurons. Upon neuronal injury, neurofilament light chain proteins (NFL) are released into blood and cerebrospinal fluid (CSF). Quantification of NFL allows the detection of pathologies in various neurological diseases including multiple sclerosis and traumatic brain injury. Since PM is associated with neuronal injury, this study characterizes NFL levels in CSF and serum in the course of experimental PM.

Materials/methods: Eleven-day old Wistar rats were infected intracisternally with 6.25 ± 5.3 x 10^3 CFU S. pneumoniae (n=20) or saline (n=8). All animals received ceftriaxone (100 mg/kg, i.p.) at 18 hours post infection (hpi). CSF and blood were sampled at 18 and 42hpi, centrifuged, supernatants were collected and stored at -80°C. NFL levels in CSF and serum were measured on a Simoa HD-1 instrument (Quanterix) using the capture monoclonal antibody (mAB) 47:3 and the biotinylated detector mAB 2:1 from UmanDiagnostics.

Results: First, we assessed whether intracisternal puncture caused an artificial increase of NFL. Results ruled out this possibility, both in CSF or serum. At 42hpi, CSF and serum levels of NFL correlated significantly in infected and mock-infected animals (p<0.0001). NFL concentrations in CSF were approximately 35 times higher than in serum. Infected animals revealed higher NFL levels in serum at 42hpi compared to mock-infected animals (p=0.0456). In addition, infected animals displayed a significant increase (p<0.0001) of NFL level in serum between 18hpi to 42hpi while no increase was observed in mock-infected animals.

Conclusions: NFL has recently been established as a biomarker in several neurological diseases. Given the strong correlation of NFL levels in CSF and serum, NFL determination in serum would be more clinically applicable and less invasive. This study showed that NFL level in serum significantly increases during the course of PM and therefore supports its use as a biomarker for neuronal damage in this disease.

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Whole genome sequence analysis of *Klebsiella pneumoniae* isolates belonging to sequence type 231 harbouring rapidly disseminating *bla*OXA-232 located on ColKP3 plasmid in Kuwait

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**Background:** The commonly encountered carbapenem-resistant Enterobacteriaceae (CRE) isolates responsible for most infections/colonization in Kuwait have been known to harbor *bla*NDM, *bla*KPC, *bla*VIM, and *bla*OXA-48 genes. Recently, a shift to OXA-48-like-producing strains such as OXA-181, has become prominent. OXA-232, another variant of OXA-48 carbapenemases have not been reported previously in Kuwait. The aim was to determine the genetic backbone of *K. pneumoniae* harboring *bla*OXA-232 genes, isolated from the rectal swabs of ICU patients in Mubarak Al Kabeer hospital.

**Materials/methods:** A total of 41 carbapenem-resistant *K. pneumoniae* (CRKP) were isolated from the rectal swabs of ICU patients during a period of 1 year. They were identified by VITEK-2 and their susceptibility to various antibiotics determined by E-test. DNA was extracted from 24-h-old culture using qiaamp DNA mini kit. The isolates were subjected to whole genome sequencing using an Illumina MiSeq platform. The genome was annotated using Rapid Annotation Subsystems Technology (RAST). Genome sequences were screened for presence of insertion sequences, mobile genetic elements, plasmid replicons, resistance genes and Multi-Locus Sequence typing (MLST) using different software tools.

**Results:** Two isolates (4.9%) were OXA-232 producers and harbored several β-lactamase genes, including *bla*CTX-M-15, *bla*TEM-1b, *bla*SHV-100, *bla*OXA-232 in conjunction with many other resistance genes such as *acc*(6′)-lb-cr, *qnr*S1, *ARR*-3, *sul*1, *aadA*2, *erm*[B], *mph*[A], *dfr*A12, *cat*A1, *aadA*2, *aqpA* and *aqpB* that confer resistance to aminoglycosides, chloramphenicol, erythromycin, fluoroquinolones, rifampicin and sulfonamides. Seven replicon plasmid types were detected in both isolates (MK-4 and MK-5), namely Col (BS51 2), Col4401, ColKP3 that carried carbapenemase gene *bla*OXA-232, IncFIA, IncFIB (pQil), IncFII(K) and IncFII (pAMA1167-NDM-5), with one extra (IncX4) in MK-5. Sequence type ST231 was confirmed in the two isolates. Insertion sequences, ISEcp1, ISKpn2, ISKpn6, ISKpn7, ISKpn13, ISKpn14, ISKpn21, ISKpn25, ISKpn26, ISKpn28, ISKpn31, ISKpn34, ISKpn38, ISKpn37, ISKpn40, ISKpn41, ISKpn49 ISKpn50, and transposons Tn903 and Tn3, were present. The *bla*OXA-232 –plasmid was 100% identical to the plasmid Pkp3-A bearing the *bla*OXA-181.

**Conclusions:** This represents the first report of CRKP harboring *bla*OXA-232 in Kuwait. This gene, being carried on ColKP3 plasmid, with insertion sequence ISEcp1 upstream, may silently spread amongst the Enterobacteriaceae populations with potentially serious clinical management challenge.

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Abstract 3412

**MRSA transmission and hospital-acquired bacteraemia in a neonatal intensive care unit in Greece**

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**Background:** Staphylococcus aureus is a common pathogen causing hospital acquired infections (HAIs) in neonates. In this study, the epidemiology of methicillin-resistant S. aureus (MRSA) transmission and infections in a 30-bed, level III university-affiliated neonatal intensive care unit (NICU) located in a children’s hospital was investigated.

**Materials/methods:** Surveillance cultures (throat and rectal samples) were routinely collected on admission and weekly thereafter to identify multi-resistant colonized neonates in order to apply contact precautions. Surveillance and clinical care cultures of neonates that grew MRSA were retrospectively reviewed for the period 2014-2018, after a case outbreak of MRSA infections from August 2017 to January 2018. Genes encoding Panton-Valentine Leukocidin (lukS/lukF-PV, PVL), toxic shock syndrome toxin (tst), exfoliative toxins (eta, etb), and the resistance genes mecA and mecC, were defined in 46 representative strains by PCRs. Relatedness of strains was assessed by MLST.

**Results:** Of 1538 neonates accounting for 26673 patient days (mean length of stay 17 days), 77 (5%) had a positive culture for MRSA [23/77 were NICU-acquired and 54/77 imported cases]. Most isolates were multi-resistant, with higher resistance observed against kanamycin (71%), macrolides (49%), lincosamides (47%) and ciprofloxacin (39%). All 46 analyzed strains were mecA-positive. One major clone was identified, ST225, among 40 tested neonatal strains (23/40, 58%). Of these, 14/23 were imported from the same maternity hospital (MH). Another clone, ST217, was predominant (4/6) among isolates from health care workers (HCWs) found colonized during screening performed on Jan18. NICU-acquired bacteremia occurred in four neonates on Nov16, Aug17, Oct17 and Jan18 due to ST217 and ST225, three and one cases, respectively [figure 1]. Four isolates classified as ST80 were PVL-positive. Additional four strains carried tst (10%), belonging to ST30 and ST225 [two strains each], and two etb (5%, ST225). The implicated MH was notified for the problem, decolonization treatment was successfully performed in HCWs and neonates. Strengthening of infection control measures with emphasis on hand hygiene was applied.

**Conclusions:** Uncovering reservoirs for on-going MRSA transmission in NICUs has proved challenging. Well known nosocomial MRSA clones are being constantly introduced and transmitted via MHS and HCWs. Effective infection prevention and control requires constant vigilance.

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Understanding the molecular history of an ancient Pseudomonas species isolated from a pharaonic Egyptian mummy: a genomic tale from the 11th dynasty of the middle kingdom

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Background: Pseudomonas spp. are highly adaptable, as evidenced by their successful colonisation in different ecological niches. Origin and evolution of the genus Pseudomonas are still not entirely clear. Herein, understanding the evolution of Pseudomonas spp. depends on the investigation of a Pharaonic Egyptian mummy dating back to ca. 2130 BC–ca. 1991 BC, preserved in the Grand Egyptian Museum, Cairo, Egypt.

Materials/methods: Samples were taken from the mummy of the Lady Amanit, Priestess of Hathor, from oral, throat, abdominal cavity, and finger toes. The samples were inoculated on Blood agar, MacConkey agar, Brain Heart Infusion agar with vitamin K and hemin for the enrichment of anaerobes, and Sabouraud agar with chloramphenicol. Identification was performed using 16S ribosomal DNA and MALDI-TOF mass spectrometry. MICs were detected by the broth microdilution method for 16 antimicrobial agents. Whole-genome sequencing was performed. The surface topography of our isolate was detected using the scanning electron microscope (SEM). Bacterial growth rates were determined using Microplate Spectrophotometer. A Galleria mellonella infection model was used to evaluate virulence.

Results: Biochemical identification showed bacterial growth; no fungi were detected. 16S ribosomal DNA and MALDI-TOF identified Pseudomonas species in the throat sample. SEM revealed that Pseudomonas spp. was rod-shaped and ∼3.00 μm in length with monotrichous flagella and pili-like structures. MICs showed resistance to ampicillin, cefotaxime, and nitrofurantoin while sensitivity to all other tested antimicrobials. Average Nucleotide Identity (ANI) analysis indicated that the ANI of our isolate was 97.63% for Pseudomonas lutea LMG 21974 and 97.62% for Pseudomonas luteola NBRC 103146. In silico MLST showed a novel sequence type. Antibiotic resistance genes were identified; only one gene was found, namely, blaLUT-1. Several virulence factors were detected. Our strain exhibited a slow-killing mode in the G. mellonella within ten days, indicating its low virulence. The growth rate of our strain was also low.

Conclusions: The absence of other microbes with our isolate confirming the probability that our strain is an ancient bacterium that colonised the mummified body thousands of years ago. Further studies are required to get more information about the role of our strain in the evolution of the genus Pseudomonas.

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Abstract 3414

Pandrug-resistant Bacteroides fragilis clinical isolates in the Netherlands: true or fiction

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Background: Antimicrobial resistance among anaerobic bacteria is increasing and multi drug resistant (MDR) strains have been published by different groups. Bacteroides fragilis is a well-studied species. It can harbour several antimicrobial resistance genes (ARGs), but resistance to both carbapenems and metronidazole is very rare, and less than five strains are reported worldwide. Within this study we report three B. fragilis isolates, derived from three different university hospitals in the Netherlands, which were resistant to carbapenems and metronidazole, besides other antibiotics.

Materials/methods: After finding a pan-resistant B. fragilis (isolate A, 2019) at the LUMC from a wound of a liver transplantation patient, a search was performed in the national antimicrobial resistance surveillance database (ISIS-AR) for similar isolates. This resulted in one more isolate from the Erasmus MC (isolate B, 2018), from a blood culture of a patient with malignancies in the urogenital region. One more isolate was identified at the UMCG (isolate C, 2014) from a young patient suffering from complicated appendicitis. Antimicrobial resistance was determined using Etest. Presence of ARGs and other mobile genetic elements (MGEs) that play a role in antimicrobial resistance was, to date, determined for isolates A and C using whole genome sequencing.

Results: The patient from which isolate C was cultured, recovered without specific antimicrobial treatment. The other two patients died due to underlying conditions. All three isolates were resistant to carbapenems, metronidazole and tetracycline. Short read sequencing of isolate A & C showed that both isolates harboured the cfiA gene with an IS-element (carbapenems), a nim gene (respectively nimE and nimA; metronidazole) and the tetQ gene (tetracycline). Isolate A harboured ermF (clindamycin) and a mefE gene (macrolide efflux protein). Isolate C also harboured the cfiA gene (beta-lactams) and a bexA gene (fluoroquinolones). Presence of ARGs in isolate B will also be assessed.

Conclusions: The finding of three pan-resistant B. fragilis isolates harbouring resistance to both carbapenems and metronidazole is worrying. To better understand these isolates we intend to perform a hybrid assembly with short and long reads, enabling us to obtain the whole genome and determine whether ARGs are located on plasmids or other MGEs.

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Whole genome sequencing: epidemiologic surveillance of carbapenemases present in Enterobacteriaceae isolated at Sant Pau Hospital (Barcelona) in 2018

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Background: Whole-genome sequencing (WGS)-based typing has emerged as a promising and highly discriminative epidemiological tool. In this study, we used a gene-by-gene allele calling approach to investigate carbapenemase-producing enterobacterial isolates and discount any outbreaks.

Materials/methods: As a routine laboratory task, WGS was applied to the carbapenemase-producing Enterobacteriaceae detected by Real Cycler OXVIKP during 2018 at Sant Pau Hospital (Barcelona). DNA was extracted using the DNeasy UltraClean Microbial Kit. The libraries were prepared using Nextera XT v.01 and sequenced on an Illumina MiSeq sequencer (Novogen Corporation). After sequencing, the reads were quality trimmed and de novo assembled using BioNumerics 7.6 software. ResFinder website was used to obtain the resistome.

Results: The incidence of carbapenemases in the hospital was 3.44% (23/669) for Klebsiella pneumoniae, 0.17% (5/2843) for Escherichia coli, 1.45% (2/138) for Enterobacter cloacae (group) and 1.17% (1/85) for Citrobacter amalonaticus. In K. pneumoniae, 3 clusters and 5 singletons were found. The predominant cluster (10 isolates) belonged to ST392, followed by ST307 (6 isolates). Both clusters included OXA-48- plus CTX-M-15-producing isolates. The third cluster, belonging to ST258, only included 2 KPC-3- plus OXA-9-producing isolates. The 3 clusters generated by core genome analysis differed by 380 to 400 loci, whereas the difference between isolates belonging to the same cluster was between 1 and 15 loci. Similar results were obtained by wgMLST. In E. coli, 4 of the 5 isolates produced OXA-181: 2 of them belonged to ST471 and 2 to ST692; the remaining NDM-5-producing isolate was nontypeable. In E. cloacae, one isolate (ST32) produced a VIM-1 and the other (ST50) an OXA-48. Finally, an OXA-48-producing C. amalonaticus was isolated. In carbapenamase-producing strains, 14 different resistomes were found in K. pneumoniae and 4 in E. coli.

Conclusions: Through WGS we were able to clearly and objectively characterize carbapenemases detected in our hospital. In addition, it allowed us to start a database including both epidemiological and multi-drug resistance data associated with Enterobacteriaceae strains, which is used to modify empiric treatment.

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**Abstract 3418**

**Enhancing fosfomycin activity via glycerol-3-phosphate transporter activation**

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**Background:** Fosfomycin disrupts the first step in peptidoglycan biosynthesis inhibiting the enzyme UDP-N-acetylgluosamine-3-enolpyruvitransferase (MurA) leading to cell death. To carry out its activity, fosfomycin enters the bacteria through a hexose phosphate (UhpT) and glycerol-3-phosphate (GlpT) transporters, which are induced by their substrates. Additionally, glycerol is transformed, intracellularly, into glycerol-3-phosphate by the glycerol kinase (GlpK). In the susceptibility assays, glucose-6-phosphate is used to induce UhpT however, the role of GlpT remains unknown. The objective of this study was evaluating fosfomycin activity under GlpT activation.

**Materials/methods:** Escherichia coli wild-type (WT) strains and five isogenic mutants (∆glpT, ∆uhpT, ∆glpT-uhpT, ∆glpK) was used. The induction of the transporters with addition of glucose-6-phosphate (25mg/L), glycerol-3-phosphate (0.1%) and glycerol (0.1%) was monitored in the wild-type strain using the reporter-plasmid pMS201 (PglpT::gfp mut2 and PuhpT::gfp mut2) and measuring the emitted fluorescence during 48 hours. Fosfomycin susceptibilities were tested using disk-diffusion method ±glycerol-3-phosphate and ±glycerol in Mueller-Hinton agar. Halo of inhibition were measured and compared using ANOVA and post-hoc test. Fosfomycin activity was quantified spectrophotometrically using M9 (succinate) supplemented ±glucose-6-phosphate, ±glycerol or both and fosfomycin ranging from 0.25 to 256mg/L. The area under the curve from de dose-viability plot was calculated and compared among the different conditions.

**Results:** Glucose-6-phosphate rapidly activated uhpT (>6 times, peak at 4h), while glpT showed a slow expression [peak at 34h and 41h] increasing 2.29 and 3 times in the presence of glycerol-3-phosphate and glycerol, respectively. With respect to the susceptibility, glycerol increased fosfomycin susceptibility significantly in WT and ∆uhpT. However, glycerol-3-phosphate increased fosfomycin resistance in WT, ∆glpT, ∆glpK and derepressed glpT strain (ΔglpR) (Figure 1). Fosfomycin activity increased against the WT and ΔglpT strains by the addition of glucose-6-phosphate, and against WT and ΔuhpT strains with glycerol. The addition of both inducers increased the activity in all strains except ΔglpT-uhpT.

**Conclusions:** Enhancing fosfomycin penetration via glpT may be a good strategy to increase its activity. The addition of glycerol-3-phosphate reduce fosfomycin susceptibility, by the competition of glycerol-3-phosphate against fosfomycin to be transported by GlpT. The use of a non-competitive inductor, as glycerol, increased fosfomycin susceptibility.

Figure 1. Fosfomycin susceptibility by disk-diffusion assay.

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Abstract 3419

Multilevel analysis of the regional variation in healthcare-associated infections and antimicrobial use prevalence in acute-care hospitals in Greece

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Background: To identify targets for quality improvement in hospital infection control (IC) and antibiotic stewardship strategies in Greece, we investigated the regional variability in the prevalence of healthcare-associated infections (HAIs) and antimicrobial use. Because regional health authorities may implement programs to foster prudent antibiotic use and strengthen IC practices in addition to those implemented by individual hospitals, we utilized multilevel statistical modelling to assess both the individual effect of hospitals and the regional effect.

Materials/methods: Data for 87 public hospitals were obtained from the second national point-prevalence survey of HAIs and antimicrobial use in November 2016. Data included patient characteristics aggregated at the hospital level (mean values for age and Charlson comorbidity score, and proportions of patients with emergency admission, recent surgery, neutropenia, intensive care unit [ICU] admission and rapidly fatal prognosis) and hospital characteristics (hospital size and type, and numbers of single rooms, IC nurses and IC physicians). Regional variation was examined in relation to the seven Regional Health Districts comprising the health authorities that supervise hospitals and public health in Greece. The regional effect was estimated using hierarchical linear regression with a random intercept on the region.

Results: Overall, the prevalence of antimicrobial use was 58.8% and the prevalence of HAIs was 9.0%. Mapping by region showed wide variation for both antimicrobials (regional range, 54.0% to 64.6%) and HAIs (regional range, 6.8% to 11.6%). In unadjusted analysis, the regional effect explained 18.6% of the variability in antimicrobial use and 14.1% of the variability in HAI prevalence. In the multivariable analysis, adjustment for patient and hospital characteristics explained 48.5% and 71.2% of the variability in the prevalence of antimicrobials and HAIs, respectively. The regional variance component was largely reduced for HAIs (explained by 56.6%), but largely persisted for antimicrobial use (explained by only 26.4%).

Conclusions: Multilevel analysis of national prevalence data proved useful in identifying targets for improvement. Differences in patient case mix and hospital characteristics explained largely the regional variation in HAI prevalence, but not use of antimicrobials. Thus, regional health authorities in Greece must sought to harmonize local antibiotic stewardship policies, dissemination of guidelines and audits.

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Abstracts 2020

Abstract 3423

Setting up antimicrobial stewardship programme in tertiary area hospitals in India
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Background: One of the best methods to prolong the shelf-life of existing and newer future antimicrobials is antimicrobial stewardship programme (AMSP). The Indian Council of Medical Research (ICMR), New Delhi, India, has launched the Anti Microbial Resistance Stewardship Initiative with an avowed purpose of rationalizing antimicrobial prescriptions. The initiative is currently limited to tertiary care hospitals in the country.

Materials/methods: Following the gaps highlighted by ICMR baselines survey of AMSP practices in hospitals in India1, capacity building efforts were initiated by ICMR. Twenty tertiary care hospitals were subsequently funded to undertake AMSP interventions like creating institution specific antimicrobial use guideline, introducing AMSP interventions like prescription audit and feedback and formulary restriction. A new software was developed to capture antimicrobial consumption. The sites also undertook education and awareness activities. One clinical pharmacist was provided to all hospitals.

Results: All hospitals formulated a multidisciplinary AMSP Committee and were able to create a treatment guideline specific to antibiogram of the hospital. All hospitals were able to initiate all the activities although the number of ICUs and wards included varied between the hospitals. Most hospitals documented decline in usage of broad spectrum antibiotics in the intensive care units(ICUs) after introduction of treatment guideline. The culture rate varied between 20 and 100 percent. Some hospitals introduced formulary restriction on prescription of antimicrobials like fosfomycin, polymyxin, colistin, linezolid and tigecycline. All hospitals organized the education and awareness workshops.

Conclusions: Through this effort we have established structure and process of AMSP in twenty tertiary care hospitals in the country. The hospitals can now use this structure for testing other AMSP interventions like adherence to treatment guidelines, de-escalation following culture report. Sustaining the efforts would require additional manpower and commitment on part of leadership to provide logistics and human resources to continue this activity.

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**Abstract 3424**

**Genomic characterisation of meropenem/vaborbactam resistant KPC-producing Klebsiella pneumoniae strains isolated from bacteraemic patients**

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**Background:** In the last years, novel antimicrobial drugs have been developed to treat infections due to KPC producers. Among them, meropenem-vaborbactam (MER-VAB) represents a promising antimicrobial option for treatment of infections caused by class A serine carbapenemase producing Enterobacteriaceae. MER-VAB is an antimicrobial combination of a carbapenem antibiotic associated with novel boronic acid-based ß-lactamase inhibitor. Recently, few cases of MER-VAB-resistant clinical isolates have been reported worldwide. Here, we described four MER-VAB-resistant KPC-producing Klebsiella pneumoniae (KPC-Kp) isolated from patients with bloodstream infection.

**Materials/methods:** Between 1st March and 31st August 2018, we collected all KPC-producing Klebsiella pneumoniae strains isolated from patients with bloodstream infection and recovered at the St. Orsola Malpighi University Hospital in Bologna, Italy. MIC values for meropenem/vaborbactam were assessed by MIC test strip and results were interpreted following EUCAST breakpoints. Carbapenemase production was investigated by MALDI-TOF MS peak-specific analysis and NG-Test CARBA S assay. Whole-genome sequencing of MER-VAB KPC-Kp strains was performed by using MiSeq platform (Illumina, USA).

**Results:** During the study period, we collected four KPC-Kp strains resistant to MER-VAB. All strains were resistant to ciprofloxacin, penicillins, cephalosporins, carbapenem and amikacin, while remained susceptible to colistin. In detail, all KPC-Kp strains exhibited high MIC values (≥256 mg/L) for MER-VAB and one out of three KPC-Kp was also resistant to Ceftazidime-Avibactam (16 mg/L). Genetic analysis demonstrated that all KPC-Kp strains belonged to the ST258 and shared similar genetic determinants for antimicrobial resistance to fluoroquinolone and ß-lactams. Analysis of porin genes showed that all MER-VAB-resistant KPC-Kp strains had truncated ompK35 and GD1 34-1 35 insertion within ompK36. Plasmid content analysis showed that all MER-VAB-resistant KPC-Kp strains shared IncFIB(pKPHS1), IncFII(K), ColRNAI and IncX3 plasmids, while two strains harbored an additional plasmid [IncFil(K)].

**Conclusions:** Here we described four MER-VAB-resistant KPC-Kp strains isolated from bacteraemic patients. Resistance to MER-VAB in KPC-Kp strains are associated to non-functional ompK35 and mutated ompK36 porins. In one KPC-Kp strain, porins mutations has been associated to ceftazidime-avibactam resistance.

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Abstract 3425

**Stool versus rectal swab for microbiome composition analysis in critical care patients**

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**Background:** Stool samples are frequently used for clinical microbiome studies. These samples are not always readily available in critical care patients, as patients may be unable to produce a faecal sample. Rectal swabs (RS) are easier to collect, transport and store. However, it is unclear if RS are representative of the stool microbiome. In this study we compared the microbiome composition of RS and faecal samples from critically-ill patients.

**Materials/methods:** Fifteen patients admitted to a 14-bed hepatic intensive care unit were randomly selected. For each patient, a RS and a stool sample were simultaneously collected. Stool samples were homogenized with PBS and all samples were stored at -80°C until processing. DNA was extracted using PureLink™ Microbiome DNA Purification kit (Invitrogen) and the V3-V4 region of 16S rRNA gene was amplified and sequenced on a MiSeq platform (Illumina). Sequences were filtered and demultiplexed using DADA2, taxonomy was assigned using SILVA-132 and statistical analyses were conducted using QIIME2 and R environments. Three patients were excluded due to low sequence counts in one of their samples (2 stools, 1 RS).

**Results:** Median Charlson comorbidity index was 5 (IQR:3.6-6.25), median age was 66 (IQR:57.75-64.25), 83.3% (10/12) were male and 91.7% (11/12) had liver cirrhosis. Microbial (alpha) diversity was not significantly different between RS and stool samples (Faith index, p-value:0.22). Figure 1A shows relative abundance of bacterial communities of analysed samples demonstrating taxonomical similarity between stool and rectal swabs from the same patient. Figure 1B shows principal coordinate analysis plot using unweighted unifrac distances. Unweighted unifrac distances between samples belonging to the same subject (median:0.46, IQR:0.27-0.57) were significantly lower than between samples belonging to different subjects (median:0.68, IQR:0.62-0.77) (p<0.0001) (Figure 1C).

**Conclusions:** RS and stool samples are comparable in terms of microbial diversity. Bacterial communities from RS and stool samples belonging to the same patient were similar and compositional differences between samples from the same patient were lower than between samples from different patients. Our results suggest that RS are adequate representative samples of gut microbiota composition in critically-ill patients. However, we recommend selecting one type of sample when designing gut microbiota studies to reduce possible sample-related variabilities.
**Figure 1**

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Abstract 3430

Emergence of multiple ESBL-producing \textit{Salmonella enterica} serovars in hospitalised horses due to an epidemic spread of a CTX-M-3 plasmid pSEIL-3

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\textbf{Background:} \textit{Salmonella enterica} is a highly important zoonotic pathogen causing human Salmonellosis. This bacterium is mainly recognized as a food-borne pathogen often associated with food animal colonization. ESBL-producing \textit{S. enterica} has emerged worldwide and currently poses therapeutic challenges and a risk for resistance spread. Considering 'one health' significance and taking into account close animal-human contact, we aimed to investigate ESBL-producing \textit{Salmonella} (ESBL-PS), and to decipher the mode of ESBL dissemination among hospitalized horses.

\textbf{Materials/methods:} ESBL-PS isolates were collected in the Koret-School of Veterinary-Medicine during a prospective ESBL-P Enterobacteriaceae survey (Dec2015-Dec2017). The isolates were recovered from fecal and clinical samples using Chromagar-ESBL plates following with identification, susceptibility testing (VITEK2), and serovar determination (Kaufmann-White-Le-Minor). ESBL genes were detected by multiplex-PCR and sequencing. ESBL-encoding plasmids were purified, transformed and sequenced (Nanopore) and WGS was performed for each serovar (Illumina-HiSeq). Conjugation experiments were performed to prove plasmid transferability.

\textbf{Results:} Twelve ESBL-PS isolates were recovered from foals (n=8) and adult horses (n=4). All Isolates produced the same ESBL gene-\texttt{bla}\textsubscript{CTX-M-3}, and showed an identical MDR profile, with co-resistance to trimethoprim/sulfamethoxazole and aminoglycosides. Three ESBL-PS serovars were identified- Cerro (n=7), Havana (n=3), and Liverpool (n=2), all reported for the first time in horses. Molecular epidemiology analysis revealed clustered-in-time clonal spread of serovar Cerro among seven horses, together with an epidemic spread of a single CTX-M-3-encoding plasmid (designated pSEIL-3), which horizontally and serovar-independently disseminated among horses. pSEIL-3, a 86.4Kb IncM2 plasmid, encoded nine antibiotic resistance genes and was highly similar (>95%) to other \texttt{bla}_{CTX-M-3} or \texttt{bla}_{NDM-1} IncM2 broad-host-range plasmids from various Enterobacteriaceae of human origin. Using a multiplex-PCR designed specifically for pSEIL-3 screening, we proved the presence of this plasmid in other ESBL-P Enterobacteriaceae co-colonizing three horses, demonstrating transfer of pSEIL-3 in horses' gut in situ. Five out of the eight foals deceased following ESBL-PS infections.

\textbf{Conclusions:} This is an alarming report on the emergence of ESBL-P MDR \textit{S. enterica} in hospitalized horses, associated with gut colonization and severe foal morbidity. We demonstrate the potential of horses to host and shed ESBL-P \textit{Salmonella} and serve as a reservoir for highly transferrable broad-host-range MDR plasmids posing a frightening 'one-health' risk.

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Abstract 3433

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**Background:** The World Health Organization recommends the use of neuraminidase inhibitors for treatment of influenza. The increasing resistance of influenza viruses against current anti-influenza drugs demonstrates the challenging need to identify new antiviral agents. At the end of the 20th century ribavirin was seen as a possible treatment. Currently novel anti-influenza drugs from nucleoside analogues like favipiravir are being researched. In the Russian Federation in 2014 riamilovir (Triazavirin®) was registered.

**Materials/methods:** In this retrospective study we evaluated the clinical effectiveness of riamilovir (53 cases) with that of oseltamivir (57 cases) for treating influenza. All included in-patients were young men (18-26 years) with moderate severe PCR confirmed influenza A (H1N1, H3N2) and B during epidemic seasons 2016-2017 and 2017-2018. The treatment was initiated within 48 hours of clinical symptoms. We compared infectious intoxication syndrome duration, total febrile period, duration of acute rhinitis, acute pharyngitis, acute laryngitis, acute tracheitis, acute bronchitis, cough duration as well as pneumonia occurrence.

**Results:** There was no statistically significant difference in the duration of developed syndromes. In riamilovir-treated group and oseltamivir-treated group mean duration of intoxication was 3.6±2.24 days vs. 3.2±2.21 days, total febrile period – 2.0±1.05 days vs. 1.8±1.19 days, acute rhinitis – 4.9±2.28 days vs. 4.6±3.09 days, acute pharyngitis – 4.2±2.77 days vs. 3.9±2.41 days, acute laryngitis – 2.5±0.71 days vs. 2.2±1.10 days, acute tracheitis – 2.4±1.28 days vs. 2.3±1.24 days, acute bronchitis – 2.7±1.53 days vs. 3.3±2.65 days, cough – 6.1±2.91 days vs. 4.6±3.15 days accordingly. No incidence of pneumonia was observed in both groups.

**Conclusions:** Riamilovir and oseltamivir were equally effective in treating adult patients with influenza. The duration of infectious intoxication syndrome, total febrile period, duration of respiratory syndromes were comparable for both medications. Thus, nucleoside analogue riamilovir (Triazavirin®) as well as neuraminidase inhibitor oseltamivir can be recommended for treatment of influenza.

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Seroprevalence of Coxsackievirus B1-6: retrospective study in an Italian population
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Background: Group B Coxsackieviruses (CVB) include 6 serotypes (CVB1-6) responsible for a wide range of clinical diseases comprising meningitis, pancreatitis, and myocarditis. Moreover, CVB infection could be a trigger for the onset of insulin-dependent diabetes. Seroepidemiologic data on CVB are limited and no recent studies are available in our geographical area. Therefore, the aim of this study was to investigate CVB1-6 seroprevalence in a wide Italian population.

Materials/methods: The study retrospectively included 2,459 subjects referring to Umberto I University Hospital (Rome) in the period 2004-2016. Information about age was available for 2,114 individuals, that were divided into 11 age-groups. Serum samples were screened with a micro-neutralization assay to detect neutralizing antibodies (nAb) against all six CVB. Statistical analysis was performed evaluating seroprevalence rates and nAb titers in relation to years of observation and subjects’ gender and age.

Results: Positivity for at least one serotype was detected in 69.1% of individuals. Overall, the prevalent serotype was B4 (45.2%), followed by B3 (33.3%), B5 (26.2%), B1 (12.7%), B2 (11.0%), and B6 (1.7%). Positivity rates of B1, B3, B4, and B5 varied over years with cyclical trends. B2 seroprevalence was the highest among CVB in 2004 (64.8%) but significantly decreased in 2005 and 2006 (50.5% and 31.2%), settling at levels lower than 8.5% starting from 2007 (p<0.0001). The percentage of seropositivity was higher in females than in males, and this difference was significant for B2 and B3 (p<0.05). Positivity to at least one virus was lowest in toddlers aged 0-2 years (25.2%), but significantly increased in pre-school (3-5 yr) (50.3%) and school (6-10 yr) children (70.4%) (p<0.0001). The number of individuals with multiple positivity also increased with age. The age-related positivity increase is significant also analyzing B1-B5 specific seroprevalence. Higher nAb responses for B3 and B4 were observed in children of 3-5 years of age (p<0.05).

Conclusions: A high overall CVB prevalence was found. Type-specific variations in prevalence over time probably reflect the fluctuations in circulation typical of Enteroviruses. Children are at greater risk for CVB infection given the high number of seronegative subjects aged less than 10 years.

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Abstract 3435

**Preliminary analysis of a pilot study using a new oral encapsulated formulation of faecal microbiota**

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**Background:** *Clostridioides difficile* infection (CDI) is the main cause of health care–associated diarrhoea, and there is an increasing in the incidence of CDI in the community. Numerous publications have demonstrated that the most effective treatment is the faecal microbiota transplantation (FMT) from a healthy donor. Oral capsules obtained from processed stool samples by adding excipients (vivapur-101 and magnesium stearate) to microbial pellet have shown high viable bacterial concentration. Here we present the preliminary results of a pilot study that evaluated the efficacy of this formulation to prevent recurrence in patients with CDI.

**Materials/methods:** All CDI cases in our institution from March to October 2019 were prospectively detected. Written informed consent was obtained from all participants. Eligible patients were female and male adults (> 18 years) presenting an acute episode of diarrhoea (> 3 unformed bowel movements every 24 hours). Exclusion criteria were oral intolerance, severe immunosuppression, pregnancy, concomitant antibiotic treatment, severe CDI and life expectancy inferior to 1 month.

**Results:** Ninety-one patients presented with an acute episode of CDI. Among them, only 17 patients met the inclusion criteria. The main reasons for exclusion were: severe immunosuppression (12 patients), concomitant antibiotherapy (27 patients), severe disease (4 patients) and short-life expectancy (13 patients). Of the 17 eligible patients, only 8 were included. The mean age was 64.75 years, 50% were female, 87% had community-acquired CDI, 62.5% had cancer, 50% had received antibiotics in the prior month and for the majority of them it was their first episode (62.5%). FMT consisted in a single dose of 20 capsule after at least 5 days of vancomycin or fidaxomicin treatment. All patients reported a good oral and gastrointestinal tolerance. The mean follow-up was 84 days. Only one patient had a CDI recurrence and two of them died more than 90 days post-FMT from underlying malignancy condition.

**Conclusions:** Our experience shows that oral FMT is well tolerated and suggests that our FMT formulation is effective in terms of reducing the recurrence rate of CDI.

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Global metabolism indicates novel mechanism of GreA-induced dormancy in Mycobacterium tuberculosis

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Background: Dormancy is a nonreplicating, reversible cellular state that enables mycobacteria to circumvent and survive adverse stresses. Our recently study has been shown that GreA, a transcription elongation factor, is involved in drug tolerance, reactive oxygen, starvation in M. smegmatis and M. tuberculosis H73Ra. Our hypothesis is that the important role of GreA in stress induced dormancy in mycobacteria.

Materials/methods: To explore the role of GreA in stress induced dormancy, we constructed strains by recombineering the native greA gene fused with gfp fluorescent protein. The intracellular distribution of GFP was measured by time-lapse microscopy. Flow cytometric analysis of fluorescence after different hours exposure to nutrient limited medium. qRT-PCR was implemented to detect the expression of greA between active and dormant mycobacteria. In addition, CFU was used to evaluate the vitality of dormant bacteria between wild-type and ΔgreA. Furthermore, GC/MS was performed to find the differential metabolites between ΔgreA strain and wild type strain in a dormant state. Finally, the phenotype of GreA was confirmed in M. tuberculosis.

Results: Both results of FCM and time-lapse microscopy revealed greA expression was increased with early starvation treatment. The analysis of RT-PCR also confirmed that the mRNA of greA was increased in M. smegmatis, suggesting a critical role of GreA in the regulation of dormancy in M. smegmatis. Loss of greA resulted in M. smegmatis becoming more sensitive to nutrient scarcity based on the CFU counts. Further the GC/MS data demonstrated that more than 40 differential metabolites were identified between M. smegmatis WT strain and ΔgreA strain under starvation and most of them were decreased in greA mutant. Notably, lipid-related metabolic pathways, were generally down regulation in ΔgreA strain compared with WT. Furthermore, the intracellular energy resource significantly declined due to deficient of greA in mycobacteria. Consistent with these results, M. tuberculosis lack of greA also exhibit a reduced survivability under starvation.

Conclusions: Our data indicate that the deletion of greA mainly down regulation of lipid metabolic pathways, caused a shift ATP concentration and a suppression of dormancy. This study would likely provide vital clues to design novel drugs for the control of dormant TB.

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Ultrasonic guidance and risk for intravascular catheter-related infections among peripheral arterial catheters. A post hoc analysis of two large randomised controlled trials

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Background: The ultrasound guidance effect on infectious risk remains controversial in short-term arterial catheters (ACs). The present study aimed to investigate the association between ultrasound guidance (US) in AC insertion and intravascular catheter-related infections or colonizations.

Materials/methods: We used individual data from two multicenter randomized-controlled trials (RCTs) in intensive care units (ICUs) that evaluated various prevention strategies regarding major catheter-related infections (MCRI), catheter-related bloodstream infections (CR-BSI) and colonization. The skin colonization at catheter removal was evaluated using semi-quantitative insertion-site cultures. Univariate and multivariate marginal Cox model for clustered data were used for the evaluation of the daily hazard rate for MCRI, CR-BSI and catheter-tip colonization.

Results: A total of 3,029 patients were included by 10 ICUs and 3,950 ACs were analyzed. The US was used for 386 catheter placements. In the univariate Cox model analysis, the risk for MCRI (HR 0.86, CI 95% 0.27–2.72, p = 0.79), CR-BSI (HR 0.87, CI 95% 0.20–3.72, p = 0.85) and catheter colonization (HR 1.31, CI 95% 0.92–1.86, p = 0.13) were similar for catheters inserted with US and without US. After adjustment on confounders, US showed similar risk to non-US for MCRI (HR 0.71, CI 95% 0.23–2.24, p = 0.56), CR-BSI (HR 0.71, CI 95% 0.17–3.00, p = 0.63) and catheter colonization (HR 0.92, CI 95% 0.63–1.34, p = 0.67, Figure). No differences between US and non-US for MCRI, CR-BSI and colonization were observed for the radial and the femoral site, respectively. The skin colonization at catheter removal was similar between US and non-US groups (p = 0.69).

Conclusions: Using the largest dataset ever collected from large multi-centric RCTs conducted with consistent catheter care, we showed that the infection risk was similar for US and non-US utilization. With regard to the infectious risk, our results support the utilization of US for ACs.
Figure: Adjusted analyses for risk of MCRI, CR-BSI and colonization for ultrasound guidance versus without ultrasound guidance.

<table>
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<tr>
<th>Outcome</th>
<th>Hazard ratio (95% CI), p-value</th>
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<tr>
<td>adjusted MCRI*</td>
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<tr>
<td>femoral (n=1,307)</td>
<td>0.71 (0.23-2.24), p=0.56</td>
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<td>radial (n=2,643)</td>
<td>0.78 (0.11-5.69), p=0.81</td>
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<td>&lt;= 7 days (n=2,672)</td>
<td>0.89 (0.20-3.96), p=0.88</td>
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<tr>
<td>&gt; 7 days (n=1,278)</td>
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<tr>
<td>adjusted CR-BSI**</td>
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<tr>
<td>femoral (n=1,307)</td>
<td>0.71 (0.17-3.00), p=0.63</td>
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<tr>
<td>radial (n=2,643)</td>
<td>1.06 (0.13-8.51), p=0.96</td>
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<td>&lt;= 7 days (n=2,672)</td>
<td>0.84 (0.11-6.41), p=0.87</td>
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<tr>
<td>&gt; 7 days (n=1,278)</td>
<td>0.67 (0.09-5.05), p=0.69</td>
</tr>
<tr>
<td>adjusted colonization***</td>
<td></td>
</tr>
<tr>
<td>femoral (n=1,307)</td>
<td>0.92 (0.63-1.34), p=0.67</td>
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<td>1.02 (0.63-1.65), p=0.93</td>
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<tr>
<td>&gt; 7 days (n=1,278)</td>
<td>0.98 (0.60-1.59), p=0.93</td>
</tr>
</tbody>
</table>

Legends: *Variables used for adjusting MCRI: SAPS II score, dressing, skin antisepsis, vasopressor at insertion. **Variables used for adjusting CR-BSI: SAPS II score, skin antisepsis and antibiotic at insertion. ***Variables used for adjusting colonization: vasopressor at admission, SAPS II score, insertion site, dressing, skin antisepsis, mechanical ventilation at insertion, vasopressor at insertion, antibiotics at insertion. A hazard ratio (HR) less than one indicated a lower risk of event of ultrasound guidance (US) compared with non-US. CI: Confidence Interval. MCRI: Major catheter-related infection. CR-BSI: Catheter-related bloodstream infection

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Role of AcrAB-TolC multidrug efflux pump in mcr-1-mediated colistin resistance

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Background: A growing number of mobile colistin resistance (MCR) proteins is threatening the renewed interest of colistin as a “last-resort” defense against carbapenem-resistant pathogens. A recent study reported that efflux pump inhibitor CCCP can reverse colistin resistance mcr-1 colistin-resistant strains, suggested the role of efflux pump in colistin resistance in the mcr-1 positive bacteria. However, the precise relationship is unclear.

Materials/methods: We focused on AcrAB-TolC, a major Escherichia coli multidrug efflux pump. The expression of AcrAB-TolC in isolates and engineering bacteria was detected by RT-qPCR. Minimum inhibitory concentration (MIC) of colistin of E. coli was conducted using the agar dilution method. The alternative of the lipopolysaccharide (LPS) was verified through MALDI-TOF.

Results: The expression of AcrAB-TolC was significantly decreased in the E. coli BW25113 strains carrying mcr-1 when compared to wild-type BW25113. ΔacrA or ΔtolC containing mcr-1 showed a reduced colistin resistance and the slower growth. As expected, overexpression of acrA or tolC enhanced the colistin resistance. Moreover, mutants for acrA or tolC does not abolish the modification of the lipid A in BW25113 strains.

Conclusions: Colistin susceptibility will be rescued when the strains carrying mcr-1 lack acrA or tolC. Given the role of AcrAB-TolC in drug efflux, we concluded that AcrAB-TolC is dispensable for mcr-1-mediated colistin-resistance.

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Combined effect of fosfomycin and amikacin against fosfomycin-heteroresistant Escherichia coli isolates

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Abstract

Background: Fosfomycin and aminoglycosides are antibiotics with activity against multidrug-resistant Enterobacteriaceae. Fosfomycin heteroresistant isolates could lead to treatment failure with fosfomycin monotherapy. Combination therapy with aminoglycosides could solve fosfomycin suboptimal efficacy. The aim of this study was to evaluate the effect of fosfomycin and amikacin alone and combined against fosfomycin-heteroresistant E. coli isolates.

Materials/methods: Fosfomycin-heteroresistant clinical E. coli isolates, hypermutable (M9, M11, M34, P86) and normo-mutable (3203, S0406), were studied. E. coli ATCC25922 was used as control. Fosfomycin and amikacin MICs were determined using gradient strip (GSA) and broth microdilution (BMD) assays. Fosfomycin (50mg/L and 200mg/L) and amikacin (32mg/L) mutant frequencies were determined. Fosfomycin (64mg/L, susceptibility breakpoint and 307mg/L, human Cmax) and amikacin (16mg/L, susceptibility breakpoint and 45mg/L, human Cmax) activity were assayed alone and combined (fosfomycin/amikacin: 64/16 mg/L) in 48h time-kill curves. Drug interactions were assessed in checkerboard assays (analyzed with SynergyFinder). Fosfomycin (8g/8h) and amikacin (15 mg/kg/24h) human regimens were assessed in 72h hollow-fiber infection model (HFIM) [M11, M34, 3203, 50406]. Total and resistant bacterial populations were quantified and susceptibility from recovered colonies were reassessed (time-kill and HFIM). Glucose-6-phosphate (25mg/L) was added in fosfomycin experiments.

Results: GSA/BMD (mg/L) fosfomycin and amikacin MICs were, respectively: M9 (0.5/16; 2/16), M11 (0.5/256; 2/16), M34 (0.25/256; 2/16), P86 (0.5/64; 1/4), 3203 (0.25/512; 2/8), 50406 (4/≥1024; 1/4), ATCC25922 (0.5/2; 1/4). Mutant frequencies >10⁻⁷ were observed in all isolates, except ATCC25922, at fosfomycin 50mg/L and in M34, 3203 and 50406 at 200mg/L. Amikacin mutant frequencies were <10⁻⁹. In checkerboard assays, synergy was found against M9, M11, M34 and 3203 isolates. In time-kill assays, all clinical strains were able to growth at 64mg/L and only M34, 3203 and 50406 at 307mg/L fosfomycin. ATCC25922, M9, M11 and 3203 survived at 16mg/L, but none at 45mg/L amikacin. Combination assays cleared all bacterial cultures. In HFIM, fosfomycin and amikacin monotherapies failed to eradicate the bacterial burden. Recovered strains showed MIC above susceptibility breakpoints.

Conclusions: Fosfomycin might be inefficacious as monotherapy to treat hypermutator and normo-mutator fosfomycin-heteroresistant E. coli infections. Combined therapy with amikacin could be a successful alternative. PK/PD studies of these combination should be performed.

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### Abstract 3444

**Comparison of the performance of two galactomannan detection tests: Platelia Galactomannan (Bio-Rad) and Galactomannan Virclia (Vircell)**

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**Background:** The reference technique for the detection of Galactomannan (GLM) is the Platelia-Aspergillus (Bio-Rad) (Plate- lia) test. In its current format, it is a technique that requires batching and makes it very difficult to be used with individual samples as a “same day test”. A new monotest for GLM [Aspergillus Galactomannan Ag VIRCLIA® Monotest] using detection by chemiluminescence, developed by Vircell SL (Granada, Spain), could improve some of the limitations of Platelia. Our study consists of comparing Platelia and Virclia performed simultaneously in blood or Broncho Alveolar Lavage.

**Materials/methods:** Adult patients with only a single sample per patient. One of the hospitals (HGM) included selected retrospective samples mainly from patients with known proven or probable IA, in order to have a greater number of positive controls. In the remaining two hospitals, samples were included prospectively along 2019. Platelia and Virclia were run in parallel, according to the manufactures recommendations. Significant indexes were 0.5 for Platelia and 0.2 for Virclia.

The results of both techniques compared were classified as Concordant (Both techniques have a positive or negative result) or Discordant. In discordant results the presence of clinical criteria of proven or probable IA of the EORTC criteria was used as reference.

**Results:** Of the 323 patients, 120 were collected retrospectively (25 from controls and 95 from patients with IA criteria) and the remaining 203 were prospectively obtained from daily requests. Globally, 102 determinations were positive for one technique or another, 78 with Platelia and 98 with Virclia. Overall, the results were concordant in 294 of the 323 samples (91%) of the patients and 29/323 (9%) were discordant. Of the 29 discordant cases 19 had IA and the remaining 10 did not. Platelia was positive in only 4 of 19 IA cases while Virclia detected 15. Of the 10 cases without IA, Platelia was negative in 9 and Virclia in 1.

**Conclusions:** Both tests showed concordant results in 91% of the cases. Virclia was more convenient for rapid detection of GLM and proved more sensitive for the detection of cases of IA when results were discordant.

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**Abstract 3449**

**In vitro activity of fosfomycin against Escherichia coli and Klebsiella pneumoniae isolates recovered from bloodstream infections (2017-2018)**

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**Background:** Among the members of the family Enterobacteriaceae, the carbapenemase-producing *Klebsiella pneumoniae* and *Escherichia coli* are within the scope of Fosfomycin.

**Materials/methods:** A total of 336 *E.coli* (*n=116*) and *K.pneumoniae* (*n=220*) isolates from nosocomial bloodstream infections were included in the study. They had been isolated between January 2017 and December 2018 in Hacettepe (800-bed), Uludag (996-bed) and Black Sea Technical (1050-bed) University Hospitals located in Ankara, Bursa and Trabzon cities, respectively. Blood cultures are processed with the Bactec FX system (BD Diagnostics, Sparks, MD, USA) according to the manufacturer’s recommendations and identification of the isolates were performed by MALDI-TOF MS (BD Diagnostics, Sparks, MD, USA) at each center. **Agar dilution method** was performed for susceptibility testing. The EUCAST MIC breakpoints were used to interpret the susceptibility results. IMP, VIM, OXA-48, NDM, KPC type carbapenemases and TEM, SHV, CTX-M type extended spectrum beta-lactamases (ESBLs) were determined. FosA3 activity of the fosfomycin-resistant ones were also screened.

**Results:** Of the total isolates, 25.8% of *E.coli* and 59.5% of *K.pneumoniae* were producing at least one of the carbapenemases. OXA-48 was the most common carbapenemase type and the frequency of NDM and KPC types were increasing. Majority of the isolates were producing at least one of the ESBLs particularly CTX-M and TEM types. None of the fosfomycin-resistant isolates were positive for FosA3 gene. In vitro fosfomycin susceptibility of *E.coli* and *K.pneumoniae* isolates were presented in Table 1:

**Conclusions:** Fosfomycin susceptibility of carbapenemase-producing *E.coli* and *K.pneumoniae* isolates was 96.6% and 76.8%, respectively showing that fosfomycin has substantial in vitro activity against these isolates, even though the majority are producing carbapenemases and ESBLs. The activity of fosfomycin did not appear to be influenced by the expression of the specific resistance genotypes. The potential clinical utility of the drug merits further evaluation.

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<table>
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<tr>
<th>Bacteria</th>
<th>N of the isolates</th>
<th>MIC₉₀ (µg/ml)</th>
<th>Range (µg/ml)</th>
<th>Fosfomycin Susceptibility N (%)</th>
</tr>
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<td><em>Escherichia coli</em></td>
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<td>Carbapenemase-negative</td>
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<td>0.5</td>
<td>128-0.5</td>
<td>84/86 (97.6%)</td>
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<td>Carbapenemase-positive</td>
<td>30</td>
<td>0.5</td>
<td>256-0.5</td>
<td>29/30 (96.6%)</td>
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<tr>
<td>Total</td>
<td>116</td>
<td></td>
<td>113/116 (97.4%)</td>
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<td><em>Klebsiella pneumoniae</em></td>
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<tr>
<td>Carbapenemase-negative</td>
<td>89</td>
<td>4</td>
<td>256-1</td>
<td>73/89 (82.0%)</td>
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<tr>
<td>Carbapenemase-positive</td>
<td>131</td>
<td>8</td>
<td>256-0.5</td>
<td>96/131 (73.2%)</td>
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<tr>
<td>Total</td>
<td>220</td>
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<td>169/220 (76.8%)</td>
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</table>
Abstracts 2020

Abstract 3450

**It’s a trap! The development of a versatile drain biofilm model**

Katarzyna Ledwoch*1,2; Jean-Yves Maillard1; Phillip Norville2

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Abstract third-party references: GAMA Healthcare Ltd.

**Background:** There is little information on the effectiveness of drain disinfection, despite the association of contaminated drains with infection outbreaks. We report the development of a complex drain biofilm model that was used for measuring the efficacy of drain disinfection.

**Materials/methods:** A complex bacterial culture from a communal sink drain was used. Identical drain biofilms were initially grown in six silicone tubes for 2 days then developed as a mature complex biofilm for 6 days, fitting the tubes into glass bottle with screw cap twin hose connector to imitate a sink trap. During the maturation phase, biofilms were exposed to periodical media flushes to mimic sink usage. Samples were taken from the front, middle and back sections of the tube corresponding to biofilm formed under the strainer, inside trap reservoir and on the pipe outlet to wastewater. Drain biofilm composition, appearance and susceptibility to disinfection was investigated with next generation sequencing (NGS), scanning electron microscopy (SEM), viability test and regrowth tests.

**Results:** Following biofilm formation, our model consisted of 84 different species with *S. marcescens*, *K. oxytoca*, *K. pneumoniae*, *S. bangori* and *E. coli* dominating. SEM revealed a dense biofilm matrix, uniformly covering the tubing surface. Diversity and composition were reproducible between the 6 concurrent biofilms and between experiments, with 8.2 ± 0.8 log10 biofilm recovered from 27 samples of 9 independent batches.

Sodium hypochlorite (NaOCl) 1,000ppm, non-ionic surfactant and sodium dichloroisocyanurate 1,000 ppm treatments were most effective in eliminating the biofilm in the front part of drain biofilm model but failed to control the biofilm in the other sections. Biofilms also fully recovered within 1 day following NaOCl treatment. NaOCl treatments eliminated or decreased *S. marcescens* and *K. oxytoca* content, further increasing *K. pneumoniae* percentage content. In contrast, peracetic acid 4,000ppm effectively eliminated biofilm in all parts of the drain and prevented regrowth for at least 4 days.

**Conclusions:** Our model mimicking sink usage showed that conventional treatments fail to eradicate drain biofilm or prevent regrowth. Our reproducible complex drain biofilm model also enabled to understand the impact of disinfectants on biofilm spatial composition, diversity, viability and recovery post-treatment.

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Abstracts 2020

Abstract 3451

Resistance patterns and serotype distribution of *Streptococcus pneumoniae* isolates responsible for respiratory tract infections in Poland, 2006-2018

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**Background:** The aim of the study was to characterise *S. pneumoniae* isolates responsible for lower respiratory tract infections [LRTIs] in Poland between 2006 and 2018, by determining their antimicrobial resistance patterns and serotype distribution.

**Materials/methods:** Pneumococcal isolates (n=2849, including 1611 from blood) were serotyped by the Pneumotest-Latex kit, PCR or the Quellung reaction. MICs were determined either by the broth microdilution or Etest method, and interpreted according to the EUCAST criteria.

**Results:** Among studied isolates, 8.5% were from children under 5 years of age and 41.0% from patients older than 65 years. The most common were isolates of serotype 3 (20.1%), 14 (9.2%), 19F (8.0%), 4 (5.0%), 23F (4.8%), 19A (4.8%), 9V (4.3%) and 6B (4.2%). The overall coverage rates of PCV10, PCV13 and PPV23 were 42.5%, 69.3% and 83.0%, respectively but they differed significantly within age groups. Penicillin MICs higher than 0.06 mg/L were found in 25.8% of all isolates and in 66.1% of isolates from children under 5 years of age, whereas MICs higher than 2.0 mg/L in 72.8% and 22.0%, respectively. The susceptibility of *S. pneumoniae* was as follow: penicillin (74.2%), oral amoxicillin (81.4%), oral cefuroxime (76.9%), intravenous cefuroxime (79.0%), ceftriaxone (83.3%), macrolides (68.7%), clindamycin (74.7%), tetracyclines (72.9%), rifampin (93.6%) and trimethoprim/sulfamethoxazole (65.7%). Among pneumococci resistant to erythromycin, 83.3% represented phenotype cMLSβ, 15.7% M-phenotype and 1.0% iMLSβ. Multidrug resistance [MDR] characterized 30.1% of all pneumococci, but it was more common in non-invasive in comparison to invasive isolates (40.1% vs 22.9%, p<0.0001) and in children under 5 years old when compared to older population (59.9% vs 27.3%, p<0.0001). MDR phenotype was the most prevalent among pneumococci of serotypes 19A (83.0%), 19F (81.5%), 6B (73.3%) and 14 (68.8%). Since 2010 to 2018 susceptibility to penicillin have increased from 65.6% to 84.2% (p<0.0001) and MDR isolates decreased from 38.8% to 20.0% (p<0.0001).

**Conclusions:** Although pneumococcal susceptibility rates differed by age groups, types of infection and serotypes, MDR isolates numbers decreased significantly during the study period. This may be explained by wider use of antypneumococcal vaccination and its introduction into vaccination calendar in 2017.

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Staphylococcus aureus pathogenicity in cystic fibrosis patients: virulence genes, phylogeny and horizontal gene transfer

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Background: Cystic fibrosis (CF) patients suffer from chronic respiratory infections. Staphylococcus aureus has the highest prevalence in the airways of CF patients and has shown to contribute to airway inflammation. However, the impact of S. aureus on lung function and disease progression especially in older patients has not yet been elucidated. This analysis aims to identify bacterial factors associated to clinical deterioration in these patients.

Materials/methods: During an observational prospective multicenter study, respiratory specimens from 195 CF-patients (16 centers in Germany, 1 center in Austria) were processed at a central laboratory. All S. aureus isolates (n=3180) were analyzed for the presence of virulence genes by single and multiplex PCR (adhesin genes: cap, clfA/B, cna, eap, emp, fnbA/B, sasG/H, sdrC/D/E; toxin genes: eta/etb, hlg, pvl, seA/B/C/D/E/G/H/I/J, tst; immune escape: chip. Molecular typing was performed by spa-typing. Clinical data related to lung disease exacerbation (4 out of 12 clinical parameters) were reported in case report forms including change of sputum, fever, decrease in pulmonary function, radiographic changes and others.

Results: The average follow-up time was 80 weeks with a mean of 7 visits. Neither the quantity of virulence genes, nor the presence of specific virulence genes characteristic for S. aureus were associated to a clinical deterioration. However, for the agr-types 1 and 4 a link to the subject’s clinical status became evident. Moreover, the agr-types showed a clear association to the clonal background of S. aureus. Further, the analyses revealed a significant longitudinal decrease regarding the number of virulence genes present in the patients’ clones. Analyses concerning the plasticity of the virulence genes revealed significantly increased plasticity rates in the presence of environmental stress.

Conclusions: These results provide evidence for the concept that rather the phylogenetic background than the presence of specific virulence genes accounts for differences in S. aureus pathogenicity. The significantly increased gene plasticity rates in the presence of environmental stress suggest a host and iatrogenic influence on S. aureus genome plasticity. The loss of virulence genes during persistence most likely reflects the adaptation process directed towards a persistent and colonizing rather than an infecting lifestyle.

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Interleukin-1α and vascular endothelial growth factor support the growth and persistence of biofilm-growing Cutibacterium acnes in individuals with acne

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Background: Acne vulgaris is a common inflammatory disorder, affecting more than 80% of young adolescents. Cutibacterium acnes plays a role in the pathogenesis of acne lesions, although the mechanism(s) are, as yet, poorly understood. The aim of the study was to measure the prevalence of C. acnes in comedogenesis and in the progression towards inflamed acne lesions; to analyze the role of C. acnes as well as the impact of biofilm production; to assess the level of different inflammatory molecules on the skin of acne patients and their role in promoting bacterial growth and persistence.

Materials/methods: Samples for microbiological analysis were collected from the skin of 10 healthy subjects, and the unaffected skin, the comedones and the papulo-pustular lesions of 30 acne patients. Samples were characterized using 16S rRNA gene sequencing. Biofilm production was measured by the clinical BioFilm Ring Test in all C. acnes isolates. Tape adsorption tests were performed on the skin of acne patients and in 10 healthy controls, to measure the levels of skin inflammatory molecules. In vitro studies were performed to evaluate the response of C. acnes isolates to different concentrations of inflammatory molecules.

Results: Microbiome analysis showed a significantly higher relative abundance of C. acnes [P < 0.05] in inflammatory (papule and pustule) compared with noninflammatory (comedones) acne lesions, unaffected skin and the skin of healthy subjects. All the strains analyzed were able to produce comparable levels of biofilm, independently from the site of isolation. The level of cutaneous interleukin (IL)-α, and vascular endothelial growth factor (VEGF) was significantly higher [P < 0.05] in the skin of acne patients as compared to control subjects. Additionally, both IL-1α and VEGF selectively promoted a concentration-dependent increase of C. acnes growth.

Conclusions: C. acnes proliferates in the inflammatory lesions of acne patients. The increased level of IL-1α and VEGF in the skin of acne patients, may play a role in promoting the growth of C. acnes. Biofilm production by C. acnes may contribute to sustaining bacterial adhesion and chronic persistence in acne.

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Abstract 3457

Impact of positive blood culture occurring in early post-operative cardiac surgery: a retrospective study

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Background: The occurrence of bacteremia after cardiac surgery is common, secondary to surgical site infection or not. The objectives of this study were to assess the complications of early postoperative bacteremia after sternotomy, their diagnosis process and therapeutic management.

Materials/methods: This monocentric retrospective study included patients over 18-year of age with bacteremia within 30 days after coronary bypass (CBP) and/or valvular surgery hospitalized at Bichat hospital in Northern Paris from January 2013 to December 2016.

Results: After excluding positive blood culture considered as contamination (n=83), 104 patients were enrolled in this study (Figure 1). Among these, 69.2% were men and the median age was 68.3 years [IQR=58.2-75.1]. The median EuroSCORE II was 4.4 [1.7-11.2]. The most common identified pathogens were Methicillin-susceptible Staphylococcus aureus (n=24, 23%) and Enterobacteriaceae (n=34, 33%). Thirty-five patients [34%] were in septic shock during bacteremia with a median IGS 2 score at 47 [38-75]. The median delay between surgery and positive blood culture was 9 days [4-18]. Infections were due to surgical site infection in 20 patients, including mediastinitis (n=13) and superficial wound infection (n=7) or secondary to other site infection with principally respiratory tract infections (n=19) or urinary infections (n=14). 19 patients had endocarditis: 15 after valvular surgery, and 4 after CBP. Endocarditis diagnosis was made by echocardiography (n=14) or WBC scintigraphy or PET/CT (n=5). Valvular surgery group was treated with higher antibiotic doses (55.8% (n=43) versus 33.3% (n=9) in the CBP group) (p=0.024) and longer median duration (21 days [14-42] against 14 days [7-21] in the CBP group) (p=0.033). Surgical treatment was done in 25 patients. Mortality at 30 days concerned 16 patients, 10 in valvular surgery group against 6 in the CBP group (p=0.404) and mortality at 1 year 32 patients, 22 in valvular surgery group against 10 in the CBP group (p=0.617).

Conclusions: Positive blood culture occurring after cardiac surgery is a complication with a high rate of mortality. Surgical site infection and endocarditis, particularly after valvular surgery, should be tracked and antibiotic therapy started immediately with high doses. As long as guidelines are lacking, prospective studies will be needed.

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Adaptation to triclosan in carbapenemase-producing Klebsiella pneumoniae clinical isolates

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Background: Carbapenemase-producing Klebsiella pneumoniae (CP-Kp) is a serious public health problem. Environmental reservoirs contaminated with biocides are acquiring increasing relevance in the dissemination of CP-Kp. Triclosan is a biocide widely used for multiple purposes (ie. antiseptic, preservative, etc.) which can accumulate in environmental reservoirs, enhancing the competitiveness and spreading ability of triclosan-adapted CP-Kp. The aim of this study was to i) determine if CP-Kp can be adapted to grow in increasing triclosan concentrations and ii) detect mutations in the gene encoding the target of triclosan (fabI; enoyl-acyl carrier reductase) in triclosan-adapted isolates.

Materials/methods: Six CP-Kp isolates representing different clones and carbapenemase types (ST15/bla VIM-1, ST11/bla OXA-48, ST258/bla KPC-3, ST15/bla OXA-48, ST147/bla VIM-1, ST405/bla OXA-48) were selected from the Andalusian reference laboratory PIRASOA and Reference and Research for Resistance to Antibiotics Laboratory of Carlos III. MICs of triclosan were determined by microdilution in MHB. Isolates were sequentially adapted by subculture in MHB containing rising subinhibitory triclosan concentrations, until MIC stabilisation. The nucleotide sequences of fabI of parental and triclosan-adapted isolates were determined by Sanger DNA sequencing (Macrogen). Aminoacid sequences of parental and corresponding adapted isolates were aligned by Clustal Omega for comparison.

Results: for parental CP-Kp isolates the MICs of triclosan were 0.1 mg/L [ST405/bla OXA-48] and ST15/bla VIM-1, 0.5 mg/L [ST15/bla OXA-48 and ST11/bla OXA-48] and 1.9 mg/L [ST258/bla KPC-3 and ST147/bla VIM-1]. In contrast, the MIC of triclosan determined against all the parental isolates after 1 week of adaptation to triclosan were ≥15 mg/L. No mutations were detected in two triclosan-adapted CP-Kp (ST15/bla VIM-1 and ST11/bla OXA-48). Mutations G93V and F203L, previously described in triclosan-resistant Escherichia coli, were detected in ST258/bla KPC-3 and ST15/bla OXA-48 (G93V), and ST147/bla VIM-1 (F203L). Mutation Y146H was detected in ST405/bla OXA-48.

Conclusions: (1) CP-Kp is able to adapt rapidly to grow in presence of triclosan, which might suppose a competitive advantageous under triclosan exposure. (2) Four out of the six triclosan-adapted CP-Kp isolates tested harbor one mutation in fabI, which could be involved in triclosan tolerance as has been previously described in E. coli. (3) The absence of mutations in fabI of two triclosan-adapted CP-Kp isolates suggest that mechanisms other than fabI mutations could be implicated in triclosan adaptation.

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Impact of restricting procalcitonin measurements on antibiotic use, clinical outcomes and costs in a Swiss tertiary care hospital: an interrupted time-series analysis

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Background: Although biomarkers such as procalcitonin (PCT) can help avoiding unnecessary antimicrobial treatments, data suggest that overuse and misuse of PCT is frequent in routine practice. The primary objective of this study was to analyse the effect of the restriction of PCT measurement on antibiotic use in the wards concerned by the prescription limitation before and after its implementation. Secondary objectives were to assess the impact of the restriction on clinical outcomes and costs.

Materials/methods: This quasi-experimental study was conducted in Geneva University Hospitals. Due to the substantial financial burden of PCT-reagent costs it was decided to restrict PCT measurements as of February 3, 2016, except for the paediatric emergency department, the intensive care and transplantation units. We conducted an interrupted time-series analysis, using a Prais-Winsten regression, of rates of monthly antibiotic use in defined daily doses [DDD] per 1000 patient-days (PD), LOS, and in-hospital mortality, before and after the start of the restriction policy. We modelled the predicted number of PCT measurements per month based on the trend before the intervention. The difference between the observed and predicted number of PCT measurements was then used to calculate cost savings from the perspective of the hospital.

Results: After the intervention, there was an immediate statistically significant decrease in level of PCT measurements per month (-637.4; 95% CI 539.7-735.0) without a statistically significant change in slope (-0.05; 95% CI -8.2 to 8.1) (Figure). Before the intervention, there was an increasing trend of monthly antibiotic use of 4.3 DDD/1000 PD (95% CI 1.4-7.1). After the intervention, there was a non-significant decrease in level of 47 DDD/1000 PD (95% CI -1.0-95.6), followed by an upward change in slope of 1.6 DDD/1000 PD (95% CI -0.2-3.5) which was not statistically significant (Figure). There was no evidence of deleterious effect on mortality or LOS, and costs decreased considerably.

Conclusions: This study shows that the restriction of PCT measurements in our hospital did not have an impact on overall antibiotic use and was not associated with increases in LOS or mortality. At the same the restriction led to significant cost savings.

Figures – Changes in (A) monthly number of PCT measurements; (B) monthly rates of antibiotic consumption (measured in DDD per 1000 patient-days) before and after restriction of procalcitonin measurements.

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Ten-year trends in Estonian ambulatory antibiotics use and comparison of ESAC quality indicators with Nordic countries

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Abstract third-party references: Project RITA1/02-75-02

Background: The ambulatory antimicrobial use in Estonia has been among the lowest in the EU. However, there has not been lately any thorough country-wide assessment of the pattern of antimicrobial prescribing. Therefore we aimed to analyse the prescribing trends of systemic antimicrobials for better guided local antimicrobial stewardship.

Materials/methods: Consumption of systemic antibiotic was based on the wholesalers annual reports from 2008 to 2018. Antibiotics were grouped according to the active substances [ATC groups, 4th level], consumption is presented as defined daily doses per 1000 inhabitants per day [DDD/1000 inhabitants/day]. ESAC [European Surveillance of Antimicrobial Consumption] quality indicators were used to describe time-trends and compare outpatient antibiotic use in Estonia and selected Nordic countries.

Results: Over the past 11 years total antibiotic consumption has been very stable in Estonia ranging from 1.28 in 2008 to 1.22 in 2018 DDD/1000 inhabitants/day. There have been, however, changes in the consumption of specific antibiotics. Most commonly prescribed antibiotics (36% in 2018) were penicillins (J01C, DDDs/1000 inhabitants/day increased from 3.8 in 2008 to 4.4 in 2018). The prescribing of wide-spectrum penicillins (J01CA) has decreased and changed to the combinations of penicillins with betalactamase inhibitors (BLI, J01CR) (Figure 1)

Figure 1. Ten years changes in the consumption of penicillins

Important changes at the ESAC quality indicators:

Ratio of the consumption of broad-spectrum [J01 [CR+DC+DD+[F-FA01]]] antibiotics to the consumption of narrow-spectrum penicillins, cephalosporins and macrolides [J01 [CE+DB+FA01]] has changed markedly. In 2008 the ratio of broad spectrum antibiotics used in Estonia was 5.42 compared to the 15.95 in 2018 [annual percent change [APC] +16.2%, p<0.05]. The respective ratios in Nordic countries were <0.6 in 2018.

Consumption of BLI/BLI [J01CR] expressed as percentage of the total consumption of antibacterials for systemic use [J01] has increased from 8.4% in 2008 to 19.4% in 2018 [APC +8.9%, p<0.05]. The respective percentages in Nordic countries in 2018 were <6.

Conclusions: The shift in consumption from narrow to broad spectrum antibiotics despite stable low rate of AMR is of concern and suggests the need for more extensive monitoring of antibiotic prescriptions and improving antibiotic stewardship.

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Abstracts 2020

Abstract 3469

**Pathogenic, antimicrobial-resistant Escherichia coli in low-income settings household soils: origins and genomic diversity**

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**Background:** Soils in households in low-income settings are reservoirs for Escherichia coli and have been suggested to be important for disease transmission, particularly in areas with inadequate sanitation. The aims of this study were to investigate the risk factors for and genomic diversity of E. coli in soils collected from household plots to gain insights into their origins.

**Materials/methods:** E. coli was enumerated and isolated from soil and human, chicken, and cattle fecal samples collected in 52 rural Bangladeshi households. Associations between E. coli concentrations in soil, household-level risk factors, and soil physicochemical characteristics were evaluated. Susceptibility to 16 antibiotics was investigated among 175 collected isolates and whole-genome comparative analyses were performed for a subset of 60.

**Results:** E. coli was detected in 44.2% of the soil samples with an average of 1.95 log10 CFU/g dry soil. Soil moisture and clay content were associated with the E. coli concentration in soil, whereas no household-level risk factor was significantly correlated. Antibiotic resistance was detected in 42.3% of the 175 isolates and amongst the 60 isolates sequenced, 23 encode at least one resistance gene. Detected virulence factor-related genes are linked not only to intestinal pathotypes but also to environmental adaptation. The number of plasmid replicons detected ranged from 1 to 7 amongst 49 isolates (81.7%). E. coli from soils were genetically diverse and located across multiple branches of the reconstructed phylogeny, intermixed with isolates from fecal sources. Analyses of the accessory genome identified 1764 protein-coding genes, including a large number with unknown functions, statistically significantly enriched in the Bangladeshi isolates relative to genomes of the nearest neighbors available in databases.

**Conclusions:** Together, these findings indicate that E. coli detection in soils, including pathogenic and antimicrobial-resistant, appears to be driven by soil physicochemical characteristics and inputs from multiple and diverse E. coli sources (human and animal) that share a common accessory gene pool. Thus, public health interventions in low-income setting settings must consider soil as an important source for the transmission of E. coli variants with the potential to cause disease in people and that could pose treatment difficulties.

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Nasal carriage of livestock-associated *Staphylococcus aureus* in Poland

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**Background:** Livestock-associated *Staphylococcus aureus* (LA-SA) draws increasing attention due to its particular ability to colonize farm animals and be transmitted to people, which in turn leads to its spread in the environment.

The aim of the study was to investigate the nasal carriage of *S. aureus*, in particular LA-SA, among people having professional contacts with pigs in Poland in 2009 vs. 2017.

**Materials/methods:** 204 and 210 nasal swabs were taken from volunteers participating in annual conferences concerning pig health and farming (risk group) in 2009 and 2017, respectively. In parallel, nasal swabs from volunteers without contact with pigs (control group), were collected. For all identified *S. aureus* isolates, PCR-detection of *mecA*, *mecC*, *lukS-PV/lukF-PV* genes and *spa*-typing was performed. In all *mec*-positive isolates SCCmec types were defined. MLST was performed on selected isolates. Resistance to antimicrobials was determined.

**Results:** Table. Comparison of *S. aureus* nasal carriage in risk and control group (2009 vs. 2017).

<table>
<thead>
<tr>
<th>Group</th>
<th>Year</th>
<th>Swabs no.</th>
<th><em>S. aureus</em> no. (% of swabs)</th>
<th>MRSA no. (% of <em>S. aureus</em>)</th>
<th>MSSA no. (% of <em>S. aureus</em>)</th>
<th>CC398-MRSA (% of swabs)</th>
<th>CC398-MSSA (% of swabs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk</td>
<td>2009</td>
<td>204</td>
<td>81 (39.7%)</td>
<td>10 (12.3%)</td>
<td>71 (87.7%)</td>
<td>9 (4.4%)</td>
<td>27 (13.2%)</td>
</tr>
<tr>
<td></td>
<td>2017</td>
<td>210</td>
<td>82 (39.0%)</td>
<td>43 (52.4%)</td>
<td>39 (47.6%)</td>
<td>42 (20.0%)</td>
<td>5 (2.3%)</td>
</tr>
<tr>
<td>Control</td>
<td>2009</td>
<td>456</td>
<td>106 (23.0%)</td>
<td>3 (2.8%)</td>
<td>102 (97.2%)</td>
<td>1 (0.2%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>2017</td>
<td>487</td>
<td>102 (21.1%)</td>
<td>3 (2.9%)</td>
<td>100 (97.1%)</td>
<td>1 (0.2%)</td>
<td>3 (0.6%)</td>
</tr>
</tbody>
</table>

All CC398 isolates identified in 2009 and 2017 were negative for *pvl* genes. The most prevalent *spa*-type among CC398 was t034 (65%), followed by t011 (17%). 61% CC398 isolates were *mec*-positive and carried element SCCmecV (91%) or SCCmecIVA (9%). The most prevalent resistance profile in 2009 was penicillin, erythromycin, clindamycin, tetracycline (62.2%) while in 2017 penicillin, erythromycin, clindamycin, tetracycline, chloramphenicol (64.7%). Increase in resistance rate for chloramphenicol (5% in 2009 vs. 98% in 2017) was observed.

**Conclusions:** Within a few years, percentage of CC398-MRSA carriers increased significantly fourfold in risk group (p<0.0001). CC398-MSSA were replaced by CC398-MRSA strains. Nasal carriage of CC398-MRSA in the control group remained at the same low level. The observed increase in incidence of CC398-MRSA among people having professional contact with pigs indicates the need to monitor *S. aureus* carriage in this risk group.

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Abstract 3473

Prevalence and genetic characterisation of Shiga toxin-producing Escherichia coli isolates from cattle in Portugal

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Abstract third-party references: Project PhageSTEC (POCI-01-0145-FEDER-029628)

Background: Shiga toxin-producing E. coli [STEC] cause significant foodborne diseases in humans. They are natural residents of ruminants and are transmitted to humans through contaminated food. From 500 STEC serotypes known to infect humans, only few groups are responsible for the majority of cases [e.g. O157, the leading serotype worldwide]. However, the epidemiological link between STEC serotypes transmitted by animals to humans remains unclear. Their prevalence varies based on the type of animal, age, region and country, being unknown in Portugal.

Materials/methods: From November 2018 to June 2019, we collected 409 faecal specimens from the rectum of healthy dairy cattle [adults lactating cows, n=254 and heifers, n=155], at 21 milk farms located across the Northern region of Portugal. After enrichment with modified TSB with novobiocin, samples were analyzed by qPCR to detect virulence genes (stx1, stx2 and eae) in accordance with ISO/TS 13136:2012(E). Conventional PCR was used to confirm the strains profile and to detect stx1 (stx1a, stx1c and stx1d) and stx2 (stx2a, stx2b, stx2c, stx2d, stx2e, stx2f and stx2g) subtypes according to VTEC European Union Reference Laboratory guidelines. Additionally, serotyping was performed to establish O (O1 -O181) and H (H1-H56) antigens.

Results: A total of 141 isolates were recovered from 114 positive animals [dairy cows and heifers]. The STEC prevalence was higher in heifers (60/155; 38.7%) than in adult cows (54/254; 21.3%) [p<0.05]. PCR showed that 69 (49.9%) isolates carried stx1 genes, 114 (80.9%) stx2 genes and 41 (29.1%) both stx1 and stx2, with several stx subtypes identified. STEC isolates have shown a great diversity in terms of O and H antigens. Although the notorious O157:H7 and O26:H11 were found, others serotypes [e.g. O29:H12, O113:H21, O15:H16] were the most prevalent.

Conclusions: The high level of STEC prevalence in Portuguese dairy cattle, demand new strategies to prevent food contamination and subsequent human infection.

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Abstract 3474

A case of recurrent Campylobacter cured by faecal microbiota transplant in an immunosuppressed patient with common variable immune-deficiency

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Background: We report a case of a 69 year old immunosuppressed patient with a 7 year history of recurrent Campylobacter infection, who was successfully treated with Faecal Microbiota Transplant (FMT) administered via nasojejunal tube.

Materials/methods: The patient was diagnosed with Common Variable Immune-deficiency (CVID) in 2000 and is treated with fortnightly intravenous immunoglobulin (IVIG). She has suffered from numerous infectious complications including EBV-driven diffuse large B-cell lymphoma, toxoplasma chorioretinitis, chronic bacterial sinusitis and recurrent Campylobacter jejuni gastroenteritis. This was first identified in 2012 following a trip to Brazil, but was isolated again (with the same sensitivity pattern so assumed to be a relapse) in 2014 which corresponds with a break in IVIG treatment. Between May 2018 and 2019 she suffered at least 6 further episodes, despite prolonged treatment with numerous courses of clarithromycin to which the isolates were sensitive. Further antimicrobial susceptibility testing revealed resistance to ciprofloxacin and doxycycline. She consented to FMT which was performed via push enteroscopy from an anonymous donor according to our standard methods. This was undertaken in May 2019 following a course of fosfomycin to treat the Campylobacter.

Results: After initial improvement in diarrhea, she suffered a further microbiologically confirmed relapse. She was treated with an extended (6 week) course of fosfomycin and her dose of IVIG was increased. She underwent a second FMT (using a different donor) at the end of July 2019, again with good response. She remains asymptomatic at the time of writing [four months after the 2nd FMT] and has gained 5kg in weight.

Conclusions: Recurrent Campylobacter infections [including gastroenteritis and bacteraemia] have previously been reported in patients with CVID and are particularly problematic to manage. To our knowledge, this is the first time FMT has been used to successfully treat such a patient.

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**Abstract 3477**

**Differentiation of the members of the Staphylococcus aureus complex by MALDI-TOF using the VITEK MS platform**

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**Background:** Staphylococcus argenteus and Staphylococcus schweitzeri have been recently described as new species within the Staphylococcus aureus complex. The need to distinguish species within the complex for routine purposes is currently questionable as no difference in morbidity, mortality or transmission between *S. aureus* and *S. argenteus* have been described and no human infections with *S. schweitzeri* have been reported so far. However, the distinction is valuable to further clarify the epidemiology and clinical impact of these two novel species. In this study, we tried to establish if their differentiation is possible using the MALDI TOF technology.

**Materials/methods:** A total of 234 spectra were acquired on 49 strains (29 *S. aureus*, 18 *S. argenteus* and 2 *S. schweitzeri* strains) obtained from different sources, including the French National Reference Center for Staphylococci. Spectra were acquired following direct deposit on a VITEK MS slide, in the 3000 to 17000 Da mass range and integrated into the next release of the VITEK MS knowledge base. Data were analyzed using Multidimensional Scaling (MDS). Performance was evaluated using a cross-validation approach.

**Results:** The cross-validation study performed on the updated database, containing 41922 spectra covering 1257 bacterial species, showed that the correct identification rates at species level reached 97.3% for *S. aureus* and 100% for *S. argenteus*. Conversely, only 8.3% of the spectra from *S. schweitzeri* were identified at species level, 66.7% were identified in low discrimination with the two other members of the complex, 8.3% were not identified while 16.7% were misidentified either to *S. aureus* or *S. argenteus*. The MDS confirmed that a clear differentiation is possible between *S. aureus* and *S. argenteus* but not between *S. schweitzeri* and the two other members of the complex.

**Conclusions:** This study demonstrates that MALDI TOF using VITEK MS platform is able to differentiate *S. argenteus* from *S. aureus* but not *S. schweitzeri* from *S. argenteus* and *S. aureus*. The identification of *S. argenteus* at species level could help to clarify its involvement in clinical infection and, if warranted, to implement future surveillance or infection control measures.

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Abstracts 2020

Abstract 3478

Coxiella burnetii DNA in cheeses and bulk milk samples of sheep and goats in Puglia and Basilicata, Italy

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Background: Coxiella burnetii is a Gram-negative obligate intracellular bacterium that is responsible for Q fever, a worldwide zoonosis. C. burnetii infects a wide range of wild and domestic mammals, including humans. Domestic ruminants are the main reservoir. Infected animals can shed C. burnetii at high concentrations in their urine, feces, milk and birth products. Consumption of contaminated raw milk and dairy products might be source of human infection, although the transmission by the oral route is still controversial.

Materials/methods: This study included a total of 200 samples of dairy products of ovine-caprine origin [71 short-seasoned cheese and 129 raw milk samples], collected from October 2018 to October 2019 by the local health services and transferred to the Istituto Zooprofilattico della Puglia e della Basilicata in Foggia. A loop-mediated isothermal amplification assay (LAMP) was performed for rapid and simple detection of the IS1111 transposon of C. burnetii. The C. burnetii Nine Mile strain strain (Ampli-run® Coxiella burnetii DNA control, Vircell Microbiologists) was used as a positive control.

Results: C. burnetii DNA was found in 14 out of 200 (7%) samples analysed. In particular, 12 of the 129 samples of raw milk (9.3%) and 2 of the 71 cheese samples (2.8%) came out to be positive for IS1111.

Conclusions: LAMP assay can rapidly detect C. burnetii DNA and does not require any specific or expensive equipment. Some studies suggest that the consumption of raw milk could be the cause of some cases of Q fever in humans. Indeed, there is epidemiological evidence that the consumption of milk and/or milk-based products contaminated by C. burnetii is associated with seroconversion in humans. Therefore, the results of this study emphasize the importance of a One Health approach to Q fever, that includes active monitoring, vaccinations and correct hygiene measures to prevent the dispersion of the bacterium in the environment, between animals and a possible transmission to humans.

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Differentiation at species level of the members of the PSC complex (Pseudallescheria boydii / Scedosporium apiospermum) involved in cystic fibrosis by MALDI-TOF MS

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**Background:** The species of the Pseudallescheria boydii/Scedosporium apiospermum complex (PSC) are ubiquitous molds reported as emerging pathogens causing invasive fungal diseases and colonization especially in cystic fibrosis (CF) patients with a prevalence of about 10%. The distinction of the species within the complex is of great importance as they show different antifungal susceptibility profiles to azoles or echinocandins.

The current molecular methods can be fastidious and time-consuming. In this study, we propose a rapid identification of these organisms at species level via an inactivation/extraction protocol followed by a MALDI-TOF MS identification.

**Materials/methods:** A total of 343 spectra from 64 well-characterized PSC strains (Pseudallescheria boydii [n=5], Pseudallescheria ellipsoidea [n=4], Pseudallescheria minutispora [n=4], Scedosporium apiospermum [n=17], Scedosporium aurantiacum [n=4], Scedosporium dehoogii [n=4], and Scedosporium prolificans [n=6]) were acquired with the VITEK MS after an inactivation/extraction protocol and within the mass range of 3,000-17,000 Da.

The spectra were integrated into the next VITEK MS knowledge base update and data were analyzed using dendrograms and multidimensional scaling (MDS). Performance was evaluated using a cross-validation approach.

**Results:** The MDS shows that a clear differentiation is possible between all species of the complex despite a very high spectrum similarity (>50%) as shown by the dendrogram analysis.

The cross validation study performed on the updated database, containing 15,557 spectra covering 327 fungal species, shows that 97.7 to 100% correct identification rates are obtained at the species level for all seven species.

**Conclusions:** This study demonstrates that MALDI-TOF MS is a rapid and reliable tool to differentiate close species within the PSC complex. It could help in the management of CF patients by improving the identification of molds responsible for colonization and by reducing the time to start appropriate antifungal therapy.

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Case report: microbiological effects of phage therapy on *Pseudomonas aeruginosa* in a pneumonia patient

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**Background:** Due to growing concerns about multi drug resistant bacteria, interest in phage therapy has increased. Especially the ESKAPE organisms are seen as a potential target for phage therapy. In this case report we present a case of adjunctive phage nebulization for a pulmonary infection with *Pseudomonas aeruginosa*. By analyzing the isolates obtained during the course of treatment, we evaluated the effect of phage nebulization on the bacterial populations in the lung.

**Materials/methods:** A 7 year old girl with recurrent pulmonary infections, was treated for a new episode of pneumonia with sputum cultures showing *Pseudomonas aeruginosa* and *Klebsiella variicola*. The isolated pathogens were susceptible for the administered antibiotics. During hospitalization, on request of the patient’s family, adjunctive phage therapy was started through nebulization of two phage cocktails from Tbilisi containing multiple phages against the *Pseudomonas* strain. Different *pseudomonas* phages were isolated based on plaque morphology and were whole genome sequenced. Daily sputum samples were taken to monitor microbiological response. *Pseudomonas* isolates were tested for phage susceptibility using plaque assays. Several isolates were whole genome sequenced for phylogenetic analysis and analysis of phage resistance mechanisms.

**Results:** 14 phages with lytic activity against the *pseudomonas* strain were isolated from the two phage cocktails. Genetic assembly revealed two phage variants: Myoviridae with genetic similarities between the isolates of >99% and Podoviridae sharing a homology of >90%. *Pseudomonas* isolates were collected till 47 days after start of phage nebulization. A varying phagogram was seen between the isolates over time. All isolates had the same antibiogram and all 7 sequenced isolates had identical MLST-types. None of the bacterial isolates carried a CRISPR system. We are still in the process of analyzing the underlying resistance mechanisms and the phylogenetic relationship between the *pseudomonas* isolates.

**Conclusions:** Current analysis indicates that there have been no major shifts in bacterial strains. We hypothesized that due to heterogeneous spread of phages through the lung, variations in phage susceptibility are seen between exposed an unexposed *pseudomonas* populations. This case report provides important insights about the microbiological response on phage nebulization which will be valuable in planning future trials.

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Abstract 3486

Widespread distribution of the acquired colistin resistance gene, mcr-9, amongst Enterobacterales in England and Wales

Matthew Ellington*1, Tim Dallman1, Daniele Meunier1, Katie Hopkins1, Neil Woodford1

1Public Health England, London, United Kingdom

Background: Colistin is a last-line treatment option for infections due to multi-resistant Gram-negative bacteria. The emergence of mobile colistin resistance (mcr) genes threatens to cause widespread colistin resistance. We determined the distribution of the most recently described variant, mcr-9, amongst large collections of Enterobacterales isolates including carbapenemase-producing Enterobacterales (CPE).

Materials/methods: PHE's National Infection Service reviewed WGS data (Illumina HiSeq 2500) for isolates of: Salmonella (N=39,697), gastrointestinal E. coli (N=13,082) isolated in 2014-17; ExPEC (N=529) referred in 2017-18 and 3089 CPE (N=3089) referred between 2010-16.

AMR genes, bacterial species and MLST were determined via PHE-genefinder, kmer-ID and MOST, respectively. Antimicrobial MICs for CPE were determined by agar dilution according to BSAC methodology and interpreted using EUCAST breakpoints.

Results: We detected mcr-9 in 210 isolates of Enterobacterales. These were comprised of 38/39,697 Salmonella, of which 24 were ST19 S. Typhimurium, and 0/13,082 gastrointestinal E. coli. Twenty-eight of the Salmonella encoded CTX-M-9 or -15 ESBLs.

HCAI/AMR mcr-9 isolates from 41 English centers comprised: 5/529 HCAI-E. coli isolates from 5 centers and 167/3089 CPE from 41 centers (three centers referred 68 isolates). CPE were dominated by Enterobacter spp. (125) belonging to 55 STs, followed by K. pneumoniae (16), K. oxytoca (7), E. coli (10) representing 24 different STs, C. freundii (4) and five isolates from four other Enterobacterales species.

Amongst mcr-9 CPE, OXA-48 isolates dominated (61 isolates) followed by KPC-2 (49 isolates), NDM-1 (24 isolates) and VIM-4 (15 isolates). Six IMP isolates encoded IMP-1, IMP-4 or IMP-10. The remaining 12 isolates were variants from these main families. All mcr-9+ CPE harboured IncHI2 replicons, except five isolates from three species, with different carbapenemases. Of the 125 mcr-9+ CPE with colistin MIC data: 99 were <=0.5mg/L, 23 were 1-2 mg/L, only three were resistant (>2 mg/L).

Conclusions: The mcr-9 gene is disseminated amongst diverse Enterobacterales and was found in more isolates than other mcr variants. Whilst its clinical significance remains unclear, we will further investigate MICs amongst populations with and without the gene.

The association of mcr-9, IncHI2 replicons and ESBLs or carbapenemases raises concern for the co-selection of mcr-9 with other resistances.

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Abstract 3488

**Carbapenem-resistant *Escherichia coli* causing neonatal sepsis: NDM-5 gains prominence**

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**Background:** *Escherichia coli* causes sepsis in neonates. Carbapenem-resistant *E. coli* (CREc) are rapidly spreading. An important family of carbapenemases are the Zn(II)-dependent –β-lactamases, known as metallo-β-lactamases (MBLs). Among them, the New Delhi metallo-β-lactamase (NDM) is a potent enzyme. This study maps the *E. coli* causing neonatal sepsis in a tertiary care hospital in India during a decade focusing on carbapenem resistance, the phylogroups, sequence types and virulence determinants of *E.coli* with a view to understand changing patterns of the prevalent variants and the corresponding sequence types.

**Materials/methods:** *E.coli* were collected from the Neonatal Intensive Care Unit (2008-2017). Isolates were confirmed, MIC for meropenem was determined by broth dilution. Presence of **bla**<sub>NDM</sub> and other resistance genes were determined by PCR followed by sequencing. Phylogroup and sequence types were determined by standard procedures.

**Results:** Thirty-four percent of the isolates were carbapenem-resistant, harbouring **bla**<sub>NDM</sub> (MIC 2-64mg/L). The different allelic variants were distributed as follows: NDM-1, 50%; NDM-5, 36%; 9% NDM-7 and one isolate possessed NDM-15. The amino acid differences of the variants in comparison to NDM-1 were V88L and M154L for NDM-5, D130N and M154L for NDM-7 and M154L and A233V for NDM-15. Most isolates co-harboured **bla**<sub>CTX-M-15</sub> along with different combinations of other resistant-genes such as **aac-(6’)-Ib-cr**, **bla**<sub>SHV</sub>, **rmtB**, AmpC. CREc also revealed diverse plasmid types (HI1, I1, FIA+FIB, FIA, FII, FIIK, FIIS, and Y). Virulence genes such as **traT**, **papC**, **fimH**, **iucC**, **usp**, **hlyA** which encoded diverse virulence traits were also present. The distribution of the phylogroups among the strains were A, B2, C, and B1, of which phylogroup A predominated. CREc were of diverse sequence types ST2, ST43, ST471, ST922 (Pasteur scheme). There was no association between any particular phylogroup or ST types and the NDM variants, their presence in a particular ST or phylogroup was random.

**Conclusions:** Carbapenem-resistance in *E. coli* in this unit has been primarily due to NDM-1. Lately NDM-1 is slowly being replaced with NDM-5.

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Assessment of ceragenin CSA-131-poloxamer for treatment of Stenotrophomonas maltophilia infections as a potential antimicrobial agent

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Background: Stenotrophomonas maltophilia is an important Gram negative opportunistic pathogen causing variety of infectious. As well as extensive intrinsic resistance, multi drug resistance was reported worldwide. Therefore, new drugs need to develop to combat S. maltophilia infections. Ceragenins were developed as alternative antimicrobial agents to antimicrobial peptides (AMPs) to improve AMPs antimicrobial and chemical properties. The aim of this study was to evaluate antimicrobial activities of ceragenin CSA-131 (Cationic Steroid Antibiotic) by formulating in poloxamer micelles as well as CSA-13 and CSA-131 against S. maltophilia isolates.

Materials/methods: S. maltophilia clinical isolates (n=40) were collected from Istanbul University, Faculty of Medicine between 2006-2016. CSA-13 and CSA-131 were synthesized from cholic acid Scaffold technique. CSA-131 was combined with Pluronic F-127 to decrease the cytotoxicity of CSA-131. Minimum inhibitory concentrations (MICs) and Minimum bactericidal concentrations (MBCs) of CSA-13 (prototype ceragenin) and CSA-131 with or without 5% pluronic F-127 were determined as well as conventional antibiotics ceftazidime, cefaperazon, sulfamethoxazole-trimethoprim (SMX-TMP) and levofloxacin. Five different isolates that have lowest MIC results were selected and time kill curve experiments were performed with 1x, 2x and 4x MICs of ceragenins. Also, Minimum biofilm eradication concentrations (MBECs) of ceragenins were investigated against four isolates that have biofilm forming ability.

Results: MIC and MBC ranges, MIC50/MIC90 and MBC50/MBC90 results were shown at Table 1. CSA-131-poloxamer displayed the lowest MICs and MBCs. While seven isolates were determined as susceptible to ceftazidime and SMX-TMP, all of the isolates tested were resistant to cefaperazon. Only one isolate was resistant to levofloxacin. According to time kill curve results, all 4xMICs of ceragenins showed bactericidal activity (3 log reduction) after four hours. CSA-131-poloxamer (320->640 µg/ml) displayed better antibiofilm activity than CSA-131 (2560->5120 µg/ml).

Conclusions: CSA-131-poloxamer with 5% pluronic F-127 had better antimicrobial properties than CSA-131 and CSA-13 against S. maltophilia. For treatment of S. maltophilia infections, CSA-131-poloxamer can be potential antimicrobial agent.

Table 1: In vitro antimicrobial activities of ceragenins

<table>
<thead>
<tr>
<th>Ceragenins</th>
<th>MIC (µg/ml)</th>
<th>MBC (µg/ml)</th>
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<tr>
<td></td>
<td>MIC Range</td>
<td>MIC50</td>
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<tr>
<td>CSA-13</td>
<td>8-32</td>
<td>16</td>
</tr>
<tr>
<td>CSA-131</td>
<td>2-4</td>
<td>2</td>
</tr>
<tr>
<td>CSA-131-poloxamer</td>
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</table>

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Abstract 3490

Heterogeneity of Clostridiodes difficile infection testing and the impact on missed diagnoses: results from COMBACTE-CDI

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Abstract third-party references: on behalf of the COMBACTE-CDI consortium

\textbf{Background:} ESCMID guidelines for CDI diagnosis largely focus on the diagnostic method, not the testing rate. Here we investigate the impact of both testing rates and methodology on detection of cases in hospitalised patients.

\textbf{Materials/methods:} Sites were recruited from 12 European countries (1 site/3 million population). On two days, all diarrhoeal faecal samples (regardless of tests requested) were sent to the European coordinating laboratory (ECL) for toxin testing and culture. The CDI results/test-not-requested at each original submitting site were compared with the ECL results to determine the number of missed cases. Additional information on testing rates and methodology was collected from the sites via an online questionnaire. Estimates of missed cases/10,000 pbds for each site, country and European region were calculated.

\textbf{Results:} There was wide heterogeneity in testing methods, and 100/105 (95\%) used more than one test to diagnose CDI; 16/105 (15\%) did not detect toxin, including 9/16 sites in France. There was wide variation in testing rates in hospital based facilities across European countries; country range 20.4-218.6 tests/10,000 pbds/site. There was also wide variation in case rates; country range 2.5-27.9 cases/10,000 pbds/site. The average number of missed cases ranged from 0.0-8.8/10,000 pbds/site, with the highest in Romania (8.8 missed cases/10,000 pbds/site) and Sweden (6.52 missed cases/10,000 pbds/site). These countries also had the highest proportion of sites using one only CDI test - Sweden (single molecular test) and Romania (standalone toxin EIA).

The site CDI rate in Northern Europe was 3-fold higher in sites using methods that did not directly detect faecal toxin, compared with those using at least one toxin detection test (18.1 vs 6.4 case/10,000 pbds/site) (Figure 1). In addition, the missed CDI case rate was twice as high in the former sites (4.9 vs 2.1 missed cases/10,000 pbds/site respectively).

\textbf{Conclusions:} Heterogeneity of testing impacts not only on reported CDI rates, but also on the number of cases that are missed. Missed CDI rates were higher in countries using single tests, or tests that did not detect toxin, suggesting important potential consequences of not following current ESCMID recommendations.
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Figure 1. Testing and CDI rate by European region in countries that use any tests (A), at least one test detecting toxin (B), and test(s) that did not detect toxin (C).

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Abstract 3492

Combined inhibition of CD14 and C5 in *Escherichia coli* and Group B streptococci induced inflammation in human cord blood

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Abstract third-party references: Nordlandssykehuset, UiT - The Arctic University of Norway, HelseNord

Background: *Escherichia coli* (*E. coli*) and Group B streptococci (*GBS*) are the main causes of early-onset neonatal sepsis (EONS). Treatment with antibiotics is not always sufficient to inhibit a massive systemic inflammatory response, associated with increased morbidity and mortality. Activation of CD14 and the complement system have important roles in this inflammatory response, and are therefore potential targets for novel therapy in order to prevent harmful effects. Studies indicate that combined inhibition of CD14 and complement (C5) may attenuate Gram-negative bacteria-induced inflammation, but less is known about their roles in Gram-positive infections. The objectives with this study are to first compare inflammatory response between *E. coli* versus *GBS*, with a focus on complement activation and cytokines, in an EONS-human cord blood model. Second, to assess the efficacy of the combined inhibition of CD14 and C5 in the same model.

Materials/methods: Human cord blood from term infants (*n* = 30) is anti-coagulated with lepirudin. A combination of anti-CD14 and eculizumab (C5 inhibitor) is added 8 min prior to or 15 min or 30 min after adding *E. coli* (ATCC 33572) or *GBS* (SO-SAG18-1). Total incubation time for the experiments is 120 min. Cytokines and the terminal complement complex (TCC) are measured using multiplex technology and ELISA.

Results: The combined regimen of anti-CD14 and Eculizumab totally blocked complement activation (TCC) when supplemented 8 min prior to adding the bacteria. For the post-challenge time-points 15 min and 30 min we found a 70-80% and 60-70% reduction in complement activation (TCC), respectively.

Conclusions: Preliminary results show that the combined CD14/C5 inhibition in this EONS-human cord blood model dramatically reduces the complement activation induced by both *E. coli* and *GBS*. The study is ongoing, and complete data on cytokine response and the results from the combined inhibition in the post-challenge experiments will be presented. Future studies in animal models are the next steps to evaluate a potential future clinical role for this therapy in severe cases of EONS.

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Abstract 3493

A quality improvement project to increase influenza vaccination uptake amongst inpatients in a tertiary care centre supported by Electronic Healthcare Records (EHR)

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Background: Influenza infection is an important cause of morbidity and mortality; vaccination remains the single best preventative public health initiative[1]. Much of the focus to date has been on community-delivered vaccination. In 2015 there was a large outbreak of nosocomial acquired influenza infection in St James’s Hospital. A subsequent audit performed in 2017 focused on the vulnerable Medicine for the Elderly inpatient cohort. This audit concluded that less than one quarter of eligible patients received vaccination and many patients had cognitive impairment. Best practice in administering vaccination to patients with cognitive impairment is to inform both patients and their next-of-kin (NOK).

The primary aim was to increase inpatient vaccination uptake amongst eligible inpatients with prolonged length of stay (LOS).

Materials/methods: An action learning quality improvement approach was used, based on iterative Plan-Do-Study-Act (PDSA) cycles. Data was collected using the EHR system for inpatients under the care of a single Medicine for the Elderly consultant. Patients included were those over 65 years old and with length of stay (LOS) greater than 21 days. Baseline characteristics collected included gender, age, LOS and documented Mini Mental State Examination (MMSE) score.

Results: 71% of patients were male, mean age was 82 (68-90). Mean LOS was 84 days (34-111). Of those with a documented MMSE score, 100% scored < 24 indicating mild cognitive impairment.

For the primary group studied, 98% of patients’ NOKs raised no objections to proceeding with influenza vaccination. 12% declined fearing an adverse reaction. Of 88% of these patients, 75% were themselves agreeable and received influenza vaccination. Opportunistic education on the benefits of influenza vaccination was provided to all patients, their NOK and staff.

Conclusions: While influenza vaccination strategies are predominantly and appropriately focused on primary care, prolonged inpatient admission necessitates consideration of this important public health intervention. EHR aided in timely and efficient identification of patients who required vaccination. The learning from this primary PDSA cycle will be extended to other patient cohorts at risk of influenza and other in-patient and out-patient vaccination programmes to include pneumococcal vaccination.

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Abstract 3496

Public health implications of prevalent antibiotic resistance genes and integrons in commensal Escherichia coli inhabiting a major Indian river

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Background: Rapid emergence of antibiotic resistance (AR) is a major global public health concern. Due to lesser clinical implications, commensal strains of Escherichia coli are less studied than pathogenic strains. The current study aimed to investigate the prevalence of AR and integrons in commensal E. coli isolated from river Yamuna, Delhi India.

Materials/methods: Eighty-three well-characterized E. coli strains of phylogroups A and B1 were studied. Antibiotic susceptibilities to major classes of antibiotics viz. β-lactams, aminoglycosides, tetracycline, quinolone/fluoroquinolone, and chloramphenicol were assessed according to CLSI guidelines. The strains were also tested for extended spectrum β-lactamases (ESBL) and AmpC production. Resistance determinants to β-lactamases (blaTEM, blaSHV, blaCTX-M, blaOXA, blaCMY-42) aminoglycosides (rmtA, rmtB, rmtC, armA, str, aacC2) tetracycline (tetA, tetR, tetM, tetW), plasmid mediated quinolone resistance (PMQR) (qnrA, qnrB, qnrC, qnrD, qnrS, qep, aac), integrons and variable gene cassette arrays were PCR-characterized.

Results: Resistance profiling revealed high prevalence of ampicillin resistance 95% (n=79) followed by cefazolin 45% (n=39). About 15% (n=12) strains were resistant to tetracycline. Approximately 19% strains were multidrug resistant and 15% (n=12) were ESBL producers. AmpC production was not detected. Co-resistance to fluoroquinolone and ESBL antibiotics was observed in 6% (n=4) of the strains. blaTEM was the most widespread (95%) gene followed by blaOXA (15%). Genes conferring resistance to aminoglycoside viz. str and armA were detected in 5 and 7 E. coli strains, respectively. Genes tetA and tetR genes which confer resistance to tetracycline were detected in 3 and 5 E. coli strains, respectively. The PMQR gene qnrS was detected in 15% of the strains investigated. The upstream of blaCTX-M had insertion sequence ISEcp1 and orf477 in the downstream region. intI gene of class 1 integron was detected in 64% (n=53) isolates. Of the 53 intI harboring strains, 7 strains had variable gene cassettes. Sequencing revealed the presence of aacA4, catb3, dfrA1, aadA1, dhfr1, and aadA2 gene arrays. None of the strains had class 2 and 3 integrons.

Conclusions: The presence of antibiotic resistance genes (ARGs) and integrons along with co-existence of ESBL and PMQR genes in aquatic E. coli suggests that these strains might serve as reservoirs for transmission of ARGs to other bacteria.

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The female reproductive tract microbiome and its relationship with infertility and hydrosalpinx

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Background: The vaginal microbiome has been thoroughly investigated but little is known on the upper female reproductive tract microbiome. Hydrosalpinx, a blocked edematous fallopian tube, is a known cause of infertility and may result from previous pelvic infections, endometriosis or post-surgical adhesions. However, the role of the microbiome in this process is yet unknown. This study aimed to describe vaginal and fallopian tube microbiota (VM, FTM) in 32 women undergoing surgery for hydrosalpinx or other indications.

Materials/methods: We studied 9 cases that underwent salpingectomy for hydrosalpinx (due to recent pelvic infection and/or infertility) and 23 controls that underwent surgery that included salpingectomy for other indications. Samples for VM and FTM were obtained and subjected to DNA extraction and high-throughput 16S rRNA gene amplicon sequencing. Bioinformatics analysis was carried out using the QIIME software package (v1.9.1). Microbial alpha-diversity was calculated using Shannon index, with Kruskal-Wallis used for group significance tests. Differences in mean taxonomical abundance were calculated using t-test.

Results: The mean age of studied women was 41 (range: 29-54). Alpha diversity as measured by Shannon index was significantly different between FTM and VM in controls (3.365 vs. 1.7 1 7, p<0.005), but not cases (2.7 vs. 2.45, p=0.77). A significant difference was found between the VM composition of cases and controls (2.45 vs. 1.77, p=0.027) as well as in the FTM composition between the groups (p=0.0002). Figure 1 shows abundance at phylum level; Firmicutes (including Lactobacillus) dominated in VM of controls. Notably, the average relative abundance of the genus Lactobacillus in all VM samples was 63% vs. 8% in FTM (p<0.0001). Lactobacillus relative abundance in cases and controls was 52% vs. 68% (p=0.3) in VM samples, and 2% vs.10% (p=0.1) in FTM samples, respectively.

Conclusions: Vaginal and fallopian tube microbiota are altered in women undergoing salpingectomy for hydrosalpinx as compared to other indications. This may reflect dysbiosis associated with recent pelvic infections or altered upper genital micro-environment of blocked fallopian tubes. This observed dysbiosis warrants further study, with particular focus on the possible contribution of microbial composition to the pathogenesis of hydrosalpinx and associated infertility.

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Improving the adequacy of empirical antimicrobial therapy at regional level in bacteraemia due to *Escherichia coli* of urinary source: an intervention of the VINCat programme (Infection control and antimicrobial stewardship Catalonian programme)

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Abstract third-party references: VINCat Program [Infection Control and Antimicrobial stewardship Catalonian Program].

**Background:** to analyze the changes in the adequacy of empirical antimicrobial therapy to local guidelines, in bacteraemia caused by *E. coli* of urinary source in Catalan hospitals along a three-year period. The impact of a voluntary survey asking for analyzing local results and implementing correction measures was also analyzed.

**Materials/methods:** Multicentric prospective observational study including all episodes of *E. coli* bacteraemia of urinary source, between May 2017 and September 2019, in adult hospitalized patients in 45 Catalan hospitals. Adequacy of the empirical therapy (AET) to local guidelines was prospectively recorded. A survey evaluating local results of 2017-2018 and asking for correcting measures was sent to the hospitals at the end of 2018. Percentages of AET in 2017, 2018 and 2019 were compared by means of chi squared test.

**Results:** 3,804 episodes of bacteraemia were recorded. 845 in 2017, 1,861 in 2018 and 1,098 until 30/09/19. Globally, AET to guidelines increased from 73.7% in 2017 to 78.2% in 2019 (p=0.06). Interestingly, in the 24 hospitals responding to the survey, the AET increased significantly from 72.9% in 2017 to 79.9% in 2019 (p=0.009), while in those who did not respond, adequacy did not change (76.7% in 2017, 75.1% in 2019, p=0.90). In the 24 responding hospitals, improvement of adequacy was especially important in ambulatory healthcare-associated infections (65.7% in 2017 vs. 72.2% in 2018, p=0.050) and in hospital-acquired infections (56.7% in 2017 vs. 79.9% in 2019, p = 0.0001). Correction measures applied were: meetings with the antimicrobial stewardship team to evaluate the results (100%), review of local resistance rates (62%), review of local guidelines (58.3%), improving guidelines diffusion (75%), education sessions for improving guidelines adherence (58%), and analysis of adherence after education (65%).

**Conclusions:** Adequacy of empirical antimicrobial therapy to local guidelines for the treatment of patients with bacteraemia caused by *E. coli* of urinary source improved from 2017 to 2019 in Catalonia, but only in hospitals answering a voluntary survey for improving adequacy. Improvement of the adequacy was more important in ambulatory healthcare associated infections and hospital-acquired infections.

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Abstract 3501

Pulmonary sparganosis: a case report with 20 months follow-up
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Background: Sparganosis is a zoonotic parasitic disease caused by the sparganum of Spirometra species. Pulmonary sparganosis had seldom been reported. Currently, the efficacy of antiparasitic therapy is uncertain, only surgical resection is recommended in Sanford Guide. However, surgical resection is unsuitable for multiple visceral lesions. Here we present a case of pulmonary sparganosis with multiple lesions, the patient was treated with praziquantel and had been followed up for 20 months.

Materials/methods: A 43-year-old woman from Guangdong China present at April 2018, complained of cough and low-grade fever for one month, and a subcutaneous nodule about 1cm x 1cm in size was palpated in the right thigh. Chest spiral computer tomography (CT) showed multiple lung lesions. Bronchoalveolar lavage and thoracoscopic pulmonary nodule biopsy were performed for suspected of pulmonary aspergillus or tuberculosis. The histologic examination of the pulmonary nodule revealed tapeworms. Antisparganum antibody was detected in serum by enzyme-linked immunosorbent assay. Next-generation sequencing (NGS) reported detecting 236 Spirometra erinaceieuropaei nucleotide sequences in bronchoalveolar lavage fluid. Meanwhile, the subcutaneous nodule resection and pathological biopsy also revealed parasite structure, which was identified as sparganum.

Results: The patient was diagnosed as pulmonary sparganosis and cutaneous sparganosis, she was administrated praziquantel 60mg/kg/day and low-dose prednisone (10mg/day) for 10 days. Fever and cough improved rapidly after the treatment, but there was little improvement in lung lesions. Eight courses of praziquantel were given at an interval of 1 or 2 months afterwards, and the last course was at April 2019. The patient is still under follow-up, pulmonary lesions improved gradually even if the treatment had been stopped (Fig 1).

Conclusions: NGS is a promising tool for the rapid and accurate diagnosis of pulmonary sparganosis. Surgical removal is recommended for the treatment of sparganosis, but is impossible for pulmonary sparganosis with multiple lesions. Multiple pulmonary lesions improved gradually after nine courses of praziquantel treatment in this case, suggests multiple courses of praziquantel may be an alternative treatment for surgically unresectable cases.

Fig 1 Sequential imaging of chest spiral CT. Sequential imaging from April 2018 to August 2019 reflects the changes of lung lesions after multiple courses of praziquantel.

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Abstract 3502

**Antibiotic utilisation and carbapenem-resistant *Acinetobacter baumannii*: a 12-year time series and cross-correlation analysis**

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**Background:** Carbapenem-resistant *Acinetobacter baumannii* (CRAB) is endemic in many hospitals causing nosocomial infections. Reducing carbapenem usage is one control strategy. We observed declining incidence density of CRAB after ten years of antimicrobial stewardship programme in a university teaching hospital in Singapore. We investigated the temporal relationship between antibiotic usage and CRAB incidence density.

**Materials/methods:** Monthly utilisation of antibiotics in defined daily doses (DDD) and CRAB incidence per 1,000 patient-days from January 2007 to December 2018 were obtained from the hospital’s database. Each time-series was pre-whitened to account for autocorrelation. An autoregressive integrated moving average (ARIMA) model was fitted to an antibiotic utilisation time-series filtered to obtain white noise residuals. The CRAB incidence time series was also filtered with the same model. We then computed the cross-correlation function (CCF) between the filtered time-series for each antibiotic use and CRAB incidence at lags up to 12 months. We investigated the lag in the CCF at which the peak correlation of statistical significance (p<0.05) occurred, so as to determine the lead time of antibiotic utilisation relative to CRAB incidence.

**Results:** The monthly incidence density of CRAB reduced significantly from 0.45/1,000 patient-days in 2007 to 0.14/1,000 patient-days in 2018, at a rate of -0.003/1,000 patient-days per month (p<0.001). CRAB incidence was correlated with beta-lactams with beta-lactamase inhibitors (BLBLI) utilisation (0.19, p=0.02) among major antibiotic groups. No significant correlation was found with fluoroquinolones (-0.14, p=0.09) and carbapenems (-0.13, p=0.13). Utilisation of individual antibiotics like co-amoxiclav (0.21, p=0.01), ceftazidime (0.20, p=0.02), ceftriaxone (0.17, p=0.04?) and clindamycin (0.18, p=0.03) were also correlated with CRAB incidence. The lead time at which peak correlation occurred was 2 months for BLBLI, co-amoxiclav and clindamycin, 10 months for ceftazidime and 11 months for ceftriaxone.

**Conclusions:** BLBLI, co-amoxiclav, clindamycin, ceftriaxone and ceftazidime correlated significantly with CRAB incidence density, but not fluoroquinolones and carbapenems. Reducing a single antibiotic class may not be effective in controlling the incidence of CRAB.

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Abstract 3504

High-level AmpC beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae in Dutch hospitals and livestock farms: results from the i-4-1-Health project

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Abstract third-party references: i-4-1-Health Study Group

Background: High-level AmpC beta-lactamase-production in Escherichia coli and Klebsiella pneumoniae (HL-AmpC-Ec/Kp) is emerging as antimicrobial resistance mechanism and is based on mutations in the promoter/attenuator of the chromosomal AmpC gene (cAmpC) or plasmid-located AmpC genes (pAmpC). This study aimed to determine the prevalence of HL-AmpC-Ec/Kp among patients in Dutch hospitals and in livestock farms.

Materials/methods: In 2017/2018, HL-AmpC-Ec/Kp prevalence surveys were performed in 2 hospitals, 16 pig farms and 14 broiler farms in the South of the Netherlands. Perianal swabs (human) or fecal swabs (livestock) (FecalSwab, CopanItaly) were pre-enriched in a non-selective tryptic soy broth (CopanItaly) and subsequently cultured on an AmpC screening agar plate (McC, cefoxitin 8mg/L, cefotaxime or ceftazidime 1mg/L, Mediaproducts). MastDiscs (D68C, MastGroup) were used to confirm AmpC-production. Whole-genome sequencing of phenotypic AmpC-producing Ec/Kp was performed on a MiSeq (Illumina), followed by de novo assembly with SPAdes v3.9.1 and whole-genome multilocus sequence typing (wgMLST) with SeqSphere (Ridom). ResFinder v3.1 (CGE) was used to detect acquired-resistance genes and chromosomal mutations.

Results: A total of 370 patients were cultured. Of those, 12 (3%) were carrier of HL-AmpC-Ec/Kp. Mutations in the cAmpC promoter were identified in 7 Ec isolates and pAmpC (blaCMY-4, blaDHA-1) in 3 Ec and 2 Kp isolates. HL-AmpC-Ec/Kp isolates from patients were clonally unrelated. From 16 pig farms and 15 broiler farms, 128 and 119 cultures were obtained, respectively. HL-AmpC-Ec was detected on 2 pig farms (prevalence 60% and 70%) and 6 broiler farms (prevalence 10% to 90%). Mutations in the cAmpC promoter were present in all 10 HL-AmpC-Ec isolates from pig farms and in 2 (10%) of 21 HL-AmpC-Ec isolates from broiler farms. The other 19 (90%) broiler Ec isolates carried pAmpC (blaCMY-2). Five within-farm wgMLST clusters of 2 to 8 HL-AmpC-Ec isolates were identified in two pig farms and one broiler farm (Figure).

Conclusions: Rectal carriage of HL-AmpC-Ec/Kp was low among patients in Dutch hospitals. The prevalence of HL-AmpC-Ec/Kp in varied between livestock farms and livestock species. The genetic diversity of HL-AmpC-Ec/Kp isolates was high, with clusters of clonally-related isolates within farms, but not between farms, patients or between the human and veterinary domain.

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Abstract 3506

Clinical and economic impact of three different strategies for the management of schistosomiasis in Sub-Saharan immigrants to Italy

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Background: Recently an increased migration flow from Sub-Saharan Africa (SSA) to Europe and Italy has been recorded. Schistosomiasis, highly prevalent in migrants from SSA, can lead to irreversible complications if left untreated. Italian guidelines and the European Centre for Disease Control and Prevention recommend a serological screening for schistosomiasis in migrants from SSA. However, studies on clinical and economic impact of this strategy in the Italian and European setting are lacking. This study aims to compare benefits and costs of different strategies to manage schistosomiasis infection in Italy in migrants from SSA.

Materials/methods: A decision tree and a Markov model was developed to assess the health and economic impacts of three interventions for schistosomiasis: a) passive diagnosis of symptomatic patients (current practice in Italy); b) serological screening of all immigrants and treating those positive; c) presumptive treatment for all immigrants with praziquantel in a single dose. The time horizon of analysis was one year, to investigate the punctual expenses, and 28 years, to consider possible sequelae, in the Italian health-care perspective. We assumed that each diagnosed patient will be managed according to the standard of good practice. Inputs data were derived by available literature; costs were taken from the pricelist of Careggi University Hospital, Florence, and from National Hospitals Records.

Results: Assuming a population of 100,000 migrants with a schistosomiasis prevalence of 21.2%, at one year passive diagnosis option is the least expensive, costing €709,042. Screening option (€4,512,018) is more expensive than presumptive treatment (€2,848,212). At 28 years the cheapest option is presumptive treatment (€6,958,223) while the passive diagnosis and screening strategy accounts for €7,775,631 and €9,331,608, respectively. Considering the cost/QALY presumptive treatment appears the more favorable intervention compared with the passive diagnosis.

Conclusions: The results of model suggests that presumptive treatment strategy compared with the current strategy are more favorable from an economic point of view.

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Abstract 3508

Which anatomic sites should be screened for carbapenem-resistant Acinetobacter baumannii?

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Background: Acinetobacter baumannii is a global, multidrug-resistant nosocomial pathogen causing severe infections in hospitals and long-term care facilities. Active surveillance for carbapenem-resistant Acinetobacter baumannii (CRAB) has been recommended to control the spread of CRAB. Early and accurate identification of carriers is important to effectively direct infection prevention measures. We aimed to identify the best anatomic sites and method of screening for CRAB.

Materials/methods: This evaluation was conducted in two centers in Israel: adult wards at Tel-Aviv Sourasky Medical Center (TASMC); and the chronic ventilation ward at Beit-Rivka (BR), a subacute care facility. CRAB screening was performed for routine active surveillance. Our sample included only patients who screened positive in at least one anatomic site. Four anatomic sites were cultured: buccal mucosa and rectum using swabs, skin using pre-moistened sponges, and sputum using tracheal aspirate (from ventilated patients only). Study specimens were transferred to the National Center for Infection Control laboratory. Samples were inoculated after overnight enrichment in brain-heart infusion broth onto CHROMagar MDR Acinetobacter plates, and incubated overnight. Suspected colonies were further identified to the species level, and susceptibility testing performed. We compared yield by anatomic site using a test of proportions.

Results: We analyzed data from 201 patients who screened positive for CRAB; 100 from TASMC and 101 from BR. Yield by body site is presented in Table 1. The site with the highest yield was skin (92%), and yield was similar in both facilities (91% at TASMC, 92.8% at BR, p=0.64). In carriers whose skin screened negative for CRAB, the buccal mucosa was positive in 9/10 (90%), rectum in 2/4 (50%), and sputum in 2/7 (28.6%). The buccal mucosa, sputum, and rectum had much lower yields, even when combined (Table 1).

Conclusions: Our data support culturing the skin using pre-moistened sponges as a single site for active surveillance of CRAB. A negative screening culture from the other sites had unacceptably high false negativity, and may not be taken as evidence for CRAB non-carriage when directing an infection control program for CRAB.

Table 1: CRAB screening yield among 201 patients positive for CRAB, by body site.

<table>
<thead>
<tr>
<th>Site</th>
<th>No sampled</th>
<th>No positive</th>
<th>Yield (%; 95% CI*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buccal mucosa</td>
<td>136</td>
<td>85</td>
<td>62.5 (54 - 71)</td>
</tr>
<tr>
<td>Sputum</td>
<td>110</td>
<td>54</td>
<td>49.1 (39 - 59)</td>
</tr>
<tr>
<td>Skin</td>
<td>197</td>
<td>181</td>
<td>91.9 (87 - 95)</td>
</tr>
<tr>
<td>Rectum</td>
<td>169</td>
<td>80</td>
<td>47.3 (40 - 55)</td>
</tr>
<tr>
<td>Buccal+Skin</td>
<td>136</td>
<td>136</td>
<td>99.3 (96 - 100)</td>
</tr>
<tr>
<td>Buccal+Rectum</td>
<td>107</td>
<td>74</td>
<td>69.2 (59 - 78)</td>
</tr>
<tr>
<td>Skin+Rectum</td>
<td>165</td>
<td>159</td>
<td>96.4 (92 - 99)</td>
</tr>
<tr>
<td>Sputum+Rectum</td>
<td>99</td>
<td>62</td>
<td>62.6 (52 - 72)</td>
</tr>
<tr>
<td>Sputum+Skin</td>
<td>106</td>
<td>101</td>
<td>95.3 (89 - 98)</td>
</tr>
</tbody>
</table>

* CI - confidence interval

Conclusions: Our data support culturing the skin using pre-moistened sponges as a single site for active surveillance of CRAB. A negative screening culture from the other sites had unacceptably high false negativity, and may not be taken as evidence for CRAB non-carriage when directing an infection control program for CRAB.

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Management and cost-analysis of a *Klebsiella pneumoniae* carbapenemase-producing cluster in the cardiac intensive care unit in Vicenza hospital, Italy  

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**Background:** *Klebsiella pneumoniae* carbapenemase-producing (KPC) is a Gram-negative bacterium resistant to a wide spectrum of beta-lactam antibiotics. It can cause infections, sepsis and deaths in immunocompromised or fragile patients. Patients can acquire this microorganism mainly through the healthcare workers' hands or through environment or devices. In December 2017, KPC was detected in several patients admitted to a Heart Rehabilitation Centre, who were previously discharged from the cardiac surgery department of Vicenza Hospital.

**Materials/methods:** The hospital infection and prevention control team immediately carried out an epidemiological investigation. The index case was identified as a patient admitted to the cardiac intensive care unit and previously hospitalized in a clinical ward where KPC cases had been detected. The screening method for KPC was implemented, adding a rectal swab at discharge to identify patients who acquired KPC colonization during the hospitalization. An on-site inspection was carried out and environmental samples were performed. Contact isolation measures were applied for all patients. Staff education and training were provided to underline the importance of hand hygiene and contact precautions. An increased number of medical equipment and devices was acquired and most of them were dedicated to single patient use. An extraordinary sanitation of the department was carried out and additional cleaning measures were adopted.

**Results:** From 1 January to 31 October 2018, 1527 rectal surveillance swabs were performed on 682 patients admitted to cardiology surgery department and 104 patients were identified as colonized (15%). Most positive patients were detected in the first four months of the year, cases gradually decreasing during the following months. The hospital had to bear huge economic costs due to environmental sanitization and cleaning measures enhancement, the purchase of medical devices and enormous quantities of equipment for contact isolation and disinfection. The total amount due to the KPC cluster was approximately € 139.282.

**Conclusions:** Some critical issues had emerged in the cardiac intensive care unit during the cluster. Staff education raised awareness on multidrug-resistant microorganisms among healthcare workers and, together with the enhancement of preventing and hygiene measures and the use of patient-dedicated equipment, it led to the successful resolution of the cluster.

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Abstract 3511

**Vertical and horizontal dissemination of an IncA/C plasmid harbouring rmtB 16S-rRNA methylase conferring resistance to amikacin and plazomicin among KPC-producing Klebsiella pneumoniae in a Brazilian tertiary centre**

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**Background:** Carbapenemase resistant KPC-producing K. pneumoniae (KPC-KP) infections are among the most important clinical challenges, and not least in middle-income countries, where novel beta-lactams/beta-lactamase inhibitors are often not available. Remaining antimicrobial options are often restricted to “old antibiotics” such as aminoglycosides and polymyxins.

**Materials/methods:** We studied a collection of 125 KPC-KP strains isolated from bloodstream infections between 2014 and 2016 at the Hospital São Paulo, a Brazilian teaching hospital, where KPC-2 KP is endemic. All isolates were typed by MLST and a subset of representative strains were fully sequenced (Illumina MiSeq, MinIon long-reads). Susceptibility to the commonly used aminoglycosides amikacin and gentamicin were determined by agar dilution according to EUCAST recommendations. Susceptibility to plazomicin (E-test), a new aminoglycoside, and to apramycin, a veterinary approved aminoglycoside were investigated to evaluate alternative treatment options.

**Results:** Forty-nine (39%) of the 125 KPC-2-KP isolates showed high resistance to both amikacin and gentamicin. Genomic analysis revealed that 95% of aminoglycoside resistant were carrying the 16S-methylase rmtB. Among the rmtB positive, 43 strains (91%) belonged to the ST258 clone, representing 95% of all KPC-ST258 isolates. Presence of rmtB was also confirmed in one ST16 isolate. Plasmid sequence assembly of the two different ST type isolates revealed that rmtB was harboured by a highly similar 175-177 kb IncA/C2 plasmid (>95% identity) suggesting clonal dissemination of a rmtB-positive, KPC-2-positive ST258 clone and horizontal transfer to the ST16 clone. All the strains carrying rmtB were fully resistant to the new aminoglycoside plazomicin [MIC >256mg/L], but remained susceptible to veterinary approved apramycin [MIC range 4-8mg/L].

**Conclusions:** Herein, we report the clonal spread of a KPC-2 producing rmtB-positive ST258 in a tertiary hospital, and we documented a case of horizontal acquisition of the IncA/C2 plasmid by an ST16 KPC-KP isolate. Dissemination of the rmtB 16S-rRNA methylase plasmid in the endemic setting for KPC-producing K. pneumoniae CC258 clones is worrisome, since it provides resistance to most aminoglycosides approved for human usage including new therapeutic options as plazomicin. Human drug development of apramycin like molecule could be of great interest for the treatment of these multi-drug resistant clones.

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Imipenem/sulbactam, a repurposed drug combination for the treatment of MDR Acinetobacter baumannii infections

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Background: Multi-drug resistant (MDR) Acinetobacter baumannii are an increasing cause of nosocomial infection in the severely ill. Limited treatment options has renewed interest in repurposing older antibiotics in unorthodox combinations. The potential of IMP / SUL as a novel β-lactam / β-lactamase inhibitor combination was assessed both in-vitro and in-vivo.

Materials/methods: Antimicrobial susceptibility testing was performed on 119 MDR A. baumannii with imipenem (IMP), sulbactam (SUL), and fixed ratios of IMP / SUL (2:1, 1:1, 1:2) by disc diffusion. Minimum inhibitory concentrations (MIC) were determined for 57 strains by agar dilution using IMP / SUL (1:1 and 1:2). Monte Carlo simulation of human pharmacokinetic (PK) / pharmacodynamic (PD) data was used to predict therapeutic success (PTA > 60% / TA≥MIC) of bolus, extended or continuous infusion dosing regimens of 3-8g / day, modelled across putative IMP / SUL breakpoints of ≤16 / ≤0.25 mg/L. In-vivo efficacy of IMP / SUL was assessed using a Galleria mellonella therapy model with humanised dosing regimens of IMP / SUL (25 mg/kg).

Results: IMP / SUL (1:1 or 1:2) displayed enhanced activity against A. baumannii with 4 - 64 fold reduction in MIC (MIC₉₀ / MIC₉₀ 8/8 – 64/128 mg/L) compared to either drug alone (MIC₉₀ / MIC₉₀ >256 mg/L). PK / PD modelling predicted up to 65% of A. baumannii with IMP / SUL MIC ≤16 / 16 mg/L may be treatable with a high-dose (8g / day) fixed-ratio (1:1 or 1:2) combination. IMP / SUL (25 / 25 mg/kg) was effective in the treatment of 2 MDR A. baumannii-strains in the G. mellonella model but only at low inocula (≤10⁴ cfu / larvae).

Conclusions: IMP / SUL has potential as a repurposed β-lactam / β-lactamase inhibitor combination therapy. If targeted at A. baumannii, MIC and PK / PD simulation data suggest a 1:1 or 1:2 fixed dose regimen of 3-8 g of IMP / SUL would be required to treat 90% of IMP resistant strains with an IMP / SUL MIC of up to 8 / 8 mg/L. Extended or continuous infusion of both compounds would be needed to optimise a precise dosing regimen.

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Non-carbapenem beta-lactams for the treatment of Acinetobacter baumannii bacteraemia: a multi-centre retrospective analysis

Giulia La Martire*, Vincent Fihman2, Adrien Galy3, Diane Le Pluart4, Latifa Noussair5, Anne Lise Lecapitaine6, Etienne Canoui7, Anne Lise Munier8, Clemence Richaud9, Charlotte Wemmert1, Raphael Lepeule1

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Background: Unlike the French and American committees (CA-SFM and CLSI), the European Committee for Antibiogram (EUCAST) does not establish clinical breakpoint (CB) for beta-lactam antibiotics other than carbapenems (BL TnC) for Acinetobacter baumannii (Ab). EUCAST considers these CB technically unreliable. On top of it, pharmacokinetic and pharmacodynamic studies highlighted theoretical potential risk for failure of BL TnC in Ab infection treatment. However, BL TnC are often prescribed for treating Ab bacteraemia (Abb) in several French centres. Our objective was to evaluate local habits for Abb treatment and to highlight eventual adverse events linked to these practices.

Materials/methods: This was a multicentre retrospective study in which all patients treated with a BL TnC or carbapenem (CP) for monomicrobial Abb between January 2015 and December 2018 were included. Clinical and microbiological failures and mortality at day 7 and 30 were analysed.

Results: Eight centres participated to this preliminary analysis. A total of 93 patients were screened for eligibility and 22 retained for analysis [details of exclusions are presented in the figure]; 18 patients were treated with BL TnC (82%). Preferred empirical treatments in BL TnC group were piperacilline/tazobactam 7/18(40%) and cefotaxime 6/18(33%) and preferred definitive treatments were cefepime 7/18(40%) and piperacilline/tazobactam 7/18(40%). Patients were relatively young (median age of 56); 10/22(45%) were immunosuppressed, mean Charlson comorbidity index was 3,4; 7/22(31%) of Abb occurred in ICU. Origin of bacteraemia was a central venous catheter in 14/22(64%) of cases. Outcome was favourable in 15/18 patients (83%) in BL TnC group. One patient on palliative care died on day 17, with a secondary NDM Klebsiella pneumoniae bacteraemia, 1 patient had persistent bacteremia cleared after infected catheter removal (he kept on BL TnC), 1 patient presented secondary ESBL E. cloacae bacteraemia. Outcome was favourable in 4/4 in CP group.

Conclusions: Abb is an uncommon event in our setting, and MDR Ab are still rare. Treating these infections with BL TnC appears to be a standard practice in several centers even if EUCAST doesn’t provide clinical breakpoints. We couldn’t highlight adverse events related to this practice in this preliminary analysis. More centers are expected to participate to this study for larger analysis.

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Trends of emerging multidrug-resistant nosocomial strains and development of antimicrobial resistance in the years 2007 - 2018

Jan Koren1, Andrea Longauerová2, Adriana Krajčíková3, Livia Slobodnikova3, Mária Blažeková3, Adriana Liptáková3, Tibor Maliar3, Vladimir Krcmery1

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Abstract third-party references: Study was supported by the project APVV-16-0173.

Background: Global spreading of multidrug-resistant strains should be related to highest national priority for preventive measures in healthcare facilities. Otherwise, developing antimicrobial resistance may be associated with treatment failure and higher mortality. We aimed to assess occurrence of MDR pathogens such as ESBL and carbapenemase-producing Enterobacteriales/Enterobacteriaceae - CPE, MRSA, VRE and Clostridioides difficile toxin A/B as well antimicrobial resistance over the last 12 years.

Materials/methods: Specimens were obtained from patients hospitalized at the University Hospital Bratislava [UHB] Old Town between 2007 and 2018. Resistance mechanisms were detected according to EUCAST guidelines and interpretive breakpoints. C. difficile toxin A/B was proved by immunochromatographic assay. Antimicrobial resistance assessment was relied upon colorimetric micro- and E-test methods including disc diffusion susceptibility testing.

Results: Emergence of ESBL producers in our hospital for investigated years was following: 131, 169, 383, 314, 269, 293, 511, 402, 400, 449, 473 and 504. Confirmed CPE numbers in last years were: 1, 6, 17 and 19. MRSA outcomes accounted for monitored years: 10, 13, 27, 29, 44, 52, 90, 62, 77, 121, 156 and 173. VRE occurrence represented data as follows: 2, 3, 5, 18 and 28 strains. Determined C. difficile toxin A/B findings were: 7, 43, 34, 16, 24, 29, 24, 44, 35, 73 and 129. Klebsiella pneumoniae meropenem resistance in the beginning of period was 1% and in last year 4%. Escherichia coli ceftazidime resistance increased from 11% (2007) to 21% (2018), in Proteus mirabilis from 12% to 15% but in Pseudomonas aeruginosa decreased from 23% to 12%. Staphylococcus aureus oxacillin resistance elevated from 5% to 19% and in Enterococcus spp. vancomycin resistance raised from 0% to 8%.

Conclusions: Analyzed period noticed increasing E. coli and P. mirabilis ESBL-producing strains with established resistance development. Higher prevalence of CPE mostly involved K. pneumoniae NDM strains resulted in resistance to carbapenems. P. aeruginosa resistance decreased to aminoglycosides and no ascertained resistance to colistin at the end of reporting period. C. difficile toxin A/B production, including MRSA and VRE demonstrated increasing trend implying that Staphylococcus aureus with Enterococcus spp. expressed higher resistance.

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Evaluation of two Aspergillus PCR assays testing of bronchoalveolar lavage fluid and serum for diagnosis of chronic pulmonary aspergillosis

Zhengtu Li*, Peiyin Zeng1, Shaoqiang Li1, Zhixian Wang2, Feng Ye1

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Background: Chronic pulmonary aspergillosis has been increasingly reported in patients with underlying respiratory disorders, such as COPD, cavitary pulmonary tuberculosis, bronchiectasis and in patients given glucocorticoids or immunosuppressants. Because of the relatively intact immune system, these patients often display atypical symptoms coupled with non-standard imaging results, making the early diagnosis difficult. Molecular biological diagnostic methods such as PCR for the diagnosis of aspergillosis have the advantages of rapidity, sensitivity and high specificity, and is a research hotspot in recent years. At present, most of the PCR research focuses on invasive aspergillosis patients with immunodeficiency in patients with hematologic malignancies, hematopoietic stem cell transplant recipients and solid organ transplant recipients. There is less research on PCR in Chronic pulmonary aspergillosis. Recently, two multiplex PCR AsperGenius® (Pathonosdics, Netherlands) and MycoMDx™ (Dynamiker, China) have been released to the market. Our purpose was to compare the performance of the two PCR assay in Chronic pulmonary aspergillosis.

Materials/methods: This diagnosis was based on [ESCMID and ERS] guidelines and IDSA guidelines for the management of CPA. All the samples from the First Affiliated Hospital of Guangzhou Medical University. The sample include 20 serum and 15 BALF samples from the CPA patient group, and 30 serum samples from the non-CPA patient group. The samples were tested in parallel using MycoMDx Aspergillus PCR assay and AsperGenius® Aspergillus PCR assay as recommended by the manufacturer.

Results: The sensitivity and specificity of Dynamiker MycoMDx Aspergillus PCR for serum sample were 60% and 77%, respectively. The sensitivity of Dynamiker multiplex PCR for BALF sample were 80%. For the AsperGenius® multiplex PCR assay the sensitivity and specificity of the serum sample in the diagnosis of CPA were 50% and 80%, and the sensitivity of the BALF sample in the diagnosis of CPA were 80%. [Table 1]

Table 1 Diagnostic performance of Dynamiker and AsperGenius multiplex PCR assay

<table>
<thead>
<tr>
<th>Kit</th>
<th>Sample</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dynamiker</td>
<td>Serum</td>
<td>60</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td>BALF</td>
<td>80</td>
<td>/</td>
</tr>
<tr>
<td>AsperGenius®</td>
<td>Serum</td>
<td>50</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>BALF</td>
<td>80</td>
<td>/</td>
</tr>
</tbody>
</table>

Conclusions: The Dynamiker MycoMDx Aspergillus PCR Assay performed satisfactorily and may be considered for routine diagnostic use by medical mycology laboratories to detect the Chronic pulmonary aspergillosis.

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**Abstract 3520**

**Effects of ceragenins to intracellular *Pseudomonas aeruginosa* infections formed in human airway epithelial cells**

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**Background:** Ceragenins are the newly investigated antibiotic candidates. They were synthesized to mimic antimicrobial peptides and it was proven that they had potential antimicrobial properties. However, there is limited information about their cytotoxicity on the human cells. As well as cytotoxicity, their effects of intracellular bacteria in human airway cell is not well known. The aim of this study is to investigate cytotoxicity of ceragenins on A549 cell and effects against intracellular *P. aeruginosa* in A549 cell.

**Materials/methods:** A549 cell which is a human airway carcinoma cell line was growth in DMEM, 10% FBS and 1% penicillin-streptomycin and 1% glutamine. IC₅₀ results of ceragenins were determined by using XTT (the second generation tetrazolium dye) assay. To investigate antibacterial activity of ceragenins against intracellular bacteria, *P. aeruginosa* PA0-1 strain, which has green fluorescent protein, was added to the A549 cell for co-infection. After co-infection, gentamycin was added to the co-culture to kill extracellular bacteria. Then, ceragenins were added and CFU counting was performed while lysising the cells by Triton-X solution. CSA-13, CSA-44, CSA-90, CSA-131, CSA-138, CSA-142, CSA-144, CSA-192 and CSA-131-poloxamer were used as antimicrobial agents.

**Results:** Whereas the most cytotoxic ceragenin was determined as CSA-90 (IC₅₀:18.76 µg/ml), the least cytotoxic agent was CSA-142 (IC₅₀: 94.54 µg/ml). According to IC₅₀ results, 20, 10 and 5 µg/ml concentrations of ceragenins were included to the study to investigate anti-intracellular bacteria activities. Among all ceragenins studied, CSA-13 showed the best activity and decreased 3 log CFU even if 10 µg/ml concentration was used.

**Conclusions:** Ceragenins especially CSA-13 displayed good activity against intracellular *P. aeruginosa* formed in human airway epithelial cells. These results make ceragenins good candidates for treatment of *P. aeruginosa* infections associated with lungs.

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Abstract 3524

Costs and impact of whole genome sequencing on tuberculosis diagnostics in a high prevalence and high MDR-TB burden country

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Background: Genetic resistance testing of tuberculosis (TB) isolates recovered from clinical samples of TB patients will soon become an indispensable tool in TB diagnostics as it is faster and more thorough than phenotypic susceptibility testing. This type of testing can be done by use of either whole genome sequencing (WGS) or targeted sequencing on next generation sequencing (NGS) platforms.

Materials/methods: We report our experiences with the implementation of NGS in the Kyrgyz Republic National Reference Laboratory (NRL), a lower-middle income Central Asian Republic with a TB incidence of 144/100,000 and 30% MDR-TB resistance. The Illumina MiSeq NGS platform was chosen after careful estimation of long-term needs based on epidemiological data. Technology and skill transfer required 68 weeks. Resistance markers were identified using WGS for the first 133 samples, and compared to phenotypic Drug Susceptibility Testing (DST) results when available.

Results: Total procurement costs were 307,157 USD (230,528 USD and 76,629 USD for equipment and consumables, respectively). Costs per sequenced genome were 277 USD during the training phase, and 167 USD and 141 USD after training using the MiSeq® Reagent kits v2 and v3, respectively. NGS was fully implemented in the Kyrgyz Republic in approximately 68 weeks. Two laboratory employees were trained by NGS experts from Forschungszentrum Borstel, they have since trained two additional sequencing technicians. Quality was externally assessed by lab-to-lab comparison of 30 WGSs with outstanding results. A total of 101 of the first 133 samples that were sequenced also had DST, of which 5 samples were identified with at least one additional antibiotic resistance marker using WGS.

Conclusions: The five major lessons we have learned were that: [1] the identification of the optimal platform is a complex process which needs to involve a team of experienced experts in the field; [2] knowledge and skill transfer to the NRL was relatively straightforward; [3] procurement was much more complicated and took longer than expected; [4] material costs per sequence were higher than expected, and [5] the transitioning process should be initiated in an early project phase and demands both financial support and strong guidance.

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Abstract 3525

Serotype, antimicrobial resistance and virulence profile of invasive Streptococcus pneumoniae isolates in a nationwide surveillance study in Lebanon

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Background: Streptococcus pneumoniae infections cause millions of deaths worldwide. Despite the introduction of pneumococcal conjugate vaccines (PCV), pneumococcal disease burden remains high. Pathogenesis of Streptococcus pneumoniae is promoted by various virulence factors providing it with pathogenic advantages. We evaluated the serotype prevalence and antimicrobial susceptibility patterns of invasive isolates in Lebanon over a 14 year period. We also assessed the carriage of seventeen virulence genes and their association with specific serotypes and sites of infection.

Materials/methods: A total of 528 isolates were collected from patients with invasive pneumococcal disease. Identification and antimicrobial susceptibility testing of the isolates were performed. Serotypes were determined using capsular multiplex PCR. Genes coding for Streptococcus pneumoniae virulence proteins were assessed by singleplex PCR including the pneumococcal surface adhesin (psaA), pneumococcal surface protein (pspC), enolase (ena), choline binding protein (cbpE) which occurs by recruitment of host proteases to the bacterial cell surface. We present evidence supporting the role of choline-binding protein E (CBPE, polyhistidine triad (phtA, B, E, D), pneumococcal adherence and virulence factor (pavA), pneumococcal choline binding protein (pcpA), plus islet (Pi-1, Pi-2), neuraminidases (nanA, B, C), immunoglobulin A1 (IgA1) protease, and high temperature requirement (htrA).

Results: Non-susceptibility rates by disc diffusion were the highest for Trimethoprim-sulfamethoxazole (56.6%), oxacillin (52.1%), and erythromycin (30.8%). For oxacillin-resistant isolates, 11.4% were resistant to penicillin (MICs ≥2.0 μg/ml). The PCV-7 and PCV-13 serotypes represented 35.1% and 65.3%, respectively. Three virulence genes (ena, psaA, and nanA) were carried by more than 85% of isolates while 9 genes (phtA, phtB, nanB, nanC, IgA1, pspC, Pi-1, cbpE and pcpA) differed significantly among the predominant serotypes (1, 14, 18, 19A, 19F, 23F, 3, 5, 6A, 9V/9A and 22F/22A). A significant difference in nanC and phtA prevalence was observed between the PCV13 and non-PCV13 serotypes. We did not find a statistical association between the presence of virulence genes and the three sites of infection (bacteremia, meningitis and pneumonia).

Conclusions: PCV13 serotypes were the most prevalent and accounted for the majority of isolates with increased antimicrobial resistance. The virulence genes carriage varied significantly among predominant serotypes without being associated with a preferential site of infection. The common virulence genes (ena, psaA, and nanA) may be evaluated as possible vaccine candidates.

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Abstracts 2020

Abstract 3526

**Unravelling the anti-biofilm mechanism of action of an antimicrobial peptide: an atomic force microscopy study**
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**Background:** Biofilms are three-dimensional communities of bacteria encased in a highly hydrated extracellular matrix that have high impact on public health given their decreased susceptibility to conventional antibiotics. Antimicrobial peptides (AMPs) have been proposed as an alternative to fight biofilm infections. For the development of new antibiofilm peptides, it is essential to understand their mechanism of action. Here, we study the mechanism of action of vCPP2319, a peptide with proven antibacterial activity against bacterial cells in the planktonic and biofilm form, by atomic force microscopy (AFM).

**Materials/methods:** In this work, we started by the optimization of the AFM imaging conditions for the visualization of the biofilm structure. For that, 24h pre-formed Staphylococcus aureus (S. aureus) biofilms were imaged in the presence and absence of glutaraldehyde, used as a fixation agent. Then, the effect of increasing concentrations of vCPP2319 on the morphology of the biofilm was visualized by AFM.

**Results:** Glutaraldehyde fixation preserves the biofilm structure and enables a better visualization of its three-dimensional assembly, thus allowing high-resolution images of the biofilm morphology. The AFM images obtained in presence of the peptide show that vCPP2319 reduce the thickness of the S. aureus biofilm and increase the roughness of their surface.

**Conclusions:** AFM images allow the visualization of vCPP2319 effect on the S. aureus biofilm structure. The peptide act on the bacterial cells, causing a perturbation of the cells membranes and a reduction in the biofilm volume.

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Abstracts 2020

Abstract 3527

**Inhibition of *Candida albicans* biofilms by Gram-negative bacteria and their cell-free supernatants**

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**Background:** Multispecies biofilms, which were mostly formed by polymicrobial species, represent an unexplained and clinically relevant health problem, as a potential infectious reservoir. The biofilm forming ability of *Candida albicans* is a major virulence factor and correlated with increasing mortality and morbidity compared to infections caused by planktonic cells and can be in relation with other microorganisms in infection site and can form biofilm together. Several studies have shown the increasing lethality in the case of polymicrobial biofilms especially *C. albicans* formed between and Gram negative microorganisms. The aim of this study was to evaluate the growth of *C. albicans* in biofilms with four clinically important Gram negative bacteria or their cell free supernatants (SNs).

**Materials/methods:** *C. albicans* (SC 5314), *Acinetobacter baumannii* ATCC 19606, *Pseudomonas aeruginosa* PA01, *Escherichia coli* ATCC 25922, and *Klebsiella pneumoniae* ATCC 700603 strains were used in this study. Polymicrobial biofilms containing *C. albicans* + Gram negative bacteria were formed in 96-well tissue culture-treated polystyrene plate. The anti-biofilm activities of SNs derived from sessile growths of these bacteria, were also tested for inhibitory properties against *C. albicans*. Viability was monitored by CFU assay and a colorimetric method utilizing MTT. Biofilms were visualized using the Olympus CKX41 fluorescence microscope and imaging with Olympus DP72 camera.

**Results:** It was shown that Gram negative bacteria negatively affected and decreased the numbers of *C. albicans* cells (more than 3 log). The anti-biofilm activity was also present in cell free SNs, especially with *P. aeruginosa* SN (near 3 log decrease). MTT test also proved that the metabolic activity of *C. albicans* during biofilm formation reduced. Inhibition of biofilm development of *Candida* cells with Gram negative bacteria and their SNs was confirmed through fluorescence microscopy images.

**Conclusions:** Overall, our study highlighted that Gram negative bacteria can negatively affect *C. albicans* biofilms even with or without cells. Additionally, reducing in *C. albicans* biofilms with cell-free SNs was less than with Gram negative cells, which is suggesting that the physical coexistence of the cells affected *C. albicans* biofilms more.

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Interpretation of WGS data for surveillance of vancomycin-resistant Enterococcus faecium in an endemic setting: challenges and limitations

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Background: The rapid spread of Vancomycin-resistant Enterococcus faecium (VRE) in Europe over the last years led to endemic regions with high colonization and infection prevalences in hospitals. High resolution VRE sequencing methods provide new information, though the interpretation still bears some difficulties. In this study we explored the potential added benefit of incorporating the patient epidemiology within the hospital and colonization status at admission to distinguish between accumulations and outbreaks.

Materials/methods: All VRE isolated from blood cultures in the year 2016, as well as admission screening results of these patients underwent whole-genome-sequencing (WGS) (n=73). Genetic relatedness was determined by SNP distance (≤10) between isolates. The patient movement data along with admission screening was analyzed to identify potential transmissions.

Results: ST177, ST80 and ST203 were the most predominant in our study population. Most patients were rectally screened positive for VRE (30/43, 70%), 60% (18/30) were colonized and infected with the identical clone. SNP analysis of infection and colonization isolates revealed 9 potential transmission clusters. 19 out of 43 (44%) belonged to 5 transmission clusters. Incorporation of prior colonization status revealed that transmission is very likely in only 63% (12/19) of patients in these transmission clusters.

Conclusions: Care should be taken, when interpreting WGS data to investigate transmission, especially in an endemic setting. Although interpretation of WGS data is challenging, incorporation of patient movement data and colonization status by admission screening of high-risk patients may have and added benefit provide additional resolution when interpreting the magnitude of an outbreak in an endemic setting. Furthermore, we urgently need further studies in a multi-center approach to investigate regional spread and local diversity of VRE with the aim to better understand emerge and transmission dynamics of Enterococci.

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Healthcare resource utilisation for treatment of Clostridioides difficile infection across 12 European countries: health economic results of COMBACTE-CDI

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Background: Clostridioides difficile infection (CDI) is one of the leading healthcare associated infections resulting in prolonged hospital length of stay and increased costs. CDI related data of healthcare resource utilization across Europe are scarce.

Materials/methods: A questionnaire to assess current CDI practices and CDI-related costs was sent out in 10/2018 to both hospital and community settings in 12 European countries. Countries were divided into four regions: West (Belgium, France, The Netherlands), North (Ireland, Sweden, United Kingdom), East (Poland, Romania, Slovakia), and South (Greece, Italy, Spain). Bootstrapped CDI related direct costs were expressed in Euro (€), year 2019 values. For international comparison of health expenditures, price level indices published by the Organisation for Economic Co-operation and Development (OECD) were used to ensure comparability of cross-country variations.

Results: Overall, 158 sites participated in the survey, predominantly hospitals (n= 109, 69%) and community physicians (n= 49, 25%). Median overall costs for one C. difficile stool sample test was €21.8 [interquartile range (IQR): €13.8 - €37.2], with lowest and highest values in Northern Europe [€15.0; IQR: €11.6 - €22.9] and Western Europe [€31.9; IQR: €16.2 - €37.6; p= 0.046], respectively. Across Europe, community physicians reported higher median drug costs for a one-day treatment with metronidazole iv [€14.4; IQR: €9.9 - €52.9 vs. €1.9; IQR: €1.4 - €9.5; p= 0.005] and vancomycin [€15.6; IQR: €7.9 - €22.0 vs. €6.5; IQR: €3.7 - €12.8; p= 0.017] compared to the hospital setting. In the pan-European hospital setting, median costs for severe CDI cases treated in intensive care units ranged from €1,437.5/day (IQR: €1,292.7 - €1,839.9) in Eastern Europe to €2,094.7/day (IQR: €1,063.8 - €3,191.5; p= 0.175) in Western Europe. Median costs for one general ward bed-day with isolation measures due to CDI was 2-fold higher in Southern Europe [€769.2; IQR: €567.9 - €1,623.9] compared to Eastern Europe [€324.0; IQR: €166.8 - €690.0; p= 0.010].

Conclusions: Healthcare costs of CDI diagnostic and treatment measures vary markedly in both hospital and community settings across Europe. The impact of the prevalence of hypervirulent strains, severity of illness, and guideline adherence are subject of future health economic evaluations of COMBACTE-CDI.

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Abstract 3530

Non-vancomycin antibiotic resistance genes in vancomycin-resistant *E. faecium*: variation linked to MLST and mismatch between aminoglycoside resistance geno- and phenotypes

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Background: Vancomycin resistant and -variable Enterococcus faecium have been endemic in the capital region hospitals during the last 4-5 years. Many of the isolates are whole-genome sequenced (WGS), enabling investigation of other antibiotic resistance genes than the van genes. We noted disappearance of chloramphenicol resistance (*cat*) and some of the aminoglycoside-resistance (*amgr*) genes, while others of the latter increased in frequency. We therefore scrutinized 232 genomes from 2014-2019 for MLST and resistance genes and studied resistance phenotypes.

Materials/methods: A total of 232 *E. faecium* strains screening isolates from hospitalized patients were collected and whole-genome sequenced in Copenhagen from 2014 to 2019. To predict resistance genes and genotypes ResFinder was used based on WGS data. We screened for phenotype performed on 22 selected VRE strains by testing for susceptibility towards nine antibiotics (streptomycin, gentamicin, tobramycin, amikacin, erythromycin, tetracycline, chloramphenicol, vancomycin) with MIC determination or agar disc diffusion method. ResFinder results were compared with antimicrobial susceptibility testing results.

Results: Amgr genes were linked to MLST, which fluctuated during the period: ST203 (*vanA, erm(B), ant(6)-Ia, tet(M), lsa(A), cat, msr(C), dfrG*) dominated in 2014-18, but was overtaken by ST17 (*vanA, erm(B), ant(6)-Ia, oac[6′]-aph(2′), aph(3′)-III, lsa(A), msr(C), or vanB, erm(B), ant(6)-la, aph(3′)-III, lsa(A), msr(C), dfrG*) and the none-MLST-typeable vancomycin-variable clone (*vanA, erm(A), erm(B), oac[6′]-aph(2′), aph(3′)-III, tet(M), lsa(A), spc, msr(C), dfrG*) as well as a mix of diverse ST80 with fluctuating resistance profile during the later years. *cat* virtually disappeared in isolates from 2015 (96% positive) to 2019 (6% positive). There was complete concordance with pheno- and genotypes for macrolides, tetracycline and chloramphenicol. Discordance with presence of amgr gene combinations and amgr resistance was seen for 14/22 isolates (*oac[6′]-aph(2′), ant(6)-la* and *aph(3′)-III*). This discrepancy was due to presence of pseudogenes, i.e. non-functional genes.

Conclusions: The fluctuation in different non-vancomycin antibiotic resistance genes is in most cases related to shifts in ST-types. The reason for this variation cannot be deduced from antibiotic use in humans alone: Chloramphenicol has not been used in humans for decades except for topical administration in ophthalmology, and aminoglycoside consumption (gentamicin and tobramycin) is decreasing.

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Abstract 3531

**New evidence-based recommendations for cefazolin prophylaxis in patients undergoing cardiac surgery with cardiopulmonary bypass**

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**Background:** Antimicrobial prophylaxis (AP) with cefazolin is central to the prevention of serious wound infections following cardiac surgery. Despite the unique conditions and complex procedures, there is limited data on whether standard AP dosing maintains adequate concentrations during cardiac surgery. Furthermore, there is no guidance on how AP dosing should be adjusted appropriately for reduced renal function. Our goal was to develop and implement a comprehensive cefazolin AP protocol for patients undergoing cardiac surgery with cardiopulmonary bypass (CPB).

**Materials/methods:** Our previous study of cefazolin AP in patients with normal renal function (CrCl > 50 mL/min) concluded that 2 g pre-operatively and every 3 hours (Q3H) during surgery was more appropriate than the Q4H recommended in clinical practice guidelines. In the current study, the pharmacokinetics of cefazolin during cardiac surgery with CPB were described using population-pharmacokinetic modelling (Pmetrics®). Next, Monte Carlo simulations were conducted with relevant patient demographic, pharmacokinetic and surgery data to investigate cefazolin AP regimens for various degrees of renal dysfunction. A new cefazolin AP protocol was constructed and further refined for feasible and practical implementation in the surgical setting.

**Results:** Simulations for the new cefazolin AP protocol are depicted below. Data for prolonged surgery was selected to show the potential for drug accumulation over time. For CrCl’s of 50 mL/min [grey line] to 100 mL/min [black line], the AP protocol incorporated our previously established standard regimen of 2 g pre-operatively and Q3H during surgery. For CrCl’s <50 mL/min, however, that regimen led to significant accumulation with twice the exposure to cefazolin over 24 hours [i.e., area-under-the-concentration curve, AUC24]. Simulation results supported a renal-adjusted regimen of 2 g pre-operatively and at 3 hours; and again at 11 hours for ongoing surgery and CrCl of 20-49 mL/min. The exposure to cefazolin was similar for the standard and renal-adjusted regimens with predicted AUC24 ranges of 1960-3560 mgxh/L and 2570-3880 mgxh/L, respectively.

**Conclusions:** The current study provides evidenced-based dosing recommendations for cefazolin AP in patients with various degrees of renal function undergoing cardiac surgery. The new cefazolin AP protocol was implemented successfully into practice by our provincial cardiac surgery program.

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**Abstract 3537**

**Antibacterial and anti-biofilm activities of mucolytics, alone and in combination with antibiotics against Gram-negative pathogens**

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**Background:** *Pseudomonas aeruginosa*, *Klebsiella pneumonia* and *Acinetobacter baumanii* are the most important Gram negative, opportunistic human pathogens. They cause infections that are difficult to treat because of forming biofilms in the airways and lungs. Because of the biofilm-associated bacteria are not affected by therapeutically achievable concentrations of antimicrobial agents, new biofilm control strategies should be carried out by the researchers. Due to their mucus lysis effects mucolytics are one of the promising agents which are medicines that used to help treatment of airway and lung infections. The aim of this study was to evaluate the antimicrobial and anti-biofilm activities of mucolytics alone and in combination with antibiotics against planktonic cells and mature biofilms of *P. aeruginosa*, *K. pneumonia* and *A. baumanii* strains.

**Materials/methods:** Among mucolytic agents; N-acetyl cysteine (NAC), Erdosteine and Ambroxol, and antibiotics colistin, meropenem, levofloxacin and ceftazime were selected and used in our study. Minimum inhibitory concentration (MIC), Minimum Biofilm Eradication Concentration (MBEC) and fractional inhibitory concentration (FIC) indexes were determined by the microbroth dilution and chequerboard techniques, respectively.

**Results:** The MIC values of mucolytics were within the 3.1-12.5, 3.1-12.5, 1.5-6 mg/L for planktonic *P. aeruginosa* ATCC 27853, *K. pneumonia* ATCC 4352 and *A. baumanii* ATCC 19616 strains, respectively. Also, the MBEC values were determined as 6.25-25, 3.1-50, 1.6->50 mg/L for *P. aeruginosa*, *K. pneumonia* and *A. baumanii* biofilms, respectively. According to these results, however the MBEC/MIC ratios of antibiotics were very high, mucolytics MBEC/MIC ratios were 1-8 fold. When we perform the checkerboard assay, we found the NAC-Colistin combination was synergistic against *K. pneumonia*, and Erdosteine-Colistin against *P. aeruginosa* strains.

**Conclusions:** In this study, we showed that the mucolytics displayed similar MIC and MBEC results due to their possible biofilm lysis effect. Among mucolytics, erdosteine was the most effective agent against not only planktonic cells but also biofilms of the isolates, and it was synergistic with colistin.

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Abstract 3538

Oral versus intravenous antibiotics in the treatment of osteomyelitis in adults: a systematic review and meta-analysis

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Background: The worldwide incidence of osteomyelitis is approximately 21.8 cases per 100,000 person-years. The cornerstone of treatment is prolonged (4-6 weeks) intravenous antibiotic administration. This entails additional cost, inconvenience, and added manpower from the healthcare system. Thus, studies have explored the possible use of oral antibiotics as alternatives to improve patient compliance and reduce costs. Our meta-analysis aimed to compare the efficacy of oral versus intravenous antibiotics in treating adult patients with osteomyelitis.

Materials/methods: Electronic databases (PubMed, Medline, EMBASE, Cochrane Central Register of Controlled Trials, Google Scholar, and Research Gate) from 1966 to November 2019 were searched using the terms "oral antibiotics", "osteomyelitis", "randomized controlled trial". Only studies that directly compared oral versus intravenous antibiotics and confirmed osteomyelitis through biopsy and/or imaging were included. Primary outcome is remission (resolution of symptoms with no relapse and bacteriologic eradication); secondary outcomes, (a) relapse (persistence of the pathogen after treatment) and (b) adverse events. The validity of included studies was assessed using the Cochrane Handbook for Systematic Reviews of Interventions. We performed a random-effects model in Review Manager Version 5.3 with 95% confidence interval. The I2 test was used to assess heterogeneity.

Results: Seven of 89 trials comprised of 1,282 patients were included in the final analysis. All studies included patients with osteomyelitis of the lower extremities. Oral antibiotics used were Ciprofloxacin, Ofloxacin, and Co-trimoxazole; intravenous antibiotics used were deemed appropriate by the infectious disease specialist. Patients were only given either oral or intravenous antibiotics. Results showed an 8% increase in remission rates [RR 1.08 (0.81 to 1.44, 95% CI, Z = 0.52, p=0.60)] with no heterogeneity (I2 = 0%) in the intravenous antibiotics group. However, this was not statistically significant. Furthermore, there was a 62% decrease in relapse rates in the intravenous antibiotics group [RR 1.62 (0.85 to 3.07, 95% CI, Z = 1.47, p = 0.14)] with no heterogeneity (I2 = 0%), but was not statistically significant.

Conclusions: Oral are comparable to intravenous antibiotics in treating osteomyelitis in terms of remission and relapse rates. However, larger and double-blinded trials should be done to generate more robust data to validate these claims.

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Evaluation and monitoring of the prevalence of ESBL-producing Escherichia coli: result from the 1st year of Tricycle Project in Madagascar

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Abstract third-party references: Centre d’Infectiologie Charles Mérieux

Background: Antimicrobial resistance is recognized as a global public health problem. The main objective of this study is to determine the prevalence of extended-spectrum beta-lactamases producing Escherichia coli (ESBL-E.coli) as an indicator of resistance in human, food chain, and environmental sectors in Madagascar, by following the protocol developed by WHO-AGISAR group.

Materials/methods: This pilot study lasted 13 months (April 2018 - April 2019). The human survey was carried out in seven laboratories from the RESAMAD network, in collaboration with local Maternity Hospitals. The rates of ESBL strains among E.coli isolated from patients with bloodstream infections documented by positive blood cultures were assessed in hospitalized patients. In the community, the rate of fecal ESBL-E.coli colonization was determined in healthy pregnant women close to delivery. The search of ESBL-E.coli in food chain was done from the ceca of chickens collected from Antananarivo markets over the year. The environmental component of the ESBL-E.coli surveillance, was realized by collecting upstream and downstream water samples of Ikopa river which crosses Antananarivo, the communal wastewater and the water of slaughterhouse. E.coli strains isolation was done on chromogenic and selective media, followed by indole test for E.coli identification, and by antimicrobial susceptibility testing for ESBL detection.

Results: In the community settings, 176 out of 535 (32.9%) samples from pregnant women, were tested positive for ESBL-E.coli. In hospitals, 310 out of 1,150 blood cultures were positive, of which 16 (5.16%) were ESBL-E.coli. The results of the food chain showed that 155 out of 274 (56.6%) tested chickens were carrying ESBL-E.coli. Seven rounds of environmental water samples were taken along one-year study. On average, ESBL-E.coli was present at a concentration of 1 CFU/100 mL in upstream water, 2.4 log CFU/100 mL in downstream, 4.2 CFU/100mL in wastewater and 4.1 CFU/100mL log in slaughterhouse water.

Conclusions: This study on antimicrobial resistance was effective in measuring a single indicator in three interdependent sectors using a “One health” approach. A follow up over time of this indicator is necessary to better understand risk factors linked to resistance propagation and to monitor the effectiveness of the fight against antimicrobial resistance.

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Clinical validation of an ELISpot-based in vitro diagnostic assay to monitor cytomegalovirus-specific cellular immunity in immunocompromised transplant recipients

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Background: Impaired cytomegalovirus (CMV)-specific cellular immunity (CMV-CMI) is a major cause of uncontrolled CMV reactivation and associated complications in solid-organ and hematopoietic stem cell transplantation (SOT, HSCT). Reliably assessing CMV-CMI is desirable to individually adjust antiviral and immunosuppressive therapy. We demonstrate here the suitability of an IFN-γ ELISpot assay (T-Track® CMV), based on the stimulation of peripheral blood mononuclear cells with pp65 and IE-1 CMV proteins, to monitor CMV-CMI in immunocompromised SOT and HSCT patients.

Methods: Two independent prospective, longitudinal, observational, multicenter studies were conducted, the first one in 86 intermediate-risk (D-/R+, D+/R+) renal transplant recipients [ClinicalTrials.gov ID: NCT02083042], the second one in 154 intermediate- and high-risk (D+/R+, D+/R-, D-/R+) HSCT recipients [ClinicalTrials.gov ID: NCT02156479]. In both studies, patients underwent pre-emptive antiviral therapy, and CMV-CMI, CMV viral load and clinical complications were monitored over approximately six months post-transplantation.

Results: In the kidney transplantation setting, CMV-specific response was reduced following immunosuppressive treatment and increased in patients with graft rejection, indicating the ability of the ELISpot assay to monitor the patients’ immunosuppressive state. Interestingly, median pp65-specific response was 9-fold higher in patients with self-clearing viral load compared to antivirally-treated patients prior to first detection of viral load (p<0.001), suggesting that reactivity to pp65 represents a potential immunocompetence marker. In HSCT recipients, 40/101 (39.6%) patients with a first CMV reactivation experienced at least one recurrent reactivation, mainly in the D-/R+ high-risk group. The positive predictive value (PPV) of T-Track® CMV (patients with a negative test after the first reactivation experienced at least one recurrent reactivation) was 84.2% (16/19) in high-risk patients. Kaplan-Meier analysis revealed a higher probability of recurrent CMV reactivation in high-risk patients with a negative test after the first reactivation [hazard ratio 2.73; p=0.007, Figure 1]. A post-hoc analysis considering T-Track® CMV measurements at day 100 post-transplantation, a time point highly relevant for outpatient care, showed a PPV of 90.0% (9/10) in high-risk patients.

Conclusions: Altogether, the standardized IFN-γ ELISpot assay (T-Track® CMV) is a highly sensitive immune-monitoring tool, suitable for the follow-up of SOT and HSCT recipients, and with a potential use for the risk assessment of CMV-related clinical complications.

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Abstract 3544

**Dual-function antimicrobial laundry supplement and textile coating for the decontamination of healthcare laundry**

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**Background:** In the UK nurses’ uniforms are domestically laundered, posing a threat of cross contamination of healthcare-associated infections. The UK Department of Health recommends washing uniforms at 60°C, however nurses most commonly wash them at 40°C. Bacteria survive on textiles washed at low temperatures; 4.28-4.62 log10 *Escherichia coli* and *Staphylococcus aureus* survived washing at 40°C and cross contaminated other textiles in the wash. Antimicrobial laundry supplements could sanitise textiles and limit cross-contamination. A supplement that deposits an antibacterial coating onto textiles could also reduce contamination between washes. This study aimed to investigate a silver-based antimicrobial textile coating product (Micro-Fresh 1911) as a dual-use antimicrobial laundry supplement and textile coating.

**Materials/methods:** Polycotton inoculated with 10⁸ colony forming units (CFU)/mL *E. coli* or *S. aureus* (type and clinical isolates) were washed with 2% Micro-Fresh 1911 in a domestic washing machine (40°C) and surviving microorganisms enumerated. Washes were conducted with and without soiling and biological detergent. Control washes were water alone.

The antimicrobial activity of polycotton washed with Micro-Fresh 1911 at 40°C was assessed against *S. aureus* and *E. coli* using International Standards Office (ISO) 20645 and ISO 20743 methods. Controls were polycotton washed in water and textile padded with Micro-Fresh 2611.

**Results:** Washing with Micro-Fresh 1911 reduced *E. coli* and *S. aureus* by 7.14-8.08 log₉₀⁰. No cells were recovered from sterile textile, whereas washing with water alone reduced *E. coli* and *S. aureus* by 2.21-4.25 log₉₀⁰ and resulted in 3.13-4.01 log₉₀⁰ CFU cross-contamination. Combining Micro-Fresh 1911 with biological detergent reduced *E. coli* and *S. aureus* by 5.56-6.65 log₉₀⁰.

Fabric washed with Micro-Fresh 1911 was antimicrobial against *E. coli* and *S. aureus* type and clinical isolates according to ISO 20645 and ISO 20743. The antimicrobial coating remained after washing the fabric in water once at 40°C and 73°C.

**Conclusions:** Micro-Fresh 1911 exhibits antimicrobial activity in a 40°C domestic wash and deposits an antimicrobial layer onto polycotton. Micro-Fresh could be employed as an antimicrobial laundering product to reduce microbial contamination of healthcare laundry washed at low temperatures.

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Can machine learning predict a positive blood culture?
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Background: The early detection of bacteria in peripheral blood is relied on to improve patient outcomes and reduce mortality rates associated with bloodstream infections. More effective screening methods for identification of patients with a suspected bloodstream infection are needed to improve on current diagnostic and treatment pipelines. The aim of this study was to evaluate the effectiveness of machine learning for the classification of blood samples, identifying those that contain clinically relevant bacteria in the blood.

Materials/methods: We conducted a preliminary, retrospective study of data from all blood samples collected from hospital patients in 2018, which were analysed by a Sysmex XN-9000 haemocytometer system. Bacteriological data from all blood cultures generated from the same patient group during corresponding hospital admissions was linked to the haemocytometer data. The combined dataset was extremely imbalanced, with blood culture-positive samples representing less than 1% haemocytometer-analysed total. The Python programming language was used, accompanied by open source libraries for machine learning and data analysis.

Results: During this preliminary study, the complete 2018 dataset was split into training, validation and unseen test sets. Classes in each of the sets represent either the absence or presence of the verifiable laboratory outcome i.e. a positive blood culture. Samples belonging to the negative class (absence of positive blood culture) were not stratified further. Only data available from complete blood counts produced by the Sysmex XN-9000 was utilized. The results from the training, validation and test sets respectively had a sensitivity of 0.9359, 0.9275, 0.8974 and a specificity of 0.6721, 0.6737 and 0.6686.

Conclusions: This study demonstrates the potential use of a machine learning-based approach as a screening method to predict the subsequent growth of bacteria in blood cultures, using routinely generated full blood count data up to 24 hours before auto analysers indicate a positive result. These results provide the foundation for future work in this field, and highlight the importance of taking advantage of readily available datasets.

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Automated surveillance of urinary tract infections in a tertiary care hospital in Stockholm

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Background: Healthcare-associated infections (HAI) pose a major burden on the healthcare system and are associated with prolonged hospital stay, increased morbidity, mortality and costs. Healthcare-associated urinary tract infections (HA-UTI) account for about one fifth of all HAI. Traditional surveillance methods are time consuming and resource intensive. We aimed to develop a fully automated surveillance algorithm for HA-UTI.

Materials/methods: The study was performed using electronic health record data from Karolinska University Hospital. Both structured and unstructured free-text data was used. Natural language processing was used for processing free text medical notes. Four algorithms were developed using data from 3700 healthcare episodes with a positive urine culture from July 2010 till March 2011: Algorithm 1) positive urine culture; Algorithm 2) positive urine culture combined with UTI ICD-10 codes; Algorithm 3) positive urine culture combined with presence of fever and/or UTI symptoms; Algorithm 4) algorithm 3 with negation for fever without UTI symptoms by non-correspondent positive blood cultures or relevant ICD-10 codes. Subsequently, these algorithms were validated in 409 episodes with a positive urine culture from January till March 2012. UTI were manually annotated according to the ECDC definitions by trained healthcare personnel.

Results: In the validation set 158/409 (39%) of episodes fulfilled the ECDC HA-UTI definition. In preliminary analyses the four algorithms classified 403, 143, 201 and 169 episodes, respectively as being an HA-UTI. In the table below the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for all four algorithms are shown.

<table>
<thead>
<tr>
<th>Algorithm</th>
<th>Sensitivity (95%CI)</th>
<th>Specificity (95%CI)</th>
<th>PPV (95%CI)</th>
<th>NPV (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Algorithm 1</td>
<td>0.99 (0.96-1.00)</td>
<td>0.02 (0.01-0.04)</td>
<td>0.39 (0.34-0.44)</td>
<td>0.67 (0.30-0.90)</td>
</tr>
<tr>
<td>Algorithm 2</td>
<td>0.41 (0.33-0.48)</td>
<td>0.69 (0.63-0.74)</td>
<td>0.45 (0.37-0.53)</td>
<td>0.65 (0.59-0.70)</td>
</tr>
<tr>
<td>Algorithm 3</td>
<td>0.78 (0.71-0.84)</td>
<td>0.69 (0.63-0.74)</td>
<td>0.61 (0.54-0.68)</td>
<td>0.83 (0.77-0.88)</td>
</tr>
<tr>
<td>Algorithm 4</td>
<td>0.73 (0.65-0.79)</td>
<td>0.78 (0.73-0.83)</td>
<td>0.68 (0.61-0.75)</td>
<td>0.82 (0.77-0.86)</td>
</tr>
</tbody>
</table>

Conclusions: Simple algorithms based on positive urine culture or ICD-10 codes only are insufficient to adequately classify HA-UTI. More advanced algorithms based on text mining of unstructured data to detect symptoms performed better. This study shows that it is feasible to develop fully automated surveillance algorithms based on text mining, with adequate performance, for surveillance of HAI.

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Management of a vancomycin-resistant Enterococcus faecium outbreak in the haematology unit of an Italian hospital

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Background: Enterococci are normally present in the intestinal flora and in the environment. Many of these bacteria develop resistance to antibiotics, such as vancomycin, thus being defined Vancomycin-Resistant Enterococci (VRE). The percentage of vancomycin resistance in E. faecium in the EU has significantly increased in the last years. In Italy, the percentage has reached 18.9% in 2018. Long-term hospitalization, immunodepression and antibiotic therapy represent some of the risk factors for developing a VRE infection. Aim of the study is to report an outbreak investigation and point out strategies to prevent or solve a new potential outbreak.

Materials/methods: VRE screening was performed with rectal swabs. A cluster of VRE colonization was detected in hematology in April 2019. The index case was found to be a patient who had sepsis from VRE in February 2019 with prolonged persistence of colonization. She was subsequently readmitted to the ward several times. Many preventive measures were adopted to avoid the spreading of VRE colonization: cohorting of patients (one filter room, swab + rooms, swab – rooms), sphygmomanometer and phonendoscope per person, oximeter per room, personal protection equipment, food consumption with single-use dishware, disinfectants trolleys outside every room, no common areas, information for patients on hand hygiene. Environmental samples were collected. Moreover, one health and social care worker was employed.

Results: 29 people were colonized in total, 3 patients had VRE sepsis (including the index case). Up to 12 colonized people were hospitalized simultaneously (on a total of 27 beds). The outbreak was contained in about 5 months [April-September], this timing being lower than the estimated average in literature [11 months]. The ward has never been shut down. All environmental samples tested were negative for VRE.

Conclusions: Early detection of colonized patients, strict preventive measures, a good communication among healthcare professionals and between staff and patients/relatives played a crucial role in solving the outbreak. Rectal swabs must be performed at admission to early detect colonized patients in order to adopt supplementary preventive measures. Hand hygiene is one of the most important infection-control measures to be adopted by patients and staff to avoid the spreading of VRE.

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Monitoring enterovirus human infections in Italy: molecular analysis of two recent outbreaks due to Echovirus 30
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Abstract third-party references: This work was partially supported by the grant from the Italian Ministry of Health, CCM, "Monitoraggio della circolazione di enterovirus a supporto delle attività di sorveglianza per il mantenimento dello status polio-free".

Background: The Regional Reference Laboratory (RRL)/WHO Collaborating Centre for polio at the Istituto Superiore di Sanità (ISS) in Italy is involved in all activities to monitor a possible reintroduction of poliomyelitis and to maintain the polio free status. To support polio eradication activities and due to the fact that there is not routine data collection on non-polio enteroviruses in Italy, the RRL started, in April 2019, with the support of the Italian Ministry of Health, the surveillance on enteroviruses that cause human diseases. Lab-capacity for the diagnosis of enterovirus through the country and two recent outbreaks due to Echovirus 30 (E-30) are, here, described.

Materials/methods: A questionnaire to explore the enterovirus diagnosis lab-capacity has been administered through the laboratories identified in each Italian Regions. For surveillance purpose, a dedicated form with the patient’s clinical information is required. Twenty-six enterovirus infections, of which 17 were aseptic meningitis, were reported by the Marche Region and the autonomous provinces of Trento and Bolzano. These enterovirus infections have been studied by sequencing the genomic region of Viral Protein (VP)1 for characterization and possible genomic correlation.

Results: Hospital laboratories in Italy carry out the diagnosis of enterovirus mostly on cerebrospinal fluids and nasopharyngeal swabs using molecular techniques. More than 50 lab-confirmed enterovirus infections have been reported to the ISS from April to September 2019. Over the period, epidemiological investigations and VP1 nucleotide sequences have identified two E-30 outbreaks: the first including 21 cases of E-30 infections in the Marche Region and the second with 5 cases occurring in the autonomous provinces of Trento and Bolzano. The two outbreaks are not correlated to each other.

Conclusions: A great heterogeneity in the lab-capacity to identify enterovirus infections has been highlighted among the Italian Regions. In the first months of surveillance, two different outbreaks of E-30 were identified and confirmed by molecular analysis. Thus underlines the need to monitor the circulation of non-polio enterovirus in the country in order to know the burden of the disease in Italy.

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Abstract 3551

**Validation of Colorex (CHROMagar) Serratia agar on WASP/WASPLab in screening for Serratia marcescens in neonatal intensive care units using the ESwab**

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**Background:** Serratia marcescens is commonly associated with outbreaks in neonatal intensive care units. Investigations of outbreaks require efficient recovery of clinical and environmental isolates to prevent potentially fatal sepsis, meningitis or pneumonia. The objective of this study was to validate a new Colorex™ (CHROMagar™) Serratia agar for neonatal Serratia screening using the WASP™ and WASPLab™.

**Materials/methods:** This study used 579 Serratia surveillance specimens collected with ESwab™ kits processed on the WASP™. Known reference strains (N=105) of Serratia marcescens were also tested. The Colorex™ Serratia agar plates were incubated in the WASPLab™ for 20 hours then imaging analysis was performed. Results were compared to current testing method which uses MacConkey agar. Positive results were confirmed with Vitek MS.

**Results:** Of the 579 samples tested, 6 were positive for Serratia marcescens by the current method using MacConkey plates, versus 24 positives for Serratia species with Colorex™ Serratia agar and the WASP™ and WASPLab™ imaging analysis. 22 identified as Serratia marcescens, 1 as S. liquefaciens and 1 as S. odifera. All 24 isolates were blue in colour and grew heavy on the Colorex™ Serratia agar. 18 specimens showed very light growth of target colour blue colonies that identified as Klebsiella oxytoca, Citrobacter freundii and Enterobacter cloacae. 11 specimens showed a light growth of non-target clear colonies that identified as Proteus, Morganella and Pseudomonas species. 102 known Serratia isolates grew well on Colorex™ Serratia agar with varying blue to blue-green colour. Interestingly, a few red pigmented strains resulted in pink to purple colonies. Colorex™ Serratia agar sensitivity: 100% (95CI 0.61-1) and specificity: 97% (95CI 0.95-0.98).

**Conclusions:** Results showed Colorex™ Serratia agar (CHROMagar™) had a significantly greater sensitivity than MacConkey agar in isolating Serratia marcescens from neonatal surveillance specimens. The use of the WASP for set up provides efficient and consistent processing and WASPLab™ imaging allows for high resolution digital imaging analysis. The WASPLab™ also has the capability to use segregation software to analyze images and put no growth images into a separate screen for rapid resulting.

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Abstract 3552

The role of the eye microbiome in health and disease states of the lacrimal system

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Background: The ophthalmic microbiome remains poorly studied. Nasolacrimal duct obstruction (NLDO), either primary or secondary, leads to stagnant fluid in the lacrimal sac, occasionally leading to dacryocystitis. Dacryocystorhinostomy (DCR) is a surgical procedure creating an alternative path for tear drainage between the lacrimal sac and nasal cavity for alleviating NLDO. We studied the microbiome of these anatomical structures in patients undergoing DCR.

Materials/methods: Samples were taken intraoperatively from 22 patients undergoing DCR, including the conjunctival fornix (F), plica semilunaris (P) and the inferior nasal turbinate (N) from both sides. Samples from the lacrimal sac (L) were taken only from the diseased side. The samples were subjected to DNA extraction and high-throughput 16S ribosomal RNA gene amplicon sequencing. Bioinformatics analysis was carried out using the QIIME software package (v1.9.1). Microbial alpha diversity was calculated using Shannon index, with Kruskal-Wallis used for group significance tests. Beta diversity was calculated using Bray-Curtis dissimilarity and principal coordinate analysis (PCoA).

Results: Of studied patients, 61% were women and the mean age was 49 (range: 19-86). A total of 156 samples were taken from both diseased and healthy sides. The dominant phylum in the ocular surface (F&P) of all studied eyes was Proteobacteria (41%), whereas nasal samples were mainly comprised of Firmicutes (40%). Figure 1 is a PCoA plot including all studied samples, showing the clustering by anatomic site. Shannon diversity did not differ between F and P microbiota, but significant differences were found between the ocular surface and the lacrimal (P=0.03) and nasal (P=0.002) sites. No difference was found between lacrimal and nasal diversities (p=0.55). Comparison between healthy and diseased sides revealed no significant difference between ocular and nasal microbiota on the healthy side (p=0.07), and a significant difference on the pathological side (p=0.01).

Conclusions: The normal nasolacrimal system demonstrates a gradient between ocular and nasal microbiota, representing an ocular surface-nasal cavity microbial continuum. This gradient appears disrupted in patients with NLDO, resulting in demarcation between microbiota of ocular and nasal structures. Whether disrupted microbiota represents an underlying cause or a result of NLDO deserves further study.

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Abstract 3553

Intestinal microbiome in critical care patients: association with patient status and outcome

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Background: Acquisition and infection by multi-drug resistant bacteria (MDRB) remains a major challenge in critical care patients. The role of intestinal microbiome in MDRB colonization resistance has been previously reported but not completely understood. Our aim was to investigate the association of diversity and composition of intestinal microbiota with MDRB colonization, infection and subsequent mortality in critical patients.

Materials/methods: We conducted a prospective study in 277 patients admitted to a 14-bed hepatic intensive care unit (hICU) between July-December 2018. Rectal swabs were obtained at admission to hICU and weekly during hICU-stay. Finally, 170 rectal swabs from 64 patients (minimum 2 rectal swabs per patient) were included for microbiome analysis. Rectal swabs were used to determine the presence of MDRB by plating them on selective media. Bacterial communities were studied by amplifying and sequencing the 16S rRNA gene V3-V4 region on an Illumina Miseq platform. Sequences were filtered and demultiplexed using DADA2, taxonomy was assigned using SILVA-132 and statistical analyses were conducted using QIIME2 and R environments.

Results: Median Charlson comorbidity index among patients was 5 (IQR:4-7), median age was 67 (IQR:55-74) and 52.7% were male. Regarding MDRB intestinal colonization, 20 patients were colonized at admission, 16 patients were colonized during hICU-stay and for 28 patients MDRB colonization was not detected. Microbial diversity and composition were not associated with MDRB colonization or time to colonization. However, lower microbial diversity indexes were significantly associated with suspected clinical infection (p<0.01), confirmed infection by a positive microbiological culture (p=0.04) and fatal outcome post-discharge (p=0.01). Microbial diversity was lower in patients with liver cirrhosis (p<0.01). Higher Enterococcaceae family relative abundance was observed in cirrhotic, infection and fatal outcome groups (Figure).

Conclusions: Despite the limited sample size and patient complexity our results show that lower intestinal microbial diversity is associated with infection and clinical outcome in critical patients. These findings are important and in line with our research hypothesis. Larger prospective studies are required to establish the role of the intestinal microbiome in MDRB colonization and infection.

Figure 1. Shannon alpha-diversity index and bacterial community composition according to clinical factors. Enterococcaceae family relative abundances are shown.

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Abstract 3556

Identification of a multidrug-resistance cluster in clinical isolates of Streptococcus pyogenes that confers resistance to macrolides, lincosamides, tetracyclines, chloramphenicol and co-trimoxazole

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Background: Acquired resistance in Streptococcus pyogenes (group A streptococci; GAS) is mainly mediated by transposons of the Tn916-family. The present study describes the characteristics of GAS with an uncommon multidrug-resistant phenotype to macrolides, lincosamides, tetracycline, chloramphenicol and co-trimoxazole (MLTChSxT).

Materials/methods: Among all GAS clinical isolates collected from 1998-2018 from adults, multidrug-resistant (MLTChSxT) isolates were selected for the present study. Antibiotic susceptibility testing was performed by microdilution. All isolates were subjected to WGS (Illumina MiSeq 2x150pb). The emm-type and MLST were deduced in silico. Acquired resistance genes were initially searched using ResFinder. The genetic environment of the resistance genes was analysed in detail.

Results: Eight out 1027 GAS shared a resistant phenotype MLTChSxT. These isolates belonged to three emm-ST types: emm25-ST350 (n=6), emm81-ST117 (n=1), emm82-ST320 (n=1). All the isolates harboured a multidrug-resistance cluster containing erm[B] (resistance to macrolides, lincosamides, and streptogramins B), aph[3’]III-ant[6]-Ia (kanamycin and streptothricin resistance), cat (chloramphenicol resistance), tet[M] (tetracycline resistance) and dfrF (co-trimoxazole resistance) genes. The erm[B] gene was found into a MAS element together with the aminoglycoside modifying enzymes cluster aph[3’]III-ant[6]-Ia. The tet[M] gene was embedded in a partial Tn916-like structure. The mobilization and replication module was highly conserved among the strains. The multidrug-resistance element was inserted downstream the hsdM or rpmH genes. All the strains harboured different genes necessary for the genetic element mobilization of the T4SS (type IV secretion system).

Conclusions: A new genetic element conferring a multidrug-resistant phenotype has been identified in GAS. The identification of this element with a conserved mobilization structure among clonally unrelated GAS suggests its ability to spread. The presence of resistance mechanisms to different antimicrobials that could be used in the treatment of GAS infections is a matter of concern.

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Delafloxacin in vitro activity in skin and soft tissue infections by methicillin-resistant and levofloxacin-resistant Staphylococcus aureus

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Background: Delafloxacin (formerly W0-3034, ABT492, RX-3341) is a novel fluoroquinolone approval for the treatment of acute bacterial skin and skin structure infections (ABSSSIs) by US Food and Drug Administration (FDA).

The objective was to determine the in vitro sensitivity of delafloxacin against methicillin-resistant Staphylococcus aureus (MRSA) strains resistant also to levofloxacin isolated from clinical samples of patients with skin and soft tissue infections at the Hospital Universitario La Paz. Madrid. Spain.

Materials/methods: Sixty-six levofloxacin-resistant MRSA isolates from clinical samples of patients with skin and soft tissue infections were studied. Microdilution panels Beckman® and delafloxacin Etest Biomerieux® were used for sensitivity study. As a quality control S. aureus ATCC 29213 was used. EUCAST 2018 cut points were used except for delafloxacin. The FDA cut-off points were used for delafloxacin considering MRSA with MIC ≤ 0.25 mg/l sensitive and MIC > 0.5 mg/l resistant. Only one isolate per patient was considered.

Results: The patients presented thirty-five abscesses (53%), twenty-seven surgical wound infection (41%) and four osteoarticular infection (6%). 63.6% of the patients were male and 36.3% female.

The resistance to levofloxacin in the MRSA studied had a MIC 90 > 4 mg/l. Forty-four (66.7%) of MRSA resistant to levofloxacin had a MIC sensitive to delafloxacin (≤ 0.25 mg/l) and fifteen (22.7%) an intermediate MIC (0.5 mg/l). Seven of the MRSA (10.6%) were resistant to delafloxacin.

Conclusions: Only 10.6 % of MRSA resistant to levofloxacin were resistant to delafloxacin.

Delafloxacin could be an alternative for the treatment of Staphylococcus aureus resistant to other fluoroquinolones.

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Surface plasmon resonance as a new tool to measure vaccine response to 13-pneumococcal conjugated vaccine

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Background: the multiserotype ELISA (enzyme-linked immunosorbent assay) pneumococcal test is usually used in clinical laboratories to measure pneumococcal vaccine response in vaccinated patients. However, this approach has some disadvantages: enzyme activity may be affected by plasma constituents, experimental time of approximately 2 hours and substantial intra and inter-laboratory variation observed in quantitative results. In this context, Surface Plasmon Resonance (SPR) could provide a relevant tool for measuring anti pneumococcal capsular polysaccharides (PnP) IgGs generated in vaccinated patients. In our study SPR and ELISA were evaluated for measuring the concentration of anti-PnP IgGs generated in patients vaccinated with the 13-pneumococcal conjugated vaccine (PCV13).

Materials/methods: fast protein liquid chromatography (FPLC) was performed for antibody purification (IgGs). PCV13 was immobilized using amine coupling chemistry. Free amines of diphtheria toxoid (contained in PCV13) were covalently immobilized to a carboxy-methylated CM5 sensor chip. Binding/stability SPR experiments were performed in serum samples.

Results: a strong correlation between anti-PnP IgGs (ELISA) and the SPR signal was obtained (Spearman’s Rho = 0.89). The approach was successfully used to measure the interaction between anti-PnP IgGs and PCV13 and offered further significant advantages over classic ELISA. Thus, it provided additional information regarding the binding and stability of the interaction between anti-PnP IgGs and PCV13, and it was possible to detect and measure sera anti-PnP IgGs in a very short experimental time (2.5 min). Figure 1 shows injection of the patient’s serum an binding between the PCV13 and the anti-PnP IgGs and the sensorgram obtained by SPR. Sensorgram 1 represents RU level obtained in a patient with poor vaccine response and Sensorgram 2 represents RU level obtained in a patient with high vaccine response.

Conclusions: SPR offered an important advantage from a clinical perspective as it was possible to regenerate the sensor and perform approximately 250 of analytical sessions on the same chip, thus resulting in cost-effectiveness over commercial ELISA kit.

Figure 1: serum injection and SPR sensorgram obtained in two patients

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Abstract 3564

Benzylpenicillin gradient tests underestimate MICs for penicillin non-susceptible Streptococcus pneumoniae

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Background: The EUCAST oxacillin 1 μg disk screening test detects all beta-lactam resistance mechanisms in Streptococcus pneumoniae, but it cannot quantify the level of benzylpenicillin (PCG) resistance and a PCG MIC must be performed for screen-positive isolates (oxacillin <20 mm). For MIC testing, gradient tests are often the first choice for clinical laboratories. The objective of this study was to evaluate the performance of commercially available benzylpenicillin gradient tests for S. pneumoniae using broth microdilution (BMD) as reference.

Materials/methods: Benzylpenicillin MICs were determined in 57 S. pneumoniae using gradient test from two manufacturers (Etest®, bioMerieux®; and MIC Test Strip (MTS)® Liofilchem®). Antimicrobial susceptibility testing was performed using MH-F agar from BD® (BBL®) and Thermo Fisher Scientific (Oxoid) in parallel. BMD was performed according to ISO standard 20776-1 on custom Sensititre plates (Thermo Fisher) using MH-F broth. In addition, PCG BMD MICs were performed on 68 S. pneumoniae from 11 external laboratories and compared with the PCG Etest® MICs submitted by the original laboratory. Results were interpreted according to EUCAST Breakpoints v 9.0. Categorical (CA) and essential agreement (EA, MICs within ± 1 dilution of reference) were calculated for each combination of gradient test brand and media.

Results: PCG BMD MICs ranged from 0.016-4 mg/L and 45 of 57 isolates had MICs above the susceptible breakpoint (0.06 mg/L). For both Etest and MTS, MICs were systematically lower than with BMD: 60.5% were 1-3 dilutions below and only 3.5% above (Table 1). There were differences related to brands of gradient test and agar, but categorical errors were observed for all combinations. The tests on isolates from external laboratories (n=68) showed similar results with 66% of the Etest MICs being 1-4 dilutions below the BMD MICs.

Conclusions: Both Etest and MTS systematically underestimate benzylpenicillin MICs in S. pneumoniae. This results in several categorical discrepancies where resistant isolates risk being categorised as false susceptible - even when a large part of the results are within EA. EUCAST has published a warning against the use of benzylpenicillin gradient tests in S. pneumoniae with beta-lactam resistance mechanisms (http://www.eucast.org/ast_of_bacteria/warnings/).

Table 1. Differences in benzylpenicillin MIC for gradient tests compared to reference BMD

<table>
<thead>
<tr>
<th>Benzylpenicillin MIC value</th>
<th>Etest</th>
<th>MTS</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>BBL MH-F</td>
<td>Oxoid MH-F</td>
</tr>
<tr>
<td>&gt;2 dilutions lower</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>2 dilutions lower</td>
<td>2</td>
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</tr>
<tr>
<td>% within EA*</td>
<td>96</td>
<td>86</td>
</tr>
<tr>
<td>mE (non meningitis)</td>
<td>10</td>
<td>13</td>
</tr>
<tr>
<td>VME (meningitis)</td>
<td>5</td>
<td>7</td>
</tr>
</tbody>
</table>

*Essential Agreement (MIC within ±1 dilution of reference BMD)
**minor Error (discrepancies between S/I and I/R)
***Very Major Error (False susceptibility)

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Abstract 3567

Is there any risk factor in terms of mortality in patients with nosocomial colistin-resistant Klebsiella pneumoniae infection?

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Background: Colistin resistance is increasing in Klebsiella pneumonia isolates. In this study, risk factors for mortality were investigated in patients with nosocomial colistin-resistant Klebsiella pneumonia (CoRKP) infections.

Materials/methods: Between January 2014 and October 2019, 105 CoRKP infections were detected in 87 patients. Only the first CoRKP infection was included in the study for each patient. Identification and antibiotic susceptibility tests were performed using VITEK-2 automated system. Colistin resistance verified by Etest. Concomitant diseases, risk factors including invasive devices and procedures were recorded. Risk factors for mortality were compared between death and survival groups.

Results: Study group included 87 patients with CoRKP infection. Of patients, 49 was female (56%), mean age was 67.3±17.457 years. Most of patients were hospitalized in intensive care units (ICU), mean length hospital stay was 84.48±77.555 days. Among CoRKP isolates, 87% had also carbapenem resistance, 95% extended spectrum beta-lactamases. The most common concomitant diseases were hypertension, diabetes mellitus, cerebrovascular disease (44%, 35%, 31%, respectively). Most commonly detected risk factors were central venous catheter, urinary catheter, H2 receptor antagonist use, nasogastric tube, mechanical ventilation (99%, 95%, 93%, 81%, 79%, respectively). Overall mortality rate was 68%. There was no statistically difference between dead and survivor patients according to the gender (p=1.000). Mean age was significantly higher in patients who died compared with survivors (70.8±14.618 versus 60.0±20.728 years, p=0.017). Staying in ward or in ICU was not detected as a risk factor for mortality (63.6% versus 68.4%, p=0.741). We didn’t find any difference in terms of mean length of hospital stay (89.75±62.580 versus 81.98±84.117 days, p=0.665). The presence of carbapenem resistance and ESBL in CoRKP isolates was not found as risk factors for mortality (p=0.741 and p=0.591). We found no difference between the groups in terms of concomitant diseases and risk factors as invasive devices and procedures (p>0.05 for each).

Conclusions: In this study, gender, staying in ward/ICU, length of hospital stay, presence of carbapenem resistance and ESBL, concomitant diseases, invasive devices and procedures were not found as risk factors for mortality in patients with nosocomial CoRKP infections. Mean age was found significantly higher in patients who died.

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Abstract 3568

Genetic diversity of *bla*KPC gene containing IncF plasmids from epidemiologically related and unrelated Enterobacteriaceae

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Background: Knowledge of the within-replicon-group genetic diversity of resistance-encoding plasmids is limited. This study aimed to compare *bla*KPC-containing IncF plasmids of epidemiologically related and unrelated Enterobacteriaceae isolates.

Materials/methods: Short-read sequence data (MiSeq, Illumina, San Diego, US) of two *Klebsiella pneumoniae*, one *Escherichia coli* and one *Enterobacter cloacae* with *bla*KPC-containing IncF plasmids (IncFII(k2) and IncFIB(pQiL)) were available from a previously described KPC-E outbreak in a Dutch nursing home (2013-2014). For the present analysis isolates were additionally sequenced on a MinION (Oxford Nanopore Technologies, Oxford, United Kingdom). Hybrid assembly was performed with Unicycler v.0.8.4, followed by extraction of circular IncF replicon and *bla*KPC-containing contigs from the assembly graph with BANDAGE v.0.8.1. Eight epidemiologically unrelated *bla*KPC-containing plasmids of similar size, GC-content, and replicon group (IncFII(k2) and IncFIB(pQiL)), but isolated in a different country (Greece, Italy, Israel and the US) and year of isolation (between 2006 and 2011), were selected from GenBank. Pairwise single nucleotide polymorphisms (SNPs) were identified using Snippy v.4.4.5. The GenBank plasmid that was first isolated was used as reference genome for the pairwise SNP analysis. All plasmids were annotated using Prokka v.1.13.3. ComParison of gene presence or absence was performed with Roary v.3.12.

Results: The number of SNPs ranged from 0 to 13 between the outbreak plasmids and from 0 to 32 between the outbreak and the unrelated plasmids (Figure 1). A total number of 132 genes were detected, of which 121 (92%) were present in all plasmids. The number of genes being either variably present or absent ranged from 0 to 2 between the outbreak plasmids and from 1 to 8 between the outbreak and unrelated plasmids (Figure 1).

Conclusions: *bla*KPC-containing IncFII(k2)-IncFIB(pQiL) plasmids isolated from epidemiologically related and unrelated Enterobacteriaceae show a high degree of sequence similarity in terms of SNP differences and the number of shared genes. Therefore, judgements on the horizontal transfer of these plasmids based on genetic identity should be made with caution.

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Abstract 3573

Serum lateral flow tests for invasive aspergillosis: a prospective cohort study

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Background: Recently, two lateral flow tests for the diagnosis of invasive aspergillosis (IA) were commercialized and have been evaluated in bronchoalveolar lavage fluid. However, there are no studies on their performance in serum.

Materials/methods: We prospectively collected screening serum samples twice a week from a cohort of hematology patients at high risk for IA, and bronchoalveolar lavage fluid whenever bronchoscopy was performed. We tested the performance of the OLM AspLFD (LFD) and the IMMY Aspergillus galactomannan (LFA) tests on serum and compared it to the serum galactomannan (Platelia Aspergillus Ag, Bio-Rad, Hercules, California, United States) with a cutoff ≥ 0.5. Results from the LFD and LFA were recorded digitally using a dedicated reader (Cube reader, Chembio Diagnostics GmbH, Berlin, Germany).

Results: Between January 2017 and June 2019, we included 266 patients: 5 were eventually classified as proven, and 36 as probable IA according to the 2008 revised EORTC/MSG definitions. Six patients were excluded as they were not classifiable and were started on mould-active therapy for suspected IA. The performance of the LFD and LFA is shown in Table 1. The LFA outperformed the LFD on all parameters (p < 0.05). Serum galactomannan had a similar sensitivity as the LFA (0.45 vs 0.52, p=0.317) and a slightly higher specificity (0.99 vs 0.96, p=0.014). In the subgroup of patients undergoing bronchoscopy due to suspected IA (n=67), we found a prevalence of IA of 61%. The negative predictive value of the LFA was slightly higher in this subgroup (0.54 vs 0.46, p=0.03), whereas the positive predictive value was equally high (0.95 vs 1.00, p = 0.48).

Conclusions: Performance of the LFA in serum was better than that of the LFD. However, in patients undergoing bronchoscopy for suspected IA, the predictive values are clinically similar.

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>LFA</td>
<td>0.49 (0.33, 0.65)</td>
<td>0.96 (0.93, 0.98)</td>
<td>0.69 (0.49, 0.85)</td>
<td>0.91 (0.87, 0.94)</td>
</tr>
<tr>
<td>LFD</td>
<td>0.24 (0.12, 0.40)</td>
<td>0.88 (0.83, 0.92)</td>
<td>0.27 (0.14, 0.44)</td>
<td>0.86 (0.81, 0.91)</td>
</tr>
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Table 1. Performance of the OLM AspLFD (LFD) and the IMMY Aspergillus Galactomannan (LFA) tests in the complete study cohort (n=266), including 95% confidence intervals

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**Abstract 3578**

**Importance of selection of nucleic acid extraction kits for viral nucleic acid extraction**

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**Background:** The extraction and purification of nucleic acids is critical for the molecular detection of viral infection. Although several RNA/DNA extraction kits are available, little information is available on the importance of the selection of viral nucleic acid extraction kits. Here, we compared the viral nucleic acid extraction efficiencies of five commercial kits using culture supernatants from rotavirus (RoV), respiratory syncytial virus (RSV), herpes simplex virus (HSV) and cytomegalovirus (CMV). We also compared the results of viral nucleic acid concentrations measured with NanoDop and Qubit.

**Materials/methods:** The nucleic acid extraction kits used were as follows: QIAamp Viral RNA Mini kit (A kit), QIAsymphony DSP Virus/Pathogen Kits (B kit), QIAamp DSP Virus kit (C kit), QIAamp DNA mini kit (D kit), and QIAamp DNA stool mini kit (E kit) (all QIAGEN, Germany). Supernatants from the cultures of RoV, RSV, HSV, and CMV were extracted in triplicates using these kits. The average yield of each sample was compared using the threshold cycle (Ct) value measured with commercialized real-time PCR assays for each virus, NanoDrop (Thermo Scientific), and Qubit (Thermo Scientific).

**Results:** Based on the results of real-time PCR, QIAamp Viral RNA Mini kit (A kit) and QIAsymphony DSP Virus/Pathogen Kit (B kit) showed higher nucleic acid extraction yield, especially for RNA viruses (average Ct values of A, B, C, D, and E kits: 30.45, 29.93, 33.35, and 34.43 for RoV; 18.48, 18.87, 21.82, 22.55, and 26.02 for RSV; 18.94, 19.60, 21.29, 20.00, and 22.41 for HSV; 28.86, 29.65, 32.61, 29.59, and 32.45 for CMV, respectively). Nucleic acid concentrations measured with NanoDrop were much higher than those measured with Qubit.

**Conclusions:** The extraction performance significantly varied depending on the extraction kit and species of viruses. Nanodrop results for DNA/RNA concentrations extracted from virus-cultured fluids were much higher than those of Qubit. These results may help laboratories to select the best extraction method for viruses and to understand the difference between NanoDrop and Qubit results for measuring viral DNA/RNA concentrations.

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Abstract 3581

Epidemiology and outcomes of microbiologically documented bacterial foodborne infections in solid organ transplant recipients: a 10-year nationwide cohort

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Background: Food-safety measures are generally recommended in solid organ transplant (SOT) recipients. However, little is known about the incidence and outcomes of bacterial foodborne infections after transplantation. We assessed the epidemiology, clinical characteristics and outcomes of bacterial foodborne infections in a nationwide cohort of SOT recipients.

Materials/methods: Patients transplanted between 2008 and 2018 and enrolled in the Swiss Transplant Cohort Study (STCS) were included. In the STCS, infection episodes are prospectively collected after transplantation. Testing for infection is performed at each center as part of routine clinical practice. Data not available in the STCS database were collected retrospectively by chart review.

Results: Among 4405 SOT recipients with a median follow-up of 4.5 years [IQR 2.2-7.3], 157 episodes of bacterial foodborne infection occurred in 143 (3.3%) patients [3.9% [98/2467] kidney, 2.1% [20/944] liver, 4.18% [14/335] heart, 1.5% [6/403] lung, 2.8% [3/106] kidney-pancreas, and 1.4% [2/38] kidney-liver]. The pathogens more frequently identified were *Campylobacter* spp. in 136 (86.6%), followed by *Salmonella* spp. in 16 (10.2%), *Yersinia enterocolitica* and *Listeria monocytogenes* in two (1.3%), and *Shigella* in one (0.6%) episode. Co-infection with enteropathogenic *E. coli* occurred in 3 (1.9%) cases. Resulting incidence rate was 6.37 (95% CI 5.43-7.60) and 0.76 (95% CI 0.46-1.23) per 1000 patient-years for *Campylobacter* and *Salmonella*, respectively. Median time from transplantation to infection was 1.6 years [IQR 0.6-3.3]. Diarrhea (92.7%, 127/137) and fever (37%, 51/137) were the most common symptoms and antibiotics were given in 74.5% (157/211) of cases. Invasive infections were diagnosed in 12 (7.6%) episodes: 9 bloodstream infections [3 *Campylobacter, 4 Salmonella, and 2 Listeria], 2 arthritis [one *Campylobacter* and one *Salmonella* arthritis with bacteremia] and one *Salmonella* aortitis. Hospital and intensive-care-unit admission were required in 42% [66/157] and 4.5% [7/157] of cases, respectively. Two patients [1.4%] died by day-30 after infection [one *Salmonella* aortitis and one *Salmonella* bacteremia] and 180-day graft loss rate was 2.1% [3/143].

Conclusions: Bacterial foodborne infections are common, occur late after transplant, and are associated with significant morbidity in SOT recipients. We observed a high rate of hospitalization and invasive infections, highlighting the essential role of education for food-safety measures in SOT recipients.

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Sputum iron metabolism in patients with cystic fibrosis as a marker of infectious complications

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Background: Today, cystic fibrosis is one of the most common hereditary diseases. The etiology of cystic fibrosis is a mutation of the gene Cystic Fibrosis Transmembrane Regulator (CFTR), which leads to a violation of the synthesis and operation of the protein of the same name. In the respiratory tract, there is a favorable environment for infection with bacteria and the development of inflammation, which can lead to complications (“cepation-syndrome”) and death of the patient. First of all, representatives of non-fermenting gram-negative bacteria such as Burkholderia cepacia complex and Pseudomonas aeruginosa have clinical significance. The aim of the study was to identify in sputum possible markers of infectious and inflammatory complications caused by non-fermenting gram-negative bacteria in the respiratory tract in patients with cystic fibrosis.

Materials/methods: The study analyzed sputum from 97 patients with cystic fibrosis. Sputum culture was carried out on dense nutrient media: 5% blood agar (Bio-Rad), universal chromogenic medium (Bio-Rad), selective medium for cultivation of B. cepacia complex (HiMedia). A MALDI-ToF mass spectrometer (Microflex LT, Bruker) was used to identify the cultures. Biochemical sputum examination was carried out on an automatic biochemical analyzer Cobas integra 400 plus (Roche, Germany).

Results: As a result, 77 (group 1) patients were identified non-fermenting gram-negative bacteria Burkholderia cepacia complex and Pseudomonas aeruginosa, 20 (group 2) other microorganisms. According to the results of biochemical sputum examination, there was a correlation between the detected microorganisms and the indicators of iron metabolism. In group 1 patients in sputum were significantly increased indicators of iron and iron-binding proteins-ferritin and transferrin, compared with patients of group 2. These differences were statistically significant. In group 1, the median iron level was 16.1 mmol/l, in group 2, 3.05 mmol/l. The median ferritin level in group 1 was 831.6 µg/l, in group 2, 45.35 µg/l. The median transferrin level in group 1 was 0.01 g/l, in group 2, 0 g/l.

Conclusions: Thus, indicators of iron metabolism in sputum can be used as additional markers of infectious and inflammatory complications caused by non-fermenting gram-negative bacteria in the respiratory tract in patients with cystic fibrosis.

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Galleria mellonella as a novel in vivo drug discovery platform using bioluminescent KAPE pathogens

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Background: Drug discovery is costly and time consuming. A major rate-limiting factor in drug development is the screening of candidate drugs in a cost effective manner through an appropriate model prior to mammalian testing. The objective of this project is to investigate the feasibility of using research grade Galleria mellonella (TruLarv) as an in vivo model for screening antimicrobials. We aim to establish a protocol for imaging intracellular Acinetobacter baumannii within TruLarv by engineering the bacterium to be bioluminescent. We would then be able to monitor A. baumannii infection within the larvae by the luminescent signal, and assess modulation of the infection when the larvae are dosed with antimicrobials.

Materials/methods: An extensively drug resistant A. baumannii strain was engineered to express the Lux operon (BV642) and a subsequent bioluminescent target mutant was produced (BV647). These strains were tested for growth, luminescence intensity and colistin resistance. BV642 and BV647Δcsm were tested in TruLarv with and without colistin (4 mg/kg). TruLarv were monitored for luminescence signal from bacteria, survival, motility and melanisation.

Results: We were able to visualise bioluminescent A. baumannii within TruLarv and monitor infection over 72 hrs. When the larvae were dosed with colistin and then challenged with either colistin-resistant or colistin-sensitive A. baumannii, we were able to visualise the infection dynamics, with the sensitive strain unable to establish an infection.

Conclusions: We have shown that we can visualise modulation of infection by antimicrobials, in real time, in an in vivo model. Within the Impact2 Eurostars project, we aim to configure the system as an in vivo high throughput drug screen for KAPE strains, allowing faster and more efficient drug discovery, which reduces the number of mammals required for screening by selecting the best drug candidates to be taken forward for further testing.

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A novel pathogenic bacteria Scardovia wiggsiae involved in early childhood caries: ultrastructural characterisation of biofilm by an original scanning electron microscopy protocol

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Background: Recently a newly identified anaerobic Bifidobacterium named Scardovia wiggsiae has been related to the Early Childhood Caries (ECC), a particularly severe manifestation of carious pathology with rapid and disruptive progression, whose microbiota includes a wide variety of bacterial species. This study aims at providing the first ultrastructural morphological characterization of S. wiggsiae and its biofilm, adopting an innovative protocol for scanning electron microscopy (SEM).

Materials/methods: S. wiggsiae DSM 22547 strain was cultivated at 35°C for 48h in anaerobic chamber, transferred in tubes containing discs of bioglass [a material that mimics dentin surface] and incubated for 120 h to allow biofilm growth. S. wiggsiae was investigated for its ability to produce biofilm on polystyrene plate, and biofilm was quantified by crystal violet staining. S. wiggsiae biofilm on bioglass discs was observed at SEM (VPSEM Hitachi SU 3500) after fixation with glutaraldehyde and treatment with a mixture of osmium tetroxide and Ruthenium Red. Samples were mounted on aluminum stubs and dried in a desiccator at 40°C

Results: Based on quantification of the total biomass at 590 nm, S. wiggsiae can be considered a strong biofilm producer. At low magnifications (1000X) in SEM we saw a well preserved biofilm aspect including areas with different surface texture. Very high magnifications (ranging from 10000X to 35000X) allowed to identify bacterial cells embedded in the matrix bulk. Focusing on matrix trabeculae, in both spongy and granular areas, it was possible to distinguish an heterogeneous density. Biofilm matrix surface was irregularly dotted with small globular aggregates. At extremely high magnifications also the surface appeared irregular due to the presence of very fine globular aggregates of matrix components. Where matrix was less dense, numerous and intimately packed bacteria were visible. In these areas the ultrastructural morphology of the individual bacterial cells could be appreciated. Cell length and diameter were measured.

Conclusions: We report the first ultrastructural description of S. wiggsiae biofilm and the morphology of the bacterial cells embedded in biofilm. To this aim an innovative and unusual protocol for SEM analysis was adopted.

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Abstract 3586

**Which is the best progressive multifocal leukoencephalopathy risk stratification strategy in natalizumab-treated patients affected by multiple sclerosis?**

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**Background:** The risk of progressive multifocal leukoencephalopathy (PML), a brain infection caused by John Cunningham virus (JCPyV), is the main limitation to the use of natalizumab, highly effective in the treatment of relapsing remitting multiple sclerosis (RRMS). Establishing the PML risk against expected benefits represents an obligatory requirement of MS treatment algorithms. In order to achieve this goal, the aims of this study were to establish if JCPyV DNA detection and NCCR arrangements could play a role of biomarkers, supporting anti-JCPyV antibodies measurement, actually the only parameter for PML risk stratification.

**Materials/methods:** Thirty RRMS patients, in treatment with natalizumab, were enrolled. Urine and blood samples were collected according to natalizumab treatment calendar (baseline or 0 infusions) and every 4, 8, 12, 16, 20 infusions. In detail, 30 urine, 30 plasma and 30 peripheral blood mononuclear cells (PBMC) samples were obtained, for a total of 540 specimens. After JCPyV-DNA extraction, a specific quantitative-PCR (Q-PCR) and arrangements’ analysis of NCCR and VP1 was carried out.

**Results:** Q-PCR detected JCPyV-DNA in urine and blood from baseline to 20 months of natalizumab treatment, although JC viral load in urine was significantly higher compared to viremia, at all selected time points. A contextual analysis of the anti-JCPyV-antibodies versus JCPyV-DNA detection displayed that viral DNA preceded the antibodies’ presence in the serum. At T0, only 1 patient exhibited anti-JCPyV-antibodies and viral DNA in plasma and in PBMC, simultaneously. At T3, although the number of anti-JCPyV-antibodies-positive patients increased, all RRMS patients presented JCPyV-DNA. Sequences isolated from blood showed an archetype JCPyV NCCR structure with the occurrence of point mutations. At T3, a NCCR reorganization was observed in plasma and PBMC with duplication of box C and deletion of box D. VP1 analysis showed a prevalence of genotypes 1A and 1B. Phylogenetic analysis suggested a stability and a similarity across different isolates of the JCPyV VP1.

**Conclusions:** Given our real-life laboratory experience we highly recommend considering JCPyV-DNA detection and NCCR reorganizations as viral biomarkers in order to accurately identify JCPyV-infected patients with a specific humoral response not yet detectable and to identify NCCR arrangements correlated with neurovirulent variants.

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Characterisation of the human cytomegalovirus genome diversity in longitudinally collected breast milk samples

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Background: Shedding of human cytomegalovirus (HCMV) into breast milk (BM) is very common in HCMV-seropositive mothers and a key transmission route for postnatal HCMV infection leading to potentially severe disease in preterm neonates. Little is known about the HCMV population composition or dynamics in BM from immunocompetent donors.

Materials/methods: We performed high-throughput sequencing (HTS) directly from 23 BM samples (obtained between day 10 and 60 after giving birth) from 13 mothers with HCMV-DNA lactia recruited for the BlooMil study (Tuebingen). Target-enriched sequencing libraries were prepared using HCMV-specific RNA baits covering the known HCMV genome diversity and HTS carried out on an Illumina MiSeq sequencer. Consensus sequences were assembled de novo. The HCMV genotype distribution and number of strains present in each sample were determined by quantifying genotype-specific sequence motifs of 12 hypervariable viral genes (RL5A, RL6, RL12, RL13, UL1, UL9, UL11, UL73, UL74, UL120, UL146, and UL139) using the Virus Analysis Tool Kit (https://github.com/centre-for-virus-research/VATK).

Results: We observed a wide range of different genotypes for the 12 hypervariable viral genes in the cohort (75 out of 109 possible genotypes). Multiple infections involving up to 3 HCMV strains were detected in 3 out of 13 mothers. In contrast to most participants, these three mothers had stated their country of origin as being outside Germany. Analysis of longitudinal time-points for individual mothers (data available for 8 women) revealed stable genotype compositions over time, i.e. shifts in the abundance ratio of the identified genotypes were observed but no superinfections.

Conclusions: HTS revealed a remarkable genotypic complexity of HCMV with longitudinally stable intra-individual population compositions in BM in this cohort of immunocompetent women of predominantly European origin. BM as a main source of transmission may serve as repository for viral diversity. In contrast to studies in transplant recipients or HIV-infected patients with a different risk pattern for acquisition of multiple HCMV infections, analyzing BM from healthy mothers with HCMV reactivation opens an opportunity to study the “natural” epidemiology of HCMV in immunocompetent adults.

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Pharmacodynamics of amikacin and fosfomycin combination therapy in neonatal sepsis modelled in a hollow fibre infection model

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Background: Antimicrobial resistant pathogens in neonatal sepsis cause an estimated 214,000 deaths annually, rendering the empiric antimicrobial regimen recommended by the World Health Organisation, amoxicillin and gentamicin, increasingly ineffective in a global context. One potential replacement combination for an empiric treatment regimen is fosfomycin and amikacin. We characterised the pharmacodynamics of this combination using a hollow fibre infection model (HFIM) of neonatal sepsis.

Materials/methods: Both amikacin and fosfomycin were assessed in a HFIM using a CTX-M14-producing E. coli and neonatal pharmacokinetic parameters. A 4x4 matrix combination HFIM experiment using dosages of amikacin and fosfomycin that achieve 20%, 50%, and 80% of maximal bacterial killing as monotherapy was performed over 96 hours. Further 7-day 2x2 matrix HFIM experiments using candidate neonatal clinical regimens were performed on six MDR Gram-negative strains (all with MICs above the EUCAST breakpoint to fosfomycin and/or amikacin) to assess the potential real-world performance of the regimen.

Results: The 4x4 matrix experiment demonstrated: (i) a dose-response relationship in terms of bacterial killing and prevention of emergence of resistance in the monotherapy arms; (ii) attainment of complete bacterial killing and prevention of emergence of resistance in the combination arms at lower doses of amikacin and fosfomycin than in the monotherapy arms.

The 2x2 matrix experiments demonstrated: (i) failure of monotherapy to kill where the minimum inhibitory concentration (MIC) was above the EUCAST breakpoint; (ii) initial killing with subsequent regrowth and emergence of resistance in 6/7 arms treated with monotherapy where the MIC was below the EUCAST breakpoint; (iii) sustained kill with no emergence of resistance with combination therapy in 3 strains with a fosfomycin MIC of <32mg/l or an amikacin MIC of <8mg/l; (iv) Failure to kill in all arms in 2/3 strains with a fosfomycin MIC of ≥32mg/l and an amikacin MIC of ≥8mg/l.

Conclusions: These experiments demonstrate the potential value of an amikacin-fosfomycin regimen for treatment of neonatal sepsis. There is a protective effect of the second antimicrobial agent in terms of prevention of emergence of resistance, enhanced antibacterial activity, even with organisms with an MIC to one agent that is above current EUCAST breakpoints.

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Abstract 3591

**Antibiotic utilisation and incidence rate of extended-spectrum beta-lactamases: a 12-year time series and cross-correlation analysis**

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**Background:** Extended-spectrum beta-lactamases (ESBL) can be selected by various antibiotics, with extended-spectrum cephalosporins (ESC) and fluoroquinolones frequently associated. We observed significant reduction in ESC and fluoroquinolone usage over ten years of antimicrobial stewardship programme (ASP) in a public university teaching hospital in Singapore. We aimed to investigate the temporal relationship between antibiotic usage and ESBL *Escherichia coli* and *Klebsiella pneumoniae*.

**Materials/methods:** Monthly utilisation of antibiotics in defined daily doses (DDD) and incidence of third-generation cephalosporin-resistant (3GCR) *E. coli* and *K. pneumoniae* per 1,000 patient-days from January 2007 to December 2018 were obtained from the hospital's database. Each time-series was pre-whitened to account for autocorrelation. An autoregressive integrated moving average (ARIMA) model was fitted to an antibiotic utilisation time-series, which was filtered to obtain white noise residuals. The incidence time series of 3GCR organisms was filtered with the same model. The cross-correlation function (CCF) was computed between the filtered time-series for each antibiotic use and 3GCR organism incidence at lags up to 12 months. We investigated the lag in the CCF at which the peak correlation of statistical significance (p<0.05) occurred, to determine the lead time of antibiotic utilisation relative to incidence of 3GCR organisms.

**Results:** The monthly incidence of 3GCR organisms fluctuated with no apparent underlying trend between year 2007 and 2018. Monthly range was 2.64/1,000 patient-days to 5.71/1,000 patient-days (mean of 3.99, standard error=0.17). Among major antibiotic groups, utilisation of ESC comprising third- and fourth-generation cephalosporins (0.22, p=0.01) was most significantly correlated with incidence of 3GCR organisms. Utilisation of antibiotics like ertapenem (0.22, p=0.01), imipenem (-0.17, p=0.04), levofloxacin (0.18, p=0.03) and ceftriaxone (0.22, p<0.01) was each correlated with incidence of 3GCR organisms. The lead time at which peak correlation occurred was 0 month for imipenem, 1 month for ESC and ceftriaxone, 5 months for ertapenem and 8 months for levofloxacin.

**Conclusions:** ESC, ceftriaxone, imipenem, ertapenem and levofloxacin usage significantly correlated with 3GCR *E. coli* and *K. pneumoniae* incidence density. Community transmission of ESBL may explain minimal impact of the ASP on ESBL incidence in the hospital.

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Abstract 3593

Detection of carbapenemases in *Pseudomonas* and *Acinetobacter* by the Mast Carba PAcE kit

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**Background:** The objective of the study was to evaluate the performance of the Carba PAcE kit, a new rapid colorimetric test proposed for the detection of carbapenemases in *Enterobacteriaceae*, *Pseudomonas* spp. and *Acinetobacter* spp. (OXA-23 positive only). This test includes a chromogenic cephalosporin, HMRZ, combined with beta-lactamase inhibitors of classes A and C, respectively.

**Materials/methods:** 164 carbapenemase-producers (104 *Pseudomonas* and 60 *Acinetobacter*), representative of the French epidemiology, were studied as well as 78 control strains, not susceptible to imipenem (58 *Pseudomonas* and 20 *Acinetobacter*). The tests were carried out according to the supplier’s recommendations and read by 2 operators after 10 and 30 minutes of incubation at 35°C. An orange or red colour was interpreted as the production of a carbapenemase, and a yellow colour as a negative result.

**Results:** After 10 and 30 minutes of incubation, the test was positive for 90 (86.5%) and 98 (94.2%) of the 104 carbapenemase-producing *Pseudomonas* strains, respectively. At 30 minutes, only 1 strain (GES-27) remained negative while 5 strains (GES-5) gave rise to an equivocal yellow-orange colour, not interpretable according to the supplier’s criteria, which turned into orange after 60 minutes. At 30 minutes, 4 control strains expressing an extended-spectrum oxacillinase (1 OXA-14, 2 OXA-35 and 1 OXA-19) were misjudged as carbapenemase producers, while 4 others could not be classified (1 GES-1, 1 OXA-17, 1 PSE and 1 VEB-1/OXA-10). In *Acinetobacter*, the sensitivity and the specificity of the test were 75% and 95%, respectively. Almost all strains positive for carbapenemase OXA-23 (n=26/27) or OXA-24/72 (n=7/8) were correctly detected, unlike those producing OXA-58 (n=3/7) and NDM-1 (n=1/9).

**Conclusions:** Carba PAcE is a reliable and rapid test for the detection of carbapenemases in *Pseudomonas*. After a prolonged incubation (60 minutes), the test was able to detect GES-5 producers, that are usually screened negative by most colorimetric assays. Furthermore, Carba PAcE could identify >95% of *Acinetobacter* harbouring class D carbapenemases found in France and Europe, but should be supplemented with a test for class B beta-lactamases in the event of negative result.

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Abstract 3601

**Systemic inflammation and activation of immunity in HIV-positive patients receiving antiretroviral therapy**

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**Background:** Antiretroviral therapy (ART) does not always lead to improvement the quality of life of HIV-positive patients due to development of systemic inflammation. Aim: to study the markers of systemic inflammation (MSI) and immune activation in HIV-positive patients receiving ART.

**Materials/methods:** The study included 276 HIV-positive patients receiving ART in the age of 39.4±8.2 years, the observation period was 5.4±2.1 years. Patients were divided into 2 groups depending on the CD4+T-lymphocyte counts after 6 months of ART: Group 1 has CD4 level less than 350, group 2 - more than 350 cells/mcL. The concentration of lipopolysaccharide-binding protein (LBP), procalcitonin and cytokines (TNF-α, IL-1β, IL-6, IL-8, IL-10, INF-γ, INF-α) was determined in serum. Parameters of the cellular immunity were detected by flow cytometry. The specific features of changes in the phenotype of CD4 + and CD8 + lymphocytes were determined by the expression of immunological markers CD38, RO, RA, HLA-DR.

**Results:** More high level of MSI and increased immune activation were detected in the 1st group compared to the 2nd. The concentration of LBP in the 1st group was 87.1±6, in the 2nd - 73.6 ± 2.8 μg/ml (p <0.05). In the 1st group, the level of IL-6, INF-γ and INF-α was significantly higher than in the 2nd group (4.9±0.7 versus 3.8±0.3 pg/ml; 32.6±2. against 23.4±3 pg/ml; 12.2±1 against 9.2±0.6 pg/ml, respectively, p <0.05). The proportion of activated lymphocytes with the phenotype CD3+/CD8+/CD38+/HLA-DR in the 1st group was also more higher than in the 2nd group (27.2±2.2% versus 21.5±1.3%, p <0.05). No significant difference was found for other studied parameters (PCT, TNF-α, IL-1β, IL-8, IL-10).

**Conclusions:** Even after several years of effective ART, immunological disorders, elevated MSI were found in a significant proportion of HIV-positive patients, which indicates the presence of additional, uncontrolled by ART, mechanisms that accelerate the progression of the disease. To predict the progression of HIV infection, it is advisable to determine the concentration of the anti-endotoxin protection marker (LBP) in the blood, the level of pro-inflammatory cytokines (INF-γ, INF-α and IL-6), as well as the percentage of activated CD3+/CD8+/CD38+/HLA-DR cells.

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Antibiotic use at the end-of-life in patients with advanced cancer: a systematic literature review

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Background: Improving the use of antibiotics across the care continuum will be necessary as we strive to protect our patients from antimicrobial resistance. One potential target for antimicrobial stewardship is during end-of-life (EOL) care of patients with advanced cancer. We aimed to perform a systematic literature review measuring the burden of antibiotic use during EOL care in patients with cancer.

Materials/methods: We searched PubMed, CINAHL, and Embase through July 2019 for studies with the following inclusion criteria in the initial analysis: (1) end-of-life patients [cancer, dementia, organ failure, frailty or multi-morbidity]; (2) antibiotic use in the EOL care; with the final analysis restricted to (3) patients with advanced cancer. Risk of bias was evaluated using the Downs and Black score.

Results: Of the 93 full-text articles, 21 studies (22.5%) met the selection criteria for further analysis. All the included studies were retrospective (n=17) or prospective (n=4) cohort studies. These studies in combination included 34,971 patients with advanced cancer. Fifteen studies (4,439 patients, [12.7%]) included patients with any type of cancer (solid or hematologic malignancy). In sixteen studies where data was available, less than one sixth of patients (12.3%, 4,317) with advanced cancer were referred to palliative care. In fourteen studies more than 50% of patients received antibiotics during end-of-life period. Fourteen studies did not report the duration of antimicrobial therapy. None of these studies reported the antimicrobial consumption in days of therapy per 1,000 patient-days. Only eleven studies examined whether the use of antibiotics was associated with beneficial outcomes [survival or comfort], and one of them evaluated potential adverse effects associated with antibiotic use. Studies had high risk of bias, with scores (up to 28 points) ranging from 4 to 20 with a median of 12.

Conclusions: There are significant gaps in the literature surrounding antimicrobial use at the EOL in patients with advanced cancer. Future studies are needed to evaluate the benefits and harms of using antibiotics for patients during EOL care in this patient population.

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Abstract 3606

**Antimicrobial activity of XF-73 against clinically relevant Gram-positive bacteria**

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**Background:** Antimicrobial resistance is a global health issue and the need for new, effective antimicrobials is crucial. The synthetic dicatonic porphyrin, Exeporfinium chloride (XF-73), is a proprietary, clinical stage drug with a novel bacterial membrane-acting mechanism of action. In addition, XF-73 is an antimicrobial agent with photosensitising potential, able to generate singlet oxygen and free radicals which may further enhance its antimicrobial activity following exposure to blue light. The aim of the current study was to determine the antimicrobial efficacy of XF-73 against a range of clinically relevant Gram-positive bacteria in the presence and absence of blue light.

**Materials/methods:** Minimum inhibition concentrations (MIC) and minimum bactericidal concentrations (MBC) were determined by micro-broth dilution in Mueller-Hinton Broth in accordance with the Clinical and Laboratory Standards Institute (CLSI) guidelines. The panel of Gram-positive bacteria consisted of: *Staphylococcus aureus* ATCC 6538, *Staphylococcus aureus* ATCC 29213, *Corynebacterium striatum* ATCC 1293, *Staphylococcus epidermidis* ATCC 12228 and *Enterococcus faecalis* ATCC 29212. Enhancement of XF-73 activity following exposure to blue light was investigated by placing the inoculated microtiter plate on the surface of a Waldmann Therapy System light box incorporating 36W Blue bulbs (emission peak 420 nm) for 15 minutes prior to incubation (light dose 13.7 J/cm²).

**Results:** XF-73 demonstrated significant intrinsic antimicrobial activity against the panel of test bacteria with MICs ranging from 0.25 – 0.125 μg/mL. MBCs recorded for all bacteria equated to the MIC values thus demonstrating bactericidal activity. Following exposure of XF-73 to blue light, the MICs and MBCs were significantly reduced with an approximate 8-fold reduction (0.25 – 0.03 μg/mL) for *E. faecalis*.

**Conclusions:** XF-73 has potent bactericidal activity against Gram-positive bacteria, which is further enhanced by 15 minute exposure to blue light. Further work is currently in progress to determine MIC/MBC values for Gram-negative bacteria, and the potential effect of XF-73 against single cell and polymicrobial bacterial biofilms with and without photoactivation.

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Escherichia coli bloodstream infections in a university hospital of northern Italy: resistance pattern and prognostic factors

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Background: Escherichia coli (Ec) is responsible for the majority of gram-negative bloodstream infections (BSIs), being isolated in one third of the episodes in our hospital. In the absence of risk factors for extended-spectrum β-lactamase (ESBL) strains, empiric therapy generally consists in a carbapenem-sparing regimen with piperacillin/tazobactam (PTZ). If a preliminary ESBL screening test on positive blood cultures is negative, the ongoing therapy is confirmed, otherwise is switched to carbapenems. Our study aimed to evaluate the 30-day mortality of Ec BSIs and identify factors related to outcome, with a specific focus on strains that are resistant to PTZ solely.

Materials/methods: We conducted a monocentric retrospective study. All consecutive cases of monomicrobial Ec BSIs between July 2018 and June 2019 were included. For every patient, demographics, source of infection, central catheter presence, Charlson comorbidity index and Pitt bacteraemia score were reported. Therapy adequacy (48h) was evaluated in ESBL and non-ESBL groups. Univariate and multivariate analysis were performed according to Poisson regression test.

Results: We collected 156 cases of Ec bacteraemia in 143 patients (mean age 71, range 25-94; males were 56.6%); resistance pattern is showed in Table 1. The most common source of infection was urinary tract (47.4%). Overall 30-day mortality was 14.7%. Multivariate analysis showed that Charlson (IRR=1.32; 95%CI 1.11-1.57; p=0.002) and Pitt score (IRR=1.51; 95%CI 1.16-1.97; p=0.003) were independently associated with mortality. When mortality was studied in separate groups, results were: 15.6% in ESBL, 13.3% in PTZ-sensitive non-ESBL and 23.1% in PTZ-resistant non-ESBL. Although mortality in the latter group was almost double the one in PTZ-sensitive cases, statistical significance was not reached (IRR=9.64; 95%CI 0.91-102.54; p=0.06).

Conclusions: We found an overall mortality of 14.7%, significantly associated with Charlson and Pitt scores. PTZ-resistant non-ESBL strains represented approximately 10% of the episodes and were associated to an increased mortality despite lack of significance. This phenomenon should be taken into account upon initiation of empiric therapy in our centre. Studies among emerging isolated PTZ-resistance are strongly awaited.

<table>
<thead>
<tr>
<th>Non-ESBL</th>
<th>ESBL</th>
</tr>
</thead>
<tbody>
<tr>
<td>PTZ-sensitive</td>
<td>PTZ-resistant</td>
</tr>
<tr>
<td>n=97; 88.1%</td>
<td>n=13, 11.9%</td>
</tr>
<tr>
<td>62.1%</td>
<td>8.3%</td>
</tr>
</tbody>
</table>

Table 1. Resistance patterns of E. coli

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Abstract 3608

**Detection of OXA-244 producing Escherichia coli of ST131 from surface water of Pavia urban area, northern Italy**

Federica Marchesini*, Melissa Spalla, Alessandra Mercato, Marika Mancinelli, Vittoria Mattioni Marchetti, Giorgio Pilla, Renato Sconfietti, Roberta Migliavacca, Elisabetta Nucleo

**Background:** The spread of multidrug-resistant microorganisms in surface water represents a risk for human health. Water samples from 12 different sampling sites in Pavia urban area (Northern Italy) have been screened for the presence of non-wild type and/or ESBL- or carbapenemase-producing Enterobacteriales.

**Materials/methods:** On May 13th-14th 2019, a total of 18 water samples were collected from four streams, two ponds, four spring waters, one sewer and one wastewater treatment plant (WWTP) in Pavia. One ml of water from each sample was filtered using 0.45 µm-pore size membranes. The filters were placed on Plate Count Agar, MacConkey (MC) and selective MacConkey containing cefotaxime (1µg/ml; 2µg/ml) of meropenem (0.25µg/ml; 4µg/ml). Species identification and antimicrobial susceptibility tests were performed by MicroScan autoSCAN-4 (Beckman Coulter). Susceptibility results were interpreted according to EUCAST 2019. Double disk (DD) test, CT103XL microarray (Check-Points), acc(6')Ibcr and blaOXA PCR, blaOXA sequencing, PFGE and MultiLocus Sequence Typing were accomplished.

**Results:** Thirty isolates belonging to Enterobacteriales grew on the MacConkey media. The 70% (n=21/30) were *E. coli*, 16.6% (n=5/30) Klebsiella spp. (n=3 *K. pneumoniae*; n=1 *K. oxytoca*; n=1 *K. aerogenes*), 6.66% (n=2/30) Citrobacter freundii and 6.66% (n=2/30) Kluyvera intermedia. A high proportion of the isolates (80%; n=24/30) resulted ESBL-positive by DD (n=21 *E. coli*; n=3 *K. pneumoniae*). The 66.6%, 66.6%, 38.0% and 19.04%, of the ESBL-producing *E. coli* were ciprofloxacin, levofloxacin, trimethoprim-sulfamethoxazole (TSX) and gentamicin resistant, respectively. Microarray detected blaCTX-M (groups 1; 2; or 9) determinants in 80% of the isolates. The 30% of the isolates resulted acc(6')Ibcr positive by PCR. A blaTEM/SHV- and blaKPC-type genes positive *K. pneumoniae* ST258, collected from a stream sample, resulted only colistin and TSX susceptible. An *E. coli* collected from a stream next to a WWTP, harboured both blaVEB- and blaMDX-2 determinants. Moreover, two blaOXA-244 positive *E. coli* strains of ST131 were detected from stream and sewer samples. PFGE typing on 21 *E. coli* ESBL-positive strains showed clonal heterogeneity.

**Conclusions:** This is the first report on the occurrence of both blaKPC-type *K. pneumoniae* and ST131 *blaOXA-244 E. coli* in the surface water of the urban area in Pavia, Northern Italy.

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Hospital lanyards: a potential reservoir for Candida auris and other Candida species identified in a hospital outbreak

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Abstract third-party references: Public Health England, Centre for Clinical Infection and Diagnostics Research, Guys and St Thomas’s NHS Foundation Trust

Background: Candida auris (CA) has been implicated in hospital outbreaks worldwide and is notable for colonising patients and causing invasive disease, being difficult to identify and treat, and its resilience in the environment.

Materials/methods: A 5 month CA outbreak was identified in two 15-bed and one 11-bed general adult intensive care units (ICU) at a UK teaching hospital. Stepwise implementation of enhanced infection prevention and control precautions were introduced including twice-weekly screening, isolation, barrier precautions, equipment and environmental cleaning. A detailed environmental screen was performed to identify potential reservoirs. This included the patient bed space, ECG leads, pulse oximeters and temperature probes as well as the key used to access controlled drugs (CDs) (eg, opiates) attached to a lanyard. Personal possessions such as mobile phones, lanyards and ID badges were also screened.

Results: The index case and 6 linked acquisitions were identified of which 1 patient had a bloodstream infection. 4/6 (67%) patients were identified with CA after discharge of all known previous cases from ICU highlighting potential for an environmental reservoir. Environmental screening was undertaken around patient beds. The areas screened and results are shown in figure 1. CA was cultured from the environment following deep cleaning with Sodium Hypochlorite and Vaporized Hydrogen Peroxide (VHP), prompting enhanced deep cleaning, although no patient knowingly acquired CA after arriving in a bed-space of a previous positive case. The CD lanyard was positive for CA, which prompted culturing of staff lanyards and discontinued use on ICU. CA was identified on 1/100 (1%) staff lanyards with Candida parapsilosis being the dominant lanyard-isolate (12/100, 12%). No mobile phones or identification badges were positive for CA.

Conclusions: This outbreak further implicates environmental reservoirs as sustaining Candida auris ICU outbreaks. Identification on the CD-key lanyard highlights need to identify commonly-handled moveable objects during an outbreak, even those that are non-patient contacting. Culture of C. parapsilosis from staff lanyards despite it being an infrequently identified isolate on patients and healthy adults, suggests preferential contamination of material by certain candida species, which could have implications for ICU outbreaks.

Figure 1: Environmental screening for Candida Auris on the ICU

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Evaluation of EUCAST rapid antimicrobial susceptibility testing (RAST) on blood cultures in a clinical laboratory
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Background: EUCAST has developed a rapid antimicrobial susceptibility testing method (RAST) based on disk diffusion to be used directly from blood culture bottles for species commonly involved in bloodstream infections. This method was introduced in our routine clinical laboratory in May 2018 and replaced a non-standardised method for antimicrobial susceptibility testing (AST) directly from blood cultures.

Materials/methods: All isolates from clinical blood cultures with RAST breakpoints were included from 25 May 2018 to 22 October 2019. One blood culture bottle per patient and sampling time was included in the analysis. Polymicrobial cultures and follow-up cultures to previously positive blood cultures were excluded (79 and 16 bottles respectively). Laboratory open hours were weekdays 07:30-17:00 and weekends 08:00-13:00. All work was performed by routine laboratory staff. Time started when the first positive bottle was removed from the blood culture instrument (BACTEC FX, BD) and ended when the first AST result was delivered (regardless of AST method used). The control group consisted of the last 100 positive consecutive blood culture isolates with RAST breakpoints immediately prior to the introduction of RAST. To further shorten reporting times reading RAST after 4 hours of incubation was prioritised from 28 May 2019 to 22 October 2019.

Results: On average more than 78% of all isolates with RAST breakpoints were reported the same day and 52% before 15:00 (fictitious time for afternoon rounds) (Table). After May 2019 this was further improved to 82% and 71%, respectively, by insisting on the 4 hour read. Median time to first AST result regardless of AST method decreased from 19 hours and 3 minutes (before RAST) to 7 hours and 13 minutes (all RAST) and even further to 5 hours and 56 minutes after May 2019. Species distributions before and after RAST were almost identical. The most frequent reason why RAST was not performed was a positive signal from the instrument late in the workday making even the 4 hour read impossible (60% of the no-shows).

Conclusions: RAST delivers a reliable and rapid way of dramatically shortening the average and median time to AST results compared to before its introduction.

<table>
<thead>
<tr>
<th>Species</th>
<th>Before RAST (n = 100)</th>
<th>RAST May 2018 to May 2019 (n = 945)</th>
<th>RAST May to Oct 2019 (n = 351)</th>
<th>All RAST May 2018 to Oct 2019 (n = 1296)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>50%</td>
<td>79%</td>
<td>84%</td>
<td>80%</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>67%</td>
<td>86%</td>
<td>80%</td>
<td>84%</td>
</tr>
<tr>
<td>S. aureus</td>
<td>40%</td>
<td>75%</td>
<td>85%</td>
<td>78%</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>13%</td>
<td>52%</td>
<td>86%</td>
<td>59%</td>
</tr>
<tr>
<td>S. pneumoniae</td>
<td>0%</td>
<td>63%</td>
<td>67%</td>
<td>63%</td>
</tr>
<tr>
<td>E. faecalis</td>
<td>33%</td>
<td>77%</td>
<td>82%</td>
<td>78%</td>
</tr>
<tr>
<td>E. faecium</td>
<td>33%</td>
<td>67%</td>
<td>60%</td>
<td>65%</td>
</tr>
<tr>
<td>Average</td>
<td>44%</td>
<td>76%</td>
<td>82%</td>
<td>78%</td>
</tr>
<tr>
<td>By afternoon rounds (15:00)</td>
<td>22%</td>
<td>45%</td>
<td>71%</td>
<td>52%</td>
</tr>
</tbody>
</table>

Table. Percentage of isolates with RAST breakpoints reported the same day (blue) respectively in time for fictitious afternoon rounds (at 15:00) on the day of the positive signal from the blood culture machine (green).

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Abstracts 2020

Abstract 3617

Presentation, treatment and natural course of severe symptoms of urinary tract infections measured by a smartphone app
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Background: Mobile phones offer new opportunities to efficiently and interactively collect real-time data from patients. Our study aim was to assess the feasibility of a smartphone app to collect symptoms of urinary tract infection (UTI) to estimates UTI symptom duration according to treatment strategy.

Materials/methods: A smartphone app was developed to collect data from adult, non-pregnant and otherwise healthy women diagnosed with suspected uncomplicated UTI. Patients were requested to record demographic information and treatment details [antibiotic and painkiller type and duration]. Push notifications remind women twice a day for seven days to submit a severity score [dysuria, frequency, urgency and low abdominal pain].

Results: The currently recruited 128 participants ranged in age from 18-72 (mean 28), 81% had at least one child and 51% were students. Complete diary entries are available for 75% of patients. Antibiotics [mainly nitrofurantoin] were prescribed to 53% of patients and a painkiller to 27%. The duration of moderately bad or worse symptoms was 2.8 days and mean symptom duration was 4.3 days. No differences were observed for those who did or did not receive an antibiotics, while painkillers did seem to be symptom free faster. 75% of patients indicated to feel cured after 4 days and 83% was symptom free on day 7. A large drop in symptom score was observed immediately after visiting the GP, suggesting a placebo effect of the consultation for all patients.

Conclusions: Our analysis showed lower mean symptom duration than indicated in previous research using paper diaries. The detail obtained through the use of a twice daily smartphone request of pain scores is providing new insights.

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Abstracts 2020

Abstract 3619

**The results of laboratory monitoring of post-vaccination measles immunity**

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**Background:** The incidence of measles in most European countries (including Russia) has increased significantly over the past year. Vaccination is the only way to achieve measles elimination. There is evidence that up to 10% of individuals do not form or maintain specific postvaccinal humoral immunity. Measles cases are also reported among vaccinated persons. The purpose of this study is to dynamically monitor postvaccinal IgG to measles virus (MV).

**Materials/methods:** A total of 1166 persons at the ages of 18 and 55 were examined, all of them had documents about vaccination and re-vaccination against measles. Determination of IgG to MV in serum was carried out by ELISA («Vector-Best», Russia). Further a group of seronegative persons (n=30) was twice vaccinated by live clumsy cultural vaccine («Mikrogen», Russia) and monitoring of content of IgG to MV was carried out by him in 1 month after vaccination and a revaccination and also in 12 months.

**Results:** The average concentration of IgG to MV was 0,741±0,025 IU/ml. Despite earlier vaccination, 27,44% of persons had no specific humoral immunity. The results of the dynamic laboratory monitoring of vaccination against MV were as follows. In one month after vaccination (V1), 28 of 30 people formed anti-measles immunity. The average IgG to MV was 1,20±0,2 IU/ml. In one month after a revaccination (V2) 29 of 30 people formed anti-measles immunity. The average IgG to MV was 1,14±0,11 IU/ml. Thus, 1 of 30 people did not have post-vaccinal anti-measles immunity. In twelve months, the average IgG to MV in the test group was 1,0±0,12 IU/ml. An individual with initially non-formed after vaccination and revaccination, immunity did not occur IgG the increase in the concentration of lead to VC. In addition, 2 individuals showed a decrease in anti-measles IgG below the values required for anti-measles immunity. However, 18 out of 30 people showed an increase in the concentration of IgG to VC compared to V2.

**Conclusions:** Interindividual variability of humoral immune responses to measles vaccination was revealed. Laboratory monitoring of vaccination efficacy should be an integral part of planned and emergency vaccine prevention.

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Abstract 3620

Commercial real-time PCR implementation for rapid diagnosis of onychomycosis: a new workflow in a clinical laboratory

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Background: Classical microbiological onychomycosis diagnosis based on culture and microscopic observation is slow and has low sensitivity. Objective: evaluate the utility of incorporating in the clinical laboratory workflow a commercial real-time PCR (qPCR) for dermatophytes detection in nails after potassium hydroxide (KOH)-based screening.

Materials/methods: Nail samples received during 4 months were observed microscopically after KOH treatment. For every 3 positive KOH samples, one negative was included. All samples were cultured in Sabouraud Gentamicine Chloramphenicol-2 (bioMérieux) and Dermatophyte solid agar (bioMérieux) [30°C, 21 days]. Identification was made by MALDI-TOF MS (VITEK MS version 3.2, bioMérieux) using VITEK® MS MOULD extraction kit. DermaGenius® 2.0 qPCR (Pathognostics) was performed using CFX96 (BioRad) using both supplied mixes. MIX-1 detects C. albicans, T. tonsurans, T. mentagrophytes, T. rubrum/soudanensi, T. interdigitale and T. violaceum and MIX-2 detects T. benhamiae, T. verrucosum, Microsporum audouinii, M. canis and Epidermophyton floccosum.

Results: 152 nail samples were included. In the negative KOH group (n=34), only one dermatophyte grew in culture and three were detected by qPCR. In the group of positive KOH (n=118), 57 dermatophytes grew in culture and 81 were detected by qPCR. In this group, 25% of diagnosed dermatophytes were detected only by qPCR (Table 1). The sensitivity of qPCR compared to culture is 92.8% and time of response decreases from days to hours.

Conclusions: Based in our results, we propose a workflow algorithm for a clinical laboratory that performs qPCR in all positive KOH samples. In this group, culture is eliminated but remains for negative KOH samples.

<table>
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Table 1. PCR results according to KOH and culture results. a,b T. rubrum/soudanensi. c T. rubrum/soudanense, 6 T. interdigitale, 1 T. rubrum/soudanense and E. floccosum co-detection. d 47 T. rubrum, 5 T. interdigitale, 3 T. violaceum, 2 C. albicans.

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Seawater: a risk for transmission of antimicrobial resistance?

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Background: Under EU bathing water regulations, bathing waters are monitored for indicators of fecal contamination between June and September each year. Seawaters are frequently used for recreational purposes and may represent a previously unrecognized risk for transmission of AMR to humans. The aim of this study was to examine seawaters for the presence of extended spectrum beta-lactamase producing Enterobacterales (ESBL-PE) and carbapenemase-producing Enterobacterales (CPE).

Materials/methods: Twenty-five samples (30L) of seawater were collected between May and September in 2018 and 2019 at two beaches (Beach A and B) in Ireland. All samples were filtered using the CapE method, and filters were enriched overnight in buffered peptone water. Enrichments were cultured on agars selective for CPE and ESBL-PE. Species were identified by MALDI-TOF, and examined for susceptibility to 16 antimicrobial agents in accordance with EUCAST criteria. Relevant isolates were screened for blaVIM, blaIMP, blaOXA-48, blaNDM, blaKPC, blaCTX-M-group1, blaCTX-M-group2 and blaCTX-M-group9 as appropriate by real-time PCR.

Results: Four CPE were isolated from individual samples. Two NDM-producing E.coli were isolated in 2019 (1 at Beach A, 1 at Beach B). KPC-producing Klebsiella pneumoniae was isolated from 1 sample collected at Beach B in 2019. One OXA-48-producing Klebsiella pneumoniae was isolated at Beach B in 2018. A total of 50 ESBL-PE were isolated from 13/14 (93%) samples collected in 2018 and from 3/11 samples collected in 2019. The majority of ESBL-PE collected in 2018 harboured blaCTX-M-group1 (n = 41 [91%]), 3 isolates [7%] harboured blaCTX-M-group9. Six ESBL-PE were isolated from 3/11 samples collected in 2019. Isolates harbouring blaCTX-M-group9 were detected at Beach A (n= 1) and in Beach B (n= 2) and 3 isolates harbouring blaCTX-M-group9 were isolated at Beach B.

Conclusions: Antimicrobial resistant bacteria were isolated from 18/25 (72%) seawater samples collected in 2018 and 2019. The isolation of CPE from 4 samples is of particular concern. These findings highlight major limitations of current EU bathing water regulations as the seawaters at the locations at which CPE and ESBL-PE were isolated were consistently designated as Good/Excellent quality. These findings also demonstrate the potential importance of seawater as a transmission route for AMR to humans.

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Genomic analysis of Panton-Valentine leukocidin-positive methicillin-resistant Staphylococcus aureus in hospitalised patients in Germany by whole genome sequencing: 2015-2018

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Background: Although the rate of MRSA infections in Germany has been declining on the past years, infections caused by MRSA remain challenging. Panton-Valentine Leukocidin (PVL) - positive isolates are often associated with recurrent skin and soft tissue or severe courses of infection. The presence of PVL is often regarded as a hallmark of community-acquired (CA) MRSA infections. Previous studies on the composition of community-onset MRSA in our hospital could show a high proportion of PVL-positive MRSA. Several reports have demonstrated the occurrence and transmission of PVL-positive strains in hospitals. However, there are very few data on the prevalence and clonal composition of PVL-positive MRSA in hospitalized patients in Germany.

Materials/methods: Patients admitted to Heidelberg University Hospital for more than 48 hours between 2015 and 2018 with detection of MRSA were included in the study. MRSA was identified according to microbiological routine diagnostic procedures and confirmed by nuc and mecA–PCR. All MRSA isolates were spa-typed and tested for the presence of PVL by PCR. PVL-positive isolates were then characterized by WGS.

Results: Between 2015 and 2018, 757 MRSA were isolated from hospitalized patients at Heidelberg University Hospital, Germany. Of these, 6.1% (n=46/757) were PVL-positive. 58.7% (n=27/46) of the patients with PVL-positive MRSA had an infection, 69.6% (n=32/46) were colonized. 15 patients (32.6%) met the criteria for nosocomial MRSA acquisition. Among the PVL-positive strains, the most frequent spa-types were t044 (n=10/46; 21.7%) and t008 (n=9/46; 19.5%). 8 of the t008 belonged to the USA300 cluster and one was the Latin American variant (USA-300-LV). SNP analysis suggested 3 possible transmission clusters involving seven patients.

Conclusions: To our knowledge, this is the first systematic study on the prevalence and characteristics of PVL-positive MRSA in hospitalized patients in Germany. As PVL is an important virulence marker for S. aureus and is associated with recurrent and severe courses of infection, the presence and composition, also in an in-hospital setting, needs to be monitored. Surveillance may help to identify and control the potential clonal spread of highly transmissible and virulent strains like ST08-USA300 in hospitalized patients.

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Imported leishmaniases in a Parisian hospital, France: a 6-year experience

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Background: Leishmaniases are regularly seen in non-endemic areas because of multiplicity of international travels. Their clinical presentations are divided in cutaneous leishmaniases (CL), muco-cutaneous leishmaniases (MCL), and visceral leishmaniasis (VL), hence the necessity of a sensitive diagnosis to exclude the differential diagnoses and the need of species identification for appropriated treatment.

Materials/methods: We reviewed our diagnostic strategy based on a quantitative PCR assay targeting a consensus 18S kinetoplasmic RNA and sequencing of the cytochrome for species identification. Skin scrapings or biopsies for suspicion of CL and MCL were performed by skilled microbiologists. For VL the search was performed on all the specimens sent (bone marrow, blood, and/or tissue biopsies). Microscopy was performed after May-Grunwald staining of thin smears. DNA was processed as already described (Foulet F et al, J. Clin. Microbiol. 2007, 45(7):2 110).

Results: Seventy-six patients had a definite diagnosis of leishmaniasis between January 1st 2013 and June 30th 2019. The sensitivity of microscopic examination was 81% in CL and CML, and 86% in VL compared to qPCR. Seven patients had VL [all with L. infantum] with known immunodepression but one [HIV n=2; lymphoma: n=3; vascularitis n=1]. Eleven patients had MCL after a trip in Latin America with four different species [6 L. guyanensis, 2 L. braziliensis; 2 L. mexicana; 1 L. panamensis]. Fifty-eight had CL from the Mediterranean basin. CL lesions were unique (41.4%) or multiple (34.5%) and occurred around 120 days after returning from endemic areas. Identification failed in 7 cases because of very low parasite burden. Leishmania major was the most frequently identified species [76%], followed by L. tropica/killicki [12%], and L. infantum [12%]. In 88% of the CL cases, the patients were of African origin resident in France. Among them, 31% of CL cases concern patients who travelled to south Tunisia, confirming the dramatic increase of CL in this region.

Conclusions: The risk of contracting leishmaniasis should be more widely known and more specifically from patients of African origin visiting relatives. Our diagnostic strategy was shown to be very satisfying for both positive diagnosis and species identification.

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Abstract 3630

Analysis of analytical performances of the new MDR/MTB ELItE MGB kit for the detection of *Mycobacterium tuberculosis* complex and rifampicin- and isoniazid-associated mutations in comparison with the MTB ELItE MGB kit

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Background: ElitechGroup has a new kit that can be used for the detection of the DNA of *Mycobacterium tuberculosis* complex and in addition identify rifampicin and/or isoniazid associated mutations. This new kit is compared to the already existing MTB ELItE MGB® kit, which is used for routine diagnostics of MTB complex in our laboratory.

Materials/methods: 48 samples have been tested, of which 38 samples were positive for MTB complex. 11 samples had a confirmed rifampicin of isoniazid resistance. All samples were tested by an Elite InGenius® system which is able to perform extraction, amplification and result interpretation.

Results: The results of the analytical performances were within predetermined parameters, no cross reaction was seen for other Mycobacterium species. An analysis of the diagnostic sensitivity and specificity resulted in a 100% agreement between the MDR/MTB ELItE MGB and the MTB ELItE MGB kit. In addition all rifampicin and/or isoniazid resistant strains were correctly identified. Interpretation of the results involves Ct values and Tm and is done by InGenius.

Conclusions: The analytical performances of the new MDR/MTB ELItE MGB kit were satisfactory. The diagnostic comparison between the new MDR/MTB ELItE MGB kit and the old MTB ELItE MGB kit resulted in no diagnostic inconsistencies. Furthermore, this kit detects mutations associated with resistance for rifampicin and/or isoniazid and can be used directly on clinical specimens. This allows faster resistance detection. This kit will be introduced into our routine diagnostics.

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Molecular biomarker to monitor NDM-producing *Klebsiella pneumoniae* outbreak in two Belgian hospitals: a whole genome sequencing-based infection control application

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**Background:** A large ST716 NDM carbapenemase-producing *Klebsiella pneumoniae* outbreak occurring in two Belgian hospitals (A and B) was previously described using whole genome sequencing (WGS) combined to epidemiological data [Heinrichs et al. CID 2018]. We developed a molecular biomarker in order: 1) to identify the putative origin of the outbreak strain circulating in hospital A; 2) to detect new NDM-producing *K. pneumoniae* isolates belonging to the outbreak strain.

**Materials/methods:** A clone-specific multiplex PCR was designed based on capsular genes alleles wzc941 and wzi89 identified in outbreak isolates. Their specificity as distinctive DNA signatures was tested by using BLASTn. Primers for PCR targeting these alleles were designed using Clone Manager Professional 9 (Sci-Ed Software). The efficiency of this PCR was evaluated on 74 fully sequenced NDM-positive *K. pneumoniae* strains recovered in Belgium in 2015, including 30 ST716 strains. A total of 393 *K. pneumoniae* resistant to 3rd generation cephalosporins (3GC-R) collected between 2010 and 2015 in hospital A were screened for the putative origin of the outbreak clone. In addition, all NDM-positive *K. pneumoniae* detected in hospital A and B in 2016 and 2017 were subjected to the clone-specific PCR.

**Results:** Out of the 74 fully sequenced NDM-positive *K. pneumoniae*, the 30 ST716 strains were positive for both targets (sensitivity 100%; specificity 100%). Among the 393 screened 3GC-R *K. pneumoniae* from hospital A, only one isolate showed a false-positive result for wzc941 and wzi89, as it belonged to ST1119 unrelated to ST716. In 2016 and 2017, 25 and 61 additional NDM-positive *K. pneumoniae* were identified in hospital A and B respectively. In hospital A, only one isolate (4%) was positive for the clone-specific PCR, while in hospital B, 22/29 (76%) and 13/32 (41%) isolates were tested positive in 2016 and 2017, respectively.

**Conclusions:** Our clone-specific PCR showed that the NDM-producing outbreak clone ST716 still circulated in hospital B in 2016 and 2017, whereas in hospital A, this epidemic clone was substituted by new genotypes. Such in-house designed PCR based on whole genome sequencing could be an useful infection control tool to follow up the local circulation of this successful clone.

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PD-L1 expressing CD4+ and CD8+ T cells as a biomarker of tuberculosis disease and treatment response

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Background: Programmed death ligand 1 (PD-L1) is involved in the response to Mycobacterium tuberculosis. It has been shown to be up-regulated in certain blood cells of patients with active tuberculosis.

Materials/methods: A set of immune cell markers was analysed by flow cytometry in peripheral blood of 29 drug susceptible, 33 multi-drug resistant tuberculosis (MDR-TB) patients, and 23 healthy donors. Mean values for percentage of cell populations among three cohorts were compared using Kruskal-Wallis and pairwise Wilcoxon rank sum tests.

Results: At baseline (TB diagnosis, therapy naïve), the percentage of T cell populations expressing PD-L1 were higher among CD4+ T cells in drug susceptible (6.07% vs 0.37%, P<0.001) and MDR-TB patients (12.79% vs 0.37%, P<0.001) compared to healthy controls. The same was observed in the population of CD8+ PD-L1-expressing cells among both drug susceptible (2.67% vs 0.33%, P<0.001) and MDR-TB (7.25% vs 0.33%, P<0.001) patients. Thus, the relative proportion of CD4+ and CD8+ PD-L1-expressing T cells was able to discriminate between TB patients and healthy controls as well as between drug susceptible and MDR-TB patients (P=0.041 for CD4+ and P=0.044 for CD8+). Over the course of anti-TB treatment, the percentage of PD-L1-expressing cells was decreasing in both CD4+ and CD8+ populations in susceptible and MDR-TB patients (P<0.001). At the end of treatment, these populations in drug susceptible patients reached levels similar to those in healthy controls (0.47% vs 0.37%, P=0.061 in CD4+ and 0.09% vs 0.33%, P=0.242 in CD8+). In MDR-TB patients the values even with a two-fold decrease compared to baseline were still higher than in the control group (6.54% vs 0.37%, P<0.001 in CD4+ and 3.37% vs 0.33%, P<0.001 in CD8+).

Conclusions: The frequency of PD-L1-expressing CD4+ and CD8+ T cells was elevated in drug susceptible and MDR-TB patients at diagnosis and decreased over the course of effective anti-TB treatment. However, this decrease was not significant in MDR-TB patients. These cell populations have a potential to be used as a clinical biomarker of TB disease, for monitoring treatment response and predicting successful therapy end. The role of PD-L1 as a potential target for host directed therapy requires further evaluation.

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Toward an improvement of the measles vaccine platform by rationalizing the muscle immune response

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Background: little is known about the immunological mechanisms involved in the muscle, although most vaccines are administered intra-muscularly. Measles vaccine (mv) is a live attenuated virus derived from the schwarz strain. This vaccine is very safe and effective; it also confers a strong and prolonged protection against measles virus. Using reverse genetic it is very easy to introduce new sequences coding for different proteins in this vector. Therefore, mv platform is currently used for the development of new vaccines against chikungunya or zika viruses with very promising results. Vaccination still remains an empiric process and there is a lack of knowledge between vaccine development and vaccine response.

Materials/methods: we used mv platform to explore cellular and molecular processes involved during vaccination. Combining two-photon microscopy and flux cytometry, we analysed the cellular immune response following vaccine injection. In parallel, we also developed a new animal model for vaccinology allowing infection by human viruses (ifnar ko), and expressing fluorescent proteins in immune cell subsets (cx3cr1gfp+/−), and albino.

Results: in our mouse model, adapted to intravital imaging, we made dynamic imaging with two-photon microscopy. We were able to visualise the muscular macrophages (cd11b+/F4/80+) as the cells infected first with the mv virus vaccine, while patrolling monocytes (cd11b+/cx3cr1+) were recruited in the muscle [at the injection site]. In the draining lymph nodes, we observed the kinetic of mv+ cells, while b and t cells were actively recruited.

Conclusions: we have shown for the first time, by using innovating tools the different cellular partners involved in the vaccine immune response. These results demonstrate that immune resident muscular cells interact with blood recruited cells to process the virus and address it at the draining lymph node. Our results provide a better understanding of the immune mechanisms involved in vaccination that can help improving the design of new vaccines.

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Antimicrobial stewardship intervention in FLU/respiratory syncytial virus adult hospitalisations: major impact on antimicrobial management of a systematic epidemiological surveillance process including training and feed-back

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Background: Influenza (FLU) and Respiratory Syncytial Virus (RSV) are known causative pathogens in adult hospitalizations for severe acute respiratory infections (SARI). While rapid molecular techniques confirm the diagnosis, the impact of patient screening at admission and viral detection on antimicrobial management remains controversial. We aimed to evaluate the setup of a systematic epidemiological surveillance process and its effectiveness as antimicrobial stewardship intervention during four consecutive epidemic seasons.

Materials/methods: Annual surveillance timelines were defined according to epidemiological criteria related to the seasonal circulation of RSV and FLU viruses in the general population during a four-year period (2015-2019). Patients were screened according to a SARI case definition at the Emergency Department (ED) of a University hospital, and enrolled for molecular assay targeting FLU/RSV viruses. Initial ED staff training, weekly national and local epidemiological updates, and hospital-wide level targeted communications were organized by the Infectious Diseases Department. Epidemiological and clinical data, microbiological investigations results and antimicrobial prescription data were reviewed.

Results: A FLU or RSV virus was documented in 316 (33%) out of 963 SARI patients. Globally, a positive viral diagnosis allowed an optimization of antimicrobial therapy in 162 (61%) out of 265 patients with no bacterial infection documented at admission (antibiotic treatment not initiated: n=111; discontinued: n=51). By contrast, 128 (28%) out of 462 patients with negative microbiological investigations had an antibiotic treatment not initiated (n=116) or discontinued (n=12). An early targeted antiviral treatment was prescribed in 197 (92%) out of 213 patients with a confirmed FLU diagnosis. The proportion of full course empirical antibiotic treatments initiated at admission was significantly lower in the FLU/RSV (+) than in the FLU/RSV (-) patients (38.9 % vs 72.3 %, respectively, P<0.0001). A yearly trend towards decrease of empirical treatments was noticeable in patients with and without a documented viral infection, while epidemiological, clinical and outcome data remain similar in both patient groups during the four-year surveillance period.

Conclusions: An epidemiological surveillance process including regular targeted communications associated with a FLU/RSV molecular diagnosis allowed an exhaustive screening and viral disease detection in SARI patients, and dramatically impacts the antimicrobial (antibiotics, antivirals) management.

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Abstract 3642

**Optimisation of duplex next-generation digital PCR assays for molecular diagnosis of infection**

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**Background:** Early diagnosis and initiation of treatment are crucial factors in handling patients with bloodstream infections (BSIs). However, the appropriate treatment for these patients is impaired due to the delay and low rentability of the gold standard microbiological diagnosis technique (blood culture). Droplet digital PCR (ddPCR) is a next-generation PCR with high sensitivity, low impact of PCR inhibitors and no need for a standard curve. Our objective was to develop a ddPCR assay for the detection of the most common pathogens in Spanish ICUs.

**Materials/methods:** Based on the ENVINE-ICU 2017 report the most common BSIs pathogens were selected for our ddPCR assay: *Escherichia coli* (Eco), *Klebsiella pneumoniae* (Kpn), *Enterococcus spp.* (Ent), and *Staphylococcus aureus* (Sau). Based on a review of the literature several genes were selected for possible identification of each of the species/genus mentioned (Eco-gad, Kpn-khe, Sau-SA442, Ent-23S). The selected genes have previously been used for bacterial identification (qPCR or ddPCR). DNA was extracted from reference strains of each pathogen obtained from the CECT using alkaline lysis. ddPCR assays were initially performed separately for each bacterial species/genus and then duplexed (Eco+Sau and Kpn+Ent). Different initial DNA concentrations (2ng/µL -0.25ng/µL) were tested to evaluate the dynamic range of ddPCR duplex assays. All assays for all DNA concentrations were performed in triplicate using the QX200 ddPCR platform (BioRad) according to manufacturer instructions.

**Results:** All ddPCR assays (simplex/duplex) were performed successfully and were highly specific for each bacterial species/genus. A quantity of 1ng of bacterial DNA was established as the lower limit of the method. Results showed high replicability for all the pathogens tested, with low SD (Figure 1). The time involved in processing all samples and assays was less than 5 hours.

**Conclusions:** Our results show that the ddPCR assays are highly sensitive and robust for the detection of pathogens, specifically Eco, Sau, Kpn and Ent. The focus of ongoing work from our group is to apply these ddPCR assays to blood from patients with BSIs.

Figure 1. ddPCR assays results for the different species analyzed: a) *Escherichia coli*; b) *Klebsiella pneumoniae*; c) *Staphylococcus aureus*; d) *Enterococcus faecalis*; e) *Enterococcus faecium*.
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**Abstract 3643**

**In vitro study of TEM inhibition by the nanobody cAbTEM-1 in view to a potential way out of the bacterial resistance**

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**Abstract third-party references**: SPF santé public, University of Liege

**Background**: The intensive use of β-lactam antibiotics lead to an increasing bacterial resistance, mainly by the production of enzymes, called β-lactamases (BLAs), which are able to hydrolyze those antibiotics. Therefore, in order to fight bacterial resistance, it is needed to develop new antibiotics and/or therapeutic approaches. In our lab, we developed a camelid antibody (nanobody) called cAbTEM-1 directed against TEM β-lactamases. A nanobody has a small size (15 KDa) and a very long CDR3 that are features very interesting in view to develop inhibitors against bacterial resistance.

**Materials/methods**: The first part of this project consists on the study of the inhibition mechanism of TEM β-lactamases by cAbTEM-1 by following the residual activity in presence of increasing concentration of the nanobody. Our second goal is to verify the specificity of cAbTEM-1 by bio-layer interferometry. Finally, structural studies of the VHH-TEM complexes by X-ray crystallography and molecular modelling were achieved in order to determine the essential factors that mediate the interaction of TEM enzymes and their inhibitor.

**Results**: Our kinetic results showed that cAbTEM-1 was able to interact specifically with members of TEM family: TEM-1 and TEM-121. Furthermore, the profile of inhibition is function of the TEM enzyme and the nature of the β-lactam considered. For example, using nitrocefin, the nanobody acts like a competitive and a non-competitive inhibitor for TEM-1 and TEM-121, respectively. We showed also that the inhibition is related to the size of the antibiotic. Finally, structural studies of the VHH-TEM complexes showed that cAbTEM-1 does not bind in the active site of the TEM enzymes. Nevertheless, its binding to the enzymes induces a steric hindrance and decreases the flexibility of the active site. The studies help us also to define the sequences of the epitope and the paratope respectively.

**Conclusions**: The complete characterization of the interaction between cAbTEM-1 and TEM give us new insights on β-lactamases inhibition. For example, the identification of the paratope sequence of VHH may lead to the synthesis of new inactivators by peptidomimetics.

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Seroprevalences of ten ToRCH infectious pathogens in women residing in Europe, Latin America and China

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Background: The determination of antibodies against ToRCH antigens before or at the beginning of pregnancy allows assessment of both the maternal immune status and the risks to an adverse pregnancy outcome. Here, we compared the seroprevalences of antibodies against ten ToRCH antigens in women of childbearing age between six countries.

Materials/methods: Seroprevalences were determined in serum samples from healthy women (N=991, 15-47 years) residing in Germany (n=202), Turkey (n=97), Mexico (n=100), Brazil (n=160), Poland (n=193) or China (n=239) using the EUROLINE Anti-TO.R.C.H. 10-Profile (IgG) (EUROIMMUN). This lineblot contains native and recombinant antigen substrates against ten pregnancy-related pathogens (Toxoplasma gondii, rubella virus, cytomegalovirus (CMV), herpes simplex viruses (HSV-1, HSV-2), parvovirus B19, varicella zoster virus (VZV), Bordetella pertussis, Treponema pallidum and Chlamydia trachomatis). The lineblot’s band intensities were evaluated with the EUROLineScan software (EUROIMMUN).

Results: Seroprevalences of IgG antibodies against VZV [seroprevalence range across six countries: 90-99%], rubella virus [range: 91-99%], and Treponema pallidum [range: 1-3%] were on comparable levels between countries. Anti-HSV-1 antibodies had seroprevalences between 74-95% across countries. Brazil showed elevated seroprevalences of IgG antibodies against HSV-2 [39%, range across the other five countries: 21-25%], Chlamydia trachomatis [48%, range across the other five countries: 5-18%] and Bordetella pertussis [59%, range across the other five countries: 0-15%] antibodies. Seroprevalences of anti-Toxoplasma gondii antibodies were in the range of 24-28% in Germany, Poland, Turkey and Mexico, but 59% in Brazil and 1% in China. Seroprevalence of anti-parvovirus B19 antibodies were low in China [12%, range across the other five countries: 36-55%]. German women had a low seroprevalence of anti-CMV antibodies [38%, range across the other five countries: 61-99%].

Conclusions: The observed seroprevalences speak in favour of global differences in immune status of women in childbearing age. This evidence advocates country-specific infection prophylaxis strategies and close monitoring as part of prenatal care. The EUROLINE Anti-TO.R.C.H. 10-Profile (IgG) is a suitable tool to assess both maternal immunity and consequent risks for an adverse pregnancy outcome.

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Ibrexafungerp demonstrates potent and consistent in vitro activity against >400 global Candida auris isolates, including isolates with elevated MIC’s to echinocandins

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Background: Candida auris is a urgent global threat; a pathogen associated with high mortality (up to 60%), multi-drug resistance, the ability to spread from person-to-person and surface-to-person, presenting high risk for outbreaks in healthcare facilities. Echinocandins are the first-line treatment for patients with Candida auris infections given the high degree of resistance to azoles and polyenes. Ibrexafungerp is a novel IV/oral glucan synthase inhibitor (triterpenoid) antifungal with activity against Candida, Aspergillus and Pneumocystis spp, in Phase 3 development. Given the potent activity of ibrexafungerp against Candida spp., Scynexis has embarked on a development program to understand the activity and effectiveness of ibrexafungerp against Candida auris. We will present a compilation of >400 Candida auris isolates from four studies, including 32 Candida auris isolates with elevated MIC’s to the echinocandins.

Materials/methods: In vitro MIC data for ibrexafungerp against Candida auris isolates were compiled from across 4 independent studies with the majority of isolates originating in the US and India. In vitro susceptibility was determined by broth micro-dilution using CLSI (M27-S3) and/or EUCAST methods. Overall, 445 isolates were evaluated including 32 isolates with elevated MIC values to one or more echinocandins.

Results: The ibrexafungerp MIC90 value against the 445 clinical isolates was 1 µg/mL; the modal and MIC50 values were 0.5 µg/mL each. These results were consistent across the four studies and no differences were observed between MIC results generated using CLSI or EUCAST methods. Similar results were obtained for the 32 isolates with elevated MIC values to one or more of the echinocandins. Among this echinocandin-resistant population, the mode, MIC50, and MIC90 for ibrexafungerp were 0.5, 0.5, and 1 µg/mL, respectively, with only 1 isolate showing reduced sensitivity.

Conclusions: This data demonstrates that ibrexafungerp possesses potent and consistent in vitro activity against Candida auris and remains highly active against C. auris isolates with high MIC’s to the echinocandins.

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Abstract 3650

**Clinical characteristics and outcomes in patients with severe West Nile neuroinvasive disease in Croatia**

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Abstract third-party references: Croatian Science Foundation, project No. IP 2016-06-7456, CRONEUROARBO.

**Background:** West Nile virus (WNV) neuroinvasive disease is a rare (<1%), but often severe manifestation of WNV infection. The clinical presentation varies and includes meningitis, encephalitis, and poliomyelitis-like syndrome. Risk factors include older age, comorbidities (arterial hypertension, diabetes) and immunosuppression. So far, 92 clinical cases of neuroinvasive WNV infection were reported in Croatia. The aim of this study was to analyze the clinical characteristics of patients with severe WNV neuroinvasive infection, hospitalized at the Department for Intensive Care Medicine and Neuroinfectology, University Hospital for Infectious Diseases “Dr Fran Mihaljevic”, Zagreb, from 2013 to 2019.

**Materials/methods:** Among 23 patients with severe WNV infection, 18 (78.2%) were male. Twenty-one patients were from Croatia, while two cases were imported from Hungary and the USA, respectively. Diagnosis was confirmed by detection of WNV RNA in cerebrospinal fluid (CSF) and/or urine samples using RT-PCR and/or detection of WNV IgM and IgG antibodies of low avidity in serum and CSF samples.

**Results:** The median patient’s age was 72 (range 33-84) years. Majority of patients reported underlying diseases, most commonly arterial hypertension (19/82.6%) and diabetes (9/39.1%). Three patients had kidney transplantation. The most common clinical presentations were encephalitis (13/56.5%) and encephalitis with acute flaccid paralysis (9/39.1%). Twelve patients (52.2%) were mechanically ventilated with the median duration of 12 (range 5-73) days. The median ICU stay was 19 days (range 5-73) while the median hospital stay was 34 days (range 7-97). Two patients (8.7%) died during the ICU treatment and 15 patients had moderate to severe disability at discharge, evaluated by modified Rankin Scale (mRS), score 3-5. The follow-up was performed in July 2019. Nineteen of 21 patients were available. Additional five patients (21.7%) died while five patients (21.7%) had moderate to severe disability. An improvement, according to mRS, was reported in 11 patients (47.8%).

**Conclusions:** WNV neuroinvasive disease affected mainly the elderly with comorbidities. These patients often need a prolonged intensive treatment and have moderate to severe neurological disability. Improvement is noted after several months in one half of the patients.

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Abstract 3656

The Mycosands initiative: exploring fungal contamination in the sand and water around the Mediterranean Sea and other water bodies of Europe: relevance to human health and well-being

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Abstract third-party references: ECMM, ISHAM

Background: Beaches are considered therapeutic for many clinical situation and are widely used for recreation purposes. In 2003, the World Health Organization (WHO) published the "Guidelines for safe recreational water environments", dedicated a chapter to sand as exposure to pathogens and opportunists, especially at latitudes where the population tends to spend less time bathing due to colder waters.

Most publications on beach sand address methodology, including microbiome characterization and its influence on human health. To date, however, there has been no clear guidance from regulation and the fungi are an under-investigated biological group, which is also not considered for regulation of the recreational water either.

Materials/methods: In order to characterize the typical mycobiota of European beach sands, a consortium of Medical Mycologists and Recreational Water Quality researchers joined in 2018 to collect samples from 28 sites representing European coasts and inland water bodies. This consortium/initiative is active during two years. The sampling sites are grouped in four different regions: Northwest, Southwest, Mediterranean and Black Sea and the number of samples of water and sand gathered until now is represented in the following table:

<table>
<thead>
<tr>
<th>Country</th>
<th>Sand</th>
<th>Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ireland</td>
<td>51</td>
<td>45</td>
</tr>
<tr>
<td>France</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>Greece</td>
<td>52</td>
<td>52</td>
</tr>
<tr>
<td>Portugal</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Israel</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>Italy</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Latvia</td>
<td>13</td>
<td>10</td>
</tr>
<tr>
<td>Netherlands</td>
<td>38</td>
<td>38</td>
</tr>
<tr>
<td>Spain</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Slovenia</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Serbia</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Turkey</td>
<td>47</td>
<td>46</td>
</tr>
</tbody>
</table>

Results: This initiative showed that there is no common mycobiota in European beaches and that the Aspergillus Fumigati complex is distributed everywhere. The same applies to Penicillium spp and other Aspergilli, with the exception of Aspergillus section Nigri which was found more frequently in warmer sands (p=0.019), Rhodotorula spp (p=0.044) follows the same pattern of latter. A. section Nigri is also associated with urban beaches (p<0.001), along with Fusarium spp (p=0.003) and Cryptococcus spp (p=0.019).

Conclusions: From these results, the initiative’s team believes that fungi in sand should be analyzed routinely because of providing relevant information to: Susceptible beach visitors, beach professionals [exposed to sand contaminants during the whole duration of their working periods], and beach managers [fungal contaminants may be used as proxy for information on causes of pollution events].

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A novel chaperone-usher pili system associated to the worldwide-disseminated high-risk clone *Klebsiella pneumoniae* ST-15

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**Background:** Emergence and global spread of carbapenem-resistant *Klebsiella pneumoniae* is considered as a dire threat to public health. The convergence of resistance and virulence determinants could promote the emergence of untreatable *K. pneumoniae* infections. Therefore, understanding the mechanisms involved in the pathogenesis and epidemiology of *K. pneumoniae* is required for managing outbreaks and developing therapeutics. We previously identify a chaperone-usher pili (CUP) operon, *kpiABCDEFG*, codifying for a novel CUP system (*Kpi*) and demonstrated the key role in adherence-related virulence functions in a *K. pneumoniae* isolate (Kp3380). The aim of this work was to perform the genetic and structural characterization of the *Kpi* system and evaluate its distribution in *K. pneumoniae*.

**Materials/methods:** Rapid Annotation using Subsystem Technology (RAST) was used for *in silico* analysis of the *kpiABCDEFG* operon. Protein structure modeling of the *Kpi* system was predicted using RaptorX. A phylogenetic analysis based on the usher amino acid sequence was performed to classify the *kpiABCDEFG* fimbrial operon. BLASTn was used to evaluate the presence/absence of the *kpiABCDEFG* operon in *K. pneumoniae*. Its sequence was used as query against 1649 *K. pneumoniae* strains isolated in 32 European countries. A core-genome MLST was performed to describe the distribution of the *Kpi* system.

**Results:** The operon *kpiABCDEFG*, consists of one usher gene (*kpiG*), 3 molecular chaperone genes (*kpiB, kpiE and kpiF*) and 3 fimbrial genes (*kpiA, kpiC and kpiD*). Protein structure modeling revealed that *Kpi* system is structurally related to CUP system type 1. The phylogenetic analysis showed that *Kpi* is included into the largest uncharacterized phylogenetic clade γ, and most of the *Kpi*-positive isolates (77%) belonged to ST-14 (9.5%), ST-15 (46%), ST-25 (4.7%) and ST-405 (16.8%). The 91.1% of ST-15 isolates shared exactly the same operon with Kp3380. The distribution of ST-15 isolates was analyzed and it was involved in outbreaks in Hungary, Croatia, Romania and Spain.

**Conclusions:** The novel *Kpi* system is associated to ST-15, which could explain the superior capacity of these clones to spread and cause outbreaks, being a specific target to control the emergence of that successful high-risk clone.

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Area of technical uncertainty for ciprofloxacin in Enterobacterales: evaluation of MIC values using the E-test method

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Background: Area of Technical Uncertainty (ATU) is a term coined by EUCAST on 2019 to warn laboratories with respect to uncertain interpretation of some antimicrobial susceptibility testing results, due to technical problems. To this regard, a MIC value of 0.5 mg/L (interpreted as Susceptible, increased exposure according to current EUCAST criteria) is classified ATU for ciprofloxacin in Enterobacterales. Different options are suggested by EUCAST to manage this result. The aim of this study was to evaluate isolates showing a MIC value of 0.5 mg/L (as routinely obtained) using the Etest method (bioMérieux).

Materials/methods: From June to October 2019, 120 non duplicated clinical isolates of Escherichia coli showing a MIC value of 0.5 mg/L for ciprofloxacin were collected at the Manzoni Hospital (Lecco, Italy). Bacterial identification was performed using matrix-assisted laser desorption ionization time-of-flight mass spectrometry (Vitek MS, bioMérieux). Antimicrobial susceptibility for ciprofloxacin was at first evaluated by Vitek2 (bioMérieux), and then re-evaluated using the Etest method. Results were interpreted according to EUCAST criteria.

Results: One hundred and fifteen isolates (95.8%) showed MIC values for ciprofloxacin ranging from 0.012 mg/L to 0.25 mg/L, thus interpreted as Susceptible, standard dosing regimen. Of them, three strains had a MIC value lower than the epidemiological cut-off (ECOFF) and were then classified as wild-type. Nine isolates showed a MIC value ranging from 0.38 mg/L (n=6) to 0.5 mg/L (n=3). Two strains had MIC values greater than 0.5 mg/L (0.75 mg/L, and 2 mg/L) thus being classified as resistant to ciprofloxacin. MIC50 and MIC90 were 0.19 mg/L and 0.25 mg/L, respectively.

Conclusions: According to EUCAST warning, our data confirm the difficulty of reproducible interpretation in case of ATU for ciprofloxacin. It is noting that most isolates appeared to be susceptible using the Etest method. However, the study shows that in most cases the strains had MIC values higher than ECOFF. Therefore, these isolates cannot be classified as wild-type and the presence of mechanism[s] of resistance to ciprofloxacin should be suspected. Additional information concerning the performances of automated systems appear essential to help microbiologists to choose the best option in case of ATU for ciprofloxacin in Enterobacterales.

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Abstract 3659

**Antifungal susceptibility description in Candida parapsilosis bloodstream infection: is there a change in the last years?**

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**Background:** To develop a profile of antifungal sensitivity of Candida parapsilosis bloodstream infection (BSI) over a period of 6 years (2013 to 2018) and compare C. parapsilosis BSI with non-parapsilosis candidemia.

**Materials/methods:** Retrospective observational study from January 2013 to December 2018 of all candidaemias diagnosed in Hospital Son Espases (Palma de Mallorca, Spain) in patients older than 18 years.

**Results:** Among 224 episodes of Candida BSI identified, 84 (37.5%) were due to C. parapsilosis. In this group, 66.7% were male, with a mean age of 63.5 years old (SD 13.8). The main baseline characteristics were: solid organ cancer (38.1%), diabetes mellitus (22.6%), renal failure (16.7%) and hematological malignancy (4.8%). The Charlson score mean was 5.3 (SD 3.1).

The main predisposing factor were: central venous catheter (CVC) (90.5%), surgery in the previous 3 months (77.4%), parenteral nutrition (46.4%), prior antibiotic therapy (90.5%), prior echinocandin therapy (34.5%), prior glucocorticoid therapy (22.6%) and previous or concurrent colonization by Candida spp. (54.8%).

The candidaemia causes were: catheter-related (56.0%), primary (35.7%), abdominal (7.1%) and urologic (1.2%). 59.5% met sepsis criteria and 27.4% septic shock. The Pitt bacteremia median was 2 [IQR: 0-4] and on the SOFA score was 3 (0-5). Echinocandins were the initial antifungal in 65.5% (67.9% caspofungin). Early CVC removal (first 48 hours) was performed in 71.1%. Appropriate management (appropriate antifungal and early CVC removal) was performed in 55.7%. The 30-day all-cause mortality was 21.4%.

The antifungal susceptibility patterns were: Amphotericin B (0%), echinocandins (29.7%), fluconazole (54.8%), voriconazole (44.0%). 21.4% [18] of the C. parapsilosis species were resistant to both fluconazole and echinocandins. The univariate analysis showed: admission to the Post-Anesthesia Care Unit (p<0.001), surgery in the previous 3 months (p: 0.001), mechanical ventilation (p: 0.014), prior echinocandin therapy (p<0.001), prior carbapenem therapy (p: 0.010) and prior linezolid therapy (p: 0.005) were associated with a higher incidence of candidaemia due to C. parapsilosis.

**Conclusions:** Currently, C. parapsilosis is the main responsible for candidaemias in our hospital. More than 50% isolated were resistant to fluconazole and almost 30% to echinocandins. Amphotericin B was the appropriate antifungal treatment in 20% of cases.

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Estrogen enhances host-pathogen interactions in ex vivo and in vitro models of the inflammatory phase of age-related impaired healing

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Background: Chronic wounds in the elderly often become infected, leading to substantial morbidity and mortality. Age-related impaired healing is mediated by age-related changes in steroid hormones, particularly declining levels of estrogen with increasing age. Although the anti-inflammatory activity of estrogen has been defined, little is known about the effects of estrogen deprivation on bacterial clearance. The aim of this study was to determine the effect of ageing (estrogen deprivation) on the ability of human monocyte-derived macrophages to eliminate bacteria via phagocytosis.

Materials/methods: Host-pathogen assays were used to measure macrophage-mediated phagocytosis of two major wound pathogens, methicillin-resistant *Staphylococcus aureus* (MRSA) and *Pseudomonas aeruginosa*, under in vitro and ex vivo conditions that model estrogen levels in the elderly, young adults and following estrogen supplementation. Fluorescence and scanning electron microscopy (SEM) were used to visualise host-pathogen interactions and protein mediators of phagocytosis were measured by immunoblotting.

Results: Estrogen at concentrations typical of youth or supraphysiological levels significantly \(P<0.05\) increased the phagocytosis of MRSA and *P. aeruginosa* in a dose-dependent manner compared to estrogen deprivation with significantly enhanced clearance of bacteria by M1 macrophages compared to M2 macrophages. Epifluorescence, confocal and SEM confirmed estrogen increases co-localisation of fluorescent GFP-*S. aureus* or mCherry-*P. aeruginosa* within macrophages and promotes bacterial internalisation. Activation of estrogen receptor-alpha (ER-\(\alpha\)) mirrored the stimulatory effect of estrogen on phagocytosis whilst ER-\(\alpha\) antagonism significantly \(P<0.01\) blocked the phagocytic effect of estrogen. In contrast, activation of ER-beta (ER-\(\beta\)) had no significant effect on phagocytosis, confirming estrogen mediates bacterial clearance via ER-\(\alpha\). Immunoblotting analysis demonstrated that estrogen-enhanced phagocytosis is associated with altered levels of mediators involved in the actin cytoskeleton of phagocytes including increased levels of FAK, Rac1, Cdc42 and RhoG, but reduced levels of RhoA.

Conclusions: Findings suggest estrogen may promote the resolution of wound infections during youth but this protection is lost as estrogen levels decline with increasing age, resulting in increased propensity and progression of age-related wound infections. Thus, novel wound dressings providing estrogen supplementation or selective activation of ER-\(\alpha\) and/or specific targeting of downstream mediators of the actin cytoskeleton may provide effective treatment options for infected wounds in the elderly.

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Abstract 3661

**Review of the hospital empiric antibiotic guideline in treating community-onset bloodstream infection in a Singapore tertiary hospital**

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**Background:** Empiric antibiotic guidelines based on the local antibiogram and suspected site of infection reduce unnecessary broad-spectrum antibiotic use. With the increasing prevalence of community antibiotic resistance, we wanted to ensure the appropriateness and safety of our hospital’s empiric antibiotic guideline. Our objectives were to determine the adequacy of our empiric antibiotic guideline and the impact of guideline adherence on patient outcomes in treating community-onset bloodstream infections (CO-BSIs).

**Materials/methods:** A retrospective study was conducted on adult patients admitted to the hospital with CO-BSI in 2018. CO-BSI was defined as positive blood cultures upon admission. Patients who were discharged from hospital in the last 48 hours, transferred to intensive care unit or another hospital within 24 hours or died within 24 hours were excluded.

**Results:** 377 patients were included in the study, 301 had Gram negative bacteraemia, 70 had Gram positive bacteraemia and 6 had both. The most common pathogens were Escherichia coli, Klebsiella pneumoniae and Staphylococcus aureus. The ESBL rates for E.coli and Klebsiella were 21.5% and 7.9% respectively while MRSA rates were 18.8%. Guideline recommended empiric antibiotics adequately covered bacteria isolated in 87.3% of the cohort. Guideline adherence was 75.9%. A significantly higher proportion of patients in the non-adherent group had Gram positive bacteraemia (31.9% vs 14.3%, p<0.001) and had escalation of empiric antibiotic (56.0% vs 18.2%, p<0.001) for broader coverage of causative bacteria. However, there was no statistical difference in 30-day mortality (8.0% vs 7.8%, p=1.00) and median length of stay (8 days vs 10 days, p=0.116) between adherent and non-adherent groups.

**Conclusions:** Our hospital empiric antibiotic guideline adequately covers for causative bacteria in CO-BSI. Adherence to guideline antibiotics was not associated with higher 30-day mortality and longer hospital stay. Results from this study can assure physicians to adhere to the empiric guideline and not to escalate antibiotics in stable patients with CO-BSI pending culture and susceptibility results. This is an evidence-based step to encourage guideline compliance and reduce unnecessary use of broad-spectrum antibiotics.

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Abstract 3666

**Estimating the burden of influenza on hospitals using severe acute respiratory infections in metropolitan France, 2012-2018**

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**Background:** In France, estimating the burden of seasonal influenza on hospital workload is restricted to influenza diagnoses in patients who present to emergency departments (ED) and are subsequently admitted, representing an hospitalization rate ranging from 2 to 15 per 100,000 over six influenza seasons (2012-2018). However, many hospitalizations for respiratory complications (e.g. pneumonia, bronchitis) occur without virological influenza confirmation, especially among the elderly. We aimed to estimate the burden of influenza on hospitals, from the proportion of severe acute respiratory infections (SARI) attributable to influenza, in order to improve health authority response.

**Materials/methods:** Using national hospital discharge data from 1/7/2012 until 30/6/2018, we extracted SARI hospitalizations based on ICD-10 codes: J09-J11 (influenza codes) in primary or associated diagnoses, and J12-J20 (pneumonia and acute bronchitis codes) in primary diagnoses. We estimated influenza-associated SARI hospitalisations, stratified by age group, as the number of influenza-coded hospitalisations plus the excess number of pneumonia- or bronchitis-coded hospitalisations using Serfling regression during influenza seasons.

**Results:** Over six influenza seasons, we identified 533,456 SARI hospitalisations and estimated 227,154 influenza-associated SARI hospitalisations (42%). Fifty-six percent had influenza as a diagnosis, 33% pneumonia and 11% bronchitis. Diagnoses varied among age groups; 14% of those 15 years and under had pneumonia or acute bronchitis, versus 59% of those 85 and older. We estimated the influenza-associated SARI hospitalization rate at 59 per 100,000 population, on average over the 6 seasons. This rate varied significantly by age group: 23 per 100,000 population in 15-64 year olds to 475 per 100,000 population among 85 year olds or older.

**Conclusions:** Compared to current influenza surveillance, analysis of SARI hospitalizations provided a much larger estimate of the true burden of influenza on hospitals, and allowed accurate assessment by age. This analysis should be implemented annually to better assess the socio-economic impact of influenza. These findings will inform the use of real-time SARI analysis from ED data, to measure the magnitude of hospital pressure during the influenza season, and support better health services planning and prompt intervention.

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A new rapid test on whole blood and on serum for the toxoplasmosis screening in pregnancy

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Background: In Italy the screening for toxoplasmosis in pregnancy is free of charge and recommended by Italian guidelines. The screening includes anti-Toxoplasma IgG and IgM antibodies at the beginning of pregnancy and monthly follow-up for seronegative women. Many studies have demonstrated the effectiveness of such a screening, but the decrease in seroprevalence of toxoplasmosis, has brought forward the cost-benefit ratio of screening itself. We wanted to evaluate the diagnostic efficacy of a new rapid test (ICT wb-TOXOPLASMA LDBIO Diagnostic Lyon France) on whole blood taken by finger puncture in comparison with clinical data and the same test on serum

Materials/methods: All the pregnant women, screened for toxoplasmosis at the Centro Unico Prelievi and at the Outpatient of Infectious Diseases department of the Fondazione IRCCS Policlinico San Matteo Pavia, were asked to take part to the study. At the same time they underwent the sampling for routine test: LIAISON® XL Toxoplasma IgG and IgM, IgG Avidity (Diasorin, Saluggia, Italy) VIDAS Toxo IgG II, IgG Avidity and ISAGA IgM (Biomerieux - Mercy l'Etoile - France) and when possible for ICT on the serum

Results: Two hundred and seventy pregnant women underwent ICT whole blood test, ICT on sera was performed on 218 sample from the same patients and the results compared with the clinical diagnosis. Concordance (Cohen’s kappa Test) was very good with K = 0.9084 for whole Blood ICT and K = 0.9599 for serum ICT. Sensitivity was 89.5% [CI 95% 87.5-98.6], specificity 99% [CI 95% 96.8-100] for whole blood. On sera sensitivity was 94.9% [CI 95% 97.4-98.6], specificity 100% [CI 95% 97.4-100]. The K value between the 2 test was 0.859. Only 30 (10%) patients refused to take part to the study

Conclusions: The use of the rapid test can be an alternative to traditional tests for ease of execution, rapid response and reduced cost. Both the tests on different matrices showed a good specificity avoiding most of IgG/IgM false positive results, but all positive cases must always be tested with routine tests to discriminate between different antibody classes and to date the infection.

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Abstract 3668

Detection of ST131, ST410 and ST69 Escherichia coli KPC-2/3, OXA-181, and VIM-1-producers from a long-term care facility in Milan, Italy

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Background: The prevalence of MDR Escherichia coli is increasing in Italian long-term care facilities (LTCFs). Objective of the study was to characterize all the carbapenemase-producing E. coli clinical isolates collected in the period 2017-18 from a LTCF of Milan, Italy.

Materials/methods: In a two years’ period, a total of 14 ertapenem and/or imipenem non-susceptible E. coli strains, were collected at the LTCF “Golgi-Redaelli” Clinical Microbiology Laboratory. Identification and susceptibility tests were performed by both Vitek-2 and Microscan Autoscan-4. Colistin and fosfomycin MICs were obtained by broth-microdilution [UMIC CO] and agar dilution methods, respectively (EUCAST 2019 guidelines). The presence of ESBLs, carbapenemases and aac-(6')Ib-cr -resistance determinants was evaluated by PCR, microarray and sequencing. Strains and plasmids characterization was accomplished by multiplex-PCR, PFGE, MLST and FBRT-kit (Diatheva), respectively.

Results: The 14 E. coli studied accounted for the 5.5% of all the MDR Gram-negative microorganisms identified in the period 2018-19 at “Golgi-Redaelli” LTCF. All the E. coli isolates, obtained from urine (n = 10/14) and rectal swabs (n = 4/14) resulted MDR. The resistance phenotypes included third generation cephalosporins, fluoroquinolones, aminoglycosides and co-trimoxazole in 100%; 86%; 78.6%; 57.1% of the E. coli, respectively. Susceptibility to colistin, phosphomycin and tigecylin was always retained, while ceftazidime-avibactam showed activity in 86% of cases. The strains harbored mainly blaKPC-2 (n=6) or blaKPC-3 (n=1) genes, followed by blaOXA-181 (n=5) and blaVIM-1 (n=2); the coexistence with aac-(6')Ib-cr, blaCTX-M-type and blaSHV-5 genes was detected in eight, six and one isolate, respectively. Eight pulsotypes, five STs and three phylogenetic groups were identified: PFGE clone A (ST69), B, C, E (ST131), D, F (ST410), G (ST1288) and H (ST648). Six/14 E. coli belonged to group A, 7/14 to D and 1/14 to B2. The plasmid characterization showed FIA, FIB and FI replicons in the KPC-2/3, X3 in OXA-181, and B/O, A/C in the blaVIM-1-positive isolates.

Conclusions: The identification of ST131 blaKPC-2/3, ST410 blaOXA-181 and ST69 blaVIM-1 positive E. coli from LTCF residents underlines an alarming scenario in the Italian LTCF. Moreover, we detected blaKPC-2-positive E. coli of ST648 and ST1288, currently of rare reporting.

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Abstract 3669

Increased risk of bacteraemia caused by Staphylococcus aureus or Escherichia coli in patients with C10X polymorphism in the NLRP3 inflammasome gene CARD8

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Background: Host genetics play an important role in susceptibility to severe infections such as bacteraemia, of which Escherichia coli and Staphylococcus aureus are the leading causes. Variations in genes encoding two proteins within the NLRP3 inflammasome, C10X within the regulatory CARD8 gene and Q705K within the NLRP3 gene, have been associated with increased risk of chronic inflammation. The present study aimed to investigate whether these specific gene polymorphisms influence the risk of contracting bacteraemia caused by E. coli or S. aureus.

Materials/methods: Samples from blood cultures displaying growth of S. aureus or E. coli, and from negative blood cultures were consecutively included between November 2013 and December 2015 at four study centers in Sweden. Human DNA was extracted, followed by genotyping of the polymorphisms Q705K in the NALP3 gene and C10X in the CARD8 gene using TaqMan® SNP genotyping assays (Applied Biosystems, Foster City, CA).

Results: Table 1 shows the prevalence of genotype distribution of C10X, with a significant association between the homozygote variant and patients with bacteraemia caused by S. aureus or E. coli compared to patients with negative blood culture (p=0.007 and p=0.002, respectively). There were no difference in genotype distribution of Q705K, neither heterozygote nor homozygote variant, between patients with bacteraemia and those with negative blood culture.

Conclusions: The prevalence of the C10X homozygote variant in the CARD8 gene was significantly higher in patients with bacteraemia caused by E. coli or S. aureus compared to patients with negative blood cultures. Individuals carrying this gene variant may have an increased risk of contracting bacteraemia.

Table 1. Genotype frequencies of C10X in bacteraemia patients compared with negative blood cultures.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Negative blood cultures n=1086 (%)</th>
<th>S. aureus bacteraemia patients n=419 (%)</th>
<th>OR (95% CI)*</th>
<th>p-value*</th>
<th>E. coli bacteraemia patients n=622 (%)</th>
<th>OR (95% CI)*</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>TT (wildtype)</td>
<td>512 (47.1)</td>
<td>172 (41.1)</td>
<td>1</td>
<td>265 (42.6)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TA (heterozygote)</td>
<td>454 (41.8)</td>
<td>182 (43.4)</td>
<td>1.2 (0.9-1.5)</td>
<td>0.15</td>
<td>256 (41.2)</td>
<td>1.1 (0.9-1.3)</td>
<td>0.43</td>
</tr>
<tr>
<td>AA (homozygote)</td>
<td>120 (11.0)</td>
<td>65 (15.5)</td>
<td>1.6 (1.1-2.3)</td>
<td><strong>0.007</strong></td>
<td>101 (16.2)</td>
<td>1.6 (1.2-2.2)</td>
<td><strong>0.002</strong></td>
</tr>
</tbody>
</table>

*S. aureus and E. coli bacteraemia compared with negative blood cultures.

*Calculated by logistic regression

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Background: Staphylococcus aureus is a commensal of the upper respiratory tract. When mechanical ventilation overcomes natural defenses, S. aureus is frequently isolated from the airways, but distinguishing between colonisation and infection is difficult. The aim of this work was to describe genotypical and phenotypical features of S. aureus isolated from mechanically ventilated patients.

Materials/methods: A set of 48 clinical isolates were selected. Patients were classified as pneumonia [10], tracheobronchitis [11] and bronchial colonization [13]. Isolates were characterized with a DNA microarray (Alere Technologies) and underwent whole genome sequencing using Illumina HiSeq4000. Minimal inhibitory concentrations for daptomycin, vancomycin and teicoplanin were determined by UMIC test (Biocentric). THP-1 cytotoxicity assay was assessed after incubating cells with bacterial supernatants and later adding a specific viability reagent. Adhesion to solid-phase fibronectin (Fn) was determined by a standardized microtitre plate assay. Detection of alpha-toxin (AT) in bacterial supernatants was performed by Western-Blot.

Results: Isolates belonged to 14 different clonal complexes (CCs). The most frequent CC for methicillin resistant S. aureus (33.3% of all isolates) was CC5 (56.25%), as well as for methicillin susceptible (15.62%). All strains were vancomycin, teicoplanin and daptomycin susceptible, with the exception of one strain daptomycin resistant. All strains were positive for hla and fibronectin binding protein A (fnbA), 80% were positive for fibronectin binding protein B (fnbB) and only one isolate was positive for pvl. Cytotoxicity was variable among isolates with 14 strains showing no cytotoxicity, with these latter presenting an unaltered Fn binding capacity. No changes on cytotoxicity were reported when comparing study groups. FN binding capacity was reported for almost all strains, with the exception of 2 strains that presented the lowest values. Strains isolated from patients with pneumonia presented a lower capacity of adhesion in comparison to those isolated during tracheobronchitis (p=0.0029). AT was detected in 35 strains (73%), and no correlation with cytotoxicity, adhesion or study group were found.

Conclusions: There is an important diversity of clonal complexes in the set of S. aureus isolates.

Cytotoxicity is variable among strains, but no association with study groups was found, whereas isolates from patients with pneumonia had lower adhesion capability.

The use of whole genome sequencing will enable a more accurate identification of genetic variations.
Abstract 3672

Impact of BD urine culture application on clinical microbiology laboratory activity
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Background: Laboratory automation and intelligent use of informatics are showing a dramatic impact on microbiology diagnostics. The development of intelligent images analysis based on algorithms tailored on type of specimens and patient characteristics represents a major innovation that has the potential to increase laboratory efficiency while reducing turn-around-time. This study evaluates the impact on the routine laboratory activity of the BD urine culture application (UCA), implemented on the BD Kiestra automated system (Becton Dickinson, Sparks, MD, USA).

Materials/methods: Ten microliters of 753 midstream and 251 permanent catheter urines were inoculated onto CHROMagar Orientation, Blood agar supplemented with colistin and nalidixic acid, and MacConkey agar (Becton Dickinson) with the BD Kiestra InoqulA using the #4 zig-zag streaking pattern. For the algorithmic analysis, plate images were acquired using the OPTISTM software, at times 0 (reference of no growth), 12 h (early positive culture workup), and 18 h (imaging endpoint). In the absence of leukocytes, growth <10,000 CFU/ml and <100 CFU/ml were considered to be negative for midstream and catheter urine samples, respectively. Other types of urine specimens were excluded from UCA analysis.

Results: During a 20-days period, 519/1004 (51.6%) urines analyzed by UCA were automatically released as negative. Sensitivity was 99.3% and specificity 74.5%. Negative Predictive Value (NPV) was 99.6%. Theoretical time to report (mean ± SD) for negative samples (i.e., negative samples released by UCA for clinical validation) was 18.65 ± 1.03 h, and actual time to report was 20.86 ± 1.73 h, due to laboratory opening hours. UCA negative samples were all reported to clinicians between 7:30 and 9:52 a.m., with 75% being reported between 7:30 and 7:58 a.m. Time-to report of negative samples excluded from the UCA was 24.87 ± 4.33 h. UCA analysis of about 50 urines per day allowed saving about 20 min per day.

Conclusions: The implementation of the BD UCA to automatically release negative urine samples decreases the time to report of negative samples, and allows to save time in the laboratory practice, with optimal NPV.

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Abstract 3673

Prevalence and impact of meropenem-resistant among nonresistant OXA-48-producing *Klebsiella pneumoniae*

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Background: OXA-48-producing *Klebsiella pneumoniae* isolates frequently show growing subpopulations within inhibition zones in meropenem diffusion assays, leading to a low agreement between diffusion and broth dilution susceptibility methods (affecting to 20-60% of isolates recovered in our region). This feature has only been studied in carbapenemase-producing isolates from a hospital outbreak-based study and was associated to mutations in the *ompK36* porin gene. The aim of this study was to assess the frequency of these subpopulations among multiple OXA-48-producing *K. pneumoniae* strains, as well as to compare the porin expression and growth rate of the clinical isolates and their resulting subpopulations.

Materials/methods: Thirty OXA-48-producing *K. pneumoniae* clinical isolates, corresponding to 12 sequence types were selected: 27 with a meropenem MIC of ≤2 mg/L and 3 with MIC of 8 mg/L, S and I categories according to EUCAST, respectively, and showing resistant subpopulations by diffusion agar methods. They were detected between 2014-2017 from 12 hospitals from Andalusia. Population Analysis Profile (PAP) was performed to calculate the frequency of these subpopulations. Stability was determined by 5 passages without antibiotic. Porin profile was studied by SDS-PAGE. The Infinite 200Pro appliance was used to compare differences in growing among native strains and subpopulations at different concentrations of meropenem for 24 hours, with optic density lecture every hour.

Results: All strains showed subpopulations with an average of 5 times higher meropenem MIC values (range: 2-7 times) than their native populations, 21 (70%) with an MIC >8 mg/L (range 1-64 mg/L), with an average frequency of 1.47x10⁻⁷ (range: 15.5x10⁻⁶-8.93x10⁻¹⁰), and all were stable. All the native populations expressed OmpK35/36 porins comparing to half of the more resistant subpopulations. Regardless of porin profiles, subpopulations showed initial growth at meropenem MIC of >8 mg/L similar to that of native populations without antibiotic.

Conclusions: 1) All OXA-48-producing *K. pneumoniae* strains show a low frequency of subpopulations, most of them into the clinical meropenem resistance category; 2) these subpopulations were observed in all the studied clones and are stable mutants; 3) loss of porin expression could explain this phenomenon in only half of them; 4) all strains showed initial heterogenic populations.

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Does our microbiome travel well? Microbiome resilience and acquisition of multidrug-resistant bacteria in travellers

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Background: The international spread of antimicrobial resistance poses a serious health risk, compounded by approximately 1.4 billion travellers in 2018, many of which to countries that are hotspots of resistance. A previous study focusing on the carriage of multidrug resistant bacteria after travel showed that there is extensive acquisition and persistence of extended spectrum beta lactamase producing Enterobacteriaceae (ESBL-E) in the gut of travellers visiting Asia and Africa.

Materials/methods: Using shotgun sequencing data from 190 of these travellers, the metagenomics profile of the gut microbiome has been analysed to understand its role in this context. A metagenomics species concept approach was used to determine the taxonomic composition, population diversity and metabolism of the microbiome at baseline (before travel) and how these are altered longitudinally. Predicted genes are clustered by their abundance profile across multiple samples, providing a more powerful signal for analysing metagenome data.

Results: Here we show that these aspects at baseline do not significantly differ between travellers that were or were not subsequently colonised by ESBL-E, so are not predictive of the risk of acquiring ESBLs. Alternatively, there were longitudinal changes detected in the taxonomy and functional profile which were specific to the travel destination.

Conclusions: The lack in predictive power of the baseline microbiome suggests that a traveller’s risk of ESBL acquisition is difficult to determine before travel. Alternatively, the longitudinal results highlight the taxa and metabolic processes that may have a role in the protection against, or clearance of, ESBL producing Enterobacteriaceae. These are therefore potential targets as a prophylactic treatment or as adjuvants in the decolonisation of ESBL-E. However, the destination of travel is be a key factor to focus on, as this is a significant contributor to how the gut microbiome is altered.

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Effectiveness and safety of utilising oral vancomycin as prophylaxis for Clostridioides difficile infections in high-risk patients

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\textbf{Background:} Reducing the incidence of \textit{Clostridioides difficile} infections (CDI) is a desirable goal for many hospitals. Recent data have shown favorable results to administer oral vancomycin as CDI prophylaxis especially in patients at high-risk of developing CDI. Purpose of this study was to determine the effectiveness of oral vancomycin prophylaxis on the incidence of CDI.

\textbf{Methods:} Retrospective, quasi-experimental, propensity-matched cohort study that examined adult patients admitted with empiric broad-spectrum antibiotics for an infection. Patients admitted from June 2017 to November 2018 were given oral vancomycin as CDI prophylaxis (VANPPX) and compared to patients admitted from June 2016 to May 2017 as the no prophylaxis (NOPPX). Primary outcome was incidence of CDI, diagnosed anytime from the initiation of antibiotics until discharge.

\textbf{Results:} Of 532 patients, 266 patients were in each group. Mean age was 71 years (±13) and 47.0% (252/532) were given more than one broad-spectrum antibiotic. Fifty-seven percent (304/532) received a proton pump inhibitor with a higher proportion in the NOPPX (66.5% vs. 47.7%; \( p < 0.001 \)). There were more admissions to intensive care unit in NOPPX (34.6% vs. 22.2%; \( p = 0.002 \)). Overall, the incidence of CDI was 2.4% (4/532); 1.5% (4/266) patients had CDI in VANPPX as compared to 3.4% (9/266) patients in NOPPX (\( p = 0.261 \)) with an unadjusted odds ratio (OR) of 0.436; 95% confidence interval (CI) (0.133, 1.433). Eighty-eight percent (468/532) patients had no history of CDI with an unadjusted OR of 0.542; 95% CI (0.165, 1.786). Propensity-matched cohort included 468 patients for analysis, 234 patients in each group. Similar results were found after propensity matching with the incidence of CDI in VANPPX and NOPPX, 1.7% (4/234) compared to 3.8% (9/234), respectively; \( p = 0.130 \).

\textbf{Conclusions:} There were no statistical differences in the incidence of CDI between groups. This study may suggest no additional benefit in the use of oral vancomycin as primary CDI prophylaxis in patients that are high risk of developing CDI. There was a larger proportion of patients without history of CDI; however, there was no effect measure modification identified with the development of CDI. Further evaluation of CDI prophylaxis is needed according to a stratification of CDI risk factors.

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Abstract 3677

**Antimicrobial susceptibility and resistance determinants in Enterobacteriaceae and Staphylococcus aureus among febrile patients hospitalised in the African region.**

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**Background:** The severe under-documentation of bacterial resistance in Africa hampers formulation of adequate treatment guidelines, antimicrobial control policies and appropriate action plans. The study presents data on bacteria the WHO has highlighted as being key antimicrobial resistance (AMR) concerns in Africa, outlining their susceptibility to standard antibiotics and the corresponding resistance determinants, with the purpose of guiding empirical treatment of common infections.

**Materials/methods:** Blood, stool and urine specimens of 3,607 febrile patients, aged between ≥30 days and ≤81 years, hospitalized in Burkina Faso, Gabon, Ghana and Tanzania, from November 2013 to March 2017 were cultured. Antibiotic susceptibility testing was performed for all Enterobacteriaceae and *Staphylococcus aureus* isolates using disk diffusion method. Extended-spectrum β-Lactamase (ESBL) production was confirmed by combined disc test and further characterized by amplifying the *bla*CTX-M, *bla*TEM and *bla*SHV genes. Ciprofloxacin resistance among *Salmonella* spp. was confirmed by E-test and non-susceptible isolates were screened for plasmid-mediated resistance genes and *gyrA*, *gyrB*, *parC*, *parE* mutations. *S. aureus* isolates were further differentiated by *spa*-typing and multi-locus-sequence-typing.

**Results:** Of 4,464 specimens, positive cultures comprised: 3.3% (N=3423) blood, 15.4% (N=629) urine and 2.2% (N=412) stool. Enterobacteriaceae were the most common isolates (88.2%, N=220), including 90 (46.4%) *Salmonella* spp., 73 (37.6%) *Escherichia coli* and 22 (11.3%) *Klebsiella pneumoniae*. The rate of ESBL-producers (all CTX-M15 genotype) was highest in Burkina Faso (n=15; 38%), followed by Gabon (n=8; 23%), Ghana (n=18; 14%) and Tanzania (n=0; 0%). ESBL positive *Salmonella* (N=3) were detected in Burkina Faso only. Similarly, ciprofloxacin resistance in Enterobacteriaceae was notably higher in Burkina Faso (53%) relative to ≥13% in the other countries.

Screening among ciprofloxacin resistant *Salmonella* revealed 2 (1.7%) isolates in Ghana with *gyrA* mutations D87G and, 7 (22%) isolates in Burkina Faso, 6 with *qnrB* genes and one with a *gyrA* mutation E133G. Methicillin resistant *S. aureus* were detected in one blood and one urine culture, only in Ghana.

**Conclusions:** Our findings reveal a distinguishable susceptibility pattern across the various African countries; thus, highlighting the need for local AMR assessments to inform empirical treatment. We additionally exhort for continued investigations of AMR in Africa, to augment the existing scarce data.

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**Enterococcus faecalis inhibits Klebsiella pneumoniae growth in polymicrobial biofilms**

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**Background:** Catheter-related urinary tract infections are one of the most common biofilm-associated diseases. Inside the biofilms, bacteria cooperate, compete or have neutral interactions according to the species involved. The aim of this investigation was to study the interspecies interactions in polymicrobial biofilms formed by *Klebsiella pneumoniae* and *Enterococcus faecalis*, two of the most common uropathogens.

**Materials/methods:** One *K. pneumoniae* and three *E. faecalis* strains were included in the study. Biofilms were evaluated by crystal violet (CV) assay, percentage of inhibition in biofilm formation, enumeration of colony-forming units (CFUs) and competitive index (CI). The competition was also studied in planktonic cultures. Antimicrobial and antibiofilm activities of lyophilized cell-free supernatants (L-CFS) from *E-faecalis* were evaluated against the *K. Pneumoniae* strain. In addition, pH and lactic acid production in *E. faecalis* L-CFS were measured at 30 minutes, 1, 2, 3, 4, 8, 24, 48 and 72 hours.

**Results:** *K. pneumoniae* was the most adherent strain, but it was not capable to maintain dominance when it grows in polymicrobial biofilms with *E. faecalis*. Furthermore, a statistically significant decrease in total biomass volume and CFUs of *K. pneumoniae* in polymicrobial biofilm was found compared with the monomicrobial biofilms. Negative CI values also indicate a competitive advantage of *E. faecalis* over *K. pneumoniae*. However, the reduction in CFUs was not statistically significant in planktonic cultures. Antimicrobial, antibiofilm, and eradication biofilm capacities against the *K. Pneumoniae* strain were observed using L-CFS collected from different *E. faecalis* biofilms. Otherwise, this effect was not present when the pH of L-CFS collected from biofilm was adjusted in 6.5. In addition, lactic acid production around 2.4 g/L was measured in biofilm supernatants, demonstrating that *E. faecalis* decreases pH in polymicrobial biofilm by lactic acid production, resulting in *K. pneumoniae* growth inhibition.

**Conclusions:** *K. pneumoniae* and *E. faecalis* interact in a competitive mode. L-CFS collected from *E. faecalis* biofilms, had an antimicrobial, antibiotic and eradication of biofilm effects over *K. pneumoniae*. For this reason, in polymicrobial biofilms, *E. faecalis* is able to modify the pH by lactic acid production, compromising the appropriate growth of *K. pneumoniae*.

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Ceftaroline fosamil for the treatment of methicillin-resistant Staphylococcus aureus bacteraemia: a real-world comparative clinical outcomes study

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Background: MRSAB is associated with significant clinical and economic healthcare system burden. This large real-world study explored whether MRSAB treatment outcomes differ with ceftaroline fosamil versus vancomycin and daptomycin.

Materials/methods: This study utilised US data from the Premier Healthcare Database (July 2011–March 2019). Adults hospitalized with MRSAB and treated with intravenous ceftaroline, vancomycin, or daptomycin were classified into three treatment groups: ceftaroline [no concurrent vancomycin or daptomycin] (Group 1); vancomycin or daptomycin [no concurrent ceftaroline] (Group 2), or combination therapy with ≥two of these three agents (Group 3). Clinical outcomes were compared using propensity score-adjusted odds ratios (ORs) from logistic regression models. Outcomes included clinical response [hospital discharge with no further need for antibiotic treatment, or with treatments indicating clinical improvement]; switch to another intravenous anti-MRSA treatment after 2 days; discharge status [expired/discharge to hospice/skilled nursing facility, discharge to health home organization/home and other/unknown]; and 30-day readmission (all-cause and MRSAB).

Results: In total, 24,479 patients were included (Group 1, n=532; Group 2, n=21,555; Group 3, n=2,392). Group 3 was, on average, younger with fewer comorbidities versus Groups 1 and 2 (mean age [SD]: 57.4 [17.4] vs. 59.6 [17.0] and 60.8 [17.5], Charlson Comorbidity Index score [SD]: 2.0 [2.8] versus 3.0 [3.2] and 2.3 [3.0], respectively; all p<0.01). Versus Group 2, Groups 1 and 3 were more likely to have clinical response (OR: 1.18 [95% CI 0.98-1.44]; p=0.08, and OR: 1.20 [95% CI 0.97 - 1.47]; p=0.09, respectively) and less likely to switch treatment (both p<0.001). However, Group 1 was more likely to have 30-day all-cause readmission (OR: 1.38 [95% CI 1.06-1.80]; p=0.02), while Group 3 was less likely (OR: 0.77 [95% CI 0.58-1.00]; p=0.05) versus Group 2. Compared with Group 1, Group 3 more often had clinical response (OR: 1.38 [95% CI 1.27-1.51]; p<0.001), was less likely to switch treatment (p<0.001), and more often discharged to home (p=0.01).

Conclusions: Ceftaroline monotherapy resulted in greater probability of clinical response versus vancomycin or daptomycin monotherapy. Combination therapy was associated with improved outcomes versus monotherapy. These results provide valuable real-world insights into ceftaroline fosamil as a potential MRSAB treatment option.

Study sponsored by Pfizer.

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Impact of positive microbiological testing on antimicrobial de-escalation and clinical outcomes in community-acquired pneumonia

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Background: We aim to determine the impact of positive microbiological (PM) testing on antimicrobial de-escalation and outcomes of patients with community-acquired pneumonia (CAP).

Materials/methods: Analysis of a prospective cohort of non-immunosuppressed adults hospitalized for CAP. Antimicrobial de-escalation was considered when the initial empirical antimicrobial therapy was narrowed to a penicillin, amoxicillin or amoxicillin/clavulanate, when microbiologically feasible; to a quinolone or macrolide in Legionella pneumonia; and to oseltamivir in cases of influenza disease. Exclusion criteria were early mortality (<72h), empirical antimicrobial therapy with an already narrow coverage, and/or lack of data regarding de-escalation. Study outcomes were time to switch to oral antimicrobial therapy, overall duration of antimicrobial therapy, ICU-admission, length of hospital stay, and 30-day case-fatality rate.

Results: Of 4393 hospitalized patients with CAP, 2257 (51.4%) had a PM testing. The three main causative agents were: Streptococcus pneumoniae (n=1479), Legionella pneumophila (n=234), and Haemophilus influenzae (n=187). Pre-hospital antimicrobial use for the acute CAP episode was associated with negative microbiological results (NM) (18.9% vs. 26.7%; p<0.001). Antimicrobial de-escalation was performed in 841 (19.2%) patients and was independently associated with PM testing (PM: 25.4% vs. NM: 12.6%; OR=3.00; p<0.001). ICU-admission was associated with PM testing (OR=1.776; p<0.001) and inversely related with antimicrobial de-escalation (OR=0.491; p<0.001). A propensity score (PS) was generated using eight variables that could have influenced the decision to de-escalate treatment [age, comorbidities, aspiration CAP, empyema, bilateral involvement, SAPS severity score>15, ICU-admission and PM testing]. Multivariate analysis adjusted by PS showed that antimicrobial de-escalation was less often associated with PM testing (OR=1.3; p=0.0051). Days to antimicrobial oral switching (OR=0.931; p=0.56) and overall length of antimicrobial treatment (OR=0.760; p=0.002) were shorter in patients who underwent de-escalation. Thirty-day mortality was not found to be independently associated with antimicrobial de-escalation (OR=0.786; p=0.414).

Conclusions: PM testing was associated with antimicrobial de-escalation in CAP, leading to shorter time to switching to oral antibiotics and overall duration of antimicrobial therapy. De-escalation was not independently associated with higher 30-day mortality. Further research is necessary to determine the potential impact of new point-of-care tests in antimicrobial stewardship strategies and outcomes in CAP.

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Abstract 3692

**Predicting the effect of single nucleotide polymorphisms on fluoroquinolone resistance in Mycobacterium tuberculosis by computational methods**

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**Background:** Multi-drug resistant (MDR) tuberculosis (TB) presents an increasing challenge for TB treatment globally. The WHO recommends fluoroquinolone antibiotics to treat MDR TB. However, fluoroquinolone resistance can be conferred by a small number of point mutations in the gyrA and gyrB genes of the antibiotic target, DNA gyrase. It is important to know whether novel mutations confer fluoroquinolone resistance in order to effectively treat patients and prevent transmission of resistant strains. Current TB drug susceptibility testing takes 6-8 weeks, yet most gyrA and gyrB mutations will result in susceptibility to fluoroquinolones. Therefore, computational approaches able to rapidly predict fluoroquinolone-susceptibility from genetic sequences would be invaluable for TB diagnostics.

**Materials/methods:** A physics-based tool, alchemical free energy methods, was applied to make susceptibility predictions based on relative binding free energy estimates. This method was tested using three control mutations, gyrA A90V (fluoroquinolone-resistant), gyrA S95T (fluoroquinolone-susceptible) and gyrA A90S (fluoroquinolone-hypersusceptible). A logistic regression model was then trained to classify previously observed gyrA and gyrB mutations as susceptible or resistant to moxifloxacin and levofloxacin. Training data included structural and chemical features of the wild type and mutant amino acids associated with the CRyPTIC catalogue of gyrA and gyrB mutations obtained from ~10,000 published genomes.

**Results:** Alchemical free energy methods made binding free energy estimates with error of +/- 1 kcal/mol, enabling confident prediction of the correct phenotype for all three test mutations, but took ~160,000 CPU hours per mutation. Logistic regression accurately classified mutants conferring fluoroquinolone-susceptibility and false positives were predicted at a low rate based on cross-validated error estimates for known mutations. Distance of the mutated amino acid from the fluoroquinolone binding site proved an important predictor. However, the phenotype of several mutants was predicted by the machine learning algorithm to be susceptible with low confidence, and additional novel mutations were predicted to be resistant. The impact of these mutations could then be predicted using more time-consuming alchemical free energy methods.

**Conclusions:** A combination of machine learning and physics-based approaches could help reduce the time needed to diagnose fluoroquinolone susceptibility in Mycobacterium tuberculosis isolates with novel or rare DNA gyrase mutations.

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Abstract 3694

**Differences in risk and outcomes for patients with Clostridium difficile toxin positive versus only cytotoxigenic culture positive faecal samples: results from COMBACTE-CDI case-control study**

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**Abstract third-party references:** on behalf of the COMBACTE-CDI consortium

**Background:** Currently reported risk factors for and outcomes of *C. difficile* infection (CDI) may be clouded by the use of different diagnostic methods in studies.

**Materials/methods:** Sites were recruited from 12 countries across Europe (1 site/3 million population). On two days, all diarrhoeal samples (regardless of tests requested, n=3613) were sent to the European coordinating laboratory for *C. difficile* toxin detection; cell-cytotoxin neutralisation testing (CCNA) ultrasensitive immunoassay (SIMOA) and cytotoxigenic culture (CTC). Cases were defined as C1 (CCNA positive n=94), C2 (CCNA-negative/SIMOA-positive n=43), C3 (toxin-negative/CTC-positive n=34), C4 controls (negative by all assays n=444). Data were collected on patient outcomes and risk factors and comparisons made according to diagnostic categories C1-4.

**Results:** C1 cases were significantly older vs C3 (median age 71 vs 47 years, p=0.013), and vs controls (C4) (71 vs 55 years p<0.0001). C2 cases were significantly older than controls (p=0.006), but not C3 (p=0.132); C3 were not significantly older than controls (p=0.859).

Mean white cell count of cases in C1 and C1+C2 (toxin positive) was significantly higher than controls (14.8x10^9/L vs 10.3x10^9/L, p=0.008 and 14.4 vs 10.3x10^9/L, p=0.002). Median length of stay (LOS) was significantly longer for C1 (12 versus 10 days, p=0.011) and C1+C2 (14 vs 10 days p=0.011) than controls. There was no significant difference in LOS between C3 and controls. 30-day mortality rate was significantly higher for C1 cases (15.9% vs 6.0%, p=0.002) and C1+C2 (13.3% vs 6.0%, p=0.007) versus controls.

The significant risk factors according to diagnostic categories are shown in Figure 1. There were no significant risk factors identified for C3 patients.

**Conclusions:** There are significant differences in outcome between patients diagnosed as toxin positive versus only CTC positive cases, when compared with controls, such as higher mortality rates and length of stay in toxin positive individuals. Risk factors for the development of toxin positive CDI were observed, but there were no risk factors identified for the presence of the organism alone, e.g. increasing age, use of antibiotics and increased co-morbidities appear to be a risk factors for toxin positive CDI, but not acquisition of the organism itself.
Figure 1. Risk factors for different CDI diagnostic categories

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**In vitro activity of imipenem/relebactam against non-Morganellaceae Enterobacterales, Pseudomonas aeruginosa and Acinetobacter baumannii isolates from patients with respiratory tract infections in the United States: SMART 2016-2018**

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**Background:** Relebactam (REL) is a diazabicyclooctane inhibitor of class A and C β-lactamases approved in the United States (US) in combination with imipenem and cilastatin for treatment of complicated intra-abdominal and urinary tract infections. A phase 3 clinical trial comparing imipenem/cilastatin/REL to piperacillin/tazobactam (TZP) for the treatment of hospital-acquired or ventilator-associated bacterial pneumonia (RESTORE-IMI 2) was recently completed. This study evaluated the in vitro activity of imipenem and REL (imipenem/REL), TZP and other comparators against organisms collected from US patients with respiratory tract infections (RTI) as part of the SMART surveillance program, including the most common pathogens identified during RESTORE-IMI 2.

**Materials/methods:** Twenty-eight medical laboratories each collected up to 100 consecutive clinically-significant gram-negative pathogens from patients with RTI. MICs were determined by broth microdilution and interpreted using CLSI breakpoints with the exception of imipenem/REL, for which US Food and Drug Administration (FDA) breakpoints were used.

**Results:** *K. pneumoniae, P. aeruginosa, A. baumannii, E. coli, and E. cloacae* were the five most prevalent gram-negative pathogens, in rank order, isolated from patients during the RESTORE-IMI 2 trial. These organisms composed 11.7%, 32.4%, 2.7%, 10.5%, and 5.8%, respectively, of isolates collected from US patients with RTI (n=5832) as part of SMART in 2016-2018. Imipenem/REL demonstrated potent *in vitro* activity against the collection of all non-Morganellaceae Enterobacterales (NME) (MIC90, 0.5 mg/L; 97.6% susceptible), *K. pneumoniae, E. coli* and *E. cloacae* isolates (MIC90, 0.25-0.5 mg/L; ≥99.7% susceptible), and *P. aeruginosa* (MIC90, 2 mg/L; 93.0% susceptible) collected in the US (Table). In contrast, imipenem/REL showed limited activity against *A. baumannii* isolates, which often harbor class D β-lactamases (MIC90, >32 mg/L; 53.9% susceptible). Similar activity was observed across US census regions, with susceptibility to imipenem/REL consistently exceeding that of TZP against individual species, the combined collected of most prevalent organisms, and all NME by 5-30 percentage points.

<table>
<thead>
<tr>
<th>Organism</th>
<th>United States</th>
<th>West</th>
<th>Midwest</th>
<th>Northeast</th>
<th>South</th>
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<tbody>
<tr>
<td></td>
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<td>75.8</td>
<td>823</td>
<td>93.7</td>
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</tbody>
</table>

**West:** California, Colorado, Utah, Washington; **Midwest:** Illinois, Indiana, Iowa, Michigan, Minnesota, Nebraska, Ohio, Wisconsin; **Northeast:** New York, Pennsylvania; **South:** Florida, Georgia, Kentucky, North Carolina, Texas. REL, relebactam; TZP, piperacillin/tazobactam; S, susceptible. NME, non-Morganellaceae Enterobacterales.

* US FDA breakpoints for imipenem/REL: ≤1/4 mg/L, susceptible; 2/4 mg/L, intermediate; ≥4/4 mg/L, resistant (Enterobacterales); ≤2/4 mg/L, susceptible; 4/4 mg/L, intermediate; ≥8/4 mg/L, resistant (*P. aeruginosa*). No FDA breakpoints were assigned for *A. baumannii*; CLSI breakpoints were applied for comparison only.

**Conclusions:** IMI/REL demonstrated potent *in vitro* activity against non-Morganellaceae Enterobacterales, including the three most prevalent species identified during RESTORE-IMI 2, and *P. aeruginosa* collected in the US. Imipenem/REL could provide an important option for treatment of RTI caused by organisms with similar resistance mechanisms.

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Accuracy of emergency department diagnosis of community-acquired pneumonia

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Background: Community acquired pneumonia (CAP) is usually diagnosed in the emergency department (ED), with patients commenced on broad spectrum antibiotics. A review of the literature indicates that around one third of these patients may not truly have CAP. Misdiagnosis leads to delays in obtaining an accurate diagnosis and commencing appropriate treatment. Additionally, unnecessary use of broad spectrum antibiotics contributes to bacterial resistance. Little research has been undertaken into the accuracy of pneumonia diagnosis in Australia.

Materials/methods: The sample was identified from coded ED data in 2017 at a tertiary hospital in Melbourne, Australia. Charts for ED visits with a code for CAP, excluding those hospitalized within 14 days, underwent a standardized chart review. A strict definition of CAP was applied using international guidelines, based on presence of radiographic chest infiltrates, accompanied by a characteristic clinical presentation. Analyses were performed using STATA 15.0.

Results: Of 133 patients with an ED diagnosis of CAP, 34% (n=45, CI: 26-42%) were found to have an alternate diagnosis when a strict definition of CAP was applied. Although symptoms consistent with a lower respiratory tract infection were present in all patients who were misdiagnosed, only 18% (n=8, CI: 9-32%) had chest X-ray (CXR) changes suggestive of CAP. When the treating physician’s interpretation of the CXR was compared with the official radiology report in the misdiagnosed group, there was a disagreement in 42% of cases (n=19, CI: 28-57%). All patients misdiagnosed received antibiotic treatment on admission. Over fifty-one percent of these patients were deemed to have received unnecessary antibiotics courses (n=23, CI: 36-66%) for a median of 4 days (IQR=3). Patients misdiagnosed with CAP were older, with a median age of 76 (IQR: 64-82) compared to a median age of 68 (IQR 48-84) in the correctly diagnosed CAP group.

Conclusions: There is a high rate of misdiagnosis of CAP in the emergency department with 34% of cases having an alternate diagnosis. Many patients misdiagnosed as having pneumonia had symptoms of an acute respiratory infection but often did not have radiological changes consistent with pneumonia. Further work is underway to determine factors that influence the rate of misdiagnosis.

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Abstract 3697

**An agent-based model to simulate the transmission of glycopeptide-resistant enterococci in hospital according to several control strategies**

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**Background:** We studied the epidemic spread of glycopeptide-resistant enterococci (GRE) between 3 specialized care units (2 conventional units and 1 intensive care unit) according to several control strategies.

**Materials/methods:** The literature review revealed that the most relevant model was the agent-based model (ABM). The parameters of ABM were derived from data observed in our hospital and from data of the literature. We simulated GRE transmission during one year under different scenarios: different rates of hand hygiene compliance for healthcare workers (HCW) in the care of all patients and particularly GRE carrier patients (scenario with contact precautions), geographical cohorting of carrier patients in one of the two conventional care units, and creation of an isolation unit with dedicated HCW.

**Results:** With less than 50% hand hygiene compliance, the spread was not under control. With 80% hand hygiene compliance in the care of all patients, there were no secondary cases in 50% of the simulations. It was the better scenario. The establishment of an isolation unit with dedicated HCW was efficient when the level of hand hygiene compliance was low. The simple geographical cohorting of GRE carrier patients was less effective.

**Conclusions:** The simulations confirmed the importance of hand hygiene in patient care regardless of their infectious status. The part of the environment remains to be studied.

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Abstract 3698

**Diagnosis of bone and joint infections using nanopore metagenomic sequencing of synovial fluids and tissue samples**

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**Background:** Metagenomic sequencing has the potential to replace culture for the microbiological diagnosis of bone and joint infection (BJI). However, the large proportion of human DNA in clinical samples reduces the extent of bacterial sequence data obtained. We assessed whether a human DNA depletion protocol improved bacterial DNA recovery sufficiently to identify bacterial species and predict antimicrobial resistance.

**Materials/methods:** Tissues and synovial fluids were processed using standard culture procedures. In parallel, DNA was extracted from 27 culture positive tissue samples, with and without saponin treatment followed by DNase exposure for host DNA depletion. Additional optimisations that aimed to improve human DNA depletion were performed on 35 tissue and synovial fluid samples, including: preexposure to dithiothreitol or mechanical lysis before saponin treatment and extension of the DNase step. Human DNA depletion was assessed by qPCR. Samples were sequenced on the Oxford Nanopore GridION platform. Bacterial species were determined to be present if ≥10% of bases classified as bacterial originated from the species.

**Results:** Human DNA depletion improved pathogen detection in tissues: 84% (26/31) versus 65% (20/31) of bacteria identified by culture were detected using sequencing when tissue samples were treated with or without saponin respectively. In these samples, mean bacterial genome coverage breadth and mean depth significantly increased using saponin (44% versus 28%, p<0.003, and 1.17-fold versus 63-fold, p<0.001, respectively, Figure 1). Extension of the DNase treatment step increased human DNA depletion in synovial fluids, but not in tissues, and correlated with improvement of the bacteria detection rate using sequencing (80% (12/15) versus 67% (10/15)). Antimicrobial resistance prediction was improved by human DNA depletion and optimisation of the protocol for synovial fluids and could be performed in total for 21/37 bacteria identified by sequencing (all with coverage breadth >70%). We detected acquired resistance genes accounting for all beta-lactams, macrolides, fusidic acid and tetracycline resistance phenotypes found by conventional sensitivity testing.

**Conclusions:** Nanopore metagenomic sequencing can provide diagnostic information for BJI from tissue and synovial fluid samples. Human DNA depletion is necessary to obtain sufficient genome coverage for AMR prediction and the protocol should be adapted depending on the sample type tested.

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Abstract 3700

Clinical development of a meningococcal group A, C, W, and Y tetanus toxoid conjugate vaccine
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Abstract third-party references: Supported by Pfizer

Background: Meningococcal serogroup W (MenW) and Y (MenY) disease has proliferated in Europe in recent years, affecting all ages. MenW cases are often associated with a hypervirulent ST-11 strain and a more recently emergent ST-9316 strain, which primarily affects children <4 years of age. In response, many countries updated their immunization programs to include quadrivalent meningococcal (MenACWY) vaccines [Figure], often replacing monovalent MenC vaccines.

MenACWY-TT (Nimenrix®) is a MenACWY tetanus toxoid conjugate vaccine licensed in the European Union and 49 other countries. It is administered to infants as a 2-dose [6 weeks–<6 months] or 1-dose [6–<12 months] primary series plus 1-dose booster in the second year of life, and as a single dose from age 12 months. Booster dosing can be administered from age 12 months if previously vaccinated with a conjugated or plain polysaccharide meningococcal vaccine.

Materials/methods: Immunogenicity and safety data from MenACWY-TT clinical studies supporting licensure are summarized.

Results: Across studies and age groups, MenACWY-TT elicited comparable antibody responses against serogroup C compared with MenC vaccines in infants/toddlers and against serogroups A/C/W/Y compared with MenACWY vaccines in other age groups, with robust antibody responses after booster dosing. Recent data demonstrate antibody persistence through 10 years after primary MenACWY-TT vaccination and 6 years after booster dosing, which were comparable to those following MenC vaccination for serogroup C. MenACWY-TT can be concomitantly administered with many typically recommended vaccines.

MenACWY-TT had an acceptable safety/reactogenicity profile in a pooled analysis of toddlers, children, adolescents, and adults [n=9621] and separate studies in older adults (>55 years; n=274), infants [n=1052], and toddlers receiving a booster dose [n=1008]. Reactogenicity profiles were generally similar across age groups and doses.

Conclusions: The MenACWY-TT clinical study program demonstrated consistency of vaccine-induced immunogenicity and safety across age groups. Immune responses persisted through 10 years after primary vaccination and 6 years after booster dosing. These data support MenACWY-TT licensure and current recommendations to prevent meningococcal group A/C/W/Y disease from age ≥6 weeks, which may help reduce the increasing burden of MenW and MenY disease in Europe.

Funded by Pfizer.

Figure: European countries with recent MenACWY vaccine recommendations.

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Abstract 3704

Modulation of antibiotic-associated virulence of Pseudomonas aeruginosa in cystic fibrosis bacterial biofilms
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Background: Bacterial biofilms are known to have high antibiotic tolerance which directly affects clearance of bacterial infections in people with cystic fibrosis (CF). Current antibiotic susceptibility testing methods are either based on planktonic cells or do not reflect the complexity of biofilms in vivo. Consequently, inaccurate diagnostics affect the treatment choice, preventing bacterial clearance and developing antibiotic resistance. This leads to prolonged ineffective treatment.

Materials/methods: In this study, we are using an ex-vivo biofilm lung model to study antibiotic tolerance of Pseudomonas aeruginosa in a single and co-infection with Stenotrophomonas maltophilia. Sections of pig bronchiol e were dissected, prepared and infected with clinical isolates of P. aeruginosa and/or S. maltophilia and incubated in artificial sputum media to form biofilms, as previously described. Then, lung-associated biofilms were challenged with antibiotics, at therapeutically relevant concentrations, before their bacterial load and virulence were quantified and detected, respectively.

Results: The results demonstrated minimal effect on the bacterial load with ciprofloxacin and meropenem, with the later causing an increased production of protease and pyocyanin of P. aeruginosa. Comparison with combination of meropenem and tobramycin did not show any additional decrease in bacterial load but demonstrated a slight decrease in total protease and pyocyanin production. In co-infection, S. maltophilia modulated the persistence and virulence of P. aeruginosa, which was strain dependent.

Conclusions: P. aeruginosa showed high levels of persistence and increased virulence production which negatively would affect lung functions. In co-infection, it was further protected even against levofloxacin, which might derive increased antibiotic resistance in mixed CF infections. Therefore, we demonstrate a realistic model for understanding antibiotic resistance and tolerance in biofilms clinically and in anti-biofilm drug development.

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Abstract 3706

Microbiological surveillance of duodenoscope reprocessing following an outbreak with OXA-48 producing *Klebsiella pneumoniae*

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**Background:** Between December 2012 and February 2013, Charité University Medicine, Berlin, a tertiary hospital with 150,000 hospital admissions a year, experienced an outbreak with OXA-48 producing *K. pneumoniae* due to ERCP which involved 12 patients. In consequence, several improvements were made to the reprocessing process of the duodenoscopes: i) strict adherence to the procedures recommended by the different manufacturers of the duodenoscopes ii) use of connectors for the duodenoscope washing machines as recommended by the manufacturers iii) implementation of Standard Operation Procedures. To increase the sensitivity of the quarterly microbiological surveillance testing, brushing of the working channel was added to the procedure recommended by German guidelines.

**Materials/methods:** Duodenoscopes were sampled by flushing the working channel with 20 ml of sterile saline solution, brushing and then flushing it again. A 10 ml sample of the each flushing solution (before / after brushing) was neutralized, filtered and incubated on Columbia agar plates at 36±1°C. After 48 hours, colony forming units (cfu) were counted. In addition, the cantilevered elevator mechanism of the duodenoscopes was swabbed. Swabs were enriched in trypticase soy broth (TSB) for 48 hours at 36±1°C. Subsequently, the enriched TSB samples were cultured on Columbia and MacConkey plates.

**Results:** Channel flushing:

![Image](image_url)

Figure 1: Number of duodenoscopes undergoing microbiological surveillance 2013 - 2018 and the cfu’s of filtered flushing solutions. A limit of < 10 cfu / 10 ml is in concordance with the German guidelines for successful reprocessing.

Elevator mechanism swabbing: No pathogens were detected.

**Conclusions:** The reprocessing procedure of duodenoscopes improved substantially. In 2018, none of the microbiological surveillance samples exceeded the limit of < 10 cfu [versus 43% in 2013].

Microbiological surveillance testing by brushing and flushing the channels had higher sensitivity than just flushing the channels [10 of 16 limit violations would have been missed without brushing].

The complex design of duodenoscopes requires accurate and stringent reprocessing and adherence to the manufacturer's recommendations.

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An opportunity for antimicrobial stewardship in urinary tract infections using rapid tests directly on urine samples

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Abstract 3707

**Background:** Time to identification and antimicrobial susceptibility testing (AST) of microorganisms causing urinary tract infections (UTIs), impacts antimicrobial treatment. We propose a “Fast Track” algorithm for early etiological diagnosis of complicated UTIs, based on rapid tests directly on urine samples, combined with antimicrobial stewardship.

**Materials/methods:** Prospective study in a 1200-bed tertiary hospital from October 2018 to June 2019. Adult hospitalized patients with blood cultures taken and a urine sample received in the Microbiology laboratory were evaluated. Patients with microorganisms seen in gram stain of uncentrifuged urine were finally included. Direct identification using MALDI-TOF and direct AST were performed. Detection of carbapenemase production was evaluated by PCR (Xpert Carba®) when *Klebsiella pneumoniae* was identified by MALDI-TOF. Rapid results were informed to physicians in charge of each patient and antimicrobial adjustment was advised by a clinical microbiologist within the working shift. Results and turnaround time (TAT) were compared for both rapid and conventional methods. Antimicrobial adjustment within 24 hours after rapid results was recorded.

**Results:** During the study period, 1535 urine samples were evaluated. Of them, 269 (17.5%) ended to have a positive urine culture (>10^5 cfu/ml). Of these 269 urines, microorganisms were seen in gram stain in 212 samples (79%) from 211 patients. Compared to standard urine culture, MALDI-TOF identified, directly on urine, 69% of gram negative bacilli (GNB), 55.5% of gram positive cocci and 0% of yeasts. Out of the 22 GNB identified as *K. pneumoniae*, 5 were OXA-48 producers and all were early detected in urine by Xpert Carba®. Mean TAT were as follows: identification by MALDI-TOF directly on urine, 4 hours; preliminary AST, 22h; identification of microorganism in standard culture, 28h; standard AST report, 94h. Empirical treatment was considered adequate in 89 patients (42%). Of the remaining 123, rapid results lead to a change in treatment within 24h in 87 episodes (70.7 %), either de-escalation or adjustment due to resistance.

**Conclusions:** The proposed diagnostic algorithm provides advanced information, within 4 hours, in 79% of all episodes of UTIs requiring admission in our Hospital, with an important impact on antimicrobial stewardship during the first 24 hours.

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Posaconazole versus voriconazole as antifungal prophylaxis for invasive fungal diseases in patients with haematological malignancies

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Background: The incidence of Invasive Fungal Diseases (IFDs) has been dramatically increased in patients with hematologic malignancies due to prolonged neutropenia. IFDs are associated with significant morbidity and mortality. Due to these risks, international guidelines have recommended antifungal prophylaxis for Acute Myeloid Leukemia (AML) and Myelodysplastic syndromes (MDS) patients. Posaconazole has been recommended as the prophylactic agent of choice in these patients. Also, voriconazole has been recommended by guidelines with different levels of recommendations. Data on a direct comparison between Posaconazole delayed-release tablets (DR) and Voriconazole for IFD prophylaxis are lacking. Therefore, we aim to compare the efficacy and safety of the fungal prophylaxis; voriconazole versus posaconazole in AML/MDS patients at Princess Nourah Oncology Center (PNOC), Jeddah.

Materials/methods: Retrospective chart review study for eligible patients from January 2017 to February 2019 to identify the breakthrough IFD rates and assess the frequency of adverse events within AML/MDS patients at PNOC, Saudi Arabia.

Results: A total of 48 patients (130 chemo cycles) were included in the study: 50 using posaconazole (DR) and 80 using oral voriconazole as antifungal prophylaxis. The incidence rates of IFD in the posaconazole group was 8.0% (4/50) of those 2 were probable, and 2 were possible infections while 6.26% (5/80) of patients in the voriconazole group have developed IFD of them 4 had a possible infection, and one had a probable infection (p=0.7325). A higher percentage of patients in the voriconazole group discontinued prophylaxis due to adverse events (5 patients vs. 2 patients). Use of voriconazole as antifungal prophylaxis for 15 days in 130 cycles in 48 AML/MDS patients would cost 1,755,500 SR in comparison to the cost of the posaconazole for the same duration of 1,350,130 SR. So, use of voriconazole would save 1.13 million SR and is more cost effective when used as antifungal prophylaxis in AML/MDS patients in comparison to posaconazole although it is category 1 recommended antifungal prophylaxis in international guidelines.

Conclusions: Our study has shown that both posaconazole and voriconazole have comparable efficacy and safety in the prevention of IFD in AML and MDS receiving chemotherapy but voriconazole is more cost effective.

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**Abstract 3710**

**French Urinary Tract Infections in Healthcare Facilities (FURTIHF): an historic cohort**

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**Background:** Urinary tract infections (UTI) are so common, including very various infections: cystitis, acute pyelonephritis (APN), prostatitis or kidney abscesses but their incidence remains unknown. UTIs could lead to hospitalization in acute care settings and a substantial UTI amount is also hospital-onset UTIs. The incidence of UTIs in France is unknown. The objective was to assess performance parameters of an UTI case definition based on the French hospital medico-administrative databases (F-DRG: PMSI) and estimate the national incidence of UTIs in acute-care settings.

**Materials/methods:** An historic cohort of adult patients with UTIs hospitalized in France was performed using the PMSI databases 2014-2018. Hospital stays with at least one ICD-10 code of UTI were selected via the F-DRG algorithm built by a multidisciplinary team (ID specialists, urologists, epidemiologists). The performance parameters were calculated by reviewing 500 medical reports as gold standard (250 cases/250 non cases according to the F-DRG definition), blindly by physicians in charge of the patients. The national incidence rate was estimated after adjusting on the predictive positive value (PPV) of the case definition.

**Results:** The internal validation of the algorithm showed: PPV 82.7% [74.1%-91.2%], predictive negative value and sensitivity 100%, specificity 85.2% [77.2%-93.3%]. From 2014 to 2018, over 2 million acute UTIs (n=2,083,973) were hospitalized in France, occurring mainly in female, and of whom 36% were device-associated UTIs. Acute cystitis represented almost 2/3 of the cases (66%), followed by APN (22%) and prostatitis (12%). The most frequent comorbid conditions were diabetes mellitus (15%), obesity (9.5%), chronic respiratory disease (9%) and chronic kidney failure (7%). The adjusted incidence rate of UTIs hospitalized in France was 67 4 cases/100,000 inhabitants, stable over the period and increasing with age.

**Conclusions:** With a validated and performant algorithm, this national cohort study is the first to date to estimate the incidence of hospitalized UTIs in France. UTIs, even if not severe, are very common, representing a substantial burden of care. Further analyzes of the French medico-administrative databases using the algorithm will provide data for more informed goals-of-care discussions and may help target hospital UTIs surveillance and prevention, especially in device-associated UTIs.

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Screening of bovine and human bacterial strains by diagnostic assays for detection of β-lactamases

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Abstract third-party references: SPF santé public, University of Liège

Background: The intensive use of β-lactam antibiotics selected resistant environmental and nosocomial bacterial strains. Among all bacterial resistance mechanisms, expression of enzymes called β-lactamases (BLA) stays the major cause of resistance in bacteria. Today, we count around three thousand bla genes. A goal of this work is to develop specific diagnostic assays in order to assess the type of β-lactamases expressed by bacteria.

Materials/methods: To develop our technologies, we focused our work on BLA TEM family. In our lab, we selected a camelid antibody (nanobody), called cAbTEM−1, and a rabbit polyclonal antibody, with high affinity and specificity, directed against TEM enzymes. We decided to screen a large panel of bovine strains from a collection of pathogenic E. coli collected from diarrheic faces, enteritis cases and blood samples. Our tests will be also developing on human bacterial strains collected by the CHU UCL Namur hospital (BE). We assessed the presence of a β-lactamase by three different methods. Firstly, we make PCR to check presence of TEM genes. Moreover, we set up a classical sandwich ELISA assay with the cAbTEM−1 for capture and the polyclonal antibody for revelation. Finally, we develop a technology based on bio-layer interferometry phenomenon (ForteBio).

Results: A panel of 46 pathogenic E. coli strains from bovines, previously characterized by PCR, micro-array and sequencing, were used in order to assess our sandwich ELISA assay. All genetically positive and negative strains for bla TEM had a positive and negative signal, respectively. That means our assay is very specific, recognizing TEM WT but also TEM IRT and TEM ESBL, and very sensitive with a limit of detection around 1 ng/mL of antigens.

Conclusions: At this stage of our work, we confirmed that our ELISA assay works for detection of TEM BLA. Finally, the presented data give us the possibility to develop our technologies for detection of other β-lactamases families such as other ESBLs and/or carbapenemases. For these reasons, we continue to select nanobodies against interesting BLAs and to develop those technologies in order to favor a rapid sensitive and robust diagnostic assays.

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Abstract 3714

**Current practices and evaluation of barriers and facilitators to surgical site infection prevention measures in Jimma, Ethiopia**

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**Abstract third-party references:** This project was funded/ partially funded through a Faculty and Staff Travel Award from the University of Wisconsin-Madison Global Health Institute

**Background:** The burden of surgical site infection (SSI) is high in low- and middle-income countries (LMIC) such as Ethiopia. In Ethiopia, SSI complicates 10-20% of surgeries. The WHO has provided guidelines for implementation of SSI prevention tools, but many barriers exist. We sought to understand the barriers and facilitators to SSI prevention in Jimma, Ethiopia.

**Materials/methods:** Interview participants and surgical procedures were selected by convenience sampling, but efforts were made to include a variety of healthcare providers and types of surgery. Theoretical saturation determined participant number. An interview guide was designed to probe knowledge, barriers, and facilitators within the SEIPS model’s five components of the work system: tools and technology, person, organization, task, and environment. Interviews were recorded, transcribed, and coded thematically using the qualitative data analysis software QSR Nvivo (Version 12.4.0). An observation checklist was created based on WHO and UW Health SSI prevention bundles.

**Results:** Twenty healthcare providers were interviewed resulting in 543 interview excerpts which were coded into themes. Of these, 64% were deemed barriers and included shortage of supplies [antiseptics, water, and gloves], lack of protocols or guidelines, low involvement of an Infection Prevention team, and lack of training on SSI prevention. Facilitators included sterile instrument indicators, culture of communication around maintenance of sterility, and knowledge about SSI prevention. In 19 total surgeries observed, 100% compliance was noted for surgical scrub, glove use, sterile instrument sterility, incision site cleaning, maintenance of sterility, fraction of inspired oxygen kept >=50%, and wound care completed post-operatively. Surgical Safety Checklist use, antibiotics given within 120 minutes of incision, and OR door kept closed during surgery were observed in 95% of cases. Peri-operative antibiotics were discontinued within 24 hours in 79%, and all patients who received antibiotics received ceftriaxone. Pre-operative bathing and glucose monitoring were rare.

**Conclusions:** While many barriers to SSI prevention exist, our findings help identify several areas towards which resources can be directed to improve patient safety. Highest priorities include improved communication with and education by the Infection Prevention team, formation of guidelines and improved access to them, and standardization of supply chain for antiseptics and gloves.

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Comparative study of two susceptibility testing methods for carbapenem-resistant Klebsiella pneumoniae clinical isolates

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Background: Carbapenem resistant Klebsiella pneumoniae (CRKP) is a leading cause of life-threatening infections. Therefore, accurate antimicrobial susceptibility testing is crucial for the adequate treatment selection. In the present study, the performance of the Vitek2 automated system [bioMérieux, France] was assessed against the broth microdilution Micronaut-S system [MN] [Merlin, Germany].

Materials/methods: 135 CRKP non-duplicate isolates collected from patients hospitalized in AHEPA University Hospital from 2017 to 2019 were included in the study. The performance of the Vitek2 AST-318 card was compared with the Micronaut-S MDR MRGN-Screening-2 panel. The latter served as reference. MICs were interpreted according to EUCAST breakpoints. Escherichia coli ATCC 25922 was used for quality control. Essential agreement (EA), categorical agreement (CA), minor errors (mE), major errors (ME) and very major errors (VME) were assessed.

Results: Overall 10 antimicrobials were evaluated with both methods. The results are presented in the Table. The overall CA ranged from 33.60% (for amikacin) to 98.45% (for trimethoprim/sulfamethoxazole) while EA varied from 12.78% (for tigecycline) to 90.69% (for ceftazidime). The rate for VME was below 5% for all antimicrobials tested with the exception of colistin (6.01%). ME were observed at >5% for amikacin, fosfomycin, imipenem, and tigecycline.

Conclusions: The MN method reported significantly higher susceptibility rates for amikacin, fosfomycin, imipenem and tigecycline suggesting that these antimicrobials should be furtherly tested with an alternatively method besides the automated one. Our study reinforce the need for further studies regarding the performance of automated systems, especially when multi-drug resistant bacteria are to be tested.

<table>
<thead>
<tr>
<th>Antimicrobial (No tested)</th>
<th>Vitek2 vs MN</th>
<th>Susceptibility rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CA (%)</td>
<td>VME (%)</td>
</tr>
<tr>
<td>Amikacin (120)</td>
<td>33.60</td>
<td>0</td>
</tr>
<tr>
<td>Cefazidime (129)</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Trim/sulf (129)</td>
<td>98.45</td>
<td>1.55</td>
</tr>
<tr>
<td>Pip/tazo (128)</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Fosfomycin (122)</td>
<td>65.60</td>
<td>2.46</td>
</tr>
<tr>
<td>Imipenem (129)</td>
<td>73.65</td>
<td>0.77</td>
</tr>
<tr>
<td>Meropenem (134)</td>
<td>74.62</td>
<td>0.49</td>
</tr>
<tr>
<td>Tigecycline (133)</td>
<td>34.59</td>
<td>0</td>
</tr>
<tr>
<td>Colistin (133)</td>
<td>93.99</td>
<td>6.01</td>
</tr>
</tbody>
</table>

Presenter email address: protonotariou@gmail.com
Abstract 3719

Systematic comparison of three commercially available combination disc tests for carbapenemase detection in Enterobacterales isolates

Janko Sattler*1,2, Anne Brunke1,2, Axel Hamprecht1,2,3

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Background: Early detection of carbapenemases in Enterobacterales is crucial for patient treatment and infection control. EUCAST guidelines propose combination disk tests (CDT) with different inhibitors (e.g. EDTA, boronic acid) for identification of carbapenemases. However, little data on the performance of these assays is available except for areas of high endemicity where only few carbapenemases prevail. In this study, we compare the performance of three commercially available CDT using a collection of molecularly characterized carbapenemase producing Enterobacterales (CPE) isolates.

Materials/methods: Mastdiscs Combi Carba plus (Mast Diagnostica, Reinfeld, Germany), KPC/MBL and OXA-48 Confirm Kit (Rosco, Taastrup, Denmark) and KPC&MBL&OXA-48 disc kit (Liofilchem, Roseto degli Abruzzi, Italy) were challenged with 103 molecularly characterized CPE and 46 non-CPE. Tests were performed according to manufacturers’ recommendations.

Results: Carbapenemases were detected in 85% (Mast), 84% (Rosco) and 88% (Liofilchem) of the CPE. Specificity was 96% (Mast and Rosco) and 85% (Liofilchem). Correct classification of the Ambler class was recorded in 80% (Mast), 81% (Rosco) and 77% (Liofilchem), see Table 1. Mast CDT performed poorly for detection of class A carbapenemases.

<table>
<thead>
<tr>
<th>Class A</th>
<th>Mast</th>
<th>Rosco</th>
<th>Liofilchem</th>
</tr>
</thead>
<tbody>
<tr>
<td>GES (n=2)</td>
<td>0%</td>
<td>50%</td>
<td>0%</td>
</tr>
<tr>
<td>IMI (n=9)</td>
<td>67%</td>
<td>100%</td>
<td>78%</td>
</tr>
<tr>
<td>KPC (n=19)</td>
<td>47%</td>
<td>100%</td>
<td>58%</td>
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</table>

<table>
<thead>
<tr>
<th>Class B</th>
<th>Mast</th>
<th>Rosco</th>
<th>Liofilchem</th>
</tr>
</thead>
<tbody>
<tr>
<td>IMP (n=4)</td>
<td>100%</td>
<td>75%</td>
<td>50%</td>
</tr>
<tr>
<td>NDM (n=27)</td>
<td>93%</td>
<td>78%</td>
<td>89%</td>
</tr>
<tr>
<td>VIM (n=17)</td>
<td>88%</td>
<td>47%</td>
<td>59%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Class D</th>
<th>Mast</th>
<th>Rosco</th>
<th>Liofilchem</th>
</tr>
</thead>
<tbody>
<tr>
<td>OXA-48 (n=8)</td>
<td>100%</td>
<td>88%</td>
<td>100%</td>
</tr>
<tr>
<td>OXA-48-like (n=15)</td>
<td>80%</td>
<td>93%</td>
<td>100%</td>
</tr>
<tr>
<td>OXA-58 (n=2)</td>
<td>0%</td>
<td>50%</td>
<td>0%</td>
</tr>
</tbody>
</table>

Table 1: Sensitivity of combination disk tests according to Ambler class and carbapenemase subtype.

Conclusions: Performance varied greatly between Ambler classes and test kits. The choice for a CDT should therefore be based on the local prevalence of carbapenemases. Mast CDT worked best for class B carbapenemases, ROSCO for class A and Liofilchem for class D. However, the overall performance of the tests included in this study was comparatively weak (sensitivity 84%-88%). These data suggest that CDT should only be used complimentary (if at all) to other assays like zCIM, colorimetric tests, immunochromatographic tests or PCR.

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Abstracts 2020

Abstract 3721

**HBV RNA and HBcrAg: two new biomarkers for monitoring chronic hepatitis B virus infection**

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**Background:** Chronic hepatitis B virus (HBV) infection is a highly dynamic process, defined by several serovirological profiles. Presently, HBV eradication is not possible for the constant presence of intrahepatic persistent form of the virus (cccDNA). The detection of cccDNA needs an invasive investigation and, at present, there are no standardized methods. Recent studies suggest new biomarkers to control the transcriptional activity of intrahepatic cccDNA, including HBV RNA and HBcrAg (*Hepatitis B core-related antigen*).

We evaluated those two biomarkers and their correlation to HBV DNA and quantitative HBsAg level in blood samples.

**Materials/methods:** Blood samples from 55 HBeAg-negative infected patients were analyzed. The level of HBV DNA was detected by COBAS AmpliPrep/COBAS TaqMan (Roche), a fully automated viral load quantitative hepatitis B test (ranging from 20 to 1.7 x 10^9 IU/mL). HBsAg was evaluated by Architect (Abbott), the limit of detection declared was 0.05 IU/mL. HBcrAg was measured by chemiluminescent enzyme immunoassay (Fujirebio, Lumipulse GHBcrAg), the range declared was from 2 to 7 Log U/mL. Finally, HBV RNA was detected by a home-made qRT-PCR.

The results were also matched to the HBV genotype and the ALT levels.

**Results:** A total of 55 patients were included in the study. All patients were negative for hepatitis delta virus co-infection.

Overall, a median HBcrAg value of 3.5 Log U/mL was detected. For quantitative HBsAg levels, a range from 2.26 to 4.45 Log IU/mL was identified, while HBV-DNA ranged from 2.42 to 8.30 Logs IU/mL. HBV RNA ranged from 1.76 to 6.82 Log copies/µL.

The HBV RNA levels significantly correlated to HBcrAg (r=0.426; P<0.01) and to ALT levels (r=0.405; P<0.01). On the contrary, we didn't find a significant correlation to HBsAg levels (P=0.658).

Nonetheless, the HBcrAg level significantly correlated with the HBV DNA level (r=0.342; P<0.05).

**Conclusions:** Chronic hepatitis B virus infection is associated with a broad spectrum of clinical profiles. These preliminary observations have been validated in a restrict cohort, the quantization of different biomarkers was also proposed as a novel tool for the monitoring of chronic infected patients.

Further studies are needed to understand and to determine the utility of these assays.

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Abstract 3723

The efficiency of antimicrobial coatings in whole blood: development of a realistic in vitro model

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Background: The serious medical consequences and cost-intensive management of catheter-associated blood stream infections have led to an enhanced interest in antimicrobial coatings. Many materials show promising performance in standard microbiological assays, but fail in animal studies. This shows the need for more realistic in vitro models to test antimicrobial coatings in a physiological environment.

Materials/methods: Experimental Design: The setup consists of a microfluidic device which allows the adjustment of shear forces equivalent to those occurring on a catheter surface. A bacterial culture was incubated on the surface for 1 hour to allow bacterial adherence, prior to the incubation with hirudin-anticoagulated whole blood.

Hemocompatibility: In a pilot study, informative parameters of coagulation and inflammation after up to 24 h incubation of bacteria \( [c = 10^4 \text{ CFU/ml}] \) with whole blood were determined.

Bacterial performance: First experiments were run with GFP labelled E. coli (MG1655 eGFP) in blood plasma. The bacterial attachment on the model surface was evaluated after 2, 4, 20 and 24 hours via fluorescence microscopy. Additional results of whole blood incubation and analysis of the biofilm with fluorescence in situ hybridization will be shown.

Results: The preliminary hemocompatibility tests revealed IL-1 \( \alpha \) and MIP-1 \( \beta \) (analyzed by ProcartaPlex) to be the most promising parameters to analyze inflammation after long-term incubation. They reflect the influence of gram-positive and negative bacteria still after 12 and 24 hours while other examined factors (e.g. cell count, CD11b-expression, IFN-\( \gamma \), TNF-\( \alpha \)) lose their significance after 4 or 8 hours.

Figure 1: cytokine expression in whole blood inoculated with S. epidermidis and E.coli in dependency of incubation time

Analysis of bacterial fluorescence signal revealed a significant decrease during the first 2 hours, presumably due to the flushing of non-adherent bacteria. Thereafter the number of bacterial cells remained constant on the used model surfaces (Thermoplastic Polyurethane).

Conclusions: The reported results suggest that our developed in vitro model will be able to evaluate antimicrobial coatings under consideration of the mutual influence of bacteria and human whole blood – an attempt existing in vitro models failed so far.

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Clinical diagnostic evaluation of a real-time PCR assay for the quantitative detection of cytomegalovirus from EDTA-plasma and urine samples

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Background: The cytomegalovirus (CMV) is a wide-spread virus and like other members of the herpes virus family, it can cause latent infection. In newborns and individuals with congenital or acquired immune deficiencies or in persons undergoing immunosuppressive therapy, the infection can cause complications and damage numerous organ systems. The aim of the study was to evaluate the clinical performance of the newly commercialized RIDA®GENE CMV assay with EDTA-plasma and urine samples.

Materials/methods: The performance of the RIDA®GENE CMV assay was compared to a reference test - FluoroType® CMV (Hain Lifescience GmbH). The diagnostic sensitivity and specificity were determined by using 100 EDTA-plasma and 104 urine samples from patients with request for CMV diagnostics. In addition, the analysis of quantitation differences in log [IU/mL] between the two assays was evaluated. All samples were pre-determined with FluoroType® CMV and retrospectively analyzed with RIDA®GENE CMV. Analysis of discrepant results was performed with the CMV R-gene® assay (bioMérieux).

Results: The overall diagnostic sensitivity and specificity of RIDA®GENE CMV with EDTA-plasma samples were 100% and 90%, respectively. By comparing to the reference assay, FluoroType® CMV, 66% of the EDTA-plasma samples quantified with RIDA®GENE CMV were within the limits of ±0.5 log difference. In case of urine samples, six were discrepant positive and after discrepant resolution, a diagnostic specificity of 91% was achieved. The overall diagnostic sensitivity of the RIDA®GENE CMV assay was of 100% and in comparison to the reference method, 63.8% of the urine samples were correctly quantified within the limits of ±0.5 log.

Conclusions: The RIDA®GENE CMV assay can be recommended as an efficient and reliable method for the direct qualitative and quantitative detection of cytomegalovirus in EDTA-plasma and urine clinical samples.

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Abstracts 2020

Abstract 3729

**Congenital toxoplasmosis: outcomes of newborns from mothers with documented seroconversion out of a multi-centre cohort in two tertiary referral hospitals**

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¹IRCCS Policlinico San Matteo, Pavia, Italy, ²Spedali Civili di Brescia, Brescia, Italy

**Background:** Primary Toxoplasma gondii infection during pregnancy can cause congenital toxoplasmosis (CT) and documented seroconversion (SC) is the only serological evidence of such event. The aim of our study was to describe the newborns outcomes from a multicenter cohort of seroconverted mothers.

**Materials/methods:** We retrospectively reviewed all T. gondii SCs among pregnant women referred to Brescia (Spedali Civili) and Pavia (IRCCS Policlinico San Matteo) from 2007 to 2017. Serologic data, amniocentesis results, neonatal outcome, antibiotic treatments and characteristics of CTs were recorded.

**Results:** 247 pregnant women were included: 12 with periconceptional infection and 235 with documented SC with a total of 238 newborns expected (3 twin pregnancies). We didn’t record the pregnancy outcome in 23.5% cases. The observed transmission rate was 25.3%; 46.7% among the 3rd trimester SCs, 8.8% among 2nd trimester SCs and 0/38 among the 1st trimester ones. Among the infected fetuses, 12/46 had clinically apparent CT (26.7%) 11 live births (5 with ocular and 7 with CNS localization – 1 newborn with CNS and retina disease localization) and 1 terminated fetus. The clinically apparent CT rate was 20% among the 3rd trimester SCs and 45.5% among the 2nd trimester ones. Two miscarriages and 1 more termination of pregnancy were recorded without any information about fetuses. All the infected newborns were treated with pyrimethamine-sulfadiazine for one year.

Spiramycin was the mother’s first choice treatment (89.8%) and in only 3 cases it was interrupted because of side effects. Six women did not receive treatment and for 4 subjects we didn’t have any records. Amniocentesis was performed in 83/235 cases (35.3%), no complication was recorded and no false positive or false negative results were registered. No CT was recorded among periconceptional infections.

**Conclusions:** The results are in line with the fetal risks reported in literature for T. gondii infection during pregnancy. In our cohort the treatment was promptly initiated after SC evidence. The incidence of CT is lower than expected. The high number of missing data on SC outcomes show how is still difficult to guarantee an efficient multidisciplinary management of such complicated pregnancies.

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Abstract 3735

Measles issue in Georgia

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Background: Measles - a vaccine-managed acute viral infection. For Georgia, as well as for many countries around the world, it remains a major health problem. Since the end of 2018 the outbreak Measles has become intense and we are currently experiencing a widespread outbreak that could turn into a full-scale epidemic.

Materials/methods: The purpose of the work was to identify the features of measles [2018-19] according to clinical material of the infectious Diseases and AIDS Center. Measles was diagnosed in 787 patients with measles-specific M antibodies.

Results: 75.2% of patients were adults and 24.8% - the children. The disease progressed in all cases with typical clinical symptoms, with cycle duration, with the development of abundant maculo-papular rash. The hemorrhagic component was reported in 6 adult patients. The most common complication of the disease was acute bacterial bronchitis and pneumonia [87 and 48 cases, respectively]. Lethality occurs in 1 case - patient died from severe distress syndrome which developed as a result of pneumonia. 3/4 of patients had no vaccination at all, and / or their vaccine status was not known.1/4 had the measles vaccine only once, and even more than 10 years ago, in childhood. In adults, hyperpyretic fever was common: intoxication - severe asthenia, appearing dazed, and sometimes somnolence. In 4/5 of patients hyperfermentemia was seemed [2.5-10 times increase], enzymes normalized when clinical signs improved. The dramatic increase in the incidence of measles was preceded by the circulation of the H1N1 virus in population because of this there was the increased incidence of bronchitis and pneumonia.

Conclusions: Our clinical cases analysis fully confirms the importance of the measures that the National Center Diseases Control provides to prevent further spread of the disease [to create a vaccinated layer of population due to fully vaccinating adults and children].

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Abstract 3739

A diagnostic accuracy study of a novel blood-based assay for identification of tuberculosis in people living with HIV

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Background: Non-sputum triage or diagnostic tests for tuberculosis disease have been identified as a high-priority need for diagnostic development to reach the End-TB targets of WHO. Such a test would aid the identification of the 3 millions of patients currently not diagnosed and reported. A combinatory score based on a novel 3-gene host-signature has shown promise in discriminating TB disease from other respiratory illnesses.

Materials/methods: We evaluated the accuracy of an early-prototype cartridge assay (Xpert Prototype, developed by Cepheid, USA) of this 3-gene signature on biobanked blood samples from people living with HIV (PLHIV) against a comprehensive microbiological reference standard (CMRS, culture and Xpert® MTB/RIF). Whole blood from symptomatic PLHIV in South Africa were collected from February 2016 to August 2017 in PAXgene tubes. We depict results based on performance targets set by WHO and compare the performance of the Xpert Prototype with that of a laboratory-based CRP assay.

Results: Of the 201 patients included, 67 were culture-positive for Mycobacterium tuberculosis. The AUC for the Xpert-Prototype was 0.89 (CI 0.83-0.94) against the CMRS. Considering the Xpert-Prototype as triage test (at nearest upper value of sensitivity to 90%), the corresponding specificity was 55.8% (CI 47.2-64.1). At fixed value of sensitivity near 95% (95.5% nearest upper value; CI 87.6-98.5), the specificity was 25.6% (CI 18.8-33.7). In comparison, the laboratory-based CRP test had AUC = 0.86 (CI 0.8-0.91), and at fixed value of sensitivity near 90% (90.9% nearest upper value; CI 81.6-95.8), would achieve a specificity of 69.0% (CI 60.6-76.3; CRP-value of 12.3 mg/L). Similarly, at a fixed value of sensitivity near 95% (95.5% nearest upper value; CI 87.5-98.4), the specificity was 45.7% (CI 37.4-54.3) (CRP-value of 6.2 mg/L). Considering the Xpert-Prototype as stand-alone diagnostic test, at a specificity of 95%, the test achieved a sensitivity of 65.7% (CI 53.7-75.9). In comparison, CRP-test performance at a specificity of 95.4% (nearest value; CI 90.2-97.9), the sensitivity is only 13.6% (CI 7.3-23.4) (CRP-value of 253.6 mg/L).

Conclusions: In this first accuracy study of a prototype blood-based host-marker assay, we show the possible value of the assay for particularly for diagnosis but also for triage in PLHIV.

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Abstracts 2020

Abstract 3742

Variables associated with higher readmission frequency in an OPAT program

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Background: Adequate selection of candidate patients intravenous for outpatient parenteral antimicrobial therapy (OPAT) is a key aspect for clinical success. The aim of this analysis was to describe the reasons of readmission during OPAT to improve the selection of candidate patients.

Materials/methods: Prospective observational study of patients admitted in OPAT in 2 Spanish university hospitals between July 2012 and August 2019. All patients were evaluated by an infectologist previous to the admission in the program. Bivariate statistical analysis using Chi-square test and Mann-Whitney U test, as well as multivariate logistic regression analysis.

Results: Of the 1,225 patients treated in our OPAT program, 128 (10.4%) had an unexpected readmission, and 12 (0.9%) died during this admission. Readmission occurred after a median of 8.5 days (IQR 4-16) in OPAT. Fifty-nine (50.9%) of the patients who had to be readmitted, continue their therapy again in OPAT once the reason for readmission was solved. The most frequent causes of readmission were: unfavorable clinical evolution (44.5%), insufficient control of the source (18%) and decompensation of comorbidity (14.8%). The mean age (p=0.012) and the mean Charlson score (p=0.001) were associated with a higher frequency of readmission. Of the variables included in Charlson score, heart failure (OR 1.78, 95%CI 1.22-2.60), neoplastic disease (OR 1.45, 95%CI 0.99-2.12), and chronic liver disease (OR 1.92, 95%CI 1.12-3.32) were associated with the outcome variable. After stratification by syndromes, abdominal source of the infection was also associated (OR 1.66, 95%CI 1.07-2.57). The clinical experience on OPAT based on the year of inclusion, the centre, and the experience of the infectologist (codified as age under or over 45 years) were not associated with higher readmission. In the multivariate analysis presence of heart failure (aOR 1.92, 95%CI 1.31-2.84), neoplastic disease (aOR 1.53, 95%CI 1.08-2.27) as well as the abdominal source interacting with chronic liver disease (aOR 3.14, 95%CI 0.95-10.35) were the variables associated with higher readmission.

Conclusions: Comorbidity and abdominal source of the infection were the circumstances associated with unexpected readmission in our OPAT cohort. It is crucial to add these variables to the selection criteria of candidate patients for OPAT.

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Considerations in the design and analysis of antibiotic duration trials in the presence of non-adherence

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Background: Non-inferiority trials have been widely adopted to evaluate whether antibiotic treatment duration can be safely reduced. They are also used in other areas of infectious disease research and account for 27% of late phase randomized trials published in leading medical journals in the past two years. However, non-adherence in non-inferiority trials often increases the chance of claiming non-inferiority under the standard intention-to-treat analysis.

Materials/methods: We performed a computer-based simulation study to: i) explore the impact of various patterns of non-adherence and analysis methods on effect estimates; ii) quantify the probability of claiming non-inferiority when long treatment duration is actually inferior; and iii) evaluate alternative analytical methods such as inverse probability weighting and instrumental variable estimation to reduce the chance of incorrectly concluding non-inferiority.

Results: We found that the probability of concluding non-inferiority when long treatment duration is actually inferior depends on whether non-adherence is due to confounding factors that influence both adherence and outcome, and on the actual treatment durations received by the non-adherent participants. Under most patterns of non-adherence, intention-to-treat analysis leads to an inflated tendency to conclude non-inferiority when long duration is actually inferior. Even when adherence is relatively high at 90%, the probability of incorrectly concluding non-inferiority can be as high as 0.1 from the nominal value of 0.025. The direction of bias for the per-protocol analysis depends on the directions of influence the confounders have on adherence and outcome. The inverse probability weighting approach can reduce bias but will only eliminate it if all confounders can be measured accurately and appropriately adjusted for. Instrumental variable estimation overcomes this and gives unbiased estimates even in the presence of unmeasured confounders, but typically requires large sample sizes to achieve acceptable power. We developed an online power calculator allowing for various patterns of non-adherence.

Conclusions: Patterns of non-adherence and potential confounders are important considerations in trial designs. These data from both adherent and non-adherent participants should be collected and analysed. Adjusted analysis of the per-protocol population with sensitivity analyses on confounders and other approaches, such as the instrumental variable estimation, should be considered when non-adherence is anticipated.

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Abstract 3748

High levels of carbapenem resistance in paediatric bloodstream infection across WHO regions influenced by variation in relative pathogen prevalence

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Background: WHO empiric antibiotic regimens for childhood sepsis do not account for regional variation in pathogen prevalence or resistance rates. Recent data suggests high use of meropenem in child sepsis treatment. This study aimed to assess pathogen variation and its influence on meropenem coverage across WHO regions.

Materials/methods: A questionnaire on aggregate paediatric (0-<18 years) blood culture data from 1 January 2018-31 December 2018 was sent to a global network of paediatric sites. Data requested included total blood cultures taken, number positive, a predefined pathogen list and resistance phenotypes for selected pathogens (e.g. CRE, ESBL, MRSA, VRE). Meropenem monotherapy coverage was estimated at site-level for centres reporting >100 isolates. Coverage was estimated using a Bayesian decision tree model for bloodstream infection antibiograms incorporating intrinsic resistance and EUCAST interpretive guidelines.

Results: A total of 252,022 blood cultures were reported from 51 sites (median: 3179/site, IQR:1395-5069, range:539-23650) across 5 WHO regions of which 6.6% (95%CI:5.7-8.5%; 19788 total) were positive. Excluding coagulase-negative staphylococci (CoNS), Klebsiella spp. was one of the most common pathogens for all regions (AFRO: median:12.1%, IQR:5.0-38.1%; EURO: median:4.0%, IQR:1.9-9.5%; PAHO: median:12.3%, IQR:9.9-12.7%; SEARO: median:11.2%, IQR:5.3-22.5%; WPRO: median:6.7%, IQR:3.7-10.3%); In three regions, S. aureus (AFRO: median:7.8%, IQR:3.4-10.8%, EURO: median:6.3%, IQR:4.1-12.0%, WPRO: median:6.9%, IQR:6.0-8.9%) and E. coli (AFRO: median:4.1%, IQR:2.8-6.1%, EURO: median:5.9%, IQR:5.2-9.8%; WPRO: median:8.1%, IQR:6.6-13.6%) were two of the most common pathogens. Acinetobacter spp. (median:8.9%, IQR:8.1-10.7%) and Salmonella typhi (median: 11.2%, IQR: 0.2-15.0%) were in the top three pathogens in SEARO and Enterococcus spp. (median:6.7%, IQR:0-7.5%) and Candida spp. (median:8.3%, IQR:8-9.5%) were in the top three pathogens in PAHO.

For the 21 sites reporting >100 isolates, meropenem coverage by site ranged between 56% (95%CI:49-62%) and 91% (95%CI:89-93%) (Figure 1). Across all 21 hospitals, Acinetobacter spp. and Pseudomonas spp. were the Gram-negative pathogens with the highest carbapenem resistance however their impact on the coverage estimate is small given their low frequency compared to other pathogens.

Conclusions: Current global high use of empiric meropenem is not supported by the coverage levels identified. Future empiric guidance should consider variation in both pathogen prevalence and resistance.

Figure 1. Carbapenem coverage estimates for 21 centres reporting >100 isolates.

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Abstract 3753

**Escherichia coli** bloodstream infections: a multinational population-based perspective

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Abstract third-party references: On behalf of the International Bacteremia Surveillance Collaborative

**Background:** *Escherichia coli* is the most common cause of blood stream infections (BSI). However, population-based multi-national comparative data is lacking. Our objective was to define the epidemiology and outcome of *E. coli* BSI in a large multi-national population-based cohort.

**Materials/methods:** All incident *E. coli* BSI occurring among residents of the western interior region of British Columbia (Canada), Calgary (Canada), Skaraborg county (Sweden), Canberra region (Australia), and Finland nationally between 2013 and 2018 were identified. Incidence rates were directly age and sex standardized to the 2018 EU-28 population. Univariable Poisson models were used to analyze temporal and regional variation in standardized incidence rates. The *E. coli* BSI were categorized as community-onset or hospital-onset, whether 30-day mortality occurred and whether they were third-generation cephalosporin (3GC) resistant. Data from all centres was available for calculation of the overall crude incidence rate but some additional analyses were based on a subset of centres.

**Results:** Overall 31,112 incident *E. coli* BSI were identified during 39 million person-years of surveillance for an annual crude incidence of 79.7 per 100,000 population. The standardized incidence rates were 64.2, 68.8, 93.6, and 115.3 per 100,000 person-years for western interior, Calgary, Skaraborg and Finland, respectively. Compared to western interior, the incidence rates from Skaraborg and Finland were significantly higher (IRR:1.46 95%CI:1.26-1.68; IRR:1.79, 95%CI:1.56-2.05, respectively). There was no significant difference in rates between western interior and Calgary (p=0.37) and no significant temporal variation in rates (p=0.35). The *E. coli* BSI were predominantly community-onset (81.6%), and this varied significantly by region (p<0.001). Resistance to 3GC was present in 7.8% and was higher in Calgary, western interior and Canberra as compared to Skaraborg and Finland. The 30-day all-cause case-fatality proportion was 9.7% and ranged from 9.3% (Finland) to 12.8% (western interior). The annual standardized mortality rate was 7.8 per 100,000 population and ranged from 8.4 to 11.2 per 100,000 population [western interior and Finland, respectively].

**Conclusions:** *E. coli* BSI are associated with a major burden of illness. The significant differences in the rates and characteristics of *E. coli* BSI between regions merits future research.

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Abstract 3754

Challenges in setting-up and conducting a global multi-centre prospective observational cohort of sepsis in hospitalised neonates: the NeoOBS study

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Abstract third-party references: on behalf of the NeoOBS study team

Background: There have been no large international pragmatic trials of the optimal antibiotic management of neonatal sepsis in the hospitalised setting. NeoOBS was designed to inform the design and conduct of trials of treatment of neonatal sepsis caused by MDR pathogens in low-middle income neonatal units.

Materials/methods: NeoOBS is a cohort study of inpatient management of neonatal sepsis in 5 WHO regions. Setting-up and conducting a multicentre, prospective observational study required a multidisciplinary team to ensure good communication and on-going management throughout the study. Web-based programs like REDCap™ (a secure web-based data collection platform hosted at SGUL) and telecommunications applications were used.

Results: Currently 1853 patients have been enrolled from 19 secondary and tertiary neonatal units in 11 countries. Setup took 12 months (Aug2018–2019) with ethics committee (EC) approvals and agreement of contracts taking on average 3½ months (range 1-8 months) and 4.4 months (range 2-7 months) respectively. REDCap™ has been used successfully at a low cost and has proven to be an excellent database due to its user-friendly application to suit the needs of the study. Piloting the database before study launch is essential. Monitoring has been conducted on-site (verification of 10% of consent forms and data at time of visit) and off-site (data verification of case report forms and REDCap from 10% of patients) to ensure data quality remains high throughout the study.

The main challenges have been navigating different EC and contractual processes (including material transfer agreements), translation requirements (>15 different languages), and use of local templates. Delays in EC approvals were due to errors in submissions, irregular/cancelled EC meetings, and additional approvals due to foreign sponsorship. Issues with consent were due to the widespread geographic and social factors of parents who are unable to be present at the hospital, and cultural mistrust of research. Regulations and requirements for exporting bacterial isolates vary widely by country and must be considered before site selection.

Conclusions: Global multicentre studies in neonatal sepsis are complex but NeoOBS has indicated that they can be achieved. Understanding the barriers that have been identified will aid setup and conduct of future sepsis trials.

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Abstract 3758

CRISPR-based rapid and ultra-sensitive diagnostic test for smear-negative or sputum-scarce tuberculosis using bronchoalveolar lavage fluid: a prospective, multi-centre study in China

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Background: Rapid and simple-to-use diagnostic methods for tuberculosis are urgently needed. Recent development has unveiled the diagnostic power of CRISPR system in the detection of Mycobacterium tuberculosis complex (MTB) infections. However, its accuracy and impact when performed on bronchoalveolar lavage fluid (BALF) obtained from patients with sputum-scarce or smear-negative TB is unclear.

Materials/methods: We conducted a prospective multicenter study (NCT04074369) in China of 272 HIV-negative patients suspected with pulmonary TB, who were sputum-scarce or smear-negative underwent bronchoscopy. The rapid CRISPR-based assay for TB detection (CRISPR-MTB) was performed on uncentrifuged BALF (300μl), in parallel with culture and the GeneXpert MTB/RIF assay (Xpert). Final clinical diagnosis of the enrolled cases was made by the attending physicians according to clinical guidelines, combining the patient’s clinical manifestations, imaging findings and patient’s responsiveness to anti-TB treatment after one month of follow-up. Patients with MTB culture-positive or Xpert-positive results for MTB would be classified as microbiologically confirmed TB cases.

Results: Of the 272 included, 101 were diagnosed with micro-confirmed TB and 42 were clinical TB cases. Among the confirmed cases, 89 were detected by CRISPR-MTB, which was similar as Xpert (n = 88), but significantly higher than culture (n = 62, p < 0.001). Among clinically diagnosed cases with negative Xpert and culture, CRISPR-MTB detected 15 cases. When evaluated in the overall cohort, the CRISPR-MTB test exhibited an overall improved sensitivity over both culture (73% vs 44%, p <0.001) and Xpert (73% vs 62%, p = 0.017), without compromise in specificity (126/129, 98%). All three CRISPR-MTB false positive patients had a history of tuberculosis. With processing time around 1.5 hours, the full turnaround time of CRISPR-MTB test in clinical practice, from the sample collection to reporting results to clinicians, was within 24h, which was same as Xpert but significantly shorter than culture.

Conclusions: The CRISPR-MTB test exhibits an improved overall diagnostic performance over culture and Xpert in patients with sputum-scarce or smear-negative TB and offers great potential as a new diagnostic technique for pulmonary tuberculosis.

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**Abstract 3764**

**In vitro activity of carbapenemase-producing Enterobacterales to mecillinam**

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**Background:** The increase in antibiotic resistance of Enterobacterales has complicated the treatment of urinary tract infections (UTI). Mecillinam (MCM) is an orally available beta-lactam antibiotic, which is also active against many Enterobacterales producing extended-spectrum beta-lactamases. *In vitro* activity in carbapenemase-producing Enterobacterales (CPE) has been discussed but data is still scarce. In this study we compare the *in vitro* activity of MCM to meropenem, imipenem and ertapenem in a collection of molecularly characterized CPE.

**Materials/methods:** The challenge collection consists of 105 isolates (Klebsiella spp. [N=49], Escherichia coli [N=30], Enterobacter cloacae [n=13], Citrobacter freundii [N=9], Proteus mirabilis [N=3], and Raoultella ornithinolytica [N=1]) producing different carbapenemases (OXA-48-like [N=36], VIM [N=21], NDM [N=22], KPC [N=11], IMI [N=9], IMP [N=6], GES [N=2] and OXA-58 [N=2]). MICs of carbapenems are determined by agar gradient diffusion using MIC test strips, MICs of MCM by agar dilution and disk diffusion methodology.

**Results:** Until 11/2019 susceptibility testing has been completed for 44/105 CPE isolates (table 1). In 6/44 isolates MCM MICs were ≤ 8 mg/L ([*E. coli* [N=4], *K. pneumoniae* [N=2] producing OXA-48-like). In 38/44 isolates (VIM, NDM, KPC, OXA-48-like and IMP producers) MCM MICs were >8 mg/L. Overall MICs for carbapenems ranged from ≤ 0.125 to >32 mg/L with a median MIC of 16 mg/L.

**Conclusions:** Our preliminary data indicate that *in vitro* activity of MCM in CPE is limited to isolates with OXA-48-like carbapenemases. MICs in different OXA-48 variants will be further assessed in this study. Most isolates with low MICs for MCM had also low carbapenem MICs. MCM could be a valuable oral alternative for the treatment of uncomplicated UTI caused by OXA-48-like producing *E. coli*, Klebsiella spp. and *P. mirabilis*.

<table>
<thead>
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Table 1 MIC (mg/L) of all isolates stratified by carbapenemase

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Abstract 3767

Diagnostic accuracy of toxoplasma Western blot test in suspected seroconversion in pregnancy: a multi-centre study


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Background: The high sensitivity of the automated screening tests, widely employed for Toxoplasma gondii serology can yield false positive results due to cross and/or non-specific reaction. On the other hand therapy with spiramycin when IgM are found to be positive could delay IgG production and mask seroconversion. There is the need of second level test to early detect real toxoplasmic seroconversions. We planned an European multicentre study with 4 reference center for the diagnosis of toxoplasmosis: [Pitié-Salpêtrière Paris, CHU Grenoble-Alpes Grenoble, La Timone Marseille, IRCCS Policlinico San Matteo Pavia] to evaluate the diagnostic accuracy of the new LDBIO-TOXO II IgG/IgM Immunoblot (IgG-IgM WB) by LDBio Lyon - France. We also looked at the immunodominant antigen in the IgM WB

Materials/methods: We retrospectively analysed the leftover of laboratory samples after clinical diagnosis of 403 sera: 234 corresponding to 96 toxoplasmic seroconversions [2 to 3 sera/patient] and 169 sera corresponding to 69 patients with cross reactions and/or non-specific IgM [1 to 3 sera/patient]. All the patients had a documented seroconversion with first IgG/IgM negative results and then either IgG/IgM positive or a false positive result. All anonymised samples were processed in blind by LDBio. To validate WB we performed two different analyses: concordance [Cohen’s kappa] with final diagnosis [seroconversion or false positive] and diagnostic accuracy [sensitivity, specificity etc]

Results: The concordance between IgM and IgG type II WB with the diagnosis was good K = 0.89 and K = 0.89, respectively. In 4 cases the appearance of IgM and 46 cases the appearance of IgG was recorded by WB before the traditional tests. Sensitivity was 100% for IgM WB and 93.8% for IgG WB. Specificity was respectively 87% and 95.7%. Looking at the most antigenic bands, P30 was recorded in all but one positive sample and P40 in all but five.

Conclusions: The IgM WB not only detected all seroconversions, and even earlier than traditional tests in four cases, but also well discriminated the false positive results. The definition of immunodominant band will be extremely helpful in the interpretation of the results.

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Abstract 3768

Neonatal screening for congenital cytomegalovirus infection: identification of a viral DNA diagnostic cut-off value in saliva samples

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Background: Congenital cytomegalovirus (cCMV) infection is the most prevalent infection-related cause of congenital neurological disability and sensorineural hearing loss. CMV-PCR in saliva has excellent sensitivity for cCMV screening. However, literature data has reported evidence that false positive cCMV diagnosis in saliva could be an issue. Viral contamination of newborn saliva samples could happen throughout the peri- and post-partum period. Our prospective multicenter study aims to determine in positive CMV-DNA saliva samples, i) if a viral DNA cut-off value can discriminate a congenitally infected newborn from a non-congenitally infected one, for which the positivity saliva samples are a result of contamination and, ii) if a repeat saliva sample is indicated as confirmatory testing for the diagnosis of cCMV infection or instead, it is mandatory to test a urine sample.

Materials/methods: We will analyze saliva swabs (COPAN UTM, IT) from a minimum of 3150 newborns up to 21 days of age in order to obtain at least 20 congenitally CMV-infected newborns (Z-test at α=0.05; power=0.80), at study sites in two Italian hospitals (Bologna and Legnano-MI). All infants will be classified as having symptomatic or asymptomatic infection. The serological CMV-maternal serostatus before or during pregnancy will be evaluated, when available. The search of CMV-DNA in saliva and urine samples will be performed with a real time-PCR (ELITe InGenius – CMV-MGB Kit, ELITechGroup, IT).

Results: To date, we have enrolled 1847 neonates and identify 13 infected infants, the rate was 0.7%. Twenty-seven (1.5%) of the saliva swabs were false positives and all with a number <250 CMV-DNA copies/ml. Out of 1847 mothers, 1728 (93.6%) knew their CMV serostatus. At birth, 11 out of 13 (84.6%) newborns were asymptomatic, 2 symptomatic newborns had severe bilateral deafness. Both mothers were primarily infected in the first trimester. Fifty-four percent of infected newborns came from maternal primary infection, 31% from non-primary infections and 15% unknown maternal CMV-serostatus.

Conclusions: The strengths of this study include the large number of prospectively collected newborn body fluids samples, the viral load data, the results of confirmatory neonatal urine and saliva tests, the identification of maternal CMV-test in pregnancy and the infant clinical information.

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Real-time sampling of travellers to Laos: epidemiology of mobile genetic elements
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Background: Antimicrobial resistance (AMR) is highly prevalent in low- and middle-income countries. International travel contributes to this substantially: of the 100 million annual visitors to tropical countries, 30–70% become colonized by MDR-GN bacteria. The phenomenon has been well documented, but since sampling has only been conducted after travellers’ return home, data on the actual colonization process are scarce. Further, genomic epidemiology of mobile genetic elements in this context is lacking.

Materials/methods: A group of 20 European volunteers visiting Lao People’s Democratic Republic for three weeks provided daily stool samples. Acquisition of extended-spectrum beta-lactamase-producing gram-negative bacteria (ESBL-GN) was examined by selective stool cultures followed by whole-genome sequencing (WGS) of isolates. Long read data was used to reconstruct plasmid sequences and identify shared mobile genetic elements.

Results: Daily sampling revealed that all participants had acquired ESBL-GN at some time point during their overseas stay, with individual colonisation status varying day to day. WGS analysis revealed a transient pattern of colonization, with sequential acquisition of new strains. All but one participant acquired multiple strains. Participants also shared conserved mobile genetic elements that were distributed across distinct bacterial strains, which conferred resistance to antimicrobials.

Conclusions: This is the first study to characterize in real time the dynamics of acquiring MDR-GN during travel. Our data show multiple transient colonization events indicative of constant microbial competition. It also highlights the importance of considering mobile genetic elements as a separate and crucial aspect of genomic epidemiology.

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Genomic and transcriptomic approach to unravel the resistance mechanisms to ceftazidime-avibactam in *Pseudomonas aeruginosa* and *Enterobacter cloacae*

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**Background:** Ceftazidime-Avibactam (CAZ-AVI) is a novel antibiotic combination effective against multidrug-resistant pathogens carrying β-lactamases from different classes. Knowledge on molecular CAZ-AVI resistance mechanisms is scarce. We use adaptive laboratory evolution combined with deep sequencing to unravel resistance mechanisms of *Pseudomonas aeruginosa* and *Enterobacter cloacae* treated with CAZ-AVI at the genome and transcriptome level. In addition we provide insights into cross-resistance to meropenem (MEM) and allow pre-estimation of the potential resistance development under therapy.

**Materials/methods:** For single-step selections, strains were grown on agar plates containing CAZ-AVI (2x to 16x MIC, fixed AVI concentration of 4mg/L). For multi-step adaptions, cultures were grown in serial passages under sub-inhibitory concentrations (0.25x MIC) of CAZ-AVI or MEM. For CAZ-AVI multistep resistance selection we used the clinical powder (Zavicefta, Pfizer®), in order to display the changes in Avibactam concentration. Changes in MICs were monitored by E-test and the antibiotic concentrations for the next passages were adapted. Three different clones of each isolate were passaged in parallel to detect different resistance trajectories (n= 24 in total). Whole genome as well as -RNA sequencing of the resistant strains was done using the Illumina platform.

**Results:** Single-step selection revealed a CAZ-AVI resistance frequency of 10⁻⁷-10⁻¹⁰ when plated on 2x and 4xCAZ-AVI MIC while no resistant *P. aeruginosa* or *E. cloacae* were isolated on 8x and 16x MIC. When *P. aeruginosa* was cultured in the presence of sub-inhibitory concentrations CAZ-AVI, resistance to CAZ-AVI (up to 42x MIC) and MEM (>1000x MIC) developed (Figure 1ab). Sub-inhibitory concentrations of MEM led to CAZ-AVI resistance at a rate that was dependent on the initial MEM MIC of the parental strain (Figure 1cd). For *E. cloacae*, CAZ-AVI and MEM in sub-inhibitory concentrations only led to intermediate resistance (42x MIC) in 1 of 12 *E. cloacae* cultures and after 60 passages. We are currently analyzing changes in the genome and the transcriptome (RNA-seq) of the resistant strains and their susceptible progenitors to present genes putatively required for elevated resistance.

**Conclusions:** This ongoing study will provide a molecular insight in CAZ-AVI resistance mechanisms and selecting agents for CAZ-AVI resistance in *P. aeruginosa* and *E. cloacae*.
c) *Pseudomonas aeruginosa* subjected to subinh. MEM

**Legend:**
- Isolate 1
- Isolate 2
- Isolate 3
- Isolate 4

**Graph:**
- Y-axis: MIC [mg/l]
- X-axis: Passages of 24h

**Annotation:**
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Abstract 3774

**Automation in full genotyping of human papilloma viruses: evaluation of the analytical performance of Anyplex HPV28 assay**

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**Background:** It becomes increasingly important to know which high-risk human papillomaviruses (HR-HPV) types are present because persistent infection is related with cervical cancer and not every type is equally carcinogenic.

Pipetting and washing steps of our current reference method – DNA extraction with MagNA Pure LC32 (Roche) and genotyping with PapilloCheck® assay (Greiner Bio-One) - require a lot of hands on time.

"Seegene All-in-One Platform" is a streamlined automation solution that in combination with the Anyplex™ HPV28 Assay can genotype 19 high-risk and 9 low-risk HPVs (four more than PapilloCheck®).

**Materials/methods:** The test was performed following the manufacturer's instructions. Barcode labelled PreservCyt® (Hologic) samples were directly placed on board of the MICROLAB STARlet platform followed by extraction (STARMag96 Universal Cartridge Kit) and PCR setup. The PCR took place in the CFX96 Cycler (BioRad). Interpretation of melting curves was done by the Seegene Viewer Software. Results were directly sent to the laboratory information system.

The assay was checked for analytical sensitivity, accuracy and precision following Belgian guidelines (Raymaekers et al., 2011).

**Results:**

**Sensitivity:**
A negative PreservCyt® sample was spiked with the WHO HPV16 and HPV18 standards to determine the limit of detection (LOD with a 95% hit rate). The lowest concentration was 10000 international units/ml, correlating with 100 copies/PCR and was lower compared to PapilloCheck® (120 copies/PCR).

**Accuracy:**
65 specimens were tested. 17 external quality controls and 13 plasmids were typed correctly. 33 out of 35 clinical samples gave a concordant result (identical HPV types were detected in single/double infections or two or three identical HPV types were detected in multiple infections with three or four types respectively). In 12 out of 35 clinical samples Anyplex™ HPV28 detected one or more extra types. Two samples with a very low viral load were missed (HPV39 and HPV73).

**Precision:**
One negative and two positive samples with a multiple infection were extracted on 3 different days. PCR was performed on two cyclers. All results were concordant.

**Conclusions:** Anyplex™ HPV28 Assay met all our validation criteria, saved hands on time, avoided pipetting errors and was therefore successfully implemented in our routine diagnostic laboratory.

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Abstract 3775

**Treatment of bacteraemia caused by *Enterobacter* spp.: should the potential for AmpC induction dictate therapy?**

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**Background:** Carbapenems are considered treatment of choice for bacteraemia caused by potential AmpC producing bacteria, including *Enterobacter* spp. Data on the effectiveness of therapy with other antibiotics are limited.

**Materials/methods:** A retrospective study, conducted in two centers in Israel, including hospitalized patients with *Enterobacter* bacteraemia treated with either third generation cephalosporins (3GC), piperacillin/tazobactam, quinolones or carbapenem monotherapy, between 2010-2017. The primary outcome was 30-day all-cause mortality. Univariate and multivariate analyses were conducted, introducing type of antibiotics as an independent variable.

**Results:** Included were 277 consecutive patients. Of these, 73 were treated with 3GC as their main antibiotics, 39 with piperacillin/tazobactam, 104 with quinolones and 61 with carbapenems. All-cause 30-day mortality was 16% (45 patients). In either univariable or multivariable analyses, type of antibiotics was not significantly associated with mortality. With carbapenems as reference for multivariable analysis - odds ratio [OR] was 0.708, 95% confidence interval [CI] 0.231-2.176, p=0.547 for 3GC; OR 1.172, 95% CI 0.388-3.537, p=0.778 for piperacillin/tazobactam; and 0.586, 0.229-1.452, p=0.242 for quinolones. Type of antibiotics was not associated with repeated growth of *enterobacter* spp., including bacteremia (p=0.520). Resistance to the treating antibiotics developed in third of isolates (3/9) in each 3GC and piperacillin/tazobactam groups.

**Conclusions:** Type of antibiotic therapy was not associated with increased mortality or repeated growth of enterobacter spp. in cases of *enterobacter* bacteraemia in our cohort. Considering our results and previous studies, using antibiotics other than carbapenems for this infection seems reasonable, though randomized controlled trials are needed to confirm these findings.

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Impact of suppression of envelope stress responses on bacterial sensitisation to antimicrobial agents

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Background: New targets are necessary to fight against multidrug resistant bacteria. Stress response pathways suppression could be an interesting strategy to get it. The aim of this study was to evaluate the impact of disbalancing envelope stress responses as ςE, Cpx, Rcs, Bae and Psp responses on bacterial sensitization.

Materials/methods: Seventeen isogenic strains belonging to KEIO collection with deletions in genes corresponding to ςE response (rseA and rseB genes), Cpx response (cpxA, cpxR, cpxP and nlpE genes), Rcs response (rcsF, rcsA, rcsC, rcsD and rcsB genes), Bae response (baeR and baeS genes) and Psp response (pspA, pspB, pspC and pspF genes) were selected. Disk-diffusion for 19 antimicrobials, including agents disturbing cell wall (penicillins, cephalosporins, carbapenems, aztreonam, colistin and fosfomycin), protein synthesis inhibitors (aminoglycosides, tetracyclines and chloramphenicol), RNA synthesis inhibitors (rifampin), DNA synthesis inhibitors (fluoroquinolones) and folic acid synthesis inhibitors (sulphonamides and trimethoprim) were used as an initial screening to select the strains whose deleted genes caused an increase in susceptibility relative to wild-type strain E. coli BW25113. Then, gradient strip tests were performed for selected antimicrobials where >3 mm increase was observed by disk-diffusion.

Results: Three hundred and twenty-three antimicrobial/strain combinations were evaluated using disk-diffusion. Fifteen knockouts showed an increase in susceptibility in any of these antimicrobials: ampicillin, ceftazidime, cefepime, aztreonam, ertapenem, imipenem, fosfomycin, amikacin, chloramphenicol and trimethoprim/sulfamethoxazole. The reduction in the MIC of fosfomycin, trimethoprim/sulfamethoxazole, aztreonam, ertapenem, cefepime, ceftazidime and ampicillin ranged from 1,3 to 2,8-fold for rcsD, pspA, pspB and pspC knockouts. The major reduction in MIC was observed for ceftazidime (up to 2,8-fold) and trimethoprim/sulfamethoxazole (up to 2-fold). rcsD, pspA, pspB and pspC knockouts showed MIC reduction for 3 or 4 antimicrobials (Table 1).

Conclusions: Suppression of envelope stress response pathways could be a strategy to sensitize bacteria. According to these results, strains mutated in Psp response showed a greater increase of susceptibility compared to other envelope stress responses. Its role for repairing extensive disruptions of the inner membrane do it essential to bacterial survival, so that it would be the best target to address sensitization.

Table 1. Fold number of Antimicrobial susceptibility changes in knockouts.

<table>
<thead>
<tr>
<th>Gradient strip test</th>
<th>E. coli BW25113 knockouts</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMPICILLIN</td>
<td>rcsD</td>
</tr>
<tr>
<td>CEFTAZIDIME</td>
<td>2</td>
</tr>
<tr>
<td>CEFEPIME</td>
<td>1,4</td>
</tr>
<tr>
<td>ERTAPEMEN</td>
<td>1,5</td>
</tr>
<tr>
<td>AZTREONAM</td>
<td>1,5</td>
</tr>
<tr>
<td>TRIMETHOPRIM/ SULFAMETHOXAZOLE</td>
<td>1,4</td>
</tr>
<tr>
<td>FOSFOMYCINE</td>
<td>1,3</td>
</tr>
</tbody>
</table>

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Abstract 3778

High clinical impact on antimicrobial stewardship using multiplex PCR syndromic panels for severe community-acquired infections: a real-life experience

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Background: The different PCR panels of Biofire FilmArray have been individually studied with a focus on etiological diagnosis accuracy. Our study evaluates the clinical impact of using several FilmArray panels for severe community acquired infections (CAI) as a part of an antimicrobial stewardship program run by a Clinical Microbiology Department.

Materials/methods: Prospective study in a 1200-bed tertiary hospital from October 2018 to September 2019. Patients with CAI requiring admission in which sepsis was suspected (blood cultures obtained) with additional samples available in the Laboratory, were included. Meningitis/Encephalitis, Respiratory and Gastrointestinal FilmArray panels were performed in Cerebrospinal fluid (CSF), nasopharyngeal swabs (NPS) and feces respectively. Rapid results were informed to physicians in charge of each patient and antimicrobial adjustment was advised by a clinical microbiologist within the working shift. Conventional methods and FilmArray panels were compared regarding diagnostic yield and turnaround time (TAT). Antimicrobial adjustment within 24 hours after rapid results was recorded.

Results: During the study period, 146 samples from 142 patients were included. Filmarray panels were applied to the following samples: 46 fecal samples, 51 NPS and 49 CSF. Overall, 119/142 patients (83.5%) were clinically diagnosed with an infection. Of them, 102 were diagnosed with an infection covered by the three panels: respiratory infection in 50, gastrointestinal infection in 25 and central nervous system infection in 27. Seventeen cases had infection of other location and the remaining 23 were finally diagnosed with a non-infectious process. Of the 102 patients with an infection covered by the panels, an etiological diagnosis was obtained in 64 (62.7%): 54 (52.9%) by FilmArray panels and 25 (24.5%) by conventional methods (both yielded positive results in 13, 12.7%). Mean TAT was 2.4 hours for FA vs 94 hours for conventional methods. Antimicrobial adjustment within 24 h of rapid results was made in 64/142 patients (45%): de-escalation in 50 (35.2%), escalation in 14 (19.8%).

Conclusions: Filmarray panels provide higher diagnostic performance than conventional methods in a TAT as short as 2 hours. A high impact on antimicrobial stewardship was observed, leading to an early adjustment of empirical treatment in almost half of the patients.

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Abstract 3779

An evaluation of an automated broth microdilution platform versus the EUCAST disk diffusion methodology
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Abstract third-party references: Supported by Thermo Fisher Scientific

Background: The objective of this study was to evaluate the results, performance and workflow of the Thermo Scientific™ Sensititre™ ARIS HiQ™ system (ARIS HiQ) when compared to the EUCAST disk diffusion methodology, using clinical isolates at University Hospital Southampton, UK.

The ARIS HiQ is an automated broth microdilution platform, which has the capacity to incubate, read and interpret up to 100 Thermo Scientific™ Sensititre™ Susceptibility MIC plates (Sensititre plates) simultaneously.

Materials/methods: Antimicrobial susceptibility testing was performed on a total of 358 clinical isolates, consisting of Staphylococcus spp. (n=165), Enterococcus spp. (n=33), Enterobacteriaceae (n=86), Pseudomonas spp. (n=66), and Acinetobacter spp. (n=8) from University Hospital Southampton. Disc diffusion was performed on all isolates using antimicrobial discs and Mueller-Hinton Agar following the EUCAST methodology. All isolates were tested using the relevant Sensititre plates on the ARIS HiQ, according to the manufacturer’s instructions.

Results: ARIS HiQ and disc diffusion results were compared and analysed following the guidelines stipulated in ISO 20776-2:2002. Results have been summarised into groups of Gram positive and Gram negative and are shown in Table 1.

Table 1. Result summary for disc diffusion vs. ARIS HiQ.

<table>
<thead>
<tr>
<th></th>
<th>Gram-positive</th>
<th>Gram-negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of results</td>
<td>1511</td>
<td>1018</td>
</tr>
<tr>
<td>Categorical agreement %</td>
<td>98.9%</td>
<td>97.2%</td>
</tr>
<tr>
<td>Intermediate result versus resistant or susceptible result</td>
<td>0.1%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Disc diffusion result susceptible vs. ARIS HiQ result resistant</td>
<td>0.9%</td>
<td>1.6%</td>
</tr>
<tr>
<td>Disc diffusion result resistant vs. ARIS HiQ result susceptible</td>
<td>1.6%</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

Conclusions: This evaluation found the ARIS HiQ to be an accurate alternative to disc diffusion. A review of results demonstrated the benefit of using an automated platform in reducing human error. In addition, automated interpretation and application of expert rules offers a more time efficient approach.

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Clinical features and outcomes of patients with *Staphylococcus aureus* bacteraemia of unknown origin

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**Background:** *S. aureus* bacteremia (SAB) of unknown origin (UO) occurs in a subset of patients and is challenging to manage as source control procedures may not be possible. We compare patients with SAB between those with known origin (KO) and UO to identify distinguishing clinical features and outcomes that could guide clinicians on optimal management.

**Materials/methods:** A multi-center, prospective, observational study of hospitalized SAB patients was conducted. Medical charts were reviewed to obtain relevant demographics, laboratory, and clinical data. Serum cytokine concentrations for TNF, IL-6, IL-8, IL-10, IL-1beta, IL-17, IFN-gamma at SAB onset and 72h after therapy initiation were measured by ELISA. Patient groups were compared on clinical features including cytokine response and outcomes.

**Results:** 1163 patients were included, 19% had UO. Overall mean age was 57y and 34% had MRSA SAB. UO group had more males (79% vs 69%, p=0.0048) and cirrhosis (17% vs 11%, p=0.027), however KO had more patients on dialysis (21% vs 12%), dyslipidemia (19% vs 13%), diabetes (43% vs 32%), anemia (11% vs 6%), and presence of hardware (32% vs 21%) (all p<0.05). UO patients had worse clinical presentation: more had Pitt bacteremia score ≥4 (17% vs 12%, p=0.03) and altered mental status (22% vs 14%, p=0.0043). All measured cytokine concentrations at SAB onset and after 72h were similar between the groups (p=ns). Initiation of effective antibiotic therapy was delayed by ≥1d in UO (38% vs 27%, p=0.0008) and duration of therapy was shorter (median 9d vs 10d, p=0.043). While duration of bacteremia >2d (UO 40% vs KO 39%, p=0.64) and length of stay (UO 13d vs KO 11d, p=0.26) were similar, 30d mortality was significantly higher in the UO group (14% vs 8%, p=0.0054).

**Conclusions:** The high proportion of UO patients presenting with altered mental status likely precluded the ability of clinicians to obtain a thorough history from the patients to ascertain the source of SAB. Prompt initiation of effective therapy and for sufficient duration is needed regardless of whether the source of SAB is known.

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Abstract 3781

**Escherichia coli ST457: an emerging pathogen with wildlife and food-producing animals’ reservoirs**

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**Background:** *Escherichia coli* ST457 is a globally dispersed lineage often reported to carry resistance to clinically important antibiotics including beta-lactams and colistin. Carbapenemase-producing strains of ST457 have also been detected in USA, Mexico, China and Italy. ST457 has been recovered from diverse sources including humans, animals and the environment.

**Materials/methods:** A high prevalence of *E. coli* ST457 was detected in two ongoing projects evaluating antibiotic resistance within Australian gulls (42 ST457 strains) and Paraguayan poultry (14 ST457 strains). All of these strains were subjected to whole genome sequencing (WGS) using MiSeq and NovaSeq Illumina platforms. Long-read sequencing using the PacBio Sequel platform was performed for three representative strains. Publicly available WGS sequences of ST457 were downloaded from EnteroBase and included in SNP-based phylogenetic analysis and to assess serotype and carriage of antibiotic resistance genes, virulence factors and plasmid incompatibility groups.

**Results:** SNP analysis of 136 ST457 strains identified five main clades. The Australian gulls partitioned in two clades reflecting their serotypes (O11:H25 or O11:H45) and most of them carried *bla*CMY-2 on IncI1/ST23 plasmids. Human strains of ST457 from Australia, New Zealand, UK, Germany and Japan clustered with the gull strains with serotype O11:H25. Notably, the O11:H45 clade contained human clinical strains from Australia which were closely related to one of the gull strains. The Paraguayan poultry strains represented a successful clonal lineage carrying *mcr-5* gene along with *bla*CTX-M-8 on IncI1/ST113 plasmids. Their clade contained several strains from poultry of US origin and human isolates from Peru and Japan. One clade comprises strains from human and food animal origin with representatives from most continents but mainly from USA and China. This clade, mostly human and food-producing animals, carried more resistance gene cargo compared with strains in the other 4 clades including *mcr-1.1*, *mcr-2.1*, *bla*CTX-M-27, *bla*CTX-M-55, *bla*CMY-2.

**Conclusions:** This is the first large-scale WGS comparison of ST457 from diverse sources. Our data indicate that *E. coli* ST457 is an emerging pathogen with potential reservoirs in wild (gulls) and food-producing animals (mainly poultry). Association of this ST with resistance to extended-spectrum beta-lactams and colistin and various virulence genes is a major concern.

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Early-onset of bloodstream infections in a burn unit

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Background: Severely burn patients are at high risk for bloodstream infections (BSI) due to loss of the skin barrier function and state of immunosuppression induced by significant thermal injuries.

Materials/methods: This retrospective study was designed to evaluate the epidemiology and risk factors for BSI in a burn intensive care unit. Additionally, we also investigated the risk factors for multi-resistant bacteria [multidrug-resistant Pseudomonas aeruginosa (MDRPA), carbapenem-resistant Acinetobacter baumannii (CRAB), carbapenem-resistant Klebsiella pneumoniae (CPKP)]. All patients with burn injury admitted to the 8-bed burn unit at CTO Hospital of Turin between January 2015 and July 2019 were enrolled in the study. All episodes of BSI were included.

Results: There were 183 episodes of BSI among 324 cases with 241 microbiological isolates. Eighty-eight patients had at least one positive BSI (27.2%). Among them, 26 patients (29.5%) had more than three episodes of BSI during their stay. The median time to first positive blood culture was 10 days. Most of the first positive blood cultures were documented during the first week of hospitalization [37/88; 42]. The leading isolate was A baumannii (24.1%), followed by P aeruginosa (20.7%). Klebsiella spp accounted for only 7% of total isolates. A large number of isolates showed antimicrobial resistance, particularly in gram-negative bacteria. Among A baumannii isolates, 93.1% of them were CRAB, while the rate of MDR strains in P aeruginosa isolates was 48%. The prevalence of BSI due CPKP was around 5% (5.5%). At multivariate analysis, the placement of central venous catheter within the first 24 hours (OR:3.576 95% CI:1.596-8.017) undergoing a surgical intervention (OR:3.608 95% CI:1.238-10.517) and a higher revised Baux score (OR:1.019 95% CI:1.008-1.031) increased the risk of acquiring BSI. Prior rectal colonization (OR: 13.543 95% CI: 3.553-51.621) was a predictor of MDR gram-negative BSI. Polymicrobial (p=0.0004) and MDR gram-negative BSI (p=0.0019) increased the risk of death.

Conclusions: In our local setting, BSI are predominantly caused by non-fermenting Gram-negative bacteria, with high rate of carbapenem resistance, since the earliest days of hospitalization. These data underscore the need for effective infection control measures.

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Unveiling the role of nisin on resistance development by diabetic foot staphylococci: mutant selection window and horizontal gene transfer

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Background: The most prevalent microorganism in diabetic foot infections (DFI) is Staphylococcus aureus, an important pathogen due to its multi-resistant profile. As such, it is mandatory to develop alternative compounds for DFI treatment. Nisin is a promising alternative, being effective against DFI S. aureus and used in food industry for 90 years. However, correct drug therapeutic doses must be established before including this peptide in new therapeutic protocols, to avoid the selection and amplification of resistant mutants.

Materials/methods: A collection of 23 S. aureus DFI isolates and the reference strain ATCC29213 were used. For mutant selection window (MSW) and mutant prevention concentration (MPC) determination, 10^10CFU/mL bacterial suspensions were inoculated in Mueller-Hinton agar supplemented with nisin at 5.63, 11.25, 22.5, 45, 90, 180, 360 and 720 μg/mL, and incubated for 72h at 37ºC. To understand if nisin could potentiate resistance transfer from Enterococcus, after inducting rifampicin resistance in the 24 S. aureus isolates, mating experiments were performed using the Vanr Rifr Enterococcus faecium CCUG 36804 strain as a donor for the vanA gene and the 24 Vans Rifr staphylococci as recipients.

Results: MSW ranged from 11.25-360 μg/mL (two isolates), 11.25-540 μg/mL (three isolates) and 11.25-720 μg/mL (one isolate). It was not possible to determine the MSW for the remaining 18 isolates since they were able to grow at the highest nisin concentration tested (720 μg/mL). Regarding the horizontal protocol, it was possible to observe that in the presence of the nisin concentrations tested no transconjugants were obtained.

Conclusions: Determining nisin MSW will contribute to avoid resistant mutants’ development. The high concentrations obtained can be applied in vivo, being lower than the acceptable daily intake dose established by EFSA. Also, similar doses were already applied in vivo on infected wounds, showing no toxic effects on patients. As vancomycin is applied in DFI treatment, it is important to understand if nisin could potentiate the transfer of vancomycin resistance genes. The horizontal gene transfer protocol performed in the presence of nisin revealed no transconjugants, indicating that, at the concentrations tested, nisin doesn’t promote vanA transfer, which supports its future application to DFI treatment.

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Abstract 3793

CXCL13: a new marker in the diagnosis of Lyme neuroborreliosis?
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Background: Lyme neuroborreliosis (LNB), early or late disseminated form of Lyme disease are caused by spirochaetes of the Borrelia burgdorferi sensu lato complex (Bb). LNB diagnosis is based on 3 criteria: neurological symptoms, intrathecal synthesis of anti-Bb IgG (IA) and CSF pleocytosis [1,2]. The CXCL13 chemokine produced by CSF monocytes has been proposed as a promising marker for early diagnosis and therapeutic efficacy in LNBs. CXCL13 is detectable at high levels in CSF before intrathecal anti-Bb Ig synthesis and is negative after effective treatment. Our study evaluated the performance of a rapid test detecting CXCL13 (ReascanCXCL13® kit) in the CSF as part of the LNB's diagnostic

Materials/methods: In this retrospective study conducted at the Institute of Infectious Agents (CHU Lyon) between July 2018 and August 2019, the CXCL13 assay was performed in the CSF of 59 patients using the ReascanCXCL13® kit according to the manufacturer’s recommendations [threshold of positivity 250 pg/mL]. For 2 patients with confirmed LNB, the CXCL13 assay was performed before and after antibiotic treatment [post-ATB]

<table>
<thead>
<tr>
<th>Diagnosis retained</th>
<th>Nb of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confirmed LNB (3 criteria)</td>
<td>15</td>
</tr>
<tr>
<td>Possible LNB (2 criteria)</td>
<td>2</td>
</tr>
<tr>
<td>Non neurological Lyme disease</td>
<td></td>
</tr>
<tr>
<td>Infectious meningitis (n=19)</td>
<td></td>
</tr>
<tr>
<td>Viral</td>
<td>11</td>
</tr>
<tr>
<td>Bacterial</td>
<td>7</td>
</tr>
<tr>
<td>Cryptococcosis</td>
<td>1</td>
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<td>Non infectious neurological diseases</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>59</td>
</tr>
</tbody>
</table>

Results: Calculated diagnostic performances were sensitivity 100%, specificity 88.6%, positive predictive value 75% and negative predictive value 100%. Five CSF of infectious meningitis contained a level of CXCL13 ≥ 250 pg/mL [2 neurosyphilis, 1 H. influenzae, 1 S. pneumoniae and 1 P. aeruginosa]. No case of viral meningitis gave rise to a positive result. For the 2 patients who had a post-ATB control, CXCL13 was negative after 1 and 2.5 months of antibiotic therapy respectively, whereas the IA remained positive

Conclusions: This is the first clinical evaluation in France of ReascanCXCL13® kit in a near-real situation. In agreement with literature, sensitivity was excellent and specificity medium. Nevertheless, the lack of specificity concerns bacterial meningitis whose clinical picture is usually different of LNBs. Thus, the CXCL13 dosage arises as a fast and complementary marker in the LNBs diagnosis. Its usefulness as a marker of therapeutic efficacy is promising but remains to be assessed on a larger cohort

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If breaking a hip feels like a concern for the elderly, then getting pneumonia should be twice as concerning!

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Background: Pneumonia is a common lung infection that can be life-threatening, especially in elderly. Despite these concerns, elderly mostly fail to accurately gauge their own pneumonia risk, leading to inadequate prevention efforts especially low uptake of existing vaccines. The mismatch between the high morbi-mortality and the low awareness of pneumonia potential severity represent a driver of unhealthy aging. On the contrary, breaking a hip is widely recognized as a major concern for the elderly. To change this trivialization of pneumonia in Elderly and help the vaccination uptake, we compared 2-year outcomes for elderly (≥80 y.o.) patients after hospitalization for acute respiratory infection (ARI) or hip fracture (HF).

Materials/methods: A 2009-15 population-based cohort study was performed in one French region (2.5 million inhabitants), using medico-administrative data collected from the French-DRG. We defined cases of patients ≥80 hospitalized for ARI or HF using ICD-10 and Current Procedural Terminology algorithms. The main outcome was the 2-year mortality of the two patient groups. Kaplan Meier curves described the overall survival and hazard ratios and 95% confidence intervals HR (95% CI) were calculated using Cox models.

Results: 16,917 patients hospitalized for ARI (n=12,159) or HF (n=4,758) were included. Patients hospitalized for ARI had more comorbidities and 3.3-fold greater in-hospital mortality (17.9% mortality for respiratory infection and 5.4% for hip fracture). The Kaplan Meier curves for elderly patients showed a significant difference in mortality for these two groups (log rank test p<0.0001). After adjusting for comorbid conditions and frailty score (as well as age and sex), the global risk of death at two years for elderly patients hospitalized for ARI compared to the HF was significantly higher (HR 1.8 [95% CI: 1.7 - 2.0]).

Conclusions: We hope that placing the consequences of pneumonia in relation to the consequences of a hip fracture may provide useful perspective for discussions of pneumonia and its prevention with aging populations. The population, but also their caregivers and clinical practitioners, should be more aware of this disease's risk and importance. Better recognition will improve the prevention of pneumonia by increasing uptake of vaccines, such as influenza and pneumococcus.

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Abstract 3795

Prevalence of *Clostridioides difficile* strains found in Texas soil
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**Background:** *Clostridioides difficile* infection (CDI) is an urgent public health threat worldwide, with known isolates existing in both humans and animals. While commonly a hospital-acquired infection, recent reports have shown that community-acquired CDI can account for up to 41% of infections. Identifying environmental sources of *C. difficile* can give the scientific community a better idea of how non-hospital reservoirs can potentially contribute to *C. difficile* exposure and subsequent gastrointestinal colonization. The objective of the study was to identify *C. difficile* and toxin genes across various soil sources.

**Materials/methods:** This was a cross-sectional study utilizing soil samples obtained throughout Texas, USA, including dry dirt, sand, and wet soil near water sources. All samples were collected between September and November 2019. Samples were taken from areas where human and animal contact are frequent, such as recreational parks, and ranged from surface collection to 3 inches deep. Samples were stored at -80°C until processing. DNA extractions were performed using the DNeasy Powersoil Pro Kit (Qiagen) per manufacturer’s instructions. Real-time PCR was also performed on extracted DNA using the Microbial DNA qPCR Multi-Assay Kit for Clostridium difficile Pathogenicity (Qiagen) for the identification of *C. difficile*, toxin A (TcdA), and toxin B (TcdB) genes.

**Results:** A total of 89 soil samples were collected and processed for the presence of *C. difficile*. These included samples from parks and trails (59.6%), water sources (26.9%), and other public spaces (13.5%). *C. difficile* was identified in 40 (44.9%) soil samples, with 3 (3.4%) showing Toxin A and 1 (1.1%) showing toxin B production. *C. difficile* was most prevalent among samples taken from water sources (70.8%), followed by parks and trails (35.8%), and other public spaces (25%). The median (IQR) Cq value for the *C. difficile* gene was 39.83 among samples that tested positive.

**Conclusions:** We identified a high prevalence of *Clostridioides difficile* in soil samples, though toxin gene detection prevalence was low. Future studies will analyze other sources, including water and varying surface samples to obtain a comprehensive view of *C. difficile* in the environment.

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Genomic analysis reveals persistence and microevolution of methicillin-resistant Staphylococcus aureus in recurrent carriers

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Background: Methicillin-resistant Staphylococcus aureus (MRSA) remains a public health problem worldwide. The duration of asymptomatic MRSA carriage is not well known. This study is aimed to investigate whether the recurrence of MRSA was caused by the same strain.

Materials/methods: Sixty-eight isolates, one each from the first and the second episode of 34 cases, were subjected to whole-genome sequencing and antimicrobial susceptibility testing. The patients had at least three negative samples between the first and the second episode of detected MRSA. The genomes of all isolates were analysed by multi-locus sequence typing (MLST), core-genome MLST (cgMLST), resistance traits and virulence factors. Broth microdilution method was applied for antimicrobial susceptibility testing.

Results: Among the 34 pairs of isolates, 27 pairs remained the same sequence type (ST) and seven pairs had different STs in two episodes. Of the 27 same-ST pairs, 26 cases presented 0 to 25 allelic difference by cgMLST, indicative of persistence of same strains, despite three negative samples between the two positive samples. Microevolution was suspected for one case, in which the paired isolates had 74 differed alleles, same ST and SCCmec type, same genomic traits for resistance and toxins. The paired isolates with different STs (n=7) had >1,000 allelic differences, indicating colonization with a new strain.

Despite persistence of the same strains, susceptibilities to clindamycin, erythromycin, tetracycline or tobramycin changed from resistant to susceptible in the second isolates in six cases. Re-sensitization to clindamycin, erythromycin or tetracycline could be explained by the loss of resistance genes ermC or tetK. All other paired isolates associated with persistence/microevolution had the same antimicrobial susceptibility patterns and genomic resistance traits.

The median span between two episodes was 25 months (1-63 months) in the persistence/microevolution cases, and 39 months (29-154 months) in the re-colonization cases.

Conclusions: The duration of asymptomatic persistent carriage could last up to 63 months among cases in the present study. Although same strains persisted over time, resistance genes could be lost which led to re-sensitization. Genomic analysis provides us a useful tool in assessing whether recurrence of MRSA carriage is due to low-level persistence or colonization with a new strain.

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Development of fungal mock community standards for mycobiome studies

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Background: To date, a significant amount of work has been performed on the human microbiome to evaluate its composition and influence on physiology; this research has led to additional studies on microbiomes localized at specific sites of the human body (e.g., skin, oral, vaginal). Given that fungi are ubiquitous and live in symbiosis with the human body, researchers are now actively looking into the role of the mycobiome in human health and disease. Recent advancements in sequencing technologies have enabled the community profiling of fungi; however, the complexities associated with metagenomics sequencing analyses have posed significant challenges toward standardization. To address this need, ATCC has developed genomic DNA and whole cell mock microbial communities comprising ten medically relevant fungal species mixed in even proportions. In this proof-of-concept study, we demonstrate the use these standards in evaluating DNA extraction and sequencing methods for mycobiome analysis.

Results:

DNA Extraction Efficiency

Conclusions: This proof-of-concept study demonstrates the utility of mycobiome standards as controls for evaluating run-to-run variability and optimizing assay performance at each stage of the mycobiome analysis workflow.

- Whole cell standards can help identify biases introduced during DNA extraction and can be used as full-process controls.
- Genomic DNA standards can be used for comparing various library preparation methods and sequencing platforms.
- The data analysis for mycobiome profiling is challenging due to the lack of complete fungal reference genomes and the limited availability of analyses pipelines.

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Background: Chronic disseminated candidiasis (CDC) occurs after profound (neutrophils < 100/mm3) and prolonged (≥10 days) neutropenia, and consists in persistent fever and multiple small (<10 mm) abscesses in liver and/or spleen. The aim of this study was to assess 18F-fluorodeoxyglucose PET/CT in the diagnosis and follow-up of CDC.

Materials/methods: A pilot prospective study was conducted in 38 French onco-hematological centers from 2013-2017 (NCT01916057). Patients ≥18 y.o. suspect for CDC on conventional imaging (40 CT and 4 MRI) were included. PET/CT and conventional imaging were performed initially and at M3. Clinical follow-up was assessed until M12. Clinical success was defined by resolution of fever attributable to CDC, complete biological response by normal liver enzymes and CRP ≤20 mg/L, and complete radiological response by disappearance of lesions compared to initial imaging. The primary endpoint was the global response to antifungal treatment at M3 defined by clinical success and extinction of hepatosplenic metabolic uptake on PET/CT.

Results: Among 44 analyzed cases (7 proven, 13 probable, 24 possible CDC), 75% had acute leukemia, 55% were male (median age 47 [21-79]). At diagnosis, 82% had fever and 82% liver enzyme abnormalities, C-reactive protein was elevated in 85%. Conventional imaging showed abscesses on liver and spleen in 66%, liver in 25%, spleen in 9%. PET/CT showed metabolic uptake at CDC diagnosis in 84% but did not match with lesion localizations on conventional imaging in 34%. Patients received in median 153 days [18-399] of antifungal drugs, combined with corticosteroids in 50%. At M3, 25% (8/32) of evaluable patients met the primary endpoint criteria. However, among 37 patients who had clinical success at M3, 32% had biological success, and 78% failed to respond on conventional imaging. Among these patients, extinction of hepatosplenic metabolic uptake on PET/CT was observed in 17% (5/29). At M6, 10% (4/40) of patients had persistent fever attributable to CDC and 6% (2/33) at M12. The 11 deaths were not attributable to CDC.

Conclusions: Clinical improvement of CDC occurs before biological and radiological normalization. In patients with clinical success at M3, kinetic of PET/CT metabolic uptake decrease is more helpful than conventional imaging and could guide antifungal duration.

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Development of electronic nano-sensors for the specific in situ detection of Escherichia coli
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Background: Detection of bacterial pathogens directly on surfaces, without resorting to nucleic acid extraction, still remains difficult. We explored a new method using nanowire technology able to fix bacteria and detect their presence by electrical variations; a chemical functionalization of the process allows a specific bacterial detection. This work describes the development of a highly sensitive bacteria biosensor using silicon nanowire-based resistors for direct detection by electrical measurements.

Materials/methods: The resistors used for bacterial detection applications are manufactured using conventional silicon technology. Comb-shaped inter-digitated electrodes are devices, fabricated using a highly doped polycrystalline silicon (polySi). Silicon nanowires are synthesized on the teeth of polySi inter-digitated electrodes by the vapour-liquid-solid (VLS) growth mechanism at 460°C using gold as a catalyst and silane as gas precursor.

Results: Nanowire functionalization was used to facilitate the attachment of bacteria to silicon nanowires through specific anti-LPS antibodies. APTES [3-Aminopropyl-triethoxysilane] and then glutaraldehyde (C5H8O2) was vapor deposited on the nanowires, allowing the antibodies grafting (Ac anti-LPS) and the E. coli-gfp binding (Fig.1).

Figure 1: Bacterial grafting protocol.

To check it, fluorescent bacteria [Escherichia coli ATCC-25922-GFP] were attached to these functionalized nanowires and the fluorescence intensity was evaluated by confocal microscope. The electrical characterization (I-V) was used to determine the variation of the resistance as a function of the concentrations of bacteria. During the first tests, this system allowed E. coli to be easily detected at a concentration of 10^5 and 10^7 CFU/ml.

By the fluorescence microscope the area was measured without bacteria [6.18] and after addition of 10^5UFC/ml E.coli [59757,65] [magnification X20; image thresholds by an “intermode” threshold], indicating a specific detection of bacteria in situ without amplification steps.

Conclusions: The next step in the project is to test the specificity and to evaluate the sensitivity of our sensors, using several species and concentrations of bacteria. A new sensor will be designed, integrating resin-based wells (by inkjet printing), in order to guarantee complete reproducibility of measurements.

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Abstract 3808

**Title:** TB screening and treatment in an Italian cohort of haematopoietic stem cell transplant recipients

**Authors:** Andrea Della Vecchia*, Carmen Di Grazia*, Alida Dominietto*, Anna Maria Raiola*, Emanuele Angelucci*, Matteo Bassetti*, Viscoli Claudio*, Malgorzata Karolina Mikulska*

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**Background:** Hematopoietic stem cell transplant (HSCT) recipients are considered at increased risk of tuberculosis (TB), but in non-endemic countries available data report a low number of latent and active infections. Current guidelines recommend latent TB screening in a low endemicity setting but supporting data are limited. The aim of this study was to report the rate of active and latent TB, the factors associated with Quantiferon (QFT) results and the use and outcome of treatment of latent TB.

**Materials/methods:** Data from 933 consecutive allogeneic HSCT recipients from Ospedale Policlinico San Martino, Genova, Italy from years 2008-2019 were collected retrospectively. Patients were screened for latent TB with Quantiferon-TB In-Tube until May 2018, QuantiFERON-TB Gold Plus thereafter. Data on patients with TB, with latent TB and those re-tested with QFT were collected. Variables associated with QFT results (positive vs. negative vs. indeterminate) were analyzed in a multinomial regression model.

**Results:** Overall, 2/933 (0.002%) patients developed active TB during 5015 person-years of follow up, with an incidence of active TB of 39.88 cases per 100,000 person-years. Among screened patients, 15/254 (5.9%) resulted QFT positive and 32 (12.6%) indeterminate. Older age was associated with QFT positivity, while a transplant from a mismatched donor was associated with an indeterminate QFT result.

Of 51 patients who were re-tested with QFT after HSCT, 17 had discordant results: 11 from indeterminate to negative, 4 from positive to negative and 2 from negative to positive (one with active TB and one with latent TB after recent exposure). No cases of LTBI reactivation were observed in a 36 person-years follow-up.

Overall, 8/15 (53%) QFT positive patients and 1 with post-HSCT latent TB were treated with isoniazid (INH) for an average of 5.7 months and 3/9 (30%) developed hepatic toxicity that required drug discontinuation.

**Conclusions:** The incidence of active TB in allogeneic HSCT was higher than in the general Italian population (39.88 cases per 100,000 person-years), but none of the cases occurred in those with latent TB at HSCT, despite INH provided to only half of them. The benefits of latent TB screening should be re-evaluated in a low endemicity setting.

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Abstract 3809

**Using metagenomics to study the impact of hospital stay on the human gut resistome**

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**Background:** Antimicrobials are vital for modern medicine. Antimicrobial use selects for antimicrobial resistant bacteria, particularly among the gut microflora. Minimising antimicrobial resistance (AMR) selection by avoiding unnecessary antibiotic use helps combat AMR. Metagenomic analyses have the potential to provide accurate detection and quantification of AMR genes (ARGs) within an individual’s gut microbiome (their gut ‘resistome’), allowing the impact of different types of antibiotic exposures to be evaluated and guide interventions to reduce AMR.

**Materials/methods:** We have developed a short-read sequencing approach to characterise the gut resistome and piloted this in two clinical sample sets. Briefly, DNA is extracted directly from faecal samples and sequenced by Illumina NovaSeq to a depth of $10^6$ million reads. The resulting reads are filtered, then mapped to known ARGs in the CARD database using the bioinformatics tool ARIBA.

**Results:** The first sample set was 25 paired stool samples from older hospitalised adults taken a median of 25 days apart (1 to 50 days). Both median ARG reads/kb/million total reads (RPKM) and median ARG count increased between first and second samples (1544 (IQR 1122 to 3062) to 2704 (IQR 1220 to 6308) and 48 (IQR 19 to 61) to 64 (IQR 23 to 72) respectively), but this did not reach statistical significance (paired Wilcoxon test, p=0.22 and p=0.19, respectively).

The second sample set comprised 168 faecal discards from *Clostridium difficile* testing at a hospital, taken over 14 months. In the first set of samples, from months 1-3 [group 1, n=11] and 12-14 [group 2, n=10], the median ARG RPKM increased from 883 (IQR 561 to 3107) to 1040 (IQR 570 to 3891), and the median ARG number increased from 18 (IQR 15.5 to 53) to 49.5 (IQR 22.5 to 54), but this did not reach statistical significance (two sample Wilcoxon test, p=0.7 and p=0.48, respectively).

**Conclusions:** Direct, deep sequencing can be used to quantify carriage of ARGs in faecal samples. Our data indicate this approach can be used to study the impact of healthcare exposure and antibiotic treatment on ARG carriage in individual patients. Large scale evaluation of this is underway within the ARK Hospital Project.

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A silent mcr-9 and a novel class A beta-lactamase in *Citrobacter telavivum* sp. nov. colonising hospital patients

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**Background:** Evolutive biomarkers and whole-genome sequencing (WGS) analysis are contributing to clarify taxonomic bacterial positions. In this study, two *Citrobacter* spp. strains (6105T and 6106) previously identified as *Citrobacter farmeri* by Vitek 2 and as *Citrobacter amalonaticus* by MALDI-TOF MS, and recovered during an epidemiological study of ESBL screening in rectal swabs of hospitalized patients at Tel-Aviv (Israel; 2010) were characterized by a polyphasic approach.

**Materials/methods:** The strains were characterized by WGS, phylogenetic analysis based on 16S rRNA or recN genes, multi-locus sequence analysis (MLSA; fusA, leuS, pyrG, rpoB), genomic comparisons [Average nucleotide identity (ANI) and digital DNA-DNA hybridization (GGDC)], and biochemical tests. Location and genetic surrounding of antibiotic resistance genes were investigated, and antibiotic susceptibility profiles were determined by disc diffusion, and broth microdilution methods.

**Results:** Phylogenetic analysis based on 16S rRNA gene sequences indicated that strains 6105T and 6106 belonged to the genus *Citrobacter*, while recN phylogeny and MLSA revealed one strongly supported clade encompassing both strains, and distinct from currently recognized species of the genus *Citrobacter*. ANI and GGDC showed 90.7% and 54.3% identity to the closest relative *C. farmeri*, respectively. The ability to metabolize different compounds also discriminated strains 6105T and 6106 from other species. Genomic analysis of strains 6105T and 6106 revealed that a novel class A beta-lactamase (TEL-1; sharing 90.5% identity with chromosomal β-lactamase CdiA of *Citrobacter koseri*), and mcr-9, flanked by two IS*Ehe*3-like elements, were chromosomally located. Sequence query of the region surrounding mcr-9 showed similarity to sequenced plasmids from other *Enterobacteriaceae*. The isolates were multidrug resistant, although colistin susceptible.

**Conclusions:** *Citrobacter telavivum* sp. nov. producing a novel class A beta-lactamase (TEL-1) is hereby described colonizing hospital patients in Tel-Aviv. Moreover, an acquired silent mcr-9 that seems to circulate among plasmids and chromosome of different *Enterobacteriaceae* was identified enlarging the species that could act as a host of this gene.

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Abstract 3811

**Anti-biofilm activity of ozenoxacin against methicillin-resistant *Staphylococcus aureus* strains**

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**Background:** Biofilm formation is an important virulence factor for methicillin-resistant *Staphylococcus aureus* (MRSA). Ozenoxacin (OZN) is an excellent option against Gram-positive cocci. We investigated the antibiofilm activity of OZN against quinolone-susceptible (QS) and -resistant (QR) MRSA compared with topical antibiotics.

**Materials/methods:** The minimal inhibitory concentration (MIC) of ozenoxacin (OZN), fusidic acid (FA) and mupirocin (MUP) was determined by microdilution in 4 MRSA-QS and 4 MRSA-QR producing biofilm. The same antibiotics were tested to determine the minimum biofilm inhibitory concentration (MBIC) and the minimum biofilm eradication concentration (MBEC) by microdilution assay. In addition, from MBEC plate was determined the frequency of resistant mutant.

**Results:** The geometric mean (GM) of the MIC of OZN was 0.031 µg/mL for MRSA-QS and 0.2 µg/mL for MRSA-QR. Values slightly higher were found for FA and MUP, showed a GM-MICs of 0.2 1 and 0.354 µg/mL for MRSA-QS and 0.07 and 0.044 µg/mL for MRSA-QR, respectively.

The GM of MBICs for OZN was 0.297 µg/mL for MRSA-QS and 1.4 µg/mL for MRSA-QR strains. The GM-MBICs of FA was 0.4 and 0.125 µg/ml for MRSA-QS and –QR, respectively. MUP showed than GM-MBICs for MRSA-QS and –QR were 0.5 and 0.2 µg/ml. GM-MBECs for OZN was 16 µg/mL and 128 µg/mL for MRSA-QS and -QR strains, respectively. FA, showed a GM-MBECs for MRSA-QS of 362 µg/ml and 512 µg/ml for MRSA-QR. Finally, MUP showed a GM-MBECs of 256 and 1024 µg/ml for MRSA-QS and –QR, respectively.

Worthy of note, OZN did not select mutant strains in this study. The selection rate of FA was 10^-10 in SA3 strain (MRSA-QS) and 10^-7 for SA-823 strain (MRSA-QR). Moreover, MUP has selected spontaneous mutant in three of four MRSA-QR strains. For SA-50 strain the mutant selection rate was 2.6x10^-10, 1x10^-10 for SA126 and 10^-10 SA-823 strain.

**Conclusions:** OZN shows an excellent *in vitro* activity against MRSA-QS and -QR strains. MBEC values to OZN in MRSA-QS were 5 and 16 times lower in comparison with other topical antibiotics and in the range of concentration achieved on the skin after topical application. In addition, OZN did not select spontaneous mutants in strains of this study.

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**Abstract 3813**

**Discrepancy results with meningitis/encephalitis panel FILMARRAY in cerebrospinal fluid**

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**Background:** CNS infections require a fast and reliable diagnosis. Filmarray® (FA) Meningitis/Encephalitis (ME) Panel (bioMérieux) is a rapid multiplex PCR platform which detects 14 pathogens in cerebrospinal fluid (CSF) in patients with ME. The aims of this study were to assess the performances of this test in comparison with routine methods (RM). In case of discrepancy an analysis based on patient records and laboratory results was performed.

**Materials/methods:** From January to November 2019 at Hospital Lozano Blesa, Zaragoza-Spain, CSF samples of patients with ME suspicion were tested with the RM: gram stain, India ink stain (IIS), bacterial culture, Herpesviridae and Enterovirus PCR (Entherpex Genomica®) and Cryptococcus sp. (Csp) antigen immunochromatography (IC) (RDT CryptoPS, BIO-RAD). Results were compared with FA.

**Results:** Fifty-three CSF from 49 patients were tested. RM global positivity rate was 14/49 (28.6%) versus 16/49 (32.7%) for FA. There was a good concordance between both methods in 10 samples (3 Enterovirus, 1 VZV, 2 HSV-1, 2 Streptococcus pneumoniae (SP) and 2 Listeria monocytogenes). Discrepancy was found in 5 samples. SP was detected by FA and not by culture in a CSF with bacterial pattern. In two samples VZV was detected by FA and not by PCR (Genomica®), in both cases, CFS had a viral pattern, and one of the patients had vesicular lesions. In one non pathological CFS, false positive HSV-2 was detected for Genomica® but not by FA. In one sample with lymphocytes, Csp was detected by IC and not with FA or IIS, this sample was FA negative at the arrival to the laboratory; however, sample showed a FA C. neoformans/gattii and IIS positive result after incubation for 48h at 37°C.

**Conclusions:** Discrepancy between FA and RM were detected for SP, VZV, HSV-2 and Csp. FA showed more sensitivity for VZV and SP FA sensitivity was deficient for Csp, requiring other methods to confirm. FA is a useful method in emergency cases; however, its results should be confirmed and always interpreted according to the CSF biochemistry results.

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Abstract 3814

**Determining the value of sequential screening to detect carbapenemase-producing Enterobacteriales**

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**Background:** When CPE carriage is confirmed in hospital inpatients, the Public Health England acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae, stipulates the patient must remain in isolation for the duration of their hospital stay and all subsequent visits.

There are few publications that have determined the value of sequential screening to establish the optimal number of samples required to demonstrate transient versus established carriage and whether there is a requirement for the patient to remain in isolation. Therefore, we aimed to demonstrate whether multiple screens could determine whether the patient reverts and remains negative for a CPE.

**Materials/methods:** Screening data was extracted from the laboratory information management system (LIMS) during a suspected outbreak of Enterobacteriales producing OXA-48 type carbapenemases over an 18 month period, from May 2016 to March 2018. During this time screening was performed on admission, followed by weekly screening.

**Results:** Of the 815 patients screened, 137 had at least one positive result, with the majority considered as carriage and 4 isolated from clinical samples and, therefore, deemed to be a cause of infection.

Of the 137 patients with at least one positive CPE screen, 60% received only one screen, 24.1% had 2 screens, 8% had 3 screens, 3% had 4 screens, 2% had 5 screens, 1.5% had 6 screens and 0.7% had 9 screens.

Based on the patients receiving at least 3 CPE screens, we can report that 85% of patients had established CPE carriage, compared to 15% demonstrating transient carriage i.e. reverting back to negative carrier status.

**Conclusions:** This research demonstrates the necessity of serial screening of CPE carriers to determine transient versus established carriage. Patients with transient carriage could remain in open wards, which would have large cost savings for the hospital.

The results of this study, therefore, do not fully support the guidelines in the PHE toolkit which state that all CPE carriers should have a positive carrier status for their lifetime and always be in an isolated facilities.

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Abstract 3818

Complex polyclonal outbreak of blaVIM-1-harbouring and mcr-9-cohabouring Enterobacter cloacae complex linked to drains in a German hospital

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Background: The dissemination of carbapenem or colistin resistance genes is a major public health threat. Over a period of 20 months a hospital-acquired extensively drug-resistant Enterobacter cloacae complex was detected in four patients in two adjacent single rooms of an intermediate care ward at a tertiary care centre in Germany.

Materials/methods: Identification, antimicrobial testing (VITEK2, colistin microdilution) and carbapenemase tests (mCIM, PCR) were performed. Genotyping was carried out by whole genome sequencing (Illumina MiSeq, analysis by Ridom Seqsphere+ with an ad hoc cgMLST scheme, JSpeciesWS, PlasmidFinder and ResFinder). Infection prevention and control measures introduced were as follows: contact precautions, screening, environmental sampling of all sinks and shower drains, change/cleaning and disinfection of the drainage, observations, and trainings.

Results: In January 2019, patient 2 was colonized in room 1 with a VIM-1-producing E. hormaechei that was related to an isolate of a prior occupant of the room (patient 1) treated 16 months earlier. Water samples were taken from all drains of the ward and the strain was found in the drains of room 1. A third patient became colonized with a VIM-1-producing E. cloacae in room 2 in March 2019. Finally, a blaVIM-1- and mcr-9-cohabouring E. hormaechei was detected in Patient 4 in room 1 in May 2019. A highly related strain was found in room 2 (shared drainage system with room 1) two weeks before the patient was admitted. Both isolates were colistin susceptible (MIC 0.1 25 mg/L, 0.25 mg/L) but the mcr-9 regulatory genes (qseC/qseB) were not detected. Observations carried out revealed possible environment-to-patient transmission events as medical equipment was stored nearby the washbasin. One hospital-acquired infections (UTI) was observed.

Conclusions: Transmissions of carbapenemase-producing Enterobacterales arising from the hospital waste-water system are complex, involving several species, genotypes and resistance genes. As the biofilm is difficult to eradicate it is important to emphasize standard precautions. To the best of our knowledge, this is the first report of a (silent) mcr-9 gene transmission in Germany. As the gene was not expressed, circulation was difficult to detect. However, further research about the transmissibility of the blaVIM-1 and mcr-9 genes is needed.

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Abstract 3822

A low-cost nanoliter droplet handling system for pathogen identification and antimicrobial susceptibility testing on microtitre plates

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Background: Antimicrobial resistance (AMR) has already threatened the effective treatment of an ever-increasing range of infections caused by bacterial pathogens due to extensive overuse and misuse of antibiotics. To correct analysis and implementation of prescription instructions, guiding patients safe, effective and rational drug use, antimicrobial susceptibility testing (AST) should be performed to evaluate the antibiotic resistance. A routine procedure usually takes 48-72 h from sampling to final report. Those laborious and time-consuming complicated steps hinder the clinicians choosing the most proper treatment timely, resulting in inappropriate prescription of antibiotics and the emergence of AMR. Shortening turn-around-time of diagnosis is notably a critical determinant of optimal treatment.

Materials/methods: We developed an automated nanoliter droplet handling system for low-cost minimum inhibitory concentration (MIC) testing and pathogenic bacteria identification suitable for early diagnosis with limited sample volumes. Nanoliter liquid handling was realized by a simple interfacial nanoliter injection (INI) method. The workflow included preparation of preloaded plates with nanoliter reagents, automated sample distribution, and results readout by a standard plate reader. For pathogen identification, the preloaded reagents were species-specific primers; while for AST, they were antibiotics. The addition of redox indicator provided the results could be read both by visual and fluorescence changing.

Results: A quality control strain (E. coli ATCC 25922) was chosen to verify this method for AST. Eight antibiotics including amikacin, ampicillin, chloramphenicol, meropenem, tetracycline, cefalotin, ceftriaxone, gentamicin were tested. The AST results obtained within 5 hours were consistent with the quality control range. The reaction volumes can be down to 20 nL. Nine strains isolated from clinical samples with four drugs were tested, and the results were comparable with those obtained from VITEK2 Compact (Table 1). Species distinctive PCR primers were designed and 17 species which are the most common cause of bloodstream infection pathogens were identified with 98.86% correspondence.

Conclusions: This system enables rapid MIC determination and species identification on the same platform, using common microtiter plates with preloaded antibiotics or PCR primers, greatly reduces the cost of reagents and saves time.

Table 1. AST results obtained from INI method and VITEK2 Compact

<table>
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<tr>
<th>Bacteria</th>
<th>PUMCH code</th>
<th>Amikacin</th>
<th>Aztreonam</th>
<th>Meropenem</th>
<th>Ceftazidime</th>
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<td>8</td>
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<td>&gt;16</td>
<td>&gt;128</td>
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<td>E. cloacae</td>
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Bacterial and fungal contamination and simultaneous analysis of chemical indoor air pollution in medical-social establishment and liberal healthcare offices

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Background: Indoor air quality of medical-social establishment and liberal healthcare offices is poorly studied. This work aimed for the first time to describe simultaneously the microbial, chemical and particulate contamination of these indoor environments.

Materials/methods: Two campaigns were conducted in Rennes (Brittany, Western France) and Nancy (Lorraine, Eastern France) in summer 2018 and winter 2019 in six liberal facilities and four nursing homes. Samples were collected for microbial detection with a cyclonic liquid air sampler and surfaces using swabs. During both campaigns, bacteria and fungi were enumerated by cultural techniques. They were also detected as well as viruses by real time PCR on air samples. Besides, a huge panel of 40 volatile organic compounds (VOCs) and 13 semi-volatile organic compounds (SVOCs) were measured. Ambient parameters (temperature, relative humidity, pressure and carbon dioxide) and the number of fine particles (PM2.5) were also measured.

Results: Low median concentrations of bacteria (45 CFU/m3 in air and 307 CFU/100 cm2 on surfaces) and of fungi (11 CFU/m3 and 9 CFU/100 cm2) were detected. Among all bacteria, Stenotrophomanos maltophilia and Citrobacter freundii at high concentrations were the most potentially pathogens found, notably on surfaces of patient rooms from a medical-social establishment. Bacillus and Chryseobacterium were detected at lower levels in air. Low concentrations both in summer and winter of Cladosporium, Penicillium and Aspergillus were detected in air, but high levels of Rhodotorula were reported on surfaces. Regarding chemical compounds, median concentrations (µg/m3) were determined for alcohols (ethanol: 372.1 and isopropanol: 28.3 respectively for and), aldehydes (formaldehyde: 11.4), ketone (acetone: 27.2) and terpenes (limonene: 5.9). For phthalates, the highest median concentrations were measured for diisobutyl phthalate (0.27).

Conclusions: Indoor air contained a complex mixture of many microorganisms and pollutants found in rather low concentrations, below the indoor air quality guidelines. Our study showed a lower pollution compared to dwelling indoor environments. However, this pollution originated mainly from healthcare activities and uses, and was higher than that measured in hospitals (same campaigns in Rennes and Nancy hospitals) that are equipped with central air conditioning systems, decreasing indoor aerosols more efficiently than in healthcare offices often not equipped.

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National outbreak of norovirus genogroup II in a sushi restaurant chain associated with an internationally distributed seaweed product

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Abstract 3826

Background: In July/August 2019, environmental health were informed of 176 reports of gastrointestinal illness linked to a sushi restaurant chain with 11 outlets nationally. A multi-agency outbreak control team was convened to investigate and implement control measures.

Materials/methods: Individuals reporting gastrointestinal illness were sent online questionnaires requesting information on demographics, symptoms, and food consumed at the restaurants. Cases were defined as having diarrhoea, vomiting, nausea, or fever within five days of dining at the restaurants. Stool samples were requested from cases and staff. Food samples were tested for pathogens. The Rapid Alert System for Food and Feed was reviewed for contaminated food sources, and links to the restaurants. A case-control study was conducted recruiting controls from the chain's online delivery service.

Results: 49/176 individuals completed the questionnaire and met the case definition. Median age was 28 years (range 12-71); 75% were female. 91% of cases reported nausea, 79% vomiting, 71% diarrhoea, and 10% bloody stools. Median incubation period was 38 hours (range 1-71). Most commonly consumed foods among cases were wakame seaweed salad (80%), soy sauce (63%), and salmon sashimi (57%). Norovirus genogroup II was detected in stool samples of two cases and two staff members. Genogroup II was also isolated from a sample of wakame seaweed salad, but no other foods samples. On 13th August, Spanish authorities reported isolating norovirus genogroups I and II in a seaweed salad product from China distributed via Germany. This product was supplied to the affected UK restaurants. The case-control study generated further evidence that the consumption of wakame seaweed salad (aOR: 50 CI: 1.2-203.0) was associated with becoming a case.

Conclusions: The epidemiological, microbiological, and food tracing investigations suggest the most likely cause of this outbreak was norovirus [genogroup II] through a contaminated seaweed product. The product was voluntarily withdrawn on 19th August 2019.

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Abstracts 2020

Abstract 3832

Comparison of vaccine opinion of parents in 5 key European countries: learnings from Vaccinoscopie Europe


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Abstract third-party references: The survey was conducted by IDM families and funded by GSK.

Background: Suboptimal vaccination coverage rates have led to vaccine-preventable disease resurgence and epidemics, such as measles in Europe these last years. Growing vaccine hesitancy is one of the key explanations of this situation. We aimed to compare vaccine opinion of parents, key target for vaccination, in 5 big European countries.

Materials/methods: Vaccinoscopie Europe is a web-based survey conducted in 2019 on a representative sample of 1,500 parents of 0-2 years old infants based in France, Germany, Italy, Spain and United-Kingdom (300 per country).

Results: Vaccination positive opinion of parents varied according to countries (from 73% for France to 94% for Spain). UK and Germany had 3% of opponents to all vaccinations versus <1% in the other countries. In all countries, more than 90% of parents were favorable to mandatory vaccination for at least certain vaccines. German and British parents were the most refractory.

In terms of vaccination knowledge, French parents felt significantly less well informed (77% of well informed) than parents from the other countries (90-94%) with less web consultations about vaccination (respectively 58% versus 70-81%). Trust level in Health authorities was highest in Spain and lowest in France (on a 10-point scale, respectively 88% and 68% with a score of 7 to 10).

Although the first source of information to decide to vaccinate their child was a health care vaccinator, the latter differed in each country based on health care system. The second source of information was Internet, with Health authorities’ websites the most consulted by all countries, followed by friends and families. Influence of these last two sources varied according to countries (respectively from 14 to 40% and from 9% to 30%).

Conclusions: Parents’ vaccination favorable opinion seemed to be linked with a better perceived vaccination knowledge. If the health care vaccinator was the first source of information, Internet was a valuable resource and friends and families might be influential. Local characteristics should be taken into account to increase confidence into vaccination. Evaluation should be harmonized at an European level, allowing to share public health best practices strategies.

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Comparative outcomes of cefazolin versus anti-staphylococcal penicillins for treatment of methicillin-susceptible Staphylococcus aureus endocarditis: a prospective multi-centre cohort study

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Background: Cefazolin has been shown to be as effective as anti-staphylococcal penicillins (ASP) in methicillin-susceptible Staphylococcus aureus (MSSA) bacteremia. Both American and European guidelines recommend cefazolin as an alternative to ASP in MSSA endocarditis despite the lack of comparative study in this context.

The objective of this study was to compare the efficacy of cefazolin versus ASP in MSSA endocarditis.

Materials/methods: In this prospective multicenter cohort study from two reference centers, all consecutive patients with MSSA endocarditis confirmed by endocarditis team and treated either by cefazolin or ASP between July 2013 and December 2018 were included. Patients were excluded if they received more than 7 days of both treatments. The primary outcome was 90-day mortality and secondary outcome were relapse, emboli under treatment, duration of bacteremia and premature antimicrobial discontinuation due to adverse events (PAD).

Results: Of 225 patients included in the study, 162 (72.0%) were in the ASP group and 63 (28.0%) in the cefazolin group. Sixty-five of 225 patients (28.9%) had a prosthetic valve endocarditis. The median duration of treatment was similar in the two groups (32 days). The 90-day mortality rate was 28.4% (64/225 patients).

In multivariate analysis, the 90-day mortality was similar between cefazolin and oxacillin group (27.0% versus 29.0%; p=0.91), while age (p<0.01), Charlson index (p=0.01), brain emboli (p<0.01) and intensive care unit admission (p=0.01) were factors significantly associated with higher mortality and surgery (p=0.04) with lower mortality.

No patients relapsed in the cefazolin group while 5/162 patients (3.1%) relapsed in the ASP group (p=0.32) and 5 patients (7.9%) had emboli under treatment in the cefazolin group versus 19 (11.7%) in the ASP group (p=0.41). We did not find a difference in bacteremia duration between the two groups (median of 3 days for both groups, p= 0.76). Rates of PAD for 1000 patients-days of treatment were 3.3 in the cefazolin group versus 2.8 in the ASP group.

Conclusions: There was no significant difference of efficacy or tolerance between cefazolin and ASP for the treatment of MSSA endocarditis. Physicians might consider cefazolin as an adequate and well-tolerated treatment for MSSA endocarditis.

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**Abstract 3835**

**Borrelia burgdorferi sensu lato in Ixodes ricinus in Slovenia**

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**Background:** Cultivation and isolation of Borrelia burgdorferi sensu lato, the causative agent of Lyme borreliosis, from any biological material are very challenging and labor-intensive but it remains the only approach for detailed genotypic characterization of strains, which is of great importance for epidemiological, clinical, and evolutionary studies.

The present study aimed to isolate and genotype B. burgdorferi sensu lato from ticks collected in different geographic areas of Slovenia in years 2017-2019.

**Materials/methods:** A total of 1007 (247, 172 and 588 in years 2017, 2018 and 2019, respectively) Ixodes ricinus ticks were collected by flag dragging. After morphological identification, ticks were washed with ethanol and sterile water, homogenized and placed in 1.5 ml MKP-F medium. Samples were incubated at 33 °C for up to 12 weeks. MluI-LRFP was used for Borrelia species determination from culture positive samples.

**Results:** B. burgdorferi s.l. was isolated from 70/1007 (7.1%) ticks (35, 5 and 30 in years 2017, 2018 and 2019, respectively). MluI-LRFP revealed the presence of 26 B. afzelii (subtypes Mla1 and Mla2), 24 B. garinii (subtypes Mlg2, Mlg4, Mlg6, Mlg8 and one new LRFP profile), 8 B. valaisiana (subtypes Mlv1 and Mlv2), and 3 B. burgdorferi sensu stricto (subtypes Mlb2 and Mlb8).

**Conclusions:** Cultivation and borrelia isolation from ticks is a technically demanding and low-yield method. Genetic diversity of B. burgdorferi s.l. strains from I. ricinus is high. All collected isolates will be available for further analysis and comparison with human isolates.

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**Abstract 3838**

**Increase of daptomycin-resistant *Staphylococcus aureus* with a possible link to antiseptic wound treatment in three medical centres in Cologne, Germany**

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¹Cologne Merheim Medical Centre, University Hospital of Witten/Herdecke, Institute of Hygiene, Cologne, Germany, ²Cologne Merheim Medical Centre, University Hospital of Witten/Herdecke, Department of Plastic Surgery, Hand Surgery, Burn Center, Cologne, Germany, ³MVZ synlab Leverkusen GmbH, Köln-Merheim, Department of Clinical Microbiology, Cologne, Germany, ⁴Robert Koch Institute, National Reference Centre for Staphylococci and Enterococci, Wernigerode, Germany

**Background:** Emergence of daptomycin resistance in *Staphylococcus aureus* (SA) during treatment is a growing concern. After an increase of daptomycin resistance especially in methicillin-susceptible SA a molecular surveillance was established at three medical centres in Cologne.

**Materials/methods:** Identification and antimicrobial testing was performed with VITEK2. Daptomycin resistance was confirmed by broth microdilution (BMD). All available SA (daptomycin-resistant or daptomycin-susceptible SA [DR-SA, DS-SA]) of the affected patients were included. Polyhexanide MICs were determined by BMD. Whole genome sequencing (WGS, Illumina MiSeq), cgMLST analysis by SeqSphere+ (Ridom) and detection of resistance mechanisms were carried out. Epidemiological and clinical data were analysed.

**Results:** From May 2016 to July 2018 DR-SA were detected in 42 patients (31 MSSA, 11 MRSA). First DR-SA isolates had daptomycin MICs of 2 to 4 mg/L. Acquisition of resistance was almost exclusively healthcare-associated (n=41). Half of the 42 patients were identified with prior and 13 patients with subsequent DS-SA colonization (same location and similar antimicrobial susceptibility profile). Only few patients were treated with daptomycin (n=2) or vancomycin (n=4) before detection. First detection, mostly from wounds (n=37), was associated with a stay in a surgical department (n=39). Wound treatment was evaluated. At least 20 patients were treated with polyhexanide which is part of the local wound management standards. 71 SA isolates were available (42 first, 10 previous and 19 consecutive isolates; 54 DR-SA, 17 DS-SA). WGS displayed a diverse genetic background of DR-SA (only three possible transmission events) and showed that daptomycin resistance evolved in a patient and was reversible. Daptomycin resistance was associated with various polymorphisms in the mprF gene except in five isolates. Elevated polyhexanide MICs in DR-SA compared to DS-SA were demonstrated.

**Conclusions:** In this study, daptomycin resistance in SA was not linked to prior antibiotic therapy. Our hypothesis is that daptomycin resistance was induced by wound treatment with polyhexanide and genetically linked to adaptive changes of a membrane protein (MprF) of the cell wall, previously described in-vitro by Renzoni et al. (2017). Further research like in-vitro selection of polyhexanide and daptomycin resistance in clinical strains is under way.

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Autochthonous human and canine Strongyloides stercoralis infection in Europe: a systematic review

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Background: Autochthonous human and canine strongyloidiasis is reported in Europe but is unclear whether the transmission of infection still occurs.

Materials/methods: We performed a systematic review of literature on autochthonous human and canine strongyloidiasis in Europe to investigate the dynamic of autochthonous transmission.

Results: Overall 109 papers published after 1987 were included and one previously unpublished Italian case was added. Eighty case reports were retrieved from 16 European countries and 42 of them (52.5%) had severe strongyloidiasis. Most of case reports described patients infected in Spain (n=21), Italy (n=17) and France (n=11). Median age was 58 and the most represented age group was 61-70 years (n=21, 26.5%). Eleven cases were diagnosed in the decade 2009-2018, including 2 cases in subjects aged <30 years. Concerning human epidemiological studies, 6 were carried out in Italy, 2 in Turkey and 1 each in Austria, France, Poland, Spain and Romania, showing prevalence ranging from 28% to 0.56%. Higher prevalence was found among elderly, farm workers and kids with characteristic symptoms of parasite infection. Data from epidemiological studies and case reports indicate that most of human autochthonous European infections have been acquired in the Valencia province, Northern Italy and several regions of France. Agriculture and mine work were the most commonly reported risk factors for infection but walking barefoot, solid organ transplantation, and homosexual male behavior were also reported. In no case there was mention of possible zoonotic transmission, but one study investigated and revealed the presence of the parasite in humans, dogs and soil in a segregated settlement in Eastern Slovakia. Canine strongyloidiasis was reported mainly in Italy (68 cases), few cases occurred also in Iceland, Finland, England, Germany, France, Switzerland, Russia, Slovakia, Romania and Greece.

Conclusions: Autochthonous strongyloidiasis is still sporadically reported in Europe. Cases in humans are mainly diagnosed in elderly subjects probably infected in the past, while recent infections are extremely rare. Health care professionals should be aware of this issue to timely identify infected subjects and avoid adverse outcome, especially in immunosuppressed patients. Further investigations are needed to clarify the zoonotic transmission of this nematode in Europe.

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Abstract 3840

**Reporting antimicrobial susceptibilities and resistance phenotypes in *Staphylococcus* spp.: a nation-wide proficiency study**

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**Abstract third-party references**: on behalf of the Spanish Group of Nosocomial Infections (GEIH) and the Study Group of Mechanisms of Action and Resistance to antimicrobials (GEMARA) from the Spanish Society of Clinical Microbiology and Infectious Diseases (SEIMC), and the Spanish Network for Research in Infectious Diseases (REIPI)

**Background**: to evaluate the proficiency of Spanish Microbiology laboratories with respect to the antimicrobial susceptibility testing (AST) of *Staphylococcus* spp.

**Materials/methods**: Eight *Staphylococcus* spp. with different resistance mechanisms were selected: CC-01 (*S. aureus/meca*), CC-02 (*S. aureus/mecC*), CC-03 (*S. aureus/BORSA*), CC-04 (*S. aureus/MLSBI*), CC-05 (*S. epidermidis/23S rRNA mutation*), CC-06 (*S. aureus/blaZ*), CC-07 (*S. aureus/cfr*), and CC-08 (*S. capitis/daptomycin-resistant*). These isolates were sent to 48 Spanish centers which were asked to report: (i) the AST system used; (ii) MICs; (iii) breakpoints used (CLSI versus EUCAST); (iv) clinical category. Minor, major and very major errors (mE, ME and VME, respectively) were determined.

**Results**: the greatest discrepancies were: (i) by automated AST method: 50.0% (Wider) and 88.2% (Vitek); (ii) by breakpoints: 3.4% (EUCAST) and 2.1% (CLSI); (iii) by antimicrobial agent: amikacin (28.4% EUCAST), fosfomycin (25.0% EUCAST) and tobramycin (10.4% EUCAST). The highest categorical error rates were: (i) by AST method: broth microdilution (EUCAST: 11.1% ME), gradient strips (EUCAST: 10.7% VME; CLSI: 12.7% VME) (ii) by breakpoints: mE (80.1% CLSI, 58.4% EUCAST), ME (3.5% CLSI, 12.4% EUCAST) and VME (16.4% CLSI, 29.2% EUCAST); (iii) by antimicrobial agent: mE (EUCAST: 25.4% amikacin; CLSI: 7.3% erythromycin, ME (EUCAST: 28.6% fosfomycin, 16.2% tobramycin, 9.5% gentamicin and 5.6% amikacin, CLSI: 14.3% quinupristin-dalfopristin) and VME (EUCAST: 21.4% linezolid, 15.4% tetracycline, 12.0% daptomycin, 11.1% fusidic acid and 8.1%. CLSI: 16.7% quinupristin-dalfopristin, 7.3% erythromycin, 4.4% linezolid, 4.1% levofloxacin and gentamicin, and 3.4% oxacillin).

**Conclusions**: (1) Clinical Microbiology laboratories must improve their ability to determine antimicrobial susceptibilities of *Staphylococcus* spp. isolates. (2) The highest discrepancies were associated to the automated AST system (Wider I and Vitek), the EUCAST breakpoints, and the antimicrobial (mE for aminoglycosides, ME for fosfomycin, aminoglycosides and oxacillin, and VME for linezolid, tetracycline, daptomycin and oxacillin).

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Abstract 3844

Understanding antibiotic prescribing behaviours among hospital physicians and exploring strategies currently used by infectious diseases physicians to influence change: a qualitative interview study

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Abstract third-party references: Ottawa Hospital Research Institute

Background: Inappropriate use of antibiotics contributes to antibiotic resistance and adverse patient outcomes. Infectious diseases (ID) physicians can act as change agents who can improve appropriate prescribing behaviours among their non-ID colleagues.

Materials/methods: A convenience sample of hospital ID and non-ID physicians participated in semi-structured interviews (Ottawa, Canada). We assessed 1) non-ID physicians’ experiences to identify determinants of antibiotic prescribing, and 2) strategies ID physicians currently use to influence others’ prescribing behaviours. Responses were coded using the Theoretical Domains Framework (TDF), a framework including modifiable factors that explain behaviour change and a catalogue of behaviour change techniques (BCTs), respectively. Both sets of responses were mapped to identify areas where BCTs could be used to more strongly effect prescribing changes.

Results: Among 16 non-ID physicians interviewed, antibiotic prescribing was influenced by 5 themes 1) knowledge and availability of resources (“what to do” problem), 2) motivation and beliefs about consequences (“worried about this patient”), 3) automatic actions and skills (“this is how I do things”), 4) social influence (“someone else prescribed it”) and 5) deferring antibiotic-related decisions to ID (“this is not my role”).

On the other hand, current strategies to improve prescribing among peers that are used by 12 ID physicians interviewed include giving clear and precise instructions [e.g. providing recommendations for treatment, discuss in person controversial cases], explaining the rationale for the recommendation, providing evidence from a credible source [e.g. guidelines], promoting autonomy of their peers [e.g. giving license for experimenting with non-ID way first, then try with ID approach] and focusing on previous positive experiences.

We identified that prescribing behaviours among non-ID physicians may be more strongly influenced by better targeting fear of undertreatment, use of non-evidence based practices, and practices influenced by the dynamics and culture of the work environment.

Conclusions: ID physicians do use strategies to improve their peers’ prescribing; however, these may not be based on awareness of barriers and facilitators perceived by their non-ID colleagues. Training ID physicians to recognize barriers non-ID physicians face, and identify strategies to surmount these barriers, could help overcome this gap and ultimately improve antibiotic prescribing among non-ID physicians.

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A five-species biofilm model for confirming the potential of a nisin-biogel aiming at canine periodontal disease control

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**Background:** Periodontal disease (PD), one of the most common diseases in dogs, is caused by the development of a polymicrobial biofilm at the tooth surface. Previous studies have shown that, when incorporated within a guar-gum biogel (nisin-biogel), the antimicrobial peptide nisin can inhibit and eradicate mono-species biofilms formed by canine oral enterococci, rendering nisin a potential agent for PD control. As the clear majority of the dental plaque biofilms in vivo are polymicrobial, we aimed to confirm the nisin-biogel antimicrobial ability against polymicrobial biofilms formed by five bacterial species frequently present in the canine dental plaque.

**Materials/methods:** Five reference strains commonly present in canine dental biofilms were used: *Neisseria zoodegmatis*, *Enterococcus faecalis*, *Corynebacterium canis*, *Porphyromonas gingivalis* and *Peptoniphilus canis*. First, strains coaggregation ability was evaluated as described by Datta et al. (2017). Then, a five-species biofilm model was established in 96-well microplates by simultaneously inoculating the strains in Brucella broth, followed by incubation in microaerophilia for 48 hours at 37ºC. After incubation, the presence of all strains in the multi-species biofilm was confirmed by Fluorescent In Situ Hybridization (FISH) using specific probes. Afterwards, the five-species biofilm model developed was used to determine the Minimum Biofilm Inhibitory (MBIC) and Eradication Concentrations (MBEC) of the nisin-biogel, as previously described by Cunha et al. (2018).

**Results:** All bacterial pairs exhibited a coaggregation percentage higher than 30% at 24 hours, showing their potential to form multi-species biofilms. The microplate assay developed allowed establishing five-species biofilms, as the presence of all PD bacterial strains on the biofilm model was confirmed by FISH. The nisin-biogel tested presented inhibitory activity against the polymicrobial biofilm, with a MBIC value of 25 µg/mL and a MBEC value > 100 µg/mL.

**Conclusions:** It was possible to develop an *in vitro* model of a periodontal polymicrobial biofilm, composed by five strains frequently present in dog’s dental plaque. This model, which better mimics the *in vivo* conditions present in the oral cavity of dogs, allowed to observe that the nisin-biogel developed by our research team can inhibit the formation of multi-species biofilms, reinforcing its potential for controlling a major disease of these animals.

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Abstract 3846

**Dissecting the single-cell heterogeneity and subpopulation dynamics of quiescence in *Mycobacterium tuberculosis***

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**Background:** Quiescence is a complex process, in which cells experience metabolic reprogramming to achieve the minimal metabolic function required for survival. *Mycobacterium tuberculosis* is known to persist in the permissive host-niche for long periods of time, under a state of quiescence. Although, several factors have been implicated in persistence, but understanding the dynamics of this phenomenon is still insufficient, and limits considerably the control of tuberculosis. Here, we target to interpret the physiology of quiescent *M. tuberculosis*.

**Materials/methods:** We identified candidate genes that are upregulated under different stress conditions, including hypoxia. We developed the dual fluorescent reporter in the background of an existing ribosomal reporter strain, which we previously used to monitor the metabolic activity in *M. tuberculosis*. Further, to determine the behavior of the dual reporter strain in the host niche, we infected different cells lines that are associated to tuberculosis. The infection experiment was monitored from early to late stage of infection. To investigate the different molecular signatures between two subpopulations, i.e., quiescent versus active bacilli, we sorted bacteria and performed the comparative transcriptomic profiling of the two subpopulations.

**Results:** By single-cell snapshot microscopy, we found that the quiescence marker was upregulated in stationary phase, starvation, fatty-acids enriched medium and combined host-mimetic conditions. We infected cell lines that constitute the typical niche of *M. tuberculosis* and found substantial intracellular variation, and upregulation of the quiescence marker in macrophages and alveolar epithelial cells during late stage of infection, as opposed to dendritic cells, lung fibroblasts and osteoblasts. To understand the quiescent cell’s physiology, we carried out comparative transcriptomic profiling of subpopulations, sorted according to the expression of the quiescence marker. We optimized sorting and RNA extraction, and carried out low-input RNA-seq of metabolically active versus quiescent subpopulations. Preliminary differential analysis suggested that the two subpopulations differ in their transcriptomic profiles.

**Conclusions:** Preliminary functional analysis of the RNA-seq transcriptional profiling reveals up-regulation of pathways important for adaptation in the quiescent subpopulation. We envisage to identify molecular signatures of quiescence, which may prove useful as biomarkers for subclinical tuberculosis.

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Abstract 3850

Leishmanial Localised Lymphadenopathy (LLL) by Leishmania infantum: a benign disease different from visceral leishmaniasis

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Background: Leishmanial localized lymphadenopathy (LLL) is an atypical form of clinical presentation of leishmaniasis as an isolated adenopathy, and only a few cases by L. infantum have been confirmed. We update our experience in the management and outcome, and propose a modified definition of LLL case

Materials/methods: We retrospectively collected clinical variables of all consecutive LLL and VL with adenopathies in Hospital Universitario de Fuenlabrada since 1st January 2004 to 1st November 2019. LLL cases and VL cases with adenopathies were compared.

Results: 30 cases of LLL were collected. 27% had cutaneous lesion associated. 57% were male, mean age 45.6, 20% not born in Spain. All of them were immunocompetent. None had systemic symptoms. Only one patient with isolated adenopathy had splenomegaly and altered hematological results and acute phase reactants elevated. Diagnosis in LLL cases was made by fine needle aspiration showing granulomatous lymphadenitis with Leishmania parasites in 87%. 3 patients were cured without treatment and they had not relapsed [mean follow up 468 weeks]. The rest received liposomal amphotericin B (L-amphB) at different doses: 10 were treated with 10mg/kg [mean follow up after treatment 322 weeks], 7 with 15 mg/kg [472 weeks], 2 with 18 mg/kg [363 weeks] and 8 with 21 mg/kg [385 weeks]. The patient with splenomegaly showed progression [new adenopathies] at the end of treatment and needed retreatment. No patient has relapsed nor presented visceral disease during follow up. By the other hand, 121 patients with VL were revised, only 3 patients with typical VL had adenopathies. 2 were HIV co-infected. All of them had fever, splenomegaly, pancytopenia and elevated ferritin and C-reactive protein.

Conclusions: Due to its clearly differentiated clinical characteristics and evolution, LLL is a different entity from VL. We propose a definition of LLL case by L. infantum if adenopathy/s is the only form of presentation, without systemic or analytical repercussion, with normal acute phase reactants, in an immunocompetent patient. In our experience, LLL by L. infantum that fit this definition is a benign disease that could be safely treated with 10mg/kg L-amphB, and even in selected cases can resolve spontaneously.

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Inter- and intra-clonal diversity in *Staphylococcus epidermidis* prosthetic joint infection

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Abstract third-party references: Damp Stiftung

**Background:** *S. epidermidis* colonizes the skin and nares of virtually all human beings. However, it is also the most important pathogen in foreign material associated infections. In the present study we collected clinical samples and data of 135 patients suffering from prosthetic joint infection, in order to investigate pathogenicity factors facilitating the establishment of infection, adaptation processes during infection and bacterial diversification in the infection.

**Materials/methods:** 135 patients suffering from a prosthetic joint infection (PJI) were prospectively included into the study. Twenty-eight were caused by *S. epidermidis* and thus selected for in-depth analysis. Multiple isolates from the patients’ nares as well as from the infected joint were analysed by PFGE and NGS. Phylogenetic trees were constructed and k-mer-based genome wide association study (GWAS) were conducted. Phenotypic tests were performed: Hemolysis as a phenotypic marker of agr-expression, biofilm formation, cell-cell aggregation, proteolysis, as well as growth phenotypes and antibiotic susceptibility were investigated. To analyze the basis for the observed differences, expression analysis of important genes like agr was conducted.

**Results:** We found evidence of marked inter- and intra-clonal phenotypic diversity. In 6/28 cases a nasal clone identical to the infectious isolate was identified. Interestingly, we observed marked intra-clonal phenotypic heterogeneity within the infection and in significant phenotypic divergence from the nasal clone. Strikingly, the scc-mec-element, conferring resistance to beta-lactams, was lost in a sub-population in 3/28 infections. This result provide important implications for resistance testing in PJI.

The GWAS provided a panel of sequences associated with infectious and commensal lifestyle.

**Conclusions:** There is pronounced inter- and intra-clonal diversity in PJI caused by *S. epidermidis*. Phenotypic and genotypic differences between commensal and infecting clones will provide new insights into the establishment and maintenance of *S. epidermidis* PJI. In a clinical context, diversity in antimicrobial resistance pattern within infections is of paramount importance for the microbiological diagnosis of PJI.

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Extreme short course therapy for chronic hepatitis C infection

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**Background:** Hepatitis C chronic infection (HCV) therapy reached in recent years surprising sustained virological response (SVR) rate with almost no side effects. Glecaprevir/Pibrentasvir (G/P) is recommended in the EASL guidelines for the treatment of Hepatitis C Chronic Infection (CHC) and has a good pharmacokinetic and pharmacodynamics (PK/PD) profile. It is approved for CHC treatment in patients on hemodialysis with a 12 weeks course. We describe here the first case in our knowledge of extreme short term course therapy to treat a well known and challenging chronic condition in difficult-to-treat patients.

**Materials/methods:** Case report.

**Case report description:** A 79-year-old man on polypharmacy with a 25 years history of CHC, diabetes, IgA nephropathy and chronic kidney disease advanced stage requiring three time/week hemodialysis consulted our ambulatory to treat CHC. He had no history of crioglobulinemia, fibrosis stage was assessed using Fibroscan as 8.2 kpa[F2], abdominal ultrasonography normal, he had no history of atopia or intolerance [alimentar nor pharmacological]. HBsAg and HIV status tested were negative. Creatinine before treatment was 1.2 mg/dl. HCV RNA 567800 UI/mL. He started treatment with (G/P) with the recommendation of taking the medication after dialysis. No apparent adverse events were observed. After seven days of treatment he started suffering uncontrollable itching; was prescribed cetirizine with previous chronic steroid therapy. Due to the lack of clinical improvement, the patient interrupted the treatment at day twelve. Itching lasted for 15 days longer. No other adverse events nor complications occurred. He underwent two blood sample testing at the end of twelve days course treatment and at week 12 (SVR12). HCV RNA tested both negative.

**Conclusions:** in this case, twelve days course therapy with G/P resulted in SVR12 in the treatment of CHC Genotype 4 in an elderly patient on three/time week dialysis for chronic kidney disease. Despite prolonged itching no other side effect were recorded. Side-effects disappeared 15 days after stopping antiviral therapy. Clinical and PK/PD studies are needed to further assess the safety and effectiveness of G/P in the management of CHC in patient with renal diseases with the chance of shorter treatment in selected cases.

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Abstract 3854

**Rapid detection of colistin resistance using a newly developed protocol for MALDI-TOF MS**

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**Background:** In the last several years, colistin resistance has increased and its emergence has caused global concern. MALDI-TOF MS can be used as a rapid complementary method to conventional antimicrobial susceptibility testing methods. It allows the detection of the drug target, i.e. the lipid A (LpA) moiety of the lipopolysaccharide, which generates resistance when modified by addition of 4-amino-4-deoxy-L-arabinose and/or phosphoethanolamine.

**Materials/methods:** A rapid MALDI-TOF sample preparation was developed using weak hydrolysis in acetic acid solution. Modified and unmodified LpA were detected using VITEK®MS Plus mass spectrometer in negative ionization mode, norharmane matrix and a m/z 1000-4000 mass window. A panel of 200 collection isolates from 20 different bacterial species (Pseudomonas aeruginosa, Acinetobacter baumannii, and Enterobacteriaceae) were tested. This panel of isolates included susceptible and resistant bacteria harbouring either chromosomal- or plasmid-mediated resistance genes. The MALDI-TOF assay was compared to the colistin susceptibility status given by broth microdilution (BMD), growth on CHROMID® Colistin R agar, PCR testing of mcr genes and whole genome sequencing (WGS).

**Results:** Detection of mcr genes by PCR was a good predictor of colistin resistance, but the significance of mutations observed by WGS in pmrA, pmrB, phoP, and phoQ genes was frequently uncertain. Some mutations appeared to be associated to the resistance whereas others were clearly not.

Prediction of colistin resistance using the MALDI-TOF LpA assay was in agreement with the BMD method and CHROMID® Colistin R agar for a large majority of isolates and species, e.g. LpA versus BMD agreement was 100% (36/36), 98% (41/42), and 100% (6/6) in Escherichia coli, Klebsiella pneumoniae, and Klebsiella aerogenes, respectively. However, for a few species, inconsistent results were observed for some strains, e.g. LpA versus BMD agreement was 83% (33/40) and 87% (27/31) in A. baumannii, and P. aeruginosa, respectively. This observation may be due to colistin hetero-resistance, a still poorly understood phenomenon, making it challenging to diagnose in clinical settings.

**Conclusions:** The usefulness of a short sample preparation for LpA extraction, associated with a VITEK®MS Plus reading, was demonstrated as a rapid alternative to conventional methods for colistin resistance detection on a large panel of bacterial species and strains.

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Abstract 3855

**Beta-lactam exposures to methicillin-resistant Staphylococcus aureus involve cell membrane and surface adaptation for daptomycin synergy**

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**Background:** The synergy of β-lactams with daptomycin (DAP) against DAP resistant (DAP-R) MRSA has been well documented in the literature, however the precise mechanism behind this phenotype has yet to be elucidated. DAP’s activity is dependent on cell wall and membrane homeostasis. Further, development of DAP-R is often caused by single nucleotide polymorphisms (SNP) in genes encoding phospholipid biosynthesis proteins. This study focused on potential cell membrane (CM) mechanisms by which β-lactam antibiotics promote DAP synergy against isogenic DAP-susceptible (DAP-S) / DAP-R MRSA strain pairs.

**Materials/methods:** Nine well characterized clinically derived DAP-S/DAP-R strain pairs were utilized in this study. CM characteristics were analyzed following growth to exponential phase in the presence of sub lethal concentrations of selected β-lactams cloxacillin (LOX), cefoxitin (FOX), meropenem (MEM), or nafcillin (NAF). Cell surface charge and CM fluidity were measured with Cytochrome C binding assay and fluorescence polarization respectively. Cardiolipin (CL) specific dye N-Acryl-amide Orange (NAO) was used to quantify CL content by spectrofluorimetry and CL localization by confocal microscopy.

**Results:** Exposure of DAP-R MRSA strains to sub lethal concentrations of LOX, FOX, MEM, and NAF lead to significant alterations in CM and surface characteristics including decreased CM fluidity and decreased net positive surface charge. NAO fluorescence indicated increased amount of CL and delocalization of CL in the membrane as shown in Figure 1. Similar trends were observed in DAP-S strains exposed to the same β-lactams, although the changes were less pronounced compared to respective isogenic DAP-R strains.

![Figure 1](image_url)

**Conclusions:** These results suggest that perturbations of the CM and cell surface may be critical for induction of β-lactam synergy with DAP in MRSA strains. In particular, the increase in CL content and distribution, reduction in positive surface charge, and alteration of membrane fluidity following β-lactam exposure could improve DAP activity, especially in DAP-R strains. Further studies correlating these data to strain specific synergy and associating genetic alterations responsible for CM and surface changes are underway.

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Analysis of the microbiological data from the delafloxacin (DLX) phase III community-acquired bacterial pneumonia (CABP) trial using European analysis sets

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Background: DLX is a novel fluoroquinolone (FQ) antibiotic with gram-positive/MRSA, gram-negative and atypical activity. It offers IV and oral treatment and no QT restrictions. In a Phase 3 study in CABP patients, DLX was non-inferior to moxifloxacin (MOX) in the primary EMA endpoint, clinical outcome at T0C (91.0 vs 89.2; 95% CI: -2.6, 6.2) in the modified Intent-to-Treat (mod-ITT = modified to exclude PORT II patients) population. A detailed microbiological analysis was conducted.

Materials/methods: CABP pathogens were identified by culture/non-culture methods. Pathogens identified by non-culture methods included Streptococcus pneumoniae (culture, urinary antigen [UA], nasopharyngeal [NP] swab lytA PCR), Legionella pneumophila (culture, UA, serology), Mycoplasma pneumoniae (culture, serology), and Chlamydia pneumoniae (serology). All other pathogens were identified using culture only. For S. pneumoniae cultured from NP, a concomitant lytA PCR value of ≥ 1000 gene copies/mL was required. All isolates underwent susceptibility testing, and a subset of isolates underwent molecular or phenotypic characterization including whole genome sequencing for FQ resistance mechanisms, PCR for PVL/mecA genes (S. aureus), β-lactamases (Haemophilus/Moraxella spp), and serotyping (S. pneumoniae).

Results:

<table>
<thead>
<tr>
<th>Pathogens</th>
<th>Baseline Frequency [All diagnostic methods] N=228</th>
<th>Micro Success in DLX Pts mod Micro Evaluable @ T0C n/N (%)</th>
<th>DLX MIC₉₀ mg/L mod MITT</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. pneumoniae</td>
<td>105 (46.1)</td>
<td>88/95 (92.6)</td>
<td>0.015</td>
</tr>
<tr>
<td>M. pneumoniae</td>
<td>32 (14.0)</td>
<td>27/28 (96.4)</td>
<td>0.5</td>
</tr>
<tr>
<td>H. parainfluenzae</td>
<td>28 (12.3)</td>
<td>24/28 (85.7)</td>
<td>0.5</td>
</tr>
<tr>
<td>L. pneumophila</td>
<td>26 (11.4)</td>
<td>25/26 (96.2)</td>
<td>-</td>
</tr>
<tr>
<td>S. aureus</td>
<td>26 (11.4)</td>
<td>24/26 (92.3)</td>
<td>0.004</td>
</tr>
<tr>
<td>H. influenzae</td>
<td>24 (10.5)</td>
<td>20/21 (95.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>C. pneumoniae</td>
<td>21 (9.2)</td>
<td>20/20 (100.0)</td>
<td>-</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>16 (7.0)</td>
<td>13/16 (81.3)</td>
<td>0.25</td>
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<tr>
<td>P. aeruginosa</td>
<td>13 (5.7)</td>
<td>11/12 (91.7)</td>
<td>4</td>
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</table>


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Serum C-reactive protein: a useful tool in the diagnosis of tuberculosis?
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Background: Tuberculosis (TB) remains a significant public health concern with an estimated 10 million cases and 1.5 million associated deaths in 2018.[1] Diagnosis is often delayed due to repeated presentations to non-specialist medical services with non-specific symptoms.[2] [3] Evidence for the use of C-reactive protein (CRP) in the diagnosis of tuberculosis is conflicting. A recent meta-analysis of patients undergoing screening for TB found a pooled sensitivity for CRP of 93% and a pooled specificity of 60%.[4] 72% of the patients in the analysis were HIV positive. In populations with lower HIV prevalence, the utility of CRP is less clear. This study examined the utility of CRP in the diagnosis of microbiologically confirmed TB in a low HIV-prevalence setting.

Materials/methods:

All patients with microbiologically confirmed TB between October 2019 and October 2017 were identified using the laboratory database. Clinical and demographic data were gathered from patient records, anonymized and transcribed into EpiData, and analysed using Stata.

Results: 150 cases of TB were identified over the study period; 117 patients (78%) had a CRP recorded at diagnosis. 65% were male, 6% were HIV positive. The median age was 36 years (range 0-79). The median CRP was 42mg/L (IQR 10-97) and was highest amongst patients with disseminated TB (87mg/L, IQR 28-123) followed by those with pulmonary TB (pTB) (50mg/L, IQR 9-118). Patients with extra-pulmonary TB (EPTB) had lower median CRP (27mg/L, IQR 3-71). Patients with smear-positive pTB had a significantly higher median CRP value than those with smear-negative pTB (57mg/L vs 23mg/L p=0.001).

36% of cases of smear-negative and 9.5% of smear-positive pTB cases had normal-range CRP (≤5mg/L). The sensitivity of an abnormal CRP for pTB was 80% (90.5% for smear-positive pTB, 64% for smear-negative pTB). For EPTB, the sensitivity of an abnormal CRP was 80.5% with 19.5% of cases having a CRP within the normal limits.

Conclusions: While elevated CRP levels was a sensitive marker of smear positive pulmonary tuberculosis, many patients with smear negative pulmonary and extra-pulmonary tuberculosis had normal CRP levels. This limits its utility as a test to exclude a diagnosis of tuberculosis.

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Assessment of the performances of the second generation of the ID NOW influenza A&B and comparison with the GeneXpert

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Background: Rapid and accurate diagnostic of flu is challenging for the management of patients, but conventional PCR methods are time-consuming and require specific competencies. Molecular methods based on isothermal amplification were developed first for point of care use. However, preliminary evaluations of the ID NOW® influenza A&B performances were heterogeneous, leading the company to improve their reagent. Therefore, we aim to:

i) assess the performances of the second generation of the ID NOW®,

ii) compare the ID NOW® influenza A&B 2 to the GeneXpert® Xpress Flu/RSV use when performed within a central laboratory.

Materials/methods: i) analytical performances of ID NOW® were assessed in comparison to a reference multiplex PCR (Allplex, Seegene®, Korea): 112 clinical samples collected in 2017, 2018 and 2019 were included of which 63 and 26 positives to influenza A and B respectively and 23 negatives for influenza viruses. All discrepant results were repeated by both methods.

ii) Invalid rate per operator and time-to-result were calculated for the GeneXpert® and the ID NOW® during 2017-2018 and 2018-2019 flu outbreaks, respectively.

Results: i) After discrepant resolution, ID NOW influenza reaches an overall sensitivity and specificity of 96.6% and 96.1% respectively. All but one false-negative results display a Ct > 37 using the reference method. A single false-positive was noticed for influenza B.

ii) Overall, the rate of invalid results was 2.02% and 1.93% for ID NOW® and GeneXpert® respectively (p = 0.86). For both instruments, a single operator was involved in about half of all invalid results. Excluding this operator, the invalid rate falls to 1.09% and 1.11% respectively (p=0.95). Time-to-result from arrival to the laboratory was significantly shorter in the ID NOW® versus the GeneXpert® group [33 vs 97 min, p < 0.01].

Conclusions: The second generation of the ID NOW® influenza A&B 2® displays high performances, comparable to conventional PCR method. In order to prevent invalid results, we highlight the need for adequate training of operators. Also, when implemented in a central laboratory, the location of the instrument could have a strong impact on time-to-results.

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Abstract 3860

**Characteristics of bloodstream infections in patients with liver cirrhosis in a general hospital**

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**Background:** Data on bloodstream infections (BSIs) in patients with liver cirrhosis are scarce. The aim of our study was to analyse clinical characteristics, and prognosis of BSIs in liver cirrhosis (LC) patients followed in our General Hospital.

**Materials/methods:** In our centre, patients with BSIs are evaluated by an ID specialist who collects prospectively clinical and microbiological characteristics, and data on empirical antibiotic treatment. These records are inserted in an anonymous database (Epidata software). An extraction was performed on the period from May 1, 2017 to August 31, 2019, and patients with LC were analysed.

**Results:** During the study period, 126 BSI (including 81 male patients, 67%) occurred in LC patients, which represented 10.4% of all consecutive BSIs episodes (n=1210). Mean age was 65 ± 11 years, LC patients were younger than patients without LC (mean age 72 ± 17 years, p<0.001). Community-acquired infections were predominant (92/126, 73%), and the most frequent portal of entry was digestive tract (n=42, 33%), followed by urinary tract (n=21, 17%). A total of 138 strains were isolated, the most frequent were *E. coli* (n=44, 32%, among which 2 [4%] were ESBL), *S. aureus* (n=22, 16%, among which 2 [9%] were methicillin-resistant), and streptococci/enterococci (n=28, 20%), which was similar to patients without LC. Overall, an empirical antibiotic therapy was prescribed in 90 patients (71%), with at least one active drug in 74 patients (59%). Severe sepsis rate was 38% (n=48), and shock septic rate was 11% (n=14), with a 7-day mortality rate of 16% (tending to be higher than patients without LC [10%], p=0.06) and a 30-day mortality rate of 25% (higher than patients without LC [16%], p=0.004).

**Conclusions:** In our centre, more than 10% of BSIs occurred in LC patients. LC patients with BSIs were younger than patients without LC, with a majority of community-acquired infections, and a predominance of digestive tract infections. Epidemiological data were similar to patients without LC, the main pathogens were *E. coli* and *S. aureus*, with low-resistance rates, thus antibiotic protocols should not be modified in patients with LC. Mortality rate was higher in LC patients.

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Abstract 3862

**Chagas disease diagnosis: performance of a new automated native antigen technique**

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**Background:** Chagas disease (CD) burden is growing in non-endemic countries due to population mobility and globalization. Spain is one of the countries with highest prevalence (up to 10-15%). Blood screening is a cost-effective strategy to prevent its transmission. CDC recommend performing two different CD diagnosis tests, ideally with both native and recombinant antigens for IgG detection. Except for chemiluminescence recombinant assays, most of commercialized native tests in Spain are not automated and manual processing is required. The rising number on CD demanded tests has made high throughput laboratories to start diagnosis algorithm with a recombinant antigen method, employing the manual native technique as confirmation test. Our aim was to compare a new automate native antigen test with our recombinant method as screening tool for CD.

**Materials/methods:** A total of 556 serums (202 retrospective and 354 prospective samples), mainly from Latin American patients, were tested by two CD tests: 1) Our reference assay, a chemiluminescence immunoassay employing a recombinant multi-antigen protein (Liaison® XL murex Chagas, DiaSorin, Italy); 2) A new chemiluminescence immunoassay based on native antigen (Vitros® Anti-T. cruzi assay, Ortho-Clinical Diagnostics, USA). Sensibility, specificity, positive and negative predictive values for the native technique over the recombinant assay were determined. Prevalence was calculated from the prospective cohort. Discrepant results between both assays were analyzed.

**Results:** Among the 556 samples, 160 (28.8%) were positive and 383 (68.9%) were negative by both assays. In the prospective cohort, 25/354 samples were positive. Therefore, our CD prevalence was 7%. Only in 1/556 samples (2.3%) discrepancies were observed. Compared to Liaison®, Vitros® sensitivity, specificity and positive and negative predictive values were respectively, 93.6%, 99.5%, 98.8% and 97.2%.

**Conclusions:** Due to lack of a unique gold-standard serological assay, combination of two tests remains to be the best approach, especially in those inconsistent results. Our data suggest that Vitros® could be a good option as CD screening assay, with a 97.7% of concordant results with our reference technique. Specifically, given its high specificity, Vitros® can be an option as confirmation assay for CD diagnose.

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Development and validation of a specific real-time PCR assay for the rapid detection of Candida auris
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Background: Since its description in 2009, Candida auris has been considered as an emerging and multidrug-resistant fungus with a high capacity to cause nosocomial infections especially in immunocompromised patients, it causes fungemia, internal organ infections, skin infections and otitis. A strong association between C. auris infection and mortality has been documented in the world. Given the recent global emergence of C. auris, a rapid detection and identification of this pathogen is necessary to control its spread. The aim of this study was to develop a specific molecular diagnostic tool able to detect the 4 emerging clades of C. auris.

Materials/methods: A RT-PCR (Real-time polymerase chain reaction) system was designed based on a GPI (Glycosyl-phosphatidylinositol) protein encoding-gene specific for C. auris. A collection of 50 bacteria and 70 fungi were tested to confirm its specificity and sensitivity. Then 2073 clinical and environmental samples from different geographical countries were tested also to detect C. auris.

Results: The in Silico analysis shows that this system was able to amplify only C. auris, it was highly specific (100%), reproducible and sensitive, with a limit of detection of 13 CFU/qPCR reaction. All clinical and environmental samples were negative.

Conclusions: To the best of our knowledge, we have developed a specific, sensitive and reproducible real time PCR system able to detect specifically C. auris.

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Abstracts 2020

Abstract 3866

**Visceral leishmaniasis by Leishmania infantum in immunocompetent adults: update of the leishmaniasis outbreak in Madrid (Spain)**

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**Background:** Visceral leishmaniasis due to *L. infantum* mainly affects children and immunosuppressed, and there is scarce information on management in immunocompetent adults. Since June 2009, an outbreak of leishmaniasis on Fuenlabrada [Madrid, Spain] was declared. We update our experience in the management of ICVL in this outbreak.

**Materials/methods:** From the beginning of the outbreak in June 2009 until November 1, 2019 we have prospectively collected clinical variables, diagnosis, treatment and follow-up of all adult patients with VL treated at Hospital Universitario de Fuenlabrada.

**Results:** Since the beginning of the outbreak we have identified 85 immunocompetent patients with visceral leishmaniasis (ICVL). 72% were male, mean age 44.1 years (18-95). 53% were of sub-Saharan origin, but residing in the area for at least one year before diagnosis. 98% presented with fever, 29% splenomegaly (95% radiological), 87% anemia, 91% leukopenia and 92% thrombocytopenia. 76% had ferritin greater than 1000 mcg/dl. 38% met criteria for hemophagocytic syndrome. PCR was positive in 91% in bone marrow and 82% in blood of ICVL and was the most reliable technique. Regarding serology, rK39 rapid test was positive in 43% of patients with ICVL, but showed a positive predictive value of 99%. 93% of patients were treated with liposomal amphotericin B (L-amphB). There were 8 relapses of which 5 were patients of sub-Saharan origin (12% vs. 8% others, p NS). Total dose of L-amphB under 21mg/kg was the only variable related to failure, OR 30.0 (4.1-200), p = 0.001. 3 of the relapses occurred beyond 6 months.

**Conclusions:** There was a high proportion of patients of sub-Saharan origin among ICVL. One third met criteria for hemophagocytic syndrome, all resolved exclusively with VL treatment. The rapid rK39 test had a low sensitivity, but a high specificity that allows confirming the diagnosis in a few minutes. In our environment, we do not recommend using less than 21mg/Kg of liposomal amphotericin B in ICVL, and even higher doses could be assessed in sub-Saharan. The follow-up in ICVL should be at least one year after treatment.

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Abstract 3867

**Health economics of nosocomial pneumonia in UK intensive care units: an exploratory study**

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**Abstract third-party references:** On behalf of the INHALE WP2 Study group

**Background:** Both Hospital-Acquired and Ventilator-Associated Pneumonia (HAP and VAP) cause considerable health care costs, as well as significantly impacting patient outcomes. The United Kingdom’s (UK’s) National Institute for Health Research-funded INHALE (https://www.ucl.ac.uk/inhale-project/) programme is exploring the use of rapid molecular diagnostics to improve the treatment of HAP/VAP patients by more swiftly identifying causative pathogens and their antibiotic resistances. Resulting changes to patient management and antibiotic use potentially have substantial resource implications, and it is important to be able to quantify these. Accordingly, to establish a baseline, a cross-sectional health economic survey of recent HAP/VAP was undertaken.

**Materials/methods:** Patients, or their representatives, from four UK hospital Intensive Care Units (ICUs) were approached for involvement if they were either i) starting a course of antibiotics or ii) having a change of antibiotics for the treatment of HAP or VAP. We collected information to allow estimates of: cost of ICU stay [length of stay (LOS) and related health resource group (HRG)], acquisition cost (from the British National Formulary) of antibiotics used in the 21-days after recruitment; and quality of life [EuroQoL EQ-5D-5L] in those alive at 21-days.

**Results:** N=143 patients were recruited. They had considerable ICU-associated LOS and hospital costs: their mean stay was 22 days and mean costs were GBP £43,100). Both LOS and costs were heavily right-skewed (most values are low but the remainder take large values resulting in a long right ‘tail’ such that the mean is greater than the median). Compared with HAP, VAP caused greater LOS and ICU costs. Antibiotics themselves formed only a tiny fraction of total costs (mean 21-day cost was £321). A total of 43 people completed the EQ-5D-5L: a wide ranges of utilities resulted, ranging from 0.8 to -0.4 (with negatives indicating states valued worse than death).

**Conclusions:** HAP, and particularly VAP, are associated with significant hospital costs. Interventions that could improve the care of individuals with HAP/VAP and reduce their LOS would significantly free up scarce ICU resources, allowing other patients to be treated.

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Intestinal colonisation by carbapenemase-producing Enterobacteriaceae detected by polymerase chain reaction in patients with negative cultures: do they really have an increased risk of infection?

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Background: Intestinal colonization detected by culture of carbapenemase-producing Enterobacteriaceae (CPE) is an important risk factor for infection. However, little is known about whether colonization detected only by polymerase chain reaction (PCR) has the same risk.

Materials/methods: Observational retrospective cohort study performed between 2017 and 2019. Adult patients admitted for any cause and screened for CPE gut colonization with cultures and multiplex PCR for blaKPC/blaOXA genes, in a University Hospital of Buenos Aires, Argentina were included. They were divided into 3 groups: Group 1 (G1) positive PCR results with negative cultures, Group 2 (G2) both positive tests, and Group 3 (G3) both negative tests. The main outcome was CPE infection episodes in the first 270 days. Categorical variables were analyzed by $\chi^2$ test and continuous variables by Kruskal-Wallis test. To analyse the PCR positive results in patients with CPE negative cultures, we performed a multivariate analysis for the main outcome using binary logistic regression analysis between G1 and G2.

Results: 477 patients were included. G1: 89 (18.7%), G2: 113 (23.7%) and G3: 275 (57.7%). Baseline characteristics were similar in all groups: Median age (IQR 25-75) 66 (54-78), 66 (56-79) and 69 (61-80), respectively; Charlson Comorbidity Index (IQR 25-75): 5 (3-7), 5 (3-6), and 5 (3-6), respectively. Risk factors for CPE acquisition were more frequent in G1 and G2 than in G3: previous antibiotic therapy: 53.9% vs 60.2% vs 21.8%, P=0.0001; previous carbapenem therapy: 29.2% vs 30.4% vs 8.3%, P=0.024; previous ICU admission: 34.8% vs 44.2% vs 25.8%, P=0.002; previous surgery: 25.8% vs 26.5% vs 9.5%, P=0.0001; length of hospitalization (IQR 25-75): 21 (7-30) vs 31 (8-32) vs 15 (5-14), P=0.0001. Finally, CPE infection episodes were more frequent in G1 and G2 than G3: 16.9% vs 27.4% vs 2.5%, P=0.0001. In multivariate analysis a positive PCR result was associated with higher risk of CPE infection: OR 4.24, P=0.008 (CI95% 1.46 - 12.3).

Conclusions: Patients that are colonized by CPE detected by PCR and have CPE negative culture results in rectal swabs have an increased risk of infection by CPE. This result is important for decision-making in clinical practice.

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Multidrug-resistant tuberculosis imported into high-income countries: a GeoSentinel analysis, 2008–2017

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Abstract third-party references: Centers for Disease Control and Prevention (CDC)

Background: Multidrug-resistant tuberculosis (MDR-TB) is a major obstacle to TB elimination. Migration contributes to TB importation to low-burden countries. The aim of this investigation was to describe epidemiologic characteristics of travellers and migrants with MDR-TB reported to GeoSentinel, a global travel and tropical medicine network.

Materials/methods: Patients with a confirmed or probable diagnosis of MDR-, pre-extensively drug-resistant (pre-XDR), or extensively drug-resistant (XDR-TB) reported to GeoSentinel between 2008 and 2017 were analysed regarding demographics, travel or migration details, and disease attributes. The analysis was stratified according to two resistance levels (MDR-TB and pre-XDR/XDR) as well as three regions of birth (Georgia, the Former Soviet Union [FSU] excluding Georgia, and non-FSU/other countries).

Results: There were 164 patients from 16 GeoSentinel sites, 98.8% of whom were first-generation immigrants. Median age was 31 years [range: 11–63]; 61% were male. HIV co-infection was uncommon [3.7%]. Twenty-five percent were born in Georgia and 24% in other FSU states. Subclassification of MDR-TB was known for 147 patients [12.2% pre-XDR and 12.9% XDR-TB]. Time from immigration to presentation was shorter in patients from the FSU [median = 86 days [interquartile range [IQR]: 9–643]] and Georgia [4 [IQR: 1–13]] than other countries [300 [IQR: 97–1018]] and correlated with degree of resistance. Symptom onset before immigration was reported more frequently by patients with pre-XDR/XDR-TB as well as three regions of birth (Georgia, the Former Soviet Union [FSU] excluding Georgia, and non-FSU/other countries).

Conclusions: The temporal relation between immigration and presentation to a GeoSentinel site may be due to the need for specialized care not available in the home country of travellers and migrants with MDR-TB. Resources should be devoted to better understanding the factors contributing to the cross-border spread of MDR-TB.

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Occurrence of sporadic human ascariasis in non-endemic regions: the importance of zoonotic transmission from swine

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Background: Ascariasis in developed countries occurs only sporadically, and usually in travelers or in children in rural settings with direct or indirect exposure to *Ascaris suum* from swine. Reciprocal transmission between humans and swine is possible given *A. suum* and *A. lumbricoides* are considered conspecific based on published mtDNA and nuclear ribosomal ITS-1 studies with recognized phenotypic/genotypic differences reflecting host-specific adaptive changes. Here we evaluated 15 cases of human ascariasis detected over 6 a year period from specimens submitted to a regional parasitology laboratory in a non-endemic region of the Upper Midwest USA.

Materials/methods: Fifteen helminth specimens spontaneously passed per rectum were submitted for laboratory identification during 2013-19 and identified morphologically as *A. lumbricoides/suum* (undifferentiated). All patients attended local clinics and brought specimens in for identification. Clinical records were available for 13 patients.

Results: Ages ranged from 14 months to 41 years with 13 cases (87%) occurring in children <=12 years and 2 (13%) >30 years; 9 patients (60%) were female. Thirteen (87%) of the *A. lumbricoides/suum* specimens were adults and 2 (13%) were juveniles. Individuals with records available either lived on or had visited a farm (5) or hobby farm (2) where pigs were currently or likely historically present; lived at a rural address (4); used animal manure for gardening (1); or lacked discernable farm connections though was active outdoors (1). International travel history was lacking in all cases. One 2-year old child from a rural address had passed 2 worms 6 months apart. All 13 patients were treated with albendazole per guideline without complication.

Conclusions: Ascariasis attributable to poor sanitation has been largely eradicated from the USA since the early 1980s. Sporadic infections in non-travelers have, however, continued to be recognized and likely represent zoonotic transmission from domesticated swine. While human and pig *Ascaris* have long been considered distinct species, recently published molecular and cross-transmission experiments point to conspecificity. This case series is a reminder of the zoonotic disease risks posed by swine-origin *Ascaris*, especially in young children, and reinforces the need for proper herd management and attention to personal hygiene for at-risk individuals.

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Biomarkers help to stop secondary prophylaxis on Leishmania-HIV co-infected patients

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Background: Secondary prophylaxis with liposomal amphotericin B (L-amphB) for HIV patients with visceral leishmaniasis (VL) is recommended, but it is not clear when to stop it. CPA-SLA (cellular proliferative assay to soluble Leishmania antigen) and interferon gamma (IFN-γ) have been tested as markers of specific cellular immunity. We update the usefulness of these tests for withdrawal of secondary prophylaxis in Leishmania-HIV coinfected patients.

Materials/methods: From January 2013 to 1st November 2019, Leishmania-HIV coinfected patients with previous or active VL were recruited after the end of treatment for VL. PCR, CPA-SLA and IFN-γ were included besides habitual test for HIV.

Results: 15 Leishmania-HIV coinfected patients were identified. 1 was lost and 3 died of events not related to leishmaniasis. 11 were recruited after standard treatment for VL with L-amph B. All of them were on HAART according guidelines, were asymptomatic when recruited and completed follow up (364 weeks).

7 patients showed negative PCR and positive CPA-SLA and IFN-γ. Prophylaxis had been stopped in 3 of them before they were recruited. These 3 patients have not relapsed during follow up. The other 4 patients were still on prophylaxis when were recruited. Prophylaxis was stopped after these results. CD4 levels were 152, 189, 243 and 359/mm3. None relapsed during follow up (mean 251 weeks, range 59-363, from the end of prophylaxis).

4 patients showed negative CPA-SLA. 1 showed negative PCR and positive IFN-γ, and prophylaxis was stopped when CD4 were 154, without relapses after 163 weeks. The other 3 showed positive PCR and negative IFN-γ. Prophylaxis were maintained but all of them relapsed and needed retreatment. After retreatment, 1 patient changed to negative PCR and positive CPA-SLA and IFN-γ. Prophylaxis was stopped (CD4 301) and this patient has not relapsed after 162 weeks of follow up. The other 2 showed still positive PCR and negative CPA-SLA and IFN-γ at the end of follow up, and are still on prophylaxis.

Conclusions: In this small sample of Leishmania-HIV coinfected patients, CPA-SLA and IFN-γ are valid markers of specific cellular immunity, and allowed withdrawal of secondary prophylaxis of leishmaniasis, not matter CD4 level.

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Abstract 3874

The effect of live attenuated influenza vaccine on pneumococcal colonisation densities among children aged 24-59 months in Gambia

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Background: Live attenuated influenza vaccine (LAIV) has been shown to increase Streptococcus pneumoniae carriage duration and colonization densities in murine and human challenge models, similar to influenza virus infection. We investigated the effect of LAIV on S. pneumoniae colonization dynamics in the upper respiratory tract (URT) of Gambian children, a population with high pneumococcal colonisation rates, as a model to study the interaction between S. pneumoniae and influenza.

Materials/methods: In a clinical trial in The Gambia (NCT02972957), children aged 24-59 months were randomised 2:1 to receive LAIV at day 0 (n=213) or remain unvaccinated until day 21 (n=108). Children were recruited during January-April in either 2017 or 2018. Nasopharyngeal swabs (NPS) were collected at day 0, day 7 and day 21. Pneumococcal colonisation prevalence and densities were determined using quantitative polymerase chain reaction targeting the autolysin gene (lytA qPCR). Presence of other respiratory viruses was determined by a multiplex RT-PCR. Generalized mixed effects models were used to assess the effect of LAIV and other variables on pneumococcal colonisation densities.

Results: Pneumococcal colonisation prevalence was high (>75%) and similar in LAIV recipients and unvaccinated controls at each timepoint (day 0: p=0.1; day 7: p=0.45; day 21: p=0.24). We observed a positive association between LAIV and pneumococcal colonisation density (p=0.009). Lower age (p=0.003), recruitment in 2018 (p=0.008) and presence of another respiratory virus at baseline (p=0.008) were other contributory factors. Within the LAIV group, children with an asymptomatic respiratory viral infection at the time of LAIV had an earlier peak of pneumococcal density at day 7, compared to those with no other virus detected. An unexpected rise in pneumococcal density was observed in the control group between day 7 and 21, which was potentially explained by acquisition of a new respiratory virus between day 0 and 7, seen in 22% of children.

Conclusions: LAIV was associated with increased pneumococcal colonisation densities in the first 21 days following vaccination. LAIV-associated increase in S. pneumoniae densities was enhanced by asymptomatic viral co-infection prior to LAIV administration, suggesting that S. pneumoniae proliferation in the nasopharynx may be driven by sequential natural and induced viral infections.

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Effect of biocides on the mobilization of plasmid-encoded OXA-48 carbapenemases from Klebsiella pneumoniae growing in biofilms

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Background: The dissemination of plasmid-encoded carbapenemases represents a serious health problem worldwide. This is particularly worrying for blaOXA-48-producing K. pneumoniae (OXA-48/Kp) that it is spreading efficiently through diverse environmental reservoirs. Biofilm formation can contribute in the survival of OXA-48/Kp under adverse conditions, preventing or reducing the activity of biocides. Recent studies suggest that plasmids can be mobilized under stress conditions [ie. biocides]. The objective of this study was to evaluate the effect of sublethal concentrations of some commonly used biocides on the mobilization of plasmid-encoded OXA-48 carbapenemases from K. pneumoniae growing in biofilms.

Materials/methods: Seven representative isolates of different ST types of OXA-48/Kp (Table) were selected. For conjugation assay, Escherichia coli J53 (azide resistant) was used as a receptor. For biofilm formation, donor and receptor mixtures [1:1] were prepared in polystyrene plates in absence [control] and presence of concentrations of chlorhexidine (CHX), ethanol (EtOH), sodium hypochlorite (NaClO), povidone iodine (POV) or triclosan (TRI) equivalents to 0.25x their respective MICs and were incubated 24 hours at 37ºC. Biofilms adhered to wells were sonicated and subcultured in chromogenic agar containing azide (100,000 mg/L) and ertapenem (0.1 25 mg/L). Conjugation frequency (CF) in biofilms was calculated as Nº of UFC of transconjugants in solid medium with azide and ertapenem / Nº of E. coli J53 in azide medium. Differences associated with a p <= 0.05 (Student test) were considered statistically significant.

Results: The table shows the fold-change in the CF in biofilms determined in presence of biocide respect to the CF determined in absence of biocide.

<table>
<thead>
<tr>
<th>Isolate</th>
<th>CHX</th>
<th>EtOH</th>
<th>NaClO</th>
<th>POV</th>
<th>TRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>ST11/OXA-245</td>
<td>-7*</td>
<td>-1</td>
<td>-25*</td>
<td>-738*</td>
<td>-64*</td>
</tr>
<tr>
<td>ST437/OXA-245</td>
<td>2</td>
<td>-1</td>
<td>1</td>
<td>27*</td>
<td>-2</td>
</tr>
<tr>
<td>ST16/OXA-48</td>
<td>4</td>
<td>11*</td>
<td>16*</td>
<td>-7*</td>
<td>1</td>
</tr>
<tr>
<td>ST846/OXA-48</td>
<td>-2</td>
<td>1</td>
<td>1</td>
<td>125*</td>
<td>87*</td>
</tr>
<tr>
<td>ST13/OXA-48</td>
<td>71*</td>
<td>16*</td>
<td>61*</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>ST899/OXA-48</td>
<td>253*</td>
<td>243*</td>
<td>396*</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>ST974/OXA48</td>
<td>61*</td>
<td>39*</td>
<td>11*</td>
<td>11*</td>
<td>4</td>
</tr>
</tbody>
</table>

* = p < 0.05

Conclusions: The tested biocides showed a variable effect on the CF in biofilms of OXA-48/Kp. This effect was also clone-dependent.

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Abstract 3881

High occurrence of Serratia spp. in abiotic surfaces at hospital intensive care unit areas during non-outbreak situations

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Background: Serratia spp. (Se) is frequently involved in clonal or multiclonal nosocomial outbreaks at ICUs, often carrying genes encoding Extended Spectrum Beta-lactamases (ESBL) or carbapenem resistance (CR). Sinks (SK) are identified as reservoirs of ESBL/CRSe but the ecology of this species in built hospital environments (BE) remains largely unexplored.

Materials/methods: We weekly collected 5 samples/patient room (sinks-SK; ventilator’s-touchscreen-VT; washbasin-WB; bedrails-BR) and 2 samples from staff-areas (keyboards) using EZ-Reach-Sponges (April-October 2019). We plated the 1,728 samples [(5x14rooms+2)x24weeks] on ChromagarOrientation and characterized bacterial colonies (1/morphotype; 10,180 colonies). Identification (MALDI-TOF-MS), antimicrobial susceptibility (disk-diffusion, DDST, Hodge test), clonal diversity (XbaI, S1-PFGE, FTIR) were analyzed by standard procedures. Metadata (clinical, microbiology, surveillance) analysis using REDCap (Research Electronic Data Capture) application was used to integrate and further exploit comprehensive metadata [clinical records, IC, microlab, BE surveillance]. ICU-metrics for the period studied includes 95% occupancy, 244 patient admissions, 28% MDR colonization-rate (23% ESCAPEm, 6.8% CPSm).

Results: MALDI-TOF-MS identified 1,026 isolates as Se with a high-score (88% S. marcescens, Sem; 12% S. ureilytica). Sem was recovered in 14/14 ICU-rooms (45 isolates/week), from SK (97.6%) and also from WB and VT (2.4%). Sem isolates clustered according the antimicrobial susceptibility to beta-lactams (aminopenicillins-AMP; amoxicillin-clavulanic-AMC; cefoxitin-FOX; 3GCephalosporins-3GC; carbapenems) in 5 groups: i) susceptible to all beta-lactam classes (S;39.5%) ii) AMPc hyperproducers (AMPc;25.1%), iii) AMP+AMC resistant (AA;17%), iv) ESBLproducers (1.9%), v) CR (1.8%), vi) other phenotypes (12.8%). ESBLSm appeared in SK of 5/14 rooms, persistently in 2/14 rooms. Isolates with S, AMPc and AA phenotypes appeared in 12/14, 6/14 and 5/14, respectively. Different Sem populations were simultaneously recovered in rooms #8 (AMPc, AA), #10 (S, AMPc, A), #12 (S, AMPc, AA) and #13 (S, AMPc) along the time. Sem were detected in patients of rooms #3, #8 and #10, eventually related to Sem from BE.

Conclusions: Sinks are common reservoirs of “resident” Sem populations in hospitals. The low occurrence and persistence of ESBL/CRSm suggest differences in the adaptation of Sm populations to humans and abiotic surfaces. Fully characterization of unusual and consistently recovered isolates susceptible to beta-lactams [in progress] will facilitate the understanding of BE ecology.

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A randomised prospective clinical trial to assess the role of procalcitonin-guided antimicrobial therapy to reduce long-term infections' sequelae [PROGRESS]

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Background: Procalcitonin (PCT) has already been introduced to guide duration of antimicrobial treatment for lower respiratory tract infections. Although data support a similar benefit in sepsis, the possible long-term benefit of this strategy has never been investigated. PROGRESS (ClinicalTrials.gov number, NCT03333304) was a multicenter randomized clinical trial in Greece, aiming to investigate long-term benefit of the PCT-guided stop of antimicrobials in sepsis.

Materials/methods: From November 2017 until January 2019, 266 sepsis (according to Sepsis-3 definition) patients with lower respiratory tract infections, acute pyelonephritis or primary bacteremia, were randomized to PCT-guided antimicrobial treatment (PCT group) or treatment according to local standard practice (SOC group). In the PCT group, PCT was daily measured starting from day 5 and physicians were advised to discontinue antimicrobials when values were lower than 0.5ng/ml or when any more than 80% baseline decrease was found. The composite primary endpoint was the change in the rate of infection-associated adverse events, i.e. infections by multidrug resistant organisms (MDRO), infection by Clostridium difficile and infection-associated death on day 180. Secondary endpoints were 28-day mortality, duration of antibiotic treatment and cost of hospitalization.

Results: The primary outcome was met in 15.3% of patients in the SOC group compared to 7.2% in the PCT group (hazard ratio, 0.45; 95% confidence intervals [CIs] 0.20 to 0.98; P=0.04) (Figure). 28-day mortality was 28.2% (95% CIs, 21.2%-36.5%) and 15.2% (95%CIs, 10.0%-22.2%) respectively (P=0.02). Median (interquartile range) treatment duration was 10 [8] and 5 [2] days respectively (P<0.001). The effect of PCT guidance on treatment duration was similar for all types of infection. Antimicrobial-associated adverse events were reported in 63.4% (95%CIs, 54.8%-71.1%) and 51.2% (95%CIs, 42.5%-59.8%) respectively (P=0.05). The mean (standard error) cost of hospitalization was 1,274.65€ (110.79) in the PCT group; this was 1,758.17€ (163.50) in the SOC group (P=0.02).

Conclusions: Use of an early PCT-guided stopping rule of antimicrobials in sepsis was proven of significant benefit by reducing secondary infections by MDRO and C.difficile, 28-day mortality and cost of hospitalization. Shorter duration of antibiotic treatment associated with lower adverse events may be a plausible explanation.

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Abstract 3883

**Detection of Enterovirus in cerebrospinal fluid 24 hours a day by a fully-automated PCR assay is associated with improved management of aseptic meningitis in adult patients**

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**Background:** Molecular techniques are recognized as the reference standard for the diagnosis of enterovirus (EV) infections and enable to simplify aseptic meningitis (AM) patient management.

The aim of our study is to evaluate impact of performing 7 days a week and 24 hours a day (24/7) the RT-PCR Xpert EV on Geneexpert (Cepheid) in cerebrospinal fluid samples (CSF) from the emergency department.

**Materials/methods:** Our observational study consists in including all patients from emergency department with AM whose CSF has been analysed by EV RT-PCR from 01/01/2015 to 30/06/2019. Medical files were analyzed to collect therapeutic attitude especially antimicrobial treatments and length of hospitalization.

**Results:** Among the 1535 CSF collected at the emergency department during the study, 165 EV RT-PCR have been performed (10.75%). 133 remained negative (1st group) and 32 were positive (2nd group). None antibiotic or antiviral treatment have been given to 47 patients of 1st group (35.3 %) and to 12 patients of 2nd group (37.5%). Others patients, in two groups, were treated by one or several anti-infectives among cefotaxim, amoxicillin, gentamicin and acyclovir.

In the 2nd group, 97% of the patients with anti-infective therapy only receive the first dose: treatment was stopped when EV RT-PCR positive result was known. A significant difference was highlighted between the 2 groups concerning the hospitalization ($p<1.10^{-3}$). In the 1st group 119 (89.5 %) patients have been hospitalized with a mean length of stay of 10.5 days whereas in the 2nd group only 17 (53.2 %) patients were hospitalized (mean length of stay: 1.8 days), the 15 others (46.8 %) were sent back to home.

**Conclusions:** From 2014, the French Health Authority recommends to perform EV detection by molecular technique in less than 48 hours. Thanks to the implementation of automatized EV RT-PCR and reorganization of our microbiology laboratory, we can provide EV result 24/7 in less than 6 hours which improves management of AM by significantly reducing anti-infective therapy, decreased hospitalizations and length of stay.

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Abstract 3887

**A surgical take on broncho-pulmonary Aspergillus: 20 years of experience**

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**Background:** *Aspergillus fumigatus* is an omnipresent opportunistic fungus causing a spectrum of pulmonary pathology from simple to complex aspergillomas, to pneumonia-like aspergillosis. Surgical resection continues to join drug- and embolization-therapy in the treatment options. This retrospective study aims to review one centre’s 20-year experience in surgical treatments of these patients, to evaluate their feasibility and safety, as well as differences in morbidity and mortality between the diagnostic groups of Pulmonary Aspergillosis (PA), Simple Aspergillomas (SA), and Complex Aspergillomas (CA).

**Materials/methods:** An existing surgical patient database of 23,244 operations was queried and reviewed to identify 47 patients that had a confirmed diagnosis of Aspergillus and were treated surgically for the purpose of fungal resection at the University Hospital of Leuven, Belgium. Patients were categorized into the main diagnostic groups: Pulmonary Aspergillosis (PA), Simple Aspergillomas (SA), and Complex Aspergillomas (CA), and subject to internal and external case analysis focusing on patient epidemiology, underlying disease, operative indication, and postoperative morbidity and mortality. A Kaplan-Meier Graph was generated to display and compare postoperative mortality.

**Results:** There was a total of 47 patients, 27 men and 20 women, with a mean age of 47.8y (range 2-82y). The most common underlying conditions for CAs and SAs were tubeculous caverns (38% and 10%), and for PAs were radio-chemotherapy (31%) and immunosuppressants (25%). The most common surgical indications were recurrent infections [56% of PAs], massive hemoptysis [52% of CAs], and preventive resection [60% of SAs]. Postoperative mortality rate (within 60 days) was 17%, with sepsis and pneumonia as the main causes of postoperative death – some, but not all, of which Aspergillus induced. The postoperative morbidity due to infection was also high, 36% fevers, 26% pneumonias, and 17% empyemas. At five-years the cumulative survival (Kaplan-Meier) dropped to 62% overall, 55% for PAs, 64% for CAs, and 77% for SAs.

**Conclusions:** In general, these results reconfirm surgery as a feasible treatment mode for SAs and CAs, with a lower threshold for surgical resection of SAs warranted. High mortality and morbidity should be taken into account for all groups, surgery of PAs in particular, continues to be controversial for this reason.

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Influence of the Built Environment (BE) microbiota on the epidemiology of antimicrobial resistance at intensive care unit of a tertiary hospital

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Background: Emergence and transmission of antimicrobial resistant (AMR) pathogens remain to be fully understood. We comprehensively analyzed the ecology and dynamics of bacteria in built environment (BE) of a large ICU fully enrolled in AMR control programs.

Materials/methods: In ICU-Intensive Medicine, 5 samples/patient room (sinks-SK; ventilator’s-touchscreen-VT; washbasin-WB; bedrails-BR) and 2 samples from staff-areas (keyboards) were weekly collected using EZ-Reach-Sponges (April-October 2019). 1,728 samples were plated [(5x14rooms+2)x24weeks] on ChromagarOrientation and bacterial colonies. Bacterial identification (MALDI-TOF-MS), antimicrobial susceptibility (disk-diffusion agar, Hodge test, PCR of bla gene), clonal diversity (XbaI, P-FGE) were studied. Population structure of BE-isolates of ESKAPE species was fully addressed (FTIR, WGS). Ward epidemiological metrics in this 6m-period were 95% occupancy (14/14 rooms), 244 patients, 65%/35%-male/female, APACHEII-score 21, SAPS-index 47, 13.47% mortality-rate and 27.9% MDR colonization-rate at admission (23.7%/15.3% ESBL-Escherichia coli (EC)/K. pneumoniae (KP), 13.6% Pseudomonas aeruginosa (PA), 6.8%/6.8% carbapenem-resistant (CR)-Serratia marcescens (SM)/KP). REDCap (Research Electronic Data Capture) application was used to integrate and further exploit comprehensive metadata (clinical records, IC, microlab, BE surveillance).

Results: 10,180 isolates were recovered from abiotic samples (56 genera, 191 species). Predominant species in SK were SM (29.2%), Staphylococcus spp. (SC, 15.7%), PA (9.7%), Achromobacter spp. (5.2%), Burkholderia cenocepacia (5.1%), Stenotrophomonas maltophilia (4.2%), Klebsiella (2.0%), Sphingomonas spp. (2.0%), Bacillus spp. (BC, 2.0%), and other Enterobacteriaceae (3.8%). Predominant species in dry surfaces (VT, WB, BR) were SC (37%), Enterococcus spp. (5.0%), BC (3.3%), Corynebacterium spp. (2.2%), and Streptococcus spp. (2.2%). Consistent BE-microbial diversity patterns were identified in ICU-rooms. Abiotic AMR isolates of Enterobacteriaceae, BGNF (ESBL+, CR), SC (MRSA) and enterococci (AMPR) were related to AMR clinical isolates but time-limited. Abiotic persistent clones in SK were reservoirs of ESBLs. Diversity and co-occurrence patterns of ESKAPE species and transmission networks were established.

Conclusions: Abiotic surfaces in ICU rooms show specific microbial diversity profiles, maintained a long time, with resident clones often influencing the spread and/or maintenance of AMR genes. Combined surveillance data greatly improved risk assessment analysis.

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Dalbavancin: to OPAT or not to OPAT

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Background: As the demand on inpatient beds increases, there is a growing emphasis on outpatient infection management and admission avoidance. The use of novel antibiotics such as dalbavancin could play a key role. Dalbavancin is a second generation lipoglycopeptide and is licensed for use in acute bacterial skin and skin structure infections, and there is increasing evidence for its use as a 2-dose antibiotic in deep seated infections such as osteomyelitis or spinal infections. Dalbavancin’s unique pharmacokinetics yields a duration of action up to 8 weeks, however, the cost of using novel antibiotics which can be up to 10 times the cost of a common antibiotic is a major barrier to their use.

Materials/methods: The clinical outcomes of dalbavancin recipients (January to October 2019) were assessed using the available microbiology, clinical diagnoses, and social circumstances of the patients, and calculated the ‘bed-day’ savings from date of discharge to the theoretical ‘end-date’ of antibiotics as if a conventional intravenous antibiotic were used.

Results: Of the 15 patients reviewed, bone and joint, aortic graft and diabetic foot infections were identified. In 10 cases, the alternative treatment option would have been hospitalisation as traditional daily or three times a week OPAT antibiotic options weren’t appropriate due to either drug user status or social/geographical circumstances. The remaining 5 cases would have also required hospitalisation as a long course of antibiotics were needed where oral options were not appropriate due to drug interactions, intolerance or complex monitoring.

A dosing regimen of 1500mg (1000mg in renal impairment) on day 1 and 8 was used in all patients. The regimen was either initiated on the wards with prompt discharge or initiated in OPAT as admission avoidance. In total 14 patients clinically improved or remained stable and 1 patient was lost to follow up.

Compared to hospitalisation the use of dalbavancin resulted in a ‘bed-day’ saving of 738 days which yields a net saving of £153,000.

Conclusions: With acceptable clinical outcomes, the use of dalbavancin in this study saved on average £10,000 per patient, making it a significant contribution to overall outpatient infection management and admission cost reduction.

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Use of a hospital-cumulative antibiogram to guide empirical antibiotics in gram-negative bloodstream infections
Charlotte Richardson*, Damien Mack1
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Background: A hospital cumulative antibiogram provides an annual summary of culture isolates and antimicrobial susceptibility rates. This has utility in surveillance of local resistance trends, empirical antibiotic choice and in formulating local antimicrobial guidelines.

Materials/methods: We extracted the first blood culture isolate of an organism per patient in the 2018 calendar year from the laboratory information system at the Royal Free Hospital, a teaching hospital in London, UK, in accordance with the CLSI cumulative antibiogram guidelines. Organism identification was performed using the Brucker Biotyper (Brucker Daltonics, Bremen, Germany). Antibiotic susceptibility testing was performed using the BD Phoenix™ instrument (BD Diagnostic Systems, Sparks, MD) in accordance with EUCAST guidelines. Isolates reported as ‘resistant’ or ‘intermediate’ were deemed non-susceptible and samples without antimicrobial susceptibility data were excluded. Only species with susceptibility testing data for at least 30 isolates were included. We report susceptibility rates of gram-negative bloodstream infections to individual antibiotics and the combination of co-amoxiclav and gentamicin.

Results: There were 1252 isolates including 225 Escherichia coli, and 51 Klebsiella pneumoniae. Significantly more K. pneumoniae than E. coli were susceptible to co-amoxiclav (66% vs. 49%, p=0.021). The addition of gentamicin to co-amoxiclav significantly increased susceptibility for E. coli compared to co-amoxiclav alone (88% vs. 49%, p<0.001) but not for K. pneumoniae (80% vs. 66%, p=0.066). Significantly more E. coli were susceptible to the combination of co-amoxiclav plus gentamicin compared to K. pneumoniae (88% vs. 80%, p=0.037). Resistance rates to gentamicin were similar (E. coli 86%, K. pneumoniae 80%, p=0.103) (Table 1).

Conclusions: In our hospital, combination prescribing of co-amoxiclav and gentamicin can increase the proportion of E. coli isolates covered. Susceptibility differed between E. coli and K. pneumoniae which may have implications for the review of antimicrobial treatment at the time of organism identification. A cumulative antibiogram can help inform antimicrobial stewardship decisions at patient and hospital level.

Table 1: Percentage of isolates susceptible to antibiotic/ antibiotic combination

<table>
<thead>
<tr>
<th>Escherichia coli</th>
<th>Co-amoxiclav</th>
<th>Amoxicillin</th>
<th>Co-amoxiclav</th>
<th>Ceftriaxone</th>
<th>Ciprofloxacin</th>
<th>Ertapenem</th>
<th>Gentamicin</th>
<th>Meropenem</th>
<th>Piperacillin/Tazobactam</th>
<th>Ticarcillin</th>
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<tr>
<td>80%</td>
<td>96%</td>
<td>49%</td>
<td>82%</td>
<td>66%</td>
<td>100%</td>
<td>86%</td>
<td>100%</td>
<td>95%</td>
<td>70%</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>80%</td>
<td>96%</td>
<td>66%</td>
<td>72%</td>
<td>68%</td>
<td>94%</td>
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<td>96%</td>
<td>72%</td>
<td>70%</td>
</tr>
</tbody>
</table>

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Abstract 3891

Chagas disease diagnosis: comparison between two different native antigen assays

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**Background:** Chagas disease (CD) is an antropozoonosis caused by the parasite *Trypanosoma cruzi* and it is mainly transmitted by reduviid bugs. Due to population mobility and globalization, the burden is growing in non-endemic countries, especially through infected pregnant women and donations. Blood screening for CD antibodies in Latin American adults living in Europe is a cost-effective strategy. Spain is one of the European countries that receives most of Latin American immigrants. WHO recommends performing two different serological tests for CD diagnosis. Our diagnosis algorithm includes a recombinant antigen method screening and a manual native assay as confirmatory test. We aimed to compare two different native CD diagnostic tests, an immunofluorescence assay and an automated chemiluminescence test for the second-step CD diagnosis.

**Materials/methods:** We compare the performance of two CD diagnostic native antigen test: 1) An indirect immunofluorescent assay (Chagas IFA IgG+IgM, Vircell microbiologists, Spain) and 2) an automated chemiluminescence immunoassay (Vitros® Anti-*T. cruzi* assay, Ortho-Clinical Diagnostics, USA). For IFA, samples that show the same fluorescence brightness as positive control were considered positive and lower or no brightness cases were considered negative. For Vitros® Anti-*T. cruzi* assay, samples with index ≥ 1 were considered positive and <1 were considered negative, following the manufacturer's recommendations.

**Results:** A total of 180 samples (148 retrospective and 32 prospective serums) were tested by both methods. Among them, 157 (87.2%) were concordant positive and 11 (6.1%) were concordant negative. Thus, overall agreement was 93%. Discrepant results between assays were found in 12 samples (6.7%); 8 were IFA negative/chemiluminescence positive result and 4 were IFA positive/chemiluminescence negative result. Discordant samples corresponded to CD treated patients in 7 cases (58.3%) and to an 8-months baby from a CD infected mother, with 2 negative microhematocrit tests at birth.

**Conclusions:** An automated and rapid native antigen test is ideal for better efficiency in high-throughput laboratories. Manual techniques are time-consuming, subjective and rely on skilled technicians. Vitros® Anti-*T. cruzi* chemiluminescence immunoassay could be a good choice as a native assay test, combined with a recombinant technique and epidemiological data, for CD diagnosis.

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Abstract 3894

Challenges in infective endocarditis: valvular infective endocarditis in patients with cardiac implantable electronic devices: clinical characteristics and outcome: analysis on a national cohort

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Background: Among patients with valvular infectious endocarditis (valvular-IE) and a cardiac implantable electronic devices (CIED), some but not all have underlying cardiac device-related infection (CDRI). Last guidelines have no specific recommendations for the management of valvular-IE with non-infected CIEDs.

The aim of this study was to assess the clinical characteristics, evolution and prognosis of valvular-IE in patients with CIED (valvular-IE+CIED) without evidence of CDRI.


Results: 3966 cases of IE were identified, 284 (7.2%) were valvular-IE+CIED without CDRI.

Patients with valvular-IE+CIED as compared to valvular-IE without CIED (N=3258) were older (age (median): 75y vs 68y, \( p<0.001 \)) and had more comorbidities (Charlson index (median): 5 vs 4, \( p<0.001 \)). Enterococcus spp. (54 [19%] vs 457 [14%], \( p=0.02 \)), CNS (59 [20.8%] vs 506 [15.5%], \( p=0.02 \)) were more frequently identified among valvular-IE+CIED. Acute heart failure (134 [48%] vs 1340 [41.1%], \( p=0.04 \)) or acute renal insufficiency (128 [45.1%] vs 1140 [35.9%], \( p<0.001 \)) were also more frequent among valvular-IE+CIED. Surgery performance (83 [29.3%] vs 1383 [42.5%], \( p<0.001 \)) was less common and inhospital mortality (131 [46.1%] vs 1087 [33%], \( p<0.001 \)) was higher in CIED-carriers.

We compared patients with (34[12%]) or without device-removal (250 [88%]). In patients without device-removal surgery indication (153 [61.2%] vs 32 [94.1%], \( p<0.001 \)) and surgery performance (51 [20.4%] vs 32 [94.1%], \( p<0.001 \)) were less common. Inhospital mortality was higher (102 [40.8%] vs 7 [20.6%], \( p=0.02 \)).

Risk factors associated with in-hospital mortality in patients with valvular-IE+CIED were Charlson index (OR 1.16 [CI 95% 1.02-1.31]), acute heart failure (5.09 [2.85-9.08]) or acute renal insufficiency (1.99 [1.11-3.56]). Device-removal surgery was associated with lower mortality (0.17 [0.07-0.54]).

Conclusions: Almost half of the patients with valvular-IE+CIED without evidence CDRI died during admission. They were older, had more comorbidities and more complications than patients with valvular-IE without CIED. Device-removal surgery was associated with lower mortality, but it may indicate the success of the surgery itself in severe patients with surgery indication.

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Microbial biosurfactants: a new approach for the control of polymicrobial biofilm development on biomedical materials

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Background: Implantable medical devices are associated with a significant risk of microbial infections caused by biofilm formation at the interface between the device and tissues. In particular, polymicrobial biofilms are associated with more aggressive forms of infection due to the synergistic interactions between the species involved, which increase their virulence, biomass and resistance to antimicrobials. Surface-treated biomaterials commonly used in clinical practice have shown limited efficacy over time and potential toxicity toward cells. In this context, biosurfactants (BSs) have recently emerged as a new generation of anti-adhesive and antimicrobial agents with higher biocompatibility.

Materials/methods: Initially, the ability of microbial strains to form polymicrobial biofilms on silicone under appropriate experimental conditions was determined. Subsequently, silicone surfaces were treated with three different BSs (rhamnolipids, lipopeptides and sophorolipids) by physical adsorption. Anti-biofilm activity was evaluated at 24, 48 and 72 hours. Complementary aspects of biofilm were considered, such as biomass, metabolic activity, viable cell count and micro-structural characterization by SEM, for a complete understanding of the observed phenomenon. Two-way ANOVA was used to compare biofilms formed on BSs treated surfaces and untreated controls. The results were considered statistically significant when \( p < 0.05 \).

Results: Total biomass and metabolic activity of polymicrobial biofilms were significantly higher than the sum of the values detected for the single species. The percentage composition of mixed biofilms, evaluated by viable count, showed a predominance of the bacterial strain (98-99%) compared to the fungal strain (1-2%). All the tested BSs demonstrated an excellent inhibitory activity (>90%) against the formation of polymicrobial biofilms on silicone, both in terms of total biomass, metabolic activity and viable count up to 72 hours of incubation. The SEM observations of the biofilms were consistent with culture data.

Conclusions: The obtained results support the idea that silicone functionalization with biosurfactants represents a promising strategy for the prevention of polymicrobial colonization on medical devices.

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Polyclonal New Delhi metallo-β-lactamase producers Acinetobacter sp. in Algerian hospital

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Background: Métallo-bêta-lactamases (MβLs) begin to play an important role in carbapenem resistance in Acinetobacter baumannii. A recent study, conducted in our hospital, estimates their prevalence at 13% of isolated CRABs (unpublished data). This work will aim to characterize at the molecular level, a collection of CRAB MβL(+) and to determine circulating clones in our hospital.

Materials/methods: One hundred CRAB phenotypically characterized as MβLs (+) was collected over a period of 13 years (2006-2018) at the CHU Mustapha in Algiers. All of them benefited from a PCR search of NDM, VIM, IMP, GIM, SIM, SPM, DIM, FIM, AIM, KHM, and oxacillinases OXA-23, OXA-24, OXA-58 and OXA-51. Each strain, according to its molecular profile, was candidate for one or more of the following techniques: PFGE with ApaI (N = 40), OXA-51 base typing (N = 60), MLST according to the Pasteur scheme (N = 20).

Results: NDM-1 was the only MβL detected. Intrinsic OXA-51 was found in 98% of strains that are distinguished into four profiles:

Profile (P1) NDM alone found in 73% of CRAB MβLs (+). All showed an OXA-94 variant and an ST85 clone. Six pulsotypes were distinguished by PFGE with a predominant profile (A) in 85% of the strains.

Profile (P2) NDM + OXA-23 found in 13 strains: All showed an OXA-64 variant and an ST25.

Profile (P3) NDM + OXA-24 found in one strain that had an OXA-64 variant and an ST25.

Profile (P4) NDM + OXA-58 found in one strain that had an OXA-66 variant and an ST63.

Finally, a last profile (P5) was found in two strains NDM (+), but OXA-51 negative. This result indicates that these species are other than A. baumannii. The MLST analysis distinguishes them in two clones: ST1309 and ST1315. We report with this work, the first world description of ST1315 clone.

Conclusions: This study demonstrates the existence of five different clones of NDM producers Acinetobacter sp in our hospital. These clones being phylogenetically distant testify to probable genetic exchanges between these species.

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Abstract 3900

Would HIV infections and AIDS cases decrease in Japan? Time series analysis using Bayesian inference
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Background: The number of newly diagnosed HIV infections and AIDS patients in Japan appears to be decreasing according to surveillance data, and some might feel optimistic to consider that Japan is catching up with other developed nations, which successfully declined number of new infections. However, whether they continue to decline or not is unclear. Therefore, we conducted a time series analysis using Bayesian inference to predict whether the number continues to decline.

Materials/methods: We used quarterly data on HIV/AIDS from the first quarter, 2001 (2001Q1) to the second quarter, 2019 (2019Q2), provided by Japan Foundation for AIDS prevention. Bayesian analyses were conducted using Markov chain Monte Carlo (MCMC) method, and local linear trend models were constructed for number of newly diagnosed HIV infection without AIDS diagnosis, AIDS cases, and their aggregate. Predictions for the following 5 years (up until the second quarter, 2024) were also made for both models.

Results: Total number of HIV/AIDS patients in the second quarter, 2024 (2024Q2) was predicted to be 214 (95% credible interval 130-443) in the local linear trend model, with declining trend from the latest reported number (295 in 2019Q2), yet with relatively wide credible interval (Figure). For HIV infections alone, cases in 2024Q2 was predicted to be 174 (95%CI 0-370). For AIDS, cases in 2024Q2 was predicted to be 53 (95%CI 0-158). Both again showed decreasing trend with wide credible interval, which could lead to either zero new infection to increased new infections.

Conclusions: Our local linear trend model suggested that number of HIV/AIDS cases in Japan could continue to decline, granted there is no significant change in the trend in future, although credible interval was quite wide. One might not be able to optimistic yet regarding future incidence of HIV/AIDS in Japan, and additional measures to further decrease it may be necessary.

Figure legend: Local linear trend model for quarterly reported data on number of HIV/AIDS patients in Japan from 2001 quarter 1 to 2019 quarter 2, with prediction for the following 5 years. Dot: actual number, solid line: forecasted number, band:95% credible interval, and gray rectangle: predicted numbers.

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Abstract 3902

**Enterovirus D68: biennial circulation and molecular epidemiology in New York, USA, 2014-2018**

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**Background:** Enterovirus D68 (EV-D68) infection has been associated with severe respiratory illness and acute flaccid myelitis (AFM). Following a nationwide outbreak in the US in 2014, only limited EV-D68 detection was reported in 2016 and no data are available thereafter. The objectives of this study were to determine whether EV-D68 continued circulating in the Lower Hudson Valley, New York, and to compare the viral strains recognized since 2014 at regional, national and global levels.

**Materials/methods:** Nasopharyngeal (NP) specimens collected from 2013 through August 2018 from patients in the Lower Hudson Valley, New York were examined for Rhinovirus/Enterovirus (RhV/EV) by the FilmArray Respiratory Panel. Selected RhV/EV-positive and negative NP specimens were analyzed using two EV-D68-specific rRT-PCR assays, Sanger sequencing and a RNA-Seq-based metagenomic next-generation sequencing. Genomic sequences of all EV-D68 strains since 1962 were also retrieved from the GenBank and analyzed for strain genotypes (clades) using genome-based algorithms.

**Results:** A total of 2,264 NP specimens from 2013 through 2018 were examined for EV-D68. EV-D68 was detected in NP samples collected in 2014 (29.4%, 94/320), 2016 (26.6%, 160/602), 2017 (0.9%, 5/562) and 2018 (14.4%, 80/556), respectively, but not in those collected in 2013 (n=25) or 2015 (n=199). Comparative genomic analysis confirmed that distinct EV-D68 strains were circulating and caused outbreaks in New York in 2014 (subclades B1 and B2) and 2016 (subclade B3) with a relatively high viral load in patient specimens. Only low levels of clade D strains were detected in 2017. The majority of EV-D68 strains (92.3%, 24/26) circulating in 2018 belonged to subclade B3. Bioinformatics analysis of 2,746 sequences worldwide (1962-2018) revealed temporal and spatial diversity in EV-D68 population but a shared global evolutionary trend.

**Conclusions:** We reported a biennial regional outbreak and circulation of EV-D68 in the lower Hudson Valley, New York, USA from 2014 to 2018. The establishment of distinct viral strains and variable levels of circulation provides essential information for surveillance, diagnosis and control of EV-D68 infection in the US and worldwide.

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Abstract 3903

Long-read compared to short-read next-generation sequencing of the 16S-23S rRNA region for the identification of bacterial species in clinical samples: a pilot study

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Background: The use of next generation sequencing (NGS) in diagnostic medical microbiology is increasing as these methods overcome limitations of culture and 16S rDNA Sanger sequencing. NGS of the 16S-23S rRNA region [16S-23S NGS] enables identification with a high taxonomic resolution of bacteria in polymicrobial infections. Here we present a pilot study comparing long read sequencing (ONT MinION) with short read sequencing (Illumina MiSeq) of the 16S-23S rRNA region for the identification of bacterial microorganisms in clinical samples.

Materials/methods: Twenty clinical samples were subjected to 16S-23S NGS using short read sequencing (NexteraXT 600-V2 kit, sequencetime 56 hours) as described previously (Sabat et al., 2017) and long read sequencing (ONTSK-LSK109, sequencetime 2 hours). The correct assignment of bacterial species was performed using de novo assembly or mapping to the RRN database (Benítez et. al, 2017) for short and long reads, respectively; this was followed by BLASTN using the NCBI database. Short read sequencing and long read sequencing were compared for length of contigs and consensus sequences. Contigs and consensus sequences with an abundancy of ≥5% were used for the assessment of bacterial identification concordance.

Results: Using Illumina, in total 53 contigs were assembled, with a medium length of 2657 bp (817–5060); in 15/53 (28%) contigs the length of the contig was >3900 bp. MinION yielded in total 46 consensus sequences with a medium length of 3949 bp (2276–4795); in 37/46 (80%) sequences the length was >3900 bp. Illumina detected bacterial species in 19/20 samples; a single bacterial species and polymicrobial communities (2-9 species) were identified in 9 and 10 samples, respectively. Using MinION in 17/20 samples bacterial species were detected; a single bacterial species and polymicrobial communities (2-8) were identified in 7 and 10 samples, respectively. Bacterial identifications using MinION was concordant with Illumina for 31/36 (86%) species. Five disconcordant identifications were only detected using Illumina.

Conclusions: This pilot study demonstrates that long read sequencing of the 16S-23S rRNA region, compared to short read sequencing, enables accurate identification of bacterial species in complex samples. Moreover, using long read sequencing the turnaround time of the application may be shortened by 54 hours.

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Abstract 3904

**Trichomonas vaginalis trends for women and men in a national reference laboratory database**

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**Background:** Trichomoniasis is a common curable sexually transmitted infection (STI), which is not reportable to public health departments in the United States. In women, Trichomonas vaginalis (TV) preferentially infects the vaginal epithelial cells. While most women with trichomoniasis are asymptomatic, others may experience vaginal discharge and/or vulvar irritation. In men, trichomoniasis may be asymptomatic or may cause non-gonococcal urethritis. The objective of this study was to evaluate molecular testing data from a large US commercial laboratory to understand national TV rates.

**Materials/methods:** A retrospective analysis of TV status from January 2014 to August 2019 was conducted using the Quest Diagnostics national database. TV positivity rates were compared to *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoea* (NG) rates overall; rates were also assessed as a function of age, sex, geographic location and co-infection.

**Results:** Greater than 60 million STI test results over 5.5 years were analyzed and TV comprised 9.6% of the total results (women: 90.6% of TV results). Using the national database, TV positivity rates were compared to *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoea* (NG) rates overall; rates were also assessed as a function of age, sex, geographic location and co-infection. Higher rates were noted in certain regions of the US: 7.3% (TV) in women and 3.3% (TV) in men in the Midwest, 5.6% (TV) in women and 2.8% (TV) in men in the Southern United States. The median age for TV-positivity was significantly higher in men than in women (39.3 [IQR: 29.6 – 51.1] years vs 31.8 [IQR: 25.0 – 41.4] years, P<0.0001). TV rates peaked in women aged 41-55 but continued to increase with age in older men (Fig. 1). Among this cohort, CT and GC co-infection rates for TV-positive patients were low (<1%).

**Conclusions:** Compared to the overall rates of TV, the noted higher rates of TV in the Southern and Midwestern United States correlate with historical reported rates of CT and NG. TV rates among older women are consistent with previous reports. While the analysis was limited due to the lack of clinical information, the increase in TV rates in older men (>41 yrs), suggests that additional screening may be warranted in targeted populations.

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**Abstract 3905**

**Intra-abdominal candidiasis after pancreatic transplantation: epidemiology, use of antifungal prophylaxis, risk factors and impact on pancreatic graft**

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**Background:** Information regarding epidemiology and risk factors of intra-abdominal candidiasis (IAC) after pancreas transplantation and its impact on pancreatic graft is scarce. In the present study we aimed to determine the epidemiology, the role of antifungal prophylaxis, risk factors and impact of IAC on pancreatic function in pancreas recipients.

**Materials/methods:** We retrospectively reviewed patients receiving pancreas transplantation from 2008 to 2018. All patients were followed up for one year or until death or pancreas graft loss. IAC was defined as a symptomatic infection in the abdominal cavity presenting with Candida isolation in intra-abdominal fluid cultures. Hospital protocol indicated fluconazole prophylaxis (200mg per day) in all recipients during the first month post transplantation. Graft loss was defined as the need for permanent insulin therapy of ≥ 0.5 units/kg/day and c-peptide levels ≤ 1. Patients presenting graft loss in the first 7 days post transplantation were excluded.

**Results:** Over the ten-year study period, 208 pancreas transplants were performed: 157 simultaneous pancreas-kidney procedures, 26 pancreas-after-kidney and 25 pancreas alone procedures. One-hundred and eight patients (86%) received prophylaxis (mean 16 days, SD ± 12). IAC was developed in 12 recipients (6%), with median days from transplantation of 38 (IQR 5-159). Seventy-five percent of the episodes were developed during the first month post transplantation. Four patients that received antifungal prophylaxis developed an IAC caused by a fluconazole non susceptible Candida species. The one-year graft loss rate for recipients with IAC was 25% compared with 9% for those without IAC (p = 0.09). In the multivariate analysis, surgical reintervention [OR 9.8 (CI 95% 1.9-48.6)] and antifungal prophylaxis [OR 0.1 (CI 95% 0.04-0.6)] were independently associated with IAC. Six patients died during the study period, none related with IAC.

**Conclusions:** Six percent of pancreas recipients developed IAC, especially in the first month post transplantation. Surgical reintervention was a risk factor to developed IAC whereas antifungal prophylaxis was a protective factor. IAC was not associated with one-year graft loss neither related with mortality.

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Performance of the sōna Aspergillus galactomannan lateral flow assay from serum samples for the diagnosis of invasive aspergillosis in patients after haematopoietic stem cell transplantation

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Background: One cornerstone for diagnosis of Invasive Aspergillosis (IA) is the detection of galactomannan (GM). So far, enzyme-immunoassays (EIA) are used for this purpose but they are usually not performed daily resulting in an undesired delay of test results. Immunochromatographic assays, like the sōna Aspergillus-Galactomannan-Lateral-Flow-Assay (Asp-LFA), may overcome this disadvantage. The Asp-LFA detects GM in serum and bronchoalveolar-lavage fluid in approximately one hour without the need for batch testing. To compare the performance of the Asp-LFA with the Platelia™ Aspergillus-Ag-EIA (Asp-EIA) we have conducted a study on sera from patients after allogeneic hematopoietic stem cell transplantation (alloHSCT).

Materials/methods: All patients that underwent alloHSCT during a one-year period were enrolled. Patients with IA were classified according to the EORTC/MSG 2008 guidelines. The Asp-LFAs were analyzed with a digital reader provided by the manufacturer.

Results: A total of 547 sera from 101 patients after alloHSCT were tested. By the end of hospitalization one proven, 10 probable and 19 possible IA cases were diagnosed. The sensitivity and specificity of a single positive Asp-LFA for proven and probable IA were 80 % and 57 %, respectively. Repeat testing of the Asp-LFA-positive serum samples revealed that the positive result was reproducible in only 58 % of samples. The sensitivity and specificity of a reproducibly positive Asp-LFA for proven and probable IA were 80 % and 77 %, respectively. The Asp-EIA and the Asp-LFA are both detecting GM. To directly compare the assays the EORTC/MSG-classification was performed with only culture and [1→3]-β-D-glucan as mycological criteria. In this case 1 proven, 8 probable and 21 possible IA cases were diagnosed. The sensitivity and specificity of a reproducibly positive GM-test for proven and probable IA were 22 % and 97 % for the Asp-EIA and 78 % and 70 % for the Asp-LFA, respectively. The GM levels determined by both tests correlated significantly (r=0.32, p<0.001).

Conclusions: The Asp-LFA shows a superior sensitivity compared to the Asp-EIA. Handling of the Asp-LFA is easy and time-to-result is below 60 min. However, it is highly recommended to use a digital reading device and to repeat testing in case of positive results.

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Abstract 3907

**The trend of changes in paranasal computed tomography of patients with haematologic malignancies and febrile neutropaenia**

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**Background:** The aim of this study was to evaluate the clinical significance of early screening of computerized tomography scan of paranasal sinuses (PNS CT) in hematologic malignancies before chemotherapy and evaluation of changes after chemotherapy and during neutropenia.

**Materials/methods:** All forty new case of hematologic malignancies with febrile neutropenia in a teaching referral hospital between 2017 and 2018 were enrolled in this study. All of these patients underwent PNS CT before chemotherapy, along with other preliminary investigations. Symptoms and signs indicating infectious process meticulously were followed and monitored before and during chemotherapy as well as occurrence of febrile neutropenia. All patients were clinically and radiologically evaluated regarding presumptive diagnosis of invasive fungal sinusitis during prolonged febrile neutropenia (more than 4 days). PNS CTs before and after chemotherapy of all patients were compared by two radiologists and were evaluated based on histopathologic findings of nasal and or paranasal biopsies.

**Results:** Around 50% of patients with paranasal abnormality suggesting inflammatory process including microbial and fungal sinusitis during prolonged febrile neutropenia (more than 4 days) were confirmed that have had similar involvement with no significant changes before starting chemotherapy. The histopathologic examination of sinuses also showed no evidence of invasive fungal infection by endoscopic biopsy. Therefore, the abnormal findings including mucosal thickening in PNS CT during prolonged febrile neutropenia were not consistent with the confirmed invasive fungal infection. The rate of mortality was 2.5% without association to invasive fungal sinusitis.

**Conclusions:** The considerable number of patients with underlying hematologic malignancies has paranasal sinus involvement such as mucosal thickening that may be misleading as probable invasive fungal sinusitis during hazardous phase of prolonged febrile neutropenia. Thus, performing PNS CT scan before initiation of chemotherapy even though in asymptomatic patients could be helpful to decrease the number of suspected and probable cases of fungal sinusitis based on abnormal findings in PNS CT scan followed by the number of cases undergoing sinus endoscopic surgery.

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Abstract 3908

**BIOFIRE FILMARRAY pneumonia panel in the evaluation of severe lower respiratory tract infections**

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**Background:** Although viruses are considered the most common detected cause of admitted cases of lower respiratory tract infections [LRITs] [Etiology of Pneumonia in the Community [EPIC] prospective, multicentre, active surveillance study], data for patients with severe LRIT are missing. This study aimed to define the epidemiology of severe LRIT using the BIOFIRE® FILMARRAY® Pneumonia plus Panel (PNplus Panel) and the association of the results with the host inflammatory state.

**Materials/methods:** This was a sub-study of the interventional PROGRESS trial where procalcitonin (PCT)-guidance for early stop of antibiotics was used to prevent infection-associated adverse events in patients with sepsis (ClinicalTrials.gov NCT03333304). PNplus Panel was performed retrospectively using frozen lower respiratory samples of 90 patients with LRIT and sepsis defined according to Sepsis-3. Primary endpoint of the present sub-study was the comparison of the detection rate of pathogens between conventional microbiology [blood, sputum, pleural fluid cultures and urine antigen detection] and PNplus Panel. Secondary endpoints were the association of the PNplus Panel with the inflammatory host response and detection of antibiotic resistance.

**Results:** 56 patients with community-acquired pneumonia (CAP) and 34 with healthcare-associated pneumonia (HCAP) were studied; median pneumonia severity index was 113 (interquartile range 88-135). PNplus detected at least one pathogen in 65 patients (72.2%) compared to 10% detected by conventional microbiology (p<0.0001); bacteria were the most common pathogens [Figure]. Median PCT was 0.49 ng/ml among patients with ≥105 copies/ml of a bacterial pathogen compared to 0.18 ng/ml in detection at lower loads (p=0.004). SOFA score, serum CRP and white blood cells did not differ between patients with undetected, bacterial, viral or bacterial-viral cause of infection. Median PCT was 0.52 ng/ml among patients with bacterial pathogens compared to 0.19 ng/ml among patients with viral pathogens (p: 0.045). At least one resistance gene was detected in 14.4% of samples, being more common in HCAP versus CAP (32.2% vs 5.1%; p: 0.001).

**Conclusions:** PNplus detects severe pneumonia pathogens at significantly greater rate than conventional microbiology. The greater circulating PCT levels reflect the true virulence of the detected pathogens.

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Failure of artemether-lumefantrine treatment for Plasmodium falciparum malaria imported from sub-Saharan Africa to the UK

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Background: Oral artemisinin combination therapy (ACT) is recommended for all uncomplicated cases of Plasmodium falciparum malaria. ACT resistance is increasingly prevalent in South-East Asia, but uncommon in Africa.

Materials/methods: We report two cases of recrudescent falciparum malaria that occurred despite full adherence to ACT in the Tropical and Infectious Diseases Unit in Liverpool. We reviewed our pharmacy dispensing records to estimate the failure rate of ACT in our institution over the preceding year.

Results: Patient 1 is a 53-year old man who had been working in wildlife conservation in Zambia. He was admitted four days after his return with a P. falciparum parasitaemia of 1.3%. He initially received intravenous artesunate, followed by a course of artemether-lumefantrine (six doses over 60 hours) as an inpatient. Repeat blood films at 48 hours showed a 0.001% parasitaemia. His symptoms recurred 19 days after discharge, with a 1% parasitaemia. He was re-treated with artemether-lumefantrine, followed by a full course of quinine and clindamycin. His parasitaemia cleared within 48 hours and remained negative 13 days later.

Patient 2 is a 51-year old man with virologically-suppressed HIV infection, who returned from visiting relatives in Mozambique. He presented five days later with a 0.9% P. falciparum parasitaemia. He completed six doses of artemether-lumefantrine as an inpatient; repeat films at 48 hours showed a parasite count of 0.1%. One month later he complained of ongoing malaise and a repeat film showed a parasitaemia of 0.01%. He was treated with atovaquone-proguanil; repeat films on treatment and two weeks later were negative.

All blood films for both cases showed P. falciparum trophozoites only. Neither patient had travelled abroad between presentation and recrudescence.

Between July 2018—July 2019, 18 patients were prescribed artemether-lumefantrine as inpatients on the unit, of whom 16 had falciparum malaria acquired on the African continent. This translates to an ACT failure rate of 12.5% [95% CI 2.2—39.6%] for the treatment of P. falciparum.

Conclusions: Monitoring of malaria treatment outcomes in real-world settings is key to detecting emerging resistance. Ongoing genotypic analysis may elucidate the mechanism of treatment failure in the two cases reported here.

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Abstract 3911

**Genetic score involving polymorphisms of innate immune receptors for predicting cytomegalovirus infection in solid organ transplant recipients: a prospective multi-centre cohort study**

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**Background:** Genetic polymorphism at the immune system may increase the risk of post-transplant infections. The aim of this study was to assess the influence of genetic variability of certain innate immune receptors on the risk of developing Cytomegalovirus (CMV) infection after solid organ transplantation (SOT) in patients at highest risk for CMV infection.

**Materials/methods:** CMV-seronegative recipients of grafts from CMV-seropositive donors undergoing heart, liver, kidney or pancreas transplantation from 7 centers in Spain during a 3-year period were included. All recipients received 100 days-prophylaxis with valganciclovir. Clinically and/or functionally relevant single nucleotide polymorphisms (SNPs) from TLR2, TLR3, TLR4, TLR7, TLR9, AIM2, MBL2, IL28, MYD88, IFI16, IRAK2 and IRAK4 were assessed by quantitative Polymerase Chain Reaction (qPCR) or sequence-based typing (PCR-SBT). The incidence of asymptomatic CMV infection and disease according to SNPs was estimated. A predictive CMV-score based on SNPs combinations was created by logistic regression analysis.

**Results:** A total of 116 patients in 7 centres were recruited. Sixty-one patients (53%) presented at least one episode of CMV infection, 33 asymptomatic and 28 had CMV disease, at a median time of 163 days. Recurrent CMV infection occurred in 11 (9%) patients. There were no differences regarding major characteristics among groups depending on receptor gene SNPs. In univariate analysis, none of the SNPs analyzed was associated with either asymptomatic CMV infection or CMV disease. According to the CMV-score, the probability of CMV disease with combined SNPs in TLR4, TLR3, TLR7, AIM2 and MBL2 was 83%, while decreased to 6% with combined SNPs in TLR9, IL28 and IFI16 (p =0.002). The AUC of the model for predicting CMV disease was 0.66, with sensitivity and specificity of 64 and 72%, respectively. In addition, the probability to develop a asymptomatic CMV infection, conferred by genetic variants of TLR4, TLR7 and AIM2 was of 68 % (p=0.07).

**Conclusions:** This genetic CMV-score was useful to calculate the risk of developing a CMV disease in CMV-seronegative recipients of grafts from CMV-seropositive donors undergoing SOT.

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Abstracts 2020

Abstract 3912

Rectal colonisation by drug-resistant bacteria in nursing home residents in Crete, Greece

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Background: Multidrug-resistant organisms (MDROs) pose important public health problem worldwide. Residents of long term care facilities (LTCFs) are at high risk of being colonized and infected by MDROs.

Materials/methods: This is a point-prevalence study detecting colonization of MDROs conducted in 6 LTCFs in Crete, Greece. Rectal swabs were cultured in order to detect MDROs, while risk factors for colonization were evaluated. Data collected included age, gender, duration of stay in LTCFs, comorbidities, antibiotic exposure, and recent hospitalization.

Results: A total of 137 LTCF residents aged 65 years or more were enrolled in this study. Mean age was 82.1 years and 19.7% were male (27 residents). In total, 255 isolates were cultured; E. coli, K. pneumoniae and P. aeruginosa were the commonest isolates cultured in 64.3%, 11.8% and 5.5% samples, respectively (164, 30 and 14, isolates respectively). Among the microbes cultured, 17.6% (45 isolates) had the extended-spectrum beta-lactamase (ESBL) phenotype, while 18% (46 isolates) were MDROs. Statistical analysis did not reveal any correlation between age, duration of stay in the LTCF and Charlson Comorbidity Index and the presence of the ESBL phenotype. However, contingency analysis identified male sex to be associated with higher possibility of ESBL production.

Conclusions: Colonization by MDROs is common in LTCFs in Crete, being in similar levels to other European countries.

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Correlation between rubella IgM positivity and detection of cytomegalovirus/parvovirus B19 primary infection in pregnant women accessing the Tuscany Reference Centre for Infectious Diseases in Pregnancy

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Background: In the majority of European countries, pregnant women are routinely tested for Rubella but not for Cytomegalovirus (CMV) and Parvovirus B19 (B19V), two potentially harmful pathogens for the fetus. Positive Rubella IgM results at screening may be due to recent Rubella infection or false positive, sometime do to cross-reactions between Rubella IgM and other intercurrent viral infections such as CMV and B19V. The aim of the study is to investigate the correlation between Rubella IgM positivity and CMV or B19V primary infection in pregnancy.

Materials/methods: Pregnant women consecutively evaluated between 2016 and 2019 at the Tuscany Reference Center for Infectious Diseases in Pregnancy for positive anti-Rubella IgM were enrolled in this retrospective observational study. All women were assessed for possible recent Rubella, CMV and B19V infections.

Results: A total of 380 pregnant women were included. The mean age was 34-years-old (16-49, SD 5.5), the mean gestational age was 14 gestational weeks (5-39, SD 6.1). 142/380 (37.4%) had a serological evidence of rubella immunity before pregnancy, 28/380 (7.4%) had been previously vaccinated. All women underwent a second serological test for Rubella, and IgM were confirmed in 119 (31.3%). No cases of Rubella acquired during pregnancy were diagnosed. Serology for CMV was performed in 327 (86.1%) women and B19V in 258 (67.9%) showing reactive IgM result in 18 (5.5%) and 6 (2.3%) cases respectively (details in Table). Only one primary CMV infection and one recent B19V infection have been detected. The patient with primary CMV infection had negative CMV IgM (despite Rubella IgM positivity at qualitative test), low CMV IgG avidity index and positive DNA in urine sample. The patient with recent B19V infection had borderline IgM and IgG (IgM antibody titer for Rubella less than 2 times the cut-off of positivity) and positive DNA in blood sample.

Conclusions: Recent CMV or B19V infections were found in 1 of 327 (0.3%) and 1 of 258 (0.4%) pregnant women with positive IgM Rubella suggesting that these infections are a rare cause of false positive Rubella IgM. However, considering the potential fetal adverse outcome of these infections, testing may be justified.

<table>
<thead>
<tr>
<th>Rubella IgM at first serology</th>
<th>Rubella IgM at indoor serology</th>
<th>CMV IgM</th>
<th>B19V IgM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Borderline or positive</td>
<td>ELFA+</td>
<td>Borderline</td>
</tr>
<tr>
<td>Borderline</td>
<td>57</td>
<td>13/57, 22.8%</td>
<td>6/13, 46%</td>
</tr>
<tr>
<td>Qualitative test</td>
<td>34</td>
<td>18/34, 53%</td>
<td>14/18, 78%</td>
</tr>
<tr>
<td>Titer &lt; 2X</td>
<td>197</td>
<td>42/197, 21.3%</td>
<td>12/42, 28.6%</td>
</tr>
<tr>
<td>Titer &lt; 3X</td>
<td>46</td>
<td>15/46, 32.6%</td>
<td>10/15, 66.7%</td>
</tr>
<tr>
<td>Titer &lt; cut-off</td>
<td>12</td>
<td>7/12, 58.3%</td>
<td>6/7, 85.7%</td>
</tr>
<tr>
<td>Titer &gt; cut-off</td>
<td>34</td>
<td>24/34, 70.6%</td>
<td>22/24, 91.7%</td>
</tr>
</tbody>
</table>

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Epidemiological characteristics of *Stenotrophomonas maltophilia*-associated lower respiratory tract infection in Qatar: a one-year retrospective study

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**Background:** Stenotrophomonas maltophilia is rapidly emerging as a multi-drug resistant nosocomial pathogen causing life-threatening opportunistic pneumonia. Incidence of infections by *S. maltophilia* has been reported as 0.07-0.4% of hospital discharges. This is the first study from Qatar indexing the epidemiological characteristics and antibiotic susceptibility of *S.maltophilia*.

**Materials/methods:** This retrospective descriptive epidemiological study was done by analyzing inpatient respiratory isolates of *S.maltophilia* during 2016-17. Out-patients, children below 14 years and non-respiratory samples were excluded. Clinical records were reviewed to identify possible risk factors. Infection and colonisation was identified using CDC algorithm for clinically defined pneumonia and statistically analyzed using chi-square test and Pearson’s correlation.

**Results:** *S.maltophilia* was isolated from 2.07% (317/15312) of all respiratory samples received in microbiology lab during our study period. 317 patients studied had a mean age of 60.5±20 years and 68% were men. Most of the isolates were from sputum (179), followed by endotracheal tube (43), tracheal aspirate (39), Bronchial wash (25), bronchoalveolar lavage (17) and blood (14). 67% of them were hospitalised for more than 2 weeks, 39.1% were on mechanical ventilation and 88% had received a broad-spectrum antibiotic prior to the event. 29.1% were deemed to have infection and 70.9% colonisation. Incidence of infection in those with Charlson’s Co-morbidity Index (CCI) ≥3 was 36.5% compared to 24.2% in those with CCI<3 (Relative Risk (RR)=1.52;95%CI:1.04,2.18; p=0.01). Patients with recent chemotherapy, immunosuppressant or steroid use had a significantly higher risk of infection compared to those without [69.2% versus23.3% (RR=2.96;95%CI:2.2,3.9; p<0.05)]. Most common symptoms in patients with infection were fever (96%) and expectoration (61.9%). Most common radiological finding was lobar consolidation (71.6%). Mean CRP and procalcitonin were 106.5±15.5mg/l and 12.3±14ng/ml. Overall mortality was 16.3%. Patients with IBMP-10 score ≥2 had 22.8% mortality compared to 5.7% in those with score<2 (RR=3.9;95%CI:0.9,16.6; p=0.015). As per CLSI break-point values, Trimethoprim-Sulphamethoxazole (TMP-SMX) showed highest sensitivity (97.8%) followed by colistin (83.3%), levofloxacin (71.6%), ceftazidime (37.8%), tigecycline (36.6%), ciprofloxacin (8.8%) and aztreonam (5.6%). 0.3% of samples were pan-drug resistant.

**Conclusions:** *S.maltophilia* causes nosocomial pneumonia in immunocompromised and patients with CCI≥3 with high risk of mortality in those with IBMP-10≥2. Strains from Qatar show good susceptibility to TMP-SMX, colistin and levofloxacin. Tigecycline, aztreonam, ceftazidime and ciprofloxacin have high rates of resistance and should never be used alone.
Prevalence of Mycoplasma genitalium and macrolide resistance in Israel

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Background: Mycoplasma genitalium (MG) is one of the leading pathogens causing urethritis, cervicitis and PID. Macrolide and quinolone resistance are increasingly reported in various parts of the world and have significant impact on treatment efficacy. We examined the prevalence of this pathogen in a large cohort of patients in Israel and looked for macrolide resistance mutations.

Materials/methods: Retrospective observational study over 7 years (2013-2019), in a Health Maintenance Organization insuring 1.2 million individuals. Urine and genital samples were examined by PCR for 5 clinically relevant pathogens (N. gonorrhoea, C. trachomatis, M. genitalium, U. urealyticum and T. vaginalis) using Allplex™ STI Essential Assay (Seegene, Seoul, South Korea). A subgroup of 191 MG positive samples were tested for mutations at positions 2058 and 2059 in the 23S rRNA gene, responsible for macrolide resistance using Segene Allplex MG & AzIIR Assay.

Results: In this study 74,000 samples were included, collected from both patients with a clinical syndrome or asymptomatic individuals going through screening. From 2013 to 2019, 8% of the samples were positive for one of the 5 clinically relevant pathogens. This rate was stable over the years. MG accounted for 22.6% of the positive samples (second only to CT, which accounted for 52%). The rate of MG increased gradually from 16% in 2013 to 27.9% in 2019. Of 191 MG positive samples (collected during the last study year) macrolide resistance mutation was found in 47 (24.6%).

Conclusions: MG is the second most prevalent pathogen identified in urine and genital samples in Israel. It is responsible for 23% of all positive tests and its prevalence has been increasing. Macrolide resistance in MG is substantial reaching 25%. These results highlight the need to reconsider current treatment guidelines of urethritis and cervicitis in Israel, considering implementation of resistance guided therapy.

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EUCAST temocillin breakpoints and antimicrobial susceptibility testing guidelines
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Background: Temocillin, a beta-lactam agent active against many ESBL-producing Enterobacterales, has primarily been used in infections originating from the urinary tract, including urosepsis caused by Escherichia coli and Klebsiella pneumoniae. Temocillin is approved in some EU countries, but was never subjected to the centralized European Medicines Agency procedure. In the absence of EUCAST breakpoints, several national breakpoints were used.

Materials/methods: The standard EUCAST processes for setting breakpoints were used. Clinical outcome and PK-PD data were assessed together with MIC distribution data. Both broth microdilution MIC testing (ISO 20776-1) using freeze-dried Sensititre™ plates and disk diffusion according to EUCAST were performed on E. coli (n=65), K. pneumoniae (n=19) and Proteus mirabilis (n=8). Disk diffusion was performed on Mueller-Hinton agar with temocillin 30-µg disks from four manufacturers (Figure 1), and for a subset of isolates, also on temocillin 5- and 15-µg disks (Mast Diagnostics). Inhibition zones were read both when i) ignoring isolated colonies within zones and ii) taking colonies into account.

Results: After assessing data on two alternative dosing schedules, clinical outcome, the PK-PD, and MIC distributions for organisms without and with resistance mechanisms, EUCAST concluded that wild-type organisms have MIC values below or equal to 16 mg/L which is the proposed susceptible breakpoint. Organisms with wild-type MIC values should be treated with the highest dose when causing complicated urinary tract infection (cUTI) [including non-severe urosepsis] whereas non-cUTI with complicated organisms can be treated with the standard dose schedule because of the high urinary concentration. The “Susceptible, increased exposure” (S≤0.001, R>16 mg/L) category is therefore appropriate. The best correlation between disk diffusion and broth microdilution MIC determination was achieved using a 30-µg disk (rather than a 5- or 15-µg disks) and when ignoring isolated colonies within zones [Figure 1]. Corresponding zone diameter breakpoints were set at S≥50 mm, R<17 mm.

Conclusions: The EUCAST breakpoints (S≤0.001, R>16 mg/L) and new disk diffusion methodology will enable to test and report temocillin for E. coli, K. pneumoniae and P. mirabilis with EUCAST methodology. The breakpoints and the category “Susceptible, increased exposure” signal the need for high exposure when treating cUTI, including non-severe urosepsis with temocillin.

Figure 1. Inhibition zone diameter distributions for temocillin 30 µg (disks from Bio-Rad, BD, Mast Diagnostics and Oxoid/Thermo Fisher Scientific) for isolates tested on Mueller-Hinton agar from BBL/BD and Oxoid/Thermo Fisher Scientific in parallel, resulting in 8 disk diffusion results per isolate for a) Escherichia coli (n=65), Klebsiella pneumoniae (n=19) and Proteus mirabilis (n=8) and b) Escherichia coli (n=65). Isolated colonies within the inhibition zones were ignored when reading zone diameters. EUCAST resistant zone diameter breakpoint (17 mm) is shown as a dotted line.

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Type I interferons mediate antiviral resistance to Zika virus in human macrophages

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Background: Since the recent emergence of Zika virus (ZIKV), major aspects of its pathogenesis remain poorly defined. ZIKV efficiently evades type I interferon (IFN-α/β) responses, which are central to innate antiviral defence: a key question is whether IFN-α/β is therefore redundant in human ZIKV immunity. Existing murine models are unhelpful as modelling ZIKV disease in mice has necessitated deletion of the IFN-α/β receptor (IFNAR). We therefore addressed this question in human macrophages, key effector cells of innate antiviral immunity, which are implicated in ZIKV persistence, transmission and neuropathology.

Materials/methods: We employed a validated model of human tissue macrophages derived from induced pluripotent stem cells (iPSC), incorporating unique patient-derived cells lacking the human IFN-α/β receptor (IFNAR2). Wild-type and IFNAR-deficient macrophages were challenged with African and Asian lineage ZIKV strains. Innate signalling, infection and cytopathic effects were quantified by qPCR, immunofluorescence, immunoblot, plaque assay and live cell viability imaging.

Results: Wild-type macrophages mounted a robust innate interferon response to ZIKV infection, resulting in the expression of key antiviral interferon stimulated genes (ISGs). This IFN-α/β-mediated antiviral state effectively restricted viral replication and limited cytopathic effects. In contrast, cells lacking IFNAR showed markedly enhanced viral infection (12.06% wild-type vs 63.75% IFNAR2/- macrophages expressing ZIKV antigen by immunofluorescence, p<0.0001) and virus-induced cell death (Figure 1). This was accompanied by an absence of antiviral ISG induction, despite normal induction of innate interferons, reflecting a failure of IFNAR signalling. This phenotype was recapitulated in wild-type control cells by (a) blockade of downstream IFNAR signalling with ruxolitinib and (b) deletion of IFNAR2 by CRISPR/Cas9 gene editing, and was partially rescued in IFNAR-deficient cells by IFNγ.

Conclusions: These data reveal that IFN-α/β is central to ZIKV resistance in human macrophages, and that despite ZIKV countermeasures, IFN-α/β plays an important role in human ZIKV immunity. Future work is needed to understand the generalisability of this mechanism in other disease-relevant cells and tissues. Nevertheless, our data raise the possibility that defects in IFN-α/β immunity may underlie some extreme clinical phenotypes of ZIKV disease.

Figure 1. Live-cell immunofluorescence. MOI = multiplicity of infection, ns = non-significant, Rux = ruxolitinib, *** = p<0.0001.

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Abstract 3921

Ceftobiprole susceptibility of European Gram-positive and Enterobacteriaceae clinical isolates from different infection sources collected in 2018

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Background: Ceftobiprole is an advanced-generation, broad-spectrum parenteral cephalosporin approved in 17 European and eight non-European countries for the treatment of adults with community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP) (excluding ventilator-associated pneumonia) caused by susceptible Gram-positive pathogens, including methicillin-resistant Staphylococcus aureus (MRSA), and Gram-negative pathogens. The present investigation reports susceptibility of European Gram-positive and Gram-negative isolates from 2018 as part of an ongoing susceptibility surveillance program.

Materials/methods: A total of 4284 clinical isolates were collected from European hospitals in 2018, including Enterobacterales, Pseudomonas aeruginosa, MRSA, MSSA, Streptococcus pneumoniae and Haemophilus influenzae. These were collected from various infection sources including respiratory, skin, genitourinary tract, body fluid and gastrointestinal infection sources. MIC determination was performed by broth microdilution and susceptibility interpreted using EUCAST clinical breakpoints.

Results: A summary of ceftobiprole susceptibilities are shown in the Table.

<table>
<thead>
<tr>
<th>Organism / Group [n]</th>
<th>Breakpoints [μg/L]</th>
<th>%Susceptible</th>
<th>MIC50</th>
<th>MIC90</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus [1813]</td>
<td>≤2 ≥4</td>
<td>99.7</td>
<td>0.5</td>
<td>2</td>
</tr>
<tr>
<td>MRSA [530]</td>
<td>≤2 ≥4</td>
<td>98.9</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>MSSA [1283]</td>
<td>≤2 ≥4</td>
<td>100</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Streptococcus pneumoniae [626]</td>
<td>≤0.5 ≥1</td>
<td>98.7</td>
<td>≤0.015</td>
<td>0.5</td>
</tr>
<tr>
<td>Enterobacterales [1845]*</td>
<td>≤0.25 ≥0.5</td>
<td>75.6</td>
<td>0.06</td>
<td>&gt;64</td>
</tr>
<tr>
<td>P. aeruginosa [570]</td>
<td>≤4** ≥1</td>
<td>63.2</td>
<td>4</td>
<td>32</td>
</tr>
<tr>
<td>H. influenzae [153]</td>
<td>≤4** ≥1</td>
<td>100</td>
<td>0.06</td>
<td>0.5</td>
</tr>
</tbody>
</table>

*seven species including Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, K. oxytoca, K. pneumoniae, Proteus mirabilis, and Serratia marcescens; **Non-species related PK/PD breakpoint

Conclusions: The susceptibility data for ceftobiprole show that the majority of Gram-positive bacterial isolates were susceptible. All MSSA isolates were susceptible to ceftobiprole, followed by 98.9% of MRSA and 98.7% of pneumococci. All MSSA and MRSA were susceptible to daptomycin and vancomycin and 100% of pneumococci were linezolid-susceptible. Susceptibility of the enteric bacteria to ceftobiprole was 75.6%. Of those resistant to ceftobiprole, resistance to ampicillin and other cephalosporins was also high, as expected, indicating the vast majority of these were probably extended-spectrum beta-lactamase producers. Almost two-thirds of pseudomonads and all H. influenzae were susceptible to ceftobiprole. Overall, the data further support the clinical utility of ceftobiprole.

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Abstract 3923

In silico and in vitro investigation of a novel putative toxin-antitoxin system in Acinetobacter baumannii

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Background: Toxin-antitoxin (TA) systems are widespread among bacteria, archaea and fungi. They play different roles, such as postsegregational killing, abortive infection, and persister formation, and have recently been identified as novel drug targets. TA systems have been classified into six types (I-VI), depending on the nature of antitoxin and its mode of action. CptAB Type IV-TA is one of the least characterized systems that remain limited to a few bacterial species, such as Escherichia coli. This study aimed to screen different Gram-negative bacteria for this Type IV-TA, especially in Acinetobacter baumannii, known for its antimicrobial resistance.

Materials/methods: BlastP similarity searches and maximum likelihood phylogenetic analysis for both CptA and CptB were used for in silico detection of the distribution and conservation of these proteins and their encoding genes among different bacteria. In vitro, real-time reverse transcription-PCR was used to determine the differential expression of the cptAB homologous system of A. baumannii ATCC 17978 upon exposure to different stresses, including high temperature (42°C), oxidative stress, and some antibiotics.

Results: BlastP analysis of CptAB showed its wide distribution among Gram-negative bacteria (amino-acid identity: 24%–100%, over 70% coverage). Maximum likelihood phylogenetic analysis for both CptA and CptB delineated two major groups, in each of which Acinetobacter spp. clustered together. Moreover, multiple sequence analysis indicated the conservation of cptA and cptB in 128 strains of A. baumannii in the same syntenic order. A slight increase in the transcription of both cptA and cptB was observed upon exposure of A. baumannii to either 42°C (by 1.3 folds) or the protein synthesis-inhibiting antibiotic, streptomycin (by 1.2 and 1.6 folds, respectively). However, exposure to oxidative stress and other classes of antibiotics, e.g., ciprofloxacin and meropenem, caused transcriptional downregulation of both genes.

Conclusions: In silico analysis suggested a potential TA system in A. baumannii, based on sequence similarity to CptAB features in E. coli. Under the influence of some antibiotics and other stresses, transcriptional changes were observed in the A. baumannii system. Taken together, these data suggest that CptAB contributes to the bacteriostatic or cidal mechanisms of antibiotics and other stress agents against A. baumannii.

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Severe cryptococcal meningoencephalitis with large vessel vasculopathy and multi-territory cerebral infarcts
Caitlyn Sun1,2, Max Kernich1,2, Nicholas Chia1,2, Renjy Nelson1,2

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Aim: To describe a unique clinical case of suspected cryptococcus induced vasculitis.

Materials/methods: Clinical case report and literature review.

Results: A 29-year-old Indigenous Australian man presented with fever and seizures on a background of alcohol misuse and HTLV-1 infection. His conscious state deteriorated despite empirical antibiotics and he was admitted to intensive care for intubation and ventilation. No toxic or metabolic aetiology was identified.

Serum cryptococcal antigen was detected at a titre of 1:1024. Lumbar puncture revealed an elevated opening manometric pressure of >35 cmH2O, polymorphonuclear cell count of 70x106/L and elevated protein at 5.59g/L. CSF microscopy identified cryptococci on India ink stain with identification of Cryptococcus neoformans var. grubii via MALDI ToF.

CT brain demonstrated moderate hydrocephalus and MRI brain unexpectedly revealed cortical diffusion restriction in bilateral insulae, right anterior and left middle cerebral artery territories [Figure 1A]. Gadolinium-enhancement was demonstrated over the cerebral convexity [Figure 1B]. CT angiography revealed widespread long segment patchy calibre reduction of all intracranial arteries without atherosclerosis or extracranial arterial disease [Figure 1C]. The patient was commenced on flucytosine and liposomal amphotericin B, and a continuous lumbar drain was inserted. Opening CSF pressure was 55 cmH2O.

Investigations for other causes of small and medium vessel vasculitis were unremarkable. There was no improvement in the patient’s severe obtundation and he died after supportive measures were withdrawn.

Cryptococcal vasculitis is rarely reported and the exact mechanism is unknown. It has been postulated that an inflammatory process leads to vessel thrombosis, compression or spasm and subsequent infarction. Stroke in patients with Cryptococcus infection usually causes small vessel infarction of the basal ganglia, internal capsule and thalamus. Large vessel ischaemic stroke appears to be rare in patients with Cryptococcal meningitis. Three such cases have described, predominantly in older patients with cardiovascular and cerebrovascular comorbidities that may have provided a separate stroke mechanism.

Conclusions: Our case is unique given the severity and extent of the multi-territory cortical infarction in a patient with cryptococcal central nervous system infection.
Abstract 3926

Oral immunotherapy with secretory IgA improves survival in the hamster model of *Clostridioides difficile* infection

William Weiss*1, Michael Simon2,3,4, Stephan Kiessing1, Estelle Chiari2, Mark Pulse1, Stephen Brown2, Christoph Von Eichel-Streiber6, Hanne Gerding5, Maurice Mandago5

1UNT System College of Pharmacy, Fort Worth, United States, 2Secretory IgA Inc, Ann Arbor, United States, 3Wayne State University School of Medicine, Detroit, United States, 4Oakland University William Beaumont School of Medicine, Rochester, United States, 5PreviPharma Consulting, Mannheim, Germany, 6tgcBIOMICS GmbH, Bingen, Germany

**Background:** We propose that IgA antibodies recovered from healthy donor plasma have the potential to be a new orally administered antibody therapy for the treatment of *C. difficile* disease. This will create a new oral immunoglobulin application based on the oral use of IgA. The current study was performed to evaluate the efficacy of IgA preparations w/wo vancomycin in the hamster *C. difficile* infection model.

**Materials/methods:** The IgA was shown by ELISA and neutralization assays to possess specific antibodies to *C. difficile* toxins A and B. Hamsters were infected with $10^4$ *C. difficile* spores followed by 10 mg/kg SC clindamycin and then administration of 5 or 10 mg/kg vancomycin QD (q24hr) for 5 days. Animals were also orally administered either secretory IgA (recombinant secretory component+IgA dimer-polymer)/monomeric IgA mixture at 7 mg/kg TID (q8hr) for 21 days or hyperimmune secretory IgA/monomeric IgA mixture at 1 mg/kg BID (q12hr) for 11 days.

**Results:** Infection resulted in 100% mortality of untreated controls by day 4. Administration of vancomycin alone, at 5 mg/kg or 10 mg/kg, resulted in 70% or 90% survival, by day 13 and 40% or 60% survival at day 21, respectively. The combination of 5 mg/kg vancomycin + secretory IgA/monomeric IgA (TID x 21 days) or 10 mg/kg vancomycin + secretory IgA/monomeric IgA + hyperimmune secretory IgA (BID x 13 days) resulted in 90% and 100% overall survival, respectively. Survival of infected hamsters was prolonged for up to 8-14 days as compared to any individual agent alone. The survival curves for the pooled secretory IgA/monomeric IgA + 5mg/kg vancomycin dose group and the hyperimmune secretory IgA/monomeric IgA + 10mg/kg vancomycin group were significantly more efficacious as compared to vancomycin alone by Log-rank (Mantel-Cox) ($p=0.018$ and 0.029) and Gehan-Breslow-Wilcoxon ($p=0.017$ and 0.030) tests, respectively.

**Conclusions:** Administration of secretory IgA/monomeric IgA from healthy human plasma in conjunction with vancomycin resulted in enhanced survival of *C. difficile* infected hamsters and demonstrated its’ potential as a possible therapeutic treatment option.

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Metagenomic antimicrobial resistance prediction from nanopore sequencing of orthopaedic implant-related infections: can we do more than detect species from sonication fluids?

Teresa Street*1, Camille Kolenda2, Nicholas Sanderson1, Carol Taunt1, Sarah Oakley1, Bridget Atkins1, Martin McNally4, Justin O’grady5, Derrick Crook1, David Eyre6

1University of Oxford, Oxford, United Kingdom, 2Hôpital de la Croix-Rousse, Lyon, France, 3John Radcliffe Hospital, Oxford, United Kingdom, 4Nuffield Orthopaedic Centre, Oxford, United Kingdom, 5Quadram Institute Bioscience, Norwich, United Kingdom, 6Big Data Institute, Oxford, United Kingdom

Background: Metagenomic nanopore sequencing is demonstrating potential as a tool for diagnosis of infections directly from clinical samples. We have previously shown nanopore sequencing can be used to determine the causative bacterial species in prosthetic joint infections (PJI). However, to make predictions regarding antimicrobial resistance, human DNA contamination must be reduced so a greater proportion of sequence data corresponds to the microbial portion of the DNA extract. Here, we optimize selective DNA extraction from sonication fluid samples to make predictions regarding antimicrobial resistance in PJI.

Materials/methods: We investigated host cell DNA depletion with 5% saponin selective human cell lysis followed by nuclease digestion. Additionally, treatment with 1% or 0.1% saponin was tested in a subset of samples. Subsequently, bacterial cells were mechanically lysed before DNA extraction. Sequencing libraries from samples treated with and without saponin were prepared with the Oxford Nanopore Technologies Rapid PCR Barcoding Kit and sequenced in multiplexes of 4-7 samples/flowcell on a GridION. Sequencing reads were analysed using the Crumpit pipeline and a threshold of ≥10% of bases classified as bacterial was used to indicate presence of a specific bacterial genus/species. Antimicrobial resistance determinants were detected using the CARD database.

Results: 193 DNA extracts from 85 individual patient sonication fluids were subjected to metagenomic sequencing, comprising 42 monomicrobial, 2 polymicrobial and 41 culture-negative samples. 5% saponin depleted human DNA contamination most consistently, reducing the number of human sequenced bases in 64/68 samples which were tested in comparison to 5µm filtration without saponin (mean depletion 2.8 log10-fold, maximum depletion 5.0 log10-fold). Bacteria observed in sonication fluid culture were identified to species-level in 37/47 cases, and to genus-level in 40/47. 36/47 species obtained a reference genome coverage breadth of >70%. Here, we identified acquired antimicrobial resistance genes accounting for all resistance phenotypes observed by laboratory sensitivity testing for beta-lactams, macrolides, fusidic acid and tetracycline resistance.

Conclusions: Nanopore metagenomic sequencing can provide species identification and antimicrobial resistance prediction in PJI. Depletion of human DNA improves depth of coverage and allows detection of acquired antimicrobial resistance genes, enabling nanopore sequencing to potentially provide a complete diagnostic tool in PJI.

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Abstract 3928

**Aetiology and antimicrobial susceptibility of anaerobic bacteria causing serious infections in a tertiary hospital of Madrid**

José María López-Pintor*, Ana Sánchez-Díaz, Patricia Ruiz-Garbajosa, Rafael Canton Moreno, Maria-Isabel Morosini Reilly, Sergio García-Fernández

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**Background:** Anaerobic culture techniques and antimicrobial susceptibility testing (AST) are both cumbersome, so recovery and susceptibility assays imply difficulties for routinely laboratory activity. Thus, the anaerobic infection management is frequently based on empirical treatment. The aim of this study was to collect identification and AST data from anaerobic isolates obtained in routine work in the Microbiology Department of a tertiary hospital of Madrid.

**Materials/methods:** The study period comprises 15 months (June 2018 to September 2019). Samples were processed in appropriate anaerobic media and incubated using the Anoxomat system (MART Microbiology BV, Holland); final identification was performed by MALDI-TOF (Bruker, Germany). AST for 3-6 antibiotics was performed with MIC gradient diffusion strips (Liofilchem, Italy) using EUCAST-2019 [penicillin (P), co-amoxiclav (AUG), imipenem (IMI), clindamycin (CD), and metronidazole (LZ)] or CLSI-2019 [cefoxitin (FOX)] breakpoints.

**Results:** 440 anaerobic microorganisms were isolated from 363 samples with positive anaerobic culture, being 29% monomicrobial and 5.2% polymicrobial; coinfection with aerobic bacteria represented 65.8%. The most common source of infection was intraabdominal (28.7%). Anaerobic gram-negative bacilli (AGNB) were predominant, (41.3%), being *Bacteroides fragilis fragilis* [13.4%] the most prevalent; anaerobic gram-positive bacilli (AGPB) represented 35.9%, anaerobic gram-positive cocci (AGPC), 17.7%; and anaerobic gram-negative cocci (AGNC), 5.1%. Percentage of susceptible isolates and MIC\text{90} values are shown in the table.

**Conclusions:** Metronidazole and imipenem were the most active agents, while anaerobes showed a reduced susceptibility to clindamycin. Selection of antimicrobial agents may be complex in anaerobic infections due to the difficulties in obtaining appropriately isolated specimens. Thus, *in vitro* surveillance studies are necessary for the election of an adequate empirical therapy.

<table>
<thead>
<tr>
<th></th>
<th>AGNB (n=184)</th>
<th><em>Bacteroides fragilis fragilis</em> (n=59)</th>
<th><em>Bacteroides</em> non-fragilis (n=52)</th>
<th><em>Aerobacillus</em> (n=155)</th>
<th>Clostridium <em>perfringens</em> (n=13)</th>
<th><em>Clostridium</em> spp (n=16)</th>
<th><em>Anaerobacter</em> (n=78)</th>
<th>AGPC (n=23)</th>
<th>AGNC (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>P</strong></td>
<td>27.3/ &gt;256</td>
<td>0/ &gt;256</td>
<td>9.8/ &gt;256</td>
<td>84.3/ 0.064</td>
<td>53.3/ &gt;256</td>
<td>88.6/ 0.75</td>
<td>30.4/ 8</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AUG</strong></td>
<td>66.9/ 48</td>
<td>63.8/ 48</td>
<td>50/ &gt;256</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>FOX</strong></td>
<td>73.2/ &gt;256</td>
<td>77.6/ &gt;256</td>
<td>44.2/ &gt;256</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>IMI</strong></td>
<td>94.3/ 1</td>
<td>93/ 1</td>
<td>96.1/ 2</td>
<td>87.5/ 0.75</td>
<td>100/ 0.125</td>
<td>81.3/ &gt;256</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>CD</strong></td>
<td>57.1/ &gt;256</td>
<td>58.5/ &gt;256</td>
<td>46.1/ &gt;256</td>
<td>90.5/ 3</td>
<td>94.1/ 2</td>
<td>87.3/ 4</td>
<td>71.1/ &gt;256</td>
<td>86.4/ 4</td>
<td></td>
</tr>
<tr>
<td><strong>LZ</strong></td>
<td>94.4/ 1</td>
<td>96.3/ 0.75</td>
<td>96.1/ 1</td>
<td>90.2/ 4</td>
<td>87.5/ 12</td>
<td>100/ 0.38</td>
<td>88.5/ 4</td>
<td>69.6/ &gt;256</td>
<td></td>
</tr>
</tbody>
</table>

*Excluding C. difficile

**Percentage SUS/MIC\text{90}**

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Peripheral venous catheter-related bloodstream infection in hospitalised children: the role of Gram-negative bacteria

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Abstract third-party references: abstract is submitted on behalf of Itay Berger

Background: Peripheral venous catheter (PVC) is the most commonly used vascular access in medicine, allowing administration of intravenous fluids and medications. Known complications associated with PVC include extravasation, phlebitis and bloodstream infection (BSI). Data regarding PVC-related BSI in children are scarce. We evaluated the epidemiology, clinical and microbiologic characteristics of pediatric patients with PVC-related BSI.

Materials/methods: This is a retrospective study conducted in a pediatric tertiary care center. Children with BSI, admitted to the general pediatric departments, between January 2010 and November 2019, were identified and their medical records examined. Patients with BSI and phlebitis at the PVC site were further characterized and included in the analysis. We excluded patients with central venous catheters, those with other identified source of infection and those with BSI upon admission. Data collected included: patients’ demographics and clinical and microbiological characteristics.

Results: Twenty-six children with PVC-related BSI were identified and included in the analysis. They constituted 0.2% of the total cases of bacteremia during the study period. Median age was 24 months (range, 1.5–396 months); male and female were equally affected. Five patients were categorized as previously healthy while the others, had prior medical conditions. The mean time from catheter insertion to bacteremia was 4.4 (±1.5) days. Eighteen (69%) patients were infected with Gram-negative bacteria and six (23%) with Gram-positive. Mixed Gram-negative and Gram-positive and Candida albicans occurred in one patient (4%) each. Polymicrobial infection occurred in four patients (15%). The most common bacteria isolated were klebsiella spp and Staphylococcus aureus.

Conclusions: Gram-negative bacteria are more commonly associated with PVC-related BSI than Gram-positive bacteria. Clinicians should consider a broad-spectrum antibiotic coverage for the empirical treatment of PVC-related BSI in hospitalized pediatric patients.

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Fail to perform a repeat ascitic tap at 48 hours is associated with poor outcome in patients with spontaneous bacterial peritonitis

Jaclyn Yizhen Tan*, Jade King1, Jennifer Ryan1, Marsha Morgan1, Rachel Westbrook1, Emmanuel Wey2,3

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**Background:** In patients with spontaneous bacterial peritonitis (SBP), acute kidney injury (AKI) and high serum bilirubin are predictors of in-hospital mortality. Impact of patient management on mortality is unknown. This study aims to identify predictors of in-hospital mortality, accounting for management of patients with SBP, according to EASL Clinical Practice Guidelines published in 2010.

**Materials/methods:** Clinico-demographic, biochemical and microbiological data from patients presenting between 2014 and 2019, with a first episode of SBP (ascitic fluid neutrophil count >250 cells/cm³) were reviewed. The primary endpoint was in-hospital mortality. Logistic regression identified predictors of outcome.

**Results:** Overall, 130 patients (median [IQR] age 58 [51–66] yr; 65% male; aetiology: alcohol 36%, MELD score 18 [13–25]) were included. Infection was nosocomial in 49%; 35 had concomitant bacteraemia (n=14), respiratory (n=16) or urinary infections (n=9). Pathogens were identified in 57 (44%) patients within 42 [36–50] hr post initial ascitic tap; antibiotic sensitivities were available by 53 [49–62] hr. Multidrug resistant pathogens (MDRP) were identified in 12 (21%) of the 57; 10 of the 12 showed <25% reduction in ascitic neutrophil count at 48 hours.

There were 29 (22.3%) in-hospital deaths; median time to death was 6 [1–8] days. A total of 31 (24%) patients were admitted to ITU – one-third (n=13) of this cohort died. On univariate analysis, admission MELD, peripheral white cell count, INR, serum creatinine, failure to culture a pathogen, failure to perform a 48-hour ascitic tap and development of AKI were predictors of in-hospital mortality. Age, nosocomial infection or the presence of a MDRP were not. Failure to perform a 48-hour ascitic tap [OR [95% CI] = 11.2 [2.9–43.7], p<0.01], acute kidney injury [9.1 [2.0–41.5], p<0.01] and MELD score [1.2 [1.1–1.3], p<0.01] retained significance on multivariate analysis.

**Conclusions:** In-hospital mortality associated with SBP is unacceptably high at 22%. Failure to repeat the ascitic tap at 48 hours, a recommendation based solely on expert opinion in the EASL guideline, was a highly significant prognostic factor allowing early identification of patients who fail to respond to empirical antibiotic therapy. This requirement should now become recommended practice.

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Tuberculosis in the elderly: a current challenge

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Background: Tuberculosis in the elderly (>65 y.o.) is a difficult-to treat disease. To decrease its high mortality, we need to improve our knowledge of the cases and their epidemiological scenario. We aim to describe current epidemiological characteristics, clinical presentation and outcome of TB in the elderly in our institution.

Materials/methods: All elderly patients with TB diagnosed by culture or PCR from 2012 to 2019 in a 1400-bed university hospital in Madrid were included. Socio-demographic characteristics, clinical findings, and outcome were recorded. One isolate from each case was genotyped and their MIRU-VNTR patterns were compared with those from a convenience sample from the same population to label which cases are likely due to recent transmission (clustered, identical patterns or SLVs, involving cases within 3 years) or to reactivation of latent TB (orphan, unique genotypes).

Results: From January 2012 to September 2019, 56/526 TB cases (10.64%) corresponded to patients aged 65-94y. Overall 29 (51.76%) were men; 8 (14.28%) migrants, 17 (30.35%) immunocompromised (mainly due to steroids). IGRA (Quantiferon TB gold) was positive in 30/39 patients (76.92%). Radiology was helpful in only 50%. Extrapulmonary disease was found in 20 patients (36%; mainly lymph node confused with tumors), and 7 presented with dissemination (12.5%). Mean diagnostic delay was 5 months (r: <1-24). For those with information about outcome (53), treatment toxicity grade 3 and 4 occurred in 25 %, 9-month mortality was 20.75% and 24-month survival was 56%.

The percentage of drug-resistant M. tuberculosis strains isolated was 10.71%, higher than in general population (7%). Isolates from 40 elderly patients were genotyped and only 2 clusters likely due to recent transmission (involving one elderly an another non-elderly case each) were identified. Six additional clusters were identified involving an elderly case with 1-3 non-elderly cases diagnosed 5-16 years before.

Conclusions: TB in the elderly is a severe disease, usually associated to diagnostic delay. Despite its prevalence decrease in our country, we must consider TB in old people, more likely associated to reactivation of latent infection than from recent transmission, though the latter should also be taken into consideration.

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Abstract 3936

Diagnosis of amoebic liver abscess by detection of Entamoeba histolytica DNA in serum using quantitative PCR

Gheffenstein Ferreira Theo*1, Maud Gits-Muselli1,2, Nicolas Guigue1, Marie-Quitterie Picat3, Samia Hamane1, Stéphane Bretagne1,2


Background: Amebic liver abscess (ALA) is regularly seen, mainly in travelers or immigrants from tropical countries. The diagnosis relies on imaging and serology, which must be performed in emergency. However, positive serology cannot distinguish acute from previous infection. We wondered whether amebic DNA detection in serum using quantitative PCR (qPCR) assay could improve the diagnosis of ALA.

Materials/methods: We retrospectively tested all serum samples available from patients with a positive serology and a final diagnosis of ALA between 01/01/2010 and 26/11/2019. The control group included patients with a diagnosis of liver space-occupying lesions with a final diagnosis other than ALA seen during the same period in our hospital and with serum sample stored available. DNA was extracted using QIAsymphony DSP Virus/Pathogen Kits spin columns. The qPCR assay was performed as already reported [1]. The oligonucleotide primers specifically amplify a 99-bp fragment inside the 16S-like small-subunit rRNA gene of E. histolytica.

Results: 80 samples were tested (ALA n=26 and control group n=54). Among them, 72 serum samples had been collected at the time of diagnosis [median: 1 day, Q1-Q3: 0-4 days] for 20 ALA and 52 controls (ALA n=20, tumor process n=21, pyogenic liver abscess n=24, cyst n=3, others n=4).

The qPCR detected E. histolytica DNA in 80% serum samples (16/20) of ALA patients and all the serum samples of control subjects were negative. Among the four negative qPCR samples in ALA, three could be explained by an ancient seropositivity due to previous amebic infection in one regular traveler and by a prior anti-amebic treatment (≥ 5 days) in two patients. Indeed, 8 serum samples available after treatment in initially positive patients demonstrated a negativation in 4 to 6 days. Thus, in the absence of treatment within 5 days, predictive negative value and positive predictive value were 100% and 96%, respectively.

Conclusions: This study demonstrates that free-circulating amebic DNA can be detected and could help both for positive diagnosis and for following treatment efficacy. This circulating-DNA could come from the blood passage of intestinal ameba or more probably from DNA released by dying hepatic ameba.


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Abstract 3939

**Staphylococcus lugdunensis**: coloniser or pathogen: outlining the clinical importance: a study of 295 clinical samples from hospital patients received for culture at the department of Medical Microbiology, SI Lillehammer, Norway, from November 2016 to November 2019

Susanne Hartvig Hartzen¹, Christoffer Dahlseide¹, Anders Hartzen²

¹Lillehammer Hospital, Lillehammer, Norway, ²University of Copenhagen, København, Denmark

**Background:** In 2018, a new initiative was set in motion by the Norwegian Working Group on Antibiotics providing recommendations for antibiotic panels and how to report cultures and susceptibility results based on information about clinical setting and signs of infection. The initiative was part of the overall strategy to limit the use of antibiotics and curb resistance. Placing the clinical presentation of the individual patient center stage, the microbiologist responsible for checking, interpreting and reporting culture results became a key player in the effort to avoid antibiotic treatment of patients with colonization states.

As growth of *S*. *lugdunensis* might represent normal skin flora or infection, we decided to study the clinical importance and impact of culture results of 295 samples with *S*. *lugdunensis* reported to hospitals in Oppland and Hedmark Fylker. Based on information on file we investigate the background for reporting the culture result, and the impact the culture result had on antibiotic treatment.

**Materials/methods:** The study used the following information sources: the requisition records, reporting cards, and hospital records concerning the 295 patient samples, where growth of *S*. *lugdunensis* was reported. Information extracted: age, sex, type of material, dominating growth of *S*. *lugdunensis*, antibiogram, symptoms of infection, and impact of culture report.

**Results:** Table 1: Information on 295 clinical samples from 280 patients where *S*. *lugdunensis* was reported.

All strains were susceptible to cefoxitin, 60% to penicillin, and 94% to clindamycin.

<table>
<thead>
<tr>
<th>280 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>153 ♂&lt;br&gt;Age mean: 54 yrs.&lt;br&gt;Age range: 0-96 yrs.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Highlighted materials (no. of samples)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage positive for</td>
</tr>
<tr>
<td>Dominating growth</td>
</tr>
<tr>
<td>Clinical infection</td>
</tr>
<tr>
<td>Impact of culture result on antibiotic treatment</td>
</tr>
<tr>
<td>Uncertain clinical importance</td>
</tr>
<tr>
<td>Impact of culture result on antibiotic treatment</td>
</tr>
</tbody>
</table>

**Conclusions:** Uncertainty concerning the clinical significance of growth of *S*. *lugdunensis* was widely present, particularly with culture of non-sterile materials. Selective reporting of susceptibility results might be well suited in both cases of uncertainty and cases with no clear infection. Empirical antibiotic therapy was generally maintained - perhaps reflecting the equivocal nature of culture results.

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Abstract 3940

Susceptibility of Gram-positive and Enterobacterales clinical isolates isolated during 2018 from France, Germany, Italy, Spain and the United Kingdom

Stephen Hawser*1, Ian Morrissey1, Nimmi Kothari1, Nowel Redder2

1IHMA, Monthey, Switzerland, 2Correvio International Sàrl, Genève, Switzerland

Background: Ceftobiprole is an advanced-generation, broad-spectrum parenteral cephalosporin approved in 17 European and eight non-European countries for the treatment of adults with community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP) (excluding ventilator-associated pneumonia. The present investigation reports susceptibility of European Gram-positive and Gram-negative isolates from 2018 as part of an ongoing susceptibility surveillance program.

Materials/methods: A total of 2784 clinical isolates were collected from European hospitals in 2018, including Enterobacterales, Pseudomonas aeruginosa, MRSA, MSSA and Streptococcus pneumoniae. These were collected from various infection sources including respiratory, skin, genitourinary tract, body fluid and gastrointestinal. Isolates were from France, Germany, Italy, Spain, and the United Kingdom. MIC determination was performed by broth microdilution.

Results: Ceftobiprole susceptibilities are shown in the Table.

<table>
<thead>
<tr>
<th>Organism / Group</th>
<th>EUCAST Breakpoints</th>
<th>FR</th>
<th>DE</th>
<th>IT</th>
<th>ES</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Total n]</td>
<td>(SMR)</td>
<td>[N]</td>
<td>[N]</td>
<td>[N]</td>
<td>[N]</td>
<td>[N]</td>
</tr>
<tr>
<td>MRSA (266)</td>
<td>≤2 ≤4</td>
<td>100 (36)</td>
<td>95 (20)</td>
<td>98.2 (115)</td>
<td>100 (67)</td>
<td>100 (28)</td>
</tr>
<tr>
<td>MSSA (716)</td>
<td>≤2 ≤4</td>
<td>100 (135)</td>
<td>100 (196)</td>
<td>100 (121)</td>
<td>100 (160)</td>
<td>100 (104)</td>
</tr>
<tr>
<td>S. pneumoniae (375)</td>
<td>≤0.5 ≤1</td>
<td>98.7 (81)</td>
<td>99 (100)</td>
<td>97.9 (48)</td>
<td>99 (100)</td>
<td>100 (46)</td>
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<tr>
<td>Enterobacterales (1427)**</td>
<td>≤0.25 ≤1</td>
<td>83 (184)</td>
<td>80.9 (330)</td>
<td>59 (336)</td>
<td>77.5 (365)</td>
<td>79.7 (212)</td>
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<tr>
<td>P. aeruginosa (376)</td>
<td>≤4* ≤1</td>
<td>76.3 (38)</td>
<td>72 (93)</td>
<td>66.7 (84)</td>
<td>59 (95)</td>
<td>65.2 (66)</td>
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</tbody>
</table>

*Non-species related PK/PD breakpoint
**seven species including Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, K. oxytoca, K. pneumoniae, Proteus mirabilis, and Serratia marcescens;

Conclusions: Only minor variations in percent susceptibility to ceftobiprole were observed between countries for MRSA (95%-100%) and pneumococci (97%-100%). All MSSA isolates were susceptible to ceftobiprole. All MSSA and MRSA were daptomycin- and vancomycin-susceptible and all pneumococci were susceptible to linezolid. Susceptibility of Enterobacterales ranged from 59% (Italy) to 83% (France), and of Pseudomonas from 59% (Spain) to 76% (France). Although not specifically evaluated, it is probable that ceftobiprole-resistant Enterobacterales were extended-spectrum beta-lactamase producers. Overall, the data further support the clinical utility of ceftobiprole against important clinical Gram-positive and Gram-negative isolates from the five countries analysed.

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**Abstract 3942**

**Clostridiodes difficile ribotypes 001 and 176 with reduced susceptibility to moxifloxacin are the main cause of healthcare-associated Clostridioides difficile infections in Slovakia**

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**Background:** In 2016, the emergence of ribotype 176 was recognized in six hospitals in Slovakia (Novakova et al., IJID, 2019). In order to obtain current data on *Clostridium (Clostridioides) difficile* infection (CDI) epidemiology in Slovakia, we aimed to perform a CDI surveillance study and to characterize *C. difficile* isolates for all CDI cases.

**Materials/methods:** Between May 2018 and May 2019, fourteen Slovakian hospitals (Figure 1) collected stool samples and epidemiological data of patients with CDI. *C. difficile* isolates were characterised by capillary-electrophoresis ribotyping, multiplex PCR toxin genes detection and antibiotic susceptibility testing to metronidazole, vancomycin and moxifloxacin using the agar dilution method. The European Centre for Disease Prevention and Control (ECDC) CDI surveillance protocol v 2.3 was followed for the CDI case, CDI origin and recurrent infection definitions.

**Results:** Of the 381 CDI cases, 75.6% (n=288) were healthcare-associated, 11.5% (n=44) were community-associated or of unknown origin and 12.9 (n=49) of CDIs were recurrent. A complicated course of CDI was reported in 12.3% (n=47). Of the 27.6% patients (n=105) that died, 25.7% (n=98) did so within 30 days after a CDI diagnosis.

A total of 370 *C. difficile* isolates were further characterized. The most prevalent PCR ribotypes (RTs) were 176 (n=185, 50.0%) and 001 (n=129, 34.9%). A total of 322 (97.0%) of the isolates showed a reduced susceptibility to moxifloxacin (>4 mg/L), and the majority belonged to the epidemic RTs 001 and 176, (n=312). A reduced susceptibility to metronidazole (>2 mg/L) was observed in 16 isolates (RTs 001 and 176).

HA CDI was associated with CDI caused by strains showing a reduced susceptibility to moxifloxacin and HA CDIs were more likely to have a complicated course of CDI (p=0.0030, 0.0455). Mortality was associated with patients of an advanced age and a complicated course of CDI (p=0.0092 and 0.0000).

**Conclusions:** We revealed a dramatic proportion of *C. difficile* isolates that showed a reduced susceptibility to moxifloxacin in Slovak healthcare settings. The spread of ribotypes 001 and 176 drives current CDI epidemiology in Slovakia. Our findings call for an urgent reduction in prescriptions of fluoroquinolones in healthcare settings in Slovakia.

**Figure 1:** Distribution of Slovak hospitals participating in surveillance of CDI. Pie charts show the representation of *C. difficile* ribotypes 001 and 176 identified per hospital. The numbers in the centre represent the number of *C. difficile* isolates cultured for molecular characterisation

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Chronic schistosomiasis and strongyloidiasis amongst Ethiopian immigrants in Netanya

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Background: Upon immigration from Ethiopia to Israel in the 1990s, very high rates of intestinal parasites were documented among immigrants. Despite this, diagnosis and treatment of these parasitic infections are still grossly inadequate. Here we describe cases of Ethiopian-born patients diagnosed with longstanding Schistosomiasis (SC) and Strongyloidiasis (SS) at Sanz Medical Center.

Materials/methods: We reviewed the medical records of adult Ethiopian-born patients hospitalized between 2012-2019 who were tested for SC/SS. Serology (ELISA and/or Western blot) and stool molecular tests were performed at the parasitology reference laboratory. Fisher’s exact and Chi square tests were used to determine significance.

Results: 82 patients were tested for antibodies against SC/SS or both. 55 (67%) were positive: 21 for SC, 20 for SS and 14 for both. The average time from immigration until diagnosis was 20 years (range 8-37). In 40 (49%) additional microbiological tests were performed: 33 stool ova and parasite microscopy tests were all negative, while 5/7 stool PCR tests were positive, 2 for SC and 3 for SS, showing 66-75% concordance with the serology tests. 73% of the study cohort had eosinophilia, which was significantly more common among patients with positive serology for SS vs SC (91% vs 68%, p=0.03). The mean maximal eosinophil count was significantly higher in SS (1481 vs 936 cells/mcl, p=0.01). Of the positive patients: 19 had respiratory complaints, 7 anemia or gastrointestinal symptoms, 4 neurological symptoms and 23 “other” symptoms. Asthma as a presenting or past symptom was observed in 53% (18/34) of SS and 37% (13/35) of SC cases (p=0.23). Treatment availability and culture barriers resulted in only 24/55 (43%) being accessed and treated.

Conclusions: Significant eosinophilia was a common finding and a trigger for testing. Nearly 70% of patients tested had serological evidence of SS/SC, neither of which is endemic in Israel. Diagnosis many years after immigration reflects chronic medical neglect of this community. Chronic significant eosinophilia, asthma-like, gastrointestinal, neurological and dermatologic symptoms, may serve as clues for diagnosis. Our results indicate the necessity of stipulating a strategy involving systematic laboratory screening for the diagnosis of helminthic infections among the Ethiopian-born community in Israel.

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Utilisation of next-generation sequencing testing for diagnostic dilemmas: experience at a tertiary care centre

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Background: Next-generation sequencing (NGS) of microbial cell-free DNA is an evolving diagnostic tool. Current diagnostic methods for infectious diseases often require organism growth, and can delay timely initiation of appropriate antimicrobial therapy. Currently available NGS assays offer an advantage of early pathogen identification and increased sensitivity compared to other methods. However, more research is necessary to determine the optimal patient population to utilize NGS, and how to correctly interpret NGS results.

Materials/methods: This was a retrospective observational study performed at a tertiary care center. A list of all NGS tests performed from February 15, 2019 to June 30, 2019 at Loyola University Medical center was obtained. Next-generation sequencing testing (Karius, Redwood City, CA) was performed as part of the routine diagnostic work up at the discretion of the infectious diseases consult team and outcomes were examined.

Results: There were 31 patients included in our analysis. The mean age of our cohort was 54 years old, and 15 patients (48%) were immunocompromised. NGS detected at least one organism in 19 patients (61.3%), with a total of 25 bacteria, 7 viruses, 4 fungi, and 1 parasite. The mean time to NGS result from send out was 2.29 days. Antimicrobial therapy was changed based on the NGS result for 19 patients (61.3%); three patients (9.7%) were started on antibiotics, seven patients (22.6%) had antibiotics discontinued, four patients (12.9%) had antibiotics escalated, and 10 patients (32.2%) had antibiotics de-escalated. The median bacterial value for immunocompromised patients was significantly lower than that of immunocompetent patients (159 vs. 905, p = 0.006), and the median bacterial value was significantly higher in those where the NGS result correlated clinically (274 vs. 26, p < 0.001).

Conclusions: NGS is a diagnostic tool that can be beneficial to patient care if used in the appropriate clinical scenarios. At our institution, NGS testing was typically faster than traditional culture methods, and resulted in antimicrobial therapy changes in the majority of the cohort. However, optimal circumstances for testing and interpreting clinical relevance of results are still to be determined.

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# Abstract 3949

**Cholera outbreak in Algeria, August-September 2018**


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**Background:** during summer 2018, cholera outbreak occurred in the northern and western regions of Algeria. This is the first epidemic recorded in Algeria for more than twenty years (the last cases have been reported in 1995). The purpose of this work is to report the epidemiological and microbiological characteristics of this epidemic.

**Materials/methods:** during the period August-October 2018, stool specimens were received for diagnosis (n=503) or screening (n=282) as well as strains for confirmation (n=23) from different departments: Bouira, Blida, Algiers, Tipaza, Ain Dèfla, Médéa and Oran. Environmental strains (n=6) were also sent. Bacteriological analysis was performed using conventional methods and/or rapid diagnostic test (Crystal VC®). The antimicrobial susceptibility testing was performed according to CLSI recommendations. Detection of cholera toxin gene and MLST were carried out on 7 selected strains [5 clinical strains of the epidemic, 1 clinical strain, isolated in 1992 and 1 environmental strain, isolated from the wastewater from Beni Azza river, Blida].

**Results:** among the clinical samples received (n=808), 118 (14.60%) were positive. 89/515 (17.28%) patients, including 44 (49.44%) cases from Blida and 29/293 (9.09%) healthy carriers were confirmed. The age of patients ranged from 2 months to 84 years (mean age: 33 years). The sex ratio was 0.85. Four deaths have been reported. All clinical strains belonged to the species *Vibrio cholerae*, el tor biovar, Ogawa serovar and showed the same antibiotic profile with resistance to aminopenicillins, nalidixic acid and cotrimoxazole. Of the environmental strains (n=06), 3 were *V. cholerae*, el tor biovar, Ogawa serovar with antibiotic profile identical to the clinical strains and were isolated mainly from wastewater. The clinical strains tested possessed the cholera toxin gene and the MLST revealed the presence of the same genotype.

**Conclusions:** although this epidemic remains limited, this alarming return highlights a decline in the actions taken in the fight against water-borne diseases. Although the epidemic strain was well identified, it was not possible to confirm the source of contamination. Further molecular investigations are needed. To maintain control of this disease, surveillance and the strengthening of vigilance must be pursued relentlessly.

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Abstract 3951

Serodiagnostic testing for Lyme borreliosis: should we believe what we see?

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Background: Two-tier serology (screening with a sensitive enzyme-immunoassay, confirmation with a specific Western blot or line immunoassay) remained the gold standard for the diagnosis of Lyme borreliosis. Remnant antibodies might be prevalent in the general population, thus recognizing relevant seropositivity might be challenging. The antibody response against Borrelia antigens is known to be sequential, which might be diagnostically utilized. We aimed to specify details which might potentially be useful in orientating the diagnostic schedule.

Materials/methods: We processed the sera of 1304 patients using a recombinant antigen-based enzyme-linked-immunosorbent assay (ELISA) between Aprils of 2017 and 2019. Reactive ELISA results (when coherent with ongoing infection according to the anamnestic data) were confirmed with a line immunoassay (LIA). Positivity was determined by the sum of the scores linked to certain antibodies according to the manufacturers recommendations. Antibody patterns and their relation with the symptoms were documented and analyzed.

Results: ELISA testing (IgG and/or IgM) was reactive in 539 cases. 107 patients with persistent postprimary symptoms tested positive or borderline with IgG ELISA. A significant difference was observed (Mann-Whitney U-test p=0.003) between the LIA scores of patients with characteristic (arthritis, acrodermatitis, neuropathy, other neurologic disorder following known exposure; n=83; median LIA score: 16) and non-specific symptoms (entirely subjective complaints, other known disease, or lone subfebrility; n=24; median LIA score: 6). 101 of the 107 patients tested positive for IgG against any specific Borrelia protein by LIA. When dividing them into two subgroups those with a LIA score reaching the group median of 15 (n=51) displayed strong anti-VlsE IgG positivity or a typical late antibody (IgG against p100, p18 or p39) response significantly more often than those with a LIA score under the group median (88,2% vs. 30% and 100% vs. 38% respectively, Chi square test p<0.0001 for both comparisons).

Conclusions: Weak LIA positivity, especially regarding the anti-VlsE IgG response, in combination with the lack of late antibodies in patients with persistent symptoms might suggest the presence of remnant antibodies and prompt scrupulous differential diagnosis, particularly in the presence of symptoms that are not characteristic for Lyme borreliosis.

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Abstract 3952

Developing a pragmatic framework for genomics-informed surveillance of endemic Salmonella Typhimurium in Australia

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Background: Salmonella enterica serovar Typhimurium is the most common serovar notified to public health authorities in Australia. In the state of Victoria, investigation of S. Typhimurium clusters is initiated based on epidemiological data and multi-locus variable-number tandem repeat analysis (MLVA). Persistent and common MLVA types representing much of the disease burden remain largely unresolved due to insufficient resolution of the methodology. Whole genome sequencing (WGS) provides a comprehensive and highly discriminatory tool for characterising pathogens. Here we present the data underpinning the development of a pragmatic framework for WGS-informed surveillance.

Materials/methods: All S. Typhimurium (n=1477) from humans in Victoria between 1st July 2018 and 30th June 2019 were sequenced on an Illumina Nextseq platform, with bioinformatic analysis using in-house pipelines. Single-linkage clustering was performed at 2, 5 and 10 single nucleotide polymorphism (SNP) thresholds. Ten outbreaks encompassing 58 epidemiologically linked cases were used to validate clustering.

Results: The maximum pairwise distance in an epidemiologically confirmed outbreak was 2 SNPs. The 2-SNP level had 139 clusters (2-104 isolates), correctly clustered the known outbreak cases and clusters provided discrimination within common MLVA types (Figure). The 5-SNP level saw a loss of resolution with the formation of large clusters of up to 370 isolates, increasing at the 10-SNP level to 440 isolates. There were observations of the same MLVA type simultaneously occurring in multiple clusters, explaining challenges with MLVA-based investigations. MLVA type could not be reliably predicted from clusters, with several instances of multiple MLVA types occurring in a cluster.

The prospective routine surveillance will involve a tiered analysis approach with clustering at 2, 5 and 10-SNP levels; the 2-SNP identifies a core of cases with high probability of epidemiological links, subsequently serving to direct investigations of additional isolates related at 5 and 10-SNP levels. Weekly analysis of a 12-month sliding window, focusing on the most recent month for immediate public health action, and the previous 11 months for context and monitoring of persistent clusters.

Conclusions: We have developed a framework for WGS-informed surveillance of S. Typhimurium, capable of both detecting point source outbreaks and resolving slow-burning outbreaks constituting a large disease burden.

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**Abstract 3953**

**In vitro modeling of patient-specific susceptibility to neurotropic flavivirus infection by using induced pluripotent stem cells**

Silvia Riccetti*, Alessandro Sinigaglia, Giovanna Desole, Monia Pacenti, Teemu Smura, Ravi Kant, Olli Vapalahti, Marta Trevisan, Luisa Barzon;

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**Background:** A characteristic feature of many infections is that only a proportion of exposed individuals develop clinical disease, such as in the case of West Nile virus (WNV) infection, which is associated with severe neuroinvasive disease in less than 1% of infected patients. The genetic basis of the inter-individual variability in the response to infections is poorly understood. Aim of this study was the development of an in vitro model based on patient-specific induced pluripotent stem cells (iPSCs) to investigate individual susceptibility to WNV and other neurotropic flaviviruses.

**Materials/methods:** iPSCs were generated from PBMCs of two patients with previous WNV encephalitis without comorbidity (cases) and two blood donors with asymptomatic WNV infection (controls). Patient-specific iPSCs were differentiated into neural stem cells (NSCs) and infected with WNV lineage 1, ZIKV Asian lineage, and USUV lineage Europe 1 at different MOI. Viral replication kinetics, cytopathic effect, and expression of host genes involved in innate antiviral response were investigated.

**Results:** USUV and WNV replicated more efficiently, yielding 10 and 100 fold higher viral load and inducing 70% and 40% higher cell mortality, respectively, in NSCs derived from cases than in NSCS derived from controls. Several genes involved in the antiviral IFN pathway were significantly upregulated after USUV, ZIKV and WNV infection, but the general trend indicated an attenuated response in NSCs derived from WNV encephalitis cases as compared to the response in NSCs derived from asymptomatic controls. Inactivating mutations of key genes involved in innate antiviral immunity were identified by genome sequencing of iPSCs from cases but not from the controls.

**Conclusions:** NSCs derived from patients with WNV encephalitis were more susceptible to WNV and USUV replication and cytopathic effect than NSCs derived from subjects with asymptomatic infection. This increased susceptibility to neurotropic flaviviruses was associated with a significantly attenuated innate antiviral response.

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**Abstract 3954**

**Efficacy of temocillin against multidrug-resistant Enterobacterales: a retrospective cohort study**

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**Background:** Temocillin is in use in some European countries as a carbapenem-sparing agent for serious MDR Enterobacterales infections based on in vitro activity and limited clinical data. We aimed to evaluate a three-year routine use regarding infection site, dosage regimen and bacterial species.

**Materials/methods:** We reviewed all ≥3 days prescriptions in a teaching hospital from 2016-19. Temocillin susceptibility was determined by disk diffusion (S≥20 mm) and when feasible by Etest (MIC ≤8 mg/L). Overall failure was defined as clinical or microbiological failure within 30 days after the end of treatment. Regimens were compared according to corresponding daily dose in a normorenal subject.

**Results:** 171 episodes were analyzed, affecting overall old (median age: 69 years; 59-76) patients with comorbidities (median Charlson index of 3). There were 137 (80%) episodes of urinary tract infection (UTI) among which 32 (23%) catheter-related, 15 bacteremia (8 catheter-related), 6 intra-abdominal infections, 6 bone and joint infections and 7 miscellaneous. Bacterial documentation was available for 164 cases (96%) for a total of 181 Enterobacterales among which 94 Escherichia coli (52%) and 46 Klebsiella spp. (25%), with 120 (67%) ESBL and 7 (4%) AmpC-producers. All strains but 4 were susceptible, with MIC50 and MIC90 values of 4 and 8 mg/L according to the 97 E-tests. Temocillin was administered for a median duration of 1.4 days (8-18), at 2 g q12h for 77%, 2g q8h for 16% and 1g q12h for 6%. Overall failure occurred in 24% of episodes, more frequently in other infections (OI) than UTI (44% vs. 19%, P<0.01) and for E. coli rather than in other Enterobacterales infections (31% vs 16%, P<0.05). By multivariate analysis, overall failure was associated to OI (ORa=3.58, CI95%=1.37-9.48), immunosuppression (ORa=2.90, CI95%=1.22-7.00) and E. coli infection (ORa=3.27, CI95%=1.36-8.66). Clinical failure at the end of treatment was also more common for OI than UTI (38% vs. 9%, P<0.01).

**Conclusions:** Our data confirm that 2g q12h temocillin regimen can treat UTIs due to MDR Enterobacterales with MICs ≤ 8 mg/L. They suggest caution and further studies for infections of other sites.

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Abstract 3955

A systematic review and meta-analysis of the risk of latent tuberculosis acquired during travel

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Background: To achieve tuberculosis (TB) elimination in low TB incidence countries, individuals at risk for latent TB infection (LTBI) will need to be identified and treated. Persons travelling to high TB burden countries, especially for prolonged periods, are at risk for TB exposure. We aimed to estimate the travel-acquired incidence of LTBI among persons travelling from low to higher TB burden countries, and the impact of travel duration and purpose.

Materials/methods: We conducted a systematic review and meta-analysis of incident LTBI [defined as either tuberculin skin test or interferon-gamma release assay conversions (negative pre-travel test and positive post-travel test)], among individuals travelling from low (<10 TB cases/100,000 population) to intermediate (50-100/100,000) or high (≥100/100,000) TB incidence countries. We searched five electronic databases from inception to September 6, 2019. Incident LTBI acquired per 1000 person-months (PM) of travel were estimated. Meta-analysis using a random effects model of log transformed rates was conducted. Sub-group analyses by travel duration, travel purpose, and TB incidence in the destination region were undertaken.

Results: Among 546 studies identified, 118 underwent full-text review, and 10 were included. These studies included 1,155,102 travellers with 13,199,330 PM of travel recruited between 1994 and 2013. There were 443 health care workers with 972 PM of travel, 1,068,636 military (11,654,495 PM) and 86,023 travellers/other volunteers (1,543,863 PM). Among individuals who travelled a median of six months or less, health care workers had the highest rate of incident LTBI (20.7/1000 PM, 95% CI 11.3-37.9), followed by military personnel [4.96 (3.9-6.3)] and leisure travellers/other volunteers [2.8 (1.8-4.5)]. There was no difference in incident LTBI for travel to high (3.4/1000 PM, 95% CI 2.1-5.4) or intermediate [4.9 (3.9-6.2)] TB incidence regions in military or leisure travellers/other volunteers. Analyses of incident LTBI in longer-term travellers (12-24 months) is ongoing and will be presented.

Conclusions: Among travellers with a median of 6 or less months of travel, health care workers had approximately a 5-fold higher risk of developing LTBI compared to other travellers and may benefit from post-travel LTBI assessment.

Figure 1: Forest plot of incident LTBI for six months of travel, stratified by travel purpose.

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**Abstract 3958**

In vitro evolution reveals mutations in Candida auris ERG6 to confer high level amphotericin B resistance

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**Background:** Candida auris is an emerging virulent pathogen of great clinical concern, associated with outbreaks of invasive candidiasis on multiple continents. When isolated, C. auris is commonly found to be multidrug-resistant, and numerous isolates have been recovered which are resistant to all available antifungals. The polyene antifungal amphotericin B (AMB) has been relied upon as an agent of last defense since its clinical introduction, possessing both a broad spectrum of activity and fungicidal activity. Unfortunately, 30% of C. auris clinical isolates are resistant to AMB, and at present the molecular mechanisms underpinning this resistance in C. auris remain completely unknown.

**Materials/methods:** AMB evolved strains were generated by passaging the AMB susceptible C. auris clinical isolate AR0387 in YPD supplemented with AMB (2 to 4mg/L) for 48 hours. AMB MIC were measured by Etest. Comprehensive sterol profiling was performed on the AMB evolved strains and the parental AR0387 to identify alterations in cellular sterols. Sanger sequencing was employed to identify mutations in AMB evolved strains relative to the parental AR0387. A Cas9 mediated transformation system was utilized to correct mutations of interest in the AMB evolved strains.

**Results:** Three AMB evolved strains were obtained following a single passage. AMB minimum inhibitory concentrations ranged from 8 to 16mg/L compared to 0.1–25mg/L in the parental AR0387. Sterol profiling revealed ergosterol to be the predominant sterol (77%) in the parental AR0387, while all three AMB evolved strains were found to have sterol profiles consisting predominantly of cholesta-5,7,24-tetraenol (55%) and zymosterol (28%) and completely lacking detectable ergosterol. Consistent with sterol profiles, sanger sequencing revealed all three AMB evolved strains to possess nonsense mutation in ERG6, the putative C. auris sterol methyl-transferase. Cas9-mediated correction of the ERG6 mutation in an AMB-evolved strain restored AMB susceptibility to the level of the parental AR0387 (MIC 0.125mg/L).

**Conclusions:** Taken together these studies demonstrate both that C. auris can rapidly acquire resistance to AMB in vitro, and that mutations in ERG6 can contribute to AMB resistance. Further research is needed to determine the extent to which mutations in ERG6 may contribute to AMB resistance among clinical isolates of C. auris.

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Abstract 3959

Activity of the β-Lactamase inhibitor LN-1-255 against ceftazidime-resistant AmpC-hyperproducing Pseudomonas aeruginosa

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Background: New therapeutic options for Pseudomonas aeruginosa, whose resistance to β-lactams is mainly due to the cephalosporinase AmpC overproduction, are urgently needed. Treatments are limited and the new combinations ceftolozane/tazobactam and ceftazidime/avibactam are frequently necessary. We propose a new antimicrobial strategy, combining ceftazidime (CAZ) and LN-1-255 [an experimental β-lactamase inhibitor] against AmpC-hyperproducing P. aeruginosa strains and comparing it to that of the CAZ/AVI established treatment.

Materials/methods: Susceptibility assays were performed using P. aeruginosa PAO1 isogenic mutants, expressing multiple combinations of the most relevant β-lactam resistance mechanisms, such as AmpC hyperproduction, OprD inactivation or plasmid-carrying PDC-1 and PDC-315 [a ceftolozane-resistance conferring AmpC], and a collection of over-expressing ampC clinical isolates. MICs to CAZ were determined by microdilution, in the presence/absence of avibactam and LN-1-255 (4 mg/L). Additionally, for PDC-1, the IC50 of both inhibitors was calculated.

Results: The isogenic mutants overexpressing ampC displayed MICs of 8-32 mg/L to CAZ, increasing the MICs of the parental strain. As expected, the combination CAZ/AVI boosted the efficacy of CAZ, lowering the MICs 4-16-fold. LN-1-255 displayed a very similar behavior and MICs to CAZ decreased 4-16-fold in its presence. Among the clinical isolates, MICs to CAZ decreased likewise in presence of both inhibitors [Table]. Finally, PDC-1 had an IC50 of 6 nM for LN-1-255 and of 51 nM for avibactam.

Conclusions: We describe the inhibitory activity of the compound LN-1-255 against the chromosomal ampC of P. aeruginosa. CAZ in combination with LN-1-255 was effective against these CAZ-resistant AmpC-hyperproducing P. aeruginosa strains. Therefore, LN-1-255 stands as a potential new therapeutic option to recover CAZ as an antibiotic treatment against AmpC-hyperproducing strains.

<table>
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<tr>
<th>P. aeruginosa PAO1 and ISOGENIC MUTANTS</th>
<th>MIC (mg/L)</th>
<th>MIC (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CAZ</strong></td>
<td><strong>CAZ+AVI</strong></td>
<td><strong>CAZ+LN-1-255</strong></td>
</tr>
<tr>
<td>PAO1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>PAO1+PDC-1</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>PAO1+PDC-315</td>
<td>32</td>
<td>1</td>
</tr>
<tr>
<td>PAO1 AmpD</td>
<td>16</td>
<td>1</td>
</tr>
<tr>
<td>PAO1 ΔOprD</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td>PAO1 ΔOprD, ΔOprDh2, ΔOprDh3</td>
<td>32</td>
<td>2</td>
</tr>
<tr>
<td>PAO1 ΔOprD, ΔampD</td>
<td>32</td>
<td>4</td>
</tr>
<tr>
<td>PAO1 ΔOprD, ΔampD, ΔampDh3</td>
<td>16</td>
<td>2</td>
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<tr>
<td>PAO1 ΔOprD, ΔampD, ΔampDh3</td>
<td>32</td>
<td>4</td>
</tr>
<tr>
<td>PAO1 ΔOprD, ΔampD, ΔampDh3</td>
<td>16</td>
<td>2</td>
</tr>
</tbody>
</table>

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Abstract 3961

**Standard-dose vs higher-dose of rifampicin in patients with tuberculosis: a meta-analysis**

Valeria Gentile*1, Lorenzo Onorato1, Antonio Russo1, Giovanni Di Caprio2, Loredana Alessio2, Nicola Coppola1

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**Background:** evidence suggests that Rifampicin doses could be increased to achieve more effective tuberculosis treatment. We compared clinical and microbiological outcomes of patients treated with either standard dose (10mg/kg) or higher dose (>10mg/kg) of Rifampicin.

**Materials/methods:** A systematic review and meta-analysis was conducted using MEDLINE, Google Scholar and the Cochrane Library. All studies included had to fulfill the following inclusion criteria: [a] reported clinical (treatment failure, mortality and ADR) and/or microbiological outcomes [culture conversion at 8 weeks] comparing standard dose and higher dose of Rifampicin;[b] were available as a full text manuscript;[c] written in English;[d] included either pulmonary or extra-pulmonary infection;[e] enrolled either children or adult HIV-positive or HIV-negative patients. The exclusion criteria were:[a] letters, case reports, meeting abstracts, or editorial comments;[b] enrolled patients with Rifampin resistant or MDR infection;[c] studies enrolling less than 5 subjects.

**Results:** Nine studies, from a total of 11686, met the inclusion criteria, allowing a meta-analysis on 1163 patients. Three studies examined treatment failure showing no significant difference in the two observed groups (RR 0.95, 95% CI 0.81-1.12). In terms of mortality, both in CNS (RR 0.92, CI 0.76-1.12) and pulmonary TB (RR 1.53, CI 0.31-7.58), there was no statistically significant difference between the intensified treated patients and the control groups. Eight studies investigated ADR grade 3 and 4, showing a higher rate in terms of events between in the intensive treated group than the control group (RR 1.51, CI 1.20-1.91, p 0.003). Similarly, investigating into ADR leading to discontinuation of therapy more patients had their treatment suspended among the intensive therapy group compared to the control group (RR 1.52, CI 1.15-2.00; p 0.003). Treatment with higher doses of Rifampin was as efficacious as treatment with a standard dose, as it showed no difference in negativization of culture at eight weeks (RR 1.06, CI 1.00-1.13).

**Conclusions:** the meta-analysis showed a higher rate of ADR leading to discontinuation in the intensified treated patients. There were no statistical difference in terms of negativization of culture at eight weeks and mortality. Further studies are needed to clarify the role of higher dose of rifampicin in patients with tuberculosis.

**Table:** Summary of meta-analysis results in the achievement of the outcomes in experimental and control groups

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Nº of studies</th>
<th>Nº of patients experimental/ control group</th>
<th>Nº of events experimental/control group</th>
<th>RR</th>
<th>95% CI</th>
<th>p</th>
<th>Heterogeneity test (I²,%; p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment failure</td>
<td>3</td>
<td>535/483</td>
<td>182/179</td>
<td>0.95</td>
<td>0.95-1.12</td>
<td>0.56</td>
<td>26.69,256</td>
</tr>
<tr>
<td>Mortality in pneumonia infection</td>
<td>3</td>
<td>686/424</td>
<td>4/1</td>
<td>1.53</td>
<td>0.31-7.58</td>
<td>0.601</td>
<td>0.00,864</td>
</tr>
<tr>
<td>Mortality in CNS infection</td>
<td>3</td>
<td>477/460</td>
<td>135/141</td>
<td>0.92</td>
<td>0.76-1.12</td>
<td>0.425</td>
<td>50.60,132</td>
</tr>
<tr>
<td>Negativization of cultures at 8 weeks</td>
<td>4</td>
<td>569/382</td>
<td>475/382</td>
<td>1.06</td>
<td>1.00-1.13</td>
<td>0.661</td>
<td>0.00,687</td>
</tr>
<tr>
<td>Grade 3 or 4 of ADR</td>
<td>8</td>
<td>1080/920</td>
<td>164/98</td>
<td>1.51</td>
<td>1.20-1.91</td>
<td>0.603</td>
<td>0.00,820</td>
</tr>
<tr>
<td>ADR leading to discontinuation</td>
<td>4</td>
<td>914/743</td>
<td>102/66</td>
<td>1.52</td>
<td>1.15-2.01</td>
<td>0.603</td>
<td>0.00,946</td>
</tr>
</tbody>
</table>

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Abstracts 2020

Abstract 3962

High prevalence of *Plasmodium falciparum* and non-falciparum infections in asymptomatic adults in forest Ghana

Melina Heinemann*1,2; Richard Phillips3; Christof D. Vinnemeier1,2; Christina Rolling1; Egbert Tannich2,4; Thierry Rolling1,2,4

1University Medical Center Hamburg-Eppendorf, Hamburg, Germany, 2Bernhard Nocht Institute for Tropical Medicine, Hamburg, Germany, 3Kumasi Center for Collaborative Research in Tropical Medicine, Kumasi, Ghana, 4German Center for Infection Research (DZIF), partner site Hamburg-Lübeck-Borstel-Riems, Hamburg, Germany

Abstract third-party references: The study was supported by a Bayer AG grant to the University Medical Center Hamburg-Eppendorf.

Background: Mass screening and treatment is one option towards eradicating malaria. Due to the limited sensitivity of rapid diagnostic tests (RDT) normally used as diagnostic tool, a substantial number of parasite carriers may not be detected. The present study analyses prevalence of asymptomatic carriage of *Plasmodium* spp. in adults in a Ghanaian forest region during the high transmission season using RDT and polymerase chain reaction (PCR).

Materials/methods: Blood from asymptomatic adults was collected in September 2018 in five villages in the Asante Akim North district in the Ashanti region, Ghana, and tested for *Plasmodium* spp. with RDT and PCR. Exclusion criteria were clinical signs of infection, clinical conditions associated with a bleeding disorder, pregnancy and puerperium. The study was approved by the Committee on human research, publication and ethics at the Kwame Nkrumah University of Science and Technology, Kumasi, Ghana (CHRPE/AP/455/18).

Results: Two-hundred-six women and 185 men with a median age of 32 years were included in the study. A total of 284 study participants (72.6%) was tested positive for *Plasmodium* spp. by PCR. While 266 (68.0%) participants were positive for *P. falciparum*, 33 (8.4%) and 34 (8.7%) were positive for *P. malariae* and *P. ovale*, respectively. Both *P. ovale curtisi* (3.1%) and *P. ovale wallikeri* (3.8%) were identified. In a few cases of low-level *P. ovale* infection, sub-species differentiation was unsuccessful. All participants were negative for *P. vivax* and *P. knowlesi*. Non-falciparum infections were mostly combined with *P. falciparum*. *Plasmodium* spp. were detected by RDT in 126 study participants (32.2%). Sensitivity and specificity of the RDT for detection of *P. falciparum* infection were 43% (122/282) and 96% (102/106), compared to PCR. A lower cycle threshold value of the screening PCR was significantly associated with a positive RDT, adjusted for age, gender and village.

Conclusions: Asymptomatic adults represent a large reservoir for malaria transmission in forest Ghana, including for non-falciparum species. To reduce the malaria burden in Ghana, screening and treatment should not only be focused on children or individuals with a positive RDT.

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**Abstract 3963**

**Vertebral osteomyelitis in patients with Staphylococcus aureus bloodstream infection: evaluation of risk factors for failure**

Norma Jung1, Angela Ernst1, Insa Joost2, Ayla Yagdiran3, Gabriele Peyerl-Hoffmann3, Martin Hellmich4, Harald Seifert4, Winfried Kern5, Achim Kaasch7, Siegbert Rieg5

1University of Cologne, Department of Internal Medicine, Division of Infectious Diseases, Cologne, Germany, 2University of Cologne, Institute of Medical Statistics and Computational Biology (IMSB), Faculty of Medicine, Cologne, Germany, 3Heinrich-Heine-University Düsseldorf, Institute of Medical Microbiology and Hospital Hygiene, Düsseldorf, Germany, 4University Hospital of Cologne, Department of Orthopedics and Trauma Surgery, Cologne, Germany, 5Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Division of Infectious Diseases, Department of Medicine II, Freiburg, Germany, 6University of Cologne, Institute for Medical Microbiology, Immunology and Hygiene, Cologne, Germany, 7Otto-von-Guericke-University Magdeburg, Institute of Medical Microbiology and Hospital Hygiene, Magdeburg, Germany

**Background:** Staphylococcus aureus is the most common cause of hematogenous pyogenic vertebral osteomyelitis (VO) in adults. Studies indicate that S. aureus VO results in a particularly poor outcome. We aimed to investigate risk factors for treatment failure in patients with *Staphylococcus aureus* bloodstream infection (SAB) associated with VO.

**Materials/methods:** We conducted a post hoc-analysis of data from a German bi-center prospective SAB cohort study (period 2006-2014). Patients were followed-up for one year. Primary outcome was treatment failure defined as relapse and/or death within one year. We performed a multivariable analysis and compared outcome of patients with VO with and without endocarditis and those with non-vertebral osteomyelitis.

**Results:** A total of 1069 patients with SAB were analyzed, with 92 patients presenting with VO. MRSA rate was 13%. Median antimicrobial treatment duration in hospital was 34 days (IQR 21-53) with all patients receiving combination therapy (cell wall-active agent plus predominantly rifampicin or fosfomycin). In addition to antibiotic treatment, surgery was performed in 60/92 (65%) patients. 44/92 patients (48%) failed (death, n=42; relapse, n=2). Multivariable analysis revealed higher age (HR 1.05 [per year], 95% CI 1.01 – 1.08), Charlson comorbidity index (HR 1.3, 95% CI 1.1 – 1.5), septic shock (HR 2.6, 95% CI 1.2 – 5.8), the presence of a neurologic deficit (HR 2.0, 95% CI 1.04 – 4.0) and secondary hematogenous foci (HR 2.0, 95% CI 1.01 – 3.9) as independent risk factors for treatment failure within one year. Patients with VO and endocarditis showed the highest rate of treatment failure (see figure).

**Conclusions:** SAB patients with VO exhibit a high treatment failure rate. Red flags are older age, comorbidities, secondary foci or neurologic deficits. Whether these patients benefit from intensified treatment (e.g. earlier radical surgery, prolongation of antibiotic treatment) should be investigated in further studies.

**Figure:** Kaplan-Meyer event-free survival plot (event defined as relapse and/or death); SAB= *Staphylococcus aureus* bloodstream infection, VO= vertebral osteomyelitis

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Evaluation of multiplex PCR for rapid detection of bacteria and antibiotic resistance in spontaneous bacterial peritonitis: a pilot study

Jaclyn Yizhen Tan*1, Niall Thomas Burke1, Noam Pinchas Gessler Roth1, Dewi Rhys Dwen1, Jennifer Ryan1, Marsha Morgan2, Rachel Westbrook1, Emmanuel Wey2,3

1University College London, UCL Institute for Liver & Digestive Health, Division of Medicine, Royal Free Campus, London, United Kingdom, 2Royal Free London NHS Foundation Trust, Centre for Clinical Microbiology, Department of Microbiology, London, United Kingdom, 3University College London, Division of Infection and Immunity, London, United Kingdom

Background: Pathogen detection rates and antibiotic sensitivities in spontaneous bacterial peritonitis (SBP) are successful in only about 50% of cases. This pilot study aims to compare the diagnostic performance of the Curetis Unyvero IAI Intra-abdominal Infection Application, a multiplex PCR-based testing system, and conventional diagnostic procedures in the diagnosis of SBP.

Materials/methods: Ascitic fluid was collected from patients with cirrhosis admitted under the hepatology service between January and May 2019. Two samples were collected from each patient, one was sent for diagnosis via conventional protocols, the other was analysed via the Unyvero. SBP was diagnosed when ascitic fluid neutrophil count was > 250 cells/mm³. Independent-samples Mann-Whitney U test was performed to compare mean differences in time to results.

Results: Sixteen patients were included within the pilot study, 11 without SBP and 5 with SBP on conventional diagnostic methods. Overall, time to pathogen identification was reduced by a mean (± SD) of 42.0 (± 16.3) hr (p < 0.01). In patients without SBP, the Unyvero correctly concluded the ascitic fluid was negative for pathogens in 11 of 11 cases, and thus provided no false positive results. Conventional culture identified a Staphylococcus epidermidis on one bottle; which was subsequently negative on retesting and thus labelled a contaminant. In patients with SBP, there was concordance between Unyvero and conventional results in 3 of 5 cases. Two patients had discordant results. In the first patient, Staphylococcus aureus was identified by Unyvero but not by conventional ascitic culture. The patient responded well to targeted antimicrobial therapy. The next patient had Serratia marcescens, identified via conventional methods but not via the Unyvero. The pathogen was not within the Unyvero’s detection range. Key first-line antibiotic resistance profiles in the detected pathogens were concordant for both diagnostic tests.

Conclusions: The implementation of multiplex PCR-based testing for pathogens in SBP significantly reduces time to pathogen identification and antibiotic sensitivities. However, it is limited by its narrow diagnostic panel. Incorporation of such methods as an adjunct in the clinical setting has potential to improve timely and appropriate antibiotic prescribing in SBP.

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The colonisation of Czech travellers and expatriates living in the Czech Republic by colistin-resistant Enterobacteriaceae including Escherichia coli harbouring mcr-1 genes on a plasmid or chromosome

Marcela Krutová¹, Alžběta Baráková¹, Elka Nycova¹, Gelbičová Tereza², Renata Karpiskova¹, Otakar Nyc¹, Pavel Drevinek¹, Jan Tkaldec¹

¹Charles University, 2nd Faculty of Medicine and Motol University Hospital, Department of Medical Microbiology, Prague, Czech Republic, ²Veterinary Research Institute, Department of Bacteriology, Brno, Czech Republic, ³Bulovka Hospital, Department of Clinical Microbiology, Prague, Czech Republic

Background: Travelers were recognized as risk cohort that can import mcr-1-mediated colistin resistant Enterobacteriaceae. We aimed to investigate the carriage of mcr-1-mediated colistin resistance in Enterobacteriaceae in Czech travelers or expatriates residing temporarily in the Czech Republic as a source of mcr-gene dissemination.

Materials/methods: Between August 2018 and September 2019, the stool samples were cultured in Enterobacteriaceae enrichment broth at 37 °C overnight. The enriched cultures were tested for the presence of mcr-1-8 genes by PCR and inoculated onto selective agar with colistin (3.5 mg/L). A minimal inhibitory concentration (MIC) of colistin was determined by using the broth microdilution method. Colistin resistant Enterobacteriaceae isolates were tested by PCR for the presence of mcr-1-8 genes and mcr-positive isolates were characterised by whole genome sequencing. The MICs of commonly used antimicrobials in Enterobacteriaceae infections were determined by the microdilution method.

Results: A total of 177 stool samples derived from Czech travelers (n=131; 74.0%) or expatriates residing temporarily in the Czech Republic (n=46; 26.0%) were investigated. Fifteen Enterobacteriaceae isolates (from 14 individuals) cultured, after enrichment, were resistant to colistin [Table]; the carriage prevalence rate of colistin resistant Enterobacteriaceae was 7.9%. Two enriched cultures proved positive for the presence of the mcr-1 gene and two colistin resistant E. coli (MIC 4 mg/L) isolates carrying mcr-1 were obtained; the carriage prevalence rate of mcr-1-positive samples was 1.1%. In the E. coli sequence type (ST) 156, the mcr-1 was located in an ISApl1-mcr-1-orf-ISApl1 (Tn6330) and incorporated into the chromosome; in the E. coli ST23 isolate, the mcr-1 was harboured by plasmid replicon type IncX4. Both, mcr-1 positive E. coli were multidrug resistant and, in addition, one isolate was an extended-spectrum β-lactamase (ESBL) producer (blaCTX-M-37).

Conclusions: Expatriates living in the Czech Republic, can be colonized by multidrug resistant Enterobacteriaceae including those harbouring mcr-1 genes on a plasmid or chromosome.

Acknowledgement: This study was supported by the Ministry of Health of the Czech Republic grant no: NV 18-09-00254. All rights reserved.

<table>
<thead>
<tr>
<th>Number of colistin resistant Enterobacteriaceae with MIC values</th>
<th>³≥4</th>
<th>³≥8</th>
<th>³≥16</th>
<th>Total n=15</th>
<th>Travelers</th>
<th>Expatriates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>7</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>0</td>
<td>1</td>
<td>6</td>
<td>7</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Enterobacter cloaceae</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Table: Number of colistin resistant Enterobacteriaceae cultured from stool samples (n=177) and and their minimal inhibitory concentration (MIC) values.

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Measles seropositivity in renal transplant recipients in the presence of ongoing outbreaks: a single centre analysis

Fabian Wagner¹, Daniel Sidler², Maria Teresa Barbani³, Franziska Suter-Riniker², Philipp Jen⁴, Cédric Hirzel⁴, Laura Walti*⁴

¹University of Bern, Bern, Switzerland, ²Bern University Hospital, University of Bern, Department of Nephrology, Bern, Switzerland, ³University of Bern, Institute for Infectious Diseases, Bern, Switzerland, ⁴Bern University Hospital, University of Bern, Department of Infectious Diseases, Bern, Switzerland

Background: Measles outbreaks are ongoing worldwide. Measles infection has a high morbidity and mortality in the immunocompromised host. Healthcare-authorities recommend measles-antibody measurements pre- and post-transplantation [in Switzerland since 2014]. Seronegative transplant candidates should be offered pre-transplant immunization. Data on uptake of these guidelines and necessity of post-transplant reevaluation of measles immunity is lacking.

Materials/methods: We performed a retrospective analysis of measles serology among all renal transplant recipients (RTRs) transplanted between 07/1981-12/2018 at our center. Until 2005 anti-measles IgG was determined using Immunofluorescence (IF) [cut-off >40], from 2006 to 2012 using Vidas Measles Index IgG [cut-off >1.1], from 2013 onwards using SERION ELISA classic Measles Virus IgG [cut-off >200 mIU/ml]. Data on immunization was not uniformly available.

Results: Since 1981, 518 patients received kidney transplantation, 388 before and 130 after 2014. Median age at transplantation was 49 years (IQR 37-59). Measles serology was available for 38% of patients pre-transplantation and for 51% of patients post-transplantation [median time from transplantation to serology 7 years (IQR 2-13.5)]. Pre- and post-transplantation serology were significantly more often performed after the implementation of the guidelines in 2014 [pre-transplantation-serology: 18.3% before- vs. 95.4% after 2014; P < 0.0001; post-transplantation-serology: 45.0% before- vs. 68.5% after 2014; P < 0.0001]. In 130 patients measles serology was available before and after transplantation. Loss of protective antibody levels post-transplantation was rare (1.6%), and occurred in two immunized pediatric patients. Nevertheless, median antibody levels dropped significantly after transplantation in the 85 patients with paired SERION IgG serum samples [pre-transplantation 2023 mIU/ml (IQR 1332-2936) vs. 1427 mIU/ml (IQR 872-1961) post-transplantation; P < 0.0001]. Overall 4.8% of patients [13/269] had non-protective antibody levels post-transplantation, therefore considered at risk of measles infection. These patients were significantly younger [median age at transplantation 23y, IQR 16-36; P < 0.001]. Correlation of measles-IgG-levels with attainment of immunity [vaccination versus infection] was not possible, due to the lack of standardized vaccination documentation.

Conclusions: Almost five percent of RTRs are potentially at risk for measles infection post-transplantation. This highlights the importance of increasing vaccine uptake pre-transplant, and cocooning strategies. Pre-and post-transplant measles serology was performed rarely before the implementation of guidelines in 2014, but thereafter serology uptake pre-and-post-transplant increased.

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**Abstract 3969**

*Investigation of intestinal parasites in immunocompromised and immunocompetent patients with diarrhoea: what About Blastocystis and Dientamoeba fragilis?*

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**Background:** *Dientamoeba fragilis* and *Blastocystis* have long been regarded as non-pathogenic gut protozoa; however, many clinical reports after 70’s indicated them, mostly *D. fragilis*, as causative agents of gastrointestinal and dermatological complaints and reported recovery in patients following antimicrobial treatment. Trials using PCR for their detection in stool indicated dramatically higher rates than microscopy, which then aroused the discussion whether *D. fragilis* and *Blastocystis* were actually pathogens or just residents of healthy gut. The aim of this study is to compare the prevalence of intestinal parasites between different patient groups with diarrhea and healthy controls, as the initial phase of a microbiota project that will investigate the gut microbiota in diarrheic patients and controls, involving the lifestyle and eating habits of participants.

**Materials/methods:** Study Group (SG) consisted of 57 diarrheic stools of immunocompromised patients that had recently received allogenic bone marrow transplantation (n=24) and immunocompetent irritable bowel syndrome patients diagnosed according to Rome IV criteria (n=33). Control Group (n=33) consisted of age and sex-matched healthy individuals. All stools were initially examined with saline-Lugol and concentration, followed by trichrome and Kinyoun acid-fast staining, and conventional PCR for *D. fragilis*.

**Results:** *Blastocystis* was found to be the leading protozoon (n=26; 31.7%), followed by *D. fragilis* (n=16; 19.5%) and *Entamoeba histolytica/dispar* (n=15; 18.3%) among all participants. *D. fragilis* DNA was identified in 12 of 82 eligible samples in PCR (14.6%), all of which were also positive in trichrome-stained smears. Half of both *D. fragilis* and *Blastocystis*-positive participants were in CG. *Taenia saginata* was the only helminth found in a patient with IBS. *Cryptosporidium spp.* (n=3) and *Cyclospora cayetanensis* (n=2) were found in 5 of 24 (20.8%) immunocompromised patients in the study.

**Conclusions:** *D. fragilis* and Blastocystis were both found to be more common in healthy controls compared to patients with diarrhea, while diarrhea was due to the coccidians in one of five immunocompromised patients in our study. Interpretation of these initial results with further microbiota analyses of the participants involving also their lifestyle and eating habits may help us better understand the roles of *D. fragilis* and *Blastocystis* in human health.

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Abstract 3973

**A phase I study in healthy volunteers to assess the absolute bioavailability of the bilayer tablet of sulopenem etzadroxil with probenecid**

Michael Dunne*1, Mei Dai2, Rong Zhou2, Steven Aronin1, Jeff Wald3

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Abstract third-party references: Iterum Therapeutics, Jeff Wald, Michael Dunne, Mei Dai, Rong Zhou

**Background:** Sulopenem etzadroxil is the oral prodrug of sulopenem. It is being studied for treatment of urinary tract and intra-abdominal infections. This study evaluated the absolute bioavailability of sulopenem by comparing the exposure achieved following oral administration in fed/fasted states of a single dose of the fixed-dose bilayer tablet to the exposure achieved following the equivalent amount of sulopenem administered as a one-hour infusion.

**Materials/methods:** 14 subjects were enrolled to examine the bioavailability of sulopenem as part of a bilayer tablet which contained 500 mg each of sulopenem etzadroxil and probenecid. Dosing in Period 1 and 3 was conducted in fasted state; Period 2 in fed state with 7-day washout between dosing.

Standard non-compartmental methods used for calculation of pharmacokinetic parameters.

**Results:** Exposures (Cmax and AUCs) of the bilayer tablet increased in fed compared to fasted state. Absolute bioavailability of bilayer tablet is 40% in fasted state; 64% in fed state. High-fat meal increased sulopenem bioavailability by 50%.

<table>
<thead>
<tr>
<th>PK Parameter (Unit)</th>
<th>Statistic</th>
<th>Sulopenem etzadroxil 500 mg + Probenecid 500 mg as bilayer tablet</th>
<th>Sulopenem 366 mg IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (ng/mL)</td>
<td>Geom. Mean (CV%)</td>
<td>1836.4 (39.1)</td>
<td>2662.1 (43.6)</td>
</tr>
<tr>
<td>AUC0-inf (h*ng/mL)</td>
<td>Geom. Mean (CV%)</td>
<td>4854.4 (25.3)</td>
<td>7411.4 (22.7)</td>
</tr>
<tr>
<td>t1/2 (h)</td>
<td>Mean (SD)</td>
<td>1.184 (0.238)</td>
<td>1.275 (0.488)</td>
</tr>
<tr>
<td>T above MIC 0.06 µg/ml (h)</td>
<td>Mean (SD)</td>
<td>7.135 (0.760)</td>
<td>7.913 (1.039)</td>
</tr>
<tr>
<td>T above MIC 0.5 µg/ml (h)</td>
<td>Mean (SD)</td>
<td>3.438 (0.538)</td>
<td>4.105 (0.780)</td>
</tr>
</tbody>
</table>

AUC0-inf = area under the plasma concentration-time curve from time 0 extrapolated to infinity; CV = coefficient of variance; SD = standard deviation; t1/2 = terminal elimination half-life. *n=12 in Period 2 for AUC and t1/2

**Conclusions:** The absolute bioavailability of sulopenem when delivered as sulopenem etzadroxil-probenecid bilayer tablet and compared to 1-hour IV infusion of 366 mg sulopenem is 40% in fasted state and increases to 64% when dosed with food. Given its low protein binding (11%), the bilayer tablet, dosed fed or fasted, should provide exposure above the MIC of target pathogens for a significant period of the dosing interval.

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Abstract 3978

Effects of fluoroquinolone-sparing empiric therapy guideline implementation in a collaborative hospital network

Elizabeth Dodds Ashley*, Travis Jones1, Melissa Johnson1, Angelina Davis1, April Dyer1, Alicia Nelson1, Deverick Anderson1, Rebekah Moehring1

1Duke Center for Antimicrobial Stewardship and Infection Prevention, Durham, NC, United States

Abstract third-party references: Iterum Therapeutics, Jeff Wald, Michael Dunne, Mei Dai, Rong Zhou

Background: Clostridiodes difficile infection (CDI) remains a significant threat in US hospitals despite ongoing infection prevention and antimicrobial stewardship program (ASP) efforts. Guidelines recommend CDI-focused interventions to reduce broad-spectrum antibiotic use, particularly avoidance of fluoroquinolones. We aimed to describe effects of implementing a centrally developed fluoroquinolone-sparing empiric guideline customized and scaled across a collaborative hospital network.

Materials/methods: Ten acute care community hospitals enrolled in the Duke Antimicrobial Stewardship Outreach Network (DASON) as part of a larger study to evaluate implementation of the CDC's Core Elements for Hospital ASPs and 7 of 10 elected to implement fluoroquinolone-sparing empiric therapy guidelines as an “Action” element. Disease-specific empiric guidelines were developed and customized for each hospital to provide non-fluoroquinolone recommendations and highlight short durations. Guidelines were reviewed and approved by committees at each hospital between 2/2017 and 1/2018. Dissemination occurred through educational presentations to clinical staff, distribution on the back of the annual antibiogram, and posting at convenient locations for prescribers. Relevant order sets were updated. Pooled rates of inpatient antibiotic use in days of therapy/1,000 patient days (PD) and hospital onset (HO) CDI cases/10,000 patient days were tracked quarterly to describe trends among the 7 hospitals. The baseline period was defined as quarter 3 and Q4 of 2016 and the post-implementation period as Q3 and Q4 of 2018. Percent change was calculated comparing baseline to post-implementation periods.

Results: Network-wide fluoroquinolone use down-trended after Q2 2018, representing a 33% decline from baseline to post-implementation (125 vs. 84 DOT/1000PD, Figure). HO CDI declined 46% (8.9 vs 4.8 HO CDI/10,000PD). During the same time period, overall inpatient antibacterial use decreased by 10.1% (905 vs 813 DOT/1000PD).

Conclusions: Hospitals who implemented fluoroquinolone-sparing guidelines in a collaborative network decreased fluoroquinolone use and experienced corresponding declines in HO-CDI. This scalable intervention was easily implemented across a network of hospitals.

Quarterly Antibiotic Use and CDI

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Employing tongue swabs and urine as clinical alternatives to sputum for *Mycobacterium tuberculosis* testing on a solid state nanopore sensor platform

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**Background:** MTB continues to be a major health problem affecting 1 in 4 people worldwide. Imperfect phenotypic screening and costs of comprehensive molecular testing methods hinder effective public health measures to control the epidemic. Sputum, the most widely used biological material for most TB tests, is not ideal given the difficulty to process it for downstream testing, it is hard to produce on demand (especially for children), and 1 in 5 TB cases are ex-pulmonary. Thus, it is highly desirable to find an alternative bio fluid that is easily attainable and processed to facilitate high sensitivity and specificity molecular tests.

**Materials/methods:** We've developed two different tests for highly specific and sensitive detection of MTB on our solid-state nanopore sensor platform. The first is a multiplexed molecular test using tongue swabs as a MTB DNA source, the second detects the complex glycan lipoarabinomannan (LAM) in urine. These tests were first developed using benchtop methods and contrived samples, and later proofed using clinical samples and portable instrumentation employing a nanopore sensor for cost effective and field deployable testing.

**Results:** Our contrived swab testing indicates assay sensitivities down to 1 CFU per reaction, while clinical sample testing had high concordance with both laboratory based molecular (qPCR) testing and culture. Contrived urine testing for the LAM analyte indicates a sensitivity (fM) that matches a highly optimized, centralized lab ELISA test. Testing on neat clinical samples indicates assay performance is maintained using patient samples and a field applicable workflow, having sensitivities that exceed the existing lateral flow test being used in the field.

**Conclusions:** Preliminary results indicate that tongue swabs and urine samples, two easily obtainable biofluids, may prove to be sufficient, and even superior, to sputum when testing for MTB. These samples paired with the fast (<20 mins) time to result delivered from the solid state nanopore based platform offers low cost, impactful molecular testing in challenging environments needed to implement effective public health monitoring needed to control the TB epidemic.

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Abstracts 2020

Abstract 3980

Direct detection of PBP2a using the high-resolution Orbitrap mass spectrometer and rapid discrimination of antibiotic resistance in Staphylococcus aureus using the Acrion system

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Background: Methicillin-resistant Staphylococcus aureus (MRSA) is a common infectious agent in community and hospital environments. Molecular and phenotypic MRSA detection strategies are labor intensive and often indirectly detect the target responsible for antibiotic resistance, penicillin-binding protein 2a (PBP2a). While current clinical MALDI mass spectrometry methods in microbial diagnostics are low resolution, have limited mass range, and have had poor success in antibiotic resistance detection, we present a novel approach that enables direct detection of the PBP2a protein using a high resolution mass spectrometer system. While these systems usually employ peptide detection strategies, this workflow relies on detection and discrimination of intact proteins ions.

Materials/methods: S. aureus protein lysates were prepared from single colonies following 18 hours of growth on agar media and lysed with a formic acid/water/acetonitrile solvent mixture. Direct detection of PBP2a was performed using a Q Exactive™ HF mass spectrometer or Acrion™ system following a short chromatographic separation of protein lysates.

Results: Two detection approaches were designed for detection of this resistance marker, isolation of the intact protein or isolation of an in source dissociated fragment of the PBP2a protein. The latter method proved to be more robust and sensitive. Both approaches were successful across all SCCmec cassettes and the most common PFGE types. This method can be modified to facilitate detection of other PBP2a isoforms (i.e. mecB, mecC, and mecD) and other rare variants (e.g. BORSA) if the resistance mechanism(s) is known. While this approach relies on the initial identification of the microbe as S. aureus, it removes any extra culturing from the workflow to identify it as MRSA and significantly reducing the time to reporting. Initial success of this method has shown to be greater than 95% for true positives and no false-positive errors.

Conclusions: Rapid detection of antibiotic resistance using this mass spectrometry approach represents a promising leap forward in diagnostics and this work represents one of many workflows that can be adapted to the clinical laboratory.

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Abstract 3981

**Legionnaires’ disease and sleep apnea devices: retrospective analysis of a 9-year-investigation and contribution of whole genome sequencing.**

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**Background:** Legionnaires’ Disease (LD) is due to inhalation of *Legionella* contaminated aerosols. Apnea therapy devices are increasingly employed for patients with obstructive sleep apnea and can represent a high risk of contamination by inhalation of aerosolized bacteria if not properly maintained or filled with tap water. However, the incidence of Lp transmission through such medical devices is not well described.

**Materials/methods:** We report a 9-year retrospective study on sleeping apnea devices (SAD) exposure in LD patients notified in France. The exposition to such devices reported on the mandatory notification and the number of microbiological and epidemiological investigations were collected. *Legionella* PCR and culture of SAD water, typing using Sequence-based typing (SBT), nested-SBT (nSBT) or whole genome sequencing (WGS) were performed on samples / strains sent to the French National Reference Centre for *Legionella*.

**Results:** A total of 12985 LD were reported in France between 2011 and 2019. SAD exposition was indicated for 106 (0.8 %) cases (0 to 1.4% per year). During this period, a comparison between SAD water and clinical samples was requested for 19/106 cases (18%). Regarding environmental samples, 1/16 *Legionella* culture and 7/12 *Legionella* qPCR were positive. Three comparisons gave results. One of them showed a difference between clinical ST [ST1] and water nSBT [ST36], another showed compatible results between water complete nSBT [ST1] and clinical nSBT [6/7 amplified genes]. For the last case, we isolated endemic ST23 strains from patient and water samples, and WGS analysis showed they were phylogenetically closely related.

**Conclusions:** SAD and any aerosolization systems are potential sources of *Legionella* infection if misused but are rarely investigated. We confirmed for the first time by WGS comparison this contamination source. Environmental investigations are often difficult to achieve, SAD water being in insufficient quantity or frequently thrown after device cleaning. However, it is important to mention that tank or rinse water could be better investigated and probably help to resolve the investigation with current qPCR and/or WGS sensitive techniques.

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Cognitive impairment following severe malaria in travellers

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Abstract:

Background: Severe malaria is a complex disease in which people infected by Plasmodium sp can express various clinical and biological signs of organ dysfunction. Among those phenotypes is the involvement of central nervous system. Providing various brain injuries directly or indirectly due to malaria and its management, long-term consequences may include neuro-cognitive impairment or behavioural problems. Widely explored in children, these sequels are poorly described in adults. In this pilot study, we report in detail cognitive impairments in returning travellers to France following severe malaria.

Materials/methods: Nine adults with initial cognitive symptoms following an episode of imported severe malaria were assessed in our neuro-rehabilitation department 2 to 4 months post-acute. Exclusion criteria were: previous neurological or psychiatric history. A detailed cognitive assessment was performed based on patient's complaints, using standardised tools.

Results: Only two patients had no complaint. Among the others, five reported fatigue, four reported disturbances in attention, three reported disturbances in working memory, two reported word finding difficulties. For the patients that had a complaint, we assessed impairment in long term memory (information retrieval) for 4 patients, impairment in working memory for 5 patients, impairment in executive functions as well as in attention for 3 patients. Four patients had anxio-depressive symptoms. One patient had visuo-constructive problems and one had pathologic processing speed. Neuropsychological rehabilitation was proposed to patients who needed.

Conclusions: In this pilot study, we report detailed results of cognitive assessment following severe malaria in returning travellers with initial cognitive symptoms. Cognitive impairments were noted for almost all patients, particularly for cognitive functions that are not very localised in the brain such as working memory, attention and executive functions. This testifies the need for a better understanding of pathological mechanisms that provide these long-term consequences to prevent them. Moreover, these results suggest there is a need for improving the healthcare network, referring more systematically travellers following severe malaria for a complete neuro-cognitive assessment in order to identify needs in neuropsychological rehabilitation.

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Assessing impact of Multiplex PCR Point-of-Care testing in patients with respiratory tract infection: a French national study

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Materials/methods: In this prospective multicentric observational study, data were collected on patients who underwent POCT on RTI admission in 10 participating centers. POCT were realized on FilmArray® BioFire® Respiratory Panel 2+ (bioMérieux) or ePlex® Respiratory Pathogen Panel (GenMark). For each patient, demographic data, admission diagnosis, potential antimicrobial treatments and the POCT results were collected. Dates and hours of admission, hospitalization, respiratory sampling, POCT results availability and, if used, antimicrobial treatment were also collected. To assess POCT impacts, comparison between test results and antimicrobial use was conducted between patients with POCT result available before and after antimicrobial prescription.

Results: Between November 2017 and December 2018 we enrolled 649 patients with a mean age of 56 yo [0;99]. Of these, 88% (n=558) were hospitalized: 58% in conventional wards and 42% in ICU. The most frequent admission causes were Influenza-like illness syndrome [26%; n=131] and pneumonia [19%; n=98]. After exclusion of patients previously treated before their admission, 52% (n=265) and 7% (n=41) of patients received antibiotics and antivirals respectively. Among them, only 30% (n=82) of antibiotic treatments were prescribed upon test result availability, with a median time to antibiotics of 7.4 hours (IQR: 2.1;22.1) and a median time from consultation to result availability of 18.9 hours [0;10.9]. The positivity rates of POCT were 49% (IC95: 37%-60%) versus 53% (IC95: 46%-60%, p=0.49) in patients with prescribed antibiotics before and after POCT results respectively. Moreover, mean durations of antibiotics were 9.9 (CI95: 8.6-11.1) days versus 10.4 (CI95: 9.0-11.7; p=0.58) when the POCT was positive versus negative respectively.

Conclusions: No association between antibiotic introduction nor antibiotic duration and POCT results were observed. Most [70%] antimicrobial treatments were introduced before POCT results. The potential lack of impact of POCT on antimicrobial therapies use could be explained by: (i) a long mean time to result incompatible with the necessities of emergency care, and (ii) limited physician reliance on POCT results.

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Abstract 3984

**Culture-negative "tuberculosis": which patients are at risk of misdiagnosis?**

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**Background:** Patients are often started on anti-tuberculosis therapy (ATT) in the absence of positive culture results. While clinical suspicion is often proved correct, the patients that remain TB culture-negative are at risk of missed or delayed alternative diagnoses and are exposed to potentially unnecessary medication side effects. There is a paucity of information regarding the alternative diagnoses these patients receive during and after ATT.

**Materials/methods:** We retrospectively analysed prospectively collected tuberculosis (TB) patient data to identify all TB culture- and PCR-negative patients commencing treatment at Northwick Park between 01.01.2015 and 01.01.2018. Clinical records, imaging and laboratory results were reviewed to identify a) alternative (non-TB) diagnoses and b) risk factors for alternative diagnosis.

**Results:** Of 897 patients notified to the London TB register, 125 (13.9%) were TB culture- and PCR-negative. 14 patients were excluded (11 lost to follow up, 3 declined treatment).

Of the remaining 111 patients, 24 (22%) received a definite alternative diagnosis. Of these alternative diagnoses, malignancy was commonest (10), then non-TB infections (6) and sarcoidosis (3).

Median days to confirmation of alternative diagnosis was 37 (range 0-1081 days). Those with an alternative diagnosis were significantly older (median age 59 vs 38, *p*<0.01) and less likely to have diagnostic histology (4% vs 23%, *p*=0.04) or a positive Mantoux or IGRA (50% vs 81%, *p*<0.01). Additionally, they were more likely to have received steroids and less likely to have resolution of symptoms at 2 months or on finishing ATT, however these values did not reach statistical significance.

**Conclusions:** Clinical caution and vigilance is advisable when managing culture-negative suspected tuberculosis patients. The 2-month clinical review, when mycobacterial culture and sensitivity results are available, is a good time to revisit a presumptive diagnosis of TB and if risk factors for misdiagnosis are present, to prompt further imaging, histology or microbiology. In our culture-negative group, an alternative diagnosis to TB was more common in those with non-resolution of symptoms, older age, lack of positive Mantoux or IGRA and lack of strongly supportive histology and radiology at diagnosis.

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Assessing Pharyngeal Respiratory virus Carriage in healthcare workers Over Time (APRICOT): a feasibility study
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Background: Nosocomial transmission of respiratory viruses is a source of excess morbidity and mortality in hospitalised patients. Evidence suggests healthcare workers are at higher risk of acquiring respiratory viruses, but their role in onward transmission is unclear. This study aimed to assess the feasibility of surveillance pharyngeal swabs to determine the prevalence of respiratory virus carriage in healthcare workers.

Materials/methods: A single centre feasibility study was conducted on the Infectious Diseases inpatient unit at St James’s University Hospital, Leeds, UK during winter 2018-2019. Eligible participants were patient-facing staff who worked on the unit for >50% of their contracted hours, including nursing, medical, housekeeping and applied healthcare professionals. Each participant submitted a weekly pharyngeal swab for 10 weeks. Swabs were collected by researchers or the participant themselves, placed in Copan UTM™ viral transport medium and later processed using a multiplex polymerase chain reaction (PCR) containing 10 respiratory viral targets and a human RNAase P target to demonstrate sample adequacy. At the time of each swab, participants completed a questionnaire recording presence and duration of respiratory symptoms.

Results: 25 participants were recruited, of whom 85% were female and 52% were ≤35 years old. Nurses or nursing support workers comprised 52% of the cohort. 23 participants (92%) completed all 10 swabs and questionnaires, with 16 participants submitting self-taken swabs throughout. 10 participants (40%) had at least one positive swab. In total, 248 swabs were collected, of which 15 (6%) were positive for a respiratory virus, including influenza A and respiratory syncytial virus. All the subjects with positive swabs reported symptoms within 72 hours of sampling. The median number of reported sickness episodes was 2 (IQR 1-3), with the median number of reported sickness days 21 (IQR 8 – 36.5 days). Most symptomatic participants had negative swabs. 98.8% of samples were taken adequately, confirmed by RNase P detection.

Conclusions: This work has demonstrated that surveillance pharyngeal swabs can establish the prevalence of respiratory virus carriage in healthcare workers, and that self-taken swabs are adequately performed and acceptable to participants. Further work is needed to determine the risks of viral transmission between healthcare workers and patients.

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Comparative virulence of respiratory viruses on the winter seasons from 2017 to 2019: a southern European multi-centre cohort study

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Background: Influenza and respiratory syncytial virus (RSV) are responsible for a great burden of disease, peaking over the winter months in Europe. This study aimed to determine which of the most frequent agents causing severe acute respiratory infections may be responsible for the worst outcomes.

Methods: Study subjects were recruited based on positive PCR results for Influenza or RSV on respiratory samples, obtained over the previous two winter seasons in three tertiary hospitals in Cyprus, Italy and Portugal. We included patients ≥ 18 years-old who were admitted to a hospital ward and/or intensive care unit for acute illness. Data on demographics, co-morbidities, viral agents, disease course and outcome were collected. Cases deemed to have possible nosocomial infection were excluded. Univariate analysis was conducted using Mann-Whitney and chi-square tests. Multivariate analysis used logistic regression and included variables which were deemed clinically relevant and/or had p values <0.25 on univariate analysis.

Results: A total of 1012 patients met the study inclusion criteria. Their median age was 75 years, 25.3% had history of diabetes, 29.8% heart failure, 29.2% chronic obstructive lung disease (COPD) or asthma, 17.8% active malignancy and 15.8% chronic kidney disease (CKD) stage 3 or worse. Influenza A was the most frequently isolated virus (n=575; 56.8%), of which 158 were further subtyped as H1N1 (15.6% of the total) and 304 as H3N2 (30.0%). Influenza B and RSV were positive respectively in 22.9% (232) and 22.3% (226) of patients. H1N1 was associated with younger age (p<0.001), while heart failure, CKD and COPD or asthma were associated with infection by RSV.

There were 106 deaths (10.5%) and 84 (8.3%) patients submitted to invasive mechanical ventilation (IMV). Median length of stay was 9 days IQR[6-15].

Patient characteristics independently associated with death were older age [adjusted odds ratio (aOR) 1.02 CI95%[1.0-0.1.04]) and solid malignancy [aOR 2.93 [1.53-5.63]. On adjusted analysis of virulence, H1N1 was associated with higher odds of death [aOR 2.01 [1.20-3.38]) and IMV [aOR 5.3 [3.2-8.8]].

Conclusions: RSV infection was associated with the presence of chronic comorbidities. Influenza A H1N1 afflicted younger patients and was associated with higher death and IMV rates.

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Flexible implementation of microbiology laboratory automation using BD's solution of standalone instruments

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Background: The implementation of total lab automation requires significant investment, ample laboratory space, as well as considerable changes to the lab's workflows. BD is introducing a Connected Solution of standalone instruments that are logically connected and controlled, using BD Synapsys™, to mitigate some of these challenges. This modular platform allows labs to adopt automated workflows at a pace that is complementary to their growth, and reduces the physical space requirements for laboratory automation by providing a smaller, more flexible footprint of individual standalone instruments. At the heart of the Connected Solution is the BD Kiestra™ ReadA Standalone containing a 25MP camera with a telecentric lens for improved visualization of cultures.

Materials/methods: Connected Solutions consisting of combinations of BD instruments, including ReadA Standalone, Standalone InoquA+™, Standalone IdentifA, BACTEC™ FX, and Work Cell Automation (WCA), were tested in BD's microbiology laboratory. A wide variety of clinical laboratory workflows was evaluated using different clinically relevant organisms.

Results: Testing began with a configuration consisting of a ReadA Standalone and a Synapsys™ workstation. Manual inoculation was performed at the workstation, the inoculated plates were either incubated in the ReadA or externally (e.g. anaerobic plates), and all plates were imaged in the ReadA at predefined time points. The 25MP camera and telecentric lens improved visualization of complex cultures by eliminating shadows and allowing high-quality magnification of plate images. To demonstrate a step-wise approach, a BD BACTEC™ FX and BD Kiestra InoquA+™ were logically connected to the solution for automated processing of blood cultures and automated inoculation of media and slides. Plates processed by the InoquA+™ were incubated and imaged in the ReadA Standalone. In addition, a Standalone IdentifA was logically connected to a WCA where plates destined for workup on the IdentifA were automatically sent to a stacker, and manually transported to the IdentifA.

Conclusions: BD's new Connected Solution offers customizable configurations consisting of different standalone instruments. This enables laboratories to automate specific aspects of their workflows, or implement a gradual step-wise approach to lab automation. These configurations also provide increased flexibility to laboratories with space limitations, while providing all the benefits of lab automation.

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Abstract 3992

The Caserta Model: an hepatitis C virus way out in persons who use drugs in Italy

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Background: The aim of the present study was to evaluate the efficacy of an innovative and simplified model to eliminate HCV infection in a high-risk population of PWUD.

Materials/methods: between January 2018 and April 2019 a prospective, interventional, before and after study, based on the active and close cooperation between all the 6 Caserta Services for the Dependence (SerD) starting from the Teano one and the corresponding 3rd level units of Infectious Diseases in Caserta, Campania, Italy, was performed. The intervention included periodic prospective audits conducted by the infectious disease consultants in the SerD to improve the knowledge on HCV infection and on the need to treat. The infectious disease consultants were responsible for writing and sharing diagnostic protocols for HCV infection to do at SerD; a simplified pathway to access the Infectious Disease Unit and to start DAA was planned and a protocol for the follow-up during and after DAA treatment with a close collaboration between SerD and ID Unit personnel was identified. The outcomes were to test the efficacy of the model. The pre-intervention period was defined as January-December 2017; the post-intervention period as January-September 2018.

Results: in this setting, in the 6 SerD, the linkage to care model, resulted in an increase of 506% of rates in DAA treatment. PWUD followed up by the Teano one in 2017 and in 2018 were 318 and 275, respectively. The Figure shows the HCV cascade in the two periods. Compared with the pre-intervention period the number of subjects tested for HCV increased, but no significantly, in the post-intervention period (78% vs. 72%, p 0.1). Compared with the pre-intervention period the number of subjects HCV Ab positive tested for HCV RNA increased (91% vs 27% p<0.05). Of the 75 HCV-RNA-positive subjects identified in post-intervention period 65 (86%) were linked to care to Infectious Disease Unit and started DAA regimen, a prevalence clearly higher than that observed in the pre-intervention period (17%, p<0.05).

Conclusions: This innovative procedures for micro-elimination of HCV infection is very effective in PWID with rates of diagnosis and linkage to care.

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**Abstract 3993**

**Predictors of vancomycin-resistant enterococci gut microbiome colonization among patients with Clostridioides difficile infection 6.4.1**

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**Background:** Vancomycin-resistant enterococci (VRE) commonly colonize patients’ gut microbiome and can cause subsequent infection. This risk is high among patients with *Clostridioides difficile* infection (CDI). Knowledge of VRE colonization can guide empiric antibiotic therapy to ensure timely appropriate therapy for patients with VRE while limiting unnecessary antibiotics in those without. The objective is to derive and compare predictive indices for VRE gut microbiome colonization in CDI patients.

**Materials/methods:** Single center, retrospective cohort study from 3/2017 to 4/2018. Inclusion criteria: age ≥ 18 years; positive CDI test. Exclusion criteria: CDI-positive stool sample unavailable for testing. VRE colonization was identified in stool samples through growth and speciation on selective antibiotic media and confirmed using resistance gene PCR. Multivariable logistic regression was used to identify factors associated with VRE colonization. A predictive index based on regression coefficients was computed for each patient. Predictive performance via area under the receiver operating characteristic curve (aROC) of this index was compared via Hanley and McNeil method with two other simplified risk stratification approaches: 1. prior healthcare exposure and/or high-CDI risk antibiotics; 2. number of prior high-CDI risk antibiotics.

**Results:** Two hundred-forty patients were included; 35 (14.6%) had a VRE-positive stool sample. The median (IQR) age and Charlson comorbidity index were 64.5 (52-74.8) years and 2 (1-3), respectively. Prior healthcare exposure (62.1%) and prior high-CDI risk antibiotics (60%) were common. In logistic regression, prior fluoroquinolone (OR 2.668, 95%CI 1.131-6.294) was independently associated with VRE colonization; prior vancomycin (OR 2.102, 95%CI 0.966-4.573), clindamycin (OR 3.291, 95%CI 0.807-13.432), and healthcare exposure (OR 2.379, 95%CI 0.900-6.289) were retained as explanatory variables. A risk index based on number of regression-derived risk factors significantly predicted VRE colonization (aROC 0.704, 95%CI 0.613 – 0.794), but was not significantly more predictive than prior healthcare exposure + prior antibiotics (aROC 0.650, 95%CI 0.564 – 0.736) or number of prior antibiotic exposures (aROC 0.641, 95%CI 0.539 – 0.742); P > 0.05 for both comparisons.

**Conclusions:** A simplified approach using prior healthcare exposure and receipt of prior antibiotics known to increase CDI risk identified patients at risk for VRE gut microbiome colonization as well as individual patient/antibiotic risk modeling.

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Moxifloxacin for the treatment of latent tuberculosis infection in liver transplant candidates and recipients: a single-centre experience

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Background: Solid organ transplant (SOT) recipients have an increased risk of developing active tuberculosis (TB). Screening for latent tuberculosis infection (LTBI) prior to transplantation and treatment with isoniazid or rifampicin is recommended. In the case of liver transplant (LT) recipients, however, this strategy is not usually feasible due to risk of anti-TB drug-induced hepatotoxicity. Fluoroquinolones are a promising alternative, although the occurrence of treatment-emergent severe tenosynovitis limited the use of a 9-month course of levofloxacin for the treatment of LTBI in LT recipients in a clinical trial previously conducted by our group.

Materials/methods: Descriptive study of the safety and efficacy of moxifloxacin (400 mg daily) for 6 to 9 months for LT candidates and recipients diagnosed with LTBI at our center between December 2015 and June 2019.

Results: A total of 31 patients received moxifloxacin for LTBI (23 males, mean age: 57 ± 8.7 years). Moxifloxacin was started prior to LT in 23 patients, and in 13 cases the transplantation was performed during the course of therapy. Main underlying conditions were chronic hepatitis C virus infection and/or alcoholic liver disease (71%). At the time of transplantation, 52.4% and 47.6% of patients showed a Child-Turcotte-Pugh class A and B, respectively. At the time of the current report, 24 (85.7%) and 20 (71.4%) patients had received moxifloxacin for more than 6 and 9 months, respectively. Overall, 15 patients (48.4%) experienced at least one treatment-emergent adverse effect, but only in 5 cases (16.1%) moxifloxacin had to be stopped permanently. In detail, such events included one case of hematological toxicity, one case of severe generalized arthralgia, and 3 cases of Clostridioides difficile infection [diagnosed at days 7, 116 and 198 from the initiation of therapy]. Six patients (19.4%) reported mild-to-moderate joint pain or tendinopathy, but only one case required for moxifloxacin to be stopped permanently. No cases of moxifloxacin-induced QT interval prolongation were detected. No cases of active TB were diagnosed during follow-up [median of 631 days].

Conclusions: Moxifloxacin appears to be a reasonably safe option in LT candidates and recipients to whom isoniazid or rifampicin cannot be administered for the treatment of LTBI.

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Abstract 3995

**Legionella pneumophila sqPCR in serum and respiratory samples as a marker of Legionnaires’ disease severity**

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**Background:** Legionnaires’ disease (LD) is a severe pneumonia, with a rate of intensive care unit (ICU) admission up to 50% and a global mortality of 8%. The aim of this study was to evaluate the prognostic value of quantitative Legionella pneumophila PCR (Lp qPCR) in serum and respiratory samples in comparison to LD clinical and biological severity markers, and to monitor the qPCR evolution during Lp infection.

**Materials/methods:** We included 82 patients from a national prospective cohort, "ProgLegio", hospitalized in ICU (n=55) or in conventional medical departments (n=27). SOFA severity score was evaluated (n=46). A Lp qPCR was performed from 24 to 48h after diagnosis (D0) on serum and respiratory samples, followed at D3, D5 and every 3 days until negativation (cohort sizes below) for respiratory samples. In parallel, 19 plasmatic inflammatory cytokines were measured by a multiplex technique on D0 (n=47).

**Results:** 14/46 patients (30%) had a positive qPCR in serum. They had a significantly higher SOFA (8 vs 2 p < 0.0001) and pro-inflammatory cytokine levels (IFNγ: 31.7 vs 7.5 pg/mL, p=0.004; IL6: 168.2 vs 36.3 pg/mL, p= 0.006; IL8: 81.6 vs 28.7 pg/mL, p= 0.002) than patients with negative qPCR and were mostly ICU patients. Serum and respiratory qPCR results were correlated on D0 (r=0.66; p<0.0001). Respiratory qPCRs were positive for 64/76 (84%) samples on D0, 34/40 (85%) on D3, 19/24 (79%) on D5, 13/20 (65%) on D8, 5/8 (62%) on D11, and 3/6 (50%) after D14. Patients with positive qPCR from D8 were all ICU patients and had a median SOFA compared to D0 median SOFA (10 vs 4, p=0.0048). One patient had positive qPCR results until D59.

**Conclusions:** qPCR on serum, is not appropriate for diagnosis but its positivity appears to be a marker of LD severity. Indeed, serum and respiratory DNA load are correlated and associated to an increased inflammatory cytokines release and high SOFA. Furthermore, respiratory qPCR is positive until D8 for most patients that were initially severe and had a prolonged ICU stay.

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Abstract 3997

**Association between the Blastocystis spp. load and patient’s socio-demographic and clinical profile in the northeastern area of Spain**

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**Background:** Blastocystis spp. is the most prevalent eukaryote parasite found in human feces; however, pathogenicity remains uncertain and it has been associated with the parasitic load. The aim of this study was to assess the relationship between the parasitic load and presence of symptoms.

**Materials/methods:** A cross-sectional study was designed, including fecal specimens collected from January 1st 2018 to December 31st 2018, at the Microbiology and Parasitology Service of the Hospital Lozano Blesa Zaragoza – Spain. From 6,478 samples, 475 (7.33%) were positive to Blastocystis spp., 2 of them from patients who had an incomplete clinical history were excluded; therefore, a total of 473 samples were included in the study. The parasite was identified by optical microscopy (400x magnification), and 10 fields per sample was considered as "load of Blastocystis" variable. To investigate the relationship between the variable load of Blastocystis spp. with the socio-demographic and clinical variables and given the non-normality of the distributions, the U Mann-Whitney statistic was used and the level of significance was set at p<0.05.

**Results:** The analysis of the socio-demographic variables showed that 55.8 % of the patients were men and 44.2% were women, also the median age was 27 years (IR=41). The load of Blastocystis spp. by field was significantly higher in patients with abdominal pain (Median = 5.3; IR=10.8 vs 3.6, IR=5.2), chronic diarrhea (Median = 6.6; IR=12.1 vs 4.0, IR=7.9), vomit (Median = 8.6; IR=11.2 vs 4.2, IR=9.3) and aerophagy (Median = 7.0; IR=15.2 vs 4.4, IR=9.0) (table 1). There was not significant relationship between the load of Blastocystis is spp. by field and the rest of the symptoms.

**Conclusions:** It was identified that the load of Blastocystis spp. by field has a significant association between some symptoms described by the patients as abdominal pain, vomit, chronic diarrhea and aerophagy. The results suggested that Blastocystis spp. could behave as a pathogen and its pathogenicity is related with the parasitic load, but further studies are needed to determine the number of Blastocystis needed to be considered pathogenic.

**Table 1. Relationship between the load of Blastocystis spp. and symptoms**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Yes Median (IR)</th>
<th>No Median (IR)</th>
<th>U Mann-Whitney</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>5.3 (10.3)</td>
<td>3.6 (5.2)</td>
<td>1564.0</td>
<td>0.01</td>
</tr>
<tr>
<td>Acute Diarrhea</td>
<td>6.3 (18.0)</td>
<td>4.0 (9.4)</td>
<td>72313.3</td>
<td>0.29</td>
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<tr>
<td>Chronic Diarrhea</td>
<td>6.6 (12.1)</td>
<td>4.8 (7.8)</td>
<td>22962.0</td>
<td>0.002</td>
</tr>
<tr>
<td>Nausea</td>
<td>7.8 (16.0)</td>
<td>4.5 (9.3)</td>
<td>6392.50</td>
<td>0.884</td>
</tr>
<tr>
<td>Constipation</td>
<td>6.8 (17.9)</td>
<td>4.0 (6.4)</td>
<td>40461.30</td>
<td>0.425</td>
</tr>
<tr>
<td>Vomit</td>
<td>8.6 (15.2)</td>
<td>4.2 (9.2)</td>
<td>19867.10</td>
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</tr>
<tr>
<td>Anaemia</td>
<td>4.4 (11.7)</td>
<td>4.7 (9.4)</td>
<td>40286.5</td>
<td>0.057</td>
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<tr>
<td>Fever</td>
<td>7.8 (13.3)</td>
<td>4.5 (9.3)</td>
<td>6224.50</td>
<td>0.187</td>
</tr>
<tr>
<td>Aerophagy</td>
<td>7.0 (15.0)</td>
<td>4.0 (6.4)</td>
<td>9427.90</td>
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<tr>
<td>Anosmia</td>
<td>5.3 (9.2)</td>
<td>4.5 (8.2)</td>
<td>9902.0</td>
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<tr>
<td>Headache</td>
<td>10.8 (27.7)</td>
<td>6.6 (11.3)</td>
<td>1325.10</td>
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<tr>
<td>Uncomfort</td>
<td>4.3 (9.8)</td>
<td>4.8 (9.6)</td>
<td>22989.3</td>
<td>0.711</td>
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<tr>
<td>Sleep disorder</td>
<td>4.5 (8.4)</td>
<td>4.0 (6.4)</td>
<td>25627.5</td>
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<tr>
<td>Chest pain</td>
<td>10.7 (14.4)</td>
<td>4.5 (9.3)</td>
<td>2119.90</td>
<td>0.647</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>4.3 (9.4)</td>
<td>4.5 (9.5)</td>
<td>7531.0</td>
<td>0.453</td>
</tr>
</tbody>
</table>

*F. Matovelle et al.*

**Presenter email address:** crismatovelle@gmail.com
Abstract 3999

Subtyping *Escherichia coli* in spontaneous bacterial peritonitis with use of IR biotyper and whole genome sequencing

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**Background:** In cases of recurrent Spontaneous Bacterial Peritonitis (SBP), conventional diagnostics show similarities in pathogen antibiograms but are unable to swiftly determine if these pathogens originated from the same isolate. This study evaluates the use of Bruker Infrared (IR) Spectroscopy Biotyper and Whole Genome Sequencing (WGS) in recurrent SBP to address this limitation and evaluate their role in directing antibiotic selection and patient management.

**Materials/methods:** Ten clinical (*n* = 2) and reference (*n* = 8) *Escherichia coli* isolates were analysed retrospectively with an IR Biotyper and the IR Biotyper Software Revision C (Bruker UK). The two clinical isolates originated from a patient with bacteraemia and recurrent SBP. Isolates were prepared by aerobic incubation at 37°C for a total for 48 hrs, with the resulting homogenous suspension strain typed. Results were compared against a control Bruker Infrared Test Standard and an empty reference spot included in the 96-spot microtiter plate. A second set of the *Escherichia coli* isolates were also sent for WGS using the Illumina and Oxford nanopore platforms.

**Results:** Hierarchical cluster analysis by the IR Biotyper showed close clustering of the clinical isolates from the patient, when compared with the 8 other reference strains. WGS data from both Illumina and Oxford nanopore platforms was compared and contrasted with the IR Biotyper results.

**Conclusions:** The use of IR biotyper and WGS may be potential diagnostic adjuncts to guide swift and efficacious management in patients with recurrent SBP as it may shed light on the source of spread and pathogen sensitives quicker than conventional diagnostics. However, cost and availability of such tools should be considered if implemented in the clinical setting.

Figure 1: Dendogram produced by the Bruker IR biotyper platform demonstrated that clinical isolates (in red box) were indistinguishable from one another.

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Abstract 4000

Template RNA loops determine aberrant RNA synthesis and innate immune activation during influenza virus infection

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Background: Influenza A virus (IAV) infections usually cause a mild to moderate respiratory disease in humans. However, infections with highly pathogenic influenza viruses can cause severe or deadly pneumonia. Severe IAV infections have been linked to a dysregulated immune response that is triggered in part by detection of viral RNA by the pathogen receptor Retinoic Acid-Inducible gene-I (RIG-I). The segmented IAV viral RNA (vRNA) genome is replicated in the nucleus by the viral RNA dependent RNA polymerase (RdRp), in the context of viral ribonucleoprotein (vRNP) complexes. In addition to making full-length copies of the vRNA segments, the RdRp generates aberrant RNA products that contain internal deletions, such as defective interfering RNAs (>200nt) and mini viral RNAs (mvRNA) (56-125nt). mvRNAs are highly immunostimulatory compared to other replication products and induce interferon (IFN)-β expression by activating RIG-I. mvRNAs are therefore likely important factors in disease, but the mechanism by which they are generated and implicated in the severity of the immune response during IAV infection remains unclear.

Materials/methods: To investigate how mvRNA are generated, we analysed RdRp replication efficiency on model vRNA templates containing various secondary structures in vitro and in mammalian cells. We also investigated the ability of different templates and endogenous mvRNAs to induce an interferon response during infection.

Results: We find that the formation of an RNA duplex around the RdRp, which we call a template RNA-loop (tR-loop), can induce replication stalling and regulate the level of aberrant RNA production. Poor replication of the templates is correlated to the sub-cellular localisation of the template and aberrant products, and the induction of IFN expression. We further find that mvRNA levels vary per IAV genome segment and are influenced by adaptive mutations in the RdRp. Finally, we find that the introduction or removal of tR-loops in genome segments affects immune activation during infection.

Conclusions: We have identified a novel mechanism involving specific RNA structures that determines the generation of aberrant RNA products and regulates innate immune induction during influenza virus infection. This work advances our understanding of the replication of the virus and helps explain immune dysregulation during severe influenza disease.

Innate immune induction by aberrant mini viral RNA

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Abstract 4002

Aspergillosis complicating severe respiratory syncytial virus in intensive care unit patients: a retrospective cohort study

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Background: There are recent reports that identify severe influenza pneumonia as an independent risk factor for the development of invasive pulmonary aspergillosis (IPA), even in patients without immunocompromise. We aimed to understand the incidence of IPA as well as other coinfections over multiple seasons in patients with RSV pneumonia in the intensive care unit (ICU).

Materials/methods: A retrospective cohort study was conducted in a single center in Chicago. Data was collected over 6 seasons [January 2012-March 2018] from adult patients admitted to the ICU at a large urban tertiary care center with severe RSV pneumonia. Patients were included if they had a positive RSV PCR test, older than 18 years, admitted to the ICU with acute respiratory failure, and had pulmonary infiltrates on imaging. IPA was defined per both the EORTC/MSG criteria as well as the revised AspICU criteria [Schauwvlieghe et al]. Descriptive statistics were calculated. In univariable analysis, we compared categorical variables by Fisher's exact test and Chi-square test, continuous variables by Student's t-test where appropriate.

Results: Patients diagnosed with invasive pulmonary aspergillosis (IPA) had an increased LoS in the hospital when [23.6 days vs. 13.9 days, p=0.03] and higher mortality [62.5% vs 18.4%, p=0.01]. History of hematological malignancy and neutropenia showed trends towards development of IPA. All patients with IPA were treated with voriconazole. Other coinfections among RSV-infected ICU patients included bacterial [39, 27.1%], viral [10, 6.9%], and non-IPA fungal [2, 1.3%] pathogens.

Conclusions: Although IPA is relatively uncommon in patients admitted to the ICU with severe RSV pneumonia, patients with IPA had significant increased LOS as well as mortality. Other coinfections with bacterial, viral, and non-IPA fungal pathogens are common in those with severe RSV pneumonia.

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Prevalence and risk factors for Histoplasma Capsulatum infection amongst HIV patients attending the Buea Regional Hospital using the Histoplasma urine antigen detection enzyme immunoassay

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1University of Buea, Buea, Cameroon, 2The University of Manchester, Manchester, United Kingdom, 3The Global Action Fund for Fungal Infections, Genève, Switzerland, 4National Aspergillosis Centre, Wythenshawe, United Kingdom, 5Université des Montagnes, Bangangte, Cameroon

Abstract third-party references: Optimum Imaging Diagnostics (OIDx)

Background: Human histoplasmosis is caused by two varieties called Histoplasma capsulatum var. capsulatum (Hcc) and Histoplasma capsulatum var. duboisii (Hcd), the latter only found in Africa. Histoplasmosis is an AIDS-related illness but can occur in both immunocompromised and immunocompetent individuals. Histoplasmosis has been reported in Cameroon, but few data on the prevalence are available. The objective of this study was to determine the prevalence of histoplasmosis in HIV patients and to investigate the risk factors associated with H. capsulatum infection.

Materials/methods: A descriptive cross-sectional study was conducted in the Buea Regional Hospital where 138 HIV positive patients, mostly outpatients were recruited. Urine samples were collected from HIV positive participants and analyzed using the Optimum Imaging Diagnostics (OIDx) antigen EIA kits, Risk factors associated with the infection were assessed using a questionnaire.

Results: Of the 138 participants, the mean age was 43.67 years (SD 12.18) and H. capsulatum antigen tested positive in 36 (26.1% [95%CI 18.77-33.43]). 5.6% [2] of the participants tested positive for H. capsulatum antigen had skin lesions. There was a significant association between the prevalence of H. capsulatum infection and a history of past chest infection [P=0.001, OR:3.632, 95%CI:1.635-8.07]. There was a marginal association between the prevalence of H. capsulatum infection and the viral load [P=0.07] and no significant correlation between viral load and the quantity of H. capsulatum antigen [P=0.371, r=-0.138].

Conclusions: H. capsulatum infection is present in HIV patients attending the Buea Regional Hospital. Awareness and management of HIV patients need to be improved with respect to H. capsulatum infection to limit the dissemination of the disease.

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Abstract 4008

Comparison of a cartridge-based host gene expression test to a manual method for use in the diagnosis of sepsis

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Background: A novel approach to sepsis diagnosis is to characterize the host immune response to infection by measuring differential expression of immune response genes. Based on this approach, SeptiCyte™ LAB was the first-in-class sepsis diagnostic to gain FDA-clearance with results reported on a scale of 1-10 based on increasing probability of sepsis. However, due to the high complexity and lengthy turnaround time (TAT) the assay was not commercialized. A second-generation assay, SeptiCyte™ RAPID (on Biocartis Idylla™), currently under development, is a fully integrated sample-to-result test that includes in-cartridge sample preparation and quantitative polymerase chain reaction (qPCR) with a TAT of 1 hour. The purpose of this study was to compare performance and output of a prototype SeptiCyte™ RAPID test to its predicate.

Materials/methods: We conducted retrospective testing of prospectively collected clinical samples to compare performance and output of SeptiCyte™ RAPID with SeptiCyte™ LAB (N=28), and to compare interoperator performance using SeptiCyte™ RAPID cartridges (N=20). Whole blood was collected into PAXgene™ blood RNA tubes prior (“VENUS”, NCT02127502, Miller et al., 2018). Retrospective samples originated from patients suspected of sepsis and admitted to an intensive care unit at Intermountain Medical Center. Residual, cryopreserved samples were selected to represent the full score range of SeptiCyte™ LAB (0-10). Testing was conducted at a clinical lab (Intermountain Healthcare Central Lab) and Biocartis. SeptiCyte™ scores were calculated using a formula and qPCR Cq values. Hands-on-time (HoT) and assay TAT were recorded.

Results: Figure 1 demonstrates the correlation ($r^2=0.97$) for 28 clinical samples run using the manual SeptiCyte™ LAB test and SeptiCyte™ RAPID. Average HoT was 2 mins, and average TAT was 65 mins. Interoperator correlation on different Idylla™ machines located at different laboratories was 0.994 for SeptiCyte™ RAPID, with a coefficient of variation of 1.25%.

Conclusions: SeptiCyte™ RAPID prototype assay results, run on the Biocartis Idylla™ instrument, correlate strongly with SeptiCyte™ LAB, and are reproducible. This is the first demonstration of a fully-integrated, rapid, reproducible sepsis test that has the potential for near patient testing.

Figure 1: Scatter Plot of scores for SeptiCyte™ LAB versus SeptiCyte™ RAPID

$r^2 = 0.97$

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Abstract 4009

Is the modified quick SOFA scale superior to quick SOFA in patients with diagnosed septic shock?

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Background: Herein, we aimed to compare the effects of qSOFA (Quick Sequential Organ Failure Assessment) score with modified qSOFA score (PLoS One. 2018 Sep 26;13(9):e0204608) for predicting one month survival (OMS) in patients with diagnosed septic shock (SS) in a tertiary-care educational university hospital in a developing country.

Materials/methods: Modified qSOFA was created by adding age factor (>50 years=1 point) to patients with qSOFA scale 1 or 2 or 3 who had SS (sepsis+hypotension+adrenergic agent) and consulted by Infectious Diseases consultants between December 2013-October 2019. Statistical analysis was performed via Chi square test and a p value <0.05 was considered significant.

Results: The number of patients with qSOFA score of 1 or 2 or 3 from 739 patients are in Table [some of the cases were diagnosed as septic shock according to elder definition (without lactate) and there was a subgroup with qSOFA score 1]. Among the >50-year aged group, OMS rate was lower in patients with qSOFA2 vs qSOFA 1 vs qSOFA 3 (Table 1, p=0.224). Among the <50 years group, OMS rate was lower in patients with qSOFA 3 vs qSOFA 2 vs qSOFA 1 (Table, p=0.047). According to modified qSOFA, there was a significant difference for OMS among SS cases with scores of 1, 2, 3 and 4 (16/28=57.14% vs 65/152=42.76% vs 143/357 -40.05 vs 101/202-50%, p<0.00001). On the other hand, there was no significant difference in terms of OMS when we performed subgroup analysis in qSOFA score 1 or 2 subgroups, as ≤50-year vs >50-year but interestingly OMS was significantly lower in <50-year old cases vs elders. (Table, 16/28 vs 46/109 p=0.202, 19/43 vs 134/323 p=0.869, 9/34 vs 101/202 p=0.014).

Table. Findings

<table>
<thead>
<tr>
<th></th>
<th>A (qSOFA 1≤50 years)</th>
<th>B (qSOFA 1&gt;50 years)</th>
<th>C (qSOFA 2≤50 years)</th>
<th>D (qSOFA 2&gt;50 years)</th>
<th>E (qSOFA 3≤50 years)</th>
<th>F (qSOFA 3&gt;50 years)</th>
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<tr>
<td>Number of patients</td>
<td>28</td>
<td>109</td>
<td>43</td>
<td>323</td>
<td>34</td>
<td>202</td>
</tr>
<tr>
<td>Mean age (min-max)</td>
<td>36.42 (20-50)</td>
<td>67.96 (51-93)</td>
<td>40.18 (23-50)</td>
<td>70.43 (51-117)</td>
<td>38.20 (19-50)</td>
<td>70.45 (51-97)</td>
</tr>
<tr>
<td>One month survival</td>
<td>16 (57.14%)</td>
<td>46 (42.2%)</td>
<td>19 (44.18%)</td>
<td>134 (41.48%)</td>
<td>9 (26.47%)</td>
<td>101 (50%)</td>
</tr>
</tbody>
</table>

Conclusions: In terms of OMS, there was significant difference between qSOFA score 1, 2, 3 and 4 subgroups. However, in patients with qSOFA 1 or 2 ≤50-year-old did not have a significant effect on OMS. Modified qSOFA may be beneficial to foresee the probable mortality but these findings need to be validated in larger cohorts. The question if mortality is higher in qsofa 3 and <50-year-old cases versus older in other cohorts needs further analysis.

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Abstract 4013

**Prevalence of high-risk human papilloma virus genotypes responsible for cervical cancer in Blida, Algeria**

Samira Oukid*1, Mohammedi Kherroubi Dhakya2, Mohamed Lotfi Boudjella1, Nabila Sadouki2, Rachid Belouni3

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**Background:** Cervical cancer is the fourth most common cancer among women in Algeria. Few Algerian data are known about high-risk HPV (HR-HPV) and cervical cancer. The purpose of our study is to determine the prevalence of high-risk Humain Pa-pillomavirus genotypes responsible for cervical cancer in Blida and to know the distribution of high-risk Human Papillomavirus by age and by cytological abnormalities.

**Materials/methods:** Cervical samples testing for HR-HPV are taken with a cytobrush and stored in transport media at +4°C. The molecular analysis for HR-HPV genotypes is carried out by real-time PCR and end-point PCR, followed by reverse hybridization at the laboratory of Papillomavirus and Herpesviridae and others- Institute Pasteur of Algeria.

**Results:** Between January 2018 and April 2019, 444 cervical samples were selected for HR-HPV testing. The average age of women was 44 years [24-84, 95% CI=43.43-45.30]. The prevalence of HR-HPV among Blidean women was 3% (13/444). The peak prevalence rate was observed in women aged between 40-49 years. Eight different HR-HPV genotypes were found: HPV 16, HPV 18, HPV 31, HPV 45, HPV 52, HPV 56, HPV66 and HPV 68. The predominant genotypes were HPV 16 followed by HPV 45, HPV 18, HPV 66 and HPV56. Two out of 13 women had an infection with several HR-HPV genotypes. HR-HPV genotypes were found in 38% of smears without abnormality. Women with high-grade lesions were 15 times more likely to have HR-HPV [OR=15.49, p<0.005]. In our study, the acquisition risk factors for HR-HPV are multiple sexual partners [OR= 6.16, p<0.007, 95% CI=5.7% - 11.0%] and nulliparity [OR= 8.53, p<0.033, 95% CI=7.9% - 17.6%]. The use of the intrauterine device [OR= 0.1, p<0.001, 95% CI=12.5% - 19.2%], the swimming pool [OR= 0.07, p<0.002, 95% CI=41.4-59.8%] and a single sexual partner [OR= 0.16, p<6.5.10-3, 95% CI=3.4% - 26.9%] do not represent a risk factor for acquisition of HPV infection.

**Conclusions:** The prevalence of HR-HPV in Blida was 3%. The highest rate is observed in women aged between 40-49 years. The predominant genotype was HPV 16. The presence of HR-HPV is strongly related to the presence of High-grade lesions.

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**Abstract 4015**

**Rapid detection of piperacillin/tazobactam resistance and extended spectrum resistance to β-lactams/β-lactamase inhibitors in clinical isolates of Escherichia coli**

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**Background:** Piperacillin/tazobactam is a β-lactam/β-lactamase inhibitor (BL/BLI) recommended for the empirical treatment of severe infections. The excessive and indiscriminate use of piperacillin/tazobactam has promoted the emergence of piperacillin/tazobactam resistant *Escherichia coli* isolates. Recently, we demonstrated that piperacillin/tazobactam may contribute to the development of extended spectrum resistance to BL/BLI (ESRI) in piperacillin/tazobactam susceptible *E. coli* isolates but with low-level resistance to BL/BLI (resistance to amoxicillin/clavulanic acid and/or ampicillin/sulbactam) [Rodríguez-Villodres et al. Epub ahead of print]. This raises the need for development of rapid detection systems. Therefore, the objective of this study was to design and validate a method able to detect quickly resistance to piperacillin/tazobactam and ESRI in *E. coli*.

**Materials/methods:** A colorimetric assay based on the β-lactam ring hidrolysis by β-lactamases was designed (ESRI test). The ESRI test was evaluated by using piperacillin/tazobactam-susceptible isolates without ability to develop ESRI (n=22), piperacillin/tazobactam-susceptible isolates but ESRI developer’s (n=45) and piperacillin/tazobactam-intermediate or resistant isolates (n=47). All the isolates were obtained from bloodstream infections and intra-abdominal sources, and characterized according to their susceptibility profiles to BL/BLI. Detection of the three more frequent β-lactamases involved in BL/BLI resistance (*bla TEM, bla OXA-1* and *bla SHV*) was performed by PCR.

**Results:** The ESRI test was able to detect all the piperacillin/tazobactam-intermediate or resistant isolates, and all the piperacillin/tazobactam-susceptible isolates but with ability for ESRI development. Their mediane time-to-result were 5 and 30 minutes, respectively. All the isolates without BL/BLI resistance were negative for the ESRI test and did not harbour β-lactamase genes. For ESRI developer’s and piperacillin/tazobactam-intermediate or resistant isolates, *bla TEM* was the most frequent β-lactamase gene detected, followed by *bla SHV* and *bla OXA-1*. Sensitivity, specificity and positive and negative predictive values were 100%.

**Conclusions:** These results demonstrate the efficacy of the ESRI test, showing a great clinical potential which would lead to a reduction of health costs, ineffective treatments, and inappropriate use of BL/BLI.


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Abstract 4018

Patient level predictors of vancomycin never events
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Background: Vancomycin, the most commonly used antibiotic in the hospital, is often inappropriately used and can commonly lead to adverse drug events. We identified vancomycin ‘Never Events’ (NE), defined as clearly inappropriate use of vancomycin, and aimed to identify patient-level factors associated with NEs.

Materials/methods: Vancomycin NE were defined as either: 1) any vancomycin use for a non-susceptible organism after susceptibility results or 2) vancomycin use exceeding 48h after susceptibility report when safe de-escalation was possible. NE and controls were identified with an algorithm using an electronic data capture strategy from unique patient encounters between 1/2014 and 10/2017 at a large academic medical center. Cases and true positive NE were adjudicated via manual chart review. A logistic regression model was built to predict NE using Stata (College Station, TX: StataCorp LLC). Model building iteratively included variables according to p<0.2 using a forward selection process. Each variable inclusion required a difference greater than 3.84 for 2 times the log likelihood between the n and the n+1 model. Relative importance of identified factors to the final model was calculated as change in log likelihood (with one variable removed) expressed as percent of total log likelihood change from final model to model with the least important variable retained.

Results: A total of 100 cases and 100 controls were available, and final analysis included 96 NE and 26 controls due to partially missing data. Predictors associated with NE (OR, 95% CI) were length of stay (LOS) (1.1, 1.01-1.15), positive culture at therapy initiation (10.5, 2.78-39.43), hospital discharge from any level ICU (20, 1.39-288.4), and hospital admission to any level ICU (0.08, 0.1-0.6). Respectively, each of these predictors contributed 28.9%, 28.5%, 24.0% and 7.7% relative importance to the model. As depicted (Figure), increasing LOS greatly increased the likelihood that a vancomycin NE would occur.

Conclusions: LOS, positive culture at therapy initiation, hospital discharge from ICU, and ICU admission were significantly associated with NE. Further assessment of additional patient level data is needed to examine internal validity of model performance and cross-generalizability for NE predictions.

Predictive Margins for LOS (95% CIs)

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Clinical metagenomic sequencing of positive blood cultures as a tool for rapid microbiological diagnosis

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Background: Bloodstream infection has a high mortality worldwide with every hour delay in correct antibiotic prescription accounting for up to 7% increased mortality. Clinical metagenomics has the potential to provide quick and accurate real-time diagnostic results potentially reducing morbidity and mortality.

Materials/methods: Positive blood culture specimens were retrieved from the Oxford University Hospital’s microbiology laboratory. We evaluated four different human DNA depletion methods (Molysis Basic5, differential centrifugation, Saponin-based cell lysis, no pre-treatment) and three DNA extraction methods (MolYsis Complete5, QIAamp UCP, BiOstic Bacteraemia kit). Ten positive blood cultures, one unused blood culture bottle, and one water control were processed using each method in combination (n=144). Bacterial and human DNA yields were compared using 16S and beta-actin qPCR. Additionally, we processed 14 positive blood cultures and one water control using the BiOstic Bacteraemia kit with and without Saponin-based pre-treatment. Sequencing libraries were prepared using the Nanopore Rapid Barcoding Kit, and sequenced on R9.4 flowcells using the GridION platform, with 2-4 libraries multiplexed per flowcell. Sequenced reads were classified using Kraken2.

Results: By qPCR, the BiOstic Bacteraemia kit extracted the most bacterial DNA, yielding a median 1.55E+08 16S copies/µL (IQR 4.11E+07 - 3.34E+08), compared to the MolYsis Complete5 3.83E+07 (5.06E+06 - 8.26E+07) and the QIAamp UCP 7.17E+06 (1.54E+05 - 4.11E+07) (p<0.01). Saponin resulted in greater depletion of human DNA, with fewer beta-actin copies than differential centrifugation (p<0.01) and no pre-treatment (p<0.01). From sequencing, the median (IQR) number of human bases sequenced without saponin was 2.9E+08 (1.2E+08 - 1.4E+09) and with saponin was 2.7E+05 (2E+05 - 1.9E+06) (p<0.01). However, the median number of bacterial bases sequenced without saponin was similar to that with saponin, 2.2E+09 (1.1E+09 - 4.2E+09) and 2.3E+09 (1E+09 - 4.1E+09) respectively (p=0.50). A threshold of >1000 bacterial reads could be used to indicate a positive blood culture. All 14 samples [processed with or without saponin] contained the cultured species as the most common bacteria sequenced, at varying proportions of the total reads [Figure]. Species identification could be made within the first hour of sequencing.

Conclusions: We demonstrate that metagenomic sequencing can provide accurate and rapid diagnostic information in bloodstream infections.

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Abstract 4024

Pharmacokinetic/pharmacodynamic simulation of cost-effective dosage regimens of ceftazidime/avibactam in patients with renal impairment

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Background: The recommended dosage of ceftazidime/avibactam (CEF/AVI) is 2000/500 mg as a 2h-infusion every 8h (q8h) when creatinine clearance (CLcr) is from 51 to 80 ml/min. It should be adjusted to renal function, using 1000/250 mg q8h, 750/187.5 mg q24h in patients with CLcr of 31 to 50 ml/min, 16 to 30 ml/min, and 6 to 15 ml/min, respectively. The objective of this study was to identify alternative, cost-effective dosage regimens of CEF/AVI in patients with renal impairment.

Materials/methods: We performed a PK/PD Monte Carlo simulation study, based on a published population PK model of CEF/AVI (Li et al. Clinical Transl Sci 2019). We simulated the recommended dosage regimens as well as alternative dosage regimens using 2000/500 mg of CEF/AVI with variations of infusion time [2h, 4h, 6h] and dose interval [q12h or q24h] for different stages of renal impairment. Steady-state concentration profiles of 1000 virtual patients were obtained using the Pmetrics software. The probability of target attainment (PTA) was estimated for each regimen. For CEF, the PK/PD target was defined as a percentage of time during which the free plasma concentration remains above the MIC (fT>MIC) ≥ 50%. For AVI, the MIC was replaced by the minimum effective concentration (MEC), resulting in target fT>MEC ≥ 50% [Nichols et al. Antimicrob Agents Chemother 2018]. A PTA ≥ 90% was considered as acceptable.

Results: The results of simulations for the reference and some alternative dosage regimens are shown in Table 1. In patients with impaired renal function, the administration of the full 2000/500 mg dose of CEF/AVI every 12 or 24h with an infusion time of 2h up to 6h was associated with PTA as high as those for recommended dosage regimens. The alternative dosage regimens were not associated with overexposure except for 2000/500 mg q24h in patients with CLcr of 6 to 15 ml/min.

Conclusions: Dosing regimens of CEF/AVI based on the full dose with larger dosing interval and/or longer infusion duration appear to meet the PK/PD requirements of efficacy and could be associated with substantial cost savings.

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<table>
<thead>
<tr>
<th>CLcr (ml/min)</th>
<th>CEF/AVI Dosage</th>
<th>Infusion time (h)</th>
<th>CEF Cmax (mg/L)</th>
<th>CEF Cmin (mg/L)</th>
<th>AVI Cmax (mg/L)</th>
<th>AVI Cmin (mg/L)</th>
<th>CEF PTA MIC = 8 mg/L</th>
<th>AVI PTA MEC = 1 mg/L</th>
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<tr>
<td>80</td>
<td>2000/500 q8h*</td>
<td>2</td>
<td>71.9 (31.8-169.1)</td>
<td>12.5 (3.9-62.8)</td>
<td>11.2 (3.3-39.2)</td>
<td>0.6 (0.1-5.2)</td>
<td>99.4</td>
<td>97.4</td>
</tr>
<tr>
<td>80</td>
<td>2000/500 q12h</td>
<td>6</td>
<td>40.3 (17.6-83.4)</td>
<td>7.5 (1.8-42.7)</td>
<td>5.3 (1.6-16.1)</td>
<td>0.3 (0.0-3.8)</td>
<td>99.3</td>
<td>94.7</td>
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<td>51</td>
<td>2000/500 q8h*</td>
<td>2</td>
<td>95.3 (41.7-226.9)</td>
<td>29.9 (11.5-107.3)</td>
<td>14.8 (4.4-53.0)</td>
<td>1.9 (0.5-11.1)</td>
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<tr>
<td>50</td>
<td>1000/250 q8h*</td>
<td>2</td>
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<td>15.4 (6.0-55.0)</td>
<td>7.5 (2.2-26.9)</td>
<td>1.0 (0.3-5.8)</td>
<td>99.6</td>
<td>96.9</td>
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<tr>
<td>50</td>
<td>2000/500 q12h</td>
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<td>79.5 (32.3-208.2)</td>
<td>13.6 (3.7-66.4)</td>
<td>13.3 (3.4-49.3)</td>
<td>0.6 (0.1-6.4)</td>
<td>99.8</td>
<td>97</td>
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<tr>
<td>30</td>
<td>750/187.5 q12h*</td>
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<td>40.5 (16.6-101.0)</td>
<td>13.2 (4.9-44.3)</td>
<td>6.5 (1.7-25.8)</td>
<td>0.9 (0.3-5.4)</td>
<td>99.1</td>
<td>93.4</td>
</tr>
<tr>
<td>30</td>
<td>2000/500 q24h</td>
<td>6</td>
<td>65.9 (27.8-135.4)</td>
<td>9.8 (2.7-66.5)</td>
<td>10.6 (3.1-36.2)</td>
<td>0.3 (0.1-6.0)</td>
<td>99.5</td>
<td>95.5</td>
</tr>
<tr>
<td>15</td>
<td>750/187.5 q24h*</td>
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<td>42.8 (18.2-106.5)</td>
<td>12.6 (4.6-44.2)</td>
<td>7.6 (2.0-30.8)</td>
<td>0.8 (0.2-5.7)</td>
<td>98.6</td>
<td>92.8</td>
</tr>
<tr>
<td>15</td>
<td>2000/500 q24h</td>
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<td>33.7 (12.2-117.7)</td>
<td>20.1 (5.4-82.2)</td>
<td>2.2 (0.6-15.3)</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

The * symbol represent dosages recommended by the manufacturer Cmax values are given as median (95% CI).

Conclusions: Dosing regimens of CEF/AVI based on the full dose with larger dosing interval and/or longer infusion duration appear to meet the PK/PD requirements of efficacy and could be associated with substantial cost savings.

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The antimicrobial stewardship in surgery (ASCHI) project: long-term follow-up

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Background: Long term compliance with antimicrobial prescription indications is often reduced after an antimicrobial stewardship (AS) intervention. We report the long term follow-up of an AS intervention in a community hospital in northern Italy.

Materials/methods: Single center prospective study conducted in the General Surgery ward of Cremona’s hospital (1250 admissions/year) based on an abilitative strategy with peer education between surgeons and infectious disease (ID) doctor by weekly discussion of ID diagnosis, prophylaxis and treatment at patient’s bed-side. Surgical antimicrobial prophylaxis (SAP) and therapy (AT) appropriateness were evaluated through repeated prevalence analysis: appropriate AT prescription (AATP); wrong AT use (WATU); potential patient damage (PPD): ineffective antibiotic; and potential ecological damage (PED) on hospital microbiota: useless antibiotic.

The project had five phases: 1) pre-intervention (P1; May-October 2014); 2) intervention (P2 - November 2014-May 2015); 3) post-intervention (P3; June 2015-January 2017); 4) follow-up (P4 - July 2018-October 2018); 5) late follow-up (P5; August 2019). Data were presented and discussed with surgeons every 6 months. We conducted statistical analysis using EpiInfo™.

Results: We collected data on 2301 patients (P1 533, P2 672, P3 836, P4 227, P5 33). Correct use of AT was of 56% at baseline, while in P4 and P5 it was 84% and 85%, respectively (<0.001). Significant inappropriate use reductions were highlighted between P1 and P4/P5: WATU (23% in P1, 11% in P4, <0.001), PPD (22% vs 6%, <0.001), PED (26% vs 11%). A significant improvement in AATP was found between P1 and P2 (70% vs 84%, <0.001, X² 18.40). An improvement of SAP use with a reduction of PPD and PED was found comparing P2 and the follow-up phase (<0.001).

Conclusions: This abilitative AS intervention was associated with a significant improvement of antibiotic prescription appropriateness. The positive results of the intervention were still present 4 years after the AS intervention. This proves the durability of the abilitative intervention and the utility of a continuous teamwork between different specialist.

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Abstract 4027

**Significant increase of CTX-M-15-ST131 and emergence of CTX-M-27-ST31 *Escherichia coli* high-risk clones causing healthcare-associated bacteraemia of urinary origin in Spain (ITUBRAS-2 project)**

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**Abstract third-party references:** Merck Sharp & Dohme [MSD]

**Background:** *Escherichia coli* (Ec) ST131 is a multidrug-resistant high-risk clone (HRC) associated with quinolone resistance, CTX-M-15 production and urinary tract infections. The emergence of a ST131-clade [C1-M27] associated with CTX-M-27 production has been recently described. The purpose of this study was to assess the microbiological characteristics and the presence of HRC-ST131 among ESBL-Ec causing healthcare-associated bacteraemia of urinary origin [HCA-BOU] (ITUBRAS-2 project) and compare these results with those previously obtained in 2011 (ITUBRAS project).

**Materials/methods:** Patients with HCA-BOU [Sep-2017 to Apr-2019] from 12 tertiary hospitals in Spain were prospectively included and blood isolates were stored. Bacterial identification (MALDI-TOF MS) and antimicrobial susceptibility (microdilution, EUCAST-2019) were performed. ESBL and carbapenemase production were confirmed by double-disk synergy and a colorimetric test (CarbaNP, BioMerieux), respectively. Genes encoding ESBLs (*bla*SHV, *bla*TEM, *bla*CTX-M) and carbapenemases (*bla*OXA-48, *bla*VIM, *bla*KPC) were characterized (PCR, sequencing). ST131 screening was performed (PCR).

**Results:** Overall, 424 BOU episodes with 449 microorganisms were included. 222 [49.4%) corresponded to Ec isolates. Prevalence of HCA-ESBL-Ec producers increased from 13.9% [30/215] in 2011 to 30.6% [68/222] in 2019 (p<0.01). One non-ESBL-Ec isolate was an OXA-48-producer. ESBL producers showed higher resistance rates than non-producers to ciprofloxacin (92.6% vs. 38.3%), tobramycin (54.1% vs. 13%), gentamicin (42.6% vs. 11.7%), piperacillin-tazobactam (36.7% vs. 14.8%) and amikacin (14.7% vs. 3.2%) [p<0.01 for all comparisons]. All ESBL-Ec isolates were susceptible to ceftolozane-tazobactam, carbapenems, tigecycline and colistin. ESBL-producing HRC-ST131 was identified in higher proportion than in the previous study [56% [17/30] in 2011 vs. 66% [45/68] in 2019; p>0.5], representing 20.3% of the total Ec population. ST131 showed higher resistance rates than non-ST131 isolates to piperacillin-tazobactam (46% vs. 17.4%, p<0.01) and ciprofloxacin (97.7% vs. 82.6%, p<0.05). CTX-M-15 was the most frequent enzyme [41/68, 60%] and was mainly associated with ST131 isolates [36/41, 87%]. CTX-M-27 (absent in the previous study) was identified in 8 ST131 isolates. Non-ST131 isolates showed a high ESBL diversity including different CTX-M and SHV types.

**Conclusions:** ESBL-Ec causing HCA-BOU has increased significantly in Spain, mainly associated with the expansion of CTX-M-15-ST131 and the emergence of CTX-M-27-ST131. Ceftolozane-tazobactam showed full coverage for ESBL-Ec isolates, including those belonging to the HRC-ST131.

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Abstract 4028

Evaluation of rapid AST in blood cultures using CHROMagar Mueller-Hinton orientation agar

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Background: Rapid antimicrobial susceptibility testing (RAST) from blood cultures (BCs) guide early appropriate antibiotic therapy of sepsis that improve patient prognosis. We aimed to evaluate the EUCAST RAST directly from BC bottles on Gram-negative rods using a chromogenic Mueller Hinton (MH) agar.

Materials/methods: A total of 40 non-duplicated positive BCs bottles (BioMerieux) from patients with Gram-negative bacteremia were tested: 15 K. pneumoniae, 8 E. coli, 12 A. baumannii and 5 P. aeruginosa having different antibiotic resistance mechanisms. RAST was performed on 2 MH agars: standard (BioMerieux MH) and chromogenic (CHROMagar™ MH Orientation) following the EUCAST recommendations for short incubation (4, 6 and 8 hours) AST directly from positive BC. A conventional AST (CAST) and identification (Vitek2 automated system) was also performed from BC subcultures after overnight incubation at 37 °C. Comparisons between the RAST and CAST methods were expressed as categorical agreement (CA), very major error (VME, false susceptibility), major error (ME, false resistance), or minor error (mE), intermediate versus susceptible or resistant) taking into account the Area of Technical Uncertainty (ATU).

Results: The RAST, performed on standard MH (BioMerieux), showed an overall categorical agreement of 95.6%, a mE rate of 0.9%, a ME rate of 0.5%, and a VME rate of 2.5% compared to the CAST method. However, the RAST, performed on CHROMagar™ MH Orientation, showed a better categorical agreement to the CAST, of 96.6%, a mE rate of 1.4%, a ME rate of 0.3%, and a VME rate of 1.2% (table 1). Moreover, the chromogenic agar helped to identify all the E. coli and Klebsiella after 6-hours incubation and facilitated the inhibition zone reading.

Of note, more than half of the reported errors (> 16 errors), especially VME, were recorded for aminoglycosids with strains harboring methylases (15 strains), which appear fully resistant only after overnight incubation.

Conclusions: Our study showed that the CHROMagar™ MH Orientation could be used effectively for both rapid orientation of identification and RAST in Gram-negative positive BC. CHROMagar™ RAST could be successfully introduced into any clinical microbiology laboratory lacking MALDI-TOF MS.

Table 1: RAST results using Standard MH and CHROMagar™ MH Orientation agars

<table>
<thead>
<tr>
<th></th>
<th>Standard MH</th>
<th>CHROMagar™ MH</th>
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<tbody>
<tr>
<td></td>
<td>4H %</td>
<td>6H %</td>
</tr>
<tr>
<td>Total tested Nb</td>
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<tr>
<td>nb ATU</td>
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<td>nb VME</td>
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<td>Nb CA</td>
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</tr>
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</table>

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Abstract 4029

Social and physical opportunities to improve surgical antimicrobial prophylaxis prescribing: utilisation of the behaviour change wheel

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Background: Surgical antimicrobial prophylaxis (SAP) is a leading indication for antibiotic use in hospitals, with demonstrated high rates of inappropriateness. A greater understanding of this behaviour is needed to inform the design of targeted antimicrobial stewardship (AMS) interventions to support the optimization of SAP. We previously published our findings on barriers and enablers to SAP decision-making. An extension of this research is to map these barriers and enablers to behaviour change interventions.

Materials/methods: A qualitative case study exploring the phenomenon of SAP decision-making. Focus groups were conducted with surgeons, anaesthetists, theatre nurses and pharmacists across three hospitals in Australia. Thematic analysis was guided by the Theoretical Domains Framework (TDF) and the Capabilities, Opportunities, Motivators-Behaviour (COM-B) model. Application of the Behaviour Change Wheel (BCW), allowed for mapping of behaviour to behaviour change interventions.

Results: Fourteen focus groups and one paired interview were completed. Two key themes were mapped to the TDF, COM-B and BCW intervention functions and 12 interventions have been proposed to address these barriers and support the enablers of appropriate SAP decision-making, summarized in Table 1.

<table>
<thead>
<tr>
<th>Themes</th>
<th>TDF (COM-B)</th>
<th>BCW Interventions</th>
<th>Proposed Interventions</th>
</tr>
</thead>
</table>
| Social codes of prescribing reinforce established practices | Social (Social opportunity) | Enablement | - Target seniors surgeons for AMS interventions  
- Engage senior surgeons in intervention development and implementation. |
| Need for improved communication, documentation and collection of data for action | Environment (Physical opportunity) | Restriction | - Computerised Physician Order Entry SAP order sets  
- Modified ‘Time-Out’ pathway for SAP cessation  
- Electronic SAP redosing prompts  
- Modified Enhanced Recovery After Surgery protocol/post-operative checklist  
- Intervention education/training  
- Guideline implementation resources  
- User evaluation of resources and training  
- Identify relevant quality indicators.  
- Continue SAP prescribing audits.  
- Increase capacity for auditing of outcomes in relation to quality of SAP prescribing. |

Conclusions: SAP prescribing is a complex process across the surgical setting. Utilisation of behaviour change frameworks identified barriers and enablers of optimal SAP prescribing and supports development of theory-informed AMS interventions. Interventions should aim to increase surgeon engagement, address underlying social factors, such as professional hierarchy and support physical infrastructure for standardisation of SAP documentation.

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Abstract 4030

How we achieved improvement in diagnosis and management of sepsis at County Durham and Darlington Foundation Trust, UK

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Background: In 2015, a national sepsis target (CQUIN) was released in the UK. NHS trusts were asked to achieve 90% compliance in screening of sepsis and antibiotics within one hour, for emergency admissions and inpatients.

Materials/methods: 50 random patients’ notes from both the emergency department (ED) and inpatients were analysed per quarter from April 2015 to March 2019. Changes in practice are summarised below.

2015

Sepsis Nurse appointed in response to the CQUIN, to support sepsis and deteriorating patient work through the cardiac arrest prevention team.

Introduction of Nervecentre, an electronic observations tool for inpatients.

2016

An acute intervention team was formed (a hybrid model of a traditional critical care and outreach service) which supported the delivery of 24-hour acute care through education and responsive review.

Quarterly Sepsis Study Days for registered nurses and doctors were introduced.

2017

A sepsis steering group was formed within the Trust. This comprised sepsis, oncology and special project lead nurses, an antimicrobial pharmacist and consultants from microbiology, intensive care, emergency medicine, anaesthetics, acute medicine, paediatrics and obstetrics. This group met every 1-2 months. The aim was to improve the care of patients with sepsis within the trust, with an accompanying improvement in compliance with the national target.

A regional sepsis screening tool was created and introduced into the North-East England region. The aim was to improve consistency of approach between NHS Trusts and compliance with national guidelines. Sepsis screen and assessment within Nervecentre was introduced.

Symphony, an electronic sepsis screening tool, was introduced into the ED.

Results: The Acute Intervention Team provided sepsis education to 142 members of staff during 2018/19.

226 healthcare workers attended Sepsis Study Days. Sepsis screening is at 100% in both emergency admissions and inpatients with suspected sepsis. (Previously 70% in ED).

From April 2018 – March 2019, receipt of antibiotics within an hour for in-patients increased from 29% to 93% and from 55% to 100% in ED.

Conclusions: Through our interventions, we have improved in all areas assessed by the CQUIN. In 2018-19 we demonstrated improvement with sepsis screening and antibiotics within 1 hour for >90% of patients.

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Abstract 4034

**Alternative, cost-effective dosage regimens of ceftolozane/tazobactam in patients with renal impairment: a simulation analysis**

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**Background:** Ceftolozane/tazobactam (TOL/TAZ) dosage should be adjusted in patients with renal impairment. The recommended dosage regimens are as follows (1h infusion): 1000/500 mg every 8h (q8h), 500/250 mg q8h, and 250/125 mg q8h in patients with creatinine clearance (CCr) from 51 to 100 ml/min, 30 to 50 ml/min and 15 to 29 ml/min, respectively. The objective of this study was to identify alternative, cost-effective dosage regimens, in this patient group.

**Materials/methods:** We performed a pharmacokinetic/pharmacodynamic (PK/PD) simulation study based on a published population PK model of TOL/TAZ [Chandorkar et al. J Clin Pharmacol 2015]. Within the R package Pmetrics, we simulated the recommended dosage regimens, and alternative dosage regimens using 1000/500 mg of TOL/TAZ with various infusion times and dosing intervals (q8h, q12h or q24h), in patients with normal, moderately impaired (CCr = 30 to 50 ml/min), and severely impaired (CCr = 15 to 29 ml/min) renal function. Steady state concentrations profiles were obtained in 1000 virtual patients. Probability of target attainment (PTA) was estimated. For TOL the target was defined as a percentage of time during which the free plasma concentration remains above the MIC [fT>MIC] ≥ 32.2% [Craig et al. Antimicrob Agents Chemother 2013]. For TAZ, the MIC was replaced by the minimum effective concentration (MEC), resulting in target fT>MEC ≥ 35% [VanScocly et al. Antimicrobial Agents Chemother 2013]. A PTA ≥ 90% was considered as acceptable.

**Results:** PTA for the recommended and some alternative dosage regimens are shown in Table 1. In patients with renal impairment, a full dose of 1000/500 mg q12h or q24h can be associated with acceptable PTA for both TOL and TAZ when the infusion time is moderately increased up to 2h or 4h. In addition, such strategy is not associated with overexposure, as Cmax remains in a usual range.

<table>
<thead>
<tr>
<th>CLcr (ml/min)</th>
<th>TOL/TAZ Dosage</th>
<th>Infusion time (h)</th>
<th>TOL Cmax (mg/L)</th>
<th>TAZ Cmax (mg/L)</th>
<th>TOL PTA MIC = 8 mg/L</th>
<th>TAZ PTA MEC = 0.25 mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>51</td>
<td>1000/500 q8h*</td>
<td>1</td>
<td>65.7 (37.8 - 107.5)</td>
<td>18.6 (9.2 - 33.7)</td>
<td>99.8</td>
<td>99.5</td>
</tr>
<tr>
<td>50</td>
<td>500/250 q8h*</td>
<td>1</td>
<td>33.1 (19.0 - 54.1)</td>
<td>9.4 (4.6 - 16.9)</td>
<td>98.2</td>
<td>98.5</td>
</tr>
<tr>
<td>50</td>
<td>1000/500 q12h</td>
<td>2</td>
<td>51.1 (29.6 - 88.8)</td>
<td>13.8 (6.9 - 26.6)</td>
<td>100</td>
<td>98.5</td>
</tr>
<tr>
<td>30</td>
<td>500/250 q8h*</td>
<td>1</td>
<td>40.8 (23.3 - 66.5)</td>
<td>10.8 (5.2 - 19.6)</td>
<td>99.7</td>
<td>99.6</td>
</tr>
<tr>
<td>30</td>
<td>1000/500 q12h</td>
<td>2</td>
<td>62.2 (36.0 - 108.3)</td>
<td>16.3 (8.3 - 31.5)</td>
<td>100</td>
<td>99.9</td>
</tr>
<tr>
<td>29</td>
<td>250/125 q8h*</td>
<td>1</td>
<td>20.7 (11.8 - 33.9)</td>
<td>5.5 (2.7 - 10.0)</td>
<td>88.8</td>
<td>99.3</td>
</tr>
<tr>
<td>29</td>
<td>1000/500 q24h</td>
<td>4</td>
<td>40.8 (25.0 - 68.3)</td>
<td>11.2 (5.5 - 21.7)</td>
<td>97.4</td>
<td>95.6</td>
</tr>
<tr>
<td>15</td>
<td>250/125 q8h*</td>
<td>1</td>
<td>28.4 (16.4 - 46.2)</td>
<td>8.8 (3.3 - 13.0)</td>
<td>99.9</td>
<td>99.8</td>
</tr>
<tr>
<td>15</td>
<td>1000/500 q24h</td>
<td>4</td>
<td>53.5 (32.1 - 90.6)</td>
<td>14.2 (7.1 - 27.1)</td>
<td>99.9</td>
<td>99.3</td>
</tr>
</tbody>
</table>

The * symbol represent dosages recommended by the manufacturer. Cmax values are given as median (95% CI).

**Conclusions:** In patients with moderate to severe renal impairment, infrequent administration (q12h or q24h) combined with prolonged infusion of TOL/TAZ appears to be as effective as recommended dosages in terms of PK/PD. This strategy also has the potential for substantial cost savings by reducing the number of vials used and the nurse labor.

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Abstract 4037

**Diagnostic utility of a novel Point-of-Care test of calprotectin for periprosthetic joint infection in total knee arthroplasty patients**

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**Background:** Recently several synovial fluid biomarkers for diagnosis of periprosthetic joint infection (PJI) are being investigated. Point-of-care (POC) tests using these biomarkers are not widely available. The purpose of this study was to test the sensitivity, specificity, positive and negative predicted values (PPV and NPV) of a calprotectin POC test for PJI in total knee arthroplasty (TKA) patients, using Musculoskeletal Infection Society (MSIS) 2013 PJI diagnosis criteria as the gold standard.

**Materials/methods:** Synovial fluid samples were prospectively collected from 107 patients who underwent revision TKA (rTKA) at two academic institutions from October 2018 to November 2019. The study was conducted under IRB approval. Patients followed hospital standards for diagnostic work-up. Data collection included demographic, clinical, and laboratory data in compliance with the MSIS 2013 PJI diagnosis criteria. Synovial fluid samples were analyzed by calprotectin POC tests for synovial fluid in accordance with manufacturer’s instructions. Quantitative calprotectin read-outs were categorized into high risk (>50 mg/L), medium risk (14-50 mg/L) and low risk (<14 mg/L) for infection by the test reader system.

Patients were categorized as septic or aseptic using MSIS 2013 PJI diagnosis criteria by two independent reviewers blinded to calprotectin results. Test performance characteristics including sensitivities, specificities, PPV, NPV, and areas under the curve (AUC) were calculated for 2 scenarios: 1) a threshold of >50 mg/mL for infection, 2) a threshold of >14 mg/L for infection.

**Results:** 51 rTKAs were MSIS positive, while 56 rTKA were MSIS negative. The corresponding calprotectin classifications were 52 high, 8 medium, and 47 low risk. Of MSIS criteria positive cases, 49 were high risk, 1 was medium risk, and 1 was low risk. In the 1) >50 mg/mL threshold scenario, POC performance showed a sensitivity, specificity, PPV, NPV and AUC, respectively, of 96.1%, 94.6%, 94.2%, 96.4%, and 0.954. In the 2) >14 mg/mL threshold scenario, there was a sensitivity, specificity, PPV, NPV and AUC, respectively, of 98.0%, 82.1%, 83.3%, 97.9%, and 0.901.

**Conclusions:** The calprotectin POC test has excellent diagnostic properties including high sensitivity and specificity for diagnosing PJI in rTKA. However, further investigations with larger cohorts are necessary to further validate these results.

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Abstract 4038

Minimizing pseudo-cluster suggestions in infection control surveillance using pathogen DNA sequencing and artificial intelligence

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Background: Infection prevention surveillance for probable cross-transmissions (PCTs) is performed by manual review of microbiologic culture results and geotemporal data to identify potentially related isolates. However, the likelihood of pseudo-clusters within this approach is uncertain. Incorporating artificial intelligence (AI)-enabled algorithms with pathogen whole-genome sequencing (WGS) can rapidly identify PCTs, improving manual efforts.

Materials/methods: We deployed a commercial precision infection prevention system that utilizes WGS (Philips IntelliSpace Epidemiology, Philips Healthcare) to compare effectiveness of two surveillance methods for identifying PCTs: (i.) a unit match (UM) algorithm utilizing antimicrobial susceptibility testing (AST) with the sample collection time and unit; vs. (ii.) a clinical matching (CM) algorithm with nuanced weighting of AST data, timing of sample collection, and shared hospital location stays. WGS was performed on unique inpatient and emergency department isolates of Enterococcus faecium, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, and Staphylococcus aureus. Single-nucleotide variants (SNVs) were compared using core genome regions on a per-species basis to determine PCTs.

Results: From August 2018 to July 2019, UM and CM data from 709 patients were paired with WGS data from 479 E. faecium, 284 E. coli, 98 K. pneumoniae, 61 P. aeruginosa and 724 S. aureus isolates. Previously published SNV-relatedness thresholds were applied to define genomically related clusters as follows: 161 patients in 48 E. faecium clusters, 54 patients in 18 E. coli clusters, 8 patients in 4 K. pneumoniae clusters, 2 patients in 1 P. aeruginosa cluster, and 85 patients in 36 S. aureus clusters. 482 isolates did not meet relatedness thresholds. The UM method categorized 349 patients in PCTs, of which 219 did not belong to genomic clusters—a rate of 45% of suggested patients in pseudo-clusters. The CM method suggested 178 patients, of which 84 were not in genomic clusters—only 17% in pseudo-clusters.

Conclusions: The UM method suggested 171 more PCTs, of which many lacked genomic relatedness. The CM method decreased pseudo-cluster suggestions by 62%, with greater specificity. Further refinement and integration of AI-enabled approaches involving clinical and WGS data will permit more specific detection of PCTs and minimize pseudo-cluster suggestions, thereby improving allocation of infection prevention resources.

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Evaluation of the implementation of diagnostic automation into the bacteriology laboratory as part of pathology modernisation

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Background: Pathology services are undergoing transformation in response to a reducing budget, changing demographics and increased infection management demands, and the growing challenges of identifying multidrug-resistant micro-organisms. Advances in diagnostic laboratory technologies form part of the future direction for the re-configuration of pathology services. The shift from manual to automated operation poses many challenges and opportunities for service design and delivery, workforce skill mix and the measurement of productivity, not least the extent to which new technologies are being implemented successfully.

Methods: The research adopted an insider research case study approach combining quantitative and qualitative mix methods to investigate service improvements in the diagnostic automation of bacteriology services, including the extent of quality and productivity gains. The case focused the impact on the workforce development of laboratory staff in the four sites, managing the shift from manual to automated procedures. A range of secondary data sets analysed using descriptive statistical methods to examine indicators of laboratory workload, laboratory productivity and workforce roles. A series of 19 individual semi-structured interviews were conducted with selected managers and frontline staff and data analysed thematically using NVivo. The research proposed a systematic model to examine the various stages specific to technology innovation.

Results:

Fig1. Automation Performance

Conclusions: The research found that the automation implementation had varied successes and challenges, cost-effectiveness was dependent on a range of technological, clinical factors. Recommendations surrounding staff development and working practices are proposed

• To implement the automation does not improve the service alone, you have to change the process so that you can take full advantages of the robotics, it won’t be efficient.

• We are continuing to deal with complex human relationships when introducing automated technology. The lessons learnt from such a complex automation implementation will cover the human factors as a vital component in terms of skills required to run the new hi-tech environment.

• We find that initial performance gradually dips in the first stage of the transition period and requires more investment in staff, and no saving. Gradually the performance will improve toward the post automation stage as showing in Fig.1

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Effectiveness of chlorhexidine dressings to prevent catheter-related infections: Does one size fit all? A systematic literature review and meta-analysis

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Background: Catheter-related bloodstream infections (CRBSIs) are associated with significant morbidity. We aimed to evaluate the effectiveness of chlorhexidine (CHG) dressings in preventing incident CRBSIs and exit-site/tunneled infections.

Materials/methods: We searched PubMed, Cochrane Library, CINAHL, Embase, and ClinicalTrials.gov through March 2019 for studies with the following inclusion criteria: (1) acute-care patients with short/long-term catheters; (2) CHG dressing was used in the intervention group and a non-antimicrobial impregnated dressing was used in the control group; (3) CRBSI was an outcome. Randomized controlled trials (RCTs) and quasi-experimental studies were included. We used random-effects models to obtain pooled RR estimates. Heterogeneity was evaluated with I2 test and the Cochran Q statistic.

Results: Twenty-one studies (15,690 catheters; 17 RCTs), without evidence of publication bias, were included. CHG dressings reduced incident CRBSIs (pooled RR, 0.67: 95%CI, 0.55–0.81), independent of the CHG dressing type used: transparent CHG dressings (8 studies, pRR, 0.64: 95%CI, 0.44–0.94) vs CHG-impregnated discs (10 studies, pRR, 0.74: 95%CI, 0.57–0.95). Significant results were limited to: adults with onco-hematological disease (3 RCTs, pRR, 0.54: 95%CI, 0.36–0.81) and ICUs (9 studies, pRR, 0.58: 95%CI, 0.41–0.81); and short-term catheters (11 studies, pRR, 0.67: 95%CI, 0.50–0.90). CHG effectiveness seemed to remain in ICUs with baseline CRBSI rates <1.5/1,000 catheter-days: (2 studies, pRR, 0.37: 95% CI, 0.15–0.90). CHG dressings did not significantly reduce CRBSIs in neonates/pediatric populations (6 studies, pRR, 0.90: 95%CI, 0.57–1.40) and long-term catheters. Conversely, CHG dressings only decreased exit-site/tunnel infections in long-term catheters (3 studies, pRR, 0.36: 95% CI, 0.21–0.61). Contact dermatitis was independently associated with CHG dressings (7 studies, pRR, 5.16: 95%CI, 2.09–12.70); particularly in neonates/pediatric populations (3 studies, pRR: 9.20, 95%CI, 2.10–40.26) in whom severe reactions were described. Two studies evaluated and did not find CHG resistant isolates on the skin.

Conclusions: CHG dressings reduce the incidence of CRBSI, but evidence is limited to adults with short-term catheters—particularly in ICU settings and in patients with an onco-hematological disease. CHG dressings reduce incident exit-site/tunneled infections in long-term catheters. Future studies should focus on non-ICU settings and monitor the risk of CHG resistance.

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Community antimicrobial stewardship programme in pregnant women with urinary tract infections in primary care service

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Abstract 4043

Background: During the last 4 decades antibiotic resistance has been on the rise, so Antimicrobial Stewardship Programs (ASP) have emerged as tools to help us regulate and optimize their use. Since urinary tract infections (UTIs) in pregnancy are one of the most prevalent infectious pathologies with high resistance rates, it of the utmost importance to optimize its management considering that it is a factor that contributes to decrease perinatal morbidity and mortality, as well as it decreases bacterial resistance.

To demonstrate that the implementation of ASP is necessary to regulate and optimize antibiotic treatment in pregnant women with UTIs at the emergency area at the Guamani health center during the first quarter of 2019.

Materials/methods: We carried out a quasi-experimental analytical study pre-post trial type, through an educational intervention at the Obstetric Emergency service of the Guamani Health Center. Our study group consisted of 11 healthcare professionals at the obstetric emergency unit and the total number of patients treated in 3 months after the intervention was of 382. Our study had three phases. The first one sought to obtain data on the characteristics of healthcare attention prior to our intervention; the second consisted of masterclass lecture and persuasive interventions directed towards the obstetricians, and finally the third phase recorded the outcomes after our intervention.

Results: Pre-intervention: it was found that 46.62% of pregnant patients with UTIs were given Cefalexin as a first-choice treatment, followed by Nitrofurantoin with 33.33%. After the educational interventions, 72.51% of patients were treated with Nitrofurantoin as the first-choice treatment, compared to Cephalexin with 21.73%. The change in post intervention prescription was statistically significant with a p: 0.00, which was obtained using the Chi2 test.

Conclusions: Community Antimicrobial Stewardship Programs (C-ASP) based on masterclass and persuasive educational interventions are necessary to regulate and optimize the management of antibiotics in primary care.

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**Abstract 4044**

**Th2 response may be deleterious to protect against Staphylococcus aureus bacteraemia**

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**Background:** Staphylococcus aureus vaccine development has been so far unsuccessful. SprD is a regulatory micro-RNA present in most of S. aureus strains. Its deletion leads to a dramatic decreased virulence of the mutant strain in an animal model. We aimed to evaluate the capacity of a SprD-deleted S. aureus strain to provide a protective immune response, as a live attenuated vaccine.

**Materials/methods:** Mice were divided into three groups, all intradermally inoculated at day (D) 0, D15 and D21: i) 0.9% NaCl solution (non-immunized control), ii) WT (immunized control, injections of wild-type (WT) S. aureus), iii) ∆SprD (inoculated with isogenic S. aureus ∆SprD). At D30, all mice were challenged with an S. aureus WT bacteremia. In all groups, we analyzed survival, weight loss, bacterial load in spleens and kidneys. Cytoxines production and anti-staphylococcal immunoglobulin G (IgG) in mice serum at different times of immunization and infection were evaluated.

**Results:** Blood cultures were all negative at D38 in the NaCl group, whereas 57.1% and 23.0% of the mice were still bacteremic in the WT and the ∆SprD groups respectively. No difference in survival was observed between the groups, as for weight losses and bacterial loads in spleens and kidneys. Serum interleukin (IL)-5, a Th2 cytokine, was significantly lower in the NaCl group (median 7.7 pg/mL, IQR 8.7) than in the WT (median 214, IQR 917, p=0.004) or in the ∆SprD groups (median 412, IQR 1496, p=0.001) during bacteremia; there was no difference for other pro-inflammatory cytokines and in cytokines of the Th1 and Th17 pathways. In all the groups the concentration of total IgG in serum increased at D38 compared to D0: 9.1 fold in the WT group, and 5.5 and 3.3 folds in the ∆SprD and the NaCl groups respectively. Neutrophils bactericidal activity decreased similarly within the three groups at D38 compared to D30.

**Conclusions:** Intradermal pre-exposure to a live-attenuated S. aureus was not protective in this mice model and lead to a longer S. aureus bacteremia duration, and increased serum level of IL-5 and total antistaphylococcal IgGs.

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Burden of viral pneumonia among patients with lung infiltrates undergoing bronchoalveolar lavage: a retrospective one-year study

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Background: The etiology of lower respiratory tract infections remains often undetermined. Although viruses account for the majority of respiratory infections, frequently viral pathogens are not even investigated in patients with pneumonia. We performed a one-year observational retrospective study to define the burden of viral pneumonia in our tertiary care hospital in North-eastern Italy.

Materials/methods: We reviewed retrospectively all consecutive cases of adult patients with lung infiltrates undergoing bronchoscopy with bronchoalveolar lavage from January to December 2018, whose specimens had been analyzed with Real-time PCR for viral pathogens in addition to culture. Chi-square test has been used to establish correlation between variables.

Results: Of the 282 BAL performed, 259 patients were included. 40.5% (n=105) tested positive for viral pathogens. 64% (n=67) of these were defined as tracheobronchial viral shedding but 36% (n=38) were proven viral pneumonia; namely 14.7% of all patients enrolled. 14 patients had influenza-related pneumonia, 8 CMV, 8 HSV-1, 2 parainfluenza virus, 2 morbillivirus, 2 RSV, 1 metapneumovirus, 1 EBV pneumonia. Seasonal distribution confirmed a higher incidence of influenza, RSV, metapneumovirus and parainfluenza virus during the winter season, while CMV and HSV were evenly distributed within the year. Among patients with tracheobronchial shedding EBV was identified in 47 cases, CMV in 19, HSV-1 in 20. Viral pneumonia was associated to CAP (p-value 0.0045) and required hospitalization (p-value 0.0031) more frequently than viral shedding and or pneumonia due to other pathogens (p-value <0.0001 for both variables). Chemotherapy (p-value 0.0052), previous mechanical ventilation (p-value 0.0003) and diabetes mellitus (p-value 0.0271) were significant risk factors in our patient population. Lymphopenia (<1,000/μL) at presentation was also linked to viral pneumonia rather than tracheobronchial shedding (p-value 0.0009). No significant correlation was found with macroscopic pathological aspect of bronchial mucosa nor with radiological patterns.

Conclusions: In our study viral pneumonia seems to be not uncommon among hospitalized patients with CAP requiring diagnostic BAL and should be investigated especially in patients previously ventilated, lymphopenic or on chemotherapy. However the single-center retrospective design and the relatively small sample size do not permit to validate our conclusions. Further studies with larger populations are needed.
Use of chemiluminescence and electrochemiluminescence in the diagnosis and monitoring of hepatitis B viral infection

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Background: Several serological markers are used in the diagnosis and monitoring of hepatitis B infection (HBV). The presence of the surface antigen of HBV (HBsAg) is the main indicator that a patient is infected and it is therefore the most suitable screening marker. Modern and innovative technologies allow for a quantitative assessment of HBsAg levels in serum (HBsAg quant). This marker has an important predictive value for the anti-HBV treatment response and an accurate differential diagnosis of the stage of infection. The aim of this study is to determine the diagnostic and prediction value of the tests for quantitative determination of HBsAg, based on chemiluminescence (CLIA) and electrochemiluminescence (ECLIA), in different clinical forms of HBV infection.

Materials/methods: For the period from 01.2016 – 10.2019, a total of 2976 serum samples were tested for HBsAg quant. A trace into dynamics was done parallel with the testing of HBeAg and anti HBe. The serum samples were analysed with two tests - LIAISON® XL MUREX HBsAg Quant. (DiaSorin) and HBsAg II Quant (Roche Diagnostics Ltd). Ten serum samples were tested parallel in MDL Cibalab and the laboratory of DiaSorin (Italy). Twenty serum samples were analysed parallel by CLIA and ECLIA methods.

Results: The results from the simultaneous analysis of the ten serum samples tested with the CLIA method in two independent laboratories showed full correlation. In the correlation analysis of twenty samples tested on LIAISON® XL and Cobas 6000 there was a correlation in nineteen and a discrepancy in only one of the serum samples for patients with CHB. The analysis of the obtained results showed high sensitivity of the tests in the low linear range.

Conclusions: HBsAg quant. with using CLIA and ECLIA is economically effective and have optimal sensitivity for early diagnosis and excellent specificity. With LIAISON® XL and Cobas 6000 was performed an exact quantitative determination of HBsAg in the clinical samples in the beginning and during the antiviral therapy. They are interchangeable and can be used for quantitative determination of HBsAg which is important when making therapeutic decisions in CHB and predict treatment response.

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**Abstract 4048**

**First report of CC5-methicillin-resistant *Staphylococcus aureus*-IV-SCCfus “Maltese clone” in bat guano**

Mairi Assia1, Abdelaziz Touati2, Alix Pantel1,3, Albert Sotto1,4, Catherine Dunyach-Remy1,3, Jean Philippe Lavigne*1,3

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**Background:** *Staphylococcus aureus* is a well-known colonizer and cause of infection among animals. This bacterium has been described from numerous domestic and wild animal species. Methicillin-resistant *S. aureus* (MRSA) remains widespread around the world. It seems that these strains established new reservoirs, being currently disseminated in the community and notably among wild animals. The aim of the present study was to evaluate the resistance and virulence of *Staphylococcus aureus* strains isolated from bat guano in Aokas’s cave, Algeria.

**Materials/methods:** From March to May 2017, a total of 98 bat guano was collected using sterile swabs in Aokas’s cave (Bejaia, Algeria). Swabs were cultured in 1mL of Trypticase Soy Broth supplemented with colistin (10 mg/L), aztreonam (10 mg/L) and amphotericin B (2 mg/L) and incubated for 24h at 37°C. A 200 μL aliquot was plated onto mannitol salt agar plates and incubated for 24-48 h at 37°C. After isolation, the strains were identified by Vitek® MS system. Antibiotic susceptibility was determined by disk diffusion method according to EUCAST-CASFM 2018. DNA microarray analysis (Clondiag®) was used to characterize the molecular and antibiotic resistance profiles of Methicillin-resistant *S. aureus* (MRSA).

**Results:** A total of eleven *S. aureus* isolates were detected from 11 bat guanos (prevalence: 11.2%). All *S. aureus* isolates were sensitive for all the antibiotic tested excepted four isolates (36.3%) that were resistant to penicillin G, cefoxitin and fusidic acid. The four MRSA isolates belonged to a same clonal complex [CC]5/ST149. They harboured an SCCmec IV element and the fusidic acid resistance element Q6GD50 (fusC). The MRSA strains carried different virulence genes including enterotoxin A (sea), egc enterotoxin locus, enterotoxins C and L (sec, sel), toxic shock syndrome toxin (tst1) and hemolysins.

**Conclusions:** Wild animals could act as a reservoir of multidrug resistant bacteria. This study shows a global dissemination of CCS-MRSA-IV-SCCfus “Maltese clone” in Bat Guano in Algeria, demonstrating that this clone was not restricted to Malta.

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Abstract 4050

**Pseudomonas aeruginosa prosthetic joint infection: results from a prospective cohort**

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**Background:** *P. aeruginosa* prosthetic joint infections (PJIs) are rare (<5%). Data on their characteristics, management and outcome are very limited. The objective of the study was to describe the epidemiological, clinical and microbiological features of *P. aeruginosa* PJIs, their medical and surgical treatment and their 2 year outcome.

**Materials/methods:** Monocentric cohort study conducted from August 2004 to October 2018 including all mono and plurimicrobial *P. aeruginosa* PJIs. Data were extracted from the prospective data base. The following events were reported: relapse, new PJI, death related to infection or treatment. Results are expressed as median [min, max].

**Results:** Forty-four patients [29F/15M], the median age was 72 [35-90] years, with 27 hip, 16 knee and 1 shoulder arthroplasty infection, were included. Ten (23%) were immunosuppressed, 13 (29%) had been treated previously for another PJI. Twelve (27%) were plurimicrobial, 19 (43%) strains were wild type, 7 resistant to ciprofloxacin, none was resistant to ceftazidime.

Duration of symptoms before surgery was 190 [5-1473] days. Most PJIs were classified as late chronic [n=33, 75%], ten were early postoperative and one was a haematogenous infection.

Forty-one patients were operated: 27 underwent one-stage exchange (65%), 5 two-stage, 3 debridement and implant retention, 6 other strategies.

All patients except one received at least two antibiotics. Thirty (73%) patients were treated with continuous IV beta-lactam and oral ciprofloxacin for 6 weeks, followed by an exclusive oral ciprofloxacin regimen for 6 weeks. Eleven received 12 weeks of IV beta-lactam therapy combined with fosfomycin or colistin during 36 [24, 62] days. An aminoglycoside was used in 19 cases for 4 [2, 21] days.

After 2 years, one relapse, 3 new PJI, 2 related deaths were observed. No event was noted in 35 patients (85%).

Three patients were treated with prolonged suppressive antibiotic therapy.

**Conclusions:** The 2 year outcome of our cohort, including a majority of chronic PJI treated with one-stage exchange arthroplasty and prolonged IV antibiotic therapy, showed a favourable outcome in 85%, a higher rate than reported previously (~70%).

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**Chemical genomics to reverse the colistin resistance of MDR *Klebsiella pneumoniae***

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1University of Copenhagen, Copenhagen, Denmark, 2Macquarie University, Sydney, Australia, 3Louisiana State University, Baton Rouge, United States

**Background:** The emergence of multidrug-resistant (MDR) *Klebsiella pneumoniae* strains resistant to last resort antibiotics such as carbapenems and colistin are a global health concern. In a previous study, we used TraDIS (Transposon Directed Insertion site Sequencing) to identify the colistin secondary resistome, colistin-specific intrinsic-resistance genes, in MDR *K. pneumoniae* ST258 (ST258). The objectives of this study were to validate one of the identified colistin secondary resistance genes (*galE*) and to discover potential colistin adjuvant compounds that target this gene product.

**Materials/methods:** To validate the contribution of *galE*, which encodes UDP-Galactose-4-epimerase and is involved in LPS biosynthesis, to colistin resistance, a ∆galE mutant of ST258 was constructed through lambda-red mediated homologous-recombination. The phenotype of the ∆galE strain was confirmed by complementation of *galE* via arabinose-induced expression from a pBAD plasmid. Minimal inhibitory concentration (MIC) of colistin for wild-type, *galE* deletion and complementation strains were determined by broth microdilution. Compounds that target GaIE were identified through literature and PubChem search. Interaction between GaIE-targeting compounds and colistin was tested by checkerboard assay. To understand the effect of *galE* deletion on the envelope integrity of *K. pneumoniae*, fluorescence assay was performed using a membrane lipid-targeted probe NPN (1-N-phenylnaphthylamine).

**Results:** The colistin MIC of ST258 ∆galE mutant was 0.5 µg/mL, which was 8-16 fold lower than the MIC (8 µg/mL) of the wild-type strain. Complementation of *galE* in the mutant strain restored the colistin MIC to wild type level. A potential compound that interferes with the function of GaIE, ciclopirox olamine, exhibited synergistic growth inhibition with colistin with fractional inhibitory concentration index 0.28-0.5. Colistin MIC reduced to 0.5 µg/mL for wild-type ST258 in the presence of 4 µg/mL of ciclopirox. Envelope permeability assay showed increased NPN fluorescence in the ∆galE mutant compared to the wild-type, indicating compromised cellular envelope integrity in the absence of GaIE.

**Conclusions:** We identified a synergistic combination of colistin and ciclopirox that reverses the colistin resistance of MDR *K. pneumoniae* ST258. The approach demonstrated here, that employs chemical genomics to identify the antimicrobial adjuvant target, can be further explored to reverse the resistance of other antimicrobials and in different species.

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Abstracts 2020

Abstract 4054

Carbapenemase-producing *Klebsiella pneumoniae* in a Tunisian university hospital: emergence of hypervirulent strains

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**Background:** Carbapenemase-producing *Klebsiella pneumoniae* (CPKP) are increasingly reported worldwide. The aim of the study was to determine the molecular epidemiology of CPK in a Tunisian university hospital.

**Materials/methods:** All CPKP isolated in the Habib Bourguiba hospital between 2009 and 2016 were studied. Antibiotic susceptibility testing was performed by the agar disc diffusion method and E-test. String test was used to determine hypermucoviscosity activity of *K. pneumoniae*. The isolates were tested for the presence of carbapenemases and virulence genes by PCR. Plasmids carrying carbapenemase genes were analyzed by conjugation experiments and replicon typing method.

**Results:** 457 non-duplicate *K. pneumoniae* isolates harbored carbapenemase genes including 316 *bla*OXA-48, 127 *bla*NDM and 1 *bla*VIM and 1 coproduced *bla*OXA-48 and *bla*NDM. A gradual increase was noted in the number of CPKP isolates, ranging from 4.5% in 2009 to 26.4% in 2016. The CPKP isolates were collected mainly from urine (36%), bloodculture (20%) and sputum (16%). Their resistance rates to gentamicin, amikacin and colistin were 80%, 37% and 15%, respectively.

385 (82%) carbapenemase replicons were transferable by conjugation: 283 OXA-48 were carried on IncL/M plasmids, 30 OXA-204 on IncA/C, 1 OXA163 on IncR, 63 NDM on IncFIIk, 5 NDM-1 on IncA/C and 1 NDM on IncN plasmids.

*kpn*, *fimH1*, *ycfM*, *mrkD*, and *entB* virulence genes were detected in more than 90% of CPK isolates, *ybtS* in 80% and *kfu* in 56% of isolates. 5% of CPKP isolates were hypermucoviscous and 1% were hypervirulent and harbored *iroN*, *rmpA* and *iutA*, of which 2 hypervirulent *K. pneumoniae* strains belonged to K1 and K2 capsular types.

**Conclusions:** Our study demonstrates the increasing trend in OXA-48 and NDM carbapenemase-producing *K. pneumoniae* in our hospital and highlights the emergence of hypervirulent carbapenemase-producing strains in Tunisia.

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Clinical features of late prosthetic valve endocarditis in a cardiac referral centre (2006-2019)

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Abstract third-party references: Faperj, Rio de Janeiro, Brazil

Background: Prosthetic valve endocarditis is a severe subset of infective endocarditis (IE); it accounts for 10 to 30% of cases in IE series, and is usually associated with greater mortality than native valve IE.

Materials/methods: This is an analysis of a prospectively implemented cohort of adult patients with definite IE. ComParison between IE affecting valve prosthesis inserted for >1 year (late PVE, L-PVE) and the remaining cohort was done using Jamovi 1.0.7 software. The International Collaboration on Endocarditis case report form was used to collect data.

Results: Late PVE accounted for 53/359 episodes of IE (14.9%). Mean age of prosthesis was 8.2 ±5.9 years. Male sex was less frequent among patients with L-PVE (52.8% vs 64.9%, p NS), less patients were referred from other hospitals (26.4% vs 58.8%, p<0.001), acute presentation was more common (64.2% vs 48.6%, pNS). L-PVE was more frequently associated with prior CABG (11.8% vs 5%, p=0.06), atrial fibrillation (31.4% vs 13.9%, p<0.002), heart failure (62.3% vs 36.5%, p<0.001), cerebrovascular disease (20.8% vs 4%, p<0.001), previous IE (20.8% vs 8.6%, p=0.008), rheumatic valvopathy (65.4% vs 27.5%, p<0.001) and age above 60 years (23.7% vs 11.8%, p=0.006). No differences were found for essential hypertension, chronic renal failure or diabetes mellitus; site of acquisition (community, hospital, or healthcare-related, non-hospital) was not different. Blood cultures were more often positive for L-PVE (79.2% vs 66.1%, p=0.059) and enterococci more frequent (18.9% vs 9.3%, p=0.037). Aortic and mitral involvement were not different between groups. Conduction disturbances (mainly AV block) were more frequent in L-PVE (25.5% vs 7.4%, p<0.001), as were myocardial/paravalvular abscess (28.3% vs 18.9%, pNS). Preoperatively patients with L-PVE presented more often cardiac arrest (19.1% vs 9.8%, p=0.058), need for inotropes (43.5% vs 22.3%, p<0.002) and mechanical ventilation (37% vs 19%, p=0.006). Surgery was indicated at similar rates ( 81.1% vs 87.7%) but was done less often in L-PVE ( 63% vs 81.9%, p=0.003). Mortality was significantly higher in L-PVE (43.4% vs 21.6%, p<0.001).

Conclusions: Patients with L-PVE presented many years after valve insertion; they had more comorbidities, preoperative critical state and higher mortality.

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Abstract 4058

Outcomes of respiratory viral infections in cancer patients receiving checkpoint inhibitors
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Background: Check point inhibitors (CPI) are commonly used for the treatment of many solid tumors (ST) and hematological malignancies (HM). By blocking PD-1 in fatigued T cells, an increase in viral clearance may be noted as evidenced in cases of JC virus. We undertook a descriptive analysis of all patients treated with CPI and diagnosed with a respiratory viral infection.

Materials/methods: All patients who were infected with either influenza, respiratory syncytial virus (RSV), parainfluenza virus (PIV), or human metapneumovirus (HMPV) from 7/2016 to 5/2019 with prior or concurrent CPI therapy were included in this study. Demographics and clinical data were collected retrospectively.

Results: A total of 192 patients were included in our study. Majority of the patients were undergoing treatment for ST, with nivolumab being the most common agent. The most common HM being treated with CPI was chronic leukemia [such as CLL and CML], whereas the most common ST being treated with CPI was lung cancer. Side effects from CPI were identified in 28% of patients. The most common side effects were related to dermatitis [10%], gastrointestinal issues [8%] and pneumonitis [8%]. Steroids were used in 44% of the cases. Lower respiratory tract infection due to respiratory viral infection was noted in 38% of cases. The 30-day mortality due to respiratory viral infection was 4%. Other outcomes are displayed in table 1. Sub analysis of patients on active therapy versus those off therapy for 6 months or greater showed no difference in outcome related to respiratory viral infections.

Conclusions: The rate of lower respiratory tract infections due to respiratory viral infections in substantial. Yet, mortality associated with respiratory viral infections in patients on CPI remains low.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total n=192</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of lower respiratory tract infections</td>
<td>72 (38)%</td>
</tr>
<tr>
<td>Use of oxygen supplementation (%)</td>
<td>58 (30)%</td>
</tr>
<tr>
<td>Discharged home supplemental oxygen (%)</td>
<td>23 (12)%</td>
</tr>
<tr>
<td>Admitted for infection (%)</td>
<td>66 (34)%</td>
</tr>
<tr>
<td>Length of hospital stay (days) (IQR)</td>
<td>5 (3-10)</td>
</tr>
<tr>
<td>Admitted to ICU (%)</td>
<td>22 (18)</td>
</tr>
<tr>
<td>Use of mechanical ventilation (%)</td>
<td>22 (18)</td>
</tr>
<tr>
<td>Adjusted 30-day mortality (%)</td>
<td>6 (4)</td>
</tr>
</tbody>
</table>

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Abstract 4059

**Antimicrobial use correlates with *Clostridioides difficile* incidence across the departments of an academic centre**

Nasstasja Wassilew*, Alexandra Zehnder2, Andrew Atkinson3, Andreas Kronenberg4, Jonas Marschall1

1 Bern University Hospital, Department of Infectious Diseases and Hospital Epidemiology, Bern, Switzerland, 2 University of Bern, Institute for Infectious Diseases, Bern, Switzerland, 3 Bern University Hospital, Department of Infectious Diseases and Hospital Epidemiology, Bern, Switzerland, 4 University of Bern, Institute for Infectious Diseases, Bern, Switzerland

**Background:** *Clostridioides difficile* is a common pathogen causing nosocomial *Clostridioides difficile* infection (CDI) in vulnerable patients. The association between broad-spectrum antibiotic consumption and the risk for CDI is well known, but the individual risk of specific antibiotic groups is less well characterized. The aim of the study was to correlate the CDI incidence in eight clinical departments of a tertiary care hospital with the total antibiotic consumption per department, and for specific antibiotic groups.

**Materials/methods:** A retrospective observational correlation study was performed over 11 years (2008 - 2018). Data on CDI and antibiotic prescriptions were collected from the Swiss Antibiotic Resistance Surveillance System (ANRESIS). First and new infections were defined as CDI episodes and duplicates and recurrent infections were excluded, according to the Centres for Disease Control and Prevention definition. CDI incidence was calculated as number of CDI episodes per 10'000 bed-days and year. The most frequently prescribed antibiotic groups were analysed individually. Antibiotic consumption data were transformed into defined daily doses (DDD) according to WHO definition. A mixed effects logistic regression model was fitted with department as random effect to determine CDI incidence as a function of year, and adjusted for antibiotic consumption.

**Results:** From a total of 1807 *Clostridioides difficile* positive samples from January 1st 2008 to December 31th 2018, 1314 episodes were considered for analysis, after exclusion of duplicates and recurrent infections. Incidence increased slightly over the years (IRR 1.03 95% CI [1.00, 1.05], p=0.01), following adjustment for antibiotic consumption. The amount of total antibiotic consumption (including all 10 antibiotic groups) correlated with a higher incidence for CDI for most departments (figure 1a). Scrutinizing each antibiotic group individually, the most notable correlation was between quinolone use and CDI incidence (figure 1b).

**Conclusions:** We found that global antimicrobial consumption correlated with C. difficile incidence for some of the clinical departments of a tertiary care hospital. There was substantial variability between the departments, both in terms of antimicrobial consumption and C. difficile incidence. Fluoroquinolones exhibited the strongest correlation and may be a first target for interventions.

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ComParison of susceptibility of rifabutin and rifampicin on Staphylococcus spp. isolated in bone and joint infections

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Background: Rifampicin (RMP) combination therapy is the treatment of choice for acute staphylococcal prosthetic joint infections (SP JIs). However, RMP-related adverse effects and drug-drug interactions are frequently observed. Rifabutin (RFB) shares many of its properties with less adverse events. The present study aims to compare the antibacterial activity of RFB and RMP on staphylococcal clinical strains isolated from SP JIs.

Materials/methods: We studied 132 clinical strains of staphylococci (51 S. aureus (SA), 48 S.epidermidis (SE), and 33 coagulase negative staphylococci (CoNS)), isolated from SP JIs. The MICs, minimal bactericidal concentrations (MBC) and minimal eradication biofilm concentrations (MBEC) of RMP and RFB were determined using broth microdilution method (MIC) or the MBEC® Assay (MBC and MBEC) and then compared.

Results: RMP MIC₅₀ (0.016µg/ml [0.004-0.064]) was lower than RFB MIC₅₀ (0.032µg/ml [0.008-0.125]) for SA (p<0.001) but there was no statistically significant difference for SE [0.016 [0.002-0.064] vs. 0.016µg/ml [0.004-0.125] ; p=0.25] and CoNS [0.032 [0.002-0.064] vs. 0.032µg/ml [0.008-0.125] ; p=0.29]. RMP MBC₅₀ (0.032µg/ml [0.016-0.056]) was lower than RFB MBC₅₀ (0.064µg/ml [0.032-0.064]) for SA (p=0.003) but higher for SE [0.016 [0.008-0.032] vs. 0.004 [0.004-0.016]; p<0.001) and CoNS [0.00.24[0.008-0.016] vs. 0.008 [0.004-0.016]; p<0.01]. RMP MBEC₅₀ was significantly higher than RFB MBEC₅₀ for all strains, SA [2 [1-7] vs. 0.5µg/ml [0.25-0.5] ; p<0.001], SE [0.5 [0.015] vs. 0.064µg/ml [0.008-0.25]; p<0.001] and CoNS [0.25 [0.064-2] vs. 0.064 [0.0140.125]; p=0.004).

Conclusions: RFB has a better antimicrobial activity than RMPin biofilms encountered in SP JIs. It seems to be an excellent alternative to RMP in this indication.

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Abstract 4061

**Urinary tract infections in children: antibiotic resistance of major pathogens in Western Attika, Greece (October 2014 to October 2019)**

Polyxeni Karakosta¹, Eleni Kalogeropoulou¹, Alexandra Vasilakopoulou¹, Evaggelia Oikonomou¹, Paraskevas Tsilikis¹, Sophia Bamianidou¹, Aikaterini Tarpazi¹, Athanasia Spiliopoulou¹, Kostas Tsekouras¹, Spyros Pournaras*¹

¹Athens Medical School/Attikon University Hospital, Clinical Microbiology Laboratory, Athens, Greece

**Background:** Urinary tract infections (UTI) in children are major drivers of antibiotic prescriptions with empirical initial therapy, which in turn drive antibiotic resistance. Knowledge of local antimicrobial resistance patterns is essential for evidence-based empirical antibiotic administration. We studied the causative uropathogens and their regional pattern of antimicrobial resistance among pediatric patients attending Attikon University Hospital, Athens, Greece during the past 5 years.

**Materials/methods:** A 5-year retrospective analysis of bacteria isolated from urine samples of children (age < 14 years) with suspected UTI was performed from October 2014 to October 2019 in Attikon University Hospital, Athens, Greece. Chi-square test was used to compare subgroups.

**Results:** 2062 non-duplicate urine cultures were screened, of which 402 were positive, and 435 isolates were found. 49.2% were males and 50.8% females. Their median (IQR) age was 1.6 (4.8) years. *Escherichia coli* was the leading uropathogen (51.3%), followed by *Proteus spp.* (15.4%) and *Klebsiella spp.* (9.3%). Among isolates of *Escherichia coli*, high susceptibility rates were recorded for gentamicin (91.4%) and ceftazidime (87.4%); the lowest frequencies were noted for ampicillin (43.4%), amoxicillin-clavulanate (71.0%), trimethoprim-sulfamethoxazole (76.7%) and cefuroxime (83.0%). Over the 5 years, we observed a significant decrease in susceptibility of *Enterobacteriaceae* to ciprofloxacin [from 95.0% (October 2014-March 2017) to 88.3% (April 2017-September 2019), p=0.03] and gentamicin [from 94.1% (October 2014-March 2017) to 84.7% (April 2017-September 2019), p=0.01]. No significant differences were observed between outpatients and inpatients.

**Conclusions:** Several first-line agents for empirical treatment of childhood UTI seem to have suboptimal efficacy in the area of this study. Regular monitoring of local antimicrobial resistance patterns is recommended to update national evidence-based guidelines on antimicrobial usage.

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<thead>
<tr>
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<tbody>
<tr>
<td>Ampicillin</td>
<td>49(40.2)</td>
<td>78(42.2)</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>94(72.3)</td>
<td>142(70.7)</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>112(80.6)</td>
<td>169(81.3)</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>125(89.9)</td>
<td>194(86.6)</td>
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<tr>
<td>Meropenem</td>
<td>138(99.3)</td>
<td>222(99.1)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>132(95.0)</td>
<td>197(88.3)</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>128(94.1)</td>
<td>188(84.7)</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>111(79.9)</td>
<td>186(83.0)</td>
</tr>
</tbody>
</table>

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Abstract 4062

Household transmission of carbapenemase-producing Enterobacteriales: a prospective case-ascertained cohort study

Kalisvar Marimuthu1,2,3,4; Yin Mo3;5;6; Moi Lin Ling7; Anastasia Koutoucheva1; Shannon Fenlon8; Denis Bertrand9; David Lye1,2,3,10; Brenda Ang11;14; Eli Perencevich12; Don Tek Ng1,15; Ben Cooper3;1; Niranjan Nagarajan3;9; Swaine Chen3;8; Timothy Barkham14

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Background: Household transmission may be an avenue for community spread of carbapenemase-producing Enterobacteriales (CPE). We studied the transmission rate of CPE in households with known CPE carriers

Materials/methods: We conducted a case-ascertained cohort study in two tertiary hospitals in Singapore. Newly identified CPE carriers and their household members were followed for one year. We collected household environmental samples and stool samples from study participants and their companion animals, weekly for 4 weeks, monthly for 5 months, and bimonthly for 6 months. We defined a transmission event (primary outcome) as when an identical carbapenemase gene was found in household contacts as the index, either by culture-PCR method or metagenomic analysis. Clinical transmission was studied further with whole-genome sequencing(WGS) to identify genomic transmission. We calculated hazard rates for CPE acquisition using a multi-state Markov model.

Results: Between October 2016 to August 2017, we recruited 10 index patients and 14 household contacts [7 households-one contact, 2 households-two contacts, and 1 household-three contacts]. Median ages of index patients and household contacts were 60 and 50 years, respectively. Index patients had a higher Charlson comorbidity index, and more antibiotics and healthcare exposures compared to household contacts. The index patients and family members provided an average of 11.4 (range, 8-13) and 10.7 (range, 6-13) stool samples respectively within a cumulative follow-up time of 9 years.

Index patients were colonized with $bla_{OXA-48-ISE}$ (n=4), $bla_{VPC2}$ (n=3), $bla_{IMP}$ (n=2), and $bla_{NDM1}$ (n=1), distributed among divergent species of Enterobacteriales. Three family members [21.4%,3/14] acquired four different types of CPE in the community. Of these four acquisitions, two [14.3%,2/14] ($bla_{OXA-48-ISE}$ and $bla_{VPC2}$) met the definition of transmission events [hazard rate, 0.22/year; 95%CI, 0.06-0.89] and classified as possible transmissions by WGS. The probability of CPE transmission from an index patient to a household contact in one year was 10% [95% CI 4.26]. All household environmental samples (n=472) and stool samples from pets (n=13) were negative for CPE.

Conclusions: We found evidence consistent with limited within-household transmission of CPE and estimated that up to about one in five index patients would be expected to transmit CPE to household contacts in one year.

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Abstract 4063

**Evaluating emerging technologies in microbiology: what if your gold-standard isn’t gold?**

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**Background:** As the Microbiology laboratory increasingly looks to emerging technologies, such as artificial intelligence, to image and interpret microbial growth, the ability to accurately evaluate this technology becomes important. This study presents an evaluation of microbiologist variability in the enumeration of urine cultures, and examines the effect that using microbiologists as the gold standard may have on instrument sensitivity and specificity parameters and on understanding its true performance.

**Materials/methods:** A randomly selected set of 480 urine culture images taken by the APAS® Independence was used to assess the variability in culture interpretation between microbiologists. The primary analysis variable was bacterial growth enumeration of a urine bi-plate (HBA/Brilliance UTI), classified as 0, 10³, 10⁴ and 10⁵+ CFU/mL. The cultures comprised 107 No Growth plates, 151 plates showing 10³ CFU/mL, 148 showing 10⁴ CFU/mL, and 74 with ≥10⁵ CFU/mL of growth, as determined by the APAS® Independence. Three microbiologists assessed the enumeration of the APAS® Independence images independently of each other in a blinded manner. The microbiologists’ enumeration values were then compared across all the microbiologists.

**Results:** Variability in growth enumerations was demonstrated across the three microbiologists. The lowest agreement between all microbiologists occurred for values of 10³ CFU/mL for both agars, whilst the highest concordance between all microbiologists for both agars occurred in the ≥10⁵ CFU/mL category. Differences could be seen between the two agars with total enumeration agreement achieved between all microbiologists in 69.6% of samples on HBA [334/480] and 72.9% on Brilliance UTI agar [350/480]. Microbiologist amalgamated enumerations in agreement with consensus was 88.6% [1,276 /1,440]

**Conclusions:** Although human assessment of bacterial cultures remains the gold standard, this evaluation has shown its subjective and variable nature. This creates a dilemma for laboratories when evaluating evolving technologies that automate culture interpretation. Whilst artificial intelligent technologies promise to standardize culture interpretation, how do laboratories perform comparative evaluations? Using the microbiologist as a gold standard will likely provide inaccurate estimates of the technology’s performance and microbiologists need to be cognisant of this when designing and interpreting results.

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Abstracts 2020

Abstract 4066

Platelet trends early during Staphylococcus aureus bacteraemia are predictive of persistence and mortality
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Background: Recent evidence suggests that platelets play key roles in the host defense against Staphylococcus aureus (SA). We have shown that persistent SA bacteremia (SAB) occurs in > 1/3 of the patients with each continued day of SAB increases the risk of death by 16%. We evaluated the relationship between platelet trends early during the course of infection and outcomes in patients with SAB.

Materials/methods: Medical charts of all hospitalized patients with SAB from 2012 to 2018 were reviewed for relevant demographics, laboratory, and clinical data. Baseline and daily platelet counts during were evaluated to assess the time course and magnitude of change. Thrombocytopenia was defined as platelet count <150 x 10^3/μL, with 100-150, 50-99, and <50 x 10^3/μL as mild, moderate, severe respectively. Patients were grouped based on platelet count and compared for clinical characteristics, and outcomes (duration of bacteremia, 30-day mortality).

Results: 378 patients were included; mean age was 66y ± 16. MRSA accounted for 34% of SAB. Comorbid conditions were primarily cardiovascular followed by diabetes and renal disease. Thrombocytopenia occurred in 29% of patients at baseline; 13% (n=5) were moderate to severe (MS). Compared to patients with normal platelet count (n=246), more in the MS group had liver disease (7%,16/246 vs 24%,12/51 p<0.05) and required ICU admission (41% vs 24%, p=<0.05). MS patients had longer duration of bacteremia (2.5 vs 3.2d, p=0.057) and higher 30-day mortality (16% vs 7%, p=0.044). Patients who had normal baseline platelet count but became thrombocytopenic by day 4 of receiving effective antibiotic therapy had worse outcomes than those who maintained normal platelet count (42% vs 22% persistence, 19.4% vs 6.5% 30-day mortality). Those with reversal of baseline thrombocytopenia on days 3 to 4 (n=75) compared to those with continued decline (n=59) had superior outcomes; shorter bacteremia duration (2.57 vs 3.02d), less day 4 persistence (23% vs 32%), and 30-day mortality (5.3% vs 20.3%).

Conclusions: Our results suggest that thrombocytopenia at baseline and platelet declines during the early course of SAB is significantly correlated with bacterial persistence and mortality. Further studies to examine S. aureus virulence on platelet dynamics during SAB is warranted.

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Rapid generation of a standard inoculum direct from positive blood cultures using electrical biosensor technology

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**Background:** Bloodstream infections are life threatening and every hour a patient is not treated with an effective antibiotic the survival chance decreases by 10%. This is aggravated by the emergence of multidrug resistant bacteria where antibiotics fail to be effective. Accelerating antibiotic susceptibility testing (AST) from a positive blood culture (PBC) to provide targeted antibiotic therapy early on is key to improving patient survival. Avails Medical uses electrical biosensor technology to generate a standardized direct from PBC inoculum (eMcFarland) in as fast as 1 hour, the eQuant method. Here we compare colony plate counts and antimicrobial susceptibility results generated with the eMcFarland to results generated using a 0.5 McFarland made from traditional PBC subcultures.

**Materials/methods:** Blood culture bottles were spiked with 40 organisms. Avails’ eQuant method was performed on each PBC. The generated eMcFarland was used to perform Vitek and disk diffusion antimicrobial susceptibility testing (AST). The PBCs were also subcultured, and following overnight incubation, used to generate a traditional 0.5 McFarland inoculum which was also tested in Vitek and disk diffusion as a reference. The eMcFarland generated from a PBC was plated for viable cell counts and compared to plate counts from direct suspension of the organism from a 18-24 hour culture plate.

**Results:** Of the 40 spiked PBCs for which an eMcFarland inoculum was generated, there were 7 *Escherichia coli*, 5 *Klebsiella pneumoniae*, 5 *Klebsiella oxytoca*, 5 Enterobacter cloacae, 5 Enterobacter aerogenes, 5 *Serratia marcescens*, 2 *Citrobacter freundii*, 3 *Staphylococcus aureus*, and 3 Enterococcus faecalis. The Avails’ eMcFarland yielded an overall AST categorical agreement of 96.1% for Vitek and 97.2% for disk diffusion. Essential agreement was 96.5% for Vitek. All eMcFarland colony plate counts were within 0.5 log difference of the colony plate counts measured using a 0.5 McFarland created direct from plate.

**Conclusions:** Avails eQuant technology provides a standardized inoculum directly from positive blood cultures in as fast as 1 hour, for use in commercial AST systems. It eliminates time-consuming subcultures and has the potential to provide physicians with AST results at least 18 hours earlier compared to current traditional methods.

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**Abstract 4070**

**In vitro activity of four lytic bacteriophages specific for OXA-72-producing Acinetobacter baumannii**

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Abstract third-party references: The São Paulo Research Foundation (FAPESP)

**Background:** Bacteriophages are viruses with the ability to infect and kill bacteria and are the most abundant organisms on Earth. They are found in different environments and in the last years have been considered an alternative to treatment of several infections caused by MDR pathogens. Here, we performed an investigation and in-vitro characterization of bacteriophages recovered from hospital sewage against OXA-producing Acb isolates.

**Materials/methods:** Sewage samples were collected from four points of São Paulo Hospital and initially tested against 32 isolates of OXA-72-producing Acb as host. After selection by double-agar methodology, phages were purified, titrated, and stored at room temperature. Host range experiments were performed at 25°C and 37°C in a collection of MDR isolates: OXA-23 Acb (n=40), OXA-143 Acb (n=10), only OXA-51 Acb (n=20), without carbapenem-hydrolysing class D-β-lactamase (n=20), and OXA-72 Acb (n=106). Posteriorly, kinetics studies of phage infection were performed using different concentrations of phage (10^2 PFU, 10^3 PFU, and 10^4 PFU) by spectrophotometry during six hours at 37°C. Synergism effect of combination of 10^2 PFU of phages and 2 µg/mL of meropenem was also verified.

**Results:** Four phages were identified (PW55550, PW50186, PW53824, and P55640). PW55550 and PW50186 demonstrated activity at 25°C and 37°C, having 37°C as the optimal lytic temperature, while PW53824 and PW55640 just at 37°C and 25°C, respectively. Host range experiments showed which the phages were able to kill just OXA-72 Acb isolates. PW55550 and PW50186 were able to kill n=46 (43.4%) and n=43 (40.6%) OXA-72 Acb isolates with similar lytic profile. The remain phages showed lytic activity just against two isolates each (1.8%). Most OXA-72 Acb isolates were typed and belonged to CC79. Kinetics experiments of PW55550 and PW50186 showed that the inhibition of bacterial growth was just noted after the third hour of incubation at 37°C, with no difference in the concentration of phages used. No synergic in-vitro activity was observed when 10^2 PFU of PW55550 and PW50186 were combined to meropenem.

**Conclusions:** Hospital sewage is a rich font of bacteriophages against MDR pathogens. Two phages showed great activity against MDR OXA-72 Acb isolates and will be further characterized.

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**Fluoroquinolone resistance in Escherichia coli isolates after exposure to non-fluoroquinolone antibiotics: a retrospective case-control study**

Linda Ernestina Chaname Pinedo\(^1\), Robin Bruyndonckx\(^2\), Boudewijn Catry\(^3\), Katrien Latour\(^1\), Steven Abrams\(^1\), Herman Goossens\(^4\), Samuel Coenen\(^1\)

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**Background:** Fluoroquinolones, a major class of antibiotics, belong to the WHO list of highest priority antimicrobials for resistance surveillance in human medicine. Although the fluoroquinolone resistance percentage in Belgium has decreased from 26.7% in 2014 to 23.8% in 2017, it was still high compared to other northern European countries, such as the Netherlands (14.2%) and Denmark (12.8%) in 2017. Identification of a causal relationship between non-fluoroquinolone antibiotic use and fluoroquinolone resistance could guide treatment options to reduce fluoroquinolone resistance and enhance our understanding of co-selection. Here, we investigated whether, in routinely collected urinary Escherichia coli (E. coli) samples from primary and secondary healthcare settings in Belgium, the risk of fluoroquinolone resistance is increased by non-fluoroquinolone antibiotic use in the year prior to the sampling date.

**Materials/methods:** This was a secondary analysis of data collected retrospectively in a case-control study linking microbiological test results (isolated bacteria and their susceptibility) of urine samples routinely collected in primary and secondary care patients in Belgium with information on prior antibiotic use at the individual patient level up to one year prior.

**Results:** In urine samples from 6125 patients, 8313 E. coli isolates were retrieved; 2489 fluoroquinolone resistant isolates (cases) and 5824 fluoroquinolone susceptible isolates (controls). After adjusting for potential confounders (including fluoroquinolone use) and correcting for multiple testing, there was a 1.8 times higher odds of fluoroquinolone resistance in E. coli after exposure to trimethoprim/sulfamethoxazole [OR = 1.81, 95%CI, 1.40 - 2.34, \(p < 0.001\)] compared to no exposure to this non-fluoroquinolone antibiotic. Similarly, there was a 1.5 higher odds of fluoroquinolone resistance in E. coli isolates after exposure to nitrofurantoin [OR: 1.49, 95%CI: 1.20 - 1.84, \(p < 0.001\)]. These results were also observed for exposure at 6 and 3 months prior to the sampling date.

**Conclusions:** Under the assumption that confounding is addressed adequately and completely, exposure to non-fluoroquinolone antibiotics, i.e. trimethoprim/sulfamethoxazole and nitrofurantoin, might be causally related to fluoroquinolone resistance in E. coli isolates from urinary samples in Belgium. Future prospective research is needed to confirm non-fluoroquinolone antibiotics as potential drivers of fluoroquinolone resistance.

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Abstract 4076

**Strategy for cytomegalovirus reactivation prevention with ganciclovir and high dose of valacyclovir in allogeneic stem cell transplantation**

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**Background:** Cytomegalovirus (CMV) infection is an important cause of morbidity and mortality after allogeneic hematopoietic stem cell transplantation (HSCT). There are limited prevention strategies, and significant toxicity associated to them in developing countries.

**Materials/methods:** A retrospective analysis was performed on patients with allogeneic HSCT in Bogotá, Colombia. Patients were exposed to three CMV prevention strategies: from 2015 until 2018: universal prophylaxis with valganciclovir or preemptive strategy (once/week CMV viral load, with valganciclovir, ganciclovir or foscarnet initiation when it was positive), and since 2018: universal prophylaxis with ganciclovir from -6 until -3 and high dose of valacyclovir (1 gr q8h) since day -2 until + 100 (GVALA), with CMV viral load follow-up twice/week and treatment initiation when positive. The rate of CMV reactivation was compared.

**Results:** 262 transplants from 258 patients (4 were second transplantations because of graft failure) were analyzed. Mean age was 35 y (15-67 y), 60.7 % were men; most frequent transplantation causes were ALL (42.37 %), AML (27.1 %) and CML (10.69 %). 45.8 % were identical intrafamilial donors, 26 % haploidentical donors and 28.2 % unrelated donors. CMV D/R risk status was low in 2.68 % (n=7), intermediate in 76.72 % (n=201) and high in 20.23 % (n=53) of the cases studied.

There were 168 [64.12 %] patients with preemptive strategy, 63 [24.05 %] with GVALA prophylaxis and 31 [11.83 %] with valganciclovir prophylaxis. Overall reactivation was 45.24 % [n=76] with preemptive strategy, 42.86 % [n=27] with GVALA prophylaxis and 38.71 % [n=12] with valganciclovir prophylaxis (p=0.783). Reactivation within 100 days post-HSCT was 38.69 % [n=65] with preemptive strategy, 34.92 % [n=22] with GVALA prophylaxis and 25.8 % [n=8] with valganciclovir prophylaxis (p=0.378).

CMV mean reactivation time was 39 days (9-432 days); for patients under valganciclovir prophylaxis reactivation was delayed [64 versus 39 and 35 days, p=0.18]. There were no differences in CMV disease rate, hospitalization due to CMV or graft dysfunction.

**Conclusions:** No significant differences were observed in CMV overall reactivation, early reactivation or CMV disease in HSCT with a strategy based on ganciclovir pre-transplant administration and high dose of valacyclovir for post-transplant prophylaxis.

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Abstract 4081

Opportunities to enhance empiric prescribing in community-acquired central nervous system infections among 187 US hospitals

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Background: Central nervous system (CNS) infections carry a high burden of morbidity and mortality, which can be mitigated by implementing early effective empiric therapy. However, shifts in microbial etiologies and associated antibiotic-resistance patterns may impair appropriateness of empiric therapy and lead to deleterious outcomes. The current US landscape of CNS bacterial infections and their real-world management are unknown. Prior studies are based on billing codes and devoid of granular microbiological data. Herein we aimed to evaluate microbiological etiology, proportion of antibiotic-resistant phenotypes, use of rapid diagnostics and empiric therapy prescription patterns among community-acquired CNS infections from a large convenience US database.

Materials/methods: Clinical characteristics, in vitro susceptibility, antibiotic and adjuvant dexamethasone therapy were examined for adult inpatients with monomicrobial CNS bacterial and yeast cultures (within 48 hours of hospital admission) who received antibiotic therapy in the Premier Healthcare Database from 2016-2019. Antibiotic-resistant phenotypes were defined as resistance to methicillin in S. aureus (MRSA), vancomycin in enterococci (VRE), penicillin or vancomycin in pneumococci (VRP, PRP), extended-spectrum cephalosporins in Enterobacteriales (ESBL phenotype) and carbapenems in Enterobacteriales, Pseudomonas aeruginosa and Acinetobacter baumannii complex (CRO). Proportion of antibiotic-resistant phenotypes were compared to community-acquired CNS infection in 2009-2011.

Results: Between 2016-2019,1926 unique patient encounters in 187 centers had a positive CNS culture. Only 7 (4%) centers utilized multiplex rapid PCR testing. Mean age was 56 and 46% were males, Enterobacteriales (30%), of which E. coli (61%) predominated, followed by S. aureus (14%) and S. pneumoniae (10%) (Figure1A). Compared to 2009-11(n=878, 109 centers) there was a decrease in proportion of MRSA (p=0.001), while PRP, VRE, ESBL and CRO (p>0.50) remained stable (Figure1B) and no VRP was detected. Empiric therapy most commonly included vancomycin (80%), followed by ceftriaxone (64%), acyclovir (29%) and adjuvant dexamethasone (31%). 12.6% of patients received all three antibiotics in combination (Figure1C). Amongst patients >65 years, 23% received ampicillin.

Conclusions: Current patterns of pathogens, resistance and real-world empiric therapy suggest that opportunities exist to enhance guideline-compliant empiric prescribing practices for suspected community-acquired CNS infections. Wider implementation of reliable, rapid CNS diagnostics may increase the proportion receiving appropriate initial empiric coverage.
Abstracts 2020

A

![Pie chart showing distribution of bacterial species.]

- Entrobacteriales: 33%
- S. aureus: 20%
- S. pneumoniae: 14%
- Enterococci: 9%
- P. aeruginosa: 7%
- Streptococcal spp.: 6%
- Fungal (Candida spp./Cryptococcus spp.): 5%
- Klebsiella: 4%
- Other spp.: 9%

B

![Bar chart showing prevalence of different bacterial species over years.]

C

![Stem-and-leaf plots showing antibiotic resistance phenotypes.]


* p<0.005, all other antibiotic-resistant phenotypes p>0.05.

Figure 1A: Distribution of species of 1926 unique monomicrobial CNS bacterial and fungal yeast cultures

Figure 1B: Antibiotic-resistant phenotypes proportions in 2016-2019 cohort vs 2009-2011.

Figure 1C: Empiric-therapy combinations among community-acquire CNS bacterial and fungal yeast cultures

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Increase of parenteral antibiotic use in Japan could be explained by the society aging

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Background: We reported that national antibiotic use, estimated by sales data, decreased between 2013 and 2017, while parenteral antibiotic use increased during this period. However, the reason for this increase is unknown.

Materials/methods: We obtained data from the National Database of Health Insurance Claims and Specific Health Checkups of Japan and calculated the defined daily doses [DDDs] and days of therapies [DOTs] for each parenteral antibiotic from 2013 to 2017. Antibiotics were defined as drugs classified as J01 according to the ATC/DDD classification. Antibiotics were sorted by the AWaRe classification and categorized into three age groups (<15 years, 15–64 years, and ≥65 years). All population data were obtained by the Statistics Bureau of Japan.

Results: Parenteral antibiotic use increased from 0.78 DDDs/1,000 inhabitants/day (DID) to 0.81 DID, which accounted for a 4% increase from 2013 to 2017. Throughout the study period, the highest DID was for the ≥65 years group [1.98–2.06], followed by the 15–64 years group [0.35–0.36]. DID increases were not observed in any age groups. In the ≥65 years group, DID and DOTs/1,000 inhabitants/day (DOTID) decreased by 2.03% and 10.4%, respectively. In the AWaRe classification, Access antibiotic use increased by 3.4%, while non-Access antibiotic use decreased by 3.2%. Moreover, population data showed that the population in the ≥65 years group increased by 10.2% during the study period.

Conclusions: The DID and DOTID for the ≥65 years group decreased. Given this decrease, the increase in parenteral antibiotic use was likely due to the growth in the population aged ≥65 years.

Table: Changes in parenteral antibiotic use according to age groups

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Therapeutic drug monitoring of levofloxacin using a mobile microvolume-UV/VIS spectrophotometer and derivative spectroscopy

Jan W. C. Alffenaar*1, Erwin Jongedijk2, Claudia Van Winkel3, Margaretha Sariko4, Scott Heysell5, Stellah Mpagama4, Daan Touw3

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Background: Therapeutic drug monitoring (TDM) of fluoroquinolones has been recommended to optimize efficacy and to reduce acquired drug resistance in the treatment of multidrug-resistant tuberculosis (MDR-TB). However, traditional TDM using liquid chromatography has not resulted in broad implementation in programmatic settings. Therefore, the aim of this study was to develop a simple, low cost, robust assay using mobile spectrophotometry to quantify levofloxacin in human saliva on site.

Materials/methods: Experiments were performed on a mobile NP80 NanoPhotometer (Implen, München, Germany) and saliva samples were collected using a salivette® (Sarstedt, Nümbrecht, Germany). Samples were filtered with a 0.22 µM syringe-driven filter from Millex (Tullagreen, Carrigtwohill, Ireland). A small drop (≥3µl) of saliva was placed on the sample surface of the nanophotometer with the use of a disposable Pasteur pipette. Derivative spectroscopy was used to increase selectivity and specificity.

Results: The levofloxacin calibration curve was linear over a range of 2.5 (lower limit of quantification [LLOQ]) to 50.0 mg/L for levofloxacin with a correlation coefficient of 0.9991. Inter-patient variance was assessed by spiking six separate blank saliva samples and ranged from 2.9% to 10.4%. The calculated accuracy ranged from -5.2% to 2.4%. Within-day precision ranged from 0.7-11.4% and between-day precision from 1.9-11.4%. Drugs frequently co-administered (analgesics, general antibiotics and anti-TB/HIV drugs) were tested for interference by spiking blank saliva at the expected maximum concentration of these drugs in saliva. Application of the Savitsky-Golay method reduced the effect of interferents on the quantitation of levofloxacin resulting in no clinically significant impact. Only a pyrazinamide peak concentration of 500mg/L caused interference of 27 ± 2.3 % with levofloxacin at LLOQ level. As for TDM of levofloxacin samples are collect at 2 and 6 hours after drug intake the level of pyrazinamide interference was found negligible (9.3 ± 0.8%).

Conclusions: A simple UV method to quantify levofloxacin in saliva has been validated. This method can be used as point of care test to detect low levofloxacin drug exposure in programmatic settings.

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Abstract 4088

**Effect of short-term carbapenem restriction on the antimicrobial susceptibility of multidrug-resistant Gram-negative bacilli in an intensive care unit in Brazil**

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**Background:** Carbapenem-resistant gram-negative bacilli (GNB) infections are a serious public health problem due to its high mortality and low number of therapeutic options. Objective: Evaluate the impact of a carbapenem restriction program on reducing bacterial resistance in an intensive care unit (ICU).

**Materials/methods:** A unicentric retrospective study conducted in two phases in the 80-bed ICU of an acute care hospital in Brazil. The pre-intervention (PE) phase lasting 16 months (Jan / 18 to April / 19) and the second phase, post-intervention (PI), lasting 4 months (May to August 2019). The intervention was defined as “carbapenem-sparing” and the use of meropenem was authorized in three situations: (1) treatment of serious infections by extended spectrum β-lactamase-producing Enterobacteriaceae (ESBL); (2) therapeutic failure with another antimicrobial; (3) infectious disease recommendation. Data collection was obtained through consultation of electronic medical records and microbiological results of patients with more than 48h in ICU and who met the criteria for healthcare-associated infection (HAI) according to the CDC definition.

**Results:** In PE, 50 cultures were obtained with positive results for multidrug resistant GNB (standard deviation – sd = 12.2) and in PI, 31 cultures (sd = 12.8; p-value = 0.010). Average carbapenem consumption decreased significantly with corresponding increase in cefepime consumption in the same period: ATB (DDD / 1000patient-day) in PE: Carbapenems = 110.6 (sd = 97.1) and Cefepime = 8.2 (sd = 5.9) and in PI: Carbapenems = 44.7 (sd = 38.5; p-value = 0.015) and Cefepime = 32.0 (sd = 20.3; p-value <0.001). In terms of multidrug resistance rate, PE x PI: Acinetobacter = 95/149 = 64% x 13/30 = 43% (p-value = 0.043); other GNB reduced the resistance rate, but without statistical significance. There was a reduction in the HAI rate per MDR-GNB, PE 22.7 (sd 5.5) X PI 16.5 (sd 7.7) p = 0.07, although not statistically significant. Nevertheless, the ICU Klebsiella infection rate showed a significant reduction: in PE = 5.5 (sd = 1.9) and PI = 2.4 (sd = 1.8), p = 0.009.

**Conclusions:** Short-term carbapenem restriction may be an effective strategy to reduce the incidence of carbapenem-resistant GNB infections in ICU.

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Discriminating bacterial and viral infection using a rapid host gene expression test

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Background: Host gene expression-based signatures can discriminate bacterial and viral etiologies of acute respiratory illness but have not been translated to a clinical test nor validated in clinically indeterminate and complex cases. We therefore developed and evaluated the performance of a host gene expression-based test in subjects with confirmed infection, coinfection, and indeterminate infection compared to procalcitonin.

Materials/methods: Subjects were prospectively recruited from 2006–2016 in 4 US emergency departments. Enrollment blood samples were obtained for measurement of a 45-host gene expression test using a research-use-only (RUO) BioFire® test. The reference standard was an expert panel clinical adjudication, which was blind to gene expression and procalcitonin results.

Results: 623 participants (mean age 46 years; 45% male) were tested: 217 bacterial, 266 viral, 104 non-infectious illness, and 36 with bacterial/viral coinfection. The test provided independent probabilities of bacterial and viral infection in 45 minutes. In the training cohort, the HR-B/V test had an average weighted accuracy of 88.3% [CI: 81.7%-92.6%] for bacterial infection and 86.1% [CI 80.1%-90.1%] for viral infection corresponding to AUC values of 93.1% [CI 88.6%-96.1%] and 91.1% [CI 85.7%-94.4%], respectively. An independent validation cohort had similar performance with an average weighted accuracy of 85.6% [CI 70.7%-91.2%] for bacterial infection and 86.1% [CI 78.3%-91.5%] for viral infection with corresponding AUC values of 91.7% [CI 83.6%-96.4%] and 91.3% [CI 85.2%-95.4%], respectively. Among all subjects with respiratory bacterial infections, the test had 92.0% positive percent agreement (PPA) [CI 80.8%-97.8%], 82.4% negative percent agreement (NPA) [CI 77.3%-86.9%], 5.24 LR+ [CI 3.98-6.90], and 0.10 LR- [CI 0.04-0.25]. For viral infections, the test had 86.9% PPA [CI 81.1%-91.4%], 92.4% NPA [CI 86.1%-96.5%], 11.5 LR+ [CI 6.11-21.6], and 0.14 LR- [CI 0.10-0.21]. By comparison, procalcitonin distinguished bacterial from non-bacterial etiologies with 77% overall accuracy [CI 72.7%-81.0%] and 82.0% AUC [CI 73.9%-88.1%] but was inherently unable to discriminate viral from non-infectious etiologies.

Conclusions: Host gene expression, as measured on the BioFire System, rapidly and accurately diagnosed bacterial infection, viral infection, co-infection, or no infection. This test offers a new strategy to mitigate inappropriate antibiotic use through rapid and accurate discrimination of bacterial and viral infection.

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**Abstract 4091**

**Shared hospital epidemiology of respiratory viruses: a 3-year analysis using multiplex PCR in a university hospital**

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**Background:** Apart from a few high-risk wards, patients with other respiratory virus (RV) than influenza and RSV, are not systematically placed into droplet precautions. Our purpose was to retrospectively describe nosocomial infections associated to several RV.

**Materials/methods:** All respiratory samples from adult patients admitted for more than 24h and tested by multiplex PCR (mPCR) in a 900-bed university hospital for 3 winter periods from 2015 to 2018 were included. Detected viruses were adenovirus, coronavirus, metapneumovirus, influenza, parainfluenza, picornavirus (enterovirus and rhinovirus) and RSV. In the absence of well-defined incubation time for several viruses, infections were arbitrarily considered community-acquired, undetermined, or hospital-acquired if at least one virus was identified before 72 h, between 72 h and 96 h or over 96 h after hospital admission, respectively.

**Results:** Of 6335 samples, 1937 (30.6%) were positive, corresponding to 1604 single stays (only the first positive sample was included), with influenza accounting for 44% of cases: 1281 community-acquired (79.9%), 70 indeterminate (4.3%) and 253 hospital-acquired (15.8%) infections (Table). The viral distribution did not significantly vary across years (p=0.26), nor between community and hospital-acquired infection groups (p=0.09). Mortality among patients with hospital-acquired infection was higher than in community-acquired infection (9.5% vs 5.5%, p=0.02). The positivity rate among hospital-acquired cases varied by specialty (p=0.01) and was correlated with the proportion of double-occupancy rooms in each clinical ward (OR, 1.22; 95%CI, 1.03-5.56; p=0.03).

**Conclusions:** With the limit of a retrospective global analysis not based on systematic sampling in case of suggestive symptoms, all RV were responsible for hospital-acquired infection, with significant variations across wards and a correlation with the proportion of double-occupancy rooms. The unadjusted proportion of death was higher among hospital-acquired cases and higher for non-influenzae viruses. In view of frequency and associated death rates, droplet precautions should be discussed more widely, regardless of the virus responsible for respiratory tract infection and across all clinical wards.

<table>
<thead>
<tr>
<th>Virus</th>
<th>Adenovirus (n=25)</th>
<th>Coronavirus (n=210)</th>
<th>MPV (n=105)</th>
<th>Influenza (n=712)</th>
<th>PIV (n=56)</th>
<th>Picornavirus (n=406)</th>
<th>RSV (n=180)</th>
<th>Total (N=1604)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nosocomial cases (%)</td>
<td>3(12.0%)</td>
<td>39(18.6%)</td>
<td>18(15.2%)</td>
<td>101(14.2%)</td>
<td>16(28.6%)</td>
<td>57(14.0%)</td>
<td>32(17.8%)</td>
<td>253(15.8%)</td>
</tr>
<tr>
<td>Death rate (%)</td>
<td>2(66.6%)</td>
<td>3(7.7%)</td>
<td>2(12.5%)</td>
<td>4(4.0%)</td>
<td>2(12.5%)</td>
<td>10(17.5%)</td>
<td>3(9.4%)</td>
<td>24(9.5%)</td>
</tr>
</tbody>
</table>

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Influenza vaccine in chronic obstructive pulmonary disease

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Abstract third-party references: Sanofi Pasteur

**Background:** Prior studies have established that elderly patients with chronic obstructive pulmonary disease (COPD) are at elevated risk for developing influenza-associated complications such as hospitalization, intensive-care admission, and death. This study sought to determine whether influenza vaccination could reduce mortality among elderly patients with COPD.

**Materials/methods:** This study included Veterans (age ≥ 65 years) who received care at the United States Veterans Health Administration (VHA) during the 2014-2015 influenza season. The predominant A(H3N2) viruses, which are associated with higher rates of influenza-associated hospitalizations among the elderly, seem to have contributed to the highest recorded rate of laboratory-confirmed, influenza-associated hospitalizations. We linked VHA electronic medical records and Medicare administrative files to Centers for Disease Control and Prevention National Death Index cause of death records. A multivariable Cox proportional hazards model was performed on propensity score matched recipients of influenza vaccination to those who did not receive influenza vaccination. We estimated hazard ratios (HRs) adjusted for vaccination time and location, age, gender, race, socioeconomic status, as well as clinical characteristics such as comorbidity, medication use (bronchodilator, steroids), smoking, oxygen therapy, and pulmonary function.

**Results:** We identified 91,509 (70.3%) COPD patients without a record of influenza vaccination and 38,539 (29.7%) COPD patients with a record of influenza vaccination. Influenza vaccination was associated with reduced risk of death: 25% all-cause (HR=0.75; 95% CI: 0.64-0.86), 51% respiratory causes (HR=0.49; 95% CI: 0.47-0.51), and 57% COPD cause (HR=0.43; 95% CI: 0.40-0.45). We identified patients with severe to very severe COPD using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria for COPD severity, and found that influenza vaccination was associated with a greater reduction in risk of cause-specific COPD deaths compared to the overall COPD study population: 70% (HR=0.30; 95% CI: 0.11-0.79).

**Conclusions:** Among patients with COPD, influenza vaccination was associated with reduced risk for all-cause and cause-specific mortality.

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This abstract is about identifying Rhodotorula mucilaginosa, an opportunistic yeast, in China from August 2010 to July 2015. The study aimed to determine the ability of MALDI-TOF MS to identify R. mucilaginosa and to understand antifungal agents susceptibility, ability of biofilm formation and phylogenetic situation of these isolates.

**Background:** Rhodotorula mucilaginosa is a rare opportunistic yeast. It often infects immunocompromised persons and most infections have been associated with intravenous catheters. In China, relatively little is known of identification of R. mucilaginosa and of its antifungal susceptibility patterns and ability of biofilm formation. In the present study, we sought to examine ability of MALDI-TOF MS to identify R. mucilaginosa and to understand antifungal agents susceptibility, ability of biofilm formation and phylogenetic situation of these isolates.

**Materials/methods:** Here we studied 50 non-duplicate R. mucilaginosa isolates from 50 patients at 18 hospitals participating in the National China Hospital Invasive Fungal Surveillance Net program (CHIF-NET; 2011-2017). Molecular rDNA ITS sequencing and matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) MS identification methods were compared for their performance in species identification. Antifungal susceptibility testing was performed using Sensititre YeastOne™ YO10 methodology. The biofilm formation assay was carried out by crystal violet staining.

**Results:** All isolates were identified correctly by the Vitek MALDI-TOF MS system (bioMérieux) and the Clin-TOF MS system (Bioyong Technology Company Inc). The Bruker MS system (Bruker Daltoniks) also correctly identified all R. mucilaginosa isolates but using a lowered (≥1.700) cut-off score for species assignment. MICs of ≥256µg/mL for fluconazole were seen for all 50 isolates, whilst MICs of ≥4 µg/mL for voriconazole, ≥4 µg/mL for itraconazole and ≥2 µg/mL for posaconazole were seen for 74.0, 12.0, and 88.0% of isolates, respectively. All sequences can be divided into 4 ITS types compared to the reference sequence NR_073296.1 from R. mucilaginosa CBS316. Differences of biofilm quantification between 50 isolates were significant (0.75±0.24, 0.41±0.07, 0.19±0.07, P<0.001) with three classification.

**Conclusions:** The study has provided a global picture of the identification, antifungal susceptibility profile, phylogenetic situation and ability of biofilm formation of R. mucilaginosa in China during the period of the study.

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Abstract 4095

Multidisciplinary engagement improves monitoring of Outpatient Parenteral Antimicrobial Therapy (OPAT) in solid tumour patients at a comprehensive cancer centre

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Background: OPAT, in place since the 1970’s, improves patient quality of life, allowing for shorter hospital stays and earlier return to normal routine. Unfortunately, up to one in five patients discharged on OPAT are readmitted, but laboratory monitoring and hospital follow up within 2 weeks of discharge have been shown to reduce hospital readmissions. Whether the benefits of OPAT apply to patients undergoing antineoplastic therapy remains unclear. We aimed to improve laboratory monitoring and follow up in Infectious Disease (ID) clinic in solid tumor patients who were discharged on OPAT, per ID consultant recommendations, from a comprehensive cancer center.

Materials/methods: We previously used fishbone analysis and process mapping to analyze barriers to patients’ completing laboratory monitoring and following up in ID clinic. We used the Plan-Do-Study-Act methodology to initiate and analyze our interventions. Our initial intervention targeted clarification of ID physician recommendations through a standardized note. We invited case management to join our interdisciplinary OPAT team. During our next intervention, we asked teams to copy our standardized note into case management consult orders.

Results: After our initial intervention, we noted more complete recommendations for follow up and labs. Our ID clinic follow up rate improved from 44% to 72%. Recommendations for laboratory monitoring by ID providers increased from 43% to 90%, but the rate of completion of all recommended laboratory monitoring only increased from 33% to 45%. The percentage of patients without any lab monitoring declined from 25% to 17%. Although 50% of patients did not complete all recommended labs, OPAT-infection related readmission rates declined from 18.5 to 12.5 readmissions per 1000 OPAT-days. Infection-related emergency center visits remained stable during the study period.

Conclusions: Although our initial rates of follow up and laboratory monitoring rates according to OPAT guidelines were low, we were able to achieve improvement by using a simple intervention. Although a high percentage of our patients are still not completing recommended laboratory monitoring recommendations, we were able to achieve further improvements by engaging additional stakeholders. This improved laboratory monitoring helped achieve reductions in OPAT-infection related readmissions, similar to what has been reported in the general patient population.

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Abstract 4096

**Factors associated with in-hospital mortality in hospitalised patients with HIV/AIDS**

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**Background:** HIV infection continues to be a public health problem and the coffee triangle in Colombia has a higher incidence and prevalence vs. other areas of the country. The objective of the study was to evaluate the factors associated with mortality in hospitalized patients diagnosed with HIV in two, third-level hospital centers of the coffee triangle in Colombia.

**Materials/methods:** Descriptive study of non-concurrent cohort. Patients older than 18 years, with old or new diagnosis of HIV who entered between 2016 and 2018 were included. 180 variables grouped in sociodemographic, clinical, laboratory and death causes were defined. A univariate, bivariate and multivariate analysis was performed. The primary outcome was death as a function of time.

**Results:** 349 patients were included, male gender 71.8%, median age of 35 years, 72.6% in antiretroviral therapy, of these, 41% had adherence to treatment. 71.6% presented some defining condition of AIDS at hospital admission, tuberculosis [35.07%], pneumonia [16.3%], bacterial infections [13.7%], disseminated histoplasmosis [11.8%], wasting syndrome [10.49%], esophageal candidiasis [9.5%] and cerebral toxoplasmosis [9.18%]. Median CD4 103 cells/mL. The variables with the highest association to mortality were: enter due to respiratory symptoms (HR 2.62 IC95: 1.48-4.62), neurological symptoms (HR 4.7 1 IC95: 2.52-8.80), presence of seizures (HR 4.0 IC95: 1.67-9.6), have dementia from any cause or associated with HIV (HR 11.9 IC95: 3.92-36.3), elevation of AST upon admission (HR 1 IC95: 0.99- 1), Charlson comorbidity index of 6 or more points (HR 1.19 IC95: 1.06- 1.33) and orotracheal intubation (HR 3.46 IC95: 2.02-5.9). The variables that presented the greatest statistical weight when adjusted for the other variables were dementia of any cause and associated with HIV with a HR of 14.27 [p = 0.001].

**Conclusions:** The patients that were included in the present study present a high percentage of advanced disease due to their low CD4 count and high percentage in defining AIDS conditions. Factors that increase the risk of in-hospital mortality were identified, which can guide models of care and clinical strategies to identify early hospital admission, patients at high risk of death and be able to perform interventions aimed at reducing such risk.

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Abstract 4099

The type of agar may affect the string test result and virulence gene detection of hyper-mucoviscous Klebsiella pneumoniae

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Background: Hypermucoviscosity (HM) phenotype is a known virulent factor of Klebsiella pneumoniae. The string test to detect HM phenotype originally measured on 5% sheep blood agar after incubation at 37 °C overnight. However, the string test often performs different method previously described in the clinical settings. Therefore, we investigated the factors affecting the string test for the detection of HM Klebsiella pneumoniae (HMKP).

Materials/methods: A total of 48 K. pneumoniae isolates were used in this study. The string test was performed using 4 types of agar, including 5% sheep blood, Bromo Thymol Blue (BTB), MacConkey and Luria-Bertani (LB). A positive string test was defined as the formation of viscous strings of >5 mm in length. In addition, we assessed virulence factors associated with hypermucoviscosity by PCR, including capsular serotype (K1 and K2) and molecular genes (rmpA, magA, mrkD, wabG, uge, kfu, alls, fimH and cfa2a).

Results: Among the 48 KP isolates, 15 (31%) had the HM phenotype on blood agar. Ten (67%) on BTB, 11 (73%) on MacConkey and 1 (7%) on LB agar were negative string test among 15 HMKP on blood agar. The positive rates of K1 and K2 of HMKP were higher than those of non-HMKP on blood agar [13 and 13%, 8 and 3%, respectively]. Within HMKP on blood agar, the positive rate of K1 on BTB and K2 on MacConkey agar were same as those of blood agar. In contrast, there were no isolates with K1 on MacConkey and K2 on BTB agar. Although the positive rates of all tested genes except for magA and alls among all HMKP on all tested agar were almost same, magA and alls on MacConkey agar were not detected among all HMKP.

Conclusions: This study demonstrates that the type of agar affects the result of the string test of HMKP. Furthermore, the type of agar also affects virulence gene detection of HMKP. The string test using BTB and MacConkey agar may be overlooked the existence of HMKP. This study suggests that type of agar should be considered prior to the string test for reliable detection of HMKP.

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**Abstract 4100**

**Metagenomic insights into the dynamics and transmission of resistance genes in poultry and human beings**

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**Background:** The overuse of antibiotics in poultry farming contributes to the enrichment and spread of antibiotic resistance genes (ARGs). Numerous ARGs were identified in both poultry and human beings, but few studies described the transmission of ARGs from poultry to human beings in the metagenomic aspect.

**Materials/methods:** We collected and sequenced the metagenomes of 131 fecal samples in the same area, including 65 chicken fecal (CF) samples, 33 fecal samples of people who work in poultry farms or chicken slaughterhouses (CHF) and 33 fecal samples of nearby residents who haven’t contact with poultry farming (NCHF) as control. Bioinformatic tools were used to assemble the metagenomes, analyze the ARG contents and predict the possibility of transfer of ARGs.

**Results:** We found a similar gene diversity between CF and CHF samples, while a significant difference between CHF and NCHF samples. No distinguishable differences were found in the ARG types in three groups, but the abundance of ARGs in the gut of people who raise or slaughter chickens was significant higher than ARGs of chicken gut, followed by the control group. Fifteen ARG types were found present in all 131 samples. Quinolones and tetracycline resistance genes were the two most prevalence ARG types in both chicken and human guts. Moreover, we predict the transmission possibility of ARGs by identify if the ARG contigs were in plasmids and the integrated conjugative elements (ICEs) in ARG contigs. The results showed that the ratio of ARG contigs in plasmids and ICEs from chicken gut was significantly higher than those from human gut.

**Conclusions:** We described a higher risk of transmission of ARGs in chicken gut microbiome than human gut microbiome, and demonstrated that the gut microbiome of people who contact with poultry farming is a repository of ARGs and shares gene diversity of poultry gut microbiome.

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Diversity of the gut microbiome before haematopoietic cell transplantation is an independent predictor of respiratory failure and sepsis requiring intensive care in the post-transplant period

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Background: Diversity and composition of the gut microbiome of allogeneic hematopoietic cell transplant (allo-HCT) recipients is associated with poor overall survival, infections, disease relapse and graft-versus-host-disease (GVHD) post-HCT. Critical illness (CI) post-HCT has high short-term mortality rates. We hypothesized that pre-HCT fecal microbiome characteristics predict development of CI post-HCT.

Methods: We analyzed fecal samples from 828 adults who received their first allo-HCT from 2009 to 2017 at a single institution, collected within 10 days prior to cell infusion. The V4-V5 regions of 16S rRNA genes of DNA extracted from fecal samples were amplified and annotated taxonomically. Patients were heterogeneous with respect to transplant indication, conditioning intensity, graft source and manipulation. We analyzed time to intensive care unit (ICU) admission using survival-analysis methods.

Results: 75 patients (9%) were admitted to the ICU between the day of cell infusion (day 0) and day +50. The most common indications for ICU admission (ICUa) were respiratory failure (RF; n=52, 66%) and sepsis/septic shock (Sp/Ss; n=24, 27%). Patients were stratified based on pre-HCT fecal microbial diversity into high (inverse Simpson index ≥4) and low (<4) groups, following a previously published cutoff. Patients with low diversity pre-HCT had a strikingly higher risk of CI from RF and/or Sp/Ss than those with high diversity (HR 2.49 [95% CI 1.45-4.28], p=0.001; figure). This association remained significant in a multivariate Cox proportional hazard model (HR 2.17 [95% CI 1.24-3.76], p=0.007) that accounted for conditioning intensity, graft source, graft manipulation, and hematopoietic cell transplantation-specific comorbidity index (HCT-CI). Higher HCT-CI was also an independent predictor of ICUa for RF and/or Sp/Ss. All other ICUa indications including hemorrhage, anaphylaxis and isolated non-inflammatory dysfunctions of the cardiac, renal or neurological systems were deemed unlikely to be affected by, and did not correlate with, pre-transplant gut microbial diversity.

Conclusions: Pre-transplant fecal microbial diversity is an independent predictor of CI from RF and/or Sp/Ss requiring intensive care in the post-HCT period. These observations highlight the pre-HCT period as a window of opportunity to assess gut microbial injury; to inform antibiotic and GVHD prophylaxis, gut-decontamination, conditioning regimens; and to intervene with remedia- tion or prevention strategies.

Pre-transplant fecal microbial diversity predicts critical illness from respiratory failure and/or sepsis/septic shock after allo-HCT

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Highly sensitive and specific detection and serotyping of five prevalent *Salmonella* serovars by multiple cross displacement amplification

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**Background:** *Salmonella* is a common cause of foodborne illness worldwide and in Australia. Over 70% of notifications of human salmonellosis in Australia are caused by five *Salmonella* serovars: Typhimurium, Enteritidis, Virchow, Saintpaul, and Infantis. Rapid, accurate and sensitive detection and identification of *Salmonella* serovars is vital for diagnosis and surveillance. Recently, an isothermal amplification technique termed Multiple Cross Displacement Amplification (MCDA) has been employed to detect *Salmonella* at the species level but not to the serovar level. We utilised seven serovar/lineage-specific gene markers for the five common Australian serovars identified through genomic comparisons from our previous study (two serovars had two lineages). An MCDA assay for each of these markers was developed and evaluated.

**Materials/methods:** Seven gene markers STM4494, SEN1384/R561 RS18155, SESV_RS06060, SeSPB_A1 7 49/SeSPA_A1 352 and L287_11 788, which were specific to the five most common *Salmonella* serovars in Australia: Typhimurium, Enteritidis, Virchow, Saintpaul, and Infantis respectively, were selected as targets. Seven MCDA primers sets were designed using Primer3 online software. The limit of detection (LoD) of the seven MCDA assays was performed on serially diluted genomic DNA template from target strains. The sensitivity and specificity of the seven MCDA assays were evaluated using 79 target strains and 32 non-target strains. Real-time fluorescence measurement was used to detect the seven MCDA products.

**Results:** The seven MCDA assays successfully amplified target gene markers from the five most common *Salmonella* serovars in Australia. The LoD of seven MCDA assays was 50 fg per reaction (10 copies of target DNA) from pure culture. Sensitivity ranged from 92.3% to 100% and specificity ranged from 93.3% to 100%. The MCDA assays can also provide test results from a minimum of 8 minutes at 5 ng concentration to a maximum of 20 minutes at 50 fg concentration.

**Conclusions:** We developed and evaluated seven rapid, accurate and sensitive MCDA assays for detection and differentiation of the five most common *Salmonella* serovars in Australia: Typhimurium, Enteritidis, Virchow, Saintpaul, and Infantis. With further validation in clinically relevant conditions these assays could be used for culture-independent serotyping of common *Salmonella* serovars directly from clinical samples.

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Abstract 4109

Outcomes of a pharmacist-led antimicrobial stewardship programme within a family medicine resident clinic
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Background: Antimicrobial stewardship programs (ASP) are crucial to guiding antimicrobial prescribing. While infectious diseases-trained physicians and pharmacists typically lead inpatient ASP initiatives, the majority of antibiotics are prescribed in outpatient settings where ASP resources may be limited. Ambulatory care pharmacists (ACP) within primary care offices may serve as important ASP extenders to lead outpatient initiatives. The purpose of this study was to determine if an ACP-led ASP intervention combining baseline education with audit-with-feedback improved antibiotic prescribing in a family medicine residency clinic (FMRC) for common infections, including upper respiratory tract (URI), urinary tract (UTI), and skin and soft tissue (SSTI) infections.

Materials/methods: This quasi-experimental study compared antibiotic prescribing 6-months before (Pre-ASP group) and after (ASP group) implementation of an ACP-led audit-and-feedback process in a single FMRC. In September 2018, the health-system ASP physician and pharmacist provided live education, including review of baseline prescribing data, local resistance trends, and where to locate online institutional guideline recommendations. FMRC staff were additionally provided with pocket cards as a quick reference containing guideline recommendations. Audit-with-feedback was delivered electronically, bi-weekly for all URI, UTI, and SSTI prescriptions by the clinic’s ACP from October 2018 through March 2019. The primary endpoint of the study was total guideline-concordant antibiotic prescribing (drug, dose, and duration of therapy). Guideline-concordance was determined based on the health system’s local outpatient ASP guidelines.

Results: 514 antibiotic prescriptions were audited (pre-ASP n=79, ASP n=435). Total guideline-concordant antibiotic prescribing at baseline was 39.2% (URI 46.7%, SSTI 26.7%, UTI 47.4%). During the 6-month intervention period, 435 antibiotic prescriptions were audited (URI 183, SSTI 125, UTI 127) with all prescriptions receiving feedback from the ACP. Total guideline-concordant prescribing improved across all three infection types to 57.9% (URI 59.6%, SSTI 49.6%, UTI 63.8%, p=0.002). Significant improvements were seen in guideline-concordant antibiotic selection (68.4% vs. 80.2%, p=0.018), dose (73.4% vs. 86.2%, p=0.004), and duration of therapy (75.9% vs. 86.2%, p=0.02).

Conclusions: A pharmacist-led audit-and-feedback process within a FMRC significantly improved guideline-concordant antibiotic prescribing for the most common infectious disease states.

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Rifampicin reduces tedizolid concentrations in healthy volunteers
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Abstract 4112

Background: Tedizolid is an oxazolidinone which is currently approved to treat skin and soft tissue infections. Rifampicin is a rifamycin antibiotic which can also treat skin and soft tissue infections such as those caused by Staphylococcus aureus. In addition, rifampicin is used to treat tuberculosis and we are investigating tedizolid for the same indication. Tedizolid and rifampicin could therefore be used concurrently to treat infections. There is currently no clinical data on whether rifampicin affects tedizolid concentrations. Rifampicin is known to be an inducer of cytochrome P450s. Tedizolid is not known to be cleared by cytochrome P450s, but other clearance mechanisms may be affected. Therefore we conducted a pharmacokinetic drug-drug interaction study to investigate whether 2 weeks of rifampicin can affect tedizolid concentrations.

Materials/methods: We conducted a healthy volunteer study in 8 subjects. Subjects were first given linezolid 600 mg on day 1, tedizolid 200 mg on day 4, rifampicin 600 mg daily from days 5 to 19 (2 weeks of rifampicin), and an additional dose of tedizolid 200 mg on day 19. Blood was obtained at pre-dose, 1, 2, 3, 4, 5, 6, 8 and 24 hours post dose on days 4 and 19. Concentrations of tedizolid were measured using a validated liquid chromatography / mass spectrometry method. Pharmacokinetic parameters were calculated by Non-Compartmental Analyses using Phoenix WinNonLin version 8.0. The bioequivalence module was used to obtain ratios of PK parameters pre- and post-rifampicin.

Results: Eight patients were included in the study. 6 were Chinese, 1 Indian and 1 Burmese. Median age [range] and weight were 34.5 (29-44) years and 64 (58.4-90.8) kg respectively. Tedizolid was well tolerated in the study. Tedizolid AUC (0-24 hours) was reduced after 2 weeks of rifampicin (GMR 0.80, 90% confidence interval 0.73-0.88), as was Cmin (0.54, 0.44-0.66) and Cmax (0.85, 0.79-0.91). Clearance / F of tedizolid was significantly increased after rifampicin (1.35, 1.21-1.50).

Conclusions: Rifampicin given for 2 weeks has the potential to reduce tedizolid concentrations, especially trough levels, which was reduced by 46%. Caution is recommended when using tedizolid together with rifampicin, especially when tedizolid MIC is high or treating difficult infections.

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Abstract 4115

**Treatment patterns and healthcare resource use among hospitalised adults with carbapenem non-susceptible Gram-negative infections in a large US electronic health record database**

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**Background:** Carbapenem non-susceptible (C-NS) Gram-negative (GN) infections are difficult to treat and can be life-threatening. Limited data exist on healthcare resource use (HCRU) associated with these infections.

**Materials/methods:** Retrospective cohort study of hospitalized adults with complicated intra-abdominal infection (cIAI), complicated urinary tract infection (cUTI), bacterial pneumonia (BP), or bacteremia (BAC) attributable to GN C-NS (resistant/intermediate susceptibility to carbapenems) bacteria from January 2013-March 2018. Treatment patterns and HCRU were examined 6 months prior to the first qualifying hospitalization (pre-admission) through 12 months post-discharge, or fewer if due to death.

**Results:** 2,862 patients were included (mean age: 63.2 years, male: 55.6%). Patients had cUTI ±BAC (38.4%), BP ±BAC (21.5%), cUTI +BP ±BAC (18.7%), any cIAI (14.7%), or BAC only (6.7%). Pseudomonas was the most common pathogen (65.4%). Renal insufficiency was observed in 47.8% of patients. During index hospitalization, 83.6% received an antibiotic (74.3% combination therapy, median antibiotic classes: 2, maximum: 7). Of those given antibiotics, 38.9% received a carbapenem despite C-NS status (86.5% empiric, 13.5% post-susceptibility result confirming C-NS); 9.0% received polymyxins. Median length of stay was 12.0 days; 49.6% of patients were admitted to intensive care (median duration: 2.0 days) and 36.1% underwent mechanical ventilation (median duration: 8.0 days). Prior to admission, between one-third and two-thirds of patients had a bacterial infection in the same site as their qualifying index infection, 60.2% had inpatient visits, 46.4% received antibiotics, and 35.8% had renal insufficiency. Of those treated with a carbapenem during their index hospitalization, 27.5% also received a carbapenem pre-admission. During post-discharge, 63.9% of patients were re-hospitalized (44.3% within 30 days post-discharge, median time to first readmission: 37.0 days) and 27.7% died within 12 months post-discharge (median time to death: 82.5 days post-discharge).

**Conclusions:** Patients with C-NS infections had high levels of comorbidity and pre-admission antibiotic exposure, often received carbapenem treatment despite having non-susceptible infections, and exhibited poor outcomes in terms of high resource use and post-discharge mortality/readmission. Such patients may benefit from novel efficacious agents to which C-NS bacteria are susceptible. High levels of renal insufficiency were observed in this population, indicating a need for newer therapies with improved toxicity profiles.

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Abstract 4116

Progressive disseminated histoplasmosis in a population with HIV/AIDS in the Colombian coffee triangle

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Background: Histoplasmosis is an endemic mycosis considered worldwide as an orphan disease, which has a very variable clinical presentation and usually is disseminated in the population with HIV/AIDS. The objective of the study is determining the signs and symptoms associated with the definitive diagnosis of disseminated histoplasmosis and mortality associated variables.

Materials/methods: Retrospective cohort study that included patients diagnosed with HIV/AIDS and suspicion of disseminated histoplasmosis in a population attended in a reference hospital in a city in Colombia's coffee triangle, between January 2015 to April 2019. Clinical and laboratory variables were taken and univariate, bivariate and multivariate analyzes were performed to determine the characteristics associated with the diagnosis of disseminated histoplasmosis. A survival analysis was performed.

Results: Of 173 patients with HIV and clinical suspicion of histoplasmosis who underwent urinary antigen for histoplasma, 50 had positive and 123 negative urinary antigens. 76.3% were male, 79.2% came from urban areas, 50.9% had recently diagnosed HIV. CD4 count with a median of 54 cells/mL and viral load of 280000 copies/mL. The commonest clinical manifestations were constitutional symptoms 86.7%, weight loss 81.5% and fever 75.1%. Anemia was present in 90.8%, and lymphopenia 82.7%. Others infections were present in 65.9%, tuberculosis in 46.2%.

The conditions associated with the diagnosis of disseminated histoplasmosis in the bivariate analysis (p <0.05) were: leukopenia, thrombocytopenia, ferritin elevation, low CD4 count, AST and ALT elevation and pancytopenia; and in the multivariate analysis were: elevation of alkaline phosphatase, lactic dehydrogenase and CD4 count less than 50 cells/mL (OR 4.7 IC95% 1.4-15). 24.9% died in the hospital. The variables associated with mortality in all patients were: elderly (OR 3.9 IC95% 1.3-11.4), dyspnea (OR 4.4 IC95% 1.4-13.2), and ferritin greater than one thousand (OR 4.5 IC95% 1.3-15.7).

Conclusions: The behavior of histoplasmosis in our population establishes some differences with the reported in studies from other regions, such as less skin involvement and lymphadenopathy, but with greater hematological manifestations. The adequate analysis of these clinical and laboratory findings can facilitate decision-making to suspect the presence of disseminated histoplasmosis in patients with HIV/AIDS in our region.

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Abstract 4118

Global dissemination of multidrug-resistant *Escherichia coli* co-expressing ESBL/pAmpC and mcr-1 genes in chicken farms in Lebanon

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**Background:** Poultry production is a main contributor of the global trend of antimicrobial resistance arising from food-producing animals worldwide. In Lebanon, abusive and inappropriate use of antibiotics is frequent in chickens for prophylactic reasons and to increase productivity. In absence of a surveillance system, the present objective is to decipher the spread of expanded-spectrum cephalosporin (ESC)-resistant *Escherichia coli* in poultry in Lebanon.

**Materials/methods:** Rectal swabs *(n=280 healthy chickens)* from 56 farms across the country were screened for the presence of ESC-resistant *E. coli* isolates. Antimicrobial susceptibility and expanded-spectrum β-lactamase (ESBL)/AmpC production were determined by the disk-diffusion method. Whole genome sequencing of a set of representative isolates *(n=221)* was performed to determine the phylogenetic diversity, acquired resistance genes and plasmids using the CGE tools suite.

**Results:** From 56 poultry farms, 51 harboured ESC-resistant *E. coli*. Nearly all ESC-resistant *E. coli* isolates were multidrug-resistant with frequent additional resistance to fluoroquinolones and aminoglycosides. Among the 221 sequenced *E. coli* isolates, the proportion of ESBL, pAmpC-producers and ESBL/pAmpC co-producers were 56%, 24%, and 20%, respectively. The most prevalent ESBL genes were *bla*$_{CTX-M-3}$, *bla*$_{CTX-M-15}$, *bla*$_{CTX-M-55}$, *bla*$_{CTX-M-27}$ (n=79; 40; 24; 21, respectively). Surprisingly, only one isolate harboured the *bla*$_{CTX-M-1}$ gene usually associated with livestock production. The pAmpC cephalosporinase gene *bla*$_{CMY-2}$ was dominant (n=91/91). The dramatic proportion of fluoroquinolone-resistant *E. coli* isolates co-expressing ESBL and/or AmpC genes and the mobile colistin resistance gene mcr-1 (n=54) is especially worrisome. These ESC-resistant isolates belonged to a great diversity of sequence-types, most being well-known avian-associated (ST-117, ST-10, ST-48 and ST-93), and sometimes pathogenic. Numerous different plasmids were identified suggesting their roles in the spread of these resistance genes in the *E. coli* population.

**Conclusions:** For the first time, this study illustrates the alarming prevalence of multidrug-resistant *E. coli*, especially to medically-important antibiotics, in broiler production in Lebanon. Further molecular studies are needed to understand the country-specific epidemiology of ESBL/AmpC and mcr-1 genes in the Lebanese poultry production. Our results also advocate the urge for surveillance programs and action plans in Lebanon to reduce the abusive use of antibiotics and to limit the spread of multidrug-resistance in food-producing animals.

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Long-term exposure to ceftriaxone sodium induces alteration of gut microbiota accompanied by anxiety-like and depression-like behaviours in mice

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Background: According to the theory of microbiota-gut-brain (MGB) axis, disturbance of the gut microbiota may affect gut-brain communication, influencing the development of brain and altering host behaviors. However, the extent to which alterations in microbiota composition and function mediate the dysregulation of the axis is unknown. Thereby we assess the effects of gut bacteria depletion on emotional behaviors and attempt to explore relevant mechanisms.

Materials/methods: Mouse in experimental group was given ceftriaxone sodium solution [250mg/ml, 0.2ml/d] and control group was given pyrogen-free saline (0.2ml/d) by gavage. Emotional behaviors were assessed by the open field test and the suspension tail test. Fecal samples were collected for 16s rRNA sequencing. Serum cytokines and corticosterone were measured by ELISA. Brain derived neurotrophic factor (BDNF) and c-Fos proteins were determined by immunohistochemistry.

Results: Eleven weeks later, we found that ceftriaxone administration led to decreased richness and diversity of gut microbiota and observed characteristic microbiota. This was accompanied by behavioral abnormalities in mice, including anxiety-like, depression-like and aggressive behaviors simultaneously. Thus, we presumed there may be an association between the above results. Next we found that pathways related to the MGB axis altered, including the activation of immune system [such as increased IL-6 and IL-10], the hyperactivity of hypothalamic-pituitary-adrenal (HPA) axis [such as elevated corticosterone] and neurochemical changes [such as down-regulated trend of BDNF and up-regulated trend c-Fos].

Conclusions: The findings highlight the important role of microbiota in the gut-brain communication and suggest the absence of conventional gut microbiota influence the development of behavior and function of the brain.

Fig.1 Heat maps of gut microbiota (a) at the phylum level and (b) at the genus level; Results of mice (c) in the suspension tail test and (d) in the open field test. *P<0.05, **P<0.01, ***P<0.001. AB: antibiotic group (n = 14), CT: control group (n = 19)

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Abstract 4124

**Characterising a novel mechanism of inducible carbapenem resistance in toxigenic Corynebacterium diphtheriae**

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**Background:** Diphtheria is a potentially fatal respiratory disease caused by toxigenic *Corynebacterium diphtheriae*. Although resistance to erythromycin has been recognised, β-lactam resistance in toxigenic diphtheria has not been described. Here we report a case of fatal respiratory diphtheria caused by toxigenic *C. diphtheriae* resistant [MIC ≥ 256 μg/ml] to penicillin and all other β-lactam antibiotics.

**Materials/methods:** Long-read whole genome sequencing was performed using Pacific Biosciences SMRT sequencing to determine the genome sequence of *C. diphtheriae* BQ11 and mechanism of β-lactam resistance. Meropenem sensitive isolates were grown, in parallel, with and without exposure to meropenem and sequenced on an Illumina Hi-Seq2000 sequencer. Sequence read coverage across the resistance locus was calculated and used to compare differences in tandem repeat copy number between resistant and susceptible isolates.

**Results:** On testing, BQ11 demonstrated high-level resistance to penicillin (benzylpenicillin MIC ≥ 256 μg/ml), β-lactam/β-lactamase inhibitors and cephalosporins (amoxicillin/clavulanic acid MIC ≥ 256 mg/L; ceftriaxone MIC ≥ 8 μg/mL) and carbapenems (meropenem MIC ≥ 32 mg/L). Genomic analysis of BQ11 identified acquisition of a novel transposon carrying the penicillin binding protein Pbp2c, responsible for resistance to penicillin and cephalosporins in *Corynebacterium jeikeium* K411. Remarkably we found that when strain BQ11 was exposed to meropenem, selective pressure drove expansion of the array resulting in multiple copies of the transposon and a corresponding change from a meropenem susceptible (MIC < 0.002 mg/L) to a meropenem resistant (MIC < 32 mg/L) phenotype.

**Conclusions:** Our research has identified a novel mechanism of inducible carbapenem resistance whereby isolates that appear to be carbapenem susceptible on initial testing can develop in vivo resistance to carbapenems with repeated exposure, which could have significant implications for treatment and may lead to clinical failure.

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Abstract 4125

Assessment of antimicrobial molecules and bacteriocins isolated from Pseudomonas species for activity against multidrug-resistant bacteria

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Background: Antimicrobial treatment failures against infections caused by multi-drug resistant (MDR) organisms are increasing globally and alternative ways to treat these infections have seen a rise in research interest. Bacteriocins, antimicrobial proteins or peptide toxins produced by bacteria to kill competition of closely related species, are an alternative method to potentially treat these infections and alleviate the pressure MDR organisms poses on healthcare. Pseudomonas aeruginosa has been previously shown to secrete antimicrobial agents which inhibit other microorganisms, giving a competitive advantage within a mixed species community. In this study we evaluated P. aeruginosa strains isolated from various environmental (healthcare water) sources for antimicrobial activity against clinically relevant pathogens.

Materials/methods: Antibiotic susceptibility tests (AST) assays were performed using piperacillin-tazobactam, ceftazidime, imipenem, meropenem, aztreonam, amikacin, gentamicin, tobramycin, ciprofloxacin and piperacillin, to eliminate potential duplicate strains. A cross-streak method on an agar interface was used to determine the antimicrobial activity of 323 P. aeruginosa isolates against 10 type and clinical target isolates including: P. aeruginosa, Staphylococcus aureus, Escherichia coli, Enterococcus faecalis, Klebsiella pneumoniae. P. aeruginosa were exposed to UV radiation, low nutrient, low temperature or low-to-high temperature conditions to stress the isolates. P. aeruginosa isolates were cultured in broth to harvest the secreted molecule(s) by membrane-filtration (0.45um pore-size). Aliquots (65μL) of the filtrate were inoculated onto blank AST-discs to determine the antimicrobial activity when placed on a bacterial lawn of the target organisms.

Results: P. aeruginosa isolates (323) demonstrated secretion of antimicrobial molecules which inhibited the growth of at least one target bacteria. S. aureus (81.5% type strain, 74.2% Methicillin-resistant) and E. faecalis (32.9% type, 35.1% vancomycin-resistant) were particularly sensitive. Minimal activity was seen against K. pneumoniae strains (type, carbapenem-resistant and pan-resistant. P. aeruginosa isolates cultured under low nutrient (99) conditions showed a significant increase in activity towards carbapenem-resistant E. coli and carbapenem-resistant K. pneumoniae (p= 0.007 and 0.003 respectively).

Conclusions: Antimicrobial molecules secreted from P. aeruginosa can inhibit the growth of clinically relevant organisms. Environmental stress-induction may further enhance the inhibitory properties of P. aeruginosa strains against MDR bacteria. Antimicrobial molecules harvested from P. aeruginosa may have therapeutic clinical application.

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**Abstract 4126**

**Candida auris** in a large healthcare system in South Florida: importance of active surveillance testing to prevent spread

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**Background:** *Candida auris* (C. auris) is a multidrug-resistant yeast of urgent concern for public health that continues to spread globally. We describe the experience of a large healthcare system in Miami, Florida for early detection and control of *C. auris*.

**Materials/methods:** The healthcare system has two major-teaching hospitals (adult and pediatric), and two community hospitals (over 2250-licensed beds). After the first *C. auris* case was identified in the adult major-teaching hospital in May 2019, strategies were implemented in all hospitals for *C. auris* early detection and control: 1. Enhanced contact precautions and environmental disinfection with bleach-based products for the duration of admission for all confirmed cases; 2. Consecutive point-prevalence surveillance cultures (PPS) from axilla/groin in units with *C. auris* cases and in those where horizontal transmission was suspected; 3. One-time PPS in all adult ICUs; 4. Admission screening questionnaire to all patients at point of entry with screening cultures and contact precautions for those with risk factors until ruled out; 5. Referral to the Antibiotic Resistance Laboratory Network (ARLN) to confirm identification and susceptibility testing of clinical isolates reported using the VITEK 2 system. The MALDI-TOF system was updated September 2019 to allow on-site identification of *C. auris*.

**Results:** In total 753 screening cultures were collected between May – November 2019 from 620 patients. Of those, 670 swabs were PPS and 83 were admission screening cultures. In total 22 (3%) patients from two hospitals were positive in surveillance cultures. Seven (32%) were community-onset and 15 (68%) were hospital-onset (Figure) with horizontal transmission within one facility. Three (14%) patients also had *C. auris* isolated from clinical cultures: blood (2), urine (1), and sputum (1). Only two patients developed clinical infections (fungemia) and were successfully treated with micafungin for 14 days. The overall in-hospital mortality among all *C. auris* cases was 23%; moreover, these patients expired for reasons unrelated to *C. auris* infection.

**Conclusions:** *C. auris* remains uncommon in Miami, Florida. Only 3% of the surveillance cultures were positive and we successfully treated two infected patients. Horizontal transmission led to 68% of the cases. These findings emphasize that early detection, multidisciplinary communication, and effective infection prevention measures are crucial to prevent *C. auris* spread.

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Abstract 4128

Analysis of resistance transmission among humans and livestock using microbiome profiling
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Background: Increase of antibiotic resistance is a huge problem of public health. Globally 70% of antibiotics are used in agricultural field including animal industry. Objective of the study is to clarify the cycle of antibiotic resistance among human and livestock by using metagenomic sequencing of gut microbiome of human, pig, cow and chicken.

Materials/methods: Metagenomic whole gene sequencing was performed for 103 stool samples of human and 118 samples from livestock. As for qnrS1 and CTX-M genes, Escherichia coli containing each gene was isolated from stools of human and chicken and whole gene sequencing was performed using NGS method to analyze the phylogeny of the isolates and plasmid structure.

Results: Chicken presented the most similar pattern of gut resistome with human. Variable antibiotic resistance genes (ARGs) of variable antibiotic group showed zoonotic distribution in gut of human and livestock. TEM and CTX-M were the most popular among beta-lactam resistance genes, and qnrS1 most successfully resided among plasmid-mediated quinolone resistance genes in gut of human and chicken. Mobile element of qnrS1 constituted with 6 genes of qnrS1, 3 transposons and 1 plasmid gene (resolvase, ISKra4 family transposase ISKpn19, IS380 family transposase ISEc9 and plasmid pRiA4b ORF-3 family protein) identically in human and chicken microbiome. Meanwhile, 2 plasmids of E. coli selected from human and chicken respectively showed the identical structure consisting with 12 genes containing transposon genes and ARGs, which suggest the recent transfer of this plasmid between human and chicken. CTX-M looked also successful zoonotic ARGs, which appeared commonly in gut microbiome of human and chicken. Among 4 groups of CTX-M genes, CTX-M-1 gene was the most important zoonotic gene

Conclusions: ARGs are transferred among human and livestock and some ARGs are especially efficient in zoonotic transfer. This research was supported by a fund (2017N-ERS407-00) by Research of Korea Centers for Disease Control and Prevention.

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Abstract 4131

The type I histidine triad protein HtpsA contributes to the capsule development and virulence of Streptococcus suis serotype 2

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Background: Streptococcus suis serotype 2 (S. suis 2) is an important swine pathogen and an emerging zoonotic agent for human. In a previous study, we reported a cell surface-exposed protein HtpsA, which confers protection in mice. In the present study, we constructed an isogenic mutant strain of htpsA and investigated its role in S. suis 2 development and virulence.

Materials/methods: Homologous recombination based method was used to construct an htpsA mutant of the S. suis 2 high virulent strain 05ZYH33. Gram staining observation and Transmission electron microscope (TEM) observation were performed to compare the morphological difference of the htpsA mutant and the wild type bacteria. Adhesion assay, phagocytosis assay and animal infection experiment were adopted to evaluate the involvement of htpsA in the virulence of S. suis 2.

Results: The results showed that the mutant strain ΔhtpsA forms shorter chains and smaller colonies comparing to the wild type strain. The mutant strain also lost typical encapsulated structures with reduced level of sialic acid content. Furthermore, the survival ratio in whole blood, the anti-phagocytosis ability to mouse macrophage cell RAW264.7 and the adherence ability to Hep-2 cell of ΔhtpsA all declined significantly comparing to the wild type strain. In addition, deletion of htpsA significantly attenuated the virulence of S. suis 2 in a mouse infection model. RNA-seq analysis revealed that 126 genes were differentially expressed between the ΔhtpsA and the wild type strains (28 up-regulated and 98 down-regulated). Among them, many down-expressed genes are involved in the carbohydrate metabolism. Some of the down-expressed genes encode evidenced virulence-associated factors.

Conclusions: Taken together, the results from this study demonstrated that htpsA is involved in the morphology development and pathogenesis of the highly virulent S. suis 2 strain 05ZYH33.

Fig. 1 Phenotypic analysis of the ΔhtpsA mutant strain.

[A] Growth caves of the ΔhtpsA and wild strains were measured spectrophotometrically at a wavelength of 600 nm. [B] Observation of the cellular morphology using gram staining and light microscopy. [C] Observation of capsular morphology by transmission electron microscopy of the ΔhtpsA and wild strains.

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Abstract 4133

**Comparative effectiveness of empiric antistaphylococcal penicillins versus cefazolin in methicillin-susceptible Staphylococcus aureus bacteraemia**

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**Background:** Treatment failure related to the cefazolin inoculum effect in MSSA bacteremia is theorized to occur during the initial period of empiric therapy. Previous comparative effectiveness studies of anti-staphylococcal penicillins (nafcillin or oxacillin) versus cefazolin for MSSA bacteremia only evaluated definitive therapy, when the bacterial inoculum has already diminished. Therefore, the potential impact of the cefazolin inoculum effect with empiric cefazolin treatment is still under debate.

**Materials/methods:** We conducted a national retrospective cohort study of MSSA bacteremia patients admitted to Veterans Affairs (VA) hospitals between January 2002 and October 2015. We included patients empirically treated with up to 4-days from initial positive blood culture with vancomycin plus nafcillin or oxacillin (VAN+NAF/OXA), or vancomycin plus cefazolin (VAN+CEF), and de-escalated to the respective beta-lactam monotherapy. Patients were excluded if death or discharge occurred within 48 hours of initial culture. The effect of empiric VAN+NAF/OXA was compared with VAN+CEF for time to 30-day mortality and discharge from the culture date, and time to 30-day readmission and 30-day *S. aureus* reinfection from the discharge date, using propensity score adjusted and matched Cox proportional hazards regression models.

**Results:** We identified 384 patients treated with VAN+NAF/OXA (n=248, 64.6%) or VAN+CEF (n=136, 35.4%). The risk of 30-day *S. aureus* reinfection was significantly higher in the VAN+CEF group [adjusted hazard ratio [HR] 0.25, 95% confidence interval [CI] 0.07-0.88; n=95 matched pairs, matched HR 0.13, 95% CI 0.02-0.999]. There were no differences in the other outcomes assessed.

**Conclusions:** Among patients with MSSA bacteremia empirically treated with nafcillin/oxacillin or cefazolin, in combination with vancomycin, and de-escalated to the respective beta-lactam monotherapy, there were no differences in mortality, readmission, or time to discharge. However, patients receiving the cefazolin empiric regimen had a higher likelihood of *S. aureus* reinfection within 30-days of discharge, supporting the hypothesized inoculum effect during initial empiric therapy.

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Control of hospital-wide outbreak of OXA-48-producing Enterobacteriaceae outbreak

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Background: An increase in healthcare onset OXA-46 carbapenemase producing Enterobacteriaceae (CRE) from an average of 3 patients per month to 5 patients in September, and then 10 in October 2019 hospital alerted the Infection Prevention team of a 1750-bedded acute tertiary care of a cluster that needed investigation.

Materials/methods: The hand hygiene and environment hygiene compliance of all the wards were noted to be around 80-90% in the affected wards. 46 samples were taken from shared equipment, sink P traps and shower drains. Environmental cleaning of affected wards were immediately enhanced with 1000 ppm sodium hypochlorite twice daily and daily audits on hand hygiene and environment hygiene were conducted. P traps were changed for sinks in affected wards after samples were collected for culture. Besides usual cleaning and disinfection by ward staff in between use, the commodes were further cleaned down by Environmental Services staff daily. Decontamination of sink traps with 250mls 5000ppm sodium hypochlorite was done 3 times a week with random sampling done to check on clearance of OXA-48.

Results: Two samples from the 46 commodes and two samples from the 27 shower drains tested were positive for OXA-48. Following the decontamination of sink traps, weekly samples confirmed clearance of the OXA-48 isolates. Whole genome sequencing of the isolates from 18 patients and 3 environmental samples confirmed that they are of the same type. The number of OXA-48 patients has since returned to the baseline norm.

Conclusions: We have successfully controlled the outbreak using the approach of biofilm control in the P traps. However, more work needs to be done to determine the optimal schedule for sink trap decontamination to mitigate possibility of CRE colonization.

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**Abstract 4137**

**CTX-M-15 and CTX-M-14 genes in UK Escherichia coli are found as often on the chromosome as they are on plasmids**

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**Background:** Several reports have described CTX-M genes in *E. coli* as being mostly plasmid and occasionally chromosomally encoded. We sought to determine the commonality of chromosome location by analysis of a large number of UK strains collected through a multi-centre project.

**Materials/methods:** 968 ESBL producing *E. coli* isolates were collected through a large multi-centre study from 5 UK regions in 2014. These included isolates from bacteraemias, faecal and sewage sources. All *E. coli* were analysed for chromosomal location by Pulsed Field Gel Electrophoresis combined by in-gel hybridization using \(^{32}\)P-labeled CTX-M-15 and CTX-M-14 radioactive probes. All isolates were whole-genome sequenced by illumina-miseq. A sub-group of 50 isolates were additionally sequenced using nanopore minion sequencing.

**Results:** Sequence analysis indicated that 534 isolates encoded CTX-M-15 and 83 isolates encoded CTX-M-14. PFGE analysis indicated that c. 50% of these resistance genes were chromosomally encoded and c. 40% were plasmid encoded with c. 10% of samples losing resistance genes during processing (fig 1). Isolates with chromosomally encoded resistance were found in numerous different *E. coli* ST and typically lacked additional plasmid copies of the gene. We determined chromosomal insertion sites for 30 isolates. Most insertions were ISEcP1 mediated with insertions into various different genes and intergenic spaces. The insertions ranged from 2971-11,384bp, appeared to have no bias for insertion site and all included the resistance gene and ISEcp1. Larger insertions contained additional plasmid genes. All ISEcP1 mediated insertions were flanked by 5bp direct repeats. Other common insertions (7/30) were IS26 mediated and of common sizes 8795 and 13104bp all in ST131 strains. These insertions were all with a hot spot in a molybedenum metabolism regulator gene and included both OXA-1 and aac6’1b-cr genes as well as other plasmid encoded genes.

**Conclusions:** Chromosomal carriage of CTX-M-15 and CTX-M-14 genes is a common occurrence in UK *E. coli* isolates belonging to many different ST groups. The observation that isolates with chromosomally encoded resistance typically lack additional plasmid copies suggests loss of plasmids subsequent to chromosomal targeting.

**Genome Position CTX-M**

- **Genomic position blaCTX-M-15**
  - Chromosomal
  - Plasmid
  - Plasmid loss

- **Genomic position blaCTX-M-14**
  - Chromosomal

534 Strains

83 Strains

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Risk factors and mortality for patients with bloodstream infections of Klebsiella pneumoniae during 2014-2018: clinical impact of carbapenem resistance in a large tertiary hospital of China

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Background: Bloodstream infection (BSI) caused by Klebsiella pneumoniae (KP), especially Carbapenem-resistant Klebsiella pneumoniae (CRKP), results in high morbidity and mortality.

Materials/methods: In this retrospective cohort study, we examined 285 inpatients with BSI caused by KP in a tertiary hospital in China between 2014 and 2018, and 46 patients were infected with CRKP. All episodes of BSI caused by KP that occurred in hospitalized patients were enrolled. The outcome measured was death within 7 and 28 days of the first positive blood culture, respectively. Survivor versus non-survivor subgroups were analyzed in order to identify predictors of 28-day mortality due to KP BSI.

Results: We identified that hematological tumor (odds ratio [OR]: 8.359, [95% CI: 2.162-33.721], P=0.002), CRKP isolation (OR: 7.766, [95% CI: 2.796-21.576], P=0.001), chronic lung disease (OR: 5.020, [95% CI: 1.275-19.768], P=0.020), and septic shock (OR: 4.591, [95% CI: 1.686-12.496], P=0.003) were independent risk factors for the death of KP BSI. A 28-day mortality of KP BSI score ranging from 0 to 22 was developed based on the above 4 independent variables. Our scoring system revealed that the 28-day mortality were 9.14%, 35.29%, 38.10%, 75% and 100% for carriers with a score of 0, 5, 6-10, 11-13 and ≥14, respectively. Additionally, CRKP infection were independently associated with intensive care unit stay (OR: 5.506, [95% CI: 2.258-13.424], P=0.001), exposure to antifungals (OR: 4.679, [95% CI: 2.065-10.063], P=0.001), exposure to fluoroquinolones (OR: 2.892, [95% CI: 1.151-7.267], P=0.020), and the number of isolated bacterial species from the patient ≥ 3 (OR: 2.414, [95% CI: 1.306-4.463], P=0.005).

Conclusions: our study may be useful for the reduction of the mortality of patients with KP BSI and the prevention of developing CRKP BSI in hospitals.

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Abstract 4143

**Laboratory evaluation of the BIOFIRE FILMARRAY pneumonia panel plus compared to standard-of-care testing at a private laboratory in Cape Town, South Africa**

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**Background:** Pneumonia causes significant mortality and morbidity worldwide. The standard method for the laboratory diagnosis of lower respiratory tract infections is culture, which has a long turnaround time (TAT), poor sensitivity and does not test for atypical bacteria and viruses. The Biofire® FilmArray® Pneumonia Panel plus (FA-PP) is a comprehensive syndromic testing molecular panel that provides rapid results for 34 targets. Our aim was to compare the FA-PP to standard-of-care testing.

**Materials/methods:** This was a prospective evaluation conducted in a private laboratory in Cape Town, South Africa. Residual sputum, tracheal aspirate and broncho-alveolar lavage specimens were tested in parallel with conventional culture and the FA-PP. Standard-of-care (SOC) testing includes culture as well as other tests that were performed on clinician order only (Biofire® FilmArray® RP2plus, Legionella urine antigen and blood cultures). Detection rates and TAT of the FA-PP were compared to culture. Percentage agreement between the FA-PP and SOC was assessed.

**Results:** Thirty* samples from unique patients were tested from August-November 2019. The FA-PP was positive in 80% (24/30) of samples (14 with bacteria only, 7 viruses only, 3 co-detections of bacteria and viruses). Co-detections for ≥2 bacteria occurred in 6 samples. The FA-PP detected 2 Mycoplasma pneumoniae and 1 Legionella pneumophila.

Culture was only positive in 53% (16/30) of samples. Detection of additional organisms on culture (n=9) were only those not included in the FA-PP (Candida species, Haemophilus species other than H. influenzae, Raoultella ornithinolytica). Bacterial detection of ≥10^7 on the FA-PP correlated best with culture-based reporting, especially in bacterial co-detections. Resistance mechanisms were detected in two samples.

The mean TAT for negative and positive cultures were 42 and 62 hours respectively, versus 2-hours for FA-PP. Overall agreement between FA-PP and SOC for at least one significant pathogen was 73% (22/30). Non-concordance was due to RP2plus not requested or the cultured organism was not included in FA-PP.

**Conclusions:** The FA-PP offers a rapid TAT and high yield of bacteria, atypical bacteria and viruses. The potential impact of this panel on antimicrobial stewardship, infection control and clinical factors needs to be evaluated in further studies.

*ongoing

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Abstract 4144

In vitro activities of β-lactam antibiotics alone and in combination with sulbactam against Acinetobacter baumannii

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Background: Sulbactam, an inhibitor of β-lactamase, displays intrinsic activity against the Acinetobacter baumannii. This study aimed to evaluate the in vitro activities of β-lactam antibiotics alone and in combination with sulbactam at different ratios against Acinetobacter baumannii clinical strains.

Materials/methods: A total of 300 clinical isolates of A. baumannii were collected from 29 hospitals across China in 2018, including carbapenem-susceptible A. baumannii and carbapenem-resistant A. baumannii isolates. Minimum inhibitory concentrations (MICs) were determined by broth microdilution method. Amoxicillin, cefoperazone and imipenem were tested alone and in combination with sulbactam at different ratios of 1:1, 1:1.5, 1:2, 1:2.5 and 1:3. Sulbactam alone was also tested.

Results: MIC50 and MIC90 values for sulbactam were 32 mg/L and 64 mg/L, respectively. High resistant rates for imipenem, ampicillin and cefoperazone were observed (85.3%, 92.3% and 93%, respectively). A stepwise increase in the ratio of sulbactam to β-lactams led to a stepwise decrease in the β-lactams MICs and a stepwise increase in the susceptible rates. The susceptible rates for imipenem-sulbactam at the ratios of 2:1, 1:1, 1:1.5, 1:2, 1:2.5 and 1:3 remained at 13.7%, 14.3%, 14.3%, 15.0%, 15.7%, and 16.3%, respectively. The susceptible rates for ampicillin-sulbactam at the ratios of 2:1, 1:1, 1:1.5, 1:2, 1:2.5 and 1:3 were 12.3%, 14.3%, 20.3%, 28.3%, 51.3%, and 58.3%, respectively. Of note, the susceptible rates for cefoperazone-sulbactam at the ratios of 2:1, 1:1, 1:1.5, 1:2, 1:2.5 and 1:3 reached to 15%, 29.3%, 66.3%, 78.7%, 86.3%, and 91%, respectively.

Conclusions: The increasing proportion of sulbactam could enhance in vitro activity of imipenem-sulbactam, ampicillin-sulbactam and cefoperazone-sulbactam combinations against A. baumannii clinical strains, with cefoperazone-sulbactam as the most potent compound.

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Abstract 4145

Retrospective analysis of the in vitro activity of imipenem/relebactam against KPC-encoding Enterobacterales

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Background: Relebactam (REL) is a diazabicyclooctane inhibitor of class A and C β-lactamases, including Klebsiella pneumoniae carbapenemase (KPC), approved in the United States (US) in combination with imipenem (IMI) and cilastatin for treatment of complicated intra-abdominal and urinary tract infections. First reported in 1996, KPC is an important mechanism of carbapenem nonsusceptibility in hospital-acquired infections. An analysis of IMI/REL in vitro efficacy for KPC encoding Enterobacterales was undertaken.

Materials/methods: The Study for Monitoring Antibacterial Resistance Trends (SMART) is an ongoing worldwide surveillance study that has evaluated consecutive clinical isolates from intraabdominal, urinary, and lower respiratory tract sources since 2002. A total of 1696 sequenced Enterobacterales KPC isolates were studied from SMART and additional referred clinical isolates. MICs to IMI and IMI/REL (fixed 4 mg/L) were determined by broth microdilution and interpreted using CLSI breakpoints, with the exception of IMI/REL, for which US Food and Drug Administration (FDA) breakpoints were used. The KPC sequence subtype was determined by PCR and sequencing.

Results: The percent IMI and IMI/REL susceptibility for all KPC isolates (N=1696) was 1.9% and 95.4% while that for KPC-2 was 1.9% and 95.0% and for KPC-3 was 0.6% and 96.4%. Of 1684 sequenced KPC-encoding Enterobacterales the most frequent sub-types were KPC-2 (67.2%) and KPC-3 (31%); all other sub-types combined were 1.8%. The geometric mean (GEOMEAN) MIC (mg/L) for IMI and IMI/REL for sub-types with N>10 isolates were: KPC-2 (N=113), 1.70 and 0.31, respectively; KPC-3 (N=522), 18.5 and 0.26, respectively; KPC-17 (N=12), 8.1 and 0.30, respectively. The co-carriage of KPC and OXA-48-like genes in Enterobacterales was rare accounting for just under 1% of the total in 2015, 2017, and 2018. Of 11 isolates encoding KPC and OXA-48-family enzymes, susceptibility was 0% to IMI and 63.6% to IMI/REL. The co-carriage of KPC and metallo-β-lactamase genes has increased, from 0 in 2015/2016 to 1.6% of KPC-encoding Enterobacterales in 2018.

Conclusions: IMI/REL could provide an important treatment option for patients with infections caused by KPC-expressing Enterobacterales. There was little difference in GEOMEAN MIC for KPC allele sub-types. Percent susceptibility remained high when OXA-48-like enzymes were co-carried with KPC.

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Abstract 4146

Optimised positioning of carbapenem-sparing options for treatment of UTIs by molecular antibiotic susceptibility testing

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Background: Escherichia coli and Klebsiella pneumoniae account for approximately 75% of all urinary tract infections (UTI) globally. Due to increasing rates of antimicrobial resistance (AMR) against first-line treatment options as well as carbapenems, the use of “old” antibiotics such as fosfomycin or drug-combinations has been identified as a promising alternative.

Materials/methods: 91 Escherichia coli and 107 Klebsiella pneumoniae from the FDA-CDC AR isolate bank were subjected to fosfomycin susceptibility testing via agar dilution. Antibiotic susceptibility profiles were additionally downloaded from the FDA-CDC AR collection as well as genetically derived by interpretation of whole-genome sequencing data via ARESdb, a unique AI-powered knowledgebase of genetic AMR prediction models trained on next-generation sequencing (NGS) data for 35,000+ isolates and susceptibility data for 100+ drugs.

Results: Fosfomycin was found to be superior over carbapenems in both multi-drug resistant target pathogens. Optimizing for negative correlation between AMR phenotypes for fosfomycin and potential combination options, amikacin was identified as promising combination candidate with the combination showing 98% and 75% efficacy in multi-drug resistant Escherichia coli and Klebsiella pneumoniae respectively (Fig. 1). Using genetic AMR prediction facilitated by ARESdb, we further show that molecular antibiotic susceptibility testing is feasible with high accuracy for common UTI treatment options exceeding 90% categorical agreement with culture-based antibiotic susceptibility testing (AST) across various antibiotic drug classes in this proof-of-concept study.

Conclusions: We here describe fosfomycin either alone or in combination with amikacin as promising carbapenem-sparing option for treatment of UTIs and show that molecular drug response detection for clinical isolates is feasible by combining NGS with AI-powered data interpretation. As a multi-disciplinary consortium, we further aim at developing a molecular test for the accurate drug response detection in UTIs. The underlying molecular marker panels will be applicable to rapid testing of native patient samples, enabling patient stratification for clinical trials and informed empirical therapy.

Fig. 1: Fosfomycin outperforms carbapenems and shows high efficacy with amikacin in multi-drug resistant Escherichia coli and Klebsiella pneumoniae. Only the last-line treatment option tigecycline was found to have higher efficacy in both major UTI pathogens, with the combination of fosfomycin and amikacin outperforming colistin in Escherichia coli.

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Subtyping of adenovirus strains isolated from pre-diagnosed patients with keratoconjunctivitis

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Background: We investigated the presence and subtypes of human adenovirus (hAdV) in conjunctival swab samples taken from patients clinically diagnosed as keratoconjunctivitis and to evaluate the efficacy of infection control measures in the polyclinics.

Materials/methods: Samples (n=113) were sent to clinical microbiology laboratory in January 2018 to November 2019. The nucleic acid extraction and amplification were performed by ELIte InGeniusTM instrument (ELITechGroup, Italy) using quantitative real-time PCR method. Sequencing primers were targeted the conserved segments of the ‘Hypervariable Region 7’ (HVR-7) of the hexon gene. DNA sequence analysis was performed with ABI PRISM® 3100 Genetic Analyzer (Applied Biosystems, USA). The obtained hAdV DNA sequences were typed by BLAST analysis and the genotypes were identified by using the reference hAdV sequences of the NCBI.

Environmental swab samples were also collected from ophthalmoscopy device, patient seat, physician desk, sink, door knob of the rooms to evaluate the efficacy of disinfection and the risk of cross-contamination. Training on disinfection procedures was given to the personnel.

Results: Of 113 conjunctivitis cases, 82 (72.5%) were HAdV positive with the median (IQR): 7,1 (4,7-7,4) log 10 copies/mL viral load. Three genotypes were identified from 72 hexon gene positive samples and the most common genotypes were hAdV-8 (n: 69, 95.8%), followed by hAdV-4 (n: 2, 2.8%) and hAdV-19 (n: 1, 1.4%). As seen in phylogenetic tree, there was no predominant genetic relatedness between strains.

Conclusions: Very high hAdV positivity rate (72.5%) in our study was related with detailed clinical examination and proved once more the importance of physician-microbiologist collaboration. Even during summer outbreaks, strains were not related with each other and probably the source was not common. We screened the environment in ophthalmology polyclinics and trained the personnel to overcome cross contamination and these precautions prevented HAdV transmission between patients.

Figure. Phylogenetic tree
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**Abstract 4150**

**Impact of hypoalbuminemia and augmented renal clearance on flucloxacillin plasma concentrations: a real-life retrospective study**

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**Background:** S. aureus is the ‘consummate pathogen’ with significant morbidity and 20-30% mortality overall whilst S. aureus endocarditis is associated with mortality rates up to 70% despite the availability of highly active anti-staphylococcal antibiotics. Flucloxacillin is the antibiotic of choice for treatment of methicillin-sensitive S. aureus in many countries. This drug is characterized by a >95% binding to plasma protein (mainly albumin) and renal excretion. Here we aimed to characterize the pharmacokinetics of flucloxacillin in patients with hypoalbuminemia or altered renal function.

**Materials/methods:** Flucloxacillin therapeutic drug monitoring (TDM) was undertaken using a validated LC/MS-MS assay. Contemporaneous renal function (glomerular filtration rate estimated using the CKD-EPI formula, eGFR) and albumin were measured in the routine chemistry laboratory. A flucloxacillin trough target range (total drug) of 20-80 mg/L was recommended in local hospital guidelines.

**Results:** 505 patients had flucloxacillin concentrations measured over a 4-year period. Overall 55% fell within the target range. 335/505 had albumin measured and 352/505 had an eGFR calculated at the time of the first flucloxacillin TDM. Whilst the average flucloxacillin concentration rose as albumin fell there was no clear relationship between serum albumin levels and flucloxacillin concentration (R=0.137, P>0.05). Conversely, a significant inverse association was found between eGFR and flucloxacillin concentration (r=-0.459, p=0.033) with augmented renal clearance (eGFR 120-180 mL/min/1.73m²) resulting in a mean flucloxacillin trough concentration of 21.3 mg/L versus 79.1 mg/L for eGFR 0-30 mL/min/1.73m² (p=0.015). 42% of patients with eGFR 0-30 mL/min/1.73m² had a concentration>80 mg/L.

<table>
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<th>Ave Fluclox</th>
<th>n</th>
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<th>%20-80</th>
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**Conclusions:** Despite being highly protein bound serum albumin concentrations did not affect the mean flucloxacillin concentration. Therefore the serum albumin at the time of presentation is not an indication to alter the standard flucloxacillin dosing regimen. Conversely the eGFR was a strong predictor of flucloxacillin concentrations. Patients with augmented renal clearance require enhanced dosing regimens to achieve therapeutic concentrations whilst patients with impaired renal function may need a dose reduction to avoid drug toxicity.

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Abstract 4152

Variations in categorical agreement between fosfomycin agar dilution and disk diffusion using standard and high inoculum protocols for Klebsiella pneumoniae testing
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Background: FOF has been used in the treatment of multidrug-resistant K. pneumoniae (KP) infections despite established susceptibility breakpoints. Using disk diffusion (DD) susceptibility testing, it has been observed that inner colonies (IC) are frequent in KP testing. Furthermore, recent discussions surrounding interpretation of DD have highlighted the differences in Clinical and Laboratory Standards Institute (CLSI) and European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines, with CLSI stating to measure from the inner-most colonies, and EUCAST stating to ignore inner colonies and measure from the edge of the full coverage zone. We sought to assess the categorical agreement between FOF agar dilution (AD) and DD susceptibility testing methods against KP isolates and to assess the presence of IC.

Materials/methods: Minimal inhibitory concentration (MIC) values were determined for a convenience collection of 55 KP isolates from 2 US institutions. MIC testing was conducted in duplicate on separate days using AD and DD methods. Fifteen isolates were also analyzed using AD at a higher inoculum of 10⁵-10⁶ CFU/mL, similar to the broth microdilution method. MIC values were categorized using CLSI interpretive criteria for E. coli (≤64 mg/L, susceptible). The frequency of IC was determined, and DD was measured in accordance with EUCAST guidelines for FOF against E. coli.

Results: MIC values varied widely, ranging from 4->256 μg/mL for AD, with zone diameters of 6-24mm for DD. AD MIC₅₀/MIC₉₀ values were 32/256 mg/L. Using E. coli criteria, susceptible/intermediate/resistant rates were 85.4%/3.6/10.9 (AD) and 87.3%/9.1/3.6 (DD). Categorical agreement was 80%. IC were present in 82% of isolates, with 22% having ≥5 IC. When using the high-inoculum AD, MIC values were on average 3-fold higher compared to standard inoculum AD. Categorical agreement with DD dropped to 28.9%, with S/I/R rates of 14.2%/42.9/42.9 for the high-inoculum AD.

Conclusions: Categorical agreement between AD and DD was low for the KP isolates resistant by AD and also significantly decreased when a higher inoculum was used. In addition, IC were frequently observed and were ignored, according to EUCAST guidelines. Based on these results, we recommend further investigation of the DD reading methods, and the susceptibility breakpoints for KP.

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Abstract 4156

30-day mortality among neonates with candidaemia in a high azole resistance setting, South Africa, 2012-2017

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Background: Candida parapsilosis is the leading cause of candidaemia among neonates in South Africa. In this setting, a large proportion of C. parapsilosis strains are resistant to fluconazole, a widely used antifungal agent. We hypothesised that, owing to inappropriate treatment, neonates with C. parapsilosis candidaemia would have a higher risk of death compared to those with bloodstream infections caused by other species.

Materials/methods: We conducted laboratory-based surveillance for neonatal candidaemia over six years (2012–2017). A case was defined as a neonate aged ≤28 days with a single-species Candida bloodstream infection. Identification and antifungal susceptibility testing of viable isolates was performed at a reference laboratory. Clinical information was collected for participants admitted to sentinel hospitals. We used multivariable logistic regression to determine if C. parapsilosis candidaemia was associated with an increased 30-day mortality.

Results: Of 1494 neonates, 1176 (78.7%) had single-species infections. The median age was 14 days (interquartile range, 9-19) and 53% (766/1445) were male. C. parapsilosis accounted for 45% (532/1176) of all cases and 68% (354/523) of C. parapsilosis isolates were fluconazole-resistant compared to 1% (5/493) of other Candida species. Among 859 neonates with treatment data, most were treated with amphotericin B deoxycholate (43%, 366), amphotericin B deoxycholate plus fluconazole (34%, 292) or fluconazole (22%, 191). Of 514 neonates with a central venous catheter (CVC) in-situ, 420 (82%) had this removed after candidaemia diagnosis. Of 620 neonates with available outcome, the crude 30-day mortality was 42% (260/620): 37% (98/262) for C. parapsilosis versus 45% (162/358) for other species (unadjusted odds ratio [OR] 0.72, 95% confidence interval [CI]: 0.52–1.49, p-value=0.05). After adjusting for sex, birth weight, type of feeding, abdominal pathology, mechanical ventilation, any surgery, CVC removal, and prior antibiotic treatment, mortality among neonates with C. parapsilosis candidaemia (versus other species) was reduced by 29% [adjusted OR 0.71, 95% CI: 0.33–1.48, p-value=0.36] though the 95% CI crossed 1.

Conclusions: Despite a very high prevalence of fluconazole resistance, the risk of death was not increased among neonates with C. parapsilosis candidaemia. This may be related to amphotericin B deoxycholate treatment and CVC removal in a majority of cases.

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Emergence of another truly multidrug-resistant yeast pathogen, Candida kefyr, in Kuwait
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Abstract third-party references: Supported by Kuwait University Research Sector grant MI01/1S

Background: Invasive fungal infections (IFI) usually affect immunocompromised and/or immunosuppressed hospitalized patients with or without other co-morbidities. Recent emergence of multidrug-resistant Candida auris, Candida glabrata and few other yeast pathogens is a matter of serious concern due to limited number of antifungal drugs and antifungal drug classes that are available to treat patients with IFI. Candida kefyr, an emerging multidrug-resistant yeast, causes invasive candidiasis in susceptible patients. This study determined the prevalence of C. kefyr among yeast isolates collected during 2011-2018 in Kuwait. Antifungal susceptibility testing (AST), genotypic heterogeneity and molecular basis of resistance to fluconazole and echinocandins among C. kefyr were also determined.

Materials/methods: C. kefyr isolates were identified by CHROMagar Candida, Vitek 2 and PCR amplification of rDNA. Genotypic heterogeneity was determined with microsatellite-/minisatellite-based primers and by PCR-sequencing of IGS1 region of rDNA. AST was performed by Etest. Molecular basis of resistance to fluconazole and echinocandins was studied by PCR-sequencing of ERG11 and FKS1 genes, respectively.

Results: Among 8257 yeast strains, 69 C. kefyr (including four bloodstream and seven other invasive) isolates were detected by phenotypic and molecular methods. Isolation from urine and respiratory samples from female and male patients was significantly different (P=0.001). Fingerprinting with microsatellite-/minisatellite-based primers identified only three types. IGS1 sequencing identified seven (A-F) haplotypes among 27 selected isolates including 18 Haplotype D isolates. Four isolates showed reduced susceptibility to amphotericin B (AMB) and one isolate to all (AMB, fluconazole, voriconazole and caspofungin/micafungin) antifungals tested. Fluconazole-resistant isolate contained wild-type Erg11 protein. Echinocandin-resistant isolate contained wild-type hotspot-1 of FKS1. Based on FKS1 data, additional genotypes were also detected among IGS1 Haplotype D isolates.

Conclusions: Although frequency of isolation of invasive and non-invasive C. kefyr was stable during the study period, four of five isolates with reduced susceptibility to antifungals were obtained during last four years indicating increasing trend of reduced susceptibility to antifungals. The invasive and AMB-resistant isolates were genotypically heterogeneous. The multidrug-resistant isolate likely resulted from mechanisms that confer resistance to multiple drugs.

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Abstract 4164

Eliminating mother-to-child transmission of hepatitis B virus in Namibia: a cost-effectiveness analysis

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Background: Although eliminating mother-to-child transmission (MTCT) of hepatitis B virus (HBV) in sub-Saharan Africa (SSA) is an achievable and laudable aim, the cost implications need consideration. The aim of the study was to determine the costs and health benefits of a screen-treat-vaccinate intervention for preventing HBV MTCT (PMTCT) in Namibia, from the provider’s perspective.

Materials/methods: This analysis was attached to a screen-treat-vaccinate intervention study performed in Windhoek, Namibia. Using a hypothetical cohort of 10 000 pregnant women, decision tree modelling was performed to explore the costs and health benefits of four PMTCT interventions: (1) Universal HBV birth dose (BD) vaccination, (2) screen + vaccinate (BD + hepatitis B immunoglobulin (HBIG)), (3) screen + HBeAg testing + treatment + vaccinate, and (4) screen + HBV viral load testing + treatment + vaccinate. Resources including consumables, healthcare workers’ time, building space and facilities, and hospital utilities were measured. Health benefits were measured as number of pediatric HBV infections averted. Incremental cost-effectiveness ratios (ICERs) were calculated to compare each intervention to the previous less expensive one, and sensitivity analyses were conducted.

Results: Universal BD vaccination was the least expensive (US$15 827.22), but 31 pediatric infections would still be recorded. Adding HBIG prevented an extra 22 infections at an incremental cost of US$98 498.74. Screen-treat-vaccinate was the most effective, with only 3 residual infections. HBeAg testing costed less than HBV viral load testing: US$114 325.96 vs US$153 053.55, respectively. HBV treatment with HBeAg testing had an ICER of US$6 262.42 per infection averted, in comparison to the screen-vaccinate intervention. The latter had an ICER of US$4 550.34 per infection averted. These ICERs were highly sensitive to the prevalence of highly infectious pregnant women, the cost of the HBeAg test, and the effectiveness of each strategy among highly infectious pregnant women. HBsAg rapid testing costed approximately US$6 in comparison to US$18 for laboratory testing.

Conclusions: This is the first study describing the costs and health benefits of antenatal HBV treatment and HBIG for HBV PMTCT in SSA. The study demonstrated that elimination of HBV MTCT is achievable in Namibia, and by extrapolation in SSA.

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A multi-national study for the treatment of enterococcal endocarditis with ampicillin-daptomycin combination therapy

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Background: Enterococcus infective endocarditis continues to pose a significant therapeutic challenge inherited in the 21st century. Traditionally, the standard of care has been combination therapy with ampicillin and an aminoglycoside. The most utilized aminoglycoside sparing combination to date is ampicillin and ceftriaxone for *Enterococcus faecalis*. The past exposure of patients to multiple antibiotics prime this versatile species’ ability to evolve into becoming multidrug-resistant, thereby leaving a therapeutic vacuum in this complicated infection and limiting the existing combination options.

The combination of ampicillin and daptomycin has been successful in a small cohort in the literature, including a solid organ transplant patient. This combination is a promising alternative bringing another regimen that spares the use of aminoglycosides, with a broader therapeutic spectrum, including vancomycin-resistant enterococci.

Materials/methods: We present 34 patients treated with ampicillin-daptomycin for enterococcal infective endocarditis in the last decade. This study is a cross-section study, including three countries. The subspecies were described (Table 1.).

A chart review of patients that met definite and possible modified Duke's criteria in where the use of ampicillin-Daptomycin combination was used as primary or salvage therapy.

Results: The regiment was very effective with 3/34 deaths during admission and 6/38 at 12 months. There were no iv drug users in this population. The data included native and bioprosthetic valves without significant difference between both groups in terms of outcomes. There were no reinfections, relapse or drug discontinuation by adverse effects.

Conclusions: The combination of ampicillin-daptomycin proved to be safe with excellent outcomes and low mortality in Enterococcus faecium infective endocarditis as the initial therapy or when other drugs failed.

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Abstract 4166

Differences in clinical characteristics and causative pathogens between central line-associated bloodstream infections and catheter-related bloodstream infections using modified definition in medical intensive care unit

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Background: The surveillance definition of central line-associated bloodstream infection (CLABSI) could overestimate the central venous catheter (CVC) as the source of bloodstream infection. The definition of catheter-related bloodstream infection (CRBSI) by the Infectious Diseases Society of America is a more specific definition that identifies the CVC as the source of infection. In this study, we used modified definitions of CRBSI and compared clinical characteristics and causative pathogens between CLABSIs and CRBSIs.

Materials/methods: We retrospectively reviewed all CLABSI data reported in the 30-bed medical intensive care unit (ICU) of Severance hospital between January 2017 and December 2018. We defined CRBSI as simultaneous positive results of blood culture drawn from the central line and peripheral site without other focus of infection and excluding mucosal barrier injury-associated laboratory-confirmed bloodstream infection.

Results: Overall, 105 episodes of CLABSI were reported over 94 patients. Among them, 37 patients meet the diagnostic criteria of CRBSI. CRBSI group had more extended ICU stay (24.00 days vs. 17.95 days) and catheter indwelling time (46.49 days vs. 26 days). Emergent catheter insertion (69.7% vs. 41%), localized sign and symptoms of insertion site (88.2% vs. 30.3%) were more frequent in CRBSI group. Whereas, catheter removal rate for suspected infection was higher in CLABSI group (71.6% vs. 32.3%). Candida species were the most frequently identified causative pathogen followed by Enterococcus species in both groups. However, the proportion of Enterococcus species was lower (21.43 vs. 32.26) in CRBSI group. Despite various efforts to prevent, CLABSI outbreak occurred in the 3rd quarter of 2018. (9.21 per 1,000 catheter line days) However, the incidence of CRBSI was not correlated with CLABSI outbreak.

Conclusions: Our data showed that the current surveillance definition of CLABSI may not always warrant clinical importance. More specified definitions may be necessary to evaluate the effectiveness of interventions or outbreak investigations.

Figure 1. Incidence rate (per 1000 catheter line days) of CLABSI(blue) and modified CRBSI(red)

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**New lean preparation method for identification of mycobacteria by MALDI Biotyper**

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**Background:** The rate of successful identifications of Nontuberculous Mycobacteria (NTM) by MALDI-TOF MS has risen over the past years due to dedicated preparation techniques and expansion of reference libraries. However, MALDI-TOF MS sample preparation of mycobacteria is still laborious and a shortened protocol will be appreciated. Recently, a very fast preparation method for mycobacteria cultivated on solid medium has been published [1]. Here, we present a similar method which also works for cultures grown in liquid medium.

**Materials/methods:** NTM strains were cultivated in MGIT™ [BD] medium. Biomass was transferred to a tube containing four small steel cylinders. After centrifugation the medium was discarded. An inactivation step in 75 % Inactivation Reagent [Bruker-Hain] for 30 minutes followed. After another centrifugation step and removal of the supernatant, 200 µl extraction reagent were added and two cycles of shaking (1 min) were performed. Following a final centrifugation step, 1 µl of supernatant was spotted onto a MALDI target plate, overlaid with 1 µL matrix solution and analyzed in a MALDI Biotyper system.

**Results:** Ten different *Mycobacterium* species, mainly from culture collections, were analyzed in one lab by three different operators. Each strain was identified at high confidence level (log(score) ≥ 1.8). Four strains from clinical samples were processed in another laboratory, all of them were identified at high confidence level as well.

**Conclusions:** Altogether, 27 cultures including 4 clinical samples were reliably identified using the new rapid preparation method. The current dataset is still limited but robustness of the method is underlined by four different operators from two labs. ComParison to the current standard preparation method for mycobacteria [MycoEX] will continue in the clinical routine laboratory.

The new preparation method avoids boiling mycobacteria for their inactivation and needs less hands-on time. This might improve the applicability of MALDI-TOF MS mycobacteria identification in routine laboratories.

**Literature**


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Abstract 4169

**Antiviral efficacy of released-active antibodies to interferon gamma against MERS Coronavirus**

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Abstract third-party references: Supported by OOO "NPF MATERIA MEDICA HOLDING"

**Background:** Antibodies (Abs) are an important component in host immune responses to viral pathogens. That is why Abs-based drugs become more and more widespread in virus-caused conditions' treatment despite the difficulty with creating finished drug formulation with high accessibility and efficacy and low toxicity. Drugs based on released—active (RA) form of Abs is a novel concept to reach these goals. The technology of these drugs' manufacture is represented by combining multiple gradual decrease of Abs to the desired dilution along with physical treatment. Drugs based on RA Abs to interferon gamma (IFNγ) are proven to have confirmed efficacy and safety. The key mechanism of drug action is the ability to regulate the functional activity of endogenous interferons by exerting an allosteric effect on IFNγ structure, which results in modulation of IFNγ affinity to its receptor. Based on this mechanism of action and the coronavirus infection pathogenesis, which affects host immune system responses, RA Abs to IFNγ could be effective against Middle East respiratory syndrome coronavirus (MERS-CoV).

**Materials/methods:** The study was performed at Viroclinics Biosciences. Capacity of RA Abs to IFNγ to suppress MERS-CoV replication was evaluated *in vitro* on Human hepatocellular carcinoma cells (Huh 7). Virus MERS-HCoV/KSA/EMC/2012 was used at the dose of 2Log_{10} TCID50/ml. The reference drug pegylated-interferon α-2b (PEG-IFNα-2b) dose was 100 ng/ml. Cells were treated with drugs 24 hours prior to viral inoculation and replaced after inoculation daily for 7 days post MERS-CoV infection. Viral load was estimated by qPCR. To assess the effects, the generalized linear model and multiple comParison, followed by Tukey-Kramer post-hoc adjustments was implemented.

**Results:** RA Abs to IFNγ were shown to statistically significantly (p<0.001) decrease viral titers in cells infected with MERS-CoV vs control and virus groups. There was no significant difference between reference drug and RA Abs to IFNγ effects.

**Conclusions:** In previous studies, RA Abs to IFNγ was proven to be safe and highly effective against different RNA- and DNA-containing viruses, including pandemic strains. Using this *in vitro* experimental model, RA Abs to IFNγ were shown to have antiviral activity against MERS-CoV that is comparable to the reference drug.

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Detection of influenza and non-influenza respiratory viruses detected in lower respiratory tract specimens of hospitalised adult patients and analysis of the clinical outcome
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Background: Lower respiratory tract (LRT) infection remains one of the most fatal infections for adults. Influenza virus has been a well-recognized cause of severe pneumonia. The outcome of LRT infections caused by other respiratory viruses (RVs), however, has been insufficiently investigated.

Materials/methods: A retrospective review of medical records was performed on adult patients whose LRT specimens, including endotracheal aspirate and broncho-alveolar lavage fluid, were positive for respiratory viruses by multiplex PCR (Luminex, Canada). Underlying comorbidities, laboratory data, and clinical outcome were analyzed.

Results: Of the total 808 LRT samples collected from 666 adult patients, 166 samples from 152 patients had at least one RV identified. After exclusion, 106 patients were included in the study. The underlying comorbidities and laboratory data were not different between patients with influenza and non-influenza RVs infection. On survival analysis, mortality rates estimated at 14 days and 30 days were higher in the influenza group than in the non-influenza-RV group (P=0.026 and P=0.020, respectively), and influenza was associated with a marginally higher 90-day mortality rate (P=0.063). The mortality rates between individual viruses were also different, although the highest mortality rate was also observed in patients with influenza (P=0.343). Diabetes mellitus, a CRP level higher than 5mg/dl upon sample collection, and shock and acute kidney injury during the hospital course predicted a higher mortality rate. Use of steroid in disease course did not show a survival benefit (P=0.916). In a multivariate Cox model, shock and acute kidney injury independently predicted a higher mortality rate (hazard ratio: 4.28, 95% CI: 1.46–12.58, P= 0.008 and hazard ratio: 2.80, 95% CI: 1.28–6.15, P=0.010, respectively).

Conclusions: Respiratory viruses other than influenza are important pathogens of LRT infection in adults and may cause significant mortality. Novel antiviral agents should be developed to combat these potentially life-threatening viral infections.

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Usefulness of escalation therapy in urinary tract infection caused by extended beta-lactamase-producing Escherichia coli with bacteremia

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Background: In Japan, the detection rate of extended spectrum beta-lactamase (ESBL)-producing Escherichia coli has been increasing yearly. For ESBL-producing bacteria, broad-spectrum antimicrobial agents are often used for empiric therapy, but there is a risk of promoting further antibiotic resistance. In this study, we investigated whether delaying the initiation of effective antibiotic administration would lead to poorer outcome in urinary tract infection (UTI) caused by ESBL-producing E. coli with bacteremia.

Materials/methods: This is a single center retrospective study on adult patients aged ≥18 years who were detected with ESBL-producing E. coli by blood and urine cultures between April 2014 and July 2018. Of the 95 patients, 43 patients who met the criteria for sepsis under Sepsis-3 were excluded in the study. The patients were classified into the following groups based on whether the E. coli was resistant or susceptible to the antibiotic selected in empiric therapy: resistant group (n=27) and susceptible group (n=25). The following outcomes were assessed: hospital mortality, length of hospital stay, and rate of discharge to home. ESBL was detected using the double-disc synergy test.

Results: In the resistant group, ceftriaxone was mainly used for empiric therapy, and it took an average of 2.4 days until effective antibiotics were administered. The hospital mortality rate was 0% in both groups. The median length of hospital stay was 11 (2–62) days in the resistant group and 17 (4–86) days in the susceptible group, and the length of hospital stay was significantly shorter in the resistant group (p<0.05). The rate of discharge to home was 44% (12/27) and 52% (13/25) in the resistant and susceptible groups, respectively, but the difference was not statistically significant (p=0.78).

Conclusions: In cases of UTI caused by ESBL-producing E. coli, even with bacteremia, if the criteria for sepsis are not met, outcomes are unlikely to deteriorate even if the patient is switched to an effective antibacterial drug after determining the susceptibility. Hence, the coverage of ESBL-producing bacteria in empiric therapy may not be necessarily required for such patients.

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Abstracts 2020

Abstract 4173

The frequency of diarrhoeagenic Escherichia coli isolates in children with acute diarrhoea under five years
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Background: The detection of diarrheagenic Escherichia coli isolates from normal intestinal microbiota is important for the diagnosis and treatment of acute diarrhea. There is no research and data about the frequency of diarrheagenic E. coli pathotypes in Turkey. This study aims to detect the frequency of diarrheagenic E. coli pathotypes [enteropathogenic E. coli (EPEC), enterotoxigenic E. coli (ETEC), enteroinvasive E. coli (EIEC) Shiga toxin-producing E. coli (STEC), enterohemorrhagic E. coli (EHEC), enteroaggregative E. coli (EAEC) and diffuse adherence E. coli (DAEC)] in children with acute diarrhea under five years in Konya/Turkey.

Materials/methods: Between January and October 2019, E. coli strains isolated from stools of 259 children without any other pathogen were identified by conventional methods and Vitek 2 automated system. DNA isolation was performed with a commercial kit. The primers of eae, pEAF, daaC, otaA, elt, est, ipaH, stx1, and stx2 genes were studied by real-time multiplex PCR method. Detection of eae plus pEAF genes was accepted typical EPEC (tEPEC), only eae atypical EPEC (aEPEC), stx1 and/or stx2 genes STEC, eae plus stx1 and/or stx2 genes EHEC, elt and/or est genes ETEC, ipaH gene EIEC, otaA gene EAEC and daaC gene DAEC. Results were confirmed by monoplex PCR and gel electrophoresis.

Results: Of the 259 specimens, 46 had single and 213 had mixed pathotypes. DAEC was detected in 232, tEPEC/aEPEC in 145, EAE in 121, EIEC in 43, EHEC in 31, ETEC in three and STEC in two samples. The most common single pathotypes were DAEC [39], and EAEC [5], and mixed types were DAEC plus tEPEC/aEPEC [49], DAEC plus tEPEC/aEPEC plus EAEC [32], DAEC plus EIEC [24], DAEC plus EHEC [13].

Conclusions: DAEC was single and DAEC plus tEPEC/aEPEC were mixed predominant pathotypes in the diarrheagenic E. coli isolates in children with acute diarrhea under five years in Konya/Turkey. This is the first study to investigate all diarrheagenic E. coli pathotypes in Turkey. The study is still ongoing and preliminary data were presented here. The most important limitation of our study is that it is single-centered. Multicentre studies are needed to determine which pathotypes are common in Turkey.

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Abstract 4174

**Fosfomycin for the treatment of neonatal sepsis**

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**Abstract third-party references:** The Global Antibiotic Research Development Program (GARDP)

**Background:** Antimicrobial resistance (AMR) is a global health problem that threatens the Sustainable Development Goals for child mortality. There are published data indicating high rates of resistance to WHO-recommended empirical regimens for treating neonatal sepsis. Fosfomycin has been identified as a ‘critically important’ antibiotic for combating AMR. An off-patent antibiotic, fosfomycin has significant potential for treating neonatal sepsis yet there are minimal published safety or pharmacokinetic (PK) data in the neonatal population, and dosing regimens are poorly evidence-based.

**Materials/methods:** As part of the Global Antibiotic Research and Development Programme (GARDP) strategy we performed a Phase 1, un-blinded, prospective randomised trial to investigate the safety and pharmacokinetics of fosfomycin in 120 hospitalised neonates with clinical sepsis in Kilifi County Hospital, Kenya (NeoFosfo; ClinicalTrials.gov: NCT03453177). Eligible participants were randomised (1:1 ratio) to receive WHO standard-of-care antibiotics (SOC; ampicillin & gentamicin) or SOC plus fosfomycin (100mg/kg/dose twice daily). Parenteral antibiotics were continued until clinically indicated, at which point participants were de-escalated to oral fosfomycin (100mg/kg/dose twice daily) to complete their treatment course. Safety endpoints were plasma sodium concentration and adverse events (any grade) experienced during a 28-day follow-up period. PK sampling followed a cross-over design; samples were analysed using population-based non-linear mixed effects modelling.

**Results:** There was no significant difference between the two treatment arms with regards to serum sodium (difference in mean change 0.75mmol/L, 95% CI -1.28 to 2.78, p=0.43), potassium (difference in mean change -0.33mmol/L, 95% CI -0.08 to 0.73, p=0.83), liver function or renal function following IV fosfomycin administration. Despite oral fosfomycin’s fructose load, only one infant (2%) experienced diarrhoea (Grade 2). Adverse events (any grade) were less frequent in the group receiving fosfomycin (n=31 v’s n=42 in SOC). There were no serious adverse drug reactions attributed to fosfomycin. PK analysis revealed a two-compartment model with standard allometric and post-menstrual scaling provided a good fit to support baseline PK parameters.

**Conclusions:** Fosfomycin appears to be a safe antibiotic for treating neonatal sepsis which does not impact serum sodium levels or increase the frequency of antibiotic-associated gastrointestinal symptoms. Population-based PK modelling has defined appropriate dosing regimens to treat neonatal sepsis.

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Abstract 4175

Lipid profile change in HIV naïve patients treated with therapy tenofovir alafenamide-based

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Background: The advent of Tenofovir alafenamide (TAF) has improved long-term bone and kidney tolerability of antiretroviral treatment. However, some data in the literature show an increase in lipids after switching from TDF to TAF. Our aim is to investigate if TAF is associated with higher lipid levels than the abacavir/lamivudine regimen in the treatment of naive HIV patients

Materials/methods: We enrolled 185 naive HIV patients who had a follow-up at least 24 weeks after starting therapy. The exclusion criteria were the use of TDF or protease inhibitors. Patients were divided in relation to the type of regime adopted: TAF/FTC/RIL [Group A], TAF/FTC/EVT/Cobi [Group B], TAF/FTC/INI [Group C] and ABC/3TC/DTV, without TAF and Cobicistat [Control Group]. We evaluated triglycerides, cholesterol, HDL and LDL levels. The groups of cases were compared with the Control group analysing the baseline data (T0), 24 weeks (T1) and 48 weeks (T2) of follow-up, although the data at T2 were incomplete. The endpoint was evidence of dyslipidemia and/or the introduction of statin treatment.

Results: There were no differences between Cases and Baseline Control. At T1 and T2, we observed a higher incidence of hypercholesterolemia in TAF groups, not associated with alteration of LDL and HDL values. At the multivariate analysis to analyse the factors associated with hypercholesterolemia in T1 and T2, only age was significantly associated with this parameter.

Conclusions: Our preliminary data show that, in HIV naïve patients, TAF can be associated with hypercholesterolemia after 48 weeks of follow-up compared to baseline values in the same group, and in any case the older age of patients plays a priority role for dyslipidemia. This figure should be confirmed in subsequent analyses and although the clinical significance is still unclear, it may be an important focus for patient management.

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Activity of ceftolozane/tazobactam against prevalent Gram-negative pathogens across Asia: PACTS 2016-2018

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Background: Ceftolozane/tazobactam (C/T) is an anti-pseudomonal cephalosporin combined with a β-lactamase inhibitor, recently approved for treatment of hospital acquired pneumonia, including ventilator associated bacterial pneumonia (VABP) in adults. The Program to Assess Ceftolozane-Tazobactam Susceptibility (PACTS) surveillance study monitors C/T resistance worldwide.

In this study, we sought to characterise susceptibility of C/T against the predominant Gram-negative pathogens in Asian countries.

Materials/methods: The susceptibility of ceftolozane/tazobactam and comparator antimicrobial agents [amikacin (AMK), cefepime (FEP), ciprofloxacin (CIP), colistin (COL), gentamicin (GEN), meropenem (MEM), piperacillin/tazobactam (P/T)] was evaluated by broth microdilution, using EUCAST criteria, against 2,545 Gram-negative clinical isolates collected from hospitals participating in the PACTS study across eight countries (Japan, Korea, Malaysia, Philippines, Singapore, Taiwan, Thailand, Vietnam) between 2016 and 2018.

Results: The most common Gram-negative pathogens identified were E. coli (n=716, 28.1%), K. pneumoniae (n=547, 21.5%), P. aeruginosa (n=376, 14.8%), and A. baumannii (n=274, 10.8%).

Susceptibility of E. coli to C/T was >84.0% in all Asian countries (93.6% overall) whereas K. pneumoniae susceptibility ranged from 42.1% in Vietnam to 100% in Japan and Singapore (67.8% overall). Susceptibility of P. aeruginosa ranged from 71.4% in Vietnam to 97.3% in Taiwan; overall susceptibility was 91.0% across Asia.

Among P. aeruginosa isolates resistant to CAZ, FEP, P/T, MEM or MDR phenotypes, C/T showed highest susceptibility of all agents tested (56.8%, 48.4%, 67.1%, 45.5%, and 56.4% respectively), except colistin.

A. baumannii was the fourth most common organism collected (n=274, 10.8%), and was the most frequently identified pathogen among patients with VAP or in the ICU. In all countries where more than 30 A. baumannii isolates were collected (Korea, Malaysia, Taiwan, Thailand, Vietnam), MEM resistance was at least 75.0%. C/T MICs reflect carbapenem resistance, being under 8 μg/ml for all MEM-susceptible and over 4 μg/ml for all MEM-resistant A. baumannii isolates.

Conclusions: Overall, C/T demonstrated consistently high activity against E. coli, but substantial variability between countries for K. pneumoniae. C/T was highly potent against P. aeruginosa and maintained good activity against P/T-resistant and MEM-resistant P. aeruginosa isolates collected in Asia. These data support consideration for clinical use in Asia, particularly for resistant P. aeruginosa infections.

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Abstract 4177

Direct identification of Candida species from positive blood culture by MALDI-TOF MS using a commercial pretreatment kit

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Background: Candidemia, induced by the presence of Candida species in blood stream, is a major cause of morbidity and mortality in clinical care. Early species identification and treatment is imperative given the disease’s invasive nature. Our hospital routinely utilizes MALDI-TOF MS identification directly from positive blood cultures. However, direct identification of Candida species nevertheless presents a significant challenge in clinical settings. In this study we evaluated a commercial pretreatment kit rapid BACpro II for direct identification of Candida species from clinical samples.

Materials/methods: Positive blood culture bottles of Candidemia were acquired from Aichi Medical University’s microbiology lab. Following standard protocol, 55 bottles were processed by rapid BACpro II (Nittobo Medical, Tokyo Japan). To improve its performance, protocol of rapid BACpro II was modified to process a larger culture volume with no alteration to reagent volume. 6 bottles were then processed by the modified protocol. MALDI-TOF MS was performed using Bruker Biotyper Smart system set to Sepsityper analysis mode.

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<tr>
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<th>Standard protocol (n=55)</th>
<th>Modified protocol (n=6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Score &gt; 1.8</td>
<td>44 (80%)</td>
<td>6 (100%)</td>
</tr>
<tr>
<td>Score &gt; 1.6</td>
<td>5 (9%)</td>
<td>0</td>
</tr>
<tr>
<td>No ID</td>
<td>6 (10%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Table: Clinical performance of rapid BACpro II in processing Candidemia blood culture bottles

Results: The rapid BACpro II gave proper ID to a majority of clinical samples demonstrating its clinical competence (Table). An increase in sample volume lead to ID scores above 1.8 for all the samples processed.

Conclusions: Efficient isolation of microorganisms by rapid BACpro II is achieved by the binding of cationic polymers to the microbes. Its performance on the clinical Candidemia samples offers a promising potential for early Candidemia intervention and opens the door to the protocol's standardization in the future.

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Abstract 4178

High prevalence of azithromycin-resistant *Mycoplasma genitalium* in both urogenital and anal samples in men and women

Joyce Fallon Braam1, David Hetem2, Jean-Marie Brand3, Martijn Van Rooijen1, Clarissa Vergunst1,6, Sophie Kuizenga-Wessel1, Alje Van Dam1,6, Sylvia Bruisten1

1Public Health Service of Amsterdam, Department of Infectious Diseases Research and Prevention, Amsterdam, Netherlands, 2Haaglanden Medical Center, Department Medical Microbiology, The Hague, Netherlands, 3 Public Health Service of The Hague, Department of Infectious diseases, The Hague, Netherlands, 4NWZ, Department of Dermatology, Den Helder, Netherlands, 5Academic Medical Center, Amsterdam, Netherlands

Abstract third-party references: Department of Infectious Diseases Research and Prevention, Public Health Service of Amsterdam, Amsterdam, the Netherlands

Background: *Mycoplasma genitalium* (MG) is a sexually transmitted bacterium associated with urethritis in men. Macrolide resistance in MG is increasing and limiting treatment options. In this study, the prevalence of macrolide resistance in MG was determined from different anatomical sample locations.

Materials/methods: In 2018, urogenital and anal samples from symptomatic and asymptomatic clients visiting STI clinics in Amsterdam or The Hague were tested for MG, *Neisseria gonorrhoeae* (NG) and *Chlamydia trachomatis* (CT) using TMA assays (Aptima, Hologic). MG positive samples were tested using an in-house validated MG macrolide resistance detection PCR.

Results: We included samples from 402 clients with MG; 256 urogenital and 237 anal samples. Co-infection with CT occurred in 56/402 (13.9%) clients and with NG in 40/402 (10.0%) clients. Macrolide sensitivity of MG infections was determined in 326/493 (66.1%) samples of different anatomical locations from 291 clients. There was no significant difference in the sensitivity of resistance determination of different anatomical sample locations (table 1). From 34 clients, macrolide resistance-associated mutations were detected in samples from two different anatomical locations. Three clients (8.8%) had macrolide sensitive MG at one location and macrolide resistant MG at the other location. Infection with resistant MG was detected in 193/291 (66.3%) clients. Prevalence of macrolide resistant MG was significantly higher in men (178/291, 72.5%) compared to women (113/291, 56.6%) (p=0.005). Macrolide resistance was higher, although not significant, in clients co-infected with NG 26/38 (68.4%, p=0.091), but not in clients with CT co-infection 25/38 (65.8%).

Conclusions: Macrolide resistance is very high in clients infected with MG, especially in men. If treatment is considered, testing for macrolide resistance is essential.

<table>
<thead>
<tr>
<th>Sample Location</th>
<th>Total</th>
<th>Typable</th>
<th>Mutants (% of typable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal</td>
<td>136</td>
<td>97 (71.3%)</td>
<td>54/97 (55.7%)</td>
</tr>
<tr>
<td>Urine</td>
<td>120</td>
<td>78 (65.0%)</td>
<td>53/78 (67.9%)</td>
</tr>
<tr>
<td>Hetero male</td>
<td>66</td>
<td>44 (66.7%)</td>
<td>30/44 (68.2%)</td>
</tr>
<tr>
<td>MSM</td>
<td>54</td>
<td>34 (63.0%)</td>
<td>23/34 (67.6%)</td>
</tr>
<tr>
<td>Anal</td>
<td>237</td>
<td>151 (63.7%)</td>
<td>106/151 (70.2%)</td>
</tr>
<tr>
<td>MSM</td>
<td>147</td>
<td>102 (69.4%)</td>
<td>77/102 (75.5%)</td>
</tr>
<tr>
<td>Women</td>
<td>90</td>
<td>49 (54.4%)</td>
<td>29/49 (59.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>493</td>
<td>326 (66.1%)</td>
<td>213/326 (65.3%)</td>
</tr>
</tbody>
</table>

*From 87 clients samples from two different sample locations were available.

Presenter email address: jbraam@ggd.amsterdam.nl
**Abstract 4179**

**Recurrence of multidrug-resistant *Klebsiella pneumoniae* ST48 at Charité, Universitätsmedizin Berlin**

Friederike Maechler¹, Anna Weber*¹, Petra Gastmeier², Axel Kola²

¹Charité - Universitätsmedizin Berlin, Institute of Hygiene und Environmental Medicine, Berlin, Germany

**Background:** In summer 2019, Charité - Universitätsmedizin Berlin (CUB), a 3 000-bed hospital with 3 facilities located in different districts of the city of Berlin, experienced an outbreak of multi-drug resistant (MDR) *K. pneumoniae* (Kpn) sequence type 48 (ST48) expressing the carbapenemase OXA-48 at one of its hospital sites located in the South of Berlin. This outbreak involved 8 patients on two ICUs transferring patients among themselves. Of note, a similar cluster of Kpn ST48 was observed at one of the other CUB hospital sites in 2014.

To understand the underlying epidemiology, we tested the following hypotheses:

1. The same strain of Kpn ST48 persisted and spread between the hospital sites of CUB since 2014
2. Kpn ST48 is (hyper)endemic within the Berlin region and was repeatedly introduced to CUB

**Materials/methods:** To investigate these two hypotheses, we used subsets of MDR Kpn ST48 isolates that were i) cultured during active surveillance admission screening (09/2018-03/2019), ii) cultured in the course of different repPCR-confirmed local outbreaks (12/2016-01/2019), and iii) which tested positive for OXA-48 with PCR (03/2017-08/2019). In total, 33 Kpn isolates underwent Whole Genome Sequencing (WGS) using Nextera XT DNA library preparation, the MiSeq system (Illumina Inc., San Diego, USA) and cgMLST (SeqSphere+ 6.0.2, Ridom GmbH, Muenster, Germany).

**Results:** Only one of the 33 MDR Kpn was classified as ST48 (isolated in 2016 from a patient with no epidemiological relation to the cluster in 2014).

<table>
<thead>
<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>ST14 [n=1]</td>
<td>ST48 [n=1]</td>
<td>ST101 [n=3]</td>
<td></td>
</tr>
<tr>
<td>ST15 [n=2]</td>
<td>ST15 [n=2]</td>
<td>ST14 [n=1]</td>
<td></td>
</tr>
<tr>
<td>ST1653 [n=3]</td>
<td>ST152 [n=1]</td>
<td>ST152 [n=1]</td>
<td></td>
</tr>
<tr>
<td>ST2010 [n=1]</td>
<td>ST17 [n=1]</td>
<td>ST2 [n=1]</td>
<td></td>
</tr>
<tr>
<td>ST231 [n=1]</td>
<td>ST29 [n=1]</td>
<td>ST307 [n=2]</td>
<td></td>
</tr>
<tr>
<td>ST307 [n=1]</td>
<td>ST307 [n=2]</td>
<td>ST35 [n=1]</td>
<td></td>
</tr>
<tr>
<td>ST405 [n=1]</td>
<td>ST36 [n=1]</td>
<td>ST377 [n=1]</td>
<td></td>
</tr>
<tr>
<td>ST45 [n=1]</td>
<td>ST628 [n=1]</td>
<td>STunknown [n=1]</td>
<td></td>
</tr>
<tr>
<td>ST?16 [n=1]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** Spread of Kpn ST48 within the Berlin region and local spread within CUB seems to be unlikely. WGS analysis did not reveal an epidemiological linkage between the cluster in 2014 and the outbreak in 2019 at CUB.

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**Nephrotoxicity during teicoplanin therapy in combination with piperacillin/tazobactam or other anti-pseudomonal β lactams**

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1National Taiwan University Hospital, Taipei, Taiwan; 2National Taiwan University, Taipei, Taiwan

**Background:** Vancomycin (VAN) and piperacillin/tazobactam (TZP) have been widely used as empirical therapy for severe infections. Recently, several studies showed the increased risk of acute kidney injury (AKI) during concomitant use of VAN and TZP when compared to the risk during concomitant use of VAN and cefepime or meropenem. The mechanism of this nephrotoxicity is unclear. Teicoplanin (TEI) is another glycopeptide sharing similar spectrum and mechanism of action with VAN. Concurrent use of TEI and TZP is common; however, whether this combination also increases the risk of AKI is unknown. Therefore, this study aimed to evaluate the AKI risk of TEI/TZP, in comparison with the combination therapy of TEI and other anti-pseudomonal β lactams (APBs).

**Materials/methods:** This was a retrospective cohort study conducted in a medical centre in Taiwan. Adult patients admitted between Jun 1, 2013 and Dec 31, 2017 and treated with TEI based combination therapy (TEI/TZP or TEI/APB) were included. APBs contained cefoperazone/sulbactam, ceftazidime, cefepime, imipenem/cilastatin, meropenem and doripenem. Propensity score matching was used to balance demographic and confounding factors (age, gender, baseline creatinine, SOFA score, presence of shock and nephrotoxic agents). The primary endpoint was AKI during combination therapy, which was determined based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria.

**Results:** There were 6,813 patients treated with TEI based combination therapy in the initial sample. After propensity score matching, 243 pairs (TEI/TZP:TEI/APB, 1:3 matched) were included for statistical analysis. Overall, the mean age was 66.3 years in the matched cohort, and 17.1% of patients had a shock. Use of nephrotoxic medications (45.7 vs. 48.7%) and the baseline eGFR (78.9 ± 31.3 vs. 81.1 ± 31.5 mL/min/1.73 m²) were similar in the two groups. The median dose of TEI was 10.7 mg/kg in both groups. There was no significant difference between the groups with respect to the risk of AKI (14.8% vs. 14.2%, P=0.815). However, mean time to AKI seemed shorter in the TEI/TZP group (4.6 vs. 6.3 days, P=0.039).

**Conclusions:** Co-administration of TEI and TZP is not associated with increased risk of AKI. This combination may provide a safe choice for patients who need broad-spectrum antibiotic therapy.

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Abstract 4182

**Improved surveillance of Shiga toxin-producing Escherichia coli after implementation of whole genome sequencing at the Belgian National Reference Centre**

Florence Crombe¹, Diarie Soetens¹, Sylvie Leenen¹, Naïma Hammami², Bavo Verhaegen⁴, Sarah Denayer⁴, Denis Pierard*¹

¹Vrije Universiteit Brussel (VUB), Universitair Ziekenhuis Brussel (UZ Brussel), Brussels, Belgium, ²Agence pour une Vie de Qualité, Département Santé, Direction Promotion de la Santé, Prévention et Surveillance des Maladies, Charleroi, Belgium, ³Agency for Care and Health, Infection Prevention and Control, Flemish Community, Gent, Belgium, ⁴Sciensano, Service of Foodborne Pathogens, National Reference Laboratory for STEC, Brussels, Belgium

**Abstract third-party references**: Part of this work was performed in the frame of the Belgian National Reference Centre for Shiga toxin-producing Escherichia coli, supported by the Ministry of Social Affairs through a fund within the National Health Insurance System.

**Background**: To date traditional typing methods are used at the Belgian National Reference Centre (NRC) for surveillance of Shiga toxin-producing Escherichia coli (STEC) infections. Yet, these methods are less discriminatory than whole-genome sequencing (WGS). The data obtained by WGS enables full characterisation of STEC isolates, which facilitates epidemiologic surveillance and facilitates data comparison in case of cross-border outbreak. In addition to traditional typing methods, we performed WGS on all STEC strains provided to the NRC in the first three quarters of 2019 in order to improve surveillance of STEC.

**Materials/methods**: Ninety-three STEC-positive faecal samples, provided on a voluntary basis by clinical laboratories to the Belgian NRC STEC between January and September 2019, were included. WGS was performed on all isolates by the Brussels Interuniversity Genomics High Throughput core (BRIGHTcore). Sequencing libraries were prepared using the KAPA Hyper Plus kit (Kapa Biosystems) and sequenced on Illumina NGS instruments. The sequencing data was analysed using the Escherichia/Shigella cgMLST typing scheme in EnteroBase.

**Results**: Overall, ten clusters of two to four cases were identified by WGS analysis. Only two of these could be identified based on traditional typing data complemented with epidemiological data. On top of this, four paediatric HUS cases could be related to two cross-border clusters, i.e. cgMLST HC5/351 79 and cgMLST HC5/65006. As the source of contamination of the latter cluster was known from EPIS inquiry UI-531, trace back investigations performed by the health inspection authorities could confirm this finding. In addition, in collaboration with the National Reference Laboratory for STEC, the probable food source of contamination of cgMLST HC5/196140 cluster could be identified based on WGS data only. Besides, one Belgian paediatric HUS case, that was identified and analysed abroad, whose WGS data was available in EnteroBase, could be linked to the national cgMLST HC5/194834 cluster.

**Conclusions**: The obtained results stress the utility of using WGS data for surveillance of STEC at the Belgian NRC. WGS data has firstly enabled clustering of cases that were not identified based on traditional typing data complemented with epidemiological data and secondly helped to identify the source of contamination.

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Abstract 4183

**The intestinal carriage of colistin-resistant *Enterobacteriaceae* in a tertiary care hospital setting and whole genome sequence data analysis of *mcr-1* positive *Escherichia coli* isolates**

Jan Tkadlec1, Eva Smelikova1, Alžběta Baráková1, Marie Cabrniocha1, Gelbícová Tereza2, Renata Karpiskova2, Otakar Nyc1, Pavel Drevinek1, Marcela Krutova1

1Charles University 2nd Faculty of Medicine and Motol University Hospital, Department of Medical Microbiology, Prague, Czech Republic, 2Veterinary Research Institute, Department of Bacteriology, Brno, Czech Republic

**Background:** The emergence of plasmid-mediated colistin resistance is now a public health topic of the utmost importance because its spread could lead to outbreaks of virtually untreatable infections. We aimed to perform a sentinel testing survey to gather data on the prevalence and/or spread of *Enterobacteriaceae* resistant to colistin carrying *mcr*-genes.

**Materials/methods:** Between June 2018 and September 2019, rectal swabs or fecal samples from patients hospitalized in Motol University Hospital, Prague, Czech Republic were enriched in 5ml *Enterobacteriaceae* enrichment broth (Mossel) overnight and the enriched cultures were tested for the presence of *mcr-1* to -8 genes by multiplex qPCR assays. The enriched cultures were also inoculated onto selective agar Brilliance UTI Clarity agar (Oxoid) supplemented with colistin (3.5 mg/L). Bacterial colonies of *Enterobacteriaceae* with confirmed resistance to colistin by broth microdilution method (BMD) were retested for the presence of *mcr-1* to 8 genes. For *mcr* positive isolates the susceptibility to common antimicrobials were determined by BMD and the isolates were subjected to whole genome sequencing (WGS) using MiSeq (Illumina) and/or MinION (Nanopore) platforms. De novo assembly was performed using Geneious R10 software and data were analysed using online tools at the website: www.genomicepidemiology.org.

**Results:** In a 15-month period, 1,922 samples were investigated. The colistin resistant *Enterobacteriaceae* (MIC >2 mg/L) were recovered from 15.24% (n=293) of samples; *Klebsiella* spp. (n=129), *Escherichia coli* (n=84), *Enterobacter* spp. (n=49), *Citrobacter* spp. (n=22), *Salmonella* spp. (n=9). Four *E. coli* isolates (0.21%) were positive for the presence of the *mcr-1* gene. Other *mcr*-genes were not detected. The results of WGS analysis of the *mcr-1* positive isolates are summarized in Table 1.

**Conclusions:** To the best of our knowledge, this is the first study on the carriage of *mcr-1* to -8 genes in hospitalised patients in the Czech Republic. The Czech hospitalised patients can be colonized by colistin resistant *Enterobacteriaceae*, including strains carrying the *mcr-1* genes.

**Acknowledgment:** Supported by Ministry of Health of the Czech Republic, grant nr. NV18-09-00254.

**Table 1: Characterisation of *mcr-1* positive *E. coli* isolates cultured during the study.**

<table>
<thead>
<tr>
<th>Isolate no.</th>
<th>Isolation (month/year)</th>
<th>MLST</th>
<th>Colistin MIC (μg/ml)</th>
<th><em>mcr</em>-gene</th>
<th>Detected plasmids</th>
<th>Additional antimicrobial resistance</th>
<th>ARGs***</th>
</tr>
</thead>
<tbody>
<tr>
<td>FG42</td>
<td>10/2018</td>
<td>ST787</td>
<td>8</td>
<td><em>mcr-1.1</em></td>
<td>IncX4**, IncFIB(AP001918); IncF1; IncQ1; IncQ1</td>
<td>AMP, AMS, CXM, TMP, SXT, TET, PIP</td>
<td><strong>bhl</strong>, <strong>ndmA1; aph(3’)-Ib; aph(3’)-Ib; qnrA; sul2; tet(A); mtd(A); mtd(A)</strong>*</td>
</tr>
<tr>
<td>F732</td>
<td>11/2018</td>
<td>ST69</td>
<td>8</td>
<td><em>mcr-1.1</em></td>
<td>IncF4**, IncFA; IncFIB(AP001918); IncQ1</td>
<td>AMP, AMS, TMP SXT, CIP, TET, PIP, LV2</td>
<td><strong>bht</strong>, <strong>aadA5; aph(6’)-Ib; aph(3’)-Ib; qnrA; catA2; sul2; sul2; tet(A17; tet(B)); mtd(A); mtd(A)</strong>*</td>
</tr>
<tr>
<td>P1201</td>
<td>5/2019</td>
<td>ST744</td>
<td>0.25*</td>
<td><em>mcr-1.1</em></td>
<td>IncF4**, IncFA; IncFIB(AP001918); IncQ1</td>
<td>CIP, OMP, TET</td>
<td><strong>aph(3’)-Ib; aph(3’)-Ib; aph(3’)-Ib; sul2; tet(B); cfr; mtd(A); mtd(A)</strong>*</td>
</tr>
<tr>
<td>P1519</td>
<td>7/2019</td>
<td>ST1193</td>
<td>4</td>
<td><em>mcr-1.1</em></td>
<td>Cfr(BSS12); Cfr156; IncFA; IncFIB(AP001918); IncH2; IncH12A; IncQ1</td>
<td>AMP, AMS, TMP SXT, CIP, TET, PIP</td>
<td><strong>bht</strong>, <strong>aadA1; aac(3’)-Ib; aph(3’)-Ib; aph(3’)-Ib; kanamycin; apr(3’)-Ib; kanamycin; aac(3’)-Ib; aac(6’)-Ib; spectinomycin; spectinomycin</strong>*</td>
</tr>
</tbody>
</table>

**ARGs** – antimicrobial resistance genes, **MLST** – Multilocus sequence type (Wirth et al, Mol Microbiol 2006); **MIC** – minimal inhibitory concentration

AMP – ampicillin; AMS – ampicillin/subactam; CXM – ceftoxime; TMP SXT – trimethoprim/sulfamethoxazole; CIP – ciprofloxacin; TET – tetracycline; PIP – piperacillin; CP2 – cefoperazone.

* Isolate cultured on non-selective media based on positive qPCR result from enriched broth

** The plasmid localization of *mcr*-1 gene, for isolate P1519 the localization of *mcr-1.1* was not determined

***Resistance genes detected by corresponding antimicrobials were not tested: ndmA1,aph(3’)-Ib; aac(6’)-Ib; apr(3’)-Ib; spectinomycin, spectinomycin.

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Abstract 4185

Clonal spread of mcr-3-carrying multidrug-resistant ST34 Salmonella Typhimurium and its monophasic 1,4,[5],12:i:- from human globally

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1South China Agricultural University, Guangzhou, China

Background: Recently, the MDR ST34 S. Typhimurium (including its monophasic variant), has become a potential threat to public health due to its global emergence of mobile colistin resistance genes, including mcr-1 and mcr-3. However, to date, it is still blank on prevalence and transmission of mcr-3 in Salmonella in China. Thus, in the present study, a retrospective study was conducted to examine the emergence of the mcr-3 gene in Salmonella Typhimurium and 1,4,[5],12:i:- isolates from patients with diarrhea, and to reveal the mechanisms involved in transmission of mcr-3.

Materials/methods: A total of 582 Salmonella Typhimurium and 2299 Salmonella 1,4,[5],12:i:- strains were recovered from faecal samples of diarrhea patient from 28 general hospitals in Guangdong province during 2015-2017. All the Salmonella isolates were screened for mcr-3, submitted to WGS sequencing and conjugation experiment.

Results: Among the 2881 Salmonella isolates, 10 (0.35%) were mcr-3 positive, including 1 Salmonella Typhimurium and 9 Salmonella 1,4,[5],12:i:-. These 10 isolates were recovered from patients in 6 different hospitals located in four cities. Most of them were resistant to 8 antibiotics, including colistin, ampicillin, cefotaxime and ciprofloxacin. A phylogenetic tree based on the core genome revealed a close relationship between all of the 10 mcr-3 positive Salmonella isolates from this study and almost all of the 41 mcr-3-positive Salmonella isolates [37 from clinical human and 4 from swine from five countries] from GenBank except for three ones (SNPs ≤ 665), and in particular, some of them showed an extremely high degree of whole-genome sequence similarity to each other [38-99 SNPs]. WGS analysis revealed that all of the 51 mcr-3-positive Salmonella isolates harbored diverse ARGs, and of note, 35 of them including 10 ones from this study showed a similarity ARGs profile, including mcr-3-blaCTX-M-55-qnrS1. mcr-3 genes were successfully transferred to the recipient strain E. coli C600 among 6 of 10 mcr-3-positive Salmonella isolates, and Each transconjugants carried a single mcr-3-positive plasmid co-bearing blaCTX-M-55 (n=6) and qnrS1 (n=5) and assigned to ST3-IncC.

Conclusions: Our findings suggested clonal spread of MDR ST34 Salmonella lineage co-harboring mcr-3 with blaCTX-M-55 and qnrS1 globally.

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**Abstract 4187**

**Vaginal microbiota in Japanese women undergoing infertility treatment**

Asami Matsumoto*1, Yuka Yamagishi2, Seiichiro Takahashi1, Yasutoshi Kuroki4, Ayaka Minemura4, Kentaro Oka1, Motomichi Takahashi1, Hiroshige Mikamo2

1Aichi Medical University, Aichi, Japan, 2Aichi Medical University Graduate School of Medicine, Aichi, Japan, 3Takahashi Ladies Clinic, Gifu, Japan, 4Miyarisan Pharmaceutical Co., Ltd., Saitama, Japan

**Background:** A healthy vaginal microbiota is typically dominated by *Lactobacillus* spp. Dysbiosis of the vaginal microbiota (VM) might be responsible for the bacterial vaginosis (BV) which causes sexually transmitted infections, low pregnancy rate, spontaneous abortion and preterm delivery. In late years it is suggested that dysbiosis of VM has been linked infertility, albeit the details do not become clear. There are few reports that analyzed comprehensively the VM of the infertility treatment patient for Japanese women. Therefore, in this study, we analyzed VM of Japanese women during infertility treatment to elucidate the association between infertility and VM.

**Materials/methods:** In February 2019, we collected the vaginal samples of 16 women during infertility treatment at Takahashi Ladies Clinic, Gifu, Japan for further assessments. Nugent score was calculated using vaginal discharges. VM was analyzed by 16S rRNA gene sequenced metagenomic analysis by Miseq (Illumina) platform. Simultaneously, we isolated vaginal lactobacilli by using selective medium.

**Results:** As a result of Nugent scoring, 9 patients were normal (score 0-3) and 4 patients were intermediate (score 4-6) whereas 3 patients were diagnosed as a BV (score 7-10). VM were clearly clustered into 2 groups. Seven patients were classified in cluster 1 and 9 patients were classified in cluster 2. Cluster 1 was characterized with *Lactobacillus* spp. dominant but cluster 2 was constituted by not only *Lactobacillus* spp. but also *Escherichia* spp., *Gardnerella* spp., *Bifidobacterium* spp. and *Streptococcus* spp. and a few other taxa. The mean Nugent score of cluster 1 was 1.7 (score 0-7) whereas that of cluster 2 was 4.1 (score 0-10). There was no significant difference of detection rate of live lactobacilli between cluster 1 and 2.

**Conclusions:** Our results showed that VM of Japanese women during infertility treatment were divided into 2 groups. Further, Nugent score was correlated with composition of VM. We are investigating the pregnancy and delivering rates to elucidate the association between these rates and composition of VM. Concurrently, we are identifying the species of vaginal lactobacilli because it is suggested that the risk of bacterial vaginosis varies according to a kind of *Lactobacillus* spp.

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Abstract 4188

**Oxacillinase-48-like (OXA-48) carbapenemases along with New Delhi metallo-β-lactamase in a neonatal unit**

Sharmi Naha¹, Subhankar Mukherjee¹, Kirsty Sands², Pinaki Chattopadhyay³, Suchandra Mukherjee³, Sulagna Basu*¹

¹ICMR-National Institute of Cholera and Enteric Diseases, Kolkata, India, ²Cardiff University, School of Medicine, Cardiff, United Kingdom, ³Institute of Post-Graduate Medical Education And Research, Kolkata, India

**Background:** Emergence of oxacillinase-48-like (OXA-48) carbapenemase-producing Enterobacteriaceae is a critical health problem. Recently, reports of OXA-48-like carbapenemases are being reported in India more frequently than New Delhi Metallo-β-lactamase (NDM). The present study analyses the prevalence of OXA-48-like carbapenemases in Enterobacteriaceae isolated from the blood of septicemic neonates during 2013-2016, their transmissibility, association with sequence types and whole genome analysis.

**Materials/methods:** Identification, susceptibility test and genotypic characterization were carried out. Whole genome sequencing (WGS) was performed for isolates with OXA-48-like carbapenemases. Resistome, virulome, sequence type (ST), IS element, phage analysis, CRISPR, etc. were done. Transmissibility of this gene was evaluated by conjugation or electroporation.

**Results:** Six percent of isolates harboured OXA-48-like carbapenemases out of 195 Enterobacteriaceae isolated. All the isolates were extensively drug resistant but were susceptible to tigecycline and colistin. WGS analysis revealed two variants of OXA-48 gene viz. OXA-181 (67%) and OXA-232 (33%) among the isolates. *bla*<sub>OXA-181/232</sub> was found to be linked with Col plasmid. Association of OXA-181/232 was found with ST14, ST15, ST23, ST48, and ST231. Co-acquisition of *bla*<sub>OXA-48</sub> and *bla*<sub>NDM</sub> was found in five isolates (ST14 and ST2) along with other resistance determinants. OXA-181/232 was flanked by ∆IS<i>Ecp1</i> on upstream and ∆lysR & ∆ereA on downstream of it in accordance with isolates from other regions. Transfer of OXA-181/232 was not successful by conjugation. Presence of CRISPR array associated-cas3 gene along with different phage protein as well as intact phage was found in the genome of the isolates. Different virulence determinants were found in the genome which makes these isolates not only a successful pathogen but also a good colonizer. All the genomes were 85%-99% similar among themselves.

**Conclusions:** Prevalence of OXA-48-like carbapenemases is low in the unit, but association of this gene with other potent carbapenemases such as NDM-5 and in diverse STs is worrisome. The linkage of *bla*<sub>OXA-181/232</sub> with non-conjugative plasmid has probably restricted its spread. Proper surveillance and appropriate antibiotic strategy is required to keep the spread of these genes under check.

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Neutrophil extracellular traps and matrix metalloproteinases are increased in TB meningitis patients with contrast enhancement, ventricular dilatation and poor neurological outcome: findings from a paediatric cohort

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Background: Immunopathology in TB meningitis (TBM) patients is driven by extensive brain inflammation and tissue destruction and may be attributed to neutrophil extracellular traps (NETs) and matrix metalloproteinases (MMPs) which we sought to investigate.

Materials/methods: The cerebrospinal fluid (CSF) of 62 paediatric patients with TBM, bacterial meningitis (BM), viral meningitis (VM) and non-infectious causes (NI) were analysed for NETs by quantitative fluorometry of extracellular DNA and MMPs by Luminex assay. Glasgow Coma Scale (GCS) for children above 3 years old and Blantyre Coma Scale (BCS) for those below 3 years old were used to assess patients on admission. The CT or MRI brain of TBM patients were assessed for radiological abnormalities including contrast enhancement and ventricular dilatation by a neuroradiologist blinded to patient outcomes. Poor clinical outcome is defined as death or survival with severe neurological deficits, while good outcome is defined as full recovery or survival with mild neurological deficits.

Results: NETs were 7.2-fold higher in TBM than BM ($p < 0.01$) and 4.9-fold higher ($p < 0.05$) compared to NI. CSF concentrations of EMMPRIN (26.6-fold, $p < 0.01$), MMP-2 (8-fold, $p < 0.05$) and -9 (12.1-fold, $p < 0.05$) were significantly increased in TBM patients compared to BM patients. NETs showed a significant negative correlation with GCS ($r = -0.46$, $p < 0.05$) and BCS ($r = -0.3$, $p < 0.05$), indicating that patients with worse neurological condition have higher CSF NETs concentrations. TBM patients who showed radiological abnormalities have increased CSF concentrations of NETs (Fig. 1), as well as MMP-3, -7 and -10. TBM patients with poor clinical outcome have increased CSF concentrations of NETs (Fig. 1) and MMP-10 than TBM patients with good clinical outcome.

Conclusions: We showed that NETs are increased in TBM compared to BM and NI patients. Patients with abnormal radiological findings and poor clinical outcomes have higher NETs and MMPs than those without, suggesting that NETs and MMPs may prognosticate outcome in TBM.

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Figure 1. Concentration of NETs in paediatric TBM patients in the presence or absence of abnormal radiological features and with poor or good clinical outcome. **, $p < 0.01$.  
Abstract 4199

Achieving sustained decolonisation of CPE in sinks

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Background: The spread of carbapenemase-producing Enterobacteriaceae (CPE) is leading to a public health crisis. Recently, the role of the hospital water environment and particularly sink-traps has been recognized. This study tested seven technologies.

Materials/methods: The study was carried out during 2017-2019, at a large tertiary Medical Center (1600-bed). Following the discovery that many of the sink-traps were persistently contaminated with CPE, seven different technologies were studied in 9 departments. Persistently contaminated sink-traps were replaced either to PVC sink-trap or to one of the tested technologies and were sampled weekly. Sink sampling was performed via vigorous swabbing of the sink-trap surface or the internal part of the sink-outlets via sterile swabs. Chromagar KPC plates and Maldi-TOF were used to identify CPE. Carbapenemase genes were identified using Xpert Carba-R PCR (GeneXpert Cepheid). The studied technologies included: 1. Weekly acetic acid treatment, 2. weekly actizyme® treatment, 3. copper sink-traps, 4. nickel sink-traps, 5. specially designed “smart siphon” sink-traps, 6. Moveo® self-disinfecting siphon, and 7. the Sheba-Hamat self-disinfecting sink.

Results: A total of 130 sinks which were found to be constantly contaminated with CPE were replaced and one of 7 technologies were tested. A total of 3138 samples were taken.

<table>
<thead>
<tr>
<th>Technology</th>
<th># sinks tested</th>
<th>Total samples</th>
<th>Time of follow-up (range in Weeks)</th>
<th># sinks ever re-contaminated (%)</th>
<th>% of all samples contaminated during follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ref Control (PVC sink-trap)</td>
<td>28</td>
<td>431</td>
<td>3-70</td>
<td>23 (82.1%)</td>
<td>24.1%</td>
</tr>
<tr>
<td>1 Acetic acid treatment</td>
<td>16</td>
<td>137</td>
<td>7-10</td>
<td>13 (81.2%)</td>
<td>27.2%</td>
</tr>
<tr>
<td>2 Actizyme treatment</td>
<td>5</td>
<td>105</td>
<td>21</td>
<td>5 (100%)</td>
<td>38.1%</td>
</tr>
<tr>
<td>3 Moveo self-disinfecting siphon</td>
<td>1</td>
<td>21</td>
<td>21</td>
<td>1 (100%)</td>
<td>28.6%</td>
</tr>
<tr>
<td>4 Smart-siphon</td>
<td>30</td>
<td>424</td>
<td>9-56</td>
<td>30 (100%)</td>
<td>43.6%</td>
</tr>
<tr>
<td>5 Copper sink-trap</td>
<td>31</td>
<td>1028</td>
<td>5-110</td>
<td>25 (83.3%)</td>
<td>14.9%</td>
</tr>
<tr>
<td>6 Nickel sink-trap</td>
<td>11</td>
<td>612</td>
<td>30-104</td>
<td>11 (100%)</td>
<td>13.4%</td>
</tr>
<tr>
<td>7 Sheba-Hamat sink</td>
<td>12</td>
<td>380</td>
<td>20-50</td>
<td>4 (33.3%)</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

Conclusions: Only three technologies reduced the contamination rate of the sink-traps. Copper and nickel sink-traps were significantly better than regular PVC sink-traps, although most of them were eventually re-contaminated. However the Sheba-Hamat sinks were extremely better and only very rarely got re-contaminated.

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Diagnostic performance and validation of two ready-to-use real-time PCR assays for the detection of *Plasmodium spp.* and the principal species capable to infect human

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**Background:** Malaria early diagnosis and treatment are crucial because of its high prevalence and mortality worldwide. Despite its limitations, identification under microscopy remains the diagnostic reference method. However, molecular methods have arisen as an available option. CerTest Biotec (Spain) has developed two real-time PCR products to detect and quantify *Plasmodium spp.* and identify the species *P. falciparum, P. vivax, P. ovale, P. malariae and P. knowlesi* in blood samples. Following, the performance and added benefits compared to clinical routine diagnosis were evaluated.

**Materials/methods:** This study performed the clinical evaluation of Viasure *Malaria* and Viasure *Malaria differentiation* real time PCR detection kits, both with internal control (IC) and extraction control (EC) variants, in comparison with routine techniques. Thus, 311 clinical samples of patients attended in Hospital Universitario Miguel Servet (Spain) and collected from July 2017 to July 2019 were used. Routine analysis was based on serological assay (Alere Binaxnow Malaria©), direct visualization under the microscope and two molecular assays RealStar Malaria PCR© (Altona) and FTD Malaria differentiation© (Fast-track diagnostics). This study was approved by the Clinical Research Ethics Committee of Aragon (PI19-381).

**Results:** A total of 226 eluates and 119 clinical samples were analysed using the product variants IC and EC, respectively. 64/226 and 35/119 samples were positive for *Plasmodium* spp. Among them, 2 samples were positive for *P. malariae*, 2 for *P. ovale*, 5 for *P. vivax* and 55 for *P. falciparum*. Comparison with routine molecular assays showed 100% overall agreement and sensitivity and specificity values of >99%. Comparison of the molecular assays with the ICT and microscopy techniques showed loss of 7.81% of the samples with ICT and 21.8% of false negatives with microscopy.

**Conclusions:** Evaluated products fulfill the criteria of accuracy, sensitivity and specificity. In addition, compared with the "reference" commercial assays, the obtained results were faster and more profitable. A highlight feature of Viasure products was that thanks to this lyophilized format, their manipulation was minimal, without intermediate mixtures, and was very useful for storage and transport at room temperature instead of using refrigerated containers and occupying place in the freezers of the hospital.

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Successful salvage therapy for mucormycosis with isavuconazole in paediatric patients: cases series

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Background: Mucormycosis is a life-threatening fungal disease that occurs primarily in immunocompromised patients with hematological malignancies, but also in other patients such as those with diabetes mellitus or trauma. Isavuconazole is a new second-generation triazole with a favorable safety profile that has shown efficacy in the adult population for primary and salvage treatment of mucormycosis. However, data regarding its efficacy and long-term safety in the pediatric population are scarce.

Materials/methods: The demographic and clinical data of pediatric patients with mucormycosis who were treated with isavuconazole in 2017-2019 were collected. Children with histopathological evidence of the disease or growth on fungal cultures from a sterile body site were included.

Results: Four children of median age 10.5 years (range 7-14) met the study criteria. Two had rhino-orbital involvement and one each had cutaneous with deep tissue involvement or disseminated infection. Three had underlying hematological malignancies, and one had sustained major trauma. Two had concomitant infection with Aspergillus spp. Isavuconazole was used as salvage therapy in all: in three patients for refractory disease, and in one after intolerance to another anti-fungal drug. Following initiation of isavuconazole, alone or combined with other anti-fungal agents, complete clinical, radiological, and mycological responses were documented in all patients. The median treatment duration was 2.5 months (range 2-4), during which no isavuconazole-related adverse events were noted. Median follow-up time was 22 months (range 3-48). There were no cases of recurrent infection or mortality during follow-up.

Conclusions: Our limited clinical experience showed that isavuconazole was well-tolerated, safe, and efficacious as salvage therapy in pediatric patients with mucormycosis. The overall end-of-treatment complete response rate was 100%. Prospective clinical trials are needed to evaluate the safety and efficacy of isavuconazole in the pediatric population and its role as first-line treatment for mucormycosis.

Figure 1 – Chest and abdominal computed tomography scans of the patient with disseminated mucormycosis demonstrating necrosis and cavitary lesions of the left lower lobe of the lung, lesions in the liver, spleen and left kidney and infiltration of the colon and abdominal wall. Despite the extensive involvement, the patient had a complete recovery after initiation of isavuconazole salvage therapy.

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Abstract 4208

Two-hours direct detection of *Mycobacterium tuberculosis* complex in clinical samples by molecular method based on real-time PCR

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**Background:** Human tuberculosis (TB) continues to be a major cause of morbidity and mortality worldwide. One essential factor for controlling the spread of this disease is the ability to diagnose infection in its early stages. The gold standard in diagnosing still relies on clinical examination combined with direct microscopic examination of clinical samples and culture of bacteria. However, the culture can take up to 8 weeks and in 10-20% of cases, the bacillus is not successfully cultured. Delay in diagnosing a non-suspected TB case means that the patient is under a non-adequate treatment and therefore remains infectious for longer time. Tools for TB diagnosis changed substantially in the last decades thanks to the development of molecular methods. Here, we evaluate the Viasure *M. tuberculosis* complex real time PCR detection kit (CerTest Biotec, Spain) comparing with traditional methods used to diagnose *M. tuberculosis*.

**Materials/methods:** The study was performed using 67 DNAs from human clinical sputum samples (collected from 2005 to 2012 in Aragon, Spain) diagnosed as positive or negative for *M. tuberculosis*. These samples included different DNA from complex genotypes from lineages 1 to 5 and DNAs belonging to the lineage of strains that affect animals. To analyse the specificity of the test, five different nontuberculous mycobacteria were included in the analysis. The test was performed according to the instruction manual. The run was performed using ViiA™ 7 Real-Time PCR System (Applied biosystems).

**Results:** All samples were correctly detected. 60/65 were detected as *M. tuberculosis* complex isolates and 5/65 were detected as negative for *M. tuberculosis* complex isolates. This real-time PCR achieved a sensitivity and specificity, positive predicted value and negative predicted value of 100% in identifying *M. tuberculosis* complex isolates.

**Conclusions:** Obtained results were optimal in sensitivity and specificity, therefore the use of this product is recommended. In addition to this, the kit is presented in ready to use lyophilized format, reducing time-consuming in the lab and avoiding possible contaminations. Moreover, the stabilized format permits to transport and storage the kit at room temperature, which we considered an important advantage.

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Abstract 4209

**Validation of new anti-staphylococcal compounds within a group of potential sortase A inhibitors**

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**Background:** Staphylococcus spp. is a causative agent of many hospital and community-acquired infections with the tendency to develop resistance to the beta-lactam antibiotics. Alternative glycopeptide and oxazolidinone antibiotics are losing their effectiveness due to the resistance spread. Thus, the search of novel effective targets and their corresponding inhibitors to develop principally new antibiotics is of urgent need. Nowadays, sortase A is considered as a promising molecular target for the development of antistaphylococcal agents. Sortase A is a membrane-bound transpeptidase which catalyzes the transfer and immobilization of essential virulence factors to the surface of the microorganism. Inhibitors of sortase A affect virulence and biofilm formation, therefore decreasing selective pressure leading to the development of antibiotic resistance.

**Materials/methods:** Phenotypic screening, rational drug design.

**Results:** The phenotypic screening of the library containing 15 512 compounds from different chemical classes against methicillin resistant S. aureus ATCC43300 was performed. As a result, 250 compounds with anti-staphylococcal activity demonstrating the MIC values in the range from 0.25 mg/L to 32 mg/L were identified. The molecular docking of these compounds into active site of this enzyme using the DOCK program was performed to identify which compounds potentially can inhibit staphylococcal sortase A. There were 10 compounds selected for the following in vitro tests based on the results of molecular docking calculations and visual inspection of the best-scored complexes. A recombinant Sortase A protein has been obtained and the in vitro enzymatic activity inhibition assay where sortase-inhibiting activity has been identified for the selected inhibitors was performed. In parallel, the biofilm growth inhibition assay was conducted for S. aureus ATCC25923 and a number of methicillin-resistant and vancomycin-resistant staphylococci isolated from Ukrainian patients. The anti-staphylococcal biofilm-inhibition activity for a number of selected compounds has been confirmed.

**Conclusions:** A number of new compounds with anti-staphylococcal activity has been identified.

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Abstract 4211

Investigation of carbapenem- and tigecycline-resistant Klebsiella pneumoniae in a Greek hospital

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Background: Tigecycline is one of the last resource antimicrobial agents for the treatment of infections caused by carbapenem-resistant K. pneumoniae (CR-Kp). The purpose of the present study was the investigation of tigecycline resistance (TIG-R) among CR-Kp in a Greek tertiary hospital during January 2017-December 2018.

Materials/methods: Identification and antibiotic susceptibility testing of the isolates was performed by the Vitek®2 Compact 15 (bioMérieux) and interpreted according to the CLSI, 2018 criteria. Minimum inhibitory concentrations (MICs) of tigecycline and colistin were determined by the gradient Liofilchem® MIC Test Strip, S.R.L. and the MIC Strip Colistin, MERLIN, Diagnostika, GmbH broth microdilution methods, respectively, and interpreted according to the EUCAST criteria. The carbapenemase content of CR+TIG-R Kp was determined by the immunochromatographic method NG-Test® CARBA. PCR amplification of the ramR gene associated with tigecycline resistance was carried out. Genotyping of selected isolates was performed by MLST, as described previously.

Results: During the study period, a total of 618 Kp isolates were recovered at the Department of Microbiology. Of the 618 Kp, 267 (43.2%) were characterized as CR, 177 (28.7%) as colistin-resistant (COL-R) and 143 (23.6%) as TIG-R. From 2017 to 2018, the rates of isolation of TIG-R Kp and CR+TIG-R Kp increased from 1.3% to 31.8% and from 3.2% to 12.8%, respectively. All CR+TIG-R Kp (52 out of 618, 8.4%) Kp were extensively-drug resistant (XDR), whereas 18 of them were COL-R, and characterized as pandrug-resistant. Among the 52 CR+TIG-R Kp, 21 KPC, 21 VIM, 5 NDM, 3 OXA-48+NDM, 1 KPC+VIM, 1 OXA-48 producers were identified. MICs of tigecycline were >4mg/L for 17 VIM, 4 KPC, 1 NDM and 1 OXA-48+NDM producers. Screening for the ramR gene has revealed that 19/19 VIM, 6/20 KPC, 2/5 NDM, and 1 KPC+VIM producers were positive, whereas no PCR products were obtained for the remaining isolates. Genotyping of bloodstream KPC and VIM producers has revealed that they belonged to MLST STs 258 and 147, respectively.

Conclusions: The spread of CR+TIG-R XDR Kp in settings with high rates of carbapenem and colistin resistance limits the therapeutic options for infections caused by this pathogen.

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Abstract 4213

Role of the Ixodidae (Acari: Ixodidae) ticks, mosquitoes, and horse-flies in the transmission of vector-borne diseases in Belarus

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Background: Ticks and mosquitoes are the most significant worldwide arthropods of the medical importance. They may transmit a broad variety of pathogens causing diseases to humans and animals. Vector-borne diseases are spread in Belarus and have raising occurrence, mainly due to climatic and environmental changes and the increase of the mobility of people and animals.

Materials/methods: 359 Ixodidae (Acari: Ixodidae) ticks (Ixodes ricinus, Dermacentor reticulatus), 34 horse-flies (Tabanus bovinus) and 1006 mosquitoes (Aedes, Culex) were collected in natural foci of the Republic of Belarus during the period of their activity from May to September 2019. 272 ticks were analyzed individually by real-time PCR amplification for the presence of Borrelia spp., TBEV, Rickettsia spp., Anaplasma phagocytophilum and Ehrlichia muris. Furthermore, part of ticks, mosquitoes and horse-flies were divided by 15-20 in pools and tested for West Nile virus (WNV) by real-time PCR.

Results: The high prevalence of DNA of Borrelia spp. in ticks from all administrative regions of Republic of Belarus (38.97%). The highest content of the pathogen 69.44% was registered in Vitebsk region. Mean Rickettsia spp. prevalence was 29.78% with active foci in Vitebsk (52.78%) and Grodno (38.89%) regions. Less spread pathogens were TBEV (15.81%), Anaplasma phagocytophilum (19.49%), Ehrlichia muris (14.71%). Comparison current data with the prior year showed increase of Borrelia spp. and TBE infected ticks (38.97% in year 2019 vs 35.7% in year 2018 and 15.81% in year 2019 vs 8.8% in year 2018 respectively). The analysis of 57 pools (857) mosquitoes collected at the end of May 2019 didn’t demonstrate the presence of WNV whereas mosquitoes and ticks collected in July conformed the locative circulation (2 from 11 pools of the mosquitoes and 5 from 44 pools of ticks were positive for WNV).

Conclusions: The study of vectors and pathogens they may transmit is an essential measure for prevention and control vector-borne diseases worldwide. The ticks - inhabitants of Belarus carry and can transmit Borrelia spp., TBEV, Rickettsia spp., Anaplasma phagocytophilum, Ehrlichia muris and WNV. The locative circulation of WNV infection in Belarus was conformed and, along with other zoonoses, needs additional attention from healthcare authorities.

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Abstract 4216

Checkpoint Plus Freiburg: performance of an on-site integrated, low-threshold sexual transmitted diseases/HIV counselling and treatment service in Germany

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Background: In Germany, number and rates of new sexual transmitted infections (STI) are steadily increasing and incidence of HIV infections remains high. In order to address this issue, Checkpoint Plus (CP+) was established in January 2018 offering low threshold access for STI/HIV counselling and testing, with integration of psychosocial and medical services including on-site treatment. Objective of this study was to analyse the performance of CP+.


Results: Over the study period, an increasing number of client contacts was registered resulting in a total of 1093 contacts (Figure 1). Clients’ median age was 29.5 year (range: 18.5-62.7), 69.5% were male, 29.0% female, 0.1% trans*woman and 1.1% not binary. Clients’ sexual orientation was heterosexual (48.8%), homosexual men (37.5%) and bisexual (10.8%). Clients were from Germany (74.9%), other European countries (12.1%), and non-European countries (13%). More than one third of clients received their first STI/HIV counselling in CP+. STI/HIV screening resulted in the diagnosis of infection with N. gonorrhoeae (GO, n=11), C. trachomatis (CT, n=18), T. pallidum (n=4), and HIV (n=1). Additionally, 115 patients with HIV pre-exposure prophylaxis (PrEP) were followed for a total of 36.6 patient years. Incidence of asymptomatic STI at PrEP-initiation was n=3 for GO and n=6 for CT, whereas during follow-up under PrEP n=7 cases of GO, n=7 of CT and n=2 of Syphilis were diagnosed.

Conclusions: Substantially more non-HIV-STIs were detected, emphasizing the need for regular and low threshold screening services for bacterial STIs. The concept of CP+ may facilitate access to STI/HIV counselling and testing for a wide spectrum of people and may prove to be an important contribution to the efforts to reduce STI and HIV incidence in Germany.

Figure 1: Number of client contacts per quarter between February 19, 2018 and September 09, 2019 at Checkpoint Plus Freiburg - an on-site integrated, low threshold sexual transmitted diseases/HIV counselling and treatment service in Germany

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Molecular epidemiology of varicella zoster virus in Pitié-Salpêtrière University Hospital, Paris, France

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Background: Varicella-zoster virus (VZV) nomenclature currently recognizes 6 established (major) clades, termed 1 to 6, and 3 provisional clades, termed VII to IX. VZV genotyping strategies rely on evaluating a panel of single nucleotide polymorphisms (SNPs) across the different open reading frames (ORFs) of the viral genome. A geographical segregation of VZV clades has been shown, with clades 1, 3 and 6 predominating in Europe, clade 5 in Africa, clade 2 in Japan and East-Asia, and clade 4 in Asia. However, this regional distribution of VZV clades is dependent on increase of immigration and travels, implementation of varicella vaccine, and recombination events. The surveillance of VZV epidemiology is therefore necessary. The aim of this work was the molecular characterization of VZV isolated from patients in our University Hospital.

Materials/methods: Fifty-three consecutive patients (31 males, 22 females, median age 49 years [1 - 87]) experiencing varicella or zoster during were included during the year 2018. Most of them originated from Europe (24; 45.3%) and Africa (14; 26.4%), and 22 (41.5%) were immunocompromised. Clinical samples consisted in 49 mucocutaneous swabs, 2 whole bloods and 2 cerebrospinal fluids. VZV genotyping was based on the identification of targeted SNPs in ORF1, 22 and 50.

Results: VZV clade 1 was detected in 16 patients (30.2%), clade 3 in 16 patients (30.2%), clade 4 in 2 patients (3.8%), clade 5 in 17 patients (32.0%), and clade 6 in 2 patients (3.8%). The distribution of VZV clades did not differ according to gender, VZV-associated pathology (varicella or zoster), or immunosuppression. Patients with varicella due to clade 5 were significantly younger than those with varicella due to other clades (14.5 versus 43 years; p=0.004).

Conclusions: This study revealed similar proportions of VZV clades 1, 3, and 5 among patients. Moreover, varicella patients with VZV clade 5 were younger than others, indicating that VZV clade 5 infects the population earlier during childhood. This result may suggest that the African VZV clade 5 is able to spread more efficiently in the population than the historically circulating European VZV clades 1 and 3.

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Abstract 4221

Microbiome analysis of faecal microbiota transplantation via lyophilised capsules for recurrent *Clostridioides difficile* infection

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**Background:** Fecal microbiota transplantation (FMT) has proven to be effective in the treatment of recurrent *Clostridioides difficile* infection (R-CDI). However, use of FMT in clinical practice continues to be very restricted, probably due to the methods of administration (colonoscopy, enema or via nasojejunal tube). Few studies have been performed with capsules containing lyophilized fecal matter. Our group has previously reported success in the treatment of R-CDI with FMT via lyophilized capsules. The objective of this study was to characterize the microbiome changes associated with the use of FMT with a novel approach using lyophilized capsules.

**Materials/methods:** Fecal samples from patients with recurrent CDI who underwent FMT via lyophilized capsules (single dose of 4-5 capsules) were collected during Jan 2018-Jul 2019. FMT recipients' stools were collected before and after the procedure. Also stool specimens from the donors and the capsule’s lyophilized content were collected. All samples underwent microbiome analysis, briefly, the hypervariable V4 region of the 16s rRNA gene was amplified, sequencing (2 × 250) was performed on a Miseq platform (Illumina; California, USA) according to standard protocols. Mothur’s bioinformatic pipeline was followed for data analysis.

**Results:** Microbiome samples (n= 57 samples) were available for 33/36 patients, nine different FMT capsule batches from 8 different donors and their original stool samples were analyzed. Bray-Curtis based non-metric multidimensional scaling (NMDS) analysis indicated that donor’s microbiomes and final lyophilized FMT capsule product were alike, whereas Pre-FMT recipients’ samples were dissimilar to both. NMDS analysis showed that recipients’ microbiome converged toward donors’ microbiome profile and capsule microbiome after FMT treatment (Figure). Before FMT (n=33), patients’ microbiomes were dominated by Gammaproteobacteria (24.3%), Bacilli (23.2%) and Negativicutes (19.0%), with low abundance of Clostridia (5.4%). After FMT (n=24), there was an increase in the number of OTUS and alpha diversity, Clostridia increased (41%), together with a decrease in Gammaproteobacteria (15.4%) and Bacilli (6.2%).

**Conclusions:** Our results show that lyophilized FMT product closely resembles donor’s microbiome. Treatment of R-CDI with FMT lyophilized capsules was associated with restorative microbiome changes that resemble donor microbiome. This form of administration will allow FMT to be more widely used.

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Risk factors for colonisation with carbapenemase-resistant Acinetobacter baumanii in hospital

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Background: Despite surveillance cultures could predict the development of Carbapenemase-resistant Acinetobacter baumanii (CRAB) infections, rectal active surveillance role in CRAB spread control remains debated. Our aim is to identify the main risk factors associated with CRAB intra-hospital rectal colonisation in endemic acute care facilities in order to drive targeted screening strategies.

Materials/methods: A matched case-control study was conducted at the Azienda Ospedaliera Universitaria of Modena from January 2017 to December 2018. According with the hospital screening policy, all underwent rectal swab during the study period on admission and weekly. A patient was defined as a case if he met all of the following criteria: isolation of a CRAB strain from rectal swab screening, hospital stay ≥ 4 days at time of screening and no isolation of CRAB from any sample in the previous 6 months. Controls were selected among patients with a negative rectal swab for CRAB on the same day as the matched case. Two controls were individually matched to each case by age, date of screening and ward at the time of screening.

Results: Forty-five patients colonized by CRAB were considered and 90 controls: 37.8% from internal medicine, 37.8% from geriatric, 8.9% from surgical and 15.6% from intensive care units. The multivariate logistic regression adjusted for the length of hospital stay (odds ratio [OR]=1.03; 95% confidence interval [CI], 1.01-1.05, p-value=0.002) show that the use of indwelling devices (OR=10.15; 95% CI, 2.27-45.39), the urinary catheter (OR=4.96; 95% CI, 1.52-16.19), the tracheostomy (OR=40.01; 95% CI, 4.05-395.10), the McCabe Score (OR=5.45; 95% CI, 1.87-15.89), and the use of carbapenems (OR=5.39; 95% CI, 1.14-25.44) were the main risk factors for colonization. Analysing the single department: in geriatric, the use of hospital devices and the McCabe Score increases the risk by 10 and 15 times, respectively, while in internal medicine disabilities or bedridden with medical devices. In ICU antibiotic exposure (carbapenems and cephalosporines) were significantly associated with outcome.

Conclusions: Antibiotic therapy associated with disabilities and medical devices play a crucial role for CRAB rectal colonisation. These findings could allow an early identification of CRAB asymptomatic carriers and prevent infection transmissions in endemic setting.

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Abstract 4227

Colistin-resistant Enterobacteriaceae in Belgian broiler and pig farms

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Abstract third-party references: i-4-1-Health Study Group

Background: Colistin is a last-resort antibiotic for the treatment of multidrug-resistant Gram-negative bacterial infections. The antibiotic has been used in veterinary medicine, especially in pigs to treat post-weaning diarrhoea caused by Escherichia coli. This study determined the burden of colistin-resistant Enterobacteriaceae (ColR-E) in Belgian broiler and pig farms

Materials/methods: As part of the i-4-1 Health project, a total of 400 broiler and 400 pig fecal samples were collected from broiler (n=15) and sow farms (n=15) in Belgium between September 2017 and April 2018. A random-stratified design was used to collect twenty to thirty samples per farm (FecalSwab, Copan Italy). The presence of non-intrinsically ColR-E was investigated using selective culturing and colistin MIC testing using broth microdilution (epidemiological cut-off: 2 mg/L). To quantify colistin use, treatment incidence was calculated in accordance with Timmerman et al. (2006). A selection of ColR-E (E. coli n=14, Klebsiella pneumoniae n=15, Klebsiella oxytoca n=2, Enterobacter cloacae n=2) was sequenced (Illumina MiSeq) to determine genotype-phenotype correlations. Core genome multilocus sequence typing (cgMLST) was used to determine clonal relatedness.

Results: The percentage of samples positive for ColR-E was higher in pigs (22%) compared to broilers (0.75%) (Figure 1A). A positive correlation was found between within-farm colistin use and presence of resistance (Kendall’s tau: 0.52, p<0.01). Of all resistant strains, 67% were E. coli exhibiting MIC between 4 and 16 mg/L. Resistance was also detected in K. pneumoniae (28%), K. oxytoca (2%) and E. cloacae complex (3%) exhibiting MIC of 4 to >64 mg/L. Plasmid-mediated resistance genes were absent in 9/33 of the ColR-E, suggesting that other mechanisms are involved. Based on PROVEAN scores, we show mutations that possibly influence colistin susceptibility. Disruption of mgrB by stop codon or insertion sequence was predominant in K. pneumoniae (Figure 1B). K. pneumoniae ST101, an emerging clone associated with increased mortality rates in humans, was detected with high-level colistin resistance in pigs.

Conclusions: This study revealed that ColR-E are found in Belgian farms. The presence of high-level colistin-resistant strains, like K. pneumoniae ST101, in pig farms is a potential public health threat.
Figure 1: Colistin resistance in broiler and pig farms. Prevalence of ColR-E and colistin use in Belgian farms (A). Phenotype-genotype correlations in colistin-resistant *Escherichia coli* (B) and *Klebsiella pneumoniae* (C). Branch numbers represent allelic differences based on cgMLST (scheme based on 3437 alleles in *E. coli* and 4785 alleles in *K. pneumoniae*). * stop codon, empty spaces are unknown resistance mechanisms and sequence types.

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High prevalence of sexually-transmitted infections among at-risk HIV-positive patients

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Background: Sexually transmitted infections (STIs) have been continuously increasing after the introduction of biomedical HIV interventions. This study aimed to investigate STI prevalence and associated factors among at-risk HIV-positive patients in a country implementing treatment as prevention and pre-exposure prophylaxis for HIV.

Materials/methods: From May to November 2019, multiplex real-time PCR detecting Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG), and Trichomonas vaginalis (TV) were prospectively performed in urine and rectal specimens collected from HIV-positive patients with a history of STIs or symptoms suggestive of STIs. Patients confirmed to have acquired STIs were treated according to treatment guidelines. Tests of cure were taken at least 3 weeks after completion of treatment.

Results: During the 6-month study period, 405 HIV-positive patients (99.0% being men who have sex with men (MSM)) with a median age of 37 years were included for analysis. The overall prevalence of CT and/or NG positivity was 27.7% (112/405), including 23.5% for CT, 10.6% for NG, and 0.2% for TV. While 96.4% (108/112) of STIs were detected from rectal swab specimens, only 16.1% (18/112) were detected from urine specimens. The clinical factors associated with acquisition of CT or NG were younger age (per 1-year decrease, adjusted odds ratio [AOR], 1.04; 95% confidence interval [CI], 1.01 - 1.08), hepatitis B virus infection (AOR, 2.42; 95% CI, 1.24-4.75), recent hepatitis C virus infection (AOR, 2.98; 95% CI, 1.35-6.58), recent rapid plasma reagin titer ≥8 (AOR, 2.11; 95% CI, 1.11 -4.04), and HIV plasma viral load >20 copies/mL (AOR, 2.33; 95% CI, 1.27 -4.34). The behavioral risk factors were lower income (AOR, 2.27; 95%CI, 1.08-4.76), oral sex in 6 months (AOR, 2.13; 95% CI, 1.01 -4.49), and inconsistent condom use (AOR, 3.03; 95% CI, 1.47-6.23). Among 60 patients completing test-of-cure visits, 56 patients (93.3%) had achieved microbiological clearance.

Conclusions: Our findings strongly support STI screening at sites of exposure for HIV-positive MSM. Patients infected with viral hepatitis and syphilis frequently were coinfected with bacterial STIs.

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Abstract 4230

**Acute bacterial prostatitis due to *Escherichia coli*: clinical characteristics and outcomes in patients treated with or without β-lactam antibiotics: a cohort study**

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**Background:** Acute bacterial prostatitis (ABP) is a common urinary tract infection (UTI) with an incidence between 10-25%. Despite its frequency, it is poorly characterized in the literature. Our objective was to describe clinical characteristics of ABP due to *Escherichia coli* in a cohort of consecutive adult men comparing outcomes in patients treated with or without β-lactam antibiotics.

**Materials/methods:** Observational retrospective study. Setting: acute-care teaching hospital. Period: January-2010 to June-2019. Cases: consecutive ≥18 year-old males, admitted to the Emergency Room of an acute-care teaching hospital, with a clinical syndrome compatible with ABP and a urine culture with a significant growth of *Escherichia coli*. Study variables: demographics, management, complications and clinical outcomes. Treatment groups: patients treated with any β-lactam antibiotic (Group 1) and patients treated with either a quinolone or Cotrimoxazole (Group 2).

**Results:** One hundred and twenty-seven patients were included. Demographics and clinical characteristics are summarized in Table 1:

<table>
<thead>
<tr>
<th>Variables</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age* 66.5 (58-74)</td>
<td></td>
</tr>
<tr>
<td>Charlson Comorbidity Index*</td>
<td>3 (2-5)</td>
</tr>
<tr>
<td>Previous UTI^1</td>
<td>42 (33)</td>
</tr>
<tr>
<td>Prostatic hypertrophy^1</td>
<td>57 (45)</td>
</tr>
<tr>
<td>Prostate malignancy^1</td>
<td>10 (8)</td>
</tr>
<tr>
<td>Indwelling urinary catheter (more than 48h)^2</td>
<td>3 (2)</td>
</tr>
<tr>
<td>Urological surgical procedure^2</td>
<td>20 (16)</td>
</tr>
<tr>
<td>Fever</td>
<td>113 (89)</td>
</tr>
<tr>
<td>Dysuria</td>
<td>97 (76)</td>
</tr>
<tr>
<td>Increased urinary frequency</td>
<td>81 (64)</td>
</tr>
<tr>
<td>Days of symptoms*</td>
<td>2 (1-3)</td>
</tr>
<tr>
<td>Acute urinary retention</td>
<td>14 (11)</td>
</tr>
<tr>
<td>Shock</td>
<td>9 (7)</td>
</tr>
<tr>
<td>CRP (mg/L)* 106.5 (46-194)</td>
<td></td>
</tr>
<tr>
<td>ESBL-producing isolates</td>
<td>16 (12)</td>
</tr>
<tr>
<td>Quinolone-resistant isolates</td>
<td>27 (21)</td>
</tr>
<tr>
<td>Cotrimoxazole-resistant isolates</td>
<td>32 (24)</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>104 (82)</td>
</tr>
<tr>
<td>30-d Mortality</td>
<td>1 (0.7)</td>
</tr>
</tbody>
</table>

*Median, interquartile interval (IQI). ^1Within the previous year. ^2In the previous 30 days.

Fifty-three patients (42%) were treated with β-lactams and 58 (46%) with either quinolones or Cotrimoxazole. Clinical cure at end of therapy (EoT) was 83% in Group 1 and 93% in Group 2 (p=0.1); reinfection and relapse rates -within 90 days after EoT- were 2% in Group 1 versus 3% in Group 2 (p=1) and 9% in Group 1 versus 0% in Group 2 (p=0.02) respectively.

**Conclusions:** ABP due to *Escherichia coli* affects middle-aged males with previous urinary tract conditions. Relapse was more frequent among patients that received directed therapy with a beta-lactam.

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Abstract 4231

**Nano chitosan effect on Plasmodium falciparum in vitro**

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**Background:** The inevitable side effects, inefficiencies and also emerging the resistances of current drugs in the treatment of Malaria have led researchers around the world to think about finding new treatments for Malaria. The aim of this work was preparation of chitosan nanoparticle delivered from fungi for treatment Malaria disease.

**Materials/methods:** In this research prepared chitosan nanoparticle from *Penicillium* fungi and investigated the effect of nano chitosan on protozoan of *Plasmodium falciparum*. Nano-chitosan was prepared from chitosan extracted from *Penicillium* fungi, and characterized by FTIR, DLS and SEM. Then chitosan nanoparticle toxicity on PC12 cells and the effect of hemolysis on erythrocytes were evaluated by MTT and spectroscopy, respectively. The *P. falciparum* protozoan was collected then species confirmed using PCR-RFLP method, and cultured in RPMI1640 medium. Finally, the antiparasitic effect of nano chitosan was evaluated by the addition of chitosan nanoparticle to the protozoan culture medium.

**Results:** Prepared nano chitosan (100 nm), demonstrated no toxic effect on PC12 cells and not hemolytic effect on human erythrocytes. The highest antiparasitic activity was observed at 50 μg/mL concentration. This concentration of nanoparticles was preventing 59.5% from the growth of *P. falciparum* in the culture medium.

**Conclusions:** The synthesized nano chitosan, due to the low side effects and acceptable effect on this protozoa, could be considered as an antiparasitic nanodrug that needs further systematic study.

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Adenovirus-associated epidemic keratoconjunctivitis outbreak in a tertiary hospital
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Background: Human adenoviruses (HAdVs) are one of the main causative agents of conjunctivitis. Epidemic keratoconjunctivitis, which usually occurs as an outbreak, is predominantly caused by HAdV-D genotypes. In this work, we describe an outbreak of keratoconjunctivitis caused by HAdV-D8 in patients attending the Ophthalmology Department of Santa Creu i Sant Pau Hospital (Barcelona) from May to September 2018.

Materials/methods: Exudates from the bottom of the conjunctival sac (one per patient) were processed for antigen detection by Light Diagnostics™ Adenovirus Antibody (Merck) direct immunofluorescence and inoculating four cell culture lines. The HAdV genotype was obtained after PCR and sequencing. The sequences were analysed by BioNumerics 7.6 software and uploaded to https://www.rivm.nl/mpf/typingtool/enterovirus/.

Results: On August 14, 2018, the Ophthalmology Department notified the Infectious Diseases Unit of a suspected outbreak of keratoconjunctivitis after an unexpected increase in diagnosis. Epidemiological data (Figure 1) show that the first case was diagnosed on July 20, with the highest number of cases (8) being detected on August 6. A total of 14 cases were diagnosed before the Infectious Diseases Unit was alerted. After August 14, one sample from each keratoconjunctivitis patient was sent to the microbiology laboratory to be characterised. A total of 22 samples were collected, and among these, 13 samples were positive for HAdV and were all genotyped as HAdV-D8. A possible focus of this outbreak was the slit lamp shared by all patients. No case was detected among the clinical staff.

Conclusions: Nosocomial outbreaks caused by HAdV-D8 are rarely described because keratoconjunctivitis can be diagnosed and treated without having to characterize the causative agent. However, the importance of describing the etiologic agent should be emphasized, as it enables more efficient epidemiological surveillance.

Figure 1. Epidemiological surveillance of the 36 patients with keratoconjunctivitis.

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Abstract 4234

**Antimicrobial resistance in Taiwan, results from Surveillance of Multi-centre Antimicrobial Resistance in Taiwan (SMART), 2019**

Po-Ren Hsueh*1

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**Background:** To investigate the rates of WHO-listed major resistant pathogens associated with bacteremia and other clinical infections in Taiwan, 2019

**Materials/methods:** A total of 2400 isolates including blood isolates of *S. aureus* (*n*=366), *E. faecium* (*n*=220), *E. coli* (*n*=423) and *K. pneumoniae* (*n*=372), *P. aeruginosa* (*n*=300), *A. baumannii* (*n*=199); invasive isolates [sterile sites] of *S. pneumoniae* (*n*=64); and various sources of non-Typhoid *Salmonella* spp. [NTS, *n*=261], *Shigella* spp. [*n*=10], *N. gonorrhoeae* (*n*=187), *Campylobacter* spp. (*n*=32), and *H. influenzae* (*n*=65) collected from 18 hospitals in different geographic regions of Taiwan in 2019. MICs were determined using the broth microdilution [Vitek 2 system]/agar dilution methods and were interpreted based on CLSI guidelines, 2019.

**Results:** Table 1 Rates of WHO-listed major resistant organisms

<table>
<thead>
<tr>
<th>Resistant organisms</th>
<th>2019. % (I+R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Priority 1: CRITICAL</td>
<td></td>
</tr>
<tr>
<td>Carbapenem-resistant <em>A. baumannii</em> (CRAB)</td>
<td>43.7</td>
</tr>
<tr>
<td>Carbapenem-resistant <em>P. aeruginosa</em></td>
<td>14.3</td>
</tr>
<tr>
<td>3rd gen. cephalosporin-resistant <em>E. coli</em> (<em>K. pneumoniae</em>)</td>
<td>33.6 (25.0)</td>
</tr>
<tr>
<td>Carbapenem-resistant <em>E. coli</em> (<em>K. pneumoniae</em>)</td>
<td>1.4 (9.9)</td>
</tr>
<tr>
<td>Priority 2: HIGH</td>
<td></td>
</tr>
<tr>
<td>Vancomycin-resistant <em>E. faecium</em> (VRE)</td>
<td>50.0</td>
</tr>
<tr>
<td>Methicillin-resistant <em>S. aureus</em> (MRSA)</td>
<td>51.1</td>
</tr>
<tr>
<td>Vancomycin-intermediate or-resistant <em>S. aureus</em></td>
<td>0</td>
</tr>
<tr>
<td>Fluoroquinolone-resistant <em>Campylobacter</em> spp.</td>
<td>89.5</td>
</tr>
<tr>
<td>Fluoroquinolone-resistant <em>Salmonella</em> spp.</td>
<td>24.5</td>
</tr>
<tr>
<td>3rd gen. cephalosporin-resistant <em>N. gonorrhoeae</em></td>
<td>0</td>
</tr>
<tr>
<td>Fluoroquinolone-resistant <em>N. gonorrhoeae</em></td>
<td>97.5</td>
</tr>
<tr>
<td>Priority 3: MEDIUM</td>
<td></td>
</tr>
<tr>
<td>Penicillin-non-susceptible <em>S. pneumoniae</em></td>
<td>17.2 (NM), 62.6 (M)</td>
</tr>
<tr>
<td>Ampicillin-resistant <em>H. influenzae</em> (<em>ß-lactamase +)</em></td>
<td>71.9 (47.7)</td>
</tr>
<tr>
<td>Fluoroquinolone-resistant <em>Shigella</em> spp.</td>
<td>70</td>
</tr>
</tbody>
</table>

A total of 17 *blaKPC* (+) isolates (*K. pneumoniae*, 16; *E. coli*, 1), 2 *blaOXA-48* (*K. pneumoniae*), 1 *blaVIM* (*K. pneumoniae*); 1 *mcr-1* harboring isolates (*K. pneumoniae*) were found. PVL (+) in 30% (57/187) of bacteremic MRSA isolates. Hyperviscosity was noted in 45.7% (165/372) *K. pneumoniae* isolates and 20.6% (34/166) belonged to K1 type.

**Conclusions:** High prevalence of PVL (+) MRSA, VRE and CRAB were noted, *blaKPC*-positive *K. pneumoniae* remained endemic and *mcr-1* and *blaOXA-48* harboring *K. pneumoniae* emerged in in Taiwan.

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Detection of low-level vanB-type vancomycin-resistant Enterococcus faecium with agar screen methods

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Abstract third-party references: Supported by the Belgian Ministry of Social affairs through a fund within the Health Insurance System.

Background: VanB-containing E. faecium show variable phenotypic resistance to vancomycin (MIC: 4-1,024 mg/L). The detection of the currently circulating low-MIC ST117 vancomycin resistant E. faecium strain is challenging as its resistance is poorly induced by vancomycin. EUCAST has recently published warnings in order to improve detection of low-MIC VRE with gradient strip tests. However, EUCAST’s advice for breakpoint agar methods has remained unchanged so far. We aimed to study the performance of an home-made and commercial agar screen method for detection of low-MIC VRE.

Materials/methods: Twenty-five low-level vancomycin resistant E. faecium strains, submitted at the Belgian National Reference Centre for Enterococci in 2017 and 2018, were selected. All strains were vanB positive (via in-house real-time PCR) and belonged to ST117 (via conventional PCR followed by Sanger sequencing or whole genome sequencing using Nextera XT (2x250bp), MiSeq [Illumina]). MIC values were obtained by gradient strip testing and ranged from 2-4 mg/L. Ten µl of 0.5 McFarland bacterial suspension of the selected strains was applied on an home-made vancomycin screen agar (VancoScreen, 6 mg/L vancomycin) and on the VREselectTM Medium (Bio-Rad, 8 mg/l vancomycin). Growth for both agars was evaluated after 24h and 48h incubation at 35°C. Ten vancomycin susceptible E. faecium strains were used as control.

Results: After 24h incubation no growth was observed for 5/25 (20%) (4x MIC 4 mg/L and 1x MIC 2 mg/L) E. faecium strains on VREselectTM and 3/25 (12%) (2x MIC 4 mg/L and 1x MIC 2 mg/L) E. faecium strains on VancoScreen. Extending the incubation time to 48h resulted in growth of all strains on both media. For one strain with an MIC of 2 mg/L only one colony was detected on the VancoScreen both after 24 and 48h incubation. None of the vancomycin susceptible E. faecium strain grew on the vancomycin screen agars after 48h incubation.

Conclusions: Detection of low-level VRE E. faecium isolates with MIC levels of ≤4 mg/l is possible with agar screen methods. However, exposure of these strains to vancomycin should be extended to 48h to fully induce their resistance (instead of 24h according to EUCAST). Furthermore, any growth should be taken into account.

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Abstract 4239

**Economic burden of recurrent *Clostridium difficile* infection (rCDI) in adult patients admitted in Spanish hospitals: multi-centre, retrospective, observational study**

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**Abstract third-party references:** Merck & Co., Inc., Kenilworth, NJ, USA

**Background:** *Clostridium difficile* infection (CDI) is the most common gastrointestinal nosocomial infection and the main cause of diarrhea in hospitalized patients in Spain. CDI is associated with an increased hospital stay and mortality and a high probability of readmission, resulting in an increased use of healthcare resources and greater costs for the National Healthcare System (NHS). The aim of the study was to estimate the economic burden of rCDI in the Spanish setting.

**Materials/methods:** Multicenter, retrospective, observational study. Hospitalized patients with at least one diagnostically-confirmed episode (primary or secondary diagnosis) of rCDI between January 2010 and May 2018 were retrospectively reviewed in 6 Spanish centers. Healthcare resources included were hospital length of stay (emergency room, general ward, isolation unit and intensive care unit) as well as tests and treatments. If the primary admission diagnosis was rCDI the entire hospital stay was considered attributable to rCDI. If the primary admission diagnosis was any other than rCDI and the secondary diagnosis was rCDI, the additional hospital stay was estimated as the difference with respect to an episode without rCDI (control group). Cases and controls were matched [1:1] using the propensity score matching. Control episodes were collected in the Spanish National Hospital Discharge Database. Total costs were calculated by multiplying the natural resource units used by the corresponding unit cost (€ 2019).

**Results:** 282 rCDI episodes were reviewed (188 as primary diagnosis). 187 (66.31%) were patients aged ≥65 years and 163 (57.80%) were female. Median rCDI hospital length of stay was 10.00 days per episode [IQR: 6.00-17.00], obtaining similar results for both, primary [10.00 (IQR: 6.00-16.00)] and secondary diagnosis [10.00 (IQR: 4.00-20.00)]. Total mean cost per rCDI episode was 10,877€ (CI 95%: 9,498€-12,777€), of which 47% was due to the need of single patient room for contact precautions.

**Conclusions:** The economic burden of rCDI managed in the hospital setting is 10,877€ per episode. At national level, rCDI episodes represent an estimated expenditure between 13.9 -21.3 million euros per year. Results suggest that healthcare resources use needed to treat rCDI and related costs have a high economic impact on the Spanish NHS.

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Abstract 4241

**Investigation of a vancomycin-resistant enterococci outbreak at a cardiothoracic-surgery department: new insights from next-generation sequencing**

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**Background:** Vancomycin-resistance among Enterococcus faecium has been increasing rapidly over the past years. At the same time, infections and deaths due to Vancomycin-resistant Enterococci (VRE) have risen, and VRE outbreaks have been reported worldwide. Both, colonization and infection with VRE are associated with higher mortality, prolonged stays in hospitals and higher costs. Appropriate infection control measures are still debatable, though. In May 2019, we observed an increased rate of VRE at the cardiothoracic-surgery department of an academic hospital; here we present preliminary results from our investigation.

**Materials/methods:** An epidemiologic investigation and molecular typing, using Next-Generation Sequencing (NGS), was conducted. In order to contain the possible outbreak, immediate infection control measures, including isolation of patients, reinforcement of hand hygiene as well as intensified cleaning and disinfection, were taken.

**Results:** From May 2019 onwards, we started the outbreak investigation installing intensified personal infection control measures, environmental cleaning and disinfection, as well as universal rectal screening at the cardiothoracic-surgery department. A VRE prevalence of 6.6% (26/394) was detected. In total, from December 2018 until November 2019, VRE were found in 38 patients. Our rigorous infection control measures seemed to be effective, as only five new cases appeared since July. By using NGS, to date, we identified six distinct VRE clusters including 31 patients; five patients appeared as independent strains. The strains belonged to the multilocus sequence types ST78, ST80, ST117 and ST787. According to our extensive epidemiologic investigation, 27 patients, who fitted to one of the genetic clusters, had had contact with each other at the wards, i.e. were admitted to the same ward at the same time.

**Conclusions:** Using NGS, we were able to cluster VRE strains genetically. In connection with our epidemiologic investigation, these results suggest inward transmissions for many of the VRE cases, while others might be a result of selection through antibiotic administration. In any case, well developed hygiene practices and infection control measures were crucial in avoiding the spread of VRE.

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Abstract 4242

Validation of Simplexa HSV 1 & 2 Direct and Simplexa VZV Direct kits for herpes simplex virus and varicella zoster virus detection from low-volume cerebrospinal fluid samples

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Background: Herpes simplex virus 1 and 2 (HSV-1 and HSV-2) and varicella-zoster virus (VZV) are major causes of infectious meningoencephalitis. Therefore, rapid and accurate detection of viral genomes in cerebrospinal fluid (CSF) is mandatory for management and treatment of patients. However, low-volume CSF may be available for molecular testing. We evaluated the sample-to-result real-time PCR assays Simplexa™ HSV 1 & 2 Direct and Simplexa™ VZV Direct on LIAISON® MDX platform with the use of 25µL of sample volume, instead of 50µL as recommended by the manufacturer DiaSorin Molecular

Materials/methods: Cycle threshold (Ct) values obtained from 50µL and 25µL of sample volume tested were compared for 60 HSV-positive and 60 VZV-positive different samples: 35 CSFs from patients, 37 CSFs spiked with different quantities of ATCC HSV-1, HSV-2, or VZV strains, and 48 QCMD samples from previous years. Reproducibility using 25µL of sample was evaluated by intra- and inter-assay comparisons

Results: All 120 positive samples were detected using either 50µL or 25µL, leading to a concordance of 100%. No PCR inhibition was observed. The difference of Ct values obtained with the 2 volumes tested for each sample (ΔCt [50-25]) was below or equal to 1.0 for 102 (85%) samples and ranged from 1.1 to 1.6 for 18 (15%) samples. Mean ΔCt [50-25] values were -0.1, -0.1, and -0.2 for HSV-1 HSV-2, and VZV, respectively. Coefficients of variation (CVs) obtained for intra-assay variability (Simplexa™ Positive Controls tested 8 times in a single Direct Amplification Disk) were 3%, 3%, and 1.9% for HSV-1, HSV-2, and VZV, respectively. CVs for inter-assay variability (Simplexa™ Positive Controls tested 10 consecutive times once a week) were 1.7%, 1.0%, and 1.3% for HSV-1, HSV-2, and VZV, respectively.

Conclusions: The results obtained in this study allow the validation of the performances of Simplexa™ HSV 1 & 2 Direct kit and Simplexa™ VZV Direct kit for the detection of HSV-1, HSV-2, and VZV genomes in CSF with the use of 25µL of sample with no loss of sensitivity. This validated protocol will be useful to perform molecular tests with low-volume CSFs, especially for pediatric patients

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Abstract 4244

**Direct acting antiviral failure in hepatitis C virus genotype not 1: virological features and efficacy of re-treatment**

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**Background:** DAA-regimens are associated with failure in about 5% of cases, due with the emergence of resistance associated substitutions [RASs] within the viral quasispecies. This study characterized the virological patterns in genotype not-1 patients failing IFN-free regimens and evaluated the efficacy of re-treatment.

**Methods:** 75 HCV patients with failure to IFN-free regimen observed at the laboratory of infectious diseases of University of Campania, Naples. Sanger sequencing of NS3, NS5A and NS5B was performed at failure by home-made protocols.

**Results:** Patients enrolled were mainly males (80%), median age 58 years [range 31-86]. HCV RNA, IU/ml median value was 4.77 x 10e5 IU/ml [range: {1.3 x 10e3 IU/ml – 3.8 x 10e8 IU/ml}], 62.6% of patients had a diagnosis of cirrhosis. 26 patients were HCV genotype 2a/2c, 44 were genotype 3 and 5 were genotype 4.

The prevalence of RASs in NS5A region were more frequently detected in genotype 4 (80%) and genotype 3 (61,3 %) than in genotype 2a/2c (38,5%). RAS in the NS5B region were identified only in genotype 3 (18,1%) and genotype 2a/2c (3,8%). Out of the 75 patients enrolled, 35 [46,6 %] patients were re-treated; 84% were relapse, 4% breakthrough and 12% non-responder at retreatment.

The 18 patients re-treated with genotype 3 less frequently (77,7%) showed an SVR than the 11 patients with genotype 2 (84,6%). 60% of patients with genotype 2, 50% with genotype 3 and 60% with genotype 4 without SVR show RASs.

SVR was more frequent in patients HCV genotype 2 treated with the latest DAAs regimen [91% vs 9%, p=0.0001]; also, for patients with HCV genotype 3 treated with the latest generation DAAs [50% vs 27,8 %] SVR was more frequent.

All HCV genotype 4 patient failed at retreatment.

**Conclusions:** The prevalence of RASs was high in our population. Failed patients have at least one RASs in one HCV region. The latest DAA regimen more frequently obtained SVR despite previous regimen for HCV genotype 2 and 3.

HCV genotype 4 remains a difficult-to-treat genotype. Patients with Resistance-Guided Therapy more frequently obtain SVR.

NS3, NS5A and NS5B sequencing seems mandatory in the choice of re-treatment DAAs.

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Abstract 4245

Investigation of linezolid resistance mechanisms of *Staphylococcus epidermidis* isolates collected in Gauteng, South Africa

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**Background:** *Staphylococcus epidermidis* are Gram-positive bacteria known to cause infections in the compromised host. Linezolid is a treatment option in *S. epidermidis* infections; however, linezolid resistance mechanisms are becoming more prevalent. Linezolid resistance is due to chromosomally- and plasmid-mediated mechanisms such as 23S rRNA gene mutations and acquisition of the chloramphenicol-florfenicol resistance (*cfr*) gene, respectively. This study identified these mechanisms of linezolid resistance in *S. epidermidis* isolates obtained from private hospitals in Gauteng, South Africa.

**Materials/methods:** *Staphylococcus epidermidis* (n=27) cultured from blood using the BACT/ALERT® 3D system (bioMérieux, France) were collected from 2016 to 2018. Inclusion criteria were *S. epidermidis* isolates that tested linezolid resistant using the VITEK® 2 instrument (bioMérieux, France) according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines. Isolates were identified using matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectrometry (MS) and speciation was confirmed using multiplex polymerase chain reaction (M-PCR) assays. Linezolid minimum inhibitory concentration (MIC) was determined using ETEST® (bioMérieux, France). A singleplex polymerase chain reaction (PCR) assay was used to detect the *cfr* gene. Pulsed-field gel electrophoresis (PFGE) was performed to determine genetic relatedness. Seven representative *S. epidermidis* isolates were selected for whole-genome sequencing (WGS).

**Results:** The PCR assays confirmed identification of the *S. epidermidis* isolates. The *cfr* gene was detected in eight (29.6%) of the 27 *S. epidermidis* isolates. The ETEST® (bioMérieux, France) MIC values ranged between 8 µg/mL and > 256 µg/mL. The PFGE showed genetic relatedness among the isolates that clustered into one major cluster, four minor clusters and five singletons across nine different hospitals. The *S. epidermidis* sequence types (ST)s found were ST23 (57.1%, n=4/7), ST2 (28.6%, n=2/7) and ST22 (14.3%, n=1/7). Mutations of the 23S rRNA gene were found at positions C2190T (ST23, ST2 and ST22 isolates), C2561T (one ST23 isolate) and G2603T (ST23 and ST22 isolates).

**Conclusions:** Isolates containing a combination of 23S rRNA gene mutations and the *cfr* gene showed higher linezolid resistant MIC values than isolates with only one of these resistance mechanisms. Therefore, the spread of linezolid resistant isolates indicates the need for judicious use of linezolid and effective infection control measures.

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Abstracts 2020

Abstract 4246

**Epidemiology of respiratory colonisations and infections caused by *Aspergillus* and non-*Aspergillus* moulds in lung transplant patients**

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**Background:** Molds are frequently isolated from pulmonary samples of lung transplant patients but few data are available on the burden of this colonization during the first post-transplantation period. The aim of our study was to describe the colonization of a cohort of lung transplant patients during this early post-transplantation period.

**Materials/methods:** All the patients who had undergone lung transplantation in 2017-2018 in our hospital were followed from their transplantation until August 2019, 31th. Pulmonary samples with mold positive cultures were analyzed. Clinical and radiological data were collected to classify the patients as colonized or infected following standard definitions (EORTC/MSG).

**Results:** Ninety-seven patients (44 in 2017 and 53 in 2018, mean age 55+/−11 years) were included: 66/97 (68%) bi-pulmonary transplanted, with mainly emphysema (31/97 [32%]) and fibrosis (41/97 [42%]) as underlying diseases. The mean delay between transplantation and the first positive culture of a respiratory sample with molds was 1.9 +/- 2.6 months. During the survey, 77 patients have had at least one positive culture with molds (81%): 75 colonizations (often with a mix of *Aspergillus* spp and other molds [55/75]) and 3 aspergillosis infections. Two hundred and fifty-four strains were isolated: 138 *Aspergillus* spp (mainly *A. fumigatus* [62] and *A. niger* [33]), and 116 other molds (mainly *Penicillium* spp [61, no *P. marneffei*], and zygomycetes [11]). There was no difference between mono- and bi-pulmonary transplanted patients. Eighteen patients died during the survey (18%), including 1 aspergillosis infection and 9 colonizations.

**Conclusions:** In our cohort, a majority of lung transplant patients were colonized during the early period after their transplantation. The colonization often associated *Aspergillus* spp and other molds, mainly *Penicillium* spp. This rise the question of the potential pathogenicity of these fungi: infections with *Penicillium* spp [other than *P. marneffei*] have already been described¹ and they are known for their inflammatory effects in the lung². Further studies are needed to evaluate the real impact of these colonizations with *Penicillium* spp. alone or associated with *Aspergillus* spp. or other molds in lung transplantation, and the impact of prophylactic antifungal treatments.

1. J Infect. 2002

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Abstract 4250

Healthcare associated infections and outcomes: changes between 2013 and 2018 in Turkey


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Background: We described the change in the epidemiology of healthcare associated infections (HAI), resistance and predictors of fatality.

Materials/methods: This retrospective multi-centric study included 25 hospitals from different geographic regions of Turkey for evaluation of the fatality. All patients with HAI in these centres in 2015 and 2018 were enrolled to the study. The diagnosis of HAIs was based on the criteria of the Centers for Disease Control and Prevention (CDC). Identification of the organisms was conducted using whichever automated system was used routinely at each centre (VITEK 2, Biome`rieux, Marcy l’Etoile, France; Phoenix, BD, Franklin Lakes, NJ, USA). Antibiotic susceptibilities were tested by disc diffusion or minimum inhibitory concentration tests according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI), resistance was defined according to CLSI criteria.

Results: In total 9100 cases with HAI were fatal (41%). A total of 4539 patients in 2015 were compared with 4586 patients in 2018. There was no difference in fatality rate between two years. Blood-stream infection (BSI) was the most common (40%) infection, followed by pneumonia (33%), surgical-site infections (SSI, 23%), urinary-tract infection (UTI, 18%), gastrointestinal infections (GI, 3%) and central nervous system infections (CNS, 1%). Although BSI and SSI were significantly higher in 2018, the percentages of patients with pneumonia were lower in 2018 (Table 1). The highest rate of fatality was detected among the patients with pneumonia (57%). The fatality rates of infections were 46% in BSI, 35% in UTI, 34% in GI, 20% in MS and 14% in SSI. Klebsiella spp. was the most common (20%) causative pathogen. The resistance against carbapenem and colistin among Acinetobacter spp, Pseudomonas spp. and E. coli was significantly higher in 2018. The highest rate of fatality was detected among the patients with Acinetobacter spp (52-63%), fatality rates were similar between years (2015-2018). Among Gram-positive organisms, the most common ones were Enterococcus spp (8%), S.aureus (6%) and Coagulase-negative staphilococcus (6%).

Conclusions: Resistant Gram negative agents are the leading problem in infection control practice of Turkey. Proportion of Acinetobacter spp. decreased, but the proportion of Pseudomonas spp. increased.

Table 1. Percentage of HAI

<table>
<thead>
<tr>
<th>Type of HAI</th>
<th>Total N=9100 (%)</th>
<th>2015 n=4539 (%)</th>
<th>2018 n=4586 (%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSI</td>
<td>3182 (40)</td>
<td>1450 (37)</td>
<td>1732 (44)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2590 (33)</td>
<td>1498 (38)</td>
<td>1092 (28)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SSI</td>
<td>1787 (23)</td>
<td>775 (20)</td>
<td>1012 (26)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>UTI</td>
<td>1344 (18)</td>
<td>705 (18)</td>
<td>639 (17)</td>
<td>0.14</td>
</tr>
<tr>
<td>GI</td>
<td>191 (3)</td>
<td>81 (2)</td>
<td>110 (3)</td>
<td>0.017</td>
</tr>
<tr>
<td>CNS</td>
<td>98 (1)</td>
<td>45 (1.2)</td>
<td>53 (1.4)</td>
<td>0.421</td>
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</tbody>
</table>

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Evaluation of the FILMARRAY pneumonia plus panel for rapid diagnosis of hospital-acquired pneumonia

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Background: Early appropriate antimicrobial therapy reduce the risk of pneumonia-related morbidity and mortality in critical care patients. Nevertheless, current culture methods take at least 48 hours to obtain antimicrobial susceptibility results. The new FilmArray® Pneumonia plus Panel (FAPP) offers advantage to rapidly detect and quantify in a single test, 18 bacteria, 9 virus, and 7 antibiotic resistance genes. This test was compared to conventional bacterial culture in 85 patients suspected of having hospital-acquired pneumonia (HAP).

Materials/methods: 207 respiratory samples from 85 patients [64 bronchoalveolar lavages (BALDs) and 74 endotracheal aspirates (ETADS) obtained at the time of HAP diagnosis, and 69 ETA obtained 2-3 days later (ETATT)], were analyzed in parallel by routine microbiology testing and FAPP at the laboratory of the Nantes University Hospital. Results of FAPP were not reported to clinicians. Routine microbiology testing were analyzed independently of FAPP.

Results: 60/85 (70.59%) patients had a positive result for at least one bacterial pathogen at the time of diagnosis by culture [43/64 (67.19%) BALDs and 46/74 (62.16%) ETADS], compared to 71/85 (83.53%) for FAPP [50/64 (78.13%) BALDs and 59/74 (79.33%) ETADS]. Among 53 patients with paired BALDs and ETADS, 77.36% had the same result for both samples with conventional method, compared to 66.04% for FAPP. Among positive samples, polybacterial results were obtained for 23/43 (53.49%) BALDs, 19/46 (41.30%) ETADS, and 7/30 (23.33%) ETATT by culture vs 30/50 (60.00%) BALDs, 37/59 (62.71%) ETADS, and 32/49 (65.31%) ETATT for FAPP. Haemophilus influenzae, the most frequent species detected by FAPP (33 patients at diagnosis), was not always identified in culture (24 patients at diagnosis). A carbapenemase and/or an ESBL were detected with both methods in 7 patients.

Conclusions: Overall, FAPP detected the main bacterial respiratory pathogens with greater sensitivity than culture. The concordance between both methods was higher for BAL, less contaminated with microbial flora. In case of polymicrobial specimen, FAPP facilitated the detection of bacterial pathogens. Implementing this strategy on BAL should improve and accelerate clinical decision and isolation care. We are currently measuring the extent to which FAPP results would have modified antimicrobial prescription and costs of care.

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Differentiate diagnosis active TB infection and latent TB infection by using Interferon-\(\gamma\) released from CD8+ T cell and HBHA antigen

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Background: There is about 1/3 of the world population infected with Mycobacterium tuberculosis (MTB). Among them, about 90-95% got latent infections, and only 5-10% of people have diseases. Interferon-\(\gamma\) release assay (IGRA) can be used to identify MTB infection, but it cannot differentiate active tuberculosis (ATB) and latent TB infection (LTBI). Because QuantiFERON-TB Gold Plus (QFT-Plus) can detect Interferon-\(\gamma\) released from CD8+ T cell in most ATB patients, and HBHA is highly expressed in latent TB, we would like to evaluate the potential differential diagnostic value between LTBI and ATB groups.

Materials/methods: 108 healthy people and 30 ATB patients were tested by QFT-Plus, and their demographic characteristics were analyzed. Meanwhile, flow cytometry was used to analyze the relationships between the QFT-Plus TB2-TB1 and the distribution of peripheral blood T lymphocyte subsets in ATB patients with positive culture results. Finally, 34 volunteers with positive QFT-Plus results were selected as LTBI group, 30 ATB patients with bacteriology confirmed as ATB group, the QFT-Plus newly added antigen and its potential differential diagnostic value between LTBI and ATB groups was evaluated by using the receiver operating curve (ROC). At the same time, 22 LTBI and 40 ATB patients were tested by using IGRA with HBHA antigen. Its potential differential diagnostic value between LTBI and ATB groups was evaluated by using ROC.

Results: In patients with ATB, TB2-TB1 was positively correlated with the proportion of CD8+ T cells in peripheral blood T lymphocytes \(r = 0.586, P = 0.004\), negatively correlated with the proportion of CD4+ T cells \(r = -0.511, P = 0.015\) and the ratio of CD4/CD8 \(r = -0.520, P = 0.013\). TB2-TB1 and HBHA has potential value for differentiating LTBI and ATB with AUC=0.771 [95%CI = 0.653-0.889] and AUC=0.886 [95%CI = 0.791-0.982]. When the cut-off value of TB2-TB1 is 0.305 IU/mL, its sensitivity and specificity for ATB are 66.7% and 79.4%. When the cut-off value of HBHA is 22.37 pg/mL, its sensitivity and specificity for LTBI are 86.4% and 82.5%.

Conclusions: Both of QFT-Plus and HBHA have the potential diagnostic value to identify ATB and LTBI.

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Abstract 4255

Evaluation of the Allplex H. pylori and ClariR Assay PCR kit on gastric biopsies
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Background: The diagnosis of *Helicobacter pylori* infection can be made by PCR in gastric biopsies. The objective of this study was to evaluate retrospectively the performance of the Allplex™ *H. pylori* & ClariR Assay PCR kit (Seegene).

Materials/methods: A collection of 180 DNAs extracted from gastric biopsies was used in this study: 90 DNAs from *H. pylori*-negative patients and 90 from *H. pylori*-positive patients (10 culture-NEG/PCR-POS and 80 culture-POS/PCR-POS) (38 *H. pylori* wild-type [WT], and 52 *H. pylori* mutated). The average age of these patients was 48.3 years (+/- 18.6 years) with a sex ratio of 0.72. Allplex™ *H. pylori* PCR was performed on a CFX96™ real-time PCR System and analyzed using the Seegene Viewer software. The real-time PCR used as reference was our in-house *H. pylori* PCR (Oleastro M et al. J Clin Microbiol 2003) and discrepant results were tested by the Amplidiag PCR *H. pylori* kit (Mobidiag).

Results: The performances of Allplex™ *H. pylori* PCR are shown on the table. Regarding the detection of *H. pylori* in the 90 expected negative samples, 10 late amplifications were obtained (Ct >39). 7 of these 10 samples were also positive using the Amplidiag PCR *H. pylori* kit and were therefore considered a true positives.


<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Specificity</td>
<td>96.7</td>
<td>100</td>
</tr>
<tr>
<td>PPV</td>
<td>96.8</td>
<td>100</td>
</tr>
<tr>
<td>NPV</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

data in %; PPV: positive predictive value; NPV: negative predictive value

Conclusions: The Allplex™ *H. pylori* PCR kit has excellent performances and can be integrated into the armamentarium of diagnostic tests for *H. pylori* infection. This kit has the advantage of differentiating the main mutations (A2142G, A2143G and A2142C) associated with macrolide resistance.

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Abstract 4256

Stopping exposing rifampicin-resistant *Mycobacterium tuberculosis* to further rifampicin may lead to reversion to wildtype, preventing the evolution of compensating mutations

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Abstract third-party references: On behalf of the CRyPTIC consortium

**Background:** Rifampicin is one of four drugs in the standard first-line regime for treating tuberculosis. Resistance arises primarily through mutations in the *rpoB* gene, notably Ser450Leu which interferes with rifampicin binding. This mutation has been shown *in vitro* to confer a fitness cost which can be compensated by mutations in the adjoining *rpoC* gene.

**Materials/methods:** 10,000 clinical tuberculosis samples from the Comprehensive Resistance Prediction for Tuberculosis: an International Consortium (CRyPTIC) project were analysed. Each sample has (i) whole genome sequencing data, (ii) rifampicin minimum inhibitory concentrations (MICs), and (iii) granular growth data. The last two were measured using 96-well broth microdilution plates with the MICs measured independently by laboratory scientist, computer software and citizen scientists.

**Results:** Rifampicin-resistant strains with no known compensatory mutations in *rpoC* grow significantly slower (19.2 ± 0.4%, 95% CI) than rifampicin-susceptible strains (20.6 ± 0.3%). Rifampicin-resistant strains that do contain an *rpoC* compensatory mutation grow significantly better (23.1 ± 0.5%). The magnitude of compensation depends on the precise mutation, with several mutations growing markedly better on the microtitre plate than wildtype (e.g. V483A 25.8 ± 1.3%, I491V 24.6 ± 1.0%). This is consistent with these mutations also being fitter *in vivo*. In addition, multiple genetic signatures of reversion to wildtype at Ser450 were present (1.3% of samples with a mutation at position 450 in *rpoB* had ≥2 base changes in the codon). Crucially, these two effects, compensation and reversion, were mutually exclusive.

**Conclusions:** The slower growth of rifampicin-resistant strains collected by CRyPTIC can be explained, in part, by the known fitness cost of the *rpoB* Ser450Leu mutation. This effect can be mitigated by an increasingly large list of mutations in the *rpoC* gene, some of which grow faster than wildtype. The reversion signatures can be explained if removing rifampicin prior to any compensatory mutation arising can lead to a reversion to susceptibility. Alternatively, continuing to expose *M. tuberculosis* to rifampicin once resistance has arisen can lead to strains that grow faster than wild-type *in vitro*, potentially "locking in" rifampicin resistance.

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Burkholderia spp. and Gram-negative non-fermenters in cystic fibrosis patients in Belgium: 2012-2018
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Background: Burkholderia cepacia complex (BCC) bacteria are human pathogens, especially infecting cystic fibrosis (CF) patients as well as hospitalized immunocompromised patients. CF patients are also infected by other Gram negative non-fermenters (GNNF). These pathogens cause frequent and recurrent infective exacerbations in CF patients that can lead to premature death. As national reference centre (NRC) of Belgium, our main purpose is the surveillance of BCC and GNNF (except Pseudomonas aeruginosa and Acinetobacter) mainly in CF patients. The current work is a survey of BCC-GNNF data from 2012 to 2018.

Materials/methods: Each year, we receive BCC and GNNF isolates from each colonized patient. The isolates are quickly identified by MALDI TOF MS (Bruker) and genotyped by Random Amplification of Polymorphic DNA. The identification and genotyping are then confirmed by sequence analysis and by MLST respectively.

Results: From 2012 to 2018 we received 788 BCC-GNNF isolates from 673 patients. A total of 183 BCC and other Burkholderia spp. were received; 59% were Burkholderia multivorans, followed by Burkholderia vietnamiensis (16%) and Burkholderia cenocepacia (12%). A total of 605 GNNF were received, 49% of which were Achromobacter spp., followed by Stenotrophomonas maltophilia (23%) and other species at lower proportions.

Of the 294 Achromobacter spp. received, 68% were Achromobacter xylosoxidans and 16% Achromobacter insuavis. Other species were present at lower proportions.

ST-739 and ST-741 were the most frequent types for Burkholderia multivorans. ST-137 and ST-175 were the most frequent types for Achromobacter xylosoxidans.

Conclusions: BCC number declined while GNNF number increased over the years.

Not all Belgian centres are referring isolates. More centres should include isolates for a better representation over the whole country.

Frequent ST such as Achromobacter xylosoxidans ST-137 should be further investigated. This type is also frequent among CF patients in France.

Presenter email address: denis.pierard@uzbrussel.be
An outbreak of scabies in the north-east region of Ghana

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¹Komfo Anokye Teaching Hospital and Kumasi Centre for Collaborative Research, Kumasi, Ghana, ²Kwame Nkrumah University of Science and Technology, Kumasi Centre for Collaborative Research, Kumasi, Ghana, ³Komfo Anokye Teaching Hospital, Kumasi, Ghana, ⁴East Mamprusi Municipal Health Directorate, Kumasi, Ghana, ⁵Kwame Nkrumah University of Science and Technology, Kumasi Centre for Collaborative Research, Kumasi, Ghana, ⁶Ghana Health Service, Accra, Ghana, ⁷University Medical Center, Groningen, Netherlands

Background: Scabies is a parasitic disease of the skin with high global burden. In September 2019, there were reports of scabies among communities in the East Mamprusi Municipality of Ghana’s North East Region. The municipal health team treated individual patients with scabies within the communities. Due to continued reports of scabies, a medical team visited the district to further assess the scabies burden.

Materials/methods: Persons were invited to participate in an interview during house and school visits. All participants underwent a standardised history and skin examination using a REDCap based questionnaire. The diagnosis of scabies was based on criteria developed by the International Alliance for the Control of Scabies (IACS). Impetigo was diagnosed based on standard criteria.

Results: In all, 283 participants were interviewed. The majority were female (n=174, 61%) and the median age of the participants was 19 (IQR 13-25) years old. Itch was reported by 79% participants with a median duration of 30 days (IQR 21-60). Twenty-five (27%) of 93 high school students with scabies were treated with benzyl benzoate in the past two months compared to 57% of 190 community members. Nevertheless, the prevalence of scabies was 7.1% based on the IACS diagnostic criteria. Only 3% of the participants had no known scabies contact in the past weeks. Ninety four (47%) of the participants had moderate and 71 (35.5%) had severe scabies and 53 (18.7%) had impetigo.

Conclusions: The prevalence of scabies was extremely high in this population. IACS diagnostic criteria of scabies were helpful to assess the burden of the outbreak. Earlier treatment of individuals without treatment of contacts, did not reduce the scabies burden. Mass drug administration (MDA) is needed to substantially reduce the burden of scabies in this population. To control such outbreaks, and to develop a global control programme, studies on optimal implementation of MDA, especially in larger, non-isolated areas are desperately needed.

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**Abstract 4260**

**Infection control, antimicrobial consumptions and incidence of hospital-acquired *Clostridioides difficile* infection in acute care hospitals in Catalonia**

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**Background:** Hospital-acquired *Clostridioides difficile* infection (HA-CDI) is a major infection control (IC) challenge. We hypothesized that variations in HA-CDI rates between hospitals could be attributable either to differences in IC policies or to antimicrobial consumption (Antimicrob-C).

To assess the association of HA-MRSA rates (a surrogate marker of IC policies) and Antimicrob-C with HA-CDI incidence from 2011 to 2018 in hospitals reporting at the VINCat-program (IC and Antimicrobial Stewardship Catalan Program)

**Materials/methods:** Data on 45 hospitals (with 70.5% of all adult acute-hospital beds) reporting Antimicrob-C, HA-MRSA and HA-CDI new cases to the VINCat-program have been analysed. To report the Antimicrob-C the ATC/DDD index 2018 was used. Participating hospitals were classified into three groups: Group-I (>500 beds): 9 hospitals, Group-II (500-200 beds): 15 hospitals, Group-III (<200 beds): 21 hospitals. The number of hospitalization-days recorded at the participating hospitals increased from 2,828,101 in 2011 to 3,201,680 in 2018.

To analyze the association between study outcome HA-CDI rate and the Antimicrob-C rate as main exposure, a Poisson regression model was used. HA-MRSA rate, year and hospital group were included in the model as confounding factors that could bias the relationship between the outcome and the main exposure. The exponents of model coefficients are equal to incidence rate ratios (IRR).

**Results:** The table shows the HA-MRSA and HA-CDI rates and DDD/100 bed-days per year.

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>New HA-MRSA cases/1000-Stays</td>
<td>0.538</td>
<td>0.537</td>
<td>0.508</td>
<td>0.5</td>
<td>0.537</td>
<td>0.602</td>
<td>0.67</td>
<td>0.725</td>
</tr>
<tr>
<td>New HA-CDI cases/10000-Stays</td>
<td>0.991</td>
<td>1.115</td>
<td>1.18</td>
<td>1.589</td>
<td>1.576</td>
<td>1.552</td>
<td>1.681</td>
<td>1.551</td>
</tr>
<tr>
<td>DDD/100 bed-days</td>
<td>63.32</td>
<td>67.03</td>
<td>64.54</td>
<td>68.47</td>
<td>69.64</td>
<td>71.13</td>
<td>73.58</td>
<td>69.75</td>
</tr>
</tbody>
</table>

The regression model showed a positive association between Antimicrob-C and HA-CDI rates (IRR = 1.01, CI 95% 1.01 – 1.02 p<0.001). The percent change in HA-CDI incident rate is by 1% for every 10 DDD increase in Antimicrob-C rate, independently of HA-MRSA rate, year and hospital group. Likewise, the incident rate for HA-MRSA was significantly associated to HA-CDI (IRR = 1.68, CI 95% 1.36-2.07 p<0.001).

**Conclusions:** This study shows a clinically relevant association between HA-CDI and Antimicrob-C rates. Results suggest that antimicrobial stewardship programs are needed to improve the control of HA-CDI in Catalonia.

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Reduced clinical improvement after treatment for urethritis in men with azithromycin resistant Mycoplasma genitalium

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Abstract third-party references: Department of Infectious Diseases Research and Prevention, Public Health Service of Amsterdam, Amsterdam, the Netherlands;

Background: Mycoplasma genitalium (MG) is associated with urethritis in men. Clinical improvement in men treated syndromically for urethritis was examined and correlated to MG positivity and macrolide resistance.

Materials/methods: Urethritis was defined as the presence of >10 leucocytes per high power field in Gram stains of urethral discharge in men with urethritis symptoms. Additional presence of intracellular gram-negative diplococci defined gonococcal urethritis. Point-of-care therapy for gonococcal urethritis was 1000mg ceftriaxone IM and for non-gonococcal urethritis 1000mg azithromycin PO. From 15th May 2018 until 4th September 2019 urine samples of all men with urethritis were tested for Neisseria gonorrhoeae (NG), Chlamydia trachomatis (CT), and MG using TMA assays (Aptima, Hologic). Macrolide resistance-associated mutations in MG were detected by PCR. Patients received a question about clinical improvement in a text message two weeks after therapy.

Results: The study included 2033 men with 2181 episodes of urethritis. Of all episodes, 584/2181 (27%) patients had NG, 666/2181 (31%) CT, and 497/2181 (23%) MG. Macrolide sensitivity of MG infections could be determined in 350 (70%) samples of which 259 (74%) were macrolide resistant. Of the 640 (31%) text message responders 509 (80%) indicated that their symptoms were reduced or gone (table 1). The improvement percentage was lower for patients infected with MG compared to those without MG infection. Patients with macrolide resistant MG (46/79, 58%) reported less often improvement compared to patients with macrolide sensitive MG (20/24, 83%) (p=0.025) especially in patients with resistant MG without CT or NG co-infection (26/53, 49%).

Conclusions: Patients with urethritis and macrolide resistant MG had a worse clinical outcome after standard treatment compared to patients with macrolide sensitive MG or without MG infection. The clinical utility of testing for MG and macrolide resistance among men with urethritis should be evaluated.

Table 1: Treatment success among 640 patients with urethritis responding to text message.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Improved or cured</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>640</td>
<td>509(80%)</td>
<td></td>
</tr>
<tr>
<td><strong>Infections, regardless of co-infections</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NG-</td>
<td>480</td>
<td>383(76%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NG+</td>
<td>160</td>
<td>146(91%)</td>
<td></td>
</tr>
<tr>
<td>CT-</td>
<td>442</td>
<td>348(78%)</td>
<td>0.46</td>
</tr>
<tr>
<td>CT+</td>
<td>188</td>
<td>181(81%)</td>
<td></td>
</tr>
<tr>
<td>MG-</td>
<td>487</td>
<td>414(83%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MG+</td>
<td>143</td>
<td>95(66%)</td>
<td></td>
</tr>
<tr>
<td>Macrolide sensitive</td>
<td>24</td>
<td>20(83%)</td>
<td>0.025</td>
</tr>
<tr>
<td>Macrolide resistant</td>
<td>79</td>
<td>46(58%)</td>
<td></td>
</tr>
</tbody>
</table>

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Prevalence of macrolide resistance mutations in *Mycoplasma pneumoniae* from patients with respiratory tract infections in European Russia

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Background: *Mycoplasma pneumoniae* (*MPN*) is the most common ‘atypical’ bacterium causing lower respiratory tract infections (LRTI). Macrolides (ML) are the drugs of choice for treating *MPN* infections, however, in recent years; there have been numerous reports of emerging ML -resistance in *MPN*. *MPN* is a fastidious, difficult to culture organism, which is why routine phenotypic detection of resistance is extremely challenging and impractical. We aimed to assess the prevalence of M-resistance in *MPN* in Russia, using real-time PCR detection of macrolide resistance-associated mutations directly from clinical specimens.

Materials/methods: We collected 1 324 non-duplicate *MPN*-positive throat swabs for by routine diagnostic PCR from patients with LRTI, mostly pneumonia (n=1052), in seven cities in the European part of Russia from 2013 to 2019 (606 samples were collected during the peak incidence of community pneumonia in 2018). ML-resistance mutations in the 23S rRNA gene were detected using real-time PCR assay and confirmed by the independent PCR and sequencing. The data on identification of ML-resistance genotypes of *MPN* were deposited to the AMRmap web site (http://AMRmap.net), an online platform for the analysis of AMR surveillance data in Russia.

Results: A total of 258 (19.5%) of the 1324 samples revealed the presence of ML-resistance mutations in the 23S rRNA gene of *MPN*. The detected genotypes were (in order of decreasing prevalence): A2058G [216/1324, 16.3%] and A2059G [33/1324, 2.5%], A2062C [2/1324, 0.2%], A2062G [1/1324, <0.1%]. Five rare double- and triple-mutation genotypes were detected for the first time: A2058G+2059G [4/1324, 0.3%], A2059G+2062C [2/1324, 0.2%], A2058G+2059G+2062C [1/1324, <0.1%], and A2058G+A2059G+A2062C [1/1324, <0.1%].

Conclusions: This study revealed high prevalence (19.5%) of macrolide resistance mutations in *MPN* in the European part of Russia, but decreased prevalence (15.3%) during the outbreak period in 2018.

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**Impact of proposed revised EUCAST breakpoints on susceptibility classification of contemporary Danish mould isolates**

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**Background:** EUCAST breakpoints v 9.0 are undergoing revision following the revised definition of the "I" category from "Intermediate" to "Susceptible, Increased exposure". An area of technical uncertainty (ATU) has been proposed for several compounds and species. For isavuconazole and posaconazole, the recommendations are to interpret an MIC in the ATU as S or R dependent on the susceptibilities to voriconazole and itraconazole, respectively. For voriconazole and itraconazole, the recommendation is to report as R with the following comment: "In some clinical situations (non-invasive infections) voriconazole/itraconazole can be used provided a sufficient exposure is ensured". Here, we compare susceptibility classifications according to the current and proposed EUCAST breakpoints.

**Materials/methods:** 639 Aspergillus isolates obtained during 2018. E.Def 10.1 screening for azole-R. A. fumigatus. E.Def 9.3.1 susceptibility testing of non-S and a selection of S A. fumigatus (N=217-253 for voriconazole, itraconazole and posaconazole) and other Aspergillus species isolates. Isolates from the same patient with identical species and susceptibility patterns were excluded if sampled less than 21 days apart. EUCAST breakpoints v 9.0 and proposed v 10.0 were compared for susceptibility classification. Fisher’s test was used for statistical analysis.

**Results:** With the proposed breakpoints, statistically significant changes in resistance were seen for A. fumigatus for isavuconazole and voriconazole. For the remaining species, no or slight increases in the numbers of resistant isolates were found. Of note, the numeric increase in itraconazole R A. terreus was due to several resistant isolates from one patient and not nationwide increased resistance. For isavuconazole and posaconazole, the breakpoint revision affected the S-category for A. fumigatus, as more (92.8% vs. 77.4%) were isavuconazole S and 11/15 isolates currently classified as posaconazole I were classified as S (93.2% vs. previously 91.3%).

**Conclusions:** Adoption of the proposed EUCAST breakpoints v 10.0 on contemporary Danish Aspergillus isolates resulted in a uniform susceptibility classification across the azoles in line with clinical experience. The ATU has been introduced to avoid misclassifications where S and R populations overlap. This has reduced the number of misclassifications of isavuconazole and posaconazole wild-type isolates as non-susceptible.

**Table.** Comparison of MICs (mg/L) and percent resistant isolates using the v 9.0 and proposed v 10.0 EUCAST breakpoints (BPs). Proposed S/R/ATU are included (mg/L) and those deviating from current ones are underlined. P-values are included in parenthesis where statistically significant (P<0.05) change in susceptibility is seen. (NA: not available, No BP: no breakpoints established for that drug and species)

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Clinical profile of patients with bacteraemia caused by Enterobacter cloacae and Klebsiella aerogenes: more similarities than differences

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Background: The genus Enterobacter is among the main etiologies of nosocomial infections, composed by species that share diverse phenotypic and genotypic features, as a constitutive β-lactamase AmpC. Historically, the most frequent Enterobacter species at the clinical setting were those belonging to the E. cloacae complex and E. aerogenes. In 2018, E. aerogenes has been classified as Klebsiella aerogenes, due to its greater genotypic similarity with the genus Klebsiella. Our objective was to characterize and compare the clinical profile [risk factors, presentation, prognosis] of the bacteraemias caused by E. cloacae and K. aerogenes.

Materials/methods: Prospective cohort study. Multicentre [five university Spanish hospitals]. Period: 3 years. All the patients with bacteraemia caused by E. cloacae or K. aerogenes were included. Species were identified with MALDI-TOF. We analysed baseline characteristics [chronic comorbidities, previous therapies, invasive devices], features of the bacteraemia [source, severity, treatment], microbiological characteristics [susceptibility to antibiotics, resistance mechanisms] and prognosis [30-days mortality]. Statistical analyses were performed with SPSS.

Results: The study included 285 patients, 196 (68.7%) with E. cloacae and 89 (31.3%) with K. aerogenes. Both groups showed no differences in age, sex, most comorbidities, previous invasive devices, place of acquisition, sources or severity, but they differed in the Charlson score and previous antibiotic therapy [table]. Venous catheter was the most frequent source [31.1% for E. cloacae and 29.2% for K. aerogenes, p=0.608]. Mortality was 19.4% for E. cloacae and 20.2% for K. aerogenes, p=0.869. Susceptibility to antibiotics was similar for both species, except for cefepime and imipenem.

<table>
<thead>
<tr>
<th></th>
<th>E. cloacae</th>
<th>K. aerogenes</th>
<th>Bivariate p</th>
<th>Multivariate OR [95% CI] p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Charlson med(IQR)</td>
<td>2 (1.4)</td>
<td>1 (0.5-3)</td>
<td>0.025</td>
<td>0.86 [0.76-0.97] 0.018</td>
</tr>
<tr>
<td>Haemodialysis n(%)</td>
<td>28 (14.3%)</td>
<td>1 (1.1%)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Previous antibiotics n(%)</td>
<td>81 (41.3%)</td>
<td>38 (57.3%)</td>
<td>0.012</td>
<td>1.97 [1.18-3.29] 0.010</td>
</tr>
<tr>
<td>Previous carbapenems n(%)</td>
<td>11 (5.6%)</td>
<td>11 (12.4%)</td>
<td>0.048</td>
<td></td>
</tr>
<tr>
<td>Severe sepsis/septic shock n(%)</td>
<td>47 (24%)</td>
<td>15 (16.9%)</td>
<td>0.207</td>
<td></td>
</tr>
<tr>
<td>ESBL n(%)</td>
<td>13 (6.6%)</td>
<td>2 (2.2%)</td>
<td>0.124</td>
<td></td>
</tr>
<tr>
<td>Carbapenemases n(%)</td>
<td>1 (0.5)</td>
<td>0 (0)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>S cefepime n(%)</td>
<td>144 (73.5)</td>
<td>75 (84.3)</td>
<td>0.050</td>
<td></td>
</tr>
<tr>
<td>S imipenem n(%)</td>
<td>164 (83.7)</td>
<td>83 (93.3)</td>
<td>0.037</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Bacteraemias caused by E. cloacae and K. aerogenes share a similar profile of patients, presentation and prognosis. Patients with E. cloacae had more comorbidities and those with K. aerogenes had received more antibiotics.

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Abstract 4269

**Respiratory co-infections by Pneumocystis jirovecii and other pathogens in non-HIV immunosuppressed patients: a retrospective review**

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**Abstract third-party references:** Fundació Docència i Recerca Mútua Terrassa

**Background:** Pneumocystis jirovecii pneumonia (PJP) is an increasing, life-threatening infection in non-HIV immunosuppressed patients. Clinical implications of coinfection with other respiratory pathogens are poorly described.

Our aim was to describe clinical characteristics and prognosis of patients with PJP and other respiratory coinfections.

**Materials/methods:** Multicentre, observational, retrospective study. Setting: five acute-care teaching hospitals. Period: January-2011 to August-2017. Cases: adult patients diagnosed with PJP and other bacterial, fungal or viral coinfection in a respiratory specimen in a susceptible host with compatible clinical syndrome and radiologic characteristics.

**Results:** One hundred and fifteen patients were included; 63 (55%) presented respiratory coinfection. Thirty-two patients (28%) presented viral coinfection, mostly cytomegalovirus (18; 56%). Nineteen patients (16%) had bacterial coinfection. Six patients (5%), fungal coinfection; all of them were Aspergillus spp. Patients with Aspergillus coinfection had a solid malignancy in 70%, received high-dosing corticosteroids in 83% and presented with serious respiratory failure (median PFR of 194, IQR 160-220).

Differences between co-infected and no-coinfected patients are shown in Table 1:

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coinfection (63; 55%)</th>
<th>No-coinfection (52; 45%)</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age*</td>
<td>65 (52-71)</td>
<td>59 (47-69)</td>
<td>0.16</td>
</tr>
<tr>
<td>Male</td>
<td>44 (70)</td>
<td>26 (50)</td>
<td>0.03</td>
</tr>
<tr>
<td>COPD/bronchiectasias</td>
<td>13 (21)</td>
<td>6 (11)</td>
<td>0.6</td>
</tr>
<tr>
<td>Solid malignancy</td>
<td>15 (24)</td>
<td>13 (25)</td>
<td>0.8</td>
</tr>
<tr>
<td>Hematological malignancy</td>
<td>28 (44)</td>
<td>21 (40)</td>
<td>0.6</td>
</tr>
<tr>
<td>Systemic autoimmune disease</td>
<td>16 (25)</td>
<td>12 (23)</td>
<td>0.7</td>
</tr>
<tr>
<td>High-dose steroids(^1)</td>
<td>41 (65)</td>
<td>25 (48)</td>
<td>0.05</td>
</tr>
<tr>
<td>Days of symptoms(^*)</td>
<td>3 (1-7)</td>
<td>7 (3-11)</td>
<td>0.003</td>
</tr>
<tr>
<td>Bronchoalveolar pattern (chest X-ray)</td>
<td>27 (43)</td>
<td>8 (16)</td>
<td>0.001</td>
</tr>
<tr>
<td>Lymphocyte count(^2) ((\text{mm}^3))(^*)</td>
<td>600 (395-1025)</td>
<td>600 (300-1100)</td>
<td>0.8</td>
</tr>
<tr>
<td>LDH(^2) (IU/L)(^*)</td>
<td>445 (7835)</td>
<td>807 (472-1151)</td>
<td>0.04</td>
</tr>
<tr>
<td>Days until diagnosis(^*)</td>
<td>5 (3-9)</td>
<td>4 (1-6)</td>
<td>0.006</td>
</tr>
<tr>
<td>ICU admission</td>
<td>30 (48)</td>
<td>20 (38)</td>
<td>0.3</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>29 (47)</td>
<td>15 (29)</td>
<td>0.05</td>
</tr>
<tr>
<td>Days of stay(^*)</td>
<td>30 (16-52)</td>
<td>15 (11-32)</td>
<td>0.001</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>25 (57)</td>
<td>14 (54)</td>
<td>0.8</td>
</tr>
</tbody>
</table>

\(^1\)Median, interquartile interval [IQR]. \(^2\)\(\geq 16-20 \text{ mg/day of prednisolone (or equivalent dose), } \geq 4 \text{ weeks.} \(^*\)At diagnosis.

**Conclusions:** More than a half of patients with PJP presented respiratory coinfection, mostly viral. Co-infected patients had longer diseases and a bronchoalveolar radiological pattern. Mechanical ventilation was more frequent and hospital stay longer in co-infected patients but in-hospital mortality was similar in both groups.

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Bloodstream infections caused by *Staphylococcus aureus* non-susceptible to daptomycin: clonal and clinical aspects

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Background: *Staphylococcus aureus* is one of the leading pathogens isolated from bloodstream infections (BSI). Vancomycin or daptomycin have been the main choice of therapy for MRSA (methicillin-resistant *S. aureus*) BSI. VISA (vancomycin-intermediate *S. aureus*), hVISA (heteroresistant-VISA), and non-susceptibility to daptomycin strains have already been described. This study aimed to evaluate clinical aspects associated with the resistance and clonality of *S. aureus* isolated from BSI, between 2016 and 2018.

Materials/methods: minimum inhibitory concentrations (MICs) were evaluated for five antimicrobials by the broth microdilution method. MICs for ceftaroline and vancomycin of the MRSA isolates were determined by the E test®. Screening with BHI agar added with vancomycin and the population profile/area under the curve (PAP/AUC) test were used to diagnose VISA/hVISA. SCCmec type was evaluated by PCR and the clonal profile by PFGE method. The patient’s clinical data were analyzed in association with the microbiological one.

Results: Among 123 *S. aureus* isolates from BSI, 31% were MRSA. MIC₅₀ and MIC₉₀ values were: 2 / 2 µg/mL to daptomycin; 1 / 1 µg/mL to linezolid; 1 / 256 µg/mL to oxacillin; 0.5 / 0.5 µg/mL to teicoplanin and 1 / 1 µg/mL to vancomycin. MIC values for ceftaroline and vancomycin by the E test® were 0.75 and 2 µg/mL. 75% of the isolates were not susceptible to daptomycin. Clonal lineages and SCCmec types found were USA100/ST5-II (50%), USA800/ST5-IV (22%), USA300/ST8-IV (16%), USA1100/ST30-IV (5%), BEC/ST239-III (5%) and one isolate carrying SCCmecV/ST1. One VISA and three hVISA isolates were found, associated with the USA100 and USA300 lineages. MRSA isolates were prevalent in patients had vascular catheter (85%). Age (67.5 versus 58 years; p=0.03) and mortality was associated with MRSA infections (55.6% versus 36.6%; p=0.04). End-stage renal disease was associated with MSSA infections (50.7% versus 27.3%; p=0.03).

Conclusions: Daptomycin non-susceptibility, VISA and hVISA phenotypes were associated with prevalent clonal lineages. These strains had no impact on mortality.

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Incidence rates of multidrug-resistant indicator pathogens increase in hospitalised horses during stay
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Abstract third-party references: Federal Ministry of Education and Research (BMBF) (project numbers 01K11727D and 01K11727F)

Background: In previous studies, veterinary clinics were recognized as hot-spots for spread of multidrug-resistant (MDR) opportunistic and zoonotic pathogens such as Staphylococcus aureus (MRSA) and extended-spectrum beta-lactamase producing Escherichia coli (ESBL-E). Strategies to decrease the MDR incidence rates among hospitalized horses include hygiene management improvements and evidence-based antibiotic stewardship (ABS). Here we present preliminary data on MDR incidence rates obtained from horses suffering from colic receiving divergent perioperative antibiotic regimes.

Materials/methods: Horses subjected to laparotomy were assigned to two distinct groups defined by the length of their antibiotic courses. The first group was treated with the conventional protocol [CP], i.e. perioperative administration of a penicillin/gentamicin combination for five days. The second group of horses received the same combination, but this protocol includes a single shot [SP] prior to colic surgery only. Fecal samples and nostril swabs were collected directly at hospital admission (t0) as well as on days three (t1) and 10 (t2) after surgery. All samples were screened for ESBL-E and MRSA using microbiological diagnostics.

Results: So far, incidence rates were available for 77 horses receiving abdominal surgery. Due to different medical conditions, mainly defecation problems and sudden death or euthanasia due to animal welfare, some fecal samples were not available. Overall, 10% of the valid fecal samples from t0 (n=50) were positive for ESBL-E. coli and 7% of the valid nostril swabs (n=76) were positive for MRSA. In the CP group, the ESBL-E incidence rate raised to 67% at t1 and t2, while the MRSA carriage rates increased to 49% (t1) and 50% (t2). With a rate of 40% for ESBL-E and 24% for MRSA, the SP group showed lower incidences at t1 compared to the CP group. However, on day ten of the hospital stay (t2), the incidences reached those of the CP group for enteral carriage of ESBL-E (65%), while the MRSA rate (30%) was still lower.

Conclusions: MDR indicator pathogen incidence rates increase in horses with laparotomy over time. Further efforts with respect to ABS and targeted hygiene regimes are needed to counteract MDR accumulation among hospitalized horses.

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Abstract 4275

Suitability of ceftazidime for continuous infusion in outpatient parenteral antimicrobial therapy

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Abstract third-party references: On behalf of Members of the BSAC Working Group on Drug Stability Testing

Background: Ceftazidime is a beta-lactam cephalosporin used to treat Gram-negative bacterial infections, including Pseudomonas aeruginosa. Ceftazidime is unstable in aqueous solution leading to the formation of pyridine, a toxic degradation product. Safe use of ceftazidime in an outpatient parenteral antimicrobial therapy (OPAT) setting relies on controlling its temperature and concentration. Administration of ceftazidime in elastomeric devices would provide a convenient option for OPAT services. This study sought to establish extending the shelf-life for ceftazidime in aqueous solution in two different elastomeric devices at two different concentrations commonly used in clinical practice. The study design was to meet the acceptance criteria of the UK National Health Service (NHS) Yellow Cover Document (YCD) requirements and for pyridine the British Pharmacopoeia (BP) limit to ensure patient safety.

Materials/methods: Stability of ceftazidime was assessed according to latest UK NHS YCD and BP requirements in two different 1 day elastomeric devices and concentrations (0.9% w/v saline at 12 mg/mL and 25 mg/mL). Devices were stored at 2-8°C for 48 hours, room temperature for 3 hours and 32°C for 12 hours. Concentrations of ceftazidime and pyridine were assayed using a validated LC method.

Results: The BP limit for loss of ceftazidime solutions for injection is 90-110%; while pyridine levels are limited to not more than (0.5% (w/w). Recorded losses of ceftazidime and pyridine levels were within these limits following storage at 2-8°C for 48 hours and 12 hours infusion.

Conclusions: Ceftazidime can be formulated and stored for 48 hours at 2-8°C followed by a 12-hour infusion period at 32°C while maintaining acceptable concentrations of active ingredient; at the same time pyridine levels did not exceed the BP limit. Our data show there is a role for ceftazidime infusion over 12 hours for OPAT services which have the capacity to prepare devices and use them within 48 hours. This model will not suit all OPAT services but provides a useful treatment option for services which can deliver it and can help to reduce the reliance on broad spectrum agents such as piperacillin/tazobactam and meropenem.

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Abstract 4276

**Increased carriage of ESBL-producing Enterobacteriaceae among men who have sex with men**

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**Background:** Carriage of rectal extended spectrum β-lactamase Enterobacteriaceae (ESBL-E) occurs in 5.0% of the Dutch population. Several studies suggest that men who have sex with men (MSM) might be at increased risk for carriage of resistant bacteria. We aimed to determine the prevalence and determinants of rectal ESBL-E carriage among MSM in Amsterdam, the Netherlands.

**Materials/methods:** We screened MSM participating in the Amsterdam Cohort Study for rectal ESBL-E carriage between April and December 2018. Self-administered questionnaires were used to measure sexual behavior and possible risk factors for antibiotic resistance. Determinants of ESBL-E carriage were identified using logistic regression analysis.

**Results:** We included 583 MSM, of whom 141 (24%) reported use of antibiotics within the last 6 months. In total, 16.3% (95%-confidence interval (CI) 13.3-19.2%) of MSM tested ESBL-E positive. ESBL-E carriage was associated with younger age (being 18-34 years old) and higher education status. Compared to having ≤1 sexual partner in the past 6 months, the odds of being ESBL-E positive were no different for MSM with 2-5 sexual partners (adjusted odds ratio (aOR) 0.86, CI 0.35-2.08), but significantly higher for MSM with ≥5 sexual partners in the same timeframe (aOR 4.32, CI 2.02-9.25; p<0.001) after adjusting for age, and antibiotic use and travel history of the preceding 6 months. Condomless receptive fellatio with casual partners was associated with ESBL-E carriage (aOR 2.23, CI 1.26-3.97; p=0.006). HIV-status, antibiotic use and travel history were not associated with ESBL-E carriage.

**Conclusions:** ESBL-E prevalence in MSM is much higher than in the overall Dutch population, which might be explained by sexual transmission. Our data imply that MSM should be considered a risk group for ESBL-E carriage, and might warrant different isolation precautions and empirical antibiotic treatment if admitted to hospitals.

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Abstract 4277

Diagnostic accuracy of VIDISCA-NGS in patients with suspected central nervous system infections

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Background: Confirming the diagnosis in viral central nervous system (CNS) infections can be difficult with current available diagnostic tools. Virus discovery cDNA-AFLP next generation sequencing (VIDISCA-NGS) is a promising viral metagenomic technique, which enables detection of all viruses in a single assay. Yet, its diagnostic accuracy to detect viruses in cerebrospinal fluid (CSF) of patients with suspected CNS infections is unknown. With this study we aimed to determine the diagnostic accuracy of VIDISCA-NGS in CSF of patients with suspected CNS infections.

Materials/methods: Between 2012-2015, all adult inpatients or patients presenting to the Emergency Department, in whom a lumbar puncture was performed for the suspicion of a CNS infection, were prospectively included in a cohort study. Patients from this cohort were included in this study if 1) they were diagnosed with a viral CNS infection, or 2) a viral CNS infection was initially suspected but eventually a different diagnosis was made. A qPCR panel of the most common causative viruses was performed on CSF of these patients as a reference standard and compared to the results of VIDISCA-NGS, the index test.

Results: We included 38 patients with viral CNS infections and 35 presenting with suspected CNS infection for whom an alternative etiology was finally established. We found an overall sensitivity and specificity of 52% (95% CI 31-73%) and 100% (95% CI 91-100%), respectively. One enterovirus that was detected by VIDISCA-NGS was only identified by qPCR upon retesting. Additional viruses identified by VIDISCA-NGS consisted of GB virus C, human papilloma virus, human mastadenovirus C, Merkel cell polyoma virus and anelloviruses.

Conclusions: In patients for whom routine diagnostic work-up does not yield a causative pathogen, VIDISCA-NGS can be of additional value as it can detect a broader range of viruses, but it does not perform well enough to replace routine PCR.

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Respiratory syncytial virus bronchiolitis and recurrent wheezing: a 1-year follow-up study

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Background: Recurrence of wheeze is common after bronchiolitis. This could be due to the infection interfering with lung development and immune maturation or the infection may be the earliest stimulus for wheezing in children with underlying genetic susceptibility. There is a wide variation in the reported incidence of recurrence of wheeze following bronchiolitis. Recent studies have suggested that rhinovirus-associated bronchiolitis is a greater risk factor for development of recurrent than respiratory syncytial virus (RSV). This study was done to assess the incidence of recurrence of wheeze, over a one year follow-up period after hospitalization for RSV or non-RSV bronchiolitis.

Materials/methods: This prospective single centre cohort study was done in children hospitalized with bronchiolitis between September 2016 and August 2018 in a university teaching hospital in South India. Those with chronic underlying diseases, congenital malformations and inability to complete a one year follow up were excluded. The clinicodemographic details were noted during the hospital stay for the first episode. Monthly structured phone interviews were done for 12 months to enquire about the number of recurrences. The primary outcome was recurrence of wheeze at the end of one year.

Results: During the study period a total of 174 children with bronchiolitis were enrolled out of which 150 completed the study. 82 (47%) were positive for RSV infection. Within the first year after hospitalization, 67% children with non-RSV bronchiolitis developed recurrent wheezing, compared with 56% of RSV bronchiolitis. The difference was statistically significant (p=0.01). The Odd’s ratio of recurrence of wheeze in children with non RSV bronchiolitis was 1.45 [95% confidence interval (CI) 1.02-1.87]. 32.8% children with Non RSV bronchiolitis and 26% children with RSV bronchiolitis developed more than one episode of recurrence thus meeting the GINA definition of asthma (>3 episodes of wheeze in a lifetime).

Conclusions: Children hospitalized with bronchiolitis caused by viruses other than RSV have higher risk recurrence of wheezing during a 1-year follow-up period than children with RSV bronchiolitis [OR 1.45 [95% CI 1.02-1.87]].

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Abstract 4279

Epidemiology and clinical characteristics of upper urinary tract infections in infectious diseases emergency department of a tertiary teaching hospital in Slovenia

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Background: Urinary tract infections (UTI) are common infections. With the aging population, we sought to explore the epidemiology of upper UTI in patients referred to our infectious diseases emergency room.

Materials/methods: We performed a retrospective review of the records of patients ≥18 years who visited emergency room of our department from March 2018 to August 2019 and were diagnosed with an upper UTI. Only patients with symptoms of upper UTI (frequency, urgency, dysuria, flank pain, pyuria or fever) were included. Healthcare-associated (HA) infections were considered in patients who were hospitalized ≥2 days in the previous 30 days or in nursing home residents, others were considered community-acquired (CA). Data were statistically evaluated using t-or chi-square test.

Results: 123 episodes were identified, of which the majority were CA (86%) and complicated (72%). Patients were admitted in 45 episodes (36.5%), median for 6 days (1 – 22 days). Antibiotics were prescribed prior referral in 47 cases (38%), most frequently a fluoroquinolone (42.5%). Urine culture most commonly yielded Escherichia coli (43%), which was pansusceptible in 47%, resistant to fluoroquinolones in 19%, and ESBL producing in 6.5%. In those with negative urine culture, 77% received prior antibiotics. Hospitalized patients had more comorbidities (median Charlson index 4 vs. 1, p = 0.01), were more often male (44% vs. 27% p = 0.04) and more often had anatomical or functional abnormalities (69% vs. 40%, p = 0.001). Cefuroxime axetil (46%) or a fluoroquinolone (31%) were most frequently prescribed to outpatients, and in hospitalized patients ertapenem (24%) or parenteral cefuroxime (20%). De-escalation was more frequent in hospitalized patients (11 vs. 3, p = 0.0005). Intravenous-oral switch was performed in 56% of hospitalized patients. There were no differences in clinical failure between hospitalized patients and outpatients (11% vs. 9%, p = 0.7).

Conclusions: Patients referred to our clinic were often prescribed antibiotics prior to the visit which thus interfered with pathogen detection. Broad-spectrum antibiotic therapy was prescribed more often in hospitalized patients, but was de-escalated more often as well. Clinical outcome was favourable in both groups.

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Characterisation and comparison of farm animal and human *Clostridioides difficile* isolates in Italy

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Background: *Clostridioides* (*Clostridium*) *difficile* is one of the prevalent causes of healthcare-associated infections worldwide. Recently, a higher incidence and severity of *C. difficile* infection in both hospitals and community has been reported. This epidemiological change has been associated with the emergence of types, such as PCR-ribotype (RT) 027 and RT078, geographically widespread and able to infect various species. In particular, farm animals are recognized as possible reservoirs of *C. difficile*. Since information in Italy are still scant, this study, funded by the Italian Ministry of Health (RC IZSLER 07/15), aimed to characterize and compare human and animal isolates from Northern Italy.

Materials/methods: *C. difficile* isolates were typed using the capillary PCR-ribotyping method. Genes encoding for toxin A, B and binary toxin (CDT) were detected by PCR assays. Susceptibility analysis for moxifloxacin (MXF), erythromycin (ERY), tetracycline (TET), amoxicillin (AMX), metronidazole (MTZ) and vancomycin (VAN) was performed by Etest.

Results: 364 strains, 267 from animals (250 swine and 17 cattle) and 97 from humans were analyzed. The most frequent toxigenic profile of human isolates was A+B+CDT- (79 strains), while A+B+CDT+ (252 strains) was prevalent in animals. A higher number of different RTs was detected in humans compared to animals (28 and 11, respectively). The predominant type identified in humans was RT018 (39%), followed by RT014 and RT078 (both 8%). Conversely, RT078-lineage (RT033, RT045, RT066/2, RT078, RT126 and RT620) was predominant in animals (92%). Seven RTs (001, 005, 078, 085, 126, 620, 569) were common to both humans and animals. Susceptibility analysis showed that 98% of animal strains resistant to both ERY and MXF belonged to RT078-lineage, while isolates RT018 of human origin are known to be resistant to multiple classes of antibiotics.

Conclusions: These results indicated an overlap of several *C. difficile* RTs between human and animal Italian isolates. RT078-lineage was confirmed as one of the most successful lineage in animals, especially swine. Our data support farm animals a potential source of highly virulent and resistant *C. difficile* strains highlighting the necessity of a close *C. difficile* surveillance in Italy, in accordance with a One Health approach.

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Real-life experience with bezlotoxumab for the prevention of recurrent Clostridioides difficile infection

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Background: Bezlotoxumab, a monoclonal antibody that blocks toxin B of Clostridioides difficile, reduce by 40% the rate of recurrent C.difficile infection (CDI) at 12 weeks (MODIFY studies). Clinical experience with bezlotoxumab out of clinical trials is very scarce. The aims of our study were to describe the characteristics of patients who received bezlotoxumab after commercialization and analyze its efficacy and safety in a real-life context of Spanish hospitals.

Materials/methods: Retrospective, multicenter observational study. All consecutive patients who receive bezlotoxumab between July/2018 to June/2019 in eleven Spanish participant hospitals were included. Recurrence was defined as the appearance of a new episode of CDI within 12 weeks after bezlotoxumab infusion. Risk factors for CDI recurrence used in MODIFY studies (age over 65, immunosuppression, previous episode, hypervirulent ribotypes and severe CDI according to Zar’s criteria) were recorded in order to compare our cohort with patients treated with bezlotoxumab in MODIFY trials.

Results: Seventy-eight patients were included. Median age was 70.5 (59-82). The next table shows percentage of patients having risk factors for CDI recurrence both in our cohort and in bezlotoxumab treated patients in MODIFY studies.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Present cohort</th>
<th>Bezlotoxumab treated (MODIFY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age≥65</td>
<td>65.4%</td>
<td>49.9%</td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>62.8%</td>
<td>22.8%</td>
</tr>
<tr>
<td>Previous CDI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypervirulent strains</td>
<td></td>
<td>27.7%</td>
</tr>
<tr>
<td>Severe episode</td>
<td></td>
<td>18.2%</td>
</tr>
</tbody>
</table>

No patients in our cohort lacked risk factors for CDI recurrence and 87.2% had 2 or more risk factors. Correspondent figures in MODIFY trials were 24% and 49.6%. Most of the patients received vancomycin (57 cases; 73.1%) as anti C.difficile treatment. Recurrence rate at 12th weeks was 14.1%, (16.5% in MODIFY trials). Median time to recurrence was 39 days (IQR:14-45). There were no adverse effects related to bezlotoxumab in opinion of the investigators, and only one patient died due to CDI. Neither age, type of risk factor for recurrent CDI nor anti CDI treatment were associated with failure of bezlotoxumab.

Conclusions: In spite of being used in patients with higher risk CDI recurrence than those included in MODIFY trial, bezlotoxumab was associated with a similar rate of recurrence in a real-life context. We were unable to find factors associated with failure of bezlotoxumab.

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Impact of antimicrobial stewardship and infection control programmes on the incidence of carbapenem-resistant Pseudomonas aeruginosa: a non-linear time-series analysis

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Abstract third-party references: supported by THRESHOLDS study group

Background: Carbapenem resistance in Pseudomonas aeruginosa (PaCRE) is an important cause of nosocomial infections associated with high level of resistance, morbidity and mortality rate. Estimate the impact of antimicrobials stewardship (ABS) and infection control programmes on the emergence of (PaCRE).

Materials/methods: A time-series analysis exploring temporal associations between sequential infection control interventions (hand hygiene [iHAND Campaign], carbapenem sparing strategy [iCARBA Campaign], ABS with periodical audit and feedback [iASP Campaign]) and Incidence Density of Carbapenem-resistant Pseudomonas aeruginosa (Di_PaCRE) in Azienda Ospedaliero-Universitaria Policlinico Modena was conducted. We used the statistical approach elsewhere described ([López-Lozano JM, et al. Nat Microbiol.1160–1172, 2019]) to adjust a non-linear model (Multivariate Adaptive Regression Splines) for the identification of possible thresholds. Moreover, a counterfactual analysis to quantify the effectiveness of the different interventions was carried out.

Results: We fit a NL-TSA model (adjusted-R²=0.539) with a threshold at 26.65 litres/1000 bed-days for alcoholic gel consumption (ALCBED) and 58 DDD/1000 bed-days of Carbapenems (CarbUse). An increase by one litre/1000 OBDs of alcoholic gel decreased Di_PaCRE by 0.01 new cases per 1000 OBDs up till a ceiling of 26.65 litres/1000 OBDs. In contrast, the Di_PaCRE increased by 0.04 new cases by 1000 OBDs per one DDD/1000 OBDs of Carbapenems, but only above 58 DDD/1000 OBDs of Carbapenems. The counterfactual analysis of the iCARBA Campaign alone revealed an average monthly decrease in Di_PaCRE of 0.053 (0.029, 0.072, CI-95%) per 1000 OBDs, a total effect 3.19. In addition, we estimated that the iHAND campaign average monthly reduced Di_PaCRE in 0.057 (0.036, 0.079, CI-95%) cases per 1,000 bed-days, a total accumulated decrease of 4.37. Combining all campaigns, we estimate an average monthly decrease by 0.16 (0.13,0.19, CI-95%), with 12.11 of total effect.

Conclusions: A significant reduction of PaCRE was obtained by the implementation of a multifaceted approach, including hand hygiene and ABS aimed to reduce nosocomial transmission and selective pressure. ASP strategies rather than hand hygiene campaigns was associated with a major reduction in PaCRE infections. PaCRE could be controlled by reducing the use of carbapenems below minimum thresholds of 58 DDD/1000 bed-days. This finding could provide an innovative approach to guide ABS strategy.

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**Abstract 4285**

**Surveillance of central venous catheter bloodstream infections in critical care units in England: April 2017-March 2019**

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**Background:** Bloodstream infections (BSI) from central venous catheters (CVC-BSI) in critically ill patients in intensive care units (ICUs) increase morbidity and mortality, have high economic impact and are potentially preventable. Substantial reductions in CVC-BSI rates have previously been reported in England in a two-year study (2009-11). A key outcome was the need for a professionally-owned, standardised, national infection surveillance programme in ICUs. Here we present the results from years two and three of the English ICU CVC-BSI surveillance programme.

**Materials/methods:** An online data capture system (DCS) was launched in May 2016 to collect patient-level data on all positive blood cultures (PBCs) in participating ICUs and unit-level data on bed-days and CVC-days. All ICUs in England were invited to participate in the voluntary surveillance programme.

**Results:** By 30/03/2019, 262 ICUs in England had registered on the DCS. For financial years (FY) 2017/18-2018/19, 110 ICUs provided data (99 adult, 5 paediatric, 6 neonatal), entering a total of 6,144, 136 and 296 PBCs, respectively. Of these, approximately half were coagulase-negative staphylococci (adult:44.4%, paediatric:55.9%, neonatal:56.4%). Among PBCs, between 25%-39% were defined as ICU-associated BSI (occurring >2 days after ICU admission, adult: n=2,312/6,144, paediatric: n=53/136, neonatal: n=76/296). Among adult ICUs, 29.5% of ICU-associated BSIs were reported as CVC-BSI (n=682/2,312), this was 39.6% among paediatric ICUs (n=21/53) and 56.6% among neonatal ICUs (n=43/76). Overall, these equate to rates of 2.2, 1.6 and 2.3 per 1,000 ICU-CVC-days, respectively. However, there was wide variation in CVC-BSI rates within ICU types, particularly in adult ICUs (0.0-30.3 ICU-associated CVC-BSI per 1,000 ICU-CVC-days).

**Conclusions:** The overall rates of microbiologically confirmed ICU-associated CVC-BSI are moderate across all age-ranges; however, the difference in rates between units highlights the importance of providing a national standardised surveillance system for benchmarking and to determine the underlying causes. With the surveillance scheme now established, linkage with antimicrobial susceptibility testing data will occur to provide enhanced epidemiological data on antimicrobial resistance patterns within ICUs in England. Furthermore, the use of data linkage with other clinical datasets to reduce the burden of data collection and thereby increase surveillance ascertainment is under investigation.

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Abstract 4290

An antibiotic stewardship intervention in the emergency department leads to improved antibiotic prescription especially during normal working hours and among younger faculty

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1Ludwig-Maximilians-Universität, Klinikum der Universität München, München, Germany, 2Ludwig-Maximilians-Universität, Max von Pettenkofer Institut, München, Germany, 3Ludwig-Maximilians-Universität, Klinikum der Universität München, München, Germany

Background: Antibiotics are among the most commonly prescribed classes of drugs in emergency departments (ED). In most EDs, high patient numbers and time pressure in combination with often seriously ill patients lead to an overprescribing of broad-spectrum antibiotics. However, the decision of the type of antibiotic in the ED is crucial as it is usually continued on the wards and is not re-evaluated when patients are discharged from the ED. Here we analysed the effect of an antibiotic stewardship intervention in our main ED.

Materials/methods: The antibiotic stewardship intervention consisted of the development of local treatment guidelines for common infections in the ED, training sessions and distribution as posters and pocket cards. Retrospective evaluation of the antibiotic prescription behaviour was performed for periods before and after the intervention. Overall 585 patients were included with one of the following diagnoses: community acquired pneumonia (CAP), pyelonephritis and cystitis. Parameters assessed were (among others): choice of drug, timepoint of treatment in the ED, status of medical training, medical specialty and Charlston Comorbidity index for disease severity. In addition, antibiotic consumption (expressed as DDD/100 patient days) was assessed for both study periods.

Results: The antibiotic stewardship intervention led to a statistically significant improvement of choice of antibiotic drug in the ED. This was shown for all patients (correct antibiotic in 47% of cases before the intervention and in 58.6% of cases after the intervention; p=0.011) and especially for the entity of CAP (30% compared to 64.6%; p=0.0002). Prescribing improved significantly during normal working hours (Monday to Friday 8 a.m. till 5 p.m.) (39.1% compared to 59.8%; p=0.006), in the group of interns and residents (47.6% versus 60%; p=0.036) and for internists (47.7% versus 62.7%; p=0.0015) and neurologists (10% compared to 41.2%; p=0.027). Overall antibiotic consumption decreased by 9%. The use of narrow spectrum penicillins increased (by 34%) whereas the consumption of broad-spectrum penicillins, cephalosporins and fluorchinolones decreased.

Conclusions: The antibiotic stewardship intervention was successful, especially with regard to CAP, antibiotic prescription within normal working hours and among younger faculty. However, implementation and sustainability of behaviour change remain a constant challenge.

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In vitro activity of ceftaroline and comparators against Staphylococcus aureus clinical isolates from a tertiary hospital in Greece

Areti Tychala1,2, Maria Arhonti2, Fotini Netsika2, Georgios Meletis2, Paraskevi Mantzana1, Olga Vasilaki2, Georgia Kagkalou2, Efthymia Protonotariou2, Lemonia Skoura2

1Thessaloniki Psychiatric Hospital, Stavroupoli, Greece; 2AHEPA University Hospital, Department of Micorbiology, Thessaloniki, Greece

Background: Ceftaroline is a new parenteral cephalosporin with bactericidal activity against serious infections caused by Gram-positive bacteria including methicillin-resistant S. aureus (MRSA). The aim of our study was to assess the in vitro activity of ceftaroline and comparators against S. aureus (SA) clinical isolates.

Materials/methods: From 7/2017 to 11/2019, 488 SA isolates were recovered from patients hospitalized in several departments of AHEPA University Hospital. 236 of them were MRSA (48.36%) and 252 methicillin-susceptible (MSSA) (51.64%). The strains were isolated from various clinical sites including blood, urine, tracheobronchial secretions, intravenous catheters, fluids and wound samples. Bacterial identification and antimicrobial susceptibility testing were performed using the Vitek2 automated system (bioMérieux, France). MIC50 and MIC90 were calculated for each antimicrobial and interpreted using the current EUCAST guidelines. Due to lack of clinical data, a strain was considered resistant to ceftaroline when the MIC was > 2 mg/L, as suggested by EUCAST for indications other than pneumonia.

Results: MIC50, MIC90 and susceptibility rates of the studied isolates are shown on the Table below. Ceftaroline showed potent antimicrobial activity against SA with MIC50/90 values being 0.5/1 mg/L for MRSA and 0.25/0.25 mg/L for MSSA. Three (3) MRSA isolates exhibited MIC = 2 mg/L to ceftaroline. Levofloxacin, moxifloxacin, clindamycin and erythromycin had the lowest activity against MRSA with susceptibility rates of 22%, 21%, 28% and 23% respectively. All antimicrobials appear to be highly active in vitro against MSSA isolates, with susceptibility rates ranging from 78% to 100%.

Conclusions: Overall, ceftaroline showed excellent in vitro activity against the tested SA isolates along with other comparators in our hospital. Therefore, it could be used as an alternative for the treatment of serious infections caused by these strains.

<table>
<thead>
<tr>
<th>Organism</th>
<th>Antimicrobial</th>
<th>Number of strains</th>
<th>MIC range (mg/L)</th>
<th>MIC50 (mg/L)</th>
<th>MIC90 (mg/L)</th>
<th>Susceptibility (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA</td>
<td>Ceftaroline</td>
<td>118</td>
<td>0.25-2</td>
<td>0.5</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Clindamycin</td>
<td>236</td>
<td>0.12-8</td>
<td>4</td>
<td>8</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Daptomycin</td>
<td>235</td>
<td>0.12-2</td>
<td>0.25</td>
<td>1</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>Erythromycin</td>
<td>150</td>
<td>0.25-8</td>
<td>8</td>
<td>8</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Gentamicin</td>
<td>252</td>
<td>0.5-16</td>
<td>0.5</td>
<td>0.25</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>Linezolid</td>
<td>236</td>
<td>1-8</td>
<td>2</td>
<td>2</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td>Moxifloxacin</td>
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<td>0.25-4</td>
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<td>4</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td>Quin/dalf</td>
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<td>0.25-16</td>
<td>0.25</td>
<td>0.25</td>
<td>99</td>
</tr>
<tr>
<td></td>
<td>Rifampicin</td>
<td>118</td>
<td>≤0.06-0.25</td>
<td>≤0.06</td>
<td>≤0.06</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td>Teicoplanin</td>
<td>236</td>
<td>0.5-8</td>
<td>0.5</td>
<td>0.5</td>
<td>97</td>
</tr>
<tr>
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<td>Tigecycline</td>
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<td>0.12-1</td>
<td>0.12</td>
<td>0.5</td>
<td>94</td>
</tr>
<tr>
<td></td>
<td>TMP-SMX</td>
<td>236</td>
<td>0.5-16</td>
<td>0.5</td>
<td>1</td>
<td>95</td>
</tr>
<tr>
<td>MSSA</td>
<td>Vancomycin</td>
<td>236</td>
<td>0.5-2</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Ceftaroline</td>
<td>139</td>
<td>≤0.06-0.25</td>
<td>0.25</td>
<td>0.25</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>Clindamycin</td>
<td>252</td>
<td>0.12-8</td>
<td>0.25</td>
<td>0.25</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>Daptomycin</td>
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<td>0.25</td>
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<td>Gentamicin</td>
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<td>0.5</td>
<td>0.5</td>
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</tr>
<tr>
<td></td>
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<td>252</td>
<td>1-2</td>
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<tr>
<td></td>
<td>Moxifloxacin</td>
<td>113</td>
<td>0.25-4</td>
<td>0.25</td>
<td>0.25</td>
<td>96</td>
</tr>
<tr>
<td></td>
<td>Quin/dalf</td>
<td>113</td>
<td>0.25-0.5</td>
<td>0.25</td>
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<td>100</td>
</tr>
<tr>
<td></td>
<td>Rifampicin</td>
<td>139</td>
<td>≤0.06-0.25</td>
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<tr>
<td></td>
<td>Teicoplanin</td>
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<td>0.5</td>
<td>0.5</td>
<td>99</td>
</tr>
<tr>
<td></td>
<td>Tigecycline</td>
<td>252</td>
<td>0.12-0.25</td>
<td>0.12</td>
<td>0.12</td>
<td>100</td>
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<td></td>
<td>TMP-SMX</td>
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<td>0.5-16</td>
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<td>98</td>
</tr>
<tr>
<td></td>
<td>Vancomycin</td>
<td>252</td>
<td>0.5-2</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
</tbody>
</table>

Image 1. quin/dalf = quinupristin/dalfopristin, TMP-SMX = trimethoprim/sulfamethoxazole

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Universal neonatal screening for congenital cytomegalovirus, the time is now?
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Background: We demonstrate the impact on patient care of universal neonatal screening for congenital Cytomegalovirus (cCMV) in our hospital.

Materials/methods: From February 2nd, 2015 onwards, a universal neonatal cCMV screening program was implemented in our Belgian secondary care hospital. At mid pregnancy, parents are informed about the program and possible preventive measures by a leaflet distributed by the gynecologist or midwife. Within 48 hours postpartum, saliva of the newborn is collected by the pediatrician using Eswab (Copan, Italy) and analyzed for CMV DNA by an in house RT-PCR. Positive saliva tests are confirmed by demonstrating CMV presence on a urine sample of the newborn and/or by comparison with CMV serology of the newborn’s mother. Results are analyzed until February 1st 2019.

Results:

<table>
<thead>
<tr>
<th>Year</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
<th>2018</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates, born</td>
<td>2450</td>
<td>2291</td>
<td>2272</td>
<td>2248</td>
<td>9261</td>
</tr>
<tr>
<td>Neonates, screened</td>
<td>2394 (97.7%)</td>
<td>2254 (98.4%)</td>
<td>2266 (99.7%)</td>
<td>2246 (99.9%)</td>
<td>9160 (98.9%)</td>
</tr>
<tr>
<td>CMV positive</td>
<td>49 (2.0%)</td>
<td>40 (1.8%)</td>
<td>17 (0.8%)</td>
<td>24 (1.1%)</td>
<td>130 (1.4%)</td>
</tr>
<tr>
<td>CMV positive, not confirmed</td>
<td>28 (1.2%)</td>
<td>28 (1.2%)</td>
<td>10 (0.4%)</td>
<td>11 (0.5%)</td>
<td>77 (0.8%)</td>
</tr>
<tr>
<td>CMV positive, no confirmation performed</td>
<td>7 (0.3%)</td>
<td>2 (0.1%)</td>
<td>3 (0.1%)</td>
<td>2 (0.1%)</td>
<td>14 (0.2%)</td>
</tr>
<tr>
<td>CMV positive, confirmed (cCMV)</td>
<td>14 (0.6%)</td>
<td>10 (0.4%)</td>
<td>4 (0.2%)</td>
<td>11 (0.5%)</td>
<td>39 (0.4%)</td>
</tr>
<tr>
<td>cCMV following primary maternal infection, detected during pregnancy</td>
<td>2 (0*)</td>
<td>3 (3*)</td>
<td>1 (0*)</td>
<td>3 (1*)</td>
<td>9 (4*)</td>
</tr>
<tr>
<td>cCMV following primary maternal infection, detected after delivery</td>
<td>5 (0*)</td>
<td>4 (3*)</td>
<td>1 (1*)</td>
<td>5 (2*)</td>
<td>15 (6*)</td>
</tr>
<tr>
<td>cCMV following non primary maternal infection</td>
<td>7 (3*)</td>
<td>3 (1*)</td>
<td>2 (0*)</td>
<td>3 (1*)</td>
<td>15 (5*)</td>
</tr>
</tbody>
</table>

*symptomatic neonates

Conclusions: Universal neonatal cCMV screening was easily adopted and has become common practice in our hospital with compliance rates of 98.9%. Overall, 130 neonates (1.4%) showed a positive screening result, and in 39 (0.4%) cCMV infection was confirmed. Without the screening program, 30/39 (76.9%) of cCMV cases, 11 of which symptomatic, would not have been detected immediately after birth. Confirmation of positive saliva CMV screening results by analysis of an independent urine sample and/or serology of the mother remains necessary as CMV contamination rate in saliva is high (0.8%).

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Evaluation of BD MAX multidrug-resistant tuberculosis assay for detection of Mycobacterium tuberculosis complex in clinical specimens and identification of genetic resistance markers

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Background: Rapid and accurate diagnosis of tuberculosis (TB) and fast detection of drug resistance are critical for successful TB control strategies. BD MAX multidrug-resistant (MDR) TB (BD MAX) is a new, highly automated molecular assay for rapid detection of Mycobacterium tuberculosis complex (MTBC) directly in clinical specimens and simultaneous identification of genetic markers for resistance towards isoniazid (INH) and rifampicin (RIF). Aim of the present study was to evaluate the diagnostic accuracy of BD MAX for cohorts of MTBC negative, paucibacillary, and multibacillary MTBC positive samples.

Materials/methods: 503 archived respiratory specimens (366 sputa, 137 bronchial aspirates) which had been processed by conventional N-acetyl-L-cysteine/sodium hydroxide method were analyzed by BD MAX in a retrospective case control study. The set of study samples comprised 257 MTBC negative samples (205 culture negative samples, 52 growing non-tuberculous mycobacteria), 93 smear negative and 153 smear positive samples growing MTBC.

Results: Based on culture as method of comparison, the overall sensitivity of BD MAX was 86.6%; the sensitivities for smear positive and smear negative samples were 100% and 64.5%, respectively. The specificity rates were 100% for both culture negative specimens and those which grew non-tuberculous mycobacteria. Sensitivity and specificity for INH resistance compared with phenotypic drug resistance testing were 58.3% and 99.3%, respectively. The five samples being phenotypically resistant to INH but susceptible by BD MAX originated from only two patients. Thus, the low sensitivity of 58.3% is caused, at least in part, by a random effect due to selection of study samples. Sensitivity and specificity for RIF resistance were 100% and 98.2%. When compared to results from Genotype MTBDRplus and Sanger sequencing, sensitivity and specificity rates for INH were 100% and 99.4%, and for RIF 100% and 99.4%.

Conclusions: BD MAX is a sensitive and highly specific assay for the diagnosis of TB and detection of genetic resistance markers. Limitations of the study include the use of frozen samples what may have negatively influenced assay sensitivity.

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Abstract 4296

**Rhamnolipid coating reduces formation of *Candida albicans*-Staphylococcus aureus mixed biofilm on titanium implants: an in vitro study**

Erica Tambone¹, Chiara Ceresa³, Devid Maniglio¹, Federico Piccoli³, Iole Caola³, Giandomenico Nollo¹⁴, Paolo Ghensi⁵, Patrizio Caciagli³, Letizia Fracchia², Francesco Tessarolo*¹⁴

¹Department of Industrial Engineering and Biotech Center, University of Trento, Trento, Trento, Italy, ²Department of Pharmaceutical Sciences, Università del Piemonte Orientale "A. Avogadro", Novara, Italy, ³Department of Medicine Laboratory, Azienda Provinciale per i Servizi Sanitari di Trento, Trento, Italy, ⁴Healthcare Research and Innovation Program (IRCS-FBK-PAT), Bruno Kessler Foundation, Trento, Italy, ⁵Center for Integrative Biology, University of Trento, Trento, Italy

**Background:** In recent years, an increased number of implant infections caused by multi-species biofilm has been reported. Within a multi-species biofilm, microorganisms can interact and cooperate with each other, increasing pathogenicity, virulence and resistance to antimicrobial agents of the individual species. New strategies to prevent implant colonization are proposing to coat the surface with antimicrobial and anti-adhesive agents, such as biosurfactants.

This study aimed at assessing the ability of the rhamnolipid R89 biosurfactant (R89BS), deposited on medical-grade titanium, to inhibit formation of *C. albicans*-S. aureus mixed biofilm.

**Materials/methods:** Titanium discs (TDs) were coated with R89BS, while uncoated TDs were used as control. TDs were dipped in 1 mL of the suspension (with a final concentration of 10⁵ CFU/mL for *C. albicans* ATCC 10231 and 10⁷ CFU/mL for *S. aureus* ATCC 6538 in YNBD+10% FBS) and incubated at 37°C at 70 rpm, renewing growth medium every 24h.

The anti-biofilm activity of R89BS-coated TDs was evaluated by quantifying, at 24, 48 and 72h, total biomass (crystal violet staining), cell metabolic activity (MTT assay) and cell viability (cell viable counting). A qualitative analysis of multi-species biofilms on TDs was carried out with scanning electron microscopy.

Data analysis was performed by t-test and statistical significance was considered for p<0.05.

**Results:** *C. albicans*-S. aureus mixed biofilm were mainly composed of fungal cells and resulted significantly inhibited by R89BS coating, with a similar effect on biofilm biomass, cell metabolic activity and viable cell count (Figure 1). A biofilm inhibition up to 96% was observed at 24h. After 48h, a less marked, but still significant inhibition was detected for cell metabolic activity in respect to biofilm biomass and viable cell count. R89BS coating resulted more effective in reducing bacterial cells rather than fungal cells.

**Conclusions:** R89BS coating is effective in reducing *C. albicans*-S. aureus mixed biofilm on titanium surfaces and can be considered as a promising strategy to prevent implants colonization.
Figure 1: Inhibition of C. albicans-S. aureus mixed biofilm biomass (a), cell metabolic activity (b), and cell viability (c) on R89B5-coated TDS, in respect to normalized controls. ***p<0.001, **p<0.01.

This research is supported by by Fondazione Cassa di Risparmio di Trento e Rovereto (Grant n 2017.0340)

Presenter email address: tessaro@science.unitn.it
Abstract 4298

Effects of spectrum of antibiotics on microbiome compositions and resistome levels
Karen Leth Nielsen*, Markus Harboe Olsen1, Albert Palleja2, Søren Reddik Ebdrup1, Nikolaj Sørensen2, Oksana Lukjancenko2, Rasmus Marvig1, Kirsten Møller1, Niels Frimodt-Moller1, Frederik B. Hertz1,3

1Rigshospitalet, København, Denmark, 2Clinical-Microbiomics A/S, København, Denmark, 3Slagelse Sygehus, Slagelse, Denmark

Background: Long-term hospitalization and treatment with antibiotics increase the risk of acquiring multidrug-resistant bacteria due to antibiotic-mediated microbial compositional shifts. This study aimed to investigate how different antibiotics affect the gut microbiome and the resistome in antibiotic naïve patients during neurointensive care.

Materials/methods: Forty patients admitted to neurointensive care unit of Rigshospitalet, Copenhagen, Denmark were treated with broad-spectrum (meropenem or piperacillin/tazo-bactam) or more specific antibiotic treatment (including ciprofloxacin, cefuroxime, vancomycin and dicloxacillin). A rectal swab was collected from each patient before and after 5-7 days of antibiotic therapy. Shotgun metagenomic sequencing was performed and composition of metagenomic species (MGS) were determined. The resistome (as collection of antibiotic resistance genes) was characterized with CARD RGI software and CARD database. As a measure for selection pressure in the patient, we used the parameter antibiotic days (∑ number of days with each antibiotic). Groups were compared with Wilcoxon signed-ranked tests.

Results: The MGS composition of the microbiome changed independent of applied antibiotic treatment. We observed an increase in diversity in patients receiving more narrow-spectrum treatment (p = 0.016) and we observed two populations among the broad-spectrum patients; some decreased in diversity and some increased. We compared patients that had gained or lost >10 species, respectively. Antibiotic days were significantly higher in patients with decreased richness (p = 0.0054) and decreased Shannon diversity (p = 0.012), and these patients received a higher number of antibiotics (richness: p = 0.063; for Shannon index: p = 0.086). Changes in resistome followed MGS composition and was independent of administered antibiotics. We observed a higher prevalence of vancomycin resistance genes in post-treatment patients (p = 0.019).

Conclusions: Antibiotic spectrum was not found to have notable differential effects on the MGS composition or resistome of the microbiome. However, we observed a significantly higher number of vancomycin resistance genes after treatment. Patients who received narrow-spectrum treatment exhibited an increase in diversity. Selection pressure (antibiotic days) was found to be higher in patients with a decreased MGS diversity. The selection pressure in the patient may be a better predictor of the effect on the microbiome than the spectrum of the antibiotics.

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Background: Lyme borreliosis (LB) is the most frequent vector-borne disease in France. Since 2009, its surveillance is based on a sentinel network of general practitioners (Sentinelles network - SGPs) completed with the surveillance of hospitalized LB cases using the national hospitalization database available from 2005. We describe surveillance data in order to estimate incidence, detect trends and identify risk groups and high-incidence regions.

Materials/methods: SGPs report new diagnoses of LB. Reported cases are validated applying the European Union Concerted Action on LB case definitions. A hospitalized LB case was a person hospitalized with a LB specific diagnosis (ICD10 codes: M01.2 or L90.4 or A69.2 in the absence of any other diagnosis or associated with code(s) compatible with LB symptoms {neurological, cardiac, articular, ocular disorders}).

Results: From 2009 to 2018, the mean yearly incidence rate of patients consulting a GP for LB was 58 cases per 100,000 inhabitants fluctuating between 41 in 2011 and 104 in 2018. In 2016 and 2018, significant increases in LB incidence were observed. The hospitalization incidence rate (HIR) increased from 1.1 cases per 100,000 inhabitants in 2005 to 1.5 in 2018 with significant trend over the period. However, the significant peaks of 2016 and 2018 observed in general practice were not observed in our hospital based surveillance. Same significant inter-regional variations were observed in both data sources. HIR peaked in 5-9 and 70-79 years old. The incidence rate of LB diagnosed at GP level peaked in 60-69 years old. Erythema migrans affected 95% of the cases at primary care level. Among hospitalized cases, the most common manifestation was neuroborreliosis with a mean of 440 cases/year (52%). Among neuroborreliosis hospitalized cases, 36% presented with facial nerve disorders.

Conclusions: These data allow to follow general trends and can be used to target public health strategies towards the high risk groups for LB and neuroborreliosis. If there is an increase of the disease incidence in France over the last years that could be explained by recent modifications of ticks’ ecology, the improved awareness towards the disease could have also participated in the recent peaks in 2016 and 2018.

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Abstract 4300

**When cold water is too warm: healthcare-associated Legionnaires’ disease associated with hot season**

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**Background:** The most common form of legionellosis is pneumonia which can be acquired by inhalation of aerosolized *Legionella* spp. most commonly from man-made water-bearing systems. *Legionella* spp. grows best at 25 – 45°C. Increasing numbers of health-care associated legionella pneumonia have been observed in our hospital region since 05/2018 which led to this epidemiologic investigation. The aim was to prevent further cases.

**Materials/methods:** Sampling of the hot and cold water reservoir of two adjacent hospital water systems was performed. Samples were incubated and concentration of *Legionella* determined. The Swiss Federal Office of Public Health defines a *Legionella* concentration of ≥100 cfu/ml as elevated in high-risk settings such as oncological wards or intensive care units, where temperature has to be <25°C in cold water and >55°C in hot water. Technical details of the water supply system were inspected including presence of inactive and unused pipes, water flow in pipes, water temperatures at exit sites and in reservoir.

**Results:** We observed six cases of health-care associated legionellosis from 05/2018 – 09/2019. Concentrations of *Legionella* ≥100 cfu/ml were demonstrated in hot and surprisingly also in cold water in both hospitals and were significantly associated with temperatures above and below those recommended in cold and hot water system (p=0.004; odds ratio 27.0 [95% confidence interval 2.5 – 284.7]). Construction work involving the water supply caused inactivation of pipes and stagnation in the hot water supply. Elevated temperatures in the cold water supply were observed during hot season and construction work. Preventive measures included daily flushing of all pipes, installation of *Legionella* filters in showers, heating up and chlorination of the hot water supply and reconstruction of the cold water system. No subsequent cases of Legionnaire’s disease were observed.

**Conclusions:** While *Legionella* are commonly found in not sufficiently hot water reservoirs, our outbreak investigation identified also an association of increased legionella concentrations with too warm cold water supplies. These occurred during the hot season and construction work affecting the water system and could be reversed with preventive measures. Cold water supply must be considered as a possible source of Legionnaire’s disease.

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Abstract 4302

In vitro activity of ceftolozane-tazobactam and comparators against beta-lactam-resistant pathogens isolates collected from patients with urinary tract, intra-abdominal and lower respiratory infections in Lebanon and Jordan [SMART Study Data 2016-2017]

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Background: The Study for Monitoring Antimicrobial Resistance Trends (SMART) has been tracking resistance among Gram-negative bacilli (GNB) since 2002. High resistance rates over the years required the use of novel beta-lactam combination agents such as ceftolozane-tazobactam. This report summarizes the susceptibility rates to ceftolozane-tazobactam versus comparators and molecular characterization of extended spectrum beta-lactamases (ESBL)- and carbapenemases producing isolates collected from patients with urinary tract (UTI), intra-abdominal (IAI) and lower respiratory tract (LRTI) infections in Lebanon and Jordan (2016-2017).

Materials/methods: 332 ESBL-producing enterobacteriaceae were collected from four centers in Lebanon (131, n=2) and Jordan (201, n=2). The isolates were then shipped to a central laboratory (IHMA, Switzerland) to confirm the identification and susceptibility testing results and perform the molecular characterization. Extended spectrum beta-lactamases (ESBLs) and carbapenemases were characterized using the Check-Points microarray, followed by PCR and sequencing. We characterized all enterobacteriaceae isolates that were non-susceptible to ertapenem (CLSI breakpoints), and 50% (due to cost constraints) of the isolates that were phenotypically ESBL-positive but ertapenem susceptible.

Results: In general, Lebanese isolates exhibited relatively high susceptibility rates to ceftolozane-tazobactam (92%, 86.7%, and 88.5% in UTI, IAI, and LRTI respectively), while susceptibility rates to other beta-lactams (except for carbapenems) were notably lower (Figure 1). Lower susceptibility rates could be noted in Jordan including to ceftolozane-tazobactam with susceptibility rates of 88.8% (UTI), 77.4% (IAI), and 55.9% (LRTI). Low susceptibility levels to carbapenems were also noted in LRTI from Jordan compared to Lebanon (57.6% versus 92.3% to ertapenem, 78% versus 96.2% to imipenem and 81.4% versus 96.2% to meropenem). The high resistance rates in Jordan could be explained among others by the emergence of carbapenemases such as blaOXA-type: 30 strains isolated in LRTI, 17 in IAI and 5 in UTI versus only 8 strains in Lebanon (all sources). The most prevalent carbapenemases remain blaOXA-48 and blaOXA-181.

Conclusions: These findings highlight the importance of this novel antibiotic in treating complicated infections caused by ESBL producing enterobacteriaceae, especially in Lebanon but not for empiric use for LRTI in Jordan. Nevertheless, the result underscore the importance of appropriate antimicrobial stewardship strategies that are urgently needed in Jordan in order to control the growth of the problem of resistance.
LEBANON-JORDAN: SMART DATA 2016-2017:
Susceptibility rates of ESBL-producing pathogens in (A): IA, (B): LRTI and (C): UTI and (D): Molecular data of carbapenemases.

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Abstract 4306

Revision of clinical guidelines for hospital-acquired pneumonia led to a reduction in carabapenem prescriptions at a Swiss cantonal hospital

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Background: Carbapenems were replaced with cefepime or piperacillin/tazobactam in our internal guidelines for empiric treatment of late onset hospital acquired pneumonia (HAP) in May 2016. The recommendation for amoxicillin/clavulanate in early onset HAP remained unchanged. Antibiotic prescribing practice was assessed before and after guideline change.

Materials/methods: Electronic records of in-patients with a clinical diagnosis of HAP, extending 18 months before (period I) and after (period II) the guideline change, were retrospectively evaluated. Clinical data and antibiotic prescriptions were recorded. Differences in antibiotic prescriptions were analysed with Fisher’s exact test.

Results: 82 patients in period I and 86 in period II were included in the analysis. Median patient age was 77 years in period I and 74 in period II. Median Charlson Comorbidity index was 4.9 in both groups. Despite treatment prescription for a diagnosis of HAP, all criteria meeting the strict HAP definition (respiratory symptoms, new radiologic findings and signs of systemic inflammation) were retrospectively fulfilled in only 59% and 48% of patients in periods I and II respectively. Empiric guideline adherence was 84% in period I and 75% in period II. Prescription of imipenem/cilastatin decreased from 40% in period I to 6% in period II (p < 0.001), use of piperacillin/tazobactam increased from 32% to 45% (p = 0.082) and use of amoxicillin/clavulanate increased from 22% to 34% (p = 0.121). Cefepime prescription increased from zero in period I to 6% in period II (p = 0.059). Treatment duration was longer than recommended in 13% of patients in period I and 8% in period II. Treatment was successful in 86% of patients in period I and 89% in period II.

Conclusions: A safe and substantial reduction in empiric use of carbapenems for presumed HAP was achieved through guideline change. Appropriate diagnosis and indication for treatment of HAP remain challenging.

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Abstract 4307

Performance of RealAccurate Quadruplex Mycobacteria PCR for detection of non-tuberculous mycobacteria in clinical samples

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Background: Simultaneous molecular detection of non-tuberculous mycobacteria (NTM) next to Mycobacterium tuberculosis complex (MTB) might be beneficial in routine microbiological practice as NTM infections are not always considered. This feature is offered by the RealAccurate Quadruplex Mycobacteria PCR kit (PathoFinder) but performance data are scarce. Our study aimed to evaluate this commercial assay specifically for NTM detection in clinical samples.

Materials/methods: The Pathofinder assay was used for MTB detection in clinical samples from patients at the Antwerp University Hospital during 2018-2019. DNA was extracted with NucliSENS® easyMAG® (bioMérieux) and amplified using the RealAccurate Quadruplex Mycobacteria PCR kit (PathoFinder) on LightCycler® 480 (Roche). Samples positive for NTM or with clinical suspicion of NTM infection (n=38; 15 respiratory samples, 10 biopsy, 8 glands, 3 pus/fluid and 2 CSF) were also analysed by culture (n=30) and/or an in-house conventional nested PCR (n=38) (reference method). Proficiency testing for NTM was performed on the 2019 NTM QCMD panel (n=10).

Results: An agreement of 100% was achieved with the Pathofinder on the proficiency panel. Of the 38 clinical samples, 26 were NTM positive by Pathofinder (Ct-values: 29.29-38.14). However only 7 of these (Ct-values: 29.29-37.7) were positive with the reference method (1 via culture, 7 via PCR). For the 19 false-positive samples (Ct-values: 33.3-38.14) NTM infection was also not suspected based on clinical evaluation and culture data. Twelve of the 38 samples were NTM negative with Pathofinder, but 3 of those were positive with the reference method (1 via culture, 3 via PCR). The treating physicians considered all 3 patients as real NTM infected and patients were successfully treated. Neither false-positive nor false-negative results could be allocated to certain sample types. A sensitivity of 70% (95%CI: 35-93%) and specificity of 32% (95%CI: 16-52%) was obtained.

Conclusions: The Pathofinder assay showed low sensitivity and poor specificity for NTM detection in clinical samples although proficiency testing results were excellent. Aspecific amplification did not result in higher Ct-values or in differently shaped amplification curves compared to real positive results and could therefore not be distinguished. We do not recommend to use the assay for NTM detection in routine practice.

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Abstract 4309

Modelling the impact of antibiotic resistance on surgical site infections: the case of hip replacements
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Background: Potential consequences of increased antibiotic resistance (ABR) include not only the increased risk of untreatable infections but also the largely unquantified effect of jeopardising the safety of surgeries reliant on antibiotic prophylaxis. Hip replacements account for approximately 30% of surgeries in England, and with antibiotic prophylaxis they have a low risk of surgical site infection (SSI). Consequently, they provide an ideal case study for evaluating the impact of a reduction in efficacy of antibiotic prophylaxis due to resistance. We present a model utilising English national surveillance data to estimate the potential burden of ABR on SSIs and apply it to the case of hip replacement surgery.

Materials/methods: Commonly used prophylactic antibiotics were identified from hospital prescribing guidelines/literature. To estimate the current prevalence of ABR, the proportion of hip swab samples from 2016-2018 that contained bacteria that were resistant to antibiotics commonly used for prophylaxis were estimated from English surveillance data using bootstrapping. The increase in infections resulting from varying levels of reduction in efficacy of prophylaxis was estimated by calculating the attributable risk reduction of infection between prophylaxis and control groups. A 100% reduction in efficacy was assumed to be the infection rate observed in the control group, derived from historical clinical trials of antibiotic prophylaxis versus placebo and groups at high risk of prophylaxis failure due to factors including obesity and diabetes in more recent published studies. We estimated this value to be in the range of 2-6%.

Results: Approximately 11% of SSIs following hip replacement surgeries were resistant to commonly used prophylactic antibiotics. Preliminary predictions estimate that, under current prophylaxis guidelines, ABR could cause up to a 10-fold increase in infections resulting from hip replacement surgery in England (Figure 1).

Conclusions: There is potential for increasing rates of ABR to considerably impact SSI incidence following hip replacement surgery, which has not previously been quantified in the European setting. Adequately defining the population that are susceptible and resistant to prophylaxis is crucial to producing accurate predictions of future impact.

Figure 1: Expected increase in infections per year resulting from hip replacement surgery at different levels of resistance

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Abstract 4310

Effect of a serum lactate monitoring recommendation policy on patients treated with linezolid

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Background: Lactic acidosis is one of the most fatal adverse effects of linezolid, an antibiotic used to treat serious infections caused by antibiotic-resistant bacteria. However, the measures to prevent lactic acidosis have not been well established. We performed a retrospective study to analyze the impact of applying a serum lactate monitoring recommendation policy in patients treated with linezolid.

Materials/methods: Since September 2011, we have recommended inpatient monitoring of serum lactate levels in patients treated with linezolid at our hospital. Patients were divided into two groups according to whether they were seen during the non-recommendation or recommendation periods. The frequency of serum lactate monitoring, linezolid-induced lactatemia, lactic acidosis, critical illness, and death were compared between the two periods.

Results: After September 2011, adherence to the recommendation to monitor serum lactate increased from 6.1% to 60.1%. No difference was observed in the incidence of linezolid-induced lactatemia and lactic acidosis between the two periods. However, there was a significant difference in the incidence of linezolid-induced critical illness between the non-recommendation and recommendation periods (3 vs 0 cases, \( p = 0.044 \)).

Table 1. Comparisons of outcomes between Pre-recommendation and Recommendation period

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pre-recommendation</th>
<th>Recommendation</th>
<th>( P ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
<td>112</td>
<td>204</td>
<td></td>
</tr>
<tr>
<td>Adherence to serum lactate monitoring</td>
<td>5/82 6.1%</td>
<td>86/143 60.1%</td>
<td>&lt;0.001</td>
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<tr>
<td>LZD-related event</td>
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<td></td>
<td></td>
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<tr>
<td>Lactatemia</td>
<td>3</td>
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<td>0.752</td>
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<tr>
<td>Lactic acidosis</td>
<td>3</td>
<td>1</td>
<td>0.129</td>
</tr>
<tr>
<td>Lactic acidosis-related critical illness*</td>
<td>3</td>
<td>0</td>
<td>0.044*</td>
</tr>
<tr>
<td>Death</td>
<td>2</td>
<td>0</td>
<td>0.125</td>
</tr>
</tbody>
</table>

*Critical illness includes shock, hemodialysis, and death

Conclusions: In patients treated with linezolid, serum lactate monitoring led to early detection of lactatemia, thus enabling rapid rescue. We recommend regular monitoring of serum lactate in all patients treated with linezolid.

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Isavuconazole for the treatment of invasive fungal infection in solid organ transplant recipients: experience from a referral centre

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Background: Invasive fungal infection (IFI) is a major complication after solid organ transplantation (SOT). Interactions with immunosuppressive agents and increased risk of azole-induced toxicity complicate treatment of post-transplant IFI. Isavuconazole (ISA) is a broad-spectrum triazole with pharmacokinetic advantages and low potential for drug-to-drug interactions. However, SOT recipients were underrepresented in pivotal trials, and real-world data on the safety and efficacy of ISA in this population are scarce.

Materials/methods: We reviewed all SOT recipients with a diagnosis of IFI according to EORTC criteria that received ISA as first-line or salvage therapy at our institution from January 2018 to October 2019.

Results: We included 14 patients: 4 kidney (28.6%), 4 heart (28.6%), 3 lung (21.4%), 2 small bowel (14.3%), and one kidney-pancreas recipient (7.1%). Median interval from transplantation to IFI diagnosis was 121 days (IQR: 71.8 – 744.3). One patient (7.1%) met criteria for possible, 8 (57.1%) for probable and 5 (35.7%) for proven IFI. Aspergillus spp. was isolated in 13 patients (A. fumigatus [8 cases], mixed infection involving A. fumigatus [2 cases], and A. lentulus, A. nidulans, A. granulosus [one case each]). Sites of infection included invasive pulmonary aspergillosis (57.1% [8/14]), isolated CNS aspergillosis (14.3% [2/14]), disseminated aspergillosis, cutaneous aspergillosis, tracheobronchial aspergillosis, and disseminated IFI due to Trichosporum inkin (7.1% [1/14] each). ISA was used as first-line therapy in 12 patients (85.7%); the remaining 2 were switched to ISA due to voriconazole-induced hepatotoxicity or drug interactions. Combination therapy (mainly with an echinocandin) was used in 7 patients (50.0%). Tacrolimus daily dose was reduced in 9 (64.3%) patients by a median of 47%, with no differences observed in blood trough levels during the first month of therapy. Complete and partial response rates were 58.3% [7/12] and 41.7% [5/12] among evaluable patients. Treatment-emergent adverse events attributable to ISA occurred in one patient (7.1%) with electrolyte imbalance that resolved after discontinuation of therapy. Among 9 patients with serial ECG recordings, 4 (44.4%) had cQT interval shortening (median of 30 mseg). There was one death (7.1%) during follow-up not attributable to IFI.

Conclusions: ISA appears to be effective and well tolerated in SOT recipients with IFI.

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Abstract 4314

**Experimental evolution of high-level azithromycin resistance in Neisseria gonorrhoeae during morbidostat culture**

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**Background:** The prevalence of azithromycin resistance in Neisseria gonorrhoeae (NG) now exceeds 5% in multiple locations around the world. We sought to characterize the genetic pathway to high-level azithromycin resistance (HL-AZMR: minimal inhibitory concentration (MIC) >256mg/L).

**Materials/methods:** A NG-morbidostat was constructed and used to subject two NG reference strains (WHO-F and WHO-X) to dynamically sustained AZM pressure. Experiments were performed in triplicate (F1 -F3, X1 -X3) and included controls that received no AZM. Cultures were sampled twice a week and MICs of azithromycin were determined using E-test (bioMérieux). Whole-genome sequencing (WGS) was performed using MiSeq (Illumina) via 2x 250b reads (Nextera XT). Reads were processed and mapped to the WHO reference genomes [LT51957 and LT519215] followed by variant analysis using CLC Genomics Workbench v 12.0.

**Results:** Within four weeks, all cultures evolved to HL-AZMR. One strain of WHO-F and all triplicates of WHO-X developed high-level resistance between day 13 and 17 (Figure 1). HL-AZMR was attained by day 24-26 in the other two strains of WHO-F. WGS revealed variants associated with low-to-mid level resistance in several genes. In the case of rplD, rplIV, mtrD and recJ, the same, or similar mutations were found in different vials. Nonsynonymous mutations in the 50S ribosomal proteins L4 (rplD) and L22 (rplIV) included G70D and R71C for L4, and a F85S and deletion of codons at 94-97 positions for L22. K823E and A443V substitutions were observed in the mtrD and the recJ gene, respectively. Variants in the pilQ and topB genes were only detected in one vial each, F1 and F3. When MICs shifted to high-level resistance, three mutations at the 23S ribosomal RNA were observed. The well-known A2059G mutations was observed in most vials. Whereas, F3 showed a mutation at position 2058 and X2 at position 2611. The controls for both WHO strains retained their low MICs.

**Conclusions:** These data show that development of low and mid-level AZMR was mainly associated with mutations in genes encoding the multidrug efflux mtrD subunit, the recJ exonuclease and the ribosomal proteins L4 and L22. High level resistance was only achieved by point mutations in the 23S rRNA.

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**Abstract 4316**

**Influenza and respiratory syncytial virus antigen diagnostic tests: do they still have a place in a routine diagnostic laboratory?**

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**Background:** Rapid diagnosis of respiratory infections can help clinical decision making easier leading to a reduction of unnecessary antibiotic use and a reduction of nosocomial infections by means of isolation procedures.

Antigen testing is a cheap method which is easy to perform and the result is obtained after only 15 minutes but the sensitivity is variable.

**Materials/methods:** The antigen detection tests were done following the manufacturers’ instructions (BinaxNOW® Influenza A &B and RSV [respiratory syncytial virus] Card - Alere/Abbott) and results were compared with an in-house RT-PCR test targeting the M-gene [matrix] for influenza and the N-gene [nucleoprotein] for RSV. Retrospective evaluation was done on data collected during five winter seasons [2014-2019] in a Belgian regional hospital. Sensitivity was compared between a pediatric and an adult population (> 16 years).

**Results:** The average sensitivity of the RSV antigen test in the pediatric population (1607 patients) was 63% which stayed more or less constant over the five seasons.

The average sensitivity of the influenza antigen test in the pediatric population (1438 patients) was almost two times higher than the sensitivity in the adult population (1262 patients): 58% versus 32%.

The sensitivity of the influenza antigen test ranged from 53 to 73% in the pediatric population and from 19 to 37% in the adult population, depending on the subtype of the influenza strains which were circulating in that particular winter season.

**Conclusions:** Our evaluation is in line with the literature (C. Chartrand et al., Ann Intern Med, 2012).

According to our opinion a cheap rapid antigen test can be performed as a first line analysis in the pediatric population when a negative result is followed by a molecular diagnostic test. In the adult population however a rapid antigen test should not be used in routine due to a lack of sensitivity and a molecular diagnostic test is the preferred method of choice.

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Abstract 4317

Whole metagenome shotgun-sequencing in a case of hyperammonaemia syndrome following lung transplantation
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Background: Mycoplasma hominis and Ureaplasma sp. are responsible for opportunistic infections in transplant patients, sometimes causing a life-threatening hyperammonemia syndrome. Both pathogens are not identified with standard microbiology techniques, resulting in missed or delayed diagnosis. We present a clinical case that illustrates the added value that Next Generation Sequencing (NGS) may offer in the diagnosis of respiratory infections in immune-compromised patients.

Results: A 55 years-old man with idiopathic pulmonary fibrosis underwent double lung transplantation. He received antibiotic prophylaxis with piperacillin-Tazobactam (TZP) and a classic immunosuppressive regimen. At day 4 post-transplantation (PTx), the patient presented an acute respiratory distress requiring re-intubation. A broncho-alveolar lavage (BAL) was performed, and TZP was switched to Cefuroxime. At day 5 PTx, the patient presented a status epilepticus due to diffuse cerebral oedema. Serum ammonia concentration was 66 1 µmol/dL. BAL bacterial culture was negative. Because of the clinical presentation, special cultures were performed and identified 100.000 CFU/mL of M. hominis and Ureaplasma sp. and specific PCRs were positive for M. hominis and U. parvum. Antibiotic therapy was shifted to azithromycin and doxycycline; within 48h ammonia serum concentrations returned to normal (< 102 µmol/dL). Clinically, the coma persisted several weeks, followed by a persistent frontal lobe syndrome.

A follow-up BAL was performed on day 11 Ptx. The Mycoplasma/Ureaplasma culture was negative, yet the specific PCRs remained positive. Bacterial culture found 100 CFU/ml of Staphylococcus aureus and viral culture was positive for Herpes Simplex Virus. These results were confirmed by whole-metagenome shotgun sequencing (WMGS) as 9.32 x10⁷ genomes were found: 3980/3906 (Forward)/(Reverse) genomes mapped Human alphaherpesvirus-1, and 3804 genomes mapped bacterial phylum of which 37.5% belonged to S. aureus. M. hominis and U. parvum genomes were amplified at 0.98% and 0.15%, in favour of microbiological cure.

Conclusions: WMGS offered added diagnostic and quantitative values compared to classic PCRs which can remain positive after resolved infections. The initiation of appropriate antibiotic therapy would have occurred earlier on, possibly resulting in a better clinical outcome if WMGS had been performed in a routine fashion. The added value of this method should be investigated in a larger cohort of patients.

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Quantification and characterisation of antibiotic resistance in greywater discharged to the environment

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Background: In disprivileged communities greywater (wastewater which does not contain effluent from toilets) is often environmentally discharged without treatment. This results in a potential human exposure to associated antibiotic-resistant bacteria (ARB) including extended spectrum beta-lactamase (ESBL)-producers, however this risk is under-studied. We sought to examine the abundance of ARBs (with a focus on ESBLs) and antibiotic-resistance genes (ARGs) in greywater from rural, off-grid Bedouin villages in Southern Israel.

Materials/methods: Greywater samples (n=21) were collected from five Bedouin villages in the Negev (March-November 2018). Serial dilution was carried out to quantify faecal coliforms. ESBL-producers were recovered on CHROMagar ESBL and confirmed by VITEK®2 for ID/AST. Genomic DNA was extracted from the samples and qPCR was used to determine the relative abundances (gene copies/16S rRNA gene) of class 1 integron-integrase intI1 and the following ARGs: blaTEM, blaCTX-M-32, sul1, and qnrS. 16S amplicon sequencing was performed on the Illumina MiSeq and sequences were processed using the QIIME pipeline.

Results: Mean count of isolates recovered by selective plating was 4.6x10⁶ CFUs/100mL (Range:3.0x10⁶-7.4x10⁶ CFUs/100mL). Of 81 presumptive isolates, 15 ESBL-producers were recovered (4 Escherichia coli, 9 Klebsiella spp., 2 Enterobacter cloacae); ESBL-producers were detected in every village. Phenotypically, 86.7% of ESBL-producers were multi-drug resistant. A high abundance of intI1 (0.14 gene copies/16S rRNA), qnrS (0.02 gene copies/16S rRNA), and sul1 (0.05 gene copies/16S rRNA) was observed, followed by blaTEM (3.5x10⁻⁵ gene copies/16S rRNA) and blaCTX-M-32 (2.2x10⁻⁵ gene copies/16S rRNA, Figure 1). Pearson’s correlation analyses showed that total faecal coliform counts were positively correlated to 16S gene copies (p-value=0.001) and total ESBL counts (p-value=0.008). Microbiome analysis showed much diversity between samples, however some commonalities were detected between spatially-related samples. Clustering was observed among some ESBL-producers.

Conclusions: Greywater can be a source of ARBs, including ESBL-producers, in settings characterised by low sanitary conditions and inadequate wastewater management. A multimodal approach combining culture, qPCR, and microbiome studies is especially useful for risk assessment in relation to environmental ARB spread and impact on human health. Such an approach could inform future studies aiming at characterising environmental resistomes in communities worldwide struggling with appropriate sewage management.

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Tracing of ESBL-producing and ciprofloxacin-resistant Escherichia coli in Belgian broiler and pig farms: a longitudinal study

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Abstract third-party references: i-4-1-Health Study Group

Background: Resistant Escherichia coli from livestock may be found in food. Retail chicken meat contaminated with ESBL-producing bacteria has been documented in several countries. In addition, ciprofloxacin resistance is found to be high in Belgian livestock. Importantly, the mechanisms of fluoroquinolone resistance in veterinary and human clinical isolates are the same. Whole genome sequencing of resistant bacteria can identify the burden of antibiotic resistance and determine relatedness of resistant bacteria in farms.

Materials/methods: In the i-4-1-Health project, presence of ESBL-producing (ESBL-E. coli) and ciprofloxacin-resistant (CiproR-E. coli) E. coli in fecal samples (FecalSwab, Copan Italy) from Belgian broiler (n=15) and pig (n=15) farms was investigated longitudinally. Per farm, three measurements with a six-month interval were performed between September 2017 and April 2019. When present, three ESBL-E. coli and three CiproR-E. coli from each farm and each measurement were sequenced (Illumina MiSeq). Bioinformatic analysis was performed with BioNumerics (Applied Maths). Core-genome multilocus sequence typing (cgMLST) was used to determine clonal relatedness. A threshold of 20 allelic differences for genetic distances was used to distinguish epidemiologically related/unrelated isolates.

Results: The most common ESBL-gene in ESBL-E. coli from broilers (37%) and pigs (38%) was blaCTX-M-1. Of all CiproR-E. coli, 14% showed plasmid-mediated quinolone resistance (oqxAB, qnrS1, qnrB19), 97% showed mutations at hotspots S83L, D87N in GyrA and/or S80I in ParC and 8% also carried an ESBL-gene. Plasmid-mediated colistin resistance was detected among ESBL-E. coli and CiproR-E. coli in four pig farms (mcr-2.1 n=2, mcr-1.1 n=1, mcr-5.1 n=2, mcr-9.1 n=5) and one broiler farm (mcr-9.1 n=1). The predominant sequence type was ST1158 (7%) in broilers and ST744 (9%) in pigs. Reoccurrence of related ESBL-E. coli and/or CiproR-E. coli within a farm over different measurements was observed in 22/30 farms, indicating recirculation of isolates within farms [Figure-1]. Clonally related E. coli were detected among different broiler farms, but not among pig farms.

Conclusions: Recirculation of clonally related E. coli suggests that resistant strains reside in the farm environment. The occurrence of related strains among different broiler farms suggests a common reservoir (e.g. at top of the pyramid in the broiler production system) or transmission of resistant bacteria.
Figure 1: Minimum spanning trees based on cgMLST of ESBL-E. coli and CiproR-E. coli from broilers (A and B) and pigs (C and D) in Belgium. Colours represent different farms (F) and measurements (M). Branch numbers represent allelic differences. Clonally related isolates are partitioned when allelic differences are ≤ 20.

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Optimal detection of multidrug-resistant Gram-negatives from stools
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Background: Early detection of multidrug-resistant (MDR) bacteria in colonized patients is becoming crucial to prevent infections. In many health care settings, screening of hospitalized patients is performed as routine for infection control measures. However, the optimal detection strategies are not well established. This study evaluated different screening strategies: non-enrichment, non-selective enrichment, and selective enrichment steps prior to inoculation on selective agar plates for the detection of seven types of clinically-relevant MDR bacteria, namely extended-spectrum β-lactamase-producing Enterobacterales (ESBL-E), carbapenemase-producing Enterobacterales (CPE), polymyxin-resistant Enterobacterales (PMR-E), carbapenemase-producing Acinetobacter baumannii (CRAB), polymyxin-resistant A. baumannii (PMR-AB), carbapenem-resistant Pseudomonas aeruginosa (CRPA), and polymyxin-resistant P. aeruginosa (PMR-PA) from spiked stools.

Materials/methods: A collection of MDR Gram negative bacteria was used to test enrichment strategies. Two procedures were compared, namely an enrichment step in tryptic soy broth (TSB) and an enrichment step using TSB supplemented with antibiotic. Different antibiotic concentrations were chosen below EUCAST and CLSI breakpoint values. Commercially-available selective agar plates were used including ChromID-ESBL, SuperPolymyxin, SuperCarba, CHROMagar-Pseudomonas supplemented with meropenem (2 mg/L), and CHROMagar-MDR-Acinetobacter agar plates. Stool suspension spiked with given MDR bacteria were inoculated in three different procedures: a) directly on the selective media, b) into 5 mL of non-selective TSB, or c) into 5 mL of TSB supplemented with antibiotic. Colony-forming units (CFU) were counted after 18h of incubation at 37°C.

Results: The impact of the three different procedures revealed significant differences. Following TSB enrichment, the detection of MDR bacteria was significantly improved when compared to direct plating on selective medium (100,000-fold). Furthermore, the use of selective enrichment containing antibiotic, respectively supplemented with cefotaxime (0.1 mg/L), ertapenem (0.1 mg/L), colistin (0.5 mg/L), and meropenem (0.1 mg/L), improved the detection of MDR bacteria compared to non-selective enrichment step (10,000 fold).

Conclusions: The use of selective enrichment broths prior to direct inoculation onto selective culture media resulted in significant increased growth of all MDR bacteria tested. This screening protocol might be the best option to improve the sensitivity of the screening process, being a relatively low-cost, easy-to-implement strategy when performing extended surveys either in human, animal or environmental settings.

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Antimicrobial stewardship and infection control programmes on the incidence of carbapenem-resistant Klebsiella pneumoniae: a nonlinear time-series analysis

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Abstract third-party references: Supported by THRESHOLDS study group

Background: There is lacking evidence for effective strategies to contain the spread of carbapenem-resistant Klebsiella pneumoniae [KLEBCRE] in highly endemic hospitals. Our aim was to quantify the effectiveness of sequential infection control and antimicrobial stewardship (ABS) programs to reduce the spread of KLEBCRE.

Materials/methods: A non-linear time-series analysis (NL-TSA) exploring temporal associations between consecutive infection control interventions [hand hygiene (iHAND Campaign) and ABS (iASP Campaign)] and Incidence Density of KLEBCRE (DI_KLEBCRE) in Azienda Ospedaliero-Universitaria Policlinico Modena was conducted. We used the statistical approach elsewhere described (López-Lozano JM, et al. Nat Microbiol. 1160–1172, 2019) in order to adjust a non-linear model (Multivariate Adaptive Regression Splines) with endogenous identification of thresholds. Moreover, we evaluate the effectiveness of different interventions with a counterfactual analysis.

Results: Previous DI_KLEBCRE, alcoholic gel consumption (ALCBED) and recent hospital antimicrobial use [carbapenems and cephalosporins] were explanatory variables in the best-fit [adjusted-R²=0.539] NL-TSA model. We identified a threshold at 12.43 liters per 1000 occupied bed days [OBDs] for alcoholic gel consumption (ALCBED) above it, each additional liter per 1000 OBDs decreased the DI_KLEBCRE by 0.005 new cases per 1000 OBDs. Regarding antimicrobial consumption, we identified two thresholds: 46 DDD/1000 OBDs for Carbapenems (CARBA) and 98 DDD/1000 OBDs for Cephalosporins (CEFARES); above these thresholds, the KLEBCRE increased by 0.035 and 0.089 new cases per 1000 OBDs, respectively (figure 1). With a counterfactual analysis, we estimate that iCARBA and iASP reduced KLEBCRE by a monthly average of 0.035 (0.008, 0.058; CI-95%) per 1000 bed-days, the total accumulated decrease being of 2.5. Combining these campaigns with iHAND we estimate a decrease of KLEBCRE by 0.06 (0.028,0.092; CI-95%), with a total accumulated decrease of 4.57.

Conclusions: Antimicrobial stewardship, hand hygiene and target screening are essential components to reduce the spread of KLEBCRE in endemic settings. Our results confirm the hand hygiene central role to reduce KLEBCRE nosocomial transmission. The DI KLEBCRE increased significantly when the hospital uses of carbapenems and cephalosporins exceeded minimum thresholds. This finding could provide quantitative targets to drive ABS strategy.
Abstract 4326

The solitary parE-type toxin gene in *Pseudomonas aeruginosa* sequence type 111 clinical isolates collected in a paediatric intensive care unit in Moscow

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**Background:** Bacteria can survive antibiotic treatment using several strategies, including adaptive resistance, tolerance and persistence. The investigation of bacterial survival strategies is an important challenge in clinical microbiology.

**Materials/methods:** This study included ten *Pseudomonas aeruginosa* sequence type 111 strains isolated from a pediatric intensive care unit in Moscow (2012-17). Minimal inhibitory concentration (MIC) values were determined using Sensititre Gram Negative MIC Plates (Thermo Fisher Scientific); the results were interpreted according to the EUCAST criteria. Whole genome sequencing (WGS) was performed on the Illumina Hiseq 2500 platform. BLAST, ResFinder service and ISsaga tool were used for analysis of WGS data.

**Results:** All *P. aeruginosa* isolates were colistin-only susceptible and demonstrated resistance to piperacillin-tazobactam, ticarcillin-clavulanic acid, ceftazidime, meropenem, imipenem, amikacin, netilmicin, ciprofloxacin. A number of resistance genes, including *bla*VIM-2*, aacA29a*, *aph(3')-IIb*, *crpP*, *fosA* and *sul1*, were found in all strains. In two isolates, an insertion sequence (IS) element containing the transposase gene and inverted repeats identical to those of ISPa40 was detected. The IS element was located within the polyketide cyclase gene (*pc* gene) at nucleotide position 59. In contrast to reference ISPa40, IS detected in the present study contained a passenger gene homologous to *parE* (*parE-type* gene) encoding RelE/ParE super-family toxin, which is known to be a part of toxin-antitoxin system and induce persister formation. The *parE-type* gene was 447 bp in length and resembled *parE* from *Pseudomonas graminis* (58% query cover, 98% identity). The genetic environment of the detected *parE-type* gene is presented in Figure 1. No corresponding antitoxin genes were found in *parE-type*-positive *P. aeruginosa* isolates, therefore *parE-type* was a solitary toxin gene.

**Conclusions:** We hypothesize the detected *parE-type* gene can spread among bacterial isolates via IS element and confer to bacteria an ability to form persister cells under antibiotic treatments.

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Global outbreak of *Mycobacterium chimaera* infections in cardiac surgery patients: tracking risk through ongoing surveillance in the UK

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**Background:** Global distribution of *Mycobacterium chimaera* contaminated heater cooler units used in open-heart surgery has resulted in one of the most widespread multicenter hospital outbreaks described to date, with cases documented in 13 countries spanning 4 continents. Prospective monitoring established in 2015 by Public Health England in collaboration with Devolved Administrations informed UK risk mitigation strategies. We assess changes in risk since implementation of these measures, including enhanced device decontamination, advice on theatre positioning and patient notification of early signs and symptoms.

**Methods:** Following initial retrospective case finding, laboratories were requested to report prospective cases meeting our case definition - *Mycobacterium chimaera* endocarditis, surgical site infection or disseminated infection within 10 years of cardiopulmonary bypass (cardiothoracic surgery, extracorporeal membrane oxygenation or other procedure involving heater cooler units). Risk to patients in England was quantified using denominators derived from NHS Digital Hospital Episode Statistics.

**Results:** 45 *Mycobacterium chimaera* outbreak cases have been identified to date in the UK. Patients had undergone surgery in 22 cardiac centres, including 2 private facilities. Most [39] had heart valve surgery, the remainder coronary artery bypass or aortic graft surgery. The earliest case underwent surgery in 2007 and the most recent in 2016. Median interval between surgery and microbiological diagnosis was 23 months (<1 month to 68 months) with a decrease from 27 to 12 months from 2007-11 to 2016. Analysis of data from England indicated a crude risk of 0.19 per 1000 patients undergoing heart valve surgery from 2007 to 2018 (1 in 5000). Assuming a 5y period of risk, incidence peaked in 2014 at 1.48 cases per 10,000 person-years of follow-up, with significant decrease from 2014 to 2018 (RR=0.51, 95% CI 0.31-0.84). To date, just over half (25) of cases have died, with deaths within 1y of diagnosis (n=16) dropping between 2007-11 and 2016.

**Conclusions:** Whilst cases linked to this global outbreak continue to be diagnosed in the UK, risk estimates suggest a substantial reduction since the implementation of control measures in 2015. With limited effectiveness of treatment, outcomes for patients remain very poor, highlighting the devastating impact of this unique outbreak.

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ABSTRACT BOOK – 30th ECCMID 2020

Abstract 4333

**Chronic mucocutaneous candidiasis in children in Saint Petersburg, Russia**

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**Background:** Chronic mucocutaneous candidiasis (CMC) is a rare hereditary disorder characterized by persistent and recurrent infections by Candida due to changes in cellular immunity and may be associated with autoimmune endocrine disorders.

**Materials/methods:** Molecular genetic studies were performed with multigenic targeted sequencing (MiSeq, Illumina, USA).

**Results:** In prospective single center study included 11 patients with CMC. Median age was – 7.5 y, range - 6 to 13 y, males - 92%. Molecular genetic study has shown heterozygous mutation in the STAT1 gene in 4 patients and mutations in autoimmune regulator (AIRE) in 7 patients. Sites of candidiasis were oral mucosa – 100%, skin – 54%, esophagus – 46%, and nails – 31%. *Candida albicans* was isolated in all patients. Recurring CMC was diagnosed more than 4 times per year in all patients. Endocrine disorders were present in patients with AIRE syndrome: primary adrenal insufficiency – 71%, hypoparathyroidism – 71%, autoimmune thyroiditis with hypothyroidism – 29%; autoimmune disorders: autoimmune gastritis – 71%, alopecia – 29%, hematological disorders: lymphopenia – 30%, pernicious anemia – 14%. In patients with impaired STAT1 were lymphopenia – 50%, autoimmune gastritis 25%, other skin infections (*Streptococcus spp.*, *Malassezia spp.* ) – 25%. On susceptibility testing one *Candida albicans* (18%) was resistant to fluconazole and voriconazole. Patients with exacerbations of CMC receive fluconazole 3 mg/kg/day for two weeks, then 3 mg/kg/day once per week for 2 months with clinical response and disappearance of symptoms in 9 patients. Patient with azole resistant *Candida albicans* received itraconazole with clinical effect.

**Conclusions:** In 100% patients with mutations in AIRE and STAT1 genes diagnosed candidiasis of oral mucosa, 54% - candidiasis of skin. Endocrine system disorders, autoimmune diseases, hematological disorders was diagnosed in patients CMC with mutations in autoimmune regulator AIRE. Lymphopenia, autoimmune gastritis, other skin infections was diagnosed in patients CMC with mutations in STAT1.

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Abstract 4335

Risk factors associated with carbapenemase-producing Enterobacteriaceae infection

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Background: In most of published studies looking for risk factors for carbapenemase-producing Enterobacteriaceae (CRE) infection, matching was exclusively based on the presence of bacteremia, regardless of the source of infection or admission department.

Materials/methods: We performed a case-control study to evaluate risk factors for CRE infection including all first episodes between 06/2013 and 12/2016. We selected episodes of infection due to non-CRE Enterobacteriaceae as controls [non-CRE], matched [1:1 ratio] by clinical syndrome, previous invasive procedure and admission department.

Results: We included 136 CRE and 136 non-CRE episodes. Baseline characteristics were similar except for cardiovascular disease, that was more frequent in cases [52.2% vs. 41.2%; odds ratio [OR]: 1.882; 95% confidence interval [95%CI]: 1.045-3.390; p=0.035]. Hospital admission in the previous 90 days was more common in cases [51.5% vs. 28.7%; OR 3.214; 95%CI: 1.764-5.856; p <0.0001], with more cumulative days of hospital stay [median: 29.0 vs. 16.0; OR: 1.047; 95%CI: 1.026-1.069; p <0.0001]. Previous infection by a multidrug resistant microorganism [16.2% vs. 2.9%; OR: 5.500; 95%CI: 1.895-15.960; p=0.002] and CRE colonization [62.5% vs. 2.2%; OR 65.289; 95%CI: 8.749-487.332; p <0.0001] were more frequent in cases. The following treatment-related variables were also more common in this group: antibiotic therapy in the previous 90 days (81.6% vs. 44.9%; OR: 13.500, 95%CI: 4.889-37.725; p <0.0001), cumulative days of therapy [median: 20.0 vs. 15.0; OR: 1.030, 95%CI: 1.005-1.057; p=0.0219], and previous use of carbapenems [40.4% vs. 14%; OR: 4.600, 95%CI: 2.321-9.115; p <0.0001], quinolones [31.6% vs. 8.8%; OR: 5.429, 95%CI: 2.424-12.156; p <0.0001] and cephalosporins [31.6% vs. 18.4%; OR: 2.125, 95%CI: 1.173-3.850; p=0.016]. After adjusting by conditional logistic regression, previous renal replacement therapy [adjusted OR [aOR]: 4.924, 95%CI: 1.283-18.898; p=0.020], cumulative hospital stay within the previous 90 days [aOR [per one-day increment]: 1.034, 95%CI: 1.010-1.059; p=0.005], and previous use of quinolones [aOR: 9.516; 95%CI: 2.997-30.213; p <0.0001] and carbapenems [aOR: 3.339; 95%CI: 1.332-8.373; p=0.010] remained as independent risk factors.

Conclusions: After matching by source of infection and admission department, previous renal replacement therapy, cumulative hospital stay within the previous 90 days and previous treatment with quinolones and carbapenems emerged as risk factors for CRE-infection.

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Host biomarkers to differentiate bacteraemias from microbiologically proven viral infection in adults with acute fever episodes attending outpatient clinics in Tanzania

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Background: Patients with bacterial and viral infections have overlapping clinical presentations. Amongst febrile patients, discriminating between both groups is paramount for correct and timely therapeutic decision-making. There have been mixed results in the study of host biomarkers to this effect. We aimed to test the predictive validity of biomarkers in a microbiologically well-characterized cohort to overcome potential overlaps.

Materials/methods: Consecutive adults with temperature >38°C were recruited and the study team collected a detailed medical history and clinical examination. Blood and nasopharyngeal samples were taken to perform rapid tests, serologies, cultures and molecular analyses for infectious pathogens.

We then identified a group of patients with microbiologically-proven infections: 1) bacterial infection defined as positive blood cultures and 2) viral infection defined as patients with fever without focus and positive dengue RDT, acute HIV infection (positive p24 antigen only), acute EBV/CMV infections (IgM positive, IgG negative) and chickenpox (positive VZV PCR on skin swab).

Plasma concentrations of markers of endothelial (Angpt-2, sFlt-1, sVCAM-1, sICAM-1) and immune (sTREM-1, IL-6, IL-8, CHI3L1, sTNFR1, PCT, CRP) activation pathways were quantified using Luminex and ELISA. We evaluated the accuracy of these mediators in discriminating bacterial from viral infections.

Results: Of 507 patients we selected 172 patients with microbiologically-proven infections. 23 with bacterial infections [12 Salmonella typhi and S. paratyphi, 4 Streptococcus pneumoniae and 7 others]. 149 with viral infections of which 134 dengue, 4 acute HIV infections and 12 herpesvirus. Chronic HIV was significantly more prevalent in the bacterial infection group (48% versus 9%; p<0.01).

The top 3 predicting biomarkers were chitinase-3-like protein-1, procalcitonin and soluble-tumour-necrosis-factor-receptor-1 (area under the receiver operating characteristic [AUROC] 0.82 [95% CI 0.81-0.94], 0.86 [0.78-0.94] and 0.85 [0.73-0.96]). Adding PCT to HIV screening significantly improved the diagnostic performance [AUROC 0.69 [0.59-0.80] versus 0.90 [0.83-0.97]; p<0.01]

Conclusions: Systematic HIV screening of febrile patients identifies patients at higher risk of bacteremia. By combining it with a commercially available biomarker point-of-care test, procalcitonin, our results showed an excellent discriminatory power between bacterial and viral infections. An algorithm based on both tests for patient management has the potential to improve outcomes and decrease inappropriate antibiotic prescriptions.

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Virological features and efficacy of re-treatment in hepatitis C virus patients: a real experience in southern Italy

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Background: direct-acting antivirals (DAA)-regimens are associated with failure in about 5%. The failure was associated with the emergence of resistance associated substitutions [RASs]. This real-life study characterized the virological patterns in patient failing to DAA and evaluated the efficacy of retreatment.

Materials/methods: all the consecutive 207 HCV patients failed to DAA observed at the laboratory of infectious diseases of University of Campania, Naples were enrolled. All the patients were treated according to HCV genotype, international guidelines and local availability. Sanger sequencing of NS3, NS5A and NS5B was performed at failure by home-made protocols.

Results: Patients enrolled were mainly males (68.1%) with median age 65[31-89]. 86% were Relapse, 8,7%no Responder,5,3% Breakthrough, 35 (17% %) were re-treated. Table 2 shows the epidemiological, clinical and virological characteristics of the 35 retreated patients. At failure, 68,5% of patients presented one RAS and 42,8 % had 2 or more RAS. 17 (48,6%) obtained SVR. The 7 re-treated patients with genotype 3 most frequently (41,2%) showed SVR than the patients with genotype 1 (29,4%), 2 (23,6%) and 4 (5,8) but without statistical significance.

We analyze the SVR prevalence according to previous/latest DAA regimen, RASs distribution and Resistance-Guided Therapy [RGT]. Patients retreated with the latest DAAs regimen most frequently obtained SVR than patients retreated with previous generation of DAA (76.6% vs 13.3%, p<0.05). Patients with SVR most frequently had RGT (63.4% vs 26.6%, p<0.05).

Conclusions: The prevalence of RASs was high in our real-life population. Failed patients have at least one RASS in one HCV region. The latest DAA regimen more frequently obtained SVR despite previous regimen. Patients with RGT more frequently obtain SVR. NS3, NS5A and NS5B sequencing seems mandatory in the choice of re-treatment DAAs.

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Abstract 4341

Extrapulmonary tuberculosis among migrants in Europe
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Background: The proportion of tuberculosis (TB) cases in Europe that occur in migrants is increasing. While not transmissible, extrapulmonary TB (affecting organs other than the lungs) poses challenges in diagnosis and treatment and causes serious morbidity and mortality. To date, there has been no in-depth exploration of extrapulmonary TB in migrants across Europe.

Materials/methods: We analysed 22 years of data from the European Centre for Disease Prevention and Control’s European Surveillance System (TESSy) for 31 EU/EEA countries collected between 1995 and 2017. We investigated whether the proportion of TB cases that were extrapulmonary varied between migrants and non-migrants, and whether this varied by a) country/region of origin, b) reporting country/region, and c) site of disease. All analyses were conducted in StataSE v15.

Results: 1,270,896 TB cases were included in the analysis, comprising 326,987 (25.7%) migrants, and 943,909 (74.3%) non-migrants. 45.2% (n=147,814) of cases among migrants were extrapulmonary, compared to 21.7% (n=204,613) among non-migrants (χ²=6.7x10⁴, p<0.001). The mean age of all included migrants with TB was 38 years, and 59.9% were male, compared with 48 years and 40.1% male in non-migrants. Among extrapulmonary TB cases, specific site varies by migrant status (χ²=1.9x10⁴, p<0.001). For migrants, 47.6% of extrapulmonary TB is lymphatic, compared with 25.3% in non-migrants. Bone/joint and peritoneal/digestive TB are also relatively more common in migrants than in non-migrants. The majority of migrant extrapulmonary TB cases were from South-East Asia (n=55,390) and Sub-Saharan Africa (n=38,319), with the highest proportions of extrapulmonary TB seen among migrants from these regions (62.0% and 54.5% respectively). A relatively low proportion of extrapulmonary TB was seen in Eastern Europe (17.4%) compared with Northern/Western Europe (38.7%), where the proportion of extrapulmonary TB is greater in foreign-origin cases (49.7% extrapulmonary in foreign-origin vs. 27.2% in native-origin, χ²=2.6x10⁴, p<0.001).

Conclusions: Among TB cases in the EU/EEA, the proportion of cases that are extrapulmonary is higher in migrants than in non-migrants, particularly among those from South-East Asia and Sub-Saharan Africa. This pattern is seen primarily in final destination countries in Northern and Western Europe, which has clinical and policy implications for patient management.

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Significant increase in the prevalence of macrolide resistance-mediating mutations in Mycoplasma genitalium from 2014 to 2019

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Background: Mycoplasma genitalium is the second cause of non-gonococcal urethritis and non-gonococcal cervicitis after C.trachomatis. The recommended first-line treatment for uncomplicated M. genitalium infection according 2016 European guideline is Azithromycin 500 mg on day one, then 250 mg od days 2–5. But the last 10 years was shown the essential decrease of azithromycin efficacy and now it is approaching 60%. The azithromycin treatment failure is caused by appearance of macrolide resistance-mediating mutations in region V of the 23S rRNA gene M.genitalium.

Materials/methods: The study objective was to compare the prevalence of macrolide resistance associated mutations in M. genitalium positive patients in 2014-2015 and in 2018-2019. Samples from 400 M. genitalium positive patients who attended non-STD clinics in Moscow were collected in 2014-2015 and 125 in 2018-2019. Among received 525 urogenital samples 353 (67%) were from females and 172 (33%) from males. The extracted DNA from the samples were amplified with primers specific for V region of 23S rRNA gene M. genitalium. Antibiotic resistance-associated mutations were identified using conventional Sanger sequencing.

Results: The prevalence of macrolide resistance associated mutations was shown about three times higher in 2018-2019 than in 2014-2015: 13.6% and 4.75%, respectively. There was no significant difference in the mutation’s prevalence between men and women. The most prevalent macrolide resistance-mediating mutation - A2059G was the same in 2014-2015 and in 2018-2019 and it’s prevalence was 68.4% and 58.8%, respectively. The second most prevalent mutation was A2058G: 26.3% in 2014-2015 and 23.5% in 2018-2019. And the rarest mutations were A2062G – 5.3% in 2014-2015 and A2058T - 17.6% in 2018-2019.

Conclusions: Study showed the macrolide resistance-mediating mutations prevalence growth by about three times over 4 years, this can lead to significant problems with M. genitalium infection treatment after 3-4 years. Our data highlights the need for optimization treatment protocol and development diagnostics assays for detection antibiotic-associated mutations in M. genitalium in Russia.

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Abstract 4347

Risk factors for Chlamydia and gonorrhoea infections and STI testing uptake amongst youth in Harare, Zimbabwe

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Background: Sexually transmitted infections (STIs) contribute to significant morbidity globally, and youth are particularly vulnerable. In low resource settings, syndromic management is recommended. There is therefore limited evidence regarding factors associated with uptake of STI testing in these settings, as well as sparse data on STI prevalence and risk factors for STIs.

Materials/methods: A cross-sectional mixed methods observational study was nested within a cluster randomised trial assessing the impact of a community-based package of sexual health services for youth aged between 16 and 24 years inclusive, in Harare, Zimbabwe. Testing for chlamydia and gonorrhoea was offered as part of this package of services. Questionnaires were used to collect data on sociodemographic characteristics, sexual and reproductive history, knowledge of STIs, attitudes towards STI testing and attitudes and perceived barriers to partner notification. Testing for gonorrhoea and chlamydia infection was performed on urine samples using the Cepheid GeneXpert platform. Univarate analysis and multivariate logistic regression was used to assess factors predicting STI testing uptake and a positive STI result.

Results: Of 350 participants accepting testing, prevalence of chlamydia and gonorrhoea infection was 16.3% and 3.7%, respectively. Number of different sexual partners in the preceding year was the only factor significantly associated with having an STI on univariate analysis. Multivariate analysis revealed a strong association between female gender and a positive STI result.

Among the 243 participants included in the testing uptake analysis, older age, female gender, being employed, being married compared to single, having no recent new sexual partners and not using a condom at the most recent sexual encounter were all significantly associated with accepting STI testing in univariate analyses. The presence of current symptoms was significantly associated with accepting testing in both univariate and multivariate analyses.

Conclusions: The high prevalence of chlamydia and gonorrhoea amongst youth in Harare demonstrate the limitations of syndromic management. Regarding testing, presence of symptoms appeared to be a driving factor for uptake. Furthermore, younger males had particularly poor uptake and so should be encouraged to test. However, this should not be at the expense of females who had higher odds of having an STI.

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**Abstract 4348**

**Outcomes of bacteraemic and non-bacteraemic patients presenting to the emergency department**

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**Background:** Bacteraemia is a major cause of sepsis and is associated with high morbidity and mortality. Delayed antibiotic treatment in the septic shock population has previously been associated with poorer outcomes. We designed this study to look at the outcomes between bacteraemic and non bacteraemic patients.

**Materials/methods:** This was a retrospective cohort study performed in two metropolitan hospitals in NSW. The first cohort included adult patients (>18 years) with positive blood cultures (bacteraemia with a true pathogen). The second cohort consisted of patients matched by age to the first without bacteraemia. Data was collected on demographics and outcomes including length of stay, ICU admission and ICU length of stay, in-hospital mortality related to sepsis and antibiotic duration. Mortality associated with time to antibiotics was evaluated in both cohorts.

**Results:** There were 251 patients in each cohort. Sepsis-related mortality was higher in the bacteraemic group (OR 0.4, p=0.03). Bacteraemic patients had longer hospital admissions (10.7 vs 7.5 days, p<0.001) and longer antibiotic duration (15.44 versus 8.20 days, p=0.001). There was no difference in ICU admission (p=0.55) or ICU length of stay (p=0.11). Antibiotics administered within an hour of triage did not improve overall mortality in the bacteraemic group (p= 0.64).

**Conclusions:** Bacteraemic patients have higher sepsis-related mortality, longer length of hospital admission and longer antibiotic duration when compared with non bacteraemic septic patients. Antibiotics administered within one hour of triage did not improve sepsis mortality related outcomes.

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Abstract 4351

**Evaluation of a multiplex PCR in genital ulceration diagnosis**

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**Background:** Genital ulcerations can be hard to diagnose because different pathogens can be involved and lesions can be atypical. The aim of this study was to evaluate the analytical performances and the clinical impact of using a multiplex PCR (Allplex genital ulceration Seegene) in genital ulceration diagnosis at laboratory.

**Materials/methods:** First, analytical performances on 38 known samples were compared, using sample positive for HSV1, HSV2 and VZV (simplex PCR Sacace), *Haemophilus ducreyi* (Vircell standard), *Chlamydia trachomatis* serovar L (genotyped by the French National Reference Center) and *Treponema pallidum* (patient presenting with positive VDRL serology, with an available swab and/or positive direct examination by immunofluorescence). Then, we studied patient samples (=38) received in Cerba laboratory from February to July 2019 with a request of only *Treponema pallidum* or *Haemophilus ducreyi* PCR, or genital ulceration multiplex PCR. We notified also those for which the evidenced pathogen was not initially prescribed.

**Results:** 38 samples have then been compared to simplex tests for analytical performance evaluation. The different samples studied were anal (n=11), genital (n=8), 4 peripherical from a newborn; urine (n=1); urethral (n=1), external quality controls (n=12), and commercial standard (n=1). Results showed 100% concordance, the discrimination between HSV1 and HSV2 and between L and no-L *Chlamydia trachomatis* was perfect. (table 1) Then, among the 38 patient samples: 16 were positive for at least one target and 22 were negative. We found 11 HSV; 3 *Treponema pallidum*; 1 VZV and 1 *Chlamydia trachomatis* serovar L. (table 2) From the 16 positive samples, multiplex PCR testing allowed to diagnose 7 pathogens which were not initially prescribed.

**Conclusions:** Analytical performances of the genital ulceration multiplex PCR (Allplex Seegene) were satisfactory, with sensitive and specific detection, and can be used as an epidemiological tool. Moreover, it allowed detection of non-prescribed pathogens.

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Abstract 4352

**Clonal spread of multidrug-resistant penicillin-nonsusceptible *Streptococcus agalactiae***

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**Background:** Penicillin is the first-line antibiotics for treatment and *S. agalactiae* is generally susceptible to penicillin. Three cases of penicillin non-susceptible *S. agalactiae* (PNSA) were isolated from respiratory specimens. Those three strains were analyzed for genomics and phenotypic characteristics.

**Materials/methods:** Antimicrobial susceptibility of 3 PNSA was analyzed using Microscan® STREP MSP6+ panel (Dade Bahning, West Sacramento, CA, USA) and penicillin minimal inhibitory concentration (MIC) was determined by Etest (BioMerieux, St Laurent, QC, France). Whole genome of 3 PNSA were obtained using PacBio 20-kb platform (Pacific Biosciences, USA), which were compared to whole genome of 16 reference strains. RNA transcriptomics of those strains were quantified compared to *Streptococcus agalactiae* ATCC13813 as the reference. Antimicrobial resistance and virulence factor genes were searched from whole genome data. Molecular epidemiology was investigated by multi-locus sequence typing (MLST), serotyping by sequencing, single nucleotide polymorphism (SNP) of penicillin-binding protein (PBP) gene and similarity of whole genomes.

**Results:** Three PNSA were susceptible to ampicillin, chloramphenicol, cefotaxime, daptomycin, linezolid, meropenem and vancomycin, and resistant to clindamycin, erythromycin, levofloxacin, and tetracycline. MICs of penicillin were 0.19 µg/ml, 0.5 µg/ml, and 0.25 µg/ml in SA1, SA2, and SA3, respectively. Three strains were all ST10. Each of three PNSA strains generated the whole genomes of 2,445,137 bp, 2,528,754 bp, and 2,486,170 bp, respectively and carried variable numbers of SNP to 16 reference genomes from minimum of 5,282 to maximum of 19,229. There were 170 SNP detected common in all PNSA and belonged to 96 coding sequences. The three isolates were differed by 214 to 603 SNPs each other and genomic similarity between 3 PNSA were more than 99.96%. All 3 isolates possessed same mutations of G398A, V405A, Q557E amino acid substitutions in pbp2x gene. There was no difference of RNA expression within genes of penicillin-binding proteins.

**Conclusions:** PNSA have been clonally spread in community. Causes of penicillin non-susceptibility of *S. agalactiae* were PBP aberration induced by deleterious amino acid substitutions and not by quantitative changes of PBP protein. Penicillin resistance should be monitored among *S. agalactiae* in Korea.

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Abstract 4362

Population pharmacokinetics of ceftriaxone administered as continuous or intermittent infusion in critically ill patients
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Background: The pharmacokinetics of beta-lactam antibiotics are altered in critically ill patients. As a result of these alterations, conventional antibiotic regimens are insufficient to reach the pharmacodynamic target of 100% T>MIC. Ceftriaxone is a beta-lactam antibiotic with a long half-life. Because of the half-life the target T>MIC was assumed to be achieved with intermittent dosing. Nevertheless, increased clearance and reduced protein binding in critically ill patients may lead to insufficient exposure. Continuous infusion could therefore be supportive in reaching a T>MIC of 100%. However, no data comparing intermittent and continuous infusion of ceftriaxone are currently available.

Objective: To describe the population pharmacokinetics of ceftriaxone in critically ill patients when administered as intermittent or continuous infusion. To determine an optimized dosing regimen.

Materials/methods: A population pharmacokinetic study was performed in the intensive care unit of a tertiary teaching hospital. Patients were treated with ceftriaxone as continuous infusion or intermittent administration. A pharmacokinetic model was developed with non-linear mixed effect analysis. Subsequently, influential patient characteristics and dosing regimens were simulated with a Monte Carlo simulation to assess the probability of target attainment (PTA) of a T>MIC of 100% in intermittent and continuous dosing.

Results: 55 patients were included. The data were best described by a one-compartment model with linear elimination and non-linear saturable protein binding. The included covariates were: estimated creatinine clearance (CLcr), serum albumin concentration and intermittent or continuous infusion. The simulation results showed that 2 g/24 hours as intermittent infusion was only sufficient to reach a PTA of 90% for an MIC of 1 mg/l in patients with a reduced CLcr (0-60 ml/min). With continuous infusion of 2 g/24 hours a PTA 100% PTA was reached in all patients (CLcr 0-180 ml/min), in patients with an increased CLcr (120-180 ml/min), intermittent dosing of 2 g/24 hours and 2 g/12 hours were not sufficient to reach a PTA of > 90%.

Conclusions: Intermittent dosing of 2 g/24 hours ceftriaxone in patients with a normal or increased CLcr may lead to subtherapeutic exposure. Treating patients at risk with continuous infusion of 2 g/24 hours is superior to increasing the dose with intermittent infusion.

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Orbitrap ultra high-resolution mass spectrometry proteomics data mirrors clinically relevant functional associations of black dematiaceous hyphomycetes (black yeast-like fungi)

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Background: Dematiaceous, or darkly pigmented fungi (namely black yeasts) are a large, phylogenetically heterogeneous group of organisms that have been associated with a wide variety of clinical syndromes. These are uncommon causes of human disease, but can be responsible for life-threatening infections in both immunocompromised and immunocompetent individuals. Due to rarity of many taxa in clinical practice, their (often) poorly defined and precise taxonomic assignment and the often inconsistently annotated clinical presentation makes affiliations of unknown strains often challenging. We present Orbitrap™ Mass Spectrometry data for a variety of genera and species and provide data for a remarkable association of functional traits (clinical presentation) in species that are genetically not related. Categorization of strains based on traits may appear highly useful when identification returns a rarely encountered microbial pathogen with unknown or poorly studied treatment options.

Materials/methods: High resolution accurate mass mass spectrometry was applied to >20 species of black yeasts with all strains being of clinical origin and obtained from pre-identified strain collections deposited at the Westerdijk Fungal Biodiversity institute, Utrecht, the Netherlands. Strains were characterised by means of standard molecular barcoding using multiple protein coding genes. Mass spectra were evaluated for the individual protein masses detected.

Results: A multi genera-species strain set comprising Cladophialophora, Exophiala, Fonsecea, S. stearothrix, Curvularia, Phaeoacremonium and Blastomyces were subjected to acquisition of Orbitrap™ mass spectrometry data. Species in black yeast-like fungi were functionally associated via different algorithmic approaches, mirroring their clinical presentation other than evolutionarily relatedness based on DNA sequences.

Conclusions: Inferring relationships between organisms and based on proteomic data which is conflicting traditionally derived classification schemes on the basis of DNA sequencing, can greatly widen our views on the evolution of microbial pathogenicity mechanisms. Associations based on traits that have functional meaning, were useful to categorize organisms according to disease outcome. Due to rarity of certain taxa in clinical practice, their (often) poorly defined and precise species identity and the often inconsistently annotated clinical presentation makes affiliations of unknowns based on traits highly useful when an identification results return a rarely encountered microbial pathogen with unknown or poorly studied treatment options.

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Abstract 4368

Rapid increase of CTX-M-producing ST152 Shigella sonnei isolates in Switzerland

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Background: Shigella sonnei (Ss) is one of the most common causes of diarrhea in returning travelers and the emergence of antibiotic resistant strains is a matter of concern. Recently, the Swiss Centre for Antibiotic Resistance (ANRESIS) has noted a significant increase of third-/fourth-generation cephalosporin-resistant (3/4GC-R) isolates at national level. Here, we characterize a collection of Ss strains to better understand this phenomenon.

Materials/methods: So far, 25 Ss (of which 12 3/4GC-R) collected during 2017-2019 in Canton Bern have been analyzed. ASTs were performed using microdilution Sensititre panels. Whole-genome sequencing (WGS) was achieved using both Illumina and Nanopore and analyzed using the Center for Genomic Epidemiology platform. Sequence type (ST) was achieved using the E. coli MLST scheme. Plasmids and core genome analyses were also performed.

Results: According to the ANRESIS database, the national prevalence of 3/4GC-R Ss strains was 3.8%, 12.8%, 15.6%, and 38.5% in 2016, 2017, 2018, and 2019, respectively. The 3/4GC-R strains belonged to ST152 or, more rarely, to its single allele variant ST1503. The non-3/4GC-R belonged to different STs not included in clonal complex 152. The 3/4GC-R strains mainly carried \textit{bla}_{CTX-M-15} in IncFII or \textit{bla}_{CTX-M-3} in IncI1 plasmids. However, plasmids of same Inc group were not always similar to each other. Core genome analysis indicated that the ST152/1503 Ss strains were almost identical, with a limited number of different SNPs and allele matches >99%.

Conclusions: Our data indicate that the increase of 3/4GC-R Ss recorded by the national surveillance system (ANRESIS) is mainly due to the spread of a clone (ST152) producing CTX-M-3/-15. Although we cannot retrieve detailed epidemiological information from the laboratory databases, we noted that some strains were isolated from the stools of travelers returning from different countries. Therefore, we speculate that ST152 is a pandemic clone. In this context, we emphasize that this ST has been already reported in USA, Iran, Brazil, and we recently described a CTX-M-3 producer in Italy imported from Albania. Since Shigellosis is subject to mandatory declaration, an active collaboration with the Swiss Federal Office of Public Health could provide further key epidemiological data to better understand this concerning phenomenon.

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Abstract 4369

**Antifungal susceptibility testing practices in mycology laboratories in France, 2018**

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**Abstract third-party references:** on behalf of the SFMM-AFST Study Group

**Background:** In vitro antifungal susceptibility testing (AFST) is important for therapeutic management of patients and to detect resistance. Commercial techniques are the most common AFST methods used by mycology laboratories. Nevertheless, the practices and potential difficulties encountered in their routine use are not well known.

**Materials/methods:** An online survey was performed to assess the practices of AFST in mycology laboratories in France. An electronic questionnaire was used for the survey. It consisted of 43 questions divided into 16 sections about the type of methods used, the strategy of antifungal testing, the way of reading the MIC, the interpretation of the MIC, the quality aspects, the technical aspects, the screening of resistance.

**Results:** The survey captured information from 45 laboratories (overall response rate of 94%). A large majority (77%) of the participating mycology laboratories (PML) performed AFST for more than 150 fungal isolates per year. The E-test was the most frequently used method (86%). For yeasts, 85% of PML tested a combination of four antifungal molecules [one echinocandin, fluconazole, voriconazole and amphotericin B]. A majority of PML declared reading the MIC results first at 24h of incubation, and then at 48h, both for Candida spp. (67%) and Aspergillus spp. (58%). Most of the PML (89%) used either an internal quality assessment (IQA) or an external quality assessment (EQA) and 62% used both IQA and EQA. Forty-six percent of the PML used the EUCAST clinical breakpoints (CBs), when available, to interpret the MIC values. Almost all the PML (98%) declared that the interpretation of MIC values was the main problem encountered during AFST and 40% reported difficulties in reading MIC values. Systematic screening of resistance was performed by very few PML (≈10%) in 2018.

**Conclusions:** A majority of French mycology laboratories routinely used E-test as AFST method, for both yeasts and filamentous fungi. If most parameters were similar between the 45 PML, two main problems emerged from this survey: reading and interpretation of MIC values. To homogenize AFST practices, detailed guidelines and instructions are needed, and could be implemented both by the manufacturer and by the French Society of Medical Mycology.

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Abstract 4370

Species delimitation of clinically challenging fungi by Orbitrap ultra high-resolution mass spectrometry: a case study in Mucor, Rhizopus and Lichtheimia

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Background: The epidemiology of invasive fungal diseases due to filamentous fungi immunocompromised patients and other host groups is shifting with changing clinical practice. After Aspergillus, Mucorales (Zygomycetes) fungi are the next most commonest pathogens in patients with haematological malignancy, haematopoietic stem cell transplantation and solid organ transplantation. Additionally Mucorales infections are increasingly recognized in individuals with diabetes mellitus, after trauma or iatrogenic injury and have been associated to outbreaks following natural disasters (eg. by global climate change). We present ultra high resolution Orbitrap™ mass spectrometry data for the most relevant causative agents of Mucormycosis and their subsequent precise classification into the most up to date taxonomic entities. The presented data aims to provide an outlook on improved diagnosis to one of the most challenging fungal groups encountered in clinical microbiology.

Materials/methods: High resolution accurate mass mass spectrometry was applied to eight species of the genera Mucor, Rhizopus and Lichtheimia. Strains were all of clinical origin and obtained from pre-identified collections deposited at the Westerdijk Fungal Biodiversity institute, Utrecht, the Netherlands. Strains were characterised by means of standard molecular barcoding using multiple protein coding genes. The protein extracts from each strain were introduced to the mass spectrometer using electrospray ionisation (ESI). Mass spectra were evaluated for the individual protein masses detected. Different identification and algorithmic approaches were compared.

Results: With the described mass spectrometry method individual protein masses of a variety of classes were detected. Across the different fungal strains of the same species the variation in the presence of proteins enabled searching for species, lineage and strain specific protein masses that were used to delimit the tested entities.

Conclusions: The presented Orbitrap™ mass spectrometry identification assay was able to identify Mucormycosis causing agents, in a time efficient and effective and precise manner. Identification accuracy could not yet be obtained by conventional mass spectrometry approaches such MALDI-ToF, and demonstrates for the first time the application of a high resolution mass spectrometry technology to resolve effectively a notoriously difficult group of clinically relevant fungi in an easy way.

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Persuading the prescriber: the impact of prospective audit with feedback on hospital antibiograms

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Background: Antimicrobial stewardship constitutes an essential element of any concerted effort to tackle rising trends of bacterial resistance. The term comprises variable strategies which aim to optimise prescribing practices through either mandatory antibiotic restrictions or prospective audits of prescriptions and subsequent feedback to clinicians. Although highly debated, the actual effect of the latter on hospital antibiograms has not been evaluated systematically. Therefore, the present study aims to review, collect and assess the available literature concerning the impact of persuasive stewardship strategies on antimicrobial resistance within hospital settings.

Materials/methods: A systematic literature review was conducted in the PubMed/Medline, Embase, Global Health and CINAHL Plus databases.

Results: Cluster randomised studies were absent and including observational designs in the dataset was the sole feasible option. Eight studies were included, seven simple before-and-after and one of an interrupted time series design. Frequency of audits and compliance rates varied within and between settings. The rationale of treatment optimization is not delineated in most cases rendering policy evaluation difficult. Overall, surveillance of sentinel microorganisms post-intervention indicates trivial results. Lack of proper theroretical reasoning causes uncertainty as to whether the few recorded successes are due to a causal effect or constitute random incidence fluctuations. The most straightforward and, thus, most informative approach targeted solely fluoroquinolone prescriptions and achieved improvements in relevant Pseudomonas susceptibilities as well as MRSA.

Conclusions: Research of higher standards is needed to address the actual effects of persuasive stewardship strategies on antimicrobial susceptibility patterns. At present, prospective audits with feedback seem inadequate to play a decisive role in bacterial resistance control within hospital environments

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Recreational waters: a reservoir for Shiga toxin-producing Escherichia coli?

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Abstract 4374

**Background:** Shiga toxin-producing *E. coli* (STEC) are pathogenic *E. coli* that can cause severe intestinal infection and haemolytic uremic syndrome (HUS) in humans, representing a major threat to public health. Since 2012, the notification rate of STEC in Ireland has been the highest in Europe. The aim of this study was to examine if recreational waters are a possible reservoir for STEC.

**Materials/methods:** Seawater (n=52), river (n=15) and lake (n=8) samples (30L) were collected from locations around Ireland between December 2018 and October 2019. Samples were processed using the CapE method and filters were enriched overnight in buffered peptone water. A boil-lysis was carried out on enrichment broth aliquots and extracts were tested using multiplex real-time PCR for *eae*, *vtx1* and *vtx2* genes. Positive samples were tested further for genes associated with serogroups O157, O26, O103, O104, O111 and O145.

**Results:** Of the 75 samples tested, 29/52 (56%) seawater samples, 14/15 (93%) river and 6/8 (75%) lake samples were positive for the *eae* gene and at least one of *vtx* genes. When these samples were tested further all samples were found to contain multiple serogroup gene targets. In seawater and lake samples the predominant serogroup was O103 and in river water samples it was O157. Two samples, both from fresh water sources were *vtx1/vtx2* positive but negative for *eae*.

**Conclusions:** To our knowledge this is the first investigation of multiple sites across Ireland for the presence of STEC in recreational waters. There was a high occurrence of STEC DNA in the samples tested, highlighting the need for further investigation to establish the scale of the problem. The findings indicate that there is a need to focus attention on the potential risk of infection from recreational waters where exposure is likely. It is worth noting that all of the seawaters tested were designated as good or excellent quality based on current EU bathing water monitoring criteria. This highlights the limitations of only assessing the total number of *E. coli* present as an indicator for quality without taking into consideration the pathogenicity of some variants.

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Abstract 4375

Comparison of different sepsis scoring systems and pathways: qSOFA, SIRS, Shapiro Criteria and CEC SEPSIS KILLS pathway in bacteraemic and non-bacteraemic patients presenting to the emergency department

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Background: Bacteraemia is a major contributor to sepsis-related morbidity and mortality, with management focused on the early identification and treatment of these patients. However, prompt identification of bacteraemia has remained challenging. We designed this study to assess the performance of existing scoring systems and pathways - CEC SEPSIS KILLS pathway, quick sequential organ failure score (qSOFA), systemic inflammatory response syndrome (SIRS), the Shapiro criteria and the SEPSIS KILLS icon.

Materials/methods: This was a retrospective cohort study performed in two metropolitan hospitals in NSW. The first cohort included adult patients (>18 years) with positive blood cultures (bacteraemia with a true pathogen). The second cohort consisted of patients matched by age to the first without bacteremia. Performance of different criteria and pathway (sensitivity, specificity and mortality prediction) - qSOFA (≥2 criteria), SIRS (≥2 criteria), Shapiro criteria (≥1 major or ≥2 minor) and CEC SEPSIS KILLS pathway (BTF derangement +/- clinical concern), in the first 4 hours following ED triage was assessed.

Results: There were 251 patients in each cohort. When the Bacteraemic and Non-Bacteraemic cohort were compared using the scoring systems and pathways, the modified Shapiro criteria had the highest sensitivity (88%) with modest specificity (37.85%), and qSOFA had the highest specificity (83.67%) with poor sensitivity (19.82%). SIRS had reasonable sensitivity (82.07%), with poor sensitivity (20.72%). The CEC SEPSIS pathway sensitivity of 70.1% and specificity of 71.1%. The SEPSIS KILLS was activated on only 14% of bacteraemic patients.

<table>
<thead>
<tr>
<th>SCORING SYSTEM</th>
<th>Area under ROC curve (95% CI)</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>Clinical Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>qSOFA</td>
<td>0.517 [0.46≤CI≤0.56]</td>
<td>19.82 [15.16≤CI≤25.4]</td>
<td>83.67 [78.50≤CI≤88.02]</td>
<td>PPV 55% NPV 49%</td>
</tr>
<tr>
<td>SIRS</td>
<td>0.514 [0.46≤CI≤0.56]</td>
<td>82.07 [76.76≤CI≤86.61]</td>
<td>20.72 [15.88≤CI≤26.26]</td>
<td>PPV 45% NPV 54%</td>
</tr>
<tr>
<td>SHAPIRO</td>
<td>0.627 [0.58≤CI≤0.68]</td>
<td>88.05 [83.38≤CI≤91.79]</td>
<td>37.85 [31.82≤CI≤44.16]</td>
<td>PPV 60% NPV 76%</td>
</tr>
<tr>
<td>SEPSIS KILLS</td>
<td>0.71 [0.66≤CI≤0.75]</td>
<td>69.72 [63.49≤CI≤75.34]</td>
<td>71.31 [65.29≤CI≤76]</td>
<td>PPV 71% NPV 70%</td>
</tr>
</tbody>
</table>

Conclusions: The performance of all scoring systems and pathways was suboptimal in the identification of patients at risk of bacteraemia presenting to the emergency department.

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Abstract 4376

**Identification of genetic factors increasing carbapenem resistance in Klebsiella pneumoniae with blaOXA-48**

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**Background:** Carbapenemase-producing Enterobacterales became the most clinically significant multi-drug resistant bacteria. In Germany, *Klebsiella pneumoniae* with *bla*OXA-48 are most frequently detected, as shown in the annual reports of the National Reference Centre for Multidrug-resistant Gram-negative Bacteria (NRC). Although all carry *bla*OXA-48 some isolates show high resistance to carbapenems while some only show low minimal inhibitory concentrations (MIC) of carbapenems and are categorized susceptible according to EUCAST breakpoints. The aim of this study was to reveal possible genetic causations for varying MICs of carbapenems in *K. pneumoniae* expressing *bla*OXA-48.

**Materials/methods:** 20 Clinical *K. pneumoniae* isolates with *bla*OXA-48 showing low MICs of carbapenems were put under gradually rising selective pressure of meropenem during broth macrodilution to select for mutants with elevated MICs. Whole genome sequencing were performed with the low MIC primary isolates and the high MIC selected mutants to check for mutations. A hybrid assembly of Illumina MiSeq and Oxford Nanopore sequencing data was carried out to generate whole genome sequences.

**Results:** Mutations possibly leading to elevated MICs were predominantly found in genes of outer membrane proteins (OMP), as already described in the literature. But not in all isolates a insertion or mutation leading to an early abortion of OMP expression can be found. Ten of twenty selected mutants had an insertion element inserted within the *ompK36*-promoter, two had a complete deletion of OmpK36 and four had mutations within the *ompK36* gene, but there were also mutations in yet unsuspicous genes associated with OMP expression or proper folding.

**Conclusions:** There are only few single mutations having huge impact on the MICs of carbapenems in *K. pneumoniae* with *bla*OXA-48 as shown by sequencing data of clinical isolates and selected mutants. To further check if these mutations lead to elevated MICs of carbapenems they will be integrated into the primary clinical isolate genomes via CRISPR/Cas system. Clinical *K. pneumoniae* isolates with high MICs of carbapenems will be screened for the found or similar mutations in the same genes to check if *bla*OXA-48 or *bla*OXA-48 in combination with an mutation in an appropriate gene leads to high MIC in clinical isolates.

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Abstract 4379

The mouse ear skin model reveals specific innate immune signatures into study of the dynamics of innate immune responses against to Staphylococcus aureus biofilms

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Background: Staphylococcus aureus (SA) is a human pathogen that frequently causes nosocomial infections and infections on indwelling medical devices, mainly due to its capacity to shift between planktonic and biofilm lifestyles. Biofilm infections pose an important problem in human medicine, as they often lead to bacterial persistence and thus to chronic infections. Furthermore, they have been shown to be more resistant towards anti-infective agents and more importantly towards host immune cell attacks. In vivo, the bilateral interactions between biofilms and myeloid cells remain poorly studied and analysis of cell dynamics in tissues inoculated with biofilms is still an unexplored field. Thus, it is essential to design biologically sound in vivo experimental approaches aimed to extract specific immune signatures elicited by biofilms in order to develop alternative forms of therapies.

Materials/methods: Here, an in vivo transgenic mouse model is used in conjunction with intravital confocal microscopy, to study the dynamics of host inflammatory responses towards bacteria. We set up culture conditions to prepare calibrated inoculums of a red fluorescent strain of SA, in its planktonic or biofilm form. Then, we set up a confocal imaging acquisition and analysis protocol to study the recruitment of green fluorescent innate immune cells in the skin, specifically the mouse ear pinna of LysM-EGFP transgenic mice. These data were correlated with FACS analysis of recruited immune cells and quantification of bacterial load in target tissues (ear tissue, auricular lymph node).

Results: We show here that inflammatory responses to SA can be quantified over time, and that the dynamics of innate immune cells can be characterized. Our first results show that, despite being massively recruited in both cases, phagocytic cells have an attenuated capacity to infiltrate the injection site in the presence of biofilms and have an altered motility when compared to cells in the presence of planktonic bacteria.

Conclusions: We developed a mouse model of infection to compare the dynamics of inflammatory responses to planktonic or biofilm bacteria at the tissue and cellular level. The mouse ear pinna model appears to be a powerful imaging system to analyze the mechanisms of biofilm resistance to immune attacks.

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Spontaneous and clinically relevant tet(A)-dependent tigecycline resistance development
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Background: Overexpression of the tetracycline efflux pump tet(A) from Tn1721 in vitro has previously been shown to give increased resistance to the last-line, third generation tetracycline antibiotic tigecycline. We have previously discovered that spontaneous, high-frequency amplification of tet(A) in clinical Escherichia coli isolates leads to tigecycline resistance, but not in isolates with a 24-basepair deletion in the repressor protein tetR(A). We aimed here to study the effect of the frequent 24-nucleotide deletion on the expression of the efflux pump and on fitness. We also determined whether tet(A) could facilitate resistance development to the new tetracycline antibiotic omadacycline.

Materials/methods: Competitions of the wild-type tet(A) (tet(A)wt) and the tetR(A) 24-basepair deletion allele (tet(A)∆tetR) were performed in presence of tetracycline antibiotics (tetracycline, tigecycline, minocycline, and doxycycline) at varying concentrations. β-galactosidase assays were performed on the two tet(A) alleles and in presence of different concentrations of tetracyclines. Omadacycline MICs were determined by broth microdilution and DNA copy numbers were determined by qPCR.

Results: Competitions between strains carrying either tet(A)wt or tet(A)∆tetR showed that at high antibiotic concentrations, tet(A)wt gave a fitness advantage. At lower concentrations, there was either no difference in fitness between the two alleles, or a slight fitness advantage for tet(A)∆tetR. Neither allele appeared to be outcompeted by a strain devoid of tet(A). β-galactosidase assays showed that induction of tetA(A) was lower for the tet(A)∆tetR allele compared to tet(A)wt for all tetracycline antibiotics tested. Our simple PCR screening could accurately differentiate the different tetR(A) alleles. An increase in omadacycline MIC was observed for isolates carrying an amplification of tet(A)wt but not for isolates carrying an amplification of tet(A)∆tetR.

Conclusions: Expression of tetA(A) was decreased in the tet(A)∆tetR allele, thus explaining the inability of isolates carrying tet(A)∆tetR to develop tigecycline resistance. Maintenance of the tet(A)∆tetR allele in a population in absence and at low concentrations of tetracyclines might partially explain the high prevalence of the tet(A)∆tetR allele in E. coli. The tet(A)-associated tigecycline resistance development pattern appears to be similar for omadacycline. A simple PCR screen can identify the tet(A) allele and potentially aid in a clinical setting.

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Abstract 4382

**Whole genome sequence analysis of antimicrobial resistance genes in Global Priority Superbugs**

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**Abstract third-party references:** American Type Culture Collection

**Background:** With over 2 million infections per year in the United States alone, antimicrobial resistance (AMR) among bacterial pathogens has become a serious threat to global health. In 2017, the World Health Organization (WHO) released a report to guide the direction of antimicrobial research and drug development that was designed to have a significant impact on public health; the criteria used to select pathogens included transmissibility and preventability, recent trends and prevalence of resistance, healthcare burden, and global mortality. A global panel of experts in infectious disease, antimicrobial resistance, drug development, and public health developed three tiers for the prioritization of pathogens: critical, high, and medium. To thwart the AMR threat via drug discovery and diagnostics research, accurate characterization of AMR gene clusters, mobile elements, insertions, and deletions in bacterial genomes is crucial. To that end, we developed the ATCC Global Priority Superbugs Collection, which comprises 57 fully authenticated, characterized, and sequenced strains representing critical level pathogens. Here, we discuss the phenotypic and genotypic characterization of these strains through antimicrobial susceptibility profiling and a standardized sequencing, assembly, and annotation pipeline.

**Materials/methods:**

**Results:**

**Conclusions:** Genotypic and phenotypic characterization of antimicrobial-resistant priority pathogens is beneficial for studies involving epidemiology, antimicrobial resistance mechanisms, and drug development. To support this need, strains in the ATCC Global Priority Superbugs collection are provided with:

- Susceptibility data – MIC values and susceptibility profiles for targeted drugs.
- Genetic data – Complete genome sequence, antibiotic resistance genes and 16S rRNA genes.
- Source information – Geography, collection date, patient age and gender, and collection site.

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Abstract 4383

Diverse populations of carbapenem-resistant Klebsiella pneumoniae isolated in rectal colonisation cultures from intensive care units of a single tertiary centre in Greece

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Background: Colonized patients with carbapenem-resistant Enterobacterales, especially those admitted to intensive care units (ICUs), are considered at high risk for developing serious infections. The aim of our study was to describe the epidemiology of rectal colonization by carbapenemase-producing Klebsiella pneumoniae (CPKP) among inpatients in the intensive care units (ICUs) in a University Hospital in Thessaloniki-Greece and to identify possible epidemiological links using molecular techniques.

Materials/methods: A total of 45 CPKP were randomly selected among isolates collected from fecal samples of 45 inpatients performing active rectal screening for multidrug-resistant Enterobacterales during hospitalization in the three ICUs of AHEPA University Hospital during a two-year period (2016-2018). Bacterial identification and susceptibility testing were performed by the automated system VITEK2 (bioMérieux, France). Carbapenem-resistant isolates were phenotypically screened for the presence of MBL, KPC or both carbapenemases with a combined disk test using meropenem disks with and without carbapenemase inhibitors (EDTA and phenyl-boronic acid). The presence of carbapenemase-encoding genes was further confirmed by PCR. XbaI-PFGE typing was used to subtype the isolates and identify possible epidemiological links. A database containing all the PFGE patterns was created using the Bionumerics software. Cut off value for cluster determination was set to 90%.

Results: The patient median age was 59 (17-87) years; 27 were male. blaKPC gene was detected in 35 (78%) of the isolates while 8 (18%) of them harbored blaVIM and 9 (20%) blaNDM suggesting the different mechanisms for strains resistant to carbapenems. The 45 CPKP isolates could be assigned to 37 PFGE patterns and 20 PFGE clusters. Dominant PFGE clusters were not detected; only eight strains isolated from different ICUs were assigned to a specific cluster, indicating heterogeneity of strains circulating in the hospital wards during the study period.

Conclusions: The detection of multiple clones of CPKP colonizing patients in the ICUs of our hospital and the risk for infection they present pose challenges for infection control in a setting with shortage of ICU beds. Furthermore, it creates an environment where bacteria may accumulate different mechanisms of resistant. Further study is required to determine the molecular epidemiology of CPKPs in our setting.
**Pathogenic potential and antimicrobial resistance genomic analysis of human gut commensal Escherichia coli**

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**Background:** Gut commensal Escherichia coli (gCEC) can cause extraintestinal infections in elderly or immunocompromised patients. Sometimes these bacteria cannot be distinguished from extraintestinal pathogenic E. coli (ExPEC) by molecular epidemiological approaches, although their genotypes and virulence content may differ. Here we analyzed gCEC genomes from healthy people to investigate their pathogenic potential and phylogeny.

**Materials/methods:** Forty-eight E. coli isolated from faeces (nT=47, two isolates from the same sample had a different susceptibility pattern) from a healthy cohort (2014, Lifelines, the Netherlands) were sequenced in a NextSeq 500 Illumina instrument, 2x150bp paired-end reads. Reads were trimmed and de-novo assembled (CLCbio). We analyzed the genomes to gather information on virulence factors (VFs) associated to ExPEC and intestinal pathogenic E. coli (EnPEC) (Abricate), CRISPR-Cas system content (CRISPRCasFinder), which limits acquisition of foreign DNA, antimicrobial resistance genes (ResFinder) and molecular typing (phylogroup, serotype, MLST and cgMLST using SeqSphere).

**Results:** One isolate (B2-unknown ST, O84:H2) harboured a verocytotoxin vt1 gene considered for enterohemorrhagic E. coli (EHEC). The remaining isolates (97.9%) had either uropathogenic E. coli (UPEC) and/or neonatal meningitis E. coli (NMEC) associated genes. Fifty percent of isolates had between 11-16 of the 27 specific ExPEC genes investigated. The most prevalent genes were related to adherence (ibeA, 97.9%;aslA, 91.7%;fimA, 100%), protection (iss, 70.1%;kpsM, 58.3%) and iron-acquisition functions (chuA, 89.5%). All isolates harboured CRISPR arrays in which 56.3% (27/48) had a Cas protein cluster [41.7% I-E subtype, 12.5% I-F subtype and 2.1% both subtypes]. The number of CRISPR repeat units varied between 1 to 10. The most common phylogenetic group was B2 (39.6%). We observed 35 different MLST-STs, ST73 (10.4%) being the most abundant and all isolates had more than 41 allele differences by cgMLST analysis. Isolates were resistant to ampicillin (10.4%) -blaTEM-1B, 1C, 1D genes-, amoxicillin and amoxicillin-clavulanic acid (20.8%), cefuroxime (2.1%) and trimethoprim-sulfamethoxasol (10.4%).

**Conclusions:** The studied human gCEC isolates were genetically very diverse and could be potential extraintestinal pathogens due to the presence of associated VFs. A low number of CRISPR repeat units has been previously associated with the presence of a higher number of VF.

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Emergence of cryptic Aspergillus species infection and importance of antifungal susceptibility testing

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Abstract third-party references: This work was partly supported by the High Level-Hospital Program, Health Commission of Guangdong Province, China (HKUSZH201902012) High-Level Hospital Development Scientific Research Nurturing Program of The University of Hong Kong–Shenzhen Hospital, China as well as the Collaborative Innovation Center for Diagnosis and Treatment of Infectious Diseases, Ministry of Education, China.

Background: Amongst the list of >360 Aspergillus species, A. fumigatus, A. flavus, A. terreus and A. niger are the predominant species that cause human infection, but the clinical spectrum of Aspergillus infections has progressively diversified, largely due to the advancement of molecular technologies, which revealed numerous clinical isolates to be cryptic species. Currently, there is a lack of knowledge on the types of disease that these cryptic species cause. Moreover, these cryptic species may exhibit dissimilar antifungal susceptibilities to the four predominant Aspergillus species.

Materials/methods: All Aspergillus strains isolated in this study were recovered from clinical specimens from five hospitals in Hong Kong, Shenzhen and Shanghai. Sequencing of two long-established markers, beta-tubulin and/or calmodulin genes was performed to ensure accurate species identification. Antifungal susceptibility testing was performed to investigate the susceptibility pattern of these cryptic species against 10 antifungal agents by the EUCAST reference protocol.

Results: During 2012–2018, 21 clinical strains from 21 patients aged 26-78 years [male:female ratio = 2:1] were found belonging to twelve cryptic Aspergillus species (A. tubingensis [n = 4], A. caelatus [n = 3], A. amoenum [n = 2], A. brunneoviolaceus [n = 2], A. sydowii [n = 2], A. tamarii [n = 2], A. aculeatus [n = 1], A. ostroafricanus [n = 1], A. nidulans [n = 1], A. neoniger [n = 1], A. quadricirratus [n = 1], A. welwitschiae [n = 1]). Sixteen of the patients (76.2%) were burdened with underlying disease related to chronic respiratory diseases [56.2%]. Infection manifested as a broad-spectrum of diseases mainly comprising of chronic pulmonary aspergillosis [33.3%], chronic otitis media [9.5%], invasive aspergillosis [9.5%], wound infection [9.5%] and onychomycosis [9.5%]. Susceptibility testing showed elevated azole MICs for A. tubingensis and A. neoniger (isavuconazole: 2 to >16 mg/L; voriconazole: 2 to >16 mg/L; itraconazole: 1 to >8 mg/L; posaconazole: 0.125 to 2 mg/L).

Conclusions: Our results demonstrated a diverse spectrum of cryptic Aspergillus species infection and the potential emergence of antifungal resistance. Accurate identification of clinical Aspergillus isolates and in vitro antifungal susceptibility testing are crucial for better patient management.

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Abstract 4386

Suspected reverse zoonosis of influenza A(H1N1)pdm09 virus infection found in Ailuropoda melanoleuca in Hong Kong Oceanarium

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Background: We confirmed a case of pH1N1 infection in an Ailuropoda melanoleuca (giant panda) kept in an oceanarium of Hong Kong in 2019. The panda developed clinical signs suggestive of respiratory infections, including nasal discharge, loss of appetite and fatigue, and was nonfebrile throughout. Complete blood picture two days after symptom onset shows significant leucocytosis. Eventually, symptoms completely resolved on day 8.

Materials/methods: Nasal swab specimens were collected in 1 mL of phosphate-buffered saline for virologic studies. Investigation of the specimens was carried out for identification of causative pathogen. Rapid antigen detection and reverse transcription PCR (RT-PCR) were performed to identify the presence of influenza A virus. Real-time RT-PCR targeting the M gene was used to monitor the daily change in viral load. Cytopathic effect of the virus was studied using cell culture inoculated with the specimen. The entire viral genome was obtained for sequence analysis. Subsequent phylogenetic studies were carried out by analysing the sequences of surface glycoproteins of the isolate.

Results: Viral detection showed positive result for influenza A and RT-PCR confirmed the findings. Viral load displayed a descending trend from 6.00 log_{10} copies/mL upon symptom onset to undetectable level four days later. Phylogenetic analysis of the entire genome revealed that the isolated strain has close relation with other known pH1N1 viruses prevalent in Hong Kong previously. In particular, this strain was most closely related to the most prevalent strain within the region when the giant panda was infected, with genetic difference of two bases.

Conclusions: Study on the phylogeny of the isolated pH1N1 strain revealed close relation with other human strains. The infection is thus possible to be originated from infected humans during the influenza season. Handlers of animals are of the greatest risk of reverse zoonosis. They should pay close attention to the prevention of transmitting infectious diseases to animals. More results will come into light as the origin of infection will be tracked in the upcoming phase of the study. Handlers of the giant panda and other animals in the proximity will be screened for influenza virus, regardless of the presence of respiratory symptoms.

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Evaluation in general practice of the patient’s feelings about a recent hospitalisation and isolation for a multidrug-resistant infection

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Background: Isolation precautions used against multidrug-resistant (MDR) organisms are responsible for many emotional side effects. We evaluated patient’s feeling after a hospitalization for an MDR infection. Deciphering patients’ emotions might help provide better answers to latent and shameful questions.

Materials/methods: We conducted a qualitative study that included 11 interviews from August 2017 to June 2018 of patients previously hospitalized and placed in isolation precautions in a single occupancy room in an infectious disease ward. We used phenomenology and verbatim transcription analysis was performed using NVivo software.

Results: Participants consisted of 3 women and 8 men. Median age was 58 (26-81) years. Median duration of hospitalization was 10 (5-21) days. Patients had been previously infected by an ESBL urinary tract infection including 3 pyelonephritis, 2 epididymitis, 4 cystitis complicating a neurologic bladder, and 1 MRSA osteomyelitis. One patient experienced a skin and soft tissue infection due to a K pneumoniae OXA-48. Median duration of the interview was 12 minutes, 8 seconds, ranging from 10.10-32.35 seconds.

No interview was interrupted by any participant. Median time between discharge from the hospital and the interview was 12 weeks (4-13). Participants were mainly convinced that the infection was strongly linked to the hospital and considered it as nosocomial that led to anxiety, especially regarding the origin of the infection and the absence of formal source of infection. Also they expressed fears of contagion to their close surroundings therefore the patient is willing to “be free from carriage” and is self-questioning about limitation or therapeutic arsenal in the future.

Conclusions: MDR infections are negatively impacting patient’s lived experience even after hospital discharge, partly owing to prior implementation of isolation precautions. We need to improve communication between specialists and general practitioners to reassure the patient and his surroundings regarding the anxiety resulting from such hospitalization.

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Direct detection of extended-spectrum beta-lactamases in bacteria isolated in blood culture bottles using a lateral flow assay

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Background: Rapid identification and susceptibility testing of bloodstream infection pathogens remain a crucial step in the early effective therapy, especially for patients with sepsis, causing high morbimortality and medical costs. Traditional methods require at least one day for susceptibility testing results. We evaluated the use of a lateral flow assay - which includes NG-test Blood Culture Prep (NGBCP) and NG-Test CTX-M MULTI Lateral Flow Test (LFT) NGbiotech® - for the detection of extended spectrum beta-lactamase (ESBL) directly from positive blood cultures.

Materials/methods: A total of 48 blood cultures positive for Enterobacterales were included in the study: 28 positive for ESBL producing strains (18 Escherichia coli and 10 Klebsiella pneumoniae) and 20 non-ESBL producing strains, which included 16 third-generation cephalosporin susceptible strains (11 E. coli, 2 K. pneumoniae, 2 K. oxytoca and 1 K. variicola) and 4 third-generation cephalosporin resistant strains due to mechanisms other than ESBL (1 E. coli, 1 K. pneumoniae and 2 K. aerogenes). Species identification was performed with direct MALDI-TOF. Blood culture vials positive for Gram-negative bacilli were stored at 4°C until antimicrobial susceptibility testing were available. Only one vial from each patient was used for NGBCP+LFT. The procedure was: 1 mL of positive blood culture was mixed with 1 mL of lysis buffer, vortexed 20 seconds, centrifuged 1 minute/15000 rpm. The pellet was resuspended with 1 mL of wash buffer, vortexed 20 seconds, centrifuged 1 minute/15000 rpm. The pellet was resuspended with 5 drops of extraction buffer to perform the LFT.

Results: Test protocol (NGBCP+LFT) and results in the Figure.

<table>
<thead>
<tr>
<th>Antibogram</th>
<th>Positive ESBL</th>
<th>Negative ESBL</th>
<th>Total</th>
</tr>
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<tr>
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</tr>
<tr>
<td>Negative ESBL, 3G Cephalosporin-S</td>
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<td>Negative ESBL, 3G Cephalosporin-R</td>
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<tr>
<td>Total</td>
<td>26</td>
<td>22</td>
<td>48</td>
</tr>
</tbody>
</table>

Sensitivity and specificity of the protocol for ESBL detection directly from positive blood cultures were 92.8% and 100%, respectively. The protocol turnaround time was one hour.

Conclusions: ESBL detection time from positive blood culture samples was reduced from one day to one hour using the described protocol. The NGBCP allows standardized sample preparation compared to in-house protocols. The reduced sensitivity was probably due to insufficient bacterial load obtained from positive blood cultures in two samples.

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Mouse colonisation by multidrug-resistant *Escherichia coli* in the absence of antibiotic selection

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**Background:** Antimicrobial resistance (AMR) is a growing health concern with pathogenic bacteria becoming increasingly resistant to clinically used antibiotics. *E. coli* account for a significant proportion of these multi-drug resistant (MDR) infections. Of particular note is *E. coli* ST1 31 which has established itself as a globally dominant MDR clone. It is unclear what has permitted this particular clone to spread so effectively. Moreover, traveller surveillance studies have indicated that MDR bacteria are capable of colonising healthy individuals in the absence of antibiotic treatment. It is therefore clear that there are additional factors controlling the spread of AMR. Here we present data illustrating the ability of *E. coli* ST131 to outcompete and displace commensal bacteria in a germ-free mouse model.

**Materials/methods:** Germ free C57/B16 mice were colonised with bacteria via oral gavage of 10⁹ CFU. For competition experiments mice were colonised with 5 x10⁸ of each strain. For displacement and co-housing strains mice were colonised for one week before challenging with a second strain or co-housing. Colonisation was monitored by CFU counts from faecal pellets for between 1 and 4 weeks. Specific strain composition at select timepoints was confirmed by qPCR. Host inflammatory response was measured by histology and cytokine mRNA profiling.

**Results:** All bacterial strains used were able to colonise germ-free mice and were stable for up to 4 weeks. When co-gavaged in a 1:1 ratio the MDR ST73 and ST131 strains were able to outcompete the commensal ST10. One day subsequent to gavage the MDR strains were dominant accounting for greater than 50% of the bacterial load. The ST131 strain achieved near 100% dominance by day 4 compared to ST73 at day 6. Furthermore both ST73 and ST131 are capable of displacing a resident ST10 commensal strain. Displacement occurs both when challenging bacteria are gavaged and when mice are co-housed. ST131 produced a bacterial ‘bloom’ in the first 5 days of challenge.

**Conclusions:** MDR strains are capable of out-competing commensals when co-gavaged into mice. Moreover, MDR strains are able to dominate over resident commensals. In both instances there was no antibiotic mediated selection.

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Clinical impact of infections caused by carbapenemase-producing Enterobacteriaceae
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Background: Carbapenemase-producing Enterobacteriaceae (CRE) infections cause major morbidity. Most previous studies were designed to detect risk factors for developing CRE infections. Nevertheless, the clinical impact of carbapenem resistance once adjusted by potential confounders remains uncertain.

Materials/methods: We performed a retrospective observational study including all episodes of CRE-infection at our institution between 01/06/2013 and 31/12/2016. A comparative cohort of infection due to non-CRE Enterobacteriaceae was assembled by matching each episode by clinical syndrome, previous manipulation and admission department. The primary outcome was clinical failure (composite of lack of clinical cure, clinical and/or microbiological recurrence and all-cause 30-day mortality), whereas 30-day attributable mortality was considered as secondary outcome.

Results: We included 334 episodes of infection (167 CRE and 167 non-CRE). Most common clinical syndromes were urinary tract infection (47.3%), surgical site infection (24%), respiratory tract infection (24%), catheter-associated bacteremia (8.4%) and intraabdominal infection (7.2%). Bacteremia was present in 76 episodes. Baseline characteristics were similar between both groups except for previous renal replacement therapy (16.2% vs. 8.0%; p=0.030). Clinical failure at 30 days was 47.3% for CRE-infection and 22.8% for non-CRE-infection (unadjusted hazard ratio [HR]: 2.017; 95% confidence interval [CI]: 1.370 – 2.970; p <0.0001). 30-day attributable mortality was 22.2% for CRE-infection and 7.2% for non-CRE-infection (unadjusted HR: 3.325; 95% CI: 1.730 – 6.391; p <0.0001). After including several variables in a Cox regression model to evaluate clinical failure (McCabe and age-adjusted Charlson scores, renal replacement therapy, cumulative days of hospitalization during actual admission, Pitt bacteremia score, source control, appropriate therapy within 72 hours from the onset of symptoms, and use of potentially nephrotoxic antibiotics), CRE-infection remained as an independent risk factor (adjusted HR: 1.862; 95% CI: 1.150 – 3.013; p=0.011). In addition, CRE-infection was also predictive of 30-day attributable mortality after adjusting for previous renal replacement therapy, Pitt score, source control, appropriate therapy within 72 hours and use of nephrotoxic agents (adjusted HR: 3.273; 95% CI: 1.675 – 6.396; p=0.001).

Conclusions: After matching by baseline characteristics and adjusting for potential clinical confounders, infections caused by CRE had higher 30-day rates of clinical failure and attributable mortality than episodes caused by carbapenem-susceptible microorganisms.

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Impact of multidisciplinary management on the outcome of aortic prosthetic vascular graft infections: a retrospective, single-centre experience

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Background: Aortic prosthetic vascular graft infection (PVGI) is a rare (up to 5%) but devastating complication in vascular surgery, burdened by high mortality and reinfection rates. Aim of this study was to evaluate the impact of a multidisciplinary management on the outcome of aortic PVGI in terms of morbidity and mortality.

Materials/methods: A monthly meeting dedicated to vascular infections has been set up in Bordeaux University Hospital since April 2011. In these meetings, infectious disease physicians, vascular surgeons, nuclear medicine physicians, microbiologists, and anaesthesists discuss about the management of all patients suffering from a vascular graft infection in our centre, in order to propose a tailored treatment strategy and to improve the prognosis of these severe infections. Patients treated in our unit for aortic PVGI infection from January 2004 to July 2018 were retrospectively reviewed and divided in two groups: period 1, P1 (from 2004 to April 2011) and period 2, P2 (from April 2011 to 2018). Mortality and reinfection rates were the primary outcomes and were calculated using Kaplan-Meier curves. Log-Rank test was used to compare the two groups.

Results: A total of 92 patients (87 males, mean age: 64 years old) were included, 31 patients during P1 and 61 during P2. Demographic and baseline disease characteristics were comparable between groups. Mean delay between index surgery and PVGI surgical treatment was six years. For each period, 21% of patients underwent an emergent surgical treatment. A conservative treatment without surgery was performed in four cases during P2. More complete excisions (48% vs 51.7%) and more revascularisation using cryopreserved allograft (0 vs 19%) were performed during P2. Mean follow-up was 4.9 and 1.2 years for P1 and P2, respectively. In-hospital mortality rate was 32.3% and 21.3% during P1 and P2, respectively. Median reinfection delay was 7.5 months. Reinfection rate was significantly reduced in P2 (47.6% vs 12.5%, p=0.02). The 2-years survival rate was 54.6% and 69%, during P1 and P2, respectively.

Conclusions: Multidisciplinary management seems to provide better results for aortic PVGI management and reduces in-hospital mortality and reinfection rates.

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Abstract 4394

Delamanid in MDR/XDR pulmonary tuberculosis in Russia: first experience
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Background: Delamanid is not approved in Russia. MSF made supply of delamanid for 2 cities.

Materials/methods: In 2015-2019 delamanid was used for 48 MDR/XDR patients. 25% were females. The age was 44.87±14.38. Forty-three (89.6%) patients had caverns. Patients’ profiles: failure of previous therapy 26(54.2%), interruption of previous treatment - 12 patients (25%), a new case - 6 (12.5%), relapse - 4 (8.3%) patients. HIV was observed in 4 (8.3%) people. Hepatitis B was in 5 (10.4%), hepatitis C in 12 (25%), both in 4 (8.3%) people, combination of 3 diseases in 1 patient. Delamanid administrated with linezolid and/or clofazimine. 22 (45.8%) patients received bedaquiline. Therapy of MDR and pre-XDR resistant to injectable aminoglycosides included levofloxacin, linezolid, clofazimine. Some XDR cases included imipenem and amoxicilline/clavulanate. Safety monitoring of clinical symptoms was performed daily, laboratory and instrumental control monthly.

Results: Positive smear microscopy was in 37 (77.1%). Resistance: MDR – 11 (23%), pre-XDR-FQ – 3 (6%), pre-XDR-AMG – 11 (23%), XDR – 23 (48%) patients. The sputum culture conversion after 6 months achieved in 22 (45.8%) patients in period from 32 to 241 (average 107) days. Delamanid administrated on an average of 223.9 days. Treatment success after 4 years follow up was registered in 68.7%. Lost of observation – 5 (10.4%) patients. Ineffective treatment - 4 (8.3%) patients. Six (12.5%) died of tuberculosis during treatment. Two (4.1%) continue to have positive culture and treatment till now. 13 (27.1%) died including 9 deaths form tuberculosis. Adverse events did not required the cancellation of delamanid or change of treatment. 12 (25%) patients had QTcF prolongation, 1 patient more 500 ms normalized with no treatment. Other adverse events: increased liver enzymes, thrombocytopenia, anemia, peripheral neuropathy, dermatitis, vomiting, heart pain, cardiomyopathy, edema of the extremities. All cases did not result in the cancellation of delamanid.

Conclusions: Delamanid in combination therapy showed a good result of treatment and good safety among the most complex MDR/XDR patients with ineffective and interrupted previous course of treatment, co-infected HIV, hepatitis B and C. The combined use of delamanid, bedaquiline, linezolid, clofazimine for XDR did not lead to serious adverse events.

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Variations in antibiotic prescribing among village doctors in rural Shandong province, China

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Abstract third-party references: On behalf of the IMPACT consortium

Background: Understanding variations in antibiotic prescribing at the prescriber-level can be valuable for exploring barriers and facilitators to rational antibiotic use, as well as for enabling individualised feedback on prescribing practices. We assessed variation in antibiotic prescribing among village doctors in rural Shandong province.

Materials/methods: Prescriptions were collected retrospectively over a 2.5 year period at eight village clinics located around a single town. A target of 60 prescriptions per month were included from each clinic, from an average total of 300. Diagnoses were coded according to the International Classification of Diseases, 10th Revision and prescribed antibiotics were coded according to the Anatomical Therapeutic Chemical classification system. Prescriptions were analysed at the aggregate level and at the individual-prescriber level, with a focus on diagnoses of likely viral acute upper respiratory tract infections [AURI], defined as J00 [acute nasopharyngitis [common cold]] and J06.9 [acute upper respiratory infection, unspecified].

Results: In total 14471 prescriptions from 23 prescribers were included, of which 5833 (40.3%) contained at least one antibiotic. A total of 5177 prescriptions were categorised as likely viral AURI, and 62.5% (3237/5177) of these included an antibiotic, accounting for 55.5% (3237/5833) of all antibiotic-containing prescriptions. At the individual prescriber-level there was very wide variation in the antibiotic prescribing rate for likely viral AURI [33.1% to 88.0%], as well as the multiple antibiotic prescribing rate [1.3% to 60.2%] and injectable antibiotic prescribing rate [3.2% to 62.1%], see Figure. Each doctor prescribed between 11 and 21 unique agents for the single diagnosis of AURI, including many broad-spectrum antibiotics. Doctors in the top quartile for antibiotic prescribing for AURI also had higher antibiotic prescribing rates for potentially bacterial upper respiratory tract infections [pharyngitis, tonsillitis, laryngopharyngitis] [92.7% vs. 72.4%, p<0.05] and for gastritis, gastroenteritis and diarrhoea [88.8% vs. 76.2%, p<0.05] compared with doctors in the lowest quartile for antibiotic prescribing for AURI.

Conclusions: All prescribers showed evidence of over-using antibiotics for respiratory tract infections. Variations in individual prescriber practices are significant even in a small homogenous setting in rural China, and these must be accounted for when developing targets and interventions to improve antibiotic use.

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Abstracts 2020

Abstract 4399

**Effect of rapid influenza detection tests on antibiotic prescriptions**

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**Background:** Antibiotic misuse is common among patients with influenza like illness (ILI), contributing to the emergence of multidrug resistant bacteria. Our primary objective was to evaluate whether the deployment of rapid PCR tests for detection of influenza viruses could lead to a decrease in antibiotic prescriptions, in comparison with classic tests. The impact of rapid tests on prescription of biological tests, X-rays and oseltamivir; hospitalizations and length of stay (LOS) was also evaluated.

**Materials/methods:** Data from patients with ILI at the emergency department (ED) of Grenoble-Alpes University Hospital were retrospectively collected over three influenza seasons: in 2016/2017 and 2017/2018 when classic influenza tests were used (Rapid RT-PCR Genexpert® [Cepheid] and RT-PCR R-DiaFlu® [Diagenode Diagnostics]), and in 2018/2019 when rapid influenza tests were used (Cobas® Liat System [Roche Diagnostics]). The primary outcome was antibiotic prescription (any versus none). A bivariate analysis compared antibiotic prescriptions between the seasons; a multivariate analysis assessed the association between influenza seasons and antibiotic prescriptions, adjusting for age, sex, influenza test result and hospitalization after ED stay. Ancillary testing (complete blood count, blood chemistry, c-reactive protein, procalcitonin [PCT] and blood culture), chest X-ray and oseltamivir prescriptions were also compared, along with hospitalizations after ED stay and LOS at the ED.

**Results:** Among 1,849 patients included, 620 had a positive influenza test result. The number of antibiotic prescriptions was significantly different between the 3 periods in the bivariate analysis (31.1% in 2018/2019 vs 44% in 2017/2018 and 48.3% in 2016/2017, p<0.0001) and in the multivariate analysis (Odds Ratio [OR]=0.48, IC95%=0.30-0.76 for 2018/2019 and OR=0.99, IC95%=0.67-1.46 for 2017/2018, in comparison to 2016/2017). There were significantly fewer prescriptions of biological tests (except PCT and blood cultures), fewer X-rays and fewer hospitalizations in 2018/2019, in comparison with the 2 previous seasons. There were significantly more oseltamivir prescriptions in 2018/2019. LOS was not significantly different.

**Conclusions:** Introducing rapid influenza tests in the ED seems to decrease antibiotic use and leads to less ancillary testing, X-rays and hospitalizations among patients with ILI. However, medico-economic studies are now necessary before a definite recommendation.

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Abstract 4402

Acceptability of selective reporting of antibiotic susceptibility testing results in primary care
Maïa Simon*, Gaelle Le Dref2, Sébastien Fougnot2, Patrice De Monchy2, Joëlle Kivits2, Céline Pulcini2, Nathalie Thilly2

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Background: Selective reporting of antibiotic susceptibility testing (AST) results is one possible antibiotic stewardship strategy. The ongoing “ANTIBIO-ciblés” pragmatic, prospective, multicenter, controlled, before-after study aims to assess the impact of selective reporting of AST for Escherichia coli positive urine cultures on the prescription of broad-spectrum antibiotics (co-amoxiclav, 3rd-generation cephalosporins and fluoroquinolones) by general practitioners (GPs) of a north-eastern region of France. Acceptability by GPs and laboratory professionals has been assessed to explore potential barriers to its implementation on a larger scale.

Methods: Twenty-one semi-structured individual interviews with a random sample of GPs and three semi-structured focus groups with laboratory professionals (biologists, technicians and secretaries) having respectively received and experienced selective reporting of AST were conducted to collect their perceptions about it. The main points discussed were their knowledge and their acceptability of the selective reporting of AST, the number and reasons of calls from primary care physicians (GPs and other specialties) to the laboratory to obtain the complete reporting of AST, and their perceptions of antibiotic resistance. Focus groups and interviews were transcribed to perform a comprehensive thematic analysis.

Results: Acceptability was high for all professionals, who considered selective reporting as an effective tool against antibiotic resistance. It was not perceived as an important constraint, neither by GPs nor laboratory staff. GPs found this tool helpful, and only complained about the time needed to obtain the complete reporting of AST in specific cases. These demands were however infrequent (1.3%). Laboratory professionals were therefore not over-solicited. Biologists expressed their desire to have more training, in order to better advise physicians when they called. According to them, making prescribers more aware of the threat of antibiotic resistance would further improve the effectiveness of selective reporting of AST. Selective reporting was also perceived positively by laboratory staff, as this highlighted their added value as antibiotic stewards.

Conclusions: Overall, selective reporting of AST was well accepted by both GPs and laboratory professionals. The results about impact of the “ANTIBIO-ciblés” study on antibiotic prescriptions will be available at the beginning of 2021.

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Virological patterns of HCV-patients with failure to second-generation direct-acting antivirals
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Background: Despite the excellent efficacy, direct-acting antivirals (DAA)-regimens are associated with failure in about 5% of cases. To characterize the virological patterns and the resistant-associated substitutions (RASs) in the patients with failure to second-line DAA-regimen. It may help to identify the best approach of new line DAA-regimen

Methods: All the consecutive 63 HCV patients (pts) with failure to IFN-free regimen observed at the laboratory of infectious diseases of University of Campania, Naples from January 2018 to February 2019 were enrolled. All the pts had been treated with DAA-regimens according HCV genotype, international guidelines and local availability. Sanger sequencing of NS3 (for genotypes 1 and 4), NS5A and NS5B (for all genotypes) was performed at failure by home-made protocols.

Results: According to therapeutic outcome, 90.5% relapse, 4.7% breakthrough and 4.7% non-response. Among the 63 patients failed at three therapeutic regimens, 19 (30.1%) were treated with Sofosbuvir+Velpatasvir, 11 (17.4%) with Glecaprevir/Pibrentasvir and 33 (52.4%) with Elbasvir/Grazoprevir. The duration of DAA in months, median (range) 12 (8-24), the timing of resistance test in months at the end of treatment, median (range) 5 (1-19). The NS5A-RASs were more frequent in Sofosbuvir+Velpatasvir (17/19, 89.5%) and in Grazoprevir/Elbasvir (32/33, 97%) failed patients than in Glecaprevir/Pibrentasvir (4/11, 36.7%) failed patients (p=0.002 and 0.000 respectively). According to Sofosbuvir/Velpatasvir regimen 36.4% pts showed at least 2 RASs in at least two HCV region including NS5A and 70.3% pts showed at least 2 RASs only in NS5A region. Considering Grazoprevir/Elbasvir regimen 27.3% pts showed at least 2 RASs in at least two HCV region including NS5A and 88% pts showed at least 2 RASs only in NS5A region. (p=0.00). All 21 re-treated patients with Sofosbuvir/Velpatasvir/Voxilaprevir, obtained with SVR. The re-treatment was guided by genotyping test.

Conclusions: Patients with failure to a second-line therapeutic regimens frequently present mutation above all in the NS5A region. At re-treatment all patients obtained SVR. According to our real-life experience, re-treatment with the new regimes is effective and safe.

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Improved diagnostic of acute gastrointestinal disease by a multiplex real-time PCR semi-automated method for the detection of enteropathogens

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Background: The identification of enteropathogens is critical for the clinical management of patients with acute gastrointestinal disease. New molecular methods have been developed to increase the diagnostic sensitivity. The aim of this study was to compare a multiplex real-time PCR analysis semi-automated platform (FLOW System®, Roche) that detects a combination of 11 enteropathogens (Table 1) with standard methods.

Materials/methods: A total of 10654 samples were analyzed. From 2013-2018 (July-September), stool samples were processed using standard microbiology methods: Culture for bacteria, microscopy for parasites and immunochromatography for viruses. In 2019, the FLOW system® was introduced.

Results: Study results are shown in Table 1. Other enteropathogens, like enteropathogenic E. coli, and parasites were not included in the table. The percentage of positive samples increased with the use of molecular methods. This trend was significant for bacterial pathogens ($P<0.001$) and G. intestinalis ($P=0.059$). Molecular methods identified 13 cases of G. intestinalis and 8 of Cryptosporidium spp unsuspected by clinicians. In 39 cases (3.62%), more than one enteropathogen was detected by FLOW.

Conclusions: FLOW system on stool samples improves diagnostic performance and is likely to modify routine microbiology protocols and clinical management. Molecular methods increase sensitivity, shorten turnaround time and may identify pathogens unsuspected by clinicians.

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<table>
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<th>2013</th>
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<th>2015</th>
<th>2016</th>
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<td><em>Shigella</em> spp</td>
<td>2(0.32%)</td>
<td>4(0.57%)</td>
<td>3(0.36%)</td>
<td>2(0.16%)</td>
<td>1(0.09%)</td>
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</tr>
<tr>
<td><em>Salmonella</em> spp</td>
<td>8(1.31%)</td>
<td>10(1.44%)</td>
<td>8(0.68%)</td>
<td>16(1.32%)</td>
<td>11(1.06%)</td>
<td>14(1.18%)</td>
<td>35(3.24%)</td>
</tr>
<tr>
<td>Campylobacter spp</td>
<td>8(1.31%)</td>
<td>11(1.58%)</td>
<td>6(0.73%)</td>
<td>5(0.41%)</td>
<td>20(2.50%)</td>
<td>48(4.06%)</td>
<td>86(7.08%)</td>
</tr>
<tr>
<td>Entamoeba histolytica**</td>
<td>7(2.13%)</td>
<td>2(0.04%)</td>
<td>4(0.77%)</td>
<td>5(0.60%)</td>
<td>3(0.36%)</td>
<td>7(0.80%)</td>
<td>3(0.28%)</td>
</tr>
<tr>
<td>Giardia intestinalis</td>
<td>7(2.13%)</td>
<td>6(1.62%)</td>
<td>14(2.69%)</td>
<td>17(2.05%)</td>
<td>15(1.83%)</td>
<td>8(0.91%)</td>
<td>29(2.69%)</td>
</tr>
<tr>
<td>Blastocystis spp</td>
<td>4(1.21%)</td>
<td>7(1.00%)</td>
<td>0(0%)</td>
<td>6(1.73%)</td>
<td>49(4.90%)</td>
<td>26(3.20%)</td>
<td>27(2.10%)</td>
</tr>
<tr>
<td>Dientamoeba fragilis**</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td>70(6.49%)</td>
<td></td>
</tr>
<tr>
<td>Cryptosporidium spp</td>
<td>1(0.30%)</td>
<td>0(0%)</td>
<td>3(0.57%)</td>
<td>0(0%)</td>
<td>10(1.2%)</td>
<td>2(0.23%)</td>
<td>8(0.74%)</td>
</tr>
<tr>
<td>Rotavirus, Adenovirus, Norovirus</td>
<td>3(7.60%)</td>
<td>2(6.0%)</td>
<td>1(2.28%)</td>
<td>2(2.89%)</td>
<td>0(0%)</td>
<td>3(5.17%)</td>
<td>45(4.26%)</td>
</tr>
</tbody>
</table>

*Nb/Np/Nv: Number of samples tested for bacterial/parasites/viruses.

**No specific methods for E. dispar/E. histolytica differentiation and for D. fragilis detection differentiation were used prior to 2019. § Norovirus was identified by Flow in 76%(35/46) of samples but it was not tested prior to 2019. ¥ Shigella spp/Enteroinvasive E. coli.
Abstract 4408

Identification of mutations in hepatitis B virus reverse transcriptase associated with a tenofovir-resistant phenotype in South African adults

Jolynne Mokaya*1, Tongai Gibson Maponga1, Marije Van Schalkwyk1, Susan Hugo2, Jantjie Taljaard2, Chikezie Nwankwo2, Joshua B Singer3, Mariateresa De Cesare1, David Bonsall1, Azim Ansari1, Wolfgang Preiser2, Monique Andersson1, Christo Van Rensburg2, Eleanor Barnes1, Anna McNaughton1, Philippa Matthews1

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Background: Tenofovir disoproxil fumarate (TDF) is widely recommended for treatment of chronic hepatitis B (HBV) infection because it has a high genetic barrier to resistance. TDF resistance associated mutations (RAMs) have been reported, but data are limited. We set out to identify RAMs in three individuals with detectable HBV viraemia on TDF treatment.

Materials/methods: We recruited adults with chronic HBV infection from Tygerberg Hospital, Cape Town, South Africa in 2018. Among 66 individuals with chronic HBV (17 HIV/HBV coinfected), 44 were on TDF, and three had persistent viraemia despite >12 months treatment. We sequenced HBV DNA for these three patients using MiSeq Illumina (whole genome target enrichment) and analysed for RAMs, applying maximum likelihood phylogenetic analysis to obtain genotypes.

Results: Consensus sequence from all three individuals contained RAMs that have been described in association with TDF resistance [Table], with at least 6 RAMs present in each. In participant 209, 12 putative TDF resistant mutations were present. Significant treatment non-adherence in this individual is unlikely as HIV-RNA was suppressed to a low level on TDF-containing antiretroviral therapy. RAMs Y9H and F122L/Y were present in all three individuals. All RAMs were present in >99% of HBV reads.

Conclusions: Our findings add to the evidence that RAMs in HBV RT can underpin a TDF resistant phenotype. This is the first time these RAMs have been reported from Africa in association with clinical TDF resistance. More data are required to determine the frequency and clinical impact of RAMs, to investigate the role of combination therapy, and to support development of new antiviral agents.

Table: Participants with persistent HBV viraemia on TDF.

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>209</th>
<th>258</th>
<th>289</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49</td>
<td>42</td>
<td>70</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
<td>Male</td>
</tr>
<tr>
<td>HIV status</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>HBV DNA Viral load (log 10)</td>
<td>8</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>HIV RNA viral load (log 10)</td>
<td>2</td>
<td>5</td>
<td>N/A</td>
</tr>
<tr>
<td>Duration of treatment (years)</td>
<td>4</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Median coverage/site</td>
<td>4262</td>
<td>1601</td>
<td>14</td>
</tr>
<tr>
<td>HBV Genotype</td>
<td>A1</td>
<td>D3</td>
<td>A1</td>
</tr>
<tr>
<td>TDF polymorphisms</td>
<td>Y9H; L911; T118N; F122Y; H126Y; R153W; V173L; L180M; M204V; C256S; Q267H</td>
<td>Y9H; F122L; Q130P; S223A; D263E; V278I; A317S</td>
<td>Y9H; L911; H126Y; F221Y; C256S; K333H</td>
</tr>
</tbody>
</table>

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Transcriptional and phenotypic responses to multidrug resistance plasmid acquisition are strain-specific in *Escherichia coli*

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**Background:** Multi-drug resistant (MDR) *Escherichia coli* are a global public health priority, and their incidence has been increasing since the start of the century. This is driven by a handful of successful MDR clones (e.g. ST-131). However, little is known regarding why some clones of *E. coli* are more able to acquire and maintain MDR plasmids. Data comparing the transcriptional and phenotypic responses of diverse *E. coli* strains to MDR plasmid acquisition are lacking.

**Materials/methods:** Using a combination of long and short read whole genome sequencing, as well as RNA-seq and phenotypic assays, several strains of *E. coli* were tested to determine their genomic and transcriptional response to novel MDR plasmid acquisition.

**Results:** Whilst very little genomic variation was detected across the dataset, the transcriptional landscape varied dramatically by strain. In general, there was a reduced transcriptional impact in MDR associated sequence types compared to environmental isolates. Genes that were differentially expressed in the dataset encompassed functions related to chemotaxis, flagellar, as well as carbohydrate, nitrogen, phosphonate and sulphur metabolism. These strains also varied by phenotype, displaying distinct effects to growth rates and conjugational efficiency.

**Conclusions:** The evolutionary cost of MDR plasmid acquisition is mitigated in a strain specific manner, with MDR associated clones displaying a reduced transcriptional impact. Further work is ongoing to characterise the effects of plasmid acquisition over long generational timeframes.

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Risk factors for intra-abdominal candidiasis in intensive care units: results from EUCANDICU study

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Abstract 4414

Background: There are no studies specifically assessing risk factors for development of intra-abdominal candidiasis (IAC) among patients admitted to intensive care unit (ICU).

Materials/methods: We performed a case-control study in 26 ICUs from 10 European countries during the period January 2015- December 2016 [EUCANDICU project]. Patients ≥18 years-old who developed an episode of microbiologically documented IAC during their stay in the ICU (at least 48 hours after admission) served as the case cohort. The control group consisted of adult patients admitted in the ICU who did not develop episodes of invasive candidiasis during admission. Matching was performed at a ratio of 1:1 according to the exposition period (i.e. the period lasting between the admission in the same ICU ward of the case and the collection of the first positive sample for Candida).

Results: During the study period, we identified 101 case patients with a diagnosis of intra-abdominal candidiasis. The most commonly isolated species was C. albicans [58.4% of the isolates], followed by C. glabrata [15.8%] and C. tropicalis [4.0%]. Overall, resistance to fluconazole was detected in 17 out of 64 tested isolates (26.5%). At the univariate analysis of the comparison between patients with ICU-acquired IAC with those without an IAC, variables associated with IAC development included severe hepatic failure (7.9% vs 1.0%, p=0.03), receiving parenteral nutrition (64.4% vs 48.5%, p=0.03), re-intervention (84.9% vs 40.9%, p<0.001), recurrent gastrointestinal perforation (31.4% vs 6.8%, p=0.002), anastomotic leakage (45.3% vs 20.5%, p=0.007), previous antibiotic therapy (69.3% vs 41.6%, p=0.0001), higher median number of abdominal surgical interventions

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Abstracts 2020

[3 vs 1, \( p=0.04 \)] and higher mean SAPS II score at the time of ICU admission (42 vs 34.6, \( p=0.007 \)). At multivariate analysis, risk factors independently associated with IAC were recurrent gastrointestinal perforation (OR 5.64; 95% CI 1.46-21.80, \( p=0.01 \)), anastomotic leakage (OR 2.86; 95% CI 1.11-7.38, \( p=0.03 \)) and receiving previous antimicrobial therapy (OR 2.91; 95% CI 1.24-6.80, \( p=0.01 \)).

Conclusions: Patients admitted to ICU have peculiar risk factors for IAC development. Prospective clinical studies are needed to identify which high-risk patients will benefit from antifungal prophylaxis.

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**Abstract 4416**

**Triaging influenza in patients attending fever clinical scoring system for a modified influenza case definition**

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**Background:** Reliable and rapid clinical predictors to assess the likelihood of influenza in the clinical practice are lacking. To develop such predictors, we undertook a prospective analysis of influenza in patients attending fever clinics.

**Materials/methods:** From 1 January 2019 to 28 March 2019, we analyzed the differences in clinical presentation and laboratory parameters between fever clinic patients with PCR-confirmed influenza infection (N = 461) and those with PCR-negative non-influenza infection (N = 204).

**Results:** In multivariate logistic regression analysis we identified four parameters, namely cough (OR 3.22, P = 0.000), sputum production (OR 1.70, P = 0.011), rhinorrhea (OR 1.73, P = 0.005) and lymphocyte counts (OR 0.313, P = 0.000), as independent predictors of influenza infection. A six point score, one point for sputum production, rhinorrhea, and two points for cough and lymphopenia (< 1.16x10^9/L) was calculated for influenza infection. The median score was significantly higher in influenza as compared to non-influenza (4 [IQR 3–5] vs 3 [IQR 2–4], P = 0.000). Receiver operating characteristics showed a moderately high diagnostic accuracy of this diagnostic score (AUC 0.74 [95%CI 0.70–0.77]), which was better as compared to each parameter alone. Of the 253 patients (38%) with a score > 4 points, 90% of patients had influenza infection, which was far superior to the influenza antigen test (89.7% vs 41.1%, P < 0.0001).

**Conclusions:** A simple and practical six point score based on cough, sputum production, rhinorrhea, lymphopenia can be used to stratify patients with influenza into different management groups.

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Abstract 4424

Comparison of two commercially available qPCR kits for the detection of Candida auris
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Background: Candida auris is an emerging fungal pathogen, which has been first described in 2009. Its emergence has become a major public health concern as this species shows resistance to several antifungals and has caused outbreaks on different continents. Identification of C. auris with standard microbiology techniques is prone to errors. So far detection of patients colonized with C. auris relies mostly on cultural methods. A quicker, molecular based detection of this pathogen could help to detect carriers of C. auris more rapidly and improve patient management. In this study, the performance of two commercially available qPCR kits for C. auris detection was assessed.

Materials/methods: The two kits Fungiplex Candida auris RUO Real-Time PCR (Bruker, Bremen, Germany) and AurisID (OLM, Newcastle Upon Tyne, GB) were challenged using genomic DNA of 29 molecularly characterized C. auris isolates belonging to five different clades. Additionally, three closely related Candida species (C. pseudohaemulonii, C. haemulonii and C. duobushaemulonii) were employed to determine specificity. Serial 10-fold dilutions of DNA starting with 60 ng genomic DNA/reaction were used to assess the qPCR kits. All PCRs were performed on an ABI 7500 Real Time PCR System.

Results: All tested C. auris strains were correctly identified by the AurisID kit in the undiluted samples and up to an amount of at least 6x10^-7 ng DNA. At 60 ng/reaction, all three non-C. auris strains gave rise to false positive results. The Fungiplex kit correctly identified the C. auris strains up to an amount of at least 6x10^-5 ng DNA; no false-positive results were recorded with this assay even at higher concentrations.

Figure 1: Detection limit of the two assays at different DNA loads.

Conclusions: Both kits show excellent analytical sensitivity and specificity at lower C. auris DNA concentrations which are expected in clinical specimen. AurisID demonstrated higher sensitivity but lower specificity. Both kits could help to rapidly detect C. auris in colonized patients, e.g. in case of an outbreak. However, future studies have to further evaluate their performance on clinical samples and their usefulness in the hospital setting.

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Abstract 4426

Human mass balance study of enmetazobactam using 14C analysed by AMS
Paola Motta*, Stephen English1, Philip Barth1

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Background: Enmetazobactam (formerly known as AAI101) is a novel penicillanic acid sulfone β-lactamase inhibitor, active against a broad range of β-lactamases, including extended-spectrum β-lactamases (ESBLs) and some carbapenemases. Enmetazobactam (500 mg) is currently in Phase 3 clinical development in combination with cefepime (2 grams) for the treatment of adult patients with complicated urinary tract infections. We report here the results of a Phase 1 mass-balance study that investigated the disposition of enmetazobactam in healthy participants.

Materials/methods: Ten healthy adult males aged 27 to 58 received a single 2-hour IV infusion of 500 mg of enmetazobactam containing 1 µCi of enmetazobactam labeled with [14C]. Subjects remained in the clinical unit for 7 days after dosing for observation and collection of whole blood and excreta samples. Samples and HPLC fractions collected during metabolic profile analyses were analyzed for [14C] by accelerator mass spectrometry.

Results: Overall, approximately 99.7% of the administered 14C was recovered in the excreta (urine and feces combined) at the termination of the 168-hour collection period, with greater than 98% recovered in urine within the first 24 hours. Human plasma and urine samples collected in the first 24 hours after administration were analyzed and metabolite profiling successfully determined. Unchanged AAI101 represented 94.7% of the total radioactivity in plasma (as AUC pool) and 90% of the total radioactivity in urine. The remaining radioactivity was almost exclusively due to a single chemical entity (sulfinic acid product) that is intrinsically inactive and is formed by the cleavage of the AAI101 thiazolidine ring. The same chemical route has been observed during enmetazobactam degradation when the test item is stored above 25°C or during some extraction processes.

Conclusions: The recovery of a single dose of enmetazobactam was complete one week after dosing. Consistently with the results of the mass-balance studies conducted in human with other β-lactamase inhibitors (i.e., avibactam, tazobactam and vaborbactam), a great percentage of the administered radioactivity was found in urine, with the majority being recovered as unchanged drug in urine within the first 24 hours. The same disposition pattern was observed for cefepime, primarily excreted unchanged in the urine.

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Abstract 4427

**Prevalence and clinical outcomes associated with viral and atypical bacterial co-infections in a large global study of adults hospitalised with influenza (INSIGHT FLU003 Plus)**

Dominic Dwyer1, Deborah Wentworth2, Norman Gerry3, Marie Hoover3, Jim Neaton2, Rick Davey4, Mark Polizzotto5, Tristan Clark6, Armando Paez7, José Ramón Paño Pardo8, Jens D. Lundgren9, Ab Babiker10, Sarah Pett11

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Abstract third-party references: on behalf of the INSIGHT Study Group

**Background:** It is unclear how viral and atypical bacterial co-infections influence clinical progression among adults hospitalised with influenza.

**Materials/methods:** Adults hospitalised with influenza enrolled in FLU003 Plus were included. A Luminex NxTAG panel (includes influenza types/subtypes, respiratory syncytial viruses A/B, coronaviruses 229E/OC43/NL63/HKU1, human metapneumovirus, rhinovirus/enterovirus, adenovirus, parainfluenzaviruses 1/2/3/4, human bocavirus, atypical bacteria (C. pneumoniae/M. pneumoniae/L. pneumophila) was performed on the enrolment nasopharyngeal specimen. Seven days after enrolment, the patient’s clinical state was described using an ordinal outcome with six categories ordered by severity (death; ICU/intubated; hospitalised on oxygen or not; discharged and back to normal activities or not). Prevalence and determinants of any co-infection were assessed, the latter with logistic regression. A proportional odds model was used to compare those with/without co-infection for the 6-category ordinal outcome at Day 7. Unadjusted and adjusted (for age, in ICU or on oxygen in the general ward at enrolment, geographic region, influenza type), proportional odds ratios (ORs), 95% CIs and 2-sided p-values are cited. Other baseline factors were included in the adjusted model if associated with co-infection. ORs by influenza type were compared by including an interaction term in the ordinal regression model.

**Results:** Among 1947 patients with Luminex-panel confirmed influenza (median age 61 years, 52% female, median five days since symptoms onset), 92 (4.7%) had a viral co-infection; 2/92 patients also had an atypical bacterium infection. Most patients (91%) had only one co-infection. Longer duration of symptoms at enrolment (p=0.02) and being immunocompromised (p<0.001) were associated with an increased co-infection prevalence. Co-infection was associated with a less favourable outcome category at day 7 (OR=0.66, 95%CI:0.45-0.98, p=0.04). After adjustment, the OR was 0.78, 95%CI:0.52-1.17, p=0.23. ORs of a favourable outcome with co-infection did not vary by influenza A/B type (p=0.87).

**Conclusions:** The prevalence of viral co-infections in hospitalised laboratory-confirmed influenza in a global study was low. Atypical bacterial co-infections were uncommon. After adjustment, the presence of co-infections considered did not significantly affect 7-day clinical status. The clinical benefit of testing for other viral pathogens in laboratory-confirmed influenza may be limited.

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**Abstract 4434**

**Dissemination of carbapenem-non-susceptible Klebsiella pneumoniae from Oman**
Maarten Coorens1,2, Hissa Al Farsi*1,3, Isak Sylvén1,4, Zakariya Al-Muharrmi5, Saleh Al-Azri3, Amina Al Jardani3, Christian Giske1,2

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**Background:** Carbapenem-resistant Klebsiella pneumoniae (CR-Kp) is considered one of the major challenges in the fight against antimicrobial resistance. While certain clonal groups, such as CG258, are currently the major cause of CR-Kp infections, new successful high-risk clones can emerge rapidly. As the prevalence of CR-Kp has not been thoroughly investigated in the Middle East, including Oman, this study aimed to identify and characterize CR-Kp in Oman.

**Materials/methods:** Two hundred and thirty-seven suspected CR-Kp isolates were collected between January-November 2015 from 11 different hospitals throughout Oman. They were examined phenotypically with disk diffusion and interpreted using EUCAST guidelines. Next, DNA extraction and Illumina-NGS were performed. Genomes were assembled using Unicycler. Resistance mechanisms were identified using the CARD database, while sequence types, species, as well as virulence factor presence were determined using Kleborate. BIGSdb database was used to assign new STs when required. SNP-based analysis was performed to determine genetic variation and classical Multidimensional Scaling (CMD-scaling) was used to plot genetic diversity within different STs.

**Results:** The majority of isolates were K. pneumoniae strictu sensu, while 2 strains were K. quasipneumoniae. Carbapenem-resistance was mostly caused by OXA-48-like enzymes (n = 86), in particular OXA-232, followed by NDM-1 enzymes (n=81). Interestingly, 18 strains co-produced NDM-1 and OXA-48-like enzymes. The most common STs identified were ST231 (32%) and ST11 (32%), followed by ST147 (15%) and ST15 (7%). Interestingly, low clonal diversity was observed within ST231 isolates compared to the other ST groups. Furthermore, an association between ST and carbapenemase genes was observed, with NDM-1 being completely absent in ST231 isolates, while most ST231 isolates expressed the OXA-232 carbapenemase. Finally, a high percentage of ST231 isolates (80%) express both aerobactin and yersiniabactin virulence genes, which could be an important contributor to its effective national dissemination.

**Conclusions:** This study showed that expression of OXA-232 and NDM-1 are the leading causes of carbapenem-resistance among K. pneumoniae in Oman. In addition, our results identified a ST231 clone co-expressing both OXA-232 as well as aerobactin and yersiniabactin virulence factors, which could be indicative of the emergence of a high-risk hypervirulent multi-drug resistant clone.

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Elucidating the role of the essential operon yajC-secD-secF in Burkholderia spp.; a possible new target for new antimicrobial molecules

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Background: Infections caused by species belonging to the *Burkholderia cepacia* complex (Bcc) have a high mortality rate among immunocompromised and Cystic Fibrosis (CF) patients, due to the high levels of intrinsic antibiotic resistance of these bacteria. Consequently, the search of new therapeutic approaches to fight Bcc infections is crucial for these patient categories. Our aim is to understand the role of SecDF proteins in Bcc species in order to evaluate the possible use of this system as a new antibiotic target.

SecDF proteins, included in the Resistance Nodulation Cell-Division Superfamily (RND) of efflux pumps, are present both in Bacteria and Archaea. Some roles have been suggested for this system in different microorganisms (from protein translocation across or into the inner membrane of prokaryotes to antibiotic resistance) but its function in bacterial cells remains elusive and, although this efflux system proved to be non-essential for cells viability in all the microorganisms in which it has been studied to date, recently, the use of the "transposon mutagenesis with next-generation sequencing", TnSeq technology, revealed that the genes coding for these two proteins are essential in a variety of different microorganisms.

Materials/methods: We developed a strategy to understand the role of SecDF, based on a multiomic characterization (transcriptomics, metabolomics and phenotypic characterization) of a SecDF conditional growth mutant.

Results: A SecDF conditional growth mutant has been obtained and a preliminary characterization of its growth has been performed. A microscope observation of the cells showed problems of cell division. All the other experiments are in progress.

Conclusions: The understanding of the exact role that SecDF proteins have in bacterial cell is crucial to evaluate the role for this system as possible target for the design of new antimicrobial molecules, directed against all the microorganisms in which this system is essential, as Bcc species.

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Abstract 4437

**High utility of Gram-stain of urine specimens for guiding empiric clinical management of pyelonephritis**

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**Background:** Gram-stain is a simple and still useful method for guiding empirical clinical management without expensive equipment. Interpretation of urine gram-stain is generally easier than that of other kinds of specimens like sputums. The current guidelines for pyelonephritis recommend starting treatment with antibiotics against gram-negative bacilli (GNB) such as *Escherichia coli*, although gram-positive cocci (GPC) are occasionally responsible. Previous studies have not reported specified conditions that require empirical antibiotic coverage against gram-positive organisms. The guidelines do not mention the utility of gram-stain of urine specimens.

**Materials/methods:** A single-center, retrospective study at a 358-bed community teaching hospital in Japan. Medical records were reviewed for adult inpatients diagnosed as pyelonephritis with positive blood cultures between 2016 and 2019. We evaluated the results of gram-stain of urine specimens, the results of urine and blood cultures, the proportion of causative organisms, the options of antibiotics as empirical therapy, and their clinical courses.

**Results:** We extracted 217 cases of pyelonephritis (mean age 78.1 years, male 30.0%). GPC proved responsible in 18 of the 217 cases (8.3%, 95%CI: 5.0-12.8%). They were streptococci in 8 cases, staphylococci in 5 cases, enterococci in 4 cases, and *Aerococcus spp.* in 4 cases, including the cases in which multiple organisms were responsible, specifically. Cefmetazole had been chosen most frequently as empirical therapy (67.3%). During empirical therapy, the GPC cases tended to receive inappropriate antibiotics compared with the GNB cases (27.8% vs. 2.5%, p<0.001). The empirical antibiotic therapies based on the results of gram-stain contributed to the adequate coverage of causative organisms (p=0.017). Regarding the interpretation of the urine gram-stain results, the proportion of GPC as causative organisms was very high when GPC were observed without GNB (97.8%), conversely, the proportion was low when GPC were observed with GNB (9.3%, p<0.001). Cox regression analysis identified independent predictors for pyelonephritis with GPC: male sex (p=0.016) and renal-ureteral stones (p=0.046).

**Conclusions:** Empirical therapies tend to be inappropriate in pyelonephritis cases caused by GPC. Gram-stain of urine specimens could lead to better decisions for adequate antibiotic regimens during empirical therapy. The guidelines should mention the potential of gram-stain.

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Abstract 4440

Comparison between visual reading, smartphone image and digital scanner interpretation of lateral flow device result for detecting Aspergillus-specific IgG

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Background: Chronic pulmonary aspergillosis (CPA) is a fungal disease with an estimated 3 million cases worldwide, and most patients are from low-middle income countries (LMIC) with limited access to diagnostic tests. A lateral flow device (LFD) is an inexpensive device that can identify an analyte in a clinical sample effortlessly. We tested an LFD prototype that is being developed for detecting Aspergillus-specific IgG using recombinant antigens and interpreted the results using three different methods: a visual reading, a smartphone image and a digital scanner.

Materials/methods: Sera from 122 CPA patient and 123 healthy controls were used for this study. All readers were blinded to the patient diagnosis at the time of interpretation. Visual reading interpretation was done by one reader immediately following incubation. After that, the device was scanned using a Qiagen ESEQuant LR3 (Lake Constance, Germany) lateral flow reader and finally, a smartphone image was taken. Smartphone image interpretation was done by three readers at different times, a third reader adjudicated if there was a difference between the interpretation of first and second readers. Sensitivity and specificity of each interpretation were recorded.

Results: Visual interpretation sensitivity and specificity were 75.4% (95% CI [66.8-82.8%]) and 63.4% (95% CI [53.4-71.9%]), respectively. Smartphone image interpretation sensitivity and specificity were 62.3% (95% CI [53.1-70.9%]) and 74.0% (95% CI [65.3-81.5%]), respectively. Optimum cut-off for the digital scanner was 41.7 mV. At this cut-off, the sensitivity and specificity for the digital scanner were 76.2% (95% CI [67.7-83.5%]) and 60.2% (95% CI [51.0-68.9%]), respectively.

Conclusions: Based on these results, the digital scanner interpretation and visual interpretation provided the highest sensitivity, followed by the smartphone image. Although the smartphone image interpretation had the lowest sensitivity, it is still suitable for recording LFD results in LMIC settings. Research to develop applications or platforms for digital reading that can be integrated with a smartphone will be very important, as developments of LFD as diagnostic tools is progressing rapidly.

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<th>Specificity (%)</th>
<th>Youden’s J statistic</th>
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Abstract 4441

Resistance trends among the common bacterial causes of community-acquired lower respiratory tract infection in the UK and Ireland, 2008-2018

Carolyne Horner, Shazad Mushtaq, David Livermore

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Abstract third-party references: The British Society for Antimicrobial Chemotherapy Standing Committee on Resistance Surveillance

Background: The BSAC Respiratory Resistance Surveillance Programme has monitored antimicrobial susceptibility of Haemophilus influenzae, Moraxella catarrhalis and Streptococcus pneumoniae from community-onset lower respiratory tract infections (CO-LRTI) in the UK and Ireland since 1999/2000. We review data for 10 surveillance seasons (Oct 2008 – Sept 2018).

Materials/methods: Consecutive isolates causing CO-LRTI were tested; participating laboratories (n=21-39) collected 14-20 isolates of H. influenzae and S. pneumoniae, and 7-10 isolates of M. catarrhalis per season. MICs were determined centrally by BSAC agar dilution. Isolates of S. pneumoniae were serotyped from Oct 2013.

Results: Among H. influenzae (n=4738), 959 (20%) produced β-lactamase. Rates of resistance to aminopenicillins and amoxicillin-clavulanate increased (amoxicillin: 19% 2008/09 – 31% 2017/18; ampicillin: 20% 2008/09 – 30% 2014/15; amoxicillin-clavulanate: 0.4% 2008/09 – 9.1% 2017/18); whereas resistance to cefotaxime remained low (mean 0.7%). Rates of resistance to ciprofloxacin, erythromycin, and tetracycline were ≤2% without trend; 27/845 (3%) H. influenzae were resistant to ceftaroline. Cefotiboprole MICs ranged from 0.004-2mg/L (median 0.06mg/L). Among M. catarrhalis (n=2266), 2188 (92%) produced β-lactamase. All isolates tested were susceptible to amoxicillin-clavulanate, cefotaxime and erythromycin. Resistances to ciprofloxacin (n=8), cefuroxime (n=4), and tetracycline (n=2) were rare. MICs of ceftaroline ranged from 0.002->4mg/L (median 2mg/L; n=38, MIC >4mg/L) and ceftobiprole from 0.008->4mg/L (median 1mg/L; n=9, MIC >4mg/L); four isolates had a MIC >4mg/L to both agents. Four S. pneumoniae isolates (n=3921) were resistant to penicillin (MIC 4-8mg/L), whilst MICs for 485 (12%) were from 0.12 – 2 mg/L (no trend). Increasing resistance was seen for tetracycline (9% 2008/09 – 14% 2017/18) and clindamycin (4% 2008/09 – 11% 2017/18); whereas resistance to erythromycin remained stable (mean 1%). Resistances to ceftaroline (1/670) and ceftobiprole (13/2416) were rare. Serotyping was completed for isolates ≥3 years into the PCV13 era; 78 serotypes were represented, most commonly 15A (8.7%), 11A (8.1%), and 23B (5.3%). There were 312 (12%) isolates with a serotype within PCV13, most commonly 3 (43%), 19F (28%) and 19A (19%).

Conclusions: M. catarrhalis remain largely susceptible to existing antimicrobials; however, an increase in the rate of resistance to first line β-lactams was identified in H. influenzae. For S. pneumoniae the rise of often-multiresistant serotype 15A is a concern.

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Abstract 4444

**Epidemiology of cardiac surgical site infection in England, 2018/19**
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**Background:** Data collected by hospitals participating in national surgical site infection (SSI) surveillance provide an invaluable tool to assess local changes in risk and national trends. We extracted data on cardiac procedures from NHS hospitals participating in the Public Health England national surveillance programme to update our understanding of current epidemiology.

**Methods:** Hospitals participating in voluntary surveillance of coronary artery bypass graft (CABG) and other cardiac non-CABG procedures (primarily valve repair/replacement) prospectively followed-up patients to detect infection (based on ECDC/CDC definitions) up to 1y after surgery. Infections were detected during the inpatient stay or on readmission. Optional patient post-discharge questionnaires (PDQ) were utilised by hospitals; patients self-completed PDQs 30d after surgery with possible signs of infection reviewed by hospital staff. Operations from 2018/19 were analysed, with sub-analysis for hospitals achieving >70% PDQ return rate.

**Results:** During 2018/19, 16 hospitals participated in cardiac surveillance submitting 9,866 procedures, 5,994 CABG and 3,872 cardiac (non-CABG). The latter included 293 paediatric procedures (<18y), 136 on infants. Inpatient and readmission-detected SSI risk was 2.27% for CABG, 1.79% with exclusion of donor incisional site SSIs. For cardiac (non-CABG), SSI risk was 1.32% overall and 2.05% in children. Most CABG SSIs were superficial infections (64%), with 28% deep incisional and 8% organ/space; equivalent breakdowns for cardiac (non-CABG) were 37%, 45% and 18%. Enterobacteriaceae were the most common causative pathogens [41.8% CABG SSI, 33.3% non-CABG]. Median time to infection (all detection methods; Figure) was 16d for CABG and 18d for cardiac (non-CABG). Inclusion of PDQ-detected SSIs increased SSI risk from 2.53% to 8.55% (IQR 6.99-11.20%) for CABG and 1.04% to 2.19% (IQR 1.04-2.40%) for cardiac (non-CABG) in 5 hospitals using this methodology. One in 200 cardiac (non-CABG) patients was readmitted for management of SSI, rising to 1 in 75 for CABG.

**Conclusions:** Surveillance data provide a valuable platform to understand the epidemiology of cardiac SSI, informing the design of local and national interventions and providing a means to assess their impact.

Figure: Onset of surgical site infection (inpatient and post-discharge detected) following coronary artery bypass graft (CABG) and cardiac (non-CABG) surgery, England 2018/19

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Quantitative detection and impact of 5’ terminally deleted Group B enterovirus populations on type I IFN response in peripheral blood or heart tissue samples from acute myocarditis pediatric patients

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Background: Group B enteroviruses (EV-B) are common causes of acute myocarditis, which can be a precursor of chronic myocarditis and dilated cardiomyopathy (DCM), leading causes of heart transplantation. Major enterovirus B populations characterized by 5’ terminal genomic RNA deletions ranging up to 50 nucleotides (5’T-D) were identified either alone or associated with low proportions of intact 5’ genomic termini (FL) in heart tissue biopsies from acute myocarditis and chronic dilated cardiomyopathy (DCM) patients [1]. Dynamics of emergence of EVB-TD populations from the acute myocarditis to chronic DCM stage remain unknown.

Materials/methods: In the present study, we used an original rapid amplification of cDNA ends (RACE) PCR assay followed by micro-electrophoresis allowing quantifying FL or 5’T-D EV-B RNA genomes in clinical samples. Using this valuable molecular approach, we analyzed seven plasma and four heart tissues samples [French Enterovirus reference centers: 2015-2017] taken from seven pediatric acute myocarditis patients.

Results: EV-B viral load levels were assessed by a specific RT-qPCR assay in peripheral blood samples [5.0×10^4 cp/mL [1.82×10^3-2.98×10^4] and heart samples [4.50×10^6 cp/µg [3.97×10^4 – 9.85×10^6] of acute myocarditis cases. Our results evidenced the detection of STD RNA genomes ranging from 37 to 50 nucleotides (90 %) associated to FL (3 %) or 5’T-D RNA genomes ranging from 8 to 36 nucleotides (7 %) in the early stage of acute myocarditis. In study samples, IFN-β mRNA levels appeared to be negatively correlated with proportions of 5’T-D RNA genomes ranging from 37 to 50 nucleotides [R^2=0.811, P=0.006] whereas a positive correlation was observed between IFN-β mRNA levels and proportions of minor 5’T-D 8-36nt forms [R^2=0.905, P=0.001]. Following transfection of EVB-TD and FL forms in human cardiomyocytes (HCM), IFN-β mRNA and cytokine levels appeared to be significantly higher for the FL and minor 5’T-D 8-36 nt forms comparatively to 5’T-D 37-50 nt forms [P=0.0087].

Conclusions: In conclusion, our RACE PCR assay allowed the identification of major 5’terminally deleted EV-B populations in peripheral blood and cardiac tissues of acute myocarditis patients. Moreover, the proportions of minor 8 to 36nt EVB-TD and FL populations could modulate the innate immune sensing mechanisms in human cardiomyocytes.

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Abstract third-party references: On behalf of the DZIF R-Net study group

Background: The increase of vancomycin resistance among Enterococcus faecium in Europe is alarming (from 10.5% to 17.3% between 2015 and 2018, ECDC). We aimed to identify the VRE prevalence upon hospital admission and to analyze risk factors for VRE colonization.

Materials/methods: From 2014 to 2018 patients were recruited within 72h of admission to seven participating German university hospitals. Screening for VRE was performed and data on potential risk factors (prior MDRO detection, current and prior antibiotic consumption, prior hospital, rehabilitation or long term care facility stay (LTCF), international travel, animal contact, and consumption of medication for gastro oesophageal reflux disease) were collected by structured interviews. VRE were detected on ChromID® VRE plates (biomerieux), phenotypical resistance was further tested by means of Vitek®2 (biomerieux) and genotypical analysis was performed by cgMLST analysis (Ridom SeqSphere+). Multivariable analysis was performed for VRE colonization and specific sequence types (ST).

Results: In five years, 17351 patients were recruited. The median age was 62 years (IQR 50-73) and 8198 were women (47.2%). In total, 270 patients were colonized with VRE on hospital admission – a prevalence of 1.6%. Risk factors for VRE colonization were antibiotic treatment at the time of screening (aOR 3.62; 95% CI 3.39-3.86), prior MDRO detection (aOR 3.19, 95%CI 2.59-3.93), stay in a LTCF (aOR 2.31, 95% CI 1.74-3.06), stay in a German hospital (aOR 3.33, 95%CI 2.41-4.60) and consumption of PPI or antacids (aOR 1.38, 95% CI 1.25-1.53). The VRE admission prevalence increased by 29% per year. cgMLST showed that 137 (50.7%) of the VRE were ST117, with a steep increase over the years (Table 1). Multivariable analysis revealed that ST117 and non-ST117 VRE differed only with respect to the admission year.

Conclusions: As vancomycin resistance rates increase, so does the VRE admission prevalence, mainly driven by the emergence of ST117. Different health care contacts seem to put patients at risk for VRE colonization.

<table>
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Table 1. Yearly increase of ST117 VRE admission prevalence in %.

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Abstract 4451

Microbiota as a marker of mucoid Pseudomonas aeruginosa and Haemophilus influenzae in non-cystic fibrosis bronchiectasis

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Background: Pseudomonas aeruginosa (PA) and Haemophilus influenzae (HI) are two of the main pathogens in non-cystic fibrosis bronchiectasis (BE) chronic colonization. However, scarce evidence exists on respiratory concomitant microbiota patterns associated to each of the two pathogens, in particular when mucoid PA is present. The purpose was to determine if Pseudomonas aeruginosa (PA) non-mucoid (group 1) or mucoid (group 2), Haemophilus influenzae (HI) (group 3), and combined presence of mucoid PA and HI (group 4) are associated to any particular pattern of concomitant microbiota also clustering by BE alone or plus Chronic obstructive pulmonary disease (BE-COPD).

Materials/methods: Sputum in BE patients with at least 1 previous PA isolation was collected prospectively. Sputum samples were isolated by Norgen DNA sputum kit. The preparation of the DNA libraries was based on the hypervariable regions V1, V2, V3, V4, V5, V6, V7, V8 and V9 regions for bacterial 16S rRNA. DNA libraries were created and purified using the QIASeq Screening Panel 16S/ITS and Agencourt AMPure XP Beads. The pool of DNA libraries was introduced into Illumina Miseq platform. The bioinformatic analyses were performed by QIIME and Mothur with GreenGenes microbiome database, the pipeline design was adjusted for our objectives.

Results: Twenty-nine sputa were included in the analysis by groups 1 to 4 (n=5, n=9; n= 5 and n=10, respectively). Twenty-seven taxonomic units were found. PA and HI were present in all groups having the highest abundance of PA or HI the group 4 (p=0.022) or group 3 (0.007), respectively. HI was higher in the BE-COPD group compared to BE alone (520.5[207.5-11629.3] vs 49.5[0.0- 175.0], p=0.007, respectively).

Interestingly, four study groups differed in terms of concomitant microbiota. For instance, Carnobacteriaceae were only found in group 1 but Leptotrichiaceae, Fusobacteriaceae, Porphyromonadaceae, Erysipelotrichiaceae and Paraprevotellaceae were only found in group 2, being the fusobacteriaceae the ones with higher abundance. Mycoplasmataceae, Gemellaceae and Pectostreptococcaceae were only found in group 4 being the Gemellaceae the ones with higher abundance.

Conclusions: The use of Fusobacteriaceae or Gemellaceae as markers of mucoid PA or mucoid PA with HI colonization needs further investigation but could impact in clinical management of BE patients.

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Abstract 4453

An outbreak of Clostridioides difficile infections due to a 027-like PCR ribotype 181

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Background: Clostridioides difficile is one of the most important healthcare-associated pathogens in Europe. Recently, a number of 027-like so-called “hypervirulent” types have been found that all belong to the Clade II, but have an unknown clinical and epidemiological presentation.

Materials/methods: We identified a rapidly spreading outbreak of nineteen episodes of C. difficile infections (CDI) in a Greek 180-bed Rehabilitation Clinic (RC) within a 28-day time-period (29 March to 25 April 2019). C. difficile PCR Ribotype (RT) 027 was presumed since a diagnostic PCR revealed the presence of a typical frame shift mutation at position 117 of TcdC. Using the ESCMID definitions, the outbreak was associated with mild to moderate disease and 6% of the patients developed a relapse. Cultured strains showed an unknown RT 027-like type and were sent to Leiden University Medical Centre for further characterization. Core genome multilocus sequence typing (cgMLST) was performed in Seqsphere and the sequence data were used to build a neighbor joining tree.

Results: The CDI incidence rate on the RC was 49 infections per 10,000 patient days (29 March-25 April 2019), which nearly quadrupled compared to previous infection rates. Of 19 cultured isolates, 15 displayed the same RT 181 profile. All clinical RT 181 isolates from Greece belonged to (MLST) ST1 and were positive for tcdA, tcdB and the binary toxin genes and also had a 18bp deletion in tcdC at position 311 together with a single nucleotide deletion at position 117, similarly to RT 027. The RT 181 Greek strains clustered with two RT181 reference strains (kindly provided by University of Leeds). The RT 181 outbreak isolates were closely related to each other, belonged to MLST Clade 2, but differed around 10% in their core genome allelic profiles from the rest of Clade 2. [Figure 1] The outbreak strain was resistant to fluoroquinolones and macrolides, but susceptible to vancomycin and metronidazole.

Conclusions: New C. difficile ribotypes still emerge at unexpected time and location without a clear source. C. difficile RT 181 was rapidly spreading but not associated with increased mortality and higher relapse rates.
**Figure 1.** Neighbor-joining tree of strains from Greece (n=18) and control samples (n=7) from other RTs. RT181 (CD181-01 – CD181-15) and RT036 (CD036-01, CD036-02) strains from Greece belong to Clade 2 (yellow). Strain with unknown *ribotype* from Greece is coded with CD999-01 and belongs to Clade 1. RTs 001, 027, 023, 017 and 078 from Clade 1, 2, 3, 4 and 5 are colored red, yellow, green, blue and purple, respectively. The distance is given as a fraction of allelic differences.

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Diversity of beta-lactamase genes carried by multidrug-resistant Enterobacteriaceae clinical isolates in Georgia

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1US Army Medical Research Directorate – Georgia (USAMRD-G), Tbilisi, Georgia, 2Evex Medical Corporation, Tbilisi, Georgia, 3The First University Clinic of the Tbilisi State Medical University, Tbilisi, Georgia, 4The National Center for Disease Control and Public Health of Georgia, Tbilisi, Georgia

Background: The prevalence of the beta-lactam resistant enterobacteriaceae, specifically the 3rd generation cephalosporins and carbapenems, is steadily increasing and spreading globally. Antibiotic resistance is supported by various molecular mechanisms, including intrinsic and acquired resistance genes. Here, we examined an antibiotic resistance phenotype and beta-lactam gene content of MDR clinical isolates of enterobacteriaceae and Pseudomonas aeruginosa, recovered from patients at intensive care units of multi-profile hospitals in the Country of Georgia.

Materials/methods: Bacterial isolates were collected between July 2017 and May 2019 from four clinical sites in Georgia. Bacterial identity and antimicrobial susceptibility were determined by the Vitek 2 automated system according to CLSI standards. Antimicrobial resistance gene content was examined by multiplex PCR (Streck Inc.), targeting plasmid-mediated AmpC and beta-lactamases, representing fifteen gene families.

Results: 168 specimens, consisting of Klebsiella pneumoniae (n=72), Escherichia coli (n=51), Serratia marcescens (n=10) and Pseudomonas aeruginosa (n=35) were selected for this study. It was found that 100%, 97%, 94% and 78% of S. marcescens, P. aeruginosa, K. pneumonia and E. coli isolates, respectively, were multi-drug (MDR) resistant. CTX-M-15 or CTX-M-14 extended spectrum beta-lactamase genes were detected in 100% of MDR K. pneumonia and E. coli strains, followed by 78% and 13% found among MDR S. marcescens and P. aeruginosa. In addition to CTX-M-15 gene, subset of K. pneumonia co-harbor OXA-48 (n=15) or NDM (n=8) carbapenem resistance genes, whereas single E. coli isolates were found to also carry OXA-48 (n=1), NDM (n=1), VIM (n=2) and IMP (n=2) carbapenem resistance genes. In addition, only two strains of S. marcescens demonstrated the presence of OXA-48. VIM and IMP were found in 11 and 2 strains of P. aeruginosa, respectively. DHA and EBC were co-harborred together by one isolate of E. coli, and CMY-2 was found in single isolate. MOX ACC and FOX genes were not detected in any of presented isolates.

Conclusions: Multi-drug resistance has been observed in bacterial isolates recovered in the country of Georgia. Detection of highly transmissible plasmid associated resistance genes indicates the high potential for horizontal spread of resistance that in combination with already existing multi-drug resistance could lead to the emergence of a novel “superbug” in Georgia.

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Hospital onset bloodstream infection (HOBSI) as a marker of the burden of hospital associated infection (HAI) in a tertiary care hospital in South India

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Background: CLABSI, though accepted, may not be a reliable marker of the burden of HAI. Hospital onset Bloodstream infection (HOBSI) is proposed to be a better indicator of the burden of HAI in a hospital. This study is an attempt at comparing HOBSI with CLABSI as a marker to determine the burden of HAI in minimal resource countries.

Materials/methods: A retrospective analysis of patient records, blood culture data and summaries with blood stream infection was carried out from 2017-2018 to determine the number of HOBSI episodes in patients admitted to the hospital. This was compared with the CLABSI rates defined for the two years of study. Standard definitions were used for HOBSI- BSI first identified on blood culture drawn >48 hours after hospital admission or within 48 hours following hospital discharge and CLABSI as per CDC NHSN criteria. An attempt was made to identify the source for HOBSI along with the core organisms causing infections.

Results: A total of 54 HOBSI episodes (0.8/1000 Patient days) were found in the two years of which 37 were detected in 2017 (1.14/1000 patient days) and 17 in 2018 (0.51/1000 patient days). The chief sources for HOBSI were urinary tract (33.3%), those related to surgical complications and procedures (25.9%), complicated stent with PTBD procedures (18.5%), lower respiratory tract infections including VAP (11.1%), CLABSI (9.25%) and dialysis catheter induced BSI in 3 (5.5%). The core organisms were found to be Klebsiella pneumonia 19 of which 14 were carbapenem resistant (CRE), E.coli 16 of which 7 were CRE, and Enterococcus faecalis in 7 episodes. The corresponding documented CLABSI rates were 4 (0.91/1000 CLT days) and 2 (0.2/1000 CLT days) in 2017 and 2018 respectively.

Conclusions: HOBSI is a better and reliable indicator of the HAI burden in a hospital in comparison to CLABSI. Episodes of BSI not attributed to CLABSI but adding to the overall burden of HAI could be determined using this indicator. A retrospective HOBSI analysis of patient data was possible which is not possible with CLABSI.

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Abstract 4458

**qPCR inhibitors/enhancers: the interference in the reaction by drugs used for patient treatment or ingested by the patients**

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**Background:** The real-time polymerase chain reaction (qPCR) has become a powerful tool for rapid diagnosis. It is well-known that diverse substances can interfere in the reaction producing unintended results. In addition, there are few studies about the affection in qPCR of diverse drugs used from patient’s treatment. This study tested 46 substances (antacids, antibiotics, antipyretics, antitussives, antivirals, expectorants, laxatives, probiotics, …), in several concentrations, used for patient treatment or ingested by the patients in order to evaluate their inhibitor/enhancer potential.

**Materials/methods:** Several concentrations of each substance were added directly over the qPCR reaction mix. The qPCR assay used in this study was VIASURE Flu A, Flu B & RSV Real Time PCR Detection Kit that detected four targets in four different reactions. qPCR assays run on thermocycler CFX96TM Real-Time PCR Detection System (Bio-Rad). The 46 compounds were evaluated with two different approaches, based on the quantification cycle (Cq) and the end-point fluorescence intensity (FI); and based on the individual amplification efficiency (EA) of each individual reaction calculated with LinRegPCR program Version 2017.1. The maximum concentration of no interference (MCNI) of each substance was calculated for both approaches.

**Results:** MCNI values for both approaches were very similar; however, the one based on Cq and FI was more restrictive. Graphical representations showed that compounds could follow four general behaviors: a total inhibition in one or several concentrations (67.4%), partial inhibition (26.1%), enhancement (4.3%) and no affectation (2.2%). In addition, two specific behaviors have been also identified; the more affection over retrotranscription compared to DNA polymerase reaction (10.9%) and the gradual fall of the fluorescence with dependence on the fluorophore (2.2%).

**Conclusions:** The comparison performed with previous studies has been made carefully due to methodologies were different. Several drugs not described in the literature to date as inhibitors of qPCR were identified, which facilitates the success of qPCR for rapid diagnosis, and particularly for developing pre-qPCR processing systems. Also, the results suggested that the qPCR assay used in the present study withstood higher inhibitors concentrations.

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Primary evaluation of three Aspergillus PCRs compared to galactomannan assay
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Background: Invasive aspergillosis remains the leading cause of invasive fungal infection in immunocompromised patients. PCR-based methods are increasingly used. Here we present preliminary evaluation results of three different kits of Aspergillus PCR.

Materials/methods: 11 bronchoalveolar lavage (BAL) and 9 serum samples from 13 patients previously tested in Aspergillus galactomannan (GM) assay were extracted using Janus Chemagic360. DNA was analysed with three commercially available PCR kits: Fungiplex (Brucker), MycoGenie (Ademtech), Aspergillus ELiT MGB (Elitech). All PCR have been done on CFX96 (Biorad).

Then, we analysed with Aspergillus ELiT 10 sterile water samples and 6 strains from Cap Survey mycology evaluation: 4 Aspergillus (ochraceus, terreus, fumigatus, flavus), 1 Penicillium and 1 Scopulariopsis spiked in sterile water and diluted 1:100.

Results: Among 17 GM positive samples, 7 were positive by Fungiplex assay, 10 by MycoGenie and Elitech assays. Four serum samples from patients GM positive in BAL were tested, three remain negative in PCR.

Detection of the 4 Aspergillus was good, Scopulariopsis was not detected but Penicillium was also detected. All 10 water samples had ct > 38, considered as negative.

Conclusions: MGB and Mycogenie show better results than Fungiplex. Discrepancies with galactomannan should be investigate to determine if PCR is more specific than galactomannan or less sensitive.

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<tr>
<th>Date</th>
<th>Patient</th>
<th>Nature</th>
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<th>MycoGenie</th>
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Abstract 4461

Hospital-based surveillance of influenza in Switzerland: a pilot study, season 2018/19
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Background: Until 2018, the national reporting system for influenza in Switzerland was limited to a Sentinella system – voluntary reports of influenza-like illnesses by primary care clinicians, and laboratory characterisation of circulating virus strains during and off the influenza season. No surveillance of hospitalised cases existed nationally, each hospital having their own surveillance system. With support from the Federal Office of Public Health, we developed a pilot study for hospital-based influenza cases in Switzerland.

Materials/methods: Six major swiss hospitals participated in the pilot study and collected data following the WHO recommendations via a standardised questionnaire [demographic data, information on the influenza episode, optional information about the patient’s health]. Data were collected in a secure REDCap database. Data quality checks and descriptive analyses were reported weekly. Another questionnaire was used to assess the quality of the pilot system and to identify staff practices.

Results: From 01.11.2018 to 31.05.2019, 1700 cases were declared. The influenza epidemic started during week 2018-47 in Western Switzerland, and three to four weeks later in other sites. Most patients were elderly (67.2% over age 65). The majority of cases (98.5%) was due to influenza A. The proportion of weekly nosocomial cases peaked to 30%, with variation between sites. The hospitals adopted security measures such as wearing of masks for patients, staff, and visitors; Droplet specific measures; and cohorting when possible. The system was deemed useful to obtain an overview of the overall situation and to get prepared for the epidemic. The workload was substantial: from a few minutes to collect the obligatory information to 1.5h for the optional information; the allowance for data collection proved important for the success of the study, but sometimes insufficient.

Conclusions: Our pilot system allowed us to get a better understanding of the distribution and spread of severe influenza cases in Switzerland. Simplification of the questionnaire, direct import of existing data, automated analysis, and additional tools for epidemic management will help to reduce the workload. In participating hospitals, the pilot system has proved feasible, but might not be sustainable without additional advantages for the sites. Inclusion of other smaller hospitals is now needed.

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Are resistance rates among bloodstream isolates a good proxy for other infections: analysis from the BSAC resistance surveillance programme

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Abstract third-party references: The British Society for Antimicrobial Chemotherapy Standing Committee on Resistance Surveillance

Background: Resistance rates in bacteraemia isolates are often used as a general measure of resistance prevalence but may not represent other infection types. The BSAC Resistance Surveillance Programme monitors antimicrobial susceptibility in the major organisms of bacteraemia and respiratory tract infections (LRTI) in the UK and Ireland. We compared resistance rates between these two settings.

Materials/methods: 24 laboratories collected isolates, to a fixed annual quota per species group. Bloodstream isolates were collected during calendar 2018 and LRTI isolates between Oct 2017 to Sept 2018. MICs were determined centrally by BSAC agar dilution.

Results: 2788 isolates were reviewed, 1670 from blood and 1118 from LRTI. Respiratory Pseudomonas aeruginosa and Streptococcus pneumoniae showed higher resistance rates than for bloodstream isolates. For P. aeruginosa (209 from blood; 179 from LRTI), respective resistance rates were ciprofloxacin (18% vs. 7%), imipenem (17% vs. 8%), meropenem (9% vs. 4%), piperacillin/tazobactam (10% vs. 4%), ceftazidime (6% vs. 2%), and gentamicin (4% vs. 2%). For S. pneumoniae (209 blood; 325 LRTI) rates were penicillin MIC>0.06 mg/L (15% vs. 6%), erythromycin (15% vs. 7%), clindamycin (11% vs. 6%), tetracycline (14% vs. 10%). The trend for S. pneumoniae persisted even when multiresistant serotype 15A isolates were excluded. In contrast, approximate parity in resistance rates among bloodstream and LRTI isolates was seen for most agents against Enterobacterales (797 blood, 424 LRTI) and Staphylococcus aureus (456 blood, 190 LRTI). Exceptions included a higher rate of amoxicillin-clavulanate resistance for LRTI Escherichia coli (61% vs. 41%, based on 475 bloodstream and 241 LRTI isolates), and a higher rate of colistin resistance in bloodstream Enterobacter cloacae (12% vs. 7%, based on 159 bloodstream and 73 respiratory isolates). MRSA comprised 7% of S. aureus from blood and 10% from LRTI.

Conclusions: Rates of resistance among bloodstream isolates are a reasonable proxy for most antibiotics for Enterobacterales and S. aureus but not for Pseudomonas or S. pneumoniae where resistance to all agents was consistently more prevalent in LRTI irrespective of agent. Collection of surveillance data for different infection types is crucial for our understanding of antibiotic resistance trends.

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Epidemiology of influenza in Thailand: findings from near real-time laboratory-based influenza system, a network of 40 hospital in Thailand, 2010-2019

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Abstract third-party references: Bangkok Dusit Medical Service (BDMS), Phramongkutklao College of Medicine

Background: Influenza is an acute viral disease of the respiratory tract which is characterized by fever, headache, myalgia, cough, sore throat and cough. Although recent efforts from some Asian countries to describe burden of influenza disease and seasonality, these data are missing for the vast majority, including the private section of Thailand. A near real-time laboratory-based influenza surveillance system, the Bangkok Dusit Medical Services surveillance system (BDMS-SS), in a network of 40 hospitals was implemented in 2017 aiming to determine influenza strains circulating in the private hospitals of Thailand and know characteristics, trend and burden of influenza viruses.

Materials/methods: We used influenza data from BDMS-SS from 2010 to 2019 for this analysis. We obtained the data by monitoring patients with influenza-like illness (ILI) at a network of 40 private hospitals across Thailand. Throat-swab specimens in viral transport media were collected and transported to the National Healthcare Systems Co., Ltd. within 24 h of collection using a cold-chain system. The respiratory samples were tested by rapid influenza diagnostic tests and real-time reverse transcription polymerase chain reaction.

Results: From January 2010 to November 2019, a total of 1,300,594 subjects were tested and 320,499 cases of influenza were identified. Of those positive cases, 116,317 (36.3%) were influenza type B, 185,512 (57.9%) were influenza A unspecified subtype, 8,833 (2.7%) were influenza A(H1N1)pdm2009 and 6,371 (1.9%) were seasonal influenza A(H3N2). Positive rate were 50.5 and 49.5 in female and male, respectively. Positivity rate was 41.4% in persons 15-49 years followed by 29.1% in 15-14 years, 17.6% in under five children and 11.7% in > 49 years. In 2018-2019 season, the highest positivity rate observed in February and March (39.3%) followed by April (34.2%), January (32.3%) and September (28.9%) while the lowest positivity rate was in May (18.1%).

Conclusions: In Thailand, seasonal Influenza A(H3N2), Influenza A(H1N1)pdm2009 and Influenza B viruses were circulating during 2010-2019. In last season, positivity rate and number of cases peaked in February and March. Influenza is one of public health problems in Thailand and the need to introduce influenza vaccine and antivirus is important to prevent and treat the disease in future.
Abstract 4467

Genomic evidence that the recurrence of Salmonella enterica serovar Weltevreden in human salmonelloses in Asia is triggered by the aquatic environment

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Background: Salmonella Weltevreden is one of the top and persistently reported cause of human Salmonellosis throughout Asian countries including Vietnam, Thailand, Singapore and China. Studies have also reported that S. Weltevreden is frequently associated with seafood. The present study aimed to determine the genetic characteristics supporting survival of S. Weltevreden in the aquatic environment and their relatedness to clinical strains.

Materials/methods: S. Weltevreden were isolated from tilapia and shrimp collected on farms in China and Vietnam and subjected to WGS. Genome-wide analyses were performed with 12 of the isolates along with a collection of 60 clinical strains.

Results: The S. Weltevreden isolates were of MLST ST-365 and harbored SPI-5, which host the major virulence genes associated with human infection. Ten of the isolates harbored the IncFII (S) plasmid with one containing resistance genes (strA/B, sul2 and tetA). Phylogenetic analysis revealed genetic relatedness between shrimp isolates from Vietnam and tilapia from China with about 20 SNPs. In a global context, our isolates clustered within the continental Weltevreden lineage, originating mostly from clinical samples with as low as seven SNPs. The pangenome analysis of clinical and environmental strains of this cluster revealed a pangenome size of 7891 genes including a core-genome of 4892 genes. The accessory genome shows that the genetic content of the environmental strains is significantly similar to clinical strains [Benjamini p>0.05]. The genome-wide comparison against S. Typhi, S. Typhimurium and S. Enteritidis, revealed that S. Weltevreden possess specific Fructose 1,6-Bisphosphatase, nucleoside triphosphate hydrolase, and DEAD/DEAH box helicases involved in adaptation to changing environments and stress response contributing to survival of S. Weltevreden in aquatic environments. Environmental strains also present molecular adaptation machinery for attachment, survival and defense like the magnesium and cobalt efflux protein (CorC), and the multidrug efflux pump component (MtrF) conversed in their defense system enabling persistence in the aquatic matrices favoring human exposure via consumption of contaminated seafood.

Conclusions: Although their reservoirs remain to be studied, S. Weltevreden are genetically fit to survive the aquatic environment and possess virulence factors like clinical strains, to which they are phylogenetically related both in the core and accessory genomes.

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Abstract 4471

Characterisation of healthy gut microbiome subjects following a mediterranean diet

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Abstract third-party references: On behalf of the HGUGM Microbiome Project

Background: It is essential to define the microbiome in a healthy status in order to establish relationships between microbiome and disease. There are few studies assessing the human gut microbiome of a healthy population following a Mediterranean diet. This type of diet might influence the composition of the gut microbiome. The objective of this study was to characterize the intestinal microbiota of healthy individuals who follow a Mediterranean diet as a control cohort for future microbiota studies.

Materials/methods: Fecal samples were collected from healthy subjects, informed consent and a dietary survey was obtained. The hypervariable V4 region of the 16s rRNA gene was sequenced on an Illumina MiSeq platform. Sequenced data preprocessing, OTU clustering and taxonomic classification were done using MOTHUR software, RDP and SILVA database. Alpha and Beta diversity analysis and statistical analysis were conducted by MOTHUR, QIIME 2 and R. Enterotype analysis was performed using www.enterotypes.org web tool. Adherence to a Mediterranean diet was evaluated using Med-DQI.

Results: A total of 60 healthy subjects were enrolled (ongoing study). We observed significant differences regarding sex, females had a higher alpha diversity (p=0.025). Across age groups (Figure), we observed significant differences regarding richness (p=0.005), alpha-diversity (p<0.001), and beta-diversity (p<0.001). Bifidobacteriaceae was more predominant in children and teenagers than in adults (p=0.045), teenagers also exhibited very high levels of Clostridiaceae (p=0.035) and Coriobacteriaceae (p=0.002). Desulfovibrionaceae was characteristically low at early and late stages of life (p=0.005) and Ruminococcaceae was significantly lower in children (p=0.032). As for Mediterranean diet adherence (n= 39 subjects), 44.7% were classified as "High" adherence with a significantly greater alpha-diversity than the "Medium" group (p=0.012). Enterotype classification was as follows: "High" [35.3% enterotype-Bacteroides, 23.5% enterotype-Firmicutes, enterotype-Prevotella 41.2%] "Medium" [36.4% enterotype-Bacteroides, 27.3% enterotype-Firmicutes, enterotype-Prevotella 36.4%].

Conclusions: Our results show that sex and age group are important factors to take into account in microbiome comparative studies including healthy controls since there are important differences in terms of microbial diversity and specific microbial group abundances. We found no predominant enterotype according to Mediterranean diet adherence. However, a high adherence to Mediterranean diet resulted in a greater alpha diversity.

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Abstract 4472

Epidemiology of nosocomial highly resistant microorganism outbreaks in the Netherlands

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Abstract third-party references: On behalf of the SO-ZI/AMR group

Background: In 2012, the Early warning and response meeting of Healthcare-associated Infections and AntiMicrobial Resistance (SO-ZI/AMR) was founded. The purpose of this national structure is to timely identify large-scale outbreaks in hospitals and long-term care facilities (LTCFs) and to prevent further spread of highly resistant microorganisms (HRMO) through early warning and notification. The SO-ZI/AMR assesses the risk of the outbreak for public health, monitors the course of the outbreak and communicates potential risks for public health. Outbreaks are categorized into one of six phases: 1 (lowest) to 5 (highest risk) and phase 0 once an outbreak is completely contained. An outbreak that lasts more than 2 months is categorized as phase 2. In case of a potential threat to public health it will be classified as phase 3; phase 4 and 5 describe potential management issues.

Materials/methods: For each outbreak the following data are collected: duration, type of HRMO involved, reason of notification, number of patients involved, phase of the outbreak, and infection control measures taken.

Results: Data were collected on outbreaks that occurred between April 2012 through October 2019. In total 395 outbreaks were reported from 156 different healthcare facilities: 76 hospitals and 80 LTCFs (mean: 4.5/month). Outbreaks with methicillin-resistant Staphylococcus aureus (MRSA, n=148) and vancomycin-resistant enterococci (VRE, n=100) were most often notified. Thirty-five outbreaks with carbapenemase-producing strains were reported. Most outbreaks (97%) were classified as phase 1 or phase 2 and were controlled quickly (within 2 months). Twelve outbreaks were evaluated as phase 3, involving MRSA (2), Clostridium difficile (2) and VRE (8). C. difficile and VRE outbreaks had the longest duration (maximum 23 months). One outbreak, in 2018, with New Delhi metallo-beta-lactamase (NDM)-producing Citrobacter freundii was classified as phase 4, but could be scaled down to phase 3 after two months, after additional control measures were taken.

Conclusions: The SO-ZI/AMR has resulted in a transparent national overview of outbreaks in Dutch hospitals and LTCFs. Outbreaks with HRMO and other pathogens occur occasionally, but are usually quickly controlled. Only one outbreak progressed to phase 4, no outbreaks progressed to phase 5.

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Abstract 4474

Urinary tract infection caused by Enterococcus spp.: risk factors and mortality
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Background: Complicated urinary tract infections (UTIs) are frequently caused by Enterococcus spp.. Antibiotics that are usually recommended in guidelines are not useful for the management of this infection. Recently, guidelines have suggested the coadministration of antibiotics in patients at risk, but the risk factors for UTIs caused by Enterococcus have not been well defined.

The objective of this work is to characterise the UTI by Enterococcus knowing its epidemiology, risk factors associated with bacteraemia and general mortality, evaluating the empirical treatment.

Materials/methods: Retrospective study in patients with a diagnosis of UTIs caused by Enterococcus spp.. We compared the results with those of a random sample of patients with complicated UTIs caused by Escherichia coli. We conducted bivariable and multivariable analyses.

Results: We found 106 in-patients with UTIs caused by Enterococcus spp., 56 of whom had positive blood cultures. Distribution by species: 83% E. faecalis and 17% E. faecium, with a Charlson comorbidity index of 5.9±2.9. Only male sex with OR 2.8(95%CI 1.2-6.4), nosocomial infection with OR2.8(95%CI 1.1-7), urinary catheter with OR4.5(95%CI 1.8-11.3), urinary cancer with OR6.4(95%CI 2.1-19.4), and previous antimicrobial treatment with OR4.3(95%CI 1.8-10.2) were independent predictors of Enterococcus infection. The only risk factors for enterococcal bacteraemia were the presence of urothelial tumor and solid organ transplantation (p<0.05). Overall, in-patient mortality was 16.5%, which was associated with a higher SOFA score (>4), severe comorbidity such as immunosuppression, malignant hemopathy and nephrostomy, or Enterococcus faecium species and its pattern or resistance to ampicillin or vancomycin (p<0.05). Appropriate empiric antibiotic therapy was not associated with a better prognosis (p>0.05).

Conclusions: Enterococcus spp. is a frequent cause of UTI characterized by a profile of risk factors: male sex, high Charlson index, urinary catheter, previous antibiotic treatment, urological cancer and several types of immunosuppression. High mortality secondary to a severe clinical setting and high comorbidity may be sufficient reasons for implementing empiric treatment of patients at risk, although we did not show a higher survival rate in patients with this treatment strategy.

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Abstract 4475

**Efficacy of extended duration use of dalbavancin in pyogenic spondylodiscitis: a preliminary report**

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**Background:** dalbavancin is a lypoglycopeptide with potent activity against gram positive microorganisms, a long half–life, a favourable safety profile, and a high concentration in bone, which makes it an interesting alternative for treatment of osteo-articular infections. Experimental studies have demonstrated that dalbavancin 1500 mg IV on days 1 and 8 determine tissue exposure over the MIC for difficult gram positive for 8 weeks, maximizing the initial exposure to treatment

**Materials/methods:** in a open label study 12 patients with pyogenic spondylodiscitis were enrolled, 6 males and 6 females, mean age 66,8 years ( range 52-84). 2/12 showed cervical localization, 6/12 dorsal e 4/12 lumbar. The etiology was: MRSA 5/12; MSSA 2/12; Staphylococcus warneri 1/12; Streptococcus gallolyticus 1/12; Propionebacterium spp. 1/12; Unknown 2/12. 10/12 vertebral biopsy were performed. Two dose of Dalbavancin 1500 mg IV on days 1 and 8 were administered, and other two doses, once weekly, were subsequently administered, after an interval of six weeks. Significative adverse events were not observed All patients before to start the treatment with Dalbavancin were submitted to SPECT or PET These were repeated after fifteen weeks

**Results:** among 12 cases of spondylodiscitis 10 were cured (83,4%), 1 were considered improved (8,3%) and 1 with initial response (8,3%) died for other cause.

**Conclusions:** our preliminary report show that dalbavancin is a well tolerated antibiotic and the regimen with 2 repeated doses with six week interval between them is associated with a high cure rate in patients with pyogenic spondylodiscitis. These data would be confirmed on numerous case studies.

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Determining the lung microbiome of chronic obstructive pulmonary disease patients from hospitals in Pretoria, South Africa using IS-Pro method and 16S rDNA sequencing

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Background: Chronic obstructive pulmonary disease (COPD) is a leading cause of death worldwide and is highly prevalent in South Africa. However, despite this, there is limited information on the lung microbiome in COPD patients. There are several different methods that can be used to study the microbiome (targeting 16S rDNA gene) including next generation sequencing and the IS-Pro method. The aim of this study was to compare the IS-Pro method and 16S rDNA sequencing for routine use in identifying the lung microbiome in COPD patients.

Materials/methods: Twenty-four sputum specimens were collected from COPD patients in Pretoria. Bacterial DNA was extracted using Isolate II Genomic DNA kit (Bioline, United Kingdom). The DNA was processed in two ways: i) V1-V3 sequencing of 16S rDNA gene on MiSeq (Illumina, USA) at Inqaba Biotec (Pretoria, South Africa) and analysed using QIIME2 and ii) using the IS-Pro method (inBiome, Netherlands and Synexa Life Sciences, Cape Town)

Results: Results were only available for 23 of the 24 samples. The IS-Pro method detected six phyla across 23 samples with the dominant phyla being Proteobacteria, Firmicutes and Fusobacteria/Bacteroidetes. Analysis with QIIME2 identified 15 phyla with the dominant phyla being Firmicutes, Bacteroidetes/Proteobacteria and Actinobacteria. The most common genera in both methods were Haemophilus and Streptococcus. The IS-Pro method was able to identify 67% of the operational taxonomic units (OTUs) to a species level (the rest of the OTUs were unclassifiable at a genus level), whereas QIIME only identified 33% of the OTUs.

Conclusions: A major limitation of the IS-Pro method is that it is only able to detect members of six phyla: Actinobacteria, Bacteroidetes, Firmicutes, Fusobacteria, Proteobacteria and Verrucomicrobia. As a result, the uncommon phyla are missed. This may result in over-reporting of some phyla, as the primers used in the kit select for these phyla; which may explain the higher prevalence of Proteobacteria using the IS-Pro method. However, the two methods performed comparatively at the genus level of identification, with the IS-Pro method performing better at species level identification. This suggests that the IS-Pro method may be more useful as a screening tool for diagnostics.

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Does cefepime require dose adjustments in critically ill patients on extracorporeal membrane oxygenation? A pharmacokinetic study

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Background: The increase use of extracorporeal membrane oxygenation (ECMO) in adult intensive care units (ICUs) has led clinicians to re-evaluate the use of conventional dosing regimens in this patient population. Neonatal studies have suggested modified antimicrobial dosing regimens are necessary in the presence of ECMO to attain PK/PD targets for optimised bacterial kill and clinical cure. However, due to significant differences in physiology, these findings cannot be safely extrapolated to the adult population. Empirical antibiotics such as ceftriaxone have no defined, titratable end-point; and this may lead to possible sub- or supra- therapeutic plasma levels in this group of critically ill patients.

The aim of this study is to describe the pharmacokinetics (PK) of cefepime in critically ill patients receiving ECMO. Also, through improved understanding of ECMO-induced PK effects, propose dosing strategies that are more likely to attain the PK/PD target of 60-70% T>MIC to optimise therapeutic outcomes.

Materials/methods: This study was a multi-national, open-label study, designed to describe the PK of cefepime over one dosing interval. Critically ill adults with severe cardiac and/or respiratory dysfunction from six intensive care units in Australia, New Zealand, Switzerland and Korea were eligible for recruitment. Serial blood samplings were taken over pre-defined time points over one dosing interval. Centralised bioanalysis occurred at the University of Queensland to determine plasma cefepime concentrations through validated chromatographic methods. The concentration-time data was then used to generate pharmacokinetic parameters through non-compartmental methods.

Results: Eight critically ill patients were recruited in the study, one was excluded due to insufficient data points collected [Table 1]. In this cohort, the median [IQR] estimates for volume of distribution, clearance, elimination half-life and elimination rate constant were 0.13 [0.12–0.25] L/kg, 0.02 [0.01–0.04] L/h/kg, 7.5 [3.5–8.7] h and 0.14 [0.10–0.20] h⁻¹ respectively. Although large variations were observed in these parameter estimates, the values are generally consistent with published studies in critically ill patients who are receiving ECMO.

Conclusions: The heterogeneity of results demonstrates significant pharmacokinetic variability. Further analysis to develop robust dosing guidelines to optimise pharmacotherapy in these patients is required.

Table 1: Patient demographics, clinical characteristics and pharmacokinetic parameter estimates

<table>
<thead>
<tr>
<th>Demographic and clinical characteristics (n = 7)</th>
<th>Age in years</th>
<th>Male, n (%)</th>
<th>Weight (kg)</th>
<th>BMI (Kg/m²)</th>
<th>ECMO duration (days)</th>
<th>Serum creatinine (µmol/L)</th>
<th>Blood urea nitrogen (mmol/L)</th>
<th>Albumin (g/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin (mg/L, h)</td>
<td>321.5 (156.5–608.6)</td>
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<tr>
<td>AUC∞ (mg/L, h)</td>
<td>803.4 (405.7–1187.9)</td>
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<td>AUC0-12h (mg/L, h²)</td>
<td>8486.4 (2198.4–15066.3)</td>
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<td>Cmax (mg/L)</td>
<td>114.2 (34.3–118.9)</td>
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<tr>
<td>K1 (h⁻¹)</td>
<td>0.14 (0.10–0.20)</td>
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<tr>
<td>t1/2 (h)</td>
<td>7.5 (3.5–8.7)</td>
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<tr>
<td>CL (L/h)</td>
<td>1.2 (0.9–3.9)</td>
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<tr>
<td>CLx(Kg (L/h/kg)</td>
<td>0.02 (0.01–0.04)</td>
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<tr>
<td>V1 (L)</td>
<td>12.9 (0.4–15.4)</td>
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<tr>
<td>V2 (L/kg)</td>
<td>0.13 (0.12–0.27)</td>
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</table>

BMI, body mass index; APACHE, Acute Physiology and Chronic Health Evaluation; SOFA, Sequential Organ Failure Assessment; ECMO, extracorporeal membrane oxygenation; AUC∞, area under a curve from time 0 to infinity; Cmax, maximal concentration; K1, elimination rate constant; t1/2, half-life; CL, clearance; V0, volume of distribution.

*Data is presented as median (IQR) or number (percentage).

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Abstract third-party references: Public Health England

Background: Whole Genome Sequencing (WGS) is a validated method for the identification of Mycobacterium tuberculosis and prediction of first-line drug sensitivities through detection of polymorphisms in the DNA sequence followed by comparison to a reference database. The database of mutations must be carefully curated as new genetic mutations are identified and information on phenotypes becomes available. These updates must be rigorously tested before adoption into routine work. This genetic data is also compared to previously sequenced isolates to determine genetic relatedness. This permits identification of clusters of transmission and allows public health teams to target at-risk individuals and contain outbreaks.

Materials/methods: In November 2018 we noted several isolates with the mutation L203L, a synonymous mutation of CTG to CTA located within the fabG1 gene, functioning as a promotor mutation to inhA. Our data supported previous evidence that this mutation conferred Isoniazid resistance but required rigorous testing before incorporation into the curated database in August 2019. Following this, in October 2019 we identified an individual who clustered (0 Single Nucleotide Polymorphisms) with two others. This new case was predicted Isoniazid resistant due to L203L by WGS, discordant from the two prior cases predicted sensitive in Spring 2019.

Results: On further analysis, these earlier two cases also showed L203L as the sole mutation present within the genomes, but these were not identified in our genetic database at time of analysis. All three cases had phenotypic isoniazid resistance when tested following WGS of the 3rd case. All cases and contacts were previously or currently being treated with isoniazid-containing regimens, which may have been inadequate, thus requiring prompt management. Our data supports the determination that this synonymous mutation confers phenotypic resistance. The overall prevalence of the L203L mutation is low, at 0.3% of sequenced isolates at Public Health England.

Conclusions: Determining genetic relatedness is important as this identifies developing clusters of transmission and can assist identification of uncommon genetic mutations that may not have been detected initially using the curated database. Regular updates to these databases are necessary as identification of rare mutations can have significant clinical and public health impact.

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Improved detection of acid-fast bacteria using an automated slide scanner with integrated deep learning analysis
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Background: Microscopy of auramine stained sputum is the most used method for the initial detection of tuberculosis (TB). However, manual microscopy of auramine slides is tedious and suffers from low sensitivity. By pre-analyzing slides and presenting the condensed, relevant information to the clinician, deep learning powered automated scanning systems promise considerable improvements of this workflow.

Materials/methods: We combined a fully automated slide scanning system (Metafer, MetaSystems) with a deep neural network (DNN) classifier in order to establish an automated workflow for detection of acid-fast bacteria in auramine slides. A binary DNN classifier was trained to detect acid-fast bacteria in small image tiles of 144 x 144 pixels from 82 routine slides. The classifier was then integrated into the scanning system, allowing it to present a gallery of the most relevant image tiles (i.e. tiles that most probably contain bacteria) and to propose a slide classification on WHO-scale. For clinical validation, 531 independent slides taken from routine workflow were scanned and pre-analyzed. The scanned area per slide is equivalent to 300 microscope fields of view using a 40x objective with 23 mm oculars. A microbiologist unaware of the reference result evaluated each slide using the information given by the system. We compared the results from the microbiologist to manual microscopy, the system’s proposal and the culture results as the reference.

Results: Pre-analysis by the DNN classifier hugely reduced the manual review time of the clinician to around 10 s per slide on average. Compared to manual microscopy, the sensitivity increased from 60,7% (34/56 positive slides detected) to 71,4% (40/56 positive slides detected). The proposed classification given by the system without the clinician’s review showed the highest sensitivity (96,4%, 54/56 positive slides detected), however at the cost of specificity.

Conclusions: Automated slide scanning with assisted classification of auramine stained bacteria by deep learning saves working time and considerably improves the sensitivity of TB microscopy. Typical for deep learning systems, the performance of the pre-analysis improved with the amount of training data. Updating the system with additional training data from time to time is expected to further boost its performance even after deployment.

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Antimicrobial susceptibility in *Clostridioides difficile* varies according to European region and isolate source

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Abstract third-party references: on behalf of the COMBACTE-CDI consortium

**Background:** *C. difficile* (CD) epidemiology continues to evolve: recent studies have identified emerging and resistant ribotypes (RT) that are country-associated. The COMBACTE-CDI project provides an ideal opportunity to examine CD epidemiology and resistance across Europe.

**Materials/methods:** All diarrhoeal faecal samples sent to 119 recruited testing facilities from 12 European countries, on two sampling days, were collected. All samples were cultured for CD on CCEY agar; isolates were typed by PCR-ribotyping and toxino/typing. Contemporaneous CD isolates were collected from animals in the same countries. Metronidazole, vancomycin, fidaxomicin, moxifloxacin, clindamycin, imipenem, tigecycline and rifampicin MICs for 215 clinical and 44 animal isolates were determined by Wilkins-Chalgren agar dilution. MICs for each antimicrobial were scored as sensitive=0; intermediate=1; resistant=2 for each isolate according to published breakpoints and added to generate a cumulative resistance score (CRS).

**Results:** Fidaxomicin was the most active treatment agent (geometric mean for both clinical and animal isolates=0.03mg/L) but reduced susceptibility was observed in n=2 (RT01 2 & RT066) isolates (1mg/L). Geometric mean metronidazole MICs (clinical isolates) were 0.3mg/L, but were elevated among predominating epidemic RT027 (2.17mg/L) and Eastern European-associated RT181 (1.03mg/L). RT027 and RT181 also had elevated geometric mean moxifloxacin MICs (16.95mg/L) and 14.25mg/L); clindamycin (9.6mg/L and 10.53mg/L) and rifampicin (20.87mg/L and 0.40mg/L). Two isolates (RT016 and RT002) were metronidazole resistant (MIC=8mg/L) and 9 (8 RT027; 1 RT198) had intermediate resistance (4mg/L). Elevated metronidazole MICs were not observed in animal isolates from Eastern Europe, and no location-linked predominating RTs were observed. Increased geometric mean vancomycin MICs were observed in RT027s, which were more commonly isolated from animals than humans (22 vs 12 respectively), but there was no resistance (MIC>4mg/L). Moxifloxacin and clindamycin resistance was seen in both clinical and animal isolates of multiple RTs. No resistance to imipenem or tigecycline was observed. Average (mean) and median CRS showed that resistance levels among clinical (but not animal) isolates were highest in Eastern Europe (Figure).

**Conclusions:** Epidemiology and resistance differs between clinical and animal CD isolates and by geographic location. Epidemic CD RT027 and highly-related emerging RT181 have increased levels of antimicrobial resistance and are associated with CD infections in Eastern Europe.

![Figure: antimicrobial resistance in clinical and animal *C. difficile* isolate by European region](image)

black line indicates median Cumulative resistance score

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Biofilms and catheter-related bloodstream infections: a tale of two kingdoms

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Abstract third-party references: FCT/487/15/01/2019/S from Fundação para a Ciência e a Tecnologia.

Background: Biofilm-associated infections are a public health concern in the context of healthcare-associated infections (HAI) such as catheter-related bloodstream infections (CRBSI). Here, we studied two top ten CRBS etiological agents, Enterobacter cloacae and Candida parapsilosis, isolated from a patient with CRBSI in order to understand the role played by biofilms on this HAI.

Materials/methods: E. cloacae and C. parapsilosis were isolated from CVC and peripheral blood by standard procedures. EUCAST guidelines were followed for antimicrobial susceptibility evaluation. Single and/or mixed biofilms were assembled on different materials in Mueller-Hinton broth with 2% glucose. Biofilm assembly was assessed by crystal violet assay and scanning electron microscopy (SEM). Fluorescence in situ hybridization (FISH) was used for identification and to assess microorganisms distribution within the biofilm (3D reconstruction). In addition, Focus Ion Beam (FIB)-SEM was used to assess biofilms assembled on inner and outer surfaces of CVCs and construct tomograms. CVC and hemoculture (HC) isolates were subjected to whole-genome sequencing (WGS).

Results: All Enterobacter and Candida isolates were antimicrobial resistant. Of note, E. cloacae-CVC revealed an additional resistance (ceftolozame-tazobactam) in comparison to the HC isolate. Both microorganisms assembled biofilms on glass, polystyrene and polyurethane. Mixed biofilms were denser when both microorganisms were present from the beginning. Biofilm phenotype was not dependent of biofilm initiation by E. cloacae or C. parapsilosis. FISH and SEM analysis showed that biofilm bottom layer was in all cases richer in E. cloacae. Environmental isolates of the same species were also tested, showing that this biofilm phenotype is not a general feature. Using polyurethane catheters [shape/material factor], we observed denser mixed biofilms richer in EPS. FIB-SEM preliminary results suggest that biofilms assembled on inner and outer catheter surface might differ on microorganisms’ distribution. WGS confirmed the genetic identity of the CVC/HC pairs while corroborating the virulence potential and antimicrobial resistant character of the CRBSI-driving pathogens.

Conclusions: The results suggest that biofilms allow interaction and adaptation of microorganisms belonging to different kingdoms [Bacteria and Fungi]. Adaptation might affect virulence in a transitory or permanent fashion, with potential impact on microorganisms’ potential to cause CRBSI.

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Contribution of new tuberculosis cases for multidrug-resistant tuberculosis cases notification in Ethiopia
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1Alert Hospital, KNCV Tuberculosis Foundation, Addis Ababa, Ethiopia

Background: The first drug resistance survey (DRS) in Ethiopia, done from 2003 to 2006, showed that 11.8% of previously treated & 1.6% of new mycobacteria tuberculosis cases have rifampcin and/or isonizaide resistant tuberculosis (RR/MDR-TB). According to WHO estimate in its 2018 global TB report, 14% of previously treated and 2.7% of new TB cases in Ethiopia would have RR/MDR-TB. Given that the proportion of previously treated patients accounts just for 4.2% of all notified TB cases, the contribution of new cases for RR/MDR-TB diagnosis would be by far higher than the previously treated if all of them had received drug susceptibility test (DST). So it can be simply estimated that number of RR/MDR TB cases from new TB cases is 3 to 4 times higher than that of the previously treated one.

This study was aimed to determine the contribution of the new TB cases towards the MDR-TB case notification in urban towns of Ethiopia during 2017 to 2018.

Materials/methods: Cross-sectional survey has been conducted on RR/MDR TB patients enrolled in Addis Ababa, Dire Dawa, and Harer during July 1, 2017 to June 30 2018.

Results: As the tables below demonstrate, RR/MDR-TB case finding steadily increasing from quarter to quarter: But the contribution of new cases is still very low (29%) as compared to the previously treated one though it should have been 3 to 4 (67-75%) times higher.

Table 1: Contribution of New TB Cases for RR/MDR-TB Case Finding in Ethiopia, 2018

<table>
<thead>
<tr>
<th>First line TB Rx Hx</th>
<th>Q1</th>
<th>Q2</th>
<th>Q3</th>
<th>Q4</th>
<th>Annual</th>
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<tr>
<td>New</td>
<td>#</td>
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<td>Previously treated</td>
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<td>Unknown treatment history</td>
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<td>%</td>
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Conclusions: Though the trend of MDR-TB case notification is increasing following introduction of gene Xpert for some prioritized new TB cases, the contribution from new TB cases is yet lower than estimated which warrants universal DST for the new TB cases.

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Effectiveness of influenza vaccine in preventing medically attended influenza virus infection among healthcare personnel: a test-negative case-control study in Bangkok, Thailand, 2018/19 season

Theethach Eamchotchawalit1*, Phunlerd Piyaraj2,3, Putt Narongdej1, Sakarn Charoensakulchai2

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Abstract third-party references: Bangkok Dusit Medical Service (BDMS), Phramongkutklao College of Medicine

Background: Influenza vaccination is the most effective way of preventing influenza infections and it is recommended for the entire health care personnel in Thailand. However, the evidence of influenza vaccine effectiveness (VE) among health care personnel is lacking in Thailand. The objective of this study was to estimate influenza vaccine effectiveness (VE) against laboratory confirmed medically attended influenza illness for the 2018/19 season among health care personnel who at risk for influenza infection in Bangkok, the capital of Thailand.

Materials/methods: Throat swab specimens were collected from patients with influenza-like illness (ILI) presenting to outpatient clinics and tested for influenza virus by RT-PCR, between October 2018 and September 2019. A test-negative case-control design was used to estimate influenza VE against medically-attended laboratory-confirmed influenza in outpatient settings. Cases were influenza-like illness (ILI) patients who tested positive for influenza, and controls were influenza negative patients.

Results: During the 2018/19 season 373 samples were collected; 57 (15.3%) were positive for influenza, 70.2% A un-subtyped and 29.8% B. Adjusted VE against all influenza viruses for this influenza season was -31.7% (95% confidence interval (CI): -40.2 to 66.4), against influenza A un-subtyped, it was 43.9% (95% CI: -30.6 to 75.9) and against influenza B, it was 52.0% (95% CI: -73.9 to 86.8).

Conclusions: The seasonal influenza vaccine was moderately effective against medically attended lab-confirmed influenza infection in health care personnel in Bangkok, Thailand in the 2018-19 influenza season. Increasing seasonal influenza vaccination among health care personnel in Thailand may decrease medically attended influenza-associated ILI cases in this population.

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Abstract 4499

Treatment of urinary tract infections in haemodialysis patients: the controversy about antimicrobial urine concentration

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Background: Urinary tract infections (UTI) are common in chronic kidney disease stage 5 requiring hemodialysis (CKD-5D). These infections represent a challenge to diagnose and treat due to lack/dearth of urine production. The Infectious Diseases Society of America (IDSA) suggests utilizing antimicrobials that achieve high urinary concentrations to accomplish sufficient drug exposure. The purpose of this study is to examine the validity of this recommendation in this patient population.

Materials/methods: A retrospective observational study was conducted at our quaternary care hospital between May 2015 and March 2019. The primary end points were to determine the clinical and/or microbiological cure defined as the time to regression of functional urinary symptoms documented by the treating physician and the time to negative culture if was done respectively. Relapse and recurrence data were documented and defined as repeat positive urine culture and/or clinical symptoms within 2 to 4 weeks and three months respectively.

Results: Eleven patients with thirteen encounters of infections were included, 10 had diabetes, and nine had hypertension. The sample mean age was 75±9 years, BMI was 32±9 kg/m², 7 were males, the average duration on dialysis was 13±13 months, and 4 patients were on immunosuppressive therapy. Cystitis was the most common infection for 12 of the patients’ encounters. ESBL E. Coli was the most common pathogen (n=6) and ertapenem 500 mg IV daily was the most frequently used antimicrobial (n=5). Clinical cure was reported in all encounters with no reported microbiological failure (repeated samples were done in 9 encounters). No relapse or recurrence occurred during the follow up period of 3 months for each patient.

Conclusions: Our findings suggest that successful management of UTI in oliguric/anuric patients could be attained through systemic antimicrobials. We hypothesize that free drug concentration equilibrates across the body fluids including the bladder lining epithelial cells and would eradicate the invading pathogens without the need for urinary drug concentration. Our findings need to be replicated in larger studies.

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Abstracts 2020

Abstract 4500

Uncovering the role of airborne transmission and asymptomatic contact shedding in outbreaks of scarlet fever
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Background: England is experiencing an upsurge in scarlet fever (SF) and associated outbreaks. Transmission mechanisms are poorly understood but thought to be driven by children with symptomatic disease.

Materials/methods: We undertook a prospective, observational study in nurseries with SF outbreaks to assess impact of antibiotic treatment on detection of Group A Streptococcus (GAS) in cases; prevalence of GAS carriage in community contacts using throat swabs; and presence of GAS in the classroom environment. Transmissibility was assessed using cough plates, hand swabs, environmental swabs and settle plates, with genome sequencing to confirm chains of transmission. Cases were tested on days 1-3 of antibiotics, then weekly for 3-4 weeks. Contacts were tested weekly over 3-4 weeks.

Results: Six classes, comprising 11 SF cases, 17 household contacts, and 142 classroom contacts were recruited. Of 10 cases on treatment, all had negative samples after starting antibiotics, however 4/10 became GAS-positive by week 2 or 3. One untreated case remained positive. GAS was identified in 3/17 household contacts.

GAS prevalence in classroom contacts was high and increased between weeks 1 and 2 in all outbreaks [week 1, 0-19%; week 2, 9-56%; week 3, 18-50%]. 27 contacts (19%) were GAS-positive on two, and 4 on three samples. Surface swabs [n=60] taken in 3 classrooms did not yield GAS except in one instance. Genome sequencing showed clonality of isolates within three classes tested, confirming recent transmission accounted for high carriage. Emergent lineage M1UK accounted for 2/3 outbreaks.

Of 28 classroom contacts with GAS-positive throat swabs, who were tested for transmissibility, 6 (21%) had positive cough plates and/or hand swabs, of whom three remained GAS-positive for 3 weeks. Settle plates were GAS-positive in 2/3 classrooms tested despite being placed in elevated locations.

Conclusions: GAS transmission within classrooms was extensive despite short-term effectiveness of antibiotic treatment. Transmission may occur prior to receipt of antibiotics, underlining the importance of rapid diagnosis and treatment. Despite exclusion of cases and guideline adherence, heavy shedding of GAS by classroom contacts, who may represent subclinical infection or carriage, likely perpetuate outbreaks. Airborne transmission appears to be a key factor, in contrast to environmental contamination.

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Abstract 4503

Comparative epidemiological study of MRSA in lactating animals, dairy products, environment and personnel of dairy processing facilities in Northern Greece

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Background: Methicillin-Resistant S. aureus (MRSA) represent a serious public-health concern due to their ability to colonize and infect both humans and animals. The handling and consumption of animal origin-food contaminated with MRSA could lead to the pathogen transmission to humans. MRSA are increasingly isolated from lactating ruminants, milk and dairy products.

Materials/methods: A total of 1059 samples [farmers: 109, cows: 124, sheep: 215, goats: 123, raw milk: 96, food handlers: 87, dairy products: 93, equipment 212] from 6 dairy plants and the associated 64 dairy farms were collected from three geographical regions of North Greece (Epirus, Central Macedonia, and East Macedonia and Thrace). All phenotypically and molecularly confirmed MRSA strains were characterized for the presence of selected virulence factors such as staphylococcal enterotoxins (sea-see) and Panton-Valentine Leucocidin (PVL) genes and their ability to produce biofilms. Finally, the genetic variability of the MRSA isolates and the presence of epidemiological clones were assessed via Pulsed-Field Gel Electrophoresis (PFGE) and spa typing.

Results: MRSA were isolated from 38/1059 (3.6%) samples: 16/196 (8.2%) from employees-farmers, 9/462 (1.9%) from animals, 4/189 (2.1%) from dairy products and 9/212 (4.2%) from dairy plants’ equipment. All isolates were able to produce biofilms and 94.7% of them carried one or more enterotoxin-coding genes, with the sec being the most prevalent. The pvl gene was not detected. Sixteen spa types were identified among the MRSA isolates, with t127 being the most prevalent 14/38 (36.8%) indicating that it represents the predominant LA-MRSA type in Greece. Furthermore, spa type t034 (CC398) was isolated for the first time from livestock (goat) in Greece. PFGE typing of MRSA isolates revealed the presence of epidemiological clones in the dairy production chain, even within the dairy plants’ facilities.

Conclusions: Our study’s findings suggest that the dairy production chain may contribute to the dissemination of MRSA in the community and highlight the need for continuous monitoring of the dairy production chain and re-evaluation of the implemented cleaning and sanitizing programs, as well as the adoption of preventive strategies along the dairy production chain in order to minimize public-health risks.

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**Viral aetiology and epidemiology of acute paediatric gastroenteritis in southern region of Saudi Arabia with Yemen borders**

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**Background:** Diarrheal diseases remain the second most important cause of death in children under five years worldwide. Globally, it had been estimated that about 1.7 billion cases of pediatric gastroenteritis occurring annually. Rotaviruses were known as the leading cause of severe gastroenteritis in children in developed and developing countries. Adenoviruses recognized as the second common agent, after rotavirus, responsible for viral diarrhea in children younger than 2 years. Astroviruses had also confirmed as potential causes of viral gastroenteritis accounting for 5-9% in children. In the tropical regions, the prevalence of these infections was observed higher during the rainy seasons. In Saudi Arabia (KSA), there had been few studies addressing the occurrence and prevalence of pediatric viral diarrheal infections in some regions of the country. However, this is the first study which focuses on the distribution and magnitudes of pediatric viral gastroenteritis in the southern region of Saudi Arabia near the borders with Yemen.

**Materials/methods:** 461 diarrheal samples collected randomly from the hospital-admitted children under five years of age in the southern region of KSA. Immunochromatographic technique (ICT) was employed to investigate the presence of rotaviral, adenoviral and astroviral antigens in these samples. The prevalence rates for each virus type was calculated. The dual (coinfection) rates, sex and age distribution of these viral infections were also assessed.

**Results:** Out of the 461 specimens, 85 (18.4%) were noted positive for at least one virus. Among the 85 positive specimens, 104 viruses were detected with the frequency of 72 (69.2%), 25 (24.0%) and 7 (6.7%) for rotavirus, adenovirus and astrovirus respectively. 19 cases (22.4%) revealed dual viral infections (co-infections) (Table 1).

**Conclusions:** Rotaviruses detected as the most common cause of acute gastroenteritis in children in the study area, followed by adenoviruses and astroviruses. ICT confirmed and suggested as a rapid, sensitive and routine serological test for detection of diarrheal viruses among pediatric patients.

Table 1: Distribution of enteric viruses co-infection in the tested samples

<table>
<thead>
<tr>
<th>Coinfection pattern</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rotavirus + adenovirus</td>
<td>14 (16.5%)</td>
</tr>
<tr>
<td>Rotavirus + Astrovirus</td>
<td>4 (4.7%)</td>
</tr>
<tr>
<td>Astrovirus + adenovirus</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Rotavirus + adenovirus + Astrovirus</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td>Total</td>
<td>19 (22.4%)</td>
</tr>
</tbody>
</table>

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Abstract 4505

Invasive pneumococcal disease in the Comunidad Valenciana, Spain, 2011-2019

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Background: Complicated disease due to Streptococcus pneumoniae is a fact in many geographical areas. In the Comunidad Valenciana (CV), Spain, invasive pneumococcal disease (IPD) is a mandatory reportable disease since 2007. The aim of this study was to describe the epidemiology and serotype distribution of the S. pneumoniae isolates causing IPD in children and adults in the CV between January 2011 and mid-November 2018.

Materials/methods: Retrospective study of IPD reported to the Public Health Department between January 2011 and September 2019. Epidemiological data from cases was obtained from the Microbiology Surveillance Network of the CV (RedMIVA). Serotyping of culture confirmed cases was done using the slide agglutination test (Denka Seiken, Tokyo, Japan) and the modified Quellung test (Statens Serum Institute) at the Microbiology Department of the University Hospital La Fe.

Results: A total of 3,368 cases of IPD were reported between 2011-2018 period in the CV – 408 in 2011, 395 in 2012, 374 in 2013, 360 in 2014, 373 in 2015, 374 in 2016, 466 in 2017 and 618 in 2018. In 2019, 287 strains of IPD have been serotyped until September. A total of 2591 strains were serotyped – 282 in 2011, 293 in 2012, 309 in 2013, 300 in 2014, 298 in 2015, 302 in 2016, 339 in 2017, 468 in 2018 and 287 until September 2019. Of the total of patients, 59.13% were men, 7.96% were less than 5 years old and 53.32% over 65 years old – 161/287 (50.09%) this last year. Figure 1 shows IPD mucous serotype distribution expressed in percentage with respect to total IPD cases (2011-2018). In 2019 the percentage was done with respect to total serotyped.

Conclusions: The incidence of mucous serotypes causing IPD has increased in the CV in recent years. Serotypes 3 and 8, both mucous, account for one third of IPD cases and the latter serotype presents as an emergent serotype that should be included in new vaccines.

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Abstract 4507

**Endotoxin activity assay as a better predictor for septic shock in critically ill cirrhotic patients**

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**Background:** Early detection remains the mainstay for improving outcomes in sepsis. Various biomarkers like procalcitonin (PCT), C-reactive protein (CRP) are available but these have limited role to play in patients with liver disease. Recently the role of Endotoxin activity is being assessed as a biomarker for sepsis in patients with cirrhosis. Hence, this study was taken up to assess the role of endotoxin activity assay (EAA) as a biomarker and to compare its activity with procalcitonin in prediction of septic shock in critically ill cirrhotic patients admitted to the intensive care unit.

**Materials/methods:** Endotoxin activity and PCT were determined, using the principle of chemiluminescence [according to manufacturer's guidelines], on the day of admission and Day-3. These values were correlated with clinical severity scores and laboratory parameters like total leukocyte count, differential leukocyte count, lactate levels, blood pH and cultures sensitivity results. Statistical analysis using Kaplan Meier survival curves was done.

**Results:** 70 critically ill cirrhotic patients admitted to ICU were enrolled. Baseline characteristics showed mean age of 45.1±4.4years, with a median MELD 35(25-40), SOFA 10(8-11), EAA 0.57(0.40-0.75) and PCT 1.23(0.66-2.79). Cultures were positive in 37 patients. Gram negative isolates (83.8%) predominated with *Klebsiella pneumoniae* (54.83%) being the most common organism. 2/3rd of patients progressed into severe sepsis or septic shock and showed high levels of EAA (p=0.001) while levels of PCT (p>0.6) did not correlate with the severity of the disease. Comparative analysis of EAA and PCT as a predictor of septic shock showed an area under ROC curve for EAA (0.778) to be statistically significant compared to PCT(0.551) which was not significant. High levels of EAA on admission were associated with an increased 28day mortality rate (57%).

**Conclusions:** EAA is a better biomarker and predictor of severe sepsis and septic shock in critically ill cirrhotic patients compared to procalcitonin. High levels of EAA on admission are associated with increased morbidity and mortality.

![ROC Curve](image)

**Figure1:** EAA & PCT for prediction of severe sepsis and septic shock

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**Detection and successful containment of a NDM-1-producing Proteus mirabilis clone spread in an Italian sub-acute care unit**

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**Background:** Aim of the study was to report an experience of prompt detection and containment of a blaNDM-positive *P. mirabilis* (Pm-NDM) clone, emerged among inpatient at “S. Angelo Lodigiano” Hospital (LO), Northern Italy.

**Materials/methods:** In April 2019, n=4 *P. mirabilis* strains were selected on CHROMagar™ CPE (BD) at Lodi Hospital Clinical Microbiology Laboratory from two infected/colonized inpatients at the Sub-Acute Care Unit of “S. Angelo Lodigiano” Hospital. Xpert-Carba-R System (Cepheid) detected *blaNDM*-type determinant. Thirty samples were obtained from room surfaces and patients’ skin using SRK Hygiene monitoring kit system (Copan), in order to assess the extent of environmental contamination and with containment purposes. Species identification and susceptibility tests were performed by Vitek-2 System (BioMérieux) and AutoScan4 System (Beckman Coulter). Susceptibility results were interpreted according to EUCAST 2019 guidelines. Microarray Check-MDR CT103XL (Checkpoints), PCR and sequencing were used for beta-lactamases genes screening and *blaNDM*-type identification. Molecular typing was accomplished by PFGE (SfiI) (BioRad). Whole Genome Sequencing (WGS) by Illumina MiSeq was carried out on CRE1 strain from urine sample, as representative.

**Results:** A total of eight Pm-NDM strains were collected from urine (n=2), rectal (n=2), skin swabs (n=2) of two inpatients and environmental swabs (n=2/30), resulted susceptible only to aztreonam, gentamicin and amikacin. The i) rapid *blaNDM*-positive *P. mirabilis* identification by phenotypic/molecular methods, ii) patients cohorting, iii) infection control measures undertaken (i.e. environmental sampling) and iv) room disinfection by a dry mist of 12% hydrogen peroxide, allowed the resolution of Pm-NDM spread within a month. Microarray, PCR and sequencing assays confirmed a *blaNDM*-1 gene variant. PFGE showed the presence of a unique profile. According to WGS, CRE1 Pm-NDM harbored a larger 99278bp plasmid codifying resistance to sulphonamide (*sul1*), trimethoprim (*dfrA14*), tetracycline (*tet(B)*), rifampicin (*arr-2*), aminoglycosides (*aadA1, aph(3')-VI*), beta-lactams (*blaOXA-10, blaNDM-1*), and a small 2555bp plasmid responsible for quinolone resistance (*qnrD1*).

**Conclusions:** This is the first report on the detection/rapid containment of a MDR Pm-NDM-1 clone emerged in a Northern Italy Hospital. The findings highlight the importance of the screening for *P. mirabilis* NDM-producer, an emerging threat in Italian area.

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**Abstract 4509**

**Effect of antiviral therapy against hepatitis C virus on gut microbiota**

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**Background:** The intestinal microbiota plays a fundamental role in physiological homeostasis and in human pathology. No study has assessed the change in gut microbiota after treatment with direct antiviral agents in patients with Hepatitis C Virus (HCV) infection. The aim of the study was to evaluate the effects of such therapy on microbiota.

**Materials/methods:** We enrolled patients with HCV-related chronic liver disease attending the Infectious Diseases Unit of the A.O.U. Federico II of Naples, from January 2017 to March 2018, treated with DAAs. Fibrosis was evaluated by the mean of Fibroscan®. For each patient, a fecal sample was collected before therapy and by SVR12 time. The fecal microbial DNA was extracted using the standard operating procedures of the IHMC. The amplicons were then normalized, combined and sequenced with the Illumina MiSeq system. Intra-sample or α-diversity was evaluated through rarefaction curves obtained with different and specific metrics. Patients who received antibiotics in the last 6 months were excluded.

**Results:** We enrolled twelve patients (6 male, 8 genotype 1 (1 subtype 1a), 4 genotype 2). Fibrosis score was F0 in 1 patient, F2 in 1 patient, F3 in 4 patients and cirrhosis in the remaining 6 (all in Child-Pugh class A). All patients received DAAs for 12 weeks (5 with Paritaprevir-Ombitasvir-Ritonavir-Dasabuvir, 3 with Sofosbuvir-Ledipasvir, 1 with Sofosbuvir-Ribavirin, 1 with Sofosbuvir-Daclatasvir, 2 with Sofosbuvir-Velpatasvir) and all achieved SVR12. In all patients, we observed a reduction of potentially pathogenic microorganisms (i.e. Enterobacteriaceae), and a shift towards a more heterogeneous and less harmful bacterial population [Figure 1]. Furthermore, a trend of increase in α-diversity was observed in patients by SVR12 compared to baseline time. This trend was markedly more evident in patients without liver cirrhosis than in those with cirrhosis.

**Conclusions:** Our study shows that viral eradication obtained with DAA is associated with a trend in restoring the heterogeneity of α-diversity and in reducing the percentage of potentially pathogenic gut microbiota species, although this benefit is less evident in patients with cirrhosis. Further studies with larger sample size are necessary to confirm these data.

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![Figure 1: Heatplot with OTU pre and post treatment.](image)

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Epidemiology of ESBL-producing Enterobacteriaceae among healthcare students, Portuguese Red Cross Health School of Lisbon, Portugal

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Background: The aim of the present study was to prospectively evaluate the prevalence of intestinal carriage by ESBL-producing Enterobacteriaceae among Portuguese students attending health care bachelors, and to determine the epidemiology and antimicrobial resistance of ESBL-producing isolates.

Materials/methods: One-hundred and eleven fecal samples recovered from Portuguese health care students were screened for either ESBL-producing, carbapenem-, colistin-, or pan-aminoglycosides-resistant Enterobacteriaceae, using respective screening media. All recovered isolates were tested for antimicrobial susceptibility and characterized by pulsed-field gel electrophoresis (PFGE) and multilocus sequence typing (MLST). Plasmid analysis was completed by plasmid-based replicon typing (PBRT). The corresponding resistance mechanisms were searched by PCR followed by sequencing.

Results: A total of 17 ESBL-positive Enterobacteriaceae (16 Escherichia coli and a single Klebsiella pneumoniae) were recovered from 16 patients, corresponding to a prevalence of 14.5%. The E. coli isolates were distributed into seven PFGE types and three sequence types (ST). The most common ESBL identified was CTX-M-1 (n=13; 76%), followed by CTX-M-15 (n=3; 18%), and CTX-M-8 (n=1; 6%). The only ESBL-K. pneumoniae carried a blaCTX-M-15 gene. The majority of the strains were resistant to sulfamides (88%), trimethoprim-sulfamethoxazole (82%), fosfomycin, and tetracycline (71%), and a few to tobramycin and kanamycin (12%). PBRT revealed four different plasmid types: IncFIA/FIB (n=13), IncFIC (n=2), IncI2 (n=1), and IncP (n=1). A major clone, ST10-blaCTX-M-1, included 12 E. coli isolates. The blaCTX-M-1 gene was located onto an IncFIA/FIB plasmid type with a size of 56 kb, which co-harbored genes encoding resistance to tetracycline, sulfamides, trimethoprim-sulfamethoxazole, and fosfomycin. Such lineage had been previously identified among pigs in Portugal, however PFGE analysis showed that human and animal isolates were not clonally related.

Conclusions: We found a high prevalence of fecal carriage of ESBL-producing E. coli among healthy health care students in Portugal, underlying this population as an important reservoir.

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Abstract 4511

Assessment the immunogenicity of UpaH autotransporter of uropathogenic Escherichia coli isolates admixed with vitamin D as a novel vaccine candidate against urinary tract infection

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Background: Urinary tract infections (UTIs) caused by Uropathogenic Escherichia coli (UPEC) are among the most common infection diseases worldwide. Furthermore, increasing rate of antibiotic resistance among the isolates will make treatment of these infections ever more complicated and costly in the future. Therefore, there is a need for designing of an efficacious vaccine against UTI. UPEC has several types of autotransporter proteins such as UpaH that play important roles in pathogenesis. Thus, UpaH could be an ideal target against UTIs. In this study, we analyzed the UpaH of UPEC by in silico studies, and then the selected fragments were expressed and purified. Finally, the immunogenicity of the designed construct was evaluated in mice model.

Materials/methods: In this study, UpaH sequence of UPEC strains was evaluated by bioinformatics studies. The UpaH was expressed in BL21 host and purified by nickel resins. The analysis of the purified protein was performed by SDS-PAGE and Western blot. LPS level of the protein was removed by Triton-X114. Balb/C mice were subcutaneously vaccinated three times with UpaH alone and admixed with vitamin D. Then, serum and urine samples were obtained from the mice on days 0 and 42 for measurement the anti-UpaH IgG and IgA immune responses by ELISA method.

Results: According to the bioinformatics results, the best domains of UpaH were selected. Analysis of purified UpaH by SDS-PAGE and Western blot showed bands 32 KDa. Mice vaccinated with UpaH alone induced significantly higher humoral immune responses in serum and urine (IgG and IgA) than the control mice (P<0.05). Furthermore, vitamin D could increase the levels of IgG in serum and urine of the vaccinated mice.

Conclusions: Our results suggest that UpaH protein of UPEC has the potential of an ideal candidate against UTIs. We observed that vitamin D tended to direct the immune responses towards both the Th1 and Th2 responses. This could be valuable in eradication of intracellular and extracellular reservoirs of UPEC. Thus, vitamin D can be considered as a safe and effective adjuvant in designing of a vaccine against UTIs. Assaying the protection efficacy of the vaccine candidate is under progress.

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Abstract 4512

Evaluation of commercial multiplex real-time PCR panels to detect bacterial, parasite and viral gastrointestinal pathogens in clinical specimens

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Abstract third-party references: University Hospitals of Leicester, Mobidiag

Background: Gastrointestinal infections are often non-specific in symptoms and can be caused by a multitude of organisms with the potential to cause outbreaks, particularly in healthcare facilities. High throughput detection methods which can identify a broad range of pathogens are of use to clinical microbiology departments for pathogen screening. The aims of this evaluation was to compare the performance Mobidiag Amplidiag Easy Bacterial, Viral, and Parasitic PCR Panels against current routine methods, including culture, antigen detection and microscopy and to assess the ease of use of the Amplidiag workflow.

Materials/methods: Two hundred and seventy one non-consecutive stool samples were tested retrospectively on the Amplidiag system for the presence of 18 pathogens. This included 105 bacterial, 120 parasitic, and 112 viral tests. Samples were inoculated in eNat tubes (Copan) before automated extraction, PCR setup, real-time PCR amplification and result interpretation using the Amplidiag Easy workflow. Results were compared to standard-of-care testing using culture, EIA or immunochromatographic lateral flow devices, as appropriate to the target pathogen.

Results: The assay demonstrated overall sensitivity and specificity of 70.6% and 98.3% respectively for the bacterial panel, 86.7% and 99.0% for the parasite panel, and 73.3% and 97.7% for the viral panel. Amplidiag gave false-negative results for four each of Salmonella spp. and Giardia lamblia, two Rotavirus, and one each of Campylobacter sp., Norovirus GII and Adenovirus. An additional 49 pathogens were detected by Amplidiag in 32 (11.8%) specimens. No instrument failures were recorded, reproducibility was within acceptable levels (<10% CoV) and all results were obtained in under 3.5 hours.

Conclusions: Specificity across all panels was high, demonstrating the ability of the Amplidiag to give adequate negative predictive values for screening. For the bacterial panel, failure to detect Salmonella spp. cultured following selenite broth enrichment was the primary cause of low sensitivity. For other assays, low numbers of positive samples in this study impacted the sensitivity analysis. The application of the single, simple Amplidiag Easy workflow covering a broader range of pathogens and improved diagnostic yield compared to routine methods make this system an attractive option as a primary screening method in diagnostic clinical microbiology laboratories.

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Abstract 4513

Diversity of ESBL- and carbapenemase-producing Enterobacteriaceae with emergence of mcr-1 and carbapenem transferable resistance in a cancer clinical setting in Egypt

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Background: Carbapenem and colistin resistant Enterobacteriaceae in the Middle East represents a severe threat. The present work studied resistance spread at an oncological hospital in Egypt.

Materials/methods: Between 2016 and 2017, 130 MDR and XDR Enterobacteriaceae isolates from hospitalized cancer patients at National-Cancer-Institute-Cairo-University were detected. Carbapenemase and ESBL phenotypic detection was complemented by PCR to carbapenemases, CTX-M ESBL, qnr, AAC(6’)-Ib-cr and mcr-1. Conjugation and typing by PFGE & MLST were also performed.

Results: In 81 K.pneumoniae and 49 E.coli, 61.8% were positive at least for one of carbapenemase detection tests (Modified-Hodge, Blue-CARBA and CIM). ESBL was detected in 37.7%. OXA-48, NDM-1 and IMP-1 were detected in 36.2%, 20.8%, 0.01% respectively, highlighting, 12.3% of isolates co-produced OXA-48 and NDM-1, while 32.4% co-produced CTX-M and OXA-48.

High percentage (67.6%) harboured CTX-M genes, being 73.9% of CTX-M-Group-1 (58.8% were CTX-M-15) and 39.1% of Group-9 including 30.4% with both genes.

Expression of qnrB(9%), qnrS(14.7%) and Aac(6’)-Ib-cr(20.6%) and cross resistance in 20.6% producing OXA-48, CTX-M and fluoroquinolone-resistance-genes (57.1% qnrS and 71.4% aac(6’)-Ib-cr).

Two ESBL-producing E.coli co-expressed mcr-1, CTX-M-15, CTX-M-GP9, one of them co-expressed qnrS and Aac(6’)-Ib-cr. Successful conjugation transfer in 11.5% showed carbapenemase and CTX-M expression (46.7% carbapenemase, 66.7% CTX-M, 20% showed carbapenemase and CTX-M co-expression). PFGE showed clonal diversity for K.pneumoniae and E.coli isolates, with similar carbapenemases and/or CTX-M present in different clusters. K.pneumoniae MLST revealed 60% clustering in three carbapenemase-producing high-risk clones [ST101 (32%), ST383 (16%) and ST147 (12%)]. High-risk ST11, ST16 were detected in 8% while high-risk ST22, ST37 were detected in 4%.

Conclusions: High prevalence of ESBL-producing isolates with carbapenem and colistin resistance emergence is reported. Mcr-1 co-expression with CTX-M-15, CTX-M (GP9), qnrS and Aac(6’)-Ib-cr in ESBL-producing E.coli showing carbapenemase and CTX-M conjugal transfer what represents a big alert of XDR bacteria spread. This is calling for alternative treatment for Enterobacteriaceae infections and infection control precautions.

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Abstract 4516

Validation of a measles virus detection assay for early clinical management

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Background: Since the end of 2017, a significant increase in measles cases was observed worldwide and in Europe. Early management (vaccination or immunoglobulins administration) requires viral genome detection by RT-PCR in salivary, nasopharyngeal, respiratory or blood samples. The objective of this work was to evaluate a CEIVD kit (FTD Measles).

Materials/methods: Several approaches were performed to assess for analytical performances. First, a 10⁷ copies/ml quantified control (Amplirun Measles RNA Control, CEIVD Vircell) was used for repeatability (n = 16), reproducibility (n=8), and sensitivity by using a method of successive dilutions (10⁻¹ to 10⁻⁷). Second, a diluted MMR vaccine was tested to assess genotype A detection. Then, 29 serum samples already characterized in Measles serology (patients at the beginning of the eruptive phase) with IgM>5 and negative IgG (LIAISON XL, Diasorin) were tested by using FTD Measles assay. Finally, 20 samples were provided by the Measle French National Reference (MFNR): different types of sample (salivary and pharyngeal sample), and viral strains: A, B3, or D8, and compared between both techniques: MFNR RT-PCR vs. FTD RT-PCR. Assays were performed by using a CFX96 device.

Results: Repeatability (mean CT=28.15) and reproducibility (mean CT=28.41) showed coefficients of variation (CV%) of 1.1% and 1.4%, respectively. At the lower dilution value (1,4 cp/μl), the four replicates remained detectable with equivalent CTs (CT=36.24, CT2=37.04, CT3=36.74, CT4=38.42; CV%=2.5%). Similarly, the MMR vaccine (genotype A) tested was well amplified (CT=22.56). Of the 29 patients with IgM+/IgG- serology for whom a positive viral load was expected a positivity was indeed observed by RT-PCR in all serum tested (CT from 31.25 to 38.72). Finally, the 20 samples of patients tested in the CNR technique and in the FTD technique were all found to be positive and had equivalent CTs (CT from 15.47 to 27.96). The observed virus level were lower in serum than in salivary and pharyngeal sample, as expected.

Conclusions: The FTD Measles technique presented satisfactory analytical performances and its use is validated for the main circulating strains in France and Europe, allowing an early patient management.

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Antibiotic combination versus monotherapy for the treatment of Pseudomonas aeruginosa bacteremia: a multicentre retrospective study

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Background: Pseudomonas aeruginosa [P aeruginosa] bacteremia is a severe clinical condition and is associated with high mortality rates. There is no agreement on the optimal antibiotic regimen for the treatment of P aeruginosa bacteremia. One of the most controversial questions is the use of combination vs. monotherapy as a definitive antibiotic treatment. We aimed to evaluate the impact of these two options in hospitalized patients with P aeruginosa bacteremia on 30-day mortality.

Materials/methods: This was a multinational, multicenter retrospective study conducted in 9 countries [25 hospitals] across Europe, Australia and Israel. Adult patients hospitalized with P aeruginosa bacteremia during the years 2009-2015 were included. The main outcome was all-cause 30-day mortality. Propensity score weighting was used to balance covariates between the treatment groups; Generalized Estimating Equation model was constructed to control for center as a random effect.

Results: We analyzed 1383 patients. Among the study cohort, 28% [392/1383] received two active antipseudomonal agents concomitantly and 72% [991/1383] received a single active agent as definitive therapy. Patients treated with combination therapy were significantly younger [median 63 years [interquartile range [IQR] 51-74] vs 68 years [IQR 57-78]]. Combination group patients were more likely to have neutropenia, baseline malignancy, and a vascular catheter at presentation. The overall 30-day mortality rate was 17.6% [244/1139]. Combination therapy was not associated with reduced 30-day mortality in both univariable and multivariable propensity adjusted analyses [OR 0.86, 95% CI 0.61-1.21]. Combination therapy group had a significantly longer length of hospital stay [16 days [IQR 10.7-27] vs 14 days [IQR 9-28], P=0.027]. Moreover, patients who received combination treatment were more prone to antibiotic adverse event [rash], [5.7% [22/383] vs 2.3% [22/940], p=0.002]. Development of resistance among subsequent P aeruginosa isolates was without significant difference between groups [combination 54/ 392 [14%], monotherapy 124/991 [13%], p=0.602].
Conclusions: In this large multicenter study, we found no significant mortality benefit for combination therapy in the treatment of *P. aeruginosa* bacteremia. Prospective studies are needed to refine clinical management and to avoid unnecessary antibiotic treatment and drug-related adverse events.

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Investigating dynamic protein binding of clindamycin in vivo by means of intravasal microdialysis in healthy volunteers

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Background: Clindamycin (CLI), a lincosamide antibiotic, is a commonly used antibiotic, in particular in patients with anaerobic bacterial infections. In addition to pharmacokinetic (PK) properties, protein binding (PB) plays a crucial role in unfolding the full antiinfective effect of antibiotics in vivo. Recently, doubt has been raised that in vitro methods like ultrafiltration can capture the dynamic and concentration depending PB of highly bound antibiotics. The following study set out to determine the PK profile, bound and unbound drug concentrations versus time profile of clindamycin in healthy subjects by means of in vivo microdialysis.

Materials/methods: Six healthy volunteers received a single i.v. infusion of CLI 900 mg, applied over 30 minutes. Antibiotic plasma concentrations were measured for up to 8 hours after drug administration. Simultaneously, unbound CLI concentrations were obtained by means of in vivo intravasal microdialysis (MD) or in vitro ultrafiltration at defined time points for up to 8 hours post dosing. CLI was assayed in plasma and MD fluid using a validated HPLC-MS/MS method. Non-linear mixed effects modelling in NONMEM® was used to quantify the PB in vivo and in vitro.

Results: Cmax was 14.95, 3.39 and 2.32 µg/ml and AUC0-inf was 41.78, 5.8 and 6.14 µg/ml*h for plasma, ultrafiltrate und microdialysate, respectively. Calculated ratio of AUCunbound/AUCtotal showed similar values of 13.9±1.8% and 14.7±3.1% for ultrafiltration and microdialysate, respectively. However, protein binding was a dynamic and concentration dependent process in vitro and in vivo. Modelling confirmed the non-linear, saturable protein binding for CLI with significantly different dissociation constants (Kd) for the alpha-1 acid glycoprotein (AAG)-CLI complex in median (CI95%) of 3.25 µM (3.1-3.41) in vitro vs. 1.16 µM (1.1-1.21) in vivo (figure 1). Moreover, the estimated number of binding sites per AAG molecule was 2.33 (2.27-10.6) in vitro vs. 1.55 in vivo (1.49-1.57).

Conclusions: Significantly different protein binding was observed in in vitro ultrafiltration vs. in vivo intravasal MD with a tendency to over-estimate the protein binding in vitro, in particular in the distribution phase.

Figure 1. Visual predictive check of the developed pharmacometric model for the matrices plasma (left), ultrafiltration (middle) and microdialysate (right).

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Abstract 4521

Evaluation of a dual therapy and a simplified, patient-centred monitoring strategy for the long-term management of HIV infection: a non-inferiority, randomised, controlled, open-label clinical trial (SIMPL'HIV)

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Background: Simplification of combination antiretroviral therapy (cART) has been studied to reduce pill burden and improve quality of life in HIV patients, while minimizing costs and potential toxicity. It also includes optimized monitoring and decentralization of health care.

Materials/methods: SIMPL'HIV is a multicentre, factorial, non-inferiority randomized trial conducted among experienced HIV-infected adults in Switzerland. Participants were randomized 1:1:1:1 to switching to dolutegravir (DTG) + emtricitabine (FTC) or to continuing cART, and to patient-centred monitoring, defined as annual immunological and safety monitoring vs continuation of 3-monthly surveillance. Patient-centred monitoring included telephone calls, medication delivered by mail, and decentralized venepuncture. Quality of life was assessed using the PROQOL-HIV questionnaire, consisting of 43 questions on a scale of 1 to 5 points. The total score was standardized on a 100-point scale. We previously demonstrated non-inferiority [non-inferiority margin: -12%] of the dual therapy arm compared to cART by maintaining HIV-RNA below 100 copies through 48 weeks. This analysis presents efficacy, safety and quality of life data by treatment and monitoring groups.

Results: Forty-eight participants were randomized to DTG/FTC+ patient-centred monitoring, 45 to DTG/FTC+ 3-monthly surveillance, 47 to cART+ patient-centred monitoring, and 47 to cART+ 3-monthly surveillance. Mean nadir CD4 count was 259 cells/mm³ [SD 187]; 17% were female. In the intention-to-treat analysis, the proportion of patients with HIV-RNA <100 copies/mL throughout 48 weeks was similar in the four groups [Table 1]. The overall proportion of adverse events and discontinuations did not differ by randomization arm. Quality of life was rated above 80 points in all arms and was statistically superior in the DTG+FTC compared to the cART arm.

Conclusions: DTG+FTC was non-inferior to cART as maintenance therapy and a simplified, patient-centred monitoring approach did not affect viral suppression in this nationwide clinical trial. Quality of life was improved in dual therapy compared to cART at week 48.

<table>
<thead>
<tr>
<th>Patient centred Monitoring</th>
<th>Standard monitoring</th>
<th>Difference (99% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTG+FCT n=48</td>
<td>cART n=47</td>
<td>DTG+FCT n=45</td>
</tr>
<tr>
<td>HIV-RNA &lt; 100 copies/ml throughout 48 weeks</td>
<td>45 (93.8%)</td>
<td>45 (95.7%)</td>
</tr>
<tr>
<td>FDA Snapshot &lt;50 cp/ml at week 48</td>
<td>42 (87.5%)</td>
<td>43 (91.5%)</td>
</tr>
<tr>
<td>Proportion of patients with at least one adverse event throughout 48 weeks</td>
<td>36 (76.0%)</td>
<td>26 (55.3%)</td>
</tr>
<tr>
<td>Quality of life</td>
<td>Change from baseline to Week 48 *</td>
<td>n = 42, +2.7 (±1.5)</td>
</tr>
</tbody>
</table>

* TABLE1: 48-week efficacy, safety and quality of life data.ITT population

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Abstract 4522

High-throughput genome sequencing highlights Pseudomonas aeruginosa adaptative evolution in the urinary tract
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Background: Pseudomonas aeruginosa (PA) is an opportunistic pathogen, associated with persistent urinary tract infections or asymptomatic bacteriuria. While adaptative evolution of PA in cystic fibrosis patients is well studied, little is known about the behaviour of PA in the urinary tract. In this context, the objective was to describe molecular diversity of sequential PA urinary isolates collected in 7 inpatients over a 27-months period.

Materials/methods: 101 PA isolates (up to 5 per sample) were collected from 22 urines and sequenced using a NextSeq 500 sequencing system (Illumina Inc.). At least 50X coverage was provided to ensure a good quality sequence. MultiLocus Sequence Typing (MLST) was performed using Center for Genomic Epidemiology database. Phylogenetic analyses were performed using ParSNP software. Clone types (defined as less than 6000 SNPs between 2 isolates) were defined using Snippy software. Genomic annotation was performed using Prokka software.

Results: The average number of contigs per genome was 85 [46-123]. Draft genomes ranged in size from 6.3 to 7.1 Mbp with a mean G+C content of 66%. Alignment of the 101 core genomes (draft assemblies) led to the definition of 6 clusters in congruence with the 6 sequence types [ST] identified. All isolates from a single patient belonged to the same ST within a given urine sample but also over time; only 2 patients had isolates with the same ST. Interestingly, the genome size of isolates of 3 patients decreased over time. These loss events affected genes involved in acute virulence, metabolic pathways, regulation (mainly two component systems), or transport of small molecules.

Conclusions: Our data highlight that even if patients are colonized or infected with a single PA clone, adaptative evolution of isolates is observed within the urinary tract. This evolution could be associated with loss events rather than gene acquisition. Further analysis of genes for which single nucleotide polymorphisms appeared over time is in progress. To our knowledge, this is the first genomic study on adaptative evolution of PA urinary isolates collected from a given urine sample and over time.

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Polybrominated diphenyl ethers disruption of human gut microbiota

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Background: Environmental health is increasingly compromised by persistent toxic substances, which may have serious implications in food safety and, thus, in human health. Polybrominated diphenyl ethers (PBDEs) are anthropogenic contaminants with endocrine disruption abilities, which have been commonly found in food. Growing evidence points out that the human gut microbiota interacts with xenobiotics, which may lead to the impairment of host homeostasis if functions of microbiota become compromised. The aim of this study was to ascertain if the physiological balance of human gut microbiome is affected by the presence and dose of exposure to PBDEs.

Materials/methods: Fermentation was performed in a batch closed-system using an inoculum made from fresh human stool. Diluted fecal inoculum was incubated (i) with PBDEs at three concentrations or (ii) without PBDEs. Enumeration of the fecal microbiota was carried out using the standard serial dilution method in buffered peptone water on the appropriate culture media. Mesophilic, Gram-negative bacteria and coliforms were quantified by classic plating methods. Changes in the gut microbiome were evaluated after DNA extraction followed by deep sequencing of the 16S rDNA V3-V4 region.

Results: The exposure to PBDEs resulted in significant statistical differences (p < 0.05) between groups, showing that “Intermediate” and “High” exposure levels reduce overall bacterial density in comparison to “Low” exposure levels. Considering Gram-negative bacteria and total coliforms, no statistically significant (p > 0.05) differences were confirmed between groups. Nevertheless, all test groups showed lower bacterial densities in comparison to control. Deviations in the microbial structure of human gut occurred in the presence of PBDEs with a reduction of 15 % of Bacteroidetes, together with a decrease of 22 % of Firmicutes at the intermediate doses of PBDEs. Significant shifts were also verified for higher amounts of PBDEs at both phylum and family levels.

Conclusions: For the first time, the impact of PBDEs on the microbial homeostasis of human gut microbiota was taken into consideration, revealing noteworthy modifications with serious health implications even at oral exposure doses considered as safe by worldwide regulatory entities.

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Fast Point-of-Care biomimetic receptor-based biosensor for detection and quantification of zoonotic Campylobacter

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Abstract 4524

Background: Campylobacter is a zoonotic pathogen that causes gastroenteritis known as campylobacteriosis, which is a major public health concern and the most frequently reported food-borne disease in the EU since 2005. Based on the last EU report on food-borne outbreaks, campylobacteriosis has a notification rate of 64.8 per 100,000 population. Foodborne infections of Campylobacter are mostly associated with poultry products. Contamination can happen along the whole poultry production chain; consequently, a fast diagnostic on-site detection tool would be of high importance.

Materials/methods: We used surface imprinted polymers (SIPs) as artificial receptors for the recognition of Campylobacter. The SIPs were embodied with surface cavities complementary to the shape and size of Campylobacter. For the fabrication of SIPs, a thin layer of polyurethane polymer [PU], composed of bisphenol A, phloroglucinol and 4,4′-diisocyanatodiphenylmethane, was deposited on stainless steel substrate by spin coating. The bacteria imprints were formed on the PU layer using the stamping method. The pattern of Campylobacter imprints is created on the surface of the PU layer, after removing the bacteria using sodium dodecyl sulfate. Those stainless steel Campylobacter-imprinted chips were inserted into the flow cell of a heat-transfer method based (HTM) sensor, which measures the thermal resistivity ($R_{th}$) of the solution inside the flow cell.

Results: We applied a novel biomimetic sensor for the detection of the most prevalent zoonotic Campylobacter species, Campylobacter coli and Campylobacter jejuni. We performed dose-response measurements on SIPs imprinted separately with C. coli (see figure) or C. jejuni, by flushing into the sensor increasing bacterial concentrations in 1X PBS buffer (pH 7.4), ranging from 5x10³ to 500x10³ CFU/ml, alternated with PBS washing to remove the unbound bacteria. We observed a concentration-dependent increase in the measured $R_{th}$. The detection limit was calculated at around 30x10³ CFU/ml for both species. No cross-reactivity between the two species was observed with the sensor.

Conclusions: The biomimetic sensor presented in this work provides a sensitive method for the quantitative detection of the two most important foodborne Campylobacter species. This proof-of-concept fast detection system opens up perspectives for fast point of care testing in the food production chain.

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Comparison of the performance of hydatid fluid and the recombinant antigen recDiPol in the diagnosis of cystic echinococcosis patients

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Background: The diagnosis of cystic echinococcosis (CE) mainly relies on imaging techniques but these are inconclusive in a percentage of patients. Therefore, there is a need for the development of immunodiagnostic tools that may complement imaging data. The aim of this study was to comparatively evaluate the diagnostic value of hydatid fluid (HF) and the new recombinant antigen recDiPol for a defined cohort of CE patients.

Materials/methods: A cohort of 79 CE patients was tested in this study. 44 patients had single cysts and 35 multiple cysts. Patients with several cysts were grouped to the most active cyst stage (number of CE1, CE2, CE3, CE4 and CE5 is 47, 11, 12, 4 and 5 respectively). Additionally, 28 sera from patients with other parasitic diseases (alveolar echinococcosis (AE) (3), fasciolosis (5), toxoplasmosis (2), taeniosis (5), trichinellosis (4), toxocariasis (16) and leishmaniasis (3)) were also tested. The new recombinant protein recDiPol containing selected epitopes from antigens B1, B2 and Ag5, was produced as a single recombinant antigen with GST. RecDiPol and HF were used in ELISA for the detection of total IgG in the above-mentioned patients.

Results: Overall sensitivity was higher for HF (89.8%) than recDiPol (83.5%). Seropositivity rate of patients with multiple cyst was higher than for patients with single cysts [94.2% vs. 86.3% against HF and 91.4% vs. 77.2% against recDiPol, respectively]. While sensitivity of HF was higher than recDiPol in active and transitional cysts (91.4% vs. 81.4%), sensitivity for patients with inactive cysts was higher for recDiPol (100%) than for HF (77.7%). In terms of cross-reactivity, HF showed false positive results for 3 AE, 1 trichinellosis and 1 teniosis patients, while only 1 teniosis patient showed positivity against recDiPol.

Conclusions: Both, HF and recDiPol showed a percentage of false negative and false positive results in this study, being recDiPol better than HF in specificity and detection of CE patients with inactive cysts. recDiPol did not reach in ELISA sensitivity levels comparable with HF, and thus new immunodiagnostic approaches should be explored for the detection and follow-up of patients with CE.

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Abstract 4532

Unravelling colistin resistance diversity in clinical Acinetobacter baumannii: in-depth analysis of COL-R strain-profiling and genomics

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Background: Although the increased use of colistin (COL) for the therapy of difficult to treat Gram-negative bacteria can promote the emergence of COL-resistant (COL-R) strains, the adaptation of the bacterial species to the colistin pressure need in-depth investigation. Our study focused the strain-profiling and genomics of colistin resistance (COL-R) diversity existing in 9 clinical Extensively Drug-Resistant (XDR) Acinetobacter baumannii (Ab).

Materials/methods: COL-susceptibility was determined by repeated (10 times) Minimum Inhibitory Concentrations (MIC). COL-R inductions were performed using up to COL 2 mg/L (resistance cut-off). Population analysis profiles (PAP) were performed to investigate the presence of COL-R subpopulations. Whole Genome Sequencing was performed by Illumina Mi-Seq and the genomic epidemiology analysed by bioinformatic tools. The Variant Calling was used to identify genomic SNPs and pmrBCA, lpxA/C SNPs on Ab ACICU as RefGenome.

Results: In-depth analysis on COL-R strain-profiling displayed stable and reproducible MIC values (Full-Resistance) in 3 Ab strains, whilst 6 strains revealed unstable and variable MICs. Among these unstable phenotypes, COL-R induction revealed an inducible COL-R phenotype in 2 Ab strains (Adaptative-Resistance).

PAP analysis evidenced different COL-R subpopulations in the remaining Ab strains. In details, 3 Ab strains showed phenotype defined as "Heterogeneous-Resistance", in which on ≥32 mg/L COL agar-plates coexisted two morphologically different colony variants having two or more-fold COL MIC variations; 1 Ab strains exhibited a so-called "Homogeneous-Resistance" in which the two colony variants differed for only one-fold MIC dilution.

The genomic Phylogeny {gPhyl}, MLSTs and resistomes categorized the 9 Ab strains in 3 main clusters [cluster-I: gPhyl lineages I, ST-OX 1839, COL Full-Resistance, Resistome-I, harbouring diverse non-synonymous pmrB SNPs; cluster-II: gPhyl lineages II, ST-OX 1816 or ST-OX 218, COL Heterogeneous-Resistance, Resistome-III, carriers or not pmrB SNPs; cluster-III: gPhyl lineages III, ST-OX 1808, COL Adaptive/Heterogeneous/Homogeneous-Resistance, Resistome-IV, pmrB SNP carriers and non-carriers].

No Ab strain harbouring lpxA/C SNPs were found.

Conclusions: Our investigation, for the first time, find out the diversity of COL-resistance profiles among clinical COL-R A. baumannii defining the 4 different COL-R phenotypes and outline some genomic traits related to specific phylogenetic, MLST, resistome and pmrB-SNP clusters.

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Abstract 4533

**Rapid nuc and mecA gene testing by polymerase chain reaction is useful to choose appropriate antibiotics in Staphylococcus aureus bacteremia**

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**Background**: Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia has a higher mortality than Methicillin-susceptible *S. aureus* (MSSA) bacteremia and is often difficult to treat due to the multiple antimicrobial resistance. It is crucial to choose an appropriate antibiotic for *S. aureus* bacteremia but is difficult to predict it before antimicrobial susceptibility tests. Rapid and accurate detection of MRSA is critical to improve the prognosis of *S. aureus* bacteremia. Here we report the accuracy of nuc and mecA gene analysis, specific for *S. aureus* and MR staphylococci, respectively, using a fully automated ultra-rapid genetic analyzer directly from blood culture bottles and their efficacy on appropriate choice of antibiotics.

**Materials/methods**: We investigated nuc and mecA using GENECUBE® (TOYOBO, Japan) that is a 35 minute automated system to conduct direct PCR from biological materials. In this report, 75 cases in which staphylococci was detected in blood culture between January 2014 and December 2016 were included and the sensitivity and specificity for each gene were calculated. Furthermore, in 24 cases with *S. aureus* bacteremia during 2016, we retrospectively examined the ratio of antimicrobial changes based on the genotype.

**Results**: GENECUBE® revealed 39 cases as nuc positive (*S. aureus*) and 36 cases as nuc negative (except *S. aureus*). The sensitivity and specificity of nuc testing to detect *S. aureus* were comparable to conventional cultures (100% and 97.2%, respectively). mecA testing also exhibited high sensitivity and specificity to detect MRSA (95.2% and 93.9%, respectively). In 24 cases with *S. aureus* bacteremia, mecA positive (MRSA) and mecA negative (MSSA) were 12 cases each. As for mecA positive, the genotyping resulted in adding vancomycin in 11 cases (91.7%) and, in 1 cases (8.3%), discontinuing empirically administered broad spectrum β-lactam antibiotic on vancomycin. In cases of mecA negative, empirically administered vancomycin was discontinued in 2 cases (16.7%), a narrow-spectrum β-lactam antibiotic was chosen in 2 cases (16.7%), and antibiotics were de-escalated in 3 cases (25%).

**Conclusions**: Our study indicates that nuc and mecA genotyping by GENECUBE® is quick and accurate to separate MRSA from MSSA, which could result in an appropriate choice of antibiotics and better outcome against *S. aureus* bacteremia.

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Microbial profile shift and miRNAs circulating in the saliva: what is their clinical correlation?

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Background: Several pathological conditions, as well as neuro-psychiatric diseases, may modify salivary molecules including metabolites, proteins, RNAs and bacterial populations. Autism Spectrum Disorder (ASD), a complex neurodevelopmental disorder whose etiopathogenesis is still unclear, is believed to be the complex result of a combination of genetic, epigenetic and environmental factors. Immune dysregulation and gastrointestinal abnormalities are of particular interest in the light of several papers reporting ASD-associated disturbances.

Many studies have reported that in ASD patients gut microbiota dysbiosis could play a key role in the alterations of brain structure and function development because of interactions between the Central Nervous System (CNS) and the gut microbiota; the so-called gut-brain axis. The aim of this study was to combine the alterations of the salivary microbiome and miRNA expression profiles in ASD and healthy subjects and their association with neuropsychological parameters to determine new biomarkers of ASD.

Materials/methods: In this experimental plan, were evaluated changes in the microbial composition of the salivary microbiome in 53 ASD and 27 HE (healthy) samples, sequenced on the Illumina MiSeq platform. To profile the circulating miRNA expression from saliva, NanoString Counter system assays were performed using the NanoString platform.

Results: The microbial profile by 16S rRNA sequencing analysis of ASD patients and HE subjects revealed statistically significant differences of abundance at the genus and species levels. In particular, Rothia, Filifactor, Actinobacillus, Weeksellaceae, Ralstonia, Pasteurellaceae, and Aggregatibacter increased their abundance rates in the saliva of ASD patients, while Tannerella, Moryella and TM7-3 decreased. In addition, 5 salivary miRNAs were statistically altered in ASD patients compared to HEs. Variations of both miRNAs and microbes were statistically correlated to different neuropsychological scores related to anomalies in social interaction and communication. Interestingly, we also found a negative correlation between salivary miR-141-3p expression and Tannerella abundance.

Conclusions: In our study, we demonstrated that miRNA and microbiome dysregulations found in the saliva of ASD children are associated with cognitive impairment of the subjects and a potential cross-talking between circulating miRNAs and resident bacteria alterations could exist. Moreover, these findings could pave the way to new potential tools for molecular diagnosis of ASD.

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Abstract 4538

**Evaluation of a new commercial fosfomycin agar dilution-kit against reference agar dilution.**

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**Background:** Fosfomycin is an anti-Gram negative antimicrobial usually used to treat uncomplicated urinary tract infection (UTI). However, its use in multi drug resistant (MDR) Gram negative bacterial infections has increased due to few alternative treatment options. Reading fosfomycin susceptibility tests, either EUCAST disk diffusion or gradient strip MIC testing, is problematic for diagnostic laboratories. Colonies inside the zone of inhibition cause uncertainty when reading. Most laboratories cannot perform the reference method agar dilution (AD) and so we have evaluated a new commercial kit for fosfomycin MIC testing by AD.

**Materials/methods:** Reference method AD was performed using Mueller Hinton agar incorporating glucose-6-phosphate and fosfomycin concentrations from 0.06 to 1024 mg/L. Inocula were prepared in saline and 1ul (10⁴ cfu/ml) spotted onto the AD plates, which were incubated at 35±1°C for 16-20 hrs. Commercial fosfomycin AD kits were performed as per manufacturer’s instructions. 99 clinical isolates were tested: 69 E. coli (EC), 27 K. pneumoniae (KPN), 1 S. marcescens (SM), 1 E. cloacae (EClo) and 1 C. freundii (CF); some containing Extended Spectrum β-lactamases (ESBLs) and carbapenemases. MICs by both methods were compared.

**Results:** Essential agreement (within 1 log₂ dilution) and categorical agreement between the commercial fosfomycin AD kit and reference AD was 97.9% and 93.9% respectively. Major Errors (ME) and Very Major Errors (VME) at 5% and 1%. Most ME & VME were within 1 log₂ dilution. The comparison of MICs from the commercial fosfomycin AD kit to the reference AD method are shown in table 1. Endpoints on both the reference AD method and commercial fosfomycin AD kit were generally good, with a few isolates exhibiting trailing endpoints.

<table>
<thead>
<tr>
<th>Fosfomycin MIC</th>
<th>-2</th>
<th>-1</th>
<th>0</th>
<th>+1</th>
<th>+2</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>34</td>
<td>54</td>
<td>9</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** The commercial AD kit for fosfomycin was easy to use and read, giving comparable MIC results to the reference method.

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Delafloxacin (DLX) in the treatment of community-acquired bacterial pneumonia (CABP): patients with PORT Risk Class III-V

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Background: DLX is an IV/oral anionic fluoroquinolone approved for treatment of serious skin infections. A global Phase 3 trial of 859 patients with CABP was recently completed comparing DLX (300mg IV/ 450mg PO BID) to moxifloxacin (MOX; 400mg IV/ 400mg PO QD). This analysis includes PORT Risk Class III-V.

Materials/methods: Multicenter, randomized, double-blind trial of adults with CABP with ≥ 2 clinical symptoms: cough, sputum, dyspnea, and chest pain; physical signs; and radiographic evidence of pneumonia. Patients were randomized 1:1 to DLX or MOX treatment for 510 days (3 days IV minimum, then oral at investigator discretion). Primary clinical endpoint was the investigator assessed response at Test of Cure (TOC) 510 days after last dose. Clinical success was defined as complete/near resolution of signs and symptoms and no further antibiotics needed. Among secondary endpoints, all-cause mortality at Day 28 was assessed.

Results: 746 patients were randomized with PORT Risk Class III-V in the Intent-To-Treat (ITT) population: 60.5% male; mean age 61.5 yrs (23.9% ≥ age 75); 30.7% were PORT class IV-V; 30.1% multi-lobar pneumonia; 65% with CrCl < 90 mL/min. Overall bacterial pathogens were identified in 60.7% at baseline. Patients received mean 8.5 days of DLX (6.4/2.1 days of IV/oral) compared to 8.6 days of MOX (6.4/2.2 days of IV/oral). Clinical Success at TOC in the ITT was 91.0% (342/376) for DLX vs 89.2% (330/370) for MOX [95% CI: 2.6, 6.2]), and in the Clinically Evaluable population 94.8% (331/349) DLX vs 93.8% (320/341) MOX (95% CI: 2.5, 4.6). All-Cause Mortality at Day 28 was reported in n=8 DLX vs n=6 MOX patients. 14.4% DLX and 12.4% MOX patients had ≥ 1 treatment-related adverse events (AEs). Most common DLX events were mild to moderate diarrhea and transaminase elevations, which did not lead to treatment discontinuation. There were no QT-related AEs in DLX patients; one MOX patient reported QT prolongation.

Conclusions: IV/oral DLX demonstrated comparable efficacy to IV/oral MOX for the treatment of patients with moderate to severe CABP (PORT class III-V). DLX confirmed its favourable safety and tolerability profile without the potential for QT prolongation, phototoxicity, or major drug-drug interactions.

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Abstract 4543

Usefulness of RAST-EUCAST directly from blood culture bottles combined with rapidly interpreted antibiogram reading to detect ESBL/carbapenemase-producing Enterobacterales

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Background: Rapid communication of antibiotic resistance phenotypes in blood culture isolates is relevant for patients' management and implies a challenge for clinical microbiology laboratories. We evaluated the possibility of infer the presence of beta-lactam resistance mechanisms directly from positive blood cultures using RAST-EUCAST disk-diffusion methodology and breakpoints interpreting subsequent antibiogram readings in Enterobacterales.

Materials/methods: 128 Enterobacterales (50 ESBL-producers, 29 carbapenemase-producers, 16 ESBL+carbapenemase-producers, 2 cepamicinase-producers, 23 wild-type and 8 ATCC) were spiked into contrived blood cultures bottles. Antibiotic susceptibility testing [amoxicillin-clavulanic, piperacillin-tazobactam, cefoxitin, ceftazidime, cefotaxime, ceftepime, aztreonam, ertapenem, imipenem, meropenem, ceftolozane-tazobactam and ceftazidime-avibactam] was performed directly from blood positive bottles by disk-diffusion according to RAST-EUCAST methodology. Reading of inhibition zones [including double-disk synergy (DDS) tests for ESBL detection] was performed at 4, 6 and 8h and RAST-EUCAST cut-off breakpoints for short incubation were applied.

Results: Detection percentages by synergy/RAST are shown in the Table. Apart from one isolate, 100% of ESBL-producing Escherichia coli and Klebsiella pneumoniae were detected at 6h. Moreover, 100% of carbapenemase-producing E. coli were recognized at 8h. Considering K. pneumoniae, 3 OXA-48 were not detected by RAST at 8h. Two false positive cefamicinase-producing K. pneumoniae were detected as ESBL-producers using RAST. As expected, wild-type isolates exhibited non-resistant phenotypes.

<table>
<thead>
<tr>
<th>Positive Synergy (ES- BL-DDS)</th>
<th>%</th>
<th>4h</th>
<th>6h</th>
<th>8h</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESBL- E. coli (n=16)</td>
<td></td>
<td>50</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>ESBL- K. pneumoniae (n=15)</td>
<td></td>
<td>60</td>
<td>93,3</td>
<td>100</td>
</tr>
<tr>
<td>aESBL other species (n=19)</td>
<td></td>
<td>11,1</td>
<td>33,3</td>
<td>38,9</td>
</tr>
<tr>
<td>Detection by RAST</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESBL- E. coli (n=16)</td>
<td></td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Carbapenemase-E. coli (n=11)</td>
<td></td>
<td>-</td>
<td>90,9</td>
<td>100</td>
</tr>
<tr>
<td>ESBL - K. pneumoniae (n=15)</td>
<td></td>
<td>100</td>
<td>100</td>
<td>93,3</td>
</tr>
<tr>
<td>Carbapenemase-K. pneumoniae (n=17)</td>
<td></td>
<td>-</td>
<td>68,7</td>
<td>81,2</td>
</tr>
<tr>
<td>aAmpC-producers: 75% (E. cloacae, K. aerogenes, M. morganii)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: Early detection of ESBL/carbapenemase resistance mechanisms from positive blood cultures is feasible using RAST-EUCAST breakpoints when combined with interpretive antibiogram reading. Carbapenemase-producing K. pneumoniae were not accurately detected at 6h using only current RAST-EUCAST recommendations, and interpreted reading using other antibiotics [e.g., ertapenem] should be included. Differences of only 1-mm can lead to errors in interpretation thus being important to perform through interpretive reading. Disk-diffusion is an easy technique but useful enough to early communicate the resistance mechanism from positive blood cultures.

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Longitudinal genomic analysis of IMP-1 metallo-β-lactamase-producing Enterobacteriaceae at a tertiary care hospital in north-east Japan

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Background: Next-generation sequencing (NGS) has become a useful tool for molecular epidemiology of carbapenem-resistant Enterobacteriaceae (CRE) and/or carbapenemase-producing Enterobacteriaceae (CPE) in healthcare settings. In Japan, CPE infections and colonization are often caused by IMP-type metallo-β-lactamase-producers. In this study, we investigated sequential transmission of CPE with resistance mechanisms using NGS through a longitudinal hospital surveillance of CRE.

Materials/methods: One hundred fifty-seven CRE cases of infection or colonization are identified at a tertiary care hospital in Northeast Japan in a nine-year period between 2010 January and 2018 December, and 20 were excluded from this study since these CRE isolates were unavailable. A total of 137 non-duplicate clinical isolates of CRE were screened by PCR for \( \text{bla}_{\text{IMP}} \), \( \text{bla}_{\text{NDM}} \), \( \text{bla}_{\text{KPC}} \), \( \text{bla}_{\text{VIM}} \), and \( \text{bla}_{\text{OXA-48-like}} \). Of these CRE isolates, 33 (24.1%) were CPE that were further analyzed using NGS. Short-read libraries from DNA of all samples were sequenced using Illumina MiSeq. Specific genes and alleles, including resistance genes, plasmid replicon types, and multilocus sequence typing (MLST), were identified via the Center for Genomic Epidemiology’s bioinformatic pipeline.

Results: All carbapenemase genes identified were \( \text{bla}_{\text{IMP-1}} \) except one from an imported case with \( \text{bla}_{\text{NDM-4}} \). The \( \text{bla}_{\text{IMP-1}} \) was detected in 20 (61%) isolates of Enterobacter cloacae complex isolates, followed by Klebsiella pneumoniae \( (N=10, 30\%) \), Pantoea spp. \( (N=2, 6\%) \), and Escherichia coli \( (N=1, 3\%) \). This transmission of IMP-1-producing Enterobacteriaceae was primarily maintained by E. cloacae complex ST730 and ST252 as well as K. pneumoniae ST17 and ST1615, mostly co-harboring multiple resistance genes [e.g., \( \text{aac}(6')\text{-Ic} \), \( \text{qnrB6} \), \( \text{tet}(B) \), \( \text{fosA} \), \( \text{sul1} \) ] [Figure]. IncHI2 and IncHI2A were detected in 28 of 32 IMP-1-producers (87.5%) by in silico plasmid replicon typing. IMP-1-producing E. cloacae complex ST730 and K. pneumoniae ST1615 were found at the hospital for six and five years, respectively.

Conclusions: Our genomic analysis suggested prolonged clonal and plasmid transmission of \( \text{bla}_{\text{IMP-1}} \) within the hospital and provided insight into complex transmission mechanisms of resistance genes among intraspecies and interspecies of CPE.
### Abstracts 2020

#### Figure. Characteristics of resistance genes among carbapenemase-producing Enterobacteriaceae

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Risk factors and outcomes associated with the carriage of tigecycline-non-susceptible vancomycin-resistant Enterococcus faecium

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Background: Vancomycin-resistant E. faecium (VREF) is a common cause of healthcare-associated infections, particularly in severely ill and immunocompromised patients. Rising VRE infection rates in Germany caused an increased use of last resort antibiotics such as linezolid, daptomycin, and tigecycline. Resistance to these antibiotics is still rare and its impact on patient outcome is not well defined. Along with the changing VREF epidemiology we observed the emergence of VREF with additional tigecycline resistance (TVREF) at our hospital.

Materials/methods: At the University Hospital Frankfurt (UHF), we retrospectively identified patients with carriage or infection with TVREF between 02/2014-04/2017. We conducted a matched pair TVREF-VREF analysis to identify risk factors for TVREF carriage. Clinical events, namely detection of Clostridioides difficile, bloodstream infections (BSI), and patient death were recorded. Further, bed-to-bed contacts of TVREF cases and potential transmission routes were reconstructed. To identify putative transmission events genome sequences of 24 TVREF were analyzed by core genome multilocus sequence typing (cgMLST).

Results: In total, during the observation period 76 TVREF-positive cases (infection or colonization) were identified and compared to 152 VREF control patients. Of note, TVREF cases were associated with an increased previous exposure to tigecycline, an increased rate of bloodstream infections (BSI) with VREF or Candida spp., and a higher mortality. Whole genome sequencing provided evidence for the presence of room occupancy-associated transmissions of TVREF.

Conclusions: This study showed that tigecycline exposure is a main risk factor for the selection of TVREF. As observed for VREF, the hospital transmission of TVREF may occur despite strict contact precautions. TVREF- and Candida-BSI are associated with worse clinical outcome. Thus, regular antimicrobial stewardship and infection control interventions are of high importance to prevent the emergence and nosocomial spread of TVREF.

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Abstract 4549

Assessing the impact of interventions designed to reduce the rate of postoperative sternal wound infection at a tertiary cardiothoracic centre

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Background: Postoperative sternal wound infection (SWI) is associated with significant excess morbidity and mortality. Since October 2012 we have introduced a series of interventions with the aim of reducing postoperative infection risk, in particular those caused by Staphylococcus aureus.

Materials/methods: Patients undergoing primary sternotomy between September 2010 and June 2018 were identified using retrospective review of local registry data. The CDC's criteria for surgical site infections was used to identify cases of SWI. Following a two-year pre-intervention observation, a phased bundle of interventions were introduced. Initially these targeted human and environmental factors and later included preoperative S. aureus decolonisation.

Results: 6903 procedures were performed of which 178 were complicated by SWI (2.6%), with 89 deep infections (1.3%). SWI was significantly associated with prolonged admission, readmission, additional operations and death. Multivariate analysis confirmed independent risk factors for SWI were CABG, non-elective procedures, female sex and seasonality, with higher rates between July and September. Prior to the introduction of any interventions, S. aureus was the most commonly isolated pathogen (46.5% of SWI). Time series analysis demonstrated a breakpoint in the infection rate corresponding to the earlier phases of intervention with a significant decrease in the intercept from 5.52 to 1.62 cases/100 patients/month. This decline was principally due to a reduction in S. aureus infection (3.9%, 95%CI 3.0-4.9 pre-intervention; 1.8,1.3-2.4 during targeted decolonisation). No significant effect was found on the rate of Gram-negative infections by any of the interventions deployed.

Conclusions: This dataset demonstrates the grave consequences of SWI for the individual and points to the additional demand this complication places on a healthcare system. A phased bundle of interventions resulted in a significant decrease in the rate of S. aureus SWI, however there was no discernible impact on SWI caused by Gram-negative bacteria. These infections tend to be more complex and often require long courses of broad spectrum antibiotics. This is of particular concern for this predominantly older cohort as they tend to have more comorbidities, are more prone to antibiotic side effects and also has wider implications for antimicrobial stewardship. Evaluation of additional preventative measures that target Gram-negative SWI are urgently required.

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The temporal dynamics of Staphylococcus aureus carriage among healthcare workers in a tertiary referral hospital with a history of endemic methicillin-resistant Staphylococcus aureus, investigated by whole genome sequencing

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Background: This study investigated the prevalence and temporal dynamics of Staphylococcus aureus colonization among healthcare workers (HCWs) in a non-outbreak setting.

Materials/methods: Nasal swabs and oral rinses were collected from HCW volunteers on nine hospital wards during at least one of three consecutive six-month study phases occurring between 2017 and 2019. Samples were cultured on SaSelect and MRSASelect chromogenic media and confirmed as methicillin-resistant S. aureus (MRSA) or methicillin-susceptible S. aureus (MSSA) using routine identification methods. If an individual yielded both a nasal and oral S. aureus isolate during the same phase, a representative was chosen provided the antibiograms of the two isolates were identical; otherwise, one isolate was investigated per S. aureus-positive HCW per phase. Isolates underwent Illumina whole-genome sequencing and whole-genome multilocus sequence typing (wgMLST; BioNumerics, Applied Maths). Persistently colonised HCWs were detected by identifying those who yielded isolates from different phases that exhibited <24 allelic differences.

Results: A total of 326 HCWs were recruited from various frontline disciplines. Overall, 107/326 (33.1%) and 10 (3.1%) of HCWs were colonised with MSSA and MRSA, respectively. Ninety-four HCWs underwent repeat sampling, i.e. they were sampled during either two or all three phases. Slightly over half (48/94, 51.1%) of these repeat-sampled HCWs failed to yield S. aureus during both/all phases. Eleven of the 94 (22.0%) repeat-sampled HCWs yielded S. aureus during the first study phase only, indicative of non-persistent colonisation. Acquisition of S. aureus during the study period was suspected in 10 individuals, whereby S. aureus was not detected in their initial screen but was detected during subsequent sampling. Twenty-five of the 94 (27.0%) repeat-sampled HCWs yielded S. aureus on more than one occasion; nine of these HCWs harboured the same strain on two sampling occasions, indicative of persistent colonisation.

Conclusions: MSSA prevalence was as expected among HCWs, with MRSA prevalence lower than anticipated. Repeat screening combined with wgMLST revealed persistent S. aureus carriage in a small proportion of HCWs. Transient carriage was observed in 22% of HCWs sampled on more than one occasion.

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Background: Recently, an increasing number of OXA-244-producing Escherichia coli producers was identified from different parts of Switzerland by the National Reference Center for Emerging Antibiotic Resistance [NARA]. OXA-244 is a carbapenemase differing from OXA-48 by a single point mutation. Molecular investigations were carried out to better appreciate the different genetic features of those isolates and possibly contribute to better understand this emerging phenomenon.

Materials/methods: Sixteen OXA-244-producing E. coli clinical isolates were recovered from 11 different Swiss laboratories during the 2017-2019 period. Antimicrobial susceptibility testing was performed as well as whole genome sequencing (WGS). Conjugation assays were performed to evaluate the putative plasmid support of the \( \text{bla}_{\text{OXA-244}} \) gene. The ability to reliably detect the OXA-244 enzyme was evaluated with biochemical tests (Rapidec CARBA NP\textsuperscript{(bioMérieux)}, β-Carba test\textsuperscript{(Bio-Rad)}, NG-test Carba 5 lateral flow test [NG Biotech]). In parallel, the performances of different screening media, namely the ChromID\textsuperscript{®} CarbaSmart and ChromID\textsuperscript{®} ESBL [bioMérieux], and the mSuperCARBA [CHROMagar], were evaluated to detect OXA-244-producing E. coli.

Results: The 16 isolates showed variable degrees of susceptibility to carbapenems and expanded-spectrum cephalosporins, with 10 isolates producing an ESBL (CTX-M-14b, CTX-M-27, TEM-1B, TEM-33), two CMY-2 producers and five being susceptible to broad-spectrum cephalosporins. The main sequence type (ST) was ST38 (n=6), but a total of 7 STs was identified. WGS revealed a perfect identity with a recently-identified strain from Germany. No plasmid was detected nor transferred by conjugation, suggesting a chromosomal location for the \( \text{bla}_{\text{OXA-244}} \) gene. Among the different tests evaluated, only the NG-test Carba 5 gave positive results, while the only screening medium on which the corresponding isolates could be detected was the mSuperCARBA.

Conclusions: We evidenced here the emergence of OXA-244-producing E. coli in Switzerland, following other reports from neighboring countries, with an identical clone being identified in Germany. This emergence was mainly due to a single clonal background, but also to some other clones. Because of the weak carbapenemase activity of OXA-244 and the variable degree of resistance to β-lactams of the corresponding isolates, their detection was challenging, with the mSuperCARBA medium and the NG-test Carba 5 being the most appropriate tools.

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Abstract 4553

Multi-centre study for the evaluation of BioFire FilmArray Pneumonia Plus for the rapid microbiological diagnosis of low respiratory tract infections

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Background: Low respiratory tract infections (LRTIs) are common and serious nosocomial infections in ICUs and are responsible for longer hospital stay, higher costs, and greater mortality. Accurate and timely microbiologic diagnostic approaches for LRTIs are urgently needed to guide targeted therapeutic choices and reduce the impact of ineffective empiric antibiotic regimens and the overuse of antibiotics. We carried out a multicentric study aimed to evaluate the performance of BioFire® FilmArray® Pneumonia Plus panel (FAP). This syndromic panel allows the rapid detection (about 1 hour), directly from respiratory samples, of 34 targets for the most common bacterial, viral, and atypical bacterial pathogens responsible for LRTIs.

Materials/methods: The study was performed on 475 low respiratory samples (sputum, BAS, BAL and ETA) from 8 microbiology laboratories in Italy. All samples were simultaneously analysed with FAP and the standard of care (SoC) consisting in culture for bacteria detection and sometimes in other molecular methods for virus/atypical bacteria detection.

Results: Three samples resulted invalid by FAP and were excluded from the analysis. A total of 52 samples resulted negative for both FAP and SoC. From the 420 remaining samples were obtained 745, 84 and 15 bacterial, viral, and atypical bacterial target identifications, respectively. Correspondences between FAP and SoC were as follow: 468 bacterial targets were identified by both FAP and SoC, 251 by FAP only, and 26 just by SoC; 19 viral targets were detected by both methods, 63 by FAP only (not always investigated by SoC) and 2 solely by SoC; 11 atypical bacterial targets, were identified by both methods, 3 just by FAP and 1 was revealed by SoC only.

Conclusions: FAP showed excellent performances in detecting almost all the main respiratory pathogens and in revealing additional pathogens. Therefore, FAP is a promising test for the rapid microbiological diagnosis of respiratory infections and could have a positive impact on patient outcome and antibiotic stewardship. The absence of some targets in the panel and the epicitical value of FAP additional detections should be considered.

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Molecular epidemiology of Acinetobacter baumannii in Sudan
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Background: Acinetobacter baumannii is listed as one of the ‘priority pathogens’ by the World Health Organization due to its multi-drug resistance and global spread. A. baumannii, however, is poorly investigated in many low- and middle-income countries, thereby creating knowledge gaps on the epidemiology of this pathogen. The data presented here is a multi-centre study of the molecular epidemiology of A. baumannii in Sudan.

Materials/methods: Seventeen A. baumannii isolates were recovered from patients in 3 hospitals in Khartoum, Sudan. Species identification was confirmed by the gyrB multiplex method [1], and presence of the intrinsic blaOXA-51-like gene [2] in comparison with the Pasteur’s multilocus sequence typing (MLST. Antimicrobial susceptibility was performed by disk-diffusion. Whole genome sequencing was performed using the Illumia Miseq platform. Molecular epidemiology was investigated by core-genome MLST (cgMLST) using Ridom® SeqSphere+. Pasteur sequence types (ST) and the resistome was extracted using the Resfinder database.

Results: cgMLST is summarized in Fig-1. The isolates clustered with international clonal lineages IC1, IC2, or IC9, of which 15 were IC2. IC2 was subdivided into three STs separated by >200 allelic differences. Within these STs was evidence of transmissions (shaded in grey, or >1 isolate in a node). All isolates were multi-drug resistant, and harboured multiple resistance genes: OXA-23 (15/17; 88%) and NDM-1 (n=6; 35%), and TEM-10 (13/17; 76%) β-lactamases. All isolates contained the aminoglycoside-modifying enzymes aph(3’)-Ia and aph(6)-Ia, and 13/17 (76%) contained mphE and/or msrE contributing to macrolide resistance. 9/17 isolates (6%) were in possession of the tetracycline resistance genes tetA or tetB.

Conclusions: IC2-OXA-23 A. baumannii clone is prevalent across Khartoum hospitals, with a high burden of MDR to a variety of drug classes. OXA-23 is frequently present with other genes such as NDM-1 and aminoglycoside modifying enzymes. A systematic genomic study of A. baumannii in the Middle East and Africa is required to understand the local dissemination of the pathogen.

Figure 1: Minimum spanning tree of A. baumannii using cgMLST


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Phage-MR003 prevents infection caused by clinical isolated methicillin-resistant Staphylococcus aureus in mouse wound model

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Background: Phage therapy is expected as an option for therapeutic tool against multi-drug resistant bacterial infections. ΦMR003, Staphylococcus aureus phage isolated from sewage influent, exhibits a broad host range against MRSA strains collected from patients at Kyorin university hospital in 2015 to 2016 (Peng et al., 2019). To assess the efficacy of ΦMR003 in vivo, bacteriological and pathological effects of phage administration were analyzed using murine wound infection model.

Materials/methods: The KYMR116 and KYMR117 strains in the present study were classified as CA-MRSA by MLST. KYMR117 was classified as a USA300 clone by the presence of pvl, arcA genes, and genotype of ST/t008 (Hanawa et al., 2019). To prepare murine wound infection model, a full-thickness cutaneous wound was created on the back of each BALB/c mouse (6 w, female). After the inoculation of KYMR116 or KYMR117 at the wounding sites, ΦMR003 was subsequently administered. The number of viable bacteria in the wounds was quantified and the localization of bacterial cells and neutrophils in the skin lesions was analyzed by Hematoxylin-Eosin and Giemsa staining or immunohistochemical staining.

Results: Abscesses were formed in both KYMR116 and KYMR117 infected mice within 48-h, and 1.4×10⁹ ± 4.0×10⁸ cfu and 2.3×10⁸ ± 1.3×10⁸ cfu of bacteria were detected in the wounds infected with KYMR116 and KYMR117, respectively. On the other hand, abscesses were not formed and the number of KYMR116 and KYMR117 bacterial cells decreased to 4.1×10⁵ ± 5.3×10⁵ cfu and 5.0×10⁵ ± 1.2×10⁶ cfu, respectively, in the mice administered ΦMR003. Additionally, fewer neutrophils were recruited in the phage-treated wounds compared to the non-treated.

Conclusions: ΦMR003 decreased bacterial load and suppressed inflammation against CA-MRSA strain, KYMR116 and KYMR117. In addition, KYMR117, the virulent strain, was equivalent to KYMR116 regarding the susceptibility to ΦMR003. These results support the potential use of ΦMR003 as a therapeutic phage against MRSA wound infection.

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Abstract 4557

**Antibacterial activity of the novel compound \([\text{Mn(bpen-cholamide)}(\text{CO})_3]\)Br versus methicillin-resistant *Staphylococcus aureus***

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**Background:** *Staphylococcus aureus* is an important nosocomial pathogen, which is commonly multidrug-resistant and can cause serious skin and soft tissue infections in animals and humans. Methicillin-resistant *S. aureus* (MRSA) has been prioritised on the World Health Organisations priority pathogens list, for the research and development of novel antibiotics. Previously, novel manganese complexes have shown potential as antibacterial agents against multidrug-resistant bacteria. The aim of this study was to assess the *in vitro* and *in vivo* activity of the novel compound \([\text{Mn(bpen-cholamide)}(\text{CO})_3]\)Br against MRSA.

**Materials/methods:** Four well characterised strains of MRSA and methicillin susceptible *S. aureus* (MSSA) were used in this study. Minimum inhibitory concentrations for \([\text{Mn(bpen-cholamide)}(\text{CO})_3]\)Br were determined via broth microdilution assays and kill kinetics versus MSSA and MRSA strains were determined over 24 h. The toxicity of \([\text{Mn(bpen-cholamide)}(\text{CO})_3]\)Br and efficacy of the compound versus MSSA and MRSA strains *in vivo*, was determined in the *Galleria mellonella* model of infection. The Log rank test (Mantel-Cox) was performed to test for significant differences in larval survival.

**Results:** Strong antibacterial activity was observed against MSSA/MRSA with mean MICs of 2-2.67 µg/mL. Data from kill-kinetic assays indicated that \([\text{Mn(bpen-cholamide)}(\text{CO})_3]\)Br was bactericidal against MRSA/MSSA strains, with >3log reduction in bacterial numbers compared to the no drug control. The compound was found to be non-toxic in *G. mellonella* at concentrations ≥100 times those required for bacterial killing. *In vivo* testing in the *Galleria* model found that treatment with \([\text{Mn(bpen-cholamide)}(\text{CO})_3]\)Br significantly increased survival of MRSA/MSSA infected larva compared to PBS (\(p = <0.013\)), with survival rates of 88% versus 46%.

**Conclusions:** Results from this study not only demonstrate that \([\text{Mn(bpen-cholamide)}(\text{CO})_3]\)Br effectively reduces MRSA/MSSA numbers *in vitro*, but also significantly reduces mortality in MRSA/MSSA infected *G. mellonella* larvae, with no compound toxicity observed. This novel compound may have potential as a treatment for MRSA/MSSA infections.

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Interspecific transfer of a bla\text{VIM-2}-containing plasmid between \textit{Pseudomonas} spp. during a nosocomial outbreak

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Background: \textit{Pseudomonas} spp. are Gram-negative bacteria found in hospital wet niches. Since 2003, carbapenemase-producing, \textit{bla}\textsubscript{VIM}\textsuperscript{-}positive \textit{P. aeruginosa} have been isolated from patients and sinks in our hospital; these isolates belonged to “high-risk” sequence types ST446 and ST111. Previously, a \textit{bla}\textsubscript{VIM-2}\textsuperscript{-}containing plasmid was identified in \textit{P. aeruginosa} S04 90, a ST446 clone isolated in 2009 from a patient admitted to intensive care (IC). Our aim was to determine if this plasmid was also present in other \textit{Pseudomonas} spp.

Materials/methods: From this IC ward, \textit{bla}\textsubscript{VIM}\textsuperscript{-}positive \textit{Pseudomonas} spp. isolated between 2013-2016 from patients/sinks were selected. MALDI-TOF (Bruker) was used for species identification, and PCR was used to confirm the presence of \textit{bla}\textsubscript{VIM}. DNA was extracted and sequenced using Illumina iSeq 100 and Nanopore MinION/GridION. Hybrid assemblies were generated using Unicycler. Assembled plasmids were visualized using Bandage, and annotated with Prokka. Resistance genes were screened using ResFinder/CARD. BLASTn and Mauve were used to identify plasmids and align sequences.

Results: Six isolates, and \textit{P. aeruginosa} S04 90 as a reference, were sequenced. These isolates comprised one \textit{P. oleovorans}, one \textit{P. gessardii}, one \textit{P. putida}, and three other \textit{P. aeruginosa} of different genotypes. \textit{P. aeruginosa} S04 90 and \textit{P. putida} were clinical isolates, while the remaining five were sink isolates. In all generated plasmid sequences, \textit{bla}\textsubscript{VIM-2} was found; additionally, \textit{bla}\textsubscript{VIM-2}\textsuperscript{-}containing plasmid sequences were identical to the reference plasmid sequence. For one \textit{P. aeruginosa} sink isolate, copper/silver resistance genes were also found in the plasmid sequence.

Conclusions: \textit{P. aeruginosa} S04 90 possessed a \textit{bla}\textsubscript{VIM-2}\textsuperscript{-}containing plasmid that matched the plasmid sequences of six other \textit{Pseudomonas} spp. isolated in the same ward; five of these were sink isolates. We hypothesize that \textit{bla}\textsubscript{VIM-2}\textsuperscript{-}positive \textit{Pseudomonas} spp. have sustained in our hospital’s sinks after possible human-environment transmission events, and have exchanged the \textit{bla}\textsubscript{VIM-2}\textsuperscript{-}containing plasmid to other \textit{Pseudomonas} spp. Copper/silver resistance genes may have contributed to their persistence in sinks, as copper and silver were added to our hospital’s tap water during the outbreak period to prevent \textit{Legionella} growth. Therefore, it is crucial for effective infection prevention and control to screen for \textit{bla}\textsubscript{VIM}\textsuperscript{-}positive \textit{Pseudomonas} spp. and for the presence of plasmids in sinks.

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**The prevalence of puerperal sepsis causing emm28 Streptococcus pyogenes in four Nordic countries**


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**Background:** Streptococcus pyogenes or Group A streptococcus (GAS) is a human pathogen which causes a wide range of infections. M-protein, encoded by the emm gene, is one of the main virulence factors of GAS. Sequencing of the hypervariable region of emm is the traditional typing method for GAS. In the Nordic countries, emm28 is one of the most common causes of invasive GAS disease. A specific feature of emm28 GAS is its association with postpartum infections. We aimed to investigate the prevalence and demographic characteristics of invasive emm28 GAS infections reported in four Nordic countries, namely Finland, Sweden, Norway and Iceland.

**Materials/Methods:** This is a retrospective, population- and register-based study on invasive emm28 GAS disease in four Nordic countries. National Infectious Disease Registers of each participating country were used to search for invasive emm28 GAS cases. Demographic data of the patients (gender, age and infection type if available) were included in the analysis. The yearly proportion of emm28 of all documented invasive GAS cases was calculated.

**Results:** Among altogether 7326 invasive GAS cases, 1352 (18.5 %) were caused by a emm28 GAS isolate in the participating countries. Due to varying reporting history, the study period varied between countries; 1990-2015 (Iceland), 2006-2016 (Norway), 2002-2015 (Sweden) and 2004-2015 (Finland). The median age of patients infected by emm28 GAS was 63 years, and 53 percent of the cases were women. The cases were divided into four age groups, <20, 20-40, 41-60 and >60 years. Within the age group of 20-40 years, women were significantly overrepresented (82.8 %, 222/268 cases, p<0.001). In this age group of women, altogether 102 cases were associated with delivery or puerperal infection (median age 31 years).

**Conclusions:** Invasive emm28 GAS infections are common in the Nordic countries. There is a clear association of emm28 GAS infections with young women of childbearing age. The underlying molecular mechanisms warrant further studies.

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Abstract 4561

**Evaluation of the diagnostic accuracy of a rapid dengue NS1 antigen lateral flow immunochromatography test in UK returned travellers**

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**Background:** Dengue Fever (DF) is an important cause of illness in travellers returning to the UK. DF is often impossible to distinguish clinically from other imported infections and most UK hospitals do not have access to an on-site test. Although there is no effective anti-viral treatment, a severe vascular leak syndrome, which carries significant mortality, occurs in a small proportion of cases. Rapid diagnosis at the point of care would help identify these patients and simplify clinical decision making. Our aim was to compare the performance of a rapid diagnostic test with the reference standard in a select UK returned traveller population.

**Materials/methods:** We tested stored frozen specimens (plasma/serum), taken from adult patients who were symptomatic following return from a dengue endemic region (defined as South-East Asia, South Asia, the Caribbean, Central and South America). Patient samples were included if they had had documented onset of an acute febrile illness within seven days of return, and sample collection had occurred within five days of illness onset. Testing was performed using the BIO-RAD NS1 antigen rapid diagnostic lateral flow immunochromatography test (NS1-RDT), following the manufacturers’ instructions. The operator was blinded to the reference standard result. The NS1-RDT result was then compared with the reference standard reverse transcriptase polymerase chain reaction (RT-PCR) result.

**Results:** 79 individuals met the inclusion criteria. Of these, 41 (51.9%) had dengue virus infection according to the reference standard (RT-PCR positive). The sensitivity of the NS1-RDT was 85.4% (95% CI: 70.8, 94.4) and the specificity was 100% (95% CI: 90.7, 100) in this cohort. The positive predictive value was 96.2% (95% CI: 81.7, 98.6) and the negative predictive value was 85.2% (95% CI: 74.1, 91.1) assuming a disease prevalence of 0.5. True positives and false negatives were compared (table).

**Conclusions:** NS1-RDT is an accurate tool for early identification of DF in a select UK returned traveller population.

<table>
<thead>
<tr>
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<th>True Positive (PCR+ NS1+)</th>
<th>False Negative (PCR+ NS1-)</th>
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<td>Positive Dengue Serology (%)</td>
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<td>28.96 [24.89, 29.75]</td>
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</table>

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Bioinformatic studies and investigation of the immunogenicity of a vaccine candidate composed of ExoS and PcrV of Pseudomonas aeruginosa against urinary tract infections in an animal model

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Background: Pseudomonas aeruginosa causes different infections such as urinary tract infections (UTIs). Antibiotics are common therapy against these infections, but the increased rate of antibiotic resistance will complicate treatment of the infections in the future. Vaccines could be an alternative approach against UTIs. Exotoxin S (ExoS) as an effector toxin and PcrV as a compartment of type III secretion system are among the most important virulence characteristics of P. aeruginosa. Thus, in the present study, we analyzed the ExoS and PcrV of P. aeruginosa by in silico studies, and then the selected fragments were expressed and purified. Finally, the immunogenicity of the purified protein was evaluated in animal model.

Materials/methods: The ExoS and PcrV sequences of P. aeruginosa were investigated by bioinformatics studies. Then, the best sequences were selected, fused together by the overlapped PCR, and cloned into expression vector. The protein was expressed in BL21 (DE3) and purified by nickel column. The purified protein was analyzed by SDS-PAGE and Western blot. Mice were subcutaneously vaccinated with the purified protein in 2-weeks intervals. Then, serum and urine samples were collected from the mice for measurement the antibody responses by ELISA.

Results: By using the bioinformatics softwares, the best immunogenic segments of ExoS and PcrV were selected as a fusion construct. The expressed fusion protein ExoS:PcrV showed band at the size of 59 KD. Mice immunized with the fusion protein induced higher humoral immune responses in both serum (IgG and IgA) and urine (IgG) than control mice that recieved PBS alone ($P<0.05$). Furthermore, it was also found that the designed fusion protein evoked production of both Th1 (IgG1) and Th2 (IgG2a) responses in the immunized mice.

Conclusions: Because of the important role of P. aeruginosa strains among UTIs, designing of an effective vaccine could have an important role in prevention or treatment of these infections, especially in hospital environments. We found that a vaccine formulation based on the most important fragments of ExoS and PcrV could be considered as an ideal vaccine candidate against UTI. However, further analyses are necessary to demonstrate the efficacy of the designed candidate against UTIs.

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PK/PD of intravenous and oral fosfomycin in neonates with presumed serious bacterial infection

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Background: Treatment of Multi Drug Resistant neonatal sepsis has become a major challenge. Fosfomycin could be part of an empiric treatment regimen in settings where there are high levels of resistance to empiric ampicillin/gentamicin [SOC] and/or ceftriaxone therapy. Fosfomycin PK data in neonates is limited, with no oral PK (PO) data. Here we report model-based estimation of fosfomycin CL, V, T1/2, F% and CSF penetration in hospitalised neonates.

Materials/methods: The NeoFosfo study (ClinicalTrials.gov: NCT03453177) was conducted at Kilifi County Hospital, Kenya. 61 neonates received SOC plus 100mg/kg q12h Fosfomycin, with sample size determined by simulation-estimation. A cross-over design with 2 samples randomized to 4 time slots after the 1st IV and 1st oral dose, respectively gave >80% power for CL, V and F% estimation. CSF sampling was opportunistic. PK modelling was performed using nonlinear mixed effects modelling with NONMEM 7.3. Covariates were selected on biological plausibility or correlation with model parameter variability. Monte Carlo based simulations (n=1000) of plasma concentrations were performed in the context of two PD targets; AUC:MIC ratio and fT>MIC.

Results: Of 238 plasma and 15 CSF concentrations, IV and PO plasma levels ranged (mean) from 7 -576 (202) and 7 -206 (70) respectively, with CSF from 16-66 (38) µg/mL.

A 3-compartment model with first order absorption and allometric scaling adequately described our data. Significant covariates were PMA and PNA in maturation functions on CL and CSF protein on uptake into CSF. Population estimates (%RSE) for CL and Vc were 8.9 L/hr (7.3) and 18.8 L (4.1). Inter-individual variability was 26% (28.6) and 14% (48.3) respectively. F% was estimated at 50% (13.1), Ka at 0.1 hr (23.1) and CSF penetration 0.32 (9.5).

Conclusions: The NeoFosfo study enabled the development of a Population PK model that adequately describes IV and oral Fosfomycin plasma and CSF levels in neonates. Alongside emerging in-vitro hollow fibre data it provides a valuable tool to inform future neonatal sepsis empiric treatment candidates.

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Abstracts 2020

Abstract 4570

**Genome-wide transcriptional responses of Escherichia coli with different levels of zinc tolerance to zinc chloride exposure**

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**Background:** The trace metal zinc is an important catalyst and structural cofactor in nearly all aspects of cell metabolism and plays an essential role in maintaining a well-balanced intracellular zinc homeostasis in most bacterial species. While zinc deprivation hampers bacterial growth, zinc excess could be lethal. We have recently reported different minimum inhibitory concentrations (MICs) for ZnCl₂ associated with commensal *Escherichia coli* mirroring a broad phylogenetic background. However, reasons for these ZnCl₂ MIC differences are not fully understood yet. To investigate whether these differences in zinc tolerance might be associated with significant differences in gene expression among closely related *E. coli*, we used an RNA sequencing (RNA-Seq) approach to characterize the global transcriptomes comparatively.

**Materials/methods:** Our study focused on comparing two distinct *E. coli* of sequence type 617 with a) 1024 µg/ml ZnCl₂ MIC (RKI6122) and b) 256 µg/ml ZnCl₂ MIC (IMT11012). Both were challenged with 1.0 mM ZnCl₂ during exponential growth in supplemented minimal medium for 10 min, while untreated cultures served as controls. Three consecutive biological replicates were subjected to RNA sequencing after total RNA isolation with RNA Snap™. We comparatively characterized the global transcriptomes and identified various differentially expressed genes using the computational pipeline SCORE, which is based on a set of established tools, including DESeq2, edgeR, limma, NOISeq and sleuth.

**Results:** Transcriptional changes for each isolate were compared to those obtained from the corresponding unchallenged controls. Zinc exposure of both *E. coli* resulted in transcriptional changes of genes involved in zinc, iron and copper homeostasis and factors involved in response to envelope stress such as the phage-shock protein A (pspA). Gene transcripts involved in amino acid biosynthesis (e.g. cobalamin-independent methionine synthase (MetE)) showed significantly reduced fold changes for both isolates. In addition, differences were detected for transcripts of the biofilm adhesin polysaccharide encoding gene (*pgaB*), which was downregulated in IMT11012 but remained unaltered in RKI6122.

**Conclusions:** The transcription of genes involved in zinc, iron and copper homeostasis of *E. coli* are affected by zinc chloride exposure. Further research is needed to investigate the putative role of biofilm formation capabilities in *E. coli* expressing increased tolerance towards zinc.

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Extended antibiotic panel to analyse the susceptibility of Enterobacteriaceae by the MALDI-TOF MS-based MBT FAST Assay

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Background: The MBT FAST (MALDI Biotyper Fast Antimicrobial Susceptibility Testing) assay has recently been suggested for rapid antimicrobial susceptibility testing of bacteria by MALDI-TOF MS. Here, we extended the previously described panel of 6 antibiotics to the 10 most common antibiotics employed for severe enterobacterial infections.

Materials/methods: A collection of 25 Enterobacteriaceae comprising different species with various resistance patterns was analysed for its susceptibility towards ten antibiotic compounds (piperacillin/tazobactam, cefotaxime, ceftazidime/avibactam, ertapenem, meropenem, ciprofloxacin, gentamicin, fosfomycin, tigecycline, and colistin) at EUCAST breakpoint concentrations in triplicate by MBT FAST. The workflow was supported by dedicated hardware tools [incubation chamber and broth removal stamp] to increase reproducibility and usability. MICs were determined by the broth microdilution method according to EUCAST as reference method. Tested incubation time for MBT FAST was 4.5 and 5 h. Spectra were evaluated by a prototype software using optimised evaluation parameters and cutoff values for each antibiotic.

Results: In general, the increase of incubation time from 4.5 h to 5 h decreased the standard deviation of the calculated score values and increased the accuracy compared to the CLSI microdilution. Incubation for 4.5 h resulted in 10 invalid growth controls in contrast to only 5 invalid samples after 5 h incubation. Compared to the reference method, the accuracy for ceftazidime/avibactam, ciprofloxacin, colistin, ertapenem, gentamicin and tigecycline was > 96% up to 98% at 5 h incubation. For piperacillin/tazobactam, cefotaxime and meropenem, an accuracy of > more than 92% was achieved. The lowest concordance of 89 % was detected for fosfomycin.

Conclusions: The MBT FAST assay determined the susceptibility pattern towards those antibiotics most commonly applied against severe enterobacterial infections with a medium concordance of 92% compared to the reference method within 5 h incubation. The use of standardised hardware equipment further increased the performance compared to previous studies. An increase of the incubation time by only 30 min increased the validity and the accuracy of the assay.

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Abstract 4576

A comparison of GenomEra GBS PCR and GeneXpert GBS PCR assays with culture of group B Streptococcus with and without broth enrichment

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Background: Preventing neonatal infection with Group B streptococci (GBS) still receives substantial attention from researchers worldwide aiming at the ideal identification and prevention of transmission of GBS from mother to baby. Early-onset GBS disease (EOD) is still the most frequent cause of early-onset infection in neonates worldwide. More than 30% of infants delivered in the United States are now exposed to intrapartum antibiotics in order to prevent vertical transmission of GBS to the baby during their passage through the birth canal. This study was designed to compare the performance of GeneXpert® and GenomEra® GBS PCR assays, held up against gold standard of culture of GBS performed with and without broth enrichment.

Materials/methods: 366 women fulfilling one or more of the following criteria for presence of risk factors for EOD were prospectively included: (1) Bacteriuria during current pregnancy; (2) Prior infant with EOD; (3) Temperature above 38.0°C during labor; (4) preterm labor < 37 gestational weeks; (5) Rupture of membranes ≥18h.

Rectovaginal sampling was performed intrapartum and were immediately tested by GenomEra® CDX system (Abacus Diagnostica, Finland as well as by GeneXpert® (Cepheid Ltd., Sunnyvale, USA) as well as by standard culture with and without broth enrichment.

Results: In all, 366 pregnant women were tested intrapartum of which 99 had samples that were positive by culture, 95 by GenomEra and 95 by GeneXpert. When compared to culture, the GenomEra had sensitivity of 91.8% and the specificity of was 97.3%. The GeneXpert had sensitivity of 91.7% and a specificity of 96.9%. When compared to a combined reference standard the sensitivity increased to 91.9% and the specificity to 99.6% for GenomEra, and 91.9% and 98.8% for GeneXpert.

Conclusions: The performance of the two PCR methods examined, was very similar and very close to the findings in culture. GenomEra and GeneXpert have high sensitivities and PPV and are both applicable in a clinical setting.

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Abstract 4577

Comparative evaluation of MAST Carba PAcE, RESIST-4 O.K.N.V. and NG-Test Carba 5 kits in the detection of carbapenemase production in clinical isolates

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Abstract third-party references: Mast Group, Hardy Diagnostics

Background: Rapid detection of carbapenemases is crucial in informing both antimicrobial stewardship and infection control interventions. Here, we present a comparative evaluation of three carbapenemase detection kits in the detection of IMP-1, OXA-48, KPC, NDM-1, VIM-1 and VIM-2. The kits used are the colorimetric test MAST CARBA PAcE (Mast Group) and the immunochromatographic lateral flow assays RESIST-4 O.K.N.V. (Coris BioConcept) and NG-Test Carba 5 (Hardy Diagnostics).

Materials/methods: One hundred previously characterised clinical gram-negative isolates were evaluated using the three kits above. The prevalence of the various carbapenemase genes were: IMP-1 n=1, OXA-48 n=26, KPC n=5, NDM-1 n=24, VIM-1 & VIM-2 n=19, OXA-48 & NDM-1 n=4, others n=21.

Results:

<table>
<thead>
<tr>
<th>Commercial kit</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Cost per test (£)</th>
<th>Time per test (mins)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAST CARBA PAcE</td>
<td>95.3</td>
<td>14.3*</td>
<td>82.2</td>
<td>33.3</td>
<td>4.69</td>
<td>20</td>
</tr>
<tr>
<td>RESIST-4 O.K.N.V.</td>
<td>94.0**</td>
<td>96.0</td>
<td>82.3</td>
<td>98.1</td>
<td>11.72</td>
<td>15</td>
</tr>
<tr>
<td>NG-Test Carba 5</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>18.75</td>
<td>15</td>
</tr>
</tbody>
</table>

Table 1: Comparison of the performance and costs of the three kits.

* The low specificity is due to many false positives, which can be related to detection of CTX-M-1 and ACT-1 and/or ACT-5 β-lactamases.

** Sensitivity of detection of NDM-1 (88.9%) and VIM (84.2%) was lower than that of IMP-1 (100%), OXA-48 (96.7%) and KPM (100%).

Conclusions: MAST CARBA PAcE kit is a relatively low-cost kit with high sensitivity for the detection of a broad range of carbapenemases, extending beyond the “big five”. However, it is unable to discriminate between the different genotypes. The more expensive lateral flow assays detect the “big five” carbapenemases with high sensitivity and specificity, with NG-Test Carba 5 being overall more sensitive and quicker than RESIST-4 O.K.N.V. These tests have the ability to distinguish between different genotypes, but their repertoire is limited to the “big five” carbapenemases.

Judicious diagnostic stewardship is essential in directing appropriate use of these kits in order to optimise their application in patient management. Whereas MAST CARBA PAcE has potential as a carbapenemase screening tool, the other 2 kits might be better suited to managing outbreaks involving the “big five” carbapenemases.

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**Abstract 4592**

**Genotyping and antifungal susceptibility of *Candida albicans* isolates from vaginal samples: are the genotypes different from blood?**

Aina Mesquida*1;2, Judith Diaz-Garcia1;2, Teresa Vicente1, Elena Reigadas Ramirez1;2, María Palomo2, Patricia Muñoz1;2, Jesus Guinea Ortega1;2, Pilar Escribano1;2

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**Background:** *C. albicans* is a common cause of vulvovaginal infection, frequently associated to relapses that may be due to acquisition of resistance to azoles. Furthermore, little is known about *C. albicans* clones potentially causing vulvovaginitis. We genotyped *C. albicans* isolates sourcing from vaginal samples and studied their antifungal susceptibility.

**Materials/methods:** Isolates from vulvovaginal samples isolated in the laboratory in 2017 were selected. Multiple *C. albicans* isolates from a single patient were further studied if separated in a period span over 1 month. Isolates, genotyped by species-specific microsatellite markers, were considered identical when showed the same alleles for all loci; clusters were identical genotypes found in ≥2 patients. Genotypes found were further compared with *C. albicans* genotypes sourcing from blood samples (n=1,134). Antifungal susceptibility to amphotericin B, fluconazole, voriconazole, posaconazole, micafungin, and anidulafungin was tested by EUCAST 7.3.1.

**Results:** We studied a total of 81 *C. albicans* isolates from 50 patients (n=29 patients with multiple isolates; 2-3 isolates per patient). From the 56 genotypes found, 53 (95%) were singleton and three were clusters (5%) that involved 8 out of the 50 patients. The majority of patients with multiple isolates [18/29, 62%] turned up with identical genotypes [5.5 months; 3-7 months] vs. the remaining 11 patients that harboured different genotypes [15 months; 9-18 months]. Singleton genotypes did not match with those from blood samples whereas the 3 clusters [5%] were further found in blood cultures; interestingly the three clusters were genotypes frequently found causing candidemia sometimes even in patients located at different hospitals. Fluconazole and posaconazole resistance was very low (2.4% of isolates from a patient); isolates were fully susceptible to the remainder drugs.

**Conclusions:** We found *C. albicans* genotypes from vulvovaginal samples rarely present in blood samples, suggesting proneness of some clones to cause vulvovaginitis. In patients with multiple isolates, isolates collected in short periods of time were identical genotypes (*P*<0.05). Furthermore, resistance to antifungal drugs was anecdotic.

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Abstract 4596

**Linezolid resistance mechanisms in Staphylococcus capitis and Staphylococcus haemolyticus isolates collected in Gauteng, South Africa**

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**Background:** *Staphylococcus capitis* and *Staphylococcus haemolyticus* are Gram-positive commensals that may cause hospital- and community-associated infections in the compromised host. The treatment of these infections with linezolid is being hampered by the emergence of resistance. Linezolid resistance is commonly mediated by chromosomal 23S rRNA gene mutations and plasmid-mediated chloramphenicol-florfenicol resistance (*cfr*) gene acquisition. In this study, investigation of these two linezolid resistance mechanisms was performed on *S. capitis* and *S. haemolyticus* isolates collected from private hospitals in Gauteng, South Africa.

**Materials/methods:** *Staphylococcus capitis* (n=43) and *S. haemolyticus* (n=9) blood culture isolates, processed using the BACT/ALERT® 3D (bioMérieux, France), were collected from 2016 to 2018. Inclusion criteria was linezolid resistance using the VITEK® 2 instrument (bioMérieux, France). Matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectrometry (MS) identified the isolates. Linezolid susceptibility results were confirmed using ETEST® (bioMérieux, France). Multiplex polymerase chain reaction (M-PCR) assays confirmed species identification and a singleplex polymerase chain reaction (PCR) assay determined *cfr* gene presence. Pulsed-field gel electrophoresis (PFGE) was performed to determine genetic relatedness and representative isolates were selected for whole-genome sequencing (WGS).

**Results:** The *cfr* gene was not detected in the *S. capitis* or the *S. haemolyticus* isolates. The ETEST® (bioMérieux, France) *S. capitis* minimum inhibitory concentration (MIC) values ranged between 1.2 µg/mL and 12.8 µg/mL and the *S. haemolyticus* MIC values ranged between 8 µg/mL and 64 µg/mL. Three major clusters and four minor clusters were detected following PFGE of the *S. capitis* isolates, showing dissemination across numerous hospitals. The *S. haemolyticus* isolates displayed two minor clusters and one singleton. The WGS found various 23S rRNA gene mutations such as T2157A, C2190T, T2346C and G2603T in three representative *S. capitis* isolates.

**Conclusions:** The presence of 23S rRNA gene mutations in the absence of the *cfr* gene showed a high (24 µL/mL) MIC value, indicating that linezolid resistance is an emerging problem even when only one resistance mechanism is present. Therefore, the monitoring of linezolid resistance is needed in an effort to prevent widespread dissemination of resistance to linezolid.

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Abstract 4597

**Active search through multiplex PCR method for sexually-transmitted infections in patients with sterile pyuria**

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**Background:** Sterile pyuria is a highly prevalent condition. While bacterial infections of the genitourinary tract are the most frequent underlying pathologies, non-infectious causes and certain atypical microorganisms must also be taken into account, among which STIs are the most commonly related cause. The aim of this study was to investigate the prevalence of STIs: *C. trachomatis* (CT), *N. gonorrhoeae* (NG), *M. genitalium* (MG) and *T. vaginalis* (TV) among those patients with sterile pyuria as well as determine if the urine sample used previously for culture is valid for this determination.

**Materials/methods:** A PCR (Anyplex™ II STI-7 Detection, Seegene) was performed in the Hospital Universitario de Canarias Microbiology Service, on selected urine samples with sterile pyuria for patients between 18 and 55 years. Patient with recent episode of UTI were excluded. Epidemiological data was collected. In those patients of whom genital swabs or urine samples have been sent, a PCR was performed in parallel to compare results. All epidemiological and microbiological data was collected in an Excel table for further exploitation in the SPSS® Statistics program.

**Results:** During the period August-October 2019, 34% [206] of the sterile pyuria urine received in our Service met the criteria for inclusion; 193 woman (93.7%) of which 52 (27%) were pregnant, mean age 33.96±10.13. We obtained 15 (7.3%) positive results (Table 1), all of them were informed for subsequent clinical management. Two mixed infections were diagnosed: 1 CT with MG and 1 CT with NG. Analysed by sex: in the women’s group: 10 (5%) positive samples (4 (7.6%) in the pregnant group) and 5 (38.4%) positive in men’s group. 20 double samples were analyzed; of these, 19/20 were concordant (same result in both PCR). The calculated kappa coefficient was 0.44 (moderate force).

**Conclusions:** We found a non-negligible number of positives in a sample that a priori is not of choice for this diagnosis. Further studies will have to be carried out in the age groups between 18-34 years and in pregnant women to expand results and determine if the urine used for urine cultures is valid for determination of STIs.

Table 1.

<table>
<thead>
<tr>
<th>Microorganisms</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>10 (4.8)</td>
</tr>
<tr>
<td>MG</td>
<td>2 (1)</td>
</tr>
<tr>
<td>TV</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>CT+NG</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td>CT+MG</td>
<td>1 (0.5)</td>
</tr>
</tbody>
</table>

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Effect of *Bdellovibrio bacteriovorus* on clinical pathogens and biofilms

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**Background:** *Bdellovibrio bacteriovorus* is a Gram-negative obligate predatory bacterium which lives by attacking other bacteria including a very wide range of human pathogens. Here, we investigated the predatory behavior of *B. bacteriovorus* HD 100 ATCC 15356 against clinical Gram-positive (*Listeria monocytogenes* and *Staphylococcus epidermidis*) and Gram-negative (*Proteus mirabilis* and *Stenotrophomonas maltophilia*) isolates.

**Materials/methods:** Identification and antimicrobial susceptibility of the clinical isolates, isolated at Ege University Hospital Bacteriology Laboratory of Medical Microbiology Department were investigated and VITEK MS and VITEK 2 Compact® automated systems. The biofilm formations of the isolates were evaluated by crystal violet method in the presence and absence of *B. bacteriovorus* HD 100 ATCC 15356. Scanning electron microscopy was also used for monitoring the biofilms of isolates and predation *Bdellovibrio bacteriovorus*. All experiments were performed in triplicate.

**Results:** According to crystal violet method, all four clinical isolates had strong biofilm formation capacities. After predation of *B. bacteriovorus* biofilm formation capacities of isolates has been reduced (Table 1).

<table>
<thead>
<tr>
<th>Isolates</th>
<th>Before predation</th>
<th>After predation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1st.</td>
<td>2nd.</td>
</tr>
<tr>
<td><em>Listeria monocytogenes</em></td>
<td>0.2337 (Strong)</td>
<td>0.2536 (Strong)</td>
</tr>
<tr>
<td><em>Proteus mirabilis</em></td>
<td>0.2259 (Strong)</td>
<td>0.1583 (Strong)</td>
</tr>
<tr>
<td><em>Staphylococcus epidermidis</em></td>
<td>0.6234 (Strong)</td>
<td>0.6534 (Strong)</td>
</tr>
<tr>
<td><em>Stenotrophomonas maltophilia</em></td>
<td>0.3384 (Strong)</td>
<td>0.476 (Strong)</td>
</tr>
</tbody>
</table>

**Table 1. OD measurements of CV method**

**Conclusions:** Strong biofilm producer isolates has been detected in our hospital. Although *B. bacteriovorus* HD 100 ATCC 15356 has an inhibitory effect on biofilm formation of all clinical isolates, it reduced biofilm formation of Gram positive isolates (*L. monocytogenes* and *S. epidermidis*) more effectively. The study will be expanded with co-culture experiments and more clinical isolates.

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Abstract 4602

Whole genome sequencing investigation into a single-site outbreak of NDM-mediated carbapenem resistance disseminated across multiple species predominantly via IncL/M plasmids

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Background: Mobile carbapenemase genes, including those of the NDM family, contribute to the increasing burden of carbapenem resistance. Plasmids encoding NDM can be highly mosaic, variable and difficult to track in large multi-species outbreaks. Using short- and long-read WGS we delineated discrete circulations of NDM-1 plasmids within a multi-species district-general hospital outbreak.

Materials/methods: Thirty-seven carbapenemase-producing isolates from 34 patients in a single hospital were submitted to PHE’s AMRHAI Reference Unit between July 2017-April 2018. MICs were determined by BSAC agar dilution methodology, interpreted with EUCAST guidelines, and isolates were short-read sequenced (illumina). Twelve genetically diverse isolates were selected for long-read sequencing (ONT). Bioinformatic tools were used on the hybrid assemblies to determine species, core genomes, resistance genes, plasmid replicons and STs. Bwa established best-fit references by mapping short-read sequences to hybrid assemblies.

Results: Thirty-four isolates of Enterobacterales (E. coli, E. cloacae, K. pneumoniae, K. oxytoca and Citrobacter) from distinct patients on 13 wards encoded NDM-1. There was little evidence of geo-temporal clustering of patients positive for clonal bactera. Nine isolates had NDM with IncF (n=4) or IncHI2 (n=5) plasmids. Twenty-five patients had IncLM NDM-1 plasmids temporally distributed across the outbreak.

IncLM-plasmid hybrid assemblies from six genetically diverse ‘outbreak’ isolates represented two variant plasmids IncLM-A and -B (86,615bp and 75,455, 87% nucleotide identity) with variable class-I integron sequence regions. Short-read mapping to the six reference assemblies revealed that these plasmids were dispersed across species; E. cloacae (IncLM-A n=6, IncLM-B n=4), E. coli (IncLM-A n=4, IncLM-B n=5), K. pneumoniae (IncLM-A n=3, IncLM-B n=1), and Citrobacter (IncLM-A, n=2).

IncLM-A and IncLM-B plasmids were first observed in weeks 2 and 8 respectively, with both being observed throughout the outbreak duration. Concurrent patients on two wards had either IncLM-A or IncLM-B plasmids. In three wards IncLM-A was observed exclusively. In one week, one ward had isolates from three species with IncLM-B. Long-read sequences indicated the migration of a NDM-1 integron from IncLM to F-/HI-2 type plasmids.

Conclusions: Long-read/short-read hybrid assemblies illuminated sub-circulations of mobile elements in a multi-species NDM-1 outbreak. Within this outbreak three additional levels of mobility were identified; plasmid-species transfer and integron/transposon-plasmid transfer.

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Abstract 4606

Comparison of ResistancePlus MG and pyrosequencing for macrolide resistance detection in Mycoplasma genitalium and evaluation of macrolide and fluoroquinolone resistance in Badalona, Spain

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Abstract third-party references: Ayuda de la SEIMC

Background: Macrolides are the first-line treatment for Mycoplasma genitalium (MG) infections, but resistant patterns have been described. Fluoroquinolones are the second-line therapy. Consequently, the 2016 European guideline has recommended studying macrolide resistance-associated mutations in all cases where MG is detected. Several commercial kits have been released lately. Our aim was to compare the clinical performance of the ResistancePlus MG kit (SpeeDx, Australia) with our in-house methods. Additionally, macrolide and fluoroquinolone resistance prevalence was determined.

Materials/methods: A total of 100 MG-positive samples, collected at the Hospital Germans Trias y Pujol, Badalona, Spain, and previously tested for MG by real-time PCR (Allplex® STI-7, Seegene) and pyrosequencing (Pyromark®, Qiagen) to detect macrolide resistance were further analyzed using the one-step ResistancePlus MG kit (SpeeDx, Australia), and tested for fluoroquinolone resistance by parC gene Sanger sequencing at the University of Bordeaux, France.

Results: Regarding MG detection, an overall agreement of 87% was obtained comparing both methods. Thirteen samples were reported as negative by ResistancePlus MG but were detected with Allplex STI-7. Macrolide resistance prevalence was 64% in our hospital according to pyrosequencing. Among the 87 MG-positive samples detected using the ResistancePlus kit, 83 results were concordant with those obtained by pyrosequencing, showing an overall agreement of 95.4%. Three samples were reported as not mutated by the ResistancePlus kit but harbored a 23S rRNA A2058G (E.coli numbering) mutation by pyrosequencing, while the fourth sample was reported as mutated but was found wild-type by pyrosequencing.

Regarding fluoroquinolone resistance, 97 samples were wild-type for parC gene and 3 (3%) samples were resistant, harboring a S80I mutation (E. coli numbering). These three samples also harbored an A2059G macrolide resistance-associated mutation. Remarkably, one case corresponded to a second sample from a MG-positive patient that was initially found macrolide-resistant and fluoroquinolone-susceptible. After azithromycin and moxifloxacin treatment failures, the test-of-cure sample harbored both A2059G and S80I mutations.

Conclusions: The ResistancePlus MG SpeeDx is easy to use and showed a good correlation with pyrosequencing for mutation detection. Macrolide resistance is high in our area whereas fluoroquinolone resistance remains low. However, fluoroquinolone resistance should be studied in cases of moxifloxacin treatment failure.

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A novel KPC-3 variant associated with CAZ/AVI resistance in an Klebsiella pneumoniae ST512 causing bacteraemia

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1Azienda Sanitaria Universitaria Integrata di Trieste, Microbiology Unit, Trieste, Italy, 2University of Florence, Department of Experimental and Clinical Medicine, Florence, Italy, 3Florence Careggi University Hospital, Clinical Microbiology and Virology Unit, Florence, Italy, 4Azienda Sanitaria Universitaria Integrata di Trieste, Infectious Diseases Ward, Trieste, Italy

**Background:** Ceftazidime-avibactam (CAZ/AVI) is a recent antibiotic which shows in vitro activity against many important Gram-negative pathogens including carbapenem-resistant Enterobacterales (CRE) producing KPC and OXA-48. Resistance to CAZ/AVI is still rarely reported, but poses a serious threat for the future. We report here the characterization of a CAZ/AVI-resistant Klebsiella pneumoniae strain carrying a novel KPC-3 variant.

**Materials/methods:** Identification was performed by VITEK® MS system (bioMérieux). Minimal inhibitory concentrations (MICs) were determined by a micro-dilution method (Sensititre Diagnostic System, Trek), and interpreted according to EUCAST clinical breakpoints v 9.0. A whole genome sequencing (WGS) approach (Illumina Miseq) was adopted to characterize the resistance mechanism to CAZ/AVI.

**Results:** A 78-year-old woman was admitted in hospital following a gluteal abscess post-arthroplasty treated with metronidazole and piperacillin/tazobactam, and developed a pneumonia caused by a KPC-producing K. pneumoniae, susceptible to CAZ/AVI. For this reason, the treatment was adjusted with CAZ/AVI in combination with tigecycline. However, a breakthrough bacteraemia occurred and a KPC-producing K. pneumoniae was isolated from blood cultures resulting resistant to CAZ/AVI (MIC >32 mg/L). A severe ischemia due to the occlusion of the iliac-femoral axis led the patient to a fatal outcome. WGS analysis showed that this isolate i) belonged to ST512, ii) had a bla_kp as the only carbapenemase gene, iii) presented a novel amino acid substitution (D179G), inside the omega-loop of KPC-3, previously associated with reduced susceptibility to CAZ/AVI as variant of KPC-2, iv) showed alterations in the outer membrane porins (OmpK35 and OmpK36).

**Conclusions:** CAZ/AVI resistance mechanisms has largely been attributed to nonsynonymous mutations in KPC-3. In this work, a CAZ/AVI resistant K. pneumoniae isolate with a new variant of KPC-3 was described after an initial treatment with this antibiotic, highlighting that a strict antibiotic-stewardship and infection control practices are necessary to preserve the drug efficacy of this recent drug.

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Live probiotic vaccine against influenza virus infection

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Background: Neuraminidase (NA) the second most important antigenic component of influenza virus. When the emergence of influenza viruses with a new subtype, antibodies to NA can play a decisive role in protecting against severe forms of infection until vaccination with a new antigenic variant is started.

Materials/methods: cDNA of influenza A17/duck/Potsdam/86/92[H5N2] virus was amplified by primers corresponding to the gene of neuraminidase [na]. Pneumococcal gene pspf was replaced by na in the integrative plasmid pent-pspf [Gupalova et al, 2019]. Resultant recombinant plasmid pent-na was isolated in the E.coli system and transformed into Enterococcus faecium L3 by electroporation. Location of the insert of the integrative plasmid in the chromosome was confirmed by PCR and DNA sequencing. CBA mice were orally immunized with a probiotic vector containing neuraminidase of subtype N2 [10 animals per group]. Blood serum was collected 4 days after the end of the second and third feeding cycles to determine IgG antibodies to NA subtype N. At 10 days after the end of the third vaccination, the mice were intranasally infected with 1 50% mouse lethal dose (MLD50) of pandemic influenza virus A/South Africa/3626/13(H1N1)pdm09.

Results: Chimeric construct with the genetic element NA for influenza vaccine was inserted in frame into enterococcal gene d2 by PCR. The resultant DNA ent-na, 1.8 kb in size was cloned in suicidal plasmid pT7ermB. An integrative plasmid was used for the electroporation of the enterococcal strain E. faecium L3. NA positive clone was selected and used in vaccine preparation for further immunization.

After the third oral immunization with E.faecium strain with na gene, serum IgG against whole A/H1N1 virus were detected. When immune mice were infected with a pandemic influenza virus, 67% of the animals were protected from mortality. The average weight of the mice treated with enterococcus without insertion was significantly less relatively to those immunized with enterococcus expressing NA.

Conclusions: Thus, oral immunization of mice with a probiotic vector containing NA of subtype N2 was shown not only to induce a virus-specific immune response, but also to provide partial protection from lethal infection with pandemic influenza virus A/South Africa/3626/13 [H1N1]pdm09.

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Emergence of CTX-M-producing Salmonella enterica serotype Typhimurium in Greece

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Background: Salmonella infections are prevalent worldwide and are considered as the leading cause of foodborne hospitalizations posing a considerable financial burden on public health. Moreover, the emergence of drug-resistant strains restricts the available treatment options. We report here the emergence of three genetically related Salmonella isolates bearing CTX-M β-lactamases.

Materials/methods: The isolates were recovered from the feces of three infants of 16, 14 and 17-months hospitalized in the Pediatric ward of our hospital for mucus-bloody diarrhea. The first was admitted on September 2016 and the other two, two years later on September 2018. Species identification and susceptibility testing were performed by the VITEK2 system (bioMérieux) and by the disc-diffusion method. The antimicrobial susceptibility results were interpreted using the EUCAST breakpoints. Sero-typing was performed by the Greek National School of Public Health. The presence of β-lactamases was detected by PCR using specific primers for blaCTX-M, blaKPC, blaVIM, blAIM and blANDM. The clonal relatedness was assessed by ERIC II PCR.

Results: The isolates belonged to Salmonella enterica serotype Typhimurium and exhibited resistance or non-susceptibility to most β-lactams including cefotaxime and amoxicillin/clavulanate. They remained however susceptible to piperacillin/tazobactam, ceftazidime and carbapenems as well as to co-trimoxazole and fluoroquinolones. All three were positive for blaCTX-M and negative for carbapenemase-encoding genes. Their ERIC II patterns were similar suggesting that they were clonally related.

Conclusions: To the best of our knowledge, this is the first time Salmonella spp. harboring blaCTX-M is found in Greece. The emergence of such strains in pediatric patients is even more worrying since the treatment options for this patient group are already restricted and quinolones are ruled out a priori. Intensification of the infection control policies inside the hospital and especially in the Pediatric ward were suggested, because blaCTX-M are commonly carried on plasmids being thus able of horizontal gene transfer, not only among Salmonella spp. but also among other Enterobacterales in the hospital setting.

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Abstract 4611

**Genetic diversity of *Pseudomonas aeruginosa* isolates colonising the lungs of cystic fibrosis patients at two academic hospitals in the Gauteng Province, South Africa**

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**Abstract third-party references:** Doctoral Research Bursary, University of Pretoria, South Africa, National Health Laboratory Service, Tshwane Academic Division, South Africa, National Research Foundation, South Africa

**Background:** The average life expectancy of a cystic fibrosis (CF) patient in South Africa is 20.5 years. A major point of health decline in these patients is the colonisation of their lungs with *Pseudomonas aeruginosa*. It is considered that CF patients are typically colonised with bacterial strains from their environment and patients sharing similar environments, such as those attending the same CF clinics are expected to be colonised with similar *P. aeruginosa* strains. Here, we used the enterobacterial repetitive intergenic consensus (ERIC)-PCR technique to determine the genetic diversity of *P. aeruginosa* strains colonising the lungs of CF patients at two academic hospitals in the Gauteng Province, South Africa.

**Materials/methods:** A total of 56 PCR identified *P. aeruginosa* were isolated from the sputum of seven *P. aeruginosa* colonised CF patients from the two academic hospitals. ERIC-PCR typing was performed on the isolates and the banding profiles were analysed using GelCompar II software (Applied Maths, Belgium). A Dendrogram clustering the isolates according to genetic relatedness was constructed using Dice co-efficient and unweighted pair group method with arithmetic mean (UPGMA).

**Results:** Cluster analysis results showed high diversity in the *P. aeruginosa* isolates among CF patients attending the same hospital. Some strains of *P. aeruginosa* were shared among patients attending the same clinic but the majority of the strains were unique to the individual patient. Limited inter-hospital spread was observed among the *P. aeruginosa* isolates. Within patient diversity was observed in three CF patients with some strains showing less than 50% similarity with the main cluster for that patient (Patients 2, 3, 4 and 6). Refer to the image below.

**Conclusions:** The majority of the CF patients in the study were colonised with multiple, genetically diverse strains of *P. aeruginosa*. Considering the impact *P. aeruginosa* colonisation has on patient health decline, genotypic characterisation is important to determine the diversity and spread of strains of this pathogen among CF patients. Further genomic sequencing of the *P. aeruginosa* strains is important to determine antibiotic resistance, virulence and sequence types.
Figure 1: ERIC-PCR typing cluster dendrogram showing genetic relatedness of the P. aeruginosa isolates from the study

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**Abstract 4613**

**Evaluation of commercial media for susceptibility testing of Neisseria gonorrhoeae**

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**Background:** There is currently no EUCAST disc diffusion method for susceptibility testing Neisseria gonorrhoeae (NG). For MIC determination, EUCAST recommends following manufacturers’ instructions along with EUCAST clinical breakpoints. Most laboratories will perform gradient strips, where the manufacturers’ media recommendations however these are not always available to routine laboratories and no Mueller Hinton (MH) Fastidious media has been shown to support good growth of NG. We have evaluated alternative commercially available media for quality of growth of NG and MIC results using the BioMerieux Etest gradient strips against the agar dilution (AD) reference method.

**Materials/methods:** Two sites, Specialist Antimicrobial Chemotherapy Unit [SACU] and AMRSTI [AntiMicrobial Resistance in STIs], Public Health England [PHE] performed the testing. Six media from three manufacturers: Oxoid GC + vitox (OxGC+V), Oxoid GC non-selective with lysed horse blood (OxGCNsel), Oxoid Chocolate with vitox (Oxch+V), Becton Dickenson GC chocolate (BDGCch), Becton Dickenson Mueller Hinton chocolate (BDMHch), E&O Mueller Hinton chocolate agar (E&OMHch) were evaluated. Quality of growth for 5 WHO strains and 5 clinical isolates “poor growers” was evaluated. MICs were determined on the same six media for 47 NG isolates and 2 WHO NG control strains using ceftriaxone and azithromycin Etests. Inocula were prepared using either saline or MH broth. MICs were compared to the AD reference method (GRASP surveillance study) using Diagnostic Sensitivity Test [DST] agar, 5% horse blood and 1% vitox.

**Results:** OxGC+V and BDGCch showed the best quality of growth. For MIC testing, percentage essential agreement can be seen below:

<table>
<thead>
<tr>
<th></th>
<th>Azithromycin</th>
<th>Ceftriaxone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SACU/PHE</td>
<td>SACU/PHE/GRASP</td>
</tr>
<tr>
<td>OxGC+V</td>
<td>98</td>
<td>94</td>
</tr>
<tr>
<td>OxGCNsel</td>
<td>86</td>
<td>74</td>
</tr>
<tr>
<td>BDGCch</td>
<td>98</td>
<td>92</td>
</tr>
<tr>
<td>BDMHch</td>
<td>87</td>
<td>80</td>
</tr>
<tr>
<td>Oxch+V</td>
<td>n/a*</td>
<td>100*</td>
</tr>
<tr>
<td>E&amp;OMHch</td>
<td>n/a*</td>
<td>78*</td>
</tr>
</tbody>
</table>

*Only data from SACU available

**Conclusions:** Two media (OxGC+V and BDGCch) performed best for quality of growth and showed comparable ceftriaxone and azithromycin MICs when compared with the reference method. The use of saline instead of recommended broth for inoculum preparation gave comparable results. Diagnostic laboratories can be assured that performing MICs on these media will produce accurate results.

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Transmission of Tn1721-like transposon harbouring CTX-M-27 between Salmonella and Escherichia coli isolates from food-producing animals in China

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Background: The aim of this study was to explore the characteristics of blaCTX-M-27 carriage and mobilization in Salmonella and Escherichia coli isolates from food-producing animals in China.

Materials/methods: A collection of 2280 E. coli and 355 Salmonella isolates from food animals between June 2003 and September 2014 in China were screened for the presence of blaCTX-M-27 genes. The blaCTX-M-27-positive isolates were characterized by replicon typing. blaCTX-M-27 harboring plasmids were sequenced to determine the genetic context of blaCTX-M-27.

Results: In total, 18 CTX-M-27-positive E. coli (0.79%) and 43 CTX-M-27-positive Salmonella (12.11%) were detected and all exhibited multidrug-resistant phenotypes. Replicon typing, S1-PFGE, and hybridization on CTX-M-27-carrying plasmids confirmed that blaCTX-M-27 gene was respectively located on IncFII (12/18), IncN (4/18), and non-typable (2/18) plasmids in E. coli, and IncP (6/43), IncFiB (4/43), IncN (2/43), IncHI2 (2/43), and IncA/C (1/43) plasmids in Salmonella. It worth noting that blaCTX-M-27 was captured by P1 bacteriophages (28/43) in the remaining Salmonella isolates. Comparison and analysis of the gene environment of blaCTX-M-27 in P1 like bacteriophage and plasmids discovered that they shared the same structure contained an identical genetic environment with Tn1721-like transposon (ΔISEcp1-blaCTX-M-27-IS9030-iroN-Δmap-Tn1721). Additionally, the fitness tests by growth and competition experiments proved that transformants carrying blaCTX-M-27 P1-like bacteriophage showed stronger viability than recipient bacteria without the pressure of cefotaxime.

Conclusions: Tn1721-like transposon harboring CTX-M-27 could mobilized between different replicon plasmids in E.coli, and could be integrated into P1 bacteriophage by which disseminated among Salmonella.

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Clinical efficacy of ceftolozane-tazobactam versus other active agents for the treatment of bacteraemia and nosocomial pneumonia due to drug-resistant *Pseudomonas aeruginosa*

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Background: Ceftolozane/tazobactam (C/T) is a new cephalosporin with enhanced activity against *P. aeruginosa*, including multidrug (MDR) or extremely drug resistant (XDR) strains. Unfortunately, there are few data comparing outcomes of patients treated with C/T versus old regimens including polymyxins or aminoglycosides.

Materials/methods: We performed a retrospective multicenter 1:2 case-control study comparing patients with nosocomial pneumonia or bloodstream infection (BSI) due to MDR or XDR *P. aeruginosa* treated with ceftolozane-tazobactam or with either polymyxin or aminoglycoside-based regimens. Matching was based according to age (± 10 years), sex, type of infection and susceptibility profile of the isolated pathogen (MDR with MDR and XDR with XDR infections).

Results: Overall, 16 patients with MDR or XDR *P. aeruginosa* infections receiving an antibiotic regimen including ceftolozane-tazobactam were selected for the analysis. These patients were compared with 32 corresponding controls who received either a colistin-based (21, 43.8%) or aminoglycosides-based regimens (16, 33.3%). Mean age (±SD) was 62.4±14.5 years old and 81.3% of patients were males. Infection types were nosocomial pneumonia in 27/48 patients (56.3%) and bloodstream infection in the remaining 21/48 (43.7%). There were no significant differences between cohort in terms of demographics, main comorbidities and severity of disease. However, combination therapy was more commonly used in polymyxin/aminoglycosides patients than those who received ceftolozane/tazobactam (90.6% vs 56.3%, P = 0.01). Clinical cure at day 14 was higher (81.3% versus 56.3%, P = 0.11) and thirty-day mortality lower among cases (18.8% versus 28.1%; P = 0.72), but differences did not reach statistical significance. Polymyxin/aminoglycosides regimens were associated with increased rates of acute kidney injury (25.0% vs 0% P = 0.04).

Conclusions: Ceftolozane-tazobactam was well tolerated and at least as effective as other alternatives for *P. aeruginosa* infections. Our data support its preferential use for treatment of MDR or XDR *P. aeruginosa* infections.

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Abstract 4620

The application of CRISPR/Cas9-based genome editing in knocking out the blaNDM-1 gene to study the mechanisms of pandrug resistance in clinical isolates

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Background: The development of antibiotic resistance in bacteria is a major public health threat. Infection rates of resistant pathogens continue to rise against nearly all antimicrobials, which has led to development of different strategies to combat the antimicrobial resistance. Recently, the clustered regularly interspaced short palindromic repeats (CRISPR)-associated protein 9 (CRISPR/Cas9) system has been applied to combat antibiotic-resistant bacteria.

Materials/methods: Plasmid pcas9 expressing Cas9 was constructed and used to clone target single-guide RNAs (sgRNAs) for knocking out the blaNDM-1 gene. The recombinant plasmid pcas9-sgRNA was transfered by electroporated at 1.8 kV, 200 Ω into three clinical isolates (2 Klebsiella oxytoca and 1 Escherichia coli). The knocking out efficiency of sgRNAs targeting conserved genes was tested. S1-PFGE was used to evaluated the difference between parent plasmids and the mutant plasmids. Furthermore, we also investigated the plasmids recombination by nanopore sequencing.

Results: The deletion of blaNDM-1 gene in three clinical isolates were successfully constructed with efficiency over 90%. In this study, we observed the 4 plasmids fused into 3 plasmids in the E.coli mutant, while in two Klebsiella oxytoca mutant, the size of plasmids which original carrying blaNDM-1 gene reduced 100k and 10k, respectively. Moreover, sequencing results revealed that different transposons, insertion sequences, and recombination sites increased the variability of knockout results.

Conclusions: CRISPR/Cas9 can be used to efficiently sensitize clinical isolates to carbapenem in vitro. For isolates with multiple plasmids, the CRISPR/Cas9 approach can cause plasmid recombination. Moreover, this approach can be used to delete the mobile elements containing the resistance gene by using only one sgRNA. However, caution must be exercised to avoid unwanted recombination events during genetic manipulation. There is still challenge to practice these methods in field against emerging antimicrobial resistant pathogens.

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Evaluation of a highly specific sample-to-result real-time PCR assay for detection and typing of *Bordetella pertussis*, *Bordetella parapertussis* and *Bordetella holmesii* in nasopharyngeal aspirates, nasopharyngeal swabs and sputum samples

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¹Bambino Gesù Children’s Hospital, IRCCS, UOC Microbiology, Virology and Parasitology, Rome, Italy

**Background:** Whooping cough is a worldwide infectious disease occurring after transmission of the bacteria from person-to-person in airborne droplets caused by *Bordetella pertussis* (BP), *Bordetella parapertussis* (BPP) and *Bordetella holmesii* (BH). Despite of vaccination, incidence reported is increasing in Europe, with severe consequences in children under five. Pertussis diagnosis is mostly done using molecular methods, but the detection of multiple targets is essential to differentiate *Bordetella* spp. This study describes the performance of the multiplex Real-Time PCR assay “Bordetella ELItE MGB® Kit” in association with ELItE InGenius® instrument, the first fully automated sample-to-result solution, for highly sensitive BP, BPP and BH detection and typing, in nasopharyngeal aspirates, nasopharyngeal swab and sputum.

**Materials/methods:** The performance evaluation studies on Bordetella ELItE MGB® Kit were carried out in association with ELItE InGenius® instrument. The diagnostic validation studies were performed by Bambino Gesù Children’s Hospital, IRCCS (Rome, Italy) after ethic committee approval on 30 positive samples and 30 negative samples of nasopharyngeal aspirates, nasopharyngeal swab and sputum. Sample analysis is on-going.

**Results:** Bordetella ELItE MGB® Kit preliminary LoD ranged between 12 and 45 CFU / mL depending on the pathogen. Inclusivity was verified on 11 different strains and cross-reactivity on 18 different pathogens of respiratory tract. Test with “QCMD 2016 Bordetella pertussis EOA Panel” (Qnostics) allowed the correct detection and identification of all species including BH typing. The preliminary diagnostic specificity was 95% in respiratory sample. The preliminary diagnostic sensitivity was tested by analyzing IS481 positive samples and resulted 100%. Furthermore, the assay allowed the differentiation of one BH positive sample. The turnaround-time was about 150 minutes.

**Conclusions:** Bordetella ELItE MGB® Kit in association with ELItE InGenius instrument constitutes a highly specific and sensitive system for rapid detection and typing of BP, BPP and BH in one single PCR reaction. This innovative solution overcomes limitations of culture and serological methods for the diagnosis of Bordetella infection and simplifies the laboratory workflow by reducing testing turnaround time from days to hours.

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Meta-analysis of accuracy of rapid influenza antigen detection tests in community-care settings accounting for antigen type, setting, population and manufacturer

Elisa Gentilotti1, Eleonora Cremonini1, Pasquale De Nardo1, Anna Gorska1, Fulvia Mazzaferr1, Mical Paul2, Herman Goossens3, Evelina Tacconelli1

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Abstract third-party references: This work has received support from the EU/EFPIA/bioMérieux SA, Janssen Pharmaceutica NV, Accelerate Diagnostics S.L., Bio-Rad Laboratories, BD Switzerland Sarl, and The Wellcome Trust Limited. Innovative Medicines Initiative 2 Joint Undertaking VALUE-Dx grant n° 820755.

Background: Evidence on the performance of point-of-care rapid influenza antigen detection tests (RIADTs) is essential to inform public health and antibiotic policy interventions. As part of the VALUE-Dx Project, we performed a systematic review and meta-analysis to determine the diagnostic accuracy of RIADTs in community-care settings.

Materials/methods: Multiple electronic databases were searched to identify published studies assessing the diagnostic accuracy of immunochromatographic RIADTs for influenza A and B virus in patients presenting with influenza-like illness at a community-care settings including primary care (PC), outpatient clinic (OC), long-term care facility (LTFC), and emergency room (ER). Viral culture and/or PCR were considered as reference standard. A bivariate random-effects model and hierarchical summary receiver-operating characteristic (HSROC) were used to estimate the pooled accuracy for influenza. Subgroup analyses were conducted by antigen type, age group, study year, WHO region, and commercial kits.

Results: After titles/abstracts screening and full-text eligibility assessment, 40 articles reporting 84 studies (56, 67% assessing influenza A and 28, 33% B) in 19,790 patients were included. The majority of studies were performed in the ER (47, 56%). No study was run in LTFCs neither tested influenza B in PC. Sensitivity ranged from 0.24 [0.17; 0.33] to 1.00 [0.91; 1.00] for influenza A and from 0.22 [0.12; 0.36] to 0.97 [0.93; 0.99] for influenza B. Specificity ranged from 0.76 [0.63; 0.87] to 1.00 [0.98; 1.00] for influenza A and from 0.90 [0.85; 0.93] to 1.00 [0.99; 1.00] for influenza B. The pooled sensitivity and specificity were 0.66 [0.59; 0.72] and 0.99 [0.99; 1.00] for influenza A and 0.53 [0.41; 0.65] and 0.99 [0.99; 1.00] for influenza B. Setting and commercial kits were the most relevant sources of heterogeneity as detailed in table.

Conclusions: RIADTs in community-care settings showed high specificity and considerable variability in sensitivity by setting and commercial kits. The pooled sensitivity seems slightly better for the detection of influenza A rather than B. These results seem to suggest that inclusion of RIADTs in clinical algorithms in community-care settings during the influenza season should consider sources of heterogeneity for appropriate cost effectiveness analyses and inclusion in stewardship interventions.

Table. Subgroup analysis.

<table>
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<td>71.2</td>
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<td>55.6</td>
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<td>97.9</td>
<td>72</td>
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<td>Emergency department</td>
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<td>93.0</td>
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<td>Outpatient clinic</td>
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<td>67.2</td>
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Abstract 4629

**Surface ocular microbiome in dry eye syndrome: a preliminary study**

Claudio Foschi¹, Piera Versura², Clarissa Consolandi³, Marco Severgnini³, Maria Carla Re¹, Antonella Marangoni*¹

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**Background:** Dry eye syndrome (DED) has become the most common ocular surface disease throughout the world. Dry eye is a multifactorial condition of the tear and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damages to the eye. The bacterial composition of the ocular surface (microbiome) has been considered among the components involved in the pathogenesis of DED. In this explorative study, we assessed the composition of the surface ocular microbiome in patients with DED, comparing the traditional culture-based techniques with new genomic approaches.

**Materials/methods:** Five lower conjunctiva swabs (E-swab, Copan) were obtained from as many patients with DED. The patients attended the Outpatient Clinic of Ophthalmology of S. Orsola-Malpighi University Hospital in Bologna (Italy) and were subdivided in two groups, on the basis of clinical signs and symptoms: moderate dryness (n=3) and severe dryness (n=2). Swabs were cultured in different solid media and grown bacterial colonies were identified by means of MALDI-TOF mass spectrometry. In parallel, ocular samples were subjected to nucleic acid extraction for amplification and sequencing of V3-V4 regions of bacterial 16s rRNA gene. Obtained reads were filtered and clustered into Operational Taxonomic Unit (OTUs) at 97% identity level. Taxonomic assignment was performed via the RDP classifier against the Greengenes database.

**Results:** By means of 16s rRNA gene sequencing, the microbial composition of the ocular surface proved to be rich in different bacterial genera, including several anaerobes, with a significant diversity between subjects. Lactobacillus, Corynebacterium and Staphylococcus genera accounted for 20-50% of all the microorganisms detected. Patients with severe dryness were characterized by significantly higher levels of Propionibacterium compared to subjects with moderate dryness (p=0.03). With the conventional culture-based approach, only a few bacterial genera were recovered, especially staphylococci and corynebactria.

**Conclusions:** The surface ocular microbiome in patients with DED is characterized by a high diversity in the bacterial composition, being enriched in anaerobic bacteria. 16s rRNA gene sequencing is far more sensitive than traditional culture-based methods in revealing the complexity of the ocular environment.

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Epidemiology and dissemination of multidrug-resistant *Pseudomonas aeruginosa* colonisation in an intensive care unit

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**Background:** Multidrug resistant *Pseudomonas aeruginosa* (MDRPA) is an emerging problem due to the global spread of defined high-risk clones. ST175 is associated with serotype O4 and 2 MALDI-TOF peaks and its underlying resistance mechanism is mostly mutational. We aimed to study the epidemiology of ICU patients who acquired MDRPA in order to develop specific control strategies.

**Materials/methods:** Patients admitted to the ICU at the Complejo Hospitalario de Navarra from January to November 2019 had weekly perianal culture samples collected. Swab samples from the ICU tap drains were collected for the detection of carbapenemase-producing strains. We defined: a) admission-positive patients when had positive cultures at ICU admission for MDRPA; b) acquisition-positive patients when had negative cultures at ICU admission but a subsequent positive culture for MDRPA; and c) endogenous microbiota when had susceptible *P. aeruginosa* at ICU admission but a subsequent MDRPA with identical PFGE patterns was detected. We characterized the resistance mechanisms by molecular PCRs. We characterized MDRPA strains by PFGE, MLST, serotyping and MALDI-TOF biomarker peaks.

**Results:** Our cohort consisted of 1867 perirectal swabs with 255 isolated *P. aeruginosa*, of which 64 (25%) were MDRPA. MDRPA were isolated in 23 patients. 2 patients were admission-positive and 21 patients were acquisition-positive MDRPA. Among the acquired MDRPA, 4 (19%) were acquired by the patients' endogenous microbiota and 17 (81%) during their stay at ICU. ST175 was the main clone detected among the 14 patients with acquired MDRPA. We detected a VIM-2 carbapenemase cluster among 2 patients and 1 tap drain samples and another VIM-2 carbapenemase cluster among 1 patient and 3 tap drain samples.

**Conclusions:** Most of MDRPA at ICU were acquired. Though cross-transmission plays the main role in MDRPA acquisition in our ICU, we cannot define them as patient-to-patient transmission without excluding an undiscovered reservoir. In fact, in 3 (14%) patients the VIM transmission was through tap drains. Therefore, it is important to implement active surveillance of MDRPA clones. Serotyping and MALDI-TOF are useful tools for early detection of ST175. In order to avoid possible outbreak sources, surveillance measures to minimize the dissemination and cleaning of environmental foci should be implemented.

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Abstract 4633

No attributable mortality due to third generation cephalosporin resistance but common risk factors for mortality in patients with infections due to Enterobacteriaceae

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Background: Third-generation cephalosporin (3GC)-resistance in enterobacteriaceae (3GCRE) challenges antimicrobial stewardship and is a potential threat to patient safety. There is no data on infections due to 3GCRE on mortality in Mainland China. This study aimed at estimating attributable mortality from infections due to 3GCRE compared to 3GC susceptible enterobacteriaceae (3GCSE) in Dongguan City, 2017.

Materials/methods: We retrospectively analyzed data of patients from three tertiary-care hospitals with infections due to both 3GCRE and 3GCSE. We measured time-to-event from first infection until discharge, either all-cause mortality or discharge/transfer. Hospitalizations were censored at 30 days. A multivariate Cox proportional-hazards model was applied to estimate the effect of 3GCRE on all-cause mortality, adjusting for the following variables: age, gender, department type, bloodstream infection (BSI), seasons, and length of stay (LOS).

Results: 1667 patients with infections due to enterobacteriaceae were eligible for analysis, including 573 3GCRE patients and 1094 3GCSE patients, respectively. Among these, 49% (278/573) 3GCRE and 42% (460/1,094) 3GCSE patients were hospitalized in surgery; and 46% (262/573) 3GCRE and 43% (465/1,094) 3GCSE patients had a urinary tract infection. The proportion of 3GCRE was statistically significantly higher in patients with healthcare-associated infections compared to patients with community-acquired infections (P=0.009). All-cause mortality was 2% in both groups. There was no statistically significant difference in the multivariate survival analysis between the two groups (HR, 0.8; 95%CI, 0.4-1.6). However, gender (HR, 2.7; 95%CI, 1.4-5.2), BSI due to enterobacteriaceae (HR, 3.2; 95%CI, 1.5-6.8), and LOS >15 days (HR, 4.3; 95%CI, 1.6-11.5) were independently associated with all-cause mortality.

Conclusions: No attributable mortality from 3GCR was found. Actionable risk factors such as BSI and prolonged LOS were also identified in patients undergoing infections due to enterobacteriaceae.

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Comparative genomics and virulence of human and animal Streptococcus agalactiae (Group B Streptococcus)

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Background: Streptococcus agalactiae (GBS) is an important pathogen with a wide host range, causing sepsis and meningitis in humans, mastitis in cattle and streptococcosis in fish. This results in much medical and veterinary morbidities and a huge economic burden to both livestock and aquaculture industries worldwide. The outbreak of adult sepsis due to consumption of raw fish with serotype III, ST283 in Singapore establishes the zoonotic nature of GBS disease. We sought to identify strain clusters that have interspecies association by comparing genomes of GBS strains isolated from human and animal hosts, and to phenotypically characterize fitness and virulence of these strains in a murine infection model.

Materials/methods: Phylogenetic relationship among 828 non-duplicate strains with whole genome data available from the public domains, including sequencing of 249 GBS strains in this study, was analysed. A phylogenetic tree inferred from core genome alignments was produced using Roary and sequence types (STs) identified and linked on goeBURST. The fitness of GBS strains was examined by their generation time at 37 °C and 39 °C, and virulence evaluated in ICR 6-wk old mice inoculated with 10^7 cfu intraperitoneally and survival monitored for 10 days. ATCC12403 [ST23 serotype III] was included as control.

Results: Closely related strains between human and animal hosts were identified in three major clusters within CC103, CC283 and CC1 suggesting possible cross-species transmission. GBS strains implicated were CC103 (ST103, sLV ST651 from humans and cows); CC283 (ST283, sLV ST491 in humans and fishes); CC1 (ST1 and sLV ST2 in humans, cows, rodents). The mean generation times (n=25) of the CC strains ranged 43.1±10.0 to 71.8±2.4 min (individual strains ranging 35 – 86 min). Strains of CC1 (ST1 and 2) gave the shortest mean generation times at both temperatures as compared to CC103 and CC283 [p<0.001]. Murine infection model revealed 90% mortality with ST283 vs 0% in other ST types [p<0.01].

Conclusions: Evidence from comparative genomic analyses reveal interspecies transmission between human and animal GBS in three major clonal clusters; CC103, CC283 and CC1. GBS shows a wide variation in generation time, with CC1 revealing its fitness while CC283 remains most pathogenic among these clusters.

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Impact of rapid molecular detection of sepsis on time to optimal antimicrobial therapy in paediatric cancer patients at the National Cancer Institute, Egypt

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Background: The clinical microbiology laboratory plays a key role in the diagnosis of bloodstream infections (BSI). Reducing the time to microorganism identification and susceptibility is crucial to improving clinical outcome and subsequently reducing length of hospital stay and associated costs.

Materials/methods: This study was conducted at National Cancer Institute (NCI) on 120 pediatric cancer patients suspected to have sepsis according to a revised consensus conference definition in 2016 (Sepsis 3). Samples were sent to the microbiology laboratory during one year extending from December 2017 to December 2018. They were divided into two groups, group I to whom only blood cultures were done (n=60); while in group II, blood cultures and rapid molecular method for detection of sepsis were done (n=60). The test used was the hospital acquired infection real-time multiplex-PCR detection kit; which detects 21 different bacterial pathogens directly from venous blood sample. Bactec 9120 and Vitek-2 (Biomerieux, France) were used for the conventional blood culture testing.

Results: Compared to the conventional approach, using the rapid multiplex-PCR detection kit showed a significantly shorter turnaround time to identification. The median turnaround time for group I blood culture was 120 hrs with IQR (96-144 hrs) compared to 5 hrs with IQR (4-6 hrs) for (p value <0.001). Shift to optimal antimicrobial therapy was effectively achieved in 75% of patients in Group II compared to 48% of cases in group I (p value 0.003). All-cause mortality was lower in the multiplex-PCR group but the difference was not statistically significant (42% versus 50%, p = 0.360). There was agreement between the results of the multiplex-PCR detection kit and blood culture in 93.3% of isolates. Four isolates were detected only by the multiplex-PCR.

Conclusions: Sepsis is a time-dependent disease that requires early diagnosis and prompt appropriate treatment to improve prognosis. The benefits of rapid diagnosis of sepsis etiology are earlier adequate antimicrobial treatment and reduction of duration of hospital stay and mortality.

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**Abstract 4637**

**Evaluation of the performance of CSF pyrosequencing in the diagnosis of TB meningitis - a single-centre retrospective diagnostic accuracy study**

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**Background:** We evaluated the performance of pyrosequencing, a rapid genotypic test which detects TB and resistance to isoniazid, ethionamide, rifampicin, aminoglycosides and fluoroquinolones in 6 hours, directly on the CSF samples in the diagnosis of TB meningitis.

**Materials/methods:** This retrospective study was conducted in a tertiary care hospital in Mumbai from May 2017 to May 2019. 101 consecutive patients with physician suspected TB meningitis for whom CSF pyrosequencing was requested were studied. 1 patient with incomplete data was excluded. Lancet consensus case definition criteria were applied to classify patients into the following categories: Definite, Probable, Possible and Alternative diagnosis. Those with Definite TB meningitis were considered to have the disease, while those with alternative diagnosis were considered to not have the disease. Sensitivity, specificity, positive predictive value and negative predictive value of pyrosequencing was determined. The sensitivity of pyrosequencing was compared to MGIT culture and Xpert MTB Rif using chi square test. Statistical results were interpreted at 5% significance. Susceptibility concordance rate of pyrosequencing with MGIT culture DST and Xpert MTB Rif were determined.

**Results:** The study cohort comprised of 100 patients [Definite (n=33), Probable(n=20), Possible(n=30) and Alternative(n=17)] with 50% males [median age: 38 years (Range, 2-87 years)]. The sensitivity, specificity, positive predictive value and negative predictive value of CSF pyrosequencing to diagnose TB meningitis was 96.7%, 100%, 100% and 94.4% respectively. This test had a higher sensitivity [statistically insignificant] compared to Gene Xpert (96.7% vs 69.6%, p=0.12) and TBMGIT (96.7% vs 70%, p=0.16). This test was positive in all patients with probable meningitis, 95% (n=19/20) of whom showed good clinical response to treatment. Susceptibility concordance rate of pyrosequencing with MGIT culture DST(n=21/23) was 91.3% and with Xpert MTB Rif (n=22/23) was 95.6%.

**Conclusions:** CSF pyrosequencing facilitates early therapeutic decision making by confirming the diagnosis of TB meningitis and providing information on the mutations of the XDR-defining drugs, within 6 hours of the sample being collected. It is more sensitive than Xpert MTB Rif and MGIT culture and may be useful in cases where both these investigations test negative in true cases of TB meningitis.

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Activity of enmetazobactam in combination with cefepime in a murine urinary tract infection model challenged with an ESBL-producing isolate of Escherichia coli

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Background: Infections caused by extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae account for more than 20'000 deaths every year in the EU and US alone. Enmetazobactam (EMT) is a novel β-lactamase inhibitor belonging to the penicillanic acid sulfone class, targeting ESBLs. Enmetazobactam, in combination with cefepime (FEP), is currently being investigated in a Phase 3 randomized controlled trial in patients with complicated urinary tract infections or acute pyelonephritis. This study investigated the efficacy of FEP-EMT in a murine urinary tract infection model challenged with a cefepime-resistant, ESBL-producing isolate of Escherichia coli.

Materials/methods: C3H/HeJ mice carrying a spontaneous mutation in the Tlr4 gene at the lipopolysaccharide response locus rendering this strain highly susceptible to infections by Gram-negative bacteria were used in this study. Animals were infected with a bacterial suspension inserted via the urethra into the bladder. Treatment started 24 h post infection by subcutaneous administration of test article on a q8h schedule for two days. Bacterial burden was determined 48 h post infection in kidneys by quantitative agar plating. MICs were determined by broth microdilution with EMT at a fixed concentration of 8 µg/ml.

Results: Broth microdilution assays identified FEP and FEP-EMT MICs of >32 and 0.05 µg/ml for the CTX-M-15-producing E. coli isolate #2014-0032. This strain demonstrated a robust infection in kidney with a 1-log10 increase in bioburden within 48 h compared to pre-treatment. FEP at 10 mg/kg administered q8h reduced kidney bioburden by 0.3 log10 units compared to pre-treatment. EMT administered at ≥1 mg/kg q8h, in combination with FEP at 10 mg/kg q8h, reduced kidney bioburden by 2.0 log10 units compared to pre-treatment, which was comparable to meropenem (MEM) administered at 20 mg/kg q8h (Figure).

Conclusions: Enmetazobactam restores the efficacy of cefepime in a urinary tract infection model challenged with a cefepime-resistant, ESBL-producing isolate of E. coli. Cefepime-enmetazobactam may qualify as novel empiric carbapenem-sparing option for the treatment of serious Gram-negative infections in settings where ESBL-producers are suspected and/or prevalent.

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Comparable resistance levels between regional networks in the Netherlands
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Background: In 2016 the Dutch Ministry of Health, Welfare and Sport requested the formation of ten regional cooperative networks. The aim is to improve the collaboration between healthcare providers and healthcare facilities in order to prevent development and spread of antimicrobial resistance on a regional level. To identify targets for interventions, insight in the resistance at regional level is necessary.

Materials/methods: We used Dutch routine medical microbiological data from the Dutch national surveillance system for antimicrobial resistance (ISIS-AR). Data of general practitioners’ patients from 34 laboratories from which data were available for the full period from 2014 to 2018 were included. We calculated resistance percentages in diagnostic urinary isolates of E. coli (n=437338) and K. pneumoniae (n=52352) for co-amoxiclav, cefotaxime/ceftriaxone/ceftazidime, ciprofloxacin, fosfomycin, trimethoprim, co-trimoxazole, and nitrofurantoin. In diagnostic wound, pus, and skin isolates of S. aureus (n=20345) we calculated resistance levels for flucloxacillin (i.e. MRSA) and clindamycin. We investigated whether resistance levels within the regions showed a significant (p<0.05) and clinically relevant difference with the mean resistance in all regions combined for at least three years. Clinical relevance was defined based on expert opinion as a difference that was larger than the square root of the national resistance percentage.

Results: Resistance levels in E. coli for all agents were not different between regions. For K. pneumoniae we found a three year lower resistance only for fosfomycin in Noord-Brabant in the years 2015 (22 versus 31% in all regions combined), 2016 (14 versus 31%), and 2017 (15 versus 26%). For S. aureus only resistance to clindamycin was higher for three years in the region Noord-Holland West; 18 versus 8% in 2014, 15 versus 9% in 2016, and 18 versus 11% in 2018.

Conclusions: As expected, since the Netherlands is a small country and national treatment guidelines are used widely, we did not find regional variation for most of the investigated organism-antimicrobial agent combinations. The few observed differences may be a result of sampling policy or population factors for which no data are available in ISIS-AR, like use of antimicrobials or foreign travel. This needs further investigation within the regions.

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Abstracts 2020

Abstract 4642

Mapping the implementation of a clinical pharmacist-driven antimicrobial stewardship programme at a tertiary care centre in India

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Background: Evidence from many settings including the UK and USA supports the role of clinical pharmacists as integral part of antimicrobial stewardship programmes (ASP). However, in many parts of the world, including in India pharmacist roles in ASP remain unexplored. We describe the evolution and effect of the role of adding clinical pharmacists to a multidisciplinary ASP at a tertiary care teaching hospital in Kerala, India.

Materials/methods: Under the championship of the hospital medical superintendent a multidisciplinary ASP Committee including hospitalist, microbiologist and intensivist was established in February 2016. A bespoke training programme (including a 2-month rotation in the ASP Committee) was created by the ASP clinicians for Doctor of Pharmacy interns. The responsibilities assigned to the clinical pharmacists included: 1) review of antimicrobial prescriptions for appropriateness [right indication, right drug, right dose, right frequency and right duration]; 2) surveillance of reserved antimicrobials; 3) providing teaching and training on ASP; 4) lead ASP quality improvement initiatives (fig1). Inappropriate prescriptions were identified, presented, discussed at the ASP Committee and the recommendation was fed back to the clinical teams verbally and in written format by the clinical pharmacists.

Results: Results discussed are between February 2016 and February 2019. Out of 1326 prescriptions reviewed in the first year 56% (742/1326) were appropriate and 54% (318/584) were compliant with ASP recommendations. By third year of ASP implementation, appropriateness and compliance to recommendations increased to 80% (1752/2190) and 70% (227/325) respectively. The Anti tubercular therapy (ATT) stewardship implemented subsequently in June 2017 reviewed 157 prescriptions within a year, of which 61% (95/157) were appropriate and 42% (25/60) recommendations showed compliance. From June 2018 to February 2019, 72% (62/86) ATT prescriptions were appropriate and 58% (14/24) were compliant with ATT recommendations.

Conclusions: A clinical pharmacist driven ASP can be effective in implementing sustainable change in low- and middle-income countries (LMIC) such as India where the shortage of Infectious Diseases physicians’ specialty is a major impediment to ASP. The multidisciplinary model in this hospital has potential for scale up to other hospitals in India and LMIC.

Fig 1: Timeline showing the evolution of clinical pharmacist role in ASP

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Laboratory-confirmed influenza infection and acute myocardial infarction

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Abstract third-party references: Sanofi Pasteur

Background: Previous studies established an association between laboratory-confirmed influenza infection (LCI) and hospitalization for acute myocardial infarction (AMI). However, they did not focus on the elderly population, and lacked detailed laboratory measures.

Materials/methods: We used a self-controlled case-series design to evaluate the effect of LCI on hospitalization for AMI among Veterans Health Administration (VHA) patients. We included elderly Veterans (age ≥ 65 years) with LCI between 2010 through 2015. Patient-level data from VHA electronic medical records were used to capture laboratory results, hospitalizations, and baseline patient characteristics. Centers for Medicare and Medicaid Services fee-for-service files were used to capture hospitalizations that occurred at non-VHA facilities. Our analysis included laboratory test results on inflammation - white blood cells count (WBC), platelet activation - platelet count (PLT), age, and concurrent diagnosis of pneumonia. We defined the "risk interval" as the first 7 days after respiratory specimen collection, and the "control interval" as 1 year before and 1 year after the risk interval.

Results: We identified 391 hospitalizations for AMI that occurred within 1 year before and 1 year after a positive test result for influenza, of which 31 (31.1 admissions per week) occurred during the risk interval and 360 (3.5 admissions per week) occurred during the control interval. The incidence ratio of an admission for AMI during the risk interval compared to the control interval was 8.9 (95% confidence interval [CI], 6.2 to 12.8). No increased incidence was observed after day 7. In the subgroup analyses, risk for AMI was elevated among those with age above the median (75) at 11.9 (95% CI, 7.6-18.7), high WBC at 12.4 (95% CI, 7.0-22.1), and high PLT at 15.9 (95% CI, 3.6-70.4). Patients with a concurrent diagnosis of pneumonia had similar risk compared to those without at 8.4 (95% CI, 2.6-27.2).

Conclusions: We confirmed a significant association between LCI and AMI. The risk was elevated among patients of older age, those with high WBC or high PLT, suggesting a potential role for inflammation and platelet activation in the underlying mechanism.

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Abstract 4645

**Presence of multidrug-resistant bacteria on uniforms of healthcare professionals in healthcare settings in Cyprus: implications for targeted infection control interventions**

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**Background:** Multidrug-resistant bacteria (MDRB) constitute one of the most important issues in public health and their transmission within healthcare settings is a significant hazard for patients. To this end, healthcare professionals’ clothing has been shown to harbor pathogens that may contribute in increasing the risk of transmission. The aim of this study was to evaluate the presence of MDRB on HCP uniforms in Nicosia, Cyprus.

**Materials/methods:** Randomized, cross-sectional sampling of consenting HCP uniforms in 9 hospital wards and 7 long-term care facilities (LTCFs) in Nicosia, Cyprus, between April-August 2019. Sampling was conducted using sterile swabs pre-moistened in MRD (maximum recovery diluent), close to the end of the first shift, from both left and right pocket. Following enrichment in Brain Heart Infusion broth and overnight incubation at 37°C, isolated strains were identified and screened via standard microbiological methods; sensitivity testing was performed using the VITEK 2 system (bioMérieux). Personal hygiene and other habits recorded during interviews with HCP.

**Results:** Among 140 sampled HCP (69 from hospitals, 71 from LTCFs), a total of 33 MDRB were identified [Table]. Presence of MDRB was higher in LTCFs [n=22] compared to hospitals [n=11] [p=0.04]. No significant differences were found in years of experience or self-reported habits between HCP in hospitals and LTCF, such as hand hygiene frequency, place or frequency of uniform laundering, or visits to other wards.

**Conclusions:** In this study, we showed that HCP uniforms harbor MDRB and constitute a target for intervention to reduce the risk of MDRB transmission in Cyprus. We identified LTCFs as an important area for application of infection control measures, to reduce the burden of MDRB. Additional factors that could influence the presence of MDRB on HCP uniforms should be sought, in order to delineate further areas that could benefit from infection control.

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<th>MDRB</th>
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<td>MRSA</td>
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<td>ESBL</td>
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Chikungunya positive reference material based on lentiviral vector system for RT-qPCR assays

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**Background:** We use the lentiviral vector system to produce RNA positive reference materials for *in vitro* diagnostic assays. These materials solve the problem of many RT-qPCR assays in which the retrotranscription step is not evaluated, since the positive control is frequently a synthetic cDNA sequence. These novel controls allow us to evaluate the whole process, from nucleic acid extraction to PCR reaction. We report here the method for generation a positive reference material for Chikungunya virus, an emerging tropical RNA virus that should be handled under biosafety level 3 conditions. This non-infectious positive control, that mimic the wildtype virus, constitutes an endless source of Chikungunya positive sample and its management does not require any specific security measure.

**Materials/methods:** Lentiviral particles were generated by transfection of HEK 293T cells using second generation lentiviral system with lipid-based reagent FuGENE6. We also performed transfection without envelope vector as a method to increase the biosafety of the process, and we analyzed the effect on transfection efficiency. The transference vector contains fragments of the NS1, NS2, NS4, E3 and E1 genes of the Chikungunya genome, which are the most frequently used targets in qPCR assays. Supernatant was harvested at 48- and 72-hours post-transfection, centrifuged and filtered. Then it was extracted with the QIAamp Viral RNA Kit (Qiagen) and subsequently treated with DNase to remove residual plasmid DNA. The extracted RNA was amplified and quantified with “VIASURE Chikungunya Real Time PCR Detection Kit (Certest Biotec)”.

**Results:** The target concentration of the enveloped virus was 1,16E+10 copies/ml and 4,50E+09 copies/ml for supernatants collected at 48h and 72h, respectively. In the non-enveloped virus, the target concentration was 1,26E+10 copies/ml and 6,24E+09 copies/ml, respectively.

**Conclusions:** We have generated a replication defective and non-infectious positive control of Chikungunya virus to monitor the whole process of nucleic acid extraction and PCR. This control contributes to improve the diagnostic accuracy of the qPCR assays. We have also demonstrated that transfecting without the envelope vector does not affect the viral particle production. This standardized and optimized lentiviral system allows to create custom viral particles for a wide variety of pathogens.

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Abstracts 2020

Abstract 4648

The dissemination and molecular characterisation of clonal complex 361 methicillin-resistant Staphylococcus aureus in Kuwait hospitals, 2016-2018

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Background: Methicillin-resistant Staphylococcus aureus (MRSA) continues to pose serious problems among patients globally and in the Gulf Cooperation countries. Since being first identified in two patients’ samples in 2010, the prevalence of CC361-MRSA obtained from patients in Kuwait hospitals has increased significantly. The aim of this study was to determine the molecular characteristics of CC361-MRSA isolated from patients in Kuwait hospitals between 2016 and 2018 to understand its population dynamics

Materials/methods: Of 6945 MRSA isolates obtained from 2016-2018, 182 (2.6%) were identified as CC361-MRSA isolates by DNA microarray analysis. These isolates, obtained in 2016 [N=55], 2017 [N=56] and 2018 [N=71], from different clinical samples in 13 Kuwait hospitals were further analyzed using antibiogram and spa typing.

Results: Most of the isolates were from nasal (N=63) and skin and soft tissue infection samples (N=33). They were resistant to fusidic acid, trimethoprim and ciprofloxacin and harbored fusC and dfrS1. The isolates belonged to 22 spa types with t13841 (N=113), t315 (N=16), t1309 (N=14) and t1375 (N=5) comprising 81.3% of the spa types. The CC361-MRSA consisted of four genotypes [strain types] including CC361-MRSA-[V/VT+fus] (N=112), CC361-MRSA-V, WA MRSA-29 (N=36), CC361-MRSA-V, WA MRSA-70/110 (N=33) and CC361-MRSA-[V+fus] variant (N=1). All CC361-MRSA isolates were positive for capB, agr1, and the enterotoxin egc gene cluster (seg, sei, selm, seln, selo, selu) while, tst-1 was detected in 22 isolates only. The immune evasion cluster (IEC) genes type B (scn, cph, sak) and type E (scn, sok) were detected in 19 and 150 isolates respectively.

Conclusions: The study has provided evidence of an ongoing transmission of a newly emerged CC361 MRSA strains with CC361-MRSA-[V/VT+fus] as the dominant genotype. The dissemination of this clone can impose different challenges for control and treatment of MRSA infections in Kuwait hospitals. Therefore, understanding the MRSA population dynamics might contribute to the development of effective approaches to control this important pathogen.

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Abstract 4651

Different age distribution of influenza B virus infection by lineage
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Background: Determining the age-specific distribution of influenza B virus infection can be helpful for establishing an infection control and prevention strategy for influenza virus, including a proper use of a tetravalent influenza vaccine.

Materials/methods: Between the 2015-2016 and 2018-2019 influenza seasons, rapid influenza diagnostic tests were performed in 13,853 patients, and 3,437 (24.8%) of them were positive for influenza viruses. Excluding 94 patients with concomitant influenza A and B virus infection, the remaining 3,343 patients (influenza A infection in 2,223 [66.5%] and influenza B virus infection in 1,120 [33.5%]) were included in this study, and their medical records were retrospectively reviewed. The median ages were compared between patients with influenza A virus infection and those with influenza B virus infection.

Results: As a whole, the median age of patients with influenza B virus infection was significantly lower than that of patients with influenza A virus infection (8 years vs 13 years, \(P<0.001\)). In influenza seasons when influenza B/Victoria lineage was dominant, the median age of patients with influenza B virus infection was still significantly lower than that of patients with influenza A virus infection (6 years vs 11 years, \(P<0.001\)). In seasons when influenza B/Yamagata lineage was dominant, the median age of patients with influenza B virus infection was not significantly different from that of patients with influenza A virus infection (14 years vs 27 years, \(P=0.155\)), but significantly higher than that of patients with influenza B virus infection in seasons when influenza B/Victoria lineage was dominant (14 years vs 6 years, \(P<0.001\)).

Conclusions: The different age distribution of influenza B virus infection by lineage seems to be resulted from different virological characteristics and infectivity of two influenza B virus lineages according to the host’s age.

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Abstract 4656

Paving the way for the implementation of a decision support system for antimicrobial prescribing in primary care in West Africa: a workshop with healthcare professionals

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Abstract third-party references: Supported by Antibioclic

Background: Clinical decision support systems (CDSS) for antimicrobial prescribing have been devised to provide the prescriber with rapid access to updated information. In low- and middle-income countries, introduction of CDSS for antimicrobial prescribing could have measurable impact. However, pre-implementation research is needed to ensure that CDSS are adapted to the context in which they are deployed and are adopted in routine clinical care.

Materials/methods: Our objective was to study the requirements for a CDSS for antimicrobial prescribing in primary care adapted to the context of West Africa and to analyse the barriers and facilitators to its use. We aimed to discuss the expected consequences and potential risks of implementing a CDSS and to co-design solutions.

Results: There were 47 participants in the workshop, 19 women and 38 men representing 9 West African countries and 6 medical specialties. Most of the participants had access to a smartphone during consultation (n=35, 74%) but only 49% had access to a computer and none used a CDSS for antimicrobial prescribing. The participants considered that a CDSS could have positive consequences such as improving clinical care and reducing AMR, updating the knowledge of practitioners on antimicrobial prescribing, encouraging the development of national guidelines and developing surveillance capabilities in primary care. The CDSS should be tailored to the local epidemiology of infectious diseases and AMR and to the availability of diagnostic tests and antimicrobials using national guidelines where available. A procedure of co-design with health professionals involved in antibiotic prescribing including nurses, midwives and pharmacists was encouraged. The participants suggested to first implement the CDSS in a pilot site and to disseminate the tool using traditional professional networks and social media. The lack of widespread internet access and computers could be circumvented by the development of a mobile application with an offline mode. The participants pointed the risk of self-medication in West Africa where antibiotics can be bought with no prescription and underlined the need to regulate access to antibiotics.

Conclusions: Our study provided valuable information to develop and successfully implement a CDSS for antimicrobial prescribing among primary care prescribers in LMICs.

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Abstract 4657

**Performance of the Xpert Carba-R assay versus the ChromID CARBA SMART for the detection of carbapenemase-producing Gram-negative bacteria from rectal swabs**

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**Abstract third-party references:** Supported by a Health Services Development Grant (19N01) from the Ministry of Health, Singapore

**Background:** Direct-from-sample real-time PCR assays allow rapid detection of carbapenemase-producing Gram-negative bacilli (CPGNB), but are limited by targets included in the assay. Culture-based methods are mechanism-agnostic, but require confirmatory testing for carbapenemase-production, and have longer turn-around-times. We evaluated the Xpert Carba-R real-time PCR assay and the ChromID CARBA SMART chromogenic agar (followed by the carbapenem-inactivation method (CIM) / conventional PCR) in parallel for the detection of CPGNB.

**Materials/methods:** From April-September 2019, 15,843 surveillance rectal swabs (ESwab, Copan) were submitted for CPGNB screening. Swabs were subject to the Carba-R assay (which detects \( \text{bla}^{KPC} \), \( \text{bla}^{NDM} \), \( \text{bla}^{OXA-48-\text{like}} \), \( \text{bla}^{IMP} \), and \( \text{bla}^{VIM} \)), and ESwab liquid Amies media was cultured on each side of the ChromID biplate. GNB isolated on ChromID were subject to MALDI-TOF MS, susceptibility testing (Vitek). Enterobacteriales (carbapenem non-susceptible) were subject to an in-house conventional PCR for \( \text{bla}^{KPC} \), \( \text{bla}^{NDM} \), \( \text{bla}^{OXA-48-\text{like}} \), \( \text{bla}^{IMI} \) and \( \text{bla}^{IMP} \) test. All meropenem-resistant non-fermenting GNB were subject to the mCIM/CIM-Tris test. Two different ‘gold-standards’ [GS] were evaluated: “GS1”: One where a true positive was considered as any sample with a positive Xpert result OR a positive ChromID result (defined as an Enterobacteriales with a carbapenemase confirmed by conventional PCR); “GS2”: Which in addition to the definition of GS1, incorporated a positive mCIM/CIM-Tris test for non-fermenting GNB as a true positive.

**Results:** A total of 432 (2.7%) of samples were positive for CPGNB (122 OXA-48 type, 94 NDM, 51 IMP, 14 IMI, 9 KPC, 18 multiple genotypes, 107 positive mCIM/CIM-Tris); 338 (46.1%) were Enterobacteriales, 283 (38.6%) were non-fermenters, 112 (15.3%) were PCR-positive only. The sensitivity of Carba-R and ChromID, based on the two gold standards GS1 and GS2 were as follows:

<table>
<thead>
<tr>
<th></th>
<th>GS1 (95% CI)</th>
<th>GS2 (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td><strong>Specificity</strong></td>
<td><strong>Sensitivity</strong></td>
</tr>
<tr>
<td>Carba-R</td>
<td>92.3 (88.7-94.8)</td>
<td>100 (98.8-100)</td>
</tr>
<tr>
<td>ChromID</td>
<td>42.2 (36.8-47.7)</td>
<td>100 (98.8-100)</td>
</tr>
</tbody>
</table>

**Conclusions:** The Carba-R assay was found to be more sensitive than a culture-based algorithm. However, the specific gold standard used can affect the interpretation of test performance. Specifically, algorithms which omit phenotypic testing for carbapenemase production or screening of non-fermenting GNB (obtained on culture) will underestimate the true magnitude of CPGNB in one’s institution.

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Abstract 4659

CRISPR/Cas9 targeting of essential herpes simplex virus type 1 genes impairs virus replication in the mammalian cell

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Background: Herpes simplex virus type 1 (HSV-1) is a widespread human virus. According to the WHO, the virus infects nearly 67% of world’s population. In the majority of primarily infected individuals HSV-1 becomes latent and resistant to all antiviral drugs. Moreover, new drug-resistant HSV strains have emerged, which urges the search for new therapeutic strategies. Genome editing technology using CRISPR/Cas9 system has been proposed as one of the perspective approaches. CRISPR/Cas9 system expressed from lentiviral vectors effectively suppresses HSV infection in a cell model. However, safety issues can arise from integrative mutagenesis of lentiviral vectors and accumulation of mutations associated with a long-term action of permanently active CRISPR/Cas9 system. In addition, cell protection against HSV provided by lentivirus-expressed CRISPR/Cas9 is lost after 24 h. This instigates further search for other effective and safe vectors and means of CRISPR/Cas9 targeting. Our goal was to evaluate the ability of CRISPR/Cas9 expressed from plasmids targeted at various HSV-1 genes to suppress HSV-1 infection in cells.

Materials/methods: The following CRISPR/Cas9 plasmids were used: empty PX458 vector coding for SpCas9 and structural fragment of sgRNA, and the vector derivatives with cloned spacers against ICP0, UL8, UL29 and UL52 HSV-1 genes. The plasmids were transfected into Vero cells using Lipofectamin 3000, and cytotoxicity was assessed by MTT assay. Then transfected cells were infected with HSV-1 and quantified by immunocytochemical staining using an anti-gB monoclonal antibody.

Results: Transfection with CRISPR/Cas9 plasmids has shown high effectiveness (>50%) in Vero cells with low cytotoxicity (>70% live cells in transfected population). Plasmids encoding for a single spacer against dispensable ICP0 gene did not inhibit HSV-1 infection in Vero cells, while plasmids encoding for two spacers and targeting CRISPR/Cas9 system at HSV-1 replication complex genes (UL8-UL29 and UL52-UL29) decreased the percentage of infected cells up to 16.5-25%. One of the plasmids targeted at UL52-UL29 genes provided a 100% inhibition of HSV-1 infection for 48 h and up to 6 days.

Conclusions: The results obtained indicate that plasmid-expressed CRISPR/Cas9 system is a perspective candidate for the development of new therapeutic strategies to combat herpesviral infections.

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Presentation, outcomes and relapse rate of patients admitted with Plasmodium vivax malaria in Karachi, Pakistan

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Background: Plasmodium vivax is the most geographically widespread species of malaria, with most cases originating from India, Pakistan, and Indonesia. There has been an increase in the severity and the number of P. vivax malaria cases in Pakistan. Moreover, relapse rates in this part of the world may vary from the South East Asian and African strains of P. vivax. We, therefore, performed a cross sectional study of patients admitted with P. vivax malaria to assess the severity of disease, outcomes and relapse rates.

Materials/methods: A retrospective cross-sectional study at a 700-bedded tertiary care hospital in Karachi, Pakistan was performed. Case files of all adults admitted with P. vivax malaria [on smear or ICT], between 2007-2016 were reviewed. Patients with co-infection with P. falciparum were excluded from the study. Severity based on the WHO definitions, treatment strategies and inpatient outcomes were assessed. Patients were contacted after discharge to assess if a relapse had occurred.

Results: A total of 539 admissions in 522 patients were assessed. Most admissions occurred between August and September (34.8%). Males were more likely to be admitted (M:F ratio 349:189) and the average age was 40.7 years. A total of 168 cases (31.2%) were assessed to have severe malaria with an overall mortality of 1.5% (n=8). High dependency care [HDU] was required by 110 patients (20.4%). The most common markers of severity were hemoglobinuria, renal failure, jaundice, acidosis and bleeding. Compared with those without severe malaria, patients with severe malaria were more likely to have diarrhea, be admitted to the HDU and had a higher mortality. Of the survivors, there were 95 patients with relapses (18.2%) of which 16 (16.8%) required readmissions.

Conclusions: Severe malaria was not uncommon in P. vivax malaria admitted to a tertiary care hospital in Karachi Pakistan and was associated with increased mortality and requirement for high dependency care

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**Abstract 4664**

**An outbreak of hepatitis A among young adult men in Cyprus**

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**Background:** Outbreaks of Acute Hepatitis A (AHA) have recently been reported in Europe among men who have sex with men (MSM). Clinicians of our team observed a notable increase in hospitalized AHA cases in Cyprus, during the second semester of 2017. The aim of this work was to evaluate, for the first time, trends in the reported cases of AHA in Cyprus over the last six years.

**Materials/methods:** We retrospectively studied all people reported with AHA to the Unit for Surveillance and Control of Communicable diseases of the Cyprus Ministry of Health between January 2013 and December 2018. Demographic data, type of transmission, vaccination status for HAV, laboratory and clinical data were analyzed.

**Results:** The analysis involved 33 AHA cases (age 32.7 ±17.4 years, 78.8% males). An increase in AHA reports was observed between July 2017 and June 2018 when more than a third (n=13) of the cases of the period 2013-2018 were reported. The distribution of the 33 cases in the six-year period, is presented in Figure 1. The cases reported between July 2017 and June 2018 were young men and four identified themselves as MSM. The reporting rate of AHA doubled from 0.52 cases per 100,000 population (before July 2017) to 1.12 cases per 100,000 population (July 2017-June 2018). The male/female (M/F) ratio increased from 1 in 2013 to 8 in 2018. All patients were negative for HIV infection by serology and one was diagnosed with syphilis at the same time. One patient with AHA during the first semester of 2017, just before the outbreak, was taking pre-exposure prophylaxis. One patient, who was simultaneously diagnosed with chronic hepatitis B, developed fulminant hepatic failure and had a successful liver transplantation. Another patient, with history of obesity, developed fulminant hepatitis A and died.

**Conclusions:** An increase in AHA reports occurred in Cyprus between July 2017 and June 2018. Many cases with AHA in that period were MSM. Enhanced surveillance of cases with AHA and timely public health interventions, like vaccination and awareness promotion, are important for preventing future outbreaks.

**Figure 1**

![Distribution of patients in semesters](image)

MSM: Men who have sex with men

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Characterisation of Neisseria gonorrhoeae isolates using a core-genome multilocus sequence typing scheme

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Background: Recent reports point to a dramatic increase in antibiotic-resistant Neisseria gonorrhoeae (NGO), but there are scarce data regarding NGO in Germany. We investigated the antimicrobial susceptibility and molecular epidemiology of NGO using a core-genome MLST (cgMLST) scheme on isolates from patients with symptoms of urethritis reporting to the University of Cologne between 11/2015 - 11/2019.

Materials/methods: In total, seventy-seven isolates were collected. Susceptibilities to azithromycin, cefotaxime, ciprofloxacin, penicillin, and tetracycline were determined by Etest. Molecular epidemiology was investigated using an ad-hoc cgMLST scheme based on 1567 alleles (Ridom® SeqSphere+). Genome sequences were queried for antibiotic resistance genes and to determine 7-loci MLST.

Results: Seventeen isolates were fully susceptible to all the antibiotics tested. Non-susceptibility based on EUCAST breakpoints (ECOFF of 1mg/L for azithromycin) was; cefotaxime (n=4), azithromycin (n=6), tetracycline (n=27), ciprofloxacin (n=45), and penicillin (n=46). Twenty-two isolates were non-susceptible to 1 antibiotic, thirteen were non-susceptible to 2 antibiotics, and twenty-five were non-susceptible to ≥ 3 antimicrobials, and we consider them to be multidrug resistant (MDR). At least one antibiotic retained activity against each isolate. Tetracycline MICs ≥ 8mg/L were associated with tetM-like. Ciprofloxacin resistance was associated with GyrA substitutions. blaTEM-1 and penA variants were detected in many isolates, but this was not always associated with penicillin or cefotaxime resistance, or elevated beta-lactam MICs. Seven-loci MLST revealed 21 sequence types (ST), two of which were represented by 11 isolates; ST-7363 and ST-8156. cgMLST delineated isolates further, and split ST-7363 into two separate clusters separated by 730-753 allelic differences. Generally there were several hundred alleles different between STs, but there are exceptions, with as low as 14 alleles different between STs, highlighting the limitations of 7-loci typing. We detected nine possible transmission clusters involving 2-4 patients where isolates were separated by ≤ 10 allelic differences, including four clusters with ≤ 2 differences.

Conclusions: cgMLST allowed us to differentiate between isolates with the same ST. We detected nine potential transmission events. Almost one third of isolates were MDR, with five of the transmission events involving these MDR isolates. Cefotaxime retained good activity against N. gonorrhoeae from the Cologne area.

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Evaluation of the potential clinical impact of BioFire FilmArray Pneumo Plus for the treatment of VAP in intensive care unit patients, Careggi University Hospital, Florence

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Background: Ventilator-associated pneumonia (VAP) is the most frequent nosocomial infection in ICUs, accounting for almost 50% of all antibiotic prescriptions. The administration of inappropriate initial antibiotic therapy is associated with greater mortality and longer hospital stay. More precise and rapid microbiologic diagnostic approaches for suspected VAP are urgently needed to guide optimal therapeutic choices. In this study we evaluated the accuracy and the potential clinical impact of BioFire® FilmArray® Pneumo Plus (FAP) compared to the standard of care (SoC).

Materials/methods: From December 2018 to February 2019, in all consecutive adult ICU patients with suspected VAP, an endotracheal aspirate was collected and sent to the laboratory for rapid microbiologic testing with FAP. The results were compared with the SoC, represented by quantitative cultures. For viral target detections, the decision whether to confirm the result with a different molecular assay was left to the judgement clinicians. The potential clinical impact of FAP was evaluated registering the changes to the empiric antibiotic therapy that could have been possible based on its results.

Results: Fifty-seven samples from 37 patients were analysed. One test (1.8%) resulted invalid. A full concordance between the two methods was observed in 25/57 (43.9%) samples. FAP detected an additional bacterial target in 31/57 samples (54.4%) and a genetic marker for methicillin resistance in 2/10 samples positive for S. aureus, resulted methicillin susceptible by SoC. There were not cases of bacterial targets missed by FAP. Fourteen viral targets were detected from 13/57 (22.8%) specimens, with Influenza virus A being the most frequent. In one case, the detection of a viral target by FAP was not confirmed by SoC. Antibiotic adjustments to the empiric therapy could have been possible in 31/56 cases (55.4%); escalation in 13/56 cases (23.2%) and de-escalation in 17/56 (30.4%). In 5 cases (8.9%), escalation would have included an antiviral agent.

Conclusions: FAP allows for a rapid and reliable detection of common pathogens for VAP in lower respiratory tract specimens. The use of FAP in patients with suspected VAP could shorten the time to a targeted and effective antibiotic treatment, reducing the inappropriate or unnecessary use of antibiotics.

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Absence of the Type I-E CRISPR-Cas system in *Klebsiella pneumoniae* clonal complex 258 is associated with dissemination of *bla*<sub>KPC</sub> plasmid in this clonal complex

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**Background:** *Klebsiella pneumoniae* carbapenemase (*KPC*)-producing *K. pneumoniae* (*KPC-KP*) have disseminated worldwide and emerged as major threats to public health. Of epidemiological significance, the international pandemic of *KPC-KP* is primarily associated with CG258 isolates and the related *bla*<sub>KPC</sub>-IncF plasmids. The CRISPR-Cas system is an adaptive immune system that can hinder gene expansion driven by horizontal gene transfer (HGT), including the spread of antibiotic resistance. Because *bla*<sub>KPC</sub>-IncF plasmids are favored by CG258 *K. pneumoniae*, it was of interest to examine the co-distribution of CRISPR and acquired *bla*<sub>KPC</sub>-IncF plasmids in CC258 *K. pneumoniae* lineages.

**Materials/methods:** The prevalence of CRISPR-Cas and *sdhCDAB* operon were investigated among 203 whole-genome sequences in GenBank and 459 clinical isolates of *K. pneumoniae*. The real-time PCR was performed to measure the expression of relative genes and the promoter activity was determined by β-galactosidase assay. The conjugation assay, plasmid stability experiments and plasmid-loss examine were applied to evaluate the function of CRISPR-Cas system in *K. pneumoniae*.

**Results:** We observed that the type I-E CRISPR-Cas system was significantly scarce in the CG258 lineage (*p* < 0.0001) and the associated host-factor (*sdhCDAB*) in these isolates differed from other *K. pneumoniae*. We demonstrated that the CRISPR-Cas system in *K. pneumoniae* could effectively hindered *bla*<sub>KPC</sub>-plasmid invasion and existence and most IncF *bla*<sub>KPC</sub>-plasmids in this study were proved to be good targets of CRISPR. Furthermore, for the first time, *sdh* was experimentally shown to be a CRISPR activator. Intriguingly, the *sdh* mutations in CG258 *K. pneumoniae* also affected the CRISPR activity, the function of mutant *sdh* is weaker. This regulatory mutation impacted the CRISPR inhibition of *bla*<sub>KPC</sub>-plasmid propagation in *K. pneumoniae*.

**Conclusions:** Overall, our work suggests that the CRISPR-Cas system, coupled with a robust activator, may play a role in antagonizing the occurrence of *bla*<sub>KPC</sub>-IncF plasmids in strains not belonging to CG258, providing a new perspective on the tricky connection between *K. pneumoniae* CG258 and *bla*<sub>KPC</sub> dissemination.

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Abstract 4673

**Antimicrobial screening of 2208 UK isolates (2003-2018) using novel Legionella Medium (LASARUS)**

Edward Anthony Reginald Portal*1, Kirsty Sands1, Baharak Afshari2, Victoria Chalker2, Brad Spiller1

1Cardiff, Division of Infection and Immunity, Cardiff, United Kingdom, 2Public Health England, London, United Kingdom

**Background:** Epidemiological Cut-Off Values (ECOFF) are not available for Antimicrobial breakpoint thresholds for Legionella. This is due to variance in Antimicrobial Sensitivity Testing (AST) results from Broth MicroDilution (BMD) and BCYE solid media. The presence of activated charcoal in BCYE media removes growth inhibitors but also chelates Antimicrobials affecting results. LASARUS (Legionella Antimicrobial Susceptibility And Resistance Universal Screening), a new charcoal-free solid medium, was validated against BMD and BCYE for Legionella AST determination. The first line therapeutic for Legionella spp. is azithromycin. The presence/absence and mutations in commonly associated genes with decreased susceptibility to Antimicrobials were investigated.

**Materials/methods:** Initial MICs for a reference panel of 10 L. pneumophila strains and 45 representative clinical isolates were determined in quadruplicate on BCYE traditional agar, LASARUS agar and compared to published gold-standard BMD methods. AST for 2208 clinical and environmental Legionella isolates (2003-2018) were performed using an automated multipoint inoculator on LASARUS agar on a 2-fold series of antimicrobial dilutions (Table 1). MIC confidence intervals and distribution were analysed by GraphPad Prism; isolates with higher MIC values were identified. Preliminary Whole Genome Sequencing (WGS) (Illumina, MiSeq) was carried out on 40 strains with elevated azithromycin MICs to determine underlying mechanisms. Fastq files were assembled by SPAdes v3.9.0 and analysed by srst2 using ARGannot resistance gene database and Geneious prime to identify resistance-mediating somatic mutations.

**Results:** LASARUS showed complete concordance for MIC50 and MIC90 values to BMD. BCYE MIC values were higher (up to 32-fold). MIC50 and MIC90 are given in Table 1 for the complete 2208 isolate archive. Between 1-11% of isolates for each antimicrobial showed elevated MICs. WGS analysis of 40 of the elevated azithromycin MIC isolates identified the lpeAB gene, for first time identified in the UK. No 23S rRNA, L4 or L22 mutations were identified and the presence of ermA, ermB, ermC, ermF, mphA, ereA or ereB genes were not found.

**Conclusions:** LASARUS gave concordant results to BMD, unlike BCYE, and is suitable for high-throughput automated AST determination. The gene lpeAB is present in UK isolates of L. pneumophila with elevated MIC to azithromycin.

<table>
<thead>
<tr>
<th>Antimicrobial tested</th>
<th>( \text{MIC}_{50} ) (µg/mL)</th>
<th>( \text{MIC}_{90} ) (µg/mL)</th>
<th>Range (µg/mL)</th>
<th>( \text{CI}_{95%} ) Range (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>0.03</td>
<td>0.06</td>
<td>0.008-0.06</td>
<td>0.04</td>
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<td>0.008</td>
<td>0.002-0.008</td>
<td>0.005</td>
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<td>0.016-1</td>
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<td>0.25-2</td>
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<tr>
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</tbody>
</table>

**Presenter email address:** portale@cf.ac.uk
Abstract 4674

**Mortality in patients with Staphylococcus aureus bacteraemia and the implications of Staphylococcus aureus bacteriuria for in-hospital: results of a monocentric retrospective cohort study**

Tobias Kramer*1,2, Beate Schlosser1,2, Frank Schwab1,2, Desiree Gruhl1, Michael Behnke1,2, Petra Gastmeier1,2, Rasmus Leistner1,2

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**Background:** Staphylococcus aureus bloodstream infection (SA-BSI) is an infection with elevated risk for morbidity and mortality. Concomitant Staphylococcus aureus bacteriuria (SABU) frequently occurs in patients with SA-BSI. The clinical implications are still under investigation. In this study, we investigated the role of SABU in patients with SA-BSI and its effect on the patients mortality.

**Materials/methods:** We performed a retrospective cohort study that included all patients at the three hospital of our university medical center (Charité Universitätsmedizin Berlin) between January 1, 2014 and March 31, 2017. We included all patients with positive blood cultures for *Staphylococcus aureus* who had a urine culture taken 48 hours before or after sampling of the first positive blood culture. We identified cases using the microbiology database and collected additional demographic and clinical parameters retrospectively from patient files and charts. We conducted univariate analyses and multivariable logistic and Cox regression analyses to evaluate risk factors for in-hospital mortality.

**Results:** Of 1139 Patients with SAB 202 patients met the eligibility criteria. Overall, 55 patients (27.5%) died during their hospital stay. Multivariable analyses showed that SABU (OR 2.2; 95%CI:1.04-4.54) and a Pitt Bacteremia Score of >1 [OR 6.11; 95%CI:2.91-12.81] as well as moderate to severe liver disease [OR 2.96; 95%CI: 1.09-8.04] were independent risk factors for in-hospital mortality.

**Conclusions:** Our data indicates that SABU in patients with concurrent SA-BSI is a prognostic marker for in-hospital death. Further studies are needed to evaluate implications for therapeutic optimization.

Cox proportional hazards regression of patients with SA-BSI.

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Abstract 4678

Clinical and bacteriological outcome in urinary tract infections caused by ESBL-producing Enterobacterales and characterisation of isolated pathogens: a prospective, multi-centre study

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Background: Oral treatment options are scarce for urinary tract infections (UTIs) caused by ESBL-producing *E.coli* and *Klebsiella spp.* and there is limited evidence to support therapeutic decisions. This study aimed to assess current treatment strategies for these infections, clinical and bacteriological outcomes, and phenotypic and genotypic characteristics of the causative bacteria.

Materials/methods: A prospective, multicentre, observational cohort study was conducted at 15 sites in Sweden during 2014-2017. Patients diagnosed with UTI and significant growth of ESBL-producing bacteria in urine were included. Clinical and bacteriological cure after 10–14 days and relapse within three months upon completion of therapy was assessed. When possible, the isolated bacteria were collected and subjected to MIC determination and genotypic characterisation using whole-genome sequencing.

Results: 236 cases (108 febrile UTI, 128 lower UTI) caused by *E. coli* (*n*=221) and *Klebsiella spp.* (*n*=15) were included. The median duration of therapy for febrile UTI was 10 days. Clinical and bacteriological cure rates were 84% and 81%, respectively. Intravenous treatment was administered ≥4 days in 57% of the cases, while 32% of the patients were prescribed only oral antibiotics. Pivmecillinam was prescribed as oral follow-up [median duration 6 days] in 20 cases following intravenous treatment [median duration 4 days]; no treatment failure was observed in this group. For lower UTI, the median duration of treatment was 5 days. Clinical and bacteriological cure rates were 81% and 85%, respectively. Clinical cure was achieved in 80% (*n*=49) of patients treated with pivmecillinam alone and in 79% (*n*=53) of patients treated with nitrofurantoin alone. Clinical success was lower in complicated and recurrent UTI. Relapse occurred in 15% of the patients. Aminoglycoside resistance genes were detected in 146 of 169 tested isolates. All but two *E.coli* strains had at least one adhesin gene; among them, ST131 was the most common. ST131 was associated with treatment failure and relapse, while ST69 was associated with clinical cure.

Conclusions: Clinical and bacteriological cure rates were generally high in this cohort despite that non-evidence-based treatment was frequently used. Co-morbidities, recurrent infection and ST131 were associated with a higher risk of treatment failure.

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Characterisation of biofilm formation by *Staphylococcus pseudintermedius* on a variety of medical devices

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Abstract third-party references: CNPq, FAPERJ, Bill & Melinda Gates Foundation, CAPES

**Background:** Health care-associated infections (HCAIs) are associated with biofilm-forming bacteria and represent a concerning problem difficult to eradicate. The genus *Staphylococcus* is responsible for majority of HCAIs cases not only in humans but in veterinary medicine as well. The capacity of biofilm formation is the main reason of persistent surgical site infection and is associated with implants in dogs, caused by *Staphylococcus pseudintermedius*, including methicillin susceptible and resistant strains (MSSP and MRSP respectively). MRSP can also be considered a public health problem, since zoonotic transmission can occur. The aim of the study was to evaluate the capacity of biofilm formation by *Staphylococcus pseudintermedius* in titanium orthopaedic material and different suture materials commonly used in small animal surgery, as well as genetically evaluate the biofilm formation.

**Materials/methods:** Sterile titanium nuts and four types of sutures were tested. Suture threads were aseptically cut into 1cm segments. Sterile titanium nuts and suture segments were incubated in tryptone soy broth supplemented with 1% glucose of standard suspensions of eight *S. pseudintermedius* isolates, in 24 well plate overnight. The biofilm production was measured by optical density (OD) after vortexing of each suture segment and titanium nuts. Then were stained with safranin, in triplicate. Bacterial adherence to suture and titanium nuts were assessed by use of scanning electron microscopy. The genes associated with biofilm formation (*icaA* and *icaD*) were identified by PCR.

**Results:** In nylon suture, all isolates were classified as non biofilm producers, but in polyglycilic acid, all isolates were able to form biofilm. In cotton, 75% (6/8) were biofilm producers and 12,5% (1/8) were biofilm producers in polypropylene. Seven isolates (87,5%) were able to form biofilm in titanium nut and only one isolate (12,5%) was classified as non biofilm producer. PCR revealed the presence of the two genes (*icaA* and *icaD*) in all the isolates.

**Conclusions:** Was observed the biofilm formation in orthopaedic material composed of titanium. Biofilm formation was observed in several types of suture, especially cotton and polyglycolic acid. There was no biofilm formation in nylon suture. All the samples evidenced the presence of the *icaA* and *icaD* genes.

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Patients presenting with malaria: are we missing opportunities to screen for other travel-associated infectious diseases?

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**Background:** British Infection Association malaria guidelines do not incorporate guidance on any tropical or travel screening. 85% of UK cases are acquired through travel to Africa, predominantly among people of African origin visiting friends and relatives¹. Screening of newly arrived migrants for HIV, hepatitis B, hepatitis C, strongyloides and schistosomiasis is recommended as it is likely to be cost-effective². We sought to determine if it is similarly cost-effective to screen patients who present with malaria.

**Materials/methods:** All cases of malaria diagnosed between January 2017 and December 2018 were identified from our in-patient electronic system. Electronic patient records were interrogated for serological results for HIV, hepatitis B, hepatitis C, strongyloides, schistosomiasis and filariasis. For cases with positive serological tests, notes were reviewed to determine treatment and follow-up.

**Results:** Over the 2-year period 131 patients were diagnosed with malaria through our emergency department. Malaria was acquired in Africa 127 (97%), mainly West Africa (90%). 111 (85%) patients underwent HIV screening; 4 (4%) positive – all were known to have HIV, and 2 (2%) indeterminate results. 98 (75%) underwent hepatitis B surface antigen screening; 7/98 (7%) positive, 5 were known and 2 were new but lost to follow-up. 44 (34%) were tested for hepatitis C IgG; all were negative. 37 (28%) had strongyloides serological screening; 3/37 (8%) positive and treated and 2/37 (5%) borderline reactive serology which were negative on repeat testing. 27 (21%) were tested for schistosoma antibodies; 4/27 (15%) positive of whom 2 were treated and 2 did not attend follow-up, and 2/27 (7%) borderline positive serology which were negative on repeat testing. 3 (2%) had filaria antibody screening; all negative. Of 14 cases aged <16 years, 2 (14%) were screened for BBV, and 1 (7%) for strongyloides and schistosomiasis.

**Discussion:** The rates of HIV, hepatitis B and hepatitis C in our local population are 0.012%, 0.5% and 1.2% respectively³. Our findings suggest seroprevalence to be 250 times and 14 times higher for HIV and hepatitis B respectively as well as significant rates of strongyloides and schistosoma seropositivity, suggesting presentation with malaria is an opportunity to cost-effectively screen for these treatable infections.

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Population-based incidence and mortality of community-acquired pneumonia in Germany

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Abstract 4684

Background: Representative data on the burden of community acquired pneumonia (CAP) in adult pneumococcal vaccine eligible populations in Germany are currently scarce.

Materials/methods: Rates of CAP population-based incidence and mortality were estimated in a retrospective cohort study using a representative healthcare claims database of approx. 4 million insured persons in 2015. Incidence according to the base case was estimated by a CAP ICD-10 code in the first coding position or a CAP ICD code in the second position in combination with a sepsis diagnosis in the first position. Outpatient CAP was defined as a CAP ICD code plus an antibiotic prescription within 7 days after incident diagnosis. Chronic underlying illness predisposing to pneumococcal disease (at-risk conditions) were defined according to STIKO.

Results: Incidence rates of CAP are described in the table. In adults ≥60 years, the incidence of hospitalized CAP was underestimated by the base case compared to the diagnosis of CAP in the primary or secondary positions (Sensitivity analysis 1; IR: 1061 vs. 1560). In contrast, incidence of outpatient CAP that required a chest x-ray confirmation underestimated CAP incidence compared to the base case (Sensitivity analysis 2; IR: 1053 vs. 413). The 30-day and 1-year CAP mortality rates was 24.5% and 47.4% in adults aged ≥60 years and 8.6% and 15.0% in at-risk adults aged 16 to 59 years.

Conclusions: The burden of CAP among adults eligible for pneumococcal vaccination in Germany remains high and mortality rates in our analysis exceeded those previously reported. Using sensitive case definitions is key to obtain full estimates of the CAP burden. Effective pneumococcal vaccination strategies for the prevention of CAP and its associated mortality is needed.

Table. Incidence rates (IR) of community-acquired pneumonia in Germany per 100,000 PYO in 2015

<table>
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<tr>
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<th>16 – 59 at risk</th>
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<th>≥18 years</th>
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<td>Hospitalized CAP</td>
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<tr>
<td>Base case</td>
<td>151</td>
<td>140-164</td>
<td>1061</td>
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<tr>
<td>Sensitivity analysis 1</td>
<td>199</td>
<td>185-213</td>
<td>1560</td>
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<tr>
<td>Outpatient CAP</td>
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<td></td>
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<tr>
<td>Base case</td>
<td>807</td>
<td>780-835</td>
<td>1053</td>
</tr>
<tr>
<td>Sensitivity analysis 2</td>
<td>ND</td>
<td>ND</td>
<td>413</td>
</tr>
<tr>
<td>Overall CAP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base case</td>
<td>937</td>
<td>908-967</td>
<td>2032</td>
</tr>
</tbody>
</table>

Sensitivity analysis 1: Base case PLUS same diagnosis codes in 2nd position. Patients with 2nd ICD-10 code indicating hospital-acquired pneumonia OR a hospital discharge ≤ 7 d were excluded. Sensitivity analysis 2: Base case PLUS health claim of chest x-ray, MRT or CT-scan in the same quarter.

Presenter email address: christof.voneiff@pfizer.com
Quantiferon-TB Gold Plus: comparison of interferon-γ detection by ELISA and CLIA assay

Giulia Lombardi1, Francesco Bisognin1, Silvia Felici1, Paola Monari1, Eleonora Gatti1, Maria Carla Re1, Paola Dal Monte*1

1S. Orsola-Malpighi University Hospital, Microbiology Unit - Department of Experimental, Diagnostic and Specialty Medicine, Bologna, Italy

Background: Latent tuberculosis infection (LTBI) is defined as a state of persistent immune response to Mycobacterium tuberculosis complex (MTBc) without clinically manifested evidence of active TB disease. About 1.7 billion people worldwide are estimated to have LTBI, and are thus at risk of developing active TB disease during their lifetime. Two tests are available for the identification of LTBI: the tuberculin skin test (TST) and the interferon gamma (IFN-γ) release assays (IGRAs). They represent indirect markers of MTBc exposure and indicate a cellular immune response to MTBc. Among IGRAs, Quantiferon-TB Gold Plus (QFT-Plus, Qiagen) measures IFN-γ released by T-cell (both CD4+ and CD8+) following stimulation by MTBc-specific antigens. Aim of this study was to compare the results of QFT-Plus obtained by ELISA with those obtained with chemiluminescence immunoassay (CLIA) on the LIAISON XL analyser.

Materials/methods: In this comparative study, 197 Quantiferon-TB Gold Plus blood samples were processed in parallel for IFN-γ detection with the routinely ELISA method (on the SKYLAB automated system, DASIT) and with CLIA system on the LIAISON XL (DiaSorin). For each patient, IFN-γ results from the 4 tubes (Nil, TB1, TB2 and Mitogen) were combined in a single qualitative (positive, negative and indeterminate) result according to manufacturer’s instruction; IFN-γ quantitative values of each tube were also recorded.

Results: Among 197 samples processed with ELISA, 20 were not tested by LIAISON due to insufficient blood volume in one or more tubes. On the remaining 177 samples, the overall agreement between ELISA and CLIA assays was 89.8% (κ=0.822). Among discordant results, 2 ELISA positive samples became Indeterminate with CLIA for high level of IFN-γ in the Nil tube; 3 negative ELISA samples (in the grey zone) became positive with CLIA; and 12 of 25 indeterminate ELISA samples for a low IFN-γ level in the Mitogen, became determinate, with a negative result, with CLIA.

Conclusions: IFN-γ detection by chemiluminescence assay on the LIAISON XL analyser is more sensitive than ELISA. Within the linearity range of the test, the LIAISON system detects higher quantitative values than ELISA assay.

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Abstract 4686

**Maraviroc in PML-IRIS associated with immunotherapies: a case series**

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**Background:** Rise of the use of immunosuppressing therapies for treatment of chronic inflammatory diseases have been associated with an increase of progressive multifocal encephalopathy (PML) cases. Treatment of PML consist in restoration of antiviral immunity that may be complicated by an immune reconstitution syndrome (IRIS). IRIS is caused by massive entry of CD8 T cells (mainly bearing the CCR5 chemokines receptor) that would clear JC virus but also lead to a disproportionate tissue damage. Maraviroc, a CCR5 antagonist, have been proposed to prevent or treat IRIS. In this work, we aimed to assess maraviroc efficacy in PML-IRIS associated to immunotherapies.

**Materials/methods:** We retrospectively collected clinical and radiological data of cases from 8 university hospital in France and one in Switzerland. We performed a meta-analysis of cases reported in the literature. Primary endpoint was clinical aggravation after maraviroc introduction.

**Results:** We identified 19 cases in France/ Switzerland and 6 from the literature. Among them 16 met inclusion criteria [12 cases from our cohort and 4 from the literature]. All patients develop PML in relation with immunosuppressive treatment for chronic inflammatory diseases [15 multiple sclerosis, 1 rheumatoid arthritis]. Mean age at onset was 43.2 [33-61]. PML presented clinically in half of cases and have been detected on control MRI in the other half. Onset was progressive in most cases (62,5%) and not associated with radiological hallmarks of inflammation (eg, Gadolinium enhancing lesions, 69%). In 50% of patients Maraviroc was introduced to prevent IRIS/ Inflammatory PML and for the rest of them to treat it. In most of them Maraviroc was given in association with corticosteroids. However, despite maraviroc 7/16 (44%) patients met primary endpoint of neurological worsening. There was no differences between prevention and treatment group. Only 2 patients (12.5%) died, one from PML progression and the other one from hematological neoplasia.

**Conclusions:** Overall, this study provide non strong evidences to support the use of maraviroc in PML-IRIS.

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Respiratory pathogens detected in children with community-acquired sepsis-like syndrome in 6 European countries

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Abstract third-party references: PREPARE Project Group, funded by the European Commission under FP7

Background: The management of infants admitted to hospital with sepsis-like syndrome (SLS) without apparent focus remains challenging. There is growing evidence indicating that this clinical picture is triggered by viral pathogens, like adenovirus, enterovirus or parechovirus with a possible respiratory point of entry. We aimed to identify an association in the presence of respiratory pathogens in nasopharyngeal swabs between children with SLS and controls.

Materials/methods: A total of 102 children (≤ 6 months old) admitted to hospital with community-acquired SLS and 308 asymptomatic controls (0-6 years old) were enrolled in a prospective case-control study as part of the MERMAIDS Trial (Multi-centre EuRopean study of MAjor Infectious Disease Syndromes, www.prepare-europe.eu) in 12 hospitals in 6 European countries. The Fast Track Diagnostics Respiratory pathogens 21 plus real-time PCR assay was used to determine the presence of respiratory pathogens in nasopharyngeal swabs.

Results: The most prevalent respiratory viral targets detected in the nasopharyngeal swabs of SLS patients were rhinovirus (28%), RSV A/B (9%), enterovirus (8%) and parainfluenzavirus (5%). All other viruses (influenzavirus, coronavirus, parechovirus, human metapneumovirus, adenovirus and bocavirus) were detected in <5%. Also bacterial targets like Staphylococcus aureus and Streptococcus pneumoniae, possibly colonizers, were often detected, both in 30% of the samples. Neither Mycoplasma pneumoniae, Chlamydophila pneumoniae nor Haemophilus influenzae type B were present. Compared to the control group, enterovirus and RSV A/B were detected more frequently in the SLS patients (8 versus 2% for enterovirus, p=0.01 and 9 versus 2% for RSV A/B, p=0.01). Adeno- and bocavirus were found more often in the control group (7 versus 1% for both viruses, p=0.02). No respiratory target was detected in 25% of the SLS samples.

Conclusions: Most (75%) of the nasopharyngeal samples from SLS patients contained one or more viral or bacterial respiratory targets. In our study, the role of influenza viruses was relatively limited. The possible role of enterovirus and RSV A/B in the pathophysiology of SLS should be further elucidated.

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Abstract 4692

Gene expression pattern analysis using dual-color RT-MLPA and integrative genome-wide association studies of expression quantitative trait loci (eQTL) for tuberculosis susceptibility

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Abstract third-party references: On behalf of Jing-wen Ai

Background: When infected with Mycobacterium tuberculosis, only a small proportion of the population will develop active tuberculosis, and the role of host genetic factors in different tuberculosis infection status were still not fully understood.

Materials/methods: Forty-three active tuberculosis patients and 49 latent tuberculosis infection individuals were enrolled in the prospective cohort. Expressing levels of 27 candidate mRNAs, which were previously demonstrated to differentially transcript between latent and active tuberculosis, were measured by dual color reverse transcription multiplex ligation dependent probe amplification assay (dcRT-MLPA). Using expression levels of these mRNAs as quantitative traits, associations between expression abundance and genome-wide single nucleotide polymorphisms (SNPs) were calculated. Finally, identified candidate SNPs were further assessed of their association with tuberculosis infection status in the validation cohort of 313 Chinese Han population.

Results: We identified 9 significantly differentially expressed mRNAs including il7r, il4, il8, tnfrsf1b, pgm5, ccl19, il2ra, marco and fpr1 in the prospective cohort. Through expression quantitative trait loci mapping, we screened out 8 SNPs associated with these mRNAs and CG genotype of the SNP rs62292160 was finally verified to be significantly associated with transcription levels of il4 in tuberculosis patients (Figure 1).

Conclusions: We reported that the SNP rs62292160 in Chinese Han population may link to the regulation expression of il4 in tuberculosis. Our findings provided new genetic variation loci for further exploration of the mechanism of tuberculosis and a possible target of tuberculosis genetic susceptibility studies, which might aid the clinical decision to precision treatment of tuberculosis.

Figure 1 (A). Manhattan plot. The expression levels of mRNAs were associated with single nucleotide polymorphisms. The p value of green plots was less than E\(^{-05}\). Figure 1 (B). Regulatory network of mRNAs and SNPs related genes. The genes were surrounded by a red rectangle and the RNAs were surrounded by a blue rectangle. Seven genes and 9 mRNAs were in this network. Figure 1 (C). We validated the identified 8 SNPs and the histogram was performed to show the variations of selected SNPs in active tuberculosis (ATB) and latent tuberculosis infection (LTBI) patients. The rs62292160 had significant differences in ATB and LTBI patients.

Presenter email address: jingwenai1990@126.com
The urinary pharmacokinetics of nitrofurantoin in patients with uncomplicated urinary tract infections: interim analysis

Rixt Anna Wijma1, Birgit Koch1, Teun Van Gelder1, Eva Van Haren2, Huda Karim2, Sander Croes3,4, Anouk Edwina Muller*1,5
1Erasmus University Medical Center, Rotterdam, Netherlands, 2University of Utrecht, Utrecht, Netherlands, 3Maastricht University Medical Center, Maastricht, Netherlands, 4CAPHRI-Care and Primary Health Research Institute, Maastricht University Medical Center, Maastricht, Netherlands, 5Haaglanden Medical Center, The Hague, Netherlands

Background: Nitrofurantoin was registered for uncomplicated urinary tract infections (UTI) in 1954. At that time, a structured process of drug development was not yet mandatory. As a consequence, nitrofurantoin is being prescribed based on very limited data supporting the currently used dosing regimen. A better knowledge of the pharmacokinetic (PK) properties would help to achieve optimal dosing regimens. Our aim was to investigate and compare the urinary PK profile of nitrofurantoin in two commonly used dosing regimens in patients with uncomplicated UTI.

Materials/methods: Urine samples were collected during 24 hours in 13 females who were prescribed nitrofurantoin 50 mg q6h (Macrodantin®/Furadantin®), and in 7 patients who were prescribed 100 mg q12h (Macrobid®/Furabid®) by their treating general practitioner for the treatment of an uncomplicated UTI. Nitrofurantoin concentrations in urine were quantified by UHPLC-UV. PK analysis was performed by PKSolver® using non-compartmental analysis.

Results: Mean peak concentrations of nitrofurantoin in urine after 100 mg were higher compared to those after 50 mg (104.2 mg/L ± 74.7 versus 84.7 mg/L ± 64.6), but the range in maximum concentrations was comparable (0.7 mg/L to 257.7 mg/L). The AUC0-24h,ss was higher (931.5 mg.h/L ± 672.3 versus 881.9 mg.h/L ± 347.1) after the 100 mg dosing regimen. The slow-release effect of the 100 mg capsule, demonstrated as a delayed peak concentration, was observed but none of the PK parameters differed significantly between the dosing regimens. Urinary concentrations exceeded the EUCAST ECOFF of nitrofurantoin for Escherichia coli of 64 mg/L in only 10 out of 119 samples in the 50 mg group and in 9 out of 78 samples in the 100 mg group. In 8 patients (n=6 in the 50 mg group), concentrations never exceeded the ECOFF.

Conclusions: The urinary PK of nitrofurantoin was comparable between the two studied dosing regimens and therefore independent of the administered dose and formulation. The amount of nitrofurantoin administered might be too low, as urinary concentrations did not exceed the ECOFF for Escherichia coli in the majority of the samples. Additional PK studies as well as determination of the PK/PD target on Macrobid®/Furabid®, are needed.

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Abstract 4696

The transmission risk of multidrug-resistant organisms between pets and humans: an exploratory case control study protocol

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1Charité - Universitätsmedizin Berlin, Institut für Hygiene und Umweltmedizin, Berlin, Germany, 2Freie Universität Berlin, Department of Veterinary Medicine, Berlin, Germany

Background: This project aims to assess the relevance of pet husbandry in the colonization of multidrug-resistant organisms (MDROs) of hospital patients. Currently, the potential role of pets as reservoirs of MDROs is still unclear. The project focuses on the most common MDROs in pet owners, methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), 3rd generation cephalosporin-resistant Enterobacterales (3GCRE) and carbapenem-resistant Enterobacterales (CRE).

Materials/methods: To assess the contact to household pets as a risk factor for the colonization with one of the above named pathogens, we perform an exploratory, unmatched case-control-study. Among questions about well-known risk factors, study participants are queried regarding their contact to dogs and cats. This includes information about the number of pets in the household, the closeness of contact and diseases as well as medical treatment of the pets. To assess the genetic relatedness of the human and pet MDROs, we collect nasal and rectal swabs of the participants in the hospital and their pets to test them for MDROs. Phenotypically matching MDROs in the samples of participants and their pets will be tested for genetic relatedness using whole genome sequencing (WGS). The study is currently being performed at the Charité Universitätsmedizin Berlin. The sample size will comprise 4,000-6,000 human participants and aims at 1,000-1,500 animal samples. The study is funded by the Federal Department of Health (BMG).

Results: Among the first 958 participants, 39% (372/958) tested positive for MDROs. 54% (518/958) of participants were male and the mean age was 62 years (18-91 years). 13% of the participants (103/958) stated to own a dog, 9% (89/958) to own a cat. Among the first 112 returned pet samples, 6% (7/112) were positive for MDROs. In two cases MDROs of dog and owner were phenotypically matching. The matching pathogens were in one case VRE and the other case 3GCRE. Further preliminary results of the first 2,000 participants will be presented at the ECCMID 2020.

Conclusions: The investigation of pet husbandry as a risk factor for colonization or infection with MDRO in this study creates an opportunity to identify patients at risk and develop potential prevention strategies.

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Carbapenem-resistant *Pseudomonas aeruginosa* in cystic fibrosis children

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**Background:** Bronchopulmonary inflammation in cystic fibrosis children is predominantly associated with carbapenem-resistant (Carba-R) *P. aeruginosa*. It is an important global healthcare problem in pediatrics.

**Materials/methods:** *P. aeruginosa* isolated from lower respiratory tract of patients with cystic fibrosis in 2015-2016 were tested for susceptibility to meropenem and imipenem by the E-test method. Carba-R isolates with a meropenem minimum inhibitory concentration (MIC) >8 and/or imipenem MIC >4 were selected for further analyses. Carbapenemase carriage was detected by Real-time PCR. Sequence type (ST) was determined using multilocus sequence typing (MLST).

**Results:** In total, 75 *P. aeruginosa* isolates were collected; among them 29 (%) isolates were resistant to meropenem and/or imipenem. Only two isolates (7%) harbored *bla*<sub>VIM</sub>. The remaining 27 isolates were negative for *bla*<sub>VIM</sub>, *bla*<sub>IMP</sub>, and *bla*<sub>NDM</sub> carriage. Overall, MLST analysis revealed 20 STs. Five leading STs included ST235 (n=5; 17.2%), ST2595 (n=3; 10.3%), ST527 (n=2; 6.8%), ST798 (n=2; 6.8%), ST2464 (n=2; 6.8%) that collectively comprised 46% proportion of the collection. The remaining STs were represented by ST2758, ST2693, ST1621 (3.4%), ST1129 (3.4%), ST1062 (3.4%), ST882 (3.4%), ST845 (3.4%), ST649 (3.4%), ST612 (3.4%), ST446 (3.4%), ST362 (3.4%), ST252 (3.4%), ST244 (3.4%), ST189 (3.4%), ST9 (3.4%) (n=1 for each ST).

**Conclusions:** Carbapenem resistance in *P. aeruginosa* isolated from lower respiratory tract in cystic fibrosis children in Moscow was not associated with the presence of metallo-beta-lactamases. The *bla*<sub>VIM</sub> gene was detected only in 2 isolates which belonged to ST235. Five lineages including ST235, ST2595, ST527, ST798 and ST2464 dominated among Carba-R *P. aeruginosa* isolates.

The obtained results indicate that further studies are necessary for investigation of the carbapenem resistance mechanisms in *P. aeruginosa* isolated from patients with cystic fibrosis.

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Abstract 4701

Contribution of microbial virulence factors on mortality in adult patients with bacteraemia due to Escherichia coli presenting with sepsis/septic shock: exploratory analysis of the PROBAC-EC cohort

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Abstract third-party references: On behalf of PROBAC REIPI/GEIH-SEIMC/SAEI Group, Supported by Instituto de Salud Carlos III (PI16/01432)

Background: The objective of this study was to analyze the impact of some genotypic factors of E. coli on mortality in patients with bacteraemia and presentation as sepsis/septic shock.

Materials/methods: A prospective cohort of 143 patients with E. coli bacteraemia and sepsis/septic shock [2016 criteria] from 21 hospitals in Spain, and their blood isolates were analyzed. Whole genome sequencing (Illumina MiSeq Inc) was performed at University Hospital Virgen Macarena. The assembly was done with the CLC Genomic WorkBench (Qiagen) software. Sequence type (ST), virulence factors and antibiotic resistance genes were assessed in MLST 2.0, VirulenceFinder 2.0 and ResFinder 3.2 databases, respectively. A multivariate model only including clinical and epidemiological variables was built by logistic regression; then, individual and grouped microbial genes and STs were added in a stepwise manner. The predictive ability of the models on observed data were measured with the area under the ROC curve with 95% confidence intervals (CI).

Results: Mortality at day 30 was 32.9% (47 patients). Isolates were grouped into 60 clonal groups, ST1 31 (n=21; 14.7%), ST69 (n=17; 11.9%), ST73 (n=14 9 8%) and ST95 (n=9; 6.3%), and 17 (11.8%) isolates were ESBL-producers. The multivariate model for mortality predictors with epidemiological and clinical variables included [OR; 95%CI]: non-urinary source (4.63; 2.06-10.42), Pitt score ≥3 (2.34; 1.05-5.12) and inactive empirical therapy (5.68; 1.37-23.47); the AUROC of this model was 0.74 (95%CI, 0.66-0.82). Microbial factors with a univariate P value <0.2 were added; the best fitted model included the presence of genes that codes for thermostable enterotoxin 1 (astA) (adjusted OR; 95%CI=4.98; 1.10-22.8) and long polar fimbrial protein (lpfA) (4.35; 0.97-19.4) as factors associated with increased risk of death, and the secreted enterotoxin (sehB) [0.19; 0.04-0.77] as protective; the AUROC for this model was 0.83 (95%CI, 0.76-0.91). No better prediction was achieved by including specific sequence types.

Conclusions: These preliminary results suggest that, in patients with bacteraemia and sepsis/septic shock due to E. coli, some specific microbial factors may significantly contribute to mortality. Additional studies are required to characterize the pathophysiological role of this virulence factors in the mortality in patients with sepsis/septic shock due to E. coli.

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Abstract 4704

Increased fusidic acid resistance among *Staphylococcus aureus* skin and soft tissue infections in Portugal

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**Background:** Fusidic acid (FD) is a first-line antibiotic widely used topically for the treatment of *Staphylococcus aureus* skin and soft tissue (SSTI) and eye infections. Resistance to FD is mainly due to the acquisition of either resistance genes (*fusB, fusC*, and *fusD*) or mutations in the housekeeping *fusA* or *fusE* genes. In Europe, resistance was reported in 10% of infection *S. aureus*, but in Portugal, where FD is commonly prescribed in the community and available over the counter, there is no data regarding prevalence and resistance mechanisms.

**Materials/methods:** To fill this gap, a retrospective collection of infection and carriage *S. aureus* isolated in Portugal were screened for FD resistance: (a) 204 methicillin resistant *S. aureus* representative of the major infection clones in hospitals between 1985 and 2016; (b) 86 *S. aureus* responsible for SSTI in children (n=32) and adults (n=54) in the community and (c) 153 *S. aureus* carriage strains from nasal swabs of homeless individuals (n=44) and nursing students (n=109). FD resistance was confirmed by disc diffusion and microdilution determination of the minimum inhibitory concentration (MIC). Resistance genes were detected by PCR and *fusA* and *fusE* mutations were identified by DNA sequencing.

**Results:** The global prevalence of FD resistance was 7% (31 out of 443 strains). Resistance was more prevalent in SSTI (15.1%, p=0.0033), namely in adults (20.4%, 11 out of 54 strains), and among infection strains (13.4%, p<0.0001). *fusC* was the prevalent determinant, detected in 71% of the resistant strains associated to MICs between 8-16 µg/mL. Five strains showed mutations in the *fusA* gene and a single strain carried *fusB*. Screening of *fusE* mutations is being performed on the remaining three strains that showed none of the previous mechanisms. Half of *fusC* strains (50%) belonged to the Pediatric clone (ST5-IV-t311/t062), whereas *fusB* was associated to the European clone (ST80-IV-t044).

**Conclusions:** In Portugal, resistance to FD in *S. aureus* is mainly related to SSTI in adults (20.4%), highly associated to specific clones and mostly due to the presence of *fusC*. A continuous monitoring of resistance is warranted to ensure the efficacy of FD in the antibiotherapy of SSTI.

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Acceptability of a public commitment charter associated with patient information leaflets on antibiotics by general practitioners

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Abstract third-party references: ARS Grand Est

Background: Antibio-Charte is a randomised controlled study aiming at evaluating the effectiveness of a toolkit promoting antibiotic stewardship on antibiotics prescribed by general practitioners (GPs) in a French northeast region. This intervention concerned 109 high prescribing French general practitioners (GPs) from October 2017 to September 2018 and included a public commitment charter, a non-prescription pad and a patient information leaflet to be used when antibiotics were prescribed.

Materials/methods: A qualitative study was performed on a sample randomly selected from the 109 GPs included in the intervention group. The semi-directed interview’s guide contained open-ended questions organised around three main themes: their use of each of the three tools, their perception about these tools, and the impact of the intervention on the relationship with patients. Interviews were transcribed and a comprehensive thematic analysis was performed.

Results: A total of 30 GPs were interviewed. The interviews revealed that the intervention was not considered as time-consuming but the GPs’ adherence was sub-optimal. The public commitment charter, displayed in the waiting room, had not created a sense of commitment in GPs as expected. Out of the three provided tools, the non-prescription pad was the most appreciated one although not systematically used. It was perceived as helpful in case of patient pressure to obtain antibiotics. A poster version of the non-prescription pad to be displayed near the consultation bed was often requested. The patient information leaflet to be used when antibiotics were prescribed was perceived as redundant with the prescription and was significantly less used. Some GPs declared being in doubt regarding the effectiveness of the intervention on their antibiotic prescribing while others expected a significant impact.

Conclusions: The perceived usefulness and declared use of the three different documents that were part of the intervention differed significantly. The impact of the intervention on antibiotics prescribed by GPs will be assessed in the near future.

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Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) are among the leading causes of opportunistic infections in human and veterinary medicine worldwide. 33 MRSA isolated from feral and companion animals with *mec* C as the resistance determinant attracted our attention by presenting a broad range of different phenotypes during routine diagnostics. Since *mec* C-MRSA are commonly associated with cattle farms, wastewater, human, wild animals and the environment, we hypothesized that phenotype variation might foster survival of non-epidemic MRSA in these particular niches. To unravel the genomic background and putative accessory gene regulator (*agr*) system variations associated with the divergent phenotypes, we thoroughly investigated the animal *mec* C-MRSA comparatively with 12 closely related isolates of human origin.

Materials/methods: Altogether 45 *mec* C-MRSA were characterized by whole-genome sequence analysis using MLST-1.6, ResFinder-2.1 and VirulenceFinder-1.6 provided by Center for Genomic Epidemiology in Denmark, while Geneious was used to comparatively investigate the isolates’ genomic make-up, including *agr* encoding regions and mobile genetic elements. Phenotype characterization included hemolysis assays, a colony spreading test and biofilm formation capabilities. We also measured protein expression of α-(Hla), β-(Hlb) and δ-hemolysin (Hld) using proteomics.

Results: The 45 isolates were found to belong to clonal complexes (CC) 599, CC49, CC130 and CC1943. While each of the CC investigated was associated with a different accessory gene regulator type (*agr* I-IV), isolates within each lineage displayed different levels of *agr* functionality including completely non-functional variants, resulting in a broad variety of phenotypes. Comparison of the regions encoding *agr* I-IV showed broad range of variation among the isolate collection for each CC, especially among the isolates of animal origin. Functionality of the *agr* system corresponded with differences in protein expression of hemolysins, especially for Hld. Biofilm capabilities differed depending on the assay employed.

Conclusions: Since adaptation is a major driver for genomic changes occurring independently in divergent lineages, our results presumably indicate that *agr* variation may enhance viability and niche adaption capacities of *S. aureus* lineages aside of the epidemic lineages, which are widespread among (wild) animals and the environment, including MRSA. Further research on the impact of phenotypic variation of *mec* C-MRSA is warranted.

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Impact of diagnostic and antimicrobial stewardship on time-to-appropriate therapy and clinical outcomes in infections caused by carbapenem-resistant Gram-negative organisms

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Background: Carbapenem-resistant Gram-negative organisms (CRGNOs) cause life-threatening infections and incidence is rising globally. Timely effective therapy in these infections has a direct impact on patient survival. We aimed to determine the impact of diagnostic and antimicrobial stewardship (AMS) on time-to-appropriate therapy (TAP) and clinical outcomes of patients with CRGNO infections utilizing novel beta-lactam/beta-lactamase inhibitors (BL/BLIs).

Materials/methods: Retrospective cohort study of adult patients with CRGNO infections at a 1,500-bed University-affiliated hospital in Miami, Florida. Included patients received ≥72 hours of ceftazidime-avibactam (C/A) or ceftolozane-tazobactam (C/T) from 12/2017-10/2019. During the pre-intervention period [12/2017-12/2018], additional susceptibilities (including C/A and C/T) were performed only upon providers’ request. In 01/2019, we implemented reflex algorithms (Figure 1) for faster identification and testing of all CRGNOs including carbapenemase producers. Results were communicated in real-time to the AMS team in order to tailor therapy. Benefit-risk outcomes involving TAP, kidney injury, and mortality were evaluated by desirability of outcome ranking (DOOR) analysis.

Results: Ninety-four patients were included; median age 61 years (IQR 40.0-68.3), 51 (54.3%) were in an intensive care unit at time of culture collection; median APACHE II score was 20 (IQR 15.0 – 27.0). CRGNOs identified included 71 (75.5%) Pseudomonas spp. and 23 (24.5%) Enterobacteriales, of which 16 (17.0%) were carbapenemase producers (KPC=10, NDM=4, VIM=2). The most common infections were pneumonia (47.9%) and bacteremia (26.6%), of which 16 (17.0%) were carbapenemase producers (KPC=10, NDM=4, VIM=2). We found a significant decrease in median TAP (102.9 [IQR 76.0–155.8] vs 75.4 [IQR 56.3–101.2] hours, \( p = 0.003 \)) and length-of-stay (64 [39.9-131.6] vs 43 [20.0-83.8] days; \( p = 0.027 \)) between groups. Median time from culture collection to final susceptibility results was shorter in the post-intervention group (122.2 vs 92.4 hours; \( p < 0.001 \)). In multiple regression analysis, our intervention demonstrated a trend towards decreased 30-day inpatient mortality (OR = 0.36, 95% CI 0.13–1.10). The probability of a better DOOR in the post-intervention group was 73.6% (95% CI 71.3–75).

Conclusions: Our study identified improvement in TAP and clinical outcomes in CRGNO infections with implementation of diagnostic and AMS initiatives. Our intervention had a positive impact on patient survival and initiation of effective therapy with novel BL/BLIs for multidrug-resistant infections.

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Antimicrobial activity of ceftobiprole against clinical Staphylococcus aureus isolates from Germany
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Background: Ceftobiprole medocaril, the prodrug of ceftobiprole, is a fifth-generation cephalosporin with activity against methicillin-resistant Staphylococcus aureus (MRSA). In most countries it is approved for the treatment of adults with hospital-acquired pneumonia (excluding ventilator-associated pneumonia) and community-acquired pneumonia.

Materials/methods: We performed susceptibility testing of ceftobiprole against (A) 219 clinical S. aureus from the strain collection of the National Reference Centre (NRC), which were isolated before ceftobiprole was introduced for clinical use and (B) 133 contemporary clinical isolates for which the NRC as a reference lab was asked to confirm a putative ceftobiprole resistance phenotype primarily diagnosed in the medical microbiology laboratories. Ceftobiprole MICs were determined by broth microdilution (BMD) and results were interpreted according to EUCAST guidelines. Ceftobiprole Etest (Bestbion) was additionally performed for the contemporary strains. Molecular characterization of isolates included spa-typing, MLST for unknown spa-types and PCR detection of mec genes.

Results: 97.4% of the strains [collection A + B] were susceptible to ceftobiprole with MICs ranging from 0.125 to 4.0 mg/L, exhibiting MIC50/90 values of 1.0/2.0 mg/L. Ceftobiprole resistance [n=9] was exclusively associated with MRSA ST228/ST239, which are at present rare in Germany and were only part of collection A. MRSA of both clonal lineages [n=58] revealed elevated MIC50/90 values of 2.0/4.0 mg/L. We could not confirm ceftobiprole resistance in any of the contemporary isolates sent to the NRC. Comparing MIC determined by Etest with those obtained by BMD revealed that Etest MICs tended to be higher, therefore being closer to the resistance breakpoint, producing false-resistant results and in many cases required a categorization as ATU (area of technical uncertainty) according to recent EUCAST guidelines (v9.0).

Conclusions: Ceftobiprole resistance is rare in S. aureus of prevalent clonal lineages circulating in Germany. Increased ceftobiprole MICs are found in MRSA ST228, disseminated in Southern Europe, and in MRSA ST239, which are described worldwide but are highly prevalent in South East Europe and Asia.

Methods for susceptibility testing of ceftobiprole in clinical microbiological laboratories have to be validated thoroughly, as inconsistent results may lead to overestimation of resistance.

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**Rapid diagnostics of Pneumocystis jirovecii: so far not good enough**

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**Background:** Pneumocystis jirovecii is an important cause of serious lung infections in immunocompromised patients. Laboratory diagnosis of Pneumocystis jirovecii is based on NAAT (nucleic acid amplification test) and microscopy. Recently rapid and simple commercial tests like eazyplex® Pneumocystis jirovecii have become available on the market, but their performance in the clinical setting is unknown.

**Materials/methods:** We tested 21 bronchoalveolar lavage samples from patients suspected to have a Pneumocystis jirovecii infection. The samples were analyzed with our conventional realtime-PCR [1] and the eazyplex® Pneumocystis jirovecii test [2]. All samples were randomly selected according to the primary results from the PCR (9 negatives /12 positives). Our PCR differentiate CT-values lower than 28 into three groups; weak positive (CT value 28-24, possible colonization), moderate positive (CT value 24-20, possible infection), and strong positive (CT value < 20, probable infection). The eazyplex® Pneumocystis jirovecii kit is based on loop-mediated isothermal amplification (LAMP) and real-time detection of the mitochondrial cox gene. The result is given as positive or negative.

**Results:** All eazyplex® runs were successful. Numbers of concordant and discordant results are presented in table 1.

The eazyplex® Pneumocystis jirovecii test captured only 4 out of totally 12 positive samples (33 %). The other eight positive samples tested negative with eazyplex® Pneumocystis jirovecii despite having CT-values 20 – 27. There were no false positive results with eazyplex® Pneumocystis jirovecii.

**Conclusions:** The eazyplex® Pneumocystis jirovecii captured 33% of the positive samples according to our in-house test, all with strong positive results whereas all of the moderate positive results tested negative with the eazyplex® Pneumocystis jirovecii. Study limitations are low sample size and no pre-analytic concentration of sample specimen. Further validation is warranted.

**References:**
2. Ref7626 Instructions for use eazyplex® Pneumocystis jirovecii. May 2019

**Table 1.**

<table>
<thead>
<tr>
<th>In-house RT PCR – Eazyplex®</th>
<th>Number of pairs (n)</th>
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<tr>
<td>Negative – Positive</td>
<td>0</td>
</tr>
<tr>
<td>Positive – Negative</td>
<td>8</td>
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<td>Positive – Positive</td>
<td>4</td>
</tr>
</tbody>
</table>

*Test of difference between correlated proportions: p < 0,005 (McNemar’s test).

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Antimicrobial activity of enacyloxin IIa and gladiolin against the urogenital pathogens Neisseria gonorrhoeae and Ureaplasma species.

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Background: Treatment of urogenital pathogens is becoming increasingly more difficult due to the emergence of multi-drug and extensively-drug resistant strains. Infection with Neisseria gonorrhoeae is increasing on a yearly basis and Ureaplasma spp are intrinsically resistant to many antibiotics.

Materials/methods: The Burkholderia polyketide antibiotics enacyloxin IIa and gladiolin were tested against 14 N. gonorrhoeae and 10 Ureaplasma sp isolates including multi-drug resistant N. gonorrhoeae strains WHO V, WHO X and WHO Z as well as macrolide, tetracycline and ciprofloxacin resistant ureaplasmas. Susceptibility testing of N. gonorrhoeae were carried out by agar dilution, whereas broth micro-dilution and growth kinetic assays was used for Ureaplasma spp.

Results: The MIC range for enacyloxin IIa against N. gonorrhoeae was 0.015 – 0.125 mg/L with MIC50 and MIC90 values of 0.03 and 0.06 mg/L, respectively. The MIC range and MIC50 and MIC90 values for gladiolin were higher at 1 - 2 mg/L, 0.03 and 0.06 mg/L, respectively. The presence of resistance to front line antibiotics had no effect on MIC values. The MIC range for enacyloxin IIa against Ureaplasma spp. was 4 – 32 mg/L with MIC50 and MIC90 values of 8 and 32 mg/L, respectively, with a clear dose-dependent effect when observed using a growth kinetic assay. Gladiolin had no antimicrobial activity on Ureaplasma spp. at 32 mg/L and limited impact on growth kinetics.

Conclusions: Enacyloxin IIa and gladiolin antibiotics have promising antimicrobial activity against a range of antibiotic susceptible and resistant N. gonorrhoeae and Ureaplasma isolates. Development of these compounds warrants further investigation.

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Proposition of a uniform methodological approach to attribution of invasive aspergillosis as a cause of death

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Background: Assessing the cause of death in patients with invasive aspergillosis (IA) is difficult. Presence of underlying disease, cytotoxic treatment as well as the immunocompromised status all may cause severe complications that lead to death. Though criteria for the response to treatment were published by the EORTC, no standard assessment method exists for attribution of mortality in patients diagnosed with IA. In this study a new protocol for the assessment of mortality in IA was constructed and evaluated.

Materials/methods: A scoring model was built based on IA death criteria extracted from the literature (e.g. by Garcia-Vidal et al. 2015). The role IA played in causing the patient’s death was categorised either as attributable, contributable, non-attributable or unknown (figure 1). The scoring model was pre-evaluated by practicing on 12 clinical scenarios. The assessment was performed by a panel of three reviewers consisting of a haematologist, an infectious disease specialist and a clinical microbiologist. Reviewers received written instructions. Each case was independently reviewed by two reviewers, all discrepancies were discussed and final results were based on a consensus among the reviewers. If no consensus was reached, the judgement of the third reviewer was decisive. All adult patients diagnosed with IA who died within 120 days post-diagnosis in the Leiden University Medical Center from 2015-2019 were included.

Results: Fifty-three patients were assessed; each reviewer assessed 36 patients. Mortality was IA-related (attributable or contributable) in 23 (43%) patients, IA-unrelated (non-attributable) in 26 (49%) patients, and unknown in 4 (8%) patients. Judgements were concordant in 29 patients (55%). Most discordant judgements were differences in opinion whether death was non-attributable or contributable (10/24). Progression of underlying haematological malignancy and diagnostic certainty of IA diagnosis (proven and probable versus possible) did not influence the concordance rate of the assessments.

Conclusions: Assessing mortality attributable to IA is complicated and warrants a standardised protocol. The concept of the described methodological approach is promising. Further refinement and validation is necessary so that it can become a standard tool in research involving IA.

Attributable
The immediate cause of death was defined as the disease process, injury, or complication immediately preceding death. IA was considered the cause of death when the immediate cause of death was due to this infection. Examples are neurological complications of a aspergillosis infection that disseminated to the brain, lung bleeding or respiratory insufficiency in a patient with pulmonary aspergillosis.

or
IA was judged to have played a major role if death would not have occurred had the patient not had IA, even though another condition was present that also contributed to death. This includes toxicity, interactions and other side effects of antifungal treatment that played a major role in the cause of death.

Another example is a pseudomonas bacteremia in a patient with a cavitating pulmonary aspergillosis in which the lungs are considered the most likely source of the bacteremia.

Contributable
IA or treatment of IA was defined as playing a minor role if it was probably not essential in explaining the patient’s death but arguably did play some role in the event. Example is a patient with an aspergillus infection as well as severe uncontrolled gastrointestinal GVHD at the time of death.

Non-attributable
Mortality was classified as not related to IA if there was a clear other cause of death.

Unknown
If insufficient data were present about the circumstances in which death occurred.

Figure 1. Attribution of mortality in patients with invasive aspergillosis

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Evaluation of analytical and clinical performances of four commercial HIV-1 viral load assays on a wide panel of HIV-1/M and HIV-1/O

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Background: Plasma viral load (VL) is usually used to monitor HIV infected patients. HIV-1 broad genetic diversity frequently affects the performances of commercial assays. Since no reference assay is available regarding HIV-1 VL, most evaluations consist in pairwise comparison. Here we compared HIV-1 VL assays developed on Abbott m2000, Roche Cobas 6800, Hologic Panther and Cepheid GeneXpert platforms, on a wide panel of samples.

Materials/methods: 263 plasma from HIV-1 positive blood donors, 77 viral supernatants (SN), and 300 dilutions of 30 SN [10 replicates of each at 50 cp/ml] representative of HIV-1/M and non-M genetic diversity, and spanning a wide range of VL, were tested for clinical and analytical sensitivity in the 4 usual commercial assays. For each sample, the mean VL obtained with the four assays (Mref) was used as reference to build Bland-Altman graph and compute Passing Bablok regression.

Results: Eight of the 340 plasma and SN were detected but not quantifiable by at least one assay: four concerned minor underquantifications with \( VL_{\text{max}} = 525 \text{cp/ml} \), and four were major underquantifications, with 1 HIV-1/M subtype D misquantified using GeneXpert \( \text{Mref} = 4.52 \text{Log cp/mL} \), and 3 distinct HIV-1/O misquantified using M2000, GeneXpert and Panther \( \text{Mref} = 4.06, 4.86 \) and 5.13 Log cp/mL respectively).

On HIV-1/M samples \( n=300 \), the quantitative analysis showed a very good correlation between the four assays regarding Mref, with means of differences between 0.13 (Cobas) and -0.11Log (M2000), and coefficients of correlation between 0.989 (M2000) and 0.991 (GeneXpert and Panther).

The same analysis on HIV-1/O \( n=32 \) showed means of differences between 0.61 (Cobas) and -0.39Log (M2000) and coefficients of correlation between 0.539 (M2000) and 0.701 (GeneXpert).

Regarding the 230 HIV-1/M dilutions, 100%, 73%, 64% and 60% were positive with Cobas, M2000, Panther and GeneXpert assay, respectively. Regarding the 70 HIV-1/O dilutions, only 46%, 9%, 3% and 0% were positives with Cobas, Panther, M2000 and GeneXpert assay, respectively.

Conclusions: The four assays exhibited very good performances regarding HIV-1/M intragroup diversity, except one major underquantification for GeneXpert system. The quantification of the HIV-1/O strains was much more problematic with moderate correlation between the assays and a decreased sensitivity.

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Abstract 4729

**Personalised prediction with machine learning approach to predict candidaemia in medical wards**

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**Background:** Candidemia is a highly lethal infection associated with mortality rates between 40 and 60%; recently several studies have shown an increasing number of candidemic patients admitted to medical wards. Prompt and accurate diagnosis of invasive fungal infection is crucial, so that appropriate antifungal therapy can be started rapidly. Aim of this work was to assess predictive performance of a random forest algorithm for early detection of candidemia in the medical ward.

**Materials/methods:** A set of 42 potential predictors was acquired in a sample of 295 patients (male: 142, 48%; age: 72±15 years; candidemia: 157, 53%; bacteremia: 138, 47%). Using ten-fold cross-validation, a random forest algorithm, with 150 different combinations of its 3 hyperparameters, and two different sets of predictor variables, was compared with a classic stepwise multivariable logistic regression model; discriminative performance was assessed by C-statistics, sensitivity and specificity, while calibration was evaluated by Hosmer-Lemeshow test.

**Results:** The best tuned random forest algorithm demonstrated excellent discrimination (C-statistics = 0.87 ± 0.003, sensitivity = 84.24% ± 0.67%, specificity=91% ± 2.63%) and calibration (Hosmer-Lemeshow statistics = 12.779 ± 1.369, p = 0.120), markedly greater than the ones guaranteed by the classic stepwise logistic regression (C-statistics = 0.829 ± 0.011, sensitivity = 80.21% ± 1.67%, specificity = 84.81% ± 2.68%; Hosmer-Lemeshow statistics = 38.182 ± 15.983, p<0.001). Random forest, in addition to using a greater number of variables, suggests a major role of in-hospital antibiotic treatment with microbioma highly impacting antimicrobials (MHIA) that are found as a fundamental risk of candidemia, further enhanced by TPN. When in-hospital MHIA therapy is not performed, PICC is the dominant risk factor for candidemia, again enhanced by TPN. When PICC is not used and MHIA therapy is not performed, the risk of candidemia is minimum, slightly increased by in-hospital antibiotic therapy.

**Conclusions:** Random forest accurately estimates the risk of candidemia in patients admitted to Internal medical wards, allowing to take advantage of the ever-increasing amount of data collected in the electronic health records. Machine learning technique might help to identify septic patients at high risk of candidemia, reduce the delay in empirical treatment and improve appropriateness.

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Abstract 4730

Vitamin D3 supplementation with a daily dose of 400 or 1200 IU results in similar antibody concentrations to measles, mumps and rubella in vaccinated 2-year-old Finnish children

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Background: Vitamin D3 supplementation is presently recommended to Finnish children from 2 weeks of age as a dose of 400 IU/day. The aim of this study performed in 2013-2016 was to assess if a higher dose of vitamin D3 in early childhood affects the antibody concentrations to the measles, mumps and rubella (MMR) vaccine.

Materials/methods: Children participating in the study were randomized (1:1) to receive a daily dose of 400 or 1200 IU of vitamin D3 between 2 weeks and 2 years of age. Serum 25-hydroxyvitamin D [25-(OH)D] -concentrations were measured at 12 and 24 months of age. In a sub study, the effect of vitamin D dose on humoral immunity has been assessed by measuring antibodies to vaccines included in the national immunization program. IgG antibodies to measles, mumps and rubella were measured with enzyme immunoassay from serum samples collected at 24 months of age. All the children included in the analysis (n=144 in the 400 IU and n=136 in the 1200 IU group) had received a single dose of MMR between the age of 11 and 19 months.

Results: Geometric mean IgG concentrations did not differ between the children who received 400 vs 1200 IU vitamin D3 supplementation to measles (2700 vs 2600 mIU/ml), mumps (790 vs 840 mIU/ml) or rubella (63 vs 71 IU/ml). The proportion of seropositive sera was equally high in both study groups. Antibody concentrations at 24 months of age did not correlate with serum 25(OH)D –concentrations (range 47-213 nmol/l) at 12 or 24 months of age. Only two children at 12 months and one at 24 months had serum 25(OH)D –concentrations below 50 nmol/l, which is considered to indicate a sufficient level.

Conclusions: Vitamin D3 supplementation in a higher dose had no significant effect on the measured antibody concentrations to the MMR vaccine antigens. Also, antibody concentrations at 24 months were not associated with circulating vitamin D3 concentrations at the same time point, or at the time of vaccination. Additional vitamin D3 supplementation in vitamin D3 sufficient children provides no further benefit for humoral immunity to the live attenuated vaccine.

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A novel deep sequencing platform for genotyping and drug resistance detection of Mycobacterium leprae

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Abstract third-party references: R2STOP, EDCTP

Background: Diagnostics and surveillance of antimicrobial resistance are particularly problematic in mycobacterial diseases, linked to the biology of the pathogens involved. Among these, M. leprae can be considered the most challenging as it is not culturable and extremely clonal. In order to circumvent these problems, a culture-free assay, based on deep sequencing of a single hi-plex amplification test for M. leprae (named Deeplex-MycLep), was developed by Genoscreen in collaboration with ITM and Fiocruz.

Materials/methods: The assay queries 42 targets in one reaction. The assay includes 18 SNP target regions for determining SNP-(sub)types combined with 17 VNTR regions for higher resolution genotyping, six main drug resistance associated gene regions, in addition to the hsp65 gene for speciation.

Results: As a proof-of-principle, 15 DNA extracts from biopsies of multibacillary patients dispersed across the island of Anjouan were tested. The prototype detected 12 different genotypes [2 SNP types and 12 different Multi-Locus VNTR Analysis (MLVA) patterns], with village level clustering [two pairs from two villages with identical genotypes], and without any drug resistance mutations [Fig. 1]. Results from extended assay validation and from analysis of 332 samples from multibacillary patients recruited in the Comlep study [Comoros] will be presented.

Conclusions: The use of this amplification assay before Next Generation Sequencing allows unique target enrichment directly on clinical samples, containing also an estimated 99.9% host DNA. Translation of multiple known hypervariable region-based typing from MLVA and drug resistance-related targets onto this platform will likely result in more robust tracking of leprosy transmission and more comprehensive drug resistance surveillance datasets. In addition to high throughput capacity, Deeplex-MycLep also provides enhanced sensitivity to detect minority populations of emerging resistant bacilli or mixed infection with multiple strains.

Figure 1: Neighbour-joining tree based on the SNP and VNTR typing of M. leprae biopsy samples from leprosy patients on the Comoros [2017] in relation to their resident village.

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First study on Giardia intestinalis assemblages in Algerian individuals

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Background: Giardia intestinalis is a common flagellate parasitizing the gastrointestinal tract of humans and animals. This study investigated the occurrence of G. intestinalis in enteroparasite-positive children and adults in Algeria, and is one of only few studies to date with molecular epidemiology data on Giardia infections in Africa.

Materials/methods: A community-based cross-sectional study was carried out in two hospitals in Algiers and two in Biskra. Faecal samples from 119 individuals suspected of intestinal parasitosis and scored enteroparasite-positive by microscopy (i.e. positive for Giardia and/or other parasites) were screened by qPCR for G. intestinalis. Positive samples were subsequently assemblage-typed using nested PCR for the triose phosphate isomerase gene (tpi). The 119 study individuals comprised 55 children, 37 adults, and 27 individuals of undetermined age (Table). Median age of those with known age was 8 years (interquartile range=4.25–24, range, 2–74).

Results: Of the 119 samples, 80 (67%) were qPCR-positive; 66 were positive by both microscopy and qPCR (mean Ct value, 27.5) and 14 were negative by microscopy but positive by qPCR (mean Ct value, 30.2). The remaining 39 samples were qPCR-negative, 32 of which were negative also by microscopy. More children (45/55, 82%) were infected than adults (11/37, 30%) (P<0.0001). Samples with Ct values <30 were submitted to typing and so, for 48 of 49 positive samples (mean Ct value, 24.5), the tpi gene was successfully amplified and sequenced (Table). Assemblage A was found in 10 children, 6 adults and 6 of undetermined age. Assemblage B was found in 15 children, 6 adults and 6 of undetermined age. Neither Giardia infection overall nor specific assemblage appeared to be associated with gender; meanwhile, assemblage B appeared more common in children than in adults.

Conclusions: Most of the enteroparasite-positive children had G. intestinalis, and children were more commonly infected by this parasite than adults. It appears likely that assemblage B is more common in children than in adults in this region. Robust amplification and sequencing of the tpi gene is feasible when highly positive samples are used.

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Abstract 4734

**Antibacterial activity of aztreonam-epigallocatechin gallate combinations versus multidrug-resistant strains of Acinetobacter baumannii**

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**Background:** Acinetobacter baumannii is an important nosocomial pathogen, often innately multidrug-resistant (MDR) and frequently associated with severe and difficult to treat infections. With the lack of anti-Gram-negative antibiotics under development, novel therapies are urgently required, to support existing drugs, or to increase their useful lifespan. Polyphenols, such as epigallocatechin gallate (EGCG), have previously shown to be synergistic with antibiotics such as aztreonam. This study aimed to determine if EGCG was able to restore the activity of aztreonam against MDR strains of *A. baumannii* in vivo and highlight potential mechanisms of action.

**Materials/methods:** Sixteen MDR clinical *A. baumannii* isolates were used to determine the in vivo efficacy of aztreonam-EGCG combinations versus monotherapy in the *Galleria mellonella* model of infection. Larval morbidity and mortality were scored over 96 h. Histopathology was undertaken to determine detailed pathological effects of the therapies on the infected larvae. To elucidate possible mechanisms of action, expression of LacZ under control of promoters for RND-type efflux pumps, outer membrane pores and their regulators, was determined using the β-galactosidase assay on solid media. Bacterial motility assays were undertaken on motility plates supplemented with increasing concentrations of EGCG.

**Results:** Synergy between aztreonam and EGCG was confirmed in vivo, with morbidity and mortality significantly reduced in the group treated with the combination versus monotherapy. Histopathology also revealed that haemocyte clustering and bacteria adipose bodies were far lower in larvae treated with the combination. Results from the β-galactosidase assay indicated that EGCG inhibited the expression of *adeRS; adeABC; adeI; adeF and oprD* and also inhibited bacterial motility at 2 mg/L, without impeding sessile growth.

**Conclusions:** Results from our investigations not only demonstrate that EGCG increases the activity of aztreonam in vivo against MDR strains of *A. baumannii*, but also highlights possible mechanisms of action, including effects on antimicrobial resistance (reduced efflux) and virulence factors, which likely increase the effectiveness of the aztreonam. This combination shows potential to treat infections caused by MDR *A. baumannii*.

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Abstracts 2020

Abstract 4735

Examining the long-term adoption of a clinical decision support system for antimicrobial prescribing in primary care

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Abstract third-party references: Supported by Antibioclic

Background: In Europe, 80-90% of all antibiotics used in humans are prescribed in primary care by General Practitioners (GP). Suboptimal use of antibiotics is a driver of antimicrobial resistance (AMR) and clinical decision support systems (CDSS) for antimicrobial prescribing have been devised to improve antimicrobial use. However, many CDSS failed to demonstrate a clinical impact because of a low uptake and poor sustainability. The aim of this study is to identify the determinants of the long-term adoption of a CDSS for antimicrobial prescribing by exploring the use of Antibioclic in primary care.

Materials/methods: We interviewed French GPs about their use of Antibioclic, a CDSS for antimicrobial prescribing in primary care. Antibioclic is a publicly funded freely available CDSS targeting 37 infectious diseases, used by more than 5000 GPs daily. The participants were recruited through the mailing list of Antibioclic or at a course of antimicrobial prescribing. Interviews were recorded, transcribed and coded using NVivo 12 and were conducted until data saturation. Data were analysed using classic grounded theory approach.

Results: There were 22 interviews with GPs, 15 women and 7 men, median age 40 [IQR, 33-44] years, median duration of practice 7 years [IQR, 3-12]. All the participants had a frequent [several times a week] and sustainable [for more than one year] use of the CDSS in their practice. Antibioclic was the most used CDSS across disciplines for all the GPs. We identified 7 key themes that explained the sustainable adoption of the CDSS: usability, confidence, routinization, convenience, improvement of practices, contextualized learning and the lack of negative consequences. The GPs pointed out the importance of co-design between engineers and primary care prescribers for the development of a CDSS. They also discussed the discrepancy between guidelines and daily clinical practice, the role that CDSS play in continuing medical education and the evolution of the doctor-patient relationship.

Conclusions: This study provided valuable information on the determinants of the long-term adoption of a CDSS for antimicrobial prescribing in primary care. The themes that we identified may relate to a broad spectrum of electronic tools in healthcare.

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Abstract 4741

Hepatitis E virus infection is a risk for liver transplant recipients in Sweden

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Background: Liver-transplant recipients with acute hepatitis E virus (HEV) infection are at risk developing a chronic infection, which may rapidly progress to severe liver damage if not treated. However, the prevalence of HEV infection after liver transplantation remains to be elucidated, and likely varies geographically. Thus, the aim of this study was to investigate the prevalence of acute and chronic HEV infection among liver transplant recipients in a highly HEV endemic region.

Materials/methods: During 2013-2018, 116 liver-transplant recipients were prospectively enrolled. They were evaluated for anti-HEV IgM and IgG antibodies, as well as HEV RNA at the time of liver transplantation, and 3 and 12 months post-transplantation. Additionally, medical records were reviewed.

Results: Eleven (9%) liver transplant recipients acquired HEV infection during the study period. One patient had an ongoing infection prior to liver transplantation that had resolved without treatment at follow-up, six patients acquired early infections detected at the 3 month follow-up sampling, and four showed signs of infection at the follow-up 12 months post-transplantation. Seven (6%) had detectable HEV RNA, and additionally 4 (3%) patients had serological markers indicative of HEV infection without detectable HEV RNA. Signs and symptoms of HEV infection were subtle, none were diagnosed in routine clinical care, and none developed a chronic HEV infection. Furthermore, 15 patients (13%) had reactive anti-HEV IgG serologies in pre-transplant samples.

Conclusions: A substantial proportion of liver transplant recipients in Sweden are at risk of acquiring acute HEV infection, both before and after transplantation. Surprisingly, no chronic HEV infection were detected in the present study. As HEV infections are often discrete and not diagnosed by current clinical practise, and as ribavirin therapy is available, the introduction of routine prospective HEV RNA screening of liver transplant recipients may be warranted.

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Abstract 4742

**Genomic analysis of *Bordetella* pertussis strains causing disease in Italy and in Argentina, 2013 - 2016**

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**Background:** Antigenic divergences among *Bordetella pertussis* strains have been described mainly in countries where acellular pertussis vaccines are widely used, leading to the supposition that the bacterial population could adapt to substantial vaccine-induced immune pressure.

Here, we compared the genetic characteristics of *B. pertussis* strains isolated between 2013 and 2016 in Italy and in Argentina, two countries that have adopted different types of pertussis vaccines and different vaccination schedules.

**Materials/methods:** Whole-genome sequencing (WGS) on the Illumina MiSeq platform was used to analyze 55 genomes of *B. pertussis* strains mostly isolated from infants less than 1 year of age, from 2013 to 2016: 38 from Italy, where acellular pertussis vaccine for primary vaccination series is currently in use, and 17 from Argentina, where whole-cell pertussis vaccine for primary vaccination series is currently in use. *De novo* assembled genomes were analyzed by multilocus antigen sequence typing (MAST) and multilocus variable-number tandem repeat analysis (MLVA). Genetic relationship between the isolates were resolved into Neighbor-Net networks based on the core genome multilocus sequence typing scheme [cgMLST, https://bigsdb.pasteur.fr].

**Results:** Among the Italian isolates, the most common MAST profile was the *ptxP3/ptxA1/prn2/fim2-1/fim3-1* (82%). Sixty-two percent of the isolates resulted pertactin-deficient (*PRN*-) mostly due to the insertion of the *IS481* element (52%), followed by the introduction of a premature stop codon (39%) and the disruption of the promoter region (9%).

Ninety-four percent of the Argentine isolates belonged to the *ptxP3/ptxA1/prn2/fim2-1/fim3-2* profile. *PRN* isolates represented the 6% of the total and were exclusively due to the *IS481* insertion.

In both countries, the MLVA Type MT27 represented the majority of the isolates (>75%).

The cgMLST analysis showed a geographic clustering.

**Conclusions:** These preliminary results suggest that the use of different pertussis vaccines in the pediatric setting (acellular in Italy and whole-cell in Argentina) may exert a selective pressure favoring the prevalence of different circulating genotypes at least among strains causing disease in infants.

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Abstract 4743

Comparison of three commercial sample-to-result platforms to an established real-time PCR assay for the detection of herpesviruses in cerebrospinal fluid

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Background: Herpes simplex viruses (HSV) and Varicella Zoster Virus (VZV) are major causes of viral encephalitis. Rapid and sensitive diagnosis in CSF is of great importance for early and adequate treatment of patients with a suspect of herpesvirus encephalitis. Real-Time PCR to detect HSV1&2 and VZV is the gold standard to diagnose herpes meningitis/encephalitis. In this study, we compared three sample-to-result systems to an established Laboratory Developed Test (LDT) to detect HSV1&2 and VZV in CSF, focusing on clinical and analytical sensitivity, CSF volume, assay turnaround and hands on times.

Materials/methods: The study involved the ARIES® M1 (Luminex), LIAISON MDX® (Diasorin Molecular) and Ingenius (Elitech) systems using the respective dedicated diagnostics reagents validated for CSF. Routine LDT for the detection of HSV1&2 and VZV in CSF was considered the gold standard. Analytical sensitivities were compared using 5-fold dilution series of cultured viral stocks.

Clinical validation involved 22 retrospective CSF specimens, positive for one pathogen and serving as a negative for the others. Moreover, 20 HSV1&2 and VZV proficiency panel samples (QCMD 2018) were included.

Results: Analytical sensitivity experiments demonstrated comparable sensitivity between the sample to result systems and a maximum 5-fold reduced sensitivity compared to the LDT. Proficiency panel results for HSV1/2 and VZV demonstrated complete correctness for all commercial assays, except for one VZV sample which tested negative for ARIES®M1. Clinical validation experiments demonstrated full agreement with LDT for both the Ingenius and LIAISON MDX® HSV1/2 and VZV assays. Two clinical samples tested negative for HSV-1 in the ARIES®M1. No false positive results were observed in any assay. Assay turnaround time/sample volume for the Ingenius, ARIES® M1 and the LIAISON MDX® were 139 minutes/200µL, 245 minutes/400µL and 60 minutes/50µL, respectively.

Conclusions: The performances of the LIAISON MDX® and Ingenius systems for detection HSV1&2 and VZV in suspected viral meningitis/encephalitis patients were comparable to LDT, whereas the ARIES® M1 missed one clinical HSV-1 positive sample and one VZV positive QCMD sample. Major differences were observed required sample volumes per assay and in assay turnaround times, which were both in favor of the LIAISON MDX®.

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Factors associated with extended-spectrum β-lactamases and carbapenem-resistant Klebsiella pneumoniae bloodstream infections: a five-year retrospective study

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Abstract

Background: Klebsiella pneumoniae bloodstream infections (BSIs) occur worldwide with varying mortality. Resistant strains, like those producing extended-spectrum beta-lactamases (ESBL) and carbapenemases, are becoming increasingly common, especially in hospital settings, posing therapeutic challenges. We aimed to study factors associated with BSIs caused by antibiotic-resistant Klebsiella pneumoniae, in the largest tertiary hospital of the Republic of Cyprus.

Materials/methods: The study involved patients with BSI due to Klebsiella pneumoniae, who were hospitalized in Nicosia General Hospital between January 2014 and December 2018. Data on demographics, co-morbidities, prior hospitalization, prior ICU-admission, previous antimicrobial use, nosocomial acquisition, the presence of prosthetic device or surgery, and primary site of infection were retrospectively recorded. Associations between ESBL Klebsiella pneumoniae BSIs and factors/covariates were examined using logistic regression. Chi-squared tests and t-tests were used to explore associations between carbapenem-resistant (CR) K. pneumoniae BSIs and factors/covariates. Statistical analysis was performed in R.

Results: The study involved 175 patients with BSI caused by Klebsiella pneumoniae. Of these, 61 BSIs were caused by ESBL strains, 101 by non-ESBL and 13 by CR strains. In univariable analyses, age, sex, heart disease, antimicrobial use during current admission, previous hospitalization (ward or ICU) and primary BSI were associated with an ESBL strain. Antibiotic use during current admission [Odds Ratio (OR) 5.63, Confidence Interval (CI) 2.1 - 17] and heart disease (OR 4.72, CI 2.23- 10.5) sustained significant association with ESBL Klebsiella pneumoniae BSI in multivariable models. Antibiotic use during current admission (p 0.008), respiratory infection (p 0.03), and recent history of surgery (p 0.04) were more prevalent among CR K. pneumoniae BSI patients than among non-CR K. pneumoniae BSI patients. There were no significant differences between patients with CR K. pneumoniae BSI and those with BSI due to an ESBL strain.

Conclusions: This is the first study in Cyprus that explored factors associated with ESBL and CR Klebsiella pneumoniae bloodstream infections. Findings of the analyses including associations of recent antimicrobial use and heart disease with BSI due to ESBL producing K. pneumoniae, should inform clinical practice in hospital settings.

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Stability studies with tigecycline in bacterial growth medium and impact of stabilising agents: a prerequisite for in vitro susceptibility testing

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**Background:** Tigecycline is used in patients with life-threatening infections and hence knowledge about bacterial susceptibility is key for therapeutic decisions. Medium-age related effects on tigecycline stability were described, which led to inconsistencies in tigecycline MIC values. The aim of this study was (i) to examine the degradation process of tigecycline over time, and (ii) to evaluate the effect of the antioxidants ascorbic acid and sodium pyruvate on tigecycline stability, which were recently recommended to stabilize tigecycline infusion solutions, but had not been tested in bacterial growth medium.

**Materials/methods:** Tigecycline in aged (7 days) and fresh cation-adjusted Mueller Hinton Broth (ca-MHB) using no stabilizing agent, ascorbic acid (0.3%), or pyruvate (1%) was incubated for 24 h at 37 °C. Stability was evaluated using high-performance liquid chromatography and time-kill studies with *Staphylococcus aureus* (ATCC 29213) were conducted to evaluate the potential impact of the antioxidants on bacterial growth and kill.

**Results:** Degradation of tigecycline was dependent on ca-MHB age. In fresh ca-MHB tigecycline remained stable 99.6% (94.5% – 103.5%, p = 0.412), whereas degradation to 80.1% (82.8% – 75.6%, p = 2.44·10^{-6}) was measured within 24 h in seven days aged broth. Using fresh ca-MHB, > 1-log killing was observed (Figure 1A), while at 1x MIC in aged ca-MHB no killing but a 1-log growth was observed after 24 h (Figure 1B). Ascorbic acid in ca-MHB caused rapid degradation to 4.7% (5.1% – 3.5%, p = 2.47·10^{-6}) and resulted in loss of antibacterial activity (Figure 1C). Sodium-pyruvate (1%) in ca-MHB stabilized tigecycline in 7 days aged ca-MHB at 37 °C (94.8% – 95%, p = 1.56·10^{-3}) and the growth and killing pattern was similar to fresh broth, but independent of ca-MHB age (Figure 1D).

**Conclusions:** Our results underline the importance of using fresh ca-MHB or the need to stabilize tigecycline for susceptibility testing. Ascorbic acid, although recommended to stabilize tigecycline infusion solution, was found not suitable to stabilize ca-MHB. Sodium-pyruvate was found to stabilize tigecycline and represents an inexpensive option to streamline the susceptibility testing of tigecycline.

**Figure 1:** Time-kill studies of *Staphylococcus aureus* in (A) freshly prepared and (B) seven days aged cation-adjusted Mueller-Hinton broth and supplemented broth containing (C) 0.3% ascorbic acid or (D) 1% sodium-pyruvate.

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Detection of virulence genes and capsule types in *Klebsiella pneumoniae* isolated from blood cultures in patients with haematological malignancies

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**Background:** *Klebsiella pneumoniae* is one of the most important pathogens responsible for serious infections such as bacteremia, pneumonia, intra-abdominal infections and urinary tract infections. Nosocomial isolates are often associated with extended-spectrum β-lactamases (ESBL) and carbapenemases. However, recently there have been many reports on the hypervirulent *K.pneumoniae* (hvKp) that draws more and more attention. The aim of this study was to evaluate the presence of hypervirulent strains among *K.pneumoniae* isolated from blood cultures in patients with haematological malignancies.

**Materials/methods:** In the current prospective multicenter study we analyzed *K.pneumoniae* isolated from blood cultures in haematological patients in 12 Russian hospitals (2003-2018). Antimicrobial susceptibility was determined by the broth microdilution method [CLSI, 2018]. Carbapenemase genes (*bla*OXA-48-like, *bla*KPC-like, *bla*NDM-like, *bla*VIM-like and *bla*IMP-like) were detected by multiplex real-time PCR. Genetic markers for hypervirulence (*iucA, rmpA, rmpA2*) were detected by PCR. Multiplex PCR was performed to detect for K1, K2, K5, K20, K54, and K57 serotype-specific alleles, that are commonly used as markers for hvKp strains.

**Results:** A total of 494 *K.pneumoniae* were examined. Of those, 83(16.8%) were carbapenemase-producing *K.pneumoniae* (CP-*K.pneumoniae*), 261(52.8%) were ESBL-producing *K.pneumoniae* (ESBL-*K.pneumoniae*, without CP-*K.pneumoniae*) and 150(30.4%) were susceptible *K.pneumoniae* (without CP- and ESBL-*K.pneumoniae*). Among these 494 isolates, 108(21.9%) carried at least one virulence gene (*iucA, rmpA or rmpA2*). These isolates were considered hvKp. The virulence genes were prevalent in CP-*K.pneumoniae* (n=40;48.2%) while among ESBL-*K.pneumoniae* and susceptible *K.pneumoniae* these genes were detected in 17.2%(n=45) and 15.3%(n=23) isolates, respectively [Table]. The virulence genes were presented both in different combinations with each other and in combination with the markers associated with the studied capsule types (n=93;86.1%). Serotype-specific alleles (K1, K2, K5, K20, K54, and K57) were detected in 117(23.7%) isolates *K.pneumoniae* [Table]. Only two (K2 and K57) capsule types were identified in CP-*K.pneumoniae* while in susceptible and ESBL-*K.pneumoniae*, respectively five and four different capsule types, were detected. The virulence genes were not presented in more than a half of the isolates (51.3%) with identified capsule types.

**Conclusions:** This study revealed that 21.9% *K.pneumoniae* isolated from blood cultures carried the virulence genes. The high percentage of the virulence genes (*iucA, rmpA, rmpA2*) among CP-*K.pneumoniae* (48.2%) is especially alarming.

**Table. The presence of genetic markers of hypervirulence in *K. pneumoniae***

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>susceptible <em>K. pneumoniae</em> (n=150), n (%)</th>
<th>ESBL-<em>K. pneumoniae</em> (n=261), n (%)</th>
<th>CP-<em>K. pneumoniae</em> (n=83), n (%)</th>
<th>Total (N=494), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Virulence genes:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>23 (15.3)</td>
<td>45 (17.2)</td>
<td>40 (48.2)</td>
<td>108 (21.9)</td>
</tr>
<tr>
<td><em>iucA</em></td>
<td>23 (15.3)</td>
<td>45 (17.2)</td>
<td>40 (48.2)</td>
<td>108 (21.9)</td>
</tr>
<tr>
<td><em>rmpA</em></td>
<td>13 (8.7)</td>
<td>36 (13.8)</td>
<td>39 (47)</td>
<td>88 (17.8)</td>
</tr>
<tr>
<td><em>rmpA2</em></td>
<td>13 (8.7)</td>
<td>13 (5)</td>
<td>7 (8.4)</td>
<td>33 (6.7)</td>
</tr>
<tr>
<td>Capsule types:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>17 (11.3)</td>
<td>63 (24.1)</td>
<td>37 (44.6)</td>
<td>117 (23.7)</td>
</tr>
<tr>
<td>K2</td>
<td>8 (5.3)</td>
<td>19 (18.8)</td>
<td>16 (19.3)</td>
<td>43 (8.7)</td>
</tr>
<tr>
<td>K1</td>
<td>4 (2.7)</td>
<td>-</td>
<td>-</td>
<td>4 (0.8)</td>
</tr>
<tr>
<td>K57</td>
<td>3 (2)</td>
<td>4 (1.5)</td>
<td>21 (25.3)</td>
<td>28 (5.7)</td>
</tr>
<tr>
<td>K54</td>
<td>1 (0.7)</td>
<td>7 (2.7)</td>
<td>-</td>
<td>8 (1.6)</td>
</tr>
<tr>
<td>K20</td>
<td>1 (0.7)</td>
<td>-</td>
<td>-</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>K5</td>
<td>-</td>
<td>3 (1.1)</td>
<td>-</td>
<td>3 (0.6)</td>
</tr>
</tbody>
</table>

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In vitro activity of beauvericin against Sarcoptes scabiei: may a mycotoxin help for the control of scabies?
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Background: Scabies is a frequent cutaneous infection caused by the mite Sarcoptes scabiei in a large number of mammals including humans. Current therapeutic options are not optimal and there is an unmet need for new acaricide molecules with greater efficacy and improved pharmacological profiles. The entomopathogenic fungus Beauveria bassiana is known to produce beauvericin, a secondary metabolite belonging to the enniatin antibiotic family. Beauvericin was proven to have many biological effects including insecticidal, antitumor, antibacterial, and antifungal activity. The objective of the study was to assess the activity of beauvericin against different evolutive stages of S. scabiei.

Materials/methods: S. scabiei mites and eggs were collected from experimentally-infected pigs. For in vitro evaluation of acaricide activity, motile stages (adults, nymphs/larvae) or eggs were placed in Petri dishes filled with Columbia agar supplemented with pig serum and different concentrations (0.5, 5, and 50 µM) of the drugs to be tested. Mites were inoculated in the middle of the plates and examined at 1, 2, 3, 4, 5, 6, 7, 8 and 24h after inoculation for survival assessment of motile stages at room temperature. Mites were considered dead when no movement occurred under the microscope during 5 min. To assess the activity against S. scabiei eggs, Petri dishes were maintained at 37°C for 5 days to promote egg development. Lethal time (LT50) necessary to kill half of the mites population was calculated using the probit regression analysis in SPSS software.

Results: Beauvericin, dimpylate, and ivermectin were highly efficient against S. scabiei motile stages. The lowest LT50 values (1.1 and 1.0h) were observed with a concentration of 50 µM of dimpylate and ivermectin against females and nymphs/larvae, respectively. The highest LT50 values (5.6 and 4.7h) were observed with a concentration of 0.5 µM of beauvericin and dimpylate against females and nymphs/larvae, respectively. Beauvericin showed higher activity against adults and eggs of S. scabiei when compared to dimpylate and ivermectin.

Conclusions: These preliminary results indicated that beauvericin may be considered as a new scabicide molecule. Further studies assessing the possibility of beauvericin application to treat scabies in humans or sarcoptic mange in animals are required.

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Abstract 4750

Predictive value of CD4+ T helper lymphocytes, associated biomarkers and procalcitonin in the prognostication of polytrauma patients with sepsis

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Background: Trauma is a growing epidemic worldwide which mainly targets the young and productive population and imposes a major burden on the health infrastructure to provide emergency and often-prolonged trauma care. A high percentage of polytrauma patients develop a post-trauma complication-sepsis that can lead to increased morbidity and mortality. This study was conducted to elucidate their unique immunological profile governed by CD4+ T helper (Th) lymphocytes & biomarkers, to ultimately salvage these critically ill trauma patients.

Materials/methods: Fifty polytrauma ICU-patients with sepsis and 50 controls (40 healthy-controls & 10 diseased-controls) were included in the study conducted at JPNA Trauma Centre, AIIMS, New Delhi. Peripheral blood samples were obtained on day 0: first laboratory confirmed bloodstream infection (BSI), day 4 (post-culture based antimicrobial treatment), day 10 and day of discharge (DD). Multi-colour flowcytometry was used to study the intracellular profiles of 12 circulating CD4+ T helper subsets (IFN-γ+Th-1, IL-4+Th-2, IL-9+Th-9, IRF4+Th-9, IL-17A+Th-17, RORγT+Th-17, IL-22+Th-22, IL-10+ Tr1, TGF-β+Th-3, C-D25+FoxP3+nTreg, and FoxP3+iTreg cells), 14 serum cytokines (sIFN-γ, sTNF-α, sIL-2, sIL-4, sIL-5, sIL-6, sIL-9, sIL-10, sIL-13, sIL-17A, sIL-17F, sIL-21, sIL-22, and sTGF-β), and serum procalcitonin (PCT). The data were statistically analyzed based on disease progression and their clinical outcome.

Results: Of the total 50 patients 25 (50%) patients were microbiologically cured and 20 (40%) had a fatal outcome. Majority 38 (76%) were males and developed sepsis 11.9 ± 8.2 days post-trauma. The percentages of Th-9, nTreg and Th-3 were higher in patients than controls. Figure 1 shows the statistically significant elevation & depression of all the markers in mid (day 4) & late (day 10) phase in patients who were microbiologically cured (who had a subsequent sterile blood culture) and those who had a fatal outcome. A very high and persistent serum PCT may be an indicator of poor prognosis. By DD the levels of CD4+ Th cells & biomarkers were comparable to those in healthy controls. All the patients were clinically followed up till their outcome at the hospital.

Conclusions: This study is based on a multi-marker (n=27) approach to identify predictive immunological markers in diagnosis and prognosis of polytrauma patients developing sepsis. It has laid a foundation for further detailed studies with more stringent inclusion criteria which would ultimately lead to the development of a definitive scoring system for prediction of sepsis progression and unfavorable outcome.

Summary figure:

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Abstract 4753

Changes occurred in immunological and molecular determinations of toxoplasmosis in pregnancy and newborn children

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Background: Toxoplasmosis is one of the most prevalent parasitic disease. The etiological agent - an obligate intracellular protozoan. The life cycle involves a definitive host (Felidae) and a wide range of intermediate hosts. Sexual reproduction: in the body of the definitive host who eliminates in the external environment the unsporulated oocysts. The asexual phase: in the body of the intermediate host, resulting tachyzoites and bradyzoites.

Materials/methods: Were collected 1 789 biological materials (serum, CSF, amniotic fluid, aqueous humour) from patients with suspected toxoplasmosis. As methods: ELISA (screening) - 1623, confirmation: western blot (WB) - 80 and RT-PCR - 86. 40 pregnant patients were monitored, 26 of whom returned to birth for dynamic monitoring of the level of antibodies in the newborn, up to the age of 1 year.

Results: Of the total samples analyzed by the screening method (1623), 1115 were tested for acute phase antibodies (IgA, IgE and IgM) and 508 for chronic phase antibodies (IgG). In 40 of those who had a recent infection, the avidity test was performed, 6/40 (15%) recent infections and 34/40 (85%) late infections. All acute infections were confirmed by western blot, and RT-PCR was definitive for confirming an infection in 5 cases. Monitoring the antibodies in pregnant patients (quarterly and in dynamics), the results showed 95/320-29.68% positive for IgA, 37/639 - 5.79% for IgE, 27/116 - 23.27% for IgM and 392/508 - 77.16% for IgG. Of the mother-newborn pairs, all children presented with specific IgG-type antibodies at birth, which are transmitted passively maternal-fetal and have a titer that decreases in dynamics until the age of 1 year.

Conclusions: In the case of the diagnosis of toxoplasmosis, the laboratory methods are of major importance in monitoring the treatment and in preventing the risk of congenital transmission. Early detection of acute-phase antibodies (IgA, IgE, IgM anti-Toxoplasma gondii) in every quarter, together with molecular diagnostics (liquid, amniotic PCR, CSF, aqueous humor) allows the clinician an early diagnosis orientation and prompt establishment of an appropriate treatment which, which leads to an increase of the quality life of the patient.

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Characterisation of relationships between *Staphylococcus aureus* and *Escherichia coli*, *Acinetobacter baumannii* and *Candida auris* and their implications for survival and persistence in the dry environment

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**Background:** Microorganisms are very diverse in their relationships with other microorganisms in the healthcare environment and these relationships may influence their survival and persistence on frequently cleaned and decontaminated dry surfaces. In this study the relationship of *S. aureus*, a frequently isolated healthcare associated infectious microorganism with other clinically relevant microorganisms such as *Escherichia coli*, *Acinetobacter baumannii* and *Candida auris* were studied.

**Materials/methods:** *S. aureus*, *E. coli*, *A. baumannii* and *C. auris* were first grown as monocultures. *S. aureus* was co-cultured with the other organisms and then as a primary or secondary coloniser with each of them. The organisms were grown in 5% tryptic soy broth at ambient temperature with sequential hydration and dehydration periods for 12 days. Biomass and cell recovery were evaluated at days 4, 6, 9 and 12 by crystal violet assay and standard plate culture.

**Results:** This study confirmed the existence of active relationships between different groups of bacteria which affected their survival and the ability to form biofilms. *S. aureus* and *A. baumannii* formed a protocooperative relationship. Biomass production increased by 19% when *S. aureus* was a primary coloniser than as a secondary coloniser. The relationship between *S. aureus* and *E. coli* was predatory resulting in reduction of biomass and cells of *S. aureus* by 58% and approximately 1.5 log10 separately. Biomass production was reduced by 21% when *S. aureus* was a secondary coloniser. *C. auris* appeared to scavenge off *S. aureus* in its effort to grow as the numbers of *S. aureus* decreased by 2 log10 while that of *C. auris* increased after 6 days of coculture by 1 log10. The position of *S. aureus* as a primary or secondary coloniser had no significant impact on biomass formation (p=0.99).

**Conclusions:** The natural interactions that exist between microorganisms affect the response of microorganisms to stressors. Cocultures of free-living organisms and biofilms may be valuable in understanding microbial persistence and tolerance to antimicrobials.

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Abstract 4761

Exfoliative toxin A-producing *Staphylococcus aureus* clonal complex 8 strains causing staphylococcal scaled skin syndrome in newborns

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**Background:** Phage-encoded exotoxin genes and related clinical syndromes are associated with certain clonal complexes (CC) of *Staphylococcus aureus*. Staphylococcal scalded skin syndrome (SSSS) in newborns is mainly associated with *S. aureus* strains of CC121 and CC15 which carry the exfoliative toxin A (ETA) gene encoded Sa1int phages. We recently reported, in a study of two outbreaks of SSSS in newborns, that *S. aureus* CC8/ST2993 strains were isolated. CC8 strains were not previously associated with SSSS in newborns. We investigated ETA production and virulence of CC8/ST2993 strains, a novel causative agent of SSSS in newborns, in compare with CC15 and CC121 strains causing SSSS.

**Materials/methods:** Fully-sequenced CC8, CC15 and CC121 strains were isolated during outbreaks of SSSS in maternity hospitals in Russia. *S. aureus* strain MW2 was used as a reference control. *S. aureus* strain virulence was determined using the neonatal-mouse bioassay, a skin deep infection mouse model, and the insect infection model *Galleria mellonella*. ETA production was studied using approaches: SDS-PAGE, MALDI-TOF analysis, quantitative real-time PCR. Genome sequences of ETA-producing *S. aureus* strains and ETA-converting bacteriophages were analyzed and aligned.

**Results:** All CC8, CC15 and CC121 strains in study produced ETA as shown by a positive Nikolsky sign in the neonatal-mouse bioassay. *S. aureus* strain virulence was different depending on CC identified and animal model choice. ETA-producing CC8 strains caused open skin lesions in older BALB/c mouse model of skin deep infection. ETA amount produced by *S. aureus* strains was different depending on CC. SDS-PAGE, MALDI-TOF analysis and quantitative real-time PCR showed increased ETA levels in CC8 strains. Full genome SNP-based phylogenetic analysis revealed that ETA-producing CC8 strains were most closely related to USA300 lineage.

**Conclusions:** ETA-producing CC8/ST2993 strains, a novel causative agent of SSSS in newborns, were characterized in increased virulence compared with common *S. aureus* strains causing the infection. The result is determined probably due to increased ETA production.

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**Abstract 4762**

**Relationship between local-area socioeconomic status and rates of bloodstream infection and *Clostridioides difficile* infection**

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**Background:** Mandatory surveillance of key pathogens (MRSA, MSSA, *Escherichia coli*, *Klebsiella* spp. and *Pseudomonas aeruginosa*) causing bacteraemia and of *Clostridioides difficile* infection (CDI) in England shows geographic disparities in rates of infection, with rates of infection for some pathogens higher in the North of England, compared to the South. We sought to test the hypothesis that local area socioeconomic deprivation was associated with higher rates of infection for these pathogens and to examine factors driving the association.

**Materials/methods:** Cases of infection covered by mandatory surveillance occurring in 2017 were extracted from Public Health England’s (PHE) Healthcare Associated Infection Data Capture System (HCAIDCS). Information on covariates at the local area level (Clinical Commissioning Group, CCG) included prevalences of diabetes, cancer and dementia as well as antibiotic prescribing. Local area deprivation was assessed using the Index of Multiple Deprivation (IMD). Multivariable linear regression was used to assess relationships between rates of infection and deprivation at the local level.

**Results:** Age- and sex-standardised rates of infection were higher in areas with higher deprivation for *C. difficile* (rate difference (RD): 8.2, 95% CI:6.4-10.0, most deprived compared to least), *E. coli* (RD: 30.2, 95% CI:27.1-33.4), *Klebsiella* spp. (RD: 5.6, 95% CI:4.2-6.9) and MSSA (RD: 11.2, 95% CI:9.5-12.9). There was no evidence of differences in rates for MRSA (RD: 0.2, 95% CI:-0.2-0.7) or *P. aeruginosa* (RD: 0.7, 95% CI:-0.2-1.6). After adjusting for covariates, there was still strong evidence for associations between higher deprivation and rates of infection for *E. coli* ($R^2 = 0.47$, $p < 0.001$), *Klebsiella* spp. ($R^2 = 0.28$, $p = 0.002$), MSSA ($R^2 = 0.38$, $p < 0.001$) and *C. difficile* ($R^2 = 0.23$, $p < 0.001$), but no evidence for association between higher deprivation and rates of infection for MRSA ($R^2 = 0.13$, $p = 0.311$) or *P. aeruginosa* ($R^2 = 0.23$, $p = 0.167$).

**Conclusions:** After adjusting for available covariates, rates of infection with *E. coli, C. difficile*, MSSA and *Klebsiella* spp. remained associated with higher levels of local-area deprivation. There was no evidence of an association for MRSA or *P. aeruginosa*. Identifying causal factors of the association remains challenging.

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Abstracts 2020

Abstract 4763

**The future of hepatitis C virus nucleic acid amplification techniques standardization?**

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**Background:** Viral load measurements by nucleic acid amplification techniques (NAT) are critical for the prevention and management of HCV infections. The International Standard (IS) for HCV NAT defines the detection and quantification specifications of these assays in terms of the International Unit (IU), thereby enabling the comparison of data generated by a broad range of assay platforms. This reference comprises HCV (genotype 1a)-positive window-period plasma which has proved difficult to source at high-titre and in large volumes. Hence, it has been replaced six times since establishment over 20 years ago. The frequency of this replacement presents problems in terms of the HCV sequence heterogenicity between different plasma sources, which can affect the RNA measurement by different NAT assays and potentially lead to drift in the value of the IU.

**Materials/methods:** Two inactivated cell cultured HCV (HCVcc) samples comprising different genotypes were included in a worldwide collaborative study towards the establishment of the 6th HCV IS, in order to evaluate their suitability as a source material for future HCV references. They were evaluated alongside two HCV plasma-derived candidates and three HCV-positive plasma samples comprising different HCV genotypes.

**Results:** The variability (SD) of HCV RNA measurements between laboratories ranged from 0.11 to 0.28 log10 IU/mL across the study samples. When potencies were expressed relative to HCV plasma candidates and HCVcc there was little change in inter-laboratory variability, suggesting that HCV NAT assays are well harmonized. The results showed that neither HCVcc sample worsened the agreement between HCV NAT-assays compared to existing HCV-plasma sources. There was no evidence for variation in the quantification of different HCV genotypes present in the study samples.

**Conclusions:** Since adoption of the IU harmonization of HCV RNA measurements has continued to improve such that existing assays can detect small changes in the value of the IU between replacement ISs. This study suggests that HCVcc could provide suitable alternative source material for this reference and would provide consistent virus for replacement batches. In addition, the ability to demonstrably inactivate HCVcc would permit increased batch sizes which are currently limited by the capacity of the infectious filling isolator at NIBSC.

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Evaluation of quality indicators in Staphylococcus aureus bacteraemia in a university hospital

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Background: We are not aware of a simple Quality of Care Score (QCS) to assess in patients with S. aureus bloodstream infections (SA-BSI). Recently, it has been published a set of 25 quality indicators (QIs) for the management SA-BSI. Our study tried to construct a QCS in SA-BSI episodes with prognostic implications.

Materials/methods: Retrospective study in adult hospitalized patients with SA-BSI. We evaluated the demographic, clinical and follow-up variables.

We determined the frequency of compliance of the 25 QIs, evaluating three possibilities: done (+1 point), not done (-1 point) or not relevant (0 point) and made a QCS with the total addition of points obtained in each case. The maximum of points for uncomplicated SA-BSI was 15, and for complicated SA-BSI 18 points. We compared the QCS in the outcome of the disease, defined as mortality within 30 days.

Results: Between January 2018 and July 2019, we selected 99 cases of SA-BSI hospitalized for 7 days or longer. The median-Charlson-index was 6 (IQR 3-8). Most of the SA-BSI were secondary (85.9%) and the acquisition was nosocomial or health-care-related in 74.7%.

The median in-hospital stay was 24 days (IQR 14-39) and 18 patients were admitted in the Intensive Care Unit. The frequency of methicillin-resistant S. aureus was 25.3%. As for the outcome, 15 patients died within 30 days and 84 patients survived.

Attending the QIs, follow-up blood cultures were done in 77.8% of the cases, echocardiography in 72.7% and catheter removal in 94.4% of the cases with catheter-related bacteremia.

Overall, the median of the QCS was 8 (IQR 4-10). There was a statistically difference in the QCS in the survivors (median 9, IQR 6-11) vs non-survivors (median 3, IQR 2-7), p 0.01. In the analysis of subgroups of uncomplicated and complicated SA-BSI, there were also a significant difference in the QCS (uncomplicated SA-BSI: survivors median QCS 8 vs non-survivors median QCS -2, p < 0.01. Complicated SA-BSI: survivors median QCS 10 vs non-survivors median QCS 6, p < 0.01).

Conclusions: In our institution a QCS for SA-BSI seems simple to obtain and has prognostic implications.

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Low Interferon gamma release assay conversion rate in healthcare workers after exposure to laryngeal tuberculosis

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Background: High infectiousness of laryngeal tuberculosis is suspected in older studies, but newer data is missing. Screening for latent tuberculosis and offering preventive treatment is recommended for healthcare workers (HCW) in the setting of exposure to tuberculosis. The risk of infection with TB is supposed to depend on exogenous factors like time of exposure, but no evidence exist about relevant exposure time.

Materials/methods: In our 780-bed hospital we identified HCW exposed to a patient with smear positive laryngeal TB and offered an Interferon Gamma Release Assay (IGRA) at time of exposure and 2 months thereafter. We used QuantiFERON® TB Gold plus by Qiagen, Hilden, Germany, considered positive with a TB1 or TB2 > 0.35 IU/ml. Baseline samples were only analysed if the 2-month IGRA was positive.

Results: We screened 63 of 70 (90%) exposed HCW. The majority had a short exposure time: 51.4% (n=36) < 1 hour, 27.1% (n=19) 1-2 hours, 21% (n=5) 2-4 hours, 5.7% (n=4) 4-8 hours and 4.3% (n=3) > 8 hours. No information was provided by 4.3% (n=3). At 2-months after exposure 1/63 (1.6%) HCW had a positive IGRA (TB1 1.48 IU/ml, TB2 1.17 IU/ml). Conversion was confirmed by the analysis of the IGRA performed initially after exposure (TB1 0.35 IU/ml and TB2 0.11 IU/ml). This HCW was a room service staff with an exposition time of 1-2 hours without previous TB exposure. Treatment for latent TB was offered and started with rifampicin. Two immunocompromised HCW had a negative IGRA > 8 weeks after exposure.

Conclusions: In our contact tracing investigation of 63 exposed HCW to a case of smear-positive laryngeal tuberculosis we observed only 1 IGRA conversion in a HCW with short exposition time.

The low IGRA conversation rate of 1.6% challenges the notion of high infectiousness of laryngeal TB. To evaluate high-priority contacts with the longest duration of exposure might not be the best way to capture new infected persons. The low conversation rate questions the cost-benefit ratio of an expanded contact tracing in low incidence countries.

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Abstract 4768

Retrospective analysis of Bordetella pertussis isolates collected by the National Reference Centre for Whooping Cough in France since 1995: focus on vaccine antigen-deficient isolates

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Background: Whooping cough is a vaccine preventable disease due to infection by Bordetella pertussis. Despite vaccination, B. pertussis (Bp) is still circulating. Acellular vaccines targeting 2 to 5 antigens, i.e., pertussis toxin (PT), filamentous hemagglutinin (FHA), pertactin (PRN) and fimbrial proteins (FIM2-FIM3) have fully replaced whole cell vaccines since 2006 in France. Antigen-deficient, in particular PRN-deficient, Bp isolates have been previously described. Surveillance of the production of the vaccine antigens by Bp isolates, and of the emergence of vaccine-escape sublineages, is essential regarding vaccine efficacy.

Materials/methods: The French surveillance of whooping cough is mainly based on a sentinel hospital-based voluntary surveillance network (called RENACOQ and coordinated by Santé Public France) covering about 30% of hospitalized pertussis pediatric cases. Part of the French national reference center (NRC) collection was retrospectively analyzed for vaccine antigen production using microbiological (Western blot or Serotyping) and genomic approaches.

Results: Among the French NRC collection, 1438 Bp isolates (1995 - 2018) were screened for PT, FHA and PRN production. Four (0.28%) PT-deficient, one (0.07%) PT/PRN-deficient, 4 (0.28%) FHA-deficient and 2 (0.14%) FHA/PRN-deficient Bp isolates were found. Some were collected before the introduction of acellular vaccination in France. Genomic events explaining loss of PT, FHA production were shown to be due to insertions, deletions or point mutations. Regarding PRN-deficient Bp isolates, their proportion has been increasing significantly, representing about half of Bp collected since 2015. Different genomic events lead to loss of PRN-production, two of which were predominant: an IS481 insertion within the prn gene, and a large inversion within the promoter region of the prn gene.

Bp isolates are usually producing either FIM2 or FIM3 fimbriae proteins. A subset of 1058 Bp isolates (2006 – 2018) were serotyped for both fimbriae proteins. Most isolates were producing FIM3, however, an increase of isolates producing FIM2 in the 4 last years has been noticed. Five (0.47%) isolates producing both FIM2 and FIM3, and only 10 isolates (0.94%) producing neither FIM2 nor FIM3 were observed.

Conclusions: These results show that except for PRN, vaccine antigens are still produced by the majority of circulating Bp isolates in France.

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Molecular detection of the \textit{mcr-1} mobile colistin resistance gene in healthy humans and a dog with skin infection from Portugal

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Background: Our aim was to investigate the occurrence colistin plasmid mediated resistance in \textit{Escherichia coli} recovered from fecal samples of humans and companion animals (CAs) in Portugal.

Materials/methods: Between February 2018 and October 2019, fecal samples were collected from CAs and their human household members. Informed consent was obtained. Samples were plated after prior pre-enrichment in peptone water onto Super-Polymyxin medium. For each fecal sample, colonies with \textit{E. coli} phenotypic aspect were isolate and identification was confirmed by PCR. Minimal inhibitory concentration (MIC) for colistin was performed by broth microdilution (Sensititre \textsuperscript{TM} FRCOL, Thermo Fisher Scientific, Wesel, Germany). All isolates were screened by PCR for the presence of five colistin resistance genes (\textit{mcr-1} to \textit{mcr-5}) and Sanger sequencing was performed.

Results: Seventy households constituted of healthy humans (\textit{N}=106) living with healthy CAs (\textit{n}=49) and CAs with skin and soft tissue (SSTI) and urinary tract (UTI) infections (\textit{N}=19, \textit{N}=16, respectively) were enrolled. Of these, 95 fecal samples (89.6\%) from humans, 45 from dogs (healthy-31, SSTIs-19 and UTI-3) and 21 from cats (healthy-18 and UTI-3), were positive for \textit{E. coli} in the SuperPolymyxin medium. Broth microdilution confirmed colistin resistance in 3.1\% (5/161) isolates (three from humans and two from dogs with skin infection), with MICs between 2-8 mg/L. Molecular analysis revealed that three of the \textit{E. coli} isolates carried the \textit{mcr-1} gene, two from two healthy humans and one from a dog with skin infection, all from different households.

Conclusions: To our best knowledge, this is the first report of the presence of the \textit{mcr-1} gene from a dog and in healthy humans in Portugal. The remaining isolates showing resistant phenotype to colistin lacking the studied resistance genes will be screened for other \textit{mcr}-gene variants (\textit{mcr-6} to \textit{mcr-9}). Further studies are needed to determine the full epidemiology of colistin resistance genes in humans and companion animals.

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Lemongrass oil: a promising acaricidal and ovicidal agent against scabies?
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Background: Scabies is a frequent cutaneous infection caused by the mite Sarcoptes scabiei in a large number of mammals including humans. Current therapeutic options are not optimal and there is an unmet need for new acaricide products. Essential oils may represent an alternative strategy for controlling scabies. Lemongrass oil is reported to possess a large panel of pharmacological properties. The aim of the present study was to assess the potential efficacy of lemongrass oil against Sarcoptes scabiei.

Materials/methods: The chemical components of lemongrass oil were identified by GC-MS analysis. We evaluated the efficacy of lemongrass oil against S. scabiei mites and eggs collected from naturally infected rabbits in China. Lemongrass oil was diluted with paraffin to get concentrations of 10%, 5%, 1%, 0.5% and 0.1%. Mite mortality was monitored and evaluated under a stereomicroscope every 10 min until 1 h, and then after 3h, 6h, 12h, and 24h of exposure to treatment. The hatchability of eggs was determined under a stereomicroscope 5 days after exposure to lemongrass oil.

Results: GC-MS analysis confirmed that the main component was citral. Lemongrass oil at concentrations of 10% and 5% killed all Sarcoptes mites within 10 and 25 min, respectively. The median lethal concentration (LC50) value was 1.37%, 1.08%, 0.91%, 0.64%, and 0.48% at 1, 3, 6, 12, and 24h, respectively. Lemongrass oil at all concentrations was able to significantly decrease the hatching rate of Sarcoptes eggs (Figure 1).

Conclusions: The results demonstrated that lemongrass oil should be considered as a promising acaricidal and ovicidal agent for scabies control.

![Figure 1. Hatching rates of Sarcoptes eggs exposed to different concentrations of lemongrass oil under laboratory conditions (35°C and ≥80% relative humidity).](image-url)

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Abstract 4771

**HIV-1 transmitted drug resistance is slowly rising in Estonia in 2017**

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**Background:** Transmitted drug resistance (TDR) prevalence in Europe has been stable around 10% for the last decade. Estonian TDR levels have been lower, however after rapid scale-up of antiretroviral therapy has occurred it started slowly increasing from 4.5% in 2010 to 6.7% in 2013. We aimed to determine the level of TDR and HIV-1 subtypes in Estonia in 2017.

**Materials/methods:** Study included all available samples of newly diagnosed HIV-1 individuals (216 samples out of 219) from January 1 until December 31, 2017. Patients’ demographic and clinical data were obtained from the Estonian Health Board and databases of clinical laboratories. HIV RNA was sequenced in protease and reverse transcriptase region, followed by the determination of transmitted drug resistance mutations (DRMs) and HIV subtypes using Stanford HIV Drug Resistance Database Calibrated Population Resistance and REGA HIV-1 Subtyping Tool, respectively.

**Results:** The majority of newly diagnosed individuals were men (146/219; 67%) with median age of 36 years. The most common transmission route was heterosexual contact (88/129; 68.2%). The median HIV-1 viral load was 16,051 copies/ml (IQR 4775-157,605) and median CD4 cell count 364 (IQR 204-544) cell/µl.

The overall level of TDR was 7.6% (11/144; 95% CI 4.0-13.5). The most common DRM was the non-nucleoside reverse transcriptase inhibitor (NNRTI) mutation K103N, found in seven cases (7/11; 63.6%). NNRTI mutations G190A and Y188L, as well as nucleoside reverse transcriptase inhibitors mutations M184V and M41L were each found in single cases, whereas only one virus possessed two DRMs (K103N and G190A). No protease inhibitor mutations were found.

The majority of the viruses belonged to the CRF06_cpx subtype (93/144; 64.6%), followed by the subtype A1 (15/144; 10%), subtype B (9/144; 6%), subtype G (6/144; 4%) and unclassified URFs (12/144; 8.3%).

**Conclusions:** TDR is rising in Estonian HIV-1 infected population, which indicates that continuous monitoring is necessary in the future. Low genetic barrier NNRTIs should not be considered as a treatment option. HIV-1 subtype distribution has remained stable, indicating no impact of immigration to developing TDR in Estonia.

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Current evidence on dose reduction of antibiotics in patients with impaired renal function: a systematic review

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Background: Inconsistency exists between many guidelines in the recommended dose reduction of antibiotics in patients with impaired renal function. We aimed to define if dose reductions are evidence-based and adequate by systematically searching the literature for clinical studies investigating drug exposure or pharmacokinetic-pharmacodynamic (PK-PD) target attainment after dose reduction of antibiotics in patients with impaired renal function.

Materials/methods: We performed a systematic review searching MEDLINE and Embase from 1946, respectively 1947 until August 2019. We included studies that reported drug exposure (maximum concentration [Cmax], minimum concentration [Cmin], area under the concentration-time curve [AUC]) and/or PK-PD target attainment after dose reduction of antibiotics in patients with impaired renal function. The reduced dose was adequate if the relevant measures of drug exposure and/or PK-PD target were comparable (within a range of 80% - 125%) with that in patients with adequate renal function receiving regular doses. Risk of bias was assessed and this study was prospectively registered in PROSPERO (CRD42019120073).

Results: We included 27 studies, mainly on beta-lactams (12/27) and fluoroquinolones (9/27) and the majority included patients with clinical infections (16/27). Quality of most studies was fair (19/27). Only for meropenem and cefepime good quality evidence from multiple studies was available. For both meropenem and cefepime drug exposure was higher in patients with impaired renal function receiving reduced doses compared to patients with adequate renal function receiving regular doses, so doses are not reduced enough. For all other antibiotics where a dose reduction is recommended good quality evidence of more than one study is lacking. Additionally, remarkable heterogeneity in the definition of renal impairment and the applied dose reductions for individual antibiotics was observed between studies.

Conclusions: Sound evidence on whether dose reductions of antibiotics in patients with impaired renal function lead to comparable drug exposure as in patients with adequate renal function receiving regular doses, is lacking, with exception of meropenem and cefepime. There is need for a clear definition of renal impairment, below which the dose per antibiotic should be reduced and need for prospective validation of the currently most general recommended dose reduction of antibiotics.

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Abstract 4781

**Prospective surveillance of invasive group A streptococcal disease in the Netherlands**

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**Background:** A re-emergence of group A Streptococcal (GAS) infections has been reported by countries across the world. In the Netherlands increasing frequencies of GAS-related postpartum fever and fatal infections among infants were reported in 2018-2019. Recently Lynskey et al. (Lancet Infect Dis 2019) described the emergence of a novel emm1 lineage in the UK, which likely caused increased disease burden both for non-invasive and invasive GAS (iGAS) disease. To improve our understanding of iGAS epidemiology in the Netherlands, a national surveillance study was initiated.

**Materials/methods:** As of January 2019, Dutch GAS isolates from normally sterile body sites and isolates from non-sterile sites from patients with a clinical picture of iGAS disease have been collected. Isolates and patient’s demographic characteristics were submitted by nine participating laboratories covering approximately 25% of the country. All isolates were emm typed.

**Results:** In 2019 up to 26/11/2019, 136 cases of iGAS were identified. The median age was 41 years (range 0-99). Gender was equally distributed, except in age group 15-45 years (78% female). Most isolates were obtained from blood (46%) and the genital tract (18%), others from the respiratory tract (5%), not further specified puncture fluid (6%), tissue (6%) or abscesses (4%), joint fluid (4%), wounds (3%) and cerebrospinal fluid (2%). Twenty-one different emm types were detected. Overall, the most prevalent emm types were emm1 (30%), emm89 (10%), emm77 (9%), emm6 (8%) and emm22 (8%). The emm type distribution per culture specimen category is shown in Figure 1. Emm1 was seen significantly more in blood than genital isolates (p=0.02). Emm89 was the most dominant emm-type among genital isolates.

**Conclusions:** Dutch iGAS surveillance data shows that emm1 was the most prevalent emm type among patients with iGAS in 2019 in the Netherlands. Emm89 was the most prevalent emm type among isolates from the genital tract, reflecting a predominance among puerperal iGAS infections. Emm3 was not detected in this surveillance, despite its predominance in Dutch iGAS surveillance data from 1994-2003. In the near future, our results will be supplemented with additional genotyping and clinical data to define high-risk populations, which might impact prophylactic antibiotic treatment guidelines.

**Figure 1. Distribution of emm types in iGAS isolated from blood, genital tract and other sites**

[Graph showing distribution of emm types]

iGAS = invasive group A streptococcal; *Other culture specimens: respiratory tract, not further specified puncture fluid, tissue, abscesses, joint fluid, wounds, cerebrospinal fluid; **Remaining emm types: 4, 11, 12, 20, 29, 76, 66, 82, 87, 84, 104, 118, 145, 168, 170 and STG 682

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Active follow-up of patients colonised with highly-resistant microorganisms to discontinue isolation measures

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Background: To prevent nosocomial transmission of highly resistant microorganisms (HRMO), preventive measures must be taken when patients colonized with HRMO are hospitalized. Contact isolation measures however, are costly and labour-intensive. Since HRMO carriage can be temporary, isolation measures are discontinued once a patient is proven to be HRMO free. In our hospital, up until 2019, follow-up cultures for HRMO carriage were not routinely taken, possibly resulting in unnecessary isolation measures. Therefore, active patient follow-up was started in 2019, aiming to quickly declare patients HRMO free to reduce costs and workload due to isolation measures.

Materials/methods: This before-and-after design study was conducted in the Erasmus University Medical Centre, Rotterdam, The Netherlands. According to the local protocol, patients were declared HRMO free after two consecutive negative rectum and throat cultures. Patients with an HRMO identified between October 2013 until December 2018 were cultured only upon request of their treating physician. Patients colonized with HRMO from January 2019 onwards were actively contacted for follow-up cultures. For evaluation of the economic impact of this active patient follow-up regimen, the extra direct costs of hospitalization days in isolation were calculated, as well as the number of hospitalization days in isolation in both the active and passive follow-up periods.

Results: From October 2013 until November 2019, a total of 3522 HRMO patients were identified. 2571 patients were included with passive follow-up and 481 with active follow-up. 219 out of 481 patients identified in 2019 were eligible for culturing. Regarding active follow-up, in total, patients were hospitalized in isolation for an average 14.3 days (median=3.0) compared to 22.5 days (median=9.0) days for patients included in the passive follow-up (P>0.001). An analysis with fixed follow-up periods will follow.

Conclusions: Patients who received active follow-up had significantly less isolation days during hospitalization. However, results are based upon a limited selection of the patients identified in 2019. To get a better estimation of the impact of active follow-up a longer follow-up time and a larger number of inclusion is needed. Therefore, this study will continue to collect additional results.

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Abstracts 2020

Abstract 4793

Transforming a multiplex laboratory developed real-time PCR for herpes simplex virus type 1 and 2 & varicella zoster virus into a sample-to-answer, cassette-based format

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Background: Viral encephalitis is a devastating infection of the central nervous system. Early diagnosis of Herpes simplex virus (HSV) or Varicella zoster virus (VZV) encephalitis allows prompt administration of acyclovir which reduces neurological damage and mortality significantly. The ARIES system (Luminex Corporation) is a fully automated sample-to-answer molecular diagnostic instrument on which CE-IVD assays and Laboratory Developed Tests (LDT) can be performed. In this study, we evaluated the LDT capabilities of ARIES by converting an existing multiplex real-time PCR for HSV 1/2 & VZV (Taqman) with extraction on Qiasymphony SP/AS (QS SP/AS) (Qiagen) and amplification on Rotorgene Q (RGQ) (Qiagen) into a cassette-based ARIES assay. The performance of these two assays was compared.

Materials/methods: Carrier RNA, proteinase K and an internal extraction and amplification control (IC) was added directly to the sample. The primers and probes were added in the same concentration as for RGQ to a tube containing lyophilized ARIES Exo+ Ready Mix (Luminex Corporation). This tube was clicked onto an ARIES extraction cassette and the sample was added to the cassette. Subsequently, the cassette was processed onto the Aries system, following completion in 2 hours. Total hands on time was 5 minutes.

Sensitivity, reproducibility and accuracy was determined and a retrospective analysis of RGQ positive and negative patient samples was performed. A Ct-value for inhibition cut-off was also established.

Results: The multiplex real-time PCR for HSV 1/2 & VZV assay on Aries showed a RGQ comparable sensitivity of 100 copies/ml, a good reproducibility (ΔCt < 2.5) and an accuracy of 100%. There was also an excellent concordance for all patient samples between Aries and RGQ. Inhibition was seen when the Ct-value for IC was > 33.

Conclusions: This study demonstrates the easy transition from a QS SP/AS followed by RGQ multiplex real-time PCR for HSV 1/2 & VZV assay to a sample-to-answer format on ARIES with an excellent performance on the ARIES. Only a minimal optimization for sample pretreatment was needed for a successful transfer to ARIES. The ARIES offers a valuable addition to the routine laboratory.

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Abstract 4795

**Antimicrobial resistance in Italy: data from the National Surveillance System AR-ISS over a 7-year period, 2012-2018**

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**Abstract third-party references:** Italian Ministry of Health

**Background:** Data from routinely collected samples from invasive isolates of eight pathogenic species were collected by the Italian antibiotic-resistance surveillance network (AR-ISS), coordinated by the Istituto Superiore di Sanità. The aim of the study was to analyse the temporal trend from 2012 to 2018 of antimicrobial resistance (AMR) for selected classes of antibiotics as well as multi-drug resistance of Gram-negative bacteria and the most important drugs/pathogen combinations.

**Materials/methods:** The percentages of AMR with 95% confidence intervals were calculated overall and by Italian Regions. Multi-level logistic regression models (clustered by hospital laboratory) were applied to evaluate the association between each of the four considered drugs/pathogen combinations (MRSA, methicillin-resistant *Staphylococcus aureus*, VRE- *faecium*, vancomycin-resistant *Enterococcus faecium*, CREC, third generation cephalosporins-resistant *Escherichia coli*, CRKP, carbapenem-resistant *Klebsiella pneumonia*) and patients’ characteristics (sex, age, hospital ward, geographical area), taking into account also the laboratory effect by calculating the percentage of variation attributable to differences among laboratories (intra-class correlation).

**Results:** A total of 128,510 isolates from blood and cerebro-spinal fluid were collected during the study period. The percentage of MRSA remained quite stable (around 34%) over the whole period, whereas a significant decline was observed in the last two years for CRKP (from 33.8% in 2016 to 29.5% and 26.8% in 2017 and 2018 respectively); conversely a sharp increase was observed for VRE-*faecium* (from 6.3% in 2012 to 18.9% in 2018). A higher risk of resistance was associated with male sex (except for VRE-*faecium*), older age (18-64 and ≥65 versus 0-17 years old), intensive care and surgery (the latter only for MRSA and CRKP) as compared to medicine units. Moreover, AMR interregional variation was observed, and only for CRKP higher values of resistance were found in southern Italy compared to the other regions.

**Conclusions:** Although in the last years AMR showed a decreasing trend in Italy, likely due to more coordinated activities in accordance to the national action plan, higher resistance rates continue to be observed as compared to the EU mean values. Appropriate antimicrobial use, infection prevention and control strategies are essential for effective interventions aiming to prevent selection and transmission of bacteria resistant to CIAs.
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The relationship between clinical outcomes and empirical antibiotic therapy in patients with community-onset Gram-negative bloodstream infection: a cohort study from a large teaching hospital

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Abstract third-party references: Supported by NIHR, Supported by The Wellcome Trust

Background: The incidence of Gram-negative bacteraemias (GNB) that are resistant to first line antibiotics is increasing. The widespread use of broad-spectrum antibiotics for suspected GNB, to avoid a delay in initiating effective therapy in patients with antibiotic-resistant GNB, in turn promotes the emergence of antibiotic-resistant strains. We set out to investigate the impact of discordant empirical antibiotic therapy on clinical outcomes in patients with GNB, to inform prescribing guidelines.

Materials/methods: An observational cohort study of patients admitted to Queen Elizabeth Hospital Birmingham between 01/09/2011-01/01/2018 due to community-onset Escherichia coli bacteraemia (ECB), Klebsiella pneumoniae bacteraemia (KPB) and Pseudomonas aeruginosa bacteraemia (PsAB). We estimated the association between concordant versus discordant empirical antibiotic therapy on the odds of in-hospital death and ICU admission, adjusting for clinical and demographic factors.

Results: 1380 patients were included in the study, of whom 1103 (79.9%) had ECB, 189 (13.7%) had KPB and 88 (6.4%) had PsAB. Discordant antibiotic therapy was not associated with increased odds of in-hospital death or ICU admission for patients with ECB. For KPB, there was an increased odds of in-hospital death with discordant treatment (adjusted OR 4.78, 95% CI 1.25-18.33). In patients with ECB, a non-urinary source and increased disease severity (standardised early warning scoring system (SEWS) score of ≥4 as compared to 0-3) were respectively associated with a 3- (adjusted OR 3.19, 95% CI 1.72-5.92) and 8-fold (adjusted OR 8.05, 95% CI 4.25-15.24) increased odds of in-hospital death.

Conclusions: Patients with non-urinary source ECB and higher severity scores were more likely to experience adverse outcomes including death and ICU admission. This emphasises the need for prompt broad-spectrum antibiotics in patients with signs of a non-urinary source or clinical markers of severe illness, in support of campaigns such as Surviving Sepsis. These findings also support the use of narrow-spectrum empirical antibiotics in low risk patients with ECB (almost 80% of our cohort) of urinary source. By contrast, in patients with KPB, discordant empirical therapy was associated with adverse outcomes. This highlights the need for tools to guide empirical prescribing decisions, which consider the likely source of infection, pathogen and disease severity.

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Abstract 4800

Pharmacokinetic evaluation of micafungin prophylaxis for invasive mould disease in childhood acute lymphoblastic leukemia: part of the OPTIMA study

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Background: The Princess Máxima Center for pediatric oncology recently introduced a new biweekly prophylactic regimen of micafungin for invasive mould disease. Extended dose intervals of micafungin could overcome the need of frequent hospital visits. As part of this new strategy, we aimed to determine the pharmacokinetics of micafungin and to simulate various dose regimens that could be deployed as a mould active prophylactic regimen.

Materials/methods: Micafungin was given biweekly at 9 mg/kg as a two hour infusion during the first five weeks of the induction treatment in pediatric patients with newly diagnosed ALL. A five-point sample curve was obtained (t=0, 2.5, 4, 5 and 24h). The PK of micafungin was analysed using non-linear mixed effects modeling, with clearance (Cl) and volume of distribution (Vd) allometrically scaled to total body weight. Monte Carlo simulations with four different dosage regimens were performed: 5 mg/kg, 7 mg/kg and 9 mg/kg with a maximum dose of 300 mg and flat dose per weight band (0-10kg received 50mg, 10-20kg received 100mg, 20-40kg received 150 mg and >40kg received 300 mg). Simulated pediatric exposure was compared to exposure in adults after 100mg daily.

Results: 62 patients were included with a total of 270 observations. Median age and weight with range were 4(1-17) years and 19.3(8.6-177.2) kg. A two-compartment model with intravenous administration and linear elimination best fitted the data. Typical parameter values with relative standard error (RSE%) were for clearance (Cl) 0.668(3%) L/h, central Vd (V1) 9.87(15%) L, peripheral Vd (V2) 7.15(17%) L and intercompartmental Cl (Q) 2.65(35%) L/h. Simulated micafungin exposure (i.e. median area under the curve (AUC)) with interquartile range (IQR)) for the 5 mg/kg, 7 mg/kg, 9 mg/kg and flat dosing regimens were respectively 783(245) mg·h/L, 1043(301) mg·h/L, 1251(380) mg·h/L and 951(323) mg·h/L. All simulated regimens exceeded the micafungin exposure in adults of 690(244) mg·h/L.

Conclusions: Our 9mg/kg biweekly dose suggests an above average micafungin exposure compared to adults receiving 100mg daily. Our clinical study has currently enrolled 100 patients and will provide the evidence for efficacy and safety of this 9 mg/kg regimen. A flat dose per weight band may be a suitable alternate.

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Abstract 4801

Prolonged viral shedding in bronchial aspirate fluids in a patient with measles-related severe pneumonia

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Background: Measles, a vaccine-preventable disease, is currently responsible for worldwide outbreaks mainly due to the lack of adequate immunization. Pneumonia is the most common, even life-threatening, complication of measles. We report a case of measles-related severe pneumonia in a 56-year-old man with history of schizophrenia, hypertension, dyslipidemia, and chronic obstructive bronchopneumopathy.

Materials/methods: The patient was admitted at the Intensive Care Unit of INMI and mechanically ventilated on April 2019, following a morbilliform rash and a severe respiratory insufficiency, with 15 APACHE II [Acute Physiology and Chronic Health Disease Classification System II] score and 4 SOFA [Sequential Organ Failure Assessment] score. Measles diagnosis, based on positive measles-specific serological tests, was confirmed by molecular test on urine.

Results: Due to the clinical progression to Acute Respiratory Distress Syndrome (ARDS), longitudinal bronchial aspirates (BAS) were performed, to assess for bacterial, viral or fungal infections in lung. No detection of respiratory pathogens by PCR or culture was demonstrated, apart from a positive MV PCR in the BAS at day 13 from admission. All previously collected BAS samples were retrospectively studied for MV PCR and all resulted positive, providing evidence of a measles-related pneumonia. A prolonged persistence of MV in BAS (27 days) was observed, peaking at day 8 and 17 following admission, corresponding to worsening of the respiratory function and febrile episodes, while MV viremia was undetectable. Since MV was still detectable in BAS when the patient was extubated and transferred to the acute care setting (day 28), measles PCR monitoring was performed on longitudinally collected pharyngeal swabs. The patient was maintained in respiratory isolation until day 33, when both clinical improvement and MV clearance in pharyngeal swab were observed. At discharge (day 47), the patient was still MV PCR positive in the urine.

Conclusions: The presence of MV RNA was observed in specimens of the lower respiratory tract, even after viral clearance from plasma, suggesting a local replication. Prolonged viral shedding in respiratory samples is to be considered in patients with measles-associated-ARDS. Concerns on the prolonged duration of respiratory isolation measures deserves careful consideration in respect of infection transmission risk in the hospital setting.

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Abstracts 2020

Abstract 4802

**Carbapenemase-producing organisms in high-risk units of a district general hospital in London**

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**Background:** The epidemiology of carbapenemase-producing organisms in district general hospitals in London has not yet been well documented. Our district general hospital serves a diverse, mobile population in North London. Here we describe the epidemiology of carbapenemase-producing organisms (CPO) in patients admitted to high-risk wards.

**Materials/methods:** A retrospective analysis was carried out of all resistant organism screens performed over a 12 month period on the Critical Care Unit (CCU), Acute Stroke Unit (ASU), Neonatal Unit (NNU) and Oncology and Haematology ward (Onc/Haem). Admission and weekly screening of patients by rectal swab is carried out on these wards.

**Results:** Over the 12 month period 5,238 resistant organism screens were performed on 2,064 patients. 71 carbapenemase-producing organisms were isolated from 60 patients. 2.9% of inpatients on the high-risk units were colonised with a carbapenemase-producing organism. Prevalence was 7.0% on ASU, 2.0% on CCU, 1.0% on Onc/Haem and 0.5% on the NNU. The most common organism isolated was Enterobacter cloacae in 39 patients. The most common enzyme identified was NDM in 45 patients, whilst OXA-48 was found in 14 patients, VIM in 1 and OXA-23 producing Acinetobacter in 2 patients.

**Conclusions:** Carbapenemase-producing organisms were found in patients throughout the high-risk units of our district general hospital. Our findings highlight the importance of regular screening on these units, particularly given the vulnerable nature of these cohorts and the extent to which they move across the regional hospital network as part of specialist service referral pathways. Documenting patients’ CPO-carrier status is crucial for implementing appropriate infection prevention and control measures as well as guiding antimicrobial choice.

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Abstract 4805

Molecular detection of *Mycoplasma amphoriforme* and *Ureaplasma* species from patient samples previously investigated for *Mycoplasma pneumoniae* infection in England and Wales between 2016 – 2017

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**Background:** *Mycoplasma amphoriforme* is associated with respiratory tract infections among patients with primary antibody deficiencies with limited prevalence data among immunocompetent individuals. *Ureaplasmas* have been associated with hyperammonemia among lung transplant patients, but little is known regarding their presence within respiratory samples among patients which are immunocompetent.

**Materials/methods:** Residual DNA samples (161) submitted for *Mycoplasma pneumoniae* testing to Public Health England (PHE), from September 2016 to December 2017 were screened by an in-house qPCR assay for the presence of *M. amphoriforme* and conventional PCR for *Ureaplasma* spp and *Mycoplasma fermentans*. *Ureaplasma* species were detected using a differential in-house PCR assay which amplified a variable region resulting in 448 bp amplicon for *Ureaplasma urealyticum* and 403 bp for *Ureaplasma parvum*. The presence or absence of macrolide resistance determining mutations within domain V of the 23s rRNA was determined by PCR and sequencing of *M. amphoriforme* positive samples.

**Results:** A total of ten samples were positive for *M. amphoriforme* (6.2%), five samples were positive for *U. parvum* (3.1%) and no samples were found to contain *M. fermentans* DNA (0%). Three out of the ten *M. amphoriforme* positive samples were previously identified as positive for *M. pneumoniae* suggesting co-infection. All ten *M. amphoriforme* were genotypically susceptible to macrolide antibiotics (100%). Of the samples which were positive for *M. amphoriforme* 9/10 were from male patients, whereas for the *U. parvum* positive samples 3/5 were male. No *M. amphoriforme* detections were seen during the summer months.

**Conclusions:** These data suggest that *M. amphoriforme* can be found among clinical samples in patients suspected to have *M. pneumoniae* and it may represent an emerging respiratory pathogen. *U. parvum* can be found in the lungs of patients with suspected lower respiratory tract infections and maybe a reservoir and source of donor-derived infection among lung transplant recipients. In both instances, further investigation of their prevalence is required.

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A new high-resolution melting PCR assay for a rapid detection of linezolid-resistance-associated mutations in Mycobacterium avium complex

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Background: Mycobacterium avium complex (MAC) is a group of slowly growing non-tuberculous mycobacteria that is emerging as major infectious threat in developing countries. The most frequent are M. avium and M. intracellulare, for which the conventional treatment is a macrolide-based multidrug regimen. However, due to the increased macrolide-resistance, alternative treatments are needed.

Linezolid, the only FDA-approved oxazolidinone for mycobacterial diseases representing 2nd line treatment for M. tuberculosis, has been shown to have a good activity against Non-Tuberculous Mycobacteria (NTM) [Winthrop et al. 2015]. However, the long-term treatment, typical for mycobacterial infections, promotes the acquisition of linezolid-resistance due to mutations in rrl, rplC and rplD.

In this study we developed a High-Resolution Melting (HRM) PCR assay to detect linezolid-resistance-associated mutations in MAC.

Materials/methods: An HRM PCR assay was performed on 55 linezolid-resistant MAC clinical isolates (50 M. avium and 5 M. intracellulare) provided by ASST Grande Ospedale Metropolitano Niguarda (selected following American Thoracic Society Criteria) to detect linezolid-resistance-associated mutations in rrl, rplC and rplD genes.

The results were analysed using Precision Melt Analysis™ software (BioRad) obtaining different clusters based on mutations presence and then verified through Sanger sequencing.

Results: Preliminary results, based on 10 MAC (5 M. avium and 5 M. intracellulare), showed in 20% of isolates mutations in rplD gene: G443A (Arg148Lys) in M. intracellulare and A439G (Thr147Ala) in M. avium, respectively, already identified in a recent study [Kim et al 2018]. We have also found new mutations, never reported before (data not shown) and under confirmation.

Conclusions: In recent years, in the Milan macroarea, MAC clinical isolates have shown low resistance to first line drugs (1.2% for clarithromycin and 4.7% for intravenously-administered amikacin), but high level of resistance for second line drugs (40.2% for moxifloxacin and 91% for linezolid). Linezolid-resistance is higher in our strains compared to that described in other parts of the world.

The HRM PCR assay is a rapid screening method to discriminate wild type from mutated sequences thanks to creation of different clusters. This can be useful to detect new and known linezolid-resistance-associated mutations both before and during treatment to monitoring the resistance onset.

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Intestinal colonisation by multidrug-resistant Enterobacteriaceae and infections in patients receiving an allogeneic haematopoietic stem cell transplantation: the ENTHERE-SCT Study [PI16/01415]

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Background: Currently, it is being discussed whether intestinal colonisation by multidrug-resistant Enterobacteriaceae (MDRE) in patients receiving hematopoietic stem cell transplantation (Allo-SCT) is a risk factor for developing systemic infections. The aim of this study was to analyze the risk factors of intestinal colonisation by MDRE and the development of infections in patients with Allo-SCT.

Materials/methods: multicenter prospective cohort study conducted at four third level Spanish hospitals between June 2017 and March 2019. A rectal swab was collected before Allo-SCT and then, weekly until day 30 after transplantation, every two weeks until day 100 after transplantation and monthly until day 180 after the transplant. Clinical and microbiological data were collected during patient follow-up.

Results: Sixty four patients were included (28 from Hospital 1, 20 from Hospital 2, 10 from Hospital 3 and 6 from Hospital 4). Twenty four (37.5%) patients were colonized by MDRE at some point in the follow-up, 4 (6.3%) of them before Allo-SCT. Colonized and non-colonized patients had similar demographic factors [sex, age and underlying disease], and risk factors such as HCT-CI score and previous invasive procedures, hospital admission and infections (Table 1). One hundred and sixteen episodes of infection were recorded in 51 patients: 55 (47.4%) in 22 colonized patients and 61 (52.6%) in 29 non-colonized patients. The most frequent type of infection was bacteremia (50.0% in colonized patients and 32.5% in non-colonized patients), followed by respiratory infections, CMV infection and urinary infections. There were only 5 episodes of MDRE infections in 4 patients: 1 patient developed a cellulitis due to ESBL-producing K. pneumoniae and a bacteremia due to AmpC-hyperproducing E. cloacae; 1 patient had bacteremia due to carbapenemase-producing E. cloacae; 1 patient a urinary infection due to carbapenemase-producing K. oxytoca and 1 patient a urinary infection due to ESBL-producing C. freundii.

Conclusions: 1. In patients with Allo-SCT, intestinal colonisation by MDRE was more frequent after transplantation than before transplantation. 2. All MDRE infections occurred in patients with intestinal colonisation either before or after of the infection episode.

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Surveillance and molecular typing of carbapenem-resistant Enterobacteriaceae in neonatal intensive care units in Italy

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Background: Infections with carbapenem-resistant Enterobacteriaceae (CRE), especially Klebsiella pneumoniae and Escherichia coli, are a serious threat for neonatal intensive care units (NICU). The under-developed immune system of patients and the limited treatment options increase the associated risk. The present study was firstly aimed to estimate the prevalence of CRE strains among the hospital settings and then to investigate their molecular aspects.

Materials/methods: Between 2017 and 2019, 100 CRE strains were isolated from rectal swabs of newborn patients at the microbiological laboratory of Bambino Gesù Children’s Hospital in Rome (Italy). Strains were identified by mass-spectrometry (MALDI-TOF, Bruker) and their antibiotic susceptibility was firstly determined with Vitek 2 system (bioMérieux) according to the EUCAST breakpoints. The Xpert Carba-R (Cepheid) assay was used to detect the resistance determinants and the PCR-based replicon typing (PBRT 2.0, Diatheva Srl) was applied to distinguish the incompatibility groups (Inc). For each strain representative of a PBRT pattern, the multilocus-sequence typing analysis (MLST) was performed.

Results: Fifty-seven strains were identified as K. pneumoniae and 43 as E. coli and all were carbapenem-resistant. \textit{bla}_{NDM} gene was the predominant with 56 single detections (56%) and in 30 strains it was combined with \textit{bla}_{KPC}. A preliminary PBRT analysis of 32 strains revealed the prevalence of IncA/C group widely distributed also in A/C, R, FIIK, FIB KQ and FIB, A/C, FII patterns detected as the predominant multireplicon patterns. Among the 14 PBRT profiles, 8 isolates were selected for MLST: 8 sequence types (ST) were distinguished showing a very high variability. Within them, the ST395 and ST131 are well-known in the global scenario whereas the ST307 and ST101 are recently described as emerging clones, also in paediatric wards.

Conclusions: Based on these data, more attention must be given to the high prevalence of CRE circulating in NICU. Their molecular features highlight the need to implement control measures to avoid their spread among the clinical wards as well as possible complications for the treatment of newborn infections. Furthermore, the application of molecular typing methods in hospitals can be helpful to monitor the diffusion of high-risk clones.

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Country-specific approaches to latent tuberculosis screening and its current effectiveness in migrants to Europe

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Background: Migrants (defined as ‘foreign born’ individuals) are disproportionately affected by tuberculosis in many low-incidence countries, with most active tuberculosis arising from reactivation of latent tuberculosis infection (LTBI). New ECDC guidance suggests systematic testing and treatment for LTBI be offered to migrants, with consideration given to effective implementation along the pathway of care ensuring treatment adherence and completion, yet there is an urgent need for more research and clarity around effectively delivering LTBI screening to migrant populations.

Materials/methods: We did a systematic review and meta-analysis to explore treatment uptake and adherence among migrants in LTBI screening programmes globally. The protocol was PROSPERO registered (CRD42019140338) and follows PRISMA guidelines. We did a semi-structured questionnaire survey of experts in 32 EU/EEA countries and Switzerland (MOH or Public Health, identified through ESGITM and ESGMYC networks) exploring views and concerns around current screening approaches, diagnosis, and management.

Results: 55 studies were included in the review, including data on 30,190 migrants. 51% (95% CI = 40-62%; I² = 99.6%) of migrants testing positive in a screening programme go on to initiate and complete treatment. 71% (95% CI = 0.68-0.75; I² = 98.3%) of migrants who do initiate treatment for LTBI ultimately complete treatment. A variety of both patient and provider-linked factors account for migrants not initiating and completing treatment.

Survey data show that many EU/EEA countries do not target LTBI screening at migrants from high-burden TB countries. Of those that do, screening is voluntary, predominantly focused on young migrants (0-18 years) originating from high-burden countries (the definition of which varies by country), involves either TST or IGRA, with first-choice treatment being RIF + INH for 3 months. Experts felt that migrants were a group with higher drop-out rates, and stressed the need to raise awareness about LTBI screening in migrant populations.

Conclusions: Migrants have low treatment completion rates for LTBI. Greater focus must be given to designing and delivering effective LTBI programmes to migrants if we are to improve health and support global TB eradication.

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Abstract 4813

**Characteristics and trends of recently HIV infected individuals in Estonia in 2013-2017**

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**Background:** The number of new HIV diagnoses in Estonia has remained high with majority of infections being diagnosed among people who inject drugs (PWID) and heterosexuals. Knowing the proportion of recent infections is essential for understanding the course of our epidemic. Thus, we aimed to determine and compare the rates of recent infections among newly HIV-diagnosed individuals using HIV-1 limiting antigen avidity assay (LAq).

**Materials/methods:** All individuals diagnosed with HIV within the years of 2013 (n=325), 2015 (n=269), and 2017 (n=219) were included in the study. Residual samples (289 in 2013, 184 in 2015, and 214 in 2017) from Estonian HIV reference laboratory were tested using LAq with a median duration of recent infection of 130 days. Clinical and demographic data were obtained from Estonian Health Board, hospital records, and Estonian HIV positive patients’ database.

**Results:** Based on LAq, 128 (44.3%), 73 (39.3%), and 73 (34.1%) individuals were classified as recently infected in 2013, 2015, and 2017, respectively (Table). During study period, the proportion of recent infections decreased (44.3% vs 34.1%, p=0.022). The median age of recently infected individuals increased (30 vs 36, p=0.001), but the proportion of men remained similar. The proportion of PWID decreased over the years (25% vs 8%, p=0.004) while the proportion of heterosexuals remained roughly the same. However, self-reported risk factor was unknown in 48% of recently infected individuals in 2017.

**Table**

<table>
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</thead>
<tbody>
<tr>
<td>Age, median(IQR)</td>
<td>30(25-40)</td>
<td>31(26-39)</td>
<td>36(30-45)</td>
<td>.703</td>
<td>.001</td>
<td>.008</td>
<td></td>
</tr>
<tr>
<td>Men, n(%)</td>
<td>71(55)</td>
<td>42(58)</td>
<td>40(55)</td>
<td>.883</td>
<td>1</td>
<td>.868</td>
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<tr>
<td>Self-reported risk factor, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Heterosexual men</td>
<td>28(22)</td>
<td>14(19)</td>
<td>12(16)</td>
<td>.720</td>
<td>.462</td>
<td>.829</td>
<td></td>
</tr>
<tr>
<td>Heterosexual women</td>
<td>41(32)</td>
<td>19(26)</td>
<td>19(26)</td>
<td>.426</td>
<td>.426</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>PWID</td>
<td>32(25)</td>
<td>12(17)</td>
<td>6(9)</td>
<td>.214</td>
<td>.004</td>
<td>.207</td>
<td></td>
</tr>
<tr>
<td>MSM</td>
<td>22</td>
<td>9(12)</td>
<td>4(6)</td>
<td>.002</td>
<td>.193</td>
<td>.245</td>
<td></td>
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<tr>
<td>Unknown</td>
<td>25(19)</td>
<td>19(26)</td>
<td>32(44)</td>
<td>.293</td>
<td>.003</td>
<td>.037</td>
<td></td>
</tr>
<tr>
<td>CD4, median(IQR)</td>
<td>400(288-577)</td>
<td>468(266-638)</td>
<td>471(304-644)</td>
<td>.443</td>
<td>.248</td>
<td>1</td>
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**Conclusions:** Our results indicate that HIV testing is efficient with around one third of newly infected individuals being discovered within the first 130 days. Heterosexual contact has remained the most common self-reported risk factor indicating an ongoing sexually driven epidemic.

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Molecular genetic analysis of population of dermatophyte fungus *Trichophyton rubrum*

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**Background:** *Trichophyton rubrum* is an important causative agent of tinea unguium and tinea pedis worldwide. It is clonal fungus with remarkably low genetic variability. We studied population structure of *T. rubrum* to facilitate epidemiological studies on a global scale.

**Materials/methods:** Species identification of *T. rubrum* isolates was done by ribosomal ITS region sequencing. We performed typing of simple sequence repeats (SSR, also known as microsatellites) in 67 clinical *T. rubrum* isolates from Saint Petersburg and Yekaterinburg, Russia by original assay including 8 previously published and 4 original loci. TERG_02941 genotype was determined by TaqMan SNP genotyping assay with allele-specific probes. Six representative strains, occupying the whole span of SSR typing-based NJ tree were selected for whole genome sequencing by Illumina MiSeq technology.

**Results:** All studied isolates from Russian sample harbored the same ITS region genotype, identical to that one deposited in GenBank under accession number KT285224. SSR typing revealed three major groups of Russian isolates. WGS-based tree of *T. rubrum* sensu stricto isolates contained well-supported monophyletic branch of TERG_02941 793A isolates and two branches of 793G isolates. The TERG_02941 793A branch included West European, Russian and North American strains. The first TERG_02941 793G clade contained East Asian, South-East Asian, North American and Russian isolates, whereas the second TERG_02941 793G clade contained West European and Russian strains.

**Conclusions:** Population of *T. rubrum* consists of cosmopolitan genetic lineages. It means that tracking global spread of *T. rubrum* genetic lines is feasible.

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Abstract 4815

Analysis of the evolution of the rate and the associated factors of antiretroviral treatment switch due to intolerance symptom on children in France

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Background: For children living with HIV, cART is recommended from diagnosis. Switch in cART may be related to toxicity or intolerance, whose rate is poorly analysed and understood for infected children. The aim of this study is to estimate rate of antiretroviral therapy switches over time, to analyze calendar effect and to derive which therapeutic strategy can be linked to a switch for toxicity or intolerance. The data source is a National ANRS EPF-C010 cohort of HIV infected children and treated from 2005 to 2018.

Materials/methods: The incidence rate of switches is estimated with Poisson models. The probability of the first switch is estimated with the Kaplan Meier method, and associated factors are identified with a competitive risk model.

Results: The incidence rate of cART switch is 31.8 [30.2-32.7] per 100 person-years. The probability of switching the first treatment is 59.7% [56.1 - 63.3] at 3 years. The incidence rate of switching for toxicity or intolerance decreases over time with an IRR per year of 0.89 [0.85-0.93], p = 0.01. In children under 6 months, the probability of switching first treatment for toxicity tends to decrease after 2007 compared to 2005-07 (3.6% versus 2.1% at 2 years, p = 0.06). Hematologic or mitochondrial toxicity represents 25% of the causes of toxicity switches, all related to AZT. The probability of switching first treatment containing old NRTIs (like AZT) is 17.2% versus 4.3% for recent NRTIs; p = 0.24.

Conclusions: The decrease over time of the risk of switching cART for toxicity or intolerance in children living with HIV, treated for the first time between 2005 and 2018, is reassuring for the care of children.

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Pharmacodynamic properties of minocycline monotherapy and combined with polymyxin B in a lung model in neutropenic mice

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Background: Antimicrobial resistance is a growing problem worldwide. Given the shortage in development of new antibiotics against multi-drug resistant bacteria, there is a growing need to optimize the use of old antibiotics. Combination therapy of existing antibiotics could be an auspicious approach. We therefore investigated the pharmacodynamic (PD) properties of the combination of minocycline and polymyxin B (PMB) against *Klebsiella pneumoniae* in a lung infection neutropenic animal model.

Materials/methods: 10⁶-10⁷ CFU of 3 *K. pneumoniae* isolates (ATCC43816, 74 and 104) with minocycline/PMB MICs 4/0.5, 2/2 and 2/2 mg/L were intranasally administrated in cyclophosphamide-induced neutropenic mice. 2h after infection mice were treated with 2-64 mg/kg q6h, 4-128 mg/kg q12h or 128-256 mg/kg q24h of minocycline alone. For combination therapy mice were treated with 4-128 mg/kg q6h minocycline and 4-16 mg/kg q6h of PMB. After 24h, mice were euthanatized and CFUs were counted with serial quantitative cultures in lung homogenates. The log₁₀ CFU/lung reduction compared to initial bacterial lung burden and 24h placebo-treated mice (dCFU) were calculated for each minocycline and PMB doses.

Results: No stasis was found at any monotherapy or combination regimens. Minocycline monotherapy did not reduce lung bacterial burden compared to placebo-treated mice at any dose except the highest dose of TDD 256 mg/kg. Mean dCFU in minocycline treated q6h vs placebo-treated mice compared to start of treatment was 2.4 vs 2.4, 1.8 vs 2.6 and 1.7 vs 2.0 in *K. pneumoniae* ATCC43816, 74 and 104 infections, respectively. Highest reduction in lung load was found with q24h regimens (mean dCFU -0.9 vs 2.0) in *K. pneumoniae* 104 infected mice. When minocycline q6h up to TDD 512 mg/kg was combined with PMB q6h up to TDD 64 mg/kg in *K. pneumoniae* 104 infected mice, slight reductions in bacterial load were observed compared to monotherapy (mean dCFU -0.8 vs 0.7).

Conclusions: Minimal efficacy of minocycline alone and in combination with PMB was found up to TDD of 256 and 64 mg/kg, respectively against *K. pneumoniae* lung infection model in neutropenic mice. This combination should be studied in more detail in other infection models to explore possible interaction.

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Abstract 4817

**Campylobacter concisus prevalence in microscopic colitis: a cultivation study**

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**Background:** Microscopic colitis (MC) is an inflammatory bowel disease. Its aetiology remains unknown; but a luminal gut factor is hypothesised to influence the inflammatory response. Any association with gut bacteria is poorly described, although one study found a possible association in patients with prior Campylobacter concisus gastroenteritis, who presented with a MC diagnosis at 6-month follow-up. *Campylobacter concisus* consists of two genomospecies (GS1 and GS2), which may differ in pathogenic potential, as GS2 is better adapted to the gut than GS1. We aimed to investigate the prevalence of *Campylobacter concisus* in clinical samples from MC patients, including the distribution of GS1 and GS2 isolates.

**Materials/methods:** Fifty-five patients with MC were included. All underwent sigmoidoscopy for the collection of mucosal biopsies; saliva and faecal samples were also collected. Samples were cultivated by the filter method for 48 hours at 37°C in both microaerobic and anaerobic conditions. Species identification was confirmed by MALDI-TOF. MC results were compared to 26 comparable healthy controls. Genome sequencing of MC faecal and biopsy isolates was performed with the Illumina MiSeq; 23S rDNA analysis divided isolates into GS1 or GS2.

**Results:** *Campylobacter concisus* was cultivated in 55/55 (100%) saliva, 14/55 (25.5%) faecal and 69/436 (15.8%) biopsy samples of MC patients; and in 18/26 saliva (69.2%, p<0.0001), 3/25 faecal (12%, p=0.17) and 23/182 (12.6%, p=0.31) biopsy samples of healthy controls. By including both microaerobic and anaerobic isolates, a total of 102 saliva, 23 faecal and 123 biopsy MC isolates were cultivated. Preliminary results show, that MC biopsy isolates dominate in GS2 (n=47) compared to GS1 (n=7) p<0.001, whereas faecal isolates divide equally into GS1 (n=9) and GS2 (n=8) p=0.84.

**Conclusions:** To date, this is the largest study to describe *Campylobacter concisus* prevalence in MC. We found a higher prevalence of *Campylobacter concisus* in MC patients than healthy controls, although only significant in saliva samples. In addition, differences in the distribution of GS1 and GS2 isolates in MC samples may lead to varying effects on the gut mucosa. This possible association should be investigated further in future studies to elucidate whether *Campylobacter concisus* contributes to the aetiology in MC.

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Abstract 4818

Pharmacogenetic approach to the antifungal drug administration: clinical case

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Background: Several international guidelines nowadays recommend voriconazole as a first choice for the treatment of invasive aspergillosis [IA]. Voriconazole is an azole antifungal drug which is extensively metabolized by several isoforms of the cytochrome P450 (CYP), mainly by CYP2C19 and to a lesser extent by CYP2C9 and CYP3A4. Genetic variations (combination of alleles inherited from each patient) in drug metabolism genes can alter the capacity for biotransformation of a drug and can affect the effectiveness and safety of therapy.

Case report: The patient R. is 73 years old male, diagnosed with chronic pulmonary aspergillosis on the background asthma and COPD for the last 2 years. During this time, the patient was prescribed thrice treatment with voriconazole in a standard dosage for three months. After 10 days of taking voriconazole, side effects appeared, such as headache, dizziness, pain in the epigastric region, which reduces patient adherence to therapy.

Materials/methods: Genomic DNA was isolated from peripheral leukocytes with “Hemolytic” reagent [InterLabService, RF]. Genotyping for the CYP SNVs was performed using real-time PCR by the RotorGene 6000 (Quagen, Germany) according to the manufacturer’s protocol [Syntol, RF].

Results: The patient R. genotyping results are presented in the table. He is homozygous for CYP2C19*4 allele and heterozygous of CYP2C19*2 and *3 variants, which are associated with lower active metabolite exposure and increased risk for serious adverse events. Based on the results of the genetic analysis, the patient is recommended to monitor the concentration of voriconazole in the blood and the selection of an individual drug dose.

<table>
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Conclusions: Genetic variants of CYP are clinically significant for drug metabolism and should be considered when prescribing antifungal drugs.

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**Protection against H9N2 Influenza A(H9N2) virus induced by recombinant M2e-HA2 fusion protein**

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**Background:** Influenza as an extremely contagious respiratory tract disease is assumed a community health problem. Influenza A virus is a member of the Orthomyxoviridae family that has segmented genome and great antigenic diversity. Influenza viruses possess multiple conserved epitopes that are designed for universal vaccines. One of these epitopes is matrix-2 protein ectodomain (M2e) and the other is HA2.

**Materials/methods:** The gene coding for M2e2-9 and HA21-9 epitopes of influenza virus which are conserved among all subtypes of influenza A viruses, stimulate immune responses of B-cells and T-cells. In this study, we have constructed new plasmids to express above-mentioned epitopes as a single recombinant product. To this aim, two peptide genes of N-terminal M2e [SLLTEVET] and HA2 [GLFGAIAGF] were linked together with a (Gly4Ser)4 peptide linker (SLLTEVETGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGAIAGF), synthesized, and cloned into pGS-21a vector. Afterwards, the construct was transferred into E. coli BL21 (DE3) cells and induced using isopropyl β-D-1 thiogalactoside (IPTG). Immunization of mice with these peptides significantly induced humoral immune responses. Three weeks after the last booster, mice were inoculated intranasally with 1×10^6 EID₅₀ of H9N2 virus.

**Results:** In the present study, the recombinant M2e-HA2 fusion protein gene was cloned into pGS-21a vector. The results of sequencing showed that this gene was properly cloned in vector. Also, SDS-PAGE electrophoresis of purified protein exhibited a strong single band. Furthermore, Western blot analysis indicated a single band in correct position. Real-time RT-PCR studies showed reduction of virus in BALB/c mice lung tissues. Our study indicated that this protein could protect mice against H9N2 virus.

**Conclusions:** The recombinant M2e-HA2 fusion protein characterizes a potential candidate for influenza vaccine studies in animal model. According to the findings, the M2e-HA2 fusion protein induced humoral immunity responses. The findings of this study suggest that the recombinant M2e-HA2 fusion peptide which is economical to yield can be used for induction specific antibodies responses. The results of the current study showed that this protein can protect mice by decreasing virus shedding.

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A new ultra-fast specimen preparation method for SEM visualization of bacterial biofilms

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Background: Fast detection of bacterial biofilms is an important problem of clinical microbiology. Scanning electron microscopy (SEM) has been known to visualize microbial biofilms with a high quality. However, the SEM’s practical application is limited to long and complex specimen preparation. The current investigation demonstrates capabilities and benefits of a new biofilm preparation method for SEM based on staining/fixation with neodymium chloride (NdCl₃).

Materials/methods: The study was performed on 48h-old Staphylococcus epidermidis ATCC 12222, Staphylococcus aureus ATCC 29213, and Pseudomonas aeruginosa ATCC 27853 biofilms. The biofilms were formed on polystyrene disks. The disks with the biofilms were rinsed with isotonic sodium chloride, treated with 1% NdCl₃ (BioRee kit, Glaucon, Russia), 20 min, 37°C, and rinsed with deionized water. No additional fixation and dehydration of the specimens were done. The specimens were analyzed using the scanning electron microscope (EVO LS10; Zeiss), the low vacuum mode (70 Pa), the BSE mode.

Results: The NdCl₃ treatment has resulted in SEM high-quality visualization of bacterial cells and extracellular matrix in S. epidermidis, S. aureus and P. aeruginosa biofilms. The bacterial cells retained their shapes and sizes despite low vacuum (70 Pa) inside of the scanning electron microscope. The staining with NdCl₃ contrasted not only the cellular borders, but also intracellular structures (intracellular septa). The image of extracellular matrix was unusual: matrix looked like a volumetric substance without discrete “building blocks”. The typical SEM image of NdCl₃-stained S. epidermidis biofilm is presented in Figure 1. The staining intensity of NdCl₃-treated bacterial cells was variable on the images. Phosphate anion is known as the most significant binding site for neodymium. Therefore, we hypothesize the intensity of cell staining directly correlates with phosphate anions, reflecting bacterial metabolic activity.

Conclusions: The NdCl₃ staining of bacterial biofilms is the fast, simple and informative method of specimen preparation for SEM visualization. The NdCl₃ treatment does not require complete dehydration and ensures biofilm stabilization under the low vacuum during SEM imaging. The most interesting findings are the SEM imaging of undersurface cellular structures and the volumetric visualization of extracellular biofilm matrix.

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Cannabidiol synergic antimicrobial activity combined with polymyxin B (PB) against PB susceptible and resistant Gram-Negative bacilli

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Background: Polymyxins have been used as agents of last resort in the treatment of bacterial infections by carbapenem-resistant Gram-negative bacilli (GNB). Cannabidiol (CBD) is a major phytocannabinoid from Cannabis sativa and it has shown antimicrobial activity against Gram-positive bacteria, but not against Gram-negative bacteria. The objective of the study was to investigate CBD synergistic/antagonistic activity combined with Polymyxin B (PB) against GNB.

Materials/methods: Carbapenem-resistant, PB susceptible, PB-resistant (plasmid-MCR-1 and chromosomal mutation) and intrinsic PB-resistant GNB were evaluated. Minimal inhibitory concentration (MIC) of PB was determined using broth micro-dilution method, two-fold serial dilution (256-0.01 mg/L), combined with ultrapure CBD (99.9%) (256 µg/mL) against GNB. A minimal three-fold difference in the PB MIC values was considered as synergistic/antagonistic CBD effect. Additionally, in vitro phagocytic capacity and/or bacterial survival was verified in U937 human macrophages, in the presence and absence of CBD (256 µg/mL), using colony forming units (CFU) to determine viable internalized bacteria after phagocytosis period (5 hours).

Results: PB combined with CBD showed highlighted synergic antimicrobial activity (PB MIC decrease) against: PB-resistant (non MCR-1) KPC-producing Klebsiella pneumoniae [32 to ≤ 0.5 µg/mL]; K. pneumoniae ATCC 13883 [8 to 0.125 µg/mL]; Stenotrophomonas maltophilia ATCC 13673 [4 to 0.06 µg/mL]; carbapenem-resistant Acinetobacter baumannii [CRAB] (0.5 to ≤ 0.01 µg/mL); Escherichia coli ATCC 25922 [0.25 to ≤ 0.01 µg/mL]; ESBL-producing E. coli [0.5 to ≤ 0.01 µg/mL]; NDM-producing K. pneumoniae NCTC 13443 [1 to 0.06 µg/mL] and A. baumannii ATCC 19606 [0.5 to ≤ 0.06 µg/mL]. Surprisingly, PB combined with CBD also demonstrated antimicrobial activity against intrinsic PB-resistant Edwardsiella tarda ATCC 15947 [≥ 8 to 0.03 µg/mL] and Serratia marcescens ATCC 13880 (> 8 to ≤ 0.01 µg/mL). Regarding the in vitro phagocytic capacity and/or bacterial survival in the presence of CBD, there was decreased CFU recovery of NDM-producing K. pneumoniae, on the other hand, increased CFU recovery of CRAB, however, further immunological studies are necessary to conclude this issue.

Conclusions: CBD shows synergic antimicrobial activity combined with PB against several GNB, showing perspective of combined antimicrobial therapy, minimizing PB inherent neurotoxicity and nephrotoxicity. Moreover, this association also showed activity against intrinsic PB-resistant bacteria.

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Use of antimicrobial stewardship smartphone applications by physicians and appropriate prescribing in hospitals: a systematic review

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Background: Antimicrobial stewardship (AMS) promotes appropriate use of antimicrobial drugs and reduces antimicrobial resistance. Technological advancements have resulted in the development of smartphone applications (apps) facilitating AMS. However, user experience, uptake and impact of AMS apps on antimicrobial prescribing is unclear.

Materials/methods: A systematic review was conducted. EMBASE, MEDLINE (Ovid), Cochrane Central, Web of Science and Google Scholar databases were searched for relevant quantitative and qualitative studies regarding AMS apps in hospital settings published until February 28th 2019. Manuscripts were independently screened, selected after reaching consensus and subsequently assessed by two investigators for eligibility.

Results: Thirteen studies met the eligibility criteria of which none were randomized controlled trials. Overall, methodological study quality was considered low to moderate. The main outcomes were process indicators such as total number of app downloads, average monthly app accessions and accessed guidelines in seven studies, guideline adherence in four studies and user experience in five studies. Guidelines were more frequently accessed by app than by desktop if available on both. Average app use increased over time in one study but decreased in another. In general, adherence to treatment guidelines increased significantly for a number of indications after app implementation. In addition, bacterial susceptibility to several Watch and Reserve antibiotics changed significantly post-intervention in one study. Most users considered app use to be easy, quick and preferred it over guideline access by web viewer or booklet. However, some physicians regarded app use in front of colleagues or patients as unprofessional.

Conclusions: The available evidence is scarce, but suggests that the use of AMS apps increased guideline adherence and appropriate antimicrobial prescribing. For optimal adherence to antimicrobial guidelines, use of an AMS app should therefore be considered as a tool in the daily workflow.

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Resistance among urinary tract infection pathogens collected in Europe during 2018

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Background: Escherichia coli (EC), Klebsiella pneumoniae (KP) and Proteus mirabilis (PM) are urinary tract infection (UTI) pathogens where increasing prevalence of extended spectrum β-lactamase (ESBL)-producing organisms continues to compromise oral agents. Many ESBL-producing pathogens exhibit co-resistance (co-R) to the fluoroquinolones (FQs) and trimethoprim-sulfamethoxazole (TMP-SMX) making the management of UTIs challenging outside the hospital. The aim of the current study was to assess the prevalence of ESBL phenotypes and the extent of co-R to the FQ’s and TMP-SMX among UTI pathogens.

Materials/methods: 766 EC, 260 KP and 104 PM collected from UTIs in 18 countries in Europe in 2018 were evaluated in the SENTRY Surveillance Program for susceptibility to various agents. All isolates were centrally tested and results interpreted according to EUCAST criteria.

Results: Among EC, KP and PM the prevalence of ESBL phenotypes were 17.5%, 32.7% and 10.6%, respectively. Among all EC, resistance (R) rates for cefuroxime (CEF), levofloxacin (LEV) and TMP-SMX were 20.0%, 21.8% and 32.7%. All EC remained 100% susceptible (S) to meropenem. ESBL EC showed R rates of 99.2%, 66.4% and 67.9% for CEF, LEV and TMP-SMX, respectively. For all KP, R rates to CEF, LEV and TMP-SMX were 46.5%, 32.2% and 40%, respectively and to MER was 7.7%. For ESBL KP the R rates to CEF, LEV, TMP-SMX and MER were 98.2%, 69.1%, 78.6% and 17.9%, respectively. Among PM, R rates for CEF, LEV and TMP-SMX were 9.7%, 26.0% and 38.5%, respectively and all isolates were 100% S to MER and for ESBL PM R to CEF, LEV and TMP-SMX were ≥90.9%.

Conclusions: EC was the most prevalent UTI pathogen where R to CEF, LEV and SXT was ≥20% for all isolates and ≥66.4% for ESBL phenotypes of EC. R to oral agents was ≥32% for all KP and ≥69% among ESBL phenotypes of KP. Among PM R to LEV and TMP-SMX was ≥34%. MER exhibited greatest activity against UTI isolates and low co-R to oral agents. New oral agents with the spectrum and potency of the carbapenems could help fulfill an unmet need for new options to treat MDR EC, KP and PM from UTIs.

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Antibiotic use prior to seeking medical care in patients with persistent fever in four low- and middle-income countries

Brecht Ingelbeen*1, Kanika Deshpande Koirala2;3, Kristien Verdonck1, Barbara Barbé1, Déby Mukendi Mulumba4;5, Thong Phe6, Sayda El Safi7, Emmanuel Bottieau1, Marianne Van Der Sande1;8, Marleen Boelaert1, François Chappuis9, Jan Jacobs1;10

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Background: Community-level antibiotic use contributes to antimicrobial resistance but is rarely monitored in low- and middle-income countries (LMIC). We describe prior antibiotic use in patients consulting with persisting fever in four LMICs.

Materials/methods: The NIDIAG project developed clinical guidance for the diagnostic work-up of patients with >1 week of fever in healthcare facilities in Cambodia (urban), DR Congo (rural), Nepal (one rural; one urban) and Sudan (rural). We recorded participants’ antibiotic use within four weeks before consultation and report its frequency and risk factors. We categorized antibiotics according to the WHO Access/Watch/Reserve (AWaRe) classification (2017).

Results: We recruited 382 patients (median 47 years; IQR 35-58) in Cambodia, 300 (median 19y; IQR 7-39) in DRC, 583 (median 34y; IQR 20-50) in Nepal and 674 (median 35y; IQR 20-48) in Sudan. Overall, 348 (17.9%) used ≥1 antibiotic: 6.0%, 7.0%, 30.0% and 19.1% in Cambodia, DRC, Nepal and Sudan respectively. Use of multiple antibiotics was more frequent in Cambodia (33.3%-38.9%) than Sudan (10.9%). 294 (84.5%) patients recalled the specific antibiotic used: most frequent were cephems (172; 40.3% of reported antibiotics), macrolides (72; 16.8%), fluoroquinolones (51; 11.9%) and beta-lactamase-labile penicillins (51; 11.9%). Cephem use was higher in Nepal (54.5%) than elsewhere (14.8%-24.3%). Beta-lactamase-labile penicillins were frequently used in Sudan (41.8%) and DRC (22.2%), but rarely/not in Nepal and Cambodia (3.2%-0%). Fluoroquinolone use ranged from 8.7% (DRC) to 21.6% (Cambodia). ‘Watch’ antibiotics use ranged from 23.7% (DRC) to 82.4% (Nepal; Figure). Parenteral administration ranged from 5.9%-66.7% between study sites. Antibiotic use was more frequent among young patients (5.17y; Risk ratio 1.5, 95%CI 1.23-1.83), patients diagnosed with urinary tract infection (RR 1.38, 95%CI 1.04-1.85) or visceral leishmaniasis (RR 1.49, 95%CI 1.03-2.14; restricted to Sudan and Nepal). Patients had started antibiotics a median 5 days (IQR 2-10) before the consultation, ranging from 3 days (DRC) to 8 days (Sudan).

Conclusions: We observed large differences in the frequency and choice of (‘Watch’) antibiotics in four LMICs. Differences between countries can only partially be explained by demography and disease burden. Healthcare seeking, health system characteristics, including training, (lack of) guidelines, and ‘Watch’ antibiotics’ availability are other likely contributors.

Fig. Community-level antibiotic use among persistent fever patients by AWaRe class.

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Abstract 4826

Molecular characteristics and clonal diversity of carbapenemase-producing *Klebsiella pneumoniae* isolated from blood culture in patients with haematological malignancies

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**Background:** Carbapenem non-susceptible *Klebsiella pneumoniae* are associated with high morbidity, mortality, prolonged hospitalization patients. The aim of this study was to evaluate the genetic variability in carbapenemase-producing *K.pneumoniae* (CP-*K.pneumoniae*), isolated from blood cultures in patients with haematological malignancies.

**Materials/methods:** This study included *K.pneumoniae* isolated from blood cultures in haematological patients [2003-2018]. Susceptibility to meropenem was determined by the broth microdilution method [CLSI,2018]. Carbenapenemase genes (*bla*<sub>OXA-48-like</sub>, *bla*<sub>KPC-like</sub>, *bla*<sub>NDM-like</sub>, *bla*<sub>VIM-like</sub> and *bla*<sub>IMP-like</sub>), *bla*<sub>CTX-M</sub> genes and genetic markers for hypervirulence (*iucA*, *rmpA*, *rmpA2*) were detected by PCR. Multiplex PCR was performed to detect for K1,K2,K5,K20,K54, and K57 serotype-specific alleles, that are commonly used as markers for hypervirulence *K.pneumoniae* [hvKp]. Multilocus sequence typing [MLST] for CP-*K.pneumoniae* were performed by PCR and sequencing of 7 housekeeping genes. Allelic profiles and sequence types [STs] were assigned at the Institut Pasteur MLST database.

**Results:** A total of 494 *K.pneumoniae* isolates were evaluated, of those 83(16.8%) isolates were CP-*K.pneumoniae*. The prevalent carbapenemase genes were *bla*<sub>OXA-48-like</sub>(76/83;91.6%) followed by co-harboring *bla*<sub>OXA-48-like</sub> and *bla*<sub>NDM-like</sub>(5/83;6%), and *bla*<sub>KPC-like</sub>(2/83;2.4%). The *bla*<sub>CTX-M</sub> genes were detected in 79.5%(n=66) CP-*K.pneumoniae* isolates. Of those 60(72.3%) isolates carried only *bla*<sub>CTX-M-1-like</sub> and 6 (7.2%) isolates harbored *bla*<sub>CTX-M-1-like</sub> and *bla*<sub>CTX-M-9-like</sub> simultaneously. Among CP-*K.pneumoniae*, 40(48.2%) carried at least one virulence gene (*iucA*, *rmpA* or *rmpA2*)[Table]. These isolates were considered hvKp. MLST revealed 13 different STs, the most common types were ST395 (25/83;30.1%) and ST23 (19/83;22.9%) following by ST11 (12/83;14.5%) and ST377 (10/83;12%). The ST14 and ST3229 were represented by five isolates each and other 7 STs (ST13,ST14,ST86,ST218,ST258,ST590,ST874) were represented by one isolate each. Virulence genes were detected in 89.5% ST23 isolates. Genes of *iucA* and *rmpA2* were identified in 89.5% ST23 vs 40% ST395(p<0.0014), 16.7% ST11(p<0.0001) and 10% ST377(p<0.0021). Significant difference in gene *rmpA* detection was not found. Capsule type K57 was identified in all ST23 isolates (100% vs 0% in ST395,p<0.0001) whereas K2 was associated with ST395 isolates (56% vs 0% in ST23,p<0.0001).

**Conclusions:** The dominant carbapenemase genes were *bla*<sub>OXA-48-like</sub>(91.6%) in CP-*K.pneumoniae* isolated from blood cultures. MLST revealed the high genetic diversity of CP-*K.pneumoniae* isolates. The prevalent STs were ST395 (30.1%) and ST23 [22.9%]. ST23 isolates carried more virulence genes then ST395, ST11 and ST377 isolates.

**Table. The presence of genetic markers of hypervirulence in *K.pneumoniae***

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<td>19 (100)</td>
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<td>21 (25.3)</td>
</tr>
</tbody>
</table>

**Presenter email address:** khrulnovas@gmail.com
Abstract 4827

Rapid molecular Chlamydia trachomatis/Neisseria gonorrhoeae testing is now a reality
Barbara Van Der Pol*, Lashonda Crane, Stephanie N Taylor, Joel Lebed, Aaron Ermel, Leandro Mena, Candice Mcneil, Adam Sukhija-Cohen

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Background: Since the first molecular tests were available, STI control programs have demanded rapid, on-site molecular diagnostics for CT/NG. The nearest solution to this problem to date is a highly accurate test that provides a result in 90 minutes. The binx io system is an easy-to-use, rapid, molecular point-of-care platform that has a sample to result time of about 30 minutes. The io is portable, fully automated and has been developed to simultaneously detect CT and NG from vaginal swabs or male urine specimens. We compared the performance of this rapid point of care molecular assay to central laboratory CT/NG tests.

Materials/methods: Female patients enrolled in the study had four vaginal swabs taken which were evenly split between self- or clinician-collected using the io vaginal swab specimen collection kit and the collection devices from three commercially available nucleic acid amplification tests (NAATs). For male samples, first-void male urine was aliquoted into the io urine specimen collection kit and similarly into those of each of the three comparator NAATs. Testing on comparators was performed in a single laboratory according to the manufacturer’s instructions for use. Patients were considered infected with CT or NG if two of the three comparator tests gave positive results for that organism. The io samples were tested on-site or sent to central laboratories. All io testing was performed within seven days of collection. Testing with the io system was performed in the vast majority by non-laboratory trained clinical personnel as well as by laboratorians.

Results: Samples were tested from 726 and 223 consenting women and men, respectively. For CT, sensitivity was 96.6% (95%CI 88.5-99.1%) and 93.9% (80.4-98.3%) for women and men, respectively, while specificity was >99.3% for both sample types. For NG, sensitivity was 100% (86.7-100%) and 100% (87.1-100%) for women and men, with specificities of 100% for both sample types.

Conclusions: A rapid, highly accurate NAAT is now available that can be performed in point-of-care clinical settings and by non-laborators. This assay has the potential to drastically improve the ability to test and treat in the same visit which will reduce transmissibility and improve antimicrobial stewardship.

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Abstract 4828

Understanding discordance between observed and WGS-predicted resistance: a study of amoxicillin-clavulanate in Escherichia coli

Timothy James Davies1, Nicole Stoesser1, Anna Sheppard1, Manal Abuoun2, Philip Fowler1, Jeremy Swann1, Mai Phuong Quan1, Dai Griffiths1, Ali Vaughan1, Marcus Morgan3, Hang Phan2, Katie Jeffery3, Monique Andersson5, Matthew Ellington4, Oskar Ekelund5, Neil Woodford4, Amy Mathers6, Robert A. Bonomo7, Derrick Crook1, Tim Peto1, Muna Anjum2, A. Sarah Walker1

1University of Oxford, Nuffield Department of Medicine, Oxford, United Kingdom, 2Animal and Plant Health Agency, Bacteriology, London, United Kingdom, 3John Radcliffe Hospital, Oxford University Hospitals NHS Trust, Headington, United Kingdom, 4Public Health England, Antimicrobial Resistance and Healthcare Associated Infections Reference Unit, London, United Kingdom, 5Region Kronoberg, Department of Clinical Microbiology, Växjö, Sweden, 6University of Virginia Health System University Hospital, Division of Infectious Diseases and International Health, Charlottesville, United States, 7Case Western Reserve University, Louis Stokes Cleveland Veterans Affairs Medical Centre, Cleveland, United States

Background: Resistance prediction from whole-genome sequencing (WGS) is increasingly seen as a viable alternative to traditional antimicrobial susceptibility testing. However, while some applications work well (e.g. predicting Mycobacterium tuberculosis resistance to first-line treatment), others, such as prediction of amoxicillin-clavulanate resistance in Escherichia coli, are more difficult. Here, resistance is complex: rather than simply being due to presence/absence of beta-lactamases, expression plays a key role. Further, phenotyping is challenging, with significant differences between EUCAST- and CLSI-endorsed reference methods.

Materials/methods: We predicted WGS-based amoxicillin-clavulanate resistance/susceptibility using 261 bacteraemic isolates of E. coli from a single centre, using not only presence/absence of beta-lactamases, but also other known mechanisms of amoxicillin-clavulanate resistance that increase beta-lactamase expression or decrease cell permeability. Resistance/susceptibility predictions were compared with reference-standard replicate phenotyping performed according to both EUCAST and CLSI guidelines.

Results: Concordance between predicted and observed resistance was similar comparing against each of CLSI and EUCAST phenotypes, as at the two reference-standard phenotypes themselves (Figure). Incorrect resistant/susceptible predictions were not random, occurring mostly in isolates with peri-breakpoint MICs (p<0.001). This finding, combined with the unimodal distribution of amoxicillin-clavulanate MICs, suggests that partitioning resistance into binary R/S categories may be poorly representative. We explored this by modelling isolate MIC as a function of its genetic resistance features using mixed models. This demonstrated that some genetic features caused small but potentially additive increases in MIC. These effects in isolation could subtly alter MICs around the breakpoints, but were often masked by the inherent variability of phenotyping, thus explaining the variable peri-breakpoint predictions of the binary WGS-based prediction. Although accurate WGS-based binary resistant/susceptible prediction was sub-optimal, MIC prediction from genotype was not. In an independent test set of 704 E. coli isolates, while WGS-predicted and observed resistant/susceptible phenotype only agreed for 632 (90%) isolates, using only known resistance mechanisms, model predicted MICs were within one doubling dilution [essential agreement] for 684 (97%) isolates.

Conclusions: For amoxicillin-clavulanate, the binary resistant/susceptible paradigm was a key driver of suboptimal prediction performance. This highlights the importance of investigating discordance between WGS-predicted and observed resistance, as it may not always be due to simple phenotype or genotype errors.

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Abstract 4832

A multi-centre analysis of the value of systematic screening of influenza virus and vaccination on emergent admissions to a cardiac intensive care unit

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1Hospital General Universitario Gregorio Marañón, Clinical Microbiology and Infectious Diseases Department, Madrid, Spain, 2Hospital General Universitario Gregorio Marañón, Cardiology Department, Madrid, Spain, 3Complejo Hospitalario Universitario de Santiago, Cardiology Department, Santiago de Compostela, Spain, 4Complejo Hospitalario Universitario de Santiago, Clinical Microbiology Department, Madrid, Spain, 5Hospital Universitario Puerta de Hierro, Infectious Diseases Department, Madrid, Spain, 6Hospital Universitario 12 de Octubre, Clinical Microbiology Department, Madrid, Spain, 7Hospital Universitario 12 de Octubre, Internal Medicine Department, Madrid, Spain, 8Hospital Universitario La Paz, Clinical Microbiology Department, Madrid, Spain, 9Hospital Universitario La Paz, Cardiology Department, Madrid, Spain, 10Hospital Universitario Puerta de Hierro, Clinical Microbiology Department, Madrid, Spain

Background: Influenza is a potential inducer of acute cardiac events. However, influenza incidence in patients admitted to a C-ICU, the accuracy of clinical suspicion and the compliance of influenza vaccination of high-risk patients, are unknown. Objectives: to evaluate influenza incidence at C-ICU admission during influenza season, the potential underdiagnosis and vaccination rate.

Materials/methods: Prospective study at 5 tertiary institutions including all patients admitted at a C-ICU during 2017-2018 and 2018-2019 flu seasons. A nasopharyngeal swab was collected at admission from all patients who consented (n=526) and were tested using Xpert® Flu/RSV assay. Clinical data were registered.

Results: Influenza was detected in 39/526 (7.4%) patients (36 FluA, 3 FluB) and initially suspected by the cardiologist in 66.7% of the cases. When compared to patients without influenza, flu positive patients had more acute decompensated heart failure (38.5% vs 23.6%, p=0.03), contact with relatives with flu-like illnesses (28.2% vs 13.9%, p=0.03), antimicrobials use (64.1% vs 31.0%, p<0.01), days of hospitalization (10d vs 5d, p=0.046) and need for non-invasive mechanical ventilation (17.9% vs 5.7%, p<0.01). Reasons for C-ICU admission between both groups were similar. All patients promptly received oseltamivir and no differences were found in mortality between both groups (5.1% vs 4.7%, p=0.36) despite a higher rate of severe presentations in flu patients: myocarditis (7.7% vs 0.8%, p=0.01), respiratory insufficiency needing mechanical ventilation (15.4% vs 5.5%, p=0.01), pericarditis (27% vs 8.8%, p=0.01), and related complications (64.1%). Flu vaccination had been received by 44.7% of the patients admitted to the C-ICU and 53.3% of patients who had a clear indication for it (n=400). Among the group of vaccinated patients those who were immunodepressed showed more flu episodes (16.7% vs 3.2%, p=0.03). Risks factors for no-vaccination despite indication were: younger age (68 vs 74y-o, p<0.01) and less comorbidity (Charlson index 4 vs 5, p<0.01).

Conclusions: Seven percent of patients admitted to the C-ICU during the influenza season had influenza. Only 67% of the influenza cases were suspected at admission and only half of the patients with indication for flu vaccination, had already received the vaccine. A clinical score to recognize influenza in these patients is needed.

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Abstract 4833

Optimization of *Mycobacterium avium* complex therapy with synergistic and bactericidal drug combinations

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**Background:** The standard drug regimen for *Mycobacterium avium* complex (MAC) disease includes 3 drugs- rifampicin, ethambutol and macrolide (REM) along with amikacin for severe or refractory infections. The culture conversion rates of this regimen are 50-70%. Moreover, this regimen is based on clinical-experience more than evidence-based studies. Hence, in this study we explore different drugs- clarithromycin (CLR), rifampicin (RIF), ethambutol (EMB), amikacin (AMK), clofazimine (CFZ), and minocycline (MIN) in two, three, four and five drug combinations to explore different synergistic and bactericidal drug combinations.

**Materials/methods:** The minimum inhibitory concentrations [MIC] of all the antibiotics used in this study against *M avium* ATCC 700898 was determined by broth microdilution. We performed Time–kill kinetic assays (TKA) of all single drugs and combinations against *M. avium* ATCC 700898. Interactions in these combinations were assessed for TK experiments based on effect size and Bliss independence.

**Results:** No single drug could sterilize *M. avium* in the TKAs. Increase in the effect size was seen in all two-drug combinations (+18.72 ± 31.86%), but antagonism was seen in some combinations relative to bliss independence. Three-drug combinations showed an increase in effect size (+12.18 ± 11.46%) than two-drug combinations especially with an addition of CLR or MIN. Three-drug combinations containing CLR and CFZ outperformed REM. In most of the combinations, the addition of a fourth drug showed a diminished increase in effect size (+4.54 ± 3.08%) however, addition of CFZ to REM showed high increase in effect size. Combinations without CLR and RIF had similar effect sizes to 3-drug regimens. The five-drug regimen had a worse effect size than four-drug regimens (-5.54%). Time-kill curves for some of the combinations are shown in the figure below.

**Conclusions:**

1) MAC-PD treatment benefits from multi-drug therapy.
2) Standard drug regimen (REM) may not be the best choice and other combinations should be considered.
3) Beyond three-drug regiments, the added effect size brought by the fourth drug diminishes. Clinical evaluation is needed to warrant the added toxicity in these regimens.

Figure: The above figure shows the TK curves for 1) one, two, three drug combinations and 2) four, five drug combinations.

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Application of whole genome sequencing for national surveillance activities

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¹Animal and Plant Health Agency, New Haw, United Kingdom, ²Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom

Background: Antimicrobial resistance (AMR) is the ability of microorganisms to resist the effects of an antimicrobial to which they were once sensitive. Increases in AMR are of global concern to human and animal populations as it can lead to treatment failures. If the issue is not addressed it is estimated that millions of lives might be at risk. Whole genome sequencing (WGS) is being implemented widely for determining AMR. This has led EFSA and ECDC to consider its use for harmonised AMR monitoring. Therefore, our aim was to test benefits of using WGS for AMR national surveillance.

Materials/methods: WGS and genomic characterisation was performed on 498 ESBL/AmpC producing Escherichia coli collected on MacConkey+cefotaxime (McC+CTX) or ESBL selective agar. To aid characterisation of mobile-genetic elements, a small subset was subjected to long-read sequencing. The E. coli originated from national and EU pig surveillance studies performed across the UK in 2013, 2015 and 2017.

Results: There was 98% concordance between genotype and phenotype in a subset of isolates, supporting implementation of WGS. The majority of isolates were genotypically multi-drug resistant [MDR]. The proportions of MDR and blaCTX-M-1 harbouring isolates from McC+CTX agar reduced over time, but isolates harbouring blaCMY-2 and AmpC promoter mutations increased. Proportions of MDR isolates from ESBL agar were variable, but numbers of blaCTX-M-1 isolates decreased with other ESBL variants increasing. Genotypic resistances to non-beta-lactam antimicrobials were present in 9-88% of isolates, depending on the antimicrobial. The isolates belonged to multiple STs, demonstrating AMR dissemination. Many AMR genes were located on plasmids showing similarity to plasmids previously isolated from humans, animals or the environment. MDR IncI1 plasmids harbouring blaCTX-M-1 were the most prevalent plasmid types, and demonstrated genomic stability, which could drive transmission and persistence of MDR.

Conclusions: Our research showed that WGS, which EFSA and ECDC are looking to integrate into national surveillance, could provide a wealth of data about trends in AMR gene prevalence, and their mode of transmission and persistence.

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Abstracts 2020

Abstract 4837

Anaemia is associated with mortality in patients with left-sided endocarditis: a POET sub-study

Mia Pries-Heje*, Nikolaj IHlemann1, Niels Bruun1, Emil Fosbøl1, Niels Tønder3, Claes Ernst Moser1, Kasper Iversen5,6, Henning Bundgaard1

1Rigshospitalet, Department of Cardiology, København, Denmark, 2Gentofte Hospital, Department of Cardiology, Hellerup, Denmark, 3Northzealnds Hospital - Hillerød, Department of Cardiology, Nefrology and Endocrinology, Hillerød, Denmark, 4Rigshospitalet, Department of Clinical Microbiology, København, Denmark, 5Herlev Hospital, Emergency Department, Herlev, Denmark, 6Herlev Hospital, Department of Cardiology, Herlev, Denmark

Background: Anemia is a common finding in patients with endocarditis – a disease with a high mortality. Despite this, very little is known about frequency, severity and prognostic impact of anemia in patients with endocarditis and treatment follows standard guidelines for treatment of anemia.

Materials/methods: In the Partial Oral versus Intravenous Antibiotic Treatment of Endocarditis (POET) trial, patients with left-sided endocarditis were randomized after stabilization to conventional IV treatment or partial oral antibiotic treatment. Only medically treated patients not undergoing surgical intervention were considered, as the Hgb level after surgery was considered to reflect local transfusion regimens. Patients were classified as having mild anemia at hemoglobin (Hgb) < 8.3 and > 6.0 mmol/l for men and < 7.3 and > 6.0 mmol/l for women, moderate anemia at Hgb between 6.0 and 5.0 mmol/l and severe anemia at Hgb < 5.0 mmol/l.

Results: Four hundred patients were randomized in the POET trial. Hgb level at randomization was available for 237 (95.6%) out of 248 medically treated patients. The median time from diagnosis of endocarditis to randomization was 17 days. In total, 205 (86%) patients had anemia; 140 (59%) patients had mild anemia, 59 (25%) moderate anemia and 6 (2.5%) patients had severe anemia. Patients with moderate or severe anemia were more likely to have renal disease (30.8% vs 11.0%) and had higher CRP concentrations. There was no difference between other baseline characteristics (Table 1). Eleven (16.9%) patients with moderate or severe anemia died within 6 months follow-up as compared to six (3.5%) patients with no or mild anemia (p=0.001).

In logistic regression analysis, moderate or severe anemia was significantly associated with 6-months mortality, with an OR of 5.6 (2.05-17.04) compared to patients with no or mild anemia, (p=0.001). After adjusting for renal disease, CRP, age and gender, moderate or severe anemia was still a significant predictor of 6-months mortality (p<0.001), OR = 4.51 (1.54-14.26), with an area under the curve of 0.79.

Conclusions: In the POET study >85% of patients with left-sided endocarditis and not undergoing surgery had anemia at randomization. Moderate or severe anemia at randomization was an independent predictor of death at 6 months.

Table 1. Characteristics of the Patients

<table>
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<tr>
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<th>Non or Mild Anemia (n=172)</th>
<th>Moderate or Severe Anemia* (n=65)</th>
<th>p-test</th>
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<tbody>
<tr>
<td>Male - n (%)</td>
<td>133 (77.3)</td>
<td>43 (66.1)</td>
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<td>Age (SD)</td>
<td>70.5 (±11.0)</td>
<td>70.9 (±11.1)</td>
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<td>Renal disease -no. (%)</td>
<td>19 (11.0)</td>
<td>20 (30.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Prosthetic heart valve - no. (%)</td>
<td>55 (32.0)</td>
<td>27 (41.5)</td>
<td>0.220</td>
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<tr>
<td>Streptococcus spp.</td>
<td>87 (50.6)</td>
<td>26 (40.0)</td>
<td>0.349</td>
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<tr>
<td>Enterococcus faecalis</td>
<td>41 (23.8)</td>
<td>19 (29.2)</td>
<td>0.494</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>40 (23.3)</td>
<td>18 (27.7)</td>
<td>0.590</td>
</tr>
<tr>
<td>C-reactive protein — mg/liter (SD)</td>
<td>16.5 (±15.7)</td>
<td>21.8 (±18.4)</td>
<td>0.029</td>
</tr>
<tr>
<td>Full IV AB-treatment - no. (%) **</td>
<td>91 (52.9)</td>
<td>28 (43.1)</td>
<td>0.228</td>
</tr>
<tr>
<td>Death within 6 months</td>
<td>6 (3.5)</td>
<td>11 (16.9)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 1. *Moderate or Severe anemia: Hemoglobin ≤ 6 mmol/l. ** Non-Intervention group in POET.

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Abstracts 2020

Abstract 4838

Automated isolation of microbial DNA from human samples
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Background: The influence of the human microbiome on health has been demonstrated in multitudes of studies and is an important area of ongoing investigation for medicine and diagnostics. For these studies it is crucial to have a reliable, reproducible extraction method which is able to extract DNA of all microorganisms with comparable efficiency, while simultaneously depleting inhibitory substances which might disturb subsequent downstream analysis. In addition, the increase in number and size of microbiome studies necessitates automation of these extraction methods. Here, we present the results of automating an established extraction method on a magnetic bead handling instrument.

Materials/methods: Human microbiome samples (stool, buccal swabs, and others) were homogenized and microbial cells (including gram-negative and gram-positive bacteria, fungi, and archaea) were rapidly and efficiently lysed by bead beating in conjunction with chemical lysis. In a subsequent step various inhibitory substances were removed from all kinds of inhibitor-rich sample types including stool and gut samples. Thereafter, inhibitor-free DNA was captured on magnetic silica beads, washed, and eluted on the QIAasympohy SP automated system. Extracted DNA quality was assessed for purity and yield, as well as tested in qPCR and 16S rDNA sequencing experiments.

Results: The automated DNA extraction method was able to efficiently extract microbial DNA from one to 96 samples per run, generating consistent results with no detectable cross-contamination. Extracted microbial DNA displayed no inhibition in qPCR with internal control. 16S rDNA sequencing revealed highly complex communities, measured by alpha diversity (observed operational taxonomic units [OTUs]), being comparable to the manual DNeasy PowerSoil Pro reference method, and higher than other tested methods. Beta diversity indicated that extraction of multiple replicates of the same sample were extremely consistent.

Conclusions: This workflow enables processing of up to 192 human or environmental samples and delivers high-quality DNA for downstream applications such as PCR amplification and NGS analysis in less than one day.

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Abstract 4839

Comparison of analytical performances of the new Qiagen NeuMoDx CT/NG assay with the Abbott RealTime CT/NG assay for detecting Chlamydia trachomatis and Neisseria gonorrhoeae

Sanela Svraka-Latifovic1, Tsira Dzebisasjvili1, Roland Doorn1, Cornelis P. Timmerman1,2, Leendert Bakker1, Roel Nijhuis1, J. Wendelien Dorigo-Zetsma1

1Tergooi - locatie Hilversum, Hilversum, Netherlands, 2Tergooi Hospital, Hilversum, Netherlands, 3Meander Medical Center, Amersfoort, Netherlands

Background: The new NeuMoDx system from Qiagen has been recently introduced. In this study the NeuMoDx CT/NG Assay was compared to the Abbott m2000 Real Time CT/NG assay for detecting Chlamydia trachomatis and Neisseria gonorrhoeae in clinical specimens. Our aim is to compare the performance of the new NeuMoDx CT/NG Assay with that of Abbott RealTime CT/NG assay for male and female clinical (urine and swab) specimen.

Materials/methods: In total 1031 clinical samples and ten quality control samples were tested, 664 were retrospectively and 367 prospectively tested. Sample types included were urine and swab specimens [genital, anal, eye, throat and urethra]. Retrospective study included 120 negative, 543 positive and 1 inhibited sample, while prospective study included 198 negative and 179 positive samples.

Results: Overall agreement between the two assays was 96.64%. In total of 722 positive samples, 27 tested negative and 5 had unresolved results, in 318 negative samples five samples had unresolved results and 313 samples were negative, one unresolved sample was negative in NeuMoDx CT/NG Assay (see table 1). Remarkably, NeuMoDx assay showed more variation in mean (and median) values of ICs between different specimen types. Mean values of 34.0, 37.4, 36.1, 37.0, 34.1 and 40.0 were found for respectively, urine, genital, throat, anal, urethra and eye swabs. Less variation of IC values in different specimen types was seen in Abbott assay.

Conclusions: Overall, the comparison between the NeuMoDx system and Abbott m2000 Real Time CT/NG assay is satisfactory. Discrepancies in results were seen in swab samples collected in guanidium thiocyanate medium. Presence of the guanidium thiocyanate medium in these samples could explain the discrepancies and variation in internal control cycle threshold values, however further investigation is needed for confirmation.

Table 1. Comparison of all CT/NG results

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<th>Reference assay (Abbott RealTime CT/NG)</th>
<th>CT</th>
<th>CT/NG</th>
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<th>NEGATIVE</th>
<th>UNRESOLVED*</th>
<th>TOTAL</th>
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<td>1 [0</td>
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<tr>
<td>CT</td>
<td>0</td>
<td>64</td>
<td>0</td>
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<td>64</td>
</tr>
<tr>
<td>CT/NG</td>
<td>0</td>
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<td>1]</td>
<td>112</td>
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<tr>
<td>NG</td>
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<td>10]</td>
<td>0</td>
<td>8 [1</td>
<td>7]</td>
<td>313</td>
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<tr>
<td>NEGATIVE</td>
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<td>2]</td>
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<td>2 [0</td>
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<tr>
<td>UNRESOLVED*</td>
<td>533</td>
<td>67</td>
<td>122</td>
<td>318</td>
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Abstracts 2020

Abstract 4840

Next-generation microscopically-observed drug susceptibility assay (NG-MODS) allows more rapid and precise phenotypic drug-susceptibility testing: preliminary results for Mycobacteroides abscessus

Winston Chiu*1, Caroline Shi-Yan Foo1, Pieter Leyssen1, Emmanuel Andre1,2

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Abstract third-party references: Laboratory of Clinical Bacteriology and Immunology, Department of Microbiology, Immunology and Transplantation, KU Leuven, Leuven, Belgium, Rega Institute, Department of Microbiology, Immunology and Transplantation, KU Leuven, Leuven, Belgium

Background: Among the pathogenic nontuberculous mycobacteria (NTM), Mycobacteroides abscessus is an emerging pathogen carrying an alarming ability to develop drug resistance. Due to the absence of EUCAST or CLSI clinical breakpoints for most antibiotics and the poor analytical performance of current phenotypic drug susceptibility tests for NTM, the treatment of NTM infections remains a major challenge.

Materials/methods: We developed the “next generation microscopically-observed drug susceptibility assay” (NG-MODS), in which high-content digital fluorescent microscopy automatically monitors bacterial growth and death in 96-well plates. This test currently runs in the Caps-It isolator system (Rega Institute, KU Leuven, Belgium). For rapidly growing mycobacteria, IC90 values are computed after 32 hours based on 70 individual measurements performed when exposing the bacteria to different concentrations of each antibiotic. Figure 1A illustrates the dose response growth curves obtained for different concentrations of amikacin while 1B illustrates microscopic images on which these curves are generated.

In this proof-of-concept study, we compared the clinical performance of NG-MODS against the Sensititre™ RAPMYCO (Thermo Fisher, USA) assay using a the M. abscessus subsp. abscessus ATCC 19977 strain and a set of 14 antibiotics (amikacin, amoxicillin-clavulanic acid, cefepime, cefotaxime, ciprofloxacin, clarithromycin, doxycycline, imipenem, linezolid, minocycline, moxifloxacin, tobramycin and trimethoprim-sulfamethoxazole). We used breakpoints available in the scientific literature (Broda et al).

Results: No major discrepancies were observed between the two methods. For 11 antibiotics, we found concordant interpretations of the results (S, I, or R). Cefoxitin, ciprofloxacin and linezolid showed a minor discordance (intermediate versus resistant). The MIC of the latter two differed one dilution with the IC90.

Conclusions: NG-MODS is a novel assay allowing high-throughput, rapid and automated interpretation of DSTs. In this analysis, NG-MODS showed comparable results with RAPMYCO while providing more precise and robust raw information. These encouraging results, which are to be consolidated in a larger comparative study, could ultimately position NG-MODS as a new validated method and support the definition and implementation of EUCAST clinical breakpoints for mycobacteria.
Figure 1: A) Growth curves of *M. abscessus* (ATCC 19977) treated with different concentrations of AMI. B) Images at 12 hours post seeding of growth control, *M. abscessus* (ATCC 19977) treated with 4 μg/mL and 16 μg/mL AMI.

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Investigation of the pro-autophagic effect of IL-36α and lipopolysaccharide in THP-1 cell line

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Background: Autophagy is an important cellular catabolic process for the removal of damaged organelles, protein aggregates, and intracellular microbes. Autophagy plays important role in various cellular processes and exerts multiple immunological functions. Microbial components and soluble inflammatory mediators regulate the activation level of this antimicrobial cellular process. The lipopolysaccharide (LPS) of Gram-negative bacteria is known to stimulate autophagy. Some cytokines are powerful autophagy inducers, while others act as inhibitors. Interleukin-36alpha (IL-36alpha) is a member of the IL-1 cytokine family. IL-36alpha is highly induced in response to a number of stimuli, and exerts pro-inflammatory effects. The effect of IL-36alpha on autophagy has not yet been fully elucidated. Thus, we investigated the pro-autophagic effect of IL-36α alone or in combination with the TLR4 agonist LPS in THP-1 cells.

Materials/methods: The levels of LC3B-I and LC3B-II proteins were measured by using western blot analysis. The autophagic flux was determined by measuring LC3B-II levels under conditions where autophagosome degradation was blocked by bafilomycin A, a pharmacological inhibitor of lysosomal hydrolase activity and autophagosome-lysosome fusion. The intracellular localization of LC3B autophagic marker protein was determined by using indirect immunofluorescence assay. The LC3B-positive autophagosomes were quantified with the Image J software. Cytoplasmic acidification was detected by acridine orange staining.

Results: The results have shown that the levels of LC3B-II protein were increased in response to IL-36alpha or LPS. THP-1 cultures treated with IL-36alpha and LPS in combination showed significantly higher increases in LC3B-II levels than that of measured in cells incubated in the presence of IL-36alpha or LPS alone. Both IL-36alpha and LPS increased the number of LC3B-positive autophagic vacuoles, the combined treatment was again more efficient that the cytokine or TLR4 agonist alone. Finally, IL-36alpha and LPS stimulated the formation of acidic vesicular organelles.

Conclusions: These results demonstrate that IL-36alpha and LPS synergistically activate autophagy in THP-1 cells, and suggest that IL-36alpha may enhance the innate immune response against certain Gram-negative bacteria.

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Novel small-molecule inhibitors of bacterial lipoprotein transport against Enterobacteriaceae

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Background: Carbapenem-resistant Enterobacteriaceae (CRE) and Extended-Spectrum β-Lactamase producing Enterobacteriaceae continue to be listed as urgent or serious threats by the World Health Organization and US Centers for Disease Control and Prevention. Through our highly innovative transposon-based technology (Discuva Platform), we identified and are developing DDS-04, a novel new mechanism antibiotic series selective for Enterobacteriaceae.

Materials/methods: High-density transposon mutant libraries were generated in target pathogens. The engineered transposons contain outward facing promoters which can influence gene expression across the entire genome (upregulation, disruption or downregulation). Following compound exposure, NGS of surviving transposon mutants informs on mechanism of action and resistance drivers. Antimicrobial activity, mutation frequencies and kill kinetics were performed according to CLSI guidelines with modifications. In vitro ADME, toxicological, PK and in vivo proof-of-concept studies were performed using standard protocols.

Results: High-throughput screening enabled the identification of a small-molecule hit compound targeting components of the lipoprotein transport complex (LolC/E), a clinically unexploited and essential bacterial molecular target. Further medicinal chemistry established an excellent understanding of the structure-activity relationships that govern permeability and potency against clinically-relevant strains. The DDS-04 series demonstrates potent and specific antimicrobial activity against Enterobacteriaceae including MDR variants (<1 mg/L against MDR E. coli and K. pneumoniae). Importantly, the series is rapidly bactericidal (2-4 h), exhibits a very low mutational frequency and rate against MDR isolates (f10-9-10-10) and no cross-resistance to standard-of-care antibiotics. Optimised compounds from the series display a promising toxicological profile with no haemolytic activity, no mammalian cell cytotoxicity, excellent stability in presence of mouse and human hepatocytes, no mitochondrial toxicity, no monoamine oxidase activity, and no glutathione adduct formation (GSH+S9). PK profile (IV dosing) shows distribution to different sites of infection with significant amounts eliminated unchanged into the urine. Importantly, following single and repeat IV dosing in various murine models of sepsis, pneumonia and urinary tract infections, DDS-04 series compounds demonstrated significant reduction of the bacterial burden compared to the vehicle control.

Conclusions: The discovery of the DDS-04 series, enabled by the Discuva Platform, represents a promising advance in the development of novel drug candidates to treat infections caused by Enterobacteriaceae and warrants continued development.

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Visceral leishmaniasis burden in Bologna province, Italy

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Background: Visceral leishmaniasis (VL) incidence has been growing in Northern Italy. A disease outbreak occurred in Bologna Province between 2012 and 2013. The aim of this study was to describe the recent VL epidemiology in the Bologna Province, Italy.

Materials/methods: We retrospectively enrolled all patients with VL aged >18 years admitted to our centre from January 2016 to January 2019. Clinical, laboratory and microbiological data were collected at BL and for 12 months follow-up (FU). VL was diagnosed in all patients by serology and/or molecular tests. Data about treatment were also collected.

Results: A total of 37 patients (84% male, aged 55.7 ± 17.5) were enrolled. Thirty-four patients (92%) were living in Bologna Province. Nineteen (51.4%) were diagnosed with VL in 2018. Twelve (32%) were immunocompromised. Presenting clinical features were fever (95%, mean body temperature 38.8 ± 0.9 Celsius degrees), splenomegaly (86%) and hepatomegaly (68%). Main laboratory findings were pancytopenia (73%), hyperferritinemia (83%) and hypergammaglobulinemia (62%). Median time between symptoms onset and diagnosis was 29 days (IQR 15-54). At admission, median Sequential Organ Failure Assessment (SOFA) score was 2 (IQR 1-3) and mean Charlson Index (CI) score 2.46 ± 2. Thirty-three out 37 patients were tested by Enzyme-Linked Immunosorbent Assay (EIA) and/or rK39-based Immunochromatographic Test (ICT); corresponding sensitivities were 91% for EIA and 83% for ICT. All patients performed Real Time Polymerase Chain Reaction on peripheral blood or bone marrow specimen, positive in all cases. All patients received liposomal amphotericin B (LAmB): 28 of them (76%) received a 10 mg/Kg single dose, globally well tolerated. At 1-year follow-up 33 patients (86%) were cured, 1 (3%) was lost, 1 (3%, immunocompromised) relapsed and 3 (8%) died during hospitalization. Median age, CI and SOFA score were significantly higher in non-survivors (p <0.001, 0.045, <0.001 respectively). No significative differences were found between cured and relapsed patients.

Conclusions: After 2013, a new VL outbreak raised again in 2018. In this area, VL should be excluded in all subjects presenting with one of the described clinical features. A single-dose of 10mg/kg of LAmB seems effective and safe in our setting.

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Colistin-resistant Gram-negative bacteria isolated from humid compartments of high risk hospital units

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Background: The healthcare water environment including sinks and drainage systems, can be a long-term reservoir of nosocomial pathogens. In this study, we aimed to investigate the presence of Colistin-Resistant Gram-negative bacteria (ColR-GN) in humid compartments of high-risk hospital units in the University Medical Center Groningen (UMCG).

Materials/methods: Samples (n=80) were collected once a month for 5 months (April-August 2019) in the neonatal, pediatric, adult intensive care units (ICUs) and the hematology unit. We sampled fourteen sink drains (neonatal-ICU = 3, pediatric-ICU = 3, adult-ICU = 3, hematology = 5) and two shower drains (hematology= 2) using FLOQSwabs (Copan). Swabs were cultured (100µl) using selective agar-media CHROMID Colistin R (bioMérieux) and the bacteria isolated were identified by MALDI-TOF MS (Bruker). Colistin MICs were determined by broth microdilution following joint EUCAST and CLSI recommendations.

Results: A hundred-thirteen isolates were recovered from selective agar-media and 59 out of them (Enterobacteriaceae= 22, non-fermenting Gram-negative bacteria= 37) were selected for broth microdilution. A total of 38.9% (n=23/59) isolates had a resistant phenotype (MIC ≥ 4mg/L): Klebsiella pneumoniae (n=1, MIC= 64mg/L), Klebsiella aerogenes (n=1, MIC= 32 mg/L), Enterobacter cloacae complex (n=12, MICs 4-64mg/L), Enterobacter bugandensis (n=1, MIC= 32mg/L) Serratia liquefaciens (n=2, MICs= 16mg/L), Morganella morgani (n=1, MIC >64 mg/L) and Stenotrophomonas maltophilia (n=5, MICs 4-64mg/L). ColR-GN were found in all investigated units, Enterobacter spp. being the most abundant bacteria.

Conclusions: The presence of ColR-GN bacteria (mostly Enterobacteriaceae) in sink and shower drains of high-risk hospital units represents a safety concern and a potential threat to immunocompromised patients’ health. Monitoring such environment for antimicrobial resistant bacteria (AMRB) allows to identify reservoirs and to prevent further spread of AMRB. Molecular mechanisms for colistin-resistant will be further investigated by whole-genome sequencing.

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Abstract 4847

**Assessing the contribution of sepsis to mortality in Oxfordshire**

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**Background:** The Sepsis Trust estimates that around 52,000 people in the UK die every year from sepsis. Identifying meaningful patterns across relevant characteristics of deaths may help assess reliability of this estimate.

**Materials/methods:** The study included 9,324 individuals with an inpatient, outpatient, or A&E admission at an Oxford University Hospital who died between 01-Jan-2016 and 30-July-2019, and had any laboratory blood test result or physiological measurement taken in the 7 days prior to death. Sepsis was defined using six published scoring systems [SIRS (1991 and 2001 versions), SOFA, qSOFA, NICE, NEWS] and calculated using individuals’ worst measurements from the 7 days prior to death. Additional indicators of potential sepsis included were prescribed in-hospital antibiotics, primary or secondary infection diagnostic codes, blood culture (any taken or pathogen positive), or fever. Fuzzy C-means clustering was carried out on the proportion of components in each sepsis score an individual met, with binary indicators for the additional factors. This estimates the probability each individual belongs to each cluster, with individuals assigned to the cluster with the largest probability.

**Results:** Four clusters were identified, with characteristics shown in Figure. Cluster-1 (n=2809, 30.1%) contained individuals who were low on all sepsis scores, and all additional factors. The remaining three clusters had high proportions of individuals meeting all sepsis scores and receiving antibiotics, however varied on the other additional factors. Cluster-2 (n=2613, 28.0%) contained few individuals with infection, blood culture, or fever. Cluster-3 (n=1574, 16.9%) had a high proportion with infection diagnostic codes, but a lower proportion of individuals with blood culture or fever. Cluster-4 (n=2328, 25.0%) had the highest proportion of individuals with all additional factors. In cluster-4, 50 individuals received no in-hospital antibiotics (2.2% of cluster-4, 0.5% of study population).

**Conclusions:** Deaths in Oxfordshire broadly fall into 4 different groups using sepsis-associated markers. Cluster-1 compromised individuals whose deaths were clearly not sepsis-related. However, all other clusters had high antibiotic use, and cluster-2 had little infection, suggesting they reflect individuals’ mechanism of dying rather than cases of preventable sepsis. The 50 individuals in cluster-4 who received no in-hospital antibiotics are potentially cases of preventable sepsis.

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Abstract 4851

Serotype and susceptibility of invasive pneumococcal disease in adult population

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Background: Streptococcus pneumoniae is the most frequent etiological agent in community acquired pneumonia (CAP).

The introduction of the new conjugate vaccines has meant an important change in the incidence and epidemiology of invasive pneumococcal disease (IPD).

We have aimed to describe the evolution of circulating serotypes after childhood vaccination, to determine the clinical and epidemiological characteristics of IPD and the pneumococcus sensitivity.

Materials/methods: Retrospective study including 376 isolates from blood culture and cerebral spinal fluid. Results were distributed in two periods according to 13-valent vaccine VNC13: 2003 – 2010 (before vaccination) and 2011 – 2019 (after vaccination). The isolates were serotyped (Instituto de Salud Carlos III) and antimicrobial susceptibility with disk diffusion method was interpreted according to CLSI(2016) and EUCAST(2017) guidelines. The statistical analysis was made by SPSS 22 program.

Results: Out of the 376 studied strains, 89.9% were isolated in blood cultures and 10.1% in CSF. 236 strains were identified before VNC13 and 139 after it. Comparing the two periods, there was a decrease in male proportion (74% vs 62%) and an increase in median age (59 vs 65 years). Out of hospital (93.4%) and emergency department (80.9%) infections remained stable. There were differences in clinical presentation: CAP (60.2% vs 67.1%), septic shock (10.6% vs 7.1%) and meningitis (11.4% vs 12.9%). Mortality was also higher (25% vs 29.5%). The sensitivity to penicillin and cefotaxime for non-meningeal localization was 91.4% vs 97.1% respectively, 78.9% and 95% for meningeal localization. Other susceptibility were: erythromycin (79%), tetracyclines (79.7%), clindamycin (85.1%), levofloxacin (98.7%).

Table. Serotypes prevalence's

<table>
<thead>
<tr>
<th></th>
<th>2003-2010</th>
<th>2011-2019</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>9.7%</td>
<td>17.9%</td>
</tr>
<tr>
<td>8</td>
<td>11.4%</td>
<td>22.9%</td>
</tr>
<tr>
<td>1</td>
<td>11.9%</td>
<td>-</td>
</tr>
<tr>
<td>19A</td>
<td>11.4%</td>
<td>6.4%</td>
</tr>
<tr>
<td>7F</td>
<td>6.4%</td>
<td>1.4%</td>
</tr>
<tr>
<td>14</td>
<td>4.7%</td>
<td>6.4%</td>
</tr>
<tr>
<td>9N</td>
<td>2.5%</td>
<td>7.9%</td>
</tr>
<tr>
<td>23B</td>
<td>0.4%</td>
<td>2.1%</td>
</tr>
</tbody>
</table>

The isolates with less susceptibility were associated to serotypes 8, 19A and 14. The serotypes with decreased sensitivity to penicillin were 19A and 14 (57%). Serotypes associated with increased mortality were 19A (33.3% vs 40%), 23B (100% vs 66.7%), 8 (15.4% vs 30.8%). Serotype 9V (66.7% mortality) has not been isolated after VCN13.

Conclusions: The decrease in the incidence of several adults serotypes indicates that childhood vaccination provides herd immunity. However, 8, 9N and 23B serotypes (not included in VCN13) are still being isolated. These are serotypes associated with high mortality.

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Abstract 4852

**Antimicrobial susceptibility of vancomycin-resistant Enterococcus faecium and linezolid-resistant Enterococcus faecium isolated from blood culture in haematological patients: results of multi-centre study in Russia**

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**Background:** The aim of this study was to evaluate the antimicrobial susceptibility of vancomycin-resistant *E. faecium* (VREF) and linezolid-resistant *E. faecium* (LREF), isolated from blood culture in patients with haematological malignancies.

**Materials/methods:** Antimicrobial susceptibility testing was performed in VREF and LREF isolated from blood in hematological patients in six Russian hospitals (2002-2018). Minimum inhibitory concentrations (MICs) were determined by broth microdilution method (CLSI), except daptomycin (Etest, bioMeriéux, France). High-level gentamicin resistance (HLGR) and high-level streptomycin resistance (HLSR) was tested by the agar dilution method (CLSI, 2018). MICs of antibiotics were analyzed using CLSI 2018, MICs of tigecycline by EUCAST, 2018. Vancomycin resistance genes were detected by PCR. Linezolid-resistant isolates were examined for the presence of the mutations in the 23S rRNA gene and ribosomal protein L4 by sequencing. Gfr and optA genes were determined by PCR.

**Results:** Out of 393 *E. faecium* isolated from blood culture 71 (18.1%) were resistant to vancomycin and two (0.5%) were resistant to linezolid (2002-2018). MICs of vancomycin ranged from 128 µg/ml to 2048 µg/ml in VREF isolates, MICs of linezolid were 8 µg/ml and 16 µg/ml in LREF. VREF carried either vanA (66.2%) or vanB (33.8%) genes. All VREF were susceptible to daptomycin (MIC90 2/3 µg/ml) and tigecycline (MIC90 0.064/0.125 µg/ml). Both LREF were susceptible to daptomycin (MIC 0.5 and 1.5 µg/ml), tigecycline (MIC 0.064 and 0.125 µg/ml) and chloramphenicol (MIC 8 and 8 µg/ml). One of them was vanA VREF (vancomycin MIC 1024 µg/ml), and the other was vancomycin-susceptible (vancomycin MIC 0.125 µg/ml). G2576T mutations in 23S rRNA were determined in both linezolid-resistant isolates. The results of susceptibility testing are presented in the table. All vanB VREF were susceptible to teicoplanin. Susceptibility of vanA VREF compared to vanB VREF was significantly lower for HLSR (42.6% vs. 79.2%, p=0.005) and chloramphenicol (74.5% vs. 100%, p=0.006), respectively.

**Conclusions:** Resistance to vancomycin among *E. faecium* was 18.1%. Two (0.5%) *E. faecium* isolates were resistant to linezolid, one of them was vanA VREF, and the other was vancomycin-susceptible. All VREF carried either vanA (66.2%) or vanB (33.8%) genes. VREF isolates carrying vanB had a more favourable susceptibility profile compared to vanA VREF. Daptomycin and tigecycline were active against all VREF and LREF.

**Table. Antimicrobial susceptibility of VREF with vanA and vanB genes**

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>vanA (n=47)</th>
<th>vanB (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Susceptible</td>
<td>Intermediate</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>47 (100)</td>
<td>0</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>47 (100)</td>
<td>0</td>
</tr>
<tr>
<td>Linezolid</td>
<td>46 (97.9)</td>
<td>0</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>35 (74.5)</td>
<td>9 (19.1)</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>32 (68.1)</td>
<td>1 (2.1)</td>
</tr>
<tr>
<td>HLSR</td>
<td>20 (42.6)</td>
<td>-</td>
</tr>
<tr>
<td>HLRGR</td>
<td>12 (25.5)</td>
<td>-</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>7 (14.9)</td>
<td>4 (8.5)</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>1 (2.1)</td>
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</tr>
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<td>Teicoplanin</td>
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<td>0</td>
</tr>
<tr>
<td>Ampicillin</td>
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</tr>
<tr>
<td>Penicillin</td>
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</tbody>
</table>

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Abstract 4853

**Clinical dilemma in patients presenting with dengue viral infection**

Memoona Irshad¹, Sher Sethi¹, Kiren Habib¹, Muhammad Zain Mushtaq¹, Faisal Mahmood¹, Bushra Jamil¹

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**Background:** Dengue is a vector borne infection caused by Arbo-virus. Due to its clinical diversity, it had gained more importance in endemic areas. Dengue was first identified in Pakistan in 1994, since then many outbreaks have been reported. There are few case reports of dengue and *Staphylococcus aureus* co-infections despite the fact that both infections individually are common.

**Materials/methods:** We are describing five cases of dengue fever associated with *Staphylococcus aureus* both Methicillin Susceptible (MSSA) and Resistant (MRSA) strain infection in a tertiary care hospital. Clinico-pathological data of every patient is collected and assessed.

**Results:** All patients presented with history of acute fever associated with myalgias. All patients had thrombocytopenia on presentation. Leucocyte counts were variable. All patients had normal hemoglobin and later due to complications (bleeding/DIC), four developed anemia. Five patients had deranged liver function tests, four had deranged renal functions. Two patients developed shock with multi-organ dysfunction. Despite appropriate management all patients were deteriorating thus investigations were sent as per clinical signs and symptoms and *Staphylococcus aureus* infection was identified. All patients were started on vancomycin which was switched to cefazolin in five patients after the finalized culture reports. Source control was done in two patients. Four patients responded well and discharged, one expired and one is still under treatment.

**Conclusions:** In last few years there are cases which reported that dengue can provide a substantial source for secondary bacterial infections. However data is rare and exact mechanism of this co-infection is still not understood. Our study depicts that this viral-bacterial co-infection has poor prognosis leading to longer duration of hospital stay, and increase morbidity. We need to analyze similar studies and case reports in order to identify certain parameters/factors that might help in early identification, management and prognosis of this co-infection. Physicians dealing with dengue infection especially in endemic areas have to be vigilant of this possible yet to be established complication.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/ gender</th>
<th>Viral Marker +ve</th>
<th>Bacterial strain</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>23/M</td>
<td>IgM</td>
<td>MSSA</td>
<td>blood</td>
</tr>
<tr>
<td>B</td>
<td>32/M</td>
<td>IgM</td>
<td>MSSA</td>
<td>blood + trach</td>
</tr>
<tr>
<td>C</td>
<td>30/M</td>
<td>IgM</td>
<td>MSSA</td>
<td>blood + wound</td>
</tr>
<tr>
<td>D</td>
<td>32/F</td>
<td>IgM</td>
<td>MSSA</td>
<td>trach</td>
</tr>
<tr>
<td>E</td>
<td>40/F</td>
<td>IgM</td>
<td>MRSA</td>
<td>blood + urine</td>
</tr>
</tbody>
</table>

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Real-life dalbavancin use in acute bacterial skin and skin-structure infections and bone and joint infections: clinical experience at Florence university hospital (Italy)

Nicoletta Di Lauria*, Filippo Bartalesi, Dario Bartolozzi, Michele Cecchi, Paola Corsi, Alessandra Ipponi, Filippo Lagi, Elisabetta Mantengoli, Alessandro Bartoloni

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Background: dalbavancin is a long-acting lipoglycopeptide antibiotic approved for treatment of ABSSSI in adults. Moreover, the unique pharmacokinetic profile, joint to the good penetration into bone and synovial fluid, offers potential opportunities for outpatient parenteral antibiotic therapy (OPAT) in patients with osteomyelitis.

Materials/methods: retrospective analysis of clinical, microbiological and post-use satisfaction data obtained from patients treated with dalbavancin, by the introduction to August 2019, for ABSSSI and bone and joint infections at Careggi University Hospital in Florence (Italy). Patient satisfaction was evaluated using a 3-item questionnaire.

Results: a total of 44 dalbavancin treatments were performed. Twenty-five patients (56.8%) were male, the median age was 62 years (IQR=34-85) and the median Charlson Comorbidity Index (CCI) was 1 (IQR=0-6). The most frequent treated infections were ABSSSI (17, 38.6%). Other infections were osteomyelitis (OM) (12, 27.2%), prosthetic joint infections (PJI) (11, 25%), orthopedic device-related infections (ODRI) (4, 9%). Twenty patients (45.4%) had positive cultures and Staphylococcus spp was the most frequent isolated pathogen (13, 29.5%). Methicillin resistance (MR) phenotype was detected in 11 (85%) of those isolates. The previous failure with other treatments (18, 40.9%) and presence of MRSA risk factors (16, 36.3%) were the main reasons for dalbavancin use. Moreover, 25% of patients had social factors potentially affecting adherence. Clinical cure was reached in 88.2% of ABSSSI, 66.6% of OM, 27.2% of PJI and 75% of ODRI. Recurrence occurred in 36.3% of PJI and in 8.3% of OM. No adverse effects were observed. At the follow-up interview, 90.2% of patients expressed satisfaction with dalbavancin treatment.

Conclusions: In our case series dalbavancin represented a safe and useful outpatient treatment both in ABSSSI and in bone and joint infections. In our setting the off-label use was high (61.2%). The use as second line treatment was frequent due to the potential efficacy against biofilms and the potent activity against MR staphylococci. This last resort use could have affected the overall cure rate. Outpatient management using this long-acting molecule surely represents a real benefit to save healthcare resources and improve quality of life, as clearly showed by the results of the post-treatment satisfaction questionnaire.

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Pharmacokinetic variability and target attainment of meropenem in critically ill patients undergoing extracorporeal membrane oxygenation: a matched-cohort analysis

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Background: Variability in pharmacokinetics and target attainment of meropenem is still unclear in patients undergoing extracorporeal membrane oxygenation (ECMO). Therefore, the aim of this matched-cohort study was to evaluate the effect of ECMO on pharmacokinetic variability and target attainment of meropenem.

Materials/methods: Patients admitted to the intensive care unit (ICU) of the University Hospitals Leuven and simultaneously treated with meropenem and ECMO were eligible. These patients were matched (based on renal function) with non-ECMO ICU patients. The variability in pharmacokinetics was studied using population pharmacokinetic modelling. Probability of target attainment, i.e. 100% fT>MIC and 100% fT>4xMIC, was simulated for different dosing regimens using the MIC breakpoint for Enterobacteriaceae, i.e. 2 mg/L. All modelling and simulation were performed using NONMEM 7.4.

Results: Nine ECMO patients were included, and matched 1:1. A two-compartment model with linear clearance adequately described our data. Creatinine clearance, based on the Cockcroft-Gault formula [CG-CLcr: median [IQR] 108 [76-155] mL/min], explained 27.1% of the interindividual variability (IIV) in meropenem clearance (CLM). Nevertheless, 18.2% and 65.2% of the IIV in CL and Vd remained unexplained. CLM increased with 0.080 L/h per mL/min increase in CG-CLcr. Estimated CLM and Vd were similar between ECMO and non-ECMO patients [CLM: 11.4 vs 11.1 L/h, p=0.899, and Vd: 22.1 vs 24.0 L, p=0.709]. Ten patients (55.6%) maintained a meropenem plasma concentration above 2 mg/L over the full dosing interval (Figure 1a). Only 3 patients (16.7%) maintained a meropenem plasma concentration above 8 mg/L. Simulations of 1000 mg meropenem every eight hours at 30-minute infusions predicted 59.0% and 14.6% of patients attaining the 2 and 8 mg/L targets (N=1000 simulated patients) [Figure 1b]. Extended infusions (4 hours) of 2000 mg meropenem every eight hours and continuous infusion at a daily dose of 3000 mg were required to reach ≥90% of patients maintaining meropenem plasma concentrations above 2 mg/L.

Conclusions: In critically ill patients, target attainment of meropenem was poor under standard dosing but was not found to be influenced by ECMO. ICU patients may benefit from optimised dosing or infusion regimens to improve MIC coverage. Our model may be used to inform meropenem precision dosing.

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Reduction of laboratory turnaround time is not the only answer for shorten length of stay at the emergency department

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Background: During the influenza season the emergency departments (ED) gets overcrowded and long waiting times are a big burden for the hospitals. At Gävle Hospital, Sweden, 24/7 use of rapid PCR testing for influenza was introduced in December 2016. Despite the introduction of the rapid PCR, ED experienced long response times from the microbiological laboratory.

The aim of the study was to investigate how the introduction of rapid PCR testing for influenza reduced the time spent at the ED and what other factors that played a role.

Materials/methods: Workflow optimization by using LEAN and A3 methodologies was done at the ED. The turnaround time was measured from admission of patients with influenza like illness to the ED until the patient was discharged from the ED. The goal is that no patients need to spend more than four hours in the ED before admission.

Some of the optimizations factors were: training off staff, flu sample was taken earlier in the process, a checklist was ceated for nurses so they could take the samples without the doctor’s prescription and the sampling instructions were more easily accessible.

Measurement was done before and after optimization of the workflow. The impact of a new even quicker rapid PCR test for influenza was also added to see if it would shorten the length of stay at the ED.

Results: The average turnaround time before the optimization of workflow were seven hours and only 8 percent of the patients were discharged from the ED within four hours. After implementation of the new workflow and onset of the new rapid PCR the turnaround time decreased to 5.3 hours and 33 percent of the patient were discharged from the ED within four hours.

Conclusions: Reduction of laboratory turnaround time is not the only answer for shorten length of stay at the Emergency Department. An interaction between lab and ER is the best way to solve the burden at the ED.

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Current diagnosis, management and control strategies for Clostridioides difficile infection in Europe

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Abstract third-party references: On behalf of the COMBACTE-CDI consortium.

Background: Diagnostic and management strategies to face C. difficile infection (CDI) are rapidly evolving over the years. The aim of our study was to show the compliance to the current CDI diagnosis, notification and management guidelines in Europe, as assessed by a survey.

Materials/methods: In 2018, in the framework of the European COMBACTE-CDI project, a questionnaire was sent to hospitals, long-term care facilities (LTCFs), residential care facilities, general practitioners (GPs) and laboratories from 12 different European countries. Questions in the survey focused on the awareness of and compliance with national/local CDI testing and CDI notification policies/guidelines and on strategies adopted to avoid CDI spread.

Results: One hundred fifty-five European centres/facilities participated in the survey. Overall, 104/155 (67%) of the participants were aware of national CDI testing policy guidelines, reported awareness was lower in the Netherlands (33%), Italy (38%) and Greece (50%). The overall percentage of compliance with national testing guidelines was 104/155 (67%) whereas it was markedly lower among LTCFs (1/4, 25%) and GPs (3/39, 8%).

Regarding CDI notification, overall 111/155 (72%) of the participants reported that they notified cases of CDI regularly; 84/107 (79%) and 15/36 (42%) of hospitals and GPs, respectively, declared notification of CDI cases. Where CDI was suspected, surveyed hospitals reported adoption of contact precautions “always” and “often” in 41/107 (38%) and 22/107 (21%) of cases, respectively. Of note, 5/107 (5%) reported never adopting contact precautions in cases of suspected CDI.

Where CDI was confirmed, 39/39 (100%) of the residential care facilities reported always adopting contact precautions. Among hospitals, 80/107 (75%) and 11/107 (10%) “always” and “often” adopted contact precautions.

Conclusions: Our survey shows that compliance with CDI testing guidelines and notification policies varies according to different settings and geographical areas. Importantly, an alarmingly low rate of compliance with contact precautions for patients with suspected CDI has been reported. Our results highlight possible areas for improvement in guideline communications.

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Abstracts 2020

Abstract 4861

**Faecal microbiota transplantation via lyophilised capsules in primary episodes of Clostridioides difficile infection: preliminary results from a randomised clinical trial (EudraCT 2017-003147-38)**

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**Background:** Fecal microbiota transplant (FMT) is highly effective for treating multiple recurrent Clostridioides difficile infection (CDI) with an efficacy rate of nearly 90%. There is few data on the efficacy and safety of FMT in the treatment of primary CDI episodes. After an initial episode, risk for recurrence (R-CDI) is high, patients have important gut dysbiosis and oral vancomycin alters the gut microbiome further. FMT administered in primary episodes could help restore the microbiome and thus reduce R-CDI. The objective of this study was precisely to evaluate the efficacy and safety of FMT versus a standard 10 day course of vancomycin for primary CDI episodes.

**Materials/methods:** A randomized clinical trial in which patients were enrolled at a 1:1 ratio to a FMT lyophilized capsule regimen (single dose of 4 capsules) that includes preparatory antibiotic treatment (vancomycin 125mg/6 hours for 5 or 10 days depending on therapeutic response) or treatment only with standard vancomycin 125mg/6 hours 10 days. The primary end point was the proportion of patients without R-CDI at 8 weeks after treatment.

**Results:** From July 2018 (ongoing study) we have enrolled 32 patients (1 patient discontinued trial prior to receiving FMT). Patients’ median age was 76.5 years [IQR 59.0-84.8] and 71.9% were female. Seventeen patients received the standard 10 day vancomycin course and 15 received lyophilized FMT capsules and preparatory vancomycin (78.6% received a 5-day course; 21.4% a 10-day course). Twenty-nine patients completed the follow-up period, prevention of R-CDI was achieved in 85.7% in the FMT capsule group and in 80.0% in the standard vancomycin alone group (p=1.000). Adverse events were 35.7% for the FMT capsule group vs 20.0% in the standard vancomycin alone group (p=0.427), no serious events were related to the CDI treatments.

**Conclusions:** Our results show that so far, among adults with primary CDI, FMT via oral lyophilized capsules was not inferior to treatment with standard vancomycin 10 day course alone for preventing R-CDI over 8 weeks. Treatment with FMT lyophilized oral capsules may be an effective approach to treating primary CDI, enabling for a shorter vancomycin course of 5 days and restoring the microbiome.

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Abstract 4863

Microbiome characterisation of patients with *Clostridioides difficile* infection and colonised patients

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Abstract third-party references: On behalf of HGUGM Microbiome Project

**Background:** *Clostridioides difficile* is the main cause of nosocomial diarrhea, although distinction between colonization and infection is sometimes difficult. Patient stratification according to risk for recurrence (R-CDI) and for those evolving to severe complicated CDI is necessary to plan the proper management, however, clinical criteria is insufficient. The objective of our study was to characterize the microbiome profile of healthy, CDI and colonized patients, in order to establish possible differences that could be of use in CDI identification and risk stratification.

**Materials/methods:** Prospective study (Jan 2019-ongoing), patients positive for *C. difficile* and healthy controls were enrolled. Clinical data and fecal samples were collected. The hypervariable V4 region of the 16S rRNA gene was sequenced on an Illumina Miseq platform. Sequenced data preprocessing, OTU clustering and taxonomic classification were done using MOTHUR software, RDP and SILVA database. Alpha/Beta diversity analysis and statistical analysis were conducted by MOTHUR, QIIME 2 and R.

**Results:** A total of 244 subjects were enrolled, 167 (n=192 samples) were analyzed and classified as follows: Healthy (54), CDI (123) and Colonized (15). Alpha-diversity and richness were significantly higher in the healthy group versus CDI and colonized (p<0.001; both). Beta-diversity was significantly different between all groups (p<0.001), as well as the abundance of specific microorganism groups (Figure). Patients with previous CDI had lower richness (p=0.036) as well as those with R-CDI (p=0.019). Beta-diversity was significantly different in R-CDI vs first episode (p=0.0079) and in those with and without previous CDI episodes (p=0.009). Severe-complicated episodes had lower abundance of *Actinomyces*, *Bifidobacterium*, *Bacteroides*, *Prevotella*, *Blautia*, *Streptococcus*, *Clostridium XIVA/b*, *Fusobacterium* and *Proteus* (p<0.001). Patients that presented R-CDI had in their first episode sample, higher abundance of *Fusobacteria* and lower levels of *Collinsella* (p=0.039), *Prevotella* (p=0.0013), *Alistipes* (p=0.022), *Lactobacillus* (p=0.022), *Blautia* (p=0.022), *Clostridium XIVA* (p=0.0014), *Roseburia* (p=0.0037), and *Veillonella* (p=0.039).

**Conclusions:** We found significant differences in the microbiome profile between CDI cases and *C. difficile* asymptomatic colonization. Prior CDI episodes and R-CDI episodes had a cumulative impact in the microbiota, traduced in less alpha-diversity and richness. We identified several groups of microorganisms that may serve as microbiological markers for CDI severity and prediction of R-CDI.

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Abstracts 2020

Abstract 4865

**Comparative protein binding in vitro and in vivo: quantitative insights into binding dynamics by pharmacometrics**

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**Background:** Ceftriaxone (CRO), a third-generation cephalosporin, is a commonly used antibiotic, in particular in patients with serious infections. For CRO, protein binding (PB) is high but non-linear and thus a critical determinant for the antibacterial effect. A recent study identified fundamental differences between protein binding determined by *in vitro* methods (ultrafiltration) and *in vivo* venous microdialysis. The objective of the present study was to quantify the different protein binding by means of pharmacometric modelling.

**Materials/methods:** A single i.v. infusion 2 g CRO was administered to six healthy male volunteers over 30 minutes. Antibiotic plasma concentrations as well as unbound CRO by means of ultrafiltration (*in vitro*) as well as venous microdialysis (*in vivo*) were measured for up to 6 hours after drug administration. Non-linear mixed effects modelling in NONMEM® 7.4 was used to characterize the protein binding quantitatively.

**Results:** A two-compartment model adequately described the total concentrations of CRO. Protein binding was best characterized by a non-linear, saturable protein binding with significant difference between *in vitro* and *in vivo*. The dissociation constants (Kd) for the albumin-CRO complex was in median [CI95%] of 44.95 µM (38.5-52.5) *in vitro* vs. 30.1 µM (27.7-33.1) *in vivo*. Moreover, the estimated number of binding sites per albumin molecule was 0.94 (0.92-1.03) *in vitro* vs. solely 0.62 (0.60-0.64) *in vivo* in vivo. In addition, a time-delay for the formation of the CRO-albumin complex of approx. 15 min was quantifiable. Median fraction unbound (range) was 0.18 (0.16-0.21) *in vitro* vs. 0.37 (0.34-0.42) *in vivo* in the distribution phase at 0.5 h or 0.083 (0.075-0.093) *in vitro* vs. 0.090 (0.080-0.101) *in vivo* at 6 h.

**Conclusions:** Significantly different protein binding was observed in *in vitro* ultrafiltration vs. *in vivo* intravasal microdialysis with a tendency to over-estimate the protein binding in *in vitro*, in particular in the distribution phase. The pharmacometric analysis revealed that ultrafiltration did not capture the highly dynamic processes of protein binding, while with *in vivo* microdialysis the onset of the formation of the albumin-CRO complex was quantifiable. The dynamics of protein binding should be considered in PK/PD studies of antibiotics to derive accurate therapeutic breakpoints.

**Figure:** Visual predictive check of the developed pharmacometric model for the matrices plasma (left), ultrafiltration (middle) and microdialysate (right). Observed data (circles) with 10th, 50th and 90th percentile of observed (black) and model-predicted data (red) with confidence intervals of the prediction (shaded areas).

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### Abstract 4866

**Invasive aspergillosis and influenza virus infection: an accidental relationship?**

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**Background:** Reports suggesting that 19% of patients with influenza virus infection (FLU) requiring admission to an ICU developed invasive aspergillosis (IA), may provide a biased vision of the problem. Data matching whole populations with either IA or FLU are required.

**Objective:** To analyse the frequency of IA in the whole population with FLU and the impact of FLU in the whole series of IA in our institution.

**Materials/methods:** In our centre, a multidisciplinary collaboration group in mycology (COMIC) is on place since 2011, which facilitates the diagnosis and treatment of all IA and maintains a prospective registry. The registry of patients with FLU diagnosed by GeneXpert is also available during the study period (Oct-2016 to July-2019).

**Results:** IA complicated 9/2911 cases of FLU diagnosed in our institution in the 3-years study period (0.31%), since GeneXpert test is available. FLU was one of the underlying comorbidities in 9/53 patients with IA (16.9%) (Table 1); Flu-A predominated (77.8%). Median age was 70 years (IQR 61.5-79.5). Regarding the 9 cases, all of them were classified as probable pulmonary IA. Previous immunosuppression was present in 7/9 and only one patient had no other risk factor than FLU for developing IA. Underlying conditions included COPD 7 (77.8%), heart disease 6 (66.7%), diabetes mellitus 4 (44.4%), solid-tumour 4 (44.4%), cirrhosis 3 (33.3%), haemodialysis 1 (11.1%), AIDS 1 (11.1%). Two patients had suprarenal insufficiency on corticosteroid treatment. None of the patients had either neutropenia (<500/mm³), haematological malignancy or were SOT recipients. Regarding microbiology results, 6 patients had *Aspergillus fumigatus*, 1 *Aspergillus nidulans* and 2 mixed-infection [1 *A. fumigatus* + *Aspergillus lentulus* and 1 *A. fumigatus* + *Aspergillus ustus*]. Calcofluor was positive in 8/8 patients. Non-culture based tests were positive in 88.9% [serum GM: 5/8, BAL GM: 2/3 and serum 1,3-β-d-glucan: 6/6].

**Conclusions:** Invasive aspergillosis is uncommon in a large population with Influenza, 0.31% in our series. However, influenza and its severity can condition the development of invasive aspergillosis when there is a predisposing condition in the patient. Influenza and aspergillosis confection can be rapidly progressive and life threatening.

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Abstract 4867

**Stigma in MDRO carriers exposed to isolation precautions: an exploratory quantitative questionnaire study**

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**Background:** Isolation precautions are applied to control the risk of transmission of multi-drug resistant organisms (MDROs). These precautions have been associated with adverse effects, such as perceiving barriers in access to healthcare and feelings of anxiety and depression. This study aims to quantify the experience of stigma among carriers of MDROs, evaluate its association with mental health and experienced quality of care.

**Materials/methods:** A quantitative questionnaire study was performed in a population of MDRO carriers, exposed to ≥ 3 days of contact precautions during hospitalization. Due to the very low frequency of self-reported stigma at interim analysis, the study was halted at 41 inclusions. Items derived from the Consumer Quality Index questionnaire (CQI) were used to assess participants perception of care. Stigma scores were calculated using the recently developed modified Berger Stigma Scale for MRSA. Mental health was measured with the five-item RAND Mental Health Inventory. The Spearman rank correlation test was used to assess the association between stigma and mental health and between stigma and CQI.

**Results:** Of the 41 included individual patients, 31 (75.6%) completed both questionnaires. The experienced quality of care by the participants was good according to the CQI score. Receiving proper explanation from healthcare workers (HCWs) about MDRO was self-reported by only 24.4% of the participants. Stigma was reported in 1/31 (3.2%). Poor mental health was observed in 3/31 (9.7%) of participants. There was no clear correlation between stigma and mental health. (Figure 1)

**Conclusions:** In this prospective quantitative questionnaire study, MDRO carriers exposed to at least three days of contact isolation precautions did not report stigma associated with this setting. This contrasts with a recent study that investigated MRSA associated stigma. However, for MRSA isolation more strict isolation protocols are in place, and the psychological impact may be of a different magnitude due to yet unknown reasons. Most probably, adequate quality of care, education of HCWs and public awareness about MDROs is important to avoid stigma.

**Figure 1 MDRO Alerts**

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Methicillin-resistant Staphylococcus aureus bacteraemia: clinical-epidemiological characteristics and evolution of oxacillin resistance in 17 years

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Background: S. aureus bacteremias are one of the main problems in infectious pathology. The variability of S. aureus, the rapid adaptive response to changes in the environment, and its acquisition of antibiotic resistance have made it a habitual resident of the hospital habitat.

Our aim is to know the clinical-epidemiological factors of MRSA bacteremias and the evolution of oxacillin resistance in the last 17 years.

Materials/methods: Retrospective study of S. aureus bacteremias from January 2001 to May 2018. Blood cultures were processed by the BACTEC-FX system [BectonDickinson®]. The identification and sensitivity study was performed with the automated system MicroScan-Walkaway [Siemens®], Vitek 2® [Biomérieux] and E-Test. The statistical study was made by SPSS 22.0.

Results: 935 patients presented bacteremias due to S. aureus, 176 (18.8%) were MRSA. 60.2% were males with average age of 64.1 (14-91 years). 58.5% were in-hospital bacteremias with average admission of 37.3 days (40% >30 days and 25% were admitted in the previous 6 months).

40.3% came from medical services, 25% from the emergency room, 20.5% from ICU. 88.6% presented monomicrobial bacteremia. The most frequent medical profile were: primary bacteremia (37.7%), sepsis and/or septic shock (25.4%), catheter-associated bacteremia (12.3%), pneumonia (7.5%) and endocarditis (1.8%).

Crude mortality was 39.8% in MRSA compared to 31.4% in MSSA (p<0.05). 83.1% of the exitus in MRSA had a MIC to vancomycin <1.5.

The main causes of mortality were: primary bacteremia (35.4%); septic shock and/or sepsis (33.3%) and catheter-associated bacteremias <5%.

Regarding sensitivity: 4.3% were sensitive to penicillin, 70.9% to gentamicin and 32% to tobramycin, 35.8% to erythromycin and 61.4% to clindamycin, 9.7% to ciprofloxacin and 97.7% sensitive to linezolid. Vancomycin sensitivity was 99.4%, 17.1% with MIC>1.5 (10.8% MIC 2 and 6.3% MIC 4).

18.8% were resistant to cloxacillin (14.28% in 2001 and 16.7% in 2016, with a peak in 2013 (31%)).

Conclusions: The bacteremia caused by MRSA in our country is more frequent in men with an average age of 64.1 years old, intrahospital and from medical services.

Cloxacillin resistance has decreased in recent years, peaking in 2013 (31%), currently reaching values similar to 2001 [2001: 14.3%; 2017: 15.3%].

In spite of the high mortality (39.8%), we have not found a relationship between it and vancomycin MIC>1.5.

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Abstract 4870

An antimicrobial stewardship program in emergency department: clinical and epidemiological study of sepsis due to multidrug-resistant organism

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Background: In the last decades the prevalence of antimicrobial resistance (AMR) in Europe represent a serious threat to patient safety. In some countries is necessary to adequate empiric antibiotic treatment for sepsis to cover infection due to MDRO. For this reason we promote a sepsis performance improvement program in the Emergency Department (ED) through the development of a surveillance system for local epidemiology in order to guide a three years antimicrobial stewardship (AMS) program in ED.

Materials/methods: This was an observational, retrospective study about patients admitted to the ED of the IRCSS ASMN, Reggio Emilia (Italy), with diagnosis of sepsis from January 2019 to June 2019. Demographics, clinical and laboratory data, risk factors for MDRO, microbiological findings, infectious source, adherence to the Surviving Sepsis Campaign (SSC) bundle, disease severity score, empiric antibiotic therapy were recorded.

Results: During the study period there were 50,045 general ED attendances. A total of 580 patients with sepsis were enrolled (50.9% males, median age was 81 (IQR,71-88). The most frequent source of infection were lung (32%) and urinary tract (28.3%). Blood cultures were performed in 493 patients (85.7%): 121 in ED (20.9%) and 327 (64.8%) in ward within 48 hours of admission. There was a total of 222 microbiological isolation from 192 patients, 20.72% of them were MDRO. The most prevalent MDRO were ESBL+ Enterobacteriaceae (65.2%). 147 patients (25%) receive antibiotics in ED (71% was appropriate to antibiogram) and 38 patients complete SCC bundle. 63.8% of patients had at least one risk factor for MDR, the most represented are: hospitalization in the previous 6 months (44.4%), antibiotic therapy in the last 90 days (28%) and medical devices (21.5%). 192 patients have qSOFA ≥2, 353 NEWS-2 ≥ 5 and 449 SOFA ≥ 2. Overall, 159 patients (27.4%) died within 30 days and 215 (37%) within 90 days of ED admission.

Conclusions: This epidemiological study shows that the prevalence of MDRO in sepsis admitted in ED are high (20%), so we decided to start an antimicrobial stewardship program with ED physicians to help them to choose the best empiric antibiotics therapy in patients with specific risk factors.

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Resistance to ceftolozane-tazobactam and ceftazidime-avibactam in extensively drug-resistant (XDR) and multidrug-resistant (MDR) Pseudomonas aeruginosa: comparing antimicrobial activity, associated risk factors and clinical outcomes

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Background: Real-world experiences designed to evaluate risk factors associated with resistance to the two-novel beta-lactam/beta-lactamase inhibitor combinations (BLBLICs) and clinical outcomes are lacking.

Materials/methods: A retrospective case-control study was conducted at the Modena University Hospital from December 2017 to January 2019 including all consecutive patients with an MDR PA isolates. To obtain relative risks (RRs) associated with resistance to Ceftolozane-tazobactam (C/T), resistance to ceftazidime-avibactam (CZA) and combined resistance to new BLBLIC, univariate and multivariate analyses were performed using log-binomial regressions.

Results: During the study period 117 PA isolates were collected: colistin was susceptible in 87.1% followed by amikacin 78.6%, CZA 64.1% and C/T 63.2%. Cefepime (FEP) retained susceptibility in 38.3% followed by ceftazidime (CAZ) 29.3%, imipenem 26.3%, piperacillin/tazobactam 23.3% and meropenem (MEM) 19.8%. Among C/T-resistant isolates, 34.9% was CZA susceptible, whereas 33.3% of CZA-resistant isolates were susceptible to C/T. The result of multivariate showed the risk factors significantly associated with resistance to C/T were Charlson score (risk ratio [RR]=1.71) previous MEM (RR =1.18), the Central Vascular Catheters (CVC) (RR=1.76), Orotracheal Intubation (IOT) (RR=1.40), MEM use (RR=1.42) and FEP (RR=3.65). The multivariate log-binomial regression for the risk factors associated with resistance to CZA show that the CVC (RR=1.71) IOT (RR =1.52), CAZ (RR =8.95; 95% CI, 1.28-62.55, p=0.027) and FEP (RR=2.77) exposure were the main risk factors for resistance. Risk factors significantly associated with combined resistance to C/T and CZA were Charlson score (RR]=1.73), MEM (RR =1.11), CVC (RR=1.55), IOT (RR=1.18) and FEP (RR=16.44). Lastly, concerning clinical outcomes, patients with combined resistance to CZA-C/T showed a longer length of hospitalization, day±Std 77.8±54.3 vs 45.9±32.1, (P=0.001) and a significant higher mortality (62.96% vs 38.33%; P= 0.033).

Conclusions: Taking into account the different C/T/CZA residual susceptibility combination, both agents may be considered complementary therapeutic resources for PA hard-to-treat infection, especially lifesaving among isolates resistant to all traditional antipseudomonal beta-lactams. Considering the role of previous carbapenems exposure as the main risk factor for resistance, we urgently need for further efforts in reinforcing antimicrobial stewardship targeted to balance the correct C/T and CZA place in therapy.

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Evaluation of two lateral-flow assays with galactomannan in BAL fluids for the detection of invasive pulmonary aspergillosis: a retrospective two-centre study

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Background: Investigation of Galactomannan (GM) in respiratory samples is used as a diagnostic tool to detect invasive pulmonary aspergillosis (IPA). In this study, two Lateral Flow Assays, OLM Aspergillus Lateral Flow Device (LFD) and IMMY sôna Aspergillus Galactomannan Lateral Flow Assay (LFA), were evaluated against the GM enzyme immunoassay (ELISA) at two tertiary hospitals in Germany.

Materials/methods: A total of 200 bronchoalveolar lavage samples (BAL) from patients with suspicion of invasive aspergillosis from two tertiary hospitals were analysed retrospectively at two sites (100 samples at Paracelsus Medical University, Nuremberg and 100 samples at the University Hospital Essen). LFD [OLM Diagnostics, Newcastle Upon Tyne, United Kingdom] and LFA [IMMY, Oklahoma, USA] were evaluated against GM ELISA [Platelia, Bio-Rad Laboratories, Marnes-la-Coquette, France]. All tests were performed according to the manufacturers’ instructions. Immunochromatographic tests were read by cube-readers. For agreement analysis GM ranges were defined as follows: GM index < 0.5 (n=35), 0.5 - 1.0 (n=29), > 1.0 – 3.0 (n=51) and > 3.0 (n=85).

Results: The agreement of LFD and LFA with negative GM values in all BAL was 74 % and 51 %, respectively. The concordance between low positive GM values (0.5 to 1.0 and > 1.0 to 3.0) correlated in 26 % and 39 % with LFD results and 83 % and 96 % with LFA results, respectively. BAL with high GM values (> 3.0) had an overall agreement of 81 % with LFD results and 100 % with LFA results. The overall agreement between GM and LFD was 61 % and LFA was 88 %. The correlation between GM and LFA was r = 0.8.

Conclusions: LFA seems to be the most promising immunochromatographic test exhibiting the best agreement with positive GM values. LFA is recommended as an alternative for the GM ELISA as a diagnostic tool for the detection of an IPA.

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Abstracts 2020

Abstract 4876

**Nosocomial bloodstream infection rates: exploration of a quality indicator for infection prevention**

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**Background:** Outcome indicators for the quality of infection prevention in hospitals are scarce and time consuming to collect. In the Netherlands, the proposed rate of bloodstream infections by highly resistant microorganisms (HRMO) is so low that it has no use as a tool for focussing interventions and comparison between hospitals and wards. Therefore, we monitored nosocomial bloodstream infections rates during a 3-year surveillance period and evaluated its use as an indicator for infection prevention.

**Materials/methods:** Between January 2016 and January 2019, we conducted an observational, prospective surveillance in a tertiary teaching university hospital. We collected data on positive blood cultures in patients admitted to the hospital for more than two days from the Laboratory of Bacteriology. Data on source of BSI, ward, specialism and other patient characteristics were collected from electronic medical records. Rates of BSI were calculated as number of BSI per 1000 patient days.

**Results:** The overall prevalence of nosocomial BSI was 2.33 per 1000 patient days. The rates varied from 2.04 in 2016, 2.14 in 2017, and 2.92 nosocomial BSI in 2018. The increased rate in 2018 is probably due to a quality improvement project to increase adherence of taken blood cultures before starting antimicrobial therapy. The most common sources of BSI were (central) line-associated bloodstream infections (35.9%) and abdominal infections (18.2%). Coagulase-negative staphylococci (27.4%) and Enterobacteriaceae (23.7%) were the most commonly pathogen. The rate of HRMO was stable over time (5.1%).

Rates of nosocomial BSI varied considerably between wards and specialisms. In addition, the distribution between sources of nosocomial BSI is variable for different wards. Time trends of nosocomial BSI were used for monitoring and feedback per ward. The department of Infection Prevention spent 2.5 hours per week on data collection and cleaning.

**Conclusions:** Rate of nosocomial BSI can be used to monitor the performance of wards over time. In our hospital, nosocomial BSI is a solid, quick, inexpensive, and easy to perform outcome indicator for infection prevention. Sub-analysis of source of BSI per ward can evaluate focus interventions to decrease nosocomial BSI rates.

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Achromobacter identification using nrdA gene phylogeny and MALDI-TOF MS

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Background: The genus Achromobacter was first described in 1981 and contains today 20 species. Species from this genus are considered as emerging nosocomial pathogens and as new species are described frequently, there is a growing need of robust identification systems with evolving databases such as MALDI/TOF. In order to update those databases, the characterization of the new species using the nrdA gene is necessary as 16S RNA sequencing is not discriminant enough. In this study, we describe the use of nrdA gene phylogeny combined with MALDI TOF to identify Achromobacter species.

Materials/methods: A set of 110 strains representing 18 species of Achromobacter, from the bioMerieux collection, including type strains of new species and strains originally identified as A.denitrificans by phenotypic methods were sequenced on a polymorphic region of 760 bp of the nrdA gene. The phylogenetic trees were constructed using UPGMA and compared to dendrograms obtained using spectra acquired on the Vitek®MS platform in the 3000 to 17000 da mass range.

Results: The analysis showed that 90.9% of the strains were identified to the genus Achromobacter. Among those 90.9%, 44.36% were identified as the expected species and 44.54% as a different one. 6.36% of the strains could not be classified at the species level and 2.74% have been reclassified in other genera (Bordetella and Cupriavidus). Concerning the historical species: 39 strains originally A.denitrificans, 5 strains A.xylosoxidans and 8 strains A.piechaudii were reclassify. The Vitek®MS spectra dendrograms were in accordance with the sequencing data.

Conclusions: The nrdA gene phylogeny and Vitek®MS spectra allow a good discrimination of Achromobacter species including species that were not discriminated by phenotypic techniques. We are waiting for strains from the two recently described species A.sediminum and A.aloeverae to complete the analysis. This study shows that phylogeny combined to MALDI TOF is necessary to characterize species of the genus Achromobacter and to allow the identification systems to be more accurate.

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Investigation of electric signaling in bacterial biofilms with the Specialised Thin Agar Method (STAM)

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Abstract third-party references: Federal Ministry of Education and Research (Grant ID 01KI1803), German Research Platform for Zoonoses

Background: Prevention or even eradication of bacterial biofilms in medical settings and devices is a continuing issue worldwide. Besides quorum sensing mediated by small signal molecules, Bacillus subtilis also communicate via electric signaling in biofilms. A gate protein (TrkA) directing potassium ion channels was recently identified as generator of potassium ion waves, supporting nutrient supplies to reach the inner biofilm layers. It is conceivable that the persistence of clinical biofilms might be associated with electric signaling mediated by a concerted potassium release.

Materials/methods: To visualize electric signaling in B. subtilis biofilms, a specialized thin agar method (STAM) was developed. Two microliter minimal medium were spotted in a µ-dish (ibidi GmbH) and covered with a thin, pre-fabricated layer of agar (1.5 mm thickness). The agar was pierced with an insect needle to inoculate the interspace between agar and dish bottom. After 5.5 h incubation at 37 °C, Thioflavin T, which migrates into the bacterial cells proportional to the negativity of the membrane potential, was added to the interspace followed by live cell imaging in the confocal laser scanning microscope for 12 h at 30°C. The obtained images were analyzed using Fiji. Bacteria were segmented by automatic thresholding and mean pixel intensities were plotted over time to evaluate the changes of bacterial membrane depolarization.

Results: Using STAM, an oscillating fluorescent signal could be captured from starving B. subtilis populations, verified by analysis of mean pixel intensities. Membrane depolarization events due to potassium release ultimately ends after 20 hours of cultivation.

Conclusions: The STAM assay is a simple method to study electric signaling in bacterial biofilms which uses comparatively cheap consumables. Since the vertical colony expansion is limited by STAM, long-term visualizing of electric communication via live cell imaging becomes possible. In the next step of our study we will investigate the electric signaling capabilities of pathogens such as Staphylococcus epidermidis and Staphylococcus aureus, which also harbor TrkA. In the long run, STAM might be useful to investigate novel approaches to combat biofilms.

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Abstract 4884

Chronic hepatitis C care cascade in France: substantial impact of direct-acting antivirals but the path to elimination is still long

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Background: The World Health Organization (WHO) has targeted the Hepatitis C Virus (HCV) elimination by 2030, to ensure that 90% of people with chronic infection are diagnosed and 80% are treated. France has planned to achieve this goal by 2025. We aimed to estimate the cascade of care (CoC) for chronic hepatitis C in mainland France in 2011 and in 2016, to initiate the monitoring of HCV elimination and to assess the impact of direct-acting antivirals (DAAs) on the CoC.

Materials/methods: The numbers of people (1) with chronic HCV infection, (2) aware of their status, (3) in care for HCV and (4) receiving antiviral treatment were estimated for 2011 (18-80 years) and 2016 (18-75 years).

Estimates for 1) and 2) were based: on modeling studies for 2011; on a national cross-sectional survey with a virological sub-study conducted among randomly selected individuals from the general population for 2016. Estimates for 3) and 4) were made from the National Health Data System, that covers the entire French population, by constructing an algorithm for identifying people in care for HCV and by taking into account all antiviral treatments.

Results: Between 2011 and 2016, the number of people with chronic HCV infection decreased by 31%, from 192,700 (95% Credibility interval: 150,900-246,100) to 133,500 (95% Confidence interval: 56,900-312,600) (Figure). The proportion of people aware of their infection rose from 58% in 2011 to 81% in 2016. In the same period, the number of people in care for HCV increased by 23% (representing 26% of those infected in 2016) while the number of people under treatment increased by 25% (representing 12% of those infected in 2016).

Conclusions: This work provides, for the first time, estimates of the HCV CoC in mainland France and suggests a substantial impact of DAAs. However, access to care and treatment for infected people remained insufficient in 2016 in order to reach WHO elimination targets. Further studies are needed to estimate the CoC among specific populations including people who inject drugs.

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Abstract 4886

**The predictive performance of a model averaging approach is superior over using distinct population pharmacokinetic models in model-informed precision dosing of vancomycin**

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**Background:** Currently, the recommendation for therapeutic drug monitoring (TDM) of vancomycin is shifting towards AUC-guided dosing through model-based precision dosing (MIPD). Selecting an inadequate model from the ‘wrong’ population leads to incorrect prediction of vancomycin exposure and therefore potentially inappropriate dose recommendations [Broeker et al. CMI, 2019]. The aim of the present study was to derive and evaluate a model averaging algorithm (MAA), which automates the model selection process and thus eases the clinical application of MIPD.

**Materials/methods:** The MAA was developed by estimating individual pharmacokinetic parameters with four population pharmacokinetic models and weighting the forecasted concentration by the individual model fit. First, a simulation study was conducted using the four models developed in diverse populations [extremely obese, trauma and critically ill]. Subsequently, the MAA was applied to 264 hospitalized and critically ill patients for which routine vancomycin TDM had been conducted. The predictive performance of the MAA using all model jointly was compared to the performance of the individual models on prospectively measured concentrations. Relative bias (rBias) and relative root mean square error (rRMSE) were used to determine accuracy and precision, respectively.

**Results:** The MAA detected the correct model in 3/4 of the simulation cases supplying samples from only one dosing interval. This pattern increased when samples from more dosing intervals was supplied.

MAA applied to the heterogenous clinical dataset resulted in an inaccuracy of less than 1% (rBias) with a higher precision than the best single model. While the predictive performance of the single models [Fig 1 left panels] varied substantially, MAA using these models jointly resulted in unbiased and most precise predictions regarding both a priori prediction [Fig 1(a)] and Bayesian forecasting [Fig 1(b)-(c)]. The MAA performed even better than the model of Goti et al. (2018) that was recently evaluated best in vancomycin Bayesian forecasting.

**Conclusions:** MAA overcomes one of the major difficulties to implementation of MIPD, which is patient-individual selection of the adequate population pharmacokinetic model. Especially if the underlying population of the individual remains unclear or the patient displays atypical pharmacokinetics, MAA can provide a more reliable Bayesian forecast. Implementation into MIPD software [e.g. TDMx] is warranted.

![Figure 1](image)

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**Abstract 4887**

**A multi-site study comparing a commercially-prepared dried MIC susceptibility system to the CLSI/ISO broth microdilution method for cefepime-taniborbactam (formerly cefepime/VNRX-5133) using Gram-negative non-fastidious organisms**

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**Background:** Cefepime-taniborbactam (FTB; formerly cefepime/VNRX-5133) (Venatorx Pharmaceuticals, Malvern, PA) is an investigational combination of a fourth generation cephalosporin and a novel boronate-based beta-lactamase inhibitor (BLI) with *in vitro* activity against serine and metallo beta-lactamases. A 4-site evaluation was performed to determine the accuracy and reproducibility of FTB susceptibility testing against non-fastidious gram negative organisms using the Thermo Scientific™ Sensititre™ dried MIC susceptibility system compared with the CLSI (M07, M100)/ISO 20776-1, ISO 20776-2 (CLSI/ISO) reference broth microdilution (BMD) method.

**Materials/methods:** The Sensititre system with FTB in the dilution range of 0.004/4-64/4 mg/L was used to test 734 recent clinical and challenge isolates and 10 reproducibility isolates. Microorganisms tested included 110 *E. coli*, 203 *Klebsiella* spp., 76 *Enterobacter cloacae*, 50 *Citrobacter* spp., 25 *S. marcescens*, 76 *Proteus* spp., 46 *Providencia* spp., 94 *M. morganii* and 54 *P. aeruginosa*. The Sensititre system was inoculated per manufacturer’s instructions. BMD was performed per CLSI/ISO guidelines. Recommended CLSI quality control (QC) organisms were tested daily and all results were within the published QC ranges.

**Results:** FTB MIC results on the Sensititre system were comparable to those determined by CLSI/ISO BMD, with rates of essential agreement (EA; MICs +/- 1 log₂ dilution) of 96.6% by autoread and 96.5% by manual read for *Enterobacteriaceae* and of 100% for both autoread and manual read for *P. aeruginosa*. Overall agreement for reproducibility (MICs +/- 1 log₂ dilution of the modal MIC) using autoread and manual read was 98.1% and 99.7%, respectively.

**Conclusions:** The Sensititre system demonstrated an equivalent level of performance compared to the CLSI/ISO BMD method when testing cefepime-taniborbactam against non-fastidious gram-negative organisms. The high level of agreement obtained by the Sensititre system and the CLSI/ISO BMD method suggests that it is an acceptable method for susceptibility testing of FTB against *Enterobacteriaceae* and *P. aeruginosa*.

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Surrogate analysis of ertapenem to predict activity of tebipenem against Escherichia coli and Klebsiella pneumoniae collected from UTIs in Europe and the United States in 2019

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Background: Tebipenem (TBP) is an oral carbapenem being developed for the treatment of complicated urinary tract infections (cUTIs). Escherichia coli (EC) and Klebsiella pneumoniae (KP) are predominant uropathogens where resistance to oral agents represent an unmet need. TBP is active against most extended spectrum β-lactamase-producing uropathogens. Development of new agents on commercial susceptibility testing devices continues to lag behind drug development and surrogate testing may be an option for microbiology laboratories until devices are commercially available. The goal of the study was to assess the ability of ertapenem [ETP] to serve as a surrogate for predicting susceptibility (S) to TBP.

Materials/methods: A total of 1910 Enterobacteriaceae (ENT) from UTIs in Europe and United States were collected in 2019 as part of the STEWARD Surveillance program. Isolates were centrally tested for S to TBP and ETP using CLSI methods. Since no breakpoints for TBP are currently available a tentative PK/PD cut off value of 0.12 μg/mL was used to assess S of isolates to TBP and the CLSI/EUCAST breakpoint of 0.5 μg/mL was used to assess S to ETP.

Results: Among ENT, TBP inhibited 95% at ≤0.12 μg/mL and ETP inhibited 96% at ≤0.5 μg/mL with MIC90 values of 0.12 and 0.06 μg/mL, respectively. A categorical agreement (CA; susceptible) rate of 97.2% was observed between ETP and TBP for all ENT. For both EC (N = 1172) and KP (N = 293) the CA S rate was 100%. Among E. cloacae (N = 77) the CA S rate was 98.3% with only one very major error for ETP S isolate that was NS to TBP. The CA S rate for P. mirabilis was 85.5% with 16 ETP S isolates with TBP MICs >0.12 μg/mL.

Conclusions: TBP and ETP achieve 95% inhibition of ENT using PK/PD cut off value of 0.12 μg/mL for TBP and CLSI/EUCAST breakpoint of 0.5 μg/mL for ETP. ETP may be a useful surrogate to predict activity of TBP especially for EC and KP where the CA S rate was 100%. Once final breakpoints have been established for TBP the CA S rates will need to be confirmed.

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Background: Chimeric Antigen Receptor T cell (CAR-T) therapy has recently been a major breakthrough in the treatment of relapsed/refractory hematological malignancies. We aimed to describe incidence and epidemiology of infections in a real life cohort of patients treated with CD19 CAR-T cell therapy.

Materials/methods: Medical chart retrospective review of hematological patients receiving CD19 CAR-T cells at one university hospital in Barcelona, from May 2017, to September 2019. Descriptive study of all infections with positive microbiological results occurring from the initial treatment day to 150 days.

Results: A total of 41 patients have been treated with CD19 CAR-T cell therapy. Median age was 32 years (IQR 23-48.5 years) and underlying hematological malignancies were acute lymphoblastic leukemia (n=28, 68.3%), non-Hodgkin lymphoma (n=11, 26.8%) and refractory CLL (n=2, 4.9%). A total of 20 (48.8%) patients had 42 episodes of infection (25 bacterial, 15 viral and 2 invasive fungal infections): 17 within the first 30 days, and 24 between 31 and 150 days. Table 1 describes infections epidemiology. There were two infection-related deaths (4.9%) in one patient with severe Clostridium difficile colitis and one patient with multidrug resistant Pseudomonas aeruginosa ventilator-associated pneumonia.

Conclusions: The incidence of proven infection in CD19 CAR-T cell immunotherapy was 48.8%, similar to that of other hematological high-risk patients with intensive chemotherapy. Serious bacterial, viral and fungal infection occurred but infection related mortality rate was low.

Table 1. Infections epidemiology

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Abstract 4890

**Laboratory-confirmed seasonal influenza virus infection in Qatar: 2016-2018 national surveillance data**

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**Background:** Despite widely available annual immunisation and antiviral therapy, seasonal influenza continues to cause considerable morbidity and mortality. Limited data are available regarding the demographic and virologic characteristics of seasonal influenza in Qatar. The aim of this study was to assess the incidence and clinical impact of laboratory-confirmed influenza infection in Qatar during the years 2016 to 2018.

**Materials/methods:** Qatar Influenza Surveillance Programme involves offering laboratory testing for all individuals who present with an influenza like illness (ILI) to any primary health centre or hospital department. Upper respiratory samples are submitted to the National Virology Laboratory based at Hamad Medical Corporation, Doha, where they are tested using RT-PCR (Xpert Flu, Cepheid, Sunnyvale, California) and multiplex PCR (FTD Respiratory pathogens 21, Fast-Track Diagnostics, Esch-sur-Alzette, Luxembourg). Surveillance results, hospital admissions and mortality data were retrieved retrospectively from electronic databases. All samples tested between January 2016 and December 2018 were included. Stata (StataCorp LLC, College Station, Texas) was used for descriptive statistics. Incidence rates (IR) are reported by 100,000 population. Population data are based on those reported by Qatar Planning and Statistics Authority. The study was approved by the Institutional Review Board at Hamad Medical Corporation.

**Results:** Over the study period, Influenza Virus was detected in 19,339 (1.3%) out of 1,444,855 specimens from individuals with ILI, corresponding to an overall IR of 244 per 100,000 population. Of those with confirmed Influenza, there were significantly more males (56% versus 46% females, P < 0.001) and younger age groups (35% from those aged 0 to 4 years and 19% from 5 to 14 years age group). Influenza A (71.0%) predominated, nearly half (48.7%) of which were H1N1pdm09 type. Significantly more cases were diagnosed during the months of October to December compared with January to March (63.0% versus 18.0%, P < 0.001) (Figure). During the year 2018, there were 315 (3.0%) admissions to critical care units due to Influenza-related complications and 7 deaths (in-hospital mortality 2.4%).

**Conclusions:** The incidence of laboratory-confirmed seasonal Influenza is high in Qatar. However, children and young adults are most commonly affected, and hence relatively low rates of severe complications and mortality are observed.

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**Abstract 4892**

**CrpP-like fluoroquinolone-modifying enzymes among *Pseudomonas aeruginosa* clinical isolates in Europe**

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**Background:** Transferable mechanisms of resistance to quinolones have been identified in Gram-negative bacteria, corresponding to Qnr-type pentapeptide proteins, AAC(6')-Ib-cr, OqxAB or QepA. Recently, a plasmid-encoded 65 amino-acid long ciprofloxacin-modifying enzyme, namely CrpP (CrpP1) was identified in *Pseudomonas aeruginosa* in Mexico. The CrpP1 enzyme conferred reduced susceptibility (7.5 fold) to ciprofloxacin once produced in *Escherichia coli*. In-silico analysis identified 37 different CrpP variants. Our aim was to evaluate the dissemination, genetic support and impact on susceptibility to quinolones of this novel resistant determinant.

**Materials/methods:** A collection of 100 multidrug-resistant and clonally-unrelated *P. aeruginosa* clinical isolates, including ESBL (n=17) and carbapenemase (n=74) producers, recovered in Europe was tested by PCR and sequencing. Whole genome sequencing (WGS) was performed in several isolate to determine the location of this gene. In order to evaluate the impact of the different CrpP enzymes identified, the corresponding *crpP*-like genes encoding CrpP1 and CrpP2 enzymes were cloned in pUCp24 and transformed either in *E. coli* TOP10 and in *P. aeruginosa* PAO1. Capacity of mobilization of the Pathogenicity Islands (PAGI) were tested by PCR including primers in the extremities of the PAGI. WGS was performed to identify the genetic location of the *crpP* genes.

**Results:** A total of 49/100 positive isolates and 5 CrpP variants were identified by PCR and sequencing. WGS showed that the positive strains carried the *crpP* genes always located on a PAGI. MICs results showed a decreased MIC for ciprofloxacin (7.5-fold), for the *E. coli* clone producing CrpP2, but not CrpP1. For that latter, a 2-fold decreased MIC value was observed in *P. aeruginosa* only. Noteworthy, a 3-fold increase in levofloxacin resistance was observed once CrpP2 was produced in *E. coli*. Instead, MICs of levofloxacin was increased by 2-fold once CrpP2 was produced by *P. aeruginosa*. PCR assays identified a circular form of the PAGI island.

**Conclusions:** We first report the occurrence of *crpP*-like genes among *P. aeruginosa* clinical isolates in Europe. We showed that susceptibility to fluoroquinolones might slightly vary depending on the nature of the Crp protein. Acquisition of those genes was mediated by a PAGI functional element.

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Abstract 4896

**IS26-mediated transfer of blaNDM-1 as the main route of resistance transmission during a polyclonal, multispecies outbreak in a German hospital**

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1Robert Koch Institute, Wernigerode, Germany, 2SLK-Kliniken, Heilbronn, Germany, 3Ruhr-University, Bochum, Germany, 4University Medicine Göttingen, Göttingen, Germany

**Background:** One of the most demanding challenges in infection control is the world-wide dissemination of multidrug-resistant bacteria in clinical settings. Especially the increasing prevalence of carbapenemase producing Gram-negative pathogens poses an urgent threat to public health, as these enzymes confer resistance to almost all β-lactam antibiotics including carbapenems.

In this study, we report a prolonged nosocomial outbreak of various NDM-1-producing Enterobacterales species due to clonal spread and cross-species exchange of blaNDM-1-carrying plasmids and transposons.

**Materials/methods:** Between July 2015 and September 2017, a total of 51 carbapenemase-positive strains were collected from 38 patients and three environmental sources in a German hospital. To investigate the clonal relationship and involved mechanisms of blaNDM-1 gene transfer, conjugation assays, molecular typing and whole genome sequence analyses were performed.

**Results:** The metallo-β-lactamase gene blaNDM-1 was found to be present in 35 of 51 carbapenemase-positive isolates of which seven additionally carried the carbapenemase gene blaKPC-2. KPC-2 could also be detected within the remaining 16 NDM-1-negative isolates. Core genome MLST revealed different clusters of closely related isolates of E. coli, K. pneumoniae, C. freundii, M. morganii or E. cloacae indicating clonal spread of NDM-1 producing bacteria. The detailed reconstruction of plasmids revealed that in all outbreak-associated isolates blaNDM-1 was located on composite transposons similar to Tn125, that has previously been described for Acinetobacter baumanii. In contrast to Tn125, these structures were flanked by IS26 elements, that might facilitate horizontal gene transfer. Moreover, identical plasmids were found to be shared by E. coli and M. morganii isolates.

**Conclusions:** Our results highlight the importance of detailed genome-based analyses for resolving complex nosocomial outbreaks that include both, clonal spread of MDR pathogens and inter-species resistance gene transfer. It remains to be elucidated if standard infection prevention precautions are as effective for preventing horizontal resistance spread as it is for controlling clonal dissemination of pathogens.

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Abstract 4898

Genomic identification of clinically relevant Mycobacterium species by target sequencing
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Background: The genus Mycobacterium contains nearly 200 species and among them, some species of clinical interest due to their severe human pathogenicity. Mycobacterium taxonomy has recently being reviewed and the genus is now divided into 5 distinct groups, Mycolicibacterium, Mycobacteroides, Mycolicibacter, Mycolicibacterium and Mycobacterium, the latter including all the human pathogens. Taken into account this new taxonomy, a molecular analysis was performed within each clade to set-up an easy molecular method to identify the best relevant species. Public genomes were analyzed by similarity and target sequences on partial genes of 16S, rpoB and hsp65 genes.

Materials/methods: Whole genome analysis was done with an ANI approach (average nucleotide identity) on 176 NCBI genomes from type strains and collection strains if available (89 Mycobacterium, 53 Mycolicibacterium and 34 Mycobacteroides), the two other clades being not clinically relevant. Target sequencing was done by phylogenetic classification using UPGMA/Neighbor-joining with public sequences of 16S, partial rpoB (711pb) and partial hsp65 (603pb) genes.

Results: The ANI study showed more than 99.9% homology between subspecies of Mycobacterium abscessus and those of Mycobacterium avium. The analysis reveals also a high similarity between some species which have recently been reclassified [M.intracellulare and M.paraintracellulare, M. bouchedurhonense and M.avium, M.intracellulare and M.chimaera]. The target sequencing analysis showed that 16S was not enough discriminant, especially for the Mycobacteroides group. Analysis of rpoB and hsp65 sequences separately allows a correct identification at the species level but is not sufficient at the subspecies level. The concatenation of rpoB and hsp65 allows the discrimination of subspecies such as those of Mycobacteroides abscessus and Mycobacterium intracellulare.

Conclusions: ANI programs on whole genomes are not discriminative enough to identify all Mycobacterium species of interest, especially at the subspecies level. Target sequencing using partial rpoB and hsp65 concatenated genes allows to identify all relevant pathogenic Mycobacterium species, at the subspecies level taken into account the new taxonomy. This in-silico analysis has to be completed with internal strains sequencing before to be used in our laboratory.

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Abstract 4903

Decision tree algorithm that differentiates dengue from other febrile illnesses at the early stage of the disease: a health centre-based prospective observational cohort study

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Background: The acute phase of dengue, a viral vector-borne disease, begins with fever and non-specific symptoms frequently indistinguishable from other febrile illnesses (OFI). Early diagnosis can reduce case fatality from 20% to <1%, but molecular diagnosis is hardly available at primary care. We aimed to identify parameters that could differentiate dengue from OFI at the early stage of the disease (≤72h from fever onset) and to design a decision-tree algorithm using clinical features and routine laboratory tests.

Materials/methods: Clinical and laboratory data from patients presenting within 72h of disease onset to three primary health centres and a tertiary hospital in a dengue hyperendemic city in Venezuela, were collected during three years. Multivariate logistic regression analysis identified parameters independently associated with a laboratory confirmed dengue infection (main outcome variable) before and after day 3 from fever onset. A diagnostic decision tree algorithm was constructed based on multivariate logistic regression analysis.

Results: Of 254 patients that met the inclusion criteria, 112 (44.1%) had an acute dengue infection while 142 were classified as OFI. We constructed a diagnostic algorithm using white blood cells (WBC) count, rash, mean corpuscular haemoglobin (MCH) levels and haemorrhagic manifestations in sequential order that distinguished dengue from OFI with a sensitivity of 88% and a specificity of 63%. Multivariate analysis determined that the presence of rash, haemorrhagic manifestations and a decrease of platelet counts, WBC count and MCH were independently associated with dengue during the first 3 days of the disease. Finally, a decrease of cholesterol and an increase of albumin were the two biochemical parameters independently associated with dengue at the early phase of the disease.

Conclusions: The proposed diagnostic algorithm may be a useful instrument to help clinicians in the early identification of dengue patients. This may substantially decrease fatalities due to timely treatment and avoid overburdening of the health system owing to misdiagnosis.

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Prevalence of resistant and virulence genes in Enterococcus faecium and Enterococcus faecalis isolated from blood culture in haematological patients in Russia

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Background: The aim of this study was to investigate the prevalence resistant and virulence genes in E. faecium and E. faecalis isolated from blood culture in haematological patients.

Materials/methods: Enterococcus spp. were isolated from blood culture in haematological patients in six Russian hospitals from 2002 to 2018. Susceptibility to glycopeptides was determined by broth microdilution method (CLSI, 2018). Virulence genes (esp, hyl, asa1, cylA and gelE) in E. faecium and E. faecalis and vancomycin resistance genes (vanA, vanB and vanD) in Enterococcus spp. were detected by multiplex PCR.

Results: A total of 487 Enterococcus spp. were evaluated, of them 393 (80.7%) were E. faecium and 94 (19.3%) E. faecalis. Resistance to vancomycin was detected in 71 (18.1%) E. faecium, of them 47 (66.2%) carried vanA genes and 24 (33.8%) vanB. One (1.1%) E. faecalis was vancomycin-intermediate [MIC 16 μg/ml] with vanD gene. The distribution of virulence genes in E. faecium and E. faecalis is presented in the table. The predominant genes in E. faecium were esp (71.2%) and hyl (53.7%), in E. faecalis were gelE (67%) and asa1 (63.8%). Differences in the detection of all genes (p<0.0001) were found between E. faecium and E. faecalis. Up to 42% of E. faecalis isolates had ≥3 virulence genes whereas 82.2% of E. faecium isolates were found to carry 1-2 virulence genes only. All investigated virulence genes were absent in 15.3% E. faecium and 3.2% E. faecalis (p<0.0001). Gene hyl was detected less frequently [43.7% vs. 55.9%, p=0.066] in vancomycin-resistant E. faecium (VREF) compared to vancomycin-susceptible E. faecium (VSEF) and gene cyl was absent in VREF. No differences in distribution of virulence genes in vanA and vanB VREF were found, except of asa1 gene, which was absent in vanB VREF.

Conclusions: The rate of vancomycin-resistance was higher in E. faecium than in E. faecalis with prevalence of vanA [66.2%] compared to vanB [33.8%]. Genes esp and hyl prevailed in E. faecium, genes gelE and asa1 in E. faecalis. Multiple virulence genes in E. faecalis were significantly more prevalent than in E. faecium isolates. In VREF compared to VSEF gene hyl was detected less frequently and cyl gene was absent.

Table. The distribution of virulence genes in Enterococcus spp.

<table>
<thead>
<tr>
<th>Enterococcus spp.</th>
<th>Virulence genes in Enterococcus spp., n (%)</th>
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<tbody>
<tr>
<td></td>
<td>esp</td>
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<tr>
<td>E. faecalis (n=94)</td>
<td>32</td>
</tr>
<tr>
<td>E. faecium, (n=393)</td>
<td>280</td>
</tr>
<tr>
<td>VSEF (n=322)</td>
<td>230</td>
</tr>
<tr>
<td>VREF (n=71)</td>
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<tr>
<td>vanA VREF (n=47)</td>
<td>32</td>
</tr>
<tr>
<td>vanB VREF (n=24)</td>
<td>18</td>
</tr>
</tbody>
</table>

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Molecular epidemiology of vancomycin-resistant enterococci: changing paradigms at the crossroads of Europe

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Abstract 4905

Background: Vancomycin-resistant enterococci (VRE) are emerging pathogens of nosocomial infections worldwide and their mortality in bloodstream infections (VREBI) can reach 50%. In Germany, vancomycin-resistance in invasive Enterococcus faecium isolates increased from 11.9% (2016) to 23.8% in 2018. To investigate the epidemiology of VREBI and of the underlying isolates, we established a network of VRE surveillance in North-Rhine Westphalia (NRW), the largest German state located centrally in the Schengen free movement area, accounting for 21.6% of the German population.

Materials/methods: Between 2016 and 2018, we included VREBI isolates from all inpatients residing or hospitalized in NRW at the time of diagnosis. We determined the multilocus sequence type (ST) and vancomycin resistance determinants. Results were geographically mapped by administrative districts according to the postcode of the place of hospitalization.

Results: In total, 493 isolates were analyzed. The incidence of VREBI increased sharply during the study period: 0.52, 0.88 and 1.36 per 100,000 inhabitants in 2016, 2017 and 2018, respectively. The distribution of the resistance determinants varied drastically over time. Whereas a predominance of vanA (64.5% of all isolates) over vanB was observed in 2016, in 2017 an inversion of this distribution occurred with vanB-positive isolates almost doubling to 68.6% and reaching 83.2% of all analyzed isolates in 2018. The overall most common ST was ST117, which carried vanB in 91.9% of the cases and showed a steadily increasing incidence (45.2% in 2016, 77.5% in 2018). Other predominant STs were ST80 and ST203.

Conclusions: VREBIs are a rising problem in NRW, a situation also reported in neighboring states and countries. This can be attributed to the increasing incidence of ST117, an ST that has rapidly spread from east to west. The common association of ST117 with vanB has led to the fundamental epidemiological change, with vanB now widely outnumbering vanA, historically the predominating resistance determinant among VRE in Europe and other regions of the world. Our data can be used for the development of infection prevention policies, as vanB-positive VRE are -until now- known to be teicoplanin-susceptible.

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Plasma population pharmacokinetic modelling of cefepime and enmetazobactam in patients with complicated urinary tract infections

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Background: Infections caused by extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae account for more than 20,000 deaths annually in the EU and US. Enmetazobactam is a novel β-lactamase inhibitor belonging to the penicillanic acid sulfone class, targeting ESBLs. The combination enmetazobactam with cefepime is currently being investigated in a Phase 3 study of patients with complicated urinary tract infections (cUTI) or acute pyelonephritis (AP). In this study, population pharmacokinetic (PK) models for cefepime and enmetazobactam were established from healthy participants and cUTI patients.

Materials/methods: Plasma PK samples were analyzed from healthy participants receiving cefepime (n=57) and enmetazobactam (n=132) in three phase 1 studies and from patients receiving cefepime (n=43) and enmetazobactam (n=29) in a phase 2 study of cUTI. Population PK characteristics were described and the relationship between different subject-specific factors and model parameters were assessed. The effect of infection on disposition was assessed by testing disease covariates on fixed and random effects for all PK parameters.

Results: Cefepime and enmetazobactam PK were similar and best described with a two-compartment, linear PK model with key parameters summarized in the table. Statistically significant covariates for cefepime disposition were estimated glomerular filtration rate (eGFR) on clearance and peripheral volume of distribution (Vₚ), body weight on central Vₖ, and albumin on peripheral Vₚ. Significant covariates for enmetazobactam disposition were eGFR on clearance and peripheral Vₚ, body weight on both central and peripheral Vₚ, and gender and infection on peripheral Vₚ. Interindividual variability for clearance and central Vₖ was larger in cUTI patients for both agents.

Conclusions: The population PK models for cefepime and enmetazobactam effectively predict exposures in cUTI patients, including subjects with renal impairment or undergoing hemodialysis. These models will support Monte-Carlo simulations and target attainment estimations in this patient population.

<table>
<thead>
<tr>
<th>PK parameters</th>
<th>Typical values for a 70 kg cUTI patient (%CV)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Cefepime</td>
</tr>
<tr>
<td>Clearance [L/h]</td>
<td>6.0 (23%)</td>
</tr>
<tr>
<td>Dialysis clearance [L/h]</td>
<td>7.4 (21%)</td>
</tr>
<tr>
<td>Central volume of distribution [L]</td>
<td>10.1 (36%)</td>
</tr>
<tr>
<td>Exchange coefficient [L/h]</td>
<td>7.2</td>
</tr>
<tr>
<td>Peripheral volume of distribution [L]</td>
<td>7.5 (26%)</td>
</tr>
<tr>
<td>Terminal half-life [h]</td>
<td>2.4</td>
</tr>
</tbody>
</table>

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Community-acquired *Clostridioides difficile* infection: a prospective study in an unselected population

Laura Villar Gomara*, Silvia Noemi Vazquez Cuesta1, Luis Alcalá1, Mercedes Marín1, Patricia Muñoz1, Emilio Bouza1, Elena Reigadas Ramirez1

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**Background:** *Clostridioides difficile* infection (CDI) is the most common cause of hospital acquire diarrhea in developed countries. However, during the last decades, there has been noted an increment in CDI cases acquired in the community (CA-CDI). These patients purportedly have less known risk factors and are frequently unrecognized or underdiagnosed. Prospectively evaluated CDI series without a restrictive criteria or selection bias are scarce. The objective of this study was to assess the epidemiology, clinical characteristics and outcome of CA-CDI in an unselected population.

**Materials/methods:** We conducted a prospective study ([Jul 2018-ongoing](https://example.com)) in which systematic testing for toxigenic *C. difficile* on all diarrhoeic stool samples was performed regardless of the clinician’s request. The microbiology laboratory receives samples from hospitalized patients and from all outpatient centers within our catchment area. All episodes of CDI were prospectively collected and classified attending to the source of acquisition. Patients aged >18 years who fulfilled criteria for CA-CDI were enrolled and monitored at least 2 months after their last episode. Epidemiological and clinical data were recorded.

**Results:** During the study period, 860 samples were positive for toxigenic *C. difficile*, corresponding to 638 patients. We identified 184 CA-CDI patients, out of which 90 have completed the study and fulfilled CDI criteria. Mean age was 56.5 years and 64.4% were female. Overall, 54.4% had community onset (CO-CA-CDI). 31.1% of the episodes would have gone undiagnosed owing to lack of clinical suspicion. Overall, only 6.7% had no underlying disease, the most frequent underlying diseases were gastrointestinal (52.2%), cardiovascular (44.4%), metabolic (43.3%), respiratory, endocrine and rheumatologic (28.9%). The most frequent risk factors were having received antibiotic treatment (68.9%) and having received PPI (67.8%). Most episodes were mild to moderate (73.3%) and 84.4% were treated for CDI. Recurrence (R-CDI) occurred in 11.9% of patients. Overall mortality was 7.8% and mortality attributable to CDI was 1.1%.

**Conclusions:** Even in a setting with optimal diagnostic tests, one third of CA-CDI cases would have gone undiagnosed due to lack of clinical suspicion. Most CA-CDI episodes were mild to moderate, however there was a significant proportion of R-CDI and a CDI-related mortality episode.

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Abstract 4911

**Clinical validation of the BD CT/GC/TV2 for BD MAX system in vaginal, endocervical and female urine specimens**

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**Background:** Rates of treatable sexually transmitted infections (STI) continue to increase globally according to national and international public health agencies. In many countries, the prevalence of trichomonas is even higher than that of chlamydia and gonorrhea. Diagnostic systems that support targeted therapy rather than syndromic management are needed in order to improve antimicrobial stewardship. Here we describe the performance of the BD CTGCTV2 assay (pending CE Marking) when using vaginal (VS) or endocervical swabs (ES), endocervical samples in liquid-based cytology (LBC), and female urine (FU) specimens.

**Materials/methods:** Specimens collected from each participant included FU, 4 VS (2 patient- and 2 clinician-collected), 2 ES and 1 LBC specimen. Hologic Aptima® AC2 and TV; and BD ProbeTec™ CTQx/GCQx and TVQx assays were used as references to determine the patient infection status (PIS) (ES/FU for chlamydia and gonorrhea PIS; and VS/ES for trichomonas PIS). For female urine, results from 3 assays were used in a composite molecular comparator reference.

**Results:** Samples were obtained from 2,547 women. Sensitivity estimates using VS were 98.4, 98.8 and 99.4% for chlamydia, gonorrhea, trichomonas, respectively. In the same order, sensitivity estimates were 94.5, 95.3, and 93.8% using ES; 92.7, 92.9 and 91.4% using LBC; and, 98.4, 100 and 100% with FU. All specificity estimates were ≥98.7%. The BD CTGCTV2 assay has dual gonorrhea targets in order to optimize specificity; both targets are required to give a signal for a positive result. The PPV based on observed GC prevalence (1.6%) was ≥91.4% for all specimen types.

**Conclusions:** The BD CTGCTV2 assay uses reagent strips that allow testing in batches up to 24 samples, without reagent loss, on a tabletop instrument. The ability to correctly identify all three of the most prevalent treatable STIs in a small platform may allow local testing to be performed in settings where testing could only be accessed via centralized reference labs previously. This could lead to a reduction in specimen shipping costs and in the total time to results. Adoption of such a system could lead to improved patient management and antimicrobial stewardship by accurately targeting treatment to manage only those pathogens detected.

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A retrospective study to evaluate the epidemiology, standard of care, outcomes and resource utilisation in patients with confirmed or suspected infection by a carbapenem-resistant Gram-negative organism in Spain: the CARBAR study part 1, epidemiology of Gram-negative organisms

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1Hospital del Mar, Barcelona, Spain, 2Hospital Universitario y Politecnico la Fe, Valencia, Spain, 3Hospital Universitario Reina Sofía, Cordoba, Spain, 4Hospital Clinico Universitario Lozana Blesa, Zoragaza, Spain, 5Hospital Universitario San Espouses, Illes Balears, Spain, 6Universitat Autònoma de Barcelona, Barcelona, Spain, 7Infectious Diseases Unit, Hospital de la Santa Creu i Sant Pau - Institut d’Investigació Biomèdica Sant Pau, Barcelona, Spain, 8Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, 9Complejo Hospitalario Universitario A Coruña [CHUC], Coruña, Spain, 10Hospital Clinico San Carlos, Madrid, Spain, 11Hospital Universitaria Donostia, Donostia, Spain, 12Former Shionogi Europe, London, United Kingdom, 13Shionogi Europe, London, United Kingdom

Background: Antimicrobial resistance is a global threat with potentially devastating consequences and significant costs to society. Carbapenems are customarily reserved for difficult-to-treat Gram-negative (GN) infections, but resistance is increasing; hence, WHO recently classified carbapenem-resistant [CR] Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacteriaceae as a critical priority.

CR-GN infections have few effective treatment options, with variable outcomes, and clinical trial evidence is scarce. In this analysis, we describe the epidemiology of patients infected with CR-GN organisms in Spain.

Materials/methods: Ongoing retrospective chart review in Spain. Adult patients admitted to hospital between April 2017-March 2018 were included if they had a confirmed GN bacterial infection and/or positive screening isolate for CR-GN bacteria colonisation. Data collection included microbiological results and patient demographics.

Results: 11,040 patients were included in 5 sites [representing 13,871 GN isolates], of which 1,292 patients (12%) had CR-GN pathogen. Mean age was 62.4 years; 51% were male.

Table 1 shows the distribution of GN pathogens identified. The most prevalent GN species were Escherichia coli representing 47% of all isolates, followed by Pseudomonas aeruginosa (13 %), and Klebsiella pneumoniae (13%).

Non-fermenters represented 63% of all CR-GN isolates. The main species identified in CR-GN was Pseudomonas aeruginosa (39%) followed by Stenotrophomonas maltophilia (19%). Enterobacteriaceae represented 37% of all CR-GN isolates.

<table>
<thead>
<tr>
<th>CR-GN (n=1,539)</th>
<th>Overall (n=13,871)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CR-GN (n=1,539)</td>
<td>Overall (n=13,871)</td>
</tr>
<tr>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Acinetobacter spp</td>
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<td>Pseudomonas aeruginosa</td>
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<td>Stenotrophomonas maltophilia</td>
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<td>Total non-fermenter spp</td>
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<tr>
<td>Escherichia coli</td>
<td>57</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>200</td>
</tr>
<tr>
<td>Total Enterobacteria</td>
<td>563</td>
</tr>
</tbody>
</table>

Conclusions: 12% of GN isolates are CR-GN across Spain, representing an important segment of this population. Understanding the real-world prevalence of GN and particularly CR-GN infections, where there is the highest unmet medical need, can help to optimise antimicrobial stewardship and infection control programmes, and ultimately improving overall patient’s and healthcare system’s outcomes, which is the focus of this study’s next phase.

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Abstract 4914

Transforming care through data transparency: impact on cellulitis therapy standardisation

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Background: Cellulitis is frequently encountered in the acute care setting, leading to over 600,000 admissions annually in the United States. Variations in care can have a substantial impact on patient outcomes including hospital admission rates, overall costs, and hospital length of stay (LOS). With many therapeutic options available to treat cellulitis and wide variety in prescriber antibiotic selection, our team hoped to investigate the benefits of data transparency with the goal of standardizing care for cellulitis.

Materials/methods: This multi-site retrospective review was conducted across 7 AdventHealth campuses in Orlando, FL. The Care Transformation team and Antimicrobial Stewardship Awareness Program developed a 2-phase process to assess the impact of unblinded physician report cards. Both phases included patients >18 years of age admitted with a primary diagnosis of cellulitis DRGs 602 and 603 who also had infectious diseases (ID) physician consultations. Phase one was conducted between January 2017 to June 2018 with phase two in July 2018 to March 2019. A total of 29 ID physicians were included with over 1800 cases included in each time frame. Results for phase 1 (Figure 1) revealed each physician’s unblinded performance compared to de-identified results of their peers. Overall hospital LOS and total cost of antibiotics per case were evaluated to identify variations and subsequent standardizations in practice.

Results: After presentation of unblinded phase 1 data, improvements in both average LOS and antibiotic cost per case were noted. In comparison to phase 1 data, 57% of providers decreased their average LOS in phase 2 from 4.63 days to 4.13 days. Additionally, 48% of providers decreased their average antibiotic cost per case by $30 per case after presentation of unblinded data ($270.11 vs $242.11). This decrease led to a total costs savings of $298,375 during phase 2.

Conclusions: This study identified a wide range of variation amongst ID consultants in phase 1, and through the presentation of unblinded data, led to improvements in standard treatment for cellulitis during phase 2. Presenting data transparently may be beneficial to explore in other infectious disease states.

Figure 1: Physician Report Card-Phase 1

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**In vivo bactericidal activity of minocycline and rifampicin combination in a lung infection model in neutropenic mice**

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**Background:** As development of new antibiotics against multidrug-resistant pathogens is limited, combination therapy may increase efficacy of antibacterial treatment. Minocycline and rifampicin have broad activity against Gram-positive and Gram-negative bacteria but their efficacies are limited because of fast development of resistance. We therefore combined minocycline with rifampicin against *Acinetobacter baumannii* and *Staphylococcus aureus* in a lung infection model in neutropenic mice and determined the bactericidal effects of combination therapy.

**Materials/methods:** Neutropenic mice were challenged with *A. baumannii* 112 or *S. aureus* MUP3199 strains with minocycline/rifampicin MICs 0.063/8 and 0.125/0.008 mg/L, respectively. Treatment was started 2h after intranasal inoculation of 10⁶-10⁷ CFU and continued for 24h. Minocycline and rifampicin were dosed 0.5-2 mg/kg q6h subcutaneously and 4-64 mg/kg q12h per os, respectively (3x5 checkerboard). Mice were euthanized 24h after start of treatment and CFUs were counted with serial quantitative cultures in lung homogenates. The log₁₀ CFU/lung reductions compared to initial bacterial lung burden were calculated for each dosing regimen in duplicate experiments. Dose combinations with statistically significant bactericidal activity (>1-log₁₀ kill) were determined using t-test.

**Results:** Lung CFU in placebo-treated mice increased by 2log₁₀ compared to baseline bacterial burden whereas minocycline monotherapy showed bacteriostatic effect at the highest doses against *A. baumannii* and *S. aureus*. No effect was found with rifampicin monotherapy. When the two drugs were combined, significant bacterial killing of >1-log₁₀compared to start of treatment was found in 5 and 6 out of 15 tested dose combinations for *A. baumannii* and *S. aureus*, respectively at minocycline/rifampicin doses 0.5-2/16-32 mg/kg. The strongest bactericidal activity (-4.5 for *A. baumannii* and -3.2 for *S. aureus*) was found when 32-64 mg/kg q12h of rifampicin was combined with 0.5 mg/kg q6h of minocycline.

**Conclusions:** The addition of rifampicin to minocycline treatment resulted in strong bactericidal activity compared to monotherapy regimens. The combination may overcome fast development of resistance against the drugs alone and therefore warrants further evaluation.

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Abstract 4919

**Risk factors for in-hospital mortality in a prospective contemporary cohort of adult patients with infective endocarditis in a cardiac surgery hospital**

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**Abstract third-party references:** Supported by Faperj, Rio de Janeiro.

**Background:** Mortality in infective endocarditis (IE) remains very high, despite availability of surgery and expertise in management.

**Materials/methods:** Risk factors were sought for in hospital mortality in a prospective cohort of adults with definite IE. The Jamovi 1.0.7 software was used for analysis. International Collaboration on Endocarditis CRFs were used for data collection.

**Results:** From January 2006-September 2019, 359 episodes of IE were included; 2/3 of patients were male; over 90% of IE was left-sided. Median age was 47.1 [IQR 34-61]. In hospital mortality was related to age: patients who died were older in all quartiles (Q1, 31 vs 44.8 years; Q2 44 vs 56.5 years; Q3, 56.8 vs 68.3 years, p<0.001), but not to sex. Heart failure, HF (53.4% vs 35.7%, p=0.003), diabetes (19.3% vs 9.3%, p=0.011), hypertension (65.8% vs 42.1%, p<0.001), chronic renal failure, CRF (36.4% vs 14.9%, p<0.001) and coronary artery disease (23% vs 9.3%, p<0.001) were associated with death. Patients who died more often presented acutely (64.7% vs 46.8%, p=0.015) and had hospital-acquired IE (37.5% vs 25.7%, p=0.033). Death was associated with paravalvular abscess (29.5% vs 17.5%, p=0.015), conduction disturbances (17.9% vs 7.9%, p=0.012), persistent bacteremia (10.8% vs 3.6%, p=0.011) and acute renal failure, ARF (50% vs 25.8%, p<0.001), but not with acute onset of HF (65.9% vs 60.1%, p NS). Regarding etiology, mortality was related to coagulase-negative staphylococci (17% vs 6.3%, p=0.002), no difference was found for S.aureus, enterococci or blood culture-negative IE. Candida etiology and Gram negative non HACEK microorganisms affected more often those who died (p NS). Pre-operatively patients who died had significantly more cardiac arrest, need for inotropes, intra-aortic balloon pumps and mechanical ventilation. Of those who died, 93.4% had a surgical indication, but only 64% were operated while of those who survived, 84.8% had surgical indication and 85% had surgery (p<0.001).

**Conclusions:** In hospital mortality was mainly related to previous HF and CRF, as well as ARF. Local infection leading to abscess and heart block were also related to death, as was persistent bacteremia. Hospital acquisition was more frequent. However, S.aureus etiology was unrelated.

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Characteristics of Resistance Associated Substitutions (RASs) in “unusual” HCV subtypes: a worldwide network of HCV resistance database

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Background: HCV is highly variable; 8 genotypes and over 100 subtypes have been identified so far. Recently, “unusual” subtypes in patients from African and Asian origin have been associated with lower response rates to DAAs. This was ascribed to polymorphisms at relevant amino acid positions as compared to the most sensitive subtype in the same genotype. Using the international SHARED network, we aimed to assess the prevalence of post-treatment failure RASs and their patterns among unusual HCV subtypes, defined as GT1 non1a/b, GT2 non2a/b, GT3 non3a, GT-4 non4a/d, GT5, and GT6.

Materials/methods: We extracted data from the SHARED database of patients who did not achieve a sustained virological response on DAA therapy. Only patients who failed DAA strategies recommended by EASL guidelines were included. Genotype and subtypes were sequence-derived, and analyses grouped by HCV subtype. RASs were analysed at positions according to the 2018 EASL guidelines.

Results: We identified a 6% prevalence (73/1176) of unusual subtypes among patients who failed NSSA inhibitor-containing regimens, including: GT1g [n=2], GT1l [n=5], GT2c [n=8], GT2i/j [n=1 each], GT3h [n=7], GT3b [n=6], GT3k [n=2], GT3g [n=1], GT4r [n=14], GT4v/4ns [n=3 each], GT-4g/4o [n=2 each], GT-4f/4k/4n/4q/4t [n=1 each], GT6q [n=3], GT-6e/6h/6p/6r/6xe [n=1 each]. Patients were treated with SOF+LDV +/-RBV [n=18], SOF+DCV +/-RBV [n=15], SOF+VEL +/-RBV [n=13], GZR+EBR [n=11], 2D/3D +/-RBV [n=11], GLP+PIB [n=5]. At failure, all patients harbored NS5A RASs, with a mean number of 3 NSSA RASs. Interestingly, failures with GT6h/p/exe carried 4 to 5 NSSA polymorphisms possibly associated with reduced NSSA inhibitors susceptibility. All GT3b/3g/3k harbored the NSSA A30K+L31M combination. Additionally, in patients failing NS3 protease inhibitor-based therapy, combinations of NS3 RASs were detected in specific subtypes: R155Q/A156T/D168N/E and Y56H+D168V in two GT4g and one GT6q patients failing GZR/EBR, and A156F/D168V in a GT6q patient failing GLP+PIB.

Conclusions: Unusual subtypes may be overrepresented among DAA failures. In-depth characterization of these subtypes is crucial, in Africa and Asia where these subtypes are common as well as in countries of immigration from these regions. Our results emphasize the need for identification of RASs in these subtypes and their in vitro drug susceptibilities.

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Persistence of Tropheryma whipplei colonisation: a longitudinal study in Italy

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Background: Whipple disease (WD) is a rare and potentially fatal illness caused by Tropheryma whipplei (TW). TW DNA can been found in biological specimens of WD patients but also of asymptomatic carriers. Its identification in faeces, saliva, urine and blood has been described as a promising non-invasive diagnostic approach to differentiate between possible WD and colonization, but very little is known about persistence of TW. In our previous retrospective, observational study (2014-2016), 6.9% [85/1240] of faeces collected from Italians and migrants resulted positive to TW. However, no clinical information was available at that time.

Materials/methods: In September 2019 we contacted the 85 subjects whose faeces had resulted TW positive for a clinical revaluation including rt-PCR for TW in faeces, saliva, urine and blood. Subjects were to be classified as having: transient colonization (rt-PCR negative on all samples), asymptomatic colonization [no symptoms and at least one positive rt-PCR], and possible WD (symptoms with a positive rt-PCR or ≥ 2 positive rt-PCR regardless of symptoms or a single positive rt-PCR on blood).

Results: We analyzed the preliminary data of 26 (31%) subjects. The median age was 26 years, 58% were male, and 58% were migrants (most from Africa). Rt-PCR resulted negative in all samples in 9 (35%) subjects (transient colonization); 17 (65%) subjects had at least one rt-PCR positive in faeces or saliva after a median of 50 months. Blood and urine specimens were negative. Out of the 17 colonized subjects, 15 (88%) were asymptomatic and 2 (12%) reported both abdominal discomfort, chronic diarrhea and weight loss (possible WD). One subject, asymptomatic, had rt-PCR positive in both faeces and saliva (possible WB).

Conclusions: This is to our knowledge the first study to prospectively follow TW colonized subjects for such a long time. More than half of subjects are still colonized after nearly 4 years, suggesting that a long colonization or a reinfection are frequent. Combined use of TW rt-PCR allowed us to identify 3 subjects with possible WD who will undergo to more invasive procedures to confirm the diagnosis.


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Abstract 4927

Efficacy of ceftolozane-tazobactam in combination with colistin against extensively drug-resistant *Pseudomonas aeruginosa* including high risk clones, in an *in vitro* pharmacodynamic model

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**Background:** Colistin has been the only treatment available for extensively drug-resistant (XDR) *Pseudomonas aeruginosa* infections, for many years, having suboptimal results. Ceftolozane/tazobactam (C/T) is a new therapeutic option that showed good antipseudomonal activity. However, data about combinations containing C/T are scarce.

**Objectives:** To analyse the efficacy of C/T and colistin alone and combined against three XDR *P. aeruginosa* ST175 isolates with different susceptibility to C/T.

**Materials/methods:** The *in vitro* pharmacodynamic chemostat model was used to validate the effect of C/T and colistin alone and combined against three XDR *P. aeruginosa* ST175 isolates with different MIC values. All strains were colistin-susceptible. The simulated C/T dosing regimen was 2/1g every 8h by intravenous infusion over 1h. A continuous infusion of colistin was simulated to achieve free steady-state concentrations of 2mg/L. Bacterial suspension was cultured onto agar supplemented with C/T or colistin at 2-fold and 4-fold the baseline MICs to assess the effect of each regimen on less-susceptible bacterial population. Pharmacokinetic samples were validated by HPLC.

**Results:** ST175 [10-023] was C/T-susceptible with a MIC of 2mg/L showing resistance to β-lactams except C/T due to OprD inactivation and AmpC hyperproduction. ST175 [09-12] was C/T-resistant with a MIC of 8mg/L and showed a specific mutation in PBP3 associated with increased β-lactam resistance. ST175 [07-016] was C/T-resistant with a MIC of 16mg/L and produced GES-5. In the PK/PD model, the scheme of C/T at 2/1g every 8h combined with colistin effectively suppressed the bacterial growth at 24h. Additive or synergistic interactions with C/T plus colistin were observed against *P. aeruginosa* isolates, including those C/T-resistant [Figure 1]. C/T-resistant isolates were not detected in any of the strains with any schemes. The emergence of a colistin-resistant population was detected at the end of the experiment with colistin alone in all the strains. No colistin-resistant populations were detected with the combination. The simulated drug exposures achieved were considered satisfactory for all regimens.

**Conclusions:** Our study showed that the combination of C/T plus colistin improved the activity of monotherapies against XDR *P. aeruginosa* infections. Our data suggested that it may be a useful treatment of these infections and highlighted its potential role against C/T-resistant isolates.
Figure 1. In vitro chemostat experiments with three selected XDR P. aeruginosa ST175 isolates with different susceptibility levels to C/F: ST175 (10-023) with an MIC of 2 mg/ml, ST175 (09-012) with an MIC of 8 mg/ml, and ST175 (07-016) with an MIC of 16 mg/ml. Mean number of CFUs over 24 h for each P. aeruginosa isolate and antibiotic.

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**Evaluation of OspC as marker for direct diagnostic of Lyme disease**

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**Background:** Lyme disease is the most common tick-born infectious disease in Europe. This infection is caused by spirochetes of *Borrelia* species. Currently, laboratory diagnostics are exclusively based on serological tests. However, these tests present a lack of sensitivity, specificity and standardization due to the absence of serum antibodies in early stage, the poor representativeness of *Borrelia* strains and the detection of antibodies cross-reacting with ubiquitous antigens. A more reliable and precise test is thus needed. In this context, our objective is to develop a direct diagnostic test based on detection of circulating bacterial antigen produced by the bacteria. We focused on the outer surface proteins C (OspC), a 22kDa lipoprotein that is potentially considered as an early marker of Lyme borreliosis, according to serologic and protein skin host analysis. Nevertheless, OspC is highly variable between *Borrelia* species so to detect all OspC variants, we decided to produce monoclonal antibodies (mAbs) directed against a highly conserved OspC motif.

**Materials/methods:** Specific mAb clone were produced by immunization of BALB/c mice with synthetic peptide coupled to a carrier protein. MAb were characterized by immunoassay, western blot against recombinant proteins or *Borrelia* lysates. Their affinity (Kd) were determined by using bio-layer interferometry biosensor technology. Then, the potential of our antibodies to detect OspC was investigated on mice tissues extract and fluid. The mice were infected with different *Borrelia* species by subcutaneous inoculation. Mice tissue proteins were extracted, enriched by on beads immuno-precipitation and analyzed by western blot.

**Results:** 13 mAbs against the conserved OspC peptide were produced. During the characterization process, the mAb affinity (Kd) was determined at 9,31E-10 molar for the antibody of higher affinity, using recombinant OspC. We selected the mAbs OspC-11, allowing for instance to reach a limit of detection close to 5pg of OspC protein by Western-Blot and to detect OspC in mouse samples.

**Conclusions:** Taking into account the variability of *Borrelia* species, mAbs against conserved motif of OspC could be very useful for diagnostic of Lyme disease early stage. We plan now to evaluate the efficiency of these mAbs in more mice tissues and in clinical patient samples.

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Rapid detection of OXA-23-, OXA-40- and OXA-58-mediated carbapenem resistance in Acinetobacter baumannii

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Background: Treatment of Acinetobacter baumannii infections can be extremely challenging owing to the wide distribution of multi-drug resistant strains. Of special concern is increasing resistance against carbapenems. The WHO published a global list of antibiotic-resistant priority pathogens with carbapenem-resistant A. baumannii as “priority 1” for research, discovery and development of new antibiotics. Colonization with carbapenem-resistant A. baumannii (CRAb) requires rapid action from an infection control perspective because the organism is known for its propensity for epidemic spread. Hence, there is an unmet medical need to rapidly identify CRAb to enable appropriate antimicrobial treatment and to prevent transmission.

Carbapenem-resistance in A. baumannii is mainly mediated by the acquired carbapenemases: OXA-23, OXA-40 like or OXA-58. In a “Proof-of-concept” study we have generated and selected anti-OXA-23 monoclonal antibodies (moAbs), which have been implemented in the commercially available OXA-23 K-SeT (Coris BioConcept).

Our aim was to expand the OXA-detection abilities of the OXA-23 K-SeT to include OXA-40- and OXA-58-like carbapenemases.

Materials/methods: We generated and selected specific anti-OXA-40 (n=8) and anti-OXA-58 (n=6) moAbs. Combinations of these moAbs, were analyzed in immunochromatographic test (ICT) format for their ability to detect recombinant OXA-40 or OXA-58, respectively. Antibody pairs showing specific and strong signals were chosen and implemented into single-OXA-40 and single-OXA-58 ICT-prototypes. Those ICT-prototypes were evaluated on clinical A. baumannii isolates (n=40) with well-defined carbapenem-resistance mechanisms.

Results: One set of antibody pairs specific for recombinant OXA-40 or OXA-58 were identified in ICT format, respectively. These moAbs were implemented into single-OXA ICT-prototypes. Furthermore, one anti-OXA-58 moAb (#C8), which shows cross-reactivity to OXA-40 and OXA-58 was implemented in additional single-OXA ICT-prototypes.

The evaluation of these single-OXA-40 and single-OXA-58 ICT-prototypes with CRAb isolates has demonstrated 100% specificity within 15 min.

Conclusions: Based on successful single-OXA ICT-prototype validation the development of a triple-OXA-23/40/58 ICT will be envisaged to detect more than 93 % of CRAb strains worldwide.

With this easy-to-use, rapid detection assay one can save 12-48 hours in diagnostics, which helps to treat patients earlier with appropriate antibiotics and allows immediate intervention to control transmission of CRAb.

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Abstract 4932

**Patient management and indication for influenza A/B and respiratory syncytial virus Point-of-Care testing in the emergency room and possible gains by syndromic respiratory testing**

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**Background:** Point-of-care testing (POCT) for Influenza A/B & RSV was implemented in the emergency room at all hospitals in the Capital Region of Denmark in 2018. To evaluate the implementation, we have verified indication for testing, effects on patient management and finally considered possible benefits of a syndromic testing approach on patients that are currently tested for Influenza A/B & RSV

**Materials/methods:** Patients samples from 555 patients tested by POCT between February and July 2018 were retested for 26 respiratory pathogens and the patient records were evaluated with respect to diagnosis, indication for POCT, hospitalisation time, antimicrobial therapy and readmission or death within one month of testing

**Results:** A valid indication for POCT was established for 502 (90.5%) of all patients. A positive POCT result significantly reduced median hospitalisation time (11.8 vs. 38.8 hours) and initiation of antibiotics (26.6 vs. 50.5%), whereas antiviral treatment was significantly increased (11.8 vs 1.6%). Risk of readmission or death was not significantly altered by a positive POCT result. Testing for 26 respiratory pathogens established that risk of co-infection drops by age and that POCT should be restricted to the season. A trend towards longer median hospitalization time (19.7 vs 11.8, p = 0.087) and initiation of antibiotics (36.6 vs 26.6%, p = 0.055) was established for patients positive for one or more respiratory pathogens not included in the initial POCT

**Conclusions:** POCT increases antiviral treatment and reduces hospitalisation time and initiation of antibiotics. Syndromic POCT may be beneficial in small children and outside the influenza season, decreasing hospitalization time and antibiotic use

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Abstract 4933

Clinical and gut microbiome characterisation of Clostridiodes difficile infection in immunosuppressed patients

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Abstract third-party references: On behalf of the HGUGM Microbiome Project

Background: Data on Clostridiodes difficile infection (CDI) in specific groups are necessary in order to assess the impact of health care programs and implementation of novel costly treatments targeted for specific groups. Immunosuppressed patients are particularly susceptible to C. difficile, however little is known about specific markers of recurrence (R-CDI). Our objective was precisely to assess the clinical and gut microbiome characteristics of CDI in immunosuppressed patients.

Materials/methods: We prospectively included patients who fulfilled criteria for CDI and immunosuppression (jan2019-on-going study). Informed consent was obtained for all patients included. Epidemiological, clinical data and fecal samples were collected. For microbiome analysis, the hypervariable V4 region of the 16s rRNA gene was sequenced on an Illumina Miseq platform. Mothur's bioinformatic pipeline was followed for data analysis.

Results: During the study period, 4,341 samples were sent for CDI diagnosis. 452 were positive, out of which, 135 (29.9%) were from immunosuppressed patients. Seventy-seven episodes (56 primary episodes; 16 first recurrences; 5 second recurrences) from 56 patients who consented to their inclusion. Median age was 61.5 years and 55.4% were females. Immunosuppression was due only to underlying disease in 61.5%, in 29.9% due to medication, and 19.6% due to both. The most frequent underlying diseases were cardiological (50.0%), endocrine (37.5%), solid tumors (33.9%), and hematological (32.1%). Severity of CDI episodes was mild-moderate (63.6%), severe (18.2%) and severe complicated (7.3%). Recurrence occurred in 31.0%, overall mortality was 3.5% and CDI-related mortality was 1.8%. Female sex was an independent risk factor for R-CDI (p=0.046). Regarding microbiota analysis, the most predominant phyla were: Firmicutes (47.7%), Bacteroidetes (30.4%) and Proteobacteria (13.7%). We found no significant difference in alpha-diversity, beta-diversity or abundance of specific microorganism groups regarding the cause of immunosuppression or the presence of R-CDI.

Conclusions: One third of CDI patients had immunosuppression condition. A significant proportion had a severe or severe-complicated CDI and recurrence rate was high. Female sex was the only independent risk factors for R-CDI in this population. We could not establish any microbiota marker for R-CDI in this population. Immunosuppressed CDI patients showed an altered microbiota composition equiparable to that of other CDI patients.

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Abstract 4934

A rapid adenosine triphosphate bioluminescence-based assay for predicting antibiotic combinations against dividing and non-dividing live carbapenem-resistant Enterobacteriaceae

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Background: Non-dividing bacteria persisters, which cannot be detected by viable plating assays, have been implicated in infection relapse and development of antibiotic resistance. Persisters are particularly problematic in CRE, as pan-drug-resistant Enterobacteriaceae can develop if persisters are not eradicated. We have previously demonstrated that flow cytometry (FCM) can detect dividing and non-dividing live cells, and can hence identify effective antibiotic combinations against CRE persisters, but require specialised equipment and laborious staining. We developed a rapid ATP bioluminescence-based assay to screen and identify effective antibiotic combinations against dividing and non-dividing live CRE in FCM.

Materials/methods: To develop the assay, we tested 19 CREs (2 bla_{KPC}, 4 bla_{NDM}, 4 bla_{OXA48}, 4 co-producers, 5 non-producers) against 74 single and two-antibiotic combinations at clinically achievable concentrations. Bacteria (10^5 CFU/ml) were incubated with the antibiotic(s) at 35°C. At 24h, samples were obtained for: (a) ATP bioluminescence after removal of extracellular ATP using apyrase (1U/ml), and (b) FCM analysis using propidium iodide to differentiate live/dead cells, SYTO-62 to visualise nucleic acid, and calibrated beads for enumeration. Receiver operating characteristic (ROC) curves were used to determine optimal bioluminescence thresholds (TRLU) for predicting combinations that were (a) at least inhibitory, (b) ≥1log_{10} bacteria/ml reduction (≥90% kill), (c) ≥2log_{10} bacteria/ml reduction (≥99% kill) in FCM. Prospective validation of the established TRLU was performed using 10 additional CREs.

Results: A total of 1,406 bacteria-drug combinations was tested [Figure 1]. As shown, high accuracy ranging 80%–91% was observed for all three TRLU. The predictive accuracy was highest in determining inhibitory and non-inhibitory antibiotic combinations (TRLU=6.67; accuracy=91%, sensitivity=91%, specificity=90%). Upon external validation, the ATP bioluminescence assay distinguished combinations that were at least inhibitory, ≥1log_{10} bacteria/ml reduction [≥90% kill], ≥2log_{10} bacteria/ml reduction [≥99% kill] in FCM. Prospective validation of the established TRLU was performed using 10 additional CREs.

Conclusions: Our ATP bioluminescence assay can be employed to screen multiple antibiotic combinations to identify useful combinations against dividing and non-dividing live CRE within 24h. It may be employed to guide the timely selection of effective antibiotic combinations.

Figure 1: Summary of predictive accuracy, sensitivity and specificity of bioluminescence thresholds

<table>
<thead>
<tr>
<th>Activity of antibiotic combinations in FCM</th>
<th>Development of predictive cut-offs (No. of CRE bacteria-drug combinations =1,406)</th>
<th>Validation of predictive cut-offs (No. of CRE bacteria-drug combinations =740)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TRLU Area under ROC (95% CI)</td>
<td>Overall accuracy</td>
<td>Sensitivity</td>
</tr>
<tr>
<td>At least inhibitory 6.67</td>
<td>0.92 (0.91 – 0.94)</td>
<td>0.91</td>
</tr>
<tr>
<td>≥1log_{10} bacteria/ml reduction [90% kill]</td>
<td>6.40</td>
<td>0.82 (0.85 – 0.89)</td>
</tr>
<tr>
<td>≥2log_{10} bacteria/ml reduction [99% kill]</td>
<td>5.11</td>
<td>0.85 (0.83 – 0.87)</td>
</tr>
</tbody>
</table>

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Abstract 4937

**Rifaximin leads to eradication of KPC *Klebsiella pneumoniae* gut colonisation in a mice model**

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**Background:** Current knowledge suggests that infection by carbapenem-resistant enterobacteria (CRE) is preceded by gut colonization. It may be hypothesized that eradication of colonization by non-absorbable antibiotics may protect the patient. Following previous in vitro data (Xenofontos E, et al. ECCMID 2018; abstract 00721) on the considerable effect of rifaximin on KPC, eradication of KPC gut colonization by rifaximin was investigated in an experimental model.

**Materials/methods:** At first stage, we developed a model of gut colonization by *Klebsiella pneumoniae*-producing carbapenemase (KPC); 40 C57Bl6 mice were pre-treated with saline, oral 40mg/kg omeprazole or subcutaneous ampicillin 50mg/kg. After 5 days, mice were fed with 10⁸ cfu KPC for 7 days. Stool samples were collected for measurement of KPC growth. At second stage, 12 mice with established KPC gut colonization received orally three times daily for 7 consecutive days either rifaximin 60mg/kg dissolved in 8% bile or vehicle. On days 0, 3 and 7 stool samples were collected; mice were sacrificed for determination of tissue outgrowth.

**Results:** Pretreatment with ampicillin led to greater KPC stool outgrowth after 3 and 7 days compared with saline (3.89 ± 0.67 vs 1.35 ± 0.21 cfu/ml, p < 0.0001 and 2.27 ± 0.45 vs 1.29 ± 0.17 cfu/ml, p: 0.019 respectively). Pretreatment with omeprazole did not affect KPC growth. Rifaximin treated mice had significantly lower bacterial load in stool and gut tissue (Figure).

**Conclusions:** Development of experimental gut colonization by KPC mandates ampicillin pre-treatment. Oral rifaximin leads to eradication of gut colonization.

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Clinical, microbiological and molecular studies of invasive pulmonary aspergillosis caused by *Aspergillus lentulus* in China

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**Background:** Here is the first study aimed at clinical, microbiological and molecular characteristics of *Aspergillus lentulus* from invasive aspergillosis (IA) patients in China.

**Materials/methods:** A panel of six non-duplicate *A. lentulus* isolates recovered from respiratory tract of patients with proven or probable IA under the China Hospital Invasive Fungal Surveillance Net (CHIF-NET) program during August 2016 to July 2017. Accurate identification and phylogenetic analysis of all the isolates were based on multi-locus sequence typing (MLST) of five genes. Seven microsatellite markers employed for *A. lentulus* genotyping. The identification of all the isolates were further explored using two MALDI-TOF MS systems. The in vitro susceptibility to nine antifungal drugs was determined by CLSI M27-A3 broth microdilution methodology.

**Results:** A total of six patients in our study were diagnosed as proven or probable IA caused by *A. lentulus*, associated with fatal outcome. Immunocompromised state, prior antifungal therapy and ICU hospitalization were obvious risk factors for invasive *A. lentulus* infection. Minor phenotypic characteristics were observed in *A. lentulus* isolates including slowly growth, reduced sporulation and inability of growth at 48°C, compared with *A. fumigatus*. ITS sequences were incompetent for distinguishing *A. lentulus* and *A. fumigatus*, while benA, CaM and rod A sequences were reliable for distinction to the species level. Phylogenetic analysis further confirmed that ITS region had little variation of *Aspergillus section Fumigati* while benA gene had highest intraspecific discrimination among the four gene. Microsatellite typing results showed that chromosome 1, 3, 5 and 6b were available for *A. lentulus*. All the *A. lentulus* isolates in our study were showed in vitro resistance to multiple drugs including amphotericin B (MIC range 4 to 8 μg/ml), itraconazole (MIC 2 μg/ml), voriconazole (MIC range 8 to 16 μg/ml) and posaconazole (MIC range 0.5 to 1 μg/ml). While the MEC range for caspofungin, micafungin and anidulafungin were 0.03 to 0.25, ≤0.08 to 0.15 and ≤0.08 μg/ml, which were classified as wild type against echinocandins.

**Conclusions:** This study points that *A. lentulus* as an emerging fatal causative agent worldwide should be concerned by clinicians and laboratories in the future.

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Abstract 4940

Bioinformatic fake news: the important but under-appreciated caveats of identifying resistance genes from whole genome sequencing data

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Background: Whole-genome sequencing (WGS) could play an important role in the surveillance of antimicrobial resistance, enabling high-throughput, cost-effective identification of high-risk transmissible resistance genes [TRGs]. However, multiple bioinformatic methods for TRG identification are in common use, and the impact of bioinformatic method on reported resistance genotypes remains unclear.

Materials/methods: We identified TRGs for five antimicrobial classes in 1818 UK Escherichia coli isolates (1321 human bloodstream infection isolates and 497 pig commensal isolates) using four widely-used bioinformatic algorithms (ABRicate, ARIBA, KmerResistance, SRST2) and a single (ResFinder) database. Discrepancies between algorithms were quantified and the causes of the most common patterns were investigated. We assessed whether benchmarking against phenotype was sufficiently discriminatory to identify true genotypes for discrepancies.

Results: There was significant discordance between the four approaches, with allelic variants in reported genotypes being different for at least one gene for 934/1818 (51%) isolates. Patterns of discordance were complex, with no single method responsible for most discrepancies (Figure). The extent of discrepancy was strongly associated with particular genes, being worst for aminoglycoside and sulfonamide resistance genes (p<0.001). However, much of the difference was artefactual. All discrepancies in 508/934 (54%) isolates were explained by two common deterministic issues arising as a result of different bioinformatic approaches. These were: programs identifying "phantom" additional alleles as an artefact of clustering approaches (encountered in 660/934 [71%] discrepant isolates), and homologous alleles differing in length being favored by different algorithms, where best match is chosen by either optimal alignment score or percentage identity (encountered in 399/934 [43%] discrepant isolates). In addition to these artefactual causes of discrepancy, algorithms also performed differently in several other scenarios, including differentiating multiple related alleles in the same isolate and identifying low coverage alleles. Pheno-type was a poor benchmark, with difference in genotypes only expecting to modify phenotype in 353/934 (38%) discrepancies.

Conclusions: Commonly used bioinformatic approaches for resistance genotyping led to highly discordant results in the specific alleles that were identified from a standard resistance database. Over half of these discrepancies were artefactual, being due to algorithm-specific assumptions. This highlights the limitations of current bioinformatic approaches to TRG identification, and has important implications for resistance surveillance.

Figure: Patterns of genotype agreement by antibiotic class

<table>
<thead>
<tr>
<th>Antibiotic class</th>
<th>ABRicate</th>
<th>ARIBA</th>
<th>KmerResistance</th>
<th>SRST2</th>
<th>ResFinder</th>
</tr>
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<tr>
<td>Aminoglycoside</td>
<td>1671</td>
<td>1236</td>
<td>1715</td>
<td>1085</td>
<td>1354</td>
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<td>45</td>
<td>21</td>
<td>135</td>
<td>81</td>
<td>135</td>
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<td>Macrolide</td>
<td>29</td>
<td>58</td>
<td>17</td>
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<td>12</td>
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<td>13</td>
<td>1</td>
<td>3</td>
<td>9</td>
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<td>Tetracycline</td>
<td>8</td>
<td>9</td>
<td>24</td>
<td>6</td>
<td>11</td>
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<tr>
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<td>52</td>
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<td>4</td>
<td>18</td>
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<tr>
<td>Dicloxacillin</td>
<td>9</td>
<td>140</td>
<td>0</td>
<td>0</td>
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</tr>
</tbody>
</table>

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Bacterial consortium: the evolution of the Faecal Microbiota Transplantation (FMT)

Gianluca Quaranta*1, Giovanni Fancello1, Rosalia Graffeo1, Gianluca Ianiro1, Giovanni Cammarota1, Maurizio Sanguinetti1, Luca Masucci1

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Background: Fecal microbiota transplantation (FMT) consists of infusion of feces from a donor to a recipient patient in order to restore the resident microbial flora. FMT has shown to be a valid option for Clostridium difficile infections (CDI). However, this approach presents technical, logistical and bureaucratic criticalities. Our aim was to evaluate the therapeutic efficacy, of a synthetic bacterial suspension, defined “Bacterial Consortium” infused in the colon of CDI patients. The suspension was composed by 15 microbial species isolated from the feces of healthy donors by culturomics protocols. Each strain was evaluated on an antibiotic susceptibility/resistance profile. Efficacy of the treatment was assessed both clinically and by metagenomics typing.

Materials/methods: “Bacterial Consortium” suspension (250 ml) was prepared on the same day of the infusion using the 15 selected strains. Fecal samples of two recipient patients were collected before and after infusion. DNA samples obtained from feces at different time point (t0, 7, 15, 30 and 90 days after infusion) were analyzed using the KIT 16S r RNA Miseq (ILLUMINA).

Results: Before infusion patient 1 showed an intestinal microbiota dominated by the Phylum Bacteroidetes. After 7 days Bacteroidetes decreased, followed in parallel by an implementation of Firmicutes and Verrucomicrobia. In the subsequent time-points, a stabilization of the intestinal microbiota, in which Bacteroidetes and Firmicutes increased and the Proteobacteria fall in minimum values, was observed. Patient 2, before infusion, showed a strong abundance of Proteobacteria, Firmicutes and a significant deficiency of Bacteroidetes and Verrucomicrobia. 7 days after infusion Proteobacteria strongly decreased, while Bacteroidetes increased to almost 50% accompanied by an implementation of Verrucomicrobia. 90 days after the infusion microbiota was stabilized with a prevalence of Bacteroidetes and Firmicutes.

Conclusions: Metagenomics revealed the presence both of the cultivated and infused bacteria and the “awakening” by microbial species absent at time t0 and present after the infusion. These evidences suggest a stimulatory action by “Bacterial Consortium” on the microbiota damaged by C.difficile. The infusion of selected bacteria, appropriately screened, would act as a trigger factor for mechanism of “bacterial repopulation”. This strategy increases biosafety and may allow to bypass FMT critical points.

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Staphylococcus aureus bacteraemia during a 2-year period in a tertiary university hospital: outcome and correlations to host- and pathogen-related characteristics

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Background: Staphylococcus aureus bacteremia is associated with a high mortality rate. We performed a retrospective analysis to assess the number and outcome of patients with S. aureus bacteremia in our tertiary University Hospital. Furthermore, we investigated virulence factors, with a possible impact on outcome.

Materials/methods: From May 2013 until July 2015, all patients with S. aureus bacteremia and complete clinical information were included in this study. Data about mortality, fever, leukocytes, CRP and antibiotic therapy were collected and transferred to SPSS. Respective S. aureus isolates were thawed and characterized by spa-typing, single and multiplex PCR to assess agr-types, pvl, etA/B/D, tsst, edinA/B/C, sea-e and seg-j. We performed a static biofilm assay to measure biofilm formation as well as a FRET assay for the quantification of nuclease activity.

Results: 178 patients with S. aureus bacteremia were included (41.6% female, mean age 58.73 years) with a mortality rate of 25%. In 19 patients (11%), no focus was identified. In most cases, bacteremia was catheter related (71 patients, 40%), due to abscess or cellulitis (23 patients, 13%), pneumonia (22 patients, 12%), or endocarditis (16 patients, 9%). 112 patients (63%) presented with fever >38°C, 159 patients (89%) with elevated CRP levels, 77 patients (43%) with increased and 20 (11%) with decreased leukocytes. Patients with S. aureus-directed antibiotic therapy died less likely (p=0.014). The highest mortality was observed for patients with S. aureus pneumonia and bone and joint infections (36%). Elder patients died more likely, had higher leukocyte and CRP values and were more often infected by MRSA. The most prevalent clonal complexes were CC084 (38 patients, 21%), CC012 (21 patients, 12%), CC015 (19 patients, 11%), CC005 (18 patients, 10%) and CC068/080 (11 patients, 6%). Eighteen patients were infected by MRSA (10%). Biofilm formation of isolates was associated with CCs and the absence of seh (p=0.021) or the presence of sec (p=0.018). Higher nuclease activity of isolates was associated with female gender (p=0.008) and the absence of see (p=0.042).

Conclusions: Our data revealed that bacteremia occurred often with a high rate of mortality, which was associated with age, number of leukocytes, antibiotic therapy and agr-type.

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Abstract 4946

Clinical validation of the BD CTGCTV2 for BD MAX system assay in male urine specimens
Barbara Van Der Pol*, Edith Torres-Chavolla1, Salma Kodsi2, Charles K. Cooper3, Thomas Davis3, Kenneth H Fife4, Stephanie Taylor5, Michael Augenbraun6, Laura Bachmann7, Charlotte Gaydos8

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Background: As rates of treatable sexually transmitted infections (STI) continue to increase globally, simple, accurate tests for screening and diagnostics are needed. In addition to chlamydia and gonorrhea, trichomoniasis is known to cause urethritis in men and asymptomatic carriage of trichomoniasis is known to be responsible for sexual transmission of this pathogen to women. Therefore, assays that detect all 3 pathogens simultaneously support the goal of reducing the burden of STI at the population level. One such platform is the BD MAX™ System using the BD CTGCTV2 assay (pending CE Marking; Not available for sale in Europe/EEA). Here we describe the performance of the MAX assay when using first catch urine (FCU) from men.

Materials/methods: Men provided an FCU that was aliquoted into the transport device used for the Hologic Aptima® AC2 and ATV assays, the BD ProbeTec™ CTQx, GCQx and TVQx assays and the Cepheid Xpert® CT/NG and TV assays. At least 2 positive results from the 3 comparator assays were required to classify men as infected.

Results: Specimens were obtained from 1,159 men. Positivity rates for chlamydia, gonorrhea and trichomoniasis were 13.6, 10.8, and 4.4%, respectively. Sensitivity estimates were 96.7% (95% CI 92.6-98.6%), 99.2% (95% CI 95.5-99.9%), and 97.9% (95% CI 89.1-99.6%) for chlamydia, gonorrhea, and trichomoniasis, respectively. All specificity estimates were ≥ 99.4%. The BD CTGCTV2 assay has dual gonorrhea targets in order to optimize specificity; both are required to give a signal in order for the result to be positive. This design did not reduce the number of positives (no impact on sensitivity) since 122/123 infected men had BD MAX GC positive reactions with both targets. The PPV based on observed GC prevalence (10.8%) was 99.2% (95.6-99.9%).

Conclusions: The BD CTGCTV2 assay has high sensitivity and specificity for detection of chlamydia, gonorrhea and trichomoniasis from FCU. Adoption of this assay can i) support local testing where smaller batch sizes increase efficiency, ii) identify asymptomatic trichomoniasis infections and thus reduce the potential for this STI to be transmitted to sex partners, and iii) ensure the specificity of positive gonorrhea results, potentially eliminating the need for confirmatory testing.

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Abstract 4948

Strongiloidiasis in patients with Chagas disease in Barcelona

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Background: Chagas disease (CD) and strongiloidiasis are neglected tropical diseases according to WHO and they can result in chronic infections even lasting throughout life with high morbidity and mortality. Recent studies in Barcelona have shown a significant association between CD and strongiloidiasis so, it is recommended to perform Strongyloides stercoralis serology in people with CD.

The aim of this study was to evaluate the implementation of a systematic program of screening of strongiloidiasis in CD patients attending Primary care centres in the Southern Metropolitan Area of Barcelona.

Materials/methods: This study was carried out in patients attending Primary care centres in the Southern Metropolitan Area of Barcelona. This area with approximately 5% of Latin American population has the highest number of people with CD in Catalonia.

In June 2018, a systematic program was implemented performing Strongyloides stercoralis serology to all patients with T. cruzi positive serology by two different techniques or antigens according to WHO recommendations for CD diagnosis. The tests used for detection of T. cruzi antibodies were BIOFLASHChagas® using recombinant antigens and Ortho®T.cruzi Elisa Test System with native antigens. The IgG anti S. stercoralis was carried out with Strongyloides stercoralis serum Microwell ELISA, IVC® or EUROINMUN Anti-Strongyloides ELISA (IgG). The period of study was from June 2018 to October 2019.

Results: Of a total of 2337 patients tested for T. cruzi antibodies, 101 (4.41%) were diagnosed with CD. S. stercoralis serology was positive in 20 patients (19.80%) and indeterminate in 4 (3.96 %). All the cases were adults with a mean age of 40.4 (SD 8.9). Out of patients with CD 78% were women. This is due to the fact that a CD screening program is carried out in Latin American pregnant women.

The countries of origin of patients with Strongyloides stercoralis positive serology related to the total number of CD patients were: Bolivia [11/68], Paraguay [1/3], El Salvador [1/2], Honduras [0/1], Colombia [0/1], Ecuador [0/1] and country not recovered [7/25].

Conclusions: Strongyloides stercoralis serology should be performed in all patients with CD attending Primary care centres due to the high prevalence of co-infection, around 20%.

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K-mer based prediction of *Clostridioides difficile* ribotypes and relatedness
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**Background:** Comparative analysis of *Clostridioides difficile* whole-genome sequencing (WGS) data enables fine scaled investigation of transmission and is increasingly becoming part of routine surveillance. However, these analyses are constrained by the computational requirements of the large volumes of data involved. By decomposing WGS reads or assemblies into k-mers and using the dimensionality reduction technique MinHash, it’s possible to rapidly approximate genomic distances without alignment.

**Materials/methods:** We have assessed the performance of MinHash, as implemented by sourmash, in predicting single nucleotide differences between genomes (SNPs) and *C. difficile* ribotypes (RTs). Genomes with known ribotypes (n = 3,937) were split into a training set (2,937) and test set (1,000) randomly. The training set was used to construct a sourmash index against which genomes from the test set were compared. If the closest 5 genomes in the index had the same ribotype this was taken to predict the searched genome’s ribotype. A random subset of *C. difficile* genomes (n = 2084) were compared pairwise with sourmash and MinHash distance thresholds tested for performance against SNP cut-offs, e.g. ≤10 SNPs. Further, 2000 simulated genomes were generated with SNPs, indels and sequencing errors to test sourmash performance with ideal data.

**Results:** Using our MinHash ribotype index, predicted ribotypes were correct in 780/1000 (78%) genomes, incorrect in 20 (2%), and indeterminant in 200 (20%, in these the closest matching genomes’ ribotypes differed). Relaxing the classifier to 4/5 closest matches with the same RT improved the correct predictions to 87%. For a set of 2084 diverse *C. difficile* genomes (0 – 168,519 SNPs different), using sourmash to screen for closely related genomes, at a sensitivity of 95% for pairs ≤10 SNPs, sourmash reduced the number of pairs from 2,170,486 overall to 117,356, i.e. by 94.6%, with a positive predictive value of 0.45. Increasing the MinHash sketch size above 2000 produced minimal performance improvement.

**Conclusions:** Using MinHash it’s possible to subsample genome k-mer hashes and use them to approximate small genomic differences within minutes, significantly reducing the search space for further analysis. By constructing a sourmash index of genomes with known ribotypes, ribotypes can be predicted from WGS data.

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Abstract 4950

**Food and clinical human isolates of Klebsiella pneumoniae: is there correlation between multidrug resistance and biofilm formation capacity?**

Dafne Díaz-Jiménez¹, Andrea Muras², Javier Fernández², Ana Parga², Luz Leston¹, Ana María Otero², Azucena Mora Gutiérrez*¹

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**Background:** Klebsiella pneumoniae is an opportunistic pathogen implicated in nosocomial and community infections. On the other hand, food production animals have been identified as the main cause of the antimicrobial-resistance increase. Biofilm formation is involved in the colonization and environmental persistence of many bacterial pathogenic species and constitutes an unspecific mechanism of resistance to antibiotic treatment.

**Materials/methods:** A collection of 47 carbapenemase- and/or extended-spectrum-β-lactamase (ESBL)-producing K. pneumoniae recovered in northwest Spain (2016-2019), 28 from poultry meat and 19 from human infections, were characterized by PCR (bla and mcr genes), MLST and PFGE. Antimicrobial susceptibility testing was conducted by disc diffusion assay. MICs for colistin were manually obtained by broth microdilution for those suspected colonies. All results were interpreted according to CLSI guidelines. Biofilm formation was determined in the Active Attachment biofilm model using glass coverslips in LB culture medium under aerobic conditions and quantified by the Crystal Violet stain method after 24-h incubation.

**Results:** The 28 meat isolates were MDR showing the highest resistances to ampicillin (100%), cefotaxime (100%), fluoroquinolones (89.3%) and sulfamethoxazole-trimethoprim (82.1%). The ESBL typing revealed that 13 isolates were CTX-M-15, being eight of those also positive for SHV-28. Eight of the 11 STs identified within the meat isolates were previously reported in human isolates: ST15, ST45, ST111, ST147, ST307, ST627, ST966 and ST1086. Among the 19 K. pneumoniae from human clinical samples, 17 were OXA-48 and 84.2% MDR with the highest resistance rates to ampicillin (100%), amoxicillin-clavulanic acid (84.2%) and fluoroquinolones (84.2%). Eleven of the 47 K. pneumoniae were colistin-resistant, but only one human SHV-28/CTX-M-15 isolate carried the plasmid-mediated colistin resistance gene mcr-1. PFGE showed high heterogeneity within the macrorestriction profiles of the same STs. Likewise, the biofilm test revealed high variability even for isolates clustering with >85% identity in the PFGE comparison. Of the 47 K. pneumoniae, 10.6% were strong biofilm producers (five meat isolates), 46.8% moderate and 42.6% weak (Figure 1).

**Conclusions:** Poultry meat and clinical human MDR K. pneumoniae isolates showed high phenotypic and molecular variability even within the same STs. Moreover, we found no correlation between multiresistance and the biofilm formation capacity.

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Abstract 4952

Antibiotic consumption in very low birth weight neonates on neonatal intensive care units in Germany: a longitudinal study 3 years of national surveillance

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Background: Antibiotic consumption is high in very low birth weight neonates (VLBW). Surveillance of antibiotic consumption is difficult in the pediatric patient population. Due to great variance of weight and dosing in these patients surveillance systems based on defined and/or recommend daily doses are inadequate. Days of treatment (DOT) are an alternative for surveillance of antibiotic consumption.

The objective of this study was to implement and evaluate the first years of a national surveillance system for consumption of antibiotics on NICUs

Materials/methods: The national surveillance system for neonates (NEO-KISS) is almost universally used by neonatal intensive care units (NICU). NICUs in Germany. In those centers all VLBW newborns with a birthweight under 1500 gram are under surveillance. For every patient under surveillance, DOT with systemic antibiotics are assessed on daily basis. We introduced the antibiotic utilization rate as a new variable. It is calculated as the quotient of total patient days at which systemically effective antibiotics (total and per substance) are administered and the total number of patient days of the department multiplied by one hundred. The antibiotic utilization rate describes the proportion of patient days in percent on which systematic antibiotics were used.

Results: Between 2013 and 2015 data on 41,569 VLBW infants from 231 neonatal intensive care units were analyzed. In total, 1,463,897 patient days were under surveillance [median 31 days per patient; IQR 21-41]. Overall 406,120 days of antibiotic treatment were recorded.

In total 75.2% of VLBW infants received antibiotics during their surveillance period. This varied greatly. In patients with a birthweight of less than 500g birthweight 90.7% received antibiotics, while it was 89% in patients with a birthweight between 500g and 999g. In patients with a birthweight higher than 999g but less then 1500g antibiotics were prescribed to 65%.

In median 1.88 (IQR 1.74-2.03) different antibiotic agents were used per antibiotic day per patient.

Conclusions: Surveillance of antibiotic consumption is an essential part of continuously improving prescription practices. Surveillance with this module is feasible and was successfully implemented into daily routine of neonatal intensive care units.

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Herpes simplex virus resistance testing: an automated interpretation platform linking genotype to phenotype

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Background: The pol and tk genes of Herpes simplex virus (HSV) types 1 and 2 comprise the viral targets of currently prescribed treatments for HSV infection – aciclovir, cidofovir and foscarnet. The number of indel and substitution mutations within these genes conferring antitherpetic resistance is large and ever-growing, as is the list of natural polymorphisms.

At Public Health England (PHE), we provide genotypic resistance testing to UK hospitals to assist in guiding clinical management of acute and chronic HSV infections. Increasing demands upon this service have necessitated automation of sequence analysis and interpretation.

Materials/methods: We have created a web-browser-based application and database allowing automated analysis of HSV tk and pol gene sequencing, to support genotypic resistance assays.

In brief, FASTA files are uploaded to a web application, implemented using Flask framework in Python programming language. Built-in subprocesses call an analysis script that aligns sequences to reference genes, and outputs a variant file in the variant call format (VCF). Each VCF record is compared to a database of variants, linked to phenotypic resistance data, and a list of the relevant references. Collated interpretation data is output in text file reports.

Variant, sequence, sample, and analysis information are passed to a dedicated SQLite database via SQLAlchemy, designed to ensure secure and reliable storage, with minimal chance for incorporation of errors and data corruption. The database also allows novel variants to be uploaded and linked to phenotypic data produced by PHE’s culture-based assays.

Results: Automated sequence analysis and storage ensures that sequences are securely, efficiently and accurately processed, and reports generated. Version control of interpretation algorithms and variant databases facilitates compliance with quality management policies, as well as re-analysis of stored sequences. The linked variant and phenotyping databases allow a wide range of sequence-variant-resistance queries, helping with interpretation of the antiviral susceptibility of clinical isolates.

Conclusions: This web application and sequence-variant-phenotype database assists scientists in the analysis of HSV tk and pol gene sequences, enables efficient, repeatable, traceable and reliable result generation and storage, and permits a wide range of queries to help with interpretation of novel variants to answer clinical and research questions.

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Abstract 4955

**Diagnosis of cutaneous leishmaniasis through shotgun metagenomics**

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**Background:** Cutaneous leishmaniasis (CL) is a vector-borne disease endemic in large tropical or subtropical areas. Improving its diagnosis (especially species identification) is important as CL lesions can vary, mimic other tropical diseases and as their treatment is species-driven. We compared shotgun-metagenomics (SM) with microscopic examination (ME) and PCR-based methods for CL diagnosis.

**Materials/methods:** From October 2018 to 2019, all patients seen at Mondor Dermatological Center (Creteil, France) with lesions evocative for CL were biopsied. ME (RAL 555) and rt-PCR targeting 18S-rRNA were performed. When positive, *Leishmania* species were identified through Sanger *cytb* sequencing (Foulet. JCM. 2007). SM was performed on positive biopsies. DNA/RNA libraries were prepared on NextSeq500 (Illumina). SM data were analyzed using MetaMIC® which identified viral, bacterial, fungal and parasitic genomes. Results of ME, PCR and SM were compared in terms of *Leishmania* detection and species identification. All CL were declared to the reference center (Montpellier).

**Results:** Over 1 year, 34 patients underwent skin biopsies for CL diagnosis, 7 were positive on ME and 3 using PCR. The median age of CL patients was 42.7 years and the M/F ratio 1.2. All patients visited endemic areas: Northern (n=6) or Sub-Saharan (n=4) Africa, India (n=1), Colombia (n=1), Israel (n=1). All patients had multiple-site lesions, except three. *Cytb* sequencing allowed the identification of 8 *L. major*, 1 *L. brasilienzis* and was non-contributory in 4 cases. SM was performed in 11/13 cases (ongoing, n=2). In 10 cases, *Leishmania* were identified at species level with a better discriminating power of RNA sequences. SM results were concordant with *cytb* sequencing but provided 2 additional species identification (*L. major*). In one case, no parasitic DNA/RNA sequences were detected. The patient presented an unusual keloid lesion persistent after meglumine antimoniate injections. Histological diagnosis was unavailable and the *Leishmania* DNA load was very low in rt-PCR. No other pathogens were identified in any of the cases using SM.

**Conclusions:** SM is a powerful tool for CL diagnosis which gives better results than Sanger sequencing for species identification. The availability of this additional tool in the diagnosis of leishmaniasis could also be an opportunity for strain genotyping.

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Abstract 4962

Mycoplasma genitalium resistance against antibiotics in a Berlin MSM cohort tested with the Allplex MG & AziR Assay and Allplex MG & MoxiR Assay

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Background: Due to high rates of sexual transmitted infections [STI] reported especially in the MSM-community there is a rise in awareness and in testing. Mycoplasma genitalium (MG) is one important cause of non-gonococcal urethritis and emerging antibiotics resistance is a major concern. Standardized NAT tests are favored for this hard to culture bacterium in routine diagnostics. We tested here the Allplex MG&AziR and the new moxifloxacin-resistance MoxiR Assay [Seegene] on MG positive samples.

Materials/methods: Screening MSM for MG from urethral/anal swabs or urine was performed with the Hologic Panther system [Aptima Mycoplasma genitalium]. 163 MG positive samples were then tested for macrolide resistance with the MG&AziR Assay and 48 of those tested for moxifloxacin resistance. The AziR Assay detects and differentiates the SNP mutations A2058C/G/T and A2059C/G/T of the 23S rRNA gene region V of MG and the MoxiR Assay detects mutations G259A/C/T, G248A/T and A247C in the ParC gene.

Results: 68.1% (N=111/163) and 70.8% (34/48) of MG positive screened samples were also positive in the MG&AziR and MoxiR Assay, respectively. In a very high proportion of these samples 82.9% (N=92) Azithromycin resistance mutations could be detected. A2059G was the mutation detected with the highest frequency (78.3%; N=72) followed by A2058G (18.5%; N=17). Three samples had an A2058T mutation (3.3%). No sample showed an A2058C or A2059C/T mutation. Six samples additionally showed Moxifloxacin resistance (3xG248A each 2xG259A and G248T). For one sample only a Moxifloxacin resistance mutation was detected. Overall a Moxifloxacin resistance rate of 20.6% was detected.

Conclusions: Due to the very high sensitivity of the TMA test not all of the MG positive pretested samples were positive with the Allplex assay. 78.3% of resistant samples showed the A2059G mutation leading to resistance against Azithromycin and Josamycin. As access to Pristinamycin is limited in Germany the usual second line option is Moxifloxacin. 4 of 25 sample positive for A2059G mutations additionally had a Moxifloxacin resistance. Resistance guided therapy is crucial for sufficient treatment success and addition of molecular resistance testing against Fluoroquinolones is an additional requirement.

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Abstract 4963

**Value of pneumococcal urinary antigen testing in a recent series of Streptococcus pneumoniae bacteraemia**

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**Background:** Streptococcus pneumoniae is the most frequently detected pathogen in community-acquired pneumonia and has high morbidity/mortality rates worldwide. As concomitant bacteremia worsens the prognosis, it is important to achieve an early identification of the pneumococcal diseases, to start appropriate antibiotic treatment. Pneumococcal urinary antigen testing (PUAT) is widely used, but still remains controversial due to its variable sensitivity in bacteremic-pneumonia episodes. The aim of this study was to describe the epidemiology of S. pneumoniae bacteraemia episodes in our hospital and evaluate the performance of PUAT.

**Materials/methods:** All S. pneumoniae bacteremic episodes detected in a tertiary hospital in Madrid over a period of 10 months (January-October 2019) were included. Demographic and clinical data were collected from patient’s clinical records and laboratory informatic system. Microbiological tests results, including performance of PUAT and sputum culture were reviewed, as well as antimicrobial susceptibility testing (AST) results [disk diffusion/Etest, EUCAST criteria] and serogroups classification of S. pneumoniae isolates.

**Results:** Forty-four episodes of S. pneumoniae bacteremia were identified (56.8% women, mean age 68±16.2 years), 31 of them (70.5%) associated with pneumonia. All episodes but two required hospitalization, [mean length 11.6 days]. Sputum culture was obtained only in 10 patients (22.7%), and showed poor profitability (in none of them S. pneumoniae was isolated). PUAT was performed in urine samples of 31 patients (70.5%) and showed low sensitivity (20 positive results, 64.5%). This value was even lower in patients with pneumonia (16/26 positive cases, 61.5%) than in those with other forms of pneumococcal disease (4/5 positive cases, 80%). Serogroup classification was available in 34 isolates (77.3%), being the most frequent serogroups 8 (29.4%), 3 (11.8%), 35 (11.8%) and 19 (8.8%). Regarding AST, susceptibility rates were: penicillin, 79.4%; erythromycin, 79.4%; cefotaxime, levofloxacin and vancomycin, 100%. Three isolates belonging to serogroup 19 showed resistance to erythromycin and susceptible, increased exposure to penicillin and cefotaxime.

**Conclusions:** Negative PUAT does not rule out S. pneumoniae bacteremia, even in patients diagnosed with pneumonia. The systematic implementation of the 23-valent vaccine could avoid a great number of cases, since 73.5% of the serogroups detected in this series are included in this vaccine.

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The external validity of an investigator-initiated randomised controlled trial comparing 7 versus 14 days for Gram-negative bacteraemia

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**Background:** External validity determines the extent to which randomized controlled trials’ (RCT) results apply to all patients in clinical practice. We aimed to compare patients included in an investigator-initiated RCT to those with the targeted infection that were not included.

**Materials/methods:** This was a pragmatic RCT showing non-inferiority of 7 vs. 14 covering antibiotic days for Gram-negative bacteraemia, with exclusion criteria deemed necessary for patient’s safety and good clinical practice. Patients were not included mainly for uncontrolled infection at day 7, inability to provide informed consent, refusal to participate or participation in another trial. The current analysis includes patients recruited at Rambam Health Care Campus (RHCC). We compared all included patients vs. patients with Gram-negative bacteraemia that did not participate. Non-participants were selected randomly from all those with Gram-negative bacteraemia that did not participate. In a subgroup analysis, we compared the RCT cohort to patients fulfilling all inclusion criteria that refused to participate in the trial.

**Results:** 251 patients included in the RCT at RHCC were compared to 292 patients with Gram-negative bacteraemia that were not included, of whom 90 were excluded due to refusal to participate. Overall, there were large differences between participants and non-participants, with non-participants being more frequently male, and having poorer functional status at baseline, more comorbidities, nosocomial infections, urinary catheters, medical devices, higher sepsis severity caused mainly by altered mental status, higher total SOFA score and more frequent need for hemodynamic support. Outcomes were correspondingly worse among non-participants, including short and long-term mortality. Participants approached for inclusion, but refusing participation were more likely to have nosocomial infections, poorer baseline functional capacity and higher McCabe than included patients, but similar sepsis severity. In this subgroup analysis, there was no difference in mortality, but the patients who refused, experienced longer in-hospital stay and more relapses.

**Conclusions:** Patients participating in the RCT were selected for clinical stability and were different from other patients with Gram-negative bacteraemia; thus the trial results apply to selected patients fulfilling the trial’s eligibility criteria. Patients with nosocomial infections and poorer functional status were less likely to agree to participate in the RCT.

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Unyvero multiplex PCR on broncho-alveolar lavage for rapid microbiologic and antibiotic susceptibility documentations in immunocompromised patients under antibiotic therapy admitted to the intensive care unit

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Background: In a specific population, immunocompromised patients admitted to our medical ICU with a diagnosis of severe pneumonia (according to clinical and radiological findings) and already treated with antibiotics, we compared the rapid (4.5 hours) microbiological documentation obtained by Unyvero multiplex PCR assay (Curetis) to those obtained by direct examination and quantitative culture. This was an observational study.

Materials/methods: We examined BAL samples performed on admission from 52 patients from July 2018 to November 2019: m/f ratio 2.1:7, age 61.9 +/- 11.7, SAPS2 score 51.5 +/- 6.8. They originated mostly from the haematology (76%) and oncology (13%) units. Informed consent was obtained from all. Because the patients were under antibiotics at admission, the threshold of clinical significance for quantitative cultures was lowered to 10^3 CFU/ml. For PCR, a positive result was considered significant whatever the qualitative score (1, 2 or 3).

Results: More than 50% of the cases (29/52, 56%) remained undocumented by culture and PCR. For the 23 cases documented by culture and/or PCR, 19 were monomicrobial, 3 bimicrobial and 1 trimicrobial. Gram stain was helpful in less than half of these documented cases (11/23). Complete documentation was obtained by culture in 19 cases; in 22 cases if a second look was performed on culture plates; by PCR in 21 cases (partial documentation, 22 cases). There were 2 major discrepancies: 1 S. aureus strain not detected by PCR; 1 S. aureus strain not detected by culture. Concerning the correlation between antibiograms and resistance genotypes, 3 discrepancies were observed: 2 penicillinase-positive enterobacteria being found TEM-negative by PCR and 1 ESBL-positive Klebsiella variicola being found ESBL-negative by PCR.

Conclusions: In this specific population, results obtained by the Unyvero assay and by culture were highly correlated. The Unyvero assay on BAL samples is useful in this specific population for rapid obtention of microbiological results and also to confirm that the negativity of cultures is not due to preexisting antibiotic treatment. It thus permits a better management of antibiotic therapy, leading to a reduction of antibiotic resistance selection pressure in the ICU.

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Abstract 4967

**Communication of rapid identification results from positive blood cultures decreases time to effective therapy**

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**Background:** Implementation of rapid bacterial identification systems, in conjunction with antimicrobial stewardship programs (ASP), has repeatedly demonstrated improvement in time to appropriate therapy, decreased mortality, length of hospital stay and cost in patients with bacteremia. Whilst these previous studies notified ASP, in this study we examined the impact of rapid MALDI-ToF identification from positive blood cultures (BC) with verbal communication of the results to the intensive care unit (ICU) instead of ASP.

**Materials/methods:** During the study period between April 2018 to December 2019, time to therapy was compared in the pre-intervention and post intervention periods for bacteremic patients admitted to the ICU. In the pre-intervention period, BCs were processed as per standard procedures, with Gram stain communication to the ICU on the day of BC positivity; MALDI-ToF identification was performed on subcultures the following day with no additional communication of results. In the post-intervention period a rapid identification from BC was performed on the day of BC positivity and the result was communicated to the ICU within 2 hours of Gram stain notification. Descriptive analytics of antimicrobial use, spectrum and patient outcomes was performed.

**Results:**

<table>
<thead>
<tr>
<th></th>
<th>Coagulase Negative Staphylococcus spp.</th>
<th>E. coli</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-intervention (N = 5)</td>
<td>Post-intervention (N = 5)</td>
</tr>
<tr>
<td>Average time from BC draw to administration of effective therapy</td>
<td>6.6 h</td>
<td>0.0 h</td>
</tr>
<tr>
<td>Average spectrum of effective therapy</td>
<td>3.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Average time from BC draw to initiation of definitive therapy</td>
<td>58.6 h</td>
<td>48.0 h</td>
</tr>
<tr>
<td>Average spectrum of definitive therapy</td>
<td>2.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Number of patients whose definitive therapy was deescalated from effective therapy</td>
<td>1.0</td>
<td>n/a</td>
</tr>
<tr>
<td>Days of therapy</td>
<td>2.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Number of deaths</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

**Conclusions:** This pilot study demonstrates that communication of rapid identification results from positive BCs can reduce time to effective therapy in ICU patients with bacteremias. Further studies are needed to determine if this is broadly applicable to other organisms, thereby reducing the burden on ASP personnel whilst achieving the goal of patients receiving optimal antimicrobial therapy as quickly as possible.

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The challenge of managing bone and joint infection in the OVIVA era: significant drug/drug interactions are much more common in patients managed with oral regimes

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**Background:** The recently published Oral Versus Intra-Venous Antibiotics (OVIVA) study demonstrated the non-inferiority of oral antibiotic regimes to intravenous equivalents in bone and joint infection (BJI). However, oral regimes may be more challenging to use with drug-drug interactions (DDI) frequently encountered.

**Materials/methods:** The medication record of consecutive patients with BJI discussed at our institution’s BJI MDT during 2018 were reviewed. DDI involving oral and intravenous antibiotics commonly used by our OPAT service were assessed using the British National Formulary (BNF). QT prolonging drugs were assessed using crediblemeds.org. DDI classed as “moderate” or “severe” were considered significant. Topical/inhaled medications were excluded.

**Results:** 178 patients were included [53% male, mean age 64]. Patients were prescribed a total of 168 different medications (median 6 [range 0-19] medications per patient). Each patient’s drug history was assessed for DDI with the commonly used antibiotics, the mean number of DDI/patient is shown in the table. 148/178 (86%) of patients had at least one potential DDI to the commonly used oral antibiotics whereas only 86/178 (48%) had at least one DDI with common parenteral drugs, usually daptomycin. DDI were found affecting drugs used to treat a wide range of conditions, but 77/1381 (64%) DDI concerned drugs found in 5 BNF subsections: Hyperlipidaemia, Pain, Depression, Pain and Inflammation in musculoskeletal conditions, and Hypertension.

<table>
<thead>
<tr>
<th>Parenteral antibiotics</th>
<th>Mean DDI/patient (Max number)</th>
<th>% Patients with at least one DDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teicoplanin</td>
<td>0 [n/a]</td>
<td>0%</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>0.01 (1)</td>
<td>1%</td>
</tr>
<tr>
<td>Ertapenem</td>
<td>0.02 (1)</td>
<td>2%</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>0.55 (3)</td>
<td>46%</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>0 [n/a]</td>
<td>0%</td>
</tr>
<tr>
<td>Piperacillin tazobactam</td>
<td>0.04 (1)</td>
<td>4%</td>
</tr>
</tbody>
</table>

**Oral antibiotics**

| Doxycycline                     | 0.28 [2]                     | 26%                             |
| Ciprofloxacin                   | 1.15 [9]                     | 54%                             |
| Levofloxacin                    | 0.90 [9]                     | 42%                             |
| Rifampicin                      | 1.71 [9]                     | 78%                             |
| Linezolid                       | 0.43 [3]                     | 37%                             |
| Co-trimoxazole                  | 0.06 [2]                     | 5%                              |
| Fusidic acid                    | 0.34 [1]                     | 34%                             |
| Clindamycin                     | 0 [n/a]                      | 0%                              |

**Conclusions:** In general, oral antibiotics used within our service for the management of bone and joint infection are associated with significantly higher rates of DDI compared to parenteral antibiotics. Many patients have multiple potential DDIs and individualisation of care with changes in anti-microbial therapy or regularly prescribed medications may be required to maximise treatment effectiveness and avoid potentially serious adverse effects.

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Abstract 4969

Treatment responses to azithromycin and ciprofloxacin in uncomplicated Salmonella Typhi infection: a comparison of clinical and microbiological data from a controlled human infection model

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Background: The treatment of enteric fever is complicated by the emergence of antimicrobial resistant Salmonella Typhi. Azithromycin is commonly used for first-line treatment of uncomplicated enteric fever, but the response to treatment may be sub-optimal in some patient groups when compared with fluoroquinolones.

Materials/methods: We performed an analysis of treatment responses with azithromycin (500mg once-daily, 14 days) or ciprofloxacin (500mg twice-daily, 14 days) in healthy UK volunteers (18-60 years) enrolled into two Salmonella human challenge studies. Study A was a single-centre, open-label, randomised trial. Participants were randomised 1:1 to receive open-label oral ciprofloxacin or azithromycin, stratified by vaccine group (Vi-polysaccharide, Vi-conjugate or control Men-ACWY vaccine). Study B was an observational challenge/re-challenge study of Salmonella Typhi infection. Outcome measures included fever-clearance-time, blood-culture clearance time and plasma drug concentrations.

Results: In 81 participants diagnosed with S. Typhi, treatment with azithromycin was associated with prolonged bacteraemia (median 90.8 hours [95% CI:65.9-93.8] vs. 20.1 hours [95% CI:78-24.3], p<0.001) and prolonged fever clearance times <37.5°C [hazard ratio 2.4 [95%CI:1.25-5.0]; p=0.02]. Results were consistent when studies were analysed independently and in a sub-group of participants with no history of vaccination or previous challenge. A prolonged treatment response was observed significantly more frequently in the azithromycin group [28/52 [54.9%]] compared with the ciprofloxacin group [1/29 [3.5%]; p<0.001]. In participants treated with azithromycin, plasma concentrations of azithromycin did not exceed the MIC, whilst predicted intracellular concentrations did exceed the MIC. In participants treated with ciprofloxacin, the measured plasma concentrations and predicted intracellular concentrations of ciprofloxacin exceeded the MIC.

Conclusions: Azithromycin at a dose of 500mg daily is an effective treatment for fully sensitive strains of S. Typhi but is associated with delayed treatment response and prolonged bacteraemia when compared with ciprofloxacin within the context of a human challenge model. Whilst the cellular accumulation of azithromycin is predicted to be sufficient to treat intracellular S. Typhi, systemic exposure may be sub-optimal for the elimination of extracellular circulating S. Typhi. In an era of increasing antimicrobial resistance, further studies are required to define appropriate azithromycin dosing regimens for enteric fever and to assess novel treatment strategies, including combination therapies.

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"Seek and ye shall find": endoscopic finding and molecular diagnosis of Trichuris trichiura

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Background: Whipworms are responsible of approximately 500 million cases of trichuriasis worldwide, with higher endemity in tropical and sub-tropical countries. At first, the infection is asymptomatic, but it can develop with variable symptoms according to parasite load. Diagnosis in mainly based on the detection of eggs at microscopy, but this technique lacks sensitivity. In non-endemic countries trichuriasis can be accidentally diagnosed by colonoscopy, often in presence of negative microscopy. Here, we describe an incidental diagnosis in non-endemic country (Turin, North-West Italy).

Materials/methods: A 52 years old HIV-positive Italian man, presenting family history for colorectal cancer, was referred for colonoscopy reporting one week diarrhoea and mild abdominal pain, without fever and bleeding, which resolved leaving no discomfort. No blood chemistry or faecal parasites examination had been done before. At first, the patient only declared raw fish consumption, suggestive for fish-borne parasites. Endoscopy showed the presence of a whitish motile nematode-like organism in the caecal region. Only a portion of the organism (7×0.5mm) could be removed.

Results: Apparently, macroscopic aspect and microscopy agreed with the caudal portion of an Anisakidae. The presence of ova overflowing from the ruptured end was the only clash. Thus, the nematode was sent to Italian Reference Centre for Anisakiasis (Palermo) for RFLP and to Parasitology Section at La Sapienza University in Rome for molecular analysis of mitochondrial cytochrome b gene.

The pattern obtained with RFLP was dissimilar from Anisakis spp and cytochrome b sequencing showed high percentage of identity with Trichuris trichiura. In a second medical interview the patient reported a travel to Antigua six months before the colonoscopy. Although asymptomatic, the patient was treated after nematode removal (two administrations 400 mg oral albendazole at time 0 and after 30 days).

Conclusions: Considering the high prevalence of Trichuris in Antigua [up to 30% in children], we may consider this case a travel-related imported infection. Endoscopy is the most diffused [often accidental] diagnostic tool for identification of trichuriasis, whereas economic conditions allow the use of this technique. This case highlights how improving parasitic diseases diagnosis is a primary goal to pursue, both laboratory diagnostic tools and microbiologists training.

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Abstract third-party references: German Research Foundation: Collaborative Research Centre 1027

Background: Catheter-related bloodstream infections (CRBSI) are a prominent cause of sepsis and are associated with high morbidity and mortality. CRBSI are usually triggered by the formation of biofilms on peripheral or central venous catheters (CVC), rendering the pathogen less susceptible to anti-infective therapy. Attachment of the pathogen to the catheter surface is a basic condition of biofilm formation, thus a pathogens ability to adhere to such a surface can be considered a fundamental virulence feature. Besides Staphylococci, the yeast *Candida albicans* is a major source of CRBSI. *C. albicans* can form two major morphotypes, the yeast stage thought to contribute primarily to distribution and dissemination, and the hyphae stage, which is believed to promote cell invasion and biofilm maturation. However, the role of these morphotypes in initial adhesion is still debated. The presence of blood serum and a temperature of 37 °C are strong triggers of a yeast to hyphae transition inducing the rapid outgrowth of initial hyphae within minutes.

Materials/methods: We utilized Single Cell Force Spectroscopy (SCFS) and flow chamber experiments to investigate the contribution of *C. albicans* yeast and hyphae cells to the adhesion to commonly used CVC.

Results: Our SCFS results showed that *C. albicans* cells in the early hyphae stage, induced by incubation of yeast cells in human blood serum, attach with a significantly higher adhesion force to serum-coated/uncoated CVCs than yeast cells. Channeling early-stage hyphae through a flow chamber, using serum-coated CVC material as a substrate for adhesion, revealed a flow directional adhesion pattern, with apical hyphae tips orientating in opposite flow direction.

Conclusions: Our results indicate that the contribution of *C. albicans* hyphae to initial adhesion is bigger than currently expected. We suggest an anchoring function of early stage hyphae tips, facilitating the adherence to CVC in the blood stream. We hope that our results will contribute to the development of medical devices less susceptible to the adherence of *C. albicans* and other biofilm-forming pathogens.

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Abstract 4973

Retrospective WGS of Acinetobacter baumannii over 6.5-year-period reveals former unknown structure of clusters and uncovers resistance profile

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Background: Multi-drug resistant Acinetobacter baumannii (MDR Ab) are known to be responsible for nosocomial outbreaks, caused by a limited number of clones that spread worldwide. Locally, we observed several clusters as identified by AFLP of MDR Ab in colonized or infected patients from February 2012 to September 2018. We could not exclude long-term circulation of particular clones to be responsible, and thus employed sequencing for higher resolution to investigate the local population structure and to analyze their resistance profile.

Materials/methods: 76 patients with MDR Ab were identified and 82 isolates collected. Sequencing was performed using an Illumina MiSeq.

Results: Most strains sequenced belonged to global clone 2 (GC2) \(n=57, 70\%\), 7 to GC1 \(9\%\), the others belonged to sequence types \(ST\) not related to these global clones \(n=13, 16\%\) as well as non-Ab but Acinetobacter calcoaceticus-Acinetobacter baumannii complex isolates \(n=4\) and 1 unclassified Acinetobacter strain.

In the GC2 group we found nine clusters. Three of these clusters were in agreement with AFLP. Sequence analysis here added higher resolution as to which strains had to be included or excluded in addition to the ones originally identified. In the GC2 group, some clusters showed clear discrimination to the other clusters \(> 105\) SNPs); however one clade contained several transmission chains, each of which had an intermediate number of SNPs \(20-50\) to the others.

In the non-GC2 group we found two clusters in agreement with the AFLP assignment indicative of recent transmission events. No direct transmission events were detected in GC1.

Genes detected for antibiotic resistances were in concordance with phenotypic resistance patterns, and were conserved within transmission chains.

Conclusions: Sequencing confirmed most previously assigned clusters but more precisely elucidated the structure of phylogeny and the position of strains that were considered to be unrelated. Additionally WGS supported the investigation of possible transmission links. We found no evidence for our suspicion of a single clone spawning a long-term transmission chain but our data show, that improvement of surveillance strategies would be needed to eliminate the risks of epidemic as well as endemic MDR clones because they pose a potential risk for future outbreaks.

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Epidemiology and antifungal susceptibility patterns of invasive fungal infections from 2012 to 2014 in a teaching hospital in central China

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Background: As participants of the national China Hospital Invasive Fungal Surveillance Net (CHIF-NET) program, we sought to describe the epidemiology and antifungal susceptibility patterns of yeast isolates obtained from patients with invasive fungal infection at the First Affiliated Hospital of Zhengzhou University, China.

Materials/methods: A total of 434 yeast isolates recovered from blood and other sterile body fluids were identified to species by matrix-assisted laser desorption ionization–time of flight mass spectrometry with or without supplementation by DNA sequencing. Antifungal susceptibilities were determined by Sensititre YeastOneTM YO10 methodology.

Results: Candida albicans was the most common causative species (33.9% of isolates) but significantly decreased in frequency from 37.2% to 27.7% from 2012 to 2014. C. tropicalis was the next most common pathogen (25.1%), followed by C. parapsilosis complex (17.3%), C. glabrata (9%) and C. pelliculosa (6.7%), with other species comprising 8% of isolates. Caspofungin, micafungin and anidulafungin exhibited potent in vitro activities against the majority of Candida isolates. Azoles demonstrated in vitro activities against C. albicans with a susceptibility rate of >95% and against C. parapsilosis complex, >95% isolates were susceptible. Amongst C. tropicalis and C. glabrata isolates, resistance rates to fluconazole and voriconazole were 11.9%, 9.1% and 7.7%, 28.2%, respectively. Of note, C. pelliculosa had a high incidence rate in newborns and high rates of resistance to fluconazole and voriconazole of 55.2% and 41.4%, respectively.

Conclusions: The present study provided valuable local surveillance data on the epidemiology and antifungal susceptibilities of invasive yeast species, which is essential for guiding antifungal treatment protocol development.

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Abstract 4978

The EUCAST Rapid AST directly from positive blood culture bottles: breakpoints for additional antimicrobial agents for Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa

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Background: The EUCAST method for rapid antimicrobial susceptibility testing (RAST) is available on the EUCAST website since November 2018. The initial limited range of antimicrobial agents for Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa needs to be extended. The objective of this study was to determine breakpoints for additional agents important in the treatment of sepsis.

Materials/methods: BC bottles, BACTEC® Plus Aerobic (BD), were inoculated with isolates of E. coli (n=65), K. pneumoniae (n=53) and P. aeruginosa (n=60) together with 5 mL defibrinated horse blood and placed in the BACTEC FX system (BD). Isolates susceptible and resistant isolates for each antimicrobial agent were included (Table). Disk diffusion was performed according to the EUCAST RAST methodology using Mueller-Hinton agar from two manufacturers (BBL/BD and Oxoid/Thermo Fisher Scientific). Inhibitions zones were read after 4, 6 and 8h incubation (6 and 8h for P. aeruginosa), on the same re-incubated plates. MIC values from broth microdilution according to ISO 20776-1 interpreted according to EUCAST breakpoints v.9.0 (2019), were used as reference. Proposed breakpoints were set to correctly categorise as many isolates as possible and to avoid false susceptible results.

Results: We were able to determine RAST breakpoints for the additional agents. The proportion of readable zones corresponded to results for other, previously investigated, agents. As previously, an Area of Technical Uncertainty (ATU) was introduced to reduce categorical errors. Less than 16% of all readable zones were categorised as ATU. RAST for ceftolozane-tazobactam was difficult for both E. coli and K. pneumoniae. With the suggested breakpoints more than 95%, 94% and 96% of all isolates were correctly categorised as susceptible or resistant for E. coli, K. pneumoniae and P. aeruginosa respectively. With the suggested breakpoints there were only two false susceptible results.

Conclusions: This study shows that the EUCAST RAST method can now be used for several additional clinically relevant antimicrobial agents for E. coli, K. pneumoniae and P. aeruginosa. As with other agents, the number of errors is low, especially false susceptible results, when testing a collection of isolates with high number of resistant isolates with varying MIC values.

Table. Theoretical and actual number of tests, the proportion of tests which could be read and interpreted after 4, 6 and 8 h, and the categorical errors with RAST at each reading time for E. coli, K. pneumoniae and P. aeruginosa.

For each table, data are presented as (letters relating to footnotes):
A. The theoretical number of tests = Total number of possible isolate-agent combinations in duplicate (since data on media from two manufacturers).
B. Number of completed tests = Number of completed test after excluding missing data (e.g. disk dropped).
C. Readable zones = Number of tests with readable inhibition zones.

<table>
<thead>
<tr>
<th>Species</th>
<th>E. coli</th>
<th>K. pneumoniae</th>
<th>P. aeruginosa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimicrobial agents</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incubation time</td>
<td>4h</td>
<td>6h</td>
<td>8h</td>
</tr>
<tr>
<td>Theoretical number of tests (n)</td>
<td>608</td>
<td>608</td>
<td>608</td>
</tr>
<tr>
<td>Completed tests</td>
<td>608</td>
<td>608</td>
<td>608</td>
</tr>
<tr>
<td>Readable zones (% of completed tests)</td>
<td>597 (98)</td>
<td>608 (100)</td>
<td>608 (100)</td>
</tr>
<tr>
<td>Not interpreted to S or R (ATU)</td>
<td>13</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Interpreted to S</td>
<td>50</td>
<td>52</td>
<td>54</td>
</tr>
<tr>
<td>Interpreted to R</td>
<td>37</td>
<td>37</td>
<td>37</td>
</tr>
<tr>
<td>Errors calculated on the total number of zones interpreted to S or R (%)</td>
<td>mE</td>
<td>1.4</td>
<td>2.6</td>
</tr>
<tr>
<td>ME</td>
<td>2.9</td>
<td>1.9</td>
<td>2.5</td>
</tr>
<tr>
<td>VME</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total errors</td>
<td>4.3</td>
<td>4.5</td>
<td>4.9</td>
</tr>
</tbody>
</table>

mE (minor Error) = Categorised as susceptible (S) or resistant (R) with RAST when susceptible with increased exposure (I) with standard method.
ME (Major Error) = False resistant.
VME (Very Major Error) = False susceptible.

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Abstract 4980

Location and numbers of handrub dispensers in Swiss hospitals: a representative survey to establish a national minimal standard

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Background: Hand hygiene (HH) using alcohol-based handrub (ABHR) belongs to the standards of care for infection control to prevent transmission of pathogens. Data on numbers and best location for ABHR dispensers (ABHR-D) are scarce. The German Office of Public Health (RKI) recommends at least one dispenser per bed in intensive care units and 0.5 dispenser per bed in general wards. WHO, CDC and ECDC do not provide exact recommendations on the number of ABHR-Ds. We investigated the actual numbers and location of ABHR-Ds in Switzerland.

Materials/methods: Between 7/19-9/19, we asked all 178 hospitals participating in the Swissnoso National surveillance Network, representing around 80% of Swiss acute care hospitals, to respond to an anonymous, standardized questionnaire on HH practices with emphasis on numbers of ABHR-Ds per bed and location. The questionnaire was addressed to board-certified infection control practitioners and hospital epidemiologists. Non-responders were reminded twice before being considered as non-compliant.

Results: 110 of 178 (61.8%) participating hospitals provided data, representing approximately 20’000 hospital beds. 66 hospitals (60%) have more than 100 beds. Pocket-sized dispensers (100ml) are used in 97.3% (n=107) of hospitals, but in only 28.2% (n=31) pocket dispensers are the preferred way of distribution. The reported median number was 2 ABHR-D per room (mean: 1.83, range 1-4). 91 out of 110 hospitals (82.7%) provided detailed data on the total amount of beds and dispensers within the building, reporting a median of 2.38 (range 0.38-22.1). A majority of hospitals (83.6%, n=92) had dispensers located at the entrance of the room; 73.6% (n=81) have a ABHR-D near the sink, 28.2% (n=31) within one-meter radius of the bed and 23.6% had a dispenser at the bottom of the bed. In total, 47.3% (n=52) hospitals reported a ABHR-D location near or at the bed. Other frequently mentioned locations were mobile devices such as computer trolleys.

Conclusions: Swiss hospitals have on average 2.38 dispensers per bed four times as many as recommended by RKI. This is the very first study evaluating the number of ABHR-Ds in hospitals and may serve as new minimal standard for HH lacking standards issued by WHO, CDC and ECDC.

<table>
<thead>
<tr>
<th>Hospital characteristics</th>
<th>All hospitals (n=110)</th>
<th>Hospitals &lt;200 beds (n=70)</th>
<th>Hospitals 200-500 beds (n=30)</th>
<th>Hospitals &gt;500 beds (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location of ABHR dispensers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entrance</td>
<td>92 (83.6)</td>
<td>58 (82.9)</td>
<td>26 (86.7)</td>
<td>7 (70.0)</td>
</tr>
<tr>
<td>Near to the sink</td>
<td>81 (73.6)</td>
<td>47 (67.1)</td>
<td>25 (83.3)</td>
<td>9 (90.0)</td>
</tr>
<tr>
<td>Within 1m radius from the bed</td>
<td>31 (28.1)</td>
<td>19 (27.1)</td>
<td>5 (16.7)</td>
<td>7 (70.0)</td>
</tr>
<tr>
<td>At the bedside</td>
<td>26 (23.6)</td>
<td>19 (27.1)</td>
<td>5 (16.7)</td>
<td>2 (20.0)</td>
</tr>
<tr>
<td>Elsewhere (for example trolleys)</td>
<td>14 (12.7)</td>
<td>10 (14.3)</td>
<td>2 (6.7)</td>
<td>2 (20.0)</td>
</tr>
<tr>
<td>Pocket dispenser use &gt;60%</td>
<td>26 (23.6)</td>
<td>18 (25.7)</td>
<td>11 (36.7)</td>
<td>4 (40.0)</td>
</tr>
<tr>
<td>Number of dispensers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Per Room, mean (SD, range)</td>
<td>1.8 (0.8; 1.4)</td>
<td>2 (0.8; 1.4)</td>
<td>1 (0.8; 1.4)</td>
<td>2 (1; 1.3)</td>
</tr>
<tr>
<td>Per Bed, mean (SD, range)</td>
<td>2.4 (3.0; 0.4, 22.2)</td>
<td>2.5 (3.6; 0.8, 22.2)</td>
<td>2.1 (1.0; 0.7, 5.3)</td>
<td>2.1 (1.5; 0.4, 4.9)</td>
</tr>
<tr>
<td>Mean ABHR-D per hospital (SD, range)</td>
<td>285 (581; 20, 3185)</td>
<td>185 (256; 20, 1250)</td>
<td>510 (282; 150, 1200)</td>
<td>1500 (1068.4; 197, 3185)</td>
</tr>
<tr>
<td>HH compliance monitoring</td>
<td>68 (61.8)</td>
<td>37 (52.9)</td>
<td>25 (83.3)</td>
<td>5 (50.0)</td>
</tr>
</tbody>
</table>

Footnote to the Table: ABHR, alcohol-based handrub

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Ceftazidime-avibactam resistance and restoration of carbapenem susceptibility in KPC-producing Klebsiella pneumoniae infections

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Background: Since the introduction of the ß-lactam/ß-lactamase inhibitor ceftazidime-avibactam (C-A), rapid evolution of resistance has been reported in different KPC-producing Klebsiella pneumoniae isolates. In this multicenter retrospective study we describe the emergence of C-A resistance and evaluate the mutations that might be responsible for the restoration of carbapenem susceptibility.

Materials/methods: During a study period of 18 months, KPC-producing K. pneumoniae isolates of five hospitalized patients were collected with phenotypic development of C-A resistance.

Results: In vitro restoration of carbapenem susceptibility during treatment was observed in 3 isolates. Whole genome sequencing of these isolates showed a D179Y mutation in the KPC gene of 2 variants and a KPC-2 with a Δ242-GT-243 deletion (KPC-14). Two KPC-3 variants showed C-A resistance with sustained carbapenemase activity without genomic adaptations in the KPC gene.

Conclusions: This study confirms the emergence of C-A resistance in KPC K. pneumoniae. The role of carbapenems in treating patients with these variants is unclear and combination therapies warrant further investigation.

Table 1. Phenotypic and molecular characterization of KPC-producing Klebsiella pneumoniae isolates before (A) and following (B) ceftazidime-avibactam treatment

<table>
<thead>
<tr>
<th>Isolate</th>
<th>Sequence Type</th>
<th>Complex Type</th>
<th>KPC Variant</th>
<th>C-A MIC1</th>
<th>MEM MIC1</th>
<th>IPM MIC1</th>
<th>KPC variants</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-A</td>
<td>307</td>
<td>3502</td>
<td>KPC-3</td>
<td>1 (S)</td>
<td>12 (R)</td>
<td>32 (R)</td>
<td></td>
</tr>
<tr>
<td>1-B</td>
<td>307</td>
<td>3502</td>
<td>KPC-31</td>
<td>96 (R)</td>
<td>0.064 (S)</td>
<td>0.38 (S)</td>
<td>D179Y</td>
</tr>
<tr>
<td>2-A</td>
<td>101</td>
<td>1400</td>
<td>KPC-2</td>
<td>6 (S)</td>
<td>32 (R)</td>
<td>32 (R)</td>
<td></td>
</tr>
<tr>
<td>2-B</td>
<td>101</td>
<td>1400</td>
<td>KPC-33</td>
<td>256 (R)</td>
<td>4 (I)</td>
<td>0.38 (S)</td>
<td>D179Y</td>
</tr>
<tr>
<td>3-A</td>
<td>512</td>
<td>4641</td>
<td>KPC-3</td>
<td>4 (S)</td>
<td>32 (R)</td>
<td>32 (R)</td>
<td></td>
</tr>
<tr>
<td>3-B</td>
<td>512</td>
<td>4641</td>
<td>KPC-3</td>
<td>32 (S)</td>
<td>32 (R)</td>
<td>32 (R)</td>
<td>None</td>
</tr>
<tr>
<td>4-A</td>
<td>512</td>
<td>4381</td>
<td>KPC-3</td>
<td>4 (S)</td>
<td>32 (R)</td>
<td>32 (R)</td>
<td>None</td>
</tr>
<tr>
<td>4-B</td>
<td>868</td>
<td>4642</td>
<td>KPC-3</td>
<td>64 (R)</td>
<td>32 (R)</td>
<td>32 (R)</td>
<td>None</td>
</tr>
<tr>
<td>5-A</td>
<td>1685</td>
<td>4642</td>
<td>KPC-2</td>
<td>3 (S)</td>
<td>32 (R)</td>
<td>32 (R)</td>
<td></td>
</tr>
<tr>
<td>5-B</td>
<td>1685</td>
<td>4642</td>
<td>KPC-14</td>
<td>256 (R)</td>
<td>1.5 (S)</td>
<td>0.5 (S)</td>
<td>Δ242-GT-243</td>
</tr>
</tbody>
</table>

KPC, Klebsiella pneumoniae carbapenemase; C-A, ceftazidime-avibactam; MEM, meropenem; IPM, imipenem; MIC, minimum inhibitory concentration; S, susceptible based on EUCAST interpretive criteria; R, resistant based on EUCAST interpretive criteria

*MICs were determined by ETEST®. EUCAST interpretative criteria were applied to define susceptibility as follows: ceftazidime-avibactam, ≤8 mg/L; meropenem, ≤2 mg/L; imipenem, ≤2 mg/L

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**Abstract 4983**

**Vaccinium macrocarpon urine metabolites inhibit Candida albicans adhesion and biofilm formation**
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**Background:** Candida albicans urinary tract infections (UTI) are increasingly common in hospital settings due to its high propensity to form biofilms on mucosal surface and plastic surface of indwelling devices. Vaccinium macrocarpon (cranberry) has been widely used for decades in the prevention of UTIs in the general population. Proanthocyanidins (PACs), in particular the A-type, are the main responsible for the in vitro activity. Nevertheless, there are controversial results on their presence in human urine after cranberry oral intake. The aim of the work was i) to identify and quantify cranberry components and metabolites in human urine after the oral intake of a highly-standardized cranberry extract (Anthocran™, Indena S.p.A.), ii) to evaluate the urine ex vivo effect on C. albicans adhesion and biofilm formation and iii) to test the in vitro activity of a mixture of metabolites identified in the active fractions.

**Materials/methods:** Ten young healthy female volunteers took 2 capsules Anthocran™/day for 7 days. Urine samples were collected before starting supplementation and at the following time-points after the last dose: 1, 2, 4, 6, 10, 12, 24 hours. An HPLC-MS/MS method was set-up using a LTQ-XL-Orbitrap working in data dependent scan mode to perform the analyses. A targeted and an untargeted approach was used to identify known metabolites and compounds hereto unreported in the literature. Urine fractions were tested in vitro against the reference strain C. albicans SC5314 and eight clinical isolates from UTIs.

**Results:** Urine fractions collected after 1 and 12 hours were found to significantly reduce the adhesion. The ex vivo effect of cranberry metabolites was then confirmed by evaluating the significant inhibitory effect of a reconstituted mixture of metabolites on C. albicans adhesion and biofilm formation.

**Conclusions:** The data reported in the present work demonstrate that i) PACs are metabolized after cranberry oral intake, ii) urines collected following one week of cranberry treatment are able to significantly reduce C. albicans adhesion and biofilm formation, iii) the activity can be due to a synergistic effect of identified cranberry metabolites including PACs metabolites.

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Abstract 4985

Direct-from-Blood-Culture NG-Test CTX-M Multi and Carba 5 assay to predict extended-spectrum β-lactam resistance of Escherichia coli and Klebsiella pneumoniae

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Background: Bloodstream infections (BSIs) caused by extended-spectrum β-lactamases and carbapenemase-producing Escherichia coli and Klebsiella pneumoniae are associated with treatment failure and increased mortality. Rapid, reliable detection of these organisms may help clinicians to provide more adequate therapy during the early period of clinical illness. We aimed to determine the feasibility of using the rapid NG-test CTX-M MULTI and the NG-Test Carba 5 immunochromatographic (ICT) assays directly from positive blood cultures (BCs) to predict phenotypic resistance to cefotaxime, ceftazidime, imipenem and meropenem.

Materials/methods: Analysis was prospectively carried out on 630 consecutively positive BCs from nonduplicate patients, in which the presence of K. pneumoniae or E. coli was detected by direct MALDI-TOF mass spectrometry analysis from positive BC broths. All BC samples were then tested with the NG-test CTX-M MULTI and the NG-Test Carba 5 according to the manufacturer’s instructions with some modifications. Test results were read by eye after 15 minutes of migration at room temperature. ICT results were compared to phenotypic resistance as determined by broth microdilution method which was performed and interpreted according to EUCAST clinical breakpoints. Carbapenemase, extended-spectrum and plasmid-mediated AmpC β-lactamase genes were further identified by PCR assay and sequencing.

Results: Overall 41.3% of the isolates were resistant to cefotaxime, 36.3% to ceftazidime, 8.6% to imipenem and 9.0% to meropenem. The sensitivity of the NG-test CTX-M MULTI and the NG-Test Carba 5 to predict ceftriaxone and ceftazidime resistance was 0.95 (95% confidence interval [CI] 0.92–0.97) and 0.95 (95%CI 0.91-0.97), respectively, while the specificity was 1 (95%CI 0.99-1) and 0.92 (95%CI 0.89-0.95), respectively. The sensitivity of the NG-Test Carba 5 to predict imipenem and meropenem resistance was 0.98 (95%CI 0.90-0.99) and 0.97 (95%CI 0.88-0.99), respectively, while the specificity was 0.99% (95%CI 0.97-0.99) and 0.98 (95%CI 0.97-0.99), respectively.

Conclusions: Although further studies are needed to assess their performance in routine diagnostics, our experience with this large series of E. coli- and K. pneumoniae-positive BCs indicates that the NG-test CTX-M MULTI and the NG-Test Carba 5 assays accurately predict resistance to β-lactam antimicrobials used in the treatment of BSIs caused by E. coli and K. pneumoniae isolates.

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Abstract 4988

Limited genetic diversity of blaCMY-2-containing IncI1-ST12 plasmids from Enterobacteriaceae of diverse human and broiler origin in the Netherlands

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**Background:** IncI1 plasmid sequence type [pST] 12 has been linked to the spread of blaCMY-2, the most common plasmid-encoded ampC gene. So far, literature is scarce on the genetic diversity of IncI1-pST12 plasmid sequences. Next-generation sequencing (NGS)-based analysis of blaCMY-2 IncI1-pST12 plasmids in Enterobacteriaceae from Dutch hospitalised patients and broilers was performed to investigate their genetic diversity.

**Materials/methods:** Short-read sequence data (Illumina, Dan Diego, US) in our local NGS database of Enterobacteriaceae cultured from humans and broilers were screened for the presence of both a blaCMY-2 gene and an IncI1-pST12 replicon. Six E. coli and one Salmonella enterica from different sequence type [ST] and origin (human or broiler) were selected the present analysis [Figure]. De novo assembly was performed with SPAdes v3.12, followed by in silico plasmid extraction using an IncI1-pST12 reference plasmid. The plasmid constructs and the IncI1-pST12 reference plasmid were aligned using progressiveMAUVE v2.4.0, creating a genome-content distance matrix reflecting the mean proportion of shared genomic content. Pairwise single nucleotide polymorphisms [SNP] were determined using Snippy v4.4.5. The plasmids were annotated using Prokka v1.13.3 and a pan-genome was constructed using Roary v3.12.

**Results:** The genome-content distance in pairwise comparisons with the reference plasmid ranged from 0.00 to 0.04. The number of SNP's detected between the plasmid constructs and the reference IncI1-pST12 plasmid ranged from 1 to 8 [Figure]. One-hundred and one genes (82%) of the pan-genome of 124 genes were present in all plasmid constructs, where the number of genes being variably present or absent between the plasmids ranged from 1 to 16 [Figure].

**Conclusions:** NGS-analysis of seven blaCMY-2-containing IncI1-pST12 plasmids isolated from epidemiologically unrelated Enterobacteriaceae shows a high degree of sequence similarity in terms of a low number of SNP differences and a high number of shared genes. Given the conserved genome of these plasmids, judgements on the horizontal transfer based on genetic identity should be made with caution.

**Figure SNP differences and variable gene presence or absence**

<table>
<thead>
<tr>
<th>Isolate</th>
<th>Species</th>
<th>MLST</th>
<th>Origin</th>
<th>Site</th>
<th>Year of Isolation</th>
<th>SNP differences / variable gene presence or absence</th>
</tr>
</thead>
<tbody>
<tr>
<td>EC1</td>
<td>E. coli</td>
<td>ST865</td>
<td>Chicken</td>
<td>Fecal</td>
<td>2017</td>
<td>x</td>
</tr>
<tr>
<td>EC2</td>
<td>E. coli</td>
<td>ST865</td>
<td>Chicken</td>
<td>Fecal</td>
<td>2017</td>
<td>2 / 9 x</td>
</tr>
<tr>
<td>EC3</td>
<td>E. coli</td>
<td>ST86</td>
<td>Chicken</td>
<td>Fecal</td>
<td>2017</td>
<td>3 / 7 1 / 1 x</td>
</tr>
<tr>
<td>EC4</td>
<td>E. coli</td>
<td>ST131</td>
<td>Human</td>
<td>Blood</td>
<td>2013</td>
<td>4 / 11 4 / 2 3 / 3 x</td>
</tr>
<tr>
<td>EC5</td>
<td>E. coli</td>
<td>ST131</td>
<td>Human</td>
<td>Blood</td>
<td>2014</td>
<td>3 / 16 3 / 9 2 / 7 1 / 7 x</td>
</tr>
<tr>
<td>EC6</td>
<td>E. coli</td>
<td>ST973</td>
<td>Human</td>
<td>Rectal</td>
<td>2017</td>
<td>8 / 10 8 / 1 7 / 2 8 / 1 7 / 8 x</td>
</tr>
<tr>
<td>SE1</td>
<td>S. enteritidis</td>
<td>ST973</td>
<td>Human</td>
<td>Fecal</td>
<td>2018</td>
<td>5 / 7 5 / 7 4 / 8 5 / 7 4 / 11 7 / 6 x</td>
</tr>
</tbody>
</table>

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Prevalence of Chlamydia trachomatis and Neisseria gonorrhoeae at extragenital sites in the north metropolitan area in Catalonia

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Background: Chlamydia trachomatis [CT] and Neisseria gonorrhoeae [NG], not only cause urethritis and cervicitis, but also can be detected at extragenital sites (rectum, pharynx). Extragenital chlamydia and gonorrhoea infections are commonly reported in men who have sex with men (MSM). Recent studies suggest the prevalence of extragenital infections in heterosexuals, mainly in women, may be increasing. We aimed to evaluate extragenital sexually transmitted infections [STIs] prevalence in our environment.

Materials/methods: This is a prospective study conducted from January-October 2019 at the Microbiology department of Laboratory Clinic Metropolitan North in Badalona [Spain]. Samples for CT and NG detection by real-time PCR came from asymptomatic and symptomatic patients. Additionally, the rectal swabs which were positive for CT, were retested by real-time PCR for Lymphogranuloma venereum [LGV] detection.

Results: A total of 550 rectal swabs were analyzed. Of them, 14% were positive for CT and 7.6% were positive for NG. LGV was positive in MSM, 35/39 (90%). Meanwhile, in heterosexual population was positive 1/37 (3%). Besides, 1255 pharyngeal swabs were analyzed. Of them, 4% were positive for CT and 3% were positive for NG. The samples received from women were 1156/1375 (84%) and from MSM were 430. Table 1.

Conclusions: MSM and women seem to have a higher risk of extragenital STIs. The prevalence of chlamydia infection in heterosexual population, which practice anal intercourse, is as high as MSM. However, the majority MSM reported were LGV, but in heterosexual population was uncommon. Due to STIs have been increasing in genital sites in the last few years; maybe they have also been rising in rectum and pharynx. We recommend analyzing all anatomical sites according to sexual behavior.

<table>
<thead>
<tr>
<th>Extragenital site</th>
<th>CT N° positive/total (%)</th>
<th>Microorganism N° positive/total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CT L1-L2 (LGV)</td>
<td>NG</td>
</tr>
<tr>
<td>Rectum (n=550)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSM</td>
<td>39/277 (14)</td>
<td>35/39 (90)</td>
</tr>
<tr>
<td></td>
<td>37/273 (13.5)</td>
<td>1/37 (3)</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>2/37 (5)</td>
<td>1/37 (100)</td>
</tr>
<tr>
<td>Men</td>
<td>35/37 (95)</td>
<td>3/10 (30)</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td>7/10 (70)</td>
</tr>
<tr>
<td>Pharynx (n=1255)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MSM</td>
<td>1/153 (&lt;1)</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>51/1102 (5)</td>
<td>11/153 (7)</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>6/51 (12)</td>
<td>--</td>
</tr>
<tr>
<td>Men</td>
<td>45/51 (88)</td>
<td>32/1102 (3)</td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td>8/32 (25)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>24/32 (75)</td>
</tr>
</tbody>
</table>

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The economic burden of carbapenem-resistant non-fermenting Gram-negative bacteria healthcare-associated infections

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Background: CRNF HAIs are a major public health threat. Quantifying the economic burden of CRNF HAIs to hospitals can assist decision makers in determining the investments for prevention and control. We determined the cost of a single CRNF HAI from a hospital’s perspective, and estimated the annual economic impact of CRNF HAIs to a Singapore hospital.

Materials/methods: We conducted a matched case-control study for CRNF and carbapenem-susceptible non-fermenting Gram-negative bacteria (CSNF) HAI patients in a 1,700-bedded tertiary hospital in Singapore, matched for organism, time at risk and admitting ward. Probabilities and outcomes were entered into a tree diagram to estimate the cost of a CRNF HAI for the duration of the infection from the hospital’s perspective, and compared to the cost of a CSNF HAI (Figure 1). Cost of individual components (e.g. bed-day cost, hourly wages, instrumentation) were obtained from nationally representative local databases. All costs were adjusted to 2016 SGD using a 3% inflation rate. Monte Carlo simulations were performed, comprising 1000 trials, varying distributions through their ranges. The annual economic burden of CRNF HAIs was determined by extrapolating the cost data to the hospital’s annual CRNF HAI incidence. Scenario analyses were further conducted.

Results: The median cost of a single CRNF HAI from the hospital’s perspective was $33,424 (90% credibility ranges (CR), $23,314-$46,556), which is markedly higher than the median cost of a single CSNF HAI [$13,030; 90% CR, $8,149-$23,562]. Approximately 50% of the cost incurred consisted of productivity losses in healthcare workers [$8,941 (90% CR, $3,011-$21,746)] and loss in opportunity costs for lost room and board [$8,207 (90% CR, $2,729-$19,834)]. The costliest CRNF HAIs are intra-abdominal infections [$46,988 ($35,804-$59,638)] and pneumonia [$39,371 ($19,127-$80,144)]. Extrapolating this to our annual CRNF HAI incidence (incidence rate of 51.10 per 10,000 admissions), CRNF HAIs will cost the hospital approximately $15.07 million/year. A reduction in CRNF incidence rates by 20% will lead to cost savings of SGD$3.01 million/year.

Conclusions: HAIs caused by CRNF were associated with substantial costs to the hospital. Efforts should be made to prevent these nosocomial infections to allow healthcare resources to be better employed for other purposes.

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Abstract 4994

A retrospective study to evaluate the epidemiology, standard of care, outcomes and resource utilisation in patients with confirmed or suspected infection by a carbapenem-resistant Gram-negative organism in the UK: the CARBAR study part 2

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Abstract third-party references: Study Sponsored by Shionogi Europe

Background: Antimicrobial resistance is a major global threat with potentially devastating consequences and significant costs to society. Carbapenems have been the main class of drugs, reserved for difficult-to-treat Gram-negative (GN) infections, but resistance is increasing worldwide; hence WHO classified carbapenem-resistant (CR) strains of Acinetobacter baumannii (CRAB), Pseudomonas aeruginosa (CRPA), and Enterobacteriaceae spp (CRE) as a critical priority. Infections by CR pathogens have few effective treatment options, with suboptimal use and scarce clinical trial evidence. In this study, we describe the diagnosis and management pathway of patients who are treated for Carbapenem non-susceptible GN (CarbNS-GN) infection.

Materials/methods: Retrospective chart review from 9 sites in UK. Eligible adult patients were randomly selected from part 1 of this study [an epidemiology survey including all patients with a GN pathogen] and included if had confirmed CarbNS-GN infection and admitted into hospital between April 2017 and March 2018. Index date was considered the first CarbNS-GN positive sample. Data collected included patient demographics, microbiology results, treatment history including pre-hospitalization, travel history, management pathway, survival and discharge status.

Results: 157 patients with CarbNS-GN infections were included, mean age was 63.3 years, 62% were male, and 17.5% patients had ≥2 Carb-NS pathogens identified. 78% of patients were from England, 15% from Scotland and 7% from Wales.

Overall, non-fermenter pathogens were identified in 72% of patients; CRPA was the most commonly identified pathogen (38%), followed by Stenotrophomonas maltophilia (27%) and Enterobacteriaceae spp (25%). At the end of this study 51% of these patients had died, of which 54% died in hospital. Mean time from index sample collection to sensitive therapy was 7.2 days, but patients had been on antibiotic treatment on average for 9.1 days before index date. Overall, mean time from first antibiotic prescribed to first active agent was 14.5 days.

Conclusions: Patients with CarbNS-GN infections were observed across the UK and represent an important population, with high mortality, significant burden, and high unmet medical need. Understanding the real-world management and outcomes of these patients, can help optimize antimicrobial stewardship and infection prevention and control programs, ultimately improving overall patients’ and NHS’s outcomes.

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**Abstract 4995**

**Genomic analysis of the subclades C2/H30Rx and C1-M27 of Escherichia coli ST131 high-risk clone across Hungary**

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**Background:** Recently burden of disease caused by third-generation cephalosporin-resistant (3rdCR) *Escherichia coli* increased the most in Europe. The ST131 high risk clone, especially C2/H30Rx subclade with *bla*\_CTX-M-15 and C1-M27 subclade with *bla*\_CTX-M-27, is the predominant lineage among 3rdCR *E. coli*. In 2018 44.6% (75/168) of invasive ESBL-producing *E. coli* isolates investigated at the National Public Health Center belonged to the ST131 clone, where the ratio of C2/H30Rx and C1-M27 was 1 to 0.8. The aim of our study was to perform genomic analysis on selected C2/H30Rx and C1-M27 ST131 *E. coli* invasive isolates in order to compare their genetic backgrounds.

**Materials/methods:** Seventeen C1-M27 and 16 C2/H30Rx ESBL-producing invasive *E. coli* isolates originated from entire country between 2015-2018 were selected. The antimicrobial susceptibility testing was performed by gradient MIC tests or broth microdilution and interpreted using EUCAST guidelines. The possible clonal relationships were investigated by core genome (cg)MLST (SeqSphere+ [Ridom]) using whole-genome sequencing (WGS) data of all isolates obtained from Illumina 251-bp paired-end sequencing. From WGS data acquired antimicrobial resistance and virulence genes were retrieved using ResFinder3.1, VirulenceFinder2.0 online tools and a pipeline based on 62 additional genes associated with extraintestinal infections.

**Results:** All the isolates proved resistant to ceftriaxone and ciprofloxacin, but susceptible to ceftazidim/avibactam, amikacin, tigecyclin, fosfomycin and carbapenems. C2/H30Rx isolates showed higher resistance rates than the C1-M27 ones to ceftazidim (87.5% vs 23.5%), tobramycin (81.3% vs 0%) and gentamicin (56.3% vs 0%). The virulome and resistome of the subclades showed high similarities, although differences were found (Fisher’s exact test, p<0.05): some adhesin genes (*sfaB, afa, dra*), some toxin genes (*cnf, astA, hylA*) and some antibiotic resistance genes (*bla*\_CTX-M-15, *gmrB19, aoC(6)-lb-cr, aoC(3)-lla*) significantly associated with C2/H30Rx; while *traD* serum-resistance gene, *senB* toxin gene and some antibiotic resistance genes (*bla*\_CTX-M-27, *sul2*) significantly associated with C1-M27. According to cgMLST, the isolates within a subclade were more closely related than between.

**Conclusions:** Despite of the similarity of their genetic background, there are differences which can associate with their phenotype in case of antibiotic resistance and virulence. The possible link between the clone dissemination, antibiotic resistance and virulence needs further investigations.

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Prevalence of haematogenous seeding at distant sites in patients with Candida bloodstream infections

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Background: Bloodstream infection (BSI) by Candida spp. can be complicated by hematogenous seeding of distant sites and development of end organ infection (complicated Candida BSI). Our study aims to define the prevalence of complicated Candida BSI.

Materials/methods: We retrospectively reviewed medical records of all adults [age ≥18 years] with Candida BSI from November, 2011 to December, 2018. Cases with positive blood cultures via catheter alone [negative peripheral blood cultures] and polymicrobial cases were excluded. Patient demographics, clinical and microbiologic data, diagnostic imaging, and autopsy reports were reviewed.

Results: A total of 250 patients were identified and 125 patients met inclusion criteria. The median age at presentation was 62 years (IQR 50-71.5 years). The majority (53%) had a non-albicans Candida spp. BSI (46%, Candida glabrata). Five percent (6/125) had a complicated Candida BSI. The median time to blood culture positivity was 47 hours (IQR 33.5-53.5 hours) and the median time of clearance was 48 hours (IQR 42-96 hours). Seventy-four patients (59.2%) had an ophthalmological assessment, with a median time to evaluation of 5 days (IQR 3-7 days). Only two cases had ocular involvement (Table 1). Most (106/125, 85%) patients had imaging looking for a source of Candida BSI. More than half of the cases (65%) had a CT of the abdomen/pelvis, followed by a TTE and a TEE (25% and 18.4%, respectively). None of the cases had hepatosplenic candidiasis or endocarditis. Two patients had infected thrombi of the superior vena cava and transjugular intrahepatic portosystemic shunt that were confirmed by PET/CT and SPECT scan, respectively. Four cases had an infection recurrence. Three of the four cases relapsed (same Candida spp.) and one case had a re-infection (different Candida spp.). The median time of recurrence was 52.5 days (IQR 33.5-67 days). One of the three cases who relapsed cleared Candida BSI after removal of a cardiac implantable electronic device (CIED). At one year of follow up, all six patients with complicated Candida BSI were alive.

Conclusions: The prevalence of complicated Candida BSI, including ocular involvement, is low. Further evaluation for hematogenous seeding may be warranted in recurrent episodes of Candida BSI.

Table 1. Ocular candidiasis

<table>
<thead>
<tr>
<th>Age (Years)/Gender</th>
<th>Host</th>
<th>Ocular symptoms</th>
<th>Diagnosis</th>
<th>Candida species</th>
<th>Duration of Candida BSI (hours)</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>48/M</td>
<td>ICH – Stage III sigmoid colon adenocarcinoma on chemotherapy</td>
<td>No ocular pain, vision unchanged</td>
<td>Bilateral retinitis and choroiditis</td>
<td>Candida albicans</td>
<td>48 hours</td>
<td>Intravitreal voriconazole plus fluconazole (lifelong suppression)</td>
</tr>
<tr>
<td>64/F</td>
<td>ICH – PSC</td>
<td>No ocular pain, new eye floaters</td>
<td>Right endophthalmitis s/p vitreous and anterior chamber tap with negative fluid cultures</td>
<td>Candida albicans</td>
<td>72 hours</td>
<td>Intravitreal voriconazole plus fluconazole (lifelong suppression)</td>
</tr>
</tbody>
</table>

Abbreviations: ICH= immunocompromised, PSC= primary sclerosing cholangitis, BSI=bloodstream infection.

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**Abstract 4997**

**Risk factors for treatment failure in patients with deep spinal SSI with foreign bodies treated with debridement, antibiotic and implant retention (DAIR): an international multi-centre retrospective cohort study**

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**Abstract third-party references:** ESCMID Study Group on Implant Associated Infections (ESGIAI)

**Background:** Deep spinal infections in patients with foreign bodies are a frequent complication. Best treatment strategies have not been evaluated, yet. Complete exchange of foreign bodies is infrequently performed. Debridement, antibiotic and implant retention (DAIR) is most frequently chosen as a treatment strategy. However risk factors for failure when performing DAIR without exchanging the implant have not yet been well studied. The objective of this study is to identify risk factors associated with failure in patients treated with DAIR.

**Materials/methods:** All consecutive cases of patient with a deep SSI between 2005-2015 treated with DAIR were included. Patients were at least 18 years of age at onset of SSI and had a follow up after initial DAIR for at least 12 months. Infections were defined as onset of symptoms and or clinical diagnosis of SSI after implant placement: Early onset infection (< 30 days); late infection infection (> 30days and < 365 days) and delayed onset (≥ 1 year). Failure was defined as either progressed, relapse or new infection within the follow up period.

**Results:** This study included 133 patients (57.5% female, median age 54) from 8 centers located in Europe and south-America. 112 (84.2%) patients had an early, 12 (9.0%) a late and 9 (6.8%) patients had delayed onset of infection. Median length of primary surgery until onset of SSI was 16 days (IQR: 10-23). Polymicrobial infections were identified in 50 patients (37.6%), *Staphylococcus aureus* was identified in 44 patients (MRSA=6), followed by 31 coagulase-negative staphylococci (19 meticillin resistant). *Enterococcus* spp. was identified in 22 patients. Of those, 33 patients failed (24.8%) during follow up, thereof 26 (19.5%) due to uncontrolled spinal infection; 6 due to relapse of infection with the same pathogen (4.5%) and one patient (0.8%) had a new infection with a different microorganism. Failure was most frequent in delayed infections (8 of 9, 88.9%).

Regression analysis of independent risk factors for failure of DAIR is pendent.

**Conclusions:** DAIR appears to be an effective strategy in spinal deep SSI associated with foreign bodies. Further studies are needed to evaluate strategies for patients at risk for failure.

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Abstract 4998

**Donor selection in the Belgian Ghent Stool Bank: a relief to help**
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**Background:** The Ghent Stool Bank was created in 2018 at Ghent University Hospital, Belgium, to meet the growing demand of stool from healthy donors for fecal microbiota transfer. Candidate donors are selected based on a questionnaire inquiring general health, bowel movements, (chronic) diseases, medication. Selected donors are asked to provide 5 donations during 1 month. Every donation is tested for several enteropathogenic bacteria, viruses and parasites, as well as multi-resistant organisms in close accordance with the guidelines published by the Belgian Superior Health Council. Serum is screened before and 3 months after donations for hepatitis A, B, C, E; HIV; CMV; EBV and Treponema pallidum antibodies.

**Results:** Since the summer of 2018 until October 2019 approximately 264 candidate donors volunteered for stool donation at the Ghent Stool Bank. Based on general criteria, 166/264 candidate donors received a questionnaire and of those 51 passed selection for donations (immediately or after waiting period). Seven candidate donors never donated due to various reasons (lost to follow-up, diarrhea). 44 candidates started donating for a total of 190 donations (128 ± 81 g/donation), 19 men and 25 women. 43/44 donors tested positive for EBV IgG and 15/44 for CMV IgG. In 4 donors ESBL producing Escherichia coli, in 1 donor Stenotrophomonas maltophilia, in 1 donor Pseudomonas putida and in 1 donor Trichosporon was cultured from stool, their donations were excluded. 2/44 donors were rejected based on stool morphology (severe diarrhea). 7/42 tested positive for Hepatitis E IgG before the donations but the virus could not be detected in the stool samples by qPCR. 2 donors only tested positive for Hepatitis E IgG after the donations and might have suffered a recent infection, these donors were rejected as well.

**Conclusions:** In total 34 donors were fully approved on a total of 264 individual reactions, a success rate of 12.9%.

Figure 1: Overview of the selection process of the Ghent Stool Bank (GSB) in 2018 and 2019. Of 264 candidates 34 donors were approved, a success rate of 12.9%. (Q = questionnaire)

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Abstracts 2020

Abstract 5000

Molecular detection of Lyme disease and Q Fever agents in Dermanyssus gallinae (Acari: Mesostigmata) mites related to outbreaks of dermatitis in city-dwellers (southern Italy)

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Background: The poultry red mite (PRM), Dermanyssus gallinae is a non-burrowing haematophagous nest-dwelling ectoparasite of birds; occasionally, it bites mammals, including humans also inducing papular dermatitis. Attacks are common in poultry workers but evidences show an increasing of urban infestations, due to presence of avian nests close to edifices and/or canarians/rodents taken as pets. The possibility that this ectoparasite may be also involved in transmission of human pathogens represents an additional medical concern; however, information is scarce with a one only documented case showing Bartonella quintana in Dermanyssus sp. mites collected during an urban outbreak of trench fever. Aim of this study was investigate for zoonotic agents PRMs involved in urban outbreaks of dermatitis.

Materials/methods: PRMs related to indoor infestations (2001-2017 years) in residentials were pooled on the basis of each outbreak and molecularly investigated for Coxiella spp. (16S rRNA), Chlamydophila spp. (16S rRNA), Rickettsia spp. (17 kDa protein-encoding gene), Bartonella spp. (16S–23S rRNA intergenic spacer) and Borrelia burgdorferi sensu lato (groEL gene). Amplicons were sequenced and nucleotide sequences compared to GenBank using BLAST.

Results: A total of 98 mites divided in 12 pools (size = from 5 to 10 mites) were tested. Out of 12 examined pools, one pool (1/12) resulted positive to Coxiella sp, two (2/12) to B. burgdorferi sensu lato and 9 (9/12) pools resulted negative. The obtained three amplicons exhibited 100% identity with Coxiella burnetii and 99% with Borrelia afzelii, respectively.

Conclusions: Among the parasites affecting synantropic birds, mainly pigeons, D. gallinae represents the principal ectoparasite that humans may acquire; feral birds/rodents are also reservoirs of a number of microorganisms, including Q fever and Lyme disease agents (DNA) for the first time herein documented in association with the PRMs. Although no study has yet been carried out to ascertain the ability of D. gallinae to transmit the detected pathogens to humans, this possibility should be no longer be neglected and previous PRM-infestations should be considered when atypically outbreaks occur in people with unlikely exposure to historical infection sources (ruminants and ticks, respectively).

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How to accelerate bacteria identification from positive blood culture in a routine microbiology laboratory with the aid of MALDI-TOF MS: a simple and rapid in-house protocol

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Background: Rapid diagnostic tests for infectious disease can lead to rapid optimization of antimicrobial therapy and subsequently improve patient outcomes. Although various methods have been developed to directly identify bacteria from positive blood culture by MALDI-TOF MS, it is necessary to develop a feasible protocol to be used in the routine microbiology laboratory. The aim of this study was to develop an even faster, simple and inexpensive in-house protocol for direct identification of bacteria from positive blood cultures.

Materials/methods: The study included hemocultures flagged as positive by bacT/ALERT®. A total of 134 bacterial samples isolated from blood cultures were obtained, 82 Gram-negative (GN) and 52 Gram-positive (GP) aerobes from August to November 2019. Rapid identification was performed as follow: 3 mL of blood was taken from positive bottle and transferred to a tube containing plasma separation gel and centrifuged [3,000 rpm/10 minutes]. After discarding the supernatant, 3 mL of saline was added and centrifuged [3,000 rpm/5 minutes]. The supernatant was discarded and 1uL was used for identification by the VITEK MS® system database v3.0 (bioMérieux, France); CHCA matrix solution was placed onto each spot and formic acid was added for samples with GP bacteria. Duplicate spots were generated for every sample. As a calibration control, the Escherichia coli ATCC 8739 strain was used. The rapid identification results were compared to those Vitek MS® results according to the manufacturer’s instructions protocol.

Results: The percentages of total correct identification of the isolates tested at species and gender level using rapid protocol were 95% and 96%, respectively, the highest identification rate at species level was for GN bacteria, 98% [81/82 were identified correctly] and for GP was 90%. No identification was obtained in only five isolates tested.

Conclusions: The in-house protocol could identified common bacteria directly from the blood samples within 30 minutes. The protocol could reduced the turn-around time at least 24h for bacteria identification in institution's workflow. This rapid method can be used to rapidly, simply, accurately and cost-effectively identify aerobic bacteria from positive blood cultures meeting the demand for rapid diagnostics tests.

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Background: Climatic factors\(^1\, 2\) may explain proportions of antimicrobial resistance (AMR) variance across Europe and in the USA. Yet, they showed poorer explanatory strength for regions with higher levels of nurse emigration. The present study investigated the contribution of healthcare workforce density to AMR variance explanation in Europe.

Materials/methods: A 30-country database observational study was conducted. The six-year prevalence of carbapenem-resistant gram-negatives (CRGN; \textit{Pseudomonas aeruginosa}, \textit{Escherichia coli}, \textit{Klebsiella pneumoniae}, and \textit{Acinetobacter} spp.) was determined using published data\(^3\). Furthermore, we calculated the fluoroquinolone (FRGN) and aminoglycoside (NRGN) resistance prevalence in these same species in addition to methicillin-resistant \textit{Staphylococcus aureus} (MRSA) and vancomycin-resistant enterococci (VRE). Multivariate regression analysis was performed to identify associations between \(\log_{10}\) CRGN and healthcare workforce (density of nurses and of physicians), in addition to factors which might confound this association.

Results: We found a significant association of nurse but not physician density with CRGN, in contrast to FRGN, NRGN, MRSA and VRE, explaining 83\% of total variance (multivariate model). Nurse-density had a higher contribution to variance explanation than outpatient antimicrobial use (DDD). This association was not confirmed in countries with an established gate-keeping role of primary care specialists. In countries without gate-keeping, nurse-density was a significant explanatory factor of CRGN variance, contributing 72\% to total variance explanation. Using these models, we estimated the influence of nurse graduation figures on CRGN in 29 countries.

Conclusions: This study contributes to the AMR debate by identifying a potential association between nurse-density and CRGN. Statistical observation might be supported by survey data on health workers’ attitudes, which identified nurses and associates as the professionals most likely to perform hand hygiene\(^4\). Including nurses in future AMR policies is most beneficial in countries without a gate-keeping system. The findings are especially relevant, since nurses are largely missing in the EU Commission’s action plan on AMR\(^5\).

\(^1\)Kaba et al., \textit{IJHEH}, 2020, 223: 151-158.
\(^2\)Kaba et al., 29th ECCMID, Amsterdam, 2019.
\(^3\)ECDC Surveillance Atlas of Infectious Diseases, 2016.
\(^4\)Survey of healthcare workers’ knowledge, attitudes and behaviour on antibiotics, antibiotic use and antibiotic resistance in the EU/EEA, ECDC, 2019.
\(^5\)A European One Health Action Plan against Antimicrobial Resistance (AMR), 2017.

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Abstract 5008

**Exploring minocycline pharmacodynamics against *Acinetobacter baumannii* and *Staphylococcus aureus* in a lung model in neutropenic mice: clinical implications on optimal dosing regimens**

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**Background:** The emergence of multi-drug resistance has increased the interest on neglected and disused antibiotics like minocycline. Given the lack of knowledge on minocycline pharmacokinetics (PK) and pharmacodynamics (PD), we determined the PK/PD of minocycline in a lung infection model in neutropenic mice and bridged these data with human PK to optimise dosing regimens.

**Materials/methods:** Neutropenic mice were intranasally challenged with *A. baumannii* or *S. aureus* strains. Treatment was started 2h after infection and continued for 24h. PK was determined for 4 subcutaneous doses of 1-64 mg/kg using a validated liquid chromatography mass spectrometry method. PD studies of minocycline administered 0.5-64 mg/kg every 6h (q6h) were performed against 4 *A. baumannii* or 4 *S. aureus* strains. Mice were euthanized 24h after start of treatment and CFUs in lung homogenates were counted. Area under concentration-time curve (AUC) over MIC ratios to reach 1-log10 kill were estimated and the target attainment for 100, 200 and 300 mg q12h dosing regimens attaining a mean±SD AUC0-24 of 72±53, 183±33, 292±25 mg*h/L, respectively in patients was used in Monte Carlo Simulations (Fagan et al. Stroke 2010).

**Results:** Mean±SD AUC0-24/MIC ratio of minocycline resulting in 1-log10 killing at q6h dosing was 43.8±8.5 and 16.5±3.7 for *A. baumannii* and *S. aureus*, respectively. For *A. baumannii* this target was attained in >95% of cases for isolates with MICs ≤0.25, 0.5-2 and 4 mg/L with the 100, 200 and 300 mg q12h dosing regimen, respectively (Figure). For strains with MIC ≥8 mg/L, doses >300 mg are required. For *S. aureus*, >95% target attainment was reached for isolates with MICs ≤1, 2-4 and 8 mg/L with the 100, 200 and 300 mg q12h dosing regimen, respectively (Figure). Doses >300 mg are required for strains with MIC ≥16 mg/L.

**Conclusions:** The standard dose minocycline is sufficient to attain the PK/PD target for wild type *S. aureus* (MICs ≤0.25 mg/L). In contrast, for wild type *A. baumannii* (MICs 0.5-16 mg/L), the standard dosing regimen minocycline is not sufficient to attain the PK/PD target. Higher doses up to 300 mg are needed for *A. baumannii* strains with MICs up to 4 mg/L.

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Abstract 5009

Pharmacokinetic variability and target attainment of fluconazole in critically ill patients

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Background: Fluconazole is an antifungal drug frequently used in the intensive care unit (ICU) but few data are available regarding its exposure in this population. A subanalysis of the DALI-study raised some concerns considering variability in exposure and inadequate target attainment in critically ill patients. We aimed to determine fluconazole variability and target attainment at the ICU.

Materials/methods: All adult, critically ill patients treated with intravenous fluconazole between May and September 2019 were included, provided that the DNR code was <2 and written informed consent was obtained. The administered dose was left at the discretion of the treating clinician. Trough samples were collected during a maximum period of 15 days. Samples were analysed using an UPLC-DAD analytic method. The intra-and intersubject variability of fluconazole trough concentrations was calculated by dividing the standard deviation by the mean*100. Moreover, the difference between the maximum and minimum fluconazole concentration within each patients was determined. For target attainment, the fAUC/MIC from clinical data amounts to 100 corresponding with trough levels >10-15 mg/L, as recommended by EUCAST and ECIL-6. The limit for toxicity was set on 50 mg/L.

Results: Seventeen patients were included, resulting in 95 fluconazole trough levels. Patients had a median APACHE-II score of 18 [16-23] and administered dose of 5.1 [4.1-7.5] mg/kg/day. The median fluconazole trough level was 26.6 [19.7-35.3] mg/L. In Figure 1, fluconazole trough concentrations are depicted in function of the dose. The mean intra-and intersubject variability (CV%) were 18,4% and 34,5%, respectively. The median difference between the maximum and minimum concentration for the 14 patients with >1 measured fluconazole level, was 14,8 [6,6-18,9] mg/L. In two patients, this difference was more than 2-fold. All trough levels were >10mg/L and 85/95 (89%) samples were >15mg/L. None of the levels exceeded the upper limit of 50 mg/L.

Conclusions: As shown in the DALI-study, a considerable intra-and intersubject variability in fluconazole levels was observed at the ICU. Despite this variability, all fluconazole trough levels were above the lower limit of 10 mg/L and most of them >15 mg/L. No toxic concentrations were observed.

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Enterovirus surveillance in an Italian paediatric hospital

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Background: Human Enteroviruses (EVs) are classified into four groups (A-B-C-D) including polioviruses and non-polioviruses. EVs are ubiquitous and a common cause of self-limiting febrile, gastroenteric or respiratory illnesses. Some EV genotypes are also responsible for serious diseases; in infants and young children. EVs can cause meningoencephalitis, paralyis, myocarditis, sepsis-like syndrome, respiratory disease and acute hepatitis. Since EV can be neurotropic and responsible for severe infections, it is necessary to monitor and to genotype it in order to correlate the EV types to the different clinical manifestations.

The aim of the study is EV surveillance to identify genotypes associated with more severe conditions, to confirm the absence of circulation and importation of the poliovirus, to monitor their molecular epidemiology and distribution and to facilitate a correct patient management.

Materials/methods: Since January 2018, we have been collecting positive samples for EV from patients admitted to the Bambino Gesù Children’s Hospital in Rome [Italy]. Up to now, sequencing part of the VP1 capsid protein gene of EV according to WHO recommendations, we have genotyped 45 Enteroviruses from: 15 cerebrospinal fluid, 14 plasma, 12 respiratory, 3 stool and 1 skin swab samples. Samples were collected from 40 children mostly younger than 1 year old [30/40].

Results: In our population, we have genotyped 20 echoviruses [6, 7, 9, 11, 18, 20, 25, 30], 14 coxsackieviruses [A6, A9, A16, B1, B2, B4, B5] and 6 enteroviruses [A71 and D68]. In particular, in patients younger than 1 year old [18/30] had meningeal symptoms attributable to echoviruses [7, 9, 11, 18, 20, 25 and 30], coxsackieviruses [A9, B4 and B5] and Enterovirus A71. Patients older than 1 year old [10/40] had mostly respiratory infections [8/10]. Only one of these patients [6 years old] had a diagnosis of meningitis due to Echovirus 6.

Conclusions: From these initial results, no epidemic outbreaks due to EV was found. With few exceptions, genotype detected were consistent with symptomatology reported on literature data. We hope that a greater number of typed EVs, will allow to establish an etiological correlation with the pathology for those genotypes for which it has not yet been described.

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Abstract 5013

Melioidosis in an Indian intensive care unit: the enigma of a ‘Silent Killer’

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Background: Melioidosis is a neglected tropical disease in India and accounts for 2-5% of all patients admitted with Community-acquired sepsis. Recent modeling on the global distribution of melioidosis predicted India to have the highest burden of the disease with an incidence of 52506 cases per year. A study from Thailand found 74% of patients undergoing sepsis (SOFA≥2), with melioidosis being the second most common cause of infection. We undertook the study to determine the clinical characteristics and outcome of patients with severe melioidosis undergone sepsis.

Materials/methods: A prospective ICU based observational study from January 2014 to November 2017 was conducted in a tertiary care hospital in India. Patients diagnosed with culture confirmed melioidosis admitted to the ICU with SOFA score >2 were recruited in the study. Comparisons of continuous variables between survivors and nonsurvivors were performed using the Mann-Whitney U test. Categorical variables were compared using χ² test or Fisher Exact Test.

Results: Forty-one adult ICU patients with microbiologically documented melioidosis were included in the study. Mean age was 51.2 ± 15.2 years with male predominance (4:1). 18 (43.9%) of the cases were associated with occupation related to soil contact. Majority of the patients were bacteremic (30/41; 73.2%) having a median Pitt Bactermia score of 3 (1-5). Pneumonia was the most common presentation (25/42; 61%) with a median CURB 65 score of 2 (1-4). 19 (46.3%) of the patients underwent Acute Kidney Injury and 8 (19.5%) were in septic shock. 5 (12.1%) patients underwent organ failure with median of 2 organ dysfunction. 31 (75.6%) of the cases had Type 2 Diabetes Mellitus. Median APACHE II score was 19.5 (14-26). The overall mortality was 29.3%. The median ICU length of stay for survivors and non survivors was 6 days and 5 days, respectively. Organ failure (OR 26.5; CI 3.8- 183.7, p<0.001) and Pitt Bacteremia score >4 (OR 2.8; CI: 1.0-7.8, p=0.03) were significant risk factors associated with mortality.

Conclusions: Death being predicted by organ dysfunction and higher PITT Bacteremia score signifies the poor outcome of melioidosis patients undergone sepsis. An earlier and rapid diagnosis of the disease to avoid systemic involvement is a requisite.

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Mycobiome sequencing reveals a high fungal diversity in patients with severe atopic dermatitis

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Background: Atopic dermatitis (AD) is a multifactorial, chronically relapsing inflammatory skin disease. Characteristics are an impaired skin barrier and an altered skin immune system, which often come along with predominant colonization by Staphylococcus aureus. The role of fungi, i.e. the mycobiome, remains poorly investigated although AD patients are frequently sensitized to Malassezia, the most abundant fungus on skin. We aim to improve the understanding of the skin mycobiome in AD.

Materials/methods: Skin swabs of 11 AD patients and 11 healthy controls (HC) were taken from 4 skin sites (antecubital crease, glabella, vertex, and dorsal neck). To assess temporal shifts in the mycobiome, AD patients were sampled at 3 time points (0, 2 and 4 weeks). HC were sampled at 2 time points (0 and 4 weeks). We assessed the relative abundance of fungal genera and species by amplicon-based next-generation sequencing (NGS) of the fungal ITS1 region.

Results: The most abundant fungi at all skin sites were Malassezia spp. The species distribution was site-dependent with high abundances of M. globosa at the neck, M. restricta at the glabella and vertex, and overall lower abundance of Malassezia at the antecubital crease. As shown exemplary for the neck (figure 1), patients with severe AD tended to be more frequently colonized with non-Malassezia fungi such as Candida. In most HCs and patients with mild to moderate AD, the mycobiome was comparable between individuals and stable over time. In contrast, in severe AD the mycobiome was different between individuals and changed over time.

Conclusions: Patients with severe AD had a high intra- and interpersonal species diversity. We speculate that the impaired skin barrier in severe AD allows colonization with more different fungi than healthy skin. Vice versa, the altered mycobiome may cause activation of the skin immune system leading to inflammation and eczema. In the next step, we will correlate these results with the bacterial microbiome in the same samples.

Figure 1: Relative abundances of fungal taxa in swabs collected from the neck in a) severe AD, b) mild to moderate AD, and c) HCs. t1: day 0; t2: day 14; t3: day 28

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Human parechovirus 3 “outbreak” at a tertiary hospital

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Background: Human parechoviruses (HPeV) remain as one of the most prevalent pathogens causing fever without a source, sepsis-like illness and meningitis/encephalitis in neonates and children under 3 months of age. Most of these cases are caused by HPeV3. The objective of this study was to describe a limited outbreak of the HPeV3 infections in our sanitary area attending a pediatric population of 55000.

Materials/methods: HPeV detection was conducted on SmartCycler® with a Progenie-Molecular® assay and the positive samples were sent to Instituto de Salud Carlos III for further typing by VP3/VP1 sequencing. We reviewed the clinical records in search of clinical manifestations and biochemical findings and antibiotic prescriptions.

Results: We identified 9 HPeV-positive patients between May and July 2019. All HPeV were typed as HPeV3. Mean age was 242 days, but the median was 51 days. The most frequent sample where HPeV3 was detected was whole blood (7), followed by nasopharyngeal swab (6), feces (4) and cerebrospinal fluid (CSF) (3). Eight children were diagnosed of fever without source, only two of them had leukocytosis (> 10000/µl) and an elevated plasmatic reactive protein C (>5 mg/L). None of them received antibiotic treatment. One of these patients presented a macular rash. None of them developed neurological symptoms during the acute illness or to the present day. One patient was diagnosed of clinical sepsis and received antibiotic therapy, but it was suspended shortly after obtaining the HPeV3 positive result. None of these nine patients had any other microbiological findings during the episode.

The CSF-biochemistry of the 3 patients with positive CSF samples was anodyne with no alterations at the leukocyte count or protein levels.

Conclusions: Almost half of the patients of our study were older than 3 months, the usual risk group to get HPeV3 infections. In our study whole blood seems to be an adequate sample for detecting HPeV3. HPeV3 detection at CSF can’t be ruled out even without biochemical alterations. The short span of time in which all cases appeared and the lack of other cases during the rest of this year cases suggest an epidemiological relationship between these cases.

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Abstract 5017

Fibronectin binding protein plays pivotal role in development of central nervous system complication of *Staphylococcus aureus* bacteremia

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**Background:** Central nervous system complications (CNS-C) in patients with *Staphylococcus aureus* bacteremia (SAB) are one of the most serious complications. Until recently, no microbiologic factors related to CNS-C have been known. The purpose of this study was to explore the microbiologic factors associated with CNS-C in SAB.

**Materials/methods:** Clinical isolates and their clinical data of SAB in four university-affiliated hospitals were collected. CNS-C were defined as any of multiple embolic infarctions, intracranial hemorrhage, or meningitis. Control cases without CNS-C were matched to the cases according to the methicillin susceptibilities, site of infection, and severity defined by SOFA score. All cases and control patients underwent the brain magnetic resonance imaging or computed tomography. We performed the polymerase chain reaction to detect virulence factors, sequencing of fibronectin binding protein A (fnbpA) to find single nucleotide polymorphisms (SNP), and multilocus sequence type analysis.

**Results:** A total of 1087 cases of SAB were occurred during the study period during 5 years. CNS-C occurred in 43 patients (4.0%). Embolic infarction accounted for 23 cases, intracranial hemorrhage, for 8 cases, and both lesions were present in 12 cases. Of these cases, experimental study was performed using 22 isolates that were stored, with isolates of their matched control cases. FnbpA was significantly higher in isolates from CNS-C, whereas fibronectin binding protein B (fnbpB) was associated with lower incidence of CNS-C. Other virulence factors did not significantly differ between two groups. In the SNP analysis of fnbpA, K786N mutation significantly increased the incidence of CNS-C. CC5 and CC30 strains were significantly associated with CNS-C, and CC30 with variant fnbpA had a high rate of CNS-C.

**Conclusions:** The presence of fnbpB was negatively associated with CNS-C in SAB. However, the presence of fnbpA was associated with CNS-C of SAB. Moreover, genetic variation in fnbpA raise the risk of CNS-C in SAB.

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Abstract 5018

The use of carbapenemase real-time PCR directly from rectal swab for control carbapenem-resistant Enterobacteriaceae cross-transmission in a kidney transplant ward

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Abstract third-party references: Conselho Nacional de Desenvolvimento Científico e Tecnológico

Background: Infection by Carbapenem resistant Enterobacteriaceae (CRE) is a great concern among solid organ transplant recipients. CRE colonization is the main risk described for CRE infections in this population.

The aim of this study was to analyze the impact of the introduction a CRE-surveillance based on real-time PCR for carbapenemases in a kidney transplant ward.

Materials/methods: We observed an increase on cases of CRE-acquisition related to KT-ward stay in the second semester-2018 (Figure). The strategies for CRE control adopted in this unit before and during intervention period were: CRE surveillance through rectal swab culture (SC) at admission and on a weekly basis; CRE-colonized patients cohorting; periodical staff training for hand-hygiene (HH), and monthly report consumption of alcohol-based hand sanitizer. The intervention occurred from March-2019 to October-2019 and consisted on collected second rectal swab during weekly surveillance. We tested in this swab carbapenemases genes (\textit{bla}\textsubscript{KPC}, \textit{bla}\textsubscript{NDM}, \textit{bla}\textsubscript{VIM} and \textit{bla}\textsubscript{IMIP}) by real-time PCR directly from swab. The results were available in the same day and patients with positive results were put on contact precaution. We analyzed the correlation between tests (real-time PCR and SC) through Kappa test, and the evolution of rates during the time through chi-square for trend.

Results: A total of 257 patients collected 518 paired SC (PCR and culture) for CRE during study period. Positivity rate of cultures was 13.2%, 34 patients. Eleven patients (11/34-32.4%) had CRE also isolated in clinical cultures, among those, 8 (8/34-23.5%) developed infection. The number of patients with positive RT-PCR in rectal swab was 46 (16.7%). Fourteen patients (14/46 – 30.4%) had positive PCR and negatives surveillance/clinical cultures. The tests agreed (PCR and SC) on 90.3%, Kappa coefficient of 0.60. The most common CRE isolated was \textit{K. pneumoniae} 85.3% [29/34] and the most common carbapenemase was \textit{bla}\textsubscript{KPC}, 80.4% [37/46].

We observed a progressive decrease on positivity rate of patients who the acquisition of CRE was related to KT ward stay (Figure) from 15.0% to 4.9% (p=0.05), the unit colonization pressure rate also decreased from 24.0% to 12.2% (P=NS) during study period.

Conclusions: Surveillance culture through real-time PCR could be an additional strategy for CRE control.

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West Nile virus 2018 season in Italy: rapid spreading of West Nile neuroinvasive disease in northwest Italy

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Background: In Italy, results from the integrated-One-HEALTH-surveillance system reported, for the year 2018, 230 West Nile neuroinvasive disease (WNND) which are equivalent to 40% of all West Nile virus (WNV) notified, with 42 deaths (18%). It is a significant higher number of WNND compared to the previous period from 2008 to 2017 (231 cases in 9 years). The majority of WNND cases occurred in Northern areas along the Po river. We report results of the human WNV surveillance in Piedmont, North-West Italy, an area crossed by the Po river (4.424 million inhabitants) where the vector, mosquito Culex spp., is widespread. The first human case was notified by the regional Reference Laboratory, Amedeo di Savoia Hospital, Torin on July, 27 (50 days after the first Italian case in Rovigo, Italy North-East).

Materials/methods: From the 1st of June to 30th November 2018, 216 patients were studied with molecular methods for WNV-RNA detection in plasma, urine and cerebrospinal fluid (CSF) when available, (ELITechGroup, Italy), serology for WNV IgG and IgM (Euroimmun AG, Lubek, Germany), and confirmation with Plaque Reduction Neutralization Tests (PRNT).

Results: Autochthonous WNV infection was identified in 61 patients (28%, 54 confirmed and 7 probable cases). WNND was present in 41 patients (67%), West Nile fever (WNF) in 12 (19,7 %); 8 were symptom-less. The most frequent condition in WNND was encephalitis and/or meningitis/encephalitis (30 patients, 73%); 3 patients died (7.3%). Comorbidities were present in 29% of patients with WNND. RT-PCR identified WNV in 26 patients with WNND: in urine and/or plasma (24 patients), some of them with a prolonged viraemia and/or viruria (until 26-28 days); CSF was positive in 7. In the remaining patients WNV infection was confirmed by serology.

Conclusions: According to the 2018 season in Europe, we confirmed the early start of WNV season in North-West Italy and the rapid spread of WNND along the Po river valley, with an unusual high number of WNND that support a strict integrated One-HEALTH-surveillance system to predict areas and periods at risk of WNV outbreaks. Further studies are required to better understand genetic and viral determinants for WNND in naïve patients.

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The resistance ratchet tightens: widespread penicillin-binding protein-3 insensitivity in carbapenemase-producing Escherichia coli

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Background: It is widely accepted that β-lactam resistance among Enterobacterales predominantly involves β-lactamases whereas resistance in Gram-positive bacteria predominantly reflects target Penicillin-Binding Protein (PBP) modification. Recent reports of PBP-3 changes in carbapenemase-producing E. coli [CPE. coli] challenge this dogma, but prevalence is unclear.

Materials/methods: Whole Genome Sequencing (WGS, by Illumina HiSeq 2500) was performed for CPE. coli submitted to PHE from Jan-2013 to Oct-2016: 97% were submitted between Jan-2014 to June-2016, when WGS was performed on CPE. coli from every new patient. Data were analysed for MLST type, resistance genes and pbp3 sequence using in-house tools. MICs were determined by BSAC agar dilution.

Results: Among 816 CPE. coli referred, from 58 hospitals, 121 (14.8%) had a 12-bp insert leading to insertion of 4-amino acid sequences in the turn between the β2b–β2c sheets of PBP-3: 110 had YRIN, 7 YRIK, 3 YRIP and 1 YTIN. Inserts were found in 67/276 (24.3%) isolates with blaNDM, 43/433 (9.9%) with blaOXA-48-like, 5/20 (25%) with both blaOXA-48-like and blaNDM, 4/68 (5.9%) with blaKPC, 1/1 with both blaOXA-48-like and blaKPC, 1/11 (9.1%) with blaVIM, but 0/3 with blaIMP and 0/3 with blaGES. Among 72 (67+5) insert-positive isolates with NDM, 44 had NDM-5 and 12 had NDM-7; among 49 (43+6) with OXA-48-like, 30 had OXA-181. Classical NDM-1 and OXA-48 dominated among insert-negative isolates. Isolates with inserts belonged to 36 STs, with ST410 (n=20, 16.5%), ST167 (n=12, 9.9%), ST940 (n=8, 6.6%) prominent. MICs that were stable to the carbapenemase produced and protected against co-produced ESBLs with avibactam, were raised for insert-positive isolates, illustrated by geometric means [tabulated].

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Geometric mean MIC, mg/l (n, no. tested)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OXA-48-like</td>
</tr>
<tr>
<td>Ceftazidime/avibactam</td>
<td></td>
</tr>
<tr>
<td>Insert-positive</td>
<td>1.22 (n=14)</td>
</tr>
<tr>
<td>Insert-negative</td>
<td>0.38 (n=80)</td>
</tr>
<tr>
<td>Aztreonam/avibactam</td>
<td></td>
</tr>
<tr>
<td>Insert-positive</td>
<td>1.59 (n=9)</td>
</tr>
<tr>
<td>Insert-negative</td>
<td>0.47 (n=11)</td>
</tr>
</tbody>
</table>

Conclusions: The wide distribution of these inserts in E. coli PBP-3, and their association with particular carbapenemases (NDM-5, -7 and OXA-181), not particular STs, is striking, as is the association with reduced susceptibility to PBP3-targeted antibiotics. The prevalence and cumulative effect of these mechanisms needs surveillance, for they have the potential to compromise otherwise promising agents.

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Abstract 5022

Cefazolin meningeal diffusion compared to cloxacillin for the treatment of methicillin-susceptible Staphylococcus meningitis

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Abstract third-party references: On behalf of NAMAP study group

Background: Cefazolin is not recommended for the treatment of methicillin-susceptible Staphylococcus (MSS) meningitis contrary to anti-staphylococcal penicillins. However, the data supporting these recommendations are limited. The main objective of the study was to assess the meningeal diffusion of cefazolin and cloxacillin in patients treated for MSS meningitis.

Materials/methods: Patients with cerebrospinal fluid (CSF) concentrations of cefazolin or cloxacillin measured at a French University Hospital between January 2009 and October 2019 were retrospectively identified. Patients with proven MSS meningitis defined by a positive culture of CSF (at least two samples in case of coagulase-negative staphylococci) and/or a polymerase chain reaction (PCR) in CSF were included. Medical charts were retrospectively reviewed. Concentrations were measured in CSF and plasma using a liquid-chromatography coupled with mass-spectrometry assay. Bacterial antibiotic susceptibilities were determined using a Vitek 2 automated system (bioMérieux, France). CSF concentrations were analyzed with respect to the latest ECOFF values for cefazolin (≤ 2 mg/L) and cloxacillin (≤ 0.5 mg/L).

Results: Among the 18 included patients, 8 (44%) received cefazolin and 10 (52%) cloxacillin. Median daily dosages of cefazolin and cloxacillin were 8 (range 6-12) and 12 (range 10-13) grams respectively. All patients received continuous infusion. All plasma samples were collected on steady state. Twelve patients (67%) were males, median [IQR] age was 60 years [51;71], 14 (83%) had post-operative meningitis and 4 (22%) hematomatous meningitis. Median [IQR] antibiotic CSF concentration was 2.8 mg/L [2.1;3.8] and 0.7 mg/L [0.5;1.7] for cefazolin and cloxacillin respectively. CSF concentration of antibiotic was above ECOFF in 11/14 (79%) samples corresponding to 6/8 [75%] patients receiving cefazolin and 10/13 [77%] samples corresponding to 7/10 [70%] patients receiving cloxacillin. Median [IQR] CSF/plasma ratio was 4.3% [2.9;8.4] for cefazolin and 1.8% [1.7;2.2] for cloxacillin. Cefazolin was discontinued in 3 (30%) patients because of failure or under dosing and antibiotic therapy was switched. All patients in both groups were cured without any recurrence.

Conclusions: In patients treated for staphylococcal meningitis cefazolin appeared as satisfying as regarding the level of CSF diffusion. Treatment failure was only observed in cloxacillin group. Cefazolin should be prospectively evaluated in this indication.

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Epidemiological typing of Neisseria gonorrhoeae with whole genome sequencing: a vital supplement in transmission surveillance

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Background: Neisseria gonorrhoeae remains a global public health concern. While traditional methods for epidemiological typing of N. gonorrhoeae are suboptimal, whole-genome sequencing (WGS) offers ultimate discriminatory power in bacterial genotyping. Hence, this study aimed to assess the potential of N. gonorrhoeae genotyping as a tool in transmission surveillance.

Materials/methods: Forty-seven isolates from 35 patients enrolled in 17 suspected epidemiological linkages were investigated using whole-genome sequencing, as well as serogroup and serovar determination. The genetic relationship of the isolates was analyzed by N. gonorrhoeae multi-antigen sequence typing (NG-MAST), multi-locus sequence typing (MLST), core-genome MLST (cgMLST) and single nucleotide polymorphisms (SNPs) using the 1928D platform. Determination of SNPs was performed on isolates belonging to the two dominating sequence types (STs).

Results: Among the 47 isolates, 24 isolates were categorized into 13 NG-MAST genogroups and 23 isolates had novel types. Fifteen different STs were detected by MLST. ST9363 and ST8156 were predominant and accounted for 40.4% of all isolates. The combination of a novel NG-MAST (porB 2999, tbpB 267) and ST9363 was the most common type, identified in seven isolates from six patients belonging to four epidemiological linkages. The second most common combination was NG-MAST S441 with ST8156. In the cgMLST, >98% of the core genes were identified in all isolates. Of 13 epidemiological linkages, at least two isolates in each linkage were found to be strongly genetically related with the same MLST and 0-1 allelic differences with cgMLST. cgMLST also suggested five transmission events including two outbreaks with 0-4 differed alleles, where epidemiological data will be further investigated. SNP analyses revealed that four ST8156 cases in December 2018 to February 2019, were strongly genetically related (1-4 SNPs), in accordance to the cgMLST results. Only in nine epidemiologic linkages, grouping of isolates with serovar were concordant with grouping by sequence types.

Conclusions: WGS-based typing method provides a useful tool in epidemiological typing of N. gonorrhoeae. However, when selecting a typing method, it is essential to consider the epidemiological context and the question that the genomic data should answer. Therefore, genomic investigation should be used to supplement, rather than replace, careful epidemiologic investigation.

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Abstract 5028

Acquired resistance to fosfomycin through acquisition of an ISEcp1-blaCTX-M-14 tandem in a Klebsiella pneumoniae clinical isolate

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Background: Acquired resistance to fosfomycin in Gram-negative bacteria may occur through chromosomal mutations or acquisition of genes encoding FosA-like enzymes that inactivate fosfomycin. Despite having a natural $\text{fosA}$ gene in its chromosome, Klebsiella pneumoniae isolates remain susceptible to fosfomycin, suggesting a low-level of expression of this gene in normal conditions. Our study aimed to decipher the genetic basis of fosfomycin resistance acquisition in a K. pneumoniae isolate recovered in Switzerland in 2017.

Materials/methods: The fosfomycin-resistant K. pneumoniae isolate with no known mechanism identified was submitted to whole genome sequencing and the resistome was studied using the CARD and ResFinder databases. Minimal inhibitory concentration (MIC) of fosfomycin was determined by agar dilution. Gene expression assays were performed by RT-qPCR. Cloning experiments were done using the plasmid pBADb carrying an L-arabinose inducible promoter.

Results: Isolate S54 presented an MIC of fosfomycin at 2,048 mg/L that dropped to 128 mg/L when phosphonoformate was added, suggesting the production of a glutathion-S-transferase. ResFinder and CARD databases did not identify any acquired fosfomycin resistance genes except the natural chromosomal $\text{fosA}$ gene. In-silico analyses identified an ISEcp1-bla-CTX-M-14 cassette inserted upstream of the natural $\text{fosA}$ gene providing a -35 box forming a novel hybrid promoter for $\text{fosA}$ expression. Once cloned in E. coli, the $\text{fosA}$ gene with this chimeric promoter had an MIC of fosfomycin at 2,048 mg/L, while the same construct but with a wild-type promoter was only at 128 mg/L. Quantitative expression experiments showed an overexpression of the $\text{fosA}$ gene of 340-fold between the two constructs.

Conclusions: We report here the acquisition of fosfomycin resistance by the acquisition of a strong hybrid promoter brought by the acquisition of an ISEcp1-bla-CTX-M-14 cassette. Hence, our study showed that acquired resistance to both cephalosporins and fosfomycin may occur through a single genetic event in K. pneumoniae.

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Impact of letermovir (LTV) on utilisation of pre-emptive therapy for cytomegalovirus after allogeneic haematopoietic cell transplantation: a single-centre experience

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Abstract 5029

**Background:** Quantitation of antiviral utilization using Pre-emptive therapy (PET) strategy for CMV is important for assessing the net value of preventive strategies. We examined a contemporary cohort managed by PET to 1) quantify CMV antiviral utilization and 2) report readmissions related to CMV and 3) report net changes in PET days after Letermovir prophylaxis.

**Materials/methods:** Retrospective review of adult, CMV R+ HCT recipients of first peripheral blood or marrow HCT from 3/2013 to 12/2017 managed by PET (PET-group) and from 12/2017 to 12/2018 who received Letermovir prophylaxis (LTV-group). Ex vivo T-cell depletion (TCD) or unmodified graft from mismatched donors defined high CMV risk (HR). All others were low risk (LR); Routine monitoring was performed by CMV quantitative PCR assay. PET was initiated per standard of care. Clinical characteristics, PET and readmission through Day 180 were extracted from the electronic medical records/databases. Inpatient charges were obtained from the Vizient database and converted to adjusted costs using cost-to-charge ratio, wage index and inflation rate.

**Results:** PET group comprised 368 R+ recipients (HR 52%). Overall, 208 (57%) patients initiated PET (Figure 1a) at median of 35 days; Interquartile range (IQR): 28-41 post HCT for a median duration of 47 days (IQR:34-70) (Figure 1b). Of 11,759 total antiviral-days 8,943 (76%) were (val)Ganciclovir and 2816 (24%) Foscarnet; 80% of antiviral-days occurred <D100 and 18% were administered in-patient. 112/208 (54%) PET recipients were readmitted compared to 53/160 (33%) of No-PET recipients (p=0.00005). Of 180 readmissions among PET recipients 67 (37%) were CMV-related with an average total cost of $185,053; standard deviation (237,099). Of 98 patients in the LTV group, 5 (5.1%) received PET (figure 1c). PET utilization by D100 was compared to 95 patients that received HCT during 2017 and managed preemptively (No LTV-group). Clinical characteristics were similar between the two groups. There was a 96% reduction in total PET-days in 2018 (LTV-group compared with 2017 no-LTV group) (figure 1d).

**Conclusions:** 1) 80% of PET-days occurred before D100. 2) CMV-related readmissions cost an average $185,053 USD per patient. 3) Implementation of LTV prophylaxis resulted in a 96% reduction in total PET days by D100 post HCT.
Abstract 5032

Escherichia coli serotype O55:H9 as a new multidrug resistant hybrid pathotype producing Shiga toxin and carrying extra-intestinal virulence plasmid

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Background: Enterohemorrhagic Escherichia coli (EHEC) are major food-borne pathogens responsible for gastrointestinal diseases which can be complicated by hemolytic uremic syndrome (HUS), first cause of acute renal failure in children. The multi-drug resistant O80 EHEC clone (ST301, fimH54) has recently emerged in Europe. It can be considered as a hybrid pathotype involved in HUS but also in extra-intestinal invasive infections potentially due to the presence of an additional virulence plasmid similar to pS88 involved in neonatal meningitis. In this study, we aim to know if such hybrid pathotype are restricted or not to O80 serogroup.

Materials/methods: To analyze the prevalence and the diversity of hybrid pathotype within the non-O80 EHEC serogroups of the French Reference National Center collection (2014-2018), we evaluated the presence of pS88 by multiplex PCR and characterized strains of interest by whole-genome sequencing (Illumina).

Results: We identified the serotype O55:H9 as another hybrid pathotype combining intestinal and extra-intestinal virulence factors characteristic of pS88. During the studied period, we identified 20 O55:H9 strains isolated from HUS cases (n=15), patients with diarrhea (n=3) or asymptomatic carriers among HUS entourage (n=2). No invasive infections were observed among these 20 cases. All strains carry Stx2 subtype (45% of Stx2d and 55% of Stx2a). A pS88-like plasmid is present in 95% of cases (n=19/20) harboring all characteristic genes except for one strain. Finally, the O55:H9 serotype appears to be phylogenetically closely related to O80 clonal group sharing the same ST301, fimH54 and eoe-. However, comparatively to O80 clone, all O55 strains carry the additional iron-uptake system yersiniabactin.

Conclusions: Our study reveals that hybrid pathotype strains combining intestinal and extra-intestinal virulence are not restricted to O80:H2 serotype but shared with O55:H9 serotype. The phylogenetic proximity between these two serotypes suggests a common origin followed by a change in somatic and flagellar loci. O80 and O55 EHEC serogroups, emerging clonal pathogens perfectly equipped to induce HUS and invasive infections, have to be strongly monitored worldwide.

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Abstract 5035

**Klebsiella pneumoniae** type VI secretion system allows the implantation and survival of the pathogen within the intestinal microbiota

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Abstract third-party references: Supported by the Agence Nationale de la Recherche of the French government through the program “Investissements d'Avenir” [16-IDEX-0001 CAP 20-25], EMERGENCE 2018.

**Background:** Intestinal carriage is a significant risk factor for infections in intensive care unit with ~50% of *Klebsiella pneumoniae* infections resulting from patients’ contamination with their own microbiota. An anti-bacterial activity mediated by *K. pneumoniae* type six secretion system (T6SS) was recently highlighted in vitro. This system allows bacterial toxic effectors delivery in either prokaryotic or eukaryotic cells, after cell-to-cell contact. The aim of this study was to better characterize the role of T6SS in *K. pneumoniae* physiopathology and especially during the process of intestinal colonization.

**Materials/methods:** After an *in silico* analysis of T6SS organization clusters in *K. pneumoniae* CH1157 strain, the role of the cluster 1 was evaluated *in vivo* during the process of murine intestinal colonization using an isogenic mutant. The composition of the intestinal microbiota (16S rRNA high-throughput sequencing) of colonized mice was statistically analyzed (DESeq2, Metacoder, and MetagenomeSeq) to determine which bacterial phylia/genus became underrepresented in the presence of wild type versus mutant. In parallel, T6SS-1 expression has been assayed by RT-qPCR under different stress conditions (temperature, pH, bile salts, biofilm).

**Results:** *In silico* analyses reveal the existence of two T6SS-like genomic islands in the genome of *K. pneumoniae* CH1157 isolate, comprising putative elements of pathogenicity. *In vivo* experiments indicate that T6SS-1 promotes *K. pneumoniae* intestinal establishment in the lower part of the gastrointestinal tract. 16S rRNA high-throughput sequencing of the mice intestinal microbiota content confirm the establishment of an intestinal microbiota dysbiosis induces by the T6SS-1 of *K. pneumoniae*. Interestingly, the expression of this gene cluster is negatively correlated to sessile bacterial mode of life.

**Conclusions:** Altogether, these data will provide new insights into the physiopathological process of *K. pneumoniae* infection beginning by the T6SS-1 role into establishment of an intestinal microbiota dysbiosis, allowing the pathogen colonization. Pathogens’ SST6 impairment represents a new strategy for limiting the implantation of opportunistic pathogenic bacteria associated with high antibiotic resistance in part due to biofilm formation capacities.

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Molecular epidemiology of invasive vancomycin-resistant Enterococcus faecium isolates
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Background: Vancomycin-resistant E. faecium (VREfm) have been listed as pathogens with high priority by the World Health Organization due to their high clinical relevance with decreasing therapeutic possibilities. Unfortunately, the VREfm prevalence has increased significantly in the last few years in Europe. In 2017, the percentage of VREfm has ranged between 10-25% in Germany. The resistance-type vanB has been detected more frequently than vanA in E. faecium since 2016.

Materials/methods: 128 invasive E. faecium isolates with vanB-type resistance were collected between 2011 and 2013 as well as between 2017 and 2018 in the University Hospital Essen and in 2018 in the Hospital Nuremberg, Germany. The isolates were characterized with the well-established microbiological methods multilocus sequence typing (MLST) and pulsed-field gel electrophoresis (PFGE).

Results: The 128 VREfm isolates were separated into 15 sequence types (ST) by MLST. All of these ST belong to the Clonal Complex 17, known to be responsible for nosocomial infections worldwide. While ST 117 was the most prevalent ST in Essen (48.2%) and in Nuremberg (36.2%), ST 192 was found solely in Essen between the years 2011 and 2012, accounting for 39.5% of the investigated isolates from Essen. ST 192 has been detected to be the second-most prevalent ST both in Essen and overall. In Nuremberg, the second leading ST was ST 78 with 23.4%. The PFGE divided the isolates included in this study into 68 PFGE types. Two local VREfm outbreaks in the cardiology 2011 and the perinatal center 2017 in the University Hospital in Essen could be confirmed. The PFGE also showed a broad genetic diversity between the VREfm isolates found in the two hospitals but also within different institutions and wards.

Conclusions: The results obtained by MLST confirmed the previously described allocation of ST in Germany. The variety of detected PFGE types might suggest a lower significance of intrahospital transmission of VREfm than expected. It rather indicates that a great part of VREfm-positive patients acquires VREfm and their corresponding PFGE type before hospitalization. More epidemiological studies are necessary to track and compare the intra- and interhospital spread and evolution of the genotypical populations.

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The unexpected stability of Group B Streptococcus clones/serotypes colonising the genitourinary tract of healthy young women

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Background: Group B Streptococcus-GBS is often part of the normal gastrointestinal and genitourinary microbiota. However, it can cause serious neonatal infections, being the leading cause of neonatal mortality worldwide. Moreover, GBS has been increasingly associated with invasive disease in elderly and immunocompromised patients. GBS population structure has been explored mainly from infections and from pregnancy colonization, based on serotype (10 sialic acid-rich capsular polysaccharide variants -CPS) and MLST. In this study we characterized the population structure and stability of GBS population in the genital and urinary tract (UT) of young healthy women.

Materials/methods: Mid-stream urine (U) and vaginal swab (VS) samples were collected from 20 healthy non-pregnant women (age:25-37) with no clinical evidence of UT disorders, and no antibiotic treatment (previous month). Within 2.5 years interval, 10 women provided U and VS second samples. Samples underwent extended culturomic analysis (blood agar and supplemented chromogenic agar/different atmospheric conditions) with colonies identification by MALDI-TOF/MS and presumptive GBS isolates confirmed by dltS gene amplification. Further characterization included MLST and CPS-genotyping.

Results: GBS was detected in 50% of women (10/20). From these donors, only 5 presented GBS in both samples (U+VS), 2 presented only in VS and 3 only in U. A total of 197 GBS isolates were distributed among 6-STs/7-CPS-types: ST2/CPS-V; ST8/CPS-VI; ST10/CPS-II; ST10/CPS-V; ST19/CPS-II; ST28/CPS-II; ST31/CPS-IV. ST10 was the most frequent and presented higher CPS diversity. The hypervirulent strain ST17/CPS-III responsible for the majority of late-onset meningitis cases in neonates was not found; however, it is of note the presence of CPS-V and ST19/CPSIII that have been linked to invasive disease in non-pregnant adults. Interestingly, although GBS colonization fluctuations have been described, the paired samples from the same individuals (U/VS) presented the same clones at both sampling points.

Conclusions: Our study revealed an unexpected GBS-ST/serotype stability over time. It is of note the GBS detection only in U and not in VS in 3 donors, reflecting the need to rethink the current GBS screening procedures in pregnancy. GBS population structure and colonization patterns knowledge are essential to early identify GBS strains changes, and to guide the development of a potential serotype-dependent prophylaxis.

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Respiratory syncytial virus and influenza virus infection in adult primary care patients: association of age with prevalence, diagnostic features and illness course

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Background: Viral respiratory tract infections (RTIs) caused by respiratory syncytial virus (RSV) and influenza virus [influenza] are a major public health problem, especially during winter months. To better target new vaccines and treatments under development, we studied the association of age with prevalence, diagnostic features and illness course for RSV and influenza in adult primary care patients.

Materials/methods: Secondary analysis of observational data on the aetiology, diagnosis and prognosis in adults presenting to primary care with acute cough in 12 European countries [2007-2010] using regression analyses corrected for clustering of patients within countries. Age groups were 18-59 years, 60-74 years, and 75 years and older (75+).

Results: Nasopharyngeal swabs for 144 (4.8%) and 307 (10.2%) out of 3104 patients were polymerase chain reaction (PCR) positive for RSV and influenza, respectively. RSV-prevalence in patients 75+ (8.5%) was twice the prevalence in those under 60 years [4.2%]. Influenza prevalence was not associated with age. For both infections the diagnostic features were neither. For RSV, symptom duration was shorter in patients aged 18-59 years, while it was not associated with age for influenza. The odds of unresolved symptoms after 28 days was associated with age for both viruses, with patients aged 18-59 years at lower risk. Illness deterioration was associated with age for RSV, with patients 75+ at increased risk, but not for influenza (Table 1).

Table 1. Unresolved symptoms after 28 days in adult acute cough patients that tested positive for respiratory syncytial virus (RSV) or influenza virus in primary care.

<table>
<thead>
<tr>
<th></th>
<th>RSV – adjusted OR (95%CI)</th>
<th>Influenza – adjusted OR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RSV</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>N (%)</em></td>
<td><strong>60-74 versus 18-59 years</strong></td>
<td><strong>75 years and older versus 18-59 years</strong></td>
</tr>
<tr>
<td><strong>Cough</strong></td>
<td>17 (14.0)</td>
<td>1.72 [0.66-5.34]</td>
</tr>
<tr>
<td><strong>Shortness of breath</strong></td>
<td>7 (6.0)</td>
<td>2.36 [1.04-5.30]</td>
</tr>
<tr>
<td><strong>Wheezes</strong></td>
<td>4 (6.3)</td>
<td>1.79 [0.76-3.76]</td>
</tr>
<tr>
<td><strong>Runny nose</strong></td>
<td>12 (11.3)</td>
<td><strong>2.44 [1.09-4.48]</strong></td>
</tr>
<tr>
<td><strong>Chest pain</strong></td>
<td>3 (5.2)</td>
<td>1.31 [0.66-2.76]</td>
</tr>
<tr>
<td><strong>Fever</strong></td>
<td>0 (0.0)</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Disturbed sleep</strong></td>
<td>6 (6.9)</td>
<td>1.91 [0.91-3.78]</td>
</tr>
<tr>
<td><strong>Interruption with normal activities or work</strong></td>
<td>8 (5.0)</td>
<td><strong>2.56 [1.08-5.39]</strong></td>
</tr>
<tr>
<td><strong>Illness deterioration</strong></td>
<td>27 (22.1)</td>
<td>1.08 [0.49-2.64]</td>
</tr>
</tbody>
</table>

OR: odds ratio; CI: [bootstrap-based] confidence interval; Numbers printed in bold indicate significance: models accounted for significant covariates (smoking status and presence of other viruses for RSV; gender, history of cardiac comorbidities, influenza vaccination, days coughing prior to consultation, presence of bacteria and presence of other viruses for influenza).

Conclusions: In adults presenting to primary care with acute cough, the diagnostic features of RSV or influenza infection are not associated with age. For RSV both the prevalence and illness course are significantly worse at higher age, for influenza only the illness course is.

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Abstract 5043

**Dynamics of *Staphylococcus aureus* in the hospital environment and in patients: is the environment identified as a reservoir?**

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**Background:** *Staphylococcus aureus* is a well-known colonizer of humans, but also an important pathogen. Little is known about the dynamics of methicillin sensitive *Staphylococcus aureus* (MSSA) in the hospital’s innate environment in relation to patient colonization. Therefore, we performed staphylococcal protein A (spa) typing of isolates from patients and the hospital environment to determine dynamics.

**Materials/methods:** Environmental samples were taken at 14 moments in a 16-month period from an old and a newly-constructed hospital. Each moment, 306 locations (e.g. nightstands) in 40 patient rooms were sampled. From January 2018 until August 2019, adult patients admitted to specific wards with an expected stay of ≥48 hours were asked to participate. Nasal swabs were obtained at admission and discharge. All samples were cultured for MSSA. Environmental samples were selected for spa typing when multiple locations in one room were positive at one moment or when one location was positive over time. Patient samples were selected for spa typing when patients were linked to MSSA-positive rooms.

**Results:** 116 out of 4082 (2.8%) environmental samples revealed MSSA. Admission and discharge cultures were taken from 690 patients. 121 patients (17.5%) were positive at admission and discharge, 64 (9.3%) were only MSSA positive at admission, and 16 (2.3%) acquired MSSA. Spa typing was performed on 74 environmental- and 36 patient samples. MSSA from multiple positive locations in one room at one moment had identical spa types. Samples from locations positive over time had different spa types. MSSA strains identified in patients were identical at admission and discharge, except for one patient. No transmissions from environment to patients or vice versa were observed. Most prevalent spa types from patients and environment were t026 (13.1%), 1012 (8.2%) and t091 (8.2%).

**Conclusions:** Based on the results, no transmission from patients to environment or vice versa is observed, although the change in MSSA type in one patient suggests this. However, since we were unable to sample all patients and rooms, possible transmissions may have been missed. Analysis of all environmental and patient isolates using additional typing methods with higher resolution is necessary for a further understanding of MSSA dynamics.

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Evaluation of the Sepsis Flow Chip kit for the molecular diagnosis of bloodstream infections

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Background: Bloodstream infections (BSI) are a major cause of death with increasing incidence and severity. Blood cultures remain the gold standard for microbiological diagnosis but are time-consuming. Rapid diagnostic testing has proven useful in the improvement of patient outcomes by speeding up microbial identification and predicting antimicrobial susceptibility.

The purpose of this study is to evaluate the performance of the Sepsis Flow Chip Kit molecular assay (Vitro) for the detection of 36 bacterial species, Candida species and 20 antibiotic resistance markers.

Materials/methods: A total of 166 positive blood culture samples were analysed with the Sepsis Flow Chip Kit assay. Time-to-result is 4 hours for a 12-sample batch. The test performance was compared to the culture-based workflow currently in place, consisting of identification (MALDI-TOF MS - bioMérieux) and antimicrobial susceptibility testing (Vitek 2 - bioMérieux).

Results: Out of 166 tested samples, 3 were excluded for lack of amplification of the external control, due to the presence of inhibitors, and 7 as positive for bacteria not included in the assay panel.

Out of 156 results suitable for comparison, 141 showed complete agreement with the reference algorithm (91%). In 2 polymicrobial samples, the molecular test yielded a concordant result with an added identification, while in 3 more polymicrobials it was in agreement with the standard diagnostic workflow for one target, but missed the second.

In 9 cases (6%), the Vitro assay tested negative with a positive culture result. Finally, Proteus mirabilis was misidentified by the molecular test as Morganella morganii within a polymicrobial sample. This was due to an incorrect software interpretation of amplified targets belonging to a second pathogen (Klebsiella pneumoniae).

Conclusions: The Sepsis Flow Chip Kit assay showed an overall ease of use and a rather short turnaround time, which would prove useful in a time-sensitive setting such as BSI diagnosis. The results obtained are generally in agreement with those of the culture-based algorithm used as a reference workflow; however, the discrepancies that emerged within the study need to be further investigated as to accurately gauge the system’s sensitivity, in light of a potential use in a diagnostic setting.

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Mutations in PBP3 conferring β-lactams resistance in Haemophilus parainfluenzae

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Background: Haemophilus parainfluenzae is an opportunistic pathogen of upper respiratory and genitourinary tract. Due to widespread and frequent use of β-lactams, resistance to these antimicrobials has been developed. One of the main mechanisms of β-lactams resistance consists on amino-acid substitutions in PBP3 encoded by ftsI gene. The aim of this study was to determine mutations in PBP3 in H. parainfluenzae which confer resistance to β-lactams by sequencing ftsI gene.

Materials/methods: 17 clinical isolates of H. parainfluenzae recovered at Hospital Universitario Marqués de Valdecilla during 2012-2019 were studied. Antimicrobial susceptibility was performed using gradient strips (Etest®) and according to EUCAST both disk diffusion guidelines and breakpoints for H. influenzae. FtsI gene was amplified by PCR using the primers described by Tristam et al (1). PCR product was sequenced and aligned with nucleotide BLAST between our isolates and H. parainfluenzae T31 (GenBank code Q312002.1). Amino-acid substitutions were obtained with Sequencher software.

Results: The most common substitutions in PBP3 were N526K/H/S and V511A, and were associated with resistance to AMC and FUR. All cefotaxime-resistant isolates presented mutations in S385T+I442F (n=11, ertapenem susceptible) or T443A+T322I (n=2, ertapenem-resistant). The single meropenem-resistant isolate showed additional mutation in D551Y, not present in any of the other isolates.

Previously described substitutions K276N, A307N and V329I, although of unclear significance, were also appeared in 5 cefotaxime resistant isolates.

Conclusions: The most prevalent mutations [N526K/H/S and V511A] described in H. influenzae conferring resistance to β-lactams, were also detected in our H. parainfluenzae isolates.

PB3 mutations T443A, T322I and D551Y were detected in carbapenem resistant isolates, but additional site-directed mutagenesis studies are needed to confirm this association.


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**Abstract 5047**

**The incremental clinical value of metagenomic next-generation sequencing when applied to microbiological diagnosis of skin and soft tissue infections**

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**Background:** Metagenomic next generation sequencing (mNGS) with its comprehensiveness has been widely applied in microbiological diagnosis. Etiological diagnosis is of paramount clinical importance in skin and soft tissue infections (SSTIs) patients. Meanwhile, the clinical application of mNGS in SSTIs is little known.

**Materials/methods:** From April 1st 2017 to October 30th 2019, 100 SSTIs cases were enrolled. The main classification was pyomyositis (n=32), followed by subcutaneous abscess (n=30) and impetigo (n=16). The positive rates of pathogens detected by mNGS and culture were compared by analyzing the tissues, pus, swabs and/or interstitial fluids of infected parts. The modification of antibiotics treatment strategy due to mNGS were also assessed.

**Results:** The sensitivity of mNGS for detecting pathogens in SSTIs cases was superior to that of culture (71.0% vs 36.0%; p=0.041). mNGS was able to identified a significantly higher rates of virus (14.0% vs 0.0%; p<0.01), anaerobe (11.0% vs 3.0%; p<0.01), mycobacterium tuberculosis (17.0% vs 11.0%; p<0.01) and non-tuberculous mycobacterium (6.0% vs 3.0%; p<0.01) compared with culture. Notably, some rare pathogens were detected by mNGS such as vibrio vulnificus and bartonella henselae. Importantly, proportion of multi-pathogens infections of SSTIs in mNGS was superior to that of culture (13.0% vs 7%; p=0.045). The rate of targeted antibiotics treatment was significantly higher in mNGS-positive cases than that in mNGS-negative cases (33.0% vs 2.0%; p<0.01). In the culture-negative and mNGS-positive cases, the improvement rate was higher than that in mNGS-negative cases, while there was no significant difference (25.0% vs 5.0%; p=0.281).

**Conclusions:** mNGS is a promising tool of etiological diagnosis for SSTIs, particularly in identifying virus, anaerobes, mycobacteria and multi-pathogens infection. Application of mNGS testing to clinical practice is able to change antibiotics treatment strategies and partly benefit clinical outcomes.

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Abstract 5051

**Sensitivity of the pneumococcal urinary antigen ImmuView in proven or probable pneumococcal pneumonia**

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**Background:** ImmuView® is an immunochromatographic test which detects pneumococcal and Legionella antigens in urine samples. The aim of this study was to evaluate the sensitivity of pneumococcal urinary antigen ImmuView® to detect probable or proven pneumococcal pneumonia. Furthermore, to analyze its sensitivity regarding the pneumococcal serotypes.

**Materials/methods:** We collected urine samples from patients with probable pneumococcal pneumonia (symptoms of infection plus a sputum or blood culture with *Streptococcus pneumoniae*). The samples were prospectively tested for pneumococcal urinary antigen with Binax® and preserved frozen. After thawed, samples were tested with ImmuView®. Clinical isolates of *S. pneumoniae* were serotyped using ImmuLex PNEUMOTEST KIT® and/or Quellung reaction. The antibiotic susceptibility was tested by microdilution following EUCAST recommendations.

**Results:** A total of 53 probable pneumococcal pneumonia episodes were detected over the study period (Jul 2018 - Jun 2019). Of them, 33 had blood cultures and 20 respiratory specimens with *S. pneumoniae*. The most frequent serotypes were 3 (11.3%) and 8 (11.3%). The antibiotic susceptibility rates were penicillin 79.2% (MIC≤0.06 mg/L), levofloxacin 98,2% and erythromycin 84.9%. The 1.9% of the isolates had a penicillin MIC >2mg/L. The Binax® urinary antigen detection was positive in 40 of 53 probable pneumococcal pneumonia episodes. While the ImmuView® test was positive in 37 out these 53 urine samples after thawing (p=0.4). No Legionella antigen was co-detected together with pneumococcal. No differences in sensitivity were found regarding serotypes.

**Conclusions:** The ImmuView® had a good sensitivity to detect pneumococcal antigen in urine samples of patients with proven or probable pneumococcal pneumonia even in frozen samples.

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**Effectiveness of single-dose of doxycycline for the prevention of tick-borne relapsing fever**

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**Background:** Tick-Borne Relapsing Fever (TBRF) can be effectively prevented by post exposure prophylaxis (PEP) with doxycycline. However, unlike PEP for Lyme disease, the traditional regimen for the prevention of TBRF consists of 5 days of treatment.

**Materials/methods:** In this observational study, data were collected from 80 spelunkers regarding their self-administered PEP habits following exposure to cave-ticks. Data were collected using a 47-item questionnaire published on social networks and on the website of the Israel Cave Research Center (February 2016 to July 2019). TBRF occurrence was compared in subjects taking a single dose PEP, defined as one dose of 100 mg doxycycline within 72 hours of tick exposure, to subjects not using PEP.

**Results:** One hundred thirty-five tick-exposure events were recorded. PEP was administered following 89 (66%) of the 135 reported events, and in 84% of these only one dose of doxycycline was used. TBRF occurred in 43% of events that were not followed by PEP administration. PEP consisting of a single dose of 100 mg Doxycycline provided 100% efficacy in preventing TBRF, p<0.0001 for between group difference of TBRF occurrence. Thirty four exposure cases took place in Borrelia persica positive caves, defined as caves where confirmed TBRF cases were acquired. Of 16 persons not taking PEP, nine TBRF cases were reported, representing an attack rate of 56%. None of the 16 individuals (57%) receiving PEP with Doxycycline were infected (13 out of 16 took 1 dose of doxycycline, for whom p<0.0002 for between group difference of TBRF occurrence).

**Conclusions:** This study, which mapped spelunkers self-administered PEP regimens after exposure to cave-ticks, demonstrated that a single dose of 100 mg doxycycline taken within 72 hours of exposure is comparable to a 5-day course, and is 100% effective for the prevention of TBRF.

**Figure 1.** Exposure events, PEP regimen and TBRF occurrence. Figure 1. 1a. Entire study population. 2a. Exposure in Borrelia positive caves (caves in which a person has been reported of acquiring TBRF).

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Evaluation of the rapid ResaPolymyxin Acinetobacter/Pseudomonas NP test for rapid screening of colistin resistance in non-lactose fermenters

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Background: Pseudomonas aeruginosa and Acinetobacter baumannii form part of the ESKAPE pathogens that are of global concern due to their ability to acquire multidrug and pandrug resistance. As colistin is used as one of the last resort antibiotics, rapid screening of colistin susceptibility is crucial for infection control and antibiotic stewardship. Recently, the Rapid ResaPolymyxin Acinetobacter/Pseudomonas NP (RPNP) test, a colorimetric assay based on the bacterial metabolism that reduces resazurin (blue) to resorufin (pink), was developed for non-fermenting Gram-negative bacteria. The aim of the study was to evaluate the performance of the RPNP test as compared to the broth microdilution (BMD) assay using a collection of clinical carbapenem-susceptible and -resistant P. aeruginosa and A. baumannii isolates.

Materials/methods: A total of 126 P. aeruginosa (106 colistin-susceptible and 20 colistin-resistant according to BMD) and 52 A. baumannii isolates (31 colistin-susceptible and 21 colistin-resistant according to BMD) with colistin minimum inhibitory concentrations (MICs) in the range of 0.125 to >64 mg·L⁻¹ were included in the study. The reference method was colistin BMD performed and interpreted according to the EUCAST/CLSI joint guidelines. Isolates were considered susceptible when colistin MICs were ≤2 mg·L⁻¹ and resistant when colistin MICs were >2 mg·L⁻¹. The RPNP test was performed and interpreted as previously described. Isolates were considered colistin-susceptible if a blue colour was observed and resistant if a purple or pink colour was observed.

Results: The categorical agreement between the reference method and the RPNP test was 69% for P. aeruginosa and 94% for A. baumannii. Very major error (false susceptibility) was observed in 45% (9/20) of P. aeruginosa isolates and 10% (2/21) of A. baumannii isolates. Major error (false resistance) was more commonly observed in P. aeruginosa isolates (28%: 30/106) than in A. baumannii isolates (3%; 1/31). The sensitivity and specificity of the RPNP test was poor in P. aeruginosa isolates (55% and 72%) but were in an acceptable range for A. baumannii isolates (90% and 97%).

Conclusions: The RPNP test is a rapid, inexpensive screening test that performs better for A. baumannii, but not for P. aeruginosa.

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Dual RNase and β-lactamase activity of a single enzyme encoded in most Archaea

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Background: β-lactamases enzymes have been so far identified thanks to their hydrolyzing activities on β-lactam antibiotic family. However, annotation of genomes of multiple living species showed that homologous β-lactamase sequences were present in most living organisms, including those for which there are no known β-lactam targets. This the case in Human but also in Archaea in which two groups of β-lactamases are present in the majority of Archaea which are not, by nature, susceptible to β-lactams, in whom alternative role of these enzymes may be suspected, such as nuclease, ribonuclease, or glyoxalase thanks to the shared motif “HxHxDH” with class B metallo-β-lactamase (MBL) enzymes. Here, we express two archaeal β-lactamases and investigate their different activities.

Materials/methods: The Archaea β-lactamases were identified by blastP analysis using as targets inferred ancestor sequences for bacterial β-lactamases. Selected sequences were synthetized by GenScript (Piscataway, USA) and optimized for protein expression in Escherichia coli in the pET24a(+) expression vector. Purified enzymes were tested for β-lactamase activity on nitrocefin and β-lactams using the Cefinase paper disc test and Liquid Chromatography-Mass Spectrometry (LC-MS). The nuclease activity was evaluated on synthetized single and double-stranded DNA whereas the ribonuclease activity was evaluated using the RNaseAlert QC System kit (Fisher Scientific, France) and on extracted bacterial RNA. Glyoxalase II activity was determined using the Glyoxalase II Activity kit from BioVision (Milpitas, USA).

Results: Class B and C β-lactamases were identified in most Archaeal genomes. Class B sequences appeared highly conserved in several classes of archaea and have been transferred into the single bacterial family, i.e. Flavobacteriaceae (especially Elizabethkingia). The expressed class B β-lactamase from Methanosarcina barkeri digests nitrocefin and penicillin G. While a weak glyoxalase activity was detected, a significant ribonuclease activity was demonstrated. The expressed class C-like β-lactamase, also from Methanosarcina sp., shows β-lactamase activity and was more closely related to DD-peptidase enzymes.

Conclusions: Our findings highlight the requalification needness of annotated enzymes as β-lactamases, either by annotating them a more neutral name or by giving them name containing at least β-lactamase-nuclease, so as not to neglect an aspect probably essential to the life of this group of enzymes.

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Infectious disease consultation reduces time to appropriate antimicrobial treatment in Gram-negative bacteraemia: data from an area of high prevalence of antibiotic resistance

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Background: Administration of appropriate antimicrobial treatment can be challenging in areas of high prevalence of antibiotic resistance. This study evaluated the impact of infectious disease consultation (IDC) on time to and risk of appropriate antimicrobial treatment (AAT) for Gram-negative bacteraemia (GNB).

Materials/methods: Retrospective observational study on patients with GNB hospitalized at San Raffaele Hospital (Milan, Italy) between January-December 2017. Patients' demographics, microbiological data and all therapeutic prescriptions for every GNB were collected from clinical records. Only the first episode of GNB was evaluated. IDC was requested at treating physician's discretion. Resistance was defined as non-susceptibility to third-generation cephalosporins, piperacillin-tazobactam and/or carbapenems. Therapy was deemed AAT if the antibiotic had the narrowest spectrum considering infection site, polymicrobial aetiology, allergies and comorbidities. In case of multiple AAT, time to first AAT was calculated. We identified a group of patients with interventional IDC (I-IDC) which included: 1) patients with the first AAT suggested by IDC; 2) patients without AAT with the last therapeutic modification suggested by IDC. Results were described as percentage, median (interquartile range). Time to AAT was evaluated by Kaplan-Meier curves. Factors associated with risk of AAT were assessed by Cox proportional-hazard models; [adjusted] hazard ratios ([a]HR) with 95% confidence intervals (95%CI) were reported.

Results: 471 patients; age 69.8 (61.0-77.4), 63% males; hospital units: Emergency Department (23.6%), Surgery (30.6%), Medicine (31.4%), Intensive Care Unit (ICU, 11.7%). GNB sustained by resistant bacteria in 38.2% of cases. Empiric therapy prescribed during IDC in 12.7% of patients.

Overall, 29.9% of patients received an I-IDC. In subjects without empiric AAT (n=263), patients with and without I-IDC had a median time to AAT of 2 days (95%CI=2-3) vs 7 (95%CI=3-10), respectively (p<0.0001; Figure). At multivariate analysis, I-IDC was associated with AAT in this subset (aHR=2.318 [1.643-3.270]) and confirmed in the whole cohort (aHR=1.339 [1.052-1.705]), after adjusting for age, sex, admission ward, previous surgery, Charlson/Pitt score, infection site, time to bacteremia, previous isolation of multidrug-resistant organisms, previous ICU stay, resistant phenotype, previous IDC.

Conclusions: In an area of high prevalence of antibiotic resistance, infectious disease consultation was associated with earlier prescription of appropriate therapy in Gram-negative bacteremia.
Abstract 5057

Utilising long-read shotgun sequencing to study the lower respiratory tract microbiome from endotracheal aspirate samples

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Background: Long-read sequencing helps to determine high-resolution species composition and the genetic context of resistance genes, although samples such as endotracheal aspirates (ETA) are enriched in host DNA. Here, we evaluate a saponin treatment on ETA samples to reduce host DNA in order to increase the number of microbial reads to answer clinically relevant questions.

Materials/methods: A set of ETA samples (n=4) were obtained from patients (n=4) in UZA (Antwerp University Hospital). The samples were liquefied with lysomucil (acetylcysteine) and subjected to metagenomic DNA extraction using ZymoBiomics DNA/RNA Miniprep Kit (Zymo Research, USA) with and without a saponin (Thermo Fisher, USA) treatment to remove host DNA from the sample. Singleplex and multiplex library preparation was performed using SMRTBell Template Prep Kit 1.0 (Pacific Biosciences, USA) and sequencing in Sequel with SMRTCell v3 (Pacific Biosciences, USA). The same samples were sequenced using short-read shotgun sequencing (MiSeq, Illumina, USA). Host reads were removed by reference mapping using CLC Genomics workbench (Qiagen, Germany). Remaining long-read sequences were analysed using WIMP (What is In My Pot) workflow and assembled with MetaFlye. Similarly, short-read sequences were assembled using metaSPAdes. All assemblies were analysed using BacPipe v.1.2.6 for annotation and resistance gene detection (Figure 1A).

Results: Multiplexing of clinical samples for shotgun metagenomics on Sequel platform was successfully validated and shown to be more cost-effective [1,066€/sample:singleplex vs 561€/sample: multiplex], producing enough coverage for all samples (Figure 1B). Saponin treatment showed 30-99% of host DNA removal in treated samples, without affecting the bacterial DNA, but significantly affecting fungal DNA (Figure 1C). The results entirely correlated with the phenotypic data (species detection, susceptibility profile). Additionally, long-read sequencing was capable of identifying the complete genetic characterisation of the beta-lactamase gene and detection of integrative conjugative elements (ICE), which was incomplete in short-read sequencing (Figure 1D).

Conclusions: We show the importance of saponin treatment to remove host DNA in ETA samples with low bacterial content and the feasibility and cost-effectiveness of multiplexing for long-read shotgun sequencing, deriving in enough coverage for taxonomaical classification and resistance genes detection.

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Abstract 5059

**Method comparison: Abbott Alinity m STI (CT, NG, MG, TV) vs Hologic Aptima CT/NG & Aptima MG**

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**Background:** High rates of sexual transmitted infections (STI) reported in the MSM population lead to a rise in awareness and in testing. The implementation of pre-exposure prophylaxis in the MSM community to prevent HIV-infections includes regularly STI screening tests leading to higher demands on STI tests. We here compare the results of two random access systems, the newly launched Abbott Alinity m STI and the established Hologic Aptima CT/NG & Aptima MG assays.

**Materials/methods:** 257 Left-over routine samples from requests for Neisseria gonorrhoeae, [NG] Chlamydia trachomatis [CT] and Mycoplasma genitalium [MG] or combinations thereof were analysed with the Aptima assay and retested on the Abbott Alinity m STI. 105 swabs (different locations: pharyngeal, anal and urethral) collected in Aptima swab specimen collection tube, 148 urine in urine specimen collection tubes and 4 urine/swab mixes were tested. Trichomonas vaginalis [TV] results were only available with the Alinity m STI assay.

**Results:** An overall concordance of 98.1% between the Aptima and the Alinity m assays could be reached when equivocal results of the Aptima assay (N=2) were defined as positive. Of 162 tested samples we observed 7 discordant results for MG which were positively detected only in the Aptima assay. NG testing revealed four discordant results with 3 positive detections only in the Alinity m assay and one only detectable in the Aptima assay. 3 discordant results for CT divide into 2 samples only detectable in the Alinity m assay vs. one only in the Aptima assay.

**Conclusions:** The Alinity m STI assay showed high concordance with Aptima CT/NG & Aptima MG assays. With random access, the ability to continuously load samples and detection of 4 STIs simultaneously the Alinity m STI is an excellent alternative to three Aptima STI assays. In addition the Alinity m STI includes a cellular control to assess the quality of the material.

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**Comparison 257 samples STI testing**

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Abstract 5064

Activity of peracetic acid against MDR Enterococcus faecium and non-typhoidal Salmonella from diverse epidemiological and genetic backgrounds

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Background: Multidrug-resistant (MDR) bacteria represent one of the greatest challenges worldwide, with antiseptic/disinfectants assuming an increasing relevance to prevent MDR-bacteria transmission in food-chain and hospital contexts. Foodborne pathogenic non-typhoidal Salmonella-NTS from emergent serotypes/clones and particular hospital-adapted clonal lineages of Enterococcus faecium-Efm cause thousands of human infections worldwide. Peracetic acid (PAA) is widely used in food-chain (20-3000mg/mL) and healthcare environments (150-2000mg/mL) to disinfect surfaces/hands, but its activity has not been tested in bacteria from diverse epidemiological and genetic backgrounds. Here we evaluated PAA tolerance of MDR Efm and NTS from diverse origins and clones/serotypes.

Materials/methods: We included 74-Efm and 60-NTS recovered from humans (n=54), food-animal production setting/foods (n=75), and environment (n=5) [1997-2018; 6-countries]. Efm strains included were from hospital [21-clade A1] and community [37-clade A2; 9-clade B] associated clonal lineages and among NTS, 17-serotypes were considered, including the most frequent 5. Typhimurium, 17. 4,[5],12:i:- and 3. Enteritidis. Most of the isolates were MDR [Efm 76%-n=56/74; NTS 73%-n=44/60]. The MICPAA was performed by broth-microdilution (ISO20776-1:2006; 37ºC/24h) followed by MBCPAA (NCCLS:1999; 37ºC/48h) (minimum 2 replicas/isolate), using a concentration range of 40-170mg/L. Induction assays were performed in 6-NTS and 6-Efm (diverse MIC/MBCPAA; genetic backgrounds), exposing bacteria (log-phase: 3-4h) to sub-inhibitory PAA concentrations (up to 10/100 times less the MICPAA) followed by MIC/MBC assay.

Results: Efm presented a MICPAA=70-120mg/L and MBCPAA=100-170mg/L [MIC90=110mg/L; MBC90=170mg/L]. NTS presented a MICPAA=50-70mg/L and MBCPAA=60-100mg/L [MIC90=70mg/L; MBC90=90mg/L]. No differences in MIC/MBCPAA were observed among isolates from diverse sources or MDR/non-MDR bacteria. Efm from clade A1 (62%-n=13/21; 70%-n=9/13 vancomycin-resistant ) showed a MBC equal or higher to the minimal concentrations recommended in ready-to-use products for hand disinfection in hospitals ([150mg/L], and all NTS a MBC higher to the minimal concentrations recommended in food/beverage industry (20mg/L). The induction with PAA did not affected the MIC/MBC in any isolates tested.

Conclusions: We unveil that MDR bacteria with clinical relevance survive to PAA concentrations used in different contexts, including most frequent NTS serotypes and Efm from hospital-adapted clonal lineages. Contrasting with other biocides, exposure to sub-inhibitory PAA concentrations seems not to have an impact on tolerance development in the few strains studied, deserving further studies.

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Abstract 5068

**HCV resistance patterns in a large international cohort of DAA-naïve and -experienced patients with GT3a infection**

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**Background:** HCV genotype 3a (GT3a) is highly prevalent worldwide. GT3a is recognized as one of the most difficult-to-cure HCV genotypes. The international SHARED consortium investigated the prevalence and characteristics of resistance patterns in GT3a-infected DAA-naïve and -experienced patients from various regions.

**Materials/methods:** Sequence and clinical data from 735 chronically infected HCV GT3a patients were collected from a database of 2656 HCV-infected patients from 17 countries. Resistance Associated substitutions (RASs) were defined according to 2018 EASL HCV guidelines.

**Results:** In DAA-naïve patients (n = 351), no NS5B RASs were detected, whereas NS3 RASs were found in 3% (e.g. Q80K/R, Q168R) and NS5A RASs in 22% of patients (with A30K and Y93H, at 5% and 7% respectively). In DAA-experienced patients (n = 384) failing NS5A inhibitor-based therapy (SOF/DCV+/-RBV, 65.1%; SOF/LDV+/-RBV, 13.3%; SOF/VEL+/-RBV, 10.7%; SOF/VEL/VOX+/-RBV, 2.3%; G/P, 2.3% and others 6.2%), 78.8% of patients harbored NS5A RASs at failure. NS5A Y93N/H was the most prevalent RAS (66.2%), present after failure of all NS5-inhibitor containing regimen except ledipasvir, followed by NS5A A30K/S (17%). NS5A A30K was more frequently present after SOF/VEL/VOX or G/P failure (33% and 44% respectively) than after SOF/DCV or SOF/VEL failures. The combination of NS5A A30K and Y93H was rarely detected, except in patients failing SOF/VEL/VOX or G/P. In contrast, the majority of NS5A A30S was frequently associated with Y93H after DCV and VEL containing regimen failures. In addition to NS5A RASs, NS3 RASs including Y56H, Q80K, A156G, and Q168R were present in 62.5% of patients failing G/P (≥2 RASs, 50%). The frequency of NS5B S282C/T was low (1.2%) in patients failing SOF-containing regimens. No NS5B polymorphisms (including at positions 150 and 206) were associated with SOF-containing regimen failures.

**Conclusions:** In this large international cohort of GT-3a infected patients, the vast majority of patients who failed to achieve SVR harbored resistant HCV variants carrying one or two NSSA RASs, the most frequent being Y93H. The frequency of the co-occurrence of Y93H with another RAS at position 30 (A30S, A30K) depended on the treatment regimen received (first versus last-generations DAA). Multiple NS3 and NSSA RASs can challenge retreatment with last-generation NSSA inhibitors.

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Detection of Borrelia burgdorferi cell-free DNA in human plasma samples for improved diagnosis of early Lyme borreliosis

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Background: Erythema migrans (EM), the skin rash of early Lyme borreliosis (LB), is a non-specific physical finding unless a classical targetoid lesion with central clearing is identified. In 80-90% of EM skin lesions, the rash is not classical, and a rash is absent entirely in approximately 20% of early LB cases. Confirmation of suspected cases is challenging, as serology and blood PCR are insensitive in early LB. Here, we demonstrate that detection of Borrelia burgdorferi (B. b.) cell-free DNA (cfDNA) in plasma can improve diagnosis of early LB.

Materials/methods: B. b. cfDNA detection in plasma samples was compared with serology and blood PCR in 40 patients with physician-diagnosed EM, 28 of whom were confirmed to have LB by skin biopsy Borrelia culture (N=18), seroconversion (N=2) or both (N=8). These 28 individuals were classified as having “laboratory-confirmed” EM.

Results: B. b. cfDNA was detected in 18/28 patients (64%) with laboratory-confirmed EM. In comparison, the sensitivity of acute-phase serology using modified two-tiered testing (MTTT), in which two different enzyme immunoassays are applied without the use of immunoblots, was 50% (P=0.45). Sensitivity of blood PCR was 7% (P=0.0002). Combining B. b. cfDNA detection and MTTT increased diagnostic sensitivity to 86%, significantly higher than either approach alone (P≤0.04). B. b. cfDNA sequences matched precisely with strain-specific sequence generated from the same individual’s cultured B. b. isolate. B. b. cfDNA was not detected in plasma from 684 asymptomatic ambulatory individuals. Among 3000 hospitalized patients tested as part of clinical care, B. b. cfDNA was detected in only two individuals, both of whom had clinical presentations consistent with LB.

Conclusions: This study demonstrates the potential clinical utility of B. b. cfDNA detection in the diagnosis of early LB. The combination of B. b. cfDNA and acute-phase MTTT improves sensitivity compared with either method alone.

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Abstract 5075

**Characterisation of resistance-increasing determinants of OXA-48-bearing clinical isolates of Klebsiella pneumoniae**

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**Background:** Nosocomial infections with multidrug-resistant Gram-negative pathogens are an emerging problem in healthcare systems worldwide. Some isolates of *Klebsiella pneumoniae*, that carry an OXA-48 carbapenemase, are carbapenemase resistant and some are not. Here we investigated an additional mutation in the *ompK36* gene, which encodes for a channel protein embedded in the outer membrane, that may increase the resistance of such isolates.

**Materials/methods:** A carbapenem susceptible *K. pneumoniae* with an OXA-48 carbapenemase was placed under selective pressure with meropenem. A mutant could be selected in vitro, which in addition to production of OXA-48 had an amino acid deletion in OmpK36 at positions V320 and G321. To investigate the effect of this deletion, this mutation was introduced into a clinical OXA-48-producing carbapenem-susceptible isolate of *K. pneumoniae* using the λ-Red recombination system. MICs of the wildtype and the porin mutant were determined using broth microdilution and interpreted according to EUCAST. The effect of the porin mutation on bacterial fitness was analysed by growth experiments.

**Results:** Resistance testing of the mutant showed increased MICs of several cephalosporins, mecillinam and carbapenems. In growth experiments, a fitness loss of the OmpK36 mutant compared to the wild type was also observed. The mutated porin also appears to alter the composition of the cell membrane or efflux of the cell, as the mutant showed a different morphology on agar plates than the wild type.

**Conclusions:** The deletion of V320 and G321 in OmpK36 seems to have a significant effect on the resistance of *K. pneumoniae* in combination with production of an OXA-48 carbapenemase. The deletion may cause a structural change of the porin, so that the influx of larger molecules such as carbapenems is decreased. The fitness loss indicates that reduced influx could also affect nutrients.

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Abstract 5078

**Large variability of unbound active fraction of ceftriaxone in contrast to ciprofloxacin in plasma of critically ill patients**

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**Abstract third-party references:** Erasmus University Medical Center

**Background:** Traditional antibiotic dosing is not designed for critically ill patients. Severe illness, frequent hypoalbuminemia, and renal failure results in aberrant pharmacokinetics. Protein binding of drugs may vary significantly in critically ill patients, which can lead to high drug clearance and therefore low plasma concentrations and therapeutic failure. Additionally, bound fractions of antibiotics have no therapeutic effect. For ceftriaxone and ciprofloxacin the unbound fractions have been described as 5-15% and 60-70%, respectively. However, data on protein binding of these antibiotics are scarce in critically ill patients. Our objectives were to determine unbound fractions of ceftriaxone and ciprofloxacin in critically ill patients, and to determine predictors affecting the unbound fractions.

**Materials/methods:** Samples were obtained from an ongoing multicentre randomized controlled trail (DOLPHIN) at the intensive care units. Peak and trough samples were collected at 1, 3, and 5 days after initiation of antibiotic therapy. Total and unbound concentrations were determined with a validated mass spectrometry (LC-MS/MS) method. For unbound fractions, we used linear regression to find predictors (p-value <0.10). These predictors were used in a multivariate linear regression (step-down) for each predictor (p-value <0.05).

**Results:** A total of 38 patients (137 samples) receiving ceftriaxone or ciprofloxacin were included. Unbound fractions that exceeded more than 3 standard deviations (outliers) were removed from analysis (N=20). The median [IQR] unbound fractions were 20.2 (15.4-29.4)% and 71.1 (69.4-76.5)% in peak concentrations for ceftriaxone and ciprofloxacin, respectively. For trough concentrations the fractions were 12.3 (8.5-20)% and 69.1 (66.8-73.5)%.

Using multivariate analysis, decreased serum albumin, increased serum creatinine, and septic shock were found to be positive predictors for the percentage of unbound fraction of ceftriaxone trough concentration. Septic shock was the major predictor. No patient characteristics were identified as predictors for unbound fractions of ciprofloxacin.

**Conclusions:** In contrast to the moderately and fairly constant bounded ciprofloxacin, the fraction of unbound concentration was extremely variable in ceftriaxone and especially for trough concentrations, higher than previously reported, resulting in fluctuations in effective exposure. At the moment unbound fraction is not considered when dosing ceftriaxone, but therapeutic drug monitoring unbound trough concentrations might increase the likelihood of therapeutic success.

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Abstract 5079

Presence and zoonotic potential of *Escherichia coli* ST131 recovered from wildlife and food-producing animals, with high prevalence of *mcr-1* within porcine isolates

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**Background:** Although the clonal group ST131 is worldwide recognized as a disseminated emerging pathogen that causes extraintestinal infections, few studies have so far analyzed its presence and zoonotic potential within intensive animal food production and wildlife. On the other hand, food production animals have been identified as the main cause of the antimicrobial resistance increase, including to colistin.

**Materials/methods:** A collection of 101 *E. coli* ST131 isolated in Spain (2006-2016) from intensive farming (28 poultry, 18 porcine), meat (29 chicken, 19 pork, two beef) and wildlife (three wild birds and three wild boars), were characterized for their serotypes, phylogroups, clonotypes (CH), sequence types (STs), virotypes, PFGE-macrolactamase profiles, and antibiotic resistances, including extended-spectrum-β-lactamases (ESBLs) and the plasmid-mediated colistin resistance gene (*mcr-1*).

**Results:** Although CH40-22 was the most prevalent clonotype (82.2%) of the 101 ST131 animal isolates, those of porcine origin showed nine different *fimH* allelic variants. Ninety-one isolates satisfied the extraintestinal pathogenic *E. coli* (ExPEC) status. According to their virulence profile, poultry ST131 isolates exhibited the virotype D4 (56 of 57 isolates); porcine isolates conformed mainly to the virotype D5 (17 of 36 isolates), but also virotypes D2 (10) and D4 (four); bovine isolates showed the virotypes D2 (one) and D4 (one), and wildlife isolates the virotypes D1 (two) and D3 (three). Ten ST131 isolates carried ESBL-genes typed as CTX-M-9 (seven poultry isolates), SHV-12 (one poultry) and CTX-M-1 (two porcine). Furthermore, 14 cefoxitin-resistant ST131 (13 poultry and one beef isolates) were carriers of the *bla_CTX-M* gene. The *mcr-1* gene was detected in one beef meat and 12 porcine isolates (seven from pig feces and five from pork meat). We found ≥85% similarity in the PFGE-macrorestriction comparison of porcine virotypes (D2, D5) and poultry virotype D4) meat isolates with ST131 isolates of human origin (Figure 1).

**Conclusions:** Intensive farming and wildlife animals represent significant reservoirs of *E. coli* ST131 potentially pathogenic for humans. Poultry and pork meat could be playing an important role in the transmission of ST131 isolates belonging to the virotypes D4 (chicken), D2 and D5 (pork). Of particular concern is the high prevalence of *mcr-1* within porcine ST131 isolates.

**Figure 1.** PFGE macrorestriction profile of 14 meat *E. coli* ST131 (in blue) compared with 15 human clinical and two avian patholgy isolates of the UREC collection (in black); association between isolation code, virotype, ESBL, year, origin of isolation (PM, pork meat; AM, avian meat; AP, avian patholgy and H, human) and virulence profile is indicated on the right. Highlighted in red clusters of similarity ≥80%.

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Abstract 5080

Whole genome sequencing of *Salmonella enterica* from Spanish hospitals with resistance to third generation cephalosporins

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**Background:** Resistance to third generation cephalosporins in *Salmonella enterica* is a cause of concern, since these antibiotics are listed by the World Health Organization as critically important with highest priority for human medicine. In the present study, whole genome sequencing (WGS) was used to thoroughly characterize cefotaxime-resistant isolates of *S. enterica* from Spanish hospitals.

**Materials/methods:** Nineteen cefotaxime-resistant isolates of *S. enterica* were recovered from patients attended at three Spanish hospitals between 2012 and 2018. Antimicrobial susceptibility was determined and the obtained results were interpreted according to CLSI guidelines. Genome sequencing was performed with Illumina (2x125 bp paired-end reads). Genome reconstruction, including reads assembly, was done with the PLACNETw pipeline. Serotyping, MLST, identification of resistance genes and plasmid detection/characterization were achieved “in silico” using SeqSero, MLST, ResFinder, CARD, ArgAnot, Plasmid Finder, pMLST and PLACNETw.

**Results:** Of the 19 cefotaxime-resistant isolates, 16 were positive for extended-spectrum \(\beta\)-lactamases (ESBL) and three for AmpC-type \(\beta\)-lactamases. The ESBL-producers carried one of the following genes: \(\text{bla}_{\text{CTX-M}}\) (ten *S. Typhimurium* ST34 isolates, of them one biphasic and nine belonging to its monophasic S. 4,12:i:- variant); \(\text{bla}_{\text{CTX-M-9}}\) (three isolates assigned to *S. Typhimurium* ST19, monophasic S. 4,12:i:- ST34 and *S. Enteritidis* ST11); \(\text{bla}_{\text{CTX-M-14}}\) (two *S. Infantis* ST32); and \(\text{bla}_{\text{CTX-M-1}}\) (one *S. Paratyphi B* ST110). In the three AmpC-producers (one monophasic S. 4,12:i:- ST34 and two *S. Bredeney* ST306), the \(\text{bla}_{\text{CMY-2}}\) gene, was detected. All except the single *S. Typhimurium* ST19 and *S. Enteritidis* ST11 isolates were MDR. Moreover, \(\text{mcr-1}\), \(\text{mcr-9}\) (for plasmid-mediated colistin resistance) or \(\text{qnrA1}\) (for plasmid-mediated quinolone resistance) coexisted with \(\text{bla}_{\text{CTX-M-9}}\) or \(\text{bla}_{\text{CMY-2}}\) in five ST34 isolates. These resistance genes were harbored by IncHI2 (\(\text{bla}_{\text{CTX-M-9}}, \text{mcr-9}, \text{qnrA1}\)), IncF/repB (\(\text{bla}_{\text{CTX-M-9}}\)), IncI (\(\text{bla}_{\text{CTX-M-9}}\) and \(\text{bla}_{\text{CTX-M-1}}\)), IncC (\(\text{bla}_{\text{CMY-2}}\)), IncP (\(\text{bla}_{\text{CTX-M-65}}\)) or IncX4 (\(\text{mcr-1}\)) plasmids, or located on the chromosome (\(\text{bla}_{\text{CMY-2}}\) in a single case).

**Conclusions:** WGS revealed that diverse *S. enterica* serotypes with resistance to third generation cephalosporins, sometimes combined with plasmid-mediated resistance to colistin or fluoroquinolones, are circulating in Spanish hospitals. Most of the detected isolates belong to highly successful clones of *S. enterica*, including the monophasic 4,12:i:- ST34 variant of *S. Typhimurium* and *S. Infantis* ST32.

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Abstract 5081

**MiSeq protocol for 16S rDNA community profiling revisited with exact ribosomal sequence variants**

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**Background:** In 2013 Illumina published a 16S rDNA amplicon sequencing protocol. Here the variable region V3 and V4 (V34) is amplified with Kapa HiFi ReadyMix polymerase and sequenced with paired 300-bp reads using standard sequencing-primers (universal tailed-tag dual index design; UTTDI). Recently algorithms using exact ribosomal sequence variants (RSVs) rather than ‘fuzzy’ OTUs have evolved quickly. Therefore, using such a de-noising approach we challenged Illumina’s protocol and compared it against a widely adopted V4 single-step amplification library preparation method using custom sequencing-primers (fusion primer dual index; FPDI).

**Materials/methods:** To assess qualitative and quantitative accuracy an even mock community with 22 bacterial species (with perfect matching amplification-primer sites) was sequenced on a MiSeq. Various libraries were produced in duplicate with paired 250- or 300-bp reads, with V34 or V4, and with UTTDI or FPDI, respectively. Cutadapt was used to remove amplification-primers from UTTDI reads. Then the DADA2 de-noising software was employed run- and library-wise with defaults (most notably zero mismatches between overlapping reads were allowed) except the following: 10-bp from the 5'-end of each FPDI read were trimmed, V4 reads were trimmed if necessary on both ends to achieve fully overlapping merged reads only, and trimmed reads with more than two expected errors were discarded.

**Results:** Each mock community species was detected in all libraries. When comparing 250- vs. 300-bp libraries it was noted that for the latter three times more reads were filtered (22.34 vs. 79.19%, \( p < 0.001 \)). Furthermore, the marginally overlapping V34 libraries had four times more false positive RSVs than V4 libraries (33.83 vs. 8.20%, \( p = 0.026 \)). Finally, the accuracy of mock community quantification expressed as root-mean-square-deviation (RMSD) between observed and expected values was better for UTTDI than FPDI. This effect was even more pronounced when a species with not perfect matching V4 primer annealing sites was added to the mock community (2.97 vs. 3.94 RMSD).

**Conclusions:** Due to possible primer editing quantification of the two-step amplification UTTDI was indeed superior to FPDI. However, for economic and quality reasons it is recommended to update Illumina’s protocol with RSV analysis to 250-bp reads and to fully overlapping V4 libraries, respectively.

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**Abstract 5082**

**Evaluation of meningococcal B vaccine antigen variants in Neisseria meningitidis: Italy 2012-2018**

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**Background:** Neisseria meningitidis of serogroup B (MenB) represents currently the leading cause of invasive meningococcal diseases (IMD) in Italy. Two protein-based vaccines are on the Italian market: the four-component vaccine, containing factor H binding protein (FHbp), Neisseria adhesin A (NadA), Neisserial heparin binding antigen (NHBA) and porin A (PorA), and the bivalent vaccine containing two FHbp-subfamily variants. Vaccine antigen variants on MenB strains responsible of IMD in Italy, from 2012 to 2018, were analyzed.

**Materials/methods:** Two-hundred and two isolates and/or clinical samples (blood or cerebrospinal fluid) from IMD were collected and characterized at the National Reference Laboratory of Istituto Superiore di Sanità in Rome. Genotypic characteristics, including serogroup identification, multilocus sequence typing (MLST), and vaccine antigen genes (FHbp, nadA, nhba and porA), were defined using the PubMLST website (http://pubmlst.org/neisseria/).

**Results:** Eighteen clonal complexes (ccs) were identified, of which the cc41/44 (22%) and the cc162 (20%) were the most frequently found. A slightly increase of cc213 was also observed. FHbp variant 1 (subfamily B) was the most commonly detected over time (54%), mostly associated with cc41/44 and cc162. FHbp variants 2 and 3 (subfamily A) were less represented (20% each one) and identified in cc41/44 and cc213, respectively. Full-length NadA peptide was detected in 8% of MenB, mostly belonging to cc32; whereas, the majority has the nadA gene interrupted by the insertion of genetic elements or by deletions. A greatest diversity was observed for NHBA peptide, with NHBA-20 being the prevalent and mainly associated with cc162. PorA VR2 14 was the most frequent, mainly identified in cc162 and cc213.

**Conclusions:** This analysis suggests that the vaccine antigen variants are quite stable over time among the MenB genomes studied. Molecular analysis need to be completed by the antigen expression measure to predict the efficacy of MenB vaccines.

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**Abstract 5083**

**Colistin-resistant bacteria in Indian raw food samples**
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**Background:** Usage of colistin as a growth promoter in livestock farms is a well-known factor contributing to colistin resistance. An earlier single publication from Chennai, India reported the presence of colistin resistant bacteria in raw food samples. Aim of the current study was to analyse the extent of the problem in a larger sample size.

**Materials/methods:** Food samples like chicken, fish, meat and vegetables were collected from multiple sources such as households, supermarkets and outlets in Chennai, between November 2018 and October 2019. Approximately one gram of minced food sample was inoculated in 9ml of Brain heart infusion broth. After overnight incubation, 1ml of suspension was enriched overnight in BHIB containing colistin (10 µg colistin disk/colistin sulfate). 50 µl of sample was inoculated in ChromID Colistin R agar plates and incubated for 24 to 48 hours. Species with intrinsic resistance to polymyxins were discarded. Colonies recovered were identified by MALDI-TOF MS and antimicrobial susceptibility testing was performed using Vitek-2 system. Colistin MIC was determined using broth microdilution method.

**Results:** A total of 381 food samples (251 vegetables, 52 fruits, 69 chicken, 8 mutton and 1 fish) were analysed. 93/381 food samples (39 chicken, 4 mutton, 41 vegetables and 9 fruits) carry colistin resistant isolates. 121 colR isolates were identified including 82 K. pneumoniae, 1 K. aerogenes, 8 E. coli, 7 Enterobacter spp, 2 Cronobacter spp., 2 Salmonella enterica, 19 P. aeruginosa. Klebsiella species showed high colistin MIC ranging from 4 to ≥256µg/ml and 51% of these are sensitive to all the tested antibiotics. E. coli shows colistin MIC of 4 to 16µg/ml with resistance to cotrimoxazole and fluoroquinolone. All Enterobacter isolates had colistin MIC of ≥256µg/ml and were susceptible to other tested antibiotics. Other species (Cronobacter, Salmonella) shows colistin MIC 4 or 8 µg/ml. Colistin MIC of P. aeruginosa ranges from 4 to 16 µg/ml.

**Conclusions:** Presence of colistin resistant bacteria in a large number of community food samples is extremely worrying. The recent Indian ban on growth promotional usage of colistin is encouraging but the implementation must be systematically monitored.

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Prevalence and molecular epidemiology of high-risk clones among third-generation cephalosporin-resistant and carbapenem-resistant Klebsiella pneumoniae in Germany

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Abstract third-party references: for the DZIF-R-NET Study Group

Background: The increase of multidrug resistant (MDR) Klebsiella pneumoniae (Kpn) reflects a complex dissemination process including mobile genetic elements and the spread of high-risk (HiR) MDR clones. We aimed to investigate the prevalence of HiR-clones and the molecular epidemiology of third-generation cephalosporin-resistant (3GCR) and carbapenem-resistant (CR) Kpn recovered from patients on hospital admission, and from bloodstream infections (BSI) in Germany.

Materials/methods: Patients were screened upon hospital admission in 2016 and 2017 for rectal colonization of 3GCR and CR Kpn at six German tertiary-care university hospitals. Isolates were selected using chromID ESBL (bioMérieux) and CHROMagar mSuperCARBA (Mast Diagnostica). 3GCR, CR and susceptible Kpn BSI isolates were included. Antimicrobial susceptibility testing for cefotaxime, ceftazidime, ertapenem, imipenem, and meropenem was performed using Vitek2 and Etest (bioMérieux). Sequencing libraries were prepared for 250bp paired-end sequencing on a MiSeq (Illumina). Core-genome MLST (Ridom® SeqSphere+) and 7-loci MLST were determined.

Results: Out of 5846 patients screened on hospital admission, 41 3GCR Kpn isolates were recovered (0.7% prevalence), of which five were additionally CR (carbapenemase negative). The most common STs were ST45 (n=4), ST14 (n=3), ST17 (n=3), ST20 (n=2) and ST307 (n=2). Among the colonizing Kpn, 22% belonged to HiR-clones (ST14, ST17, ST37 and ST307). A total of 47 3GCR Kpn isolates were recovered from BSI, of which two were also CR (OXA-48-encoding). The most prevalent STs among the BSI were ST15 (n=5), ST48 (n=5), ST307 (n=5), ST13 (n=3), and ST101 (n=3), while, 43% belonged to HiR-clones (ST14, ST15, ST17, ST101 and ST147). By cgMLST, an unambiguous separation of isolates was observed with only a few clusters detected among colonizing and infecting isolates. A total of 26 susceptible Kpn from BSI were investigated. Here, ST37 (n=4) was the most prevalent ST followed by ST14 (n=2) while no transmission clusters were detected and 31% belonged to HiR-clones (ST14, ST17, ST37, and ST101).

Conclusions: Our data demonstrate that the prevalence of 3GCR Kpn carriage on hospital admission remains low, and that CR is still rare. Clusters were rarely observed among colonizing and infecting isolates. Finally, our results indicate that international HiR-clones are circulating in Germany forming small clusters.

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Clinical efficacy of echinocandins in the treatment of candidiasis in cirrhotic patients: retrospective multi-centre study

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Background: To date comparative studies on the efficacy of echinocandins compared to azoles in patients with liver cirrhosis are lacking. Patients affected by liver cirrhosis represent a particular setting as they present a higher risk of fungal infections and an altered pharmacokinetic and pharmacodynamics.

Materials/methods: A retrospective multicenter study base on four Italian tertiary hospitals has been conducted including adult patients with liver cirrhosis and candidemia between 2014 and 2018. Patients were followed-up for 30 days after infection onset. Patients receiving antifungal regimen containing or non-containing echinocandins were compared. Factors associated to 30-day mortality were evaluated with a propensity-score adjusted multivariable analysis.

Results: Ninety patients were included. Of these, 63% were male with a median age (interquartile range) of 63 years (52-68). The cirrhosis etiologies were HCV infections (50%) and alcoholic abuse (29%). The main species of Candida spp. found in these patients were Candida albicans (64%), Candida parapsilosis (14%) and Candida glabrata (9%). Of the 90 cases analyzed, 76 had performed adequate targeted therapy, 41 out of 76 had been treated with fluconazole, 32 out of 76 with an echinocandin and 3 out of 76 with liposomal amphotericin-B. Overall, the 30-day mortality rate from candidemia was 42%. Survival analysis using Kaplan-Meier curves showed a significant lower mortality among patients treated with echinocandins (25% vs 50%; p 0.038). In the multivariate analysis the 30-day mortality predictive factors were: MELD calculated at the time of diagnosis of candidemia [HR 1.058 (95% CI 1.004- 1.117); p 0.035], septic shock [HR 3.084 [95% CI 1.422- 6.686]; p 0.004], whereas echinocandin therapy was associated with a better survival rate [HR 0.415 [95% CI 0.165-0.983]; p 0.046]. Echinocandin therapy remained highly associated with a better survival rate also after propensity score adjustments [HR 0.271 [95% CI 0.096-0.772] p = 0.014].

Conclusions: Despite the limitations related to population size and the retrospective study design, we have been able to show a greater clinical efficacy of echinocandins in the treatment of candidiasis in patients affected by liver cirrhosis.

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Are large cities at higher risk for tuberculosis drug resistance? A French appraisal

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Background: Tuberculosis burden in France is low (<10 cases/100 000), but the national average conceals regional disparities, with some parts of Ile-de-France at higher risk. These differences are mainly linked to immigration from high-burden countries or rates of human immunodeficiency virus (HIV) infection. We sought to investigate if Paris or large French cities had a higher prevalence of drug resistance, and, eventually, reasons for epidemiological disparities.

Materials/methods: Socio-demographic and microbiological data were routinely collected from 1998 to 2017 via a sentinel network of 36 laboratories of University Hospitals (AZAY-Mycobacteria network) that complied with the international recommendations for the surveillance of drug resistance and performed drug susceptibility testing. Participating laboratories were divided into 4 groups according to the region or the size of the city: Paris, Ile-de-France except Paris [sub-urban Paris], and cities larger or smaller than 200 000 inhabitants. Paris was considered the reference for comparisons.

Results: Overall, the network collected data on 30 727 patients; globally, 34% were diagnosed in Paris. Compared to the 3 other regional groups, patients from Paris were younger, more likely to be male, HIV-positive and foreign-born. Resistance to at least one first-line anti-tuberculosis drug (14% in Paris vs 11% in Ile-de-France, 11.4% in big cities, 10% in small cities), and multidrug-resistant tuberculosis (MDR-TB) (3% vs 1.5%, 2%, 2%, respectively) were significantly higher in Paris. In multivariable analysis, being diagnosed in Paris was independently associated with primary and secondary resistance to at least one first-line drug. Being diagnosed in large cities was associated with secondary resistance. Other factors independently linked to resistance were age <41 years, sputum smear positivity and being foreign-born (Table 1).

Conclusions: Resistance rates to anti-tuberculosis drugs are higher in Paris than in other large or small French cities. Moreover, Paris was independently linked to a higher risk of primary and secondary drug resistance. This risk is not explained by traditional risk factors such as treatment history and country of birth. Specific socio-demographic features should hence be sought to explain the higher burden of resistant tuberculosis in Paris compared to other districts in France.

Table 1. Results of multivariate analysis [logistic regression]

<table>
<thead>
<tr>
<th>Variables</th>
<th>Any resistance OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRIMARY RESISTANCE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;41</td>
<td>1.3 (1.2-1.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Foreign-born</td>
<td>1.6 (1.5-1.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sputum smear positive</td>
<td>1.1 (1.0-1.2)</td>
<td>0.03</td>
</tr>
<tr>
<td>Paris</td>
<td>1.2 (1.0-1.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>SECONDARY RESISTANCE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &lt;41</td>
<td>1.6 (1.3-1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Foreign-born</td>
<td>2.3 (1.8-2.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sputum smear positive</td>
<td>1.7 (1.4-2.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Paris</td>
<td>2.7 (1.7-4.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Large cities</td>
<td>3.2 (1.9-5.2)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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Abstract 5088

Trends in Gram-negative bacteraemia in adult febrile neutropaenic cancer patients in a high-resistance setting during the last decade

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Background: We analyzed the trends in gram-negative (GN) bacteremia and changes in antimicrobial resistance patterns in febrile neutropenic (FEN) patients with hematological malignancies (HMs) and/or hematopoietic stem cell transplantation (HSCT). Antibiotic resistance profile was determined for extended spectrum beta lactamase (ESBL) production, carbapenem resistance (CR), multidrug-resistant phenotype (MDR) and colistin resistance.

Materials/methods: 296 blood isolates from 286 patients hospitalized between 1.1.2010 and 31.5.2019 at Hacettepe University were evaluated. Only the first bacteremic episode for each patient was included in analysis. BD Phoenix™, VITEK-MS (BioMérieux) and Bruker Biotyper Matrix-Assisted Laser Desorption/Ionization-Time of Flight automated identification systems were used to identify bacteria over the years. VITEK® 2 Compact System and BD Phoenix was used for antibiotic susceptibility, if necessary conventional methods were also employed. ESBL detection was performed by E-test until 2017 and double disk synergy test+combine disk test were used after 2017. MDR phenotype was as described previously (Magiorakos et al. Clin Microbiol Infect 2012;18:268). Kruskal-Wallis test was used to calculate the ratios between resistance mechanisms that changed between years and Jonckheere-Terpstra test was used to evaluate the changing trends between these ratios.

Results: 153 E. coli, 52 K. pneumoniae, 36 P. aeruginosa, 31 A. baumannii and 26 other GN bacteria were isolated during study period. A significant increase was detected in ESBL-production (p=0.05) and MDR phenotype [p<0.001] in E. coli related bacteremia. ESBLs production [p<0.001], MDR phenotype [p<0.001] and CR [p<0.001] have also increased in K. pneumoniae isolates. The variation of antimicrobial resistance over the years in all bacteria is shown in the Figure. Colistin resistance was rare and detected in one each E. coli (0.6%), P. aeruginosa (2.7%), A. baumannii (3.2%) and, 2 K. pneumonia (3.8%) strains. No significant difference was found in other bacteria.

Conclusions: In our center, high-risk HM and HSCT patients have exposed to an increased rate of resistant enteric and non-fermentative GN bacterial pathogens. Since standard empirical regimens may not work in such a high-resistance setting, strategies should be regularly updated according to current epidemiological data.

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Sequential time-kill curve to distinguish polymyxin-induced resistance and hetero-resistance in Acinetobacter baumannii

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**Background:** Resistance to polymyxins, the last therapeutic option for multidrug-resistant A. baumannii, is increasingly reported. In this study, sequential time-kill experiments were used to describe the adaptive resistance to colistin and polymyxin B in A. baumannii and modifications of genes involved in polymyxin resistance were characterized by sequencing and RT-qPCR.

**Materials/methods:** Two A. baumannii clinical isolates from the same patient were used in this study: a colistin-susceptible (ColS) and a colistin-resistant after colistin treatment (ColR). Two sequential time-kill curve (TKC) were performed using colistin (CST) and polymyxin B (PMB) at concentration from 0.25x to 64x MIC. The bacteria that regrowth in presence of polymyxins from 1st TKC were directly used for the next 2nd TKC inoculum. In parallel, heteroresistance was quantified by population analysis profiles (PAPs). Alongside, bacteria were analyzed by sequencing and RT-qPCR to determine the change of genes involved in lipopolysaccharide (LPS) modifications (pmrA, pmrB, pmrC, lpxM) and LPS biosynthesis (lpxA, lpxC, lpxD).

**Results:** Sequential TKC have shown that after 2nd TKC, ColS could growth up to 8-fold MIC to CST, but not with PMB. Also, high-level colistin resistant population was shown by ColR after 2nd TKC with the highest regrowth up to 16-fold MIC for CST but only 4-fold for PMB observed from their respective MICs value. Before the contact with polymyxins, genes sequences of pmrA, pmrC, lpxM, lpxA, lpxC, and lpxD for both isolates were identical except for pmrB that shown the addition of 10-amino acid followed by an overexpression of pmrA (5-fold), pmrB (8-fold) and pmrC (3.9-fold) for ColR. PAPs confirmed the presence of resistant subpopulation with dissimilarity genetic expression in ColR but not in ColS. No other mutations were found in ColS and ColR after 2nd TKC. However, after 2nd TKC, a significant overexpression of lpxC was shown by ColR regrowth isolates only with CST (5-fold) but not with PMB.

**Conclusions:** The colistin-susceptible A. baumannii was able to develop resistance under colistin pressure while it remains susceptible to polymyxin B. We also showed that the high-level colistin resistant in ColR was presumably caused by heteroresistance population associated to loss of LPS production.

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Abstracts 2020

Abstract 5090

Rapid detection of bacteria resistant to the last resort antibiotics using MALDI Biotyper Sirius: the MALDIxin test

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Background: Resistance to polymyxins in most Gram-negative bacteria arises from chemical modifications to the lipid A portion of their lipopolysaccharide [LPS] mediated by chromosomally-encoded mutations or the recently discovered plasmid-encoded mcr genes that have further complicated the landscape of colistin resistance. MIC determination by broth microdilution, the gold standard for the detection of polymyxin resistance, is time consuming (24 hours). This is why there is a need for fast, robust, accurate, easy to use and affordable diagnostics solutions to detect polymyxin-resistant bacteria, providing a same-day-result after species identification.

Materials/methods: 40 E. coli clinical isolates and a collection of 23 Salmonella enterica clinical strains were used in this study. Briefly, bacteria grown on Mueller-Hinton agar were submitted to mild-acid hydrolysis (1 % acetic acid, 98°C for 10 min). Washed hydrolyzed cells were loaded onto the MALDI target plate and immediately overlaid with 1.2 μL of matrix (super-DHB matrix, dissolved in chloroform/methanol 90:10 v/v to a final concentration of 10 mg/mL). The bacterial suspension and matrix were mixed directly on the target by pipetting and the mix dried gently under a stream of air. MALDI-TOF mass spectrometry analysis were performed with a MALDI Biotyper Sirius (Bruker Daltonics) using the linear negative-ion mode.

Results: We calculated Polymyxin resistance ratio (PRR) values from the acquired spectra. The percentage of modified lipid A was calculated by dividing the sum of the intensities of the lipid A peaks attributed to addition of pETN (m/z 1919.2 and m/z 2157.2) and L-Ara4N (m/z 1927.2 and m/z 2165.2) by the intensity of the peaks corresponding to native lipid A (m/z 1796.2 and m/z 2034.2); a PRR value of zero, indicating polymyxin susceptibility, was obtained for all colistin-susceptible isolates, whereas positive PRR values, indicating resistance to polymyxins, were obtained for all resistant strains. In Salmonella the average percentage of modified lipid A remained significantly lower in chromosome-encoded colistin resistant isolates (18.25% ± 3.23%) compared to MCR-producers (51.12% ± 3.38%).

Conclusions: Thanks to its speed of execution, affordability and ease to use, the MALDIxin test using MALDI Biotyper Sirius might be a game changer in antimicrobial susceptibility testing and patient management.

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Abstract 5091

**Design of a varicella zoster virus PCR combined with a herpes simplex virus PCR in a multiplex assay: a diagnostic evaluation study**

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**Background:** Herpes simplex virus 1 and 2 (HSV-1/-2) and varicella zoster virus (VZV) typically infect the skin and mucosa. They can also affect the nervous system and lead to serious neurological complications. These infections have a wide spectrum of differential diagnoses. Thus, a fast and reliable detection is crucial. For this purpose, we evaluated a new VZV PCR and its combination in a multiplex format with an existing HSV-1/-2 assay to form a vesicular rash PCR.

**Materials/methods:** We designed primers and probes for VZV and an internal control and combined them with existing primers and probes for HSV-1/2 [Corey et. al. J Med Virol; 2005; 76. 350-355]. DNA extracts from 276 skin and mucosal swabs were tested with the new multiplex PCR and the commercial Artus VZV and HSV-1/-2 PCR kits, which were considered as gold standard.

**Results:** None of the samples was inhibited. Results of the new PCR and the commercial kits are compared in the 2x2 contingency table [table 1]. The overall concordance was >99%. Sensitivity, specificity, PPV and NPV of the new PCR were perfect for VZV and HSV-2 (100% each), and 100%, 99.4%, 97.0% and 100% for HSV-1, respectively.

**Conclusions:** The new VZV-HSV-1/-2 vesicular rash multiplex PCR has excellent sensitivities, specificities, PPVs and NPVs for diagnosing the three herpesviruses and is suitable for usage in routine clinical practice.

<table>
<thead>
<tr>
<th></th>
<th><strong>VZV</strong></th>
<th></th>
<th><strong>HSV-1</strong></th>
<th></th>
<th><strong>HSV-2</strong></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>New multiplex PCR</strong></td>
<td><strong>Positive</strong> (%)</td>
<td><strong>Negative</strong> (%)</td>
<td><strong>Total</strong> (%)</td>
<td><strong>Positive</strong> (%)</td>
<td><strong>Negative</strong> (%)</td>
<td><strong>Total</strong> (%)</td>
</tr>
<tr>
<td>Positive</td>
<td>117 (100)</td>
<td>0 (0)</td>
<td>117 (42)</td>
<td>32 (100)</td>
<td>1 (1)</td>
<td>33 (21)</td>
</tr>
<tr>
<td>Negative</td>
<td>0 (0)</td>
<td>159 (100)</td>
<td>159 (58)</td>
<td>0 (0)</td>
<td>124 (99)</td>
<td>124 (79)</td>
</tr>
<tr>
<td>Total</td>
<td>117 (100)</td>
<td>159 (100)</td>
<td>276 (100)</td>
<td>124 (100)</td>
<td>125 (100)</td>
<td>157 (100)</td>
</tr>
</tbody>
</table>

Table 1: 2x2 contingency table comparing the new multiplex PCR to commercial PCRs (gold standard)

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Abstract 5096

**The REAnimation Low Immune Status Markers study: phenotypic and functional alterations of innate immune response in critically ill patients**

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1EA 7426 « Pathophysiology of Injury-Induced Immunosuppression » (Université Claude Bernard Lyon 1 - Hospices Civils de Lyon - bioMérieux), Joint Research Unit HCL-bioMérieux, Immunology Laboratory & Anesthesia and Critical Care Medicine Department, Edouard Herriot Hospital, Lyon, France, 2Bioaster Technology Research Institute, Lyon, France, 3Sanofi Aventis, Chilly-Mazarin, France, 4GladSmithKline, Cambridge, United Kingdom, 5Sanofi Pasteur, Marcy-l’Étoile, France, 6ESPCI Paris, PSL Research University, Paris, France

**Background:** Immune response to sepsis is complex. Several alterations of the innate response have been described and some even observed in other severe injuries. However, the comprehensive description of immune alterations development overtime in a large cohort of patients has never been done so far. In addition, it is not known whether these alterations depend on the type of injury (infectious vs sterile) and if they are associated with an increased risk of deleterious outcomes.

**Materials/methods:** A prospective longitudinal observational study was set up in Edouard Herriot Hospital (Lyon-France, December 2015 - March 2018). A total of 354 ICU patients suffering from sepsis, severe trauma or after major surgery, and 175 healthy volunteers were enrolled. Blood specimens were collected once for volunteers and three times for patients during the first week of ICU stay. Systemic inflammation was monitored by measuring IL-6 and IL-10 plasma concentrations. The innate response was measured by assessing cell numbers, phenotypes (immature neutrophils, MHC class II expression on monocytes), functions (cytokine production), and mRNA levels (S100A9, CD74, CX3CR1) with standardized tests.

**Results:** Injury-induced innate immune profile was similar in the 3 groups of patients and characterized by a major rise of circulating immature neutrophils number and proportion whereas the number of circulating monocytes was not modified. However, starting from D1 after injury, monocytes were characterized by a major decrease in MHC class II expression correlated with altered TNFalpha production to LPS ex vivo. Intensity of these injury-induced alterations was maximal at D1, inversely correlated with systemic pro and anti-inflammatory responses and decreased overtime. The persistence at the end of the first week after injury of profound monocyte alterations was associated with an increased risk of death and secondary infections.

**Conclusions:** Our results show the complexity and overtime evolution of the innate immune response after injury. This response combines an initial physiologic stress immune response with the concomitant development of monocyte alterations. When persisting, these alterations are associated with deleterious outcomes in accordance with the development of delayed injury-acquired immunodeficiency. Our data support the rational for an immune intervention to restore functional immune response in these patients.

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**Abstract 5097**

**Human polyomaviruses in the cerebrospinal fluid of neurological patients**

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**Background:** Human Polyomavirus (HPyVs) infections are common, ranging from 60% to 100% of the general population, depending on the virus. After primary infection, which occurs asymptptomatically during childhood, HPyVs can establish a life-long latency in different body compartments. A profound immunological impairment is a risk factor for their reactivation that may lead to clinically severe polyomaviruses-induced diseases. Central nervous system (CNS) tropism is well defined for JC Polyomavirus (JCPyV) while data regarding other HPyVs, such as BK Polyomavirus (BKPyV), Merkel Cell Polyomavirus (MCPyV) and Polyomaviruses 6, 7 and 9 (HPyV6-7-9) are only sporadic in the literature.

**Materials/methods:** A total of 234 cerebrospinal fluid (CSF) samples were collected from patients affected or with suspected different neurological disorders. DNA was isolated and subjected to real-time PCR for the detection of six HPyVs: JCPyV, BKPyV, MCPyV, HPyV6, HPyV7 and HPyV9. When possible, viral strains molecular characterization of JCPyV, BKPyV and MCPyV positive samples was carried out by nested PCR and automated sequencing.

**Results:** Overall, HPyV genomes were detected in 41/234 (17.5%) CSF samples. JCPyV was detected in 3/234 (1.3%), BKPyV in 15/234 (6.4%), MCPyV in 22/234 (9.4%), and HPyV6 in 1/234 (0.4%) CSF samples. BKPyV and MCPyV were significantly more frequently detected than JCPyV (p<0.05). JCPyV was detected at the highest (p<0.05) mean load (3.7 x 10^7 copies/mL), followed by BKPyV (1.9 x 10^6 copies/mL), MCPyV (1.9 x 10^5 copies/mL), and HPyV6 (3.3 x 10^4 copies/mL). Viral protein 1 gene (VP1) gene sequence analysis showed one 1b strain for JCPyV, four Ia strains and three Ib-I strains for BKPyV. Noncoding control regions (NCCRs) gene sequence analysis showed two rearranged strains for JCPyV, four rearranged strains for BKPyV, four rearranged strains for BKPyV and five IIC strains for MCPyV.

**Conclusions:** HPyVs other than JCPyV were found in the CSF of patients affected with different neurological diseases suggesting that HPyVs are latent in the CNS of immunosuppressed patients probably as bystanders, rather than etiological agents of the disease. Furthermore, the description of CNS-infecting viral strains represent an additional benefit allowing the definition of the genotype and/or the rearrangements of HPyVs, other than JCPyV, circulating in the CSF.

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Haemophilus influenzae as the causing pathogen of epididymo-orchitis: a case report

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**Background:** Haemophilus influenzae is a Gram-negative opportunistic coccobacillary pathogen of the respiratory tract. This case study reports the rare finding of *Haemophilus influenzae* in the urine of a patient suffering from scrotal pains and mictalgia. At the emergency department of a tertiary hospital in Belgium, the 44 years old patient presents afebrile with inguinal bilateral pain and pus secretion at the start of micturition. The diagnosis of epididymo-orchitis was based on clinical findings; a urine sample was collected for molecular detection of sexual-transmitted disease and bacterial culture. He was released from the ward with anti-inflammatory medication and ciprofloxacin.

**Materials/methods:** Urine sediment analysis was conducted on the Sedimax [Menarini] automated microscope. Next, the urine sample was cultured on a cysteine lactose electrolyte deficient agar. After overnight aerobic incubation at 35°C, primary detection of suspicious colonies from the axenic culture was performed and a subculture was incubated overnight at 5% CO2 at 35°C on a haemophilus agar. Identification of the species was conducted, applying the Biotyper matrix assisted laser desorption/ionisation time-of-flight analyzer [Bruker] together with hemin and nicotinamide-adenine-dinucleotide growth factors verification. Susceptibility testing was subsequently performed.

**Results:** The microscopic urine analysis depicted a pyuria with 2761 leucocytes / µL, with a negative molecular assay for *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. After overnight incubation the cysteine lactose electrolyte deficient agar revealed a massive (> 100,000 colony-forming units / mL) growth of small, opaque colonies. Identification of *Haemophilus influenzae* with the Biotyper device was achieved with a matching score >2. Next, confirmation of the species *Haemophilus influenzae* was achieved applying both hemin and nicotinamide-adenine-dinucleotide growth factors on the haemophilus agar. The strain of *Haemophilus influenzae* tested susceptible for ampicillin (MIC = 0.75 mg/L) and resistant for trimethoprim/sulfamethoxazole (MIC = 3 mg/L). The patient’s antibiotic treatment was adapted.

**Conclusions:** Routine urine culture at our laboratory does not include a haemophilus agar, although it provides the necessary nutrients to support growth of *Haemophilus* spp. As such the incidence of the species in urinary samples could be underestimated, yet a literature search does not support the incidence of Haemophilus-associated urinary tract infection to be greater than 1%.

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Abstract 5105

**Immunochromatographic detection of quorum-sensing autoinducers, an innovative strategy to diagnose infections by identifying Staphylococcus aureus strains**

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**Background:** Staphylococcus aureus is one of the most commonly isolated microorganisms in both healthcare-associated and community-acquired infections. Most common routine diagnostic methods rely on culture-based techniques which can take up to 72h in order to obtain conclusive results. Many bacterial identification alternatives have emerged as potential alternatives of the gold standard culture plate techniques. Particularly, bacterial Quorum Sensing (QS) has attracted the attention as potential diagnostic and therapeutic target. This communication system is based on the release and sensing of low molecular weight chemical signals, called autoinducers (AIs). They control its own biosynthesis and the genetic expression of virulence factors and survival mechanisms. In S. aureus these molecules correspond to cyclic thiolactone peptides (AIPs), encoded by a specific locus, responsible of the phenotypic variability between the different strains.

**Materials/methods:** Monoclonal antibodies against the AIP-4 of S. aureus have been produced after appropriate hapten design and synthesis followed by preparation of the immunogen. A competitive indirect microplate-based ELISA has been developed and implemented to the analysis of biological samples. Clinical isolates from patients proven to be infected by agr-IV strains of S. aureus have been cultured and the profile of AIP-4 secreted to the media has been investigated.

**Results:** The microplate-based ELISA developed with the antibodies produced has shown a limit of detection below the AIP-4 concentration levels in culture broth samples. Quantifiable AIP-4 levels can be detected only after two hours of culture of clinical isolates obtained from patients infected with this pathogen. Culture samples from different agr strains did not show significant immunoreactivity, indicating the potential of the technology to discriminate between the different agr strains.

**Conclusions:** The specific quantification of this QS molecule could provide valuable information regarding the strain type and disease status. The diagnostic tool here presented may significantly contribute to improve diagnostic efficiency and current therapeutic strategies. Immunochemical techniques might be able to fulfill the requirements and demanding challenges of the infectious diseases diagnostic field through the study of QS.

![Figure 1: AIP-IV concentration in culture growth samples from a clinical isolate of S. aureus.](image)

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Polyethylene glycol (15)-hydroxystearate enhances amphotericin B activity against Mucorales

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Background: Amphotericin B (AmB) is the first line therapy recommended to treat mucormycosis. Despite treatment, mortality reaches 40 to 60%. Increasing the efficacy of AmB by using it in combination with an adjuvant could help address this issue. Polyethylene glycol (15)-hydroxystearate (PEG15HS), an FDA-approved surfactant for parenteral use, could destabilize fungal membrane by surfactant activity and thus promote AmB activity which acts through pore formation at the fungal membrane. The aim of our study was to evaluate in vitro the combination of AmB and PEG15HS on several Mucorales strains using this model.

Materials/methods: Chequerboard in RPMI following EUCAST guidelines were used to test interaction between PEG15HS and AmB. AmB diluted in RPMI (4 to 0.002 mg/L) and PEG15HS diluted in sterile water (2752 to 0.042 mg/L) were used. Twelve clinical strains of Mucorales were used: Rhizopus arrhizus (5), Lichtheimia corymbifera (3), Lichtheimia ramosa (1), Rhizopus microsporus (1), Mucor circinelloides (1), Rhizomucor pusillus (1). MIC of AmB were read after 24H at 37°C. The modeling of the effect of PEG15HS on the antifungal efficacy of AmB was performed using an inhibitory Emax model with WinNonlin software.

Results: All strains presented MIC ≤ 1 mg/L for AmB and MIC > 1024 mg/L for PEG15HS. PEG15HS enhanced efficacy of AmB against all strains with 2.5 to 38-fold MIC decrease depending on strain. Potency of PEG15HS was high, with EC50 varying from 0.13 to 1.54 mg/L for 10 strains but was lower for the two others (8.57 and 53.45 mg/L).

Conclusions: PEG15HS highly enhanced AmB activity against Mucorales with high efficacy and potency. Due to PEG15HS low toxicity, high potency, and the need of low concentrations, AmB - PEG15HS combination could improve mucormycosis treatment. Further studies are needed to evaluate pharmacokinetics of PEG15HS and its efficacy in vivo.

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Abstract 5107

**Distribution of mecA in Staphylococcus aureus isolates in a multi-centre clinical study**

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**Background:** The mecA gene encodes the penicillin-binding protein 2a (PBP2a) that confers resistance to methicillin and other penicillinase resistant beta-lactams.¹ Most molecular diagnostic tests which detect Staphylococcus spp. and S. aureus, include detection of mecA to alert the laboratory to the presence of resistant Staphylococcus. In the instance of multiple Staphylococci present in a sample, some nucleic acid tests cannot delineate which species carries the mecA. In this study, we evaluate the distribution of mecA among isolates identified as S. aureus by standard of care laboratory methods (SOC) in samples collected from 10 sites to determine how often MRSA was associated with the detection of mecA and how often another Staphylococcus spp. was present using the ePlex® Blood Culture Identification Gram-Positive (BCID-GP) Panel.

**Materials/methods:** There were 1,195 evaluable samples for S. aureus in the clinical study. Each organism was identified by MALDI-TOF MS, automated identification systems, or manual methods and tested by phenotypic antimicrobial susceptibility testing (AST). Samples were tested with qPCR and bidirectional sequencing to determine presence of the mecA. There were 160 prospective and 122 retrospective samples determined to be true positive for S. aureus.

**Results:** The BCID-GP Panel detected S. aureus with mecA in 78 prospective samples. SOC AST results confirmed 90% were MRSA. 98% of S. aureus with no mecA detected were confirmed as MSSA by corresponding AST. No additional Staphylococci were present in prospective samples. In the retrospective samples, S. aureus with mecA was detected in 103 samples and confirmed by AST as MRSA in 99% of samples. One S. aureus and S. epidermidis co-infection with mecA was confirmed as MSSA. In 15 samples with S. aureus with no mecA detected, 14 were confirmed as MSSA including one co-infection with S. capitis.

**Conclusions:** The ePlex BCID-GP Panel exhibits high correlation for the detection of S. aureus and mecA for MRSA and MSSA. Amongst prospective samples collected across 7 major laboratories, no instances of S. aureus with another Staphylococci were found by SOC, whereas only 2 instances were found in retrospective samples from 8 major laboratories. This suggests that prevalence of co-infections may be low.

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Evaluation of 16S rRNA metagenomics workflow performance by spike-in and in silico experiments

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Background: Microbiota profiling by metagenomics is establishing as a standard analysis in clinical microbiology. Despite wide and rapid developments, there is still a great heterogeneity in applied methods. Laboratories must carefully set their workflow since variations in protocols significantly impact results. We present a 16S rRNA metagenomics workflow validation study focusing on DNA extraction methods and taxonomic classification.

Materials/methods: Our workflow was evaluated on the ATCC-2002 mock-community, a commercial control composed of 20 bacteria in even proportions. Samples were prepared in triplicates by spiking serial 10-fold dilutions of this community (5x10^6 to 10^3 bact/ml) into A549 pneumocytes (10^4 cells/ml). DNA was extracted with Ultra-Deep Microbiome (Molzym), QIAamp DNA Microbiome (Qiagen) and NucleoSpin Soil (Macherey-Nagel) kits. V3V4 16S rRNA libraries were sequenced on Illumina MiSeq. Paired-end 300bp reads were processed into Amplicon Sequence Variants (ASVs) by an in-house pipeline based on DADA2. Sequences were classified by RDP against the EzBioCloud database. Moreover, simulated V3V4 amplicons were extracted from reference genomes by in silico PCRs and classified with the same pipeline.

Results: DNA extraction kits induced systematic but distinct biases [Figure]. Best analytical sensitivity was obtained with the NucleoSpin Soil kit, with 18/20 (90%, in green) bacteria of the mock-community and no contaminants representing more than 1% of the reads. Conversely, less expected bacteria and more contaminants [in red] were recovered by the two host-DNA depleting kits, especially in dilutions below 10^4 bacteria/ml. Six bacteria [30 %] were erroneously classified at the species level, even in absence of wet-lab artifacts, in the in silico simulation. For example, Bacillus cereus was classified as B. anthracis and E. coli as Shigella sonnei. Taxonomic classification improved in 4/6 cases by concatenation of the taxonomic annotation for taxa with identical V3V4 sequences in the EzBioCloud database. Wide range of 16S rRNA copies per genome (2 - 14) and a 3'-end mismatch with Cutibacterium acnes contribute to explain with extraction biases the discrepancies between the observed and expected relative taxa abundances.

Conclusions: These spike-in and in silico experiments based on the ATCC-2002 mock community exemplify the potential impact of DNA extraction and reference databases pre-processing for 16S rRNA metagenomics.

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Abstract 5110

**MYCO-TB kit: rapid and efficient digestion and decontamination method for the detection of mycobacteria in extrapulmonary specimens**

Francesco Bisognin*1, Silvia Felici1, Giulia Lombardi1, Caterina Vocale1, Giampaolo Biundo1, Maria Carla Re1, Paola Dal Monte1

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**Background:** Mycobacteria require long incubation time allowing contaminating organisms to overgrow in cultures and preventing their detection. Therefore, processing specimens by digestion and decontamination is necessary before culture.

MYCO-TB is a ready to use sample digesting and decontaminating kit developed by Copan, that requires shorter time for sample processing than other commercial kit. The aim of this study was to compare performance of MYCO-TB with MycoPrep (Becton Dickinson, BD), the latter actually used in our routine flowchart, in terms of detection of mycobacteria and culture contamination on extra-pulmonary samples.

**Materials/methods:** In this prospective study extra-pulmonary samples of a volume greater than 10 ml sent to the microbiology laboratory of the S. Orsola-Malpighi University Hospital (Bologna, Italy) for the detection of mycobacteria have been included. Specimens have been processed both with MYCO-TB and MycoPrep for digestion and decontamination, before culture on solid (Lowenstein-Jensen, with and without PACT antibiotic mix; Biolife) and liquid media (MGIT Bactec 960, BD).

**Results:** Up to date 130 extra-pulmonary samples have been processed: 28.5% cavitary fluid, 22.3% swab, 21.5% urine, 15.4% biopsy, 5.4% purulent exudates, 4.6% lymph-node and 2.3% gastric aspirate. *Mycobacterium tuberculosis* complex (MTBC) was detected in 2 liquid cultures after decontamination with both systems with an average detection time of 23.0±8.0 days for MYCO-TB and 22.2±6.9 days for MycoPrep.

Proportion of contaminated liquid cultures was 3.9% for MYCO-TB and 10.0% for MycoPrep. Contamination of solid media without PACT was 10.8% for MYCO-TB and 6.9% for MycoPrep, while proportion of contaminated LJ PACT was 5.4% with both systems.

**Conclusions:** The MYCO-TB kit has been shown to have a stronger activity than MycoPrep in the digestion and decontamination of extra-pulmonary specimens for the detection of mycobacteria. In addiction ready to use reagents made it possible to reduce and optimize required manual skills and avoid errors during processing. The rapid protocol (5 vs 23 minutes of MycoPrep) and the formulation for single sample of MYCO-TB allow to reduce the time and the risk of contamination of samples, supporting the mycobacteriology laboratory activity.

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Abstract 5113

Direct-from-blood-culture disk diffusion to determine antimicrobial susceptibility of *Escherichia coli* and *Klebsiella pneumoniae*

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**Background:** Multidrug-resistant *Escherichia coli* and *Klebsiella pneumoniae* emerged as a relevant cause of bloodstream infections (BSIs) in several countries, including Italy. Prompt initiation of targeted antimicrobial therapy depends on availability of antibiotic susceptibility testing (AST) results. At the end of 2018, EUCAST has validated a method for performing a Rapid AST (RAST) directly from positive blood culture (BC) bottles. The aim of this study was to evaluate the EUCAST RAST method for testing susceptibility to β-lactams, aminoglycosides and ciprofloxacin of *E. coli* and *K. pneumoniae*.

**Materials/methods:** Analysis was prospectively carried out on 101 consecutively positive BCs from nonduplicate patients, in which the presence of *K. pneumonia* or *E. coli* was detected by direct MALDI-TOF mass spectrometry analysis from positive BC broths. RAST was performed as indicated by EUCAST guidelines. Disk diffusion results were compared to reference broth microdilution method. AST results were interpreted according to EUCAST clinical breakpoints. The category agreement (CA) and error rates were calculated as described by the International Organization for Standardization (ISO) guidelines and also considering the new EUCAST definition.

**Results:** The CA values at 4 h, 6 h and 8 h of incubation were 77.2%, 87.7%, 93.5%, respectively using the ISO criteria and 77.5%, 88.0% and 93.8%, respectively according to the modified EUCAST criteria. No very major error was observed, and major error rates were 4.3%, 0.4%, and 0.4% at 4 h, 6 h and 8 h, respectively, using the ISO criteria and 5.1%, 0.9% and 0.9%, respectively, according to the modified EUCAST criteria. Rates of ATU (area of technical uncertainty) were 18.4%, 11.3% and 5.5% at 4 h, 6 h and 8 h, respectively. High ATU rates were observed for gentamicin and amikacin. With the EUCAST RAST method, ESBL and carbapenemase production was correctly detected in all CTX-M (*n*=18), KPC (*n*=7) and OXA-48 (*n*=1) producers, with reading at 4 h and 6 h, respectively.

**Conclusions:** These preliminary data demonstrate the potential feasibility of using RAST to guide antibiotic treatment decisions for patients with life-threatening infections.

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Background: Carbapenem-resistant Enterobacteriaceae (CRE) is an urgent challenge in the treatment of bloodstream infections (BSIs). The objective of this study was to investigate the effect of carbapenem resistance on outcomes of bloodstream infections caused by Enterobacteriaceae in China.

Materials/methods: Ten tertiary hospitals located in Guangdong province, China were involved in this study, with a median of 2,040 beds (IQR 1,375-2,850). We performed a retrospective cohort study of 117 patients to explore the association of carbapenem resistance with outcomes of BSI patients. A total of 1,391 Enterobacteriaceae were isolated from the blood of BSI patients. Preliminary species identification was achieved by MALDI-TOF MS and 16s rRNA sequencing. The underlying diseases or comorbid conditions, location before admission, health-care exposures before BSI onset and risk factors source were compared between patients with BSIs due to CRE or carbapenem-susceptible Enterobacteriaceae (CSE). MICs were detected by the broth microdilution method for 16 antimicrobial agents.

Results: Out of the 1,391 isolates, 81 (5.8%) were carbapenem-resistant. Predominant pathogens included K. pneumoniae (n=425; 72 carbapenem-resistant K. pneumoniae [CRKP], 16.9%), and Escherichia coli (n=925; 3 carbapenem-resistant E. coli [CREC], 0.3%). CRE isolates had a more extensive antimicrobial resistance profile than in CSE isolates. All CRE isolates were non-susceptible to cephalosporins. And CRE isolates were most frequently susceptible to colistin (80/81, 99%), followed by tigecycline (67/81, 83%), amikacin (39/81, 48%). A retrospective cohort study of 117 patients found that in-hospital mortality was 35% (22 of 62 patients) for patients with CRE BSI and 16% (9 of 55 patients) for patients with CSE BSI. Exposure to health-care before BSI onset was more frequent among CRE patients than CSE patients. ICU admission within 30 days, transfer from another hospital, central vein catheterisation, and change in antibiotic treatment after the positive culture were independent risk factors determined to be significantly associated with CRE BSI.

Conclusions: Our data demonstrated that the carbapenem resistance was associated with higher mortality of patients with BSI in Guangdong province, China.

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Background: Patients in whom blood cultures (BC) are performed are heterogeneous group; while those with positive BC have been extensively studied, data from patients with negative BC are scarce. However, this group of patients might be a suitable population for antimicrobial stewardship (AS) purposes. The NOBACT study aims to characterize this population. The objective of this analysis is to identify the mortality predictors in patients in whom blood cultures are obtained, and specifically in those with negative results.

Materials/methods: The first phase of the NOBACT study is a prospective cohort of randomly selected patients from whom BC were obtained from October 2018 to July 2019 in 3 Spanish University Hospitals. Demographic data, clinical and therapeutic characteristics were studied. The dependent variable was the 30-day mortality after BC. Bivariate and multivariate analysis of factors related to mortality were performed. The adequacy of antimicrobial treatment was defined according to local guideline, considering demographic data, source and severity.

Results: Overall, 622 patients with obtained BC were included; in 123 (19.7%), BC were positive. Mortality was 12% (76 patients). The variables associated with mortality in bivariate analysis are shown in figure 1. By logistic regression, positive blood culture (OR 3.87; 95% CI 1.68-8.95) and inadequate treatment due to lack of appropriate coverage according to local guidelines at day 2 after the blood culture obtainment (OR 3.59; 95% CI 1.49-8.66) were independently associated with mortality. No interactions were relevant. When only patients with negative blood cultures were included, the independent predictors of death were age (OR 1.04; 95% CI 1.01 - 1.07) and inadequate treatment due to lack of appropriate coverage (OR 4.65; 95% CI 1.74-12.40).

Conclusions: These results reinforce the importance of bacteraemia programmes to guarantee adequate treatment in patients with positive blood cultures, and provide novel data suggesting the idea that AS interventions in certain subgroup of patients with negative blood may be considered.

Figure 1. Bivariate analysis of factors associated with 30-days mortality.

<table>
<thead>
<tr>
<th></th>
<th>30-day mortality, n (%)</th>
<th>OR (CI 95%) or P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR)¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No (68) (56-78)</td>
<td>Yes (72) (65-84)</td>
</tr>
<tr>
<td>Previous antimicrobial treatment</td>
<td>223 (41)</td>
<td>0.01 (57)</td>
</tr>
<tr>
<td>Charlson score ≥3</td>
<td>135 (25)</td>
<td>30 (40)</td>
</tr>
<tr>
<td>Immunocompromised patient</td>
<td>180 (33)</td>
<td>40 (52)</td>
</tr>
<tr>
<td>Nosocomial/healthcare-related acquisition</td>
<td>546 (60)</td>
<td>58 (76)</td>
</tr>
<tr>
<td>qSOFA ≥2 (day0)</td>
<td>58 (11)</td>
<td>16 (21)</td>
</tr>
<tr>
<td>Serum CRP¹ at day in 2 mg/L, median (IQR)</td>
<td>78 (16-163)</td>
<td>91 (16-255)</td>
</tr>
<tr>
<td>Inappropriate coverage at day 2</td>
<td>75 (14)</td>
<td>18 (24)</td>
</tr>
<tr>
<td>Positive blood culture result</td>
<td>98 (18)</td>
<td>25 (32)</td>
</tr>
</tbody>
</table>

¹Interquartile range; ²C reactive protein concentration

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Abstract 5117

Colistin resistance in human Salmonella spp. isolates collected from Italian Enter-Net surveillance during the period 2016-2018

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Abstract third-party references: Istituto Superiore di Sanità

Background: Colistin is used in human to treat multidrug-resistant bacteria infections and in veterinary medicine for therapy and growth promotion in farming animals. Reports of plasmid-mediated colistin resistance mcr genes are increasing worldwide in different bacterial species, including Salmonella. ECDC-EFSA reported a 4.7% colistin resistance in human Salmonella isolates in 2017 in Europe. In this study colistin susceptibility and its molecular mechanisms were investigated in a collection of human Salmonella spp. isolates, provided by the Enter-Net laboratory surveillance network for enteric pathogens in Italy.

Materials/methods: From 2016 to 2018, 330 Salmonella spp isolates were tested for colistin susceptibility by broth microdilution method. Four previously (2009-2015) colistin-resistant Salmonella isolates were included for comparison. Multiplex PCR for detection of mcr-1 to mcr-5 genes was performed. WGS was carried out on 4 susceptible and 8 colistin resistant strains. In silico analysis of MLST, cgMLST, resistant genes, plasmid typing and pMLST were performed. mcr carrying plasmids were completely assembled. Known and unknown hypothetical chromosomal colistin resistance mechanisms were searched.

Results: Colistin resistance (MIC≥4 µg/ml) was reported in 26 out of 330 (7.9%) strains: 23 S. Enteritidis (24.1%), 1 S. Typhimurium (5.5%), 2 S. Typhimurium monophasic variant (3.3%). mcr genes were found in only 3 strains. WGS analysis revealed mcr-1 and mcr-5 in a ST-4 IncHI2 plasmid harbored by a S. Typhimurium monophasic variant strain (2016) and a mcr-1-IncX4 plasmid in a S. Enteritidis and in a S. Typhimurium monophasic variant isolated in 2009 and 2015, respectively. In one S. Napoli isolate a new amino acidic mutation was identified in sapC gene (S241A), involved in colistin resistance.

Conclusions: Salmonella isolates from humans revealed a low proportion of colistin resistance in Italy. S. Enteritidis showed the highest proportion of resistant isolates, probably due to chromosomal gene mutations. The mcr-1 gene was present in our country at least since 2009. A novel IncHI2 plasmid presenting both mcr-1 and mcr-5 genes was detected in this study in a S. Typhimurium monophasic variant. A possible chromosomal colistin resistance mechanism was identified in a S. Napoli isolate.

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Abstract 5122

The impact of shortening antibiotic treatment duration on antimicrobial resistance carriage: a modelling study

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Background: Shortening treatment duration is a key component of antibiotic stewardship interventions. However, the effectiveness of this approach in reducing antimicrobial resistance is uncertain and a clear theoretical rationale for the approach is lacking. We performed a modelling study in order to better understand the circumstances under which reducing antibiotic duration would represent a high impact intervention.

Materials/methods: We constructed three increasingly complex stochastic models to simulate nosocomial transmission and within-host selection of antibiotic-resistant and sensitive bacteria. Antibiotic exposure was assumed to act on within-host processes by modifying bacterial growth and death rates and to act on between-host processes by modifying susceptibility to carriage acquisition and transmission. The primary outcome was the difference in the proportion of carriers of resistant bacteria between the wards receiving long and short antibiotic treatment durations. We performed sensitivity analysis to understand under which circumstances shortening antibiotic duration would reduce the prevalence of resistance carriage. Using parameters appropriate for multidrug-resistant Enterobacteriaceae, we quantified the expected magnitude of the reductions in resistance with shortened antibiotic duration under different scenarios.

Results: The three models reached broadly similar conclusions. Shortening antibiotic duration is most effective at reducing resistance carriage when two conditions hold: individuals not exposed to antibiotics have a minimal probability of acquiring resistant bacteria; and decolonization of resistant bacteria is rapid without antibiotic selective pressure. In addition, longer antibiotic treatment may decrease or increase prevalence of resistance carriers depending on the availability of effective antibiotics targeting particular resistance mechanisms. In low resistance prevalence settings, antibiotic duration has a substantial impact on the prevalence of resistance only when the number of antibiotic prescriptions is already low. In high resistance prevalence and transmission settings, shortening duration rather than the number of prescriptions and narrowing the spectrum of antibiotics contributes more to the reduction of resistance carriage.

Conclusions: Our models suggest that shortening duration is effective at reducing prevalence of resistance carriage only when antibiotics are the key drivers for acquisition and persistent carriage of resistance. The magnitude of reduction in resistance carriage depends on the baseline resistance prevalence, rate of transmission, and the number of antibiotic prescriptions.

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Abstract 5123

Characterisation of carbapenemase-producing Enterobacter spp. isolates recovered in a tertiary hospital in Madrid, Spain between 2005 and 2018

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Background: Carbapenemase production is constantly increasing in Enterobacterales species. We analyzed the microbiological characteristics and population structure of carbapenemase-producing Enterobacter spp. (Ent-CP) isolates recovered at the Ramón y Cajal University Hospital, Madrid, Spain (2005-2018).

Materials/methods: Bacterial identification was performed (MALDI-TOF MS, Bruker; hsp60 amplification/sequencing). A maximum-likelihood tree was constructed with hsp60 genes (MEGA-6). Antimicrobial susceptibility (microdilution, Microscan, Beckman-Coulter; MIC-strips, Liofilchem) was interpreted using EUCAST 2019 criteria. Carbapenemase production was phenotypically confirmed (KPC/MBL/OXA-48 Confirm kit, Rosco Diagnostica and Hodge modified test). Carbapenemase and ESBL genes were detected (PCR, sequencing). Population structure (PFGE, Bionumerics) and clonal diversity (SDI) were determined. Patient’s clinical charts were reviewed.

Results: Overall, 181 Ent-CP were detected (59.1% colonizations; 39.2% clinical; 1.7% environmental) in medical (61.3%), surgical (20.8%) and ICU (17.3%) areas. Clinical samples were mainly from urinary (n=26) and respiratory tracts (n=12). Median LOS (length of stay) was 31 days (IQR=16-64). 59 cases were considered as hospital acquired and median LOS until Ent-CP detection was 34 days (IQR=13-47), being longer in infected than colonized patients (45 days vs 19 days, p<0.001). Most frequent MALDI-TOF identified species were E. cloacae (n=85) and E. asburiae (n=49). hsp60 gene-sequencing showed a higher diversity: 70 E. hormaechei-clusters III,VI, VII, VIII, 69 E. roggenkampii-IV, 15 E. kobei-II, 9 E. asburiae-I, 3 E. ludwigii-V, 1 E. cloacae subsp. dissolvens-XII. 9 K. aerogenes were also identified. A high clonal diversity (SDI>0.90) was determined except in cluster III (SDI=0.73). VIM-1 (n=133) and OXA-48 (n=34) were the most frequent carbapenemases. KPC-2 (n=9), KPC-3 [n=2], VIM-2 (n=1) and two co-producers (VIM-1+KPC-2, VIM-1+KPC-3) were also present. A fecal carriage increase was observed between 2011-2018 (p<0.001), mainly due to VIM-1 and OXA-48-Ent-CP (p<0.001). OXA-48-E. ludwigii (p=0.006) and KPC-E. kobei (p=0.001) associations were established. ESBL co-production (14.2%) was detected, frequently associated with blaTEM122 (p<0.001), E. roggenkampfi (p<0.001), colonization (p=0.03) and medical areas (p=0.02). Resistance to ertapenem (96.1%), imipenem (37.0%), meropenem (35.0%) and co-resistance to other antimicrobials were observed.

Conclusions: Ent-CP incidence is increasing in our hospital, mainly due to VIM-1 and OXA-48-Ent-CP fecal carriage. Interestingly, hsp60 gene-sequencing showed a higher discriminatory power for Enterobacter spp. identification than MALDI-TOF.

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Abstract 5125

**Association between susceptibility to quinolones in Escherichia coli and tetracycline use in the community: analysis with community-specific ARIMA models**

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**Background:** Tetracyclines are extensively used in the community. We previously found that tetracycline use was associated with resistance to quinolones in E. coli in a French community (FC), but this association was not described in other communities. Our aim was to assess the association between tetracycline use and E. coli susceptibility to quinolones in 3 distinct communities, by using community-specific models.

**Materials/methods:** Monthly time series of proportions of quinolone susceptible E. coli and uses of quinolones and tetracyclines were obtained from a FC, a Spanish community (SC) and an Israeli community (IC). The study period ranged from 2009 to 2018. The association between antimicrobial use and resistance was tested in each community using multivariate auto-regressive integrated moving average models including time, tetracycline and quinolones uses as explanatory variables, and proportion of susceptible isolates as outcome.

**Results:** Proportions of susceptible isolates in FC, SC and IC were 86%, 60% and 78%, respectively. Median (range) quinolone use in FC, SC and IC were 37 (22 to 54), 74 (43 to 172) and 51 (41 to 60) DDD/1000 inhabitants/month, respectively. Median (range) tetracycline use in FC, SC and IC were 77 (36 to 104), 22 (10 to 36) and 40 (31 to 59) DDD/1000 inhabitants/month, respectively. In the FC, use of quinolones 2 months earlier (estimate [SD], -0.099 [0.031]) and tetracyclines 12 months earlier (estimate [SD], -0.014 [0.005]) were significantly associated with quinolone susceptibility. In the SC, use of quinolones 7 months earlier (estimate [SD], -0.076 [0.022]) and tetracyclines 4 months earlier (estimate [SD], -0.252 [0.093]) were significantly associated with quinolone susceptibility. In the IC, tetracycline use 7 months earlier was significantly associated with quinolone susceptibility (estimate [SD], -0.100 [0.028]) whereas quinolone use was not.

**Conclusions:** In 3 communities that differed greatly by susceptibility to quinolones and antimicrobial use, community-specific ARIMA models showed that there was a significant association between tetracycline use and quinolone susceptibility in E. coli. These results suggest that decreasing tetracycline use in the community may decrease quinolone resistance in community isolates of E. coli.

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Preclinical efficacy, pharmacokinetics and safety of CD377, a novel antiviral Fc-conjugate against influenza

Voon Ong1, James Levin1, Allen Borchardt1, Thanh Lam1, Wantong Jiang1, Zhi-Yang Chen1, Quyen-Quyen Do1, Tom Brady1, Alain Nencovich1, Joanne Fortier1, Makia Nakamura1, Karin Amundson1, Jeffrey Locke1, Amanda Almaguer1, Nicholas Dedeic1, Grayson Hough1, Jason N. Cole1, Simon Döhrmann1, Rajvir Grewal1, Elizabeth Abelovski1, James M. Balkovec1, Michael Schlosser1, Ken Bartizal1, Leslie W. Tari*1

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**Background:** CD377 is a novel antiviral Fc-conjugate (AVC) comprising a potent small-molecule antiviral and the Fc domain of human IgG1. CD377 is long-acting and demonstrates robust efficacy in lethal mouse models of influenza. Studies were conducted to confirm its stability and characterize CD377 pharmacokinetics, safety/tolerability, and efficacy in a mouse influenza prevention model.

**Materials/methods:** CD377 stability was assessed after 0-24 h incubations at 37°C in mouse/human plasma and human liver hepatocytes using MALDI-TOF mass spectrometry. Single-dose pharmacokinetics/tolerability were studied in the mouse (1-100 mg/kg), rat (5-50 mg/kg), and monkey (5-20 mg/kg). Plasma concentrations were measured by a neuraminidase (NA)-capture or Fc-capture with Fc-detection ELISA. In this case, Fc-capture/Fc-detection measured the total concentration of Fc-related species while NA-capture/Fc-detection measured the concentration of intact NA-linked–Fc species. Two-week safety/toxicology was evaluated in monkeys (5-20 mg/kg SC) on days 1 and 8 with necropsy on day 15; clinical signs, chemistries, hematology, cytokines, and histopathology were evaluated. Preventative efficacy was studied in a lethal influenza mouse model using a single dose of CD377 [0.3–3 mg/kg] 28 days prior to intranasal challenge with 3x the LD95 of A/California/07/2009 (H1N1) [3E4 pfu], A/Hong Kong/1/68 (H3N2) [3.6E4 pfu], or B/Malaysia (Victoria lineage) [1E4].

**Results:** CD377 was stable after incubations in plasma and liver hepatocytes. Further, plasma exposures from both Fc-capture/Fc-detection and NA-capture/Fc-detection were comparable, indicating that the molecule remained intact in vivo. In the mouse, rat, and monkey, CD377 t1/2 was 5–10 days. Dose-proportional increases in exposure were observed in each species, notably from 1–100 mg/kg in mouse. High bioavailability (77%) was observed after subcutaneous or intramuscular administration. A single SC dose of 1 mg/kg administered 28 days prior to infection provided 100% protection from death against H1N1 \( P=0.0020 \) (Figure 1) and B \( P=0.0031 \) subtypes. H3N2 required only a 0.3 mg/kg dose for 100% protection \( P=0.0007 \). The 2-week monkey toxicology study showed no adverse effect on bodyweight, clinical chemistry, hematology, coagulation, cytokines, or urinalysis.

**Conclusions:** CD377 was well-tolerated and stable in vitro and in vivo; its extended half-life support its potential as a long-acting, novel AVC for prevention of influenza.

**Figure 1.** Efficacy of CD377 in a 28 Day Prevention Model. A, survival; B, body weight

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Abstract 5127

**Automated rapid antimicrobial susceptibility testing from positive blood cultures using Copan WASPLab**

Cees Verduin¹, Sebastiaan Derksen², Jitske Stalpers*¹, Theo Liebregts³, Martijn Nijs¹, Arjan Jansz¹

¹PAMM laboratories, laboratory for medical microbiology, Veldhoven, Netherlands

**Background:** In 2018, EUCAST published recommendations for Rapid AST (RAST) from positive blood culture bottles (BCb) for several species, with direct plating for disk diffusion. Reading of inhibition zones is performed after 4, 6 and 8 hours of incubation with only ±5 minutes of tolerance (*Pseudomonas aeruginosa* only after 6 or 8 hours).

The Copan lab automation can support this workflow: WASP® streaks the plate and dispense the antibiotic disks; WASPLab takes a very high-resolution picture (48Mp) autonomously at stated reading time and an algorithm for the automatic measurement of the inhibition zone supports the plate evaluation.

**Aim of this study is to describe the implementation and validation of the Rapid AST directly from positive BCb manually processed and with the use of automation.**

**Materials/methods:** *Escherichia coli* ATCC25922 and *Staphylococcus aureus* ATCC29213 were used to standardize disk diffusion AST procedure as per EUCAST guideline.

Quality control strains (QC), following EUCAST protocol, and clinical blood culture samples (CBCS) were incubated in bioMérieux BACT/ALERT®. Samples from positive bcbb were inoculated on Mueller Hinton plates using both the manual method and with WASP®. After 4, 6 and 8 hours of incubation, inhibition zones were measured manually with a ruler and automatically read using WASPLab software.

**Results:** All QC was within the ranges for both methods suggesting a good implementation of the RAST as per EUCAST indication.

CBCS for Gram negative bacteria (N=140; not for *P. Aeruginosa*) were 100% readable at 4h, the majority of Gram-positive bacteria (N=60) were readable at 6h or 8 hours. No major/very major errors (S instead of R and vice versa) were found for both methods.

Complete results will be shown at ECCMID.

**Conclusions:** The data collected show an excellent correlation between the manual method and automatic method on WASP and WASPLab. The RAST directly from positive BCb can be easily implemented on the automated platform and has important advantages. These advantages are: 1) standardized reading time points, 2) fully automated workflow, e.g. not hands-on time for technicians 3) High Resolution Images, with automated reading and interpretation 4) Images are always available for evaluation at a later time.

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Abstract 5128

**A radiologic score for pulmonary non-tuberculous mycobacterial infection: preliminary results**

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**Background:** Nontuberculous mycobacteria (NTM) can cause hard to treat pulmonary infections. These bacteria are ubiquitous in the environment, and it is difficult to differentiate between colonization and infection. Moreover, a tool to assess the lung damage objectively and measure the consequences of treatment is lacking. We aim to develop and validate a reproducible and objective radiologic score and to assess how this score is influenced by treatment.

**Materials/methods:** The score was developed modifying previously published scoring systems on the same pathology. It evaluated: consolidation, solid nodules, ground-glass opacities, bronchiectasis, bronchial wall thickening, atelectasis, bronchial filling and distal bronchiolar filling, pleural alterations and thoracic lymphadenopathies. As preliminary study we retrospectively identified five treated and five untreated adult patients affected by pulmonary NTM infection in our hospital. Their HRCT scans at baseline [time of diagnosis] and follow-up (6-12 months later) were collected and reviewed by four radiologists unaware of patient treatment. The overall scores at baseline and follow-up were matched in order to objectively compare the progress of lung involvement in treated and untreated patients over time.

**Results:** Mean radiological score values at baseline and follow-up were 28.5 (SD 24.5) and 26.1 (SD 25.1), respectively. Overall, the radiological score values did not vary significantly between baseline and follow-up (P=0.6). When stratified according to treatment, the radiological score variation between baseline and follow-up was not different between those treated compared to those who did not receive treatment (p=0.35). Interestingly, when stratified according to the NTM species a difference in the mean of the radiological score values was noted both at baseline and follow-up, although it did not reach significance.

**Conclusions:** The preliminary results show a trend in the difference in the mean of the radiological score values. Further analysis on a larger cohort of patients are needed to validate its capacity to assess changes due to treatment and eventually the presence of a correlation with the species of NTM involved.

![Figure 1](image-url) (A) Differences in radiological score between baseline and follow-up in treated vs untreated patients. (B) Radiological score results according to mycobacterial species at baseline and follow-up. [MAC: *Mycobacterium avium* complex]

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Abstract 5129

Optimising pharmacokinetics/pharmacodynamics of β-lactam/β-lactamase inhibitor combinations against high inocula of extended-spectrum β-lactamase-producing bacteria

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Background: Reduced in vitro β-lactam activity against a dense bacterial population is well recognized. It is commonly attributed to the presence of β-lactamase(s) and it is unknown whether the inoculum effect could be diminished by a β-lactamase inhibitor. We evaluated different β-lactam (BL) / β-lactamase inhibitor (BLI) combinations in suppressing a high inoculum of extended-spectrum β-lactamase (ESBL)-producing bacteria.

Materials/methods: Three clinical isolates (2 K. pneumoniae and 1 E. coli) expressing representative ESBL (CTX-M-15 and SHV-12) were examined. The impact of escalating BLI (tazobactam or avibactam) concentrations on BL (piperacillin or ceftazidime) MIC reduction was characterized by an inhibitory sigmoid E_{max} model. The effect of various dosing regimens of BL/BLI combinations was predicted using a novel PK/PD index (%T>MICi), and selected dosing exposures (n=10) were experimentally validated in a hollowfibre infection model over 120 hours. The threshold exposure necessary to suppress a high inoculum of bacteria (approximately 10^8 CFU/ml at baseline) and to prevent regrowth was identified using classification and tree regression analysis.

Results: With escalating BLI concentrations, a reduction in BL MIC was observed and well characterized in all isolates (r² >= 0.93). Regardless of the BL/BLI pairings, regrowth over time could be suppressed using T>MICi >= 73.6%. The exposures to suppress bacterial regrowth were higher than that (55.5%) we reported previously for 10^6 CFU/ml at baseline. These exposures might be attained using the clinical dose of avibactam (0.5 g), but a much higher than the standard dose would be needed for tazobactam (>= 2g).

Conclusions: A dense population of ESBL producing bacteria could be suppressed by an optimized dosing regimen of selected BL/BLI combinations. The reversibility of enzyme inhibition could play an important role in diminishing the inoculum effect. In vivo investigations to validate these findings are warranted.

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Background: In 2006 the UK introduced 7-valent pneumococcal conjugate vaccine (PCV-7) into the routine childhood immunisation programme which was replaced with the 13-valent pneumococcal conjugate vaccine (PCV-13) in 2010. Since 2003 adults aged 65+ years and all adults at increased risk of pneumococcal infection have been recommended to receive a single dose of the 23-valent pneumococcal polysaccharide vaccine (PPV23). Next generation higher valent PCVs (PCV-15 and PCV-20) are now in advance development and could shortly become available for use in adults.

Materials/methods: Peer reviewed publications (published post 2017) containing data describing the contemporary IPD and pneumococcal pneumonia disease burden in UK adults with insight into epidemiological trends and the individual pneumococcal serotype distribution were identified. The proportion of IPD and pneumococcal pneumonia in adults covered by the serotypes included in PCV-13, PCV-15 and PCV-20 was determined.

Results: Three articles were identified. Overall the incidence of both IPD and pneumococcal pneumonia in UK adults has been rising post 2013/14 though trends vary by individual serotype. Despite herd effects induced by the infant PCV programme the burden of both IPD and pneumococcal pneumonia in adults living in the UK continues to be substantial with no discernible impact of PPV23 at the population level. In 2016/17 the proportion of PCV-13, PCV-15 and PCV-20 type IPD in adults in England and Wales aged 65+ years was 21%, 32% and 63% respectively. Between 2013/14 and 2017/18 the average proportion of PCV-13, PCV-15 and PCV-20 pneumococcal pneumonia identified in English adults aged 16+ years was 35%, 40% and 66% respectively (36%, 39% and 64% in 2017/18).

Conclusions: Vaccinating older UK adults with PCV-13 could address a significant proportion of the current pneumococcal disease burden affecting this population. However, PCV-15 and PCV-20 could provide progressively increased coverage of those pneumococcal serotypes currently causing both IPD and pneumococcal pneumonia in UK adults, with PCV-20 potentially addressing ~65% of the pneumococcal disease burden.

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Abstract 5134

Clinical outcomes with the use of telavancin for methicillin-resistant Staphylococcus aureus bacteraemia with minimum inhibitory concentration >1 mcg/mL for vancomycin

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Background: The management of methicillin-resistant Staphylococcus aureus (MRSA) bacteraemia is becoming increasingly challenging, as minimum inhibitory concentrations (MICs) to vancomycin and daptomycin are consistently rising. This study aims to evaluate the efficacy and safety of telavancin in the treatment of MRSA bacteraemia with an MIC >1 mcg/mL to vancomycin.

Materials/methods: This study was an Institutional Review Board approved retrospective chart review of patients who received telavancin at an academic, tertiary care medical centre between 2015 January 1 and 2019 May 31. Electronic medical charts were reviewed for: clinical cure; 30- and 60-day relapse; criteria for the Acute Physiology and Chronic Health Evaluation (APACHE) II, the updated Charlson Comorbidity Index (uCCI), and the Pitt Bacteremia scores (PBS); prior antibiotic use; bacteraemia and endocarditis diagnostic criteria; source of infection; microbiological culture clearance; time to discharge; patient mortality; and adverse effects. The primary outcome was clinical cure at discharge, which was defined as the resolution of clinically significant signs and symptoms and clearance of blood cultures.

Results: Thirty-eight charts were identified and eleven met inclusion criteria for this analysis. The average BPS and uCCI scores for included patients were 1.7 and 3, respectively. APACHE II scores were calculated for five patients with an average score of 9.2. Vancomycin or daptomycin were given for an average of 5.4 and 2.6 days, respectively, prior to the initiation of telavancin. The average telavancin dose used for all patients was 7.5 mg/kg. All patients achieved clinical cure at discharge. The average duration of the bacteraemia before and after telavancin therapy was 6.2 and 2.1 days, respectively, with an average treatment length of 37 days; there were no instances of 60-day mortality. Two patients relapsed: one patient after 268 days and another after 467 days. Four patients experienced either significant QTc prolongation or acute renal failure.

Conclusions: The use of telavancin in MRSA bacteraemia demonstrated clinical cure and minimal relapse in our patient population. Telavancin may be a potential treatment option for patients with a vancomycin MIC >1 mcg/mL for MRSA bacteraemia. Large prospective randomised controlled trials are warranted to confirm these observations.

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Abstract 5135

**In vitro activity of novel biofilm-disrupting agents against Candida auris and other Candida species**

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**Background:** *C. auris* is a multi-drug resistant, globally emerging fungal pathogen. In fact, it has been recovered from environmental surfaces and is linked to recalcitrant candidal infections. Chlorhexidine (CHD) appears to be an effective surface disinfectant. Biofilm disrupting agents (BDAs) are novel molecules with a broad spectrum of antibacterial and antifungal activity. BDAs have been used in the treatment of chronic wounds and to sterilize environmental surfaces. The goal of this study was to evaluate BDA technology against *C. auris* and other *Candida* spp.

**Materials/methods:** We evaluated the in vitro efficacy of several BDA agents [topical gel, wound wash solution, and surface disinfectants] vs. CHD against *C. auris* isolates 0381 and 0386, *C. albicans* 90028 and *C. glabrata* 200918 by both agar plate zone inhibition and time kill assays. The efficacy was evaluated based on the magnitude of the inhibition zone and the quantitative reduction of CFU when compared to the control.

**Results:** All 3 BDAs and CHD inhibited *C. auris* growth effectively in a concentration dependent manner. A comparative analysis of the BD agents and CHD against *C. glabrata* and *C. albicans* using time-kill curves not only demonstrated a 99.99% killing at conventional concentrations at 30 minutes, but they also revealed early efficacy with a > 1 log decrease in just 10 min. Regarding *C. auris*, the BDAs demonstrated a 99.99% bactericidal effect within 60 seconds of contact. Furthermore, both CHD and the BD agents showed excellent activity against pregrown *C. auris* cells. BDAs were highly effective against both *C. auris* isolates, whereas CHD was only moderately effective against one of the *C. auris* 0386, suggesting the possible emergence of resistance/tolerance to CHD among different *C. auris* species.

**Conclusions:** All three BD agents and CHD have excellent activity against different *Candida* species, including *C. auris*. In addition, certain isolates of *C. auris* showed increased resistance/tolerance to chlorhexidine, but not to the BD agents. The rapid fungicidal activity of the BD novel agents are extremely valuable in eradicating surface colonization of *Candida* spp, especially *C. auris*. This should be able to decrease the spread of this multi-drug resistant *Candida* spp.

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Molecular epidemiology of colonising and infecting vancomycin-resistant Enterococcus faecium in Germany

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Abstract third-party references: for the DZIF-R-NET Study Group

Background: The emergence of vancomycin-resistant Enterococcus faecium (VREfm) is an important public health problem, creating an urgent need to gather detailed surveillance data. We aimed to investigate the molecular epidemiology of colonizing and infecting VREfm and compare them to vancomycin-susceptible Enterococcus faecium (VSEfm).

Materials/methods: Patients were screened upon hospital admission in 2016 and 2017 for rectal colonization of VREfm at six German tertiary-care university hospitals using chromID VRE (bioMérieux). Isolates were also collected from patients with bloodstream infections (BSI) caused by VREfm and VSEfm. Antimicrobial susceptibility testing for linezolid, teicoplanin and vancomycin was conducted using Vitek2 and Etest. Sequencing libraries were prepared using Nextera XT kit (250bp paired-end) and whole genome sequencing was performed on a MiSeq (Illumina). cgMLST (Ridom® SeqSphere+), 7-loci MLST, and Van-type were determined.

Results: Out of 5846 patients screened, 101 VREfm colonizing isolates were identified (1.7% prevalence), of which 77 harboured the vanB and 22 isolates the vanA operon. Two isolates harboured both vanA and vanB. Sequence type (ST) 117 (n=61) was the predominant clone, forming a large multi-centre complex of closely related isolates dispersed across all study centers. In contrast, ST80 (n=22) formed individual study-center clusters, with no overlapping between centers, and similar clustering patterns were observed for ST78 (n=10) and ST17 (n=3). Examination of the VREfm bloodstream isolates (n=79) revealed a similar pattern; the most prevalent ST was ST117 (n=50), forming a large multi-center complex, followed by ST203 (n=11) and ST80 (n=9) forming smaller clusters. In total, 49 VREfm BSI isolates harboured the vanB, 29 the vanA, and one had both the vanA and vanB operon. Additionally, two colonizing and three BSI isolates were linezolid-non-susceptible. No predominant clone was identified among the 27 VSEfm BSI isolates. The most prevalent STs were ST78 (n=6), ST117 (n=5), ST17 (n=4) and ST80 (n=3) forming small clusters.

Conclusions: These data demonstrate that ST117 was the predominant VREfm clone colonizing patients on admission and among patients with VREfm BSI. ST117 isolates form a large VREfm multi-center cluster expanding in the six study centers. This study provides epidemiological data about VREfm and may contribute to more effective infection control interventions.

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**Abstract 5137**

**Comparison of methods to evaluate the activity of ceftolozane/tazobactam against clinical isolates of carbapenem-resistant *Pseudomonas aeruginosa* from Chile**

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**Background:** The widespread dissemination of carbapenem-resistant *P. aeruginosa* (CR-PAE) is considered a major global public health threat. C/T is a recently approved combination of a novel cephalosporin (ceftolozane) and tazobactam (a β-lactamase inhibitor). The activity of C/T against CR-PAE remains high. However, recent reports have raised concerns about susceptibility testing methods to evaluate the in-vitro activity of C/T, due to discrepancies between them. Therefore, we aimed to evaluate the activity of C/T against Chilean clinical isolates of PAE using different susceptibility methods.

**Materials/methods:** We analyzed 66 PAE isolates (50 CR and 16 carbapenem-susceptible [CS]) collected during 2017 from 5 tertiary care institutions in Santiago, Chile. All isolates exhibited a negative Blue-Carba result. C/T susceptibility was performed by broth microdilution (BMD), E-test (Biomerieux), MIC test strip (Liofilchem), and disk diffusion ([DD], Hardy Diagnostics, 30ug discs), following CLSI-2019 recommendations. All tests were performed using the same inoculum and ATCC® 27853 was used as a reference. Results were compared to the reference method (BMD). Essential and categorical agreement (EA, CA), very major, major and minor errors (VME, ME, MiE) were determined.

**Results:** The BMD MIC₅₀/₉₀ for CR and CS-PAE were 1/16, and 0.25/1 μg/mL, respectively. All CS-PAE isolates were susceptible to C/T. For CR-PAE, 40/50 (80%) isolates were susceptible, 1/50 (2%) intermediate and 9/50 (18%) resistant to C/T. All C/T-resistant isolates were multidrug-resistant [7 of them extremely-drug-resistant] and 3/9 were found to harbor a carbapenemase by qPCR [1 *bla*KPC, 1 *bla*VIM, and 1 *bla*NDM]. For CR-PAE, the MIC₅₀/₉₀ with E-test, and MIC strips were 1.5/24 and 2/8 μg/mL, respectively. Susceptibility to C/T reached 88%, 78%, and 78% for E-test, MIC strips, and DD, respectively. The EA between BMD and both E-test and MIC test was 82%. The CA for E-test, MIC test, and DD was 92%, 88%, and 90%, respectively. The VME/MiE for E-test, MIC strip and DD were 33%/2%, 22%/6%, and 11%/6%, respectively. No ME were found.

**Conclusions:** In this multicenter study, C/T was highly active against clinical isolates of CR-PAE. All evaluated methods exhibited a good CA, however, the observed rates of VME were worrisomely high.

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Abstract 5138

Incidence and predictors of *Chlamydia trachomatis*, *Ureaplasma urealyticum*, *Mycoplasma hominis* and *Mycoplasma genitalium* in patients with sterile pyuria

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**Background:** Sterile pyuria has various infectious and non-infectious causes, posing a major diagnostic challenge and warrants detailed evaluation. Genital mycoplasmas usually remain asymptomatic. These are not detected by routine microbiological diagnosis, hence are often left undetected in most resource limited laboratories in India and left untreated.

**Materials/methods:** A prospective observational study - Oct 2017 to August 2019, adults admitted to Medicine wards were screened for sterile pyuria, detected within 24 hours of admission, irrespective of their primary presentation. Sterile pyuria was defined as urine microscopy showing > 10 WBC/HPF and no growth on blood and/or MacConkey agar. Polymerase Chain Reaction (PCR), for the detection of *C. trachomatis* and genital mycoplasmas, was performed on the urine samples as described (fig 1). Culture was also performed for *M. hominis*, and Ureaplasm spp. Patients were evaluated for other causes of sterile pyuria. They were treated with doxycycline and azithromycin and followed up.

**Results:** Occurrence of sterile pyuria in our hospital was found to be 72 (17.5%) out of 410 patients. Out of these, *C. trachomatis* and genital mycoplasmas were tested positive in 22/72 (30.5%) (*M. hominis* was 5 (6.9%), *U. urealyticum* 12 (16.7%) and *C. trachomatis* 13 (18.1%)). No patient was tested positive for *M. genitalium* or genitourinary tuberculosis. Risk factors such as chronic kidney disease (*p* = 0.008) and past history of urinary tract infection (*p* = 0.022) were significantly associated with these patients [22/72]. Due to underlying illness 4/22 patients expired. After treatment with doxycycline 12/22 (54.5%) and azithromycin 6/22 (27.2%), all patients showed complete resolution of pyuria on repeat testing at 2 weeks.

**Conclusions:** This is the first study from India to test occurrence and predictors of atypical organisms in sterile pyuria (17.5%) as compared to [1-10%] found in others. *C. Trachomatis* and genital mycoplasmas are important causes of sterile pyuria, with predisposing risk factors being CKD or history of UTI, warranting screening and evaluation. Contrary to the previous studies, genitourinary tuberculosis was not a cause.

**ORGANISM** | **PRIMER**
--- | ---
*M. genitalium* | MgPa-1
*M. genitalium* | MgPa-3
*Ureaplasma urealyticum* | U4
*Ureaplasma urealyticum* | U5
*M. hominis* | RNAH1
*M. hominis* | RNAH2
*C. trachomatis* | KL1
*C. trachomatis* | KL2

**FIG1:** Primers for polymerase chain reaction

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Hepatitis E virus genotype 3 subtype-dependent clinical outcomes in Belgium 2010-2018

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Background: Immunosuppression, male, age >50 and chronic liver disease are risk factors for Hepatitis E Virus (HEV) disease. In Belgium, diagnosis of HEV is centralized at Sciensano. We aimed at identifying risk factors and clinical outcomes associated with HEV genotype (gt) 3 subtypes in a nationwide cohort of HEV patients.

Materials/methods: Demographic, clinical and biochemical parameters of HEV infections between 2010-2018 were collected. Serum HEV – IgM, – IgG and HEV RNA were determined by ELISA and RT qPCR. HEV was subtyped by Sanger sequencing of an ORF2 fragment. Odds ratios (OR), risk ratios (RR) and 95% confidence intervals (95% CI) were calculated using STATA.

Results: Among 300 HEV cases with clinical data, the median age was 57 years and 69% were males. Viremia was detected in 211 patients, with a genotype identified in 177. HEV gt3 infections predominate [93% [165/177]] with subtypes 3c [38% [67/177]] and 3f [44% [78/177]] almost equally represented. The percent of immunocompromised patients [30% vs 16%, ORa=2.2 [1.0-4.7] p=0.045] was higher among patients with a clade-3c [achi] virus compared to a clade-3f [elg], while a similar tendency was observed for pre-existing liver cirrhosis [9.9% vs 3.4%, ORa=3.4 [0.8-12.5]]. Among patients with a clade-3f virus, higher peak values of ALT [mean of 2199 vs 1528 U/L; p=0.005] and bilirubin [mean of 8.6 vs 4.1 mg/dl; p=0.001] were identified, compared to patients with clade-3c virus. In addition, the risk of hospitalization for patients with a clade-3f virus was almost twice that of patients with clade-3c virus [36% for 3c; 61% for 3f; RR=1.7 [1.2-2.4] p=0.003]. There was a non-significant tendency towards higher mortality for clade-3f infections [1.4% vs 4.8%; RR=3.4 [0.4-30]], but no differences in intensive care unit admissions [5.7%], hospitalization durations (median of 4.0 weeks) or in chronicity [18% vs 14%, RR=0.8 [0.4-2.0]].

Conclusions: A similar number of HEV-gt3c and -gt3f infections have been diagnosed in Belgium. Despite more pre-existing comorbidity among patients with HEV-gt3c, patients with HEV-gt3f are associated with higher risks for hospitalization and high liver enzyme values. Our nationwide analysis is the first to identify a correlation between HEV-gt3 subtypes and these clinical outcomes.

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Abstract 5142

**Intact bacteria species-specific lipid profiling using the MALDI Biotyper Sirius can identify mycobacteria in one step**

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**Background:** Over the last decades, MALDI mass spectrometry has become the workhorse of clinical laboratories for Gram-Negative and Gram-positive bacterial diagnostics. For mycobacteria, an adapted and validated MALDI methodology, based on cytosolic protein profiling, has been established. Although this method is able to identify and differentiate a very broad spectrum of mycobacteria, a number of limits in species- and intra-species differentiation has been observed. Identification without culture is largely being performed by DNA-based methodologies which are relatively expensive and limited in species coverage. Here, we propose another alternative based on species-specific lipid profiling of heat inactivated bacteria, with very limited preparation using routine MALDI Biotyper Sirius.

**Materials/methods:** A collection of 27 reference strains from ATCC and ECDC were used to evaluate the use of species-specific lipids as discrimination markers. The method we have developed is fast (<5 mins after heat inactivation) and uses MALDI-TOF MS combined with a suitable matrix (super-2,5-dihydroxybenzoic acid solubilized in ethanol 70%) to analyze lipids of heat-inactivated mycobacteria. Cultured mycobacteria are heat-inactivated and loaded directly onto the MALDI target followed by addition of the matrix. Acquisition of the data has been done in both positive and negative ion mode using a MALDI Biotyper Sirius system (Bruker Daltonik).

**Results:** We have been able to build a database and the following glycolipid family were identified: i) glycopeptodilipids and phenolglycolipids, the immunoreactive glycolipids species-specific ii) phosphatidyl-myo-inositol mannosides as ligand of TLR2 receptors and antigens of CD1 restricted αβT cells. Thank to use of species-specific lipids, we were able to unlock key challenges associated with mycobacterial ID such as one-step samples preparation as well as discrimination within the M. abscessus and Tuberculosis complex, in the positive and negative ion mode, which was not currently possible.

**Conclusions:** Thanks to its speed of execution, intact bacterial lipid profiling provide a unique route for mycobacterial identification using the MALDI Biotyper Sirius. It may complement the broad identification capabilities of the protein-based mycobacteria identification by MALDI-TOF MS, enabling the resolution of closely related species complexes. Further, the high sensitivity of the method might lead to a route to direct sample analysis.

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Background: resistance to antibiotics can change over time due to consumption and adequacy of its use, among other factors. Cumulative antimicrobial tests data have great epidemiological and clinical impact, since they show trends over time and guide the selection of empirical treatment. Antimicrobial resistance surveillance is the first step, together with days of treatment determination, to implement a paediatric antibiotic stewardship program in Catalonia. Our objectives were to analyse the susceptibility of the main microorganisms causing paediatric infections in an area covered by 13 health-care centers and to compare that to the global susceptibility testing results (>95% from adults).

Materials/methods: susceptibility data refer to isolates identified from clinical samples collected from children under 18y, including neonates, during 2018. Isolates reported as intermediate or resistant were classified as resistant. All centers used EUCAST breakpoints. Different microorganisms/antibiotics were included depending on their origin (hospital or community). Resistance percentages for specific pathogens-antibiotics were calculated.

Results: the percentage of extensively drug-resistant Pseudomonas aeruginosa (XDR) was 5.8% in children versus 10.1% in adults. Escherichia coli and Klebsiella pneumoniae results are shown in the table. No isolates of vancomycin resistant Enterococcus spp. were detected. There was no difference in the MRSA percentage between hospital and community (10%) but it was lower than in adults (24.1%). Penicillin non-susceptible Streptococcus pneumoniae percentage was 19.2% in children vs 20.2% in adults and macrolide resistance was 19.7% vs 23.1% respectively. Streptococcus pyogenes macrolide and clindamycin resistance was 5.7% and 3.5% respectively in children and 7.7% and 5.4% in adults.

Pathogen/antibiotic | Escherichia coli (n=2999) | Klebsiella pneumoniae (n=461) |
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pediatrics (%)</td>
<td>Adults (%)</td>
</tr>
<tr>
<td>ESBL</td>
<td>5.3 (4% community)</td>
<td>10.6</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>19.4</td>
<td>21.4</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>7.8</td>
<td>-</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>10.6</td>
<td>-</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>0</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Conclusions: percentages of multiresistant ESBL-E.coli, ESBL/CP-K.pneumoniae and XDR-Pseudomonas were lower in Pediatrics compared to adults and in the community compared to the hospital setting, in the case of ESBL-E. coli. For Gram-positive bacteria, lower percentages of resistance were detected in children compared to adults. Surveillance of antimicrobial resistance is essential to guide infection control and antimicrobial stewardship objectives.

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Abstract 5145

**Mechanism of ceftazidime-avibactam resistance in carbapenem-resistant Escherichia coli isolated in the Arabian Peninsula**

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**Background:** The aim of the study was to reveal the molecular mechanism of ceftazidime-avibactam non-susceptibility in four carbapenem resistant carbapenemase non-producer Escherichia coli (CREC) isolated in four different hospitals in the Arabian Peninsula.

**Materials/methods:** Whole genome sequencing reads of isolates obtained using Illumina MiSeq (250 bp paired-end) were assembled using SPAdes and annotated by RAST. ResFinder was used to investigate antibiotic resistance genes. Clonality was assessed by cgMLST using Ridom SeqShere+. MIC of ertapenem (ERT), ceftazidime (CAZ), ceftazidime-avibactam (CAZ-AVI) alone and in the presence of phenylalanylarginine β-naphthylamide (PAβN) efflux inhibitor was determined by broth microdilution.

**Results:** The molecular features and susceptibility of the four CREC are shown in the Table.

<table>
<thead>
<tr>
<th>Isolate</th>
<th>Isolation year</th>
<th>MLST</th>
<th>Beta-lactamase genes</th>
<th>PBP2</th>
<th>AAs inserted into PBP2</th>
<th>ompC</th>
<th>ompF</th>
<th>MIC (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERT</td>
<td>CAZ</td>
<td>CAZ-AVI with PAβN</td>
<td>CAZ-AVI with PAβN</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ABC148</td>
<td>2015</td>
<td>ST410</td>
<td>blaCTX-M-18, blaCMY-42, blaOXA-1</td>
<td>WT</td>
<td>YRIK</td>
<td>Nonsense mutation</td>
<td>IS26 insertion</td>
<td>64</td>
</tr>
<tr>
<td>ABC610</td>
<td>2016</td>
<td>ST405</td>
<td>blaCTX-M-23, blaOXA-1, blaTEM-1B</td>
<td>WT</td>
<td>YRIK</td>
<td>Nonsense mutation</td>
<td>Nonsense mutation</td>
<td>120</td>
</tr>
<tr>
<td>RHH8</td>
<td>2016</td>
<td>ST410</td>
<td>blaCMY-42, blaTEM-1B</td>
<td>WT</td>
<td>YTD</td>
<td>Nonsense mutation</td>
<td>IS1 insertion</td>
<td>120</td>
</tr>
<tr>
<td>SAS0</td>
<td>2015</td>
<td>ST1702</td>
<td>blaCTX-M-18, blaCMY-42, blaTEM-1B</td>
<td>WT</td>
<td>YRIN</td>
<td>ompC20</td>
<td>WT</td>
<td>4</td>
</tr>
</tbody>
</table>

The isolates were non-clonal, even the two E. coli ST410 exhibited 106 differences over 2513 alleles by cgMLST. All isolates possessed an insertional mutation in the *ftsI* gene leading to a four amino-acid insertion into their PBP3, although the amino acids inserted were not identical. The isolates had either disrupted ompC, or ompC20 variant previously proven to lead to elevated beta-lactam MIC. PAβN efflux inhibitor lowered the MIC of CAZ-AVI two to eight-fold in all four isolates, suggesting that an efflux mechanism also played a role in the CAZ-AVI resistance.

**Conclusions:** In four, clonally unrelated carbapenem resistant E. coli isolated in the Arabian Peninsula the combination of three resistance mechanisms, including PBP3 modification by insertional mutations previously associated with elevated aztreonam-avibactam MIC, loss or modification of ompC and ompF porins and efflux mechanism, resulted in ceftazidime-avibactam resistance prior to the introduction of avibactam combinations into clinical practice in the region.

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Perinatal hormones favor CC17 Group B Streptococcus intestinal translocation through M cells and hypervirulence in neonates

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Abstract 5146

**Background:** Group B Streptococcus (GBS) is the leading cause of invasive bacterial neonatal infections. Late-onset diseases (LOD) occur between 7 and 89 days of life and are largely due to the CC17 GBS hypervirulent clone. Remarkably, this clone is less responsible for Early Onset Diseases (EOD, 0 to 7 days of life) and largely underrepresented in GBS adult diseases, implying that specific host factors might be involved in CC17 GBS invasiveness in > 7 day-old neonates.

**Materials/methods:** We studied the impact of estradiol (E2) and progesterone (P4), which impregnate the fetus during pregnancy, on GBS neonatal infection. One CC17 and one non-CC17 representative GBS isolates, both of capsular serotype III and responsible for neonatal disease were studied in cellular and mouse models of hormonal exposure corresponding to concentrations found at birth (E2-P4 C0) and over 7 days old (E2-P4 C7).

**Results:** We show that E2-P4 C7 concentrations specifically favor CC17 GBS meningitis following mice oral infection. CC17 GBS crosses the intestinal barrier through M cells. This process is mediated by the CC17 GBS-specific surface protein Srr2 and is enhanced by E2-P4 C7 concentrations which promote M cell differentiation, CC17 GBS intestinal translocation and CC17 GBS invasiveness.

**Conclusions:** Our findings provide an explanation for CC17 GBS responsibility in LOD in link with neonatal gastrointestinal tract maturation and hormonal imprint.

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Abstract 5147

eHealth use in tuberculosis: results from a systematic review and focus group interviews in six countries worldwide

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Abstract third-party references: GGD Groningen, the Netherlands, Pronkewail Project, Horizon 2020, Marie Skłodowska Curie Action, Beatricoord Clinic, UMCG, Groningen, the Netherlands, Sotiria Thoracic Diseases Hospital of Athens, Greece, Iasi Pulmonology Hospital, Romania, Presbyterian Hospital Agogo, Ghana, Fundación Instituto Carabobeño para la Salud, Venezuela, Central General Hospital Dr. Sardjito, Indonesia

Background: With the constant expansion of internet and mobile technologies, new opportunities arise for digitally delivering healthcare services, namely eHealth. Tuberculosis (TB) is an attractive field for eHealth implementation. We aimed to examine the use and perceptions of eHealth by performing a systematic review and interviews performed in six countries amongst TB experts and patients.

Materials/methods: The systematic review protocol was registered on PROSPERO (CRD42018115440) and adhered to PRISMA guidelines. The WHO Digital health guideline was used as a framework to present results. The focus group interviews were performed in Romania, the Netherlands, Greece, Ghana, Indonesia and Venezuela.

Results: Out of the 3154 screened studies, 85 were included. Most interventions focused on diagnosis (n=44) and treatment (n=38) and least contained an educational component (n=5). The likelihood of a patient to be diagnosed was higher with eHealth (95% CI, OR 2.80 [1.60, 4.86], I²=91%) and eHealth patients tended to be more adherent (95% CI, OR 1.53, [1.14-2.05], I²=74%). eHealth users found interventions useful (483/529, 91.3%). eHealth saved 9.56 - 14321 euros per patient (664 patients) and there were zero privacy breaches for 631 patients. Most frequent challenge was hardware-related (24/246, 17% users).

The most frequent theme in the focus group interviews was how eHealth could improve education in TB (144/911, 15% of quotes), followed by the potential of eHealth to streamline communication (67/911, 7% of all quotes). Participants in any of these six countries think eHealth would be a positive addition to TB management, provided that the app is user-friendly, translated, and free. Groups in the low-income countries reported being concerned about needing training and access to hardware.

Conclusions: A wide array of eHealth solutions has been successfully implemented. Our study suggests the main gap between literature and expectation is the TB health care workers and patients’ opinion that eHealth’s maximum potential lies in delivery of information and education. Literature as well as potential users expect eHealth to be beneficial.

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Doctor I’ve been bitten: a smart phone application to identify arthropod bites and stings
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Abstract third-party references: Natural history museum London, Imperial College London, Hospital For Tropical diseases London

Background: Arthropod related injury including bites, stings and allergic reactions to body parts are extremely common in the UK and indeed most parts of Europe. Stings in Europe are one of the commonest causes of severe allergic reaction and each year the number of large scale biting epidemics by flies, mosquitoes and lice, leading to multiple cases of infection, are increasing. Alongside this, dramatic ongoing changes in our climate mean that species carrying diseases that used to be solely associated with travelling to the tropics are now being found here on European shores. Many of these arthropod species are not well recognised and this can often lead to poor identification, misinformation and incorrect treatment.

Materials/methods: To combat this, our group consisting of London Natural History Museum and Imperial College University researchers and I created an identification smart phone application to help firstly identify UK arthropods that have caused injury and secondly provide information on those arthropods regarding the injuries they commonly cause and first line treatments. Arthropod recognition is completed using matrix key identification plus visual images, which then links to factsheet information for the commonest 51 species that harm people in the UK.

Results: The smart phone application contains an alphabetical list of the 51 species with each linked to the corresponding fact sheet, the aforementioned matrix key search function that narrows down possible arthropod culprits as questions are answered and finally treatment information is also provided in an easy to access fact sheet format for each specific injury inflicted. The app is designed in a modular format so data from other European countries can be added and used to provide advice for their arthropods specifically.

Conclusions: Lessons from this study emphasize the compromise between science and usability that is needed to create a well-functioning app and highlight the expanding scope that technology like this can provide for further health related animal and plant group identification beyond just simply arthropods.

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Cluster of invasive Mycobacterium chimaera infection in a single cardiac surgery unit: clinical features and management
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Background: In the last years a growing cases of disseminated infections due to Mycobacterium chimaera has been seen in patients undergoing open cardio-thoracic surgery with the use of Heather-Cooler Units (HCUs) for extracorporeal circulation. Airborne transmission is the source of infection due to the aerosolization of water containing M. chimaera from the HCUs. Invasive M. chimaera infection can lead to systemic or local manifestation, the latency is long and the outcome is poor.

Materials/methods: In our study we reported 7 cases of invasive M. chimaera infection observed in the Reggio Emilia Hospital. We followed ECDC criteria to identify probable or confirmed cases in patients having undergone cardiac surgery with implantation of prosthesis or devices in local cardiac surgery between 2010 and 2017.

Results: The incidence of invasive M. chimaera infection in the period 2010-2017 was 0.35%. Patients were all males with a median age of 57-years-old. All our cases had devices or prosthesis that increased the risk of disseminated form of the disease. The median period of latency between cardiac surgery and onset of symptoms was 26 months with a range of 11-45 months. All patients have shown signs of disseminated disease affecting more organs associated with: prosthetic valve endocarditis (n=3), prosthetic vascular graft infection (n=1), spondylodiscitis (n=1), chorioretinitis (n=2). Symptoms and signs reported were fever, weight loss, asthenia and splenomegaly. Laboratory test alterations were pancytopenia, renal impairment, hepatitis and liver cholestasis. In 5 patients the positivity of blood cultures was immediately attributed to M. chimaera, in one patient to MAC and in another patient to M. intracellulare, only subsequently typed as M. chimaera. Genotypic drug resistance both for macrolide and aminoglycoside was negative. In 6 patients histopathology demonstrated non-necrotizing granulomas in examined tissues. Anti-mycobacterial multidrug regimen included a macrolide, a rifamycin, ethambutol plus/minus amikacin, levofloxacin or moxifloxacin. Two patients underwent a cardiac re-operation. Mortality was 43%.

Conclusions: This study describes a local outbreak in a single cardiac surgery unit. M. chimaera infection should be strongly suspected in patients with a history of cardiac surgery who develop compatible and unexplained manifestations and clinicians should exclude both disseminated and localized infections.

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Systematic review: transmission inference using single nucleotide polymorphism [SNP] differences between isolates of ESBL and CR-Enterobacteriaceae. Can a SNP cutoff be defined?

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Background: Whole-genome sequencing and phylogenetic analyses are increasingly used to investigate transmission. However, the number of SNP differences that defines a transmission event for Enterobacteriaceae is unclear. This systematic review summarizes SNP differences reported between ESBL-producing and carbapenem-resistant (CR)-Enterobacteriaceae isolates in transmission clusters.

Materials/methods: MEDLINE, MEDLINE In-Process, MEDLINE Epub Ahead of Print, and Embase (OvidSP) databases (Jan. 1995-Jul. 2019) were searched using subject headings and textword terms for whole-genome sequencing and beta-lactam-resistant Enterobacteriaceae. 7,618 reference were retrieved; 1,465 duplicates were removed. 6,153 unique references were reviewed against inclusion criteria (epidemiological data and SNPs used in transmission inference).

Results: 525 titles and 161 abstracts met inclusion criteria. Data have been extracted from 43 full-texts reporting 69 transmission clusters. Table shows cluster characteristics. Among 62 clusters with person-person transmission, median (IQR) number of cases per cluster was 4 (2-9). Among 7 clusters with only environment-person transmission, number of cases linked to the environment per cluster was 1 (5), 2 (1), and 3 (1). Between isolates of cases deemed to be linked, the median (IQR,range) minimum SNP difference and median (IQR,range) maximum SNP difference was: 1 (0-4,0-94) to 11 (4-22,1-131) for K. pneumoniae, 0 (0-3,0-7) to 6 (3-12,0-28) for E. coli, and 0 (0-2,0-19) to 7 (3-11,0-142) for E. cloacae. In 24 clusters, investigators had a pre-defined cutoff for SNP differences indicating possible transmission; organisms and cutoffs were E. coli (≤10, ≤12, ≤58), K. pneumoniae (≤12, 151, <300), and E. cloacae (<10, <15).

Conclusions: In reported clusters of E. coli, K. pneumoniae, and E. cloacae colonization/infection, SNP differences were <12 and 142 at most, with similar distributions between different species. These data may inform guidelines for interpreting relatedness in outbreak investigations.

<table>
<thead>
<tr>
<th>Cluster characteristics</th>
<th>Number of clusters, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Setting</td>
<td></td>
</tr>
<tr>
<td>Acute care hospital[s]</td>
<td>65 (94)</td>
</tr>
<tr>
<td>Acute care hospital and rehabilitation hospital</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Long-term care facility</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Community</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Type of transmission</td>
<td></td>
</tr>
<tr>
<td>Person-person</td>
<td>57 (82)</td>
</tr>
<tr>
<td>Environment-person</td>
<td>7 (10)</td>
</tr>
<tr>
<td>Both</td>
<td>5 (7)</td>
</tr>
<tr>
<td>Transmitted organism</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>36 (52)</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>19 (28)</td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td>8 (12)</td>
</tr>
<tr>
<td>Other</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Organism resistance</td>
<td></td>
</tr>
<tr>
<td>CR-Enterobacteriaceae</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Carbapenemase-producing</td>
<td>49 (71)</td>
</tr>
<tr>
<td>ESBL-producing</td>
<td>18 (26)</td>
</tr>
</tbody>
</table>

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Investigating a cluster of community-acquired methicillin-resistant *Staphylococcus aureus* infections in a school in Eastern Switzerland

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**Background:** A cluster of infections with community acquired Methicillin-resistant *Staphylococcus aureus* (CA-MRSA), positive for Panton-Valentin leucocidin and characterized by efflux-mediated MLSB-resistance, was detected at a paediatric tertiary hospital in Switzerland since 2018. Outbreak investigation was started with the aim of identifying the source of the cluster and preventing further transmissions.

**Materials/methods:** Confirmed cases were defined as an infection with CA-MRSA of identical sequence type (ST) as revealed by whole genome sequencing (WGS) with ≤5 single nucleotide polymorphisms (SNP) within core genome multilocus sequence type. Probable cases were defined as infection with CA-MRSA without confirmation by WGS but with identical antibiotic susceptibility pattern (macrolide resistant/ clindamycin susceptible). Risk factors were evaluated by a questionnaire for confirmed and probable cases. Since most cases were children, questions regarding care facilities, schooling, activities and pets were included.

**Results:** The clustering involved 27 cases (22 confirmed cases with ST5 and 5 probable cases) of which 24 were children <18 years (median age 10.5 years [interquartile range 9 – 12 years]), the remainder being 2 teachers and 1 father of a child. 37% of cases were females. Clinical presentation of MRSA infection was skin or tissue infection in >90% of cases and septic arthritis with bacteraemia in one case. The return of the questionnaires was 63%. 74% of cases were linked to the school of which six cases attended the local child care facility (p=0.94). No link to the school could be evaluated in seven cases (six attended other schools in the same city, one did an apprenticeship). None of the activities clustered in relation to recreational or school activities, animal contact or exposure to the health care system.

**Conclusions:** This MRSA cluster was associated with one school. We hypothesize that transmission occurred during school activities and that transmissions are ongoing. Seven secondary cases were observed with probable transmission out of the school. A cross-sectional study with swabing and a modified questionnaire is already scheduled to evaluate the prevalence of colonisation and infection in the affected school, to confirm the hypothesis, identify the possible route of transmission and to define measures against further transmissions.

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Innovative antibacterial agents eradicate bacteria including persisters within mature biofilms

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Background: Prosthetic joint infection (PJI), a severe complication of joint replacement surgery, is difficult to treat due to biofilm- and persister formation on the surface of the implanted device and in the peri-implant tissue. As antibiotics often fail to clear the bacteria within biofilms, innovative antibacterial strategies are needed. Therefore, we compared the efficacy of the synthetic antimicrobial and antibiofilm peptide 148 (SAAP-148), bacteriophage ISP, and antibiotics on methicillin-resistant Staphylococcus aureus (MRSA) in mature biofilms in vitro.

Materials/methods: MRSA biofilms were grown for seven days on plastic surfaces and thereafter exposed to (I) high dose (10x MBC) of antibiotics (rifampicin and ciprofloxacin), (II) SAAP-148, (III) bacteriophage ISP, and (IV) the combination of antibiotics and bacteriophage ISP, daily for three days [Figure 1A]. At 24 hours after each daily application of these agents, the numbers of surviving bacteria were determined microbiologically. In addition, to assess the efficacy of these antibacterial agents on biofilms enriched in persisters, mature biofilms were first exposed to antibiotics for three days and then exposed to (I) SAAP-148, (II) bacteriophage ISP, (III) a combination of antibiotics and bacteriophage ISP or (IV) antibiotics, as a control [Figure 1B].

Results: SAAP-148 dose-dependently eradicated bacteria within mature biofilms on plastic surfaces. In contrast, bacteriophage ISP up to 7x10^8 PFU/ml did not efficiently reduce bacterial counts within mature biofilms. As expected, the antibiotics reduced the bacterial counts by 3-logs, but did not eradicate the bacteria in mature biofilms. Interestingly, the combination of bacteriophage (7x10^8 PFU/ml) and antibiotics almost completely eradicated the bacteria residing in biofilms within 24 hours [Figure 1A]. SAAP-148 as well as the combination of bacteriophage and antibiotics completely eradicated bacteria residing in 3 days antibiotics-exposed mature biofilms, while antibiotics alone were unable to further reduce bacterial counts in biofilms [Figure 1B]. Interestingly, bacteriophage ISP rapidly (within 1 day) and dose-dependently reduced the number of bacteria within the antibiotics-exposed mature biofilms.

Conclusions: SAAP-148 or bacteriophage ISP in combination with antibiotics are promising antimicrobial strategies in the battle against biofilm-associated infections like prosthetic joint infections.

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Abstract 5159

Healthcare-associated infections, antibiotic use and resistance in Swiss long-term care facilities: a multi-centre point prevalence study

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Abstract third-party references: Swiss National Science Foundation, Federal Office of Public Health

Background: The burden of healthcare-associated infections (HAI) and antimicrobial resistance in Swiss long-term care facilities (LTFC) is unknown. We assessed the prevalence of HAI, antibiotic use and resistant pathogens among Swiss LTFC residents.

Materials/methods: From August to October 2019, we performed a point-prevalence study in LTFCs in Eastern and Western Switzerland according to the “Healthcare-associated infections in Long-Term Care Facilities” (HALT) protocol. LTFC residents were screened for HAI and current antibiotic treatment. Characteristics of residents (age, sex, wounds, dementia, medical devices, use of proton-pump-inhibitors [PPI]) and institutions (geographic region) were registered. In addition, consenting residents underwent rectal screening for extended-spectrum β-lactamase (ESBL), carbapenemase-producing Enterobacterales (CPE) and vancomycin-resistant enterococci (VRE). For residents undergoing rectal screening, we also collected: years in institution; Katz-Score; hospital admission/antibiotic use within last 6 months; prior colonization with resistant pathogens. Risk factors for colonization with resistant pathogens were assessed using logistic regression. Whole-genome sequencing (WGS) was performed on resistant isolates.

Results: We screened 1185 residents from 16 LTFCs (8 per geographic region) for HAI and antibiotic treatment. HAI-prevalence was 4.1%, with (muco)-cutaneous mycoses (28%) and urinary tract infections (25%) being most common; 2.9% received antibiotics on the day of the survey, 35% received a PPI. Screening for resistant pathogens was done in 605/1185 (51%) residents. ESBL-prevalence was 9.1% [31/340] in Eastern and 13.6% [36/265] in Western Switzerland (P=0.08) [87% Escherichia coli]. No CPE or VRE were detected. Independent risk factors for ESBL-carriage were previous colonization with resistant pathogens [OR 6.1, 95% CI 2.7-13.6], male gender [OR 2.6, 95% CI 1.6-4.5], and PPI use [OR 2.2, 95% CI 1.3-3.8] (Figure). Preliminary WGS analysis showed a high diversity of E. coli sequence types (ST) in Eastern (10 different STs, 42% ST131), but less so in Western Switzerland (3 different STs, 89% ST131).

Conclusions: HAI prevalence in Swiss LTFCs is similar compared to other European countries, whereas antibiotic consumption and antibiotic resistant pathogens are less common. More than one third of the LTFC population received a PPI on the day of the survey. Given the independent association with ESBL-carriage of this potentially modifiable risk factor, this finding merits further study.
Multivariable logistic regression for ESBL carriage

Previous colonization with resistant pathogen

Male gender

Current proton-pump inhibitor use

Antibiotic treatment in previous 6 months

Age (per year)

Odds Ratios

6.07 ***

2.59 ***

2.18 **

1.37

0.9

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A wide spread of sexually-transmitted infections among users of pre-exposure prophylaxis attending the dedicated outpatient clinic in Modena, Italy

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1Azienda Ospedaliero-Universitaria di Modena, Università di Modena e Reggio Emilia, Modena, Italy

**Background:** Pre-exposure prophylaxis (PrEP) with the association of tenofovir (TDF)/emtricitabine (FTC) is effective in the prevention of HIV transmission. This study aims to investigate the epidemiological characteristics of the users, the effectiveness and security of PrEP, the incidence of sexually transmitted infections (STIs), as well as the adequacy of PrEP requirement.

**Materials/methods:** It is a prospective observational study conducted enrolling all the users attending our PrEP outpatient Clinic from July 2018 until September 2019. We collected epidemiological and clinical data at baseline and during follow-up visits at 1, 3 months and then every three months. We performed serological test for HIV, HBV, HCV, HAV, *Treponema pallidum* and PCR research for *Chlamydia trachomatis* and *Neisseria gonorrhoeae* on urine, rectal and pharyngeal swabs and we measured blood creatinine.

**Results:** 35 people used Prep with a follow-up of at least one month (median 6 months). 97% of them were male, all MSM, 83% Italian, median age of 37 years. Among indications, 12 people (34.3%) reported an inconstant condom use, 11 (31.4%) a previous STI, 2 (5.7%) practiced chemsex, 1 (2.9%) received post-exposure prophylaxis, 2 (5.7%) people didn’t report risky behavior. 30 (85.7%) of them chose on-demand regimen and 5 (14.3%) the daily scheme. At baseline, 13 people (37.1%) were diagnosed with at least one STI. During follow-up, 12 (34.3%) contracted at least one STI, with a median time of 4 months from the beginning of the prophylaxis, 4 users (11.4%) were diagnosed repeatedly. Figure 1 shows the proportion of diagnosed STIs. No new HIV infection was observed. Adhesion to the chosen regimen was 85.7%. Condom use in PrEP was mostly discontinuous. 12 users (34.3%) reported side effects, mostly minor gastrointestinal except for 1 acute renal failure which required PrEP suspension.

**Conclusions:** In our experience, PrEP request is limited to MSMs only. PrEP is effective in preventing new HIV infections. More than 30% of the users at the baseline already had a STI and more than 30% of them developed a STI during the prophylaxis. We recommend PrEP distribution under medical supervision to detect and cure eventual side effects as soon as possible.

<table>
<thead>
<tr>
<th>STIs at baseline</th>
<th>STIs at follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total of STIs diagnosed</strong></td>
<td>16</td>
</tr>
<tr>
<td><strong>Total of users diagnosed</strong></td>
<td>13 (37.1%)</td>
</tr>
<tr>
<td><strong>Users with multiple STIs</strong></td>
<td>3 (8.6%)</td>
</tr>
<tr>
<td><strong>HIV</strong></td>
<td>0</td>
</tr>
<tr>
<td><strong>Chlamydia trachomatis</strong></td>
<td>4 (25%)</td>
</tr>
<tr>
<td>Rectal</td>
<td>3</td>
</tr>
<tr>
<td>Pharyngeal</td>
<td>1</td>
</tr>
<tr>
<td>Urine</td>
<td>0</td>
</tr>
<tr>
<td><strong>Neisseria gonorrhoeae</strong></td>
<td>7 (43.7%)</td>
</tr>
<tr>
<td>Rectal</td>
<td>4</td>
</tr>
<tr>
<td>Pharyngeal</td>
<td>1</td>
</tr>
<tr>
<td>Urine</td>
<td>0</td>
</tr>
<tr>
<td><strong>Treponema pallidum</strong></td>
<td>5 (31.3%)</td>
</tr>
<tr>
<td>Rectal</td>
<td>4</td>
</tr>
<tr>
<td>Pharyngeal</td>
<td>3</td>
</tr>
<tr>
<td>Urine</td>
<td>0</td>
</tr>
<tr>
<td>HAV IgG</td>
<td>18 (51.4%)</td>
</tr>
<tr>
<td>Previous vaccination</td>
<td>12</td>
</tr>
<tr>
<td>HAV IgM</td>
<td>0</td>
</tr>
<tr>
<td>HCV Ab</td>
<td>1 (HCV RNA neg)</td>
</tr>
</tbody>
</table>

Fig. 1 Proportion of STIs

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Abstract 5161

Clinical experience with ceftazidime-avibactam (CAZ-AVI) in the treatment of infections caused by XDR Klebsiella pneumoniae producing OXA-48 carbapenemase

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Background: In the ICUs of our hospital more than 50% of K. pneumoniae strains show resistance to carbapenems as a result of the production of carbapenemases, mainly OXA-48 type. The aim of our study was to investigate the efficacy of the new antibiotic ceftazidime-avibactam (CAZ-AVI) in infections caused by carbapenem-resistant K. pneumoniae producing OXA-48 carbapenemase.

Materials/methods: In open-label prospective study we analyzed the results of the use of CAZ-AVI in patients with various infections. We included patients who met the following criteria: 1) isolation of K. pneumoniae, resistant to carbapenems, 2) XDR strains, characterized by sensitivity to a maximum of two antibiotics, 3) ineffectiveness of previous potentially adequate therapy. The MIC of antibiotics was studied by broth microdilution method, determination of the type of carbapenemases was carried out by PCR.

Results: We enrolled 22 patients with confirmed infection caused by K. pneumoniae producing OXA-48 carbapenemase. The most common infections were VAP (40.9%) and intra-abdominal infection (22.7%), half of the patients had bacteremia. In most patients the infection was severe [sepsis or septic shock was in 21 patients], the average value of SOFA score was 8.9±3.6. All patients had received antibiotics before CAZ-AVI [median 3] and had failed treatment. The most commonly prescribed agents were carbapenems and polymyxin B. The duration of treatment with CAZ-AVI ranged from 4 to 23 days [an average of 9.3 days]. CAZ-AVI was used in monotherapy or in combination with other antibiotics [in 10 patients with polymyxin B and 5 with tigecycline], since along with K. pneumoniae in 16 patients a second significant pathogen was isolated – P. aeruginosa or A. baumannii. All tested isolates were sensitive to CAZ-AVI with MIC\textsubscript{90} level of 0.06 mg/l. During CAZ-AVI treatment eradication of the pathogens was noted in 90.5% of patients, a clinical cure/improvement was achieved in 72.7%. CAZ-AVI was prescribed an average of 12.9 ± 9.6 days from the beginning of infection; interestingly, CAZ-AVI was prescribed on average 5.4 days earlier to the surviving patients than died patients (P<0.012).

Conclusions: CAZ-AVI has demonstrated good clinical and microbiological efficacy in infections caused by OXA-48 producing K. pneumoniae, for which therapy options are extremely limited.

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Rural and urban dogs as a source of ESBL-producing Enterobacteriaceae in northwest Spain

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Background: Antimicrobial resistance represents a threat to animal and human health worldwide. Dogs constitute a reservoir of antimicrobial resistances and a vehicle for their transmission to humans. Carbapenem- and extended-spectrum-β-lactamase (ESBL)-producing Enterobacteriaceae are categorized as critically important in the World Health Organization list. The aim of this study was to evaluate the fecal carriage of these bacteria among rural and urban dogs.

Materials/methods: Fecal samples from 179 healthy dogs from rural and urban environments in northwest Spain were recovered during May-June 2019 and plated on CHROMagar ESBL (bioMérieux), CHROMID CARBA SMART (bioMérieux) and CHROMagar OXA-48 (bioMérieux) for selection of ESBL- and carbapenemase-producing Enterobacteriaceae. Bacterial identification was performed by MALDI-TOF/MS (Bruker Daltonik). Antimicrobial susceptibility testing of suspicious colonies was carried out with the Microscan system (Beckman Coulter) and interpreted according to EUCAST guidelines. Screening of ESBLs, plasmid-mediated AmpC-beta-lactamases (pAmpCs) and plasmid-mediated colistin resistance encoding genes (mcr1 to mcr5), as well as identification of virulence genes and Escherichia coli phylotypes, were performed by PCR. MLST of E. coli and Klebsiella pneumoniae followed the respective PubMLST schemes.

Results: Forty-six enterobacterial isolates from 33 individuals (18.4%) were positive for ESBLs. They were identified as E. coli (39), K. pneumoniae (3), Enterobacter cloacae (2) and Serratia fonticola (2). All isolates were multidrug resistant (MDR), with resistances to narrow and broad spectrum β-lactams (100%), ciprofloxacin (65.2%) and tobramycin (36.9%), being the most frequent. Among the 39 ESBL-producing E. coli, 27 (69.2%) carried a blaCTX-M gene (blaCTX-M-1, blaCTX-M-14, blaCTX-M-15, blaCTX-M-27), while the remaining nine (23.0%) were positive for blaSHV-12. Furthermore, four E. coli, each from a different dog, were positive for the blaCMY-2-type pAmpC gene. Eight ESBL-producers conforming the ExPEC status belonged to O1:H45-Clade I-ST770 (5), O18:H11-A-ST93 (CC168) (1), O23:H16-B1-ST453 (CC86) (1), and O83:H42-F-ST1485 (CC648) (1) which also satisfied UPEC status. All isolates were negative for mcr-1 to mcr-5 and no carbapenemase-producers were recovered in the study.

Conclusions: Our results showed that healthy rural and urban dogs represent a significant reservoir of MDR Enterobacteriaceae resistant to critical antibiotics. Thus, they should be a key point of epidemiological surveillance in the fight against antimicrobial resistance.

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Abstracts 2020

Abstract 5166

Prophylactic antibiotics administration in low- and middle-income countries: what are the consequences on antibiotic resistance? A systematic review

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Background: Antibiotic resistance is one of the greatest threats to global health, particularly in low- and middle-income countries (LMICs). Antibiotic consumption is an important driver of antibiotic resistance and its consumption in LMICs reached 24.5 billion daily doses in 2015 for both treatment and prevention. Despite the ubiquity of prophylactic antibiotic treatment, no systematic review has yet been conducted to provide a global overview of prophylactic antibiotic use and its impact on the emergence and spread of antibiotic resistance in LMICs.

Materials/methods: We conducted a systematic review of studies using prophylactic antibiotics in LMICs published after 2000. We considered both mass drug administration or systematic prophylactic use. If investigated, data on antibiotic resistance following prophylactic antibiotics administration were reported.

Results: In total, 2193 articles were identified and 54 were eligible, comprising 34 unique studies conducted primarily in Africa (85%). Three main populations receiving prophylactic antibiotics were identified and stratified into subpopulations: children under 15 years old (healthy under 2 years old, HIV-exposed or malnourished), pregnant women (healthy, HIV-infected or with risk factor at delivery) and communities (outbreak situations or HIV-infected). Fifteen different antibiotics were prescribed, mainly co-trimoxazole (47%), azithromycin (18%) and amoxicillin (12%).

Sixteen studies (47%) evaluated the impact of prophylactic antibiotic use on antibiotic resistance following administration of co-trimoxazole (50%), azithromycin (38%), amoxicillin (12%), ciprofloxacin (6%) and doxycycline (6%).

Following co-trimoxazole administration, increases were observed in: overall expression of resistance genes (sulfonamide and trimethoprim), rates of co-trimoxazole resistance in S. pneumoniae, and rates of resistance to five different antibiotics in E. coli.

For azithromycin, increases were observed in: overall expression of resistance genes (macrolide), rates of macrolide resistance in S. pneumoniae, and rates of azithromycin resistance in S. aureus and S. pneumoniae.

No changes in resistance rates were detected after ciprofloxacin or doxycycline administration.

Conclusions: We identified a substantial proportion of the global population receiving prophylactic antibiotics in LMICs, with links to increased antibiotic resistance identified in the few studies reporting resistance data. However, consequences of all prophylactic use across target populations have never been evaluated. For future antibiotic prophylaxis implementation, studies should investigate consequences on antibiotic resistance.

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Omadacycline in a comparative analysis of *in vitro* activity on *Clostridioides difficile* isolates from Stockholm, Sweden

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**Background:** *Clostridioides difficile* is a Gram-positive, anaerobe, spore-forming bacillus that is involved in intestinal infections (CDIs) with a high rate of recurrences. CDI is the most common diarrhea-causing infection in Sweden, with one of the highest incidences amongst European countries. Moreover, the global rise of hypervirulent clones belonging to ribotypes (RT) 027 and 078 increased morbidity and mortality. Although *C. difficile* antimicrobial resistance has decreased recently in Sweden, the burden of finding novel and more efficient antimicrobial drugs is still present. One of the latest options available is omadacycline (OMC), a synthetic modified tetracycline approved by FDA. In this study, OMC has been compared to commonly used antimicrobials for CDI, using a Swedish strain collection.

**Materials/methods:** A total number of 221 *C. difficile* isolates were collected from unique patients during the period 2015-2018 from Karolinska University Hospital, Huddinge, Sweden. Blood agar plates containing antimicrobials were used for agar dilution assay, following CLSI guidelines. The isolates were tested for clindamycin (0.25 – 16 mg/L), erythromycin (0.25 – 2 mg/L), fidaxomicin (0.008 – 1 mg/mL), linezolid (0.25 – 4 mg/L), metronidazole (0.03 – 2 mg/L), moxifloxacin (0.5 – 4 mg/L), vancomycin (0.25 – 2 mg/L) and omadacycline (0.008 – 8 mg/L).

**Results:** A selection of isolates among the most common RTs in Sweden and the hypervirulent RT027 resulted in 57 strains, of which 17 (29.8%) belonged to RT014, 10 (17.5%) to RT002, 9 (15.8%) to RT023, 8 (14%) to RT001, and 13 isolates comprising other RTs including 078, 078/126, 005, 020 and 027. Median (IQR) MIC values (in mg/L) for each of the antibiotics tested were 8 (8-16) for clindamycin, 2 (2-2) for erythromycin, 0.12 (0.06-2) for fidaxomicin, 4 (2-4) for linezolid, 0.5 (0.5-2) for metronidazole, 4 (4-4) for moxifloxacin, 2 (2-4) for vancomycin and 0.5 (0.25-1) for omadacycline. MIC\(_{50}\) and MIC\(_{90}\) values for omadacycline were 0.25 and 2 mg/L respectively.

**Conclusions:** Omadacycline exhibited potent antimicrobial activity, *in vitro*, against the contemporary ribotypes of *C. difficile* causing infections in Sweden. Clinical evaluation of omadacycline in comparison with other antimicrobials agents currently used for treatment of CDI is warranted.

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Abstract 5169

Building a predictive score for local risk of respiratory syncytial virus hospitalisation: Normative Outcome Hospitalisation Assessment for Newborns (NOHAN)

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Abstract third-party references: On Behalf The VRS Study Group in Lyon

Background: Respiratory syncytial virus (RSV) infection is the predominant cause of lower respiratory tract infection (LRTI) during the first year of life. There is a strong need for a predictive model for RSV-associated hospitalization (RSVh) in the general pediatric in order to guide future preventive actions. We aimed to develop and validate a risk predictive model for RSVh within the first three months of life.

Materials/methods: Elaboration of the predictive model was based on a development cohort comprising 55180 infants and 594 laboratory-confirmed RSVh between 2012 and 2017. For validation purpose, a prospective cohort of 9268 infants born in 2018 was employed. A retrospective cohort analysis was conducted using univariate and multivariate logistic regression on demographic, laboratory, and clinical data.

Results: Prematurity under 37 weeks of amenorrhea, multiparity, socioeconomic factors, and month of birth were identified as independent risk factors for RSVh and included in the final model. The predictive model showed excellent discrimination performance with an area under the receiver operating characteristic curve of 0.847 [95% CI: 0.833–0.861] in the development cohort and 0.860 [95% CI: 0.834–0.887] in the validation cohort.

Conclusions: It is possible to build-up simple and efficient score that predict RSVh at birth using data commonly available in electronic medical records. Preventive pharmacological and non-pharmacological interventions should target the parents of at-risk infant during the pregnancy follow-up or during the birth hospitalization.

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Dalbavancin treatment for prosthetic joint infections in real-life: a national cohort study
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Background: Dalbavancin is a novel long lasting antibacterial agent with bactericidal activity against gram positive cocci. There are emerging data on bone and joint infections, but none exclusive to prosthetic joint infections (PJI). We aimed to describe the efficacy of dalbavancin on a homogenous cohort of PJI.

Materials/methods: A national retrospective study was performed from July 2017 to November 2018. Eligible patients must have presented PJI and received at least one dose of dalbavancin. We collected patients’ characteristics, indication for treatment, and outcome. Cure was defined as the absence of new antibiotic treatment, and/or new surgical intervention, and/or death from any cause.

Results: Overall, 17 patients from 8 hospitals were included in the study. Mean age was 69.1±11.0 yo; sex ratio (M/F) was 1.43. A total of 6 (35.3%) patients were immunocompromised. Associated infections were abscesses (n=2) and endocarditis (n=1).

Dalbavancin was used after a median of 2.0 lines [range 0-4] of antimicrobial treatment. Bacteria were identified in 16 cases. Main bacteria involved were: Staphylococcus aureus (n=10; 62.5%), with methicillin-resistant S. aureus (n=1; 6.3%); Staphylococcus epidermidis (n=7; 43.8%), with methicillin-resistant S. epidermidis (n=4; 25.0%); other coagulase-negative staphylococci (n=3; 18.8%); Enterococcus faecalis (n=1; 6.3%). Median MIC to dalbavancin was 0.064 mg/L for S. aureus and 0.023 mg/L (IQR 0.011 -0.079) for S. epidermidis. Median MIC to vancomycin was 0.750 mg/L (IQR 0.196-1.0) for S. aureus and 1.5 mg/L (IQR 1.0-2.0) for S. epidermidis. No Dalbavancin-resistant strain was isolated.

Dalbavancin was given as single-drug regimen in 8 (47.1%) patients. Main treatment regimens for Dalbavancin were a weekly 2-dose regimen (1500mg each) in 8 (47.1%) cases, and a single-dose regimen (1500mg) in 3 (17.6%) cases. However, the number of injections varied from 1 to 10 doses.

Clinical cure was observed in 8 (47.1%) patients [median follow-up 42.7 weeks], and all-cause mortality was 11.8%, with 2 patients classified as clinical failures. Finally, 5 (29.4%) patients were on suppressive antibiotic treatment [doxycycline n=3, dalbavancin n=2], with 2 who then presented clinical failure.

No adverse events were reported.

Conclusions: In our experience, Dalbavancin seems safe and effective for treating PJI even in salvage therapy.

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**Abstract 5174**

**Combination testing of avibactam against multidrug-resistant Gram-negative bacteria**

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**Background:** Inappropriate and excessive use of broad-spectrum antibiotics has led to a high prevalence of multidrug-resistant (MDRGN) bacteria especially of Enterobacteriaceae. These pathogens are often responsible for nosocomial infections such as bacteremia, hospital-acquired pneumonia, as well as intraabdominal and urinary tract infections. Avibactam (AVI) is a broad-spectrum β-lactamase inhibitor which prevents the degradation of beta-lactam antimicrobials and is currently available in a fixed combination with ceftazidime for treatment of Gram-negative nosocomial infections.

**Materials/methods:** In this in-vitro study, antimicrobial susceptibility testing was performed using the checkerboard assay and MIC test strips with agar plates containing avibactam. Not frequently used β-lactam antibiotics such as ceftobiprole (BPR), cefoxitin (FOX) and temocillin (TMO) as well as non β-lactam antibiotics such as fosfomycin (FOF) and tigecyclin (TGC) were tested in combination with AVI (4µg/mL) against clinical multidrug-resistant Enterobacteriaceae (20 E. coli and 22 K. pneumoniae) isolates, including 3/4MGRGN, with the respective resistances. The results were interpreted in accordance with the EUCAST breakpoints except for Cefoxitin and Temocillin for which CLSI and BSAC breakpoints were used, respectively. Characterization of the isolates was accomplished by using whole genome sequencing to identify possible resistance genes.

**Results:** MIC reductions below the susceptibility breakpoints were observed in 14/14 (BPR-AVI), 5/7 (FOX-AVI), 8/9 (TMO-AVI), 1/3 (FOF-AVI) for E. coli and in 11/21 (BPR-AVI), 1/13 (FOX-AVI), 3/11 (TMO-AVI), 5/8 (FOF-AVI) and 0/6 (TGC-AVI) for K. pneumoniae.

**Conclusions:** This study demonstrates the restoration of the antimicrobial activity of all tested agents when combined with AVI except for TGC. BPR-AVI, FOX-AVI, TMO-AVI displayed better activity against E. coli, whereas FOF-AVI was more effective against K. pneumoniae. Future clinical studies are warranted to investigate the value of these antibiotics paired with AVI as a carbapenem sparing alternative for treatment of nosocomial MGRGN infections.

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Abstract 5177

Compliance to the WHO moment 2 in German hospitals: first evaluation of detailed hand hygiene before aseptic tasks and procedures in national surveillance module HAND KISS

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Background: Hand hygiene (HH) is one of the most effective measures to prevent healthcare associated infections in healthcare settings. Especially compliance to WHO’s moment 2 (HH prior to aseptic procedures and tasks) is of crucial importance. While compliance generally increased in German hospitals since introduction of direct observation, compliance with moment 2 remained stable on a lower level in comparison. Healthcare workers are often not aware of the proper characterization of aseptic tasks in regards to hand hygiene. Therefore the goal of this study was to identify variation in compliances among different aseptic task and enable a more direct-ed feedback.

Materials/methods: Direct observation to the 5 moments is a voluntary tool of the German national hand hygiene campaign. Observations are performed by trained local IPC staff according to protocol by the WHO and documented in the hand hygiene element of the national hospital infection surveillance system [HAND-KISS]. Aseptic procedures were stratified according to different types of frequent tasks.

Results: Between 2016 and 2018 overall 1320947 indications were observed. 213959 Indications prior to moment 2 were observed (16.2%) on 1907 wards in 422 hospital. While overall median compliance was 57% compliance to moment number 2 was 53%. Since its implementation an increasing number of facilities are observing compliance aseptic procedures with the new stratification. Detailed evaluation showed that there is great variance of compliance among different aseptic tasks (table 1).

Conclusions: Direct observation of compliance is helpful for identifying areas for improvement. Detailing of aseptic procedures in direct observation forms increases insight on barriers and potential lack of knowledge for certain tasks. Thus enabling tailored interventions to improve compliance to hand hygiene prior to aseptic procedures.

<table>
<thead>
<tr>
<th></th>
<th>hospitals (n=)</th>
<th>wards (n=)</th>
<th>opportunities observed (n=)</th>
<th>Median compliance (%)</th>
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<tr>
<td>Overall</td>
<td>422</td>
<td>1907</td>
<td>1320947</td>
<td>57</td>
</tr>
<tr>
<td>Moment 2</td>
<td>422</td>
<td>1907</td>
<td>213959</td>
<td>53</td>
</tr>
<tr>
<td>Manipulation on respirator</td>
<td>268</td>
<td>480</td>
<td>9379</td>
<td>57</td>
</tr>
<tr>
<td>Preparation of i.v. drugs</td>
<td>356</td>
<td>1306</td>
<td>30493</td>
<td>61</td>
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<tr>
<td>Manipulation of PVC/PAC/CVC</td>
<td>376</td>
<td>1482</td>
<td>25824</td>
<td>52</td>
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<tr>
<td>Dressing change</td>
<td>363</td>
<td>1353</td>
<td>28797</td>
<td>59</td>
</tr>
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<td>Puncture/blood sampling/</td>
<td>358</td>
<td>1342</td>
<td>22493</td>
<td>56</td>
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<tr>
<td>placing i.v. line</td>
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<tr>
<td>Contact with mucous membrane</td>
<td>305</td>
<td>917</td>
<td>11588</td>
<td>62</td>
</tr>
</tbody>
</table>

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Abstract 5180

A new Lichtheimia corymbifera mouse model close to human pathophysiology to test antifungal drugs
Kevin Brunet*1,2,3, Jean-Philippe Martellosio1,2, François Arrive1,2, Thomas Brunet1,2, Isabelle Lamarche1,2, Sandrine Marchand1,2,3, Blandine Rammaert1,2,3
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Background: Most of the published mucormycosis animal models for antifungal studies are not representative of the human pathophysiology. Drugs are administered 30 min to 24h after spore inoculation, leading to treat spores and not hyphae, the invasive form of the fungus. The aim of our study was to develop and characterize a mouse model of Lichtheimia corymbifera pulmonary infection to test antifungal drugs.

Materials/methods: Male BALB/c mice were immunosuppressed with different corticosteroid (cortisone acetate 250 mg/kg to 500 mg/kg at different times) and/or cyclophosphamide (150 mg/kg to 200 mg/kg at different times) regimen, then intratracheally inoculated with 105 to 107 spores/mouse of Lichtheimia corymbifera. Lungs were collected at various times from one day post-inoculation (dpi) to 4 dpi, and presence of hyphae in tissue was assessed by calcofluor white staining. Intraperitoneal liposomal Amphotericin B (L-AmB; 15 mg/kg/d) was administered at 3 dpi for 4 days. Comparison of fungal load and pulmonary inflammatory cells recruitment between L-AmB treated and untreated mice was studied by quantitative PCR (qPCR) on lung parenchyma, and flow cytometry on bronchoalveolar lavage fluid (BALF) at 6 dpi, respectively. Statistical comparisons were performed using Mann-Whitney test.

Results: Mice receiving 500 mg/kg of intraperitoneal cortisone acetate 3 and 1 day before inoculation of 2.5x10⁵ spores/mouse developed an invasive infection at 3dpi (highlighted by presence of hyphae colored by calcofluor), contrary to mice immunosuppressed with cyclophosphamide alone that did not. All animals died before 10 dpi. Using L-AmB, survival was 60% at 21dpi. Lung fungal load was not different for L-AmB treated and untreated mice at 6dpi due to incapacity of qPCR to differentiate DNA from dead and living fungi. L-AmB induced a significant decrease in neutrophil recruitment in BALF of infected mice at 6dpi compared with untreated mice (4.9% vs 20.4%, p=0.02) but no difference in alveolar macrophage recruitment.

Conclusions: Survival of untreated and L-AmB treated mice in our model was in accordance with outcome of human mucormycosis. Immunomodulation effect of L-AmB could be responsible of changes in BALF cell recruitment and need further investigations.

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Impact of immunosuppression on *Clostridioides difficile* infection

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**Background:** Immunocompromised patients present a higher incidence of *Clostridioides difficile* infection (CDI) and an increased risk for adverse outcomes. Data from large prospective cohorts are sparse for this population. In a prospective observational study, we compared the characteristics, severity factors, treatment and outcomes in immunocompromised and non-immunocompromised patients.

**Materials/methods:** This prospective observational study included all consecutive cases of CDI in adult patients, between December 2018 and November 2019, in the University Hospital of Lausanne. CDI was defined as presence of diarrhea or ileus with a positive test. The tests used were an Xpert *C. difficile* polymerase chain reaction (PCR) assay (Cepheid Xpert\(^\text{®}\) C. difficile BT) followed by a C.DIFF QUIK CHEK COMPLETE\(^\text{®}\) enzyme immunoassay (EIA) (Labolife). Severity criteria according to ESCMID (2014) and IDSA (2018) guidelines were assessed. Recurrence was defined as a new episode within 8 weeks after the initial episode.

**Results:** From a total of 87 cases included, at least one factor of immunosuppression was identified in 43 cases (49%), and > 1 factors in 4 cases (hematologic malignancy \(n=18, 38\%), solid tumor \(n=20, 43\%), Solid Organ Transplant \(n=3, 6\%), other immunosuppression \(n=6, 13\%\)). There was no statistically significant difference in age, gender or the Charlson Comorbidity Index between groups. Toxin EIA was more frequently positive in the immunocompromised group (65% vs 42%, \(p=0.053\)). While only 30% of episodes in the immunocompromised group were classified as severe according to the IDSA guidelines, 71% were identified using the ESCMID criteria (vs 58% in the immunocompetent group, \(p=0.159\)). Fever and low albumin were significantly more common in the immunocompromised group (37.5% vs 14%, \(p=0.008\) and 30.4% vs 8%, \(p=0.06\), respectively). Fidaxomicin was more frequently used in the immunocompromised group (39% vs 11%, \(p<0.001\)). The rate of recurrence was higher in the immunocompromised group, but this difference was not statistically significant.

**Conclusions:** Fever and low albumin due to CDI were more frequently present in the immunocompromised group and could be of value in detecting severe disease in this population. The recurrence rate was numerically higher in the immunocompromised group, but this was not statistically significant.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Immunocompromised (N=43)</th>
<th>Immunocompetent (N=44)</th>
<th>(p)</th>
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</thead>
<tbody>
<tr>
<td>EIA Toxin pos</td>
<td>28 (65.1%)</td>
<td>19 (43.2%)</td>
<td>0.053</td>
</tr>
<tr>
<td>Recurrence D90</td>
<td>10 (23.3%)</td>
<td>5 (11.4%)</td>
<td>0.166</td>
</tr>
<tr>
<td>Death (all cause) D90</td>
<td>5 (11.6%)</td>
<td>3 (6.8%)</td>
<td>0.484</td>
</tr>
<tr>
<td>All episodes ((N=106))</td>
<td>(N=66)</td>
<td>(N=60)</td>
<td></td>
</tr>
<tr>
<td>Severity IDSA ((\geq 1))</td>
<td>17 (30.4%)</td>
<td>19 (38%)</td>
<td>0.420</td>
</tr>
<tr>
<td>Severity criteria ESCMID ((\geq 1))</td>
<td>40 (71.4%)</td>
<td>29 (58%)</td>
<td>0.159</td>
</tr>
<tr>
<td>Fever &gt; 38.5°C</td>
<td>21 (37.5%)</td>
<td>7 (14%)</td>
<td>0.008</td>
</tr>
<tr>
<td>Creatinine &gt; 133 (\mu)mol/l</td>
<td>6 (10.7%)</td>
<td>10 (20%)</td>
<td>0.277</td>
</tr>
<tr>
<td>Albumine &lt; 30 g/l</td>
<td>17 (30.4%)</td>
<td>4 (8%)</td>
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</table>

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Predictors of mortality in patients with bloodstream infections caused by metallo-ß-lactamases Enterobacterales

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Background: Metallo-ß-lactamases (MBL)-producing Enterobacterales are increasingly reported in Europe and represent a challenge due to limited treatment options. Few studies have been conducted in patients with bloodstream infections (BSIs) due to MBL-producing Enterobacterales. The aim of this study is to identify predictors of 30-day mortality in patients with BSI by MBL-producing strains.

Materials/methods: This observational study included patients admitted to 3 hospitals in Italy (Pisa and Livorno) and Greece (Athens) from 2018 to 2019. Clinical data, treatment regimens and outcome were collected. Species identification and susceptibility testing were performed by MALDI TOF MS [Bruker Daltonics] and SensiTitre [Thermo Fisher Scientific]. MICs were classified according to breakpoints established by EUCAST. The presence of bla genes was determined by PCR and sequencing. A Cox-regression analysis was performed to identify factors associated with 30-day mortality. Hazard ratio (HR) and 95% confidence interval (CI) were calculated.

Results: A total of 96 episodes of BSI by MBL-producing strains were observed. Of these, 17 (17.7%) were caused by VIM and 79 (82.3%) by NDM-producing Enterobacterales. Forty two patients (43.7%) received ceftazidime-avibactam (CAZ-AVI) plus aztreonam (AZT), 25 (26%) colistin-containing regimens and 22 (22.9%) other combinations containing tigecycline/fosfomycin whereas seven patients (7.4%) received no active antibiotic therapy. Thirty-day mortality rate was 36.5%. Compared to survivors, patients who died were older (75 vs 65 years, p=0.001), had higher Charlson Comorbidity index (6 vs 3, p=0.001), history of solid organ transplantation (SOT) (17.1% vs 1.6%, p=0.05), cardiovascular disease (57.1% vs 24.6%, p=0.001), and septic shock (48.6% versus 18%, p=0.002). At Cox regression analysis, cardiovascular disease (5.257 [2.247 - 12.298], p<0.001), SOT (3.312 [95% CI 1.253-8.756], p=0.016) and septic shock (2.646 [1.251-5.594], p=0.011) were independent predictors of 30-day mortality. Conversely, CAZ-AVI plus AZT was associated with improved survival compared to colistin-based regimen (0.194 [95% CI 0.078-0.482], p<0.001). Figure 1 shows the Kaplan Meier curve according to treatment regimens.

Conclusions: Among patients with BSIs due to MBL-producing Enterobacterales, patients with cardiovascular disease and SOT recipients are at higher risk of poor outcome, while antibiotic regimen with CAZ-AVI plus AZT is associated with reduced 30-day mortality compared to colistin-containing regimens.

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Acylated homoserine lactone- (AHL) mediated quorum sensing in dental plaque: an opportunity for novel antimicrobial treatment of oral diseases

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Background: Quorum sensing (QS) processes play a key role in the formation and maturation of bacterial biofilms. In the case of dental plaque, this role has been confirmed for the QS signals AI-2 and the autoinducer peptides (AIPs) in pure cultures of oral pathogens, but so far, the production of acyl-homoserine lactones (AHLs) by relevant oral bacteria could not be confirmed. Therefore, the current paradigm excludes a role of AHLs in dental plaque formation and in the development of oral diseases. In the view of the existence of indirect evidences in the literature indicating a role of AHLs in dental plaque, we have studied the presence and role of AHLs in in vivo and in vitro oral biofilm models.

Materials/methods: We have combined biosensor-based detection techniques with HPLC-MS analysis for the detection of AHLs in different oral samples and in vitro biofilm models and quorum quenching (QQ) activity in oral isolates. We have also studied the effect of the QQ enzyme Aii20J on in vitro oral biofilm formation.

Results: The results that support an important role of AHLs in dental plaque formation are:

- Presence of AHLs in saliva samples of healthy donors and patients suffering different oral pathologies (tooth decay and/or gum disease) and in dental plaque obtained from extracted tooth.
- Presence of a high abundance of oral strains with the ability to quench C6-HSL isolated from a periodontal patient (37.42%) and from a healthy donor (23.20%).
- Effect of the addition of the QQ enzyme Aii20J on different oral biofilms models, reaching up to an 80% of biofilm reduction measured with the xCELLigence® Real Time Cell Analyser (Acea Biosciences, Inc).

Conclusions: These data clearly support a role of AHLs in the formation on dental plaque indicating that the QS network in the oral cavity may be much more complex than the accepted paradigm and opening a new opportunity to find alternative therapies in order to prevent and control oral infections. Further studies are required in order to evaluate the role of AHLs in Gram-negative oral pathogen prevalence and in the equilibrium of the oral microbiome.

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Abstracts 2020

Abstract 5185

Markers of inflammation, neural injury and regeneration in a neonatal mouse model of Listeria monocytogenes meningoencephalitis

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Background: Bacterial infections of the central nervous system remain a substantial cause of mortality and long-term sequelae in neonates. To gain more knowledge about the pathogenesis of late-onset listeriosis, a recently developed intranasal neonatal mouse infection model was used (Pägelow D et al, Nat Commun 2018; 9: 4269). The present study analyses neuropathological alterations in brains of neonatal mice suffering from meningoencephalitis caused by Listeria (L.) monocytogenes with a focus on neural repair.

Materials/methods: The brains of 14 neonatal mice with L. monocytogenes meningoencephalitis without antibiotic treatment and 14 controls were analysed by histology, immunohistochemistry and in-situ tailing for neural proliferation and differentiation into neurons, densities of apoptotic neurons, microglia and astrocytes and morphological signs of microglial activation in the dentate gyrus of the hippocampal formation. Moreover, infiltrating blood cells, axonal injury and ischemic lesions were assessed in the brain tissue.

Results: Compared to uninfected controls, mice with L. monocytogenes meningoencephalitis showed a decreased density of dividing cells in the dentate gyrus and less neurogenesis analyzed by staining with anti-PCNA ($p < 0.0001$), anti-Calretinin ($p < 0.0001$) and anti-Calbindin ($p = 0.01$) antibodies, respectively, and an increased density of apoptotic neurons visualized by in-situ tailing ($p < 0.0001$). In infected mice, the density of microglia was higher ($p < 0.0001$), while no difference in the density of astrocytes was detected. Meningeal and/or intracerebral infiltrates were found in sections from 13 of 14 brains of infected animals. The infiltrating monocytes and neutrophilic granulocytes probably contributed to tissue damage. No ischemic injuries and no axonal damage were observed.

Conclusions: In the brains of L. monocytogenes-infected mice a strong immune response was observed which led to tissue injury and an impaired neural regeneration.

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Abstract 5188

Plasmid-mediated colistin resistance among human clinical Enterobacterales isolates: surveillance in the Czech Republic, 2018-2019

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Background: The prevalence of colistin resistance has increased rapidly among Enterobacterales. National surveillance of plasmid-mediated colistin resistance started in the Czech Republic in 2018. The aim of this study was to determine the prevalence and characteristics of isolates with mcr genes from human clinical samples.

Materials/methods: During 2018 and 2019, a total of 704 colistin-resistant isolates (MIC>2mg/l) from human clinical materials were examined for the presence of mcr-1 to mcr-8 genes. Isolates carrying mcr genes were tested for susceptibility to 18 antimicrobials substances by broth microdilution and subjected to whole genome sequencing (WGS) using MiSeq platform. Raw reads assembly was performed by SPAdes v3.12.0 to generate contigs that were used to identify antibiotic resistance genes, bacterial sequence types, and plasmid replicons using ResFinder, MLSTFinder and PlasmidFinder. Transferability of mcr-carrying plasmids was determined by conjugation experiments.

Results: So far, twenty-four mcr-1 (3.7%) and one mcr-4 (0.14%) positive isolates were obtained; other mcr genes were not detected. Isolates carrying mcr-1.1 or mcr-1.2 were identified as Escherichia coli (n=22), Klebsiella pneumoniae (n=2) and Enterobacter cloacae complex (n=1). A total of 18.9% colistin-resistant E. coli isolates subjected to PCR screening carried mcr genes. Most mcr-positive isolates showed resistance to aminopenicillins (n=24), quinolones (n=18) and trimethoprim-sulphamethoxazole (n=15). E. coli isolates belonged to various sequence types and showed diverse antibiotic resistance and plasmid content. The mcr-1 gene was predominantly located on 33 kb IncX4 (n=17) with high level of nucleotide similarity (>99.9%) to each other as well as to plasmids available at GenBank database. The gene was also carried by 60 kb IncI2 (n=4) or large (>150 kb) multidrug-resistant IncHI2 (n=3) plasmids. mcr-4.3 was identified in E. cloacae complex on 8 kb CoIE plasmid. Resistance to colistin was transferred to recipient E. coli laboratory strains via conjugation in the majority of the isolates.

Conclusions: Although this study demonstrated a low prevalence of mcr-positive isolates in patients in the Czech Republic (3.5% in 2018 and 4% in 2019), the occurrence of colistin-resistant bacteria should be considered as a possible risk for public health.

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Abstract 5191

Detection of antimicrobial resistance in Mycobacterium abscessus complex by MALDI-TOF MS

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Background: Species of the Mycobacterium abscessus complex (MABSC) are opportunistic pathogenic bacteria which are difficult to cure because of natural inducible resistance to clarithromycin (CLA) in certain subspecies. Phenotypic assessment of susceptibility to CLA, which is a major prognostic factor, currently requires 14 days of incubation. The objective of this work was to evaluate the performance of mass spectrometry (MALDI-TOF MS) for MABSC CLA susceptibility determination.

Materials/methods: Eleven MABSC strains genotypically and phenotypically characterized were cultured in liquid medium in absence and presence of CLA. According to our hypothesis, a strain susceptible to CLA would have a significant reduction in the Area Under the Curve (AUC) of the mass spectrum in the presence of CLA compared to control without CLA. Each strain was cultured at initial inoculum of 10^4 or 10^6 CFU/mL for 2 or 4 day incubation. The post-acquisition signal processing, including the AUC normalization, was performed with a program encoded in the R environment. Relative Growth (RG) ratio equal to the normalized AUC in the presence of CLA on the normalized AUC in the absence of CLA was calculated. The RG giving the best separation of strains according to their resistance phenotype was determined.

Results: For the 7 smooth strains but none of the 4 rough strains of MABSC, there was a proportional relationship between densitometry, colony count, and AUC. Normalization method encoded in the R environment resulted in robust and repeatable AUCs. The separation of the strains according to their phenotype was reproducible after a four-day incubation time and a 2.02 RG cut-off. After 4 days of incubation, for the strains studied that were extracted (19/22 strains [86%]), the CLA resistance phenotype was in agreement with reference technique for 17 of them [77% of tests performed].

Conclusions: This inexpensive technique which reduces the diagnosis of CLA resistance in MABSC from 14 to 4 days, appears promising.

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Abstract 5192

**Vanco-Test: a rapid test for detection of vancomycin-resistant enterococci**

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**Background:** Enterococci represent an important cause of nosocomial infection. Vancomycin resistant Enterococci (VRE) are microorganism subjected to screening to avoid transmission. The aim of the study was to set up a rapid and inexpensive diagnostic phenotypic test able to detect and/or vancomycin resistant Enterococci in 4 hours or less.

**Materials/methods:** The study was conducted on 59 strains, namely 44 *E. faecium*, and 15 *E. faecalis*. 23 out of 44 *E. faecium* and 2 out 15 of *E. faecalis* were vancomycin resistant, the other were vancomycin susceptible. The pattern of susceptibility or resistance was confirmed by both antimicrobial susceptibility test (broth micro dilution and Etest) interpreted following the EUCAST criteria, and Multiplex PCR for *vanA*, *vanB* and *vanC1/2* as determinant of resistance (1). The principle underlying the test is a change in the phenol red indicator following the fermentation of glucose by microorganisms which causes a lowering of the pH and a consequent color change from red to yellow. The Vanco-Test protocol was defined considering different variables: vancomycin concentration, phenol red solution concentration, amount of bacteria, medium, colonies freshness.

**Results:** Antimicrobial susceptibilities and molecular detection of resistance determinant confirmed the pattern of the strains under study. Vancomycin resistant strains showed the presence of *vanA* determinant, that is representative of our epidemiology. Two resistant strains and two susceptible strains of both species were used to set up the test conditions. Once the conditions were defined the Vanco-Test was performed for all strains under study. The results showed a 100% concordance with antimicrobial susceptibilities and molecular detection of resistance. All results were obtained in a maximum time of 4 hours. Sensitivity and specificity of Vanco-test were of 100%.

**Conclusions:** Vanco-test allows the rapid detection, 4 hours, of VRE microorganisms. It is a very cheap test that not need supply and can be done also home-made. Test must be validated with a largest number of strains, including also other determinants of resistance and with strains isolated directly from clinical samples.

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Neurodevelopment outcomes at 24 months of age in ZIKV-exposed and ZIKV-unexposed infants in French territories in the Americas: preliminary results from the ZIKA-DFA-BB cohort study

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Background: In utero exposure to Zika virus (ZIKV) is known to be associated with birth defects and neurological complications, collectively known in its most severe presentation as congenital Zika syndrome (CZS). Yet, neurodevelopment outcomes beyond birth remain unclear. The objective of this study was to determine the impact of in utero ZIKV exposure on neurodevelopment at 24 months of age among children born to women who were pregnant during the 2016 ZIKV outbreak in French territories in the Americas.

Materials/methods: ZIKA-DFA-BB is a prospective cohort study of infants born to mothers who were pregnant during the 2016 ZIKV outbreak in Guadeloupe, Martinique and French Guiana. From June 2018 to August 2019, 309 infants who had been enrolled in ZIKA-DFA-BB and had no neurological abnormalities detected at birth completed standardized neurodevelopment assessments at 24 months of age: 213 infants born to women with PCR or serological evidence of ZIKV infection during pregnancy; 96 infants born to women with no evidence of ZIKV infection at the time of delivery. Neurodevelopment assessments included the Ages and Stages Questionnaire (ASQ) for five domains of general development – communication, gross motor, fine motor, problem solving, and personal-social skills; the French MacArthur Inventory Scales (IFDC) for French language acquisition; and the Modified Checklist for Autism on Toddlers (M-CHAT) for behavior. Abnormal ASQ and IFDC outcomes were described as being below validated -2SD and 10th percentile threshold, respectively.

Results: 69 (32.4%) ZIKV-exposed infants and 38 (39.6%) ZIKV-unexposed infants had an ASQ result for at least one of the five domains below the -2SD cutoff (p=0.27). The domains most frequently scoring below threshold in the ZIKV-exposed infants were problem solving and personal-social skills. For the IFDC, there were no differences between ZIKV-exposed and ZIKV-unexposed infants in mean language acquisition (p=0.29) nor in the proportion below the 10th percentile threshold (p=0.19). No difference in M-CHAT behavior disorder screening risk between ZIKV-exposed and ZIKV-unexposed infants was observed (p=0.43).

Conclusions: In the largest cohort of in utero ZIKV-exposed infants without abnormalities at birth to date, there were no apparent differences in neurodevelopment outcomes compared to ZIKV-unexposed infants at 24 months of age.

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First vancomycin-variable enterococci from France: molecular mechanisms of phenotypic susceptibility

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Background: Over the last decade, a few studies have reported the emergence of vancomycin-variable enterococci (VVE), vanA-positive Enterococcus faecium strains phenotypically susceptible to vancomycin. In France, no VVE have been reported so far. The aim of the study was to characterize the first VVE strains isolated in France and to decipher the genetic basis of mechanisms of phenotypic susceptibility.

Materials/methods: Three strains of E. faecium received at the National Reference Center for Enterococci were included: 2 VVE isolates (17-364.1 and 18-086) and 1 vancomycin-resistant enterococci (VRE) isolate (17-364.2). Note that 17-364.1 and 17-364.2 corresponded to isogenic strains recovered from the same patient. MICs of vancomycin and teicoplanin were determined using the broth microdilution method according to EUCAST guidelines. Detection of van genes was performed by PCR. Genomes were entirely sequenced by Illumina technology (MiSeq), and bioinformatic analysis was done using the CLC Genomics Workbench software (Qiagen). Phylogenetic analysis was carried out using the E. faecium core genome as reference.

Results: Both 17-364.1 and 17-364.2 isolates were positive for vanA. However, 17-364.1 was susceptible to vancomycin and teicoplanin (MICs = 1 mg/L) whereas 17-364.2 was resistant to both antibiotics (MICs >64 mg/L). Phylogenetically, the strains were indistinguishable (0 SNP) and belonged to a new ST close to ST263. The strain 18-086 was positive for vanA and exhibited a susceptible phenotype to vancomycin [MIC = 2 mg/L] and teicoplanin [MIC = 1 mg/L]. It belonged to the ST80 and was not clonally related to the two other strains (3,599 SNPs). The Tn1546 was complete in 17-364.2, which was consistent with the resistant phenotype. By contrast, the transposon was interrupted in both VVE isolates. In 17-364.1, an IS1216 was inserted in vanS deleting the 330-bp 5’ end of the gene. In 18-086, an IS1251 was present in the intergenic sequence upstream of vanH while vanS was not detected. Note that vanR was not detected in both VVE strains.

Conclusions: This is the first description of VVE clinical isolates in France. The molecular mechanism of phenotypic susceptibility relies on the inactivation/deletion of vanRS. The risk of reversion to a resistant phenotype is under investigation.

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Abstract 5196

Vaccination uptake in sickle cell disease: results from a London teaching hospital

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Background: Sickle Cell Disease (SCD) is common in the UK with an incidence of 1 in 2000 live births. Around 12,500-15,000 people in the UK are living with SCD. People with SCD are at increased risk of infections with encapsulated organisms due to functional asplenia. Public Health England (PHE) and the UK Sickle Cell Society publish recommendations for additional vaccinations required by people with SCD above and beyond those given as part of the National Immunisation Programme (NIP).

Materials/methods: Details of all patients under regular follow up with the Haematology department at a South London teaching hospital were extracted from an electronic database and the patients’ General Practitioners (GPs) were contacted for their vaccination history. 355 patients’ GPs were contacted in writing. Data recorded were Influenza vaccine uptake for the last three years, Pneumococcal Conjugate Vaccine (PCV) uptake, Pneumococcal Polysaccharide Vaccine (PPV) uptake, Meningococcal C (MenC), Haemophilus influenzae B (HiB), Meningococcal ACWY Conjugate (MenACWY-Conj), Meningococcal B (MenB) and Hepatitis B vaccine uptake. For children, the uptake of their routine vaccinations according to the UK NIP was also recorded.

Results: 268/355 records were received (75.5% response rate). The age range of the patients was 0-84 years (median 22 years). Overall uptake of NIP vaccines for those under 18 years was 90%. In children under 18 years, vaccination uptake for additional vaccinations was much lower ranging from 59% for PPV to 13% for MenACWY. Vaccination uptake in adults ranged from 53% for PPV and most recent Influenza vaccines, to 0.7% for the MenB vaccine.

Conclusions: Overall uptake of additional vaccinations in people with SCD is poor. The best uptake was seen for Influenza vaccines and the PPV vaccine. Additional vaccinations in the UK are given by the patient’s GP due to the organisation of funding within the NHS. As a result, the patient must visit their GP separately to receive additional vaccines and the GP must be aware of the additional requirements. We propose that this is a significant contributor to the poor vaccination uptake and intend to explore whether opportunistic vaccination in hospital is an acceptable and effective alternative.

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Automated detection of antimicrobial-resistant bacteria based on real-time microbiological data

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Background: The spread of antimicrobial resistance (AMR) is a global public health threat, exposing patients to difficult-to-treat infections. An effective program to prevent the spread of AMR in hospitals includes: early detection of carriers, contact precautions for infected and colonized patients, strict hand hygiene (HH) compliance, environmental cleaning and disinfection, appropriate use of antimicrobials, and early intervention to halt outbreaks. Here we describe implementation of an automated process for AMR detection and assistance with infection control (IC) measures.

Materials/methods: The system was implemented in July 2019 in one tertiary-care hospital in Israel. We defined 6 target organisms: methicillin-resistant Staphylococcus aureus (MRSA), carbapenem-resistant Acinetobacter baumannii (CR-AB), carbapenemase-producing (CP) Enterobacteriaceae, non-CP carbapenem-resistant Enterobacteriaceae, vancomycin-resistant Enterococci, and Clostridium difficile [clinical infection only]. For each target organism, we created a generic algorithm that automatically detects positive results from the microbiology laboratory. We also created an easy-to-use system to manage the IC process upon discovery of a new carrier. The workflow starts with detection of a positive result (performed by the algorithm), automatic creation of an investigation protocol to assist the IC staff, and automatic notification of the patient’s ward regarding the required actions (e.g., isolation, screening of contacts). Finally, we developed an online dashboard that displays each wards’ data regarding the prevalence of resistant bacteria carriers, HH compliance and environmental cleaning audits, and incidence of hospital acquired cases.

Results: Compared to manual review of lab reports, the algorithm correctly detected 99% of the positive samples. As of October 2019, time to patient isolation (from lab result) has decreased significantly from 30h to 2h (for MRSA) and from 34h to 4h (for CR-AB). Standardized investigation of all new cases now occurs within 24h of the positive lab result (72h on weekends). HH compliance increased from 74% to 84%. Overall rates of hospital acquired infections by the 6 target organisms showed slight improvement (from 7.6 to 7.1 cases per 10,000 hospital days, July-Oct 2018 vs July-Oct 2019, respectively).

Conclusions: Full automation of management of resistant bacteria carriers allows focused and timely interventions. It also allows standardized and efficient work processes within the IC unit.

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Factors associated with non-vaccination against human papilloma virus among girls aged 14-15 years in France: a pooled cross-sectional analysis

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Abstract third-party references: The Vaccinoscopie® study group

Background: HPV vaccine is recommended in France in girls since 2007, but vaccine coverage remains very low. The aim of this study was to identify factors associated with non-vaccination against HPV in 14-15 year-old girls in France.

Materials/methods: We used the 2015, 2016, 2017 and 2018 Vaccinoscopie® data sets, a web-based survey conducted by IDM families and funded by GSK on a national sample of mothers selected through quota-sampling to monitor the annual evolution of vaccine coverage, perception and attitudes towards vaccination since 2008. Over the 4 years, a total of 2038 mothers of girls aged 14-15 years answered a self-administered online questionnaire reporting on their daughters’ HPV vaccination. The sample was weighted to ensure representativeness of the target population. Associations between non-vaccination against HPV and potential risk factors were analyzed using univariable and multivariable models. All variables with a p-value <0.25 in the univariate analysis were included in the multivariate logistic regression.

Results: HPV vaccine initiation rates (receiving at least one HPV vaccine dose) among 14-15 year-old girls were 23.4% (95%CI: 19.4-27.4), 23.4% (95%CI: 19.6-27.3), 31.1% (95%CI: 26.9-35.2) and 33.2% (95%CI: 29.1-37.2) in 2015/2016/2017/2018, respectively. Multivariate analyses showed that the use of internet as a source of vaccine-related information when mothers hesitate to vaccinate their child was significantly associated with non-vaccination against HPV compared with mothers who did not use the Internet (adjusted Odds Ratio (aOR)=1.47, 95%CI: 1.04-2.07). Protective factors against non-vaccination included: physician advice (aOR=0.11, 95%CI: 0.05-0.26), perception of HPV vaccination as ‘essential’ (aOR=0.04, 95%CI: 0.02-0.08), and a higher level of education (aOR=0.49, 95%CI: 0.32-0.75). Geographic disparities of HPV vaccine uptake across the five geographic regions of France were observed (p=0.0002), with the highest coverage in the West region (35.2% [95%CI: 29.8-40.6]), and the lowest in the Mediterranean region (17.0% [95%CI: 11.9-22.3]).

Conclusions: These findings will help to inform the design of future interventions to increase HPV vaccine uptake and address geographic disparities in France. Specific education campaigns are required to help vaccine-hesitant parents use the Internet safely when they seek information on vaccination.

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Abstract: Time-to-result quantification for different blood culturing workflows in an external microbiology laboratory setting
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Background: Microbiology laboratories are focused on a quick turn-around of diagnostics on patient materials, in particular for blood cultures. Therefore, blood culturing machines on location and rapid antimicrobial susceptibility testing are of interest to shorten the time between sampling and availability of culturing results. We determined and visualised the time of the different components in a blood culturing workflow in four different hospital settings, to evaluate and inform on optimal, tailored workflow choice.

Materials/methods: From our laboratory information system, we extracted the time elapsed between the times at which: the sample was drawn; sample was received; sample was placed in the incubator; a positive signal for growth was measured; a gram staining was performed; a determination was performed; the resistance pattern was determined; and a phone consultation with the clinician about the results. To establish a robust analysis of our daily practice, we evaluate both total overviews as well as medians and the inner 90-percentile of time-differences between the different blood culturing steps. To get an accurate impression of the regular workflow, we only analyse the first blood culturing event for a patient.

Results: A dashboard visualises the time between the different steps in a blood culturing process, for four different hospitals and with the possibility to select all or subsets of micro-organisms.

Figure: Example dashboard histogram displaying the number of hours between sample collection and positive blood culturing signal for E.coli.

The differences between the four hospitals were substantial: the median time between sample collection and positive incubation signal ranged between 11.2 and 23.2 hours. This is largely due to the additional use of a blood culturing system on location in two hospitals

Conclusions: Detailed analysis of the different steps in a blood culturing workflow allows for the investigation of the result of different interventions, such as the use of the blood incubation machines on location for an external laboratory, or the effect of rapid susceptibility testing on the total time to result for the patient. This allows the quantification of the diagnostic steps and deeper insight into different laboratory workflows.

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Abstract 5206

Pro-protein convertase subtilisin/kexin type 9 (PCSK9) is elevated in bloodstream infections and correlates with c-reactive protein

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Background: Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a protease involved in low density cholesterol (LDL) metabolism. Moreover, it can reduce lipopolysaccharide (LPS) and lipoteichoic acid (LTA) clearance by LDL-receptor down-regulation. The aim of this study is to compare PCSK9 concentration in patients with laboratory confirmed bloodstream infection (LCBSI) and healthy controls and to evaluate the variations of PCSK9 in patients with LCBSI according to aetiology and outcome.

Materials/methods: We enrolled 92 patients with LCBSI – retrospectively from 2014 to 2018 and then prospectively until September 2019 – and 31 healthy volunteers as controls. LCBSI was defined according to CDC definitions. PCSK9 plasmatic concentration was measured using a commercial ELISA test at admission and, for prospectively enrolled patients, at discharge too.

Results: Mean PCSK9 concentration was 611 ng/ml and 212 ng/ml in patients and controls, respectively (p<0.00001). In patients with negative outcome, PCSK9 was comparable to that seen in patients with positive outcome (623 vs 609 ng/ml, respectively). Patients with a S. aureus infection had a significantly higher concentration of PCSK9. Table 1 show the main characteristics of the study population and the 2 subgroups per aetiology (S. aureus vs other aetiology). The 25 prospectively enrolled patients were tested for PCSK9 at admission and before discharge with a significative reduction of PCSK9 concentration (796 vs 613 ng/ml, p=0.001).

As a post hoc analysis, we made a Paerson’s correlation between PCSK9 and CRP concentrations at admission; it showed a correlation with moderate strength (r=0.54) but significative (p<0.00001).

Conclusions: PCSK9 significantly increased in the inflammatory response to LCBSI, especially in S. aureus infections. Larger studies would better clarify the role of PCSK9 in this disease.

Table 1

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<tbody>
<tr>
<td>Age years, median (IQR)</td>
<td>68 (51-75)</td>
<td>69 (54-75)</td>
<td>62 (43-73)</td>
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<td>Male sex n (%)</td>
<td>59 (64.1%)</td>
<td>41 (63.1%)</td>
<td>18 (66.7%)</td>
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<td>Charlson comorbidity index median (IQR)</td>
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<td>5 (3-7)</td>
<td>4 (1-5.5)</td>
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<td>SOFA score median (IQR)</td>
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<td>1 (0-4)</td>
<td>1 (1-3)</td>
<td>&gt;0.1</td>
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<tr>
<td>Negative Outcome n (%)</td>
<td>16 (17.4%)</td>
<td>11 (16.9%)</td>
<td>5 (18.5%)</td>
<td>&gt;0.1</td>
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<td>PCSK9 ng/ml, mean±SD</td>
<td>611±236</td>
<td>571±314</td>
<td>709±247</td>
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**Abstract 5207**

**Nasopharyngeal carriage of methicillin-resistant Staphylococcus aureus in newly HIV-diagnosed, antiretroviral therapy naïve adults, Dar es Salaam, Tanzania**

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**Background:** Methicillin-resistant *Staphylococcus aureus* (MRSA) are difficult to treat and of concern to public health. Nasal colonization with MRSA is a risk factor for active disease and a particular threat to HIV-positive people who are more susceptible to severe bacterial disease. This is the first study to provide data on nasopharyngeal carriage of MRSA in newly HIV diagnosed adults in a community-setting in Tanzania.

**Materials/methods:** Individuals newly diagnosed with HIV were recruited at six sites in Dar es Salaam, Tanzania, from April 2017 to May 2018, as part of the randomized clinical trial CoTrimResist (ClinicalTrials.gov identifier: NCT03087890). Nasopharyngeal swabs were collected and cultured on sheep blood agar for isolation of *Staphylococcus aureus*. Species identity and methicillin-resistance was confirmed by polymerase chain reaction targeting the *nuc* and *mecA* genes, respectively. Antimicrobial susceptibility was performed by disk diffusion and E-test.

**Results:** Overall nasopharyngeal carriage rate of *Staphylococcus aureus* was 15% (79/537). One-third (n=27) of the isolates were MRSA, corresponding to a 5% MRSA carrier rate among all participants. MRSA isolates were significantly more resistant than methicillin-susceptible *S. aureus* (MSSA) towards gentamicin, ciprofloxacin and erythromycin. While overt clindamycin-resistance was rare in both MRSA (0%) and MSSA (2%), inducible clindamycin-resistance was much more common in MRSA (70%) than in MSSA (27%). The majority of *S. aureus* isolates (85%) were susceptible to cotrimoxazole. All MRSA isolates were fully susceptible to vancomycin and linezolid. In multivariate analysis, residence in Kigamboni and age <30 or ≥60 years were significant risk factors for MRSA carriage.

**Conclusions:** Our finding that MRSA constitute as much as one-third of *S. aureus* isolates calls for prudent antibiotic use. The majority of MRSA isolates were susceptible to cotrimoxazole. While WHO’s strategy for long-term cotrimoxazole preventive therapy may eradicate nasal carriage of MRSA in the short term, it remains to see whether this strategy will promote the emergence of increasingly resistant MRSA in the future.

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Antibiotic-metal complexes: where microbiology meets bio-physics

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Background: The misuse and overuse of fluoroquinolones (FQs) have triggered the development of bacterial resistance mechanisms. A strategy to circumvent this problem is the complexation of FQs with divalent metal ions and phenanthroline (phen). These stable complexes, known as metalloantibiotics, show different activity. Antimicrobial activity of FQs and metalloantibiotics was determined against several multidrug-resistant (MDR) isolates of *Escherichia coli* and *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA). Biophysical results on the membrane fluidity in absence and in presence of FQs and their complexes were also obtained.

Materials/methods: The minimum inhibitory concentration (MIC) of five FQs and their metalloantibiotics was assessed, by the broth microdilution method. 30 MDR clinical isolates were tested: four of *P. aeruginosa*, eight of *E. coli* and 18 of MRSA. The membrane fluidity of some clinical isolates was evaluated in absence and presence of different concentrations of FQs and metalloantibiotics, using fluorescent probes. The fluorescence anisotropy (r) of 1,6-diphenyl-1,3,5-hexatriene (DPH) and the generalized polarization (GP) of Laurdan (6-dodecanoyl-2-dimethylaminonaphthalene) were analyzed in ATCC controls and clinical isolates.

Results: Similar MIC values were obtained for FQs and metalloantibiotics against the Gramnegative MDR isolates. Nevertheless, in 15 out of the 18 MRSA isolates, metalloantibiotics exhibited a greater antimicrobial activity compared to pure FQs. The MIC values of metalloantibiotics were 4 to 28-fold lower than the ones of pure FQs. The r values obtained for the DPH were very similar among ATCC controls and clinical isolates although it is possible to state that Grampositive bacteria are in a more fluid lipid phase (smaller r). GP experiments evidenced much higher values for Grampositive bacteria, both in ATCC controls and clinical isolates. In presence of antibiotics the GP values varies little but preliminary results suggest that they are slightly smaller in presence of metalloantibiotics.

Conclusions: Metalloantibiotics exhibited an improved antimicrobial activity against MRSA isolates, suggesting that these compounds may be a promising alternative to FQs against *S. aureus*. Biophysical results show that GP values can be a valuable tool to discriminate between Grampositive and Gramnegative strains and seem promising in clarifying the interaction of the metalloantibiotics with bacterial membranes, especially in Grampositive isolates.

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Abstract 5211

**Epidemiology and comparative genomics of clinical isolates of Salmonella enterica serotype Typhimurium carrying the virulence-resistance plasmid pUO-StVR2**

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**Background:** Among more than 2,600 serovars of Salmonella enterica, S. Typhimurium is one of the most prevalent. This is mainly due to the widespread of a limited number of multidrug-resistant clones, including S. Typhimurium pUO-StVR2, which carries a virulence-resistance plasmid derived from pSLT. In the present study, we focused on the epidemiology, genomic variability and phylogenetic relationships of human clinical isolates belonging to this clone.

**Materials/methods:** All clinical S. Typhimurium isolates (532) received at the “Laboratorio de Salud Pública” (LSP) Asturias, Spain, between 2008 and 2018, were tested for antimicrobial susceptibility according to CLSI. The ampicillin-resistant isolates (416) were screened for the presence of blaOXA-1 and alterations in the nfsA gene conferring resistance to nitrofurantoin, both characteristically associated with the S. Typhimurium pUO-StVR2 clone. Isolates fulfilling these criteria were sequenced by Illumina. Typing of the isolates, as well as identification of resistance and virulence genes, plasmids and prophages were accomplished with “on line” bioinformatic tools [SeqSero, MLST, ResFinder, SPIFinder, VFBD, PlasmidFinder, pMLST, PLACNETw and PHASTER]. A phylogenetic tree was constructed with RAxML, based on SNPs in the core genome.

**Results:** Fifty out of the 416 isolates (12%) were assigned to the S. Typhimurium pUO-StVR2 clone and their genomes were sequenced. Most of them showed the ACSSuT/blaOXA-1-cataI-aadA1-sul1-tet(B) resistant profile conferred by pUO-StVR2, but two variants of this plasmid, lacking tet(B) or cataI, were also detected. pUO-StVR2 (IncFII) appeared either alone or together with plasmids of the incompatibility groups IncX1, IncI1 or IncO1, in which additional resistance genes were located [aadA5, strA-strB, dfrA1P and sul2]. According to phylogenetic analysis, the isolates were closely related and probed to be highly homogeneous with regard to SPIs and virulence genes. However, they showed great variability in prophage content, with 22 prophages distributed into 35 profiles. Of them, only Fels-1, Gifsy-1 and N15 were common to all isolates.

**Conclusions:** Together with other major MDR clones of S. Typhimurium, the pUO-StVR2-harbouring clone has substantially contributed to human salmonellosis in our region along the last decade. During this period, isolates carrying this plasmid have remained relatively stable, with prophages being responsible for the greatest diversity.

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Genetic diversity and possible recombination of Rs-BatCoV HKU32 related viruses in southern China
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Background: Coronavirus (CoV) belongs to viral subfamily Orthocoronavirinae and further subdivided into four genera, Alphacoronavirus to Deltacoronavirus. Bats are known for being the gene source for both Alphacoronavirus and Betacoronavirus. Novel alphacoronavirus Rs-BatCoV HKU32 was discovered in Rhinolophus sinicus, the same bat reservoir for SARS-related CoV (SARSr-CoV). Recombination of Rs-BatCoV HKU32 with SARSr-CoV was observed in one accessory gene. Similar viruses were found in China with significant genetic diversity, suggesting this virus is more diverse than expected. Further analyses of Rs-BatCoV HKU32 related viruses might reveal its evolutionary history and potential for zoonotic transmission.

Materials/methods: Anal swabs from different bat species were collected and subjected to viral RNA extraction and RT-PCR for CoVs detection. Two samples with Rs-BatCoV HKU32 were subjected to complete genome sequencing. Genomes of Rs-BatCoV HKU32 related viruses were obtained from Genbank. Complete genomes and selected functional genes were further subjected to phylogenetic analyses. To look for possible recombination among these viruses, bootscan analysis was performed using aligned whole genomes.

Results: Complete genome analysis showed that Rs-BatCoV HKU32 shared around 71 to 75% nucleotide identity towards Bt-CoV/Rh/YN2012 strains Rs3376, Rs4259, Rs4125 and Ra13591. According to the species demarcation criteria from International Committee on Taxonomy of Viruses (ICTV), the concatenated 7 domains of Rs-BatCoV HKU32 showed 85.5 to 89.5% amino acid identity towards the viral strains from China, representing Rs-BatCoV HKU32 was a novel viral species sharing close genetic relationship with other alphaCoVs.

Phylogenetic analyses of the whole genomes of Rs-BatCoV HKU32 related viruses revealed that viruses collected from Rhinolophus sinicus clustered together while the one collected from Rhinolophus affinis formed an outlier branch. However, different phylogenetic clustering pattern was observed in spike gene. Two strains of Rs-BatCoV HKU32 clustered closely with BtCoV/Rh/YN2012 Rs3376 followed by BtCoV/Rh/YN2012 Ra13591, suggesting possible recombination among these viruses. Bootscan analysis was carried out using Rs-BatCoV HKU32 as query and breakpoints were found at the genomic position around 20500 and 25500.

Conclusions: Rs-BatCoV HKU32 represented a novel species and was evolutionarily close to BtCoV/Rh/YN2012 viruses from China. Recombination events were found among these viruses, suggesting the possibility of novel emerging AlphaCoVs.

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**Abstract 5220**

**Worldwide dissemination of linezolid-resistant *Staphylococcus epidermidis* clones**

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**Background:** Linezolid is an important antibiotic for treatment of the nosocomial pathogen methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant Enterococci (VRE), where linezolid resistance has remained low. However, emergence of linezolid-resistant *Staphylococcus epidermidis* (LRSE) raises concern, as this species is gaining clinical relevance and represents the possibility of resistance transfer to MRSA and VRE. In spite of its clinical significance, LRSE clonal lineages and resistance mechanisms contributing to linezolid resistance spread are poorly explored.

**Materials/methods:** Ninety-three LRSE isolates from infection and colonization, collected in 2004-2016, from six different countries [Germany, Greece, Japan, Spain, Poland and USA], were analyzed. Linezolid susceptibility was evaluated by disk diffusion and minimum inhibitory concentration (MIC). Whole genome sequencing was performed with NextSeq Illumina. Raw data were assembled with INNUca v3.1 pipeline and molecular characterization performed using available resources in CGE and/or ABRIcate. Phylogenetic analysis was performed by C5Phylogeny v1.4.

**Results:** More than 75% of the isolates belonged to sequence types (ST) ST2 (49.5%) and ST22 (28.6%), while the remaining ST5, ST23, ST185, ST186 and ST797 ranged between 1.1 and 6.6%. SCCmec III was present in 80% of the isolates, while SCCmec IV was found in 7.5%. ST2-III and ST22-III clones were distributed across five countries, and some clones isolated in different countries differed by less than 12 SNPs.

All *S. epidermidis* presented a multidrug resistance profile, where high resistance rate (>89%) was observed for beta-lactam, quinolones, aminoglycosides, sulfonamides, mupirocin and phenicols. High-level mupirocin resistance was identified in 60% of the population; however *mupA* gene was only present in 25% of the isolates. Half of the isolates presented a minimum inhibitory concentration (MIC) for linezolid above 256 µg/ml; the remaining isolates had MIC varying from 6 to 128 µg/ml. The *cfr* resistance gene was identified in two ST22 isolates, suggesting mutation as the main mechanism responsible for linezolid resistance.

**Conclusions:** Linezolid-resistant *Staphylococcus epidermidis* clones are multidrug resistant and mainly associated with two clones related to clonal complex 2 (ST2-III and ST22-III), which were disseminated geographically. Mutation was identified as the main mechanism generating linezolid resistance worldwide.

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Abstract 5222

Clinical characteristics and prognosis of Staphylococcus aureus Bloodstream Infections in a French General Hospital

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Background: This study aimed to evaluate prospectively clinical characteristics and prognosis of SA BSIs in a French General Hospital.

Materials/methods: In our centre, patients with BSIs are evaluated by an ID specialist who collects prospectively clinical and microbiological characteristics, and data on empirical antibiotic treatment. These records are inserted in an anonymous database (Epidata software). An extraction was performed on SA BSIs which occurred during the period from May 1, 2017 to August 31, 2019.

Results: During the study period, 191 SA BSI occurred, which represented 16% of all consecutive BSIs episodes (n=1210). Mean age was 68.3 ± 16.6 years, and 73% of patients were immunosuppressed (mainly diabetes mellitus [n=71, 30%], and neoplasia [n=39, 17%]). There were a high proportion of health care-associated episodes (44%). The most frequent portal of entry was catheter-related infections (22%), followed by BSIs of unknown origin (20%) and bone and joint infections (17%).

Overall, the methicillin resistance rate was 16.3%. Rapid PCR based identification of methicillin resistance SA was performed in 112 episodes (59%).

Severe sepsis rate was 32% (n=62), and shock septic rate was 12% (n=23), with a 7-day mortality rate of 15% and a 30-day mortality rate of 22%.

Age, Vancomycin MICs, methicillin resistance rate, and inadequate empirical antibiotic therapy were not associated to 7-day mortality, whilst Teicoplanin MICs were significantly higher in patients who died (0.64 ± 0.48 vs 0.45 ± 0.24 mg/l in survivors, p=0.02), and a teicoplanin MIC ≥ 0.5 mg/l was associated to a higher 7-day mortality rate than a teicoplanin MIC < 0.5 mg/l (20% vs 7% respectively, p=0.01). The 7-day mortality was lower in patients with PCR use for methicillin resistance SA detection (7% in PCR group vs 25% in No-PCR group, p<0.001).

Conclusions: In our centre, SA-related BSIs are frequently associated to immunosuppression and health care-associated infections. The early mortality rate was lower in case of use of PCR for methicillin resistance SA detection, and surprisingly for strains with a teicoplanin MIC < 0.5 mg/l. Further larger prospective clinical studies are warranted to confirm the impact of teicoplanin MIC on SA BSIs survival.

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Abstracts 2020

Abstract 5223

**Interest of a systematic surgical mask wearing policy to decrease nosocomial flu burden at hospital**

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**Background:** Wearing a surgical mask is individually recommended to caregivers in presence of a patient suffering from flu to limit the risk of droplet transmission. However, no hygiene guideline suggests implementing a systematic policy of surgical mask wearing by all caregivers and visitors at hospital to decrease the occurrence of nosocomial flu. The main objective of our study was to evaluate whether such a policy could be effective.

**Materials/methods:** A prospective observational study was performed in a non-university tertiary care hospital (1 200 beds, including medical, surgical, rehabilitation wards and long term care facilities [LTCF]) during the 2018/2019 flu season. Wearing a surgical mask was asked to all caregivers and visitors during the entire period in voluntary services. Nosocomial flu cases, defined as influenza proven by PCR occurring more than 3 days after the beginning of patient’s hospitalization, were prospectively investigated in all hospital wards. The rates of hospital-acquired flu cases were compared between services which had implemented the mask wearing policy (MWP) and the others [non MWP].

**Results:** There were 37 MWP and 47 non MWP services. In MWP services, 12 patients (0.58%) developed nosocomial influenza among 2056 patients hospitalized more than 3 days, compared to 48 among 3525 hospitalized patients (1.36%) (p=0.0066) in non MWP services. A total of 65 (3.16%) and 131 (3.17%) patients were hospitalized during the same period because of a community-acquired influenza in MWP and non MWP services, respectively. In medical, surgical and rehabilitation wards, 11 cases of nosocomial flu occurred on 1584 patients (0.69%) in MWP services compared to 43 on 3266 patients (1.32%) (p=0.0528) in non MWP services. In LTCF, only 1 case on 472 patients (0.21%) was recorded in MWP services versus 5 on 259 patients (1.93%) (p=0.0231) in non MWP wards.

The flu vaccination rates among caregivers were similar in MWP and non MWP services (33% versus 30%, p=0.27).

**Conclusions:** A systematic surgical mask wearing policy by all caregivers and visitors at hospital during the flu season could decrease the risk of nosocomial influenza in a context of low caregivers’ flu vaccination coverage.

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Conserved host transcriptomic responses to acute infection are observed in the presence of multiple fungal pathogens

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Background: Invasive fungal infections frequently lead to serious critical illness in patients, however current diagnostic assays have significant limitations. Biomarkers based on pathogen-specific host gene expression patterns in peripheral blood offer potential to improve our diagnostic approaches to these devastating diseases.

Materials/methods: We have studied the transcriptional responses of circulating white blood cells utilizing animal models of Aspergillus, Cryptococcus, and Candida infection, in vitro human models of Candida and Cryptococcus, and human cases of invasive candidiasis. Logistic regression models were applied to gene expression data (RNA sequencing or microarray) to identify transcriptomic classifiers capable of identifying each type of infection as well as to assess for common antifungal response pathways.

Results: We have independently developed host gene expression classifiers for each pathogen, and shown that separate biomarker sets are capable of diagnosing infections with each of these 3 organisms. An Aspergillus classifier diagnoses aspergillosis despite variable immunosuppression (auROC 0.94). A Cryptococcus classifier distinguishes fungal from bacterial infection with 94% sensitivity and 89% specificity, while the murine candidemia classifier was able to discriminate between fungal and bacterial infection with 98% sensitivity and 96% specificity. Furthermore, we derived a transcriptomic classifier in human subjects that was capable of simultaneously and accurately differentiating multiple infectious phenotypes (auROC for Candida 0.98, bacteria infection 1.0, viral 1.0, and healthy 0.99).

However, when combining data across these different studies we were able to discover common aspects of the antifungal response shared across these very different infections. Thus, despite non-overlapping gene lists a cryptococcal classifier accurately identifies Candida infection and vice versa. Furthermore, we show that the host responses to Cryptococcus and Aspergillus share 15% of their top genes, including CXCR4 and IL10.

Conclusions: Host gene expression classifiers can accurately discriminate fungal infection from other illness phenotypes and show promise as novel diagnostic tools. These data demonstrate that there are also conserved host responses observed at the level of the transcriptome in the presence of a variety of fungal pathogens. These shared responses offer the potential for broad applicability of such assays in real-world practice.

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Variability in ceftazidime exposure and probability of target attainment of different dosing regimens of ceftazidime in critically ill patients with a proven or assumed Pseudomonas aeruginosa infection

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Background: Ceftazidime is a third generation cephalosporin antibiotic with time dependent activity (T>MIC) used as first line treatment option in the treatment of Pseudomonas aeruginosa infections in critically ill patients in the Netherlands. Optimization of dosing may improve the outcome of these high mortality infections. Aim was to investigate the magnitude of the variability in ceftazidime exposure and its causes, as well as the PK/PD target attainment (PTA) of different dosing regimens of ceftazidime in critically ill patients with a Pseudomonas aeruginosa infection. Secondary objective was to explore associations between PTA and microbiological cure.

Materials/methods: In this retrospective observational population pharmacokinetic study, blood samples were collected for ceftazidime concentration measurement and P. aeruginosa isolates were collected for MIC measurement. With the collected data a population PK model was constructed to estimate variability in exposure and PTA for the targets 100%T>MIC and 100%T>4xMIC.

For the secondary objective, patients with at least two subsequent P. aeruginosa isolates were enrolled for microbiological cure analysis.

Results: Ninety six patients yielded 368 ceftazidime concentrations. In a 1-compartment model, the use of continuous veno-venous hemofiltration was negatively associated with ceftazidime clearance. Furthermore, creatinine clearance and comorbidities including hematologic malignancy, trauma or head injury (factor 1.57, 1.19 and 2.07 respectively) were found to have a positive correlation with ceftazidime clearance, explaining 84% of variability in ceftazidime clearance.

MIC values from P. aeruginosa isolates were measured for 32 treatment courses. PTA was 100% for the 100% T>MIC, and 59% for the 100% T>4xMIC target. Patients receiving loading doses before continuous infusion demonstrated higher target attainment rates in the first 24 hours of treatment compared to other patients for 100%T>4xMIC [0% vs 64%; P=0.017].

For 17 patients the endpoint microbiological cure could be assessed. Only one patient (5.9%) achieved microbiological cure. 9 (53%) isolates of patients became resistant (≥2 dilution steps MIC increase) during therapy.

Conclusions: Critically ill patients may be at risk for underexposure to ceftazidime. A loading dose is recommended for target attainment within the first 24 hours of treatment. Furthermore, development of resistance of P. aeruginosa against ceftazidime is common during therapy with ceftazidime.

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Abstract 5230

Activity of ANT2681, a Novel metallo-beta-lactamase inhibitor in Combination with meropenem against metallo-beta-lactamase-positive Enterobacterales collected from hospitals world-wide in 2018

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Background: The spread of MBLs world-wide, especially NDM, is well documented and represents an unmet medical need. ANT2681 is a novel MBL inhibitor with a specific, non-chelating, mechanism of action involving competitive binding to conserved regions on MBLs. ANT2681 is currently in pre-clinical development in combination with meropenem. This study investigated the activity of meropenem/ANT2681 against MBL-positive Enterobacterales clinical isolates collected in 2018.

Materials/methods: MICs were determined by broth microdilution against MBL-positive isolates from Europe (n=231), Latin America (n=80), Asia-pacific (n=111), Africa (n=75), the Middle East (n=30) and North America (n=11). These included 452 NDM, 78 VIM, 5 IMP and 3 NDM+VIM (Citrobacter spp. (14), Enterobacter cloacae (90), other Enterobacter spp. (9), Escherichia coli (60), Klebsiella pneumoniae (294), K. oxytoca (15), K. aerogenes (4), Morganella morganii (5), Proteus mirabilis (9), Providencia rettgeri (5), P. stuartii (19), and Serratia marcescens (14).

Results: A summary of MIC data (mg/L) for meropenem/ANT2681 and comparator antimicrobials is shown below.

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td></td>
<td>MIC₅₀/MIC₉₀</td>
<td>Range</td>
<td>MIC₅₀/MIC₉₀</td>
<td>MIC₅₀/MIC₉₀</td>
<td>MIC₅₀/MIC₉₀</td>
</tr>
<tr>
<td>Meropenem/ANT2681¹</td>
<td>0.25/8</td>
<td>1-4</td>
<td>0.25/4</td>
<td>2/32</td>
<td>All 0.5</td>
</tr>
<tr>
<td>Meropenem</td>
<td>&gt;32/32</td>
<td>4-8</td>
<td>&gt;32/32</td>
<td>&gt;32/32</td>
<td>16/32</td>
</tr>
<tr>
<td>Cefepime</td>
<td>&gt;32/32</td>
<td>16-&gt;32</td>
<td>&gt;32/32</td>
<td>&gt;32/32</td>
<td>All &gt;32</td>
</tr>
<tr>
<td>Cefepime/taniborbactam²</td>
<td>2/32</td>
<td>8-&gt;32</td>
<td>2/32</td>
<td>0.5/8</td>
<td>All 16</td>
</tr>
<tr>
<td>Cefiderocol</td>
<td>2/8</td>
<td>0.12-2</td>
<td>2/8</td>
<td>1/4</td>
<td>2-4</td>
</tr>
</tbody>
</table>

MIC₅₀/MIC₉₀ concentration required to inhibit 50%/90% of the bacterial population.

¹ANT2681 [fixed 8 mg/L]. ²taniborbactam [fixed 4 mg/L].

Conclusions: Meropenem/ANT2681 was the most active against NDM sub-populations and the most active jointly with cefiderocol against all MBL combined plus the IMP isolates but it was less active against the VIM strains. Meropenem/ANT2681 was also active against most cefiderocol non-susceptible NDM-positive isolates (71 of 73 strains). Meropenem/ANT2681 is a promising potential therapeutic option for the treatment of MBL-positive Enterobacterales, especially those carrying NDM, and warrants further development.

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Use of N-acetylcysteine in critically ill patients with septic shock caused by carbapenem-resistant Klebsiella pneumoniae and Acinetobacter baumannii: a case-control study

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Background: Carbapenem-resistant Klebsiella pneumoniae (CR-Kp) and Acinetobacter baumannii (CR-Ab) represent nowadays an important cause of severe infections in Intensive Care Unit (ICU) patients and mortality rates are significantly associated to septic shock. N-acetylcysteine (NAC) is a mucolytic agent with antioxidant and anti-inflammatory properties, showing also in-vitro activity against several microorganisms including CR-Kp and CR-Ab and a synergistic interaction with colistin or meropenem. Aim of the study was to evaluate the effect on 30-day mortality of the addition of intravenous NAC to antibiotic therapy in ICU patients with septic shock caused by CR-Kp or CR-Ab.

Materials/methods: Retrospective, observational case:control study (1:2) in patients with septic shock caused by CR-Kp or CR-Ab hospitalized in two different ICUs with a dedicated Infectious Diseases consultant [IRCCS Neuromed, (Pozzilli) for cases and Sapienza University (Rome) for controls]. Cases included patients receiving NAC (1500 to 3000 mg/die divided q12h) in combination with antimicrobials, controls included patients not receiving NAC. Cases and controls were matched for age, SAPS II score, causative agent and source of infection. Univariate and multivariate analyses for risk factors associated with 30-day mortality were performed.

Results: No differences in age, sex, SAPS II score, cause of ICU admission (except for stroke) or time to initiate definitive therapy were observed between cases and controls. Colistin was more frequently used as definitive therapy in cases as compared to controls (80% vs 55%, respectively, p=0.02). Pneumonia (66.7%) and central lines related bacteremia (30%) were the leading infections, mostly caused by CR-Kp (60%). Overall, mortality was 48.9% [33.3% in cases vs 56.7% in controls, p=0.051]. At the univariate analysis, risk factors for mortality were age (p=0.015), time to initiate definitive therapy (p=0.017), CR-Ab infection (p=0.001), no definitive therapy with ≥2 antibiotics displaying in-vitro activity (p=0.002). At the multivariate analysis, independent risk factors for mortality were not receiving NAC (p=0.002) and CR-Ab infection (p=0.034) whereas therapy with 2 in-vitro active antibiotics (p=0.014) and time to initial definite therapy were protective (p=0.026) (Table 1).

Conclusions: A combined use of NAC plus antibiotics might reduce the 30-day mortality rate in ICU patients with septic shock caused by CR-Kp and CR-Ab.

Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (NAC not administered)</td>
<td>3.617</td>
<td>1.591</td>
<td>0.002</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.357</td>
<td>0.682</td>
<td>0.385</td>
</tr>
<tr>
<td>Age</td>
<td>1.020</td>
<td>0.991</td>
<td>0.175</td>
</tr>
<tr>
<td>SAPS II</td>
<td>1.019</td>
<td>0.986</td>
<td>0.259</td>
</tr>
<tr>
<td>CR.-A. baumannii infection</td>
<td>2.795</td>
<td>1.079</td>
<td>0.034</td>
</tr>
<tr>
<td>Therapy with 2 active antibiotics</td>
<td>0.210</td>
<td>0.060</td>
<td>0.014</td>
</tr>
<tr>
<td>Number of drugs</td>
<td>0.656</td>
<td>0.391</td>
<td>0.109</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0.799</td>
<td>0.328</td>
<td>0.621</td>
</tr>
<tr>
<td>Colistin containing regimen</td>
<td>0.501</td>
<td>0.190</td>
<td>0.163</td>
</tr>
<tr>
<td>Time to initial definitive therapy</td>
<td>0.826</td>
<td>0.698</td>
<td>0.026</td>
</tr>
</tbody>
</table>

Presenter email address: alessandra.oliva@uniroma1.it
Abstract 5233

Therapy directly observed by video for the supervision of tuberculosis treatment: experience in a series of patients from Cali, Colombia, 2019

María Elena Tello-Cajiao1, Jose Fernando Garcia-Goez2, Nelson Romero-Rosas3, Santiago Ardila-Giraldo*3, Juan Camilo Mosquera-Hernández3, Luis Gabriel Parra-Lara3

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Abstract third-party references: Secretaria de Salud Municipal de Cali, Fundación Valle del Lili, Universidad Icesi

Background: Tuberculosis (TB) programs have performed treatment supervision by Direct Observation Treatment (DOT) strategy, because the adherence needs to be guaranteed to avoid unfavorable outcomes. Adequate adherence to TB treatment with DOT strategy has been reported (90%), but in some contexts it can lead to catastrophic expenses in time and money for patients. As an alternative, the Video Directly Observed Therapy (VDOT) arises, which consists in the use of a videophone or other equipment to monitor the medications ingestion remotely. This work described the experience of the implementation of VDOT strategy for TB treatment supervision in a group of patients from Cali, Colombia.

Materials/methods: a description of a prospective case series of patients with new TB diagnosis between February 2019 and December 2019 was performed at Cali, Colombia. Subjects were recruited until May 2019 and were followed every day during the first and second phase of the treatment through video calls made with smartphones. The participants were characterized according to sociodemographic, clinical, laboratory variables, perception of the strategy and costs. The categorical variables were summarized in frequency tables and the quantitative variables according to their distribution. Significant p values <0.05 have taken and 95% Confidence Intervals were used for the analysis of the proportions.

Results: 221 potentially eligible patients were evaluated, of which 23 were recruited. 60% were men, with median age in 37 years old; the youngest patient was 19 years old and oldest patient was 82 years old. All subjects had health insurance, 91% were full-time workers and came from the urban area. 73% had pulmonary TB, 17% pleural TB and one had lymph node TB. During the first phase, a median of 47 doses were monitored by VDOT, achieving an adherence of 99.81%. Patient had to make an average of 3 visits for dispensing medications in the first phase, spending a median of $ 6.00 US on transportation. The second phase follow-ups are continued.

Conclusions: up to now, the strategy has been well tolerated and accepted. VDOT is proposed as a flexible and viable alternative to DOT therapy in selected patients from Cali.

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Abstract 5234

Experience after analysing a ceftazidime/avibactam national registry of infections caused by KPC-producing Klebsiella pneumoniae

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Abstract third-party references: Hellenic Society of Chemotherapy Hellenic Institute for the Study of Sepsis

Background: Invasive infections caused by KPC-Kp are associated with high mortality and new treatment options are urgently needed. A prospective multicenter observational study was conducted to evaluate the therapeutic efficacy of CAZ/AVI against serious KPC-Kp infections.

Materials/methods: The study was conducted under a National Registry in 15 tertiary-care hospitals between January 2018 and April 2019. Inclusion criteria were infections caused by KPC-Kp and treatment with CAZ/AVI >72h. A sub-cohort among these patients with KPC-Kp bacteremia was matched with a historical cohort with bacteremia treated with other antimicrobial agents using propensity score.

Results: A total of 168 patients were enrolled and 146 were included in the analysis. Mean patients age was 60.6 (±17.1) with Charlson co-morbidity index 2.9 ± 2.8, APACHE II 12.8 ± 7.5, SOFA score 7.0 ± 4.4 and Increment Score: 6.9 ± 3.7. Patients were suffering from bacteremia (102), VAP/HAP (27), cUTIs (15) and other infections [2]. Fifty had septic shock and 96 sepsis (by Sepsis-3). By McCabe scoring, 47 patients had ultimately fatal and 22 rapidly fatal underlying disease. For empirical treatment, 58 patients received no active agent and the remaining received at least one active drug. For definitive therapy 65 patients received monotherapy with CAZ/AVI and 81 patients received CAZ-AVI in combination with at least another active agent. At 14-day, clinical success was observed in 87.2% of participants and eradication of the infecting organism occurred in 56.4%. Resistance to CAZ/AVI was observed in 3 isolates during treatment. Mortality rates at 14-day and 28-day was 7.1% and 15.5% respectively. The 28-day mortality among the 71 KPC-Kp bacteremia patients treated with CAZ/AVI was significantly lower than that observed in the 71 patients used as controls [18.3% versus 40.8%, p=0.005]. In multivariate analysis, among the 142 KPC-Kp bacteremia cases, ultimately fatal [odds ratio [OR], 3.4; 95% confidence interval [CI], 1.2-9.5; p=0.02], and rapidly fatal disease [OR, 6.4; 95%CI, 2.0-20.5; p=0.002] were independent predictors of mortality whereas treatment with CAZ-AVI [OR, 0.3; 95%CI, 0.13-0.71; p=0.006] was the only variable associated with survival.

Conclusions: CAZ-AVI appears to be an effective treatment against serious infections caused by KPC-Kp.

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Epidemiology and risk factors of CC398 Staphylococcus aureus bone and joint infections

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Background: Staphylococcus aureus (SA) is the leading pathogen implicated in bone and joint infections (BJI). The clonal complex 398 (CC398) has emerged worldwide for several years. CC398 MRSA lineage is associated with livestock and most often responsible of colonization and mild infection in humans and animals. In contrast, CC398 MSSA is a frequent source of infections in humans, and was described frequently in serious infections such as blood stream infections. A particular ability of this clone to cause BJIs remains questionable, since some studies have described CC398 MSSA in prosthetic joint infection (PJI) and diabetic foot infection. Here, we described the long-term epidemiology of CC398 among SA isolated from BJI and identified risk factors associated with CC398.

Materials/methods: We screened all bone and joint samples (per-cutaneous joint fluid aspiration, bone or joint surgical sample) with SA-positive culture in our university hospital (France) between January 2010 and December 2017. CC398 isolates were detected with MALDI-TOF MS and confirmed by a specific PCR. We retrospectively extracted clinical informations from patients medical records. Conditional logistic regression was used for univariate and multivariate analysis.

Results: We identified 124 CC398 isolates among the 958 BJI-associated SA. The proportion of CC398 among SA increased steadily from 3% in 2010 to 28% in 2017. All the 124 BJI-associated CC398 were susceptible to methicillin. The distribution of BJI types due to CC398 and non CC398 isolates was similar. In multivariate analysis, age (p=0.034, OR=3.9), McCabe score (high comorbidity score; p=0.005, OR=5) and inoculation mechanism (p=0.020, OR=3.7) were associated with PJI-related CC398. The year of infection (p<0.001, OR=1.6), Charlson’s score (p=0.001, OR=1.5) and grade 4 (severe) of the International Working Group of the Diabetic Foot classification (p<0.001, OR=8.5) were associated with DFI related CC398.

Conclusions: We showed here the emergence and spread of CC398-MSSA in BJI, suggesting a well-adapted fitness of this clone to humans and bone. Patients with comorbidities are at high risk of CC398 MSSA PJI and DFI. The spread of CC398 in the community and hospital settings remains unclear and further epidemiological studies are needed to identify the determinants of its success.

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**Abstract 5238**

**Phage susceptibility testing with lensless imaging technique**

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**Background:** With the rise of antibiotic resistance, phage therapy is seen as a promising alternative to cure infection to multi-resistant bacteria strains. However, phage susceptibility tests currently carried out are time-consuming and are not compliant with the automated environment of hospital laboratories. In this work, we present a method for phage susceptibility testing through optical density measurement with the use of lensless imaging technique.

**Materials/methods:** Liquid samples containing bacteria and phages are loaded in a custom-made microfluidic card. The card has been machined in a 5-mm thick aluminum sheet and is composed of 8 wells of 3 mm diameter. It is sealed on one side by a MicroAmp adhesive film and on the other side by a PDMS film to insure optical transparency of the wells. Moreover, the use of PDMS, a material permeable to oxygen, enables better growth condition of the bacterial culture. The microfluidic card is put on a 3.3 cm2 CMOS imaging sensor, extracted from a CANON dslr camera. It is illuminated by a screen paired with a 560 nm spectral filter to provide a homogeneous monochromatic lighting over the whole sensor area. The large imaging area of the sensor, enables to simultaneously monitor the level of light transmitted through the entire set of wells of the microfluidic card and hence to compute the optical density of a dozen sample without the need of mechanical elements.

**Results:** With this prototype, we can monitor the decay or increase of the optical density suspension to determine respectively the lysis or growth of the bacteria under test. A first proof of concept has been done using *Pseudomonas putida* ATCC1 2633 bacteria with phage gh-1. We are able to provide a reliable result of optical phage susceptibility testing in less than 4 hours.

**Conclusions:** The prototype shown here is compact, inexpensive (<1k€) and is compliant with automated environment of hospital laboratories. Moreover, it is versatile and can be used for other application such as lysis plaque imaging to provide a fast measurement of a viral titer of a bacteriophage suspension.

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(a) Custom-made fluidic card. (b) Illustration and (c) picture of the set-up used for phage susceptibility testing

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Abstract 5240

Sequential time-kill experiments to characterize lipopolysaccharide-modifying genes involved in polymyxin resistance in *Escherichia coli* and *Klebsiella pneumoniae* carrying mcr-1

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**Background:** Resistances of Gram-negative bacteria to the last resort drugs polymyxins are on rise. It was previously reported that a MCR-1 plasmid encoding a phosphoethanolamine transferase lead to low-level resistance. Sequential time-kill study to determine the role of MCR-1 in the development of additional adaptive resistance to colistin and polymyxin B was presented at ECCMID 2019 (P1383). To determine the mechanisms involved in the impact of MCR-1 during exposition to polymyxins, genes leading to lipopolysaccharide modifications were analyzed by RT-qPCR and sequencing.

**Materials/methods:** *In vitro* selection of high-level polymyxin resistance in MCR-1 transconjugants of *E. coli* J53 (EC_MCR-1) and *K. pneumonia* R2292 (KP_MCR-1) were obtained by sequential time kill-curve (TKC) experiments in presence of colistin (CST) and polymyxin B (PMB). Expression of 11 genes (*pmrA, pmrB, phoP, phoQ, pmrC, pmrE, lpxM, arrT, cptA, lpxT* and *eptB*) assumedly involved in polymyxin resistance were analyzed quantitatively by Real-Time PCR method. The efficiency of amplification and the relative expression were analyzed by *t*-tests and 2^-∆∆CT method. In parallel, these genes were sequenced to determine the mutations occuring during polymyxins exposition.

**Results:** For all genes in highly resistant EC_MCR-1 and KP_MCR-1 strains, no mutations were found compared to the wild type strains. In comparison to wild type isogenic strain, the expression of 11 genes was increased in EC_MCR-1 before contact with antibiotic but not in KP_MCR-1. After contact with PMB and CST, all genes were down-expressed in EC_MCR-1. Otherwise, in KP_MCR-1, regulator genes *pmrA/B* and two effector genes, *pmrC* and *pmrE*, were slightly over-expressed. Moreover, in KP_MCR-1, *arrT* was significantly over-expressed up to 29-fold in CST, but only 4.5-fold in PMB (*P*<0.05).

**Conclusions:** The presence of MCR-1 in *E. coli* induced an overexpression of genes involved LPS modification pathway without polymyxins. However, the adaptation in presence of polymyxins was mainly due to the presence of MCR-1. In *K. pneumoniae*, the role of *arrT* in the adaptative resistance of polymyxins is of importance. Our findings suggest that plasmid MCR-1 favor selection of another resistance mechanism by different pathways for each strain leading to develop high-level resistance especially under colistin pressure but less in polymyxin B.

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**Abstract 5241**

**Penicillin-binding protein 2a temperature-sensitive folding defect: a new path to tackle methicillin resistance in *Staphylococcus aureus***

Melanie Roch*, Emmanuelle Lelong¹, Roberto Sierra¹, Olesya Panasenko¹, Adriana Renzoni¹, William Kelley¹

¹University of Geneva, Geneva, Switzerland

**Background:** *Staphylococcus aureus* is a major human pathogen and represents a clinical challenge because of widespread antibiotic resistance. Methicillin resistant *S. aureus* (MRSA) originates by the horizontal acquisition of *mecA* encoding PBP2a, an extracellular membrane anchored transpeptidase which confers resistance to β-lactam antibiotics by allosteric gating of its active site channel. Protein folding in the extracellular hostile environment is a critical step to assure proper enzyme configuration and activity.

**Materials/methods:** We studied the biochemical proprieties of purified PBP2a including its unfolding profile by thermal shift assay using Sypro orange and its allosteric mechanism by in vitro competition with bocillin-FL, a fluorescent β-lactam. In parallel, we performed the double knock out of PrsA and Htra1, two extracellular folding factors upregulated in presence of cell wall active antibiotics, in the MRSA strain COL. β-lactam susceptibility testing and PBP2a western blot were used to monitor methicillin resistance. We looked for additional factors involved in PBP2a quality control, by screening double mutants of *htrA1* combined with 25 other proteases using the Nebraska Transposon Mutant Library.

**Results:** Purified PBP2a showed a pronounced unfolding transition initiating at physiological temperatures leading to irreversible precipitation and complete loss of activity. Dual disruption of PrsA and Htra1 synergistically restored sensitivity to β-lactam and was enhanced by minor temperature shift, consistent with folding defect at physiological temperature. Additional experiments demonstrated that the extracellular chaperone PrsA provides anti-aggregation activity and that the Htra1 protease cleans up misfolded PBP2a and its degradation fragments created by other unknown proteases. Screening for additional factors revealed that at least 2 other proteases, respectively CtpA and PrsS, play a role in PBP2a quality control. Inspection of the PBP2a 3D-structure revealed two potential folding weak points composed of non-sequential anti-parallel β-sheets including the key allosteric domain regulating the active site opening.

**Conclusions:** The concordance of biochemical and genetic data highlights the necessity of extracellular protein folding factors for expression of MRSA β-lactam resistance. Targeting the PBP2a folding pathway represents a new particularly attractive adjuvant strategy to combat antibiotic resistance.

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Identification and discrimination of *Mycobacterium tuberculosis* and *Mycobacteroides abscessus* complex species directly from *Mycobacteria* Growth Indicator Tube (MGIT) culture media by Orbitrap ultra high-resolution mass spectrometry

Amol Bajaj¹, Joanna Freeke²*³, Mark Hutchins⁴, Benjamin Stielow²³, Adam Barker¹

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**Background:** Tuberculosis (TB) is one of the world’s deadliest diseases. In 2018, >10.0 million people around the world became sick with TB disease and there were 1.3 million TB related deaths. It is clinically important to differentiate *Mycobacterium tuberculosis* (MTB) complex organisms as members can possess differing antimicrobial susceptibility profiles and transmission rates, which in turn will aid in patient management. Unlike MTB, *Mycobacteroides abscessus* has emerged as an important respiratory pathogen in patients with cystic fibrosis. *M. abscessus* complex species cannot be differentiated by single gene sequencing and differentiating these species complexes is time consuming, highly subjective and expensive to perform. MALDI-TOFs ability to discriminate these organisms is limited. Therefore, Ultra high-resolution mass spectrometry employing nano-liquid chromatography coupled with the Orbitrap™ mass analyzer was used to obtain the discriminatory power necessary to identify the relevant species members.

**Materials/methods:** Four reference species from *M. tuberculosis* complex: *M. tuberculosis* (ATCC 27294), *M. microti* (ATCC 19422), *M. africanum* (ATCC 25420), *M. bovis* BCG (ATCC 19210) were grown for 18-21 days on 7H11 agar plates (Hardy Diagnostics, USA). Four reference species from *M. abscessus* complex *M. abscessus* (ATCC 19977), *M. massiliense* (DSMZ 45103), *M. bolletii* (DSMZ 45149), *M. chelonae* (ATCC 35752) were grown for 4-5 days on 7H11 agar plates. An approximate 0.5 McFarland dilution of all species was prepared and these samples incubated in the MGIT system (BD BACTEC). The protein extract was purified and then subjected to intact protein analysis using a Q Exactive™ HF mass spectrometer (Thermo Scientific) using a rapid gradient liquid-chromatography.

**Results:** The developed assay is simple, rapid, and reliable for discriminating *M. tuberculosis* and *M. abscessus* species complex members. ESI-MS patterns were highly reproducible and the assay identified approx. 70-100 proteoforms with a gradient elution program. Protein masses ranged from 3-30 kDa. Identified proteoforms are unique to individual members of the species complexes.

**Conclusions:** A rapid high-resolution accurate mass spectrometry technique for species-level identification was developed, which is very time efficient, demonstrating promise for more accurate, early diagnosis and reduce treatment costs. Also, provides scope to evaluate many more clinical species in future.

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Factors associated with inadequate intravenous colistin dosages: results from a multi-centre, cross-sectional study

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Background: Colistin is a last-resort agent for the treatment of severe infections due to multidrug resistant Gram-negative bacteria (MDR-GNB).

Materials/methods: This is a post-hoc analysis of a multicenter, cross-sectional study, describing colistin use in 22 Italian hospitals (COLI-CROSS study). The primary objective of this post-hoc analysis was to assess factors associated with inadequate intravenous colistin dosage. Inadequate dosage was defined as absence of an adequate loading dose (i.e., 9 million units of colistimethate) and/or absence of adequate maintenance dosages according to the Committee for Medicinal Products for Human Use of the European Medicines Agency, adjusted to renal function. Demographic and clinical variables were tested for their association with inadequate dosage in univariable logistic regression models. Then, variables potentially associated with inadequate dosage in univariable models (p<0.10) were included in an initial multivariable logistic regression model, and further selected for the final model using a stepwise backward procedure.

Results: Overall, 187 patients receiving intravenous colistin were included in the analyses. Their median age was 63 years (interquartile range 49-74), and 60% were males (113/187). Inadequate colistin dosages were administered in 27% of cases (50/187). In multivariable analyses, acute kidney injury (AKI) according to KDIGO criteria (dummy variable with stage 0 as reference, odds ratio [OR] 9.9 with 95% confidence intervals [CI] 1.6-60.2 for stage 1, OR 2.5 with 95% CI 0.3-17.7 for stage 2, OR 2.4 with 95% CI 0.3-21.4 for stage 3, overall p 0.002) and chronic obstructive pulmonary disease (COPD, OR 3.1 with 95% CI 1.3-7.4; p 0.013) were independently associated with inadequate colistin dosage, whereas presence of a central venous catheter (OR 0.4, 95% CI 0.2-0.8, p 0.001) was conversely associated with adequate colistin dosage.

Conclusions: An increased risk of inadequate intravenous colistin dosage was observed in patients with chronic or acute co-morbid conditions, such as COPD and AKI. In particular, the association between AKI and inadequate dosage may reflect the perception of an increased risk of nephrotoxicity in patients with impaired renal function, which nonetheless should not be accompanied by further dosage reductions beyond those recommended and might represent the target of dedicated antimicrobial stewardship efforts.

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Risk of infection in patients with carbapenem-resistant Enterobacterales (CRE) rectal carriage: a comparative study of KPC and NDM CRE (CHIMERA Study)

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Background: KPC-producing carbapenem-resistant Enterobacterales (CRE) are endemic in several European countries but NDM are becoming more and more frequent. The aim of this study is to identify specific risk factors for nosocomial infections among KPC and NDM-rectal carriers.

Materials/methods: This prospective observational study included patients with CRE rectal carriage admitted to an academic hospital in Italy from January 2019. Rectal swab cultures were performed in all patients at the time of hospital admission and every week thereafter. Molecular analyses on rectal swab specimen were performed using the Xpert Carba-R assay (Cepheid, Sunnyvale, USA). Patients carrying NDM or KPC CRE who developed infection were compared with colonized patients who did not. Infections included urinary-tract infections (UTI), pneumonia, intra-abdominal infections (IAI), ABSSSI, bloodstream infections (BSI). The attack rate of infections caused by the same colonizing CRE were defined as the number of infections divided by the size of the population at risk (rectal carriers). A multivariate analysis to identify risk factors for infection was performed in KPC and NDM-rectal carriers.

Results: 303 patients with CRE rectal carriage were included in the study. Among them, 161 (53.1%) were NDM and 142 (46.9%) KPC-rectal carriers. The most common infections were UTI (12.9%), pneumonia (6.6%), IAI (5.6%), ABSSSI (5%), BSI (8.6%). Attack rates of infections were higher in NDM compared to KPC-rectal carriers (Figure 1). Time from positive rectal swab to infection was shorter among NDM (5 [1-14] days) compared to KPC-rectal carriers (10 [2-15] days, p=0.024). At multivariate analysis, number of colonized sites besides stool (OR 11.948 [5.042-28.315], p<0.001) and intravascular devices (OR 2.843 [1.120-7.214], p=0.028) were factors independently associated with the risk of infection in KPC-rectal carriers. Conversely, urinary-tract diseases, including urinary-stenting or nephrolithiasis, (OR 22.638 [4.144-123.658], p<0.001), number of colonized sites besides stool (OR 4.056 [2.217-7.422], p<0.001), intravascular device (OR 3.115 [1.363-7.121], p=0.007) and steroids (OR 2.771 [1.2-6.395], p=0.017) were independently associated with infection among NDM-rectal carriers.

Conclusions: Patients with NDM-rectal carriage have higher risk of infections compared to KPC-rectal carriage. Although some risk factors for infections are shared in KPC and NDM-rectal carriers, urinary disease was the strongest risk factor among NDM-carriers.

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Abstract 5249

Distinguishing clinical characteristics and outcomes in patients with polymicrobial Staphylococcus aureus bacteraemia

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Background: Staphylococcus aureus is a common cause of bacteraemia and is often monomicrobial in nature. However, the clinical significance of polymicrobial S. aureus bacteraemia is not well-studied. We sought to determine clinical characteristics and outcomes that distinguished between patients hospitalized with polymicrobial (P-SAB) and monomicrobial (M-SAB) S. aureus bacteraemia.

Materials/methods: Retrospective chart review of patients ≥18 years old hospitalized with S. aureus bacteraemia from 2014-2019 was conducted. 465 patients were screened for polymicrobial bacteraemia, defined as growth of additional organism(s) besides S. aureus in the same blood culture. P-SAB and M-SAB patients were matched 1:2 by age, gender and bacteremia type (MRSA vs. MSSA). Relevant demographic and clinical data were recorded.

Results: 69 patients were included: 23 P-SAB and 46 M-SAB. Median age (72y), gender (78% male), and ethnicity did not differ between groups. P-SAB patients were more likely to be admitted from a long-term care/skilled nursing facility (52% vs. 24%, p=0.039), whereas M-SAB patients were more likely to be admitted from home (72% vs. 39%, p=0.039). MRSA predominated in P-SAB patients, with source of bacteremia most commonly being pneumonia (22% vs. 7%, p=0.106) and urinary tract infection (26% vs. 4%, p=0.014) in P-SAB group compared to M-SAB group. In the P-SAB group E. faecalis was isolated most frequently (n=6, 26%), followed by K. pneumoniae (n=4, 17%). While length of stay (9d P-SAB vs. 10d M-SAB, p=0.448) and requirement for ICU stay (43% P-SAB vs. 30% M-SAB, p=0.298) did not differ significantly between groups, more P-SAB patients were discharged to LTCF/SNF (70% vs. 39%, p=0.024). P-SAB patients took twice as long to achieve clinical stability (median 8d vs. 4d, p=0.009), although readmission rate (39% P-SAB vs. 41% M-SAB) and 30d mortality (9% P-SAB vs. 7% M-SAB) did not differ.

Conclusions: Healthcare setting exposure (i.e. residence in LTCF/SNF) appears to predispose patients to bloodstream infection with multiple organisms. Polymicrobial bacteremia is associated with high overall healthcare burden as evidenced by prolonged time to reach clinical stability and eventual discharge to LTCF/SNF.

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Abstract 5250

Genomic analyses of carbapenem-resistant Klebsiella pneumoniae in Singapore: resistance and virulence determinants

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Background: Kp is a versatile organism that can carry/acquire a variety of virulence and resistance genes. Hypervirulent Kp (hvKp) has higher propensity of causing severe diseases than classical Kp. However, there is still a lack of understanding of the contribution of virulence genes in pathogenesis. We characterised the resistance and virulence determinants of CrKp in Singapore and determined if virulence genes were associated with infection and mortality.

Materials/methods: 301 CrKp isolated between 2009-2018 from a Singapore tertiary hospital were subjected to Illumina whole genome sequencing and genotyped using the Kleborate software. Infections were classified according to CDC surveillance definitions. Virulence determinants were compared between isolates causing: (a) colonisation and infection; (b) mortality and no mortality using chi-square/Fisher’s exact tests.

Results: CrKp belonged to 75 different sequence types (ST); ST14 (n=39), ST11 (n=25) and ST16 (n=21) were most prevalent. All were multi-drug resistant and had ≥1 resistant gene [median=11, IQR=7–13]. Carbapenemase genes were detected in 260 isolates, with blaKPC being predominant (n=129), followed by blaoxa48-like (n=73), blaNDM (n=40) and co-producers (n=18). 53 distinct K capsule types were observed. The K1 and K2 capsule types, which are traditionally associated with hvKp, accounted for 3 and 35 isolates respectively. The frequencies of virulence genes were as follows: ybt (n=137), iuc (n=34), iro (n=19), clb (n=16), rmpA (n=17) and rmpA2 (n=26) (Figure 1). Isolates harbouring all 6 virulence genes were either K1 ST23 (n=5) or K2 ST65 (n=7). No virulence genes were detected in 155 isolates. 132 CrKp were implicated in infections, with bloodstream infections (n=60) being the commonest. The proportions of the individual virulence genes in colonisation and infection isolates were largely similar (p>0.05). Of the 12 isolates with all 6 virulence genes, only 7 were infection-causing. 38/132 CrKp resulted in 30-day mortality. No single virulence gene was associated with 30-day mortality (p>0.05).

Conclusions: Our genomic analyses suggest that known virulence determinants are low amongst CrKp in Singapore. There appears to be no clear association with disease severity and known virulence determinants in our population. Further studies are required to identify genetic factors predicting hvKp to inform clinical management.

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A widespread toxin-antitoxin system exploiting growth control via alarmone signalling

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Background: Under stressful conditions, bacterial RelA-SpoT Homologue enzymes synthesise the alarmone \((p)pGpp\), a nucleotide messenger. This alarmone is present in most bacterial species, including major pathogens. \((p)pGpp\) is essential for bacterial pathogens to become virulent, when bacteria face stress-inducing environments during infection. Therefore, the \((p)pGpp\)-mediated signalling is a promising target for the development of antibacterial agents subsequently its regulatory mechanism plays a central role in bacterial virulence and tolerance to antibiotics. We discovered that Small Alarmone Synthetases (SASs) that contain the \((p)pGpp\) synthesis domain, can be part of Toxin-Antitoxin (TA) systems. Here we investigate the distribution of this type of regulatory systems.

Materials/methods: Toxicityneutralisation assays were performed in \(E.\ coli\) BW25113 expressing toxin and antitoxin on LB medium plates with 0.2% arabinose and 1 mM IPTG (induction conditions). Nucleotide pools analysis were performed on HPLC. Cell cultures were grown in defined MOPS medium supplemented with 0.5% glycerol at 37 °C with induction conditions.

Results: We have discovered that multiple SAS subfamilies can be encoded in broadly distributed conserved bicistronic operon architectures in bacteria and bacteriophages that are reminiscent of those typically seen in toxin-antitoxin operons. We have validated five of these SASs as being toxic (toxSASs), with neutralisation by the protein products of six neighbouring antitoxin genes. The toxicity of \(Cellulomonas\ marina\) toxSAS FaRel is mediated by \((p)pGpp\) accumulation combined with depletion of cellular ATP and GTP pools, and this is counteracted by its HD domain-containing antitoxin.

Conclusions: The ToxSAS-antiToxSAS system is a novel TA paradigm comprising multiple different antitoxins that exemplifies how ancient nucleotide-based signalling mechanisms can be repurposed as TA modules during evolution.

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Abstract 5260

From DNA to diagnosis: a rapid, next-generation sequencing pipeline for detecting multidrug-resistant *Mycobacterium tuberculosis* mutations


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Background: Next-generation sequencing (NGS) has become a routine approach for detection of gene regions known to harbor resistance-conferring mutations in *Mycobacterium tuberculosis* (MTB). We performed a complete MTB DNA-to-diagnosis pipeline using targeted streamlined NGS library preparation coupled with standardized, web-based bioinformatic analysis to deduce antibiotic resistance profiles from a panel of contemporary clinical isolates from South Africa and Ethiopia.

Materials/methods: Clinical isolates were collected and shipped at ambient temperature from Africa to the United States in PrimeStore Molecular Transport Medium® (PS-MTM). After DNA extraction, rapid targeted-PCR library preparation (PrimeSeqTB) and NGS (Illumina MiSeq) were performed. FASTQ files were uploaded using a web-based bioinformatics pipeline (Hyrax Biosciences) and the resulting drug resistance profiles were generated within hours and compared to WGS results obtained using LaserGene (DNAStar) analysis.

Results: A panel of MTB clinical isolates from South Africa (N=16) and Ethiopia (N=20) revealed a variety of antibiotic resistance-conferring mutations. Antibiotic resistance to rifampin, conferred by S-450-L in the *rpoB* gene, and isoniazid, conferred by *katG* mutation at position S-350-T were most frequently reported. However genetic resistance to fluoroquinolone and pyrazinamide, conferred by mutations in the *gyrA* and *pncA* genes, respectively, were also reported. There was concordance in the TB resistance mutations identified by TGS and web-based reporting compared to genetic analysis determined using WGS and DNAStar analysis.

Conclusions: A complete MTB DNA-to-diagnosis system that incorporates laboratory methods for rapid targeted sequencing and a bioinformatics pipeline for standardized reporting of drug resistance data will guide patient care and global surveillance.

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**Abstract 5262**

**Adapting technology to provide nationwide testing for highly-resistant infections in the United States: aztreonam-avibactam susceptibility testing of metallo-β-lactamase-producing Enterobacteriaceae**

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**Background:** Metallo-β-lactamase (MBL)-producing Enterobacteriaceae can cause significant morbidity and mortality, largely because treatment options are limited. Aztreonam-avibactam, not approved by the U.S. Food and Drug Administration (FDA) and still undergoing clinical trials, has demonstrated good in vitro activity and case reports indicate successful treatment of MBL-producing Enterobacteriaceae infections. Aztreonam-avibactam can be used to treat these infections by administering aztreonam and ceftazidime-avibactam. In 2019, the U.S. Centers for Disease Control and Prevention (CDC) piloted aztreonam-avibactam antimicrobial susceptibility testing (AST) of MBL-producing Enterobacteriaceae using digital dispensing technology. We describe the problem of MBL-producing Enterobacteriaceae in the United States, the technology used to perform aztreonam-avibactam AST, and the pilot program offering this unique testing.

**Materials/methods:** State and local public health laboratories in the Antibiotic Resistance Laboratory Network (AR Lab Network) characterized carbapenem-resistant Enterobacteriaceae (CRE) isolates by performing organism identification, AST, and PCR-based detection of blaKPC, blaNDM, blaOXA-48-like, blaVIM, and blaIMP carbapenemase genes. Testing results were reported to CDC at least monthly. In March 2019, a subset of AR Lab Network labs adopted the HP D300e Digital Dispenser to create custom broth microdilution (BMD) panels for aztreonam-avibactam AST. Enterobacteriaceae displaying resistance to all β-lactams (including either ceftazidime-avibactam or meropenem-vaborbactam), or those carrying an MBL gene (blaVIM, blaNDM or blaIMP), were eligible for aztreonam-avibactam AST to inform patient treatment decisions. Aztreonam-avibactam AST results were reported to submitters within three working days.

**Results:** From January 2017 to June 2019, the AR Lab Network tested 30,537 CRE isolates. At least one targeted carbapenemase gene was detected in 36% (n=10,838) of CRE tested; 10% (n=1104) of the carbapenemase genes identified encoded MBLs. From March through October 2019, 38 CRE isolates from 17 states were sent for aztreonam-avibactam AST. All confirmed MBL-positive CRE isolates (n=36) tested against aztreonam-avibactam carried the blaNDM gene. Elevated aztreonam-avibactam MICs (>8/4 µg/mL) were detected in 14% (5/36) of MBL-positive isolates tested.

**Conclusions:** Increased testing of CRE by the AR Lab Network has improved our ability to detect MBL-producers. Using digital dispenser technology, we can now perform aztreonam-avibactam AST and inform therapeutic decision making, which may improve patient outcomes for those infected with MBL-producing Enterobacteriaceae.

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Antimicrobial combination activity of vancomycin and antimalarial quinacrine against methicillin-resistant Staphylococcus aureus isolated from infected diabetic foot ulcers

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**Background:** The emergence of multidrug-resistant pathogens is a major cause of infection-related mortality and poses therapeutic failures that have led to an increase in antimicrobial resistance. Due to a lack of therapeutic options, studies have focused on the combination of antibiotics as an alternative treatment to eradicate these infections and allow, earlier stabilization of patients and decrease the length of antimicrobial therapy. The aim of the study is to determine different combinations of the antibiotic vancomycin (VAN) and an antimalarial, quinacrine (QUI) against MRSA from infected diabetic foot ulcers.

**Materials/methods:** The minimum inhibitory concentrations (MICs) of VAN and QUI against eleven clinical MRSA isolates were determined according EUCAST guidelines (2019). The tests were performed using broth microdilution method on 96-well plates on duplicate. Referring to the MICs of the two agents, checkerboard assay was designed to determine the combinations against the MRSA isolates according to previous method. The following combinations were tested: MICVAN-MICQUI; MICVAN-MICQUI; MICVAN-MICQUI; MICVAN-MICQUI; MICVAN-MICQUI; MICVAN-MICQUI and MICVAN-MICQUI.

**Results:** The MICs of VAN in the eleven MRSA strains were 2 µg/mL for ten strains and 4 µg/mL for one strain. The MICs of QUI were 250 µg/mL for four strains, 500 µg/mL for three strains and 2000 µg/mL for four strains. VAN in combining with QUI showed inhibition of growth in all isolates. When we combined MICVAN and MICQUI there was significant inhibitory effect in 45.7% of the isolates. In combination of MICVAN with MICQUI a large percentage of inhibition of isolates was observed (72.7%), the same did not happen when combined MICVAN with MICQUI in this combination only 45.4% of the isolates inhibited, which suggested that they can be used together. In combinations MICVAN-MICQUI; MICVAN-MICQUI; MICVAN-MICQUI and MICVAN-MICQUI most isolates grew at these concentrations. Relatively to the combination MICVAN-MICQUI varied among strains.

**Conclusions:** The antimalarial quinacrine when combine with vancomycin suggest a relevant synergistic effect against MRSA from infected diabetic foot ulcers. This combination offers a potential option to treating several infections, when conventional therapeutic options are absent.

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Whole genome sequencing of heterochronous isolates of Burkholderia cenocepacia and B. contaminans from two patients with cystic fibrosis using Nanopore and Illumina platforms

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Background: Burkholderia cenocepacia and Burkholderia contaminans are members of the environmentally-derived Burkholderia cepacia complex which can be opportunistic pathogens causing chronic lung infections particularly in cystic fibrosis patients. The objective of this study was to use whole genome sequencing of heterochronous isolates from two patients to evaluate the genomic changes occurring in these pathogens during chronic infection of human hosts.

Materials/methods: Six strains of B. cenocepacia (ST28) isolated over 8 years from the same patient, and eight isolates of B. contaminans (ST482) taken over 4 years from the same patient were investigated. STs were determined by traditional MLST. The initial strain from each patient was sequenced using both MinION (Oxford Nanopore) and NexteraXT (Illumina, MiSeq) DNA libraries to generate long read and hybrid assemblies. These reference chromosomes were circularized and polished. Draft genomes for the remaining heterochronous isolates were assembled from Illumina MiSeq reads using SPAdes. Annotation was done using Prokka. Single nucleotide variants and insertions/deletions (indels) were identified using SNVPhyl and Snippy workflows and phylogenetic trees were produced. Phaster was used to identify phage, and MICs were assessed according to CLSI guidelines. Antimicrobial resistance genes were identified using the Comprehensive Antimicrobial Resistance Database (CARD).

Results: All strains were multidrug resistant, with MICs to several antimicrobials increasing over time. Genes encoding aminoglycoside, fluoroquinolone and tetracycline efflux pumps were identified in all strains of both species. The B. cenocepacia strains harboured three phages, and the complete genome consisted of three circular chromosomes and one plasmid with a total of 7.9 Mb, 7279 CDS and a G+C content of 67%. The complete genome of B. contaminans consisted of three circular chromosomes and two plasmids with a genome size of 8.6 Mb, 7781 CDS and a G+C content of 66.4%. All strains of B. contaminans harboured one intact phage. Comparative genomics identified a progressive increase in the number of indels and snps over the course of time in both species.

Conclusions: Complete whole genomes of B. cenocepacia and B. contaminans will allow us to gain insight into the changes that occur during chronic lung infections of cystic fibrosis patients.

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Abstract 5266

Whole genome sequencing to investigate genetic diversity in HBeAg-positive and HBeAg-negative hepatitis B virus infection

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Background: Hepatitis B virus (HBV) e-antigen (HBeAg) is a short, secretory protein encoded by pre-Core (pre-C), typically expressed early in infection. HBeAg has immunomodulatory properties, inducing host tolerance to HBV, resulting in conserved viral populations and high viral loads. During HBeAg seroconversion, the immunomodulatory effect of HBeAg declines and increased immune selection pressures are exerted on the viral population, with potential impact on clinical endpoints (clearance, transmission and liver disease). To investigate the impact of these varying immune environments, we performed HBV sequencing on HBeAg-positive and HBeAg-negative adults with chronic HBV (CHB) infection.

Materials/methods: Blood samples from a heterogeneous cohort of HBeAg-positive (n=11) and HBeAg-negative (n=18) CHB patients were collected from hospital clinics in London, UK. DNA was extracted and sequencing libraries prepared (Nextera). Samples were pooled and underwent a whole genome (WG) target enrichment approach with Illumina. Data were analysed using a pipeline based on the GLUE platform (http://glue-tools.cvr.gla.ac.uk/).

Results: Viral loads were higher among HBeAg-positive patients (median 6.3log10 IU/ml, IQR 5.6-7.5log10 IU/ml) than in HBeAg-negatives (median 5.0log10 IU/ml, IQR 4.3-5.7log10 IU/ml) (p=0.006). WG sequences were returned for 11/11 HBeAg-positive patients and 17/18 HBeAg-negative patients, representing genotypes A, B, C, D and E. Median coverage was higher in HBeAg-positive (1530 read/site) than HBeAg-negative samples (394 reads/site) (p<0.001). 10/11 HBeAg-positive and 14/18 HBeAg-negative samples with median coverage ≥50 reads/site were included in a comparative analysis of intra-host diversity. Median diversity was higher in the HBeAg-negative samples (p<0.001). Highly polymorphic sites (Shannon entropy score >0.4) were more common in HBeAg-negative samples (median 11 sites/sequence) than HBeAg-positive samples (median 2 sites/sequence). In HBeAg-positive samples, 61% of highly polymorphic sites were located in pre-S1, pre-S2 or S compared with just 37% in HBeAg-negative samples (p=0.01) [see Figure].

Conclusions: Highly polymorphic sites are more common in HBeAg-negative samples, in which they are distributed widely throughout the genome. Deep sequencing can provide insight into the changing host-viral interplay during different phases of CHB infection, with potential to inform better understanding of immune responses, pathophysiology, and therapeutic interventions.

Figure: Location of highly polymorphic sites in the HBV genome in HBeAg-positive (n=10) and HBeAg-negative patients (n=14).

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A One Health approach identifies the environment surrounding food animals as a potential reservoir of blaCTX-M genes in the community in Vietnam

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Background: The global emergence of extended-spectrum beta-lactamase-producing Escherichia coli (ESBL-E) is a significant threat to public health. In context of a “One Health” approach, we investigated the prevalence and transmission dynamics of blaCTX-M-carrying ESBL-E (blaCTX-M-E) isolated from patients, food-animals, their carcasses, and the slaughterhouse environment in Hanoi, Vietnam.

Materials/methods: During 2014-2015, we collected samples from patients with uncomplicated urinary tract infections (n=2,015), pigs and chickens from farms and slaughterhouses (n=365), and environmental samples in slaughterhouses (surface and wastewater, n=78) all within a 20-33 km radius from each other. UriSelect-4 (Biorad, USA) and MacConkey agars were used to identify ESBL-E from the collected samples. Antimicrobial susceptibility to 16 antibiotics was tested using Vitek, E-test (BioMérieux, France), and macro-broth dilution; results were interpreted according to the CLSI-M100-S29 guideline. Strains were typed by multi-locus sequence typing and screened for blaCTX-M genes by PCRs. blaCTX-M-E strains were subjected to 2x250bp paired-end plasmid sequencing (Miseq, Illumina Inc., USA). Additionally, 15 strains were selected for multiplexed long-read sequencing (MinION, Oxford Nanopore, UK).

Results: A total of 225 ESBL-E and 198 blaCTX-M-E strains were identified. Approximately 97% of blaCTX-M-E strains were multi-drug-resistant (MDR), including resistance to colistin (15%, n=29) and carbapenems (3%, n=5). From the different sample sources, we identified high clonal diversity and 8 blaCTX-M variants belonging to two CTX-M groups: CTX-M group 1 (blaCTX-M-1, blaCTX-M-11, blaCTX-M-15, blaCTX-M-55) and CTX-M group 9 (blaCTX-M-14, blaCTX-M-24, blaCTX-M-27, blaCTX-M-65) (Figure A). ST1193 and ST155 were dominant clones carrying blaCTX-M-27 and blaCTX-M-55 in humans and in animals, respectively. Utilizing long-read sequencing, we identified highly similar IncFII plasmids carrying blaCTX-M-55 in a lairage surface swab from a pig slaughterhouse and a human sample collected almost 2 years later. Moreover, identical fusion IncN-IncHI2 plasmids carrying blaCTX-M14 were commonly identified in a water sample collected from a chicken slaughterhouse and a chicken carcass swab from another slaughterhouse 16 km away (Figure B).

Conclusions: Our study emphasised high prevalence of MDR ESBL-E across sample sources in Vietnam. While no direct transmission routes could be established, we show the potential role of the slaughterhouse environment as an intermediate reservoir for dissemination of blaCTX-M-carrying plasmids.
Figure. (A) Prevalence of of \textit{bla}_{CTX-M} \ genes distributed between sample sources. (B) Potential transmission of \textit{bla}_{CTX-M} \ genes between sample sources identified by long-read sequencing; red arrows represents sharing plasmids between sample sources

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Modulation of the immune status in pyelonephritis caused by *Pseudomonas aeruginosa* in children with hydronephrosis

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**Background:** Among kidney diseases in children, the leading place occupied by hydronephrosis, which developed against the background of urinary tract obstruction and complicated by pyelonephritis. The purpose of the study was to identify immunological features of pyelonephritis due to *Pseudomonas aeruginosa* in children with hydronephrosis.

**Materials/methods:** The determination of T- and B- subpopulations performed by immunofluorescence reaction (RIF). The phagocytic activity of neutrophils investigated for its ability to absorb polystyrene latex particles. Cytokine levels (IL - 1, TNF-α) and IgM and IgG were determined by ELISA. The metabolic activity of neutrophils evaluated in the nitroblue tetrazolium restoration (NTR test) using light microscopy.

**Results:** Studies have shown pronounced changes of immunological reactivity parameters in pyelonephritis due to *Pseudomonas aeruginosa* in children with hydronephrosis in the active stage of the disease. Shifts in the indices of the cellular component of immunity manifested as a decrease in the relative number of T-lymphocytes with an increase in the absolute number of T-cells. In addition, the relative number of CD4-lymphocytes and immunoregulatory index CD4/CD8 were decreased, and shifts in the indicators of the humoral immunity, as a decrease in the relative and absolute number of B-lymphocytes, a low level of IgG and a high level of IgM, an increase in the concentration of CIC (circulating immune complexes). At the same time, were present signs of decrease of nonspecific antibacterial resistance as a low neutrophil activity index, decreased phagocytic number and the RNT (restoration of nitroblue tetrazolium) test, but high level of pro-inflammatory cytokines (IL-1β and TNF-α).

A research results showed that after the use of complex therapy with an immunomodulatory, was detected a higher relative number of CD4 lymphocytes IgG level and indicators of phagocytic activity, a decrease in the concentration of CIC, lower levels of IL-1β and TNF-α in serum.

**Conclusions:** Thus, it was noticed that complex treatment with immunomodulating therapy of pyelonephritis caused by *Pseudomonas aeruginosa*, in children with hydronephrosis, led to normalization of indicators of cellular and humoral immunity, nonspecific resistance and levels of pro-inflammatory cytokines in the blood serum with subsequent normalization of immunological reactivity parameter.

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Performance of the NTM Elite agar for the detection of non-tuberculous mycobacteria in sputum samples of patients with cystic fibrosis

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Abstract third-party references: Investigational Use Only. Performances establishment ongoing Sponsored by bioMérieux

Background: Nontuberculous mycobacteria (NTM) are emerging pathogens among people with cystic fibrosis (CF). Particularly Mycobacteroides abscessus has been associated with accelerated clinical decline. Nevertheless, NTM colonization and infection is under-reported due to other bacteria resisting the NALC-NaOH decontamination used prior to conventional mycobacterial cultures, possibly resulting in masking of NTM. The NTM Elite agar [bioMérieux, France] is a novel selective agar aiming to facilitate the culture of NTM without prior decontamination of sputum samples.

Materials/methods: We performed a prospective, multi-center study to compare the performance of NTM Elite agar with conventional culture methods for mycobacteria including Löwenstein-Jensen (LJ, bioMérieux, France) and Bactec MGIT (Becton Dickinson, USA). NALC-NaOH decontamination method was used prior to culture on LJ and in MGIT, while sputum samples were inoculated on the NTM Elite agar directly or after non-selective fluidization. Compared to MGIT and LJ which are incubated at 35-37°C, NTM Elite plates are incubated at 30°C, under which conditions the growth of M. tuberculosis is inhibited. This new medium can therefore be incubated and processed in conventional level 2 biosafety conditions.

Results: These preliminary results are based on 153 sputum samples from 117 patients. NTM Elite agar allowed to recover 8 positive NTM cultures (5 M. chelonae, 1 M. abscessus, 1 Mycobacterium avium, 1 other NTM), compared to 3 positive cultures for MGIT (1 M. chelonae, 2 M. avium), and no positive cultures with the LJ medium. Overall, 12% of cultures on NTM Elite agar presented an overgrowth with other micro-organisms, while this proportion was 40% on MGIT and 56% on LJ.

Conclusions: NTM Elite agar, a mycobacterial culture agar which does not require prior NALC-NaOH decontamination, outperforms conventional mycobacterial culture methods for the recovery of NTM from the sputum of CF patients. Therefore, this new medium may be considered as a suitable alternative to current time-consuming methods which still need to be considered when tuberculosis is suspected, and which are typically performed in strict level 3 biosafety conditions, what is not required for working with NTM.

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Genomic analysis of ciprofloxacin-resistant Salmonella enterica serovar Kentucky ST198 from Spanish hospitals

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Background: Salmonella enterica serovar Kentucky sequence type (ST) 198 resistant to ciprofloxacin (CipR) has emerged as a global food-borne human pathogen, posing a threat to public health. In the present study, whole genome sequencing (WGS) was applied to characterize CipR S. Kentucky isolates from Spain.

Materials/methods: Ten CipR S. Kentucky isolates were recovered between 2009 and 2018 from patients attended at hospitals in northern Spain and primary care centers associated with them. Susceptibility to antimicrobial agents was determined by automated minimal inhibitory concentration (MIC) and/or disk diffusion assays, and results were interpreted according to CLSI guidelines. Genome sequencing was performed with Illumina in a HiSeq 1500 to generate 2x125 bp paired-end reads. Serotyping, MLST, identification of resistance genes and plasmid analysis were performed with “on line” bioinformatic tools. A phylogenetic tree based on SNPs in the core genome was constructed with RAxML.

Results: All CipR isolates detected were ST198 and carried point mutations in the quinolone resistance-determining regions (QRDRs) of both gyrA (resulting in Ser83Phe and Asp87Tyr or Asp87Asn substitutions in GyrA) and parC (Thr57Ser and Ser80Ile substitutions in ParC). Resistances to other antibiotics [ampicillin, amoxicillin-clavulanic acid, chloramphenicol, aminoglycosides, sulfonamides and tetracycline], arranged in different combinations, and mediated by blaTEM-1B, cmlA1, aac(6)-Iaa, aac(3)-Id, aph(6)-Ia, sul1, tet[A] and tet[C], were also observed. Although plasmids were found in some of the isolates, all resistance genes were chromosomally located. The observed diversity of resistance genes, together with preliminary characterization of the chromosomal regions, supports the existence of different variants of Salmonella genomic island-1 (SGI1). Phylogenetic analysis revealed a close relationship of the S. Kentucky isolates from Spain with S. Kentucky ST198 CipR isolates from other countries. Finally, consistent with the African origin of the clone, travel to Africa was documented for three of patients.

Conclusions: Detection of the epidemic CipR S. Kentucky ST198 clone in Spanish hospitals is a cause of concern, which warranted further surveillance as well as implementation of control strategies to limit further spread. WGS has provided comprehensive information on the antimicrobial resistance genes of the isolates, and is presently being used to determine their virulence gene content.

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Interest of follow-up imaging examinations in patients with pyogenic vertebral osteomyelitis: a retrospective study

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**Background:** Pyogenic vertebral osteomyelitis (PVO) represents 2 to 4\% of osteo-articular infections and their incidence is steadily increasing. Magnetic Resonance Imaging (MRI) is currently the most efficient technique for diagnosis. No recommendations are established for monitoring PVOs, particularly in imaging. Although some recommend the use of systematic imaging, its use is controversial.

**Materials/methods:** We conducted a retrospective cohort analysis of patients with PVO who had both baseline and follow-up imaging results available in a French university hospital during the period of 2010-2018. We have classified the follow-up images into two groups, improvement/stability and deterioration, compared with the baseline findings. For each patient, we compared their imaging follow-up to their clinical-biological condition assessed at the same time.

**Results:** We have collected 95 patients. The median age was 68 years, 58 men, 21 patients had a history of spinal surgery. The most frequently reported germ was methicillin-sensitive \textit{Staphylococcus aureus} and the level of spinal involvement was predominantly lumbar. At diagnosis, 95 images were performed, including 26 Computerized Tomography (CT) and 69 MRI. We identified 105 follow-up images, 73 MRIs, 32 CTs. The median delay of realisation was 82 days. Of the 35 patients with clinical and biological recovery, 23 patients (66\%) showed improved imaging and 12 patients (34\%) showed radiological worsening [new abscesses \(n=4\), extension of soft tissue infiltration \(n=2\) and/or epiduritis \(n=2\) or appearance of new locations \(n=1\)]. Among the 50 patients considered as unhealed, on the contrary, imaging shows an improvement in radiological lesions in 39 patients (78\%) and an aggravation in 11 patients (22\%) [new abscesses \(n=4\), extension of soft tissue infiltration \(n=1\) and/or epiduritis \(n=3\) or appearance of new localisations \(n=1\)].

**Conclusions:** Our study showed that there was no correlation between the clinical condition of patients and their follow-up imaging in the context of PVO. Clinical and biological evaluation seems sufficient to determine whether or not the patient is cured. Many images are made during the follow-up with a questionable cost/effectiveness ratio. A standard radiograph may be sufficient to provide a basic structural condition at the end of antibiotic therapy.

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Evaluation of integrase strand transfer inhibitors on weight gain and body mass index
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Background: Recent data has linked integrase strand transfer inhibitors (INSTIs) to weight gain. Correctional facilities provide the ideal setting to evaluate the true effect on INSTIs on weight gain and BMI since they are controlled environments with consistent medication access.

Materials/methods: A retrospective cohort study evaluated incarcerated adults receiving HIV telemedicine care in 26 prisons in Illinois, USA, from 1/1/2011-12/31/2018. Included subjects were living with HIV/AIDS, receiving stable [i.e. ≥6 months] antiretroviral therapy [ART], virologically suppressed, and had weight monitoring ≥6 months prior and post INSTI switch. Subjects were excluded if previously on INSTIs, ART-naïve, released before 6 months of weight monitoring, reincarcerated, or in segregation. The primary objective was to evaluate average weight change [kg] of INSTIs [bictegravir, dolutegravir, elvitegravir, raltegravir] from baseline. Secondary objectives assessed change in body mass index (BMI) and BMI categorization for all INSTIs. Statistical analysis included Paired Student t-test and descriptive statistics.

Results: Among 117 individuals analyzed, 87% were Black men with an average age of 42.3 years. On average, subjects were stable on ART for 45.4 and 17.2 months prior and post INSTI switch, respectively. All INSTIs were significantly associated with weight gain and increased BMI (Table 1). No significant difference in change in weight or BMI was observed based on baseline regimen (NNRTI [p=0.3208] or PI-based [p=0.7960]), suspected or documented resistance [p=0.0939], single versus multiple tablet regimens [p=0.7469], tenofovir formulation [p=0.1864], or tenofovir disoproxil fumarate (TDF) versus non-TDF use [p=0.1864].

Conclusions: All INSTIs were associated with significant increases in weight and BMI in virologically suppressed patients. Dolutegravir was associated with the highest weight gain while raltegravir was associated with the lowest in this controlled population. Future research should assess long-term impacts of weight gain on morbidity and mortality.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Bictegravir</th>
<th>P-value</th>
<th>Dolutegravir</th>
<th>P-value</th>
<th>Elvitegravir</th>
<th>P-value</th>
<th>Raltegravir</th>
<th>P-value</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Average change in weight from baseline, kg</td>
<td>4.9</td>
<td>4.7</td>
<td>P=0.0036</td>
<td>6.5</td>
<td>P=0.0001</td>
<td>4.8</td>
<td>P=0.0001</td>
<td>3.6</td>
<td>P=0.0090</td>
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<tr>
<td>Average change in BMI from baseline, kg/m²</td>
<td>1.6</td>
<td>1.4</td>
<td>P=0.0111</td>
<td>2.8</td>
<td>P=0.0001</td>
<td>1.0</td>
<td>P=0.0273</td>
<td>1.2</td>
<td>P=0.0227</td>
<td></td>
</tr>
<tr>
<td>Increase in BMI categorization from baseline, n (%)</td>
<td>23</td>
<td>5/13 (38.5)</td>
<td></td>
<td>8/30 (26.7)</td>
<td></td>
<td>8/41 (19.5)</td>
<td></td>
<td>2/19 (10.5)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Perspective of the phage mini-antibodies for virus detection by using electro-acoustic sensor

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Abstract third-party references: This work was partially supported by the Russian Foundation for Basic Research [grants № 19-07-00300 and 19-07-00304].

Background: Viruses of bacteria are an excellent natural material for the investigation of polyvalent interactions with specific phage mini-antibodies. This is the promise basis for the development of new systems for the detection of viral particles and is of great practical importance, since today viral infections are a global problem. Furthermore the development of new methods for detection of bacterial viruses in various samples, which can provide a result in a short time, is important.

Materials/methods: Obtaining the phage mini-antibodies to bacteriophages from Azospirillum lipoferum Sr65 (FAl-Sp59b) as example, and their use for detection of viral particles by using the developed acoustic sensor. All experiments were conducted by specially manufactured sensor based on a resonator with a lateral electric field in the frequency range 6 - 7 MHz. An approximate criterion for the specific interaction between bacteriophages and mini-antibodies in the analyzed suspension can be defined as follows: the change in the modulus of electrical impedance of the sensor should not be less than ~5% after the addition of a certain number of mini-antibodies to bacteriophage suspension.

Results: The possibility of detecting bacteriophages using phage mini-antibodies by the electro-acoustic analysis method using bacteriophages FAl-65 was shown. It was found that the frequency dependence of the real and imaginary parts of the electrical impedance of a resonator with a suspension of phages and the appropriate antibodies significantly differed from that of the resonator with a control virus suspension without addition of mini-antibodies. The amount of FAl-Sp59b bacteriophage in the analyzed suspension varied from 10^10 to 10^6 phage/mL and the analysis time was not longer than 5 min. The change in the real or imaginary parts of the electrical impedance at the fixed frequency near the resonance after addition of specific mini-antibodies in the suspension can be used as an optimal parameter to obtain the reliable information.

Conclusions: These results demonstrate the possibility of recording the interaction of bacteriophages with mini-antibodies and serve as the basis for the development of a biological sensor for the identification and detection of viruses directly in the liquid phase.

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Abstract 5286

**Progress towards the targets for the elimination of viral hepatitis in the European Union**

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**Background:** The concept of elimination for viral hepatitis is based on global targets for reducing the incidence of chronic infections by 90% and attributable mortality by 65% by 2030. The European Centre for Disease Prevention and Control (ECDC) developed a monitoring system to support European Union (EU)/European Economic Area (EEA) Member States (MS) assessing progress towards elimination.

**Materials/methods:** Key indicators relevant for monitoring hepatitis B and C across EU/EEA MS were identified in consultation with an expert advisory group. Mapping of the indicators and sources of data was undertaken to identify existing validated sources of data and gaps where data would need to be collected from countries. ECDC developed a data collection tool to collect data directly from national authorities and data were collected and validated in 2018/9.

**Results:** Data on the indicators were incomplete, with only two countries providing data for all stages of the continuum of care for hepatitis B and ten countries for hepatitis C. Hepatitis related mortality is estimated to be 68,000 in 2015 with increasing trends in mortality rates due to hepatocellular carcinoma but decreasing rates from cirrhosis (all trends not significant). For hepatitis B, 25% (3/12) countries with data achieved the 2020 target of having 50% of persons with chronic infection diagnosed and for hepatitis C, 43.8% (7/16) of countries with data achieved the target. One country of the six with data achieved the target of having over 75% of the diagnosed patients with chronic hepatitis B on treatment but none of the 13 countries reporting hepatitis C data had reached the target.

**Conclusions:** Significant gaps in the availability of data in relation to the prevention, testing and treatment of hepatitis B and C in EU/EEA Member States present a major challenge towards being able to monitor progress towards the targets of elimination. Despite these gaps, available data indicate that countries need to significantly scale up prevention, testing and treatment programmes to impact on incidence and mortality. In order to guide national responses, countries should prioritise improving the quality of their monitoring systems, especially data along the continua of care.

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Risk of failure in dual vs. triple therapy in naive HIV patients: a meta-analysis

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Background: The objective of this meta-analysis is to evaluate the relative risk of failure of two-drug therapies compared to three-drug therapies in HIV-naive patients.

Materials/methods: A systematic review and meta-analysis conducted using MEDLINE Google Scholar and the Cochrane Library. All studies included had to fulfill the following inclusion criteria: present original data from randomized or non-randomized trials; investigate in antiviral therapy-naive HIV subjects the efficacy of a conventional triple ARV [control group], versus a dual ARV [experimental group]; report the primary outcomes clearly defined as regimen failure; report data allowing the odds ratio estimates of relative risk [RR] to be calculated for the different outcomes of therapy with triple versus dual therapy; be published from January 2007 up to January, 2019.

Results: Thirteen studies, from a total of 4,743, meet the inclusion criteria allowing a meta-analysis of 5,205 patients. The meta-analysis performed on study presenting data at 48 weeks, 10 studies, 3495 patients, reveals: in study without maraviroc-based therapy at 48 weeks, the RR of treatment failure [TF] in 6 study on 2428 patients was 1.14 [95%CI: 0.91-1.44]; the RR of virological failure [VF] in 4 studies on 2132 patients was 1.69 [95%CI: 0.96-2.96]. The RR of adverse drug reaction leading to discontinuation of regimen at 48 weeks in 8 study, on a total of 3204 patients, was 0.78 [95%CI: 0.52-1.17]. In patients with less of 200 CD4+, the RR of TF in 2 studies without MRV on 172 patients, was 2.09 [95%CI: 1.09-4.39]; in patients with equal or greater than 200 CD4+, the RR of TF in 2 studies without MRV on 1467 patients, was 1.06 [0.74-1.52]. Regarding the studies at 96 weeks, the RR of TF in 2 papers on 1558 patients, was 1.08 [95%CI: 0.84-1.39]; the VF in 2 papers on 1558 patients, was 1.05 [95%CI: 0.82-1.33].

Conclusions: Dual therapy, excluding those based on maraviroc, are as effective as those with three drugs, showing no difference according different dual therapy, except in patients with less than 200 CD4.

| Outcomes | Nº of No. of | Nº and (%) | RR | 95% CI | p | Heterogeneity test (I², %)
|-----------|---------------|------------|-----|--------|---|----------------
| Treatment failure at week 48 | Nº of patients experimental/control group | Nº of patients experimental/control group |   |       |   |       |
| Total     | 10            | 324/178    | 1.32 | 0.86-1.99 | 0.195 | 64.3%
| Using PDI-2D in dual | 2            | 56/30     | 0.79 | 0.44-1.42 | 0.414 | 54.9%
| Using TDF in dual | 5            | 116/72    | 0.75 | 0.49-1.14 | 0.194 | -
| Using TDF in dual | 1            | 116/72    | 0.75 | 0.49-1.14 | 0.194 | -
| Using TDF in dual | 4            | 116/72    | 0.75 | 0.49-1.14 | 0.194 | -
| Treatment failure at week 48 | Nº of patients experimental/control group | Nº of patients experimental/control group |   |       |   |       |
| Total     | 7             | 120/85    | 1.40 | 0.76-2.71 | 0.516 | 69.2%
| Using TDF in dual | 1             | 120/85    | 1.40 | 0.76-2.71 | 0.516 | 69.2%
| Using TDF in dual | 1             | 120/85    | 1.40 | 0.76-2.71 | 0.516 | 69.2%
| Treatment failure at week 48 without MRV | Nº of patients | Nº of patients |   |       |   |       |
| Total     | 4             | 262/207   | 1.02 | 0.76-1.21 | 0.622 | 19.29%
| Using TDF in dual | 1             | 262/207   | 1.02 | 0.76-1.21 | 0.622 | 19.29%
| Treatment failure at week 48 without MRV | Nº of patients | Nº of patients |   |       |   |       |
| Total     | 5             | 155/120   | 1.35 | 0.85-1.94 | 0.225 | 67.95%
| Using TDF in dual | 1             | 155/120   | 1.35 | 0.85-1.94 | 0.225 | 67.95%
| Treatment failure at week 48, by CD4 | Nº of patients | Nº of patients |   |       |   |       |
| CD4<200 | 3             | 165/132   | 1.23 | 0.89-1.65 | 0.306 | 39.25%
| CD4>200 | 3             | 125/100   | 1.23 | 0.89-1.65 | 0.306 | 39.25%
| Treatment failure at week 48 without MRV, by CD4 | Nº of patients | Nº of patients |   |       |   |       |
| CD4<200 | 2             | 170/170   | 1.09 | 0.84-1.39 | 0.624 | 54.63%
| CD4>200 | 2             | 170/170   | 1.09 | 0.84-1.39 | 0.624 | 54.63%

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Abstract 5292

**Systematic review on estimated rates of nephrotoxicity and neurotoxicity in patients treated with polymyxins**

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Abstract third-party references: Supported by Shionogi D.V.

**Background:** A systematic review was conducted to explore the incidence of nephrotoxicity and neurotoxicity from polymyxin treatment and whether any factors influence these.

**Materials/methods:** Searches of Pubmed and EMBASE were undertaken on 17 June 2019 to identify randomised controlled trials, cohort studies and case-control studies reporting nephrotoxicity and/or neurotoxicity rates in hospitalised patients with infections treated with polymyxins. Where appropriate, raw data of event numbers were pooled and analysed using a random-effects model. Subgroup analyses were performed using mixed effects models. The protocol is registered on PROSPERO (CRD42019134926).

**Results:** Data from 223 studies (29,729 patients) contributed to nephrotoxicity analyses. Across all studies, the rate of nephrotoxicity was 27.6% [95% CI 25.1–30.3%]. When restricted to studies using internationally recognised criteria for nephrotoxicity (AKIN, KDIGO or RIFLE), the rate was 37.8% [95% CI 35.0–40.8%], higher than studies using other criteria [15.4% [95% CI 12.7–18.5%]; p<0.001]. In a meta-analysis of head-to-head studies, polymyxins were associated with a higher rate of nephrotoxicity than non-polymyxin-based comparators (odds ratio 1.962 [95% CI 1.321–2.914]; p=0.001). Subgroup analyses showed that nephrotoxicity rate was significantly affected by polymyxin (polymyxin B: 33.1%; colistin: 26.9%; p=0.026), administration route [inhaled: 15.4%; intravenous: 37.0%; intravenous plus inhaled: 27.8%; p=0.001], dose [low: 26.1%; normal: 32.7%; high: 43.3%; p=0.006] and patient age [neonates: 7.6%; paediatrics: 10.1%; younger adults: 30.4%; older adults: 45.0%; p<0.001], but was unaffected by use of a loading dose [p=0.584], ICU setting [p=0.337], sex [p=1.000] or baseline renal impairment [p=0.145]. Nephrotoxicity rates varied by concomitant nephrotoxin [p=0.004] and were highest in patients receiving vasoressors, diuretics or glycopeptides. Cumulative nephrotoxic effects were observed with multiple nephrotoxins [p=0.001].

Seventy studies (5,464 patients) contributed to neurotoxicity analyses. The overall neurotoxicity rate was 2.9% [95% CI: 2.0–4.3%] and was not significantly affected by polymyxin type [p=0.480]. Across head-to-head studies, polymyxins were associated with a numerically, but not significantly, higher rate of neurotoxicity than non-polymyxin-based comparators [odds ratio 3.906 [95% CI 0.996–15.331]; p=0.051].

**Conclusions:** Polymyxin therapy is associated with a greater risk of nephrotoxicity than other therapies. Further data are required to confirm whether polymyxins are associated with neurotoxicity.

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Evaluation of the NeuMoDx HPV assay
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Background: High-risk human papillomavirus (HPV) testing provides better protection against cervical cancer compared to cytology. Consequently, cervical screening by primary HPV testing has or will be implemented in multiple countries or regions thereof. This emphasizes the need for robust, high-throughput HPV testing solutions. The QIAscreen HPV PCR Test is a clinically validated CE-IVD in vitro real-time PCR-based assay for the qualitative detection of HPV DNA, targeting the E7 region of 15 HPV genotypes (i.e., 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 67 and 68) and provides separate genotype information for HPV16 and HPV18. Implemented on the fully automated, random access NeuMoDx Molecular System in a high throughput, “sample to result” manner, the NeuMoDx HPV Assay enables significant improvements to the HPV testing workflow. This study reports on the analytical and clinical performance of the NeuMoDx HPV Assay.

Materials/methods: The following analytical performance metrics of the NeuMoDx HPV Assay were studied: limit of detection (LoD) of each genotype, specificity against non-target organisms, reproducibility, and impact of interfering substances. Agreement and clinical performance for CIN2+ was determined against a reference assay on 253 cervical scrapes collected in PreservCyt™ collection media, comprising 63 cases (CIN2+) and 190 controls (≤CIN1).

Results: All the reagents and consumables used for the NeuMoDx HPV Assay are stable at ambient conditions and have ready-to-use configurations requiring no user mediated steps. The LoD of the NeuMoDx HPV Assay was determined to be equivalent or better than the reference QIAscreen HPV PCR Test. No cross-reactivity was observed against relevant non-target microorganisms. No interference was demonstrated in the presence of endogenous and exogenous interfering moieties as well as commensal organisms. Turnaround time for the complete test was ~60 minutes, with no user monitoring required once the samples and reagents were loaded. Agreement on clinical specimens was 96.4% (244/253; kappa value 0.93) compared to reference and relative clinical sensitivity and specificity for CIN2+ were both 98%.

Conclusions: The NeuMoDx HPV Assay as implemented on the NeuMoDx Molecular System is a rapid, easy to use, and effective test for detection of high-risk HPV with HPV16 and HPV18 genotype information from cervical scrapes.

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Impact of pretransplant norfloxacin prophylaxis on multidrug-resistant post–liver transplant infections


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Background: Bacterial infections are major causes of morbidity and mortality after liver transplantation (LT). We are currently facing a progressive increase in the rate of MDR microorganisms. Norfloxacin is widely used for the prophylaxis of spontaneous bacterial peritonitis. The effect of norfloxacin on post-LT MDR infections is unknown. The aim of our study was to determine the effect of norfloxacin prophylaxis on MDR infections within the first 30 days after LT.

Materials/methods: All adult patients who underwent LT at two institutions (Vall d’Hebron and Bellvitge University Hospitals, Barcelona, Spain) were included in this prospective cohort study from January 2015 to December 2016. Norfloxacin prophylaxis was considered if the recipient received it during the three months before transplantation. Infections were defined by the isolation of any bacterial microorganism with clinical signs of infection. Patients were stratified into 2 groups based on the presence or absence of MDR infection as defined by Magiorakos AP et al. Student t and chi-square tests and multivariate regression analysis were used to compare the 2 groups.

Results: We included 157 patients. 54 (34.6%) LT recipients were on norfloxacin before LT. The norfloxacin group had a higher median MELD score (20, IQR 14-24, vs 11, IQR 8-19; p<0.001). There were 17 infections due to MDR bacteria, mainly urinary tract infection (9/17, 52.9%). The most isolated MDR microorganism was ESBL Klebsiella pneumoniae (8/17, 47.1%). MDR infection was more frequent in the norfloxacin group (12/54, 22.2% vs 5/97, 4.9%, p=0.002). In the univariate analysis, MELD score (23 vs 13, p=0.001), administration of antibiotics other than norfloxacin prophylaxis (82.4% vs 31.4%, p<0.001) and renal replacement therapy (29.4% vs 5.7%, p=0.004) and ICU admission before LT (35.3% vs 8.6%, p=0.004) and norfloxacin prophylaxis (70.6% vs 30.2%, p=0.002) were associated with MDR infection. In the multivariate analysis, only the use of norfloxacin (OR 3.25; CI 1.02-11.63) and the administration of antibiotics within 3 months prior to LT (OR 5.54; CI 1.53-26.51) showed relationship with the appearance of MDR infection.

Conclusions: The use of norfloxacin as prophylaxis was associated with an increased risk of MDR bacterial infection in the early post-LT period.

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Molecular diversity of carbapenem-resistant Enterobacteriaceae (CRE) in Singapore

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Background: Active surveillance is a key strategy in our combat against CRE. In addition to classical surveillance based on phenotypic methods, whole genome sequencing (WGS) has allowed greater resolution in deciphering the CRE resistome. We described the molecular epidemiology of CRE in a large public healthcare institution across 10 years.

Materials/methods: 824 non-duplicate CRE isolated from inpatients admitted to a large tertiary Singapore hospital between 2008-2018 were sent for paired-end Illumina WGS. Antibiotic susceptibilities were determined using microbroth dilution. Multi-locus sequence typing (MLST) and antibiotic resistance genes analyses were performed. Cultures were classified as infection or colonisation based on the CDC surveillance definitions.

Results: 814 (99%) CRE were MDR. Resistance to last-line agents were detected [resistant rates: fosfomycin – 22%; polymyxin B – 14%; tigecycline – 9%]. Majority of the CRE harboured genes mediating resistance to multiple antibiotic classes. The prevalence of plasmid-mediated resistance genes was high [carbapenemases – 91%, aminoglycoside genes – 89%, fluoroquinolone genes – 73% and ESBLs – 63%]. The predominant carbapenemase genes were \( \text{bla}_{KPC} \) (50%) and \( \text{bla}_{NDM} \) (33%). There was a shift from \( \text{bla}_{NDM} \) to \( \text{bla}_{KPC} \) over the study period. Amongst ESBLs, CTXM-15 was frequently detected (56%). The phenotypic and genotypic susceptibility profiles of colonisers and infection-causing isolates were different. Infection-causing CRE had significantly higher amikacin, aztreonam, levofloxacin, and tigecycline resistance rates and higher proportions of \( \text{bla}_{OXA-48} \) and ESBLs, while \( \text{bla}_{NDM} \) was more common in colonisers. MLST revealed significant genetic diversity in the isolates, with multiple distinct STs and clonal complexes detected. Of note, ST14, the OXA-48 and NDM co-producing clone responsible for several outbreaks, was commonest amongst our \( K. \) pneumoniae (11%). ST131 occurred most frequently in \( E. \) coli (13%). Compared to the \( K. \) pneumoniae and \( E. \) coli, the dominant strain in \( E. \) cloacae (ST93) and \( C. \) freundii (ST22) appeared to be more genetically similar (Figure 1).

Conclusions: CRE in Singapore were MDR and genetically diverse. Resistance to last-line antibiotics has emerged. Genomic analyses suggest that the incidence of CRE was unlikely due to the expansion of single clones nor widespread outbreaks, although there were populations within \( E. \) cloacae and \( C. \) freundii which appeared genetically similar.
**Figure 1:** Distribution of commonly found antibiotic resistance genes in major CRE strains. KP – *K. pneumoniae*; EC – *E. coli*; ENT – *E. cloacae*; CF – *Citrobacter freundii* ST22.

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Abstract 5303

**European Centre for Disease Prevention and Control system for cluster detection and interactive exploration of WGS data**

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**Abstract third-party references:** ECDC

**Background:** ECDC has been collecting WGS data for outbreak investigations since 2015, and has launched continuous WGS surveillance for multi-country outbreak detection and trend monitoring for *Listeria monocytogenes* in 2019. The ECDC strategic framework for the integration of genomic typing into European surveillance and multi-country outbreak investigations foresees that several additional pathogens will be implemented in 2020, including Salmonella, Shiga-toxin producing *E.coli*, *Neisseria meningitidis*, and multidrug-resistant *Mycobacterium tuberculosis*.

**Materials/methods:** ECDC is building a database and web service with very fast WGS data upload, matching and phylogenetic tree building capabilities for large number of isolates. The system does not perform raw data processing steps such as assembly and allele calling; instead, it collects derived results from several sources and optimizes the data for fast exploration. ECDC is also developing a web page with an interactive user interface to allow nominated national public health reference laboratory users in the EU Member States to explore their data in context of other users' data and reference data from public sources such as NCBI and pubMLST. The fast matching uses pre-calculated clusters and a pre-calculated distance matrix based on cgMLST that is stored in a SQL database; the system performs matching and reconstructs the distance matrix using SQL stored procedures, achieving very high performance, enabling real time data exploration.

**Results:** Searching for matches within seven cgMLST allelic differences in a database containing ~20,000 isolates, constructing a phylogenetic tree for ~100 isolate hits and presenting the tree together with epidemiological data to the user in a web browser, as an annotated tree image, an epicurve, a line list and an interactive MicroReact dataset takes less than 2 seconds.

**Conclusions:** ECDC has developed a high-performance interactive WGS data exploration interface for nominated EU Member State users. This system will enable fast and user-friendly contextualization of national WGS data as multi-country outbreak detection and investigations.

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Performance of the new random access molecular diagnostics analyser Alinity m

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Background: Molecular diagnostics is an essential part of diagnosis and treatment monitoring in infectious disease. Short turn-around-times are a requirement for rapid initiation of treatment and fast identification of treatment failures. New molecular diagnostic platforms allow to perform multiple parallel tests like detection of HIV, Hepatitis C Virus (HCV), Hepatitis B Virus (HBV) without the restriction of batching samples. We compare the assay performance of the new Abbott Alinity m system with the Abbott m2000 and the Hologic Panther platform.

Materials/methods: We tested 1841 clinical samples on the Alinity m system and compared the results to either the m2000 or the Panther. 1089 samples were tested for HIV viral load, 307 for HBV viral load and 445 for HCV viral load. Regression and Bland-Altman analysis was performed for samples with quantitative results. Turn-around-times (TAT) were analysed as time difference between sample arrival in the laboratory and availability of results in the laboratory information system with the same samples tested in parallel.

Results: 198 samples showed quantitative results for HIV (HBV: 151, HCV: 225). Comparison between Alinity m and m2000 showed high coefficients of correlation (HIV: R²=0.96, HCV: R²=0.96, HBV: R²= 0.95) with similar results between Alinity m and Panther (HIV: R²=0.94, HCV: R²=0.99, HBV: R²= 0.90). TAT analysis showed in 1125 samples with one Alinity m 90% of results were available after 11:09 hours compared to 7:12 hours with three m2000. A second set of 1033 samples was compared between one Alinity m and two Panther showing 90% of results were available after 5:46 hours (Alinity m) and 5:13 hours (Panther).

Conclusions: Our analysis shows excellent performance of the Abbott Alinity m system compared to Abbott m2000 and Hologic Panther with high levels of correlation. The analysis of turn-around-time shows a relevant reduction of duration until results can reported to the clinicians compared to the m2000 system, while both random access systems with an optimized pre-analytic workflow showed similar turn-around-times. The Abbott Alinity m allows to run 20 different assays in parallel as compared to 4 on Panther. This increase in automation leads to faster reportable results with less hands-on-time.

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**Abstract 5311**

**Title:** Molecular epidemiology and genetic characteristics of New Delhi metallo-β-lactamase among Gram-negative bacteria in a tertiary care hospital of north India

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**Background:** Infections caused by Gram-negative bacteria harbouring NDM poses a serious challenge to clinicians and has become a major public health concern. Co-occurrence of multiple resistant genes with blaNDM further complicates the treatment regimen. Presence of blaNDM on transferable plasmids is responsible for its rapid and global dissemination. The present study evaluated the prevalence of blaNDM gene, types of blaNDM variants circulating, genetic location of blaNDM gene and whole genomic analysis of five *K. pneumoniae* harbouring blaNDM gene.

**Materials/methods:** A total of 2000 consecutive isolates of GNB recovered from different clinical specimens from patients admitted to SGPGIMS, Lucknow were included in the study. Susceptibility testing against carbapenems, cephalosporins, aminoglycosides, ciprofloxacin and colistin were performed. PCR was performed for detection of blaNDM and followed by sequencing of selected ninety isolates to determine blaNDM variants. Other resistance genes were also determined in ninety isolates. Conjugation studies and southern hybridisation was performed to determine transfer ability and their genetic location. Whole genome-sequencing of five blaNDM harbouring *K. pneumoniae* was done to understand the genomic dynamics.

**Results:** Out of 2000 isolates 813 (40.6%) isolates were found carbapenem (Imipenem/Meropenem/Doripenem/Ertapenem) resistant. Among 813 carbapenem resistant isolates, 334 (41.8%) were NDM positive by PCR. Sequencing of PCR products revealed the presence of four different variants of blaNDM-1 namely blaNDM-3, blaNDM-5, blaNDM-7, blaNDM-11. Among the ninety blaNDM harbouring GNB other resistance genes were also detected (75% blaIMP, 28.8% blaVIM, 44.4% blaOXA-48, 46.6% blaSHV, 74.4% blaCTX-M, 63.3% ampC, 30% armA, 42.2% Rmt B, and 9% RmtF). Successful conjugation assay proved the transfer ability of blaNDM genes in recipient *E. coli* J53 cells. Southern blot analysis showed that blaNDM genes were located on multiple plasmids of variable sizes. WGS analysis showed presence of genes responsible of resistance to diverse antibiotic groups. Multiple plasmids and virulence factors were also present in the blaNDM producers, and upstream and downstream element of blaNDM gene were also analysed.

**Conclusions:** NDM-positive strains are continuing to spread worldwide despite continuous efforts and remain a critical challenge for public health across the world. Targeted measures are needed to control the spread of blaNDM producers.

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Impact of alternative dosing infusions of ceftolozane-tazobactam monotherapy against extremely-resistant *Pseudomonas aeruginosa* sequence type 175 isolates with different susceptibility profile ranging from 2 to 16 mg/L in a hollow-fibre infection model

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**Background:** The optimization of antimicrobial pharmacokinetics/pharmacodynamics (PK/PD) in infections due to XDR *P. aeruginosa* is a constant concern in our environment. As ceftolozane/tazobactam (C/T) is a time-dependent antimicrobial, the use of prolonged infusion could improve the probability of achieving an optimal PK/PD target.

**Objectives:** To compare the alternatives of human-simulated dosing infusions of C/T monotherapy against ST175 *P. aeruginosa* isolates with different C/T MIC values in a hollow-fiber model.

**Materials/methods:** A hollow-fiber model was employed to compare human-simulated exposures of C/T alternatives dosing infusions against three XDR ST175 *P. aeruginosa* clinical isolates with MIC values ranging from 2 to 16 mg/L. C/T dosing regimen simulated was 2/1g every 8h as a 1h (intermittent), 4h (extended) and 24h (continuous) infusion. Bacterial suspension was cultured onto agar supplemented with C/T at 2-fold, 4-fold and 8-fold the baseline MIC to assess the effect of each regimen on at less-susceptible bacterial population. Pharmacokinetic samples were collected and analysed by HPLC.

**Results:** Regarding the susceptibility profiles and resistance mechanisms of the isolates studied, ST175 [10-023] was C/T-susceptible with a MIC of 2mg/L and showed resistance to all β-lactams except C/T caused by OprD inactivation and AmpC hyperproduction. ST175 [09-12] was resistant to C/T with a MIC of 8mg/L and it had a specific mutation in PBP3 associated with increased β-lactam resistance. ST175 [07-016] was C/T-resistant with a MIC of 16mg/L and produced a GES-5. Figure 1 shows the total CFU/mL for the different regimens of C/T in the PK/PD model. The scheme of C/T as a continuous infusion showed greater overall reduction in the bacterial burden against the three isolates, particularly those resistant to C/T. Resistant strains to C/T were not selected with any scheme during the experiment. The simulated drug exposures achieved in this model were considered satisfactory for all regimens.

**Conclusions:** Our study shows that a dosing regimen of 2g/1g of C/T every 8h in a 1h infusion, as currently recommended, did not provide adequate coverage to achieve a good target attainment against *P. aeruginosa* isolates with MICs>2 mg/L. A continuous infusion regimen for C/T should be considered as a useful strategy, especially against C/T-resistant *P. aeruginosa* isolates.
Figure 1. Total CFU/mL using C/T alternatives dosing infusions (1h, 4h and continuous infusion) against three XDR ST175 *P. aeruginosa* clinical isolates, ST175 (10-023), ST175 (09-12) and ST175 (07-016), with MIC values ranging from 2 to 16 mg/L in a hollow-fiber infection model.

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Predicted risk and observed occurrence of *Clostridioides difficile* infection in patients with community-acquired bacterial pneumonia treated with omadacycline or moxifloxacin

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**Background:** *Clostridioides difficile* infection (CDI) is the leading cause of healthcare-associated infections and is associated with an average economic burden of $42,000 per case. Use of antibiotics such as fluoroquinolones, cephalosporins, and clindamycin is associated with increased risk of CDI. In this analysis, we compared the risk and number of cases of CDI in patients with community-acquired bacterial pneumonia (CABP) treated with omadacycline or moxifloxacin in the phase 3 OPTIC trial, using the validated Davis scoring index.

**Materials/methods:** Patients were randomized 1:1 to received 100 mg intravenous (IV) omadacycline every 12 hours for two doses then every 24 hours (q24h) or 400 mg IV moxifloxacin q24h, with optional transition to oral after 3 days (omadacycline: 300 mg q24h; moxifloxacin: 400 mg q24h). Total treatment duration, 7–14 days. Risk of CDI (score: 0–10) was calculated per patient using the following factors: number of high-risk antibiotics received (1 point each, maximum 5 points); age (40–55 years: 1 point; >55 years: 2 points); Charlson Comorbidity Index (1 comorbidity: 1 point; >1 comorbidity: 2 points); receipt of proton-pump inhibitors (1 point). Distribution of CDI risk scores was assessed for each treatment group using logistic regression and observed CDI cases were compared using Fisher’s exact test.

**Results:** The omadacycline and moxifloxacin groups included 386 and 388 patients, respectively. Risk of CDI was balanced across the two treatment groups, with overlapping mean and variance distributions. Mean risk score was 4.02 (standard deviation, 1.35) in the omadacycline group and 4.12 (standard deviation, 1.45) in the moxifloxacin group. Risk was also balanced for individual CDI risk scores, with overlapping 95% confidence intervals between treatments (Figure). Observed occurrence of CDI was not balanced between treatment groups: eight cases of CDI were reported in the moxifloxacin group, versus no cases in the omadacycline group (p=0.0037).

**Conclusions:** Despite equal risk across the two treatments, no cases of CDI were seen with omadacycline treatment, whereas eight cases occurred in the moxifloxacin group. The results from this analysis may indicate a lower propensity to induce CDI with omadacycline compared with moxifloxacin treatment.

**Figure:** Predicted risk (95% confidence intervals) of *Clostridioides difficile* infection (CDI) by Davis risk index score for patients with community-acquired bacterial pneumonia, treated with omadacycline or moxifloxacin in the phase 3 OPTIC clinical study

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Antibiotic penetration and bioavailability of vancomycin alone and in combination with rifampin in Staphylococcus epidermidis biofilms

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Background: Despite frequent clinical use, a research gap exists regarding the efficacy and interplay of rifampin combination therapy for staphylococcal prosthetic joint infections (P JIs). Questions remain regarding the potential formation of a vancomycin-rifampin molecular complex that may hinder penetration through biofilm matrixes. Our lab’s previous time-kill results utilizing combination vancomycin + rifampin, identified persister cells after 48 hours of antibiotic pressure. Penetration and bioavailability of vancomycin alone, and with rifampin must be determined to elucidate interactions within biofilms.

Materials/methods: S. epidermidis isolate ATCC® 35984, a known biofilm forming bacteria, was grown on polyurethane coupons and stained with FilmTracer™ Sypro® biofilm matrix stain. Simulated humanized concentrations of BODIPY-vancomycin (BODIPY-van) [25 µg/mL] ± rifampin [1.4 µg/mL] were added to biofilm samples and observed over 60 minutes with confocal fluorescence microscopy. Drug diffusion rate was quantified as mean fluorescence intensity (FI) over time with color histograms. Separately, fluorescence recovery after photobleaching (FRAP) was performed at three depths within the biofilm to determine antibiotic bioavailability.

Results: Mean fluorescence intensity increased over 60 minutes in biofilm treated with BODIPY-van but decreased after 30 minutes in biofilm treated with BODIPY-van + rifampin [max FI: 16.25, 13.14 respectively] (figure 1). Generation of a FRAP curve revealed partial fluorescence recovery for BODIPY-van + rifampin at three depths within the biofilm; lower layer: 24%, middle layer: 32%, upper layer: 36%.

Conclusions: Antibiotic diffusion and bioavailability were reduced for BODIPY-van ± rifampin in S. epidermidis biofilms. The addition of rifampin did not improve vancomycin penetration. These data may explain the presence of persister cells identified in time-kill studies with vancomycin + rifampin, that were not observed with vancomycin alone. Further investigation into the molecular interactions with rifampin and other antibiotics, as well as the role of rifampin for biofilm associated P JIs is warranted.

Fig 1: Orthogonal images of S. epidermidis ATCC® 35984 biofilm treated with FilmTracer™ Sypro® biofilm matrix stain (red) at T1min and T60min after antibiotic administration. BODIPY-vancomycin (BODIPY-van) diffusion was incomplete after 60 min and did not reach the lowest layers of the biofilm as confirmed with color histogram. A) Biofilm treated with 25µg/mL BODIPY-van (green) + 1.4 µg/mL rifampin (rif). B) Biofilm treated with 25µg/mL BODIPY-van (green) alone.

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Usefulness of qPCR for the assessment of vectorial competence of wild caught sand flies species: preliminary results

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Background: Leishmaniases are vector-borne diseases caused by a protozoan parasite of Leishmania (L.) genus and transmitted to humans by the bite of infected female phlebotomine sand flies. In Tunisia, south Mediterranean basin, three pathogenic taxa were described: L. infantum, L. killicki and L. major. The parasite detection in infected sand flies is based especially on the molecular detection using conventional PCR. The aim of this study is to demonstrate the usefulness of qPCR for the assessment of vectorial competence of infected sand flies.

Materials/methods: Sand flies were collected using CDC traps, individual specimens were dissected the head and posterior third segments of the abdomen were served for morphological identification. The abdomen was used for DNA extraction and molecular analysis. Firstly parasite was detected using conventional PCR, then parasite loads were quantified using a qPCR of the kinetoplast minicircle primers JW11 [5'-CCTATTTTACACCAACCCCCAGT-3'] and JW12 [5'-GGGTAGGGGCGTTCTGCGAAA-3']. Parasite typing was performed with nested PCR of the ribosomal internal transcribed spacer 1.

Results: In total 1,029 females were screened for the presence of Leishmania DNA, giving a positive rate of 8.26%. The parasite load was quantified using qPCR in 17 infected sand flies. Among them, seven were engorged and ten were unfed. The highest parasite load was observed in unfed Phlebotomus (Ph.) perfiliewi infected with L. infantum [10,000 parasites] and the lowest one was observed with Ph. perfiliewi infected by L. infantum with 19.9 promastigotes/ reaction. The mean parasite burden in unfed sand flies was 1,174 promastigotes/ reaction, while in engorged females was 90 promastigotes/ reaction.

Conclusions: Our preliminary findings, showed that the high parasite loads are correlated with a persistent feeding pattern and lead to an increase in Leishmania transmission.

Real time PCR results

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Antimicrobial activity of plazomicin and old aminoglycosides against clinical isolates of Enterobacterales collected worldwide in 2018

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Background: Plazomicin is a new-generation aminoglycoside developed to overcome common aminoglycoside-resistance mechanisms and was approved by the United States Food and Drug Administration (US FDA) to treat complicated urinary tract infection (cUTI), including pyelonephritis. We evaluated the activity of plazomicin and comparator agents against Enterobacterales isolates collected worldwide in 2018.

Materials/methods: A total of 5,519 Enterobacterales isolates were consecutively collected from 92 medical centres located in Europe [38 centres in 18 countries], US [31 centres], Asia-Pacific region [APAC; 13 centres in 7 countries] and Latin America (LATAM; 10 centres in 6 countries), and tested for susceptibility by reference broth microdilution methods in a central monitoring laboratory (JMI Laboratories). MIC results for plazomicin and comparators were interpreted as per US FDA and EUCAST criteria, respectively. Isolates were mainly from cUTI (46.3%) bloodstream infections (BSI; 22.5%), and pneumonia (17.8%).

Results: Plazomicin (MIC₅₀/₉₀, 0.5/2 mg/L) was 4-fold more active than amikacin (MIC₅₀/₉₀, 2/4 mg/L), based on MIC₅₀ values. Plazomicin inhibited 95.0% of isolates at the US-FDA susceptible (S) breakpoint of ≤2 mg/L, whereas amikacin inhibited 95.6% of isolates at the current EUCAST susceptible breakpoint of ≤8 mg/L. Plazomicin activity was consistent across the geographic regions with susceptibility rates ranging from 92.9% in Europe to 96.5% in APAC (table). Moreover, plazomicin was 8- to 64-fold more active than amikacin against ESBL-phenotype, carbapenem-resistant (CRE), multidrug-resistant (MDR), and extensively-drug resistant (XDR) isolates, and retained activity against 83.4% of gentamicin-resistant isolates. CRE rates were highest in LATAM (6.5%) and Europe (6.3%), and lowest in the US (0.7%). The Enterobacterales species most susceptible to plazomicin were E. coli, E. cloacae, K. aerogenes, K. oxytoca, S. marcescens, C. freundii and C. koseri, with MIC₉₀ values of 0.5–1 mg/L and susceptibility of 98.3–100.0%. Plazomicin was also highly active against K. pneumoniae (n=1,819; MIC₉₀, 0.25/0.5 mg/L), with susceptibility ranging from 89.8% in Europe to 99.7% in the US (95.2% overall). Plazomicin activity was very consistent among isolates from cUTI (95.1%S), BSI (95.3%S), and pneumonia (94.3%S).

Conclusions: Plazomicin demonstrated potent activity against contemporary (2018) Enterobacterales isolates collected worldwide, including CRE, MDR, XDR, and gentamicin-resistant isolates.

<table>
<thead>
<tr>
<th>Region</th>
<th>Plazomicin</th>
<th>Amikacin</th>
<th>Gentamicin</th>
<th>Tobramycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (5,519)⁹</td>
<td>0.5/2 (95.0)</td>
<td>2/4 (95.6)</td>
<td>0.5/≤16 (83.9)</td>
<td>0.5/16 (79.6)</td>
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<td>Europe (1,940)</td>
<td>0.5/2 (92.9)</td>
<td>2/8 (93.4)</td>
<td>0.5/≤16 (82.3)</td>
<td>0.5/16 (77.0)</td>
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<td>United States (1,951)</td>
<td>0.5/2 (96.2)</td>
<td>2/4 (98.8)</td>
<td>0.5/≤16 (90.9)</td>
<td>0.5/4 (83.5)</td>
</tr>
<tr>
<td>Asia-Pacific (795)</td>
<td>0.5/1 (96.5)</td>
<td>2/8 (96.5)</td>
<td>0.5/≤16 (86.2)</td>
<td>1/16 (81.1)</td>
</tr>
<tr>
<td>Latin America (827)</td>
<td>0.5/1 (95.4)</td>
<td>2/8 (92.7)</td>
<td>1/≥16 (68.9)</td>
<td>1/16 (63.5)</td>
</tr>
<tr>
<td>ESBL-phenotype (1,233)⁹</td>
<td>0.5/2 (91.6)</td>
<td>4/&gt;32 (63.5)</td>
<td>2/&gt;16 (50.0)</td>
<td>8/16 (34.8)</td>
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<tr>
<td>CRE (227)⁹</td>
<td>0.25/&gt;128 (72.2)</td>
<td>16/&gt;32 (46.7)</td>
<td>&gt;16/&gt;16 (40.1)</td>
<td>&gt;16/&gt;16 (15.9)</td>
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<tr>
<td>MDR (1,010)⁹</td>
<td>0.5/8 (94.9)</td>
<td>4/&gt;32 (77.3)</td>
<td>&gt;16/&gt;16 (35.2)</td>
<td>&gt;16/&gt;16 (15.1)</td>
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<tr>
<td>XDR (246)⁹</td>
<td>0.5/&gt;128 (60.7)</td>
<td>16/&gt;32 (44.7)</td>
<td>&gt;16/&gt;16 (30.9)</td>
<td>&gt;16/&gt;16 (4.9)</td>
</tr>
</tbody>
</table>

* All regions combined

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Booster dose of trivalent inactivated influenza vaccine is superior to double- and standard-dose regimens in kidney transplant recipients: a randomised controlled parallel pilot study

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Background: Solid organ transplant recipients are at high risk for influenza-associated complications, but immune responses to routine standard-dose trivalent inactivated influenza vaccination (SDTIIV) are unsatisfactory, thus prompting further research on double- (DDTIIV) and booster- (BDTIIV) dose trivalent inactivated influenza vaccination regimens.

Materials/methods: We conducted a randomised controlled trial in stable kidney transplant recipients (KTRs) at the University of São Paulo Medical School. We enrolled and randomised 176 KTRs: 59 to SDTIIV, 59 to DDTIIV and 58 to BDTIIV. Fifteen health-care workers were enrolled as a standard-dose controls. Blood was drawn on D0 and D21 to determine pre- and post-vaccination antibody titres. The BDTIIV group was referred for second vaccination on D21 and returned on D42 for blood drawing. Immune responses were measured by seroconversion, seroprotection and geometric mean ratios. Statistical analyses were done by modified intention to treat (mITT) and per protocol (PP). Baseline characteristics, seroconversion and seroprotection rates were compared using Chi-square test. Continuous non-normal variables and geometric mean ratios were compared using Kruskal-Wallis. Age was analysed by analysis of variance. Multivariate analyses were done adjusting for vaccine dose and age.

Results: BDTIIV induced better immune responses in both mITT and PP analyses. In the PP analysis, seroconversion rates (A/H1N1 – 37.5% vs 9.1%, p=0.024; A/H3N2 – 43.8% vs 18.2%, p=0.052; Influenza B – 31.3% vs 25.0%, p=0.758) and geometric mean ratios (A/H1N1 – 2.4 vs 1.3, p=0.013; A/H3N2 – 3.1 vs 1.7, p=0.132; Influenza B – 2.4 vs 2.0, p=0.252) were higher after BDTIIV than SDTIIV, respectively. Additionally BDTIIV induced better seroprotection rates, with statistical significance for A/H3N2 (96.9% vs 70.5%, p=0.002), and was independently associated with seroconversion to A/H3N2 (PR=2.99, 95%CI=1.42-6.26, p=0.003). DDTIIV induced better responses than SDTIIV, albeit without statistical significance.

Conclusions: BDTIIV was superior to DDTIIV regimen. In our view, both regimens require head-to-head multicentre comparisons of their efficacy, while SDTIIV should be unutilized in immunosuppressed individuals due to lower immunogenicity.

Graph 1. Comparison of seroconversion rates per vaccine antigen by vaccination group (per protocol analysis)

Legend: BDTIIV – booster-dose trivalent inactivated influenza vaccination; DDTIIV – double-dose trivalent inactivated influenza vaccination; SDTIIV – standard-dose trivalent inactivated influenza vaccination; HC – healthy control who received SDTIIV

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Abstract 5328

**Microbial epidemiology of acute graft pyelonephritis**

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**Background:** Acute graft pyelonephritis (AGPN) is a very common infection in renal transplantation. However, there is no specific practice guideline for the management of urinary tract infections (UTI) in kidney transplant recipients. Third generation cephalosporin or fluoroquinolone are recommended for empirical antibiotic therapy of community-acquired pyelonephritis; fourth-generation cephalosporin or piperacilline-tazobactam are recommended for the empirical antibiotic therapy of healthcare associated UTI. We suspect a higher rate of resistance to those drugs in kidney transplant recipient than in general population.

The aim of this study was to described microbial epidemiology of AGPN in our center and thus assesses the applicability of French guidelines for management of UTI in a kidney-transplant recipient.

**Materials/methods:** We conducted a single-center retrospective observational study on a population of kidney transplant recipients who were diagnosed with AGPN between January 2017 and December 2018. We defined AGPN as the association of fever and/or urinary tract symptoms and significant leucocyturia and bacteriuria (according to French guidelines).

**Results:** We retrospectively identified 106 AGPN in which 110 bacteria were involved. The rates of community-acquired and healthcare associated AGPN were respectively 54.7% (n=58/106) and 45.3% (n=48/106). Enterobacteriaceae were the most frequent pathogen encountered representing 87.2% of bacteria involved (n=96/110). Among these, 27.1% (n=26/96) were resistant to third-generation cephalosporins. This resistance was due to extended spectrum beta lactamase (ESBL) in 84.6% (n=22/26) and cephalosporinase in 15.3% (n=4/26). Concerning fluoroquinolones, 42.7% (n=41/96) of Enterobacteriaceae were resistant to this class of antibiotic.

**Conclusions:** Due to high rates of resistance to third-generation cephalosporins and quinolones, French practice guidelines for empirical antibiotic therapy of acute pyelonephritis do not seem applicable to a kidney-transplanted population. We need to repeat this study on a larger and prospective scale. If these results are confirmed, we propose the systematic addition of aminoglycosides to third-generation cephalosporins for the empirical antibiotic therapy of AGPN.

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Piglets as a potential reservoir of atypical enteropathogenic *Escherichia coli* (aEPEC) with serotypes of human enterohaemorrhagic *Escherichia coli* (EHEC), including the O80:H2-A-ST301 (CH27-54) eae-ξ clone

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**Background:** For aEPEC, both animals and humans can be reservoirs and are known as pathogenic for children and pigs. The concept of interconversion between EHEC and aEPEC have been previously suggested. Thus, the aim of the present study was to define porcine aEPEC clones and its comparison with clinical human aEPEC.

**Materials/methods:** Ninety-two porcine aEPEC isolates were characterized with regard to their serotypes, phylogroups, clonal types (CH), sequence types (ST), verotoxins, intimin types, and pulsed field gel electrophoresis (PFGE). In addition, porcine aEPEC were compared with aEPEC isolated from human patients with diarrhea.


**Conclusions:** Our results show that piglets with diarrhea represent a significant reservoir of aEPEC potentially pathogenic for humans. Importantly, the recently described O80:H2-A-ST301 (CH27-54) eae-ξ clone was detected in nine (9.8%) isolates. This highly virulent clone has been associated with hemolytic uremic syndrome and hemorrhagic colitis.

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**Abstract 5335**

**Pathogenic determinants of the Mycobacterium kansasii complex: an unsuspected role for distributive conjugal transfer**

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**Background:** The former *Mycobacterium kansasii* species, comprising six major subtypes, was recently reclassified into six species-level lineages. Together with *Mycobacterium gastri*, they form the *M. kansasii* complex. *M. kansasii* (subtype 1) is the most frequent and most pathogenic species of the complex. *M. persicum* (subtype 2) is classically associated with diseases in immunosuppressed patients. The other species are mostly found as lung colonizers and only very rarely reported to cause disease. To unravel the genetic determinants contributing to their different pathogenicity, we performed a comparative genomics study of the *M. kansasii* complex.

**Materials/methods:** Genomes of 51 isolates collected from patients with and without disease were sequenced and compared with 24 additional publicly available genomes. The pathogenicity of each isolate was determined based on clinical records or public metadata. Comparisons of virulence factor homologs were performed using Orthofinder-defined groups loaded in a MySQL database. Genome-wide association study (GWAS) was done using matrices of presence/absence of single-copy homolog and of core genome SNPs. Distributive conjugal transfers (DCTs) were detected using sequence-identity approaches.

**Results:** *M. persicum* (subtype 2), *Candidatus M. fractum* (subtype 4), *M. innocens* (subtype 5) and *M. gastri* isolates lacked the ESX-1-associated EspACD locus that is thought to play a crucial role in the pathogenicity of *M. tuberculosis* and other non-tuberculous mycobacteria. Furthermore, *M. kansasii* was the only species exhibiting a 25Kb-large genomic island encoding for 17 type-VII secretion system-associated proteins. The GWAS revealed that two genes encoding a hemerythin-like and a nitroreductase-like proteins were significantly associated with pathogenicity. These genes may be involved in resistance to reactive oxygen and nitrogen species, an essential mechanism for intracellular survival of bacteria. Three non-pathogenic *M. kansasii* isolates lacked these genes likely due to two distinct DCTs between *M. attenuatum* (subtype 6) and *M. kansasii*, and one DCT between *M. persicum* and *M. kansasii*.

**Conclusions:** Large differences in virulence gene content were observed in the *M. kansasii* complex, all of which could contribute to the observed differences in pathogenicity. In addition, this study links for the first time DCT – a recently-described mycobacterial type of horizontal gene transfer – to bacterial virulence modulation.

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Abstract 5338

Carbapenemase-producing Enterobacterales among urinary isolates from community in Belgrade, Serbia

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Background: Urinary tract infections represent the main cause of antibiotics prescription and consumption in primary healthcare settings. Despite that, the data about acquired resistance among community bacterial isolates remains largely unknown. The aim of this study was to determine the prevalence and the types of carbapenemases among urinary isolates of Enterobacterales from community patients in Belgrade, Serbia.

Materials/methods: Study was conducted in 2016 and 2017 in two community-serving microbiology laboratories, which receive samples from primary care settings for the local population of around 1.6 million. Urinary tract isolates were identified by MALDI-TOF MS (VITEK MS, bioMerieux). Enterobacterales isolates were screened for carbapenemase production with meropenem 10 µg disk (BioRad, France), according to the EUCAST recommendations. For screening-positive isolates, multiplex PCR for bla_KPC, bla_NDM, bla_IMP, bla_OXA-48-like was performed. Susceptibility to colistin was determined with the broth microdilution method. The detection of mcr-1 to mcr-5 genes was done for the colistin resistant isolates.

Results: In total, 39117 Enterobacterales urinary isolates were screened for carbapenemase production. Screening was positive for 159 (0.41%) isolates, and the carbapenemase genes were confirmed in 131/159 (82.4%) isolates. The most common species was Klebsiella pneumoniae (105/131, 80.1%), with the most frequent carbapenemase genes bla_OXA-48-like (81.9%), bla_KPC (8.6%) and bla_NDM (7.6%), respectively. All 17 Enterobacter cloaceae/asburiae isolates were carbapenemase producers, with 70.6% harboring bla_NDM and bla_OXA-48-like genes. Four Providencia spp., 3 Escherichia coli and 2 Proteus mirabilis isolates were bla_NDM positive. Two isolates (Providencia stuartii and P. mirabilis) were positive for the bla_VIM carbapenemase gene. bla_OXA-48-like was not found. Resistance to colistin was detected in 17/131 (13%) strains of K. pneumoniae exclusively, but no mcr-1-5 genes were confirmed.

Conclusions: Previous researches in Serbia, all based in hospital settings, found bla_NDM as the most common carbapenemase in K. pneumoniae and E. coli. In our study, bla_OXA-48-like was the most frequent one among community Enterobacterales isolates. This may suggests the shift in carbapenemases types in Enterobacterales, as community patients could be reservoirs of carbapenemase-producing bacteria with the potential to spread to hospital settings.

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Co-production of KPC and SPM carbapenemases by *Pseudomonas aeruginosa* in same hospital in northern Brazil

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**Background:** *Pseudomonas aeruginosa* is one of the most common opportunistic pathogens associated with nosocomial respiratory infections. Its adaptation to the hospital environment coupled with the high level of intrinsic resistance and the ability to acquire additional resistance mechanisms make antimicrobial therapy challenging in hospitals around the world. Among these mechanisms, carbapenemases are particularly important because of the ease of intra and interspecies dissemination.

**Materials/methods:** The isolates are part of the collection of cultures of the Section of Bacteriology and Mycology of the Evandro Chagas Institute, received from hospitals in the northern region of Brazil, from January 2018 to May 2019, for epidemiological surveillance of bacterial isolates resistant to carbapenens. The detection of genes encoding carbapenemases was performed by PCR, where the presence of the genes blaKPC, blaNDM, blaOXA-48-LIKE, blaIMP, blaVIM and blaSPM were investigated.

**Results:** Of the total of 84 *P. aeruginosa* isolates, 10 (12%) were producers of SPM type carbapenemases. Among these, in five isolates of the same hospital, obtained from tracheal secretion and urine, the simultaneous presence of the blaKPC and blaSPM genes was observed. It is worth noting that the phenotypic test using EDTA and phenylboronic acid was negative in these isolates.

**Conclusions:** We report the presence of two different carbapenemases (KPC and SPM) in five clinical isolates of *P. aeruginosa*. The production of carbapenemases in *P. aeruginosa* is still relatively rare in the Northern region. However, these findings demonstrate the ability of this microorganism to act as reservoir and dispersion vector of resistance determinants. This coproduction points to a possible change in the genetic context that can confer a high level of resistance to carbapenems, and it is necessary to evaluate their impact on patients’ morbidity and mortality. We also emphasize the importance of monitoring these pathogens as a strategy to minimize the circulation and dissemination of these resistance mechanisms in hospitals.

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Abstract 5340

TLR4-independent effects of LPS identified using longitudinal serum proteomics
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Background: Sepsis remains one of the most lethal and costly conditions treated in hospitals worldwide, with about 50% of reported cases caused by Gram-negative bacterial infections. Gram-negative septic shock is largely induced by signaling of LPS, a main component of the outer bacterial membrane, through the innate immune receptor toll-like receptor 4 (TLR4). We used label-free quantitative [LFQ] proteomics to analyze changes in serum proteomes of mice that were either susceptible or resistant to LPS induced endotoxemia.

Materials/methods: WT and TLR4-/- C57BL/6 mice were injected with a lethal dose of Escherichia coli LPS (30 mg/kg) or PBS and serum collected every 6 hours post injection (n=3 per group). Tryptic digestion of 2 µL serum from each sample was subjected to LC-MS/MS followed by MaxQuant analysis. Data were analyzed longitudinally with global ANOVA and Ingenuity Pathway Analysis [IPA].

Results: PBS treated WT mice and LPS treated TLR4-/- mice showed no clinical signs of septicemia, while WT LPS treated mice showed symptomatic and molecular phenotype over 24 hours. Longitudinal serum proteome analysis [baseline = 0h] identified 182 out of 324 proteins in LPS injected WT mice were significantly changed across four time points (0, 6, 12 and 18h). From these 182 proteins, known sepsis biomarkers were validated by ELISA and showed similar trends to the LC-MS/MS data. No significant changes were identified in the two control groups. A global analysis found 69 significantly changed proteins unique to the WT injected LPS group, and 51 significantly changed proteins common among the WT and TLR4-/- LPS injected groups.

Conclusions: These studies validate proteomics and data analyses approaches for use in longitudinal studies and support the use of longitudinal comparisons for complex animal models of disease rather than traditional pair-wise comparisons. The global analysis of WT and TLR4-/- mice identified pathways activated independent of TLR4 which represent possible compensatory mechanisms that allow for control of Gram-negative bacterial infection regardless of host immune status.

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Abstract 5341

**Population structure dynamics of *Escherichia coli* ST131 over time**

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**Background:** *Escherichia coli* ST131 is one of the most successful global antimicrobial drug resistant (AMR) clones among human isolates. Limited information is available regarding the population structure dynamics of ST131 over extended time periods. A study was designed to characterize ST131 responsible for blood stream infections over an 11 year period in a large well-defined Canadian geographical region.

**Materials/methods:** All *E. coli* from blood (n=1784) obtained in the Calgary region during 2006, 2012 and 2016 were screened with a ST131 PCR. Isolates positive for ST131 (n=344) underwent Illumina whole genome sequencing.

**Results:** Overall 19% of *E. coli* were PCR positive for ST131; the prevalence of ST131 increased from 11% in 2006 to 24% in 2012 and 21% in 2016. The majority of ST131 belonged to clade C (81%) followed by clades A (10%) and B (9%). Clade C (n=278) belonged to subclades C1-nonM27 (44%), C1-M27 (6%) and C2 (50%). ST131 clades were associated with different *fimH* alleles (e.g. A with *fimH*41, C with *fimH*30), IncF replicons (e.g. A with IncFII; B with IncFIB; C with IncFIA) and AMR determinants (e.g. A with *aph(3")*-Ib; B with *aadA*2; C1-nonM27 with *aph(3")*-Ia; C1-M27 with *bla* _CTX-M-27_ and *aph(3")*-Ib; C2 with *bla* _CTX-M-15_ and *aac(6")*-Ib-cr). The frequencies of clades A, C1-M27 and C2 increased while clades B and C1-nonM27 decreased over time. C1-nonM27 was the dominant subclade in 2006 while C2 with *bla* _CTX-M-15_ and C1-M27 with *bla* _CTX-M-27_ were responsible for the increase of ST131 among *E. coli* during 2012 and 2016.

**Conclusions:** This study demonstrates that the population structure of ST131 in a large Canadian geographic health care region is dynamic with the continuous interplay and emergence of different clades and subclades with various AMR determinates over time.

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The diagnostic impact of adding a molecular-based algorithm to routine mycobacterial testing for non-respiratory samples at a reference Saudi Arabian laboratory

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Abstract third-party references: Mycobacteriology Reference Laboratory in Riyadh, Diagnostic Microbiology, Riyadh Regional Laboratory & Blood Bank

Background: Extrapulmonary tuberculosis poses microbiological challenges due to the paucibacillary nature of the disease leading to low diagnostic yields. Here we sought to evaluate the impact of adding a rapid molecular diagnostic tool to the routine testing algorithm for extrapulmonary mycobacterial infections at a reference laboratory setting in a country with an intermediate prevalence of the disease.

Materials/methods: This cross-sectional study was conducted at the Mycobacteriology Reference Laboratory in Riyadh, Saudi Arabia. All non-respiratory specimens routinely received between 2012-2019 from patients suspected of having tuberculosis were included. Specimens were subjected to smear microscopy, liquid MGIT culture and susceptibility testing, direct Xpert MTB/RIF (Xpert) assay. The diagnostic accuracy of Xpert was calculated along with the incremental yield compared to microscopy.

Results: Among 2985 non-respiratory specimens investigated, 255 turned to be culture positive (38 tissue biopsies, 90 pus from lymph nodes, 15 gastric aspirate, 9 urine, 77 pleural, 11 cerebrospinal and 15 other body fluids). The pooled sensitivity and specificity of Xpert were 69.4% (95% CI 57.9-88.9%) and 100% (95% CI 98-100%) respectively when compared to the culture. The highest sensitivity was documented for pus (94%; 95% CI 86.5-97.3%) and urine specimens (88.9%; 95% CI 75-93.4%) with an incremental yield of 78.9 and 88.9% compared to microscopy. Moderate sensitivity for cerebrospinal fluid (81.9%; 95% CI 58.7-89.2%) pleural fluid (68.8%; 95% CI 47-77.9%) and tissues (57.9%; 95% CI 36.8-65.4%), with an incremental yield of 63.6, 41.1 and 47.4%, while the sensitivity was lowest for other body fluids (40%; 95% CI 0-57%). The rate of isoniazid monoresistance, multidrug resistance and polydrug resistance were 11, 5.8 and 3.2% respectively. Xpert detected rifampicin resistance in all but one patient and gave 1 false positive result showing an overall agreement of 77.7% (95% CI 68.5-83.7%) with phenotypic susceptibility testing.

Conclusions: Xpert can be an initial diagnostic tool for testing suspected cases of renal TB and tuberculous lymphadenitis. The added value to diagnose other forms of TB needs to consider the inferior sensitivity. Future evaluation of molecular assays needs to compare them to a composite reference standard considering the clinical and laboratory limitations.
A prediction model for identification of patients at high risk for Staphylococcus aureus intensive care unit pneumonia and implications for trial design

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Abstract third-party references: This research project receives support from the Innovative Medicines Initiative Joint Undertaking under grant agreement n° 115523, 115620, 115737 resources of which are composed of financial contribution from the European Union Seventh Framework Programme (FP7/2007-2013) and EFPIA companies in kind contribution.

Background: Staphylococcus aureus (SA) is an important cause of pneumonia acquired in the intensive care unit (ICU). Identifying patients at high risk of developing SA ICU-acquired pneumonia (SAIP) is essential for targeting preventive strategies and enhancing the efficiency of clinical trials. The aim of this study was to derive a prognostic prediction model to quantify the risk of acquiring SAIP by using a composite score of independent risk factors and assess its implications to trial design.

Materials/methods: We used data from ASPIRE-ICU, a prospective observational cohort study conducted at 30 European ICUs enrolling SA colonized and non-colonized subjects in a 1:1 ratio. SAIP development was assessed daily and was defined as pneumonia occurring >48 hours after ICU admission with SA was cultured from the lower respiratory tract or blood. A logistic regression model for SAIP was fitted using information available at ICU admission. Pre-defined predictors were selected based on the Akaike’s Information Criterion. Predictive performance, discrimination and calibration of the final model were assessed. Internal validation was performed using bootstrapping.

Results: Of 1,929 patients analyzed, 131 (6.8%) developed SAIP. The final logistic regression model included the following predictors: SA colonization status [OR: 3.20, 95%CI: 2.15-4.91, p<0.01], neurotrauma, defined as patients admitted with trauma and a Glasgow Coma Scale <8, [OR: 1.67, 95%CI: 1.02-2.66, p=0.04], and antibiotic use in the two weeks preceding ICU admission [OR:0.55, 95%CI: 0.31-0.90, p=0.03]. The area under the receiver operating characteristic curve was 0.73 (95%CI: 0.67-0.79) and decreased to 0.71 after internal validation. Model calibration was moderate [Brier score 0.063]. The model demonstrated that 9 subjects are needed to identify one SAIP case when using SA colonization at admission and/or neurotrauma (SAIP risk: 10.9%) as inclusion criteria, compared to 19 subjects needed to identify one SAIP when enrolling from the overall ICU population [SAIP risk of 5.3%].

Conclusions: S. aureus colonization status at ICU admission, neurotrauma, and antibiotic use in the two weeks preceding ICU admission performed moderately in predicting the risk of developing S. aureus pneumonia during ICU stay. Colonization status would be the most relevant predictor in terms of trial design and execution efficiency.

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**Abstract 5345**

**Standardisation and validation of the PCR technique for detection of ST16-KL51 serotype among Klebsiella pneumoniae isolates**

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**Background:** Recently, bloodstream infections caused by KPC-2-producing KPN Sequence type (ST) 16 were associated with high mortality rates. Interestingly, all ST16 KPN belonged to capsular serotype KL51. MLST have been considered an important methodology to characterize bacterial isolates because sequence data are unambiguous, and the allelic profiles of isolates can easily be compared to those in a large central database. However, it requires 7 PCR and 14 DNA sequencing reactions. We aim to develop a single PCR reaction to easily identify ST16-KL51 in KPN clinical isolates.

**Materials/methods:** For selection of PCR targets, genomes of KP-ST16 available on GenBank, were aligned by Genious Prime to identify a single locus just present in this background. Thus, an inner portion of hpKL51 capsule was selected. The following primers were used for PCR assay: 1. hpKL51internalF: 5’-AGCATCTCTGGCCAACGATAA-3’, 2. hpKL51internalR: 5’-CTGTCTTACCTGGCGTACCT-3’ (product size, 500pb). The study included 132 KPN isolates either characterized by MLST or WGS. The PCR reaction contained: 5ul de Top Taq® Master Mix Kit, Qiagen, 3ul of water, 1ul of loading and 0.25 ul of the primers (0.2 uM/L). To evaluate PCR accuracy, data were submitted to the MedCalcv19.1 statistical test to construct the ROC curve. The higher the AUC value (over 0.9), closer the curve approaches upper left corner, indicated higher sensitivity and lower proportion of false positives.

**Results:** Genomic analysis revealed that, in our collection only the ST-16-KPN (all associated to human infections) and ST231 (animal infections) have the K51 capsule, and consequently the pkL51 gene. PCR was highly discriminatory being positive with all KP-ST16 isolates (n=21/21) and KP-ST231 (n=1/1). The other 110 isolates that presented negative PCR belonged to other STs as following: ST11 (n=34), ST258 (n=44), ST437 (n=14), ST15 (n=8), ST101 (n=5), ST307 (n=2), ST29 (n=1), ST20 (n=1) and non-typed ST (n=1). The ROC curve showed AUC value of 0.995 and p<0.001, presenting 100% of sensitivity and 99.1 of specificity to detect the ST16.

**Conclusions:** This PCR showed excellent discriminatory power to identify ST16-KL51 in KP clinical isolates, since ST231 is not frequent in human specimens and could constitute an alternative option to MLST.

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Frequency and impact of differences across Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) and Cockcroft-Gault (C/G) estimations of glomerular filtration rate on antimicrobial dosing

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Background: Estimation of glomerular filtration rate (GFR) is the most commonly used patient-specific parameter to determine medication dosing. However, the EMA and FDA recommend different GFR estimation methods, CKD-EPI and C/G, respectively. Further, an electronic medical record (EMR) in the United States may provide both, potentially yielding differences across renal dosing thresholds leading to discordance in dosing selection. We sought to quantify the frequency of these discordant results, and further describe associations which may allow for greater opportunities for education and antimicrobial stewardship interventions.

Materials/methods: A one-month retrospective snapshot of select new intravenous antimicrobial starts were queried using decision support software (TheraDoc). Antimicrobials included were comprised of the greatest frequency of use by institution-specific days of therapy (DOT) along with novel agents including meropenem; ciprofloxacin; piperacillin-tazobactam; cefepime; ceftolozane-tazobactam; ceftazidime-avibactam; and meropenem-vaborbactam. Patient demographics, EMR provided CKD-EPI and C/G calculations, and infectious disease service consults were collected. Patients were excluded from analysis due to renal-replacement therapies, one-time orders, unstable renal function, and missing data. Duplicate patients were excluded unless different antibiotics were represented. Patient comparisons of GFR data across methods were performed and evaluated based on discordance with FDA approved renal dosing threshold recommendations and antimicrobial dosing regimens selected.

Results: Of the 622 patients initially identified, 388 remained after exclusion criteria applied. When evaluating for patient renal dosing threshold categorical discordance by comparing CKD-EPI with C/G lean body mass; C/G ideal body weight; and C/G actual body weight, results were 62 (15.9%), 28 (7.2%); and 43 (11%), respectively. Renal dosing threshold discordance between CKD-EPI and C/G lean body mass lead to dosing selections in 37 (59.7%) and 25 (40.3%) instances, respectively. GFR discordance by renal dosing thresholds were more likely to occur in females (p<0.00001) and older patients (p<0.00001).

Conclusions: The observed differences in dosing selection by GFR method is significant and may yield under- or over-dosing of renally eliminated antimicrobials with clinical outcome implications. Institutions should minimize the number of reported GFR methods in the EMR, and provide recommendations to clinicians regarding an endorsed GFR estimation approach. Antimicrobial stewardship programs are well positioned to incorporate GFR estimation as part of ongoing educational efforts.

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Successful introduction of a bundle of measures to reduce surgical site infection by *Staphylococcus aureus* in patients undergoing coronary artery bypass grafting

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**Background:** *Staphylococcus aureus* is the major cause of surgical site infection (SSI) after coronary artery bypass grafting (CABG) worldwide. We observed in our institution that *S. aureus* SSI rate increased in the last year, mainly in patients undergoing CABG.

**Materials/methods:** Quasi-experimental study conducted at a Brazilian public teaching and research hospital, reference in cardiovascular surgery, aiming the reduction of SSI by *S. aureus* in CABG. Intervention measures were carried out from January to October 2019, consisting in (1) bath on the day of surgery with chlorhexidine digluconate 2% wipes; (2) screening for *S. aureus* nasal carriage and use of nasal mupirocin ointment if positive test; (3) change in antimicrobial prophylaxis from vancomycin and ceftriaxone to vancomycin and cefuroxime. The definition of SSI was according to CDC criteria.

**Results:** There were 630 surgeries before and 513 after the intervention starts. In the pre-intervention period (12 months) the CABG SSI rate caused by *S. aureus* was 3.49% and in the intervention period (10 months) the rate was 0.97%, representing a 73% reduction (P = 0.006). We observed a reduction in superficial, deep incisional and organ / space SSI, but only superficial incisional reduction was significant [Table 1]. The positivity of *S. aureus* in nasal swab was 10.35% (47/454) and 90% was methicillin-susceptible. In 59 patients the screening for *S. aureus* carriage was not performed.

**Conclusions:** The implementation of a multifaceted perioperative surgical site infection prevention bundle was associated with a significant reduction in surgical site infection rate by *S. aureus* in patients undergoing CABG.

**Table 1** – Outcomes of patients undergoing CABG, before and after intervention

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-intervention [January to December/2018]</th>
<th>Intervention [January to October/2019]</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG surgeries</td>
<td>630</td>
<td>513</td>
<td>...</td>
</tr>
<tr>
<td>SSI by <em>S. aureus</em></td>
<td>22</td>
<td>5</td>
<td>0.006</td>
</tr>
<tr>
<td>MRSA</td>
<td>3</td>
<td>1</td>
<td>0.42</td>
</tr>
<tr>
<td>MSSA</td>
<td>19</td>
<td>4</td>
<td>0.009</td>
</tr>
<tr>
<td>Superficial incisional</td>
<td>7</td>
<td>0</td>
<td>0.017</td>
</tr>
<tr>
<td>Deep incisional</td>
<td>7</td>
<td>3</td>
<td>0.34</td>
</tr>
<tr>
<td>Organ/Space</td>
<td>8</td>
<td>2</td>
<td>0.115</td>
</tr>
<tr>
<td>Mean between surgery and SSI</td>
<td>24.9 days [median 24]</td>
<td>30 days [median 28]</td>
<td>...</td>
</tr>
</tbody>
</table>

MRSA: methicillin-resistant *S. aureus*; MSSA: methicillin-susceptible *S. aureus*, *chi-squared

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Abstract 5352

**Feasible approach to reduce antibiotic overuse in preterm neonates**

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**Background:** Empiric antibiotics in early onset sepsis (EOS) in neonates are used to improve outcome. They are generally started based on maternal risk factors and clinical presentation of the neonate shortly after birth. This leads to an overuse of antibiotics with well described adverse effects in this age group. The use of biomarkers to guide the initiation of antibiotics is controversial whereas their use to support treatment discontinuation after sepsis is ruled out is well described.

We use a combination of maternal risk factors, clinical presentation and biomarkers (WBC, I/T ratio, CrP and IL-6) to start empiric antibiotics in newborns. This study aims to evaluate this approach for preterm infants with premature rupture of membranes (PROM) who are at high risk for EOS.

**Materials/methods:** Retrospective chart review and analysis of clinical, epidemiological and microbiological data of all infants < 37 weeks gestation and rupture of membranes at least 1h prior to delivery at our institution between January 2015 and March 2019. Clinical sepsis (CS) was defined as antibiotic treatment of at least five days with sterile blood culture, blood culture positive sepsis (BCxS) as antibiotic treatment of at least five days and growth of any bacteria but coagulase negative staphylococci.

**Results:** 456 infants were identified using these criteria. 120 (26%) received empiric antibiotics whereas 336 (74%) did not. Of those receiving empiric antibiotics 13 (11%) had a BCxS, 46 (38%) a CS and in 61 (51%) sepsis was ruled out and antibiotics were stopped after 48-96h. All infants with BCxS were identified and treated within the first 24h of life using this approach and none of the 336 infants who were not started on empiric antibiotics needed antibiotic therapy within the first 5 days of life. Only 9 premature infants were treated with empiric antibiotics to treat one BCxS. There were no deaths, IVH > grade 1, NEC or BPD observed in the group that did not receive empiric antibiotics.

**Conclusions:** A combination of clinical presentation and biomarkers at birth can safely be used in a high risk population for EOS to reduce the overuse of antibiotics.

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**Abstract 5353**

**A systematic literature review of the efficacy and tolerability of polymyxins in resistant Gram-negative infections**

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**Background:** The development of antibiotic resistance in Gram-negative bacteria is a serious global problem. Resistance limits the number of antibiotics which can successfully treat bacterial infections; consequently, clinicians are increasingly reintroducing polymyxins into clinical practice despite evidence of toxicity. This review summarizes current published literature reporting the efficacy/tolerability of polymyxins in patients with carbapenem-, multidrug-, or extensively-drug resistant Gram-negative infections.

**Materials/methods:** Eligibility criteria were developed using the PICOS framework. Searches of MEDLINE®, MEDLINE® In-process, Embase®, and Cochrane were conducted in November 2018. Eligible studies reported efficacy and/or tolerability outcomes for patients with resistant infections who were treated with polymyxins. Data were descriptively summarized.

**Results:** 2,219 identified articles; 48 articles representing 46 unique studies met eligibility criteria (four randomized controlled trials [RCTs], 42 observational studies). All RCTs evaluated colistin; of the observational studies: colistin (n=35), polymyxin B (n=4), multiple polymyxins (n=3). Studies were heterogenous with respect to size, causative pathogens, and antibiotic susceptibility definition. One RCT reported infection-related mortality: 26.6% [monotherapy] vs. 21.2% [combination]. Three RCTs reported Day 28-30 all-cause mortality rates of 24%-45%; there were no significant differences by formulation or monotherapy/combination therapy. All-cause mortality reported in 12 observational studies ranged from 11%-83%. Clinical response rate in one RCT: 21% [monotherapy] vs. 27% [combination], 10 observational studies: 20%-87% (median: 53%), one of which showed significantly lower rates with low-dose vs. high-dose colistin; clinical cure rates in one RCT: 67% (aerosolized) vs. 72% [intravenous], 11 observational studies: 18%-82% (median: 55%); microbiological cure in two RCTs: 45%-69%, 15 observational studies: 32%-88% (median: 67%). Nephrotoxicity (per RIFLE criteria) was measured in three RCTs, ranging from 15%-48%; a similar range was seen in three observational studies [7%-51%]. Neurotoxicity was measured in 17 observational studies but was less common, with reported rates of 0%-15%.

**Conclusions:** Published literature demonstrates acceptable response rates but unacceptably high mortality rates. Clinically and economically impactful adverse events such as nephrotoxicity were also observed. Although a large degree of heterogeneity exists in the identified evidence base, available data suggest that polymyxins may be sub-optimal treatments for serious bacterial infections, with a need for alternative treatments with better efficacy and tolerability profiles.

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Abstract 5355

**Nocardia Infection over 10 years (2009-2019) in a Greek tertiary university hospital**

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**Background:** *Nocardia* spp. usually are Gram(+), slow-growing, opportunistic microorganisms, that cause rare and severe infections mainly in immunocompromised individuals.

**Materials/methods:** We analyzed the clinical and laboratory features in 56 patients affected by nocardiosis over 10 years (2009-2019) in the University Hospital of Athens "Attikon". We retrospectively reviewed the medical data of the patients with culture–proven *Nocardia* infection, including demographics, underlying diseases, antibiotic treatment and outcome. Species identification was performed by sequencing analysis of 16S rDNA (1500-bp) gene. Drug susceptibility testing was performed according to the CLSI recommendations and results were interpreted based on CLSI breakpoints [documents M24 and M62, 2018].

**Results:** We identified 56 patients (32 men, mean age 61.3 years), with clinical evidence of nocardiosis and one or more positive cultures from various specimens. Among these patients, 42 (75%) had a Physician’s high level of suspicion, 44 (78.6%) had an underlying immunosuppressive disease and 12 (21.4%) were immunocompetent. The most common underlying immunocompromising condition was hematological and solid tumor neoplasm (59%), followed by autoimmune diseases (18.1%). In this group, most of the *Nocardia* strains were isolated from the lungs (27/44) or from subcutaneous abscesses (17/44). In one patient, the same strain of *Nocardia* was isolated from bronchial and blood culture. In the group of immunocompetent, 9 patients had Chronic Obstructive Pulmonary Disease (COPD) with frequent pulmonary infections (8 patients and 1 from brain abscess). In the last 3 immunocompetent patients, *Nocardia* strains were isolated from subcutaneous tissue. *Nocardia* strains belonged to 9 species. *Nocardia cyriacigeorgica* was the most frequently isolated (35.7%), followed by *N. abscessus* (12.5%) and *N. farcinica* (10.7%). *Nocardia* strains were highly susceptible to trimethoprim-sulfamethoxazole, linezolid and amikacin [susceptibilities 94.6-100%] and highly resistant to ciprofloxacin [resistance 75%]. Treatment was based on susceptibility data (when available). Long–term prognosis was good, with a treatment success rate of 92.9%

**Conclusions:** Nocardiosis is a common opportunistic infection in patients with underlying immunosuppressive conditions or in patients with COPD and frequent pulmonary infections. In our study, trimethoprim-sulfamethoxazole remains effective in treating nocardial infections. High level of clinical suspicion, timely species identification and antimicrobial susceptibility tests may guide treatment.

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Epidemiology and antifungal susceptibility of *Rhodotorula* spp. in a tertiary care hospital

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**Background:** *Rhodotorula* spp. have been recognised as emerging yeast pathogens in humans in the last two decades. While no cases of *Rhodotorula* infection were reported in the medical literature before 1985, the number of infections increased after that time, most likely because of the increase of immunocompromised patients and wider use of intensive treatments. Our aim was to evaluate the epidemiology and the antifungal susceptibility of *Rhodotorula* infection in our hospital during 5-year period

**Materials/methods:** Clinical reports of patients with *Rhodotorula* infection attended at our institution from 2015 to 2019 were included in the study. *Rhodotorula* spp were identified by MALDI-TOF MS. In vitro activities of amphotericin B (AMB), fluconazole (FZ), itraconazole (IZ), voriconazole (VZ), posaconazole (PZ), isavuconazole (ISV), anidulafungin (AND), caspofungin (CAS), micafungin (MYC) and terbinafine (TB) were determined by the broth microdilution method following CLSI criteria.

**Results:** During the study period, 125 isolates of *Rhodotorula* spp (125 patients) were isolated, being the distribution each year as follows: 2015 (18), 2016 (25), 2017 (35), 2018 (22), 2019 (23). From 125 cases, 4 (3.2%) were invasive mycoses (3 fungemia and one peritonitis) from onco-haematological patients (two solid tumors and two leukemias). The remaining sites of isolation were: skin 62 (49.6%), nails 31 (24.8%), wounds/abscess 12 (9.6%), conjunctival 4 (3.2%), ear 4 (3.2%), genital 4 (3.2%), oropharyngeal 3 (2.4%), and respiratory tract 1 (0.8%).

Globally, the antifungal susceptibility (range/geometric mean µg/ml) of 45 available *Rhodotorula* isolates, were as follows: AMB (0.25-1/0.605), FZ (8-128/44.121), IZ (0.06-2/0.591), VZ (0.03-2/0.508), PZ (0.015-1/0.344), ISV (0.03-0.5/0.137), AND (4-8/6.755), CAS (4-32/12.208), MYC (8-128/62.927) and TRB (0.125-32/7.476).

**Conclusions:** Invasive mycoses due to *Rhodotorula* is a rare clinical entity, but it has to be kept in mind in onco-haematological patients, due to its multiresistance profile. Amphotericin B and isavuconazole showed to be the most active antifungal agents.

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Abstract 5360

**The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS): the results of antimicrobial prescribing in 33 hospitals in Guinea**

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**Background:** Since 2015, Guinea is participating in the Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (www.global-PPS.com). We aimed to evaluate the quantity and quality of antimicrobial prescriptions and resistance at 30 Hospitals in the Republic of Guinea

**Materials/methods:** A cross-sectional point prevalence survey (Global-PPS) was conducted in 2017 and 2018, including all adult and pediatric medical and surgical services in 33 different Guinea’s hospitals. Detailed data were collected for all patients receiving anti-infective agents present at 8.00 am on the day of the survey. Data included details on antimicrobial agents, reasons and indications for treatment as well as set of quality indicators. The information was extracted from the patient’s medical and nursing records. The missing data were supplemented by information obtained directly from the professionals in charge of the patients.

**Results:** Out of the 33 hospitals, 2834 patients were present in the facilities on the day of the PPS, of which 2107 (74%) were on at least one anti-infectious drug. Of the 3925 antimicrobial prescriptions, 80.6% (n = 3165) were systemic antibiotics, 16.7% were antiprotozoal. The most commonly prescribed antibiotics were ceftriaxone (n = 671) and metronidazole (n = 574). Community acquired infections were the main indication for the prescription of antibiotics (50%), followed by surgical prophylaxis (30.2%).

The medical prophylactic prescribing was (2.4%). Documentation of the reason for the prescription was written in 67.8% of the prescriptions, but a revision date was not documented.

Guidelines were missing in 33.2% of cases. If guidelines were existing, most antimicrobials were prescribed according to these (34.5%).

**Conclusions:** This study has shown high prevalence’s of antimicrobial use in hospitals in Guinea. We aim to draft a national policy against antimicrobial resistance and further develop a guide to the appropriate use of antibiotics in Guinea. As part of antimicrobial stewardship (AMS) programs, which will be crucial to develop, feedback of the Global-PPS results and education of the different hospitals will enhance creating global awareness amongst physicians and staff. We aim to repeat the Global-PPS after the initiation of these AMS programs.

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Abstract 5363

Prevalence of and risk factors for extended-spectrum beta-lactamase genes carriernship in a middle-aged and elderly population-based cohort

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Background: The increasing resistance to beta-lactam antibiotics is an alarming development worldwide. Especially the worldwide spread of CTX-M and other plasmid encoded β-lactamases such as TEM, SHV and CMY-variants contribute to the increasing resistance. The prevalence of these genes has been reported to vary between populations but only a few of these were studied in community-dwelling populations.

Materials/methods: We studied the prevalence of TEM, SHV, CTX-M and CMY genes in stool samples of middle-aged and elderly individuals of the Rotterdam Study, a population-based cohort. We isolated DNA from these samples, followed by RT-PCR using previously published primer and probe sequences. We calculated the prevalence of these genes in stool and studied the association with several potential risk factors, such as use of antimicrobial drugs, use of proton pump inhibitors, diet and factors describing the composition of the microbiota.

Results: From the studied targets, the gene with the highest prevalence was TEM (61.3%), followed by SHV (18.1%). The prevalence of the extended beta-lactamase genes CTX-M (5.3%) and CMY (3.5%) was relatively low. Use of proton pump inhibitors was associated with a higher prevalence of carriernship of TEM, SHV and CMY genes [TEM: OR 1.38; 95%CI 1.06-1.79; SHV: OR 1.93; 95%CI 1.44-2.57; CMY: OR 2.10; 95%CI 1.15-3.85]. There was an association between beta-lactamase resistant penicillin use and CMY carriernship, but no other associations between use of beta-lactam antibiotics and carriernship of these genes was found.

Conclusions: The prevalence of carriernship of TEM, was substantial, but the prevalence of carriernship of the extended-spectrum beta-lactamase genes CTX-M and CMY was low in this healthy population-based cohort. Interestingly, use of proton pump was associated with carriernship of three of these genes, whereas use of antimicrobial drugs showed little associations. Our approach is feasible in determining the prevalence of carriernship of known resistance genes and may be used to compare different populations. Further studies are needed to determine the role of the composition of the microbiota on the prevalence of resistance genes and to determine the linkage to specific micro-organisms.

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Antimicrobial drug resistance, molecular typing and whole genome sequencing of *Salmonella enterica* serovar Derby from human clinical samples and pork products

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**Background:** *Salmonella* Derby is among the 10 most prevalent serovars of *S. enterica* in Europe and is the predominant serovar in pigs. Accordingly, it can be transmitted to humans through the food chain by consumption of pork-derived products. In the present study *S.* Derby isolates recovered in Spain from humans and pork products were investigated using traditional techniques and whole genome sequencing (WGS).

**Materials/methods:** Fifty-five *S.* Derby isolates collected between 2006 and 2018 from human clinical samples (26) and pork products (29) in a Northern Spanish region were characterized regarding to antimicrobial resistance, detection of mobile genetic elements (integrons, transposons and plasmids), and pulsed-field gel electrophoresis (PFGE). Besides, four representative isolates (2 from each source) were sequenced with Illumina and their sequences analyzed using “on line” bioinformatic tools.

**Results:** Thirty-nine isolates (71%) were resistant to at least one antimicrobial and 22 (40%) were multidrug-resistant, sharing nearly all of them (20 isolates) resistance to streptomycin (*aadA*), sulphonamides (*sul1*) and tetracycline (*tet(A)*). The *aadA* and *sul1* genes were located in a class 1 integron and Tn1721 was detected in 15 *tet(A)*-positive isolates. In relation to other resistant genes, *tet(B)* was associated with Tn10 in three tetracycline-resistant isolates and *bla*TEM-1 was identified in five ampicillin resistant isolates, one of them positive for Tn3. The Asp87/Asn substitution in GyrA was detected in isolates resistant to nalidixic acid. The characterized isolates displayed a high diversity of plasmid and PFGE profiles, with each of the PFGE profiles being common to human and pork isolates. The four sequenced isolates belonged to ST40 and carried the *Salmonella* Pathogenicity Island SPI-23 (both features associated with pig origin), and presented the fosfomycin resistance gene *fosA7*. A high number of prophages and virulence genes implicated in fimbriae biosynthesis were also identified. ColE10 plasmids, carrying *tet(C)*, were detected in two isolates, and an IncI1 ST134 plasmid was present in a susceptible isolate.

**Conclusions:** Molecular typing and WGS support that the same *S.* Derby isolates are circulating in pork products and humans in our region, a fact that calls for control measures to prevent further dispersion of this serovar through the food chain.

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Abstract 5369

Characterisation of ceftobiprole’s cerebrospinal fluid penetration in patients with external ventricular drainage

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Background: Healthcare-associated meningitis (HAM) is associated with significant morbidity and mortality. HAM treatment is challenging because of antibiotics resistance and the difficulty to achieve a therapeutic dose of antibiotics in the CNS. Ceftobiprole is a novel broad-spectrum cephalosporin with excellent activity against multi-drug resistant (MDR) pathogens. Since ceftobiprole is bactericidal, well-tolerated and it has anti-biofilm activity, it could be useful in case of HAM. Nowadays there are no human studies concerning the penetration and the efficacy of ceftobiprole in the cerebrospinal fluid (CSF). The present study aims to fill these gaps in the literature.

Materials/methods: We enrolled 5 patients with and implanted EVD who received Ceftobiprole for other reasons than HAM, in a single-center pilot study. Exclusion criteria were: patients < 18, cephalosporine allergy, end-stage renal insufficiency, BMI >30, pregnancy and end-stage diseases. We have measured the ceftobiprole concentration in 8 blood samples and 11 CSF samples from each patient (95 samples in total), as described at www.coqualab.it. We calculate the maximum serum (Cmax-s) and CSF concentration (Cmax-csf) and the percentage of CSF penetration of ceftobiprole, after the third infusion of Ceftobiprole (500mg e.v. every 8hr).

Results: The mean Cmax-s was 12.02 mg/L, reached after 2hr from drug infusion, whereas the mean Cmax-csf was 0.6 mg/L. In Figure 1 the mean concentrations [and the relative standard deviations] of serum and CSF ceftobiprole concentration for each time point are represented. The mean Ceftobiprole CSF penetration was 15.3%.

Conclusions: For the first time we studied the CSF ceftobiprole’s penetration in humans, founding a mean value of 15.3%. Although we cannot conclude anything about the Ceftobiprole CSF efficacy, its meningeal penetration is in line with other cephalosporines and it is higher than Vancomycin, posing the base for a possible role of Ceftobiprole in HAM treatment.

![Figure 1: Mean serum and CSF ceftobiprole concentration in the five patients studied, with the relative standard deviation. It is possible to note either the lower CSF concentration (15.3%) and the lower variability of CSF concentration. To: steady-state, before ceftobiprole administration, at the third dose; T1-T10 are respectively at 2-2.5-3-4-4.5-5-6-8-10-12 hours after ceftobiprole administration.](image)

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Abstract 5374

**Insights in the resistome of multidrug-resistant *Pseudomonas aeruginosa* strains isolated in Romania from nosocomial infections and wastewater**


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**Background:** Hospitals generate an impressive amount of wastewater per day, the hospital effluents being loaded with pathogenic microorganisms, antibiotics and pharmaceutical or toxic substances, which are partially removed during wastewater treatments, contributing to the pollution of the natural environments, including selection and dissemination of antibiotic resistance (AR). We aimed to examine the antibiotic resistant genes (ARGs) in multidrug resistant *Pseudomonas aeruginosa* (MDR *Pa*) strains isolated in the same temporal sequence from hospital infections (HI) and hospital sewages (HS) from Bucharest, the capital city of Romania.

**Materials/methods:** *Pa* strains were isolated in the same temporal sequence, plated on carbapenem and third generation cephalosporin supplemented culture media were identified using automatic and genetic methods and their resistance profiles (RPs) were investigated by disc-diffusion, automatic, and chromogenic methods. Selected strains were subjected to whole genome sequencing (WGS) (Illumina MiSeq pair end sequencing). For bioinformatic analyses SpaDES, ResFinder MLST and CARD Database were used.

**Results:** Following the RP results, a total of 30 MDR *Pa* strains were isolated and screened for the presence of ARGs. WGS revealed that one HI *Pa*, two Pa from the effluent (EF) and one from influent (IN) of the HS were assigned to ST 357 clone harboring *bla*IMP-13, *bla* OXA-10, *bla* VEB-9, and additionally the aminoglycoside ARGs aac(6’)-I1, aadA1 and ant(3’)-Ia, tetracycline resistance tet[A], ciprofloxacin resistance crpP1, qacEdelta1 (efflux), trimethoprim resistance drfB2 and sulphonamide resistance sul1. Another two Pa ST 357 from HS EF were positive for a different ESBL gene, i.e. *bla* VEB-1. Pa assigned to ST 62 isolated from HS IN harbored *bla* IMP-13, *bla*OXA-494, *bla* PDC-55, and additionally, sul1 and fosA. Three HI Pa strains were assigned to the high-risk sequence type ST 233, harboring *bla* VIM-2, *bla*GES-1 (n=2)/*bla* VEB-9 (n=1) (additional ARGs: crpP-1, tetG, sul1, cmlA6, drfB5, drfA6, qnrVC1, aph(3’)-Iib, aadA2 and ant(3’)-Ia) and one HI Pa to the ST 395 clone (*bla* OXA-488, *bla* PDC-113, aph(3’)-Iib and fosA).

**Conclusions:** We report here the first comparative description of the genetic background of AR in MDR *Pa* high risk clones circulating between the hospital wastewater and the hospital environment in Bucharest, Romania.


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Abstract 5376

**Endemic extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* ST48 in a hospital setting and genomic plasticity driven by transposable elements**

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**Background:** Multidrug resistant (MDR) *Klebsiella pneumoniae* (*Kp*) are leading causes of severe hospital-acquired infections. Here, we report an endemic MDR *Kp*-ST48-clone with multiple chromosomally integrated copies of *blaCTX-M-15* (*Chr-blaCTX-M-15*) from a tertiary hospital in Berlin, Germany.

**Materials/methods:** From 2014-2016, we conducted a retrospective study in 8 wards of the hospital within a larger European study involving 4 countries. Rectal swabs were collected from patients at admission, weekly during hospitalization, and at discharge. Extended-spectrum beta-lactamase-producing *Kp* (*ESBL-Kp*) was isolated (CHROMID ESBL, BioMérieux, France) and identified (MALDI-TOF). Antimicrobial susceptibility to 15 antibiotics was determined by disk diffusion (Rosco, Denmark), E-test (BioMérieux, France), and CarbaNP using EUCAST-2019 breakpoints. During the study period, 49 ESBL- *Kp* were isolated from 46 patients across the 8 wards. Short- and long-read sequencing was performed on these ESBL- *Kp* using MiSeq (Illumina Inc., USA) and PacBio Sequel II (Pacific Biosciences, USA), respectively. Subsequent analyses were performed using an in-house bioinformatics pipeline (Bacpipe v.1.2.6), and ISFinder. Phylogenetic analysis was performed on core-genome SNPs using ME-GA-X and pairwise SNP distances were calculated using CLC Genomics Workbench v.9.5.1 (Qiagen, Germany). The presence of *Chr-blaCTX-M-15* genes was validated by long-range PCR using in-house designed primers.

**Results:** A total of 14 ESBL- *Kp* belonging to ST48 were isolated from 14 patients residing in 2 wards. All these strains were MDR defined by ECDC as non-susceptibility to at least 1 agent in ≥3 antimicrobial categories (Figure A). The first and the last ESBL- *Kp*-ST48 strains were isolated 535 days apart with only 16 SNP differences, suggesting the circulation of a single endemic clone in these wards. Core-genome SNP analysis revealed three clusters with a maximum of 20 intra-cluster SNP differences. A total of 7 regions of plasticity (RGPs) were identified (Figure B). Two to five copies of *Chr-ISEcp1-blaCTX-M-15* were found in these RGPs. Amongst the 14 clonal strains, one (P125A, Figure-A) was resistant to ertapenem and was isolated from a patient who received meropenem therapy. Resistance was due to IS1R-mediated *ompK36*-gene-inactivation.

**Conclusions:** Our results highlight the remarkable genomic plasticity, evidenced by multiple IS element integrations, and the persistent circulation of the ESBL-*Kp*-ST48 clone in a hospital setting.
Figure. (A) Phylogenetic tree constructed by Maximum Likelihood method based on 2142 core genome SNPs between 14 studied ESBL Kp ST48 strains and three publicly available reference strains (ERR025104, ERR025108 and ERR1740561), only bootstrap values >70% were shown. Strain clusters were defined as strains with ≤21 core-gene SNP differences. The presence and absence of the region of plasmidic (RGP), with 5 RGP contained blaCTX-M-15 (RGP1, RGP2, RGP4, RGP5, RGP6), are depicted by green and red cells, respectively. Antimicrobial susceptibility of studied strains were interpreted according to EUCAST-2019 breakpoints, susceptibilities indicated by light-green cells and resistances indicated by light-red cells. AM: Amoxicillin, XL: Amoxicillin-climoxil, CT: Cefotaxime, XM: Cefuroxime, TZ: Trimethoprim/Sulfamethoxazole, CL: Chloramphenicol, CI: Ciprofloxacín, NX: Norfloxacin, GM: Gentamicin, FM: Fosfomycin, MP: Meropenem, ETP: Ertapenem, IP: Imipenem, TC: Tetracycline (B) Seven RGP contained resistance genes (red) and mobile genetic elements (green); chromosomal genes are represented in blue.

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Abstract 5378


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**Abstract third-party references:** Supported by Hospital Clinic, IDIBAPS

**Background:** Epidemiological changes in infective endocarditis (IE) have been described in the 21st century. There is an increase in complexity, nosocomial or healthcare-associated acquisition and more involvement of vascular prostheses and cardiovascular implantable electronic devices (CIED). We aimed to describe the epidemiological and clinical changes and outcomes of CIED-IE in a reference center during the last 40 years.

**Materials/methods:** Retrospective analysis of prospectively collected CIED-IE cases from 1979 to 2018. Only definite CIED-IE cases were included (Duke criteria). Clinical and microbiological characteristics and outcomes (mortality, surgery) were analyzed comparing the period of diagnosis (1979-1999 vs. 2000-2018) and whether or not the patients had the device removed.

**Results:** Of 1,605 IE cases, 147 (9%) were CIED-IE. 21 episodes [3%] in 1979-1999 and 126 [13%] in 2000-2018 [p <0.001]. The distribution between pacemakers, defibrillators and cardiac resynchronization therapy was 75%, 24% and 1%, respectively. In the recent period, there were significantly more transfers, nosocomial infections, and fewer lead-vegetations. Staphylococci were the most frequent causative microorganism in both periods, but in the latter, there was a greater proportion of Streptococcus, Enterococcus, non-HACEK gram-negative bacilli and negative culture. CIED was removed in most patients [90.5% first period and 84.1% second]. There were no differences in-hospital mortality and one-year follow up between both periods but the recurrence rate was higher in the second period. Patients without device removal were significantly older [76 vs. 66 years, p <0.01] and had more recurrences [16% vs. 2%, p = 0.12]. The extraction of CIED was the only factor associated with a higher hospital mortality [10% vs. 44%, p <0.01] and at one year follow up [16% vs. 59%, p <0.01].

**Conclusions:** There were important epidemiological and clinical changes in CIED-IE in the last 40 years. In the last two decades there was an increase of lead-associated IE in patients with defibrillators and cardiac resynchronization therapy and an important proportion of cases were health-care related. Staphylococci was the most common etiological agents in both periods. Overall mortality was 14% and CIED extraction reduced relapses and was the only variable associated with survival.

**Table 1.** Comparison of CIED-IE cases by period and by surgical treatment (removal or non-removal)

<table>
<thead>
<tr>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>64 (66%)</td>
<td>69 (64%)</td>
<td>0.192</td>
<td>76 (59%)</td>
<td>66 (52%)</td>
<td>&lt;0.01</td>
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<tr>
<td>Male gender</td>
<td>76 (73%)</td>
<td>60 (59%)</td>
<td>0.73</td>
<td>45 (38%)</td>
<td>60 (52%)</td>
<td>0.65</td>
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<tr>
<td>Community acquired</td>
<td>67 (68%)</td>
<td>67 (64%)</td>
<td>0.22</td>
<td>36 (29%)</td>
<td>71 (61%)</td>
<td>0.44</td>
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<tr>
<td>Nosocomial acquired</td>
<td>22 (21%)</td>
<td>20 (18%)</td>
<td>0.04</td>
<td>4 (3%)</td>
<td>24 (21%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Health-care acquired</td>
<td>19 (19%)</td>
<td>15 (15%)</td>
<td>0.67</td>
<td>4 (3%)</td>
<td>19 (17%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Microorganisms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CoNS</td>
<td>11 (22.8%)</td>
<td>12 (23.1%)</td>
<td>0.14</td>
<td>4 (18%)</td>
<td>50 (44%)</td>
<td>0.07</td>
</tr>
<tr>
<td>SS</td>
<td>9 (23.8%)</td>
<td>8 (23.8%)</td>
<td>0.70</td>
<td>11 (22.3%)</td>
<td>32 (29%)</td>
<td>0.17</td>
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<tr>
<td>Enterococci</td>
<td>0 (2.5%)</td>
<td>4 (7.8%)</td>
<td>0.04</td>
<td>1 (2.9%)</td>
<td>6 (5.3%)</td>
<td>0.59</td>
</tr>
<tr>
<td>Enterococcus faecalis</td>
<td>0 (0%)</td>
<td>6 (11%)</td>
<td>0.01</td>
<td>2 (8.2%)</td>
<td>4 (3.5%)</td>
<td>0.71</td>
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<tr>
<td>non-HACEK gram-negative bacilli</td>
<td>2 (9.5%)</td>
<td>7 (14.3%)</td>
<td>0.04</td>
<td>9 (8.2%)</td>
<td>4 (3.5%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Negative culture</td>
<td>0 (0.0%)</td>
<td>1 (0.9%)</td>
<td>&lt;0.01</td>
<td>2 (1.9%)</td>
<td>11 (0.9%)</td>
<td>0.62</td>
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<tr>
<td>Outcome</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>19 (90.9%)</td>
<td>109 (84.8%)</td>
<td>0.36</td>
<td>0 (0%)</td>
<td>125 (100%)</td>
<td>NA</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>4 (20%)</td>
<td>18 (15.9%)</td>
<td>0.54</td>
<td>8 (32%)</td>
<td>44 (37.5%)</td>
<td>0.01</td>
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<tr>
<td>Recurrences</td>
<td>4 (20%)</td>
<td>2 (1.9%)</td>
<td>0.04</td>
<td>3 (12.5%)</td>
<td>3 (2.6%)</td>
<td>0.12</td>
</tr>
<tr>
<td>One-year mortality</td>
<td>5 (31.3%)</td>
<td>29 (23.5%)</td>
<td>0.57</td>
<td>10 (43.5%)</td>
<td>16 (13.8%)</td>
<td>&lt;0.01</td>
</tr>
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</table>

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Impact of antimicrobial stewardship and infection prevention interventions on a cluster of VIM-producing Pseudomonas aeruginosa in a large, academic health system in Miami, Florida

Gemma Rosello*1, Adriana Jimenez1,2, Kailynn Deronde1, Ana Vega1, Octavio Martinez1,5, Biagio De Pascale4, Kathleen Sposato1, Armando Perez-Cardona4, Steven Marshall6, Mohamad Yassin7, Robert A. Bonomo6,7, Lilian Abbo1,8

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Abstract

Impact of antimicrobial stewardship and infection prevention interventions on a cluster of VIM-producing Pseudomonas aeruginosa in a large, academic health system in Miami, Florida

Gemma Rosello*1, Adriana Jimenez1,2, Kailynn Deronde1, Ana Vega1, Octavio Martinez1,5, Biagio De Pascale4, Kathleen Sposato1, Armando Perez-Cardona4, Steven Marshall6, Mohamad Yassin7, Robert A. Bonomo6,7, Lilian Abbo1,8

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Background: Pseudomonas aeruginosa (PA) is a water-associated, environmental pathogen frequently implicated in nosocomial infections. PA is known to exhibit a wide range of resistance mechanisms, including carbapenemase production. We encountered a cluster of PA isolates harboring blaVIM (VIM-PA) and sought to describe the clinical characteristics, outcomes, and infection control strategies associated with these infections.

Materials/methods: A total of 12 patients with positive cultures for VIM-PA were identified between 12/2018-06/2019. An infection control bundle was introduced to decrease horizontal transmission. Measures included: changing sink P-traps, installing point-of-use sink filters (changed bimonthly), cohorting patients, and decreasing the nurse-to-patient ratio. A reflex-testing algorithm was implemented in the microbiology laboratory to enhance rapid identification and improve antimicrobial stewardship. Testing methodology for carbapenemase genes was modified from CarbaNP to Carba-R PCR. A new surveillance protocol allowing for timely identification of new cases, early provider notification, and immediate contact isolation was implemented. Mechanism based susceptibility testing (MBST) using combination antimicrobial double and triple disk diffusion assays guided therapy.

Results: Nine patients developed infections with VIM-PA, three of which were identified retrospectively. Three additional patients were colonized with PA. The median age was 63.6 (IQR 51 -74) years and the average length of stay was 37.8 days. Nine patients were admitted from home; three transferred from nursing homes. Organisms were isolated from the respiratory tract (59%), urine (9%), rectal surveillance (16%), and wound (16%) cultures. MBST was successful in identifying an effective antibiotic combination regimen against VIM-PA among prospectively identified patients (n=6). Four patients were treated with a regimen consisting of ceftazidime/avibactam, aztreonam, and polymyxin b (Figure 1). Three had follow-up cultures. One patient with urosepsis had microbiological clearance. Two patients with pneumonia had persistent colonization despite clinical improvement. No patients died from infection and incident cases did not emerge over the following five months.

Conclusions: We describe a cluster of VIM-PA encountered in Miami. Until recently, there was no single effective antimicrobial on the market for this organism. We report success utilizing rapid identification and MBST to guide combination therapy, resulting in low attributable mortality. An infection prevention control bundle was successful in preventing further transmission.

Figure 1: Targeted VIM Therapy, Prospectively Identified

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Abstract 5386

Mural endocarditis from a prospective national registry: the GAMES series

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Abstract third-party references: GAMES study group

Background: Mural endocarditis (MIE) is a rare but severe condition. There are no published MIE series and information about its characteristics and outcome is scarce.

Materials/methods: Consecutive patients with IE according to Duke criteria were prospectively included in the registry “Spanish Collaboration on Endocarditis (GAMES)” between January 2008 and December 2017 in 35 Spanish hospitals. Multidisciplinary teams completed a standardized case report form. Patients with mural endocarditis (endocarditis involving non-valvular native endocardium) were analysed and compared with patients with valvular (VIE) or device-associated (DIE) endocarditis in the database.

Results: During the study period, 28 cases out of 3830 fulfilled the inclusion criteria (0.7% of IE during the same period). Vegetations were more frequently located in the right heart (atrium 46.4%, ventricle 10.7%, ventricular outflow tract 10.7%, superior cava vein 10.7%) than in the left heart (atrium 10.7%, ventricle 3.6%, ventricular outflow tract 3.6%) or other (persistent ductus 3.6%).

The most frequent etiology was staphylococcal (32%), followed by Streptococci and fungi (25% each), Enterobacteriaceae and polymicrobial (7% each) and Enterococci (4%).

When compared with VIE or DIE endocarditis, patients with MIE were younger (median age 59y [46 - 57] versus 69 [57 – 77], p <0.01). Transplant and hemodialysis were more common (12.9% versus 1.7% and 12.9% versus 4.3%, p<0.01 and p=0.008 respectively) and Charlson comorbidity index was lower (4 [2 - 6] versus 5 [3 – 7], p=0.06) among them. Endocarditis originated in catheters was significantly more frequent among patients with MIE (57% versus 9.6%, p <0.01) and right heart endocarditis was more prevalent (85.7% versus 15.2%, p <0.01). Surgery was indicated less often (35.7% versus 66.8%, p<0.01), but therapy was longer (42 (30 - 52) versus 38 (25 – 45), p= 0.01).

In-hospital mortality and one-year mortality were similar to that of VIE and DIE.

Conclusions: Mural endocarditis accounts for 0.7% of endocarditis. It is often a complication of catheter use and usually involves right heart. It appears in immunocompromised patients and fungal etiology is common. Surgery is less commonly indicated, but medical therapy is longer, to achieve a similar mortality.

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Lamb meat as a source of dissemination of cephalosporin-resistant Escherichia coli

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Background: The presence of Escherichia coli in food suggests faecal contamination, and indeed several studies have reported the transmission of bacteria and antimicrobial resistance genes through the food chain. Third-generation cephalosporin (3GC)-resistance is an important threat to public health, and bacteria presenting such phenotype points out to the transmission of resistance genes from and to the intestinal microbiota. Antimicrobial resistant bacteria from sheep are a still neglected field in Brazil despite the exponential increase in the meat consumption. Thus, this study aimed to characterize the 3GC-resistant E. coli isolated from lamb meat.

Materials/methods: Twenty-five retail lamb meat were purchased in the State of São Paulo, Brazil, and analyzed with 4 mg/L ceftiofur as selective agent. Suggestive colonies of E. coli in MacConkey agar were identified and submitted to antimicrobial susceptibility test by disk-diffusion or broth microdilution. Genes responsible for 3GC-resistance and 27 virulence genes were screened by PCR. bla-carrying plasmids were characterized. Isolates were typed by phylogenetic group, XbaI-PFGE and MLST.

Results: Twenty-six E. coli were isolated from 60% of federal service inspected lamb meats, and 13 harboured IncI1-bla_{CTX-M-8} plasmids [73 kb to 97 kb] as responsible for 3GC-resistance. Ten isolates harboured IncHI2-bla_{CTX-M-2} plasmids [242.5 kb to 290 kb], two presented the bla_{CTX-M-55} in a not typed plasmid (< 48.5 kb), and one carried a bla_{CTX-M-14} in a not typed plasmid (97 kb). The majority of isolates was considered commensal, but one carried the vat gene of extraintestinal pathogenic E. coli. The XbaI-PFGE revealed general dissimilarity among isolates, with exception of four clusters formed by isolates recovered from different samples originated from animals slaughtered at the same slaughterhouse. The MLST also revealed the majority as commensal bacteria, with exception of the potentially pathogenic lineages ST58, ST106, ST117, ST205, and ST349.

Conclusions: Genes and plasmids responsible for 3GC-resistance in E. coli from lamb meat are the ones also prevalent in food-producing animals in the country, which supports that intestinal bacteria in animals could contaminate the ensuing products. This study also demonstrated slaughterhouses as a source of meat contamination by 3GC-resistant E. coli.

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Abstract 5390

Invasive pneumococcal disease among adults in Germany, nine years after PCV13 introduction

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Background: Streptococcus pneumoniae remains a leading cause of infectious disease among children and the elderly. In July 2006, vaccination with pneumococcal conjugate vaccine was generally recommended in Germany for all children ≤24 months. Apart from a strong direct effect, pneumococcal conjugate vaccination has shown herd protection effects among non-vaccinated children and adults.

Materials/methods: The GNRCs has monitored the epidemiology of IPD in adults in Germany since 1992. All isolates were serotyped using the Neufeld Quellung reaction.

Results: Since 2006/2007, the amount of IPD isolates sent to the GNRRCS has steadily increased from 2000 to over 3000 per season. Before childhood PCV vaccination, 40-45% of IPD cases among adults were caused by PCV7 serotypes. After the start of childhood vaccination, this percentage was gradually reduced to 5.4% in 2018-2019. In 2009, higher valent vaccines [PCV10, PCV13] were introduced among children. Among adults, a reduction of the percentage of IPD caused by the six additional serotypes from 42.1% in 2010-2011 to 28.0% in 2014-2015 was observed, and percentage has remained stable until 2018-2019 (30.2%). In the last five seasons, PCV13 serotypes, 3, 4, 19F and 19A have remained at prevalences over 1%. In 2018-2019, prevalences were 20.3% [3], 2.1% [4], 3.7% [19A] and 1.5% [19F], whereas 19A has slightly decreased in the last season. Serotype 4 has increased and 19F and 3 have remained stable. The prevalence of serotype 3 has reached its highest point ever since the introduction of PCVs. Among non-PCV13 types, 8 [14.0%], 22F [7.2%], 9N [6.4] and 12F [5.0%] are most prevalent. New PCV formulation would have a theoretical coverage of 38.7% [PCV15 and 65.2% [PCV20].

Conclusions: The herd protection effect of PCV7 and PCV13 on serotype distribution of IPD among adults in Germany has reached its limit. PCV13 serotypes have remained at a prevalence of about 30% during the last five seasons. Serotype 3 shows no herd protection, with prevalence increasing to 20.3% in 2018-2019. The data implicate circulation of PCV13 serotypes among adults, which might only be interrupted by direct vaccination.

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Abstract 5391

Comprehensive analysis of evolutionary dynamics of circulating strains and immunopathogenesis of respiratory syncytial virus-associated acute lower respiratory tract infections in children

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Background: The study aimed to explore the role of circulating genotypes, evolutionary dynamics, viral load and host cytokines in RSV mediated ALRTI.

Materials/methods: NPAs were collected from children (n=349) between December 2013-March 2017. RSV positive samples were subjected for viral load estimation by RT-PCR. IL-17A, IFN-Ɣ, TNF-α, IL-10, IL-6 levels in NPA samples were determined by CBA and MMP-9 and TIMP-1 levels by ELISA. The viral load and cytokine levels were correlated with the WHO criteria for ALRTI severity. ‘G’ gene region of RSV (n=77) was sequenced for phylodynamics analysis. Potential N-glycosylation and O-glycosylation sites and Selective pressure were predicted.

Results: RSV positivity was 41.38% (146/349). Of 59 RSV-A strains, 58 belong to RSV A ON1 genotype with 72 bp nucleotide (24aa) duplication. AA mutation analysis identified four most frequented mutations in duplicated region, E295K (42.1%; 24/57) followed by G284S (36.84%; 21/57) and V303A/I (28.07%; 16/57). Evolutionary rate of RSV A ON1 strains was 5.29X10⁻³ substitution/rate/year. The ON1 strains studied were seen to be sharing a similar profile of O-glycosylation sites and contained 40—50 O-glycosylation predicted sites and the 24 AA duplication resulted in 8 potential O-glycosylation site introduction in the duplicated site. Two codon sites were under positive selection pressure L310P by SLAC method and L298P by IFEL method and comparison with NIV1114046 strain isolated from Pune, India, observed that only a single codon was found to be under positive selection pressure L310P by SLAC method and L298P by IFEL method and with 60bp nt duplication in the second hypervariable region of G gene. The RSV viral load of severe ALRTI patients was significantly higher than the ALRTI patients. Pro-inflammatory cytokine TNF-α level [p<0.001], IL-6 [p<0.01] and MMP-9 was secreted in significantly higher levels in severe ALRTI patients than ALRTI patients [<0.001] leading to higher MMP-9/TIMP-1 ratio in severe ALRTI patients [p<0.001].

Conclusions: This comprehensive study on the phylodynamics of circulating RSV strains in Indian subcontinent. The study highlights Th2 cytokine bias in the pathogenesis of RSV disease with the possible contribution of MMP-9 towards disease severity.

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Leptospira spp. in rodents and environmental samples from Lisbon and Setubal districts (Portugal): what are the risks for public health?

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Background: Leptospirosis is an infectious zoonotic disease of worldwide importance. Rodents are the most common reservoirs in Leptospira spp. dissemination. When excreted in the urine, spirochetes can survive for several weeks or months under favorable conditions (wet soil, water with neutral or slightly alkaline pH). Thus, contaminated water and soils become essential vehicles of transmission to humans, which can be infected by penetration of these infectious agents into intact mucous membranes (nose, mouth, eyes), or to healthy or injured skin. Thus, this study aimed to evaluate the presence of Leptospira spp. in soils, freshwater collections, and rodents from two districts of Portugal mainland (Lisbon and Setubal).

Materials/methods: Environmental samples (N=250), of which 161 were obtained from different freshwater collections (surface of lakes, rivers, and public fountains), and 89 soil samples (near freshwater collections, dustbins, or wooded areas) were collected in nine cities from Lisbon and Setubal districts. At the collection sites, chemical and physical parameters (e.g., pH, nitrates, temperature) were evaluated. In parallel with environmental samples, it was trapped rodents (N=18) for the analysis of blood, urine, and organs (kidneys, liver, spleen, and lungs).

After DNA extraction from all samples, two nested-PCR protocols with different primers were used. At first, it was applied a nested-PCR protocol with universal primers from the rrs (16S) gene, for Leptospira spp. detection. Each sample with leptospiral DNA amplification was submitted to a second nested-PCR protocol, with specific primers (targeting lipL32 gene) for detection of pathogenic species.

Results: Assessment with “LipL32” protocol, revealed pathogenic Leptospira DNA in 38+/100 water samples (38%), 7+/75 soil samples (9%) and in 14 rodents (78%), being observed that the kidneys (n=13+/14; 93%), liver, and lungs (n=12+/14; 86%) were the more colonized organs. No Leptospira DNA was detected in any blood samples.

Conclusions: The amplification of Leptospira spp. DNA in more than half of the rodents and water samples, as well as in the majority of soil samples, represents a disturbing result, leading to a significant public health concern about the risk that it poses to population health.

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The necessity of testing for diarrhoea-causing intestinal parasites on broad indications

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Background: Testing faecal samples for parasites have traditionally been done by microscopy. The limited capacity of this technology has necessitated strict indications for testing, mostly severe immunosuppression or travel history. Many laboratories have now replaced microscopy by molecular techniques, which are more sensitive and economical affordable, and allow high throughput in a short time. Access to molecular testing allows implication of a less restricted visitation of samples and calls for a re-evaluation of which patients to test for intestinal parasites.

Materials/methods: 5006 stool samples from 2249 patients (on average 2.2 samples per patient) were examined for Giardia duodenalis, Cryptosporidium species and Entamoeba histolytica from 5th November 2017 to 4th November 2018. The investigation was performed by microscopy and strict visitation (specific requisition, a history of diarrhoea > 14 days, travel outside Europe or immunosuppression). 5686 stool samples from 4706 patients (on average 1.2 samples per patient) were examined for the same three parasites from 5th November 2018 to 4th November 2019. The investigation was performed by RT-PCR and broad visitation (specific requisition, all children <17 years old, macroscopic watery stool samples, a history of travelling, bloody diarrhoea or immunosuppression).

Results: The rates of patients with G. duodenalis increased from 0.4 % to 0.8 %, and patients with Cryptosporidium spp. increased from 0.2 % to 1.5 %. The total number of tested samples/patients and detected parasites are shown in table 1.

Conclusions: Replacing microscopy by species-specific RT-PCR and introducing a broader visitation, more than doubled the number of patients tested with only a small increase in the total number of tests. The positive rate for G. duodenalis was doubled and for Cryptosporidium spp. it was seven times higher in the samples tested. It shows very clearly that there is a need for an extended visitation than most frequently used in the investigation of diarrhoea-causing intestinal parasites.

Table 1: Number of tested samples/patients and detected parasites

<table>
<thead>
<tr>
<th></th>
<th>Microscopy and Strict visitation</th>
<th>RT-PCR and Broad visitation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of samples/patients tested during a year</td>
<td>5006/2249</td>
<td>5686/4706</td>
</tr>
<tr>
<td>Number of positive samples/patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G. duodenalis</td>
<td>28/9</td>
<td>52/38</td>
</tr>
<tr>
<td>Cryptosporidium spp.</td>
<td>6/4</td>
<td>81/72</td>
</tr>
<tr>
<td>E. histolytica</td>
<td>0/0</td>
<td>3/2</td>
</tr>
</tbody>
</table>

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Successful treatment of osteoarticular infections caused by quinolone-resistant Gram-negative bacilli with colistin plus β-lactams: preliminary results of a prospective multi-centre clinical study

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Abstract third-party references: REIPI (Red Española de Investigación en Patología Infecciosa), Instituto de Investigación "i+1", Hospital 12 de Octubre, GEIO-SEIMC (Grupo de Estudio de Infeccion Osteoarticular - Sociedad Española de Enf. Infecciosas y Microbiología Clínica)

Background: The prognosis of OAI caused by QR-GNB is poor, especially when an orthopaedic device (OD) is retained or when caused by MDR/XDR microorganisms. C+BL could be an effective alternative treatment, but experience is lacking. Our aim was to prospectively assess the safety and efficacy of this antimicrobial regime.

Materials/methods: Prospective (February 2018-September 2019), observational, multicentre (14 hospitals), non-comparative study of patients with OAI caused by QR-GNB treated with C+BL after surgery (if indicated). The primary outcome was the absence of clinical relapse or persistence due to the same QR-GNB.

Results: 45 patients were included (median age 73y [IQR 52-79]; 51% women; Charlson 1[IQR 0-2]). Thirty-three cases (73%) involved OD: 18 prostheses and 15 osteosynthesis; the rest were 9 osteomyelitis and 3 arthritis (table). Median treatment duration was 42d (IQR 36-53), it being with C+BL during 28d (IQR 22-36). Most-employed β-lactams were meropenem (40%), ceftazidime (24%), ceftriaxone (18%) and piperacillin-tazobactam (7%), administered as continuous/extended infusion in 22 cases (49%). Toxicity led to treatment withdrawal in 13 patients (29%), it being always reversible. Colistin-related toxicity happened after median treatment duration of 16d (IQR 7-24) in 9 patients (20%): renal-failure (AKIN≥1) in 6 (13%), neurological in 2 (4%) and digestive in 1 (2%). It was associated with higher drug plasmatic levels (2.2mg/L -vs- 1.0mg/L, p<0.001). β-lactam-related toxicity occurred in 7 episodes (16%): neurologic in 3 (7%), hematologic, digestive, dermatologic and renal in 1 (4%) each. Seven (16%) cases were not-evaluable: 3 (7%) are under-treatment, 3 (7%) due to not-related-to-infection-death and 1 (2%) lost to follow-up.

Absence of microbiologic-failure was reported in 37 cases (82%, CI95% 69-91%) in the overall cohort, after a median follow-up of 190d (IQR 99-320). Non-failure by subgroups: OD-retention 13/16 (81%); MDR/XDR 21/26 (81%); non-MDR/XDR 16/19 (84%).

Conclusions: Our preliminary data shows C+BL to be an effective treatment for complex OAI caused by QR-GNB, including MDR/XDR strains and the need for OD retention. Toxicity is a concern but seems to be reversible and potentially preventable by colistin concentration monitoring.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>OAI without OD</th>
<th>OAI+OD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=12</td>
<td>OD-removal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>n=17</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas spp</td>
<td>6 (46%)</td>
<td>11 (65%)</td>
</tr>
<tr>
<td>MDR/XDR</td>
<td>8 (57%)</td>
<td>9 (53%)</td>
</tr>
<tr>
<td>PK/PD-optimized BL</td>
<td>8 (67%)</td>
<td>8 (47%)</td>
</tr>
</tbody>
</table>

| Days of antibiotics    |                |                    |                    |
|                        | 39 (28.5-43)   | 42 (36-54)         | 42.5 (38.5-81.5)   |
|                        | 28.5 (21-37.5) | 25 (22-35)         | 27.5 (19.5-38.5)   |
|                        | 8 (67%)        | 16 (94%)           | 13 (81%)           |

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**Abstract 5398**

**Polymyxin B broth disk elution as a screening test to determine polymyxin B susceptibility in Enterobacterales**

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**Background:** Infections caused by carbapenem-resistant Enterobacterales are challenging and treatment may be restricted to limited drugs, including polymyxins. Detection of susceptibility to polymyxins is a nightmare due to physicochemical properties of the drug. EUCAST recommends Broth Microdilution (BMD) as reference method. However, it is a laborious and expensive technique. Polymyxin B Broth Disk Elution (PBDE) test, based on the elution of the polymyxin B disk content, is an easy and cheap methodology. We aimed to evaluate PBDE accuracy as a screening test.

**Materials/methods:** 196 non-duplicated Enterobacterales including mainly *K. pneumoniae* (88.6%) were tested. Minimal Inhibitory Concentration (MIC) of polymyxin B was defined by BMD and interpreted according to EUCAST. PBDE was performed in duplicate using a 300 IU-polymyxin B disk eluted for 30 minutes at room temperature on 15 mL of cation-adjusted Mueller-Hinton Broth (final polymyxin B concentration: 2 µg/mL). After elution, 75 µL of 0.5 McFarland bacterial suspension was added (final concentration 7.5 x 10⁵ UFC/mL) and tube was incubated for 16-20h. A tube containing only broth (growth control) was used for each isolate. Visual growth of bacteria indicated positive result (MIC > 2 µg/mL). A subset of 40 resistant isolates were tested using shorter periods of incubation (6h, 7h and 8h).

**Results:** Polymyxin B MICs varied from 0.125 to >64 µg/mL, with 34 (17.3%) presenting borderline MICs (2 and 4 µg/mL). Ninety (45.9%) were resistant to polymyxin B. PBDE demonstrated 98.9% of sensitivity and 100% of specificity when standard incubation time was applied. One *K. pneumoniae* presenting MIC 4 µg/mL gave negative result in PBDE. Shorter incubation reduced sensitivity (57.5%, 67.5% and 82.5% after 6h, 7h and 8h, respectively). However, when excluding isolates presenting MICs borderline (4 µg/mL), sensitivity increased significantly (65.6%, 78.1% and 96.9% after 6h, 7h and 8h, respectively).

**Conclusions:** PBDE proved to be a cheap, easy to perform and accurate screening test for determining polymyxin B susceptibility in Enterobacterales. Reduced incubation compromised sensitivity although it seems to be dependent of MIC values. Moreover, the limited number of isolates tested (n=40) may had influenced the sensitivity.

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Abstract 5402

**Retrospective study of cytomegalovirus infection in orthotopic liver transplantation recipients receiving low dose valganciclovir prophylaxis**

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**Background:** Prophylaxis with valganciclovir has shown efficacy in reducing the rate of cytomegalovirus (CMV) infection post solid organ transplantation (SOT), although there is a lack of consensus regarding optimal use and dosing in liver transplantation. Some centres advocate a low dose prophylaxis regimen of 450mg once daily to reduce complications related to myelosuppression. The aim of the study was to demonstrate the rate of CMV DNAemia in the context of universal low dose valganciclovir prophylaxis and evaluate the timing and severity of CMV infection when it occurred.

**Materials/methods:** A retrospective study was carried out in the National Liver Transplant Unit, St Vincent’s University Hospital, Dublin between 2017 and 2018. Data was collected from clinical charts and the laboratory information management system.

**Results:** 63 orthotopic liver transplantations (OLT) were performed between 2017 and 2018. 13 patients (21%) experienced CMV DNAemia post OLT; 3 donor positive, recipient negative (D+/R-), 4 D-/R+ and 3 D+/R+. One D-/R- patient, who did not meet criteria for prophylaxis with valganciclovir, experienced primary CMV infection. Seven patients had early CMV DNAemia (within three months of transplant). Eleven patients experienced uncomplicated asymptomatic DNAemia. One patient (D-/R+), experienced biochemical hepatitis coincident with a high CMV viral load although liver biopsy did not confirm CMV disease. Two patients with CMV DNAemia died. In one, the cause of death was bowel ischaemia. The second patient, (D-/R+) had common variable immunodeficiency syndrome with profound immunosuppression, experienced prolonged CMV DNAemia and died of pneumonia.

**Conclusions:** No high risk (D+/R-) patient developed CMV disease. CMV infection was observed in two patients, both D-/R+, (one late onset). Studies suggest a higher incidence of CMV disease once prophylaxis with valganciclovir 900mg OD has been discontinued (12.1 – 24.6%), this may be due to delayed recovery of specific T cell responses. This was not observed with low dose prophylaxis, the overall incidence of CMV disease being 3%. Low dose prophylaxis is safe and efficacious, whilst facilitating asymptomatic seroconversion in high risk patients.

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MoCaT as first option in the cystic echinococcosis treatment: what we have obtained
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Abstract third-party references: Clinic of General Surgery, “Colentina” Teaching Hospital, Bucharest, Romania, “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

Background: According to the last recommendations of the WHO-IWGE, published since 2008 in various guidelines, the minimally invasive approach has become the first choice in treating cystic echinococcosis (CE), whenever is possible, starting with the well-known PAIR procedure. Furthermore, the other or non-PAIR percutaneous techniques gained an important place, moving from the lower position “rarely used” (but accepted) to the top: “recommended”. We prefer in our surgical clinic the MoCaT technique, developed by Prof. O. Akhan in Turkey.

Materials/methods: During 01.01.2014 – 31.05.2019, 126 patients diagnosed with CE have been admitted and treated in our surgical clinic, 88 of them being treated using minimally invasive techniques. 42 patients have had cysts considered feasible for MoCaT technique, the indications being: type CE2 and CE3b cysts, as the original technique claims, but we have used also for selected cases of type CE3a and CE4 cysts. MoCaT was performed in 40 patients, the technique failed in one case (cyst’s wall too rigid), or there was an anesthetic contraindication. 43 cysts were treated in this manner.

Results: In 10 (25%) cases the cyst’s cavity has been re-filled due to bile, lymph or mixed amount of secretion, so we needed a percutaneous drainage performed in the same way. Finally all cases have a favorable evolution; none of them would need to be treated by open surgery.

Conclusions: Using MoCaT as first option in minimally invasive treatment CE is definitely correct, but we have to choose accurately the type of CE assigned for MoCaT and to maintain the drainage as long as it is necessary. Re-filling of the cavity with bile and lymph is one way of evolution and not an error of this technique, neither an important complication; it is easily solved using a percutaneous drainage. Finally the results are optimal, obtaining the imagenistic appearance of scar.

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Carbapenemase-producing Pseudomonas from Bulgarian hospitals: spread of ST233 with multiple virulence factors

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Abstract third-party references: Supported by The Bulgarian National Science Fund under Grant No H23/H24

Background: Carbapenem-resistant Pseudomonas spp. has been classified as a highest priority concern according to WHO. MDR strains often express multiple virulence factors which pose additional problem. In this study we have characterized various MDR and XDR Pseudomonas spp. carbapenemase producers (PCP) collected over 9 year period.

Materials/methods: 178 MDR Pseudomonas spp. isolates from the collection of the National Reference Laboratory for AMR (2011-2019) were screened for carbapenemase activity by Carba NP test and antimicrobial susceptibility (AST) to 16 drugs was determined according to EUCAST. PCP were subjected to multiplex PCRs detecting 21 carbapenemase genes and associated integrons were further sequenced. Bi- and triparental mating was performed to assess transmissibility of plasmids containing bla genes. A newly devised PCR-based replicon typing scheme targeting 10 replicon types [IncP-1αβγδεζ, P-2, P-3, P-4, P-6, P-7, P-9, P-10, IncN and IncW] as well as the recently described pMOS94 and pKLC102-like plasmid families was applied for studying plasmids. MLVA9 and MLST were performed to assess clonal relatedness in P. aeruginosa. Virulence determinants (algD, aprA, fliC, toxA, lasAB, plcHN, rhlR,) were studied by PCR and biofilm formation quantified by the crystal violet assay.

Results: Overall 24 PCP (20 P. aeruginosa, 3 P. putida and 1 P. pseudoalcaligenes) were confirmed. Three blaVIM variants were identified: blaVIM-2 (n=12), blaVIM-4 (n=6), one blaVIM-5 (n=1) as well as blaNDM-1 in one isolate. All blaVIM genes were located as casettes in six different class I integrons. Interestingly none of the 21 targeted carbapenemase genes were found in four isolates. AST revealed that 22/24 isolates were XDR, resistant to ceftazidime-avibactam and ceftolozane-tazobactam and 4/24 were colistin resistant. None of the targeted replicon types were registered except the novel pMOS94-like replicon in one of the unidentified carbapenemase gene producers. Mating experiments failed suggesting chromosomal location of the carbapenemase genes. Overall six MLVA9 types were differentiated distributed in ST111, ST233 and ST235. Moderate to strong biofilm production was detected in 18/24 isolates and virulence factors (algD, plcH, toxA, rhlR) were evident in all P. aeruginosa strains.

Conclusions: XDR Pseudomonas spp. is sporadic in Bulgaria however recent tendencies suggest inter-hospital clonal spread of highly virulent blaVIM-2 ST233.

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Abstract 5409

**Investigating the microbiological growth of donor organ preservation fluid in liver and kidney transplantation**

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**Background:** Recipient infection after organ transplantation is a major cause of morbidity and mortality. Culture of donor organ preservation fluid (PF), may be used as a surrogate of possible graft infection. However, there is currently no published UK method for its microbiological evaluation. At our centre, PF was initially sampled using blood culture bottles. This appeared to have a high isolation rate of non-pathogenic organisms.

The aim of this evaluation was to compare microbiological growth from PF using two different collection methods: blood culture bottles and universal containers. We also aimed to determine the impact of positive PF on any subsequent clinical infection post-transplantation.

**Materials/methods:** This was a tertiary hospital service evaluation in Leeds. Part 1 included all liver and kidney transplants between August 16-June 17 where PF was sampled using blood culture bottles. Part 2 included transplants between August 18-August 19. PF was sampled using universal containers and processed using a plate-based culture method.

The microbiological results of PF were evaluated to determine the isolation of recognised pathogenic and non-pathogenic organisms. Recipient data was collected including microbiological growth from all post-operative samples.

**Results:** Amongst 136 samples taken using blood culture bottles, 117 (86.0%) had positive microbiological growth, and 44 (32.4%) grew pathogenic organisms, including: *Staphylococcus aureus* (n=19), *Enterobacteriaceae* (n=11), *Enterococcus spp.* (n=5), *Pseudomonas spp.* (n=4), *Candida spp.* (n=3), *Acinetobacter spp.* (n=2) and pyogenic streptococci (n=1).

Of the 148 samples taken using universal containers, 27 (18.2%) had positive microbiological growth and 18 (12.2%) grew recognised pathogenic organisms, including: *Enterobacteriaceae* (n=7), *Candida spp.* (n=6), *S. aureus* (n=3) and *Pseudomonas spp.* (n=3).

In no cases, were the pathogenic organisms isolated in PF subsequently identified in post-operative microbiological specimens from the recipient.

**Conclusions:** Microbial growth in PF is common after liver and kidney transplantation, with a large proportion of these being due to non-pathogenic organisms. A change in sampling method from blood culture bottles to universal containers reduced isolation of non-pathogenic organisms, whilst still allowing isolation of recognised pathogens. Identification of concurrent pathogens in recipient samples did not occur, suggesting transmission via the donor organ leading to clinical infection in our population was uncommon.

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Identification of recently acquired tuberculosis infection using QuantiFERON-TB Gold Plus: an exploratory study

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Background: It has been shown that specific CD8+ T-cell response to Mycobacterium tuberculosis is higher in RC-TBI than that of remotely acquired infection. A surrogate marker for CD8+ T-cell response can be retrieved by subtracting the TB1 from TB2 interferon (IFN-γ) tube concentrations (ΔTB2-TB1). Therefore, ΔTB2-TB1 may be useful to differentiate RC-TBI from remote TBI.

Materials/methods: Retrospective, multicenter study (19 centers in 7 countries). We included individuals screened for TBI with positive QFT-plus results. Participants were grouped according to the risk for RC-TBI (high risk: contacts of pulmonary TB, and low risk: subjects with immune-mediated inflammatory diseases [IMID] before biologics, without risk factors for RC-TBI). Patients with HIV infection, advanced chronic liver or renal disease, organ transplant, or chemotherapy for cancer were excluded. We compared ΔTB2-TB1 between the two groups, and between smear-positive and smear-negative TB cases. Ethics clearance was obtained at all centers.

Results: 726 individuals were included: 405 (55.8%) TB contacts [close or frequent (74.1%), sporadic (15.3%), unknown closeness of the exposure (10.6%)], and 321 (44.2%) candidates to biologics.

<table>
<thead>
<tr>
<th>Contacts</th>
<th>IMD screening</th>
<th>P</th>
<th>Contacts (*1)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n= 405)</td>
<td>(n= 321)</td>
<td></td>
<td>(n= 300)</td>
<td>62</td>
</tr>
<tr>
<td>TB1-NIL UI/mL, median</td>
<td>2.72</td>
<td>1.83</td>
<td>0.03</td>
<td>2.78</td>
</tr>
<tr>
<td>TB2-NIL UI/mL, median</td>
<td>2.66</td>
<td>1.94</td>
<td>0.03</td>
<td>2.63</td>
</tr>
<tr>
<td>Mytagen UI/mL, median</td>
<td>10.00</td>
<td>10.00</td>
<td>0.97</td>
<td>10.00</td>
</tr>
<tr>
<td>ΔTB2-TB1 UI/mL, median</td>
<td>0.00</td>
<td>0.00</td>
<td>0.54</td>
<td>0.00</td>
</tr>
<tr>
<td>TB2/TB1, N (%)</td>
<td>18 (46.2)</td>
<td>14 (45.5)</td>
<td>0.91</td>
<td>12 (43)</td>
</tr>
<tr>
<td>ΔTB2-TB1≥0.6 UI/mL, N (%)</td>
<td>65 (16.0)</td>
<td>42 (13.1)</td>
<td>0.31</td>
<td>39 (13)</td>
</tr>
</tbody>
</table>

(*1) 362 in which the closeness of the exposure was known. There were no significant differences in ΔTB2-TB1 between contacts of smear-positive and smear-negative TB cases (p=0.65). Twelve contacts had QFT-Plus conversion (IFN-γ concentration was higher in TB2 than in TB1, but only in 1 the difference was ≥0.6 UI/mL).

Conclusions: We did not find any relevant differences in ΔTB2-TB1 IFN-γ production between individuals with or without risk for RC-TBI. Our results put into question the potential role of the QFT-Plus for distinguishing recent from remote TB infection, as had previously been suggested.

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Abstract 5412

**Microbial aetiology of prosthetic joint infections: what’s growing in the cultures?**
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**Background:** Prosthetic joint infections (P JIs) are a tremendous burden for patients and healthcare systems. The Veterans Health Administration is the largest healthcare system in the United States of America (USA), and is comprised of over 170 medical centers. The objective of this study was to describe the organisms isolated from patients diagnosed with P JIs across this national healthcare system.

**Materials/methods:** Our retrospective cohort study included patients with a diagnosis code for prosthetic joint infection between January 2016 and December 2018 who were admitted to a Veterans Affairs (VA) hospital. Cultures obtained from one day prior to admission through date of discharge were included. Cultures were only included if the site of culture could be specifically attributed to a joint and may have included more than one organism.

**Results:** We identified 692 positive joint cultures from 3,660 admissions among 2,216 unique patients. The sources of cultures were from the knee (78%), hip (17%), and other/unspecified joint site (6%). Only 7.9% (n=55) of all cultures were polymicrobial. *Staphylococcus aureus* was the most frequently identified organism (49%, n=339), followed by other staphylococci (22%, n=153), and streptococci (12%, n=83). Methicillin resistance was identified in 27% (n=92) of the *S. aureus* isolates, and the majority of methicillin-resistant *S. aureus* (76%, n=70) were isolated from the knee. Gram-negative organisms were identified in 18% (n=123) of all cultures and *Pseudomonas aeruginosa* was the most frequently implicated gram-negative organism (23%, n=28).

**Conclusions:** Prior studies have reported coagulase-negative staphylococci to be the most common pathogens in PJI, but our study found that *S. aureus* was the most frequently isolated organism in the largest healthcare system in the USA. While gram-positive pathogens are more commonly associated with PJI and are targeted in surgical prophylaxis, gram-negative organisms were present in 18% of cultures, which is concerning due to increasing virulence and antimicrobial resistance.

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Antifungal prophylaxis in acute myeloid leukaemia patients receiving chemotherapy is cost-effective in a resource-limited country

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Background: Invasive fungal infections (IFI) cause high morbidity and mortality in acute myeloblastic leukemia (AML) patients receiving chemotherapy. Antifungal prophylaxis is recommended in this setting. However, due to the healthcare reimbursement policy, this intervention is not widely implemented in resource-limited countries. We aimed to investigate the cost-effectiveness of antifungal prophylaxis in Thailand.

Materials/methods: A model estimating costs and outcomes from a hypothetical cohort of 1,000 AML patients receiving antifungal prophylaxis was established. Due to local high incidence of aspergillosis, anti-mold agents available in Thailand were included in this study; itraconazole (capsule and solution), posaconazole (solution) and voriconazole (tablet). Clinical efficacies of the antifungal drugs were obtained from a network-meta analysis study. The model accounted for the incidence rate, cost of care, healthcare resource utilization and 100-day outcomes of patients with IFI. These were based on previous local studies, a hospital registry, expert opinions, and a national healthcare price list. Results represented the extrapolated cost, life-year saved (LYs) and health outcome with quality-adjusted life-years (QALYs). The probabilistic incremental cost-effectiveness ratios (ICERs) were calculated from a provider's perspective. A one-way sensitivity analysis was also performed.

Results: Itraconazole capsule, solution, and voriconazole were dominant and cost-saving options. They resulted in LYs and QALYs gaining when compared to no prophylaxis. In a sensitivity analysis, at willingness to pay (WTP) threshold of the nation's per-capita gross domestic product per QALY gain (160,000 THB; 5291.01 USD), the probabilities that providing voriconazole would be cost-effective is highest followed by itraconazole capsule and solution. Posaconazole was also cost-effective (ICERs of 118,514 THB; 3924.31 USD/QALY gain) and gave the highest LYs and QALYs gain (0.19, 0.15).

Conclusions: Itraconazole, voriconazole, and posaconazole were all cost-effective with the itraconazole capsule being the most cost-saving. Overall, voriconazole would be considered the most cost-effective option for IFI prevention during AML treatment in this model. Antifungal prophylactic therapy, although considered expensive in Thailand, may improve clinical outcomes and reduce the economic burden of AML treatment.

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Comparative evaluation of the Bruker Biotyper and Vitek MS MALDI-TOF MS systems for identification of non-albicans Candida and uncommon yeast isolates

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Abstract third-party references: Marmara University, Department of Medical Microbiology, Becton, Dickinson and Company, Bioeksen, Terra Analysis and measurement Equipment Trade Co.Inc, bioMerieux

Background: Rapid and accurate identification of causative agent is critically important for invasive and disseminated fungal infections. The present work aims to compare two MALDI-TOF MS systems for the rapid identification of non-albicans Candida and uncommon yeast species.

Materials/methods: This study includes 157 isolates representing 23 yeast species (of 15 non-albicans). All isolates were identified by Bruker MALDI Biotyper [Bruker Daltonics], VITEK MS [bioMérieux] and BD Phoenix automated system [Becton Dickinson]. An isolate was considered correctly identified if two MALDI-TOF MS systems yielded the same results with acceptable confidence values or scores. ITS sequencing and VITEK MS Saramis database testing were performed on isolates with discordant/no identification results.

Results: Using a revised threshold of ≥1.7, Bruker MALDI Biotyper identified 155 isolates, VITEK MS IVD identified 153 isolates. Two MALDI-TOF MS systems gave 152 concordant and five discrepant results which were further clarified by ITS sequencing and VITEK MS Saramis database testing (see Table). ITS sequencing revealed that VITEK MS IVD misidentified one Meyerozyma caribbica isolate so correctly identified isolate number dropped to 152. Phoenix automated system correctly identified 128 isolates with 20 misidentifications and nine no-identification. The sensitivities of Bruker MALDI Biotyper, VITEK MS IVD and BD Phoenix in the identification of yeasts were 98.7%, 96.8%, and 81.6% respectively.

Conclusions: Both of the MALDI-TOF MS performed well in terms of rapid and accurate identification of clinical yeast isolates. Meyerozyma caribbica isolates either identified as Candida guilliermondii (closely related species) or not identified at all by MALDI-TOF MS systems. Both of MALDI-TOF MS was superior to a conventional automated identification system for identification of clinically relevant uncommon yeast species and can improve the diagnosis of infection as well as the patient management.

<table>
<thead>
<tr>
<th>No</th>
<th>ITSequencing</th>
<th>Bruker Biotyper</th>
<th>VITEK MS IVD</th>
<th>VITEK MS Saramis</th>
<th>BD Phoenix</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Meyerozyma caribbica</td>
<td>No identification</td>
<td>Candida guilliermondii</td>
<td>Candida guilliermondii</td>
<td>No identification</td>
</tr>
<tr>
<td>2</td>
<td>Meyerozyma caribbica</td>
<td>No identification</td>
<td>No identification</td>
<td>Candida guilliermondii</td>
<td>No identification</td>
</tr>
<tr>
<td>3</td>
<td>Candida dubliniensis</td>
<td>Candida dubliniensis</td>
<td>No identification</td>
<td>No identification</td>
<td>Candida albicans</td>
</tr>
<tr>
<td>4</td>
<td>Cyberlindnera fabianii</td>
<td>Cyberlindnera fabianii</td>
<td>No identification</td>
<td>Cyberlindnera fabianii</td>
<td>Candida pelliculosa</td>
</tr>
<tr>
<td>5</td>
<td>Not tested</td>
<td>Cyberlindnera fabianii</td>
<td>No identification</td>
<td>Cyberlindnera fabianii</td>
<td>Candida pelliculosa</td>
</tr>
</tbody>
</table>

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Abstract 5416

Susceptibility to Group A Streptococcus invasive infections in children: preliminary results of a multi-centre prospective study in France: the STREPTOPEDIA study

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Background: Group A Streptococcus (GAS) is associated with a broad clinical spectrum ranging from common benign to severe invasive infections (iGASI). Though iGASI can be associated with specific emm genotypes or virulence factors, the variability of disease severity in patients infected by the same strain suggests a role of host immunity. The primary objective of this study was to identify specific virulence factors and primary immunodeficiencies in children with iGASI, compared to children with non-invasive GAS infection (niGASI).

Materials/methods: A national multicenter prospective study recruited children ≤ 15 years old with iGASI in 19 hospitals between 2015 and 2018. All strains were analyzed by emm and PCR genotyping of virulence genes (speA, speB, speC, sso, sic, smeZ). They were compared to strains isolated in matched children for age and period diagnosed with niGASI in a pediatric outpatient network. An immunological work-up was performed in children with iGASI (WBC count with blood smear, lymphocyte phenotyping, plasma Ig dosage, vaccinal serologies, complement analysis and abdominal ultrasound) and whole exome sequencing (WES) in those with no risk factor.

Results: We included 107 children hospitalized for iGASI, of which 70 had a risk factor for iGASI (mainly chickenpox or immunosuppression). Toxic shock or severe sepsis were more common in children without risk factor compare to children with risk factor [21/67 vs 3/33, p=0.01] whereas age and sex ratio were similar. Emm1 was more frequent in iGASI (38 vs 12%) and emm89 in niGASI (22 vs 7%). SpeA was more frequently found in iGASI than niGASI strains (47 vs 18%). Among strains of iGASI, the diversity of emm genotypes measured by the Shannon index was significantly greater in the group with no risk factor [2.22 vs 1.66, p=0.009]. So far, a primary immunodeficiency has been identified in two patients (one asplenia, one GATA2 mutation).

Conclusions: The greater diversity of emm genotypes in children with risk factor-free iGASI may suggest host involvement. WES of children with no risk factor along with genome sequencing of their GAS strain are ongoing to further characterize the association between bacterial virulence and host immunity in iGASI.

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Abstract 5417

Healthcare-associated Staphylococcus aureus bloodstream infection (HA-SABSI): clinical practice variation in its management

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Background: Previous studies assessing physician practices in the management of SABSI have shown there is considerable practice variation.

Materials/methods: Retrospective study of HA-SABSI diagnosed from 01/08/2015 to 31/07/2019 in Son LLàtzer Hospital, a 350-bed university hospital in Majorca (Spain). Epidemiological, clinical and microbiological data, treatment prescribed, and outcomes were collected and analysed.

Results: After excluding patients who were transferred while on therapy and those who died before microbiological results were obtained, 82 patients were included. Median age was 73y [0-93] and mean Charlson comorbidity index was 5.9 [SD: 3.1]. SABSI was associated with peripheral venous catheters (n=36), central venous catheters (CVC) (n=11), port or tunnelled CVCs (n=12), and unknown sources/other foci (n=24). Repeated blood cultures (BCs), transthoracic, and transoesophageal echocardiographies were performed in 60 (73.2%), 53 (64.6%), and 16 (19.5%) patients, respectively. Complicated SABSI (c-SABSI) were observed in 30 (36.6%) patients and infectious endocarditis diagnosed in 11 (13.4%). MRSA was isolated in 19 (23.2%) cases. Patients with MRSA-HA-BSI were hospitalised in the Intensive Care Unit more frequently than patients with MSSA-HA-BSI (5/19 versus 5/63, p≤0.005), and 8 had complicated BSIs. MRSA-HA-BSI was treated with: vancomycin in 4 (21.1%) cases, linezolid in 5 (26.3%), and daptomycin alone or in combination in 9 (47.4%). MSSA-HA-BSI was treated with: cloxacillin in 34 (54%) cases, daptomycin alone or in combination in 14 (22.3%), linezolid in 5 (7.9%), vancomycin in 4 (9.5%), and other antibiotics in 4 (6.3%). Vancomycin MIC was >1 μg/mL in 6 cases (Etest®). Mean duration of antibiotic therapy was 13.8 days [SD: 5.6] for uncomplicated SABSIs and 21.1 days [SD: 7.1] for c-SABSI [p≤0.05]. With regard to outcomes, 2 patients were readmitted due to persistent BSI and 24 patients died. Death was related to c-SABSI in 8/30 of the cases versus 5/52 for uncomplicated SABSI [p≤0.05] and to MRSA-BSI in 2/19 of the cases versus 11/63 for MSSA-BSI [p=ns].

Conclusions: Adherence to guidelines on HA-SABSI management is poor, especially for the performance of repeated BCs, echocardiographies, and selection and duration of antibiotic therapy in complicated BSIs. The high mortality observed in complicated MSSA-HA-BSI may be related to these factors.

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Abstract 5418

**Novel lipid A mimetics (BECC438 and BECC470) act as potent adjuvants in bacterial and viral subunit vaccines**

Erin Harberts¹, David Varisco¹, Akshay Jain², Charles Middaugh², Robert Ernst*¹

¹University of Maryland - Baltimore, Baltimore, United States, ²University of Kansas, Lawrence, United States

**Background:** Infectious diseases continue to be the leading cause of morbidity and mortality worldwide, and therefore, an urgent need exists to develop effective vaccines against a variety of pathogens. Effective vaccines contain appropriate antigens from the vaccine target and adjuvant(s) to potentiate the magnitude, duration and nature (humoral and/or cellular) of the generated immune response. Bacterial enzyme combinatorial chemistry (BECC) was developed to create bacterial lipid A that are partial agonists for innate immune receptor Toll-like receptor 4 (TLR4). Specifically, BECC allows for the synthesis and characterization of custom lipid A structures, the lipid anchor of lipopolysaccharide. These defined modifications have the potential to control the quality of specific activating immunity while avoiding excessive adverse host reactions. BECC is used to establish a robust mechanism for adjuvant/vaccine design.

**Materials/methods:** From initial screenings, two lead adjuvant candidates were identified, BECC438 and BECC470 that were subsequently formulated with bacteria and viral antigens, including *Yersinia pestis* (rF1-V), *Staphylococcus* alpha toxin, and human papillomavirus (VLPs). Mice were immunized using a two-week interval prime-boost-boost, prime-boost, or prime alone vaccination strategy with several different formulations. Antigen-specific antibody titers were measured by ELISA for total IgG, IgG1, and IgG2c(2a) isotypes and levels of efficacy/survival were determined using murine pathogen challenge models. Subsequently, vaccination with ovalbumin was used to further characterize the longevity of the adjuvant-driven immune responses.

**Results:** Vaccine formulation adjuvanted with BECC438 or BECC470 result in durable and IgG1/IgG2c(2a) balanced antibody production, as compared to alhydrogel or the TLR4 agonist PHAD, for all antigens tested. For all antigens, both BECC compounds allowed for durable antibody production, antigen sparing, dose sparing, adjuvant sparing, production of T follicular helper cells, and interestingly provided protection against a heterologous challenge in viral infection models.

**Conclusions:** Adjuvants play a critical role in enhancing and directing adaptative immune responses to vaccine antigens. Our data demonstrate that the BECC molecules induce strong T₁,1 and T₁,2 immune responses and so will be effective adjuvants in vaccines using purified protein, peptide, and DNA antigens. Data presented provide evidence that BECC molecules will be effective as a component in next-generation vaccine formulations.

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Clinical epidemiology of Lyme disease in Quebec, Canada and compliance with American and European guidelines
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Background: Little is currently known about the management and clinical evolution of patients with Lyme disease (LD) in Canada. This study aimed to describe the management of LD in Quebec, Canada, and assess compliance to the Infectious Disease Society of America and European guidelines.

Materials/methods: We conducted a retrospective multicenter cohort study of patients with serologically confirmed LD seen in acute care facilities in two endemic regions of Quebec from 2004 to 2017. Our main outcome was a favourable clinical evolution, defined as the resolution of all clinical signs, 3 months following initiation of a LD treatment. Two clinicians assessed clinical evolution and guidelines adherence independently.

Results: Over the study period, 614 serologically confirmed LD cases were identified through the provincial laboratory database. Medical charts for 272 patients from 14 institutions were available and complete for data collection. The median age of patients was 51 years [interquartile range (IQR) 32-64]. Infection led to hospitalization of 48 patients (17.7%) for a median duration of 4 days [IQR 1-4]. Early localized LD was recorded in 33% of cases [90/272], early disseminated LD in 52% [140/272] and late disseminated LD in 15% of patients [42/272]. A favourable outcome was observed in 266/270 (98.5%) patients for whom follow-up visits were documented, while 10% of patients (28/270) developed a Post-Lyme Disease Syndrome. One death unrelated to LD occurred 589 days after diagnosis. Compliance to IDSA guidelines was observed in 219/243 (90.1%) patients for whom data on antimicrobial therapy was complete, and did not vary throughout time [2004-2013: 54/60 (90%); 2014-2015: 61/68 (90%); 2016-2017: 104/115 (90.4%); p=0.99]. The main reason for noncompliance was a duration of therapy superior to recommendations [14/24, 59.3%]. Compliance to the 2018 National Institute for Health and Care Excellence [NICE] guidelines was lower [110/243, 45.2%], mainly because of a duration of therapy superior to recommendations [73/133, 54.9%; p<0.001].

Conclusions: Most patients had complete resolution of the objective clinical signs at three months following the initiation of treatment. We did not observe changes in the compliance to IDSA guidelines over 13 years. This study also emphasizes significant differences between European and American guidelines.

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Early microbiome changes associated with the novel, targeted-spectrum antibiotic ACX-362E compared to oral vancomycin

Kevin Garey1, Khurshida Begum1, Chris Lancaster1, Anne Gonzales-Luna1, Dinh Bui1, Ming Hu1, Michael Silverman2, M. Jahangir Alam1

1University of Houston, Houston, United States, 2Acurx Pharmaceuticals, White Plains, United States

Background: The mechanism by which a healthy microbiome loses colonization resistance, leading to gut colonization with Clostridioides difficile and multidrug-resistant organisms after antibiotic use is poorly understood. Oral vancomycin has broad-spectrum activity against all major phyla of the human gut microbiome including Firmicutes, Bacteroidetes, and Actinobacteria. ACX-362E is a DNA polymerase IIIC inhibitor in development for the treatment of C. difficile infections that specifically targets low G+C Gram positive bacteria, including some Firmicutes. The purpose of this study was to compare early microbiome changes associated with use of these antibiotics in healthy volunteers.

Materials/methods: As part of the completed phase I clinical study of ACX-362E, stool samples were collected daily from volunteers given a ten-day course of ACX-362E (300 or 450 mg given twice daily) or vancomycin (125 mg given four times daily). DNA was extracted from stool and sequenced using shotgun metagenomics (Illumina HiSeq). Daily antibiotic concentrations were measured by LC-MS/MS. Phylum- and family-level changes in microbiota were compared from baseline.

Results: Eighteen subjects (female: 33%) aged 30±8 years were enrolled. Baseline microbiota were similar between study groups and comprised of Firmicutes (62%), Actinobacteria (23%), and Bacteroidetes (11%). Concentrations of all antibiotics exceeded 2,000 ug/g of stool by day 5 of therapy. In subjects given vancomycin, host microbiota had been replaced by two distinct families, Lactobacillaceae or Enterobacteriaceae, by day 10 of dosing. At day 10, subjects given either dose of ACX-362E had replacement of Firmicutes by an expansion of existing baseline Actinobacteria microbiota, primarily Bifidobacteriaceae.

Conclusions: Early microbiome changes after antibiotic therapy were associated with the pharmacologic activity of the antibiotic. A targeted-spectrum agent ACX-362E was associated with replenishment of host microbiota while a more-broad spectrum antibiotic led to replacement with novel microbiota.

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**Abstract 5421**

**Vancomycin for patients with MRSA bloodstream infections (BSIs) is nephrotoxic even within the recommended area under the curve (AUC) therapeutic exposure range**

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**Abstract third-party references:** Marmara University, Department of Medical Microbiology, Becton, Dickinson and Company, Bioeksen, Terra Analysis and measurement Equipment Trade Co.Inc, bioMerieux

**Background:** Vancomycin remains the standard of care for serious MRSA infections, but optimal dosing is constrained by a tradeoff between clinical effectiveness and acute kidney injury (AKI) at higher vancomycin exposures. Draft consensus vancomycin dosing guidelines recommend targeting a daily AUC of 400 to 600 mg-h/L to minimize AKI while preserving effectiveness. To investigate AKI risk within this range, we evaluated the relationship between day 2 AUC and change in serum creatinine (SCr) from baseline among patients who were enrolled in PROVIDE, a multicenter prospective cohort study of patients with MRSA BSIs who received vancomycin [PMID: 31157370].

**Materials/methods:** Data from previously completed prospective, multi-center (n=14), observational study (2014-2106) of hospitalized adults with confirmed MRSA BSI treated with VAN ≥ 72 hours who had a Scr ≤ 2 mg/dL were analyzed. Vancomycin day 2 AUC were estimated using maximum a posteriori Bayesian procedure in ADAPT 5 (Bayesian Estimator). Maximum change in SCr was calculated by subtracting the maximum recorded SCr value during vancomycin therapy from baseline SCr value. Univariable negative log binomial generalized linear regression (NLBGLR) was used to assess the relationship between Day 2 vancomycin AUC and change in SCr. Multivariable NLBGLR was performed and included covariates which had previously demonstrated associations with AKI. All analyses were performed with SAS version 9.4.

**Results:** Of the 265 patients in PROVIDE, 212 had a Scr < 2 mg/dL. Mean (SD) baseline SCr was 1.0 (0.4), mean (SD) age was 60 (18), mean (SD) APACHE II score was 11 (5); 124 (58.5%) subjects were male. In the univariate NLBGLR analysis, the mean change in SCr from baseline increased as a function of the day 2 AUC (figure). In the multivariable regression analysis, each 100 incremental increase in was associated with a 9% increase in the mean SCr change after adjusting for clinically relevant covariates.

**Conclusions:** Among patients with MRSA BSIs, SCr increased as a function of the day 2 vancomycin, even with vancomycin exposures that is within the recommended AUC therapeutic range of 400-600.

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Abstract 5423

**Botulism early recovery: one-decade experience in a referral centre**

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**Background:** Botulism is a rare and fatal disease that has various forms that food-borne botulism is often identified as an outbreak. About 1000 cases of foodborne botulism are reported annually worldwide. We reviewed all clinical features, lab data and outcome of patients who have referred to our tertiary center.

**Materials/methods:** All cases of proven botulism at an academic referral center and teaching hospital were retrospectively reviewed between 2009-2019.

**Results:** During 10 years, 53 cases of clinical or laboratory confirmed botulism (mean age 36.6 (14-74) and 56.6% males/43.4% females) were extracted. In seven cases, source of botulism was unclear and in 2 patients systemic symptoms were occurred after iatrogenic injection of botulinum toxin. The most of cases (83%) had an obvious food source, including conserved foods, tuna fish and corn (the most prevalent), 28.3% homemade dairy products, 5.7% red meat, 5.7% sausage and 1.9% salty fish.

In 66% of patients initial symptoms were presented in less than 36 hours and in 20.8% of them ≥36 hours; in 7 indeterminate source, the onset time could not be estimated. All patients had cranial involvement, including 66% ptosis, 75.5% diplopia, 71.7% dysphagia, 43.3% dysarthria, 49.1% impaired gag reflex and 28.3% mydriasis. About 47.2% of patients had autonomic manifestations [dizziness, constipation, dry mucosa, etc.] and 49.1% had gastrointestinal symptoms [abdominal pain, nausea, vomiting, etc.]. Some patients had diarrhea due to other concomitant cause of food poisoning.

Except for two patients who were unable to be prescribed due to immediate drug reaction, the rest were treated with trivalent antitoxin (A, B, E) according to our center protocol. About 17% of patients were intubated due to impaired intercostal muscle tone. Eventually, two patients died due to massive embolism and cardiac asystole. Surprisingly, in 50.9% of patients complete resolution of symptoms were documented.

**Conclusions:** Early treatment in most cases resulted in a favorable clinical outcome. Although the duration of complete resolution of symptoms usually last for several weeks and is dependent to half-life of regeneration of neural synapses, in our experience, most of patients revealed at least partial relief in early phase after treatment.

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**Epidemiology of pyrazinamide-resistant tuberculosis in a low-incidence setting**

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**Background:** Pyrazinamide (PZA) is a central component of first-line and second-line regimens for treatment of both susceptible and multidrug-resistant (MDR) tuberculosis (TB). Spain is a low-incidence TB country with an increase burden of MDR TB cases but little is known regarding the prevalence of PZA monoresistance, and PZA resistance in drug susceptible as well as MDR-TB isolates. We aimed to investigate the prevalence of PZA mono-resistance and PZA resistance among susceptible and MDR-TB isolates.

**Materials/methods:** we carried out a search of all isolates reported as PZA resistant in a tertiary referral hospital in Madrid, Spain, between 2016 and 2019. PZA susceptibility testing of these isolates was performed by using the automated BACTEC MGIT 960 system. Isolates with an initial result of PZA resistance were sent to the national reference laboratory for repeat susceptibility testing and for pncA sequencing.

**Results:** During the study period a total of 256 culture-positive TB cases were reported in our hospital. Of these, we identified 15 PZA resistant strains (5.9%). 11/15 were PZA-monoresistant and 4/15 were PZA-resistant MDR cases. Of the 11 PZA-monoresistant isolates, 9 were identified as *M. bovis* and 1 was identified as *M. bovis* BCG. The remaining isolate was identified as PZA-monoresistant *M. tuberculosis*. Among the 15 PZA-resistant strains, 3 different mutations were detected; C169G (H57D), A29G (Q10B), and A422C (Q141P). C169G (H57D) was only detected in *M. bovis* species. The remaining two mutations were found in MDR strains. No mutation was detected in the PZA-monoresistant *M. tuberculosis* isolate.

**Conclusions:** This study demonstrates that, in our setting, PZA monoresistance is a reliable marker of *M. bovis* species since only one isolate of *M. tuberculosis* was identified as PZA-monoresistant. Consistent with that reported in the literature, PZA resistance was mostly detected in MDR strains.

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Nanoparticles loaded with extracts of Brucella abortus vaccine (strain RB51) trigger protective immune responses in murine macrophages and splenocytes

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Background: Brucella sp. is a facultative intracellular pathogen able to survive within macrophages by inhibiting phagolysosome fusion and perturbing the early immune response to infection. This in vitro study evaluated the protective effect of hydrogel nanoparticles (NP) containing Brucella abortus vaccine (strain RB51) in murine macrophages and splenocytes.

Materials/methods: The protein extracts were obtained by the hot water extraction method and characterized by LC-MS/MS prior to its encapsulation by supercritical anti-solvent method. Peritoneal macrophages and splenocytes were obtained from 8-12 weeks old C57BL/6 mice. Macrophages were seeded at 5x105 /well in 24-well plates. Splenocytes were seeded at a density of 4x106/ml in 6 well plates. Cells were cultured in the presence of NP [20 µg/mL protein equivalent] and collected at different time points [6 hours, 1, 2 and 3 days]. Total RNA was extracted and reverse-transcribed to generate cDNA for SYBR-Green based qPCR analysis of the following genes: IL-2, IL-4, IL-6, IL-10, IL-12a, IL-17a, IL-23a, IFN-gamma, TNF-alpha and Tgfb1. 18S and beta-actin genes were used for the normalization of the qPCR data.

Results: Macrophages: NP strongly induced the upregulation of IL-6, TNF-alpha and IL-12a mRNAs [1777, 104 and 373 fold increase, respectively] after 6 hour incubation, and also led to a mild upregulation of IL-23a mRNA [20 fold increase] and very slight upregulation of IL-10 [4 fold increase]. Upregulation of these transcripts peaked at 6 hours. Splenocytes: NP induced the expression of IL-2, IFN-gamma and IL-17 transcripts gradually increased up to a maximum level on day 3 [8.6, 13.1 and 25.7 fold increase, respectively]. The levels of mRNA for Th2 cytokine IL-4 remained unaltered.

Conclusions: NP were able to trigger a pro-Th1 response (IL-12a, p<0.001), pro-Th17 response (IL-23a, p<0.001) and pro-inflammatory response (IL-6, p<0.001) in mouse macrophages, and a Th1 response (IL-2 and IFN-γ, p<0.001) and a Th17 response in mouse splenocytes. Both Th1 and Th17 responses are key to the elimination of Brucella sp.

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Abstract 5426

**Prospective observational study of antimicrobial stewardship programmes in Brazil: preliminary results**

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**Background:** The worldwide trend of the clinical management of antimicrobial use through the Antimicrobial Stewardship Program (ASP) aims to rationalize therapy. The need to diagnose the Brazilian national scenario is essential to define strategies due to regional differences and standardize governmental norms. In this context, the lack of national hospital data contributed to the study performance.

**Materials/methods:** This is a national, cross-sectional prospective study, containing preliminary data from 954 (56.0%) hospitals with Adult Intensive Care Unit (ICU), corresponding to 25,565 beds, from all 27 Brazilian states, including the variables that contributed and favored the implementation of ASP. Data collection was carried out from July to August 2019.

**Results:** Of the 954 hospitals, 453 (47.5%) declared that they had the ASP implemented and among the most frequent factors that contributed to the program were: 369 (81.5%) had support from the hospital’s senior management; 343 (75.7%) had availability of clinical protocols based on the institutional profile; 276 (60.9%) had support and adherence from prescribing physicians and 259 (57.2%) had the official definition of a multiprofessional group (managing team) responsible for the creation of the ASP. Among the main reasons that delayed the implementation were: 202 (44.6%) components of the operational team had not defined or enough time to perform the ASP activities; 134 (29.6%) lack of information technology support; 173 (38.2%) met resistance or opposition from the hospital prescribing physicians and 116 (25.6%) lacked commitment of the hospital teams to implement the ASP norms.

**Conclusions:** ASP is a viable strategy for the optimization and rational use of antimicrobials in developing countries. In Brazil, this plan is still under development, but will contribute to objective actions in the ICUs led by the government, with an important impact on the sustainability of antimicrobial resistance dissemination control in the country.

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Background: Diabetes Mellitus (DM) increases the risk of developing Tuberculosis (TB) infection up to 3 times and causes unfavorable treatment outcomes. It has been described that the association between DM/TB reaches 15.3% worldwide and in Latin America it can be 7.7%. This work described the clinical presentation and the outcomes to treatment of patients with a history of DM and active TB infection treated in a health institution in Cali, Colombia between 2011-2018.

Materials/methods: a cases series of patients with diagnosis of TB and history of DM reported in the institutional registry of Mycobacteria at University Hospital Fundación Valle del Lili, Colombia, between 2011 and 2018 were described. The exploratory analysis of data for evaluation of outliers and lost data was carried out. Categorical variables were summarized in tables of absolute and relative frequencies; the quantitative variables were reported according to their distribution using measures of central tendency and dispersion.

Results: Of the 1097 records of patients examined during the study period, 69 were found with a history of DM and TB infection (6.2%); the majority of patients were men (54%), of mixed-race (61%) with a median age of 63 years old (Interquartile Range - RIC: 55-77 years old); smoking was the most outstanding antecedent (27%). The pulmonary location of the infection was the most frequent presentation (72%); Fever (61%), weight loss (58%) and cough (55%) were the most commons symptoms. In 81% of the patients, microbiological confirmation was achieved, mostly by smear microscopy (53.6%). 70% of the subjects with known outcomes met the cure criteria, 13% failed and 10.14% died.

Conclusions: we recommend to develop models of differential integral health care in diabetics patients, to assess the risk of developing TB, since almost a quarter of the diabetic population may have unfavorable treatment outcomes.

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Abstract 5432

**Evaluation of the performance of the Dynamiker Fungus (1-3)-β-D-glucan assay for the diagnosis of invasive aspergillosis in high-risk patients with haematological malignancies**

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**Background:** Non-culture-based methods, like detection of circulating galactomannan (GM) and (1-3)-β-D-glucan (BDG), are important adjunctive diagnostic tools for invasive aspergillosis (IA). Until recently, only the Fungitell® assay (Associates of Cape Cod) has been commercially available (CE marking and FDA approval) for BDG testing. This changed with the release of the Dynamiker® Fungus BDG assay (CE marking), which contains detachable microplate rows allowing the test to be performed on a few clinical samples. We therefore evaluated the performance of the Dynamiker® Fungus assay in serum of high-risk haematological patients for the diagnosis of IA providing comparative data with the Fungitell® assay.

**Materials/methods:** During 4/2013-7/2015, a total of 173 serial blood specimens from 62 patients with haematological malignancies (35 AML, 9 ALL, 2 MDS, 2 NHL, 14 other) were collected twice-weekly and tested for GM (Platelia Aspergillus EIA) and BDG (Fungitell®/Dynamiker®). 19/62 (31%) patients had probable IA and received voriconazole, while 43 had no IA according to the EORTC/MSG criteria. The BDG assays were performed following the manufacturer’s instructions and the samples were considered positive, indeterminate/inconclusive or negative based on the BDG levels of <60, 60-79, ≥80 pg/mL (Fungitell®) and <70, 70-95, >95 pg/mL (Dynamiker®), respectively. The BDG values generated by the two assays were compared quantitatively (Spearman analysis) and qualitatively (3x3 x² analysis). Sensitivity/specificity rates and positive/negative predictive values (PPV/NPV) were calculated for each BDG assay.

**Results:** The mean absolute and relative difference between the BDG values of the assays tested was 50 pg/mL and 14%, respectively. BDG concentrations generated by the two assays were linearly correlated (slope 0.65±0.03, r²=0.73) with high degree of correlation [Spearman r (95%CI)=0.91 (0.88-0.94), p<0.0001]. Sensitivity, specificity, PPV and NPV was 73%, 50%, 23%, 90% for Fungitell® and 68%, 63%, 28%, 91% for Dynamiker®, respectively. Statistically significant correlation was found between the assays [χ²(4)=121.7, p<0.0001] with 85% agreement and 6% major discrepancies [Fungitell® negative/positive → Dynamiker® positive/negative and vice versa].

**Conclusions:** The Dynamiker® Fungus BDG assay is a useful complementary test for diagnosing IA, with technical flexibility to assist laboratories that process a small number of samples.

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Abstract 5433

Performance of VITEK 2 AST-GN meropenem/vaborbactam for antimicrobial susceptibility testing of Enterobacteriaceae and Pseudomonas aeruginosa: a multi-centre study

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Background: Meropenem/Vaborbactam (MEV), a β-lactam combination antimicrobial consisting of meropenem, a carbapenem, and vaborbactam, a beta-lactamase inhibitor, is indicated for treatment of patients 18 years and older with complicated urinary tract infections (cUTI) including pyelonephritis caused by designated susceptible bacteria. In this study, the performance of VITEK® 2 AST-GN MEV with Enterobacteriaceae and Pseudomonas aeruginosa was evaluated against the CLSI broth microdilution (BMD) reference method.

Materials/methods: A total of 526 clinical and challenge isolates, including 449 Enterobacteriaceae and 77 Pseudomonas aeruginosa were tested by VITEK® 2 AST-GN MEV and BMD reference at four clinical trial sites. Results were analyzed for essential agreement (EA), category agreement (CA), major error (ME) and very major error (VME) rates following the ISO performance criteria and (EA and CA ≥90%, ME and VME ≤3.0%) and using EUCAST breakpoints for Enterobacteriaceae and Pseudomonas aeruginosa (S ≤ 8µg/mL, I = N/A, R ≥ 16µg/mL).

Results: VITEK® 2 AST-GN MEV clinical trial performance is summarized below for Enterobacteriaceae and Pseudomonas aeruginosa. VITEK® 2 AST-GN MEV met the ISO susceptibility performance criteria for EA, CA, ME and VME, when applying EUCAST breakpoints.

<table>
<thead>
<tr>
<th>Claimed Species</th>
<th>EA%</th>
<th>CA%</th>
<th>mE%</th>
<th>ME%</th>
<th>VME%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacteriaceae</td>
<td>98.2</td>
<td>99.6</td>
<td>N/A*</td>
<td>0.2</td>
<td>3.0</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>93.5</td>
<td>98.7</td>
<td>N/A*</td>
<td>1.5</td>
<td>0.0</td>
</tr>
<tr>
<td>Enterobacteriaceae and Pseudomonas aeruginosa combined</td>
<td>97.3</td>
<td>99.4</td>
<td>N/A*</td>
<td>0.4</td>
<td>2.2</td>
</tr>
</tbody>
</table>

*Minor errors (mE) are not applicable as there is no intermediate category.

Conclusions: When compared to the reference BMD method, results of this multi-center study support the acceptable performance of VITEK® 2 AST-GN MEV for determining the susceptibility of Enterobacteriaceae and Pseudomonas aeruginosa in a clinical setting.

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The importance of CXCL13 cytokine as a biomarker in the molecular diagnosis of Lyme neuroborreliosis versus multiple sclerosis

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Abstract third-party references: Leptospirosis and Lyme Borreliosis laboratory, Medical Microbiology Unit, Tropical Medicine Global Health and Tropical Medicine (GHTM), Institute of Hygiene and Tropical Medicine (IHMT), Universidade NOVA de Lisboa (UNL), Lisbon, Portugal

Background: Lyme Borreliosis (LB) is a multisystemic disease caused by spirochetes, belonging to the *Borrelia burgdorferi* sensu lato complex, which includes different pathogenic species. The transmission of these spirochetes occurs by ixodid ticks bite. In Portugal, LB is often under-diagnosed due to the clinical polymorphism. Diagnosis is mostly clinical and epidemiological. When untreated, the disease can progress to Lyme Neuroborreliosis (LNB). Sometimes it is difficult for the laboratory to help the clinician in the diagnosis of this disease. Thus, it is crucial to develop/testing methods that support a more efficient diagnosis. The goal of this work was to understand the role of CXCL13 as a biomarker for diagnosis of LNB vs. Multiple Sclerosis (MS) in cerebrospinal fluid (CSF) samples from patients suspected or diagnosed of LB since it is known that human-specific cells (monocytes, macrophages, and dendritic cells) produce this cytokine.

Materials/methods: CSF samples (N=327) were used, and the concentration of the CXCL13 in CSF (cut-off 30pg/ml) was determined using an ELISA assay. For detection of anti-*B. burgdorferi* s.l., antibodies, and amplification of its DNA, the samples were analyzed by immunofluorescence (IFA) and nested-PCR [intergenic space 23S (rrl)-5S (rrf) and flaB gene], respectively.

Results: The CXCL13 cytokine was quantified in 88/327 samples [6/88, corresponding to LNB patients (>250pg/ml) and 82/88 to probable cases (>30pg/ml) if neurological symptoms were present], and in 24/327 the results were borderline (20-30pg/ml). Samples with high concentrations of CXCL13 were associated with LNB, or MS. IFA results showed (5+/197) and six borderline samples. The evaluation by nested-PCR targeting flaB gene and intergenic space, showed (2+/125) and (9+/323), *Borrelia* DNA detection, respectively. Overall, the results of the various laboratory approaches showed the presence of anti-*B. burgdorferi* antibodies in 6% (11/197), while the test under study quantified the CXCL13 cytokine by 34% (112/327) of the total CSF samples. On the other hand, *Borrelia* DNA detection was only 2-3%.

Conclusions: This cytokine proved to be an important and promising biological marker for late LB, supporting namely the diagnosis of LNB vs. MS, as well as distinguishing several diseases from Central Nervous System (CNS).

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Clinical features related to \textit{blaKPC} versus \textit{blaNDM} carbapenem-resistant \textit{Enterobacteriaceae} bacteraemia: are we talking about the same?

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\textbf{Background}: Carbapenem-resistant Enterobacteriaceae (CRE) infections are a significant public health issue. CRE-\textit{blaKPC} events are predominant, even though other CRE infections (e.g.: CRE-\textit{blaNDM}) are arising in several countries. Hence, understanding their particular clinical features could be an important tool for their proper management. Our aim was to compare clinical characteristics between CRE-\textit{blaKPC} vs. CRE-\textit{blaNDM} bacteraemia. The secondary objective was to contrast 14-day mortality.

\textbf{Materials/methods}: Retrospective and observational study which included patients with CRE-\textit{blaKPC} or CRE-\textit{blaNDM} bacteraemia from a tertiary hospital of Buenos Aires Province (Argentina) from January 2016 to September 2019. Consecutive episodes were matched 1:1 by each mentioned CRE. Patients who died before 48h of bacteremia onset and those who did not receive empiric therapy were excluded. Any antimicrobial combination with at least one active drug or scheme based on time-killed curve were taken into account for the analysis. Cultures and susceptibility tests were performed according to CLSI guidelines. Molecular techniques were used to confirm resistance mechanisms. Univariate analysis and logistic regression were executed by EPI-INFO™7.2.

\textbf{Results}: Out of 54 infections, 31 were eligible (51.6% CRE-\textit{blaKPC}, 48.4% CRE-\textit{blaNDM}). 64.5% were male and median age was 71 years (IQR23). 38.7% (n=12) died before 14 days. Previous carbapenem use was related to CRE-\textit{blaNDM} (OR 6.5 [95% CI 1.3-33.0] \textit{p} 0.03). On the other hand, time to institution of definitive therapy was longer in CRE-\textit{blaNDM} episodes, albeit that, it did not reach statistical significance (8 vs. 7 days \textit{p} 0.07). Differences in shock at bacteremia onset, source of infection and effective empiric therapy were not evident. After adjusting analysis, only prior prescription of carbapenem (aOR 96.7 [95% CI 2.2-4169] \textit{p} 0.02) was linked to CRE-\textit{blaNDM} (Hosmer-Lemeshow \textit{chi}2 14.2 df 8 \textit{p} 0.07). None specific factor was associated to 14-day mortality, even more, this outcome was similar between both groups (OR 0.6 [95% CI 0.2-2.8] \textit{p} 0.5, logrank \textit{p} 0.9).

\textbf{Conclusions}: Our findings suggest that previous carbapenem use was strongly associated to CRE-\textit{blaNDM} bacteraemia. Nevertheless, no other differences could be spotted between both groups, including 14-day mortality. For the reasons given, we do not recommend guiding empirical treatments only by clinical features.

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Abstract 5439

**Value of soluble programmed death-1 (sPD-1) and sPD-ligand-1 (sPD-L1) as early biomarkers for the post-surgical monitoring of cystic echinococcosis in Tunisian paediatric patients**

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**Background:** Cystic echinococcosis (CE) is a major health problem in African countries, including Tunisia. The post-surgical management of CE is facing relatively high rates of recurrences, which often could not be early detected by imaging techniques or available serological tests. Here, we evaluated the prognostic accuracy of laboratory tests including soluble programmed death-1 (sPD-1) and sPD-1 ligand (sPD-L1) in CE.

**Materials/methods:** A total of 62 Tunisian children (186 sera), surgically treated for CE and monitored for 1 post-operative year, were included in this prospective study. Twenty-six young patients presented pulmonary cysts, 18 and 16 cases had hepatic and multiple CE, respectively. Unusual localizations were detected only in two children (1 peritoneal lesion and 1 cyst located in spleen). Based on post-surgical outcomes and clinical courses of CE infection, patients were clustered into the cured CE group (CCE; n = 40) and the non-cured CE (NCCE; n = 22). For each patient, 3 plasma samples were obtained at the main time points of the follow-up period; 1 pre-operative sample (D0), 1-month (D30) and 1-year (D365) post-surgery specimens. Concentrations of sPD-1 and sPD-L1 were measured using ELISA commercial kits (Invitrogen, Thermo Fischer Scientific, Austria). We applied the Wilcoxon test to compare the expression levels of sPD-1 and sPD-L1 between the three points of time in the CCE and NCCE groups.

**Results:** Our results showed significant increase in sPD-1 levels 1-month after surgery compared to pre-operative titers (p = 0.004), followed by a considerable decrease after 1-year (p < 0.001), exclusively in CCE. Soluble PD-L1 exhibited significant decrease of levels 1-year in CCE group compared to 1-month concentrations (p = 0.04) but no significant difference was observed between pre-operative and 1-month levels. In contrast to CCE, the kinetics of both sPD-1 and sPD-L1 in NCCE group exhibited a similar pattern marked by unchanged levels throughout the whole monitoring period.

**Conclusions:** Our study revealed that sPD-1 showed a better performance than sPD-L1 for the post-surgical follow-up of CE cases, since it could clearly provide an early information regarding the effectiveness of therapy and the most probable clinical outcome of CE patients.

**Figure:** Evolution of sPD-1 (A) and sPD-L1 (B) levels during the monitoring period in CCE and NCCE patients. A. Median sPD-1 levels compared in CCE. a. D0 versus D30. b. D0/D30 vs D365. B. Median of sPD-L1 levels. c. compared in CCE D0/D30 vs D365. *P < 0.05; **P < 0.01, ***P < 0.001

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Differences in the lower respiratory tract microbiota in patients with severe pneumonia of viral or bacterial origin

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Background: Composition of pulmonary microbiota of patients with severe pneumonia is still poorly known.

Materials/methods: Patients were involved in the study on the basis of clinical and radiological findings. Conventional microbiological studies included urinary antigen test for Streptococcus pneumoniae and Legionella pneumophila detection, blood and respiratory samples cultures and PCR for the detection of respiratory virus and some bacterial (atypical pneumonia) pathogens.

Mini-BAL samples of 11 patients with severe pneumonia admitted to the ICU between January and June 2019 were collected in the first 24 hours since initiation of antimicrobial treatment. Nucleic acids from 1 mL of the mini-BAL samples were extracted using the NUCLISENS easyMAG platform (bioMérieux). Microbiome was studied using the Ion 16S Metagenomics Kit (Thermo Fisher Scientific) that amplifies 7 hypervariable regions of the 16S rRNA gene. Libraries were sequenced in the Ion PGM sequencer and data analysed with the Ion Reporter software 5.1 using the consensus data of all variable regions. The study was approved by the regional Ethics Committee

Results: In 3 cases Influenza virus AH1 was detected, in 1 Influenza virus AH3, in 1 Respiratory syncytial virus (RSV), in 1 Rhinovirus, in 1 L. pneumophila and in 4 S. pneumoniae.

In the lung microbiome of patients with Influenza pneumonia there was a predominance of Firmicutes (mainly Streptococcus, Staphylococcus and Veillonella at the genus level) and Proteobacteria [Moraxella and Pelomonas at the genus level] [Figure]. Patients with RSV and Rhinovirus pneumonia showed more bacterial diversity at the phylum level. Patient 7, with L. pneumophila pneumonia showed 97.5% of Proteobacteria [95% Legionella]. Patient 8, with pneumococcal pneumonia showed a high proportion of Proteobacteria, but at the genus level had the same proportion of Streptococcus and Enterobacteria. The other 3 patients with pneumococcal pneumonia showed a clear predominance of Firmicutes [Streptococcus].

Conclusions: Severe bacterial pneumonia resulted in a respiratory microbiota characterized by the predominance of one phylum, the one causing the infection. The respiratory microbiome in patients with viral severe pneumonia showed a higher diversity. These differences can aid in the diagnosis and prognosis of severe pneumonia.

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Microbiological features of vulvovaginitis in prepubescent girls

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Background: Vulvovaginitis is one of the most common gynecological conditions encountered in pediatric outpatient units. Aim of this study was to evaluate the prevalence of various microorganisms involved in the pathology of vulvovaginitis in girls of prepubertal age over a six-year period.

Materials/methods: A total of 442 girls were included, aged 1–10 years (mean age 6.7 years), presented in the outpatient department of pediatric and adolescent gynecology of our hospital, from January 2013 to December 2018, with signs and symptoms of vulvovaginitis. Vaginal swabs were placed in Stuart transport medium for culture and in normal saline for wet preparation. All samples were referred to microbiology laboratory where standard microbiological diagnostic procedures for bacterial and fungal pathogens were performed. Isolated microorganisms were identified using conventional methods. A rapid latex agglutination test was performed for identification of Lancefield A, B, C, D, F and G group antigens of streptococci (Avipath Strep, Omega Diagnostics). The microorganisms detected were classified as specific pathogens and potential pathogens (bacteria of fecal origin).

Results: Causative agents were isolated in 139/442 (31.4%) of girls studied, whereas in 303/442 (68.6%) no pathogens were identified. Of 139 culture-positive cases, specific pathogens were isolated in 52 (37.4%) and potential pathogens in 87 (62.6%). Specific pathogens were S. pyogenes 29/139 (20.9%), Haemophilus influenzae 11/139 (7.9%), S. aureus 5/139 (3.6%), Candida spp 4/139 (2.9%), Haemophilus parainfluenzae 3/139 (2.1%). Potential pathogens were Enterococcus spp 27/139 (19.4%), Escherichia coli 26/139 (18.7%), other Enterobacterales 23/139 (16.6%), S. agalactiae 9/139 (6.5%), Pseudomonas aeruginosa 2/139 (1.4%).

Conclusions:
1. In a high percentage (68.6%) of symptomatic cases of prepubertal vulvovaginitis no infectious pathogen was isolated.
2. The most common specific pathogen of pediatric vulvovaginitis is S. pyogenes followed by Haemophilus spp.
3. Bacteria of fecal origin are often found in vaginal cultures of prepubescent girls with vulvovaginitis and in these cases treatment should include counseling on vulvovaginal hygiene.
4. Candida spp is a rare cause of vulvovaginitis in prepubescent girls in the absence of predisposing factors.

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Abstract 5442

Improvement of blood cultures processing with full automation in microbiology

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Background: Sepsis is associated with an in-hospital mortality greater than 10%, which increases up to 40% in case of septic shock. The early administration of appropriate antibiotics in patients with severe sepsis and septic shock improves mortality, reduces length of hospital stay, and limits the development of antibiotic resistance. Our objective was to evaluate the impact of fully automation (WASPLab™ COPAN) to reduce the manual work and the turnaround time (TAT) for the preparation of Gram smears and culture set up for all positive BC bottles (BCs).

Materials/methods: a total of 100 BCs bottles from patients with suspected bacteremia were inserted 24/24 h into the BD Bactec®. On positive BCs, using a vacuum tube [COPAN BC+™] an aliquot of 2.5 mL was transferred from positive BC bottle to the BC+™ tube. The BC+™ tube was uploaded on WASPLab™ and Gram smears and culture set up (4 agar plates) was performed. Automatic streaking was performed with 10 µl loop and 4 quadrant streaking patterns. Only for Gram-negative bacteria, a preliminary AST (Vitek 2 CARD) was performed collecting an aliquot of blood culture from BC+™ tube to prepare a 1.5 Mac-Farland dilution. On the same tube, Real Time PCR molecular assays [CRE and Colistin-R ELITe MGB® kit, ELITechGroup Molecular Diagnostics] were performed. For the manual method, two drops of blood culture were used to inoculate each agar plate and one drop of BC was used to prepare manual smears.

Results: to process one BC bottle, the TAT monitored for whole process was 4 min while for manual procedure was exactly the double (8 min). To fill in the BC+™ tube the technician took 20 sec while with the routine method 1 min and 20 sec. Plate seeded by WASP™ had well isolated colonies and usually did not require a subculture. Good agreement between Manual and Automated smears was observed.

Conclusions: the introduction of BCs on WASPLab™ has significantly reduced manual work, has improved the quality of BCs streaking, and reduced the time to reporting. An automated protocol has a clear impact on quality and traceability.

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Emergence of mcr-1 among diverse multidrug-resistant Escherichia coli in gulls from a coastal city uncovers potentially underestimated transmission routes

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Background: The emergence and spread of multidrug-resistant (MDR) bacteria to last-resource antibiotics like colistin is a global and multi-factorial phenomenon transversal to human-animal-food-environmental sectors. Mobile colistin resistance (mcr) genes have been detected in diverse ecological niches, including foodstuffs (e.g. pigs/rabbits/turkey/poultry), hospitalized patients, and sewage/effluents. However, the role of migratory birds as a source of mcr genes is missing. Gulls are increasingly present in big coastal cities, like Oporto, living as opportunistic scavengers in high contact with humans, raising new opportunities for bacteria transmission. This study investigates the presence and genetic background of mcr-carrying E. coli among gulls.

Materials/methods: Gull faecal samples (n=14) obtained in Matosinhos beach, between September 2018 and February 2019, were analysed. Resuscitation of samples (25 g) were performed in Buffered-Peptone-Water-BPW (37°C/1 h) before spreading in TBX-agar+colistin-3 mg/L. The identification of selected colonies (1-5/sample) were performed with MALDI-TOF MS and E. coli were screened for mcr-(1-5) genes. Isolates’ relatedness was examined by phylogenetic groups (PhG) and FT-IR spectroscopy. Antibiotic susceptibility profiles of mcr-1-positive isolates were determined by disk-diffusion or reference broth microdilution method (colistin) (EUCAST/CLSI). Plasmid characterization and location was performed by PCR-PBRT and S1-PFGE-hybridization.

Results: The occurrence of mcr-1 in gull samples was 28% (n=5/14), with 9 colistin-resistant E. coli isolates (MIC=4mg/L) recovered. Those isolates were distinguished in 7 FT-IR-groups belonging to PhG A (n=1), A/C (n=4; 3 samples), B1 (n=1), B2 (n=2; 1 sample) or F (n=1). Three commonly described mcr-associated plasmids were identified: IncHI2 (n=7), IncX4 (n=1) and IncI2 (n=1). Seven isolates were MDR, including to other clinically-relevant antibiotics (e.g. extended-spectrum cephalosporins and fluoroquinolones).

Conclusions: Gulls are an underestimated reservoir of E. coli carrying mcr-1 gene and potential vehicles for their dispersal to other bacteria and ecological niches. Transmission of mcr-1 gene from gulls to humans through contamination of bathing water sources [e.g. beach sand and sea water], food-chain [e.g. fish market] and urban environments [e.g. public water supplies, sewage/effluents] should not be disregarded. Global re-assessment of colistin use in food-animal production, monitorization of mcr in sentinel species, sewage/effluent treatments and programs for control of gull population are urgently needed in a One Health context.

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Comparison of Hospital Resource Utilisation (HRU) among patients who received either ceftolozane-tazobactam (C/T) or meropenem in ASPECT-NP: a randomised, controlled, double-blind study of adult patients with Ventilated Nosocomial Pneumonia (V-NP)

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Background: In ASPECT-NP, C/T 3000 mg q8h was non-inferior to meropenem 1000mg q8h for both 28-day all-cause mortality and clinical cure for the treatment of patients with V-NP. Given the substantial economic burden associated with V-NP, assessments of HRU were prospectively incorporated in the trial. This analysis compares HRU measures in patients who received C/T or meropenem in ASPECT-NP.

Materials/methods: Patients in the microbiological intent to treat (mITT) population (received ≥1 dose of study drug and had ≥1 Gram-negative pathogen[s] isolated from the lower respiratory tract at baseline, susceptible to at least one of the study drugs) were included. HRU measures collected post-randomisation until day 28 were hospital length of stay (LOS), ICU LOS, duration of mechanical ventilation (MV), and discharge/extubation status. HRU comparisons by key baseline covariates were also performed; results reported % and mean days.

Results: 511 patients (C/T=264, meropenem=247) were included. At enrollment, 100% were receiving MV, 385 (75.3%) had ventilator-associated pneumonia, and 474 (92.8%) were in the ICU. Average hospital LOS was approximately a day longer for C/T-treated patients (C/T: 22.0 days vs. meropenem: 21.1 days). There were fewer deaths in C/T versus meropenem (20.1% vs. 24.3%). More C/T-treated patients were discharged from the ICU (C/T: 57.3% vs meropenem: 54.6%). Among ICU discharged patients, C/T-treated patients were discharged earlier (C/T: day 13.7 vs. meropenem: day 15.2). A higher proportion of C/T treated patients were extubated by day 28 (51.9% vs. 48.2%). Among those extubated, C/T treated patients were extubated earlier (C/T: day 8.5 vs. meropenem: day 9.8). Fewer C/T-treated were re-intubated during the 28-day study period (C/T: 7.5% vs. meropenem: 10.0%). Among VABP (n=385), C/T-treated patients had a shorter ICU LOS (C/T: 16.5 days vs. meropenem: 18.1 days) and MV duration (C/T: 15.1 days vs. meropenem: 16.8 days). Among patients with Pseudomonas sp. (n=128), C/T treated patients had a shorter ICU LOS (C/T: 15.7 vs. meropenem: 18.5) days and MV duration (C/T: 13.3 vs. meropenem: 15.2) days.

Conclusions: Results suggest that C/T was associated with lower day 28 HRU relative to meropenem in the mITT population and among patients with VABP and Pseudomonas sp in ASPECT-NP.

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Abstract 5448

Improvement of self efficacy and problem solving abilities in infection prevention staff, link nurses and physicians. Evaluation of a national workshop tour by the national hand hygiene campaign “AKTION SAUBERE HAENDE” in Germany

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Background: Effective sustainable implementation of infection prevention and control (IPC) often relies on designated link nurses and physicians. Those are usually healthcare workers (HCW) which are trained in a 40 hour course. We evaluated if a workshop primarily targeted at link staff performed on site could empower the target audience.

Materials/methods: We performed an anonymous online survey with a validated questionnaire consisting of 54 items in 31 German hospitals. The survey was sent to the local organizing committee for distribution to participants three months prior and after the date of the workshop. Only answers by HCW working either as IPC or in a link position were included into the analysis. In addition to structural parameters the questionnaire consisted mostly of closed questions with 5 step Likert scales. Those items were grouped into five different topics.

1. Knowledge on hand disinfection as an infection prevention measure
2. Capability to support HCW in improving their compliance to hand hygiene
3. Identifying risks for patient safety and providing adequate solution strategies
4. Persuasion that a constructive feedback culture is beneficial to patient safety
5. Awareness of the influence of communication on improvement of patient safety.

Scores for each topic were calculated and multivariate regression analyses were performed for each of the five topics to identify independent factors influencing scores.

Results: Of an approximate number of 918 participants, 389 answered prior to and 185 after the workshop. The majority of HCW chose the link position by themselves (69%) and was not select by superiors (70%). They identify with the link role (96%). While scores increased significantly for all five topics in the group after the workshop. Regression analysis identified timing of the survey after the workshop only to be independent factor for higher scores in topics 2-4. Being a link physician was independently associated with lower scores when compared to IPC staff.

Conclusions: The workshop was effective in empowering link HCW in areas. We identified that IPC staff in our sample were highly motivated and have chosen position on their own will. Link physicians were identified as a potential target group for future interventions.

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Abstract 5449

**Duration of antibiotic prescription in the management of prosthetic joints infection in France: a national audit**

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**Background:** Prosthetic joint infections (PJI) are one of the most serious complication of arthroplasty. The management of PJI needs a multidisciplinary collaboration between, at least, orthopaedic surgeon, infectious disease specialist and microbiologist. The management of PJI in France is organized around reference centres named CRIOACs. Considering the heterogeneity of PJI and the global low level of evidence available, our main objective was to perform an audit through a questionnaire survey based on clinical case, to evaluate how French physicians manage in daily care PJI.

**Materials/methods:** Eligible participants were all physicians involved in care of patients presenting a PJI. Physicians could answer individually, or collectively during a multidisciplinary team meeting dedicated to PJI. The survey consisted as three questionnaires organized in a total of six clinical cases.

**Results:** Answers from the CRIOACs to the three questionnaires were 92%, 77%, and 53%. Respectively 65%, 58%, and 86% of respondents were answering as individuals.

After a 1-stage exchange surgery for a late *S. aureus* PJI, total antibiotic regimen duration was 4-6 weeks (16%), 6-8 weeks (49%), 8-12 weeks (33%), or six months (1%); and for a late *S. agalactia* PJI six weeks (37%), eight weeks (4%), or 12 weeks (59%).

After a 2-stage exchange surgery for a late *E. faecalis* PJI, total antibiotic regimen duration was eight weeks (six weeks between explantation and implantation, and two weeks after implantation) (45%), 10 weeks (5%), or 12 weeks (six weeks between explantation and implantation, and six weeks after implantation) (24%).

After a debridement without any exchange of the mobile components for an acute *S. aureus* PJI, total antibiotic regimen duration was six weeks (26%), three months (68%), or suspensive (4%). After arthroscopic lavage for *S. aureus* native joint septic arthritis, total antibiotic regimen duration was three weeks (6%), four weeks (35%), six weeks (53%), eight weeks (1%), or 12 weeks (3%).

**Conclusions:** Despite PJI is a common infection, its medical management is still heterogenous, reflecting the lack of evidence and the numerous different possible combinations depending on the clinical presentation and the pathogen involved.

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Abstract 5452

Regional lymphadenopathy caused by Bartonella henselae among children: a single-centre study

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Background: The aim of this study was to analyze lymphadenopathy caused by B. henselae among children treated at the University Hospital for Infectious Diseases, Zagreb, from January 2014 until June 2019.

Materials/methods: We retrospectively analyzed epidemiology, clinical and laboratory characteristics along with ultrasound features of lymphadenopathy among children with positive indirect immunofluorescence assay for B. henselae IgM and IgG or positive B. henselae polymerase chain reaction (PCR) from lymph node aspirate.

Results: A total of 95 patients were enrolled in this study, 52 (54.7%) males and 43 (45.3%) females. A history of cat contact was present in 92 (96.8%) children. Acute infection was serologically confirmed in 78 (82.1%), in 5 (5.3%) with PCR while both methods were positive in 12 (12.6%) patients. Lymphadenopathy without fever was present in 51 (53.6%) patients. Axillary lymph nodes were most often affected (42 patients, i.e. 44.2%), followed by cervical in 37 (38.9%), inguinal in 15 (15.1%) and supraclavicular in 1 (1.0%) patient. Average lymph node size according to ultrasound was 2.8 cm (range, 1.8 to 5.5 cm).

Fine-needle aspiration of the affected lymph nodes was performed in 47 (49.5%) patients. The lymph node aspirate was assessed histopathologically and microbiologically, as well as by molecular methods. Histopathologically, 20 (42.5%) were cases of lymph node hyperplasia, 11 (23.4%) lymph node hyperplasia with granulomatous inflammation, 12 (25.5%) supplicative inflammation and 4 (8.5%) were cases of suppurative necrosis. Cultured lymph nodes aspirate were positive for Staphylococcus aureus in 3 and coagulase-negative staphylococci (CoNS) in 2 patients. Along with lymphadenopathy, hepatosplenomegaly was found in 5 (5.3%) and Parinaud's syndrome in 1 (1.05%) patient. The average white blood cell count was 9.9 x 10⁹/L, while the average value of C-reactive protein was 23.02 mg/L. Azithromycin was the most commonly prescribed antibiotic (76.8%, n=73). Surgical drainage of the lymph node was performed in 10 (10.5%) patients. Full recovery was the most frequent outcome (98.9%, n=94).

Conclusions: B. henselae infection among children is usually a mild disease often presenting as regional lymphadenopathy. Serology and PCR are useful tests for diagnosis. Treatment duration and choice of therapy depends on clinical manifestations and developed complications.

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Impact of the FILMARRAY gastrointestinal polymerase chain reaction panel on the clinical management of children with suspected acute bacterial diarrhoea

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Background: The FilmArray Gastrointestinal polymerase chain reaction panel (GI-PCR) is a multiplex molecular assay allowing simultaneous detection of 22 pathogens in 1 hour (13 bacteria, 5 virus and 4 parasites). The objective was to assess the impact of the results of the GI-PCR on the clinical management of children with acute diarrhea consulting in a pediatric emergency department of a tertiary care center.

Materials/methods: All children admitted in the pediatric emergency department of Robert-Debré, universitary hospital, Paris, France, from May to October 2019, for an acute diarrhea with medical indication for stool culture were included in this prospective monocentric study. Indications for stool culture followed European guidelines. A GI-PCR was performed on each stool sample. Data on children initial care and on changes in their medical management following GI-PCR results were collected.

Results: 176 children were included. The median age was 1 year and 10 months old, IQR (6 months; 6 years old). The main indications for stool culture were bloody diarrhea and/or traveller’s diarrhea (74% of cases). The GI-PCR was positive in 70% of cases. Enteroaggregative Escherichia coli (22%), enteropathogenic E. coli (20%), Shigella/ enteroinvasive E. coli (15%) and Campylobacter (12%) were the most commonly detected pathogens. PCR-GI compared to stool culture detected respectively 21 versus 19 Campylobacter, 12 versus 10 Salmonella and 27 versus 13 Shigella/ enteroinvasive E. coli.

Results of the GI-PCR resulted in a change of medical care for 60 patients (34%) before stool culture results (28 initiations, 4 changes and 1 discontinuation of antibiotic therapy; 2 hospitalizations; 4 specific Clostridium difficile isolations; 36 decisions to call parents by phone; 7 additional test prescriptions and 3 test cancellations). The most prescribed antibiotic following the GI-PCR results was azithromycin (22 cases) for Shigella/ enteroinvasive E. coli (n=11), Campylobacter (n=6) and Shigatoxin-producing E. coli (n=5) infections. A cost analysis was carried out.

Conclusions: The GI-PCR has a significant impact on the prescription of antibiotics before the results of stool culture in children with bacterial suspected acute diarrhea. Further studies are needed to better assess the cost-effectiveness of this assay.

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Impact of early carbapenemase notification on infection control management and antimicrobial stewardship

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Background: The worldwide spreading of carbapenemase-producing Enterobacterales (CPE) is a matter of concern due to the limited therapeutic options available. In severe infections, an early carbapenemase detection and notification is crucially important.

Materials/methods: During a one-year follow-up survey (August 2017 to August 2018), an observational study was performed in patients at a tertiary hospital from Porto Alegre, Brazil. Enterobacterales isolates recovered from any clinical specimen were submitted to blue-carba test (BCT) for phenotypic carbapenemase detection. Isolates were identified using Vitek 2 and antimicrobial susceptibility testing determined by disc-diffusion or broth microdilution. Carbapenemase characterization was carried out by phenotypic tests using specific inhibitors. The main objective was to determine the time from culturing sample until CPE notification in comparison with the time to report a final microbiology result (bacterial identification plus antimicrobial susceptibility testing), also, we aimed to evaluate the burden of this notification for the infection control measures and antimicrobial resistance predictability.

Results: A total of 300 CPE notifications were made, including 155 distinct patients. Average time was 1.19 days for CPE notification vs. 2.38 days for final report (Figure). KPC-producing Klebsiella pneumoniae was the most prevalent agent (97%; 291/300) and no other carbapenemase than KPC was detected in this period. Apart from that, antimicrobial resistance was observed as follow: meropenem 97.7%, gentamicin 77.6%, fosfomycin 31.6%, polymyxin 29%, amikacin 7.3% and tigecycline 5%. For the infection control point of view, 16% and 78% patients were previously clustered in standard and contact precaution, respectively, based on a BCT notification.

Conclusions: CPE notifications allow an earlier intervention (at least 24h). Additionally, the knowledge of the susceptibility profiles [and carbapenemase type] promoted an empirical adjustment with greater likelihood of adequacy, particularly by use of a combined therapy in cases of a BCT positive. An active communication between laboratory and clinical services is necessary to better explore this notification, significantly reducing the time for a first intervention.

Average time: 2.38

Average time: 1.19

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Evaluation of the efficacy of vaccination programmes in HIV-positive patients against vaccine-preventable diseases

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Background: Retrospective evaluation of before and after immune responses among the HIV positive patients by the vaccination against vaccine-preventable diseases was the main objective of our study.

Materials/methods: HIV positive patients who were admitted to outpatient or vaccination clinic between the dates of January 1st 2016 – October 8th 2018, were screened retrospectively in a tertiary-care educational hospital. HIV positive patients whose serological results were available before and after the vaccination against Pneumococcus, Hepatitis B and Hepatitis A, were recorded in the terms of demographic features, immune deficiency status and immune responses to vaccinations together with affecting factors. Statistical analysis was performed via Chi square test, p value less than 0,05 was considered significant.

Results: Total number of 128 patients were included in this study. Pre-vaccination and post vaccination immune status was evaluated in 36, 69 and 48 patients for pneumococcal vaccine, hepatitis A and B vaccine, respectively. There was statistically significant increase in pneumococcal antibody titers after the vaccination in HIV positive patients (p=0,000) (Graphic). There was no correlation between the CD4 titer with basal pneumococcal antibody titer and pneumococcal antibody titer after the vaccination. Antibody response rate via vaccination was 81.8% for the patients with CD4 < 350 cell/mm³ whereas 84% for the patients with CD4 ≥ 350 cell/mm³ (p=0,609). On the other hand, Hepatitis B antibody response rate via vaccination was 56,3% for the patients with CD4 < 350 cell/mm³ whereas 88,7% for the patients with CD4 ≥ 350 cell/mm³ which was found as statistically significant (p=0,008). There was no correlation between the HIV RNA levels and Hepatitis B vaccine response rate (p=0,350).

46 out of 48 (95%) Hepatitis A vaccinated HIV positive patients had the immunity after the vaccination.

Conclusions: Pneumococcal vaccination should be done for HIV positive patients according to our study results which shows the enough efficacy of vaccination in HIV positive patients. Although there was no relationship between the CD4 level and pneumococcal vaccine response in HIV positive patients, CD4 level was shown to affect the Hepatitis B vaccine response rate. Finally, vaccination should be performed according to guidelines for the immunocompromised patients.

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Abstract 5458

Rapid diagnosis of seasonal influenza virus and cohorting of hospitalized patients on a ‘flu ward': a prospective analysis of outcomes

Brendan O’Kelly1, Adam Kelly2, Aileen Conway3, Sam Mcconkey2,3, Cora McNally3, Eoghan De Barra2,3

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Background: The influenza season of 2017/2018 was burdensome which was in part due to high incidence of Influenza B compared to previous years. In-patient management of seasonal influenza patients is poorly described.

Materials/methods: A prospective cohort study with enrolment from Jan 1st to Feb 1st 2018. Laboratory Influenza PCR testing was performed on patients seen in the Emergency Department (ED) with possible influenza, with a turn-around time of 1 hour. Patients diagnosed with influenza in the ED were cohortated under an infectious disease (ID) firm or a general internal medicine (GIM) firm on a 35 bed influenza ward. At times of maximum capacity some patients were managed on other wards in single isolation rooms by other firms ‘non flu ward’.

Results: 91 patients were admitted to the influenza ward from ED (64 ID, 27 GIM), 38 of whom had influenza A. 64 (70.3%) received antibiotics, initial route was intravenous in 45 (49.5%). Patients managed by ID were more likely to be switched to oral antibiotics sooner median 3 vs 5 days p=0.049. Antibiotic duration was shorter for patients managed by the ID firm median 7 vs 9 days p=.016. LOS was shorter for patients managed by the ID firm on the flu ward vs ‘non flu ward’, median 5 vs 9 days p=.007. No significant difference was seen between ID and GIM LOS on the flu ward median 5 vs 7 days p=0.30.

Conclusions: Influenza patients managed by an infectious disease service on an influenza ward had a reduced length of intravenous (IV) and total antimicrobial use compared to a GIM service and had reduced LOS compared to the standard of care, ‘non flu ward’ influenza patients. HAI incidence was lowest on record for the hospital.

<table>
<thead>
<tr>
<th></th>
<th>ID</th>
<th>GIM</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>64</td>
<td>27</td>
<td>0.99</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>45 (70.3%)</td>
<td>19 (70.4%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Intravenous (% of initial abx)</td>
<td>32 (71.1%)</td>
<td>13 (68.4%)</td>
<td>0.83</td>
</tr>
<tr>
<td>Days of IV antibiotics (mean)</td>
<td>3.20</td>
<td>4.52</td>
<td>0.049</td>
</tr>
<tr>
<td>Days of IV antibiotics (median)</td>
<td>3</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Days of total antibiotics (mean)</td>
<td>6.74 [SD 3.47]</td>
<td>8.72 [SD 3.56]</td>
<td>.016</td>
</tr>
<tr>
<td>Days of total antibiotics (median)</td>
<td>7</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Deaths</td>
<td>2 (2.2%)</td>
<td>1 (3.7%)</td>
<td>0.89</td>
</tr>
<tr>
<td>Readmission ≤4 weeks</td>
<td>1 (1.1%)</td>
<td>1 (3.7%)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

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**Abstract 5459**

**Candidemia management: can we do better?**

Jorge Calderón*, Jesús Herraiz Jiménez1, Antonio Ramos Martínez1, Elena Muñez Rubio1, Alejandro Callejas1, A. Díaz De Santiago1, Isabel Sanchez Romero1, Marcos Lopez Dosíl1,2, Ana Fernandez-Cruz1

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**Background:** Recently, several scores to quantify candidemia management according to guidelines (EQUAL, GEMICOMED, Valerio) have been developed. We aim to evaluate impact of outcome of candidemia guidelines adherence using these scores and identify improvement opportunities.

**Materials/methods:** Our institution is a 613-bed tertiary teaching hospital in Madrid. We recorded retrospectively epidemiological, clinical and microbiological data from candidemia episodes (January 2017-December 2018). We analyzed candidemia management according to EQUAL, GEMICOMED and Valerio scores, and correlated those to outcome.

**Results:** Fifty-four first episodes of candidemia were retrieved during the study period. Five patients who died < 48h after bloodcultures were not included. Evaluable patients 30-d mortality was 18.4%.

Median adherence to guidelines according to EQUAL score [maximal score 22 if catheter, 19 if no catheter] was 17 (IQR 15-19), and median adherence to GEMICOMED was 86% (IQR 72.5-100%). Least followed recommendations were: daily bloodculture (12.2%), initial echinocandin (57.1%), adjustment to MIC (75.5%), catheter withdrawal <24h (82.1%) [EQUAL]; initial echinocandin in septic or neutropenic patients (71.4% and 37.5%, respectively), change of antifungal class (47%) [GEMICOMED]. Adequacy of antifungal prescription was 8.5/10 (SD 1.9); areas of improvement were: antifungal selection (30.6%), adjustment to antifungigram (26.5%), change to oral route (26.2%) and duration (15.9%) [Valerio].

Patients who died had lower EQUAL score and adherence to GEMICOMED (15 vs 17.1, p=0.041, and 67.7% vs 86.2%, p=0.002, respectively). A cut-off of >=17 for EQUAL, or compliance of <70% of GEMICOMED were associated with inferior 30-d mortality (71% vs 33.3%, p=0.028, and 7.9% vs 54.5%, p=0.002, respectively).

Infectious Diseases Unit [IDU] evaluated 65.3% of patients in 3d (IQR 1-8). IDU-evaluated cases obtained a better EQUAL score (>17) [82.1% vs 42.9%, p=0.006] and had less 30-d mortality (9.4% vs 35.3%, p=0.049)

**Conclusions:** Adherence to guidelines for candidemia management evaluated according to EQUAL and GEMICOMED was associated with a decreased 30-d mortality. There is room for improvement in initial antifungal therapy with echinocandins in septic patients, early catheter withdrawal and antifungal adjustment according to MIC. Adequacy of antifungal prescription can be improved regarding antifungal selection, adjustment to MIC, duration and switch to oral. IDU evaluation improves guideline adherence and mortality.

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Abstract 5461

**Epidemiology and outcomes of *Clostridioides difficile* infections among allogeneic haematopoietic cell transplant recipients in Switzerland: 2009-2019**

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**Background:** *Clostridioides difficile* infection (CDI) represents the leading cause of healthcare-associated diarrhea. Patients undergoing allogeneic hematopoietic cell transplantation (allo-HCT) are a highly susceptible population. In contrast to international treatment recommendations, metronidazole is considered as first line treatment for CDI in Switzerland. We therefore assessed outcomes of CDI among allo-HCT recipients in Switzerland.

**Materials/methods:** Multicenter retrospective cohort study of adult patients with allo-HCT included in the Swiss Transplant Cohort Study (STCS) from 2009-2018. The STCS includes all Swiss centers (University Hospitals of Basel, Zürich, and Geneva) performing allo-HCT. Clinical and laboratory data of all transplant recipients, including CDI episodes and follow-up information in the post-transplant period, are prospectively collected. CDI severity was classified using the Zar score. Preliminary results are presented using descriptive statistics.

**Results:** Overall, 155 episodes of CDI occurred in 134 patients. CDI incidence was 10% (range 5-16% according to center). Median age was 54 years (interquartile range 43-63) and 60% were male. The most frequent underlying hematological diseases were acute myeloid leukemia (44%), acute lymphoid leukemia (17%), and myelodysplastic syndrome (12%). CDI was healthcare-associated in 66% of the cases and was classified as severe in 24 patients (15%). Severe complications occurred in 6 patients (4%): ileus 3, hypotension/shock 2, toxic megacolon 1. Seventy-nine percent of all patients were exposed to antibiotics in the 3 months before CDI diagnosis; 80% were under therapy with proton-pump inhibitors. Thirty-nine patients (25%) were neutropenic at the time of CDI diagnosis. Other predisposing factors were the receipt of immunosuppressant therapy (73%) and/or chemotherapy (37%). Thirty-six patients (23%) suffered concomitantly from gastrointestinal GVHD. Ninety-eight patients (63%) were treated with oral metronidazole, 38 (25%) were managed with a regimen that included oral vancomycin. At least one recurrence occurred in 27 (17%) patients. Overall 30-day mortality was 5% and 1-year mortality 29%.

**Conclusions:** The vast majority of CDI episodes were classified as mild and the most frequently administered therapy was metronidazole. The recurrence rate was 17%, similar to that reported in other populations. These data support further analyses aiming to identify patients likely to benefit most from novel treatment options targeting recurrent CDI.

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Abstract 5464

**Impact of artificial intelligence on time to result in culture-based MRSA screening**

Angela Nowag\(^1\), Nathalie Jazmati\(^1\), Steven Giglio\(^3\), Sarah Wirth\(^1\), Barbara Pohl\(^1\), Xenia Quante\(^3\), Hilmar Wisplinghoff\(^*^1,2,5\)

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**Background:** Introduction of artificial intelligence (AI) has shown to be a way to increase reliability and throughput in culture based MRSA-screening. However, time to result remains a problem in culture-based methods due to the time the organisms need to grow. This study was conducted to evaluate the possibilities of decreasing time to result using AI-based classification of solid culture media.

**Materials/methods:** The APAS\(^\text{®}\) Independence in combination with MRSA Analysis Module was evaluated reading time-series (2-24 hours) of dedicated samples (n= 50). MRSA Screening was performed using the chromID\(^\text{®}\) MRSA (bioMerieux). Samples were processed using the AutoPlak\(^\text{®}\) (Beckman Coulter) and evaluated every 1-2 hours up to 24 hours of incubation. Results of AI-based classification were compared to conventional plate reading by experienced medical technicians and microbiologists.

**Results:** There was high agreement between AI-based and conventional reading. Sensitivity and negative predictive (NPV) value estimates at 24 hours were both 1.0, increasing from 0.65 (NPV, 0.45) at 2 hours to 0.90 (NPV, 0.75) at 7 hours. Specificity varied between reads, increasing from 0.75 at 2 hours to 0.87 at 7 hours. Performance did not vary between individual runs.

**Conclusions:** In this study, sensitivity of the AI-based APAS\(^\text{®}\) Independence system at 2-7 hours was comparable to conventional reading at 18-24 hours suggesting that the time to result can be considerably shortened when AI-based systems are used.

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Faecal calprotectin could help distinguish Clostridioides difficile infection from C. difficile colonisation.

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Abstract 5469

Background: Distinguishing among colonized and infected patients with Clostridioides difficile (CD) is not always an easy task. The availability of NAAT has increased the overdiagnosis and overtreatment. Patients with CD infection (CDI) show higher faecal calprotectin (fCP) concentrations than patients without CDI. Also, patients with severe CDI show higher fCP than patients with mild CDI. Nevertheless, the role of fCP in distinguishing CDI from CD colonization has not been addressed.

Materials/methods: Prospective cohort study. Patients with IBD were excluded. An infectious diseases specialist (IDS), blind to fCP, evaluated and gave recommendations to all cases with toxigenic CD detection from January to June 2019. Patients were classified in group I (presumed CDI) when anti-CD treatment was prescribed without doubts; group II (doubtful CDI) when either the IDP had doubts but gave anti-CD antibiotics or recommended not to treat, but the responsible physician decided to treat; and group III (CD colonization) when the IDP recommended not to treat and the patient did not receive anti-CD treatment during the next month. Original faecal samples were frozen for ulterior Calprotectin ELISA Assay. fCP were compared among group I and III by Mann-Whitney test. Sensitivity, specificity, likelihood ratios and ROC curve were calculated.

Results: 114 patients were diagnosed having toxigenic CD during the study period. Sixty-nine (52.3% women; mean age 68.8 years) were evaluated. Thirty-seven (53.3%) presented positive direct toxin test and 32 (46.7%) presented toxin test negative but NAAT positive for toxigenic CD. Median fCP concentrations was 382.7 μg/g, IQR (126.6-833.9) in group I (44 cases), 126.5 μg/g, IQR (57.4-273.9) in group II (14 cases) and 34.3 μg/g, IQR (20.0-115.4) in group III (11 cases); (p<0.001 for comparison among group I and III). ROC curve value was 0.855. With a cut off of 100 μg/g, sensitivity was 81.8%, specificity 72.7% and positive and negative likelihood ratios were 3 and 0.25, respectively. Fifteen cases in group I and II had fCP levels below 100 μg/g.

Conclusions: fCP could be useful in distinguishing patients that do not need anti-CD antibiotics. If results are confirmed, interventional studies should be performed to demonstrate the utility of fCP in the clinical decision process.

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Abstracts 2020

Abstract 5470

Catheter-related and non-catheter-related bloodstream infections in oncological patients

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Background: Information regarding catheter-related bacteremia (CRB) in oncological patients is scarce. We studied retrospectively all admitted oncological patients who presented an episode of bloodstream infection (BSI) and compared CRB with non-CRB.

Materials/methods: Our institution is a 613-bed tertiary teaching hospital in Madrid, with a 20-bed Oncology ward. We recorded epidemiological, clinical and microbiological data from all BSI from January 2015 to December 2018. We considered CRB both according to IDSA definition and to CDC definition (CLABSI).

Results: We recorded 124 BSI in 107 patients (33 per 1000 oncological admissions) during the study period.

BSI was healthcare-associated in 42.7% and hospital-acquired in 46.8%. Catheter was the main bacteremia source (29%; 46% among 77 patients with central venous line). Gram negative microorganisms were the most prevalent (34.7%), followed by Staphylococci (29.8%), Enterococci/Streptococci 11.3% and anaerobes (0.8%). Polymicrobial BSI accounted for 21.7% episodes. Among 155 isolated microorganisms, 8.4% were MDR. Complications occurred in 5.6% (arthritis 3, endocarditis 2, thrombophlebitis 1, liver abscess 1). ICU admission was required in 4%. In-hospital mortality was 12%, attributable mortality (according to treating physician) and 10-day mortality were both 4%.

When patients with CRB and non-CRB episodes were compared, the independent differential characteristics were as follows: in CRB patients, the most prevalent microorganisms were gram positive (77.8%, vs 38.6%, OR 5.2, p =0.001), persistence of BSI was more common (33.3% vs 11.4%, OR 3.2, p =0.032) and so was recurrence (13.9% vs 1.1%, 16.4, p=0.022).

There were not differences according to sex, age, place of acquisition, kind of underlying neoplasia or tumor stage, neutropenia at the moment of the infection, admission to ICU, empirical therapy, infectious complications or presence of antimicrobial resistance.

Conclusions: The main source of BSI in admitted oncological patients in our centre is catheter, and the most frequent microorganisms involved are gram positives. Furthermore, patients with CRB present persistent and recurrent bacteremia more often. Bacteremia attributable mortality in our study was 4%. To prevent bacteremia and its complications, catheter management should be optimized.

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Abstract 5472

Therapeutic innovation in bone and joint infections: evaluation of the activity of exebacase (CF-301 lysin) on clinical strains belonging to Staphylococcus epidermidis species

Aubin Souche*1,2, Camille Kolenda1,2, Céline Dupieux1,2,3, Raymond Schuch4, Tristan Ferry2,5,6, Frédéric Laurent1,2,3,6, Jérome Josse6

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Background: Staphylococcus epidermidis is one of the main pathogens responsible for bone and joint infections (BJI) and is more prevalent in case of prosthetic material infections. Although not highly virulent, Staphylococcus epidermidis can be involved in chronic infections because of its ability to form biofilm, which protects bacteria from antibiotics and host immune cells and plays a key role in therapeutic failures. Moreover, the prevalence of antimicrobial resistance in Staphylococcus epidermidis strains is worrisome. In this context, the development of additional or alternative therapies for antibiotics targeting the biofilm is a priority.

Materials/methods: The objective of this study was to evaluate, in vitro, the activity of phage lysin exebacase on biofilms formed by a panel (n=19) of Staphylococcus epidermidis clinical strains responsible for BJI. We determined the remaining viable inoculum inside biofilm (plating counting) and the biomass (crystal violet staining) after 24h of exposition to different concentrations of exebacase The effect of exebacase was compared to that of antibiotics currently used to treat BJI at different concentrations (rifampin, vancomycin, daptomycin) and we assessed if synergistic effects could be observed when combining exebacase with these antibiotics.

Results: Our results demonstrate that exebacase had a significant anti-biomass effect against Staphylococcus epidermidis biofilms from the concentration of 0.5 mg/L of exebacase, with a decrease in biomass of up to 90% with the concentration of 150 mg/L. A bactericidal effect on biofilm was also highlighted from the concentration of 50 mg/L, however this effect was heterogeneous among the tested strains. Synergistic effects for the association with rifampin and daptomycin were observed using low exebacase concentrations (5mg/L).

Conclusions: Exebacase appears as a promising adjuvant therapy for rifampin and daptomycin in the context of BJI. Further studies are needed to understand the mechanism of action on Staphylococcus epidermidis biofilm and the heterogeneity of strain behavior.

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Abstract 5474

Infectious complications during anti-CD19 targeted chimeric antigen T cell receptors (CAR-T) immunotherapy in relapsed/refractory aggressive B cell non-Hodgkin lymphomas (NHL): observational retrospective study in one centre

Roberta Di Blasi*, Sylvie Chevret¹, Jerome Paillassa¹, Blandine Denis¹, Lorea Aguinaga¹, Sophie Bernard¹, Hannah Moatti¹, Matthieu Lafaurie³, Elie Azoulay¹, Michael Darmon⁴, Eugenio Galli¹, Catherine Thieblemont¹


Background: Aim of present study is to describe infectious complications (IC) between day 0-90 in patients receiving CAR-T treatment for NHL.

Materials/methods: We retrospectively collected data about IC in 52 patients undergoing CAR-T in Saint-Louis Hospital from June 18th, 2018 until July 31st, 2019. Patients completed at least day 90 follow up.

Results: Median age was 54 y.o. (22-76). Male patients were 32 (61%). Most patients (42-80%) received CAR-T for DLBCL. The mean number of previous lines of treatment was 4 (range 2-9). 14 patients underwent auto-SCT (27%), and 2 allo-SCT (4%). High-intensity bridging chemo-immunotherapy was administered to most patients (33;63%). 20 patients presented hypogammaglobulinemia at admission (≤ 4g/l, 38%, 1.7-9.3). Tisagenlecleucel was used in 28 patients (54%) while 24 (46%) received Axicabtagene-ciloleucel. At reinjection, median lymphocytes count was 0.36G/L (0-1.3). Anti-Pneumocystis prophylaxis was administered in 50 patients (96%), antiviral in 49 patients (94%). One patient received antibacterial prophylaxis by azithromycin and antifungal prophylaxis was not prescribed. 87% of patients presented fever and mean onset was day 3 (1-13). IC occurred in 17 patients. 92% presented neutropenia, severe (≤0.5G/L) in 90% of cases, with mean duration of 11 days (1-180). 26 IC were microbiologically documented. During d0-30, 17 infections occurred in 14 patients (9 bacterial, 8 viral); during d31-60, 6 infections in 5 patients [2 bacterial, 4 viral]; during d61-90, 4 infections in 2 patients [1 bacterial, 2 viral, 1 fungal]. Most patients received antimicrobial empiric treatment (44/S2,85%). Hospitalization in intensive care unit was necessary for 21/52 patients (40%). Most episodes occurred at d0-30, hence we evaluated outcome of infection at d30 from CAR-T injection. Only 3/14 patients presented poor outcome. In 2 patients death occurred because of haematologic disease progression with infection, 1 patient had positive CMV at D30 while receiving Foscarnet. No mortality was attributable to IC alone. Univariate analyses of infection selected age (p=0.009), PS≥2 (p=0.02), LDH (p=0.035), allo-SCT (p=0.05), use of GCSF (p=0.03) as associated with the outcome.

Conclusions: Febrile neutropenia is frequent during CAR T-cell treatment. IC are usual in the first 30 days and bacterial and viral infections are most frequent. IC appear mild and not fatal.
**Abstracts 2020**

<table>
<thead>
<tr>
<th><strong>Age, median (range)</strong></th>
<th>54 y.o. (22-76)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>M/F</strong></td>
<td>32/20; 61%/39%</td>
</tr>
<tr>
<td><strong>DLBCL</strong></td>
<td>42; 80%</td>
</tr>
<tr>
<td><strong>PMBL</strong></td>
<td>5; 10%</td>
</tr>
<tr>
<td><strong>tFL</strong></td>
<td>5; 10%</td>
</tr>
<tr>
<td><strong>Previous lines of treatment, median (range)</strong></td>
<td>4 (2-9)</td>
</tr>
<tr>
<td><strong>Stem cell transplantation (SCT)</strong></td>
<td>14; 27%</td>
</tr>
<tr>
<td><strong>Autoalogous</strong></td>
<td>14; 27%</td>
</tr>
<tr>
<td><strong>Allogeneic</strong></td>
<td>2; 4%</td>
</tr>
<tr>
<td><strong>Hypo-gammaglobulinemia (≤4g/L)</strong></td>
<td>20; 38%</td>
</tr>
<tr>
<td><strong>Reinjected product</strong></td>
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</tr>
<tr>
<td><strong>Tisagenlecleucel</strong></td>
<td>28; 54%</td>
</tr>
<tr>
<td><strong>Axicabtagene ciloleucel</strong></td>
<td>24; 46%</td>
</tr>
<tr>
<td><strong>Lymphocytes count D0 (G/L), median (range)</strong></td>
<td>0.36 (0.1-3)</td>
</tr>
<tr>
<td><strong>Prophylaxis</strong></td>
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</tr>
<tr>
<td><strong>Anti-pneumocystis</strong></td>
<td>50; 96%</td>
</tr>
<tr>
<td><strong>Antiviral</strong></td>
<td>49; 94%</td>
</tr>
<tr>
<td><strong>Antibacterial</strong></td>
<td>1; 2%</td>
</tr>
<tr>
<td><strong>Antifungal</strong></td>
<td>-</td>
</tr>
<tr>
<td>**Pts with previous infections **</td>
<td>8; 15%</td>
</tr>
<tr>
<td>**Pts with colonisation **</td>
<td>6; 11%</td>
</tr>
<tr>
<td><strong>Neutropenia (occurring between D0-D30)</strong></td>
<td>48; 92%</td>
</tr>
<tr>
<td><strong>≤1G/L ANC</strong></td>
<td></td>
</tr>
<tr>
<td><strong>≤0.5 G/L ANC</strong></td>
<td>42; 81%</td>
</tr>
<tr>
<td><strong>Duration of severe neutropenia (ANC ≤ 0.5 G/L), days (median, range)</strong></td>
<td>11 (1-180)</td>
</tr>
<tr>
<td><strong>Pts presenting G3/4 cytopenia by D90</strong></td>
<td>16; 30%</td>
</tr>
<tr>
<td><strong>Neutropenia</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Anemia</strong></td>
<td>8; 15%</td>
</tr>
<tr>
<td><strong>Thrombocytopenia</strong></td>
<td>8; 15%</td>
</tr>
</tbody>
</table>

Table 1. Characteristics of the patients and risk factors for infection

* 1 pt: *Candida* spp peritonitis + HBV infection, non-replicative; 1 pt PCP, 1 pt indwelling catheter infection, 1 pt polymicrobial bloodstream infection (BSI), 1 pt G- BSI, 1 pt *E. coli* cystitis + indwelling catheter infection+ HSV/VZV reactivations, 2 pts non microbiologically documented pneumonias

** 3 *E.coli* extended spectrum beta lactamase (ESBL), 1 *K.pneumoniae* ESBL, 1 *P.aeruginosa* ESBL, 1 Methicillin-resistant *S.aureus* (MRSA)

*** at least one episode by D90

DLBCL= Diffuse Large B Cell Lymphoma; PMBL= Primary mediastinal B-cell lymphoma; tFL= Transformed Follicular Lymphoma; PS= performance status; G-CSF= granulocyte-colony stimulating factor

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**Abstract 5478**

### In vitro activity of imipenem-relebactam plus aztreonam against metallo-β-lactamase producing Pseudomonas aeruginosa

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**Background:** There are limited treatment options for MBL-producing *Pseudomonas aeruginosa* infections. IMI-REL plus ATM may be an option for these organisms.

**Materials/methods:** Ten OprD deficient *P. aeruginosa* isolates (3 parent strains; 7 MBL-producers) were evaluated using checkerboard methodology and Fractional Inhibitory Concentration Index (FICI) (Table 1). Isolates exhibiting synergy in checkerboard studies (FICI ≤0.5) were evaluated using 24-hour static concentration time-kill. Bacteria in late log-phase growth were diluted to 1x10⁶ cfu/mL and incubated at 37°C for 24 hours. Samples were drawn at 0, 2, 4, and 24 hours. Physiologic \( f_{\text{Cmax}} \), \( f_{\text{Cmin}} \) and \( f_{\text{Css}} \) of IMI (26.7, 5.6, 0.5 mg/L), REL (13.1, 4, 0.8 mg/L) and ATM (62, 29, 8 mg/L) were used for time-kill studies. Synergy in time-kill studies was defined as >2 log₁₀ cfu/mL reduction compared to the most active individual agent.

**Results:** Synergy was observed in five isolates in checkerboard studies, including 3/7 MBL-producing isolates. No antagonism was observed. Isolates which were OprD(-) and harbored inducible AmpC did not show synergy as defined by FICI, however individual agent MICs were significantly reduced with the combination. In time-kill studies, synergy was observed at \( f_{\text{Cmax}} \) concentrations for CL5701, MB10480, MB10620. The combination improved bacterial killing at \( f_{\text{Cmin}} \) concentrations for MB10480 and \( f_{\text{Css}} \) concentrations for CL5702 (-1.69 and -1.51 log₁₀ cfu/mL reductions, respectively). No synergy was observed for MB10481; bacterial killing was driven by ATM.

**Conclusions:** IMI-REL plus ATM appears to exhibit synergy for some MBL-producing *P. aeruginosa* at physiologic concentrations. Further study of the effect of dynamic concentrations is needed to fully understand the utility of this combination.

**Table 1. Isolate Characteristics and Susceptibility**

| Isolate | IMI-REL MIC (mg/L) | ATM MIC (mg/L) | AmpC Status | MBL | Combination MIC (IMI-REL|ATM) | FICI |
|---------|--------------------|----------------|-------------|-----|-------------------------|------|
| CLB24228 | 4                  | 32             | Inducible   | 2[16] | 1                       |      |
| MB10640 | 512                | 32             | Inducible   | ViM-1 | 1[16] | 0.502 |
| MB10641 | 512                | 32             | Inducible   | ViM-2 | 256[0.5] | 0.516 |
| CL5701  | 2                  | 32             | Constitutive| 0.5[4] | 0.375 |
| MB10480 | 128                | 32             | Constitutive| IMP-1 | 32[8] | 0.5 |
| MB10620 | 256                | 32             | Constitutive| ViM-1 | 64[4] | 0.375 |
| CL5702  | 1                  | 16             | Deleted     | 0.25[2] | 0.375 |
| MB10481 | 128                | 4              | Deleted     | IMP-1 | 16[1] | 0.375 |
| MB10621 | 256                | 8              | Deleted     | ViM-1 | 16[4] | 0.563 |
| MB10622 | 256                | 16             | Deleted     | ViM-2 | 32[8] | 0.625 |

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Genetic characterisation of virulence factors of non-O1 non-O139 Vibrio cholerae strains from clinical and environmental origin isolated in Chile between 1992 and 2018

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Background: Non-O1 non-O139 V. cholerae generally lack cholera toxin (Ctx) and toxin-coregulated pilus (Tcp). However, some non-O1 non-O139 strains are capable of causing human infections due to virulence factors such as: thermostable toxins, hemolsins, pore-forming toxin and type III secretion system [found in a genomic island homologous to Vibrio parahaemolyticus VPAI-7]. Our objective was to genetically characterize virulence factors of Chilean clinical and environmental strains of non-O1 non-O139 V. cholerae strains isolated between 1992 and 2018.

Materials/methods: 58 strains were included; 30 from environmental origin (provided by the National Public Health Institute, I.S.P.) and 28 from diarrheal episodes. End-point PCR was used to detect the following virulence genes in all strains: cholera toxin (ctxA); colonization factor (tcpA); hemolysin (hlyA); pore-forming protein (rtxA); regulatory protein (toxR) [a prominent transcriptional regulator of virulence genes]; ocludens zonule toxin (zot); cholix toxin (chxA); accessory choleric enterotoxin (ace); mannose sensitive type IV hemagglutinin (mshA); F protein (vopF) [important in intestinal colonization]; type secretion system proteins III or SST3-2 (vspD, vscN2, vscV2, vscC2) and gene segments homologous to pathogenicity island VPaI-7, previously described in Chilean strains of non-O1 non-O139 V. cholerae.

Results: ctxA, tcpA and ace virulence genes were not detected in our group of strains. In contrast, hlyA and rtxA genes were present in all strains. The mshA and chxA genes were found in different proportions in clinical and environmental strains; mshA: 14.29% vs. 23.33% and chxA: 14.29% vs. 10%, respectively. The zot gene was detected only in environmental strains with a frequency of 10%. The 4 SST3-2 genes were more frequently found in clinical strains (78.57% vs. 36.62%; p = 0.0177), as well as toxR (92.6% vs. 76.6%) and vopF (82.14% vs. 50%; p = 0.0355). Finally, homologous segments of pathogenicity island VPaI-7 [5’, middle segment and 3’] were found in 52.14% of clinical strains and 40% of environmental strains.

Conclusions: Higher prevalence of SST3-2, toxR and vopF in clinical strains, as well as homologous segments [5’, middle segment and 3’] of pathogenicity island VPaI-7, suggests a role of these virulence factors in human pathogenicity.

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Neisseria gonorrhoeae transcriptome analysis: profiling molecular determinants of resistance

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Abstract third-party references: Department of Diseases of Chronic Conditions and STI/MoH/Brazil

Background: Neisseria gonorrhoeae (NG) is the etiological agent of gonorrhea, a sexually transmitted infection that affects about 78 million people per year. Since the implementation of the treatment, gonococcus rapidly developed resistance mechanisms to the multiple classes of antimicrobials used to treat the infection. Nowadays, ceftriaxone (CRO) is the drug used as a first-line treatment recommended by the World Health Organization (WHO), although resistance to this drug was already described. Owing to the possibility of the gonococcal infection becoming untreatable, there is a need to understand the molecular and phenotypic mechanisms related to antimicrobial resistance mainly to ceftriaxone. In this study, we sequenced some genes and performed RNA sequencing to evaluate resistance mechanisms.

Materials/methods: To perform the transcriptome analysis, the NG isolate [MIC CRO 0.125mg/mL] was cultured in both GC medium plates and GC medium plates with CRO subinhibitory concentration [0.06mg/mL]. Illumina RNA sequencing was performed (Novaseq 100bp paired-end) in biological triplicates. RNAseq data analysis was performed in Rockhopper system. The mutations analysis corresponded to the sequencing of the isolate’s mtrR, porB, penA and ponA genes and analysis of mutation patterns were performed on the NGSTAR platform.

Results: The patterns for each gene for the isolate were: mtrR: -35A del, ponA: L42P, penA: mosaic, porB: G120K/A121D. The SNPs of the respective genes revealed an identical pattern of mutation in the clinical isolate [CRO MIC 0.125 mg/mL] with resistant strains [MIC CRO ≥0.250 mg/mL], leading to the absence of genotypic differentiation between strains with unequal susceptibility to CRO. Analysis of RNAseq data presented 115 differentially expressed genes showing fold-change (FC) > 1.68 and q-value <0.05, of these 53 upregulated and 62 downregulated in the condition of presence of CRO. Of those genes, only 14 have a defined molecular function, 46 are predicted RNAs [no coding RNAs], 28 are hypothetical and 26 had their function automatically annotated.

Conclusions: These results show a major lack of knowing about NG phenotypic status and how NG cell deal with CRO, calling for deep analysis of NG transcriptome. The great proportion of predicted RNAs suggests that no coding RNAs may regulate CRO resistance mechanisms.

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**Abstract 5483**

**Molecular characterisation of Fusarium oxysporum species complex isolates from the United States and susceptibility profile of the investigational antifungal olorofim**

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**Background:** Fusariosis is one of the most serious non-Aspergillus mold infections among immunocompromised patients, and members of the *Fusarium oxysporum* species complex (FOSC) are major etiologic agents of this opportunistic infection. Recently, members of the FOSC have been distinguished into more than 20 phylogenetic species. Our objective was to evaluate the species distribution and antifungal susceptibility profiles of FOSC isolates in the U.S, including the investigational agent olorofim.

**Materials/methods:** 49 clinical FOSC isolates received by the Fungus Testing Laboratory at the UT Health Science Center San Antonio for identification and antifungal susceptibility testing were included. Identification was performed by DNA sequencing and phylogenetic analysis of translation elongation factor 1-alpha (TEF1α) and RNA polymerase II second largest subunit (RPB2). Antifungal susceptibility testing was performed by CLSI M38 broth microdilution. MICs for olorofim were determined after 48 hours of incubation at the 50% and 100% inhibition endpoints, while those of amphotericin B, posaconazole, voriconazole, itraconazole, and isavuconazole were determined at 100% inhibition.

**Results:** Of the 49 isolates, 40 were identified to the species level, including 20 *F. veterinarium*, 12 *F. nirenbergiae*, 5 *F. fabacearum*, 2 *F. triseptatum*, and 1 *F. cugenangense*. Nine isolates were unnamed species. Olorofim demonstrated good in vitro activity against FOSC isolates (MIC range 0.03 - 0.5 and 0.06 - >4 mg/L at 50% and 100% inhibition, respectively). Of the antifungals, olorofim also had the lowest GM MIC values (0.107 and 0.559 mg/L at 50% and 100% inhibition) followed by amphotericin B (1.59 mg/L), posaconazole (6.11 mg/L), voriconazole (6.94 mg/L), and itraconazole and isavuconazole (>16 mg/L for each). Interestingly, olorofim GM MICs were higher against *F. nirenbergiae* (0.177 and 1.19 mg/L at 50% and 100% inhibition) compared to *F. veterinarium* (0.081 and 0.391 mg/L; p < 0.01).

**Conclusions:** Olorofim demonstrated potent in vitro activity against FOSC isolates, and this activity was maintained regardless of the specific species. Interestingly, differences in olorofim activity was observed between the two most prevalent species, *F. veterinarium* and *F. nirenbergiae*. Further studies are needed to determine how these findings may translate into in vivo efficacy.

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Abstract 5484

Real-world multi-centre experience of meropenem-vaborbactam in patients treated for serious Gram-negative bacterial infections

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Background: Gram-negative bacteria (GNB) resistance, particularly carbapenem-resistant Enterobacteriaceae (CRE), is a critical challenge in infectious diseases. The combination of meropenem with vaborbactam (MVB) received Food and Drug Administration (FDA) approval for the treatment of complicated urinary tract infections (cUTI) and acute pyelonephritis (AP) caused by susceptible organisms in August 2017. MVB combines a carbapenem with a novel beta-lactamase inhibitor and has potent in vitro activity against CRE. Unfortunately, evidence regarding MVB use in non-FDA approved indications is limited. We aim to evaluate the efficacy and safety of MVB when used to treat patients with serious GNB infections.

Materials/methods: Multi-center, retrospective cohort study from October 2017 to October 2019. We included adult patients treated with MVB for ≥ 72 hours. CRE was defined according to the Centers for Disease Control and Prevention. Clinical success was defined as survival, absence of recurrence at 30 days following the onset of infection and resolution of signs and symptoms of infection. Susceptibility was defined per Clinical and Laboratory Standards Institute minimum inhibitory concentrations (MIC) interpretive criteria.

Results: A total of 75 patients were included from over 10 institutions across the United States: median age 55 (IQR:37-66) years, 65% were male, 45% were Caucasian. Median APACHE II and Charlson Comorbidity index scores were 16 (IQR:10-24) and 4 (IQR:2-6), respectively. Common sources of infection were respiratory (33%), intra-abdominal (20%), urinary (16%), skin and soft tissue (11%) and primary bacteremia (8%). CRE were the most common pathogens isolated (81%). Specifically, Klebsiella pneumoniae (56%) followed by Enterobacter cloacae (20%). MVB MICs of 0.06 (range;0.02-4.00) mcg/mL and 0.38 (range;0.05-6.00) mcg/mL, respectively. MVB was started within 90 (IQR:25-142) hours and median therapy duration was 12 (IQR:6-15) days. 31% had combination therapy ≥ 48 hours, primarily minocycline and amikacin. Clinical success was achieved in 72%; with 30-day survival of 88%. Three patients experienced a probable MVB-adverse event; 2 nephrotoxicity and 1 skin reaction.

Conclusions: MVB demonstrated a high clinical success rate and appears to be well-tolerated in patients with GNB infections. Studies with longer follow-up and larger sample sizes are required to assess the role of MVB compared to other anti-GNB agents.

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Abstract 5486

End-to-end Workflow for HIV-1 drug resistance genotyping of protease and reverse transcriptase in major group-M subtypes

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Background: To meet the UNAIDS 90-90-90 goal, low-cost, robust drug resistance (DR) genotyping solutions for HIV are urgently needed. Moreover, the ability to extract viral RNA from Dried Blood Spots (DBS) as well as plasma provides greater flexibility for sample collection in low and middle-income countries (LMICs). Most on-market DR genotyping solutions demonstrate variable performance on non-B subtypes, and existing workflows for DBS are expensive and/or insensitive. We have created an end-to-end DR genotyping workflow that includes RNA extraction from either plasma or DBS using a modified version of the MagMAX Viral/Pathogen Nucleic Acid Isolation Kit followed by sequencing using the HIV-1 Genotyping Kit and data processing using secondary analysis software.

Materials/methods: DBS research samples containing various subtypes at varying viral loads (VLs) were extracted using the new MagMAX workflow or the bioMérieux EasyMAG system, and the samples were subjected to amplification using the HIV-1 Genotyping Kit.

Results: Both the MagMAX and EasyMAG systems successfully extracted amplifiable viral RNA across all VLs tested to <2,000 copies/mL. The HIV-1 Genotyping Kit, originally developed by the U.S. Centers for Disease Control and Prevention, achieved a Limit of Detection of 1,000 copies/mL from plasma samples and 2,000 copies/mL from DBS on subtypes A, B, C and D and CRF01 AE and CRF02 AG. DR mutation detection sensitivity was 98.1% for plasma and 98.4% for DBS, and specificity was 99.6% for both sample types at a VL of 10,000 copies/mL.

Conclusions: Overall, the DBS sample prep protocol, genotyping kit and analysis software provide lower-cost but robust alternatives to existing on-market solutions for HIV-1 drug resistance research and are specifically designed for the needs of LMICs.

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The role of genomics in typhoid control: sentinel traveller surveillance, in-host evolution and transmission dynamics

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Background: Salmonella Typhi is the causative agent of typhoid fever, a systemic human infection with a burden exceeding 10 million cases annually, occurring disproportionately among children in LMIC. Pathogen whole genome sequencing (WGS) is increasingly used for genomic surveillance and transmission modelling, however, most routine WGS of S. Typhi is conducted in non-endemic countries, and it is unclear whether the evolutionary rate of typhoid pathogens is sufficient to resolve transmission chains in outbreak scenarios. We investigated whether S. Typhi from travellers returning from endemic areas are representative of pathogen populations at the destination of travel, and measured the evolutionary rate in vivo during human challenge.

Materials/methods: WGS was used to identify SNPs, type S. Typhi into genotypes, infer phylogenies, and detect molecular determinants of antimicrobial resistance (AMR). AMR and genotype profiles of travel-associated isolates collected by public health laboratories in the United Kingdom and Australia were compared with those collected locally in India, Bangladesh, Samoa, and Papua New Guinea. Genomes from isolates obtained from human challenge study participants were compared with the complete genome of the inoculating strain to identify mutations arising in vivo.

Results: For all endemic countries examined, travel-associated isolates were intermingled in the phylogeny with those collected locally across similar sampling periods, and were significantly positively correlated in terms of both the genotypes present (Pearson correlation, 0.94, p=1.1x10^-15) and AMR determinants (Pearson correlation 0.96, p=2.22x10^-07). Of 200 post-challenge isolates, n=11 (~1 in 18) harboured de novo DNA base substitution mutations compared with the inoculating strain, yielding an estimate of in-host evolution of 5.70x10^-7 [95% CI, 3.18x10^-7 – 1.02x10^-6] substitutions/site/genome/year, in line with substitution rates estimated from Bayesian phylogenomic analyses of WGS data on natural infections.

Conclusions: Genomic surveillance is highly informative for typhoid control strategies, revealing transmission dynamics, AMR mechanisms, regional strain circulation patterns, and resolving point source outbreaks, although the substitution rate of S. Typhi is too low to resolve individual transmission events during outbreaks. Similarity between travel-associated and locally isolated S. Typhi demonstrates the utility of the former as a source of routine sentinel surveillance for regions where local genomic surveillance is not yet available.

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Abstract 5491

**Cardiac 18F-fluorodeoxyglucose Positron Emission Tomography (18F-FDG-PET/CT) use in infective endocarditis: a 10-year multi-centre cohort study**

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**Background:** Cardiac 18F-fluorodeoxyglucose Positron Emission Tomography Computed Tomography (18F-FDG-PET/CT) has recently been included as a major diagnostic criterion of prosthetic valve endocarditis (PVE) in the 2015 European Society of Cardiology (ESC) infective endocarditis (IE) guidelines. The aim of this study was to know the influence of those guidelines on the implementation of 18F-FDG-PET/C and the variables associated with 18F-FDG-PET/CT performance in a ten-year multicenter cohort study.

**Materials/methods:** All IE consecutive episodes in one reference cardiac center and nine non-cardiac central-Catalonian community hospitals were retrospectively collected for 2009 to 2018. Two centers performed 18F-FDG-PET/CT using the same protocol. We analyzed the performance of cardiac 18F-FDG-PET/CT according to the calendar year and compared the characteristics of patients with and without a cardiac 18F-FDG-PET/CT.

**Results:** From 872 consecutive episodes of IE, 165 (19%) had a cardiac 18F-FDG-PET/CT performed. The rates of cardiac 18F-FDG-PET/CT done in 2009-11, 2012-14 and 2015-19 were 5%, 15% and 31%, respectively (see Figure) and this trend was statistically significant (p<0.001). Comparing both cohorts, PVE was more frequent in patients with cardiac 18F-FDG-PET/CT performed (46% vs. 22% p<0.001) and less frequent in patients with *Viridans group streptococci* (19% vs. 13% p<0.02); mitral valve involvement (33% vs 44.5% p<0.004) and patients with severe valve regurgitation (23% vs. 39% p<0.001). There were no differences between other causative microorganisms nor within surgery indication and surgery actually performed. In-hospital mortality and one-year-mortality rates were lower in patients with cardiac 18F-FDG-PET/CT. The variables associated with cardiac 18F-FDG-PET/CT performance in the multivariate analysis were being transferred from a community hospital to the reference cardiac center (OR 1.93 [1.27 , 2.92]), suspicion of PVE (OR 2.22 [1.27 , 3.89]) and the most recent calendar year (2014-2018 period, OR 4.26 [2.79, 6.50]). In the multivariate analysis of predictors of in-hospital and one-year mortality, after adjusting for classical variables, performing cardiac 18F-FDG-PET/CT was independently associated with survival (OR, 95%CI, 0.20 [0.17-0.49] and 0.29 [0.15-0.54], respectively).

**Conclusions:** The use of cardiac 18F-FDG-PET/CT for diagnosis of IE has increased since the 2015 ESC IE guidelines, especially in patients with PVE, and identifies a subset of patients with better prognosis.

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Abstract 5493

**Interest of immunoblotting with Aspergillus fumigatus western blot IgE assay for the differential diagnosis of IgE sensitisation and allergic broncho pulmonary aspergillosis**

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**Abstract**

**Background:** Allergic Broncho-Pulmonary Aspergillosis (ABPA) diagnostic is complex and based on a multi-criteria definition. One of the major criteria is the presence of specific immunoglobulin E (sIgE) to *Aspergillus fumigatus* (*Af*), but sIgE also reflects sensitization to *Af*. Discrimination between *Af* sensitization and ABPA is complex, and no diagnostic test allows a clear distinction between these two entities to date. We recently reported that a Western Blot detecting IgE antibodies specific for *Af* could separate those two entities. This work aimed to evaluate the LDBIO *A. fumigatus* WB IgE assay for differentiating ABPA from *Af*-sensitization.

**Materials/methods:** 229 sera (2014-2018 period, Marseille, France) with known sIgE reactivity (23 ABPA, 206 *Af*-sensitized) were assayed with the LDBIO *A. fumigatus* WB IgE. All had been previously assayed with ImmunoCap® for sIgE. We evaluated the ability of WB to detect *Af* sensitization and to discriminate between ABPA and *Af*-sensitized patients, relying on ImmunoCap® and clinical chart conclusions as a reference.

**Results:** Samples displayed 0 to 10 bands in the 10-37 kDa range. The 4 most frequent bands were considered as major bands (16, 18-20, 22 and 30 kDa) and the others as minor bands (10, 17, 33, 34, 36 and 37 kDa). *A. fumigatus* WB IgE positivity was defined by the presence of 2 major bands. This WB was thus positive in 23/23 ABPA and 124/206 *Af*-sensitizations sera (64% sensitivity). WB positivity was strongly correlated to sIgE level; it was positive in 95% (98/103) of the sera with sIgE >1.5 kUa/l.

The ABPA WB IgE profile was defined by the presence of at least 2 major bands and 2 minor bands with 96% sensitivity (22/23) and 93% specificity (192/206) for ABPA diagnostic.

**Conclusions:** This study highlights the interest of the WB *A. fumigatus* IgE assay in the work-up of IgE responses to *Af* in asthmatics and cystic fibrosis patients: WB could discriminate ABPA from *Af*-sensitized patients with a sensitivity of 96% and a specificity of 93%. These encouraging results must now be reproduced in a multicentric evaluation.

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Blood virome in febrile Tanzanian children

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Background: The full characterization of the human blood virome in different continents and/or populations could contribute to identify new infectious agents and possibly predict virus emergence. We performed metagenomics next-generation sequencing (mNGS) on blood samples from a paediatric cohort with fever to identify clinically pertinent viruses not routinely screened in low-resource setting, variants not detected by available diagnostic assays, or viruses unknown to infect humans.

Materials/methods: mNGS was performed on 816 serum collected between 2014 and 2016 from a large paediatric cohort (2-59 months of age) presenting with fever at nine outpatient clinics in Dar es Salaam, Tanzania. Raw data were analysed in all cases using in parallel a bioinformatics pipeline and a new database specifically developed in the context of this study to report any known vertebrate viruses and by de novo.

Results: The mNGS analysis reported the detection of a large diversity of RNA and DNA virus sequences. Of the 816 children, 394 (48.3%) were found positive for at least one virus recognized as causing infection or diseases in humans. Among the 35 viral species detected and considered of clinical significance, we observed a predominance of human enteroviruses (113/816, 13.8%), rotaviruses (98/816, 12%), human herpesvirus type 6 (90/816, 11%) and 7 (36/816, 4.4%). Anelloviridae were detected in all except one samples and up to 92.2% of samples were co-infected by three anellovirus genus. In addition, a large number of sequences related to 33 arthropod, vertebrate or mammalian virus species and so far unknown to cause human infections were detected; the most frequent being dicistroviruses, porcine parvoviruses 4-6 and ambidensoviruses.

Conclusions: We have extensively characterized the human virome of children living in Tanzania and presenting a febrile illness. Beyond the usual viral agents, we reveal the presence of a large number of human enterovirus and rotavirus infections. The prevalence and diversity of Anelloviridae observed is far higher than expected. In addition, we observed a large number of viruses of unknown clinical significance for humans. The later ones deserve specific attention and further studies in the febrile paediatric population in Africa.

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Abstract 5495

**Enterovirus-C99 associated with cases of acute flaccid paralysis in the south-eastern region of Brazil**

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**Background:** Enteroviruses (EV) are members of the genus *Enterovirus* within the order *Picornavirales*, family *Picornaviridae*, and have been assigned to four species: *Enterovirus* A, B, C, and D. Acute flaccid paralysis (AFP) is the most common clinical presentation of acute poliovirus infection. Although polio eradication to be a public health emergency of global interest, non-polio enteroviruses (NPEV) detection amid polio surveillance to be considered. NPEV requires attention as potential causative agents of many AFP cases. The aim of this study was to provide further insights into the circulation of NPEV in children with AFP, in São Paulo State, southeastern region of Brazil.

**Materials/methods:** During nineteen years of poliovirus surveillance, January 2001 to October 2019, sixty-nine samples were analysed from AFP cases that had previously been confirmed as NPEV by the WHO-recommended RD-L20B cell culture-based algorithm. Total RNA was extracted on the RD cell culture supernatant from each sample by QIAamp Viral RNA Mini Kit (QIAGEN, Hilden, Germany) and reverse transcription polymerase chain reaction RT-PCR was applied to amplify a partial region of viral protein 1 (VP1) followed by sequencing for identifying, using the enterovirus genotyping tool and phylogenetic analysis.

**Results:** Among 69 samples NPEV positive, *Enterovirus B* was the most frequently detected species, followed by *Enterovirus A* and *Enterovirus C*, 62.3%, 27.6% and 10.1%, respectively. No *Enterovirus D* was detected. In total, we found 27 different genotypes. Within EV-B, the most frequently detected genotypes were Echovirus 11 (7/43, 16.3%) and Echovirus 6 (6/43, 14.0%). EV-A71 (5/19, 26.3%) was the genotypes most frequently detected within EV-A. In EV-C, EV-C99 (4/7, 57.1%) was the most frequently detected genotypes.

**Conclusions:** This is the first report of EV-C99 in AFP case in South America. Continuous surveillance of EV is important to afford further information on the circulation NPEV in the Brazil. This study shows the importance of increasing NPEV monitoring in order to understand the etiological role of EV-C99, as well as other EV associated with AFP. Financial Support: FAPESP (#2017/05350-0).

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Background: Catheter-associated urinary tract infection (CA-UTI) is one of the leading healthcare-associated infections (HAIs) in Latvia. CA-UTI threatens patient safety, imposes an additional burden on health care costs and contributes to the spread of antimicrobial resistance. It is acknowledged that CA-UTI may be potentially avoided by limiting unnecessary and prolonged urinary catheterization by implementing a number of preventive strategies. The aim of the conducted study is to estimate and decrease unjustified urinary catheter (UC) use during two-year period in university hospital in Riga, Latvia.

Materials/methods: Prospective interventional study was performed in university hospital in December 2017 through October 2019. To assess the frequency and appropriateness of UC use in the hospital, the first Point Prevalence Survey (PPS) was carried out in December 2017, after which three departments with a high UC use were selected for multifaceted interventions using a breakthrough series model. Main activities involved staff engagement, education and documenting the number of catheterized patients and all new catheterization cases on a daily basis. A PPS protocol was developed based on the local hospital’s guidelines, ECDC PPS protocol and in close collaboration with partners from EU-JAMRAI [European Union Joint action on antimicrobial resistance and HAI]. Specific departments were repeatedly surveyed to evaluate the impact of interventions. The primary outcome indicators were catheter-days per patient-days and number of new catheterizations per 1000 patient-days.

Results: The study sample of the first PPS consisted of 609 patients, of whom 107 (17.6%) had an UC. Urology, neurology and neurosurgery departments were identified as high-risk and were selected for further interventions and repeated PPS. Significant improvement was observed only in neurology department where the recorded prevalence of catheterized patients was 64.5% in 2017, 14.8% in 2018 and 25.4% in 2019; catheter-days per patient-days were reduced from 0.27 to 0.19 and new cases of catheterizations per 1000 patient-days gradually decreased from 28.0 to 19.9 during the study period.

Conclusions: An interventional approach managed to achieve a significant reduction of unjustifiable catheter use and prolonged catheterization although long term effect remains to be assessed. The best model of collaboration with clinical departments still has to be established.

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**Abstract 5500**

**Acute rheumatic fever in children in Morocco: a prospective study**
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**Background:** Acute rheumatic fever (ARF) is a major problem of public health in developing countries like Morocco, because of the high prevalence of its principal complication "carditis". The objective of this study is to find out the clinical manifestations and laboratory features of patients with ARF in Fez city in Morocco.

**Materials/methods:** A prospective study was conducted from January 2016 to July 2019 in the pediatric ward of the university hospital Hassan II of Fez. We included patients with age less than 18 years. A total of 152 children diagnosed ARF, based on modified Jones criteria, was studied.

**Results:** The mean age of ARF cases were 12 years and 10 months. The sex ratio male/female was 0.7. The most represented age class was the class between 5 and 15 years (76.16%). Urban residence was found in 78.8% of cases and the majority of patients with and without carditis were admitted in winter and autumn respectively. Cases of ARF with carditis was documented in 78.3% and without carditis in 21.7%. In the groups with/without carditis, arthritis was the major criterion most represented (24.4% and 12.1% respectively) and arthralgia was the minor criterion most represented (67.2% and 78.8% respectively). In the two groups, History of sore throat presented the same percentage. Penicillin A was the most antibiotic prescribed in the two groups. Commonest valvular lesions among ARF with carditis cases was mitral regurgitation (69%). A high ESR level is found in 29.4% and the ASO was positive in 37.2% of cases. Corticosteroids were prescribed in 42.8% of cases with carditis and in 30.3% of cases without carditis.

**Conclusions:** ARF continues to occur in Morocco, despite the progress made in the socioeconomic development of the country, often associated with severe cardiac involvement.

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Abstract 5504

Analysis of causes of death and mortality risk factors in extreme elderly patients with sepsis

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Background: Extreme elderly patients (+80 years-old) are admitted to hospitals with sepsis / septic shock, and the mortality rate for such cases is high.

Materials/methods: The subjects were patients admitted to our hospital with sepsis / septic shock from October 2017 to October 2019. In addition to analyzing their causes of death, the following factors were compared with cases that showed improvement: comorbidities, physical examination, laboratory parameters, gravity scores at hospital admission, infection source, compliance with sepsis protocols [3 hours and 6 hours goals], length of hospital stay and outcomes. An multivariate analysis by logistic regression was utilized for identification of mortality risk factors.

Results: A total of 346 cases (mean age; 80.9 years) were targeted for analysis (table 1). Most prevalent comorbidities of the patients were hypertension [65%], diabetes [27.5%], chronic pulmonary obstructive disease [11.3%], and hypothyroidism [13.1%]. Most patients were previously hospitalized [3 month] [24.6%]. The main sources of infection were lung [47.4%] and urinary tract [32.8%]. Many patients were admitted in septic shock [19.9%]. The mean sequential organ failure assessment score [SOFA] and quick-SOFA were 4.7 and 2.01 respectively. Compliance with institutional sepsis protocols were 83.3% and 73.1% in the 3 hours and 6 hours bundles, respectively. All-causes mortality were high [39.0%], being at < 48 hours in low proportion [7.8%]. In the multivariate analysis were independent associated with mortality the necessity for hemodialysis [Risk ratio [RR]: 2.0; 95% Conf. Interval [CI]: 1.4-2.7; p=0.05]; Pneumonia like source of sepsis [RR: 1.44; 95% CI: 1.14-1.87; p=0.005], and the presence of septic shock at admission [RR: 2.07;95% CI 1.64-2.61; p<0.05]. Otherwise, survival were associate with adequate initial volemic resuscitation with 30 ml/kg [RR:0.55;85% CI:0.4-0.71;p<0.05].

Conclusions: In extreme elderly patients with sepsis/septic shock, the presence of septic shock at hospital admission, acute kidney insufficiency requiring hemodialysis, pneumonia like source of sepsis, and lack of adequate volemic resuscitation were risk factor strongly associated to in-hospital mortality, knowing these characteristics would be useful when making decisions regarding the intensity of treatment.

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Abstract 5505

**High-throughput culture-based vancomycin-resistant enterococci screening using artificial intelligence**

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**Background:** Reading of culture media is one of the most demanding and time consuming parts of conventional microbiology. Even with the use of chromogenic media there is still considerable subjectivity. Introduction of artificial intelligence (AI) has shown to be a way to increase reliability and throughput in culture based MRSA-screening. This study was conducted to evaluate the accuracy of AI-based classification of solid culture media designed for VRE-detection.

**Materials/methods:** The APAS® Independence in combination with VRE Analysis Module was trained using 1500 routine specimens over a 3 month period. VRE Screening was performed using the Brilliance VRE® (ThermoFisher). Routine samples were processed using the AutoPlak® (Beckman Coulter) and evaluated after 24 and 48 hours of incubation. Results of AI-based classification were compared to conventional plate reading by experienced medical technicians and microbiologists.

**Results:** There was high agreement between AI-based and conventional reading. After adoption to the specific chromogenic media, sensitivity of the VRE-detection algorithms was consistently high (>95%) while specificity varied between 70% and >85% in stool and swab specimens, respectively. However, these numbers are expected to increase due to continuous training during further clinical evaluation was observed. Performance did not vary between individual runs. Using plates from routine samples the throughput averaged approximately 200 plates per hour.

**Conclusions:** In this study, accuracy of the AI-based APAS® Independence system was comparable to conventional reading, while the system was able to maintain an average throughput of 200 plates per hour. AI-based systems may provide a great addition to current practices in cultural microbiology.

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Abstracts 2020

Abstract 5508

Outcome of community-onset extended-spectrum β-lactamase-producing Escherichia coli bacteraemia and urinary tract infection: a historical population-based cohort study

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Background: Extended-spectrum β-lactamase-producing Escherichia coli (ESBL-EC) infection is increasingly acquired in the community, leaving the patients at an increased risk of receiving inappropriate empirical antibiotics. Yet, the prognostic impact of infections with ESBL-EC in our low prevalence region remain sparse. Therefore, we investigated mortality and length of hospital stay (LOS) in patients with community-onset ESBL-EC and non-ESBL-EC infections.

Materials/methods: We conducted a population-based cohort study of all adult patients hospitalised with a first-time community-onset E. coli bacteraemia or urinary tract infection (without concurrent bacteraemia) in the North Denmark Region between 2007 and 2017. We computed hazard ratios as a measure of mortality rate ratios (MRR) using cox proportional hazards regression and compared short-term (30-day) and long-term (one-year) mortality between patients with ESBL-EC and non-ESBL-EC infections. We adjusted for age, gender and co-morbidity. LOS was investigated separately for survivors and non-survivors and overall with a cumulative incidence function considering death a competing risk.

Results: A total of 21,667 patients were hospitalised with a first-time community-onset E. coli infection during the study period of which 4,085 (18.9%) had bacteraemia. ESBL-EC accounted for 810 (3.7%) of the infections. The 30-day cumulative mortality in patients with bacteraemia was 16.1% in patients with ESBL-EC and 14.0% in non-ESBL-EC, for an adjusted MRR of 1.09 (95% confidence interval [CI], 0.76-1.57). The one-year cumulative mortality was 37.1% and 31.9% respectively, adjusted MRR 1.11 (95% CI, 0.88-1.42). The 30-day cumulative mortality for patients with urinary tract infection was 9.8% in ESBL-EC and 8.9% in non-ESBL-EC. The median LOS among survivors of bacteraemia was 9 days (interquartile range [IQR], 6-13) for patients with ESBL-EC compared to 7 days (IQR, 5-11) for patients with non-ESBL-EC, which was significantly longer for an overall adjusted hazard ratio of being discharged of 0.79 (0.68-0.93). The corresponding LOS for patients with urinary tract infection was 5 days (IQR, 3-10) compared to 5 days (IQR, 2-9).

Conclusions: Patients hospitalised with community-onset infections with ESBL-EC did not experience a higher short- or long-term mortality compared to patients with non-ESBL-EC, but a longer LOS among patients with bacteraemia.

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Comparison in vitro activity of ceragenins for treatment of Burkholderia cepacia complex infections
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Background: Burkholderia cepacia complex (Bcc) is a Gram negative pathogen bacteria which cause severe infections in immunocompromised patients and fatal chronic respiratory tract infections in cystic fibrosis patients. Burkholderia species are intrinsically resistant to antibiotics such as penicillin, cephalosporin, aminoglycosides and polymyxin. Ceragenins [Cationic Steroid Antibiotic-CSA] designed to mimic the activities of antimicrobial peptides, are a new class of antimicrobial agent. In this study, we examined in vitro activities of ceragenins CSA-13, CSA-131 and CSA-131 poloxamer (P) form against Bcc isolates.

Materials/methods: Bcc clinical isolates (n=36) were collected from Hacettepe University Faculty of Medicine, between 2007-2017. CSA-13 and CSA-131 were synthesized from cholic acid Scaffold technique. Pluronic F-127 was purchased to obtain CSA-131 in poloxamer micelles in order to decrease the cytotoxicity of CSA-131. Minimum inhibitory concentrations (MICs) were determined for levofloxacin, meropenem, trimethoprim-sulfamethoxazole, ceftazidime by using broth microdilution technique according to CLSI guidelines. CSA-13 (prototype ceragenin) and CSA-131 with or without 5% pluronic F-127 were determined, as well. Five different isolates that have lowest MIC results were selected and time kill curve experiments were performed with 1x, 2x and 4x MICs of ceragenins.

Results: The MIC (µg/ml) results of CSA-13, CSA-131 and CSA-131P were between 2-128, 4-128, 2-128. The MIC50 values were determined 16 µg/ml for all ceragenins tested. The results of time-kill curve analysis indicated that CSA-131P showed bactericidal effect in two hours against all isolates, whereas CSA-131 has bactericidal effect for only two isolates at 2x and 4x concentrations. For two isolates, after rapid initial killing, regrowth was observed for CSA-131P.

Conclusions: Although CSA-13, CSA-131 and CSA-131P had similar MIC results, CSA-131P showed bactericidal activity against more isolates. The results demonstrated that CSA-131 in poloxamer micelles formed with pluronic F-127 can make it better candidate than CSA-131 and CSA-13 against Bcc infections.

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Mechanisms of resistance in *Pseudomonas aeruginosa* against ceftazidime-avibactam and ceftolozane-tazobactam from Qatar

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**Background:** Infections with multidrug-resistant organisms and its corresponding increase in morbidity and mortality is a global healthcare challenge. Ceftolozane/tazobactam (C/T) and ceftazidime/avibactam (CZA) have been approved for the treatment of serious infections caused by Gram-negative bacteria including multidrug-resistant *Pseudomonas aeruginosa* (MDR-PA). Resistance to both CZA and C/T has been increasingly reported but the mechanisms have not been fully explored. This study aims to investigate the associated genetic diversity and molecular mechanisms of resistance to CZA and C/T in clinical MDR-PA isolates from Qatar.

**Materials/methods:** A total of 525 MDR-PA isolates were collected from various clinical specimens between 2014 and 2017. Microbiological identification and antimicrobial susceptibility testing were performed by both automated BD Phoenix™ system and manual Liofilchem MIC Test Strips. A total of 75 isolates were resistant to CZA and/or C/T and subsequently processed for genomic analysis using Next-generation sequencing. To identify the potential antibiotic resistance genes (ARGs) responsible for the resistance to CZA and/or C/T, Pearson's correlation between ARGs.

**Results:** The 75 isolates belonged to 29 different sequence types; the resistant ST-235 was predominant at 13% (10/75), followed by ST-357 at 10.7% (8/75), ST-389 at 8% (6/75), ST-1284 at 8% (6/75), and others; 60% (45/75). The isolates carried multiple β-lactamase genes from all Ambler classes: class A β-lactamases including *bla*<sub>TEM-1</sub>, *bla*<sub>TEM-87</sub>, *bla*<sub>TEM-96</sub>, *bla*<sub>TEM-15</sub>, *bla*<sub>TEM-25</sub>, *bla*<sub>TEM-51</sub> and *bla*<sub>TEM-57</sub>; class B including *bla*<sub>IMP-1</sub>, *bla*<sub>VIM-2</sub>, *bla*<sub>VIM-5</sub> and *bla*<sub>PDC-2</sub>, class C including *bla*<sub>PDC-1</sub>, *bla*<sub>PDC-3</sub>, *bla*<sub>PDC-7</sub> and *bla*<sub>PDC-10</sub>, and class D including *bla*<sub>OXA-1</sub>, *bla*<sub>OXA-50</sub>, *bla*<sub>OXA-114</sub>, and *bla*<sub>OXA-129</sub>. Among the β-lactamase genes, the predominant was OXA-50 at 97% (73/75), followed by *bla*<sub>PDC-2a</sub>, *bla*<sub>VIM-2</sub>, *bla*<sub>VEB-9</sub>, *bla*<sub>PDC-3a</sub>, and *bla*<sub>VIM-2</sub>. Pearson’s correlation showed that resistance to both CZA and C/T was associated with the presence of *bla*<sub>PDC-2a</sub>, *bla*<sub>VIM-2</sub>, *bla*<sub>VEB-9</sub>, *bla*<sub>PDC-2</sub>, and *bla*<sub>PDC-7</sub>; while *bla*<sub>KPC-3</sub> presence was associated with resistance to C/T.

**Conclusions:** In MDR-PA, the mechanisms of resistance to CZA and CT is highly correlated to the presence of multiple β-lactamase genes, ie *bla*<sub>PDC-2</sub>, *bla*<sub>VIM-2</sub>, and *bla*<sub>VEB-9</sub>. The analysis was based on genomics and statistical correlation, however the relative contribution of the individual β-lactamase genes is yet unclear.

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Pentameric IgM does not improve clinical outcome in adults with sepsis after major abdominal surgery

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Background: Sepsis still represents a major public health issue worldwide, and the immune system plays a main role during infections and therefore its activity is mandatory to resolve this clinical condition. In this report we aimed to retrospectively verify in real life setting the possible usefulness of Pentameric IgM plus antibiotic in recovering patients with sepsis after major abdominal surgery.

Materials/methods: We reviewed, from January 2013 until December 2018, all adult patients admitted in ICU for Sepsis or Septic shock (2) after major abdominal surgery. Among these patients, were identified those that according to legal indication and licence in Italy, were treated with Pentameric IgM plus antibiotic (Group A) or with antibiotic alone (Group B). We analysed the following parameters were evaluated: Blood gas analysis, Lactate, CRP, Procalcitonin, Endotoxin activity, Liver and Renal Function, Coagulation, Blood Cell count at different time points (Every 48 hrs for at least 7 days). Differences between groups have been analysed by Fisher’s exact test or Chi square test for categorical variables. Mann–Whitney U test or Kruskal–Wallis test have instead been performed to compare continuous variables. Univariate and Multivariate analysis were also performed.

Results: Over a period of 30 months 24 patients were enrolled in Group A and 20 patients in Group B. In those subjects no statistical differences have been found in terms of bacterial or fungal infection isolates, when detected in a blood culture test, or in inflammatory index, SOFA score, lactate levels and mortality rate. A 48hrs response was statistically more frequent in Group B than in Group A, while no differences were found in the other clinical and laboratory evaluation.

Conclusions: Based on our results, the use of pentameric IgM do not seem to give any clinical advantage in sepsis after to major abdominal surgery.

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Abstract 5516

Comparison of different platforms and analysis tools in microbiome analysis

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**Background:** Recent findings from microbiome analyses underscore the importance of bacterial community composition at various body sites for human well-being. Next-generation sequencing (NGS) is now routinely used for community assessment, however, the lack of widely accepted standards in wet-lab protocols, sequencing and data analysis is a considerable source of variation in microbiome profiles.

**Materials/methods:** We assessed microbiota from stool (n=12), oral (n=12) vaginal swabs (n=16) and stool-like samples of known bacterial composition (n=2) with commercial 16S rDNA amplicon sequencing methods (Illumina and Ion Torrent) and analysis tools (Qiime2 and Ion Reporter). Multiparametric maximization of the sensitivity vs. precision trade-off was used to find an optimal cross-platform post-processing method for platform output. Microbiome profiles from sampling materials were characterized by alpha and beta diversities and compared between platforms using an empirical Bayesian approach; results were subjected to multi-level visualization.

**Results:** Removal of taxa with unresolved genus level or detection frequencies below 0.05% greatly improved precision of microbiome profiles while maintaining sensitivity. Independent of assessment platform, alpha diversities from oral samples were around 2.9, from stool around 3.0 and from vaginal swabs around 0.03. Between-sample heterogeneity was lowest in vaginal, and highest in stool microbiomes. In the latter we detected a total of 77 genera; thereof, only 36 were quantified equally well by all platforms, while 41 displayed platform-specific preferential detection. This effect was attributable to data generation for 23 genera and to analysis methods for 14 genera. Similar observations were made with other sampling materials, thus, the choice of wet-lab processes and sequencing method had greater impact on profiling than selection of the data analysis pipeline.

**Conclusions:** Diagnostic application of NGS-based microbiome profiling requires post-processing of output from assessment platforms and consideration of their sampling material-specific detection biases.

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Abstract 5518

Daptomycin and pulmonary eosinophilia: An unrecognised opportunity
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Background: Daptomycin pulmonary eosinophilia (DPE) has been described as a rare event. The diagnosis is uncommon since peripheral eosinophilia (EOS) may be absent and bronchoalveolar lavage (BAL) is rarely performed for suspected pneumonia. As Daptomycin (DAP) is not used for pneumonia treatment, stopping DAP often resolves the symptoms. We evaluated 331 patients who received DAP from 1/1/10-9/30/18 for DPE using the US Food and Drug Administration (FDA) criteria for proven and probable cases.

Materials/methods: Retrospective chart review of 331 patients who received DAP (inpatient and outpatient). Data collected was age, gender, weight, dosing/duration of DAP, EOS, and infection diagnosis. Pneumonia was recorded per FDA criteria with EOS and DPE. Chi-square analysis compared patients with and without EOS and DPE. Univariate analysis assessed duration and re-exposure of DAP with EOS and DPE.

Results: Overall there were 110 patients [33%] with EOS and 98 [30%] cases of DPE based on inclusion criteria. There was no difference in DPE with EOS or non-EOS groups. It was statistically significant for presence of EOS with longer durations of DAP P<0.001 [OR 4.2 CI 3.6-16.6]. Re-exposure of DAP with prior EOS was associated with severe early onset DPE P<0.05 [OR 1.5, CI 0.7-1.3]. This onset with re-exposure to DAP occurred with a median duration of 14 days compared to the initial DAP median of 25.5 days. There was no association with weight, age, or dose of DAP.

Conclusions: EOS is common with DAP usage especially with longer durations but absence of EOS does not preclude DPE. Previous EOS and re-exposure to DAP was significantly associated with early onset DPE. We recommend monitoring EOS with DAP usage as a predictor for future DPE on re-exposure.

Table 1: Comparison of eosinophilic and non-eosinophilic patients

<table>
<thead>
<tr>
<th>Factor</th>
<th>Eosinophilia (n=110)</th>
<th>Non-Eosinophilia (n=221)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (median)</td>
<td>62.6</td>
<td>64</td>
<td>n/a</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>106 (99%)</td>
<td>214 (97%)</td>
<td>0.28</td>
</tr>
<tr>
<td>BMI (median)</td>
<td>28.9 (15.54)</td>
<td>28.5 (13.60)</td>
<td>0.37</td>
</tr>
<tr>
<td>Days of DAP initial (median)</td>
<td>25.5 (1-154)</td>
<td>7 (1-102)</td>
<td>0.001</td>
</tr>
<tr>
<td>Total DAP Re-exposures</td>
<td>40</td>
<td>43</td>
<td>0.001</td>
</tr>
<tr>
<td>Days of DAP (Re-exposure) median</td>
<td>14</td>
<td>7</td>
<td>0.001</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>34 (31%)</td>
<td>56 (25%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Re-exposure DPE</td>
<td>6 (15%)</td>
<td>2 (5%)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

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Abstract 5520

Prevalence of azole resistance in clinical Aspergillus fumigatus isolates in Greece

Maria Siopi*, Olga Rivero-Menendez2, Athanasios Chatzimoschou3, Aristea Velegraki1,5, Ana Alastruey-Izquierdo2, Emmanuel Rolides3, Georgia Vrioni4, Spyros Pournaras1, Joseph Meletiadis1,6

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Background: We have recently shown that azole-resistant Aspergillus fumigatus (AR-Af) with an environmental signature is present in Greece (Siopi ECCMID2019). Nevertheless, the prevalence of azole resistance in Greek clinical isolates remains uncertain. We therefore investigated the prevalence of clinical AR-Af in Greece.

Materials/methods: A total of 140 A. fumigatus species complex (SC) strains recovered from respiratory specimens of 133 patients (64 hematological, 16 hospitalized in ICU, 53 other) were collected from 5 centers (4 Athens, 1 Thessaloniki) and were retrospectively tested. Isolates were macro-/microscopically identified and were subcultured on Sabouraud+chloramphenicol plates at 48°C to differentiate A. fumigatus sensu stricto (SS). In vitro susceptibility testing of A. fumigatus SC strains to amphotericin B (AMB), itraconazole (ITC), voriconazole (VRC), posaconazole (POS), isavuconazole (ISA), anidulafungin (AFG), caspofungin (CAS) and micafungin (MFG) was performed according to EUCAST E.DEF9.3.1. Isolates exhibiting reduced susceptibility to azoles were subjected to confirmatory molecular identification (White 1990, Balajee 2005) and were further studied for the detection of specific mutations in the cyp51A gene, including its promoter region associated with azole resistance (Mellado 2007).

Results: All isolates grew at 48°C indicating that they belonged to A. fumigatus SS. Antifungal susceptibility patterns among all strains are summarized in Table. In total, all isolates were AMB-susceptible and exhibited echinocandin wild-type phenotypes. POS was the most potent azole in vitro (geometric mean MIC 0.11 mg/L), followed by ITC, VRC and ISA (geometric mean MIC 0.46, 0.59 and 0.70 mg/L, respectively). Overall, 1/133 (0.8%) AR-Af SS from 1/133 (0.8%) patient was detected. Particularly, the isolate was recovered from a pleural fluid culture of an ICU patient, did not have mutations in cyp51A, showed resistance to ITC and POS (MIC >8 and 0.5 mg/L, respectively) and was susceptible to VRC and ISA (MIC 1 mg/L for both drugs).

Conclusions: All clinical A. fumigatus isolates were sensu stricto. We report the detection of an azole-resistant clinical A. fumigatus without cyp51A mutations. The rate of AR-Af in Greece seems to be low (0.7%).

<table>
<thead>
<tr>
<th>Antifungal agent</th>
<th>Geometric mean (mg/L)</th>
<th>MIC/MEC₉₀ (mg/L)</th>
<th>MIC/MEC₉₀ (mg/L)</th>
<th>Range (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMB</td>
<td>0.44</td>
<td>0.5</td>
<td>0.5</td>
<td>0.25-0.5</td>
</tr>
<tr>
<td>ITC</td>
<td>0.46</td>
<td>0.5</td>
<td>0.5</td>
<td>0.125-0.75</td>
</tr>
<tr>
<td>VRC</td>
<td>0.59</td>
<td>0.5</td>
<td>0.5</td>
<td>0.25-2</td>
</tr>
<tr>
<td>POS</td>
<td>0.11</td>
<td>0.125</td>
<td>0.25</td>
<td>0.03-0.5</td>
</tr>
<tr>
<td>ISA</td>
<td>0.70</td>
<td>0.5</td>
<td>0.5</td>
<td>0.5-2</td>
</tr>
<tr>
<td>AFG</td>
<td>0.01</td>
<td>0.008</td>
<td>0.008</td>
<td>0.004-0.015</td>
</tr>
<tr>
<td>CAS</td>
<td>0.23</td>
<td>0.25</td>
<td>0.25</td>
<td>0.125-0.5</td>
</tr>
<tr>
<td>MFG</td>
<td>0.01</td>
<td>0.015</td>
<td>0.015</td>
<td>0.008-0.015</td>
</tr>
</tbody>
</table>

Presenter email address: marizasiopi@hotmail.com
A multi-centre evaluation of the US prevalence and regional variation in macrolide-resistant Streptococcus pneumoniae from blood or respiratory cultures among adult patients

Vikas Gupta1, Kalvin Yu1, Jennifer Schranz1, Hanna Jokinen-Gordon1, Steven P. Gelone2

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Abstract third-party references: Nabriva Therapeutics US, Inc.

Background: S. pneumoniae continues to be designated by the 2019 CDC Antibiotic Resistance Threats Report as a "Serious Threat", underscoring need for rapid detection and prevention strategies. Additionally, the 2019 IDSA/ATS community acquired pneumonia (CAP) guidelines revised recommendations for macrolide use only in those areas where outpatient macrolide resistance is < 25%. This study sought to quantify the prevalence and rates of macrolide resistant S. pneumoniae from blood or respiratory cultures in adult ambulatory and hospitalized patients.

Materials/methods: All adults with a positive S. pneumoniae blood or respiratory culture (first isolate of a species per 30 day period) in the ambulatory and inpatient setting from 329 US hospitals from Q4 2018-Q3 2019 were evaluated [BD Insights Research Database, Becton, Dickinson & Company]. Macrolide resistance was defined as resistant to S. pneumoniae per commercial panels. Macrolide resistance was calculated overall, by source (blood vs. respiratory), by setting (ambulatory vs. inpatient), and by U.S. Census geographic region. The Chi square test was used to test for significance.

Results: There were 3,626 non-duplicate S. pneumoniae isolates across 3,510 patients; 43.8% were from the blood and 56.2% were from respiratory source. The majority of isolates were collected in the inpatient setting (n=2,798) as compared to the ambulatory setting (n=828). Overall, macrolide resistance was 39.5% and was significantly higher in respiratory versus a blood source (47.3% vs. 29.6%, respectively, p < 0.0001). Macrolide resistance was also higher in ambulatory isolates as compared to inpatient isolates (45.3% vs. 37.8%, respectively, p < 0.001). Regional differences in macrolide resistance are summarized below (p < 0.0001).

<table>
<thead>
<tr>
<th>US Census Region</th>
<th>Facilities</th>
<th>Blood</th>
<th>Respiratory</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>% R (n/Tested)</td>
<td>% R (n/Tested)</td>
<td>% R (n/Tested)</td>
</tr>
<tr>
<td>East North Central: IL, IN, MI, OH, WI</td>
<td>56</td>
<td>29.0% (63/217)</td>
<td>49.7% (159/320)</td>
<td>41.3% (222/537)</td>
</tr>
<tr>
<td>East South Central: AL, KY, MS, TN</td>
<td>49</td>
<td>38.0% (87/229)</td>
<td>55.6% (140/252)</td>
<td>47.2% (227/481)</td>
</tr>
<tr>
<td>Middle Atlantic: NJ, NY, PA</td>
<td>50</td>
<td>28.3% (54/191)</td>
<td>39.8% (94/236)</td>
<td>34.7% (148/427)</td>
</tr>
<tr>
<td>Mountain: AZ, CO, ID, MT, NM, NV, UT, WY</td>
<td>10</td>
<td>4.2% (1/24)</td>
<td>33.3% (6/12)</td>
<td>13.9% (5/36)</td>
</tr>
<tr>
<td>New England: CT, MA, ME, NH, RI, VT</td>
<td>5</td>
<td>4.0% (1/25)</td>
<td>25.0% (13/52)</td>
<td>18.2% (14/77)</td>
</tr>
<tr>
<td>Pacific: AK, CA, OR, WA</td>
<td>36</td>
<td>13.2% (34/257)</td>
<td>25.3% (48/190)</td>
<td>18.3% (82/447)</td>
</tr>
<tr>
<td>South Atlantic: DE, DC, FL, GA, MD, NC, SC, VA, WV</td>
<td>40</td>
<td>30.3% (44/145)</td>
<td>60.8% (121/199)</td>
<td>48.0% (165/344)</td>
</tr>
<tr>
<td>West North Central: IA, KS, MN, MO, ND, NE, SD</td>
<td>12</td>
<td>52.1% (25/48)</td>
<td>55.0% (72/131)</td>
<td>54.2% (97/179)</td>
</tr>
<tr>
<td>West South Central: AR, LA, OK, TX</td>
<td>71</td>
<td>35.6% (162/455)</td>
<td>48.5% (312/643)</td>
<td>43.2% (474/1,098)</td>
</tr>
<tr>
<td>Total</td>
<td>329</td>
<td>29.6% (471/1,591)</td>
<td>47.3% (963/2,035)</td>
<td>39.5% (1,432/3,626)</td>
</tr>
</tbody>
</table>

Conclusions: This large, contemporary database study helps quantify the national burden of S. pneumoniae resistance in respiratory and blood isolates. About 5 in every 10 respiratory and 3 out of every 10 blood cultures are macrolide resistant. Regional variances occur per source, and highlight the need for continued susceptibility testing to help inform empiric CAP therapy. Evaluating risk factors for resistance such as geographic region and source of pathogen identification is a key critical first step to evaluating empiric macrolide therapy in patients with CAP.

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Do we really have to worry about acyclovir-induced nephrotoxicity?

Imran Hasanoğlu*, Ayse Kaya Kalem, Bircan Kayaaslan, Zeynep Atalay Altinkaynak, Rahmet Guner

Yıldırım Beyazıt University Ankara City Hospital, Ankara, Turkey

Background: Acyclovir remains the only treatment option for herpes encephalitis but can potentially cause nephrotoxicity. Aim of this retrospective cohort study was to evaluate acyclovir-induced nephrotoxicity.

Materials/methods: The study population consisted of adult patients who received ≥ 48 hours acyclovir for treatment of viral encephalitis between 2010 and 2018. Acute kidney injury (AKI) was defined according to RIFLE criteria.

Results: Among 260 patients, AKI was observed in 27 (16.8%) of the patients. There were 9 (5.6%), 11 (6.9%), and 7 (4.4%) patients in Risk, Injury, and Failure categories respectively. No loss of function and end-stage renal disease were observed. Mean time to AKI was 5.2 days. We found no correlation between treatment time and AKI development. Rates of concomitant nephrotoxic agent use were similar between AKI and non-AKI group. In AKI group, 92% of the patients’ creatinine decreased after dose reduction. Two (1%) patients received hemodialysis. Characteristics of the patients are given in Table. Hypertension and diabetes are found to be significant risk factors for AKI. We found no statistically significant difference between two groups in terms of age, sex, clinical improvement, and mortality rates.

Conclusions: Nephrotoxicity is an important but manageable side effect of acyclovir. But still clinicians should be more careful in patients with hypertension and diabetes.

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>AKI group</th>
<th>Non-AKI group</th>
<th>Relative Risk (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers (%)</td>
<td>160</td>
<td>27 (16.8%)</td>
<td>133 (83.13)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &gt;65</td>
<td>38 (24.38)</td>
<td>10 (37.04)</td>
<td>28 (21.80)</td>
<td>1.82 [0.91–3.65]</td>
<td>0.0788</td>
</tr>
<tr>
<td>Female</td>
<td>62 (39.75)</td>
<td>11 (40.74)</td>
<td>51 (38.35)</td>
<td>1.09 [0.54–2.18]</td>
<td>0.4892</td>
</tr>
<tr>
<td>Baseline Creatinine</td>
<td>0.8 [0.1–3.4]</td>
<td>0.95 [0.4–2.2]</td>
<td>0.8 [0.1–3.4]</td>
<td></td>
<td>0.2791</td>
</tr>
<tr>
<td>Concomitant nephrotoxic agent use</td>
<td>16 (10.16)</td>
<td>2 (7.41)</td>
<td>14 (10.53)</td>
<td>0.71 [0.18–2.70]</td>
<td>0.8043</td>
</tr>
<tr>
<td>Diabetes</td>
<td>22 (13.75)</td>
<td>9 (33.33)</td>
<td>13 (47.77)</td>
<td>3.14 [1.62–6.08]</td>
<td>0.0034</td>
</tr>
<tr>
<td>Hypertension</td>
<td>35 (21.88)</td>
<td>10 (37.04)</td>
<td>25 (18.80)</td>
<td>2.10 [1.06–4.17]</td>
<td>0.0375</td>
</tr>
<tr>
<td>Kidney Disease</td>
<td>6 (3.75)</td>
<td>0 (0)</td>
<td>6 (4.51)</td>
<td></td>
<td>1.0000</td>
</tr>
</tbody>
</table>

Presenter email address: imran.solak@gmail.com
Epidemiology of sexually-transmitted infections in women with suspected pelvic inflammatory disease admitted to gynaecology emergency unit of an Italian hospital

Simona Fiorentini*, Annalisa Pirozzi1, Alberto Matteelli2, Valentina Marchese1, Roberto Stellini2, Marilena Traversi2, Francesca Caccuri3, Sabrina Rubessa2, Maurizio Gulletta2

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Background: Pelvic inflammatory disease (PID) is an acute inflammation of female upper genital tract, often resulting in long-term sequelae. The majority of PID cases (85%) are caused by sexually transmitted pathogens or bacterial vaginosis-associated pathogens, so there is no single diagnostic test as gold standard and clinical diagnosis remains the primary practical approach. Our objective was to evaluate the epidemiology of PID in a population of symptomatic patients admitted to the Gynecology Emergency Unit using a new sampling approach (Self Vaginal FLOQSwab™, COPAN Italia) combined with molecular diagnostic methods to detect Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG) and Mycoplasma genitalium (MG).

Materials/methods: From December 2017 to August 2019 a total of 14,623 women were admitted at the Gynecology Emergency Unit with clinical signs of PID. PID was confirmed only in 101 patients (age 18 to 74 years old). Depending on symptoms severity, women were hospitalized or discharged with indications for empirical treatment at home. Clinicians performed a double sample collection: cervical sampling with regular FLOQSwab™ and vaginal collection using a new Self-Vaginal swab (COPAN Italia). Both samples were then processed by molecular assays for detection of CT, NG (Xpert CT-GC, Cepheid) and MG (Elitech assay).

Results: 18 on 101 patients were positive respectively for Mycoplasma genitalium (n=4), Chlamydia trachomatis (n=7) and Neisseria gonorrhoeae (n=7). Two patients had a co-infection, one was CT/MG and one was CT/NG. In negative STIs patients others bacteria have been identified: Bacterial Vaginosis (10.3%), E.coli (20.6%) and H.influenzae (4.4%). Vaginal samples demonstrated 100% of overall agreement with the cervical collection. Post-therapy self-made sampling resulted negative and concordant with control routinary tests.

Conclusions: NG, CT and MG are the primary cause of symptomatic PID but STIs proportion among PID women was lower than expected. This is in agreement with the observation that milder symptoms occur more frequently in patients with STIs. In acute PID, the presence of other microbes should always be considered. Self-collected swabs would be a good alternative in populations that may not go for testing at all, do not have the option of clinical testing, or refuse a clinical examination.

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**Abstract 5530**

**Cycle of quantification (Cq) does not differentiate colonisation from *Pneumocystis jirovecii* pneumonia, using real-time PCR**

Peter Paul Basazemajja1, Theo A. Schuurs2, Age Jan Stellingwerff2, Aziz Al Moujahid*

1Martini Hospital, Groningen, Netherlands, 2Izore, center for infectious diseases friesland, Leeuwarden, Netherlands

**Background:** Real-time PCR shows high sensitivities (97–99%) and specificities (90–94%) in the detection of *Pneumocystis jirovecii* in clinical samples. Due to the biological nature of the pathogen and PCR targets used in differing laboratories, different quantification cycle (Cq) cut-off values have been proposed to distinguish colonization from infection. This study aimed to determine a cut-off Cq-value to distinguish colonization from *P. jirovecii* pneumonia (PJP) in the province of Friesland (the Netherlands).

**Materials/methods:** A retrospective study was conducted on respiratory samples that were sent to Izore because of clinical suspicion of PJP (study group: n=150).

Diagnostic consisted of real-time PCR. Patient’s clinical symptoms were gathered from the hospital information systems and/or the Izore application form, after informed consent. Symptoms of fever, cough, dyspnoea and clinical findings of low oxygen saturation, arterial hypoxia, chest X-ray or computed tomography abnormalities were used as symptoms associated with the clinical diagnosis of PJP in the study group.

The reference group (n=92) consisted of immunocompetent patients with lung conditions, without clinical suspicion of PJP, for which further diagnosis using deep respiratory material was required.

**Results:**
- In the study group (n=150), 54 samples (36%) were PJP positive with a mean Cq-value of 27.9 (SD ± 3.40).
- To assess correlation between the number of PJP-related symptoms and Cq-value, the 54 PJP PCR-positive samples were divided into two groups. Group A consisted out of samples with 3 or less symptoms and group B consisted out of 4-7 symptoms (strongly indicative for PJP). There was no significant difference in Cq-value between group A and B (P=0.59).
- In the reference group, 3 samples (3%) were positive with a mean Cq-value of 30.4 (SD ± 4.07). These were termed as colonization. There was no significant difference between the mean Cq-values of the immunocompetent reference group and the immune-incompetent PJP-positive group (P=0.48).

**Conclusions:**
- No Cq-value was found to differentiate colonization from PJP using real-time PCR. There was no correlation between number of symptoms and Cq-value.
- There is a low prevalence of colonization (3%) in the immunocompetent yet chronically sick population

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Abstract 5531

The recombinant NP-HA2 fusion protein as a candidate for designing of universal influenza vaccines

Maryam Zeinolabedin1, Masoud Moghadaszadeh2*, Payam Zeinolabedini3

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Background: Influenza is as an extremely contagious respiratory tract disease. Influenza A virus is a member of the Orthomyxoviridae family that has segmented genome and great antigenic diversity. Influenza viruses possess multiple conserved epitopes that are designed for universal vaccines. These epitopes are the nucleoprotein (NP) and HA2.

Materials/methods: In this survey, we have constructed new plasmids to express above-mentioned epitopes as a single recombinant product. To this aim, two peptide genes of N-terminal NP and HA2 were linked together with a (Gly4Ser)4 peptide linker, synthesized, and cloned into pET26b vector. Then, the construct was transferred into E. coli BL21 (DE3) cells and induced using isopropyl β-D-1 thiogalactoside (IPTG). Immunization of mice with above peptides significantly induced humoral immune responses. Three weeks after the last booster, mice were inoculated intranasally with 1×106 EID50 of H9N2 virus.

Results: The recombinant NP-HA2 fusion protein gene was cloned into pET26b vector. The results of sequencing displayed that gene was properly cloned in vector. Also, SDS-PAGE showed a strong single band. Moreover, Western blot analysis indicated a single band in correct position. Real-time RT-PCR studies exhibited reduction of virus in BALB/c mice lung tissues. Our study revealed that this protein could protect mice against H9N2 virus.

Conclusions: The recombinant NP-HA2 fusion protein characterizes a potential candidate for influenza vaccine studies in animal model. According to the findings, the NP-HA2 fusion protein induced humoral immunity responses. The findings of this study suggest that the recombinant fusion peptide which is economical to yield can be used for induction specific antibodies responses. The results of the current study showed that above protein can protect mice by decreasing virus shedding.

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Abstract 5534

**Accurate discrimination of *Shewanella algae* from *Shewanella putrefaciens* with Acrion system: an under-reported marine pathogen**

Jake D’Addiego1, Jarkko Räbinä2, Soniya Gurung1, Juha Knuuttila2, Jason Chew1, Mark Hutchins1, Attaybenes Socas1, Pirjo Wacklin2, Naomi Chant1

1Thermo Fisher Scientific, Basingstoke, United Kingdom, 2Thermo Fisher Scientific, Vantaa, Finland

**Background:** *Shewanella* species are a group of Gram-negative bacteria associated with marine environments. The only two reported species of clinical relevance are *Shewanella algae* (which causes around 80% of all *Shewanella* infections in humans) and *Shewanella putrefaciens*. The most common clinical manifestations are skin and soft tissue infections associated with ulcers or trauma, ear infections present as acute infections or acute exacerbations in chronic otitis media and bacteraemia. The accurate identification of *Shewanello* species by MALDI-TOF technologies has been challenging in the past due to the lack of representation of *S. algae* in their database, resulting in misidentifications. The inclusion of *S. algae* into the database of Acrion™, a novel automated diagnostic platform based on high-resolution mass spectrometry, will likely reduce the misidentifications of these marine pathogens.

**Materials/methods:** Five (5) strains each of *Shewanella algae* and *Shewanella putrefaciens* were obtained from culture collections and clinical laboratories and cultivated on two media types in appropriate conditions. Each strain was prepared for Acrion™ analysis using high resolution mass spectrometry from each cultivation condition. Analysis of all strains was carried out using intact protein analysis (MS1) to discriminate strains to species level, and the results were further confirmed through 16S rRNA sequencing.

**Results:** Using the high-resolution mass spectrometry technology employed by Acrion™, all strains of *S. algae* and *S. putrefaciens* were accurately discriminated which was in accordance with 16S rRNA sequencing results.

**Conclusions:** This study shows Acrion™ allows accurate and reliable discrimination of *S. algae* and *S. putrefaciens* through high-resolution mass spectrometry technology. The addition of these taxa in Acrion™ database will allow the identification of these emerging marine pathogens.

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Analysis of *Escherichia coli* phylotypes and known sepsis-causing sequence types in UK sewage reveals a direct link between sepsis rates and carriage of pathogenic sequence types in the community

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1Cardiff University, Cardiff, United Kingdom, 2Karaganda Medical University, Karaganda, Kazakhstan

**Background:** UK *Escherichia coli* sepsis rates have been rising for the last 20 years. However, the reason behind this consistent year on year increase is an enigma. The sepsis rate also varies greatly between NHS geographic regions and considerably between London (64/100K) and South Wales (85/100K). We hypothesized that the different rates could be due to differing prevalence of pathogenic *E. coli* types in the different UK NHS regions.

**Materials/methods:** Sewage was collected from Longreach, Marlow, Reading, Bristol, Ponthir and Cardiff sewage works from 19/9/2019-26/9/2019. We diluted and streaked these samples on chromogenic UTI agar (no antibiotics) and randomly chose c. 100 *E. coli* isolates from each location. Species was confirmed by Maldi-TOF-MS and susceptibility determined by disc diffusion (EUCAST methodology). The phylotype was determined by multiplex PCR (Clermont method). Each pathogenic B2 isolate was further tested for known common sepsis sequence types (ST): ST131, ST73, ST95 and ST69 by multiplex PCR (Doumith method).

**Results:** The prevalence of pathogenic B2 phylotype *E. coli* was considerably higher in South Wales than in England, 31.5% verses 1.2%, reflecting the higher sepsis rates in Wales as compared to England. B2 phylogenetic prevalence at each location was: Ponthir (33%), Cardiff (31%), Bristol (24%), Reading (6%), Marlow (4%), Longreach (14%) with prevalence lowest in the London region (8% overall). The multiplex PCR for detecting known sepsis causing pathogenic *E. coli* ST95, ST131, ST73 and ST69 detected one or more of these ST at all locations (Table 1). The prevalence of these specific ST was also considerably higher in S. Wales than in England, 10.5% verses 6.25%. The highest rate of specific sepsis *E. coli* ST was found in Bristol mostly due to a very high prevalence of ST95 (9%) in the Bristol community.

**Conclusions:** Our results show that regions of the UK with high *E. coli* sepsis rates correlate with high levels of group B2 *E. coli* carriage in the community and vice versa. It is reasonable therefore to suggest that the UK sepsis is due to increasing carriage rates of sepsis causing strains in the community.

<table>
<thead>
<tr>
<th>Location</th>
<th><em>E. coli</em></th>
<th>B2</th>
<th>ST95</th>
<th>ST73</th>
<th>ST131</th>
<th>ST69</th>
<th>Known ST</th>
<th>B2 other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ponthir</td>
<td>117</td>
<td>39 (33%)</td>
<td>2</td>
<td>4</td>
<td>7</td>
<td>-</td>
<td>13 (11%)</td>
<td>26</td>
</tr>
<tr>
<td>Cardiff</td>
<td>63</td>
<td>20 (31%)</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>6 (10%)</td>
<td>14</td>
</tr>
<tr>
<td>Bristol</td>
<td>114</td>
<td>27 (24%)</td>
<td>10</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>17 (15%)</td>
<td>10</td>
</tr>
<tr>
<td>Marlow</td>
<td>95</td>
<td>4 (4%)</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>4 (4%)</td>
<td>-</td>
</tr>
<tr>
<td>Reading</td>
<td>62</td>
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**Abstract 5546**

**A novel variant of CTX-M β-lactamase in a clinical strain of Serratia marcescens**

Piotr Celejewski-Marciniak¹, Renata Wolinowska², Marta Wroblewska*¹,³

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**Background:** Gram-negative rods classified in the genus *Serratia* are widely distributed in the external environment – in soil and water. Simultaneously, these bacteria may cause opportunistic healthcare-associated infections, particularly in immunocompromised patients. In humans, the most common etiological agent of infections is *Serratia marcescens*. Strains within this species are characterised by resistance to many antibiotics and other antimicrobial agents, which may be determined by both the genes localised on the bacterial chromosome, as well as by mobile genetic elements (plasmids and integrons). The aim of the study was to characterise mobile genetic elements present in clinical strains of Gram-negative rods classified in the genus *Serratia*, and to determine their role in the transfer of the genes determining resistance to antibacterial agents.

**Materials/methods:** Analysis comprised 120 clinical strains of Gram-negative rods *Serratia* spp., obtained from 7 clinical microbiological laboratories located in Warsaw and Otwock (Poland). Identification of the isolates was done with three techniques – MALDI-TOF MS, Vitek 2 Compact and API 20E. Sequencing was performed of the amplification products of the genes coding for type CTX-M β-lactamases.

**Results:** Identification of 112 strains was confirmed as *Serratia* spp., including 103 isolates of *S. marcescens*, 7 – *S. liquefaciens*, 1 – *S. fonticola* and 1 – *S. ureilytica*. Nucleotide sequences encoding type CTX-M-15 β-lactamase were present in over 75% of the analysed strains which were ESBL-positive. An isolate of *S. marcescens* no. 120 was characterised by the presence of a plasmid pPM120-1, classified in the incompatibility group IncL/M (IncM), which was encoding a CTX-M β-lactamase of the structure not described so far. It was determined that this novel variant of CTX-M β-lactamase was a hybrid of CTX-M-19 and CTX-M-3 β-lactamases.

**Conclusions:** 1. Over 75% of ESBL-positive strains of *Serratia* spp. contained nucleotide sequences coding for β-lactamase type CTX-M-15. 2. For the first time in the world, a novel variant of CTX-M β-lactamase was detected, which constitutes a hybrid of CTX-M-19 and CTX-M-3 β-lactamases. A unique nucleotide sequence *bla*\textsubscript{CTX-M-22} was deposited in the GenBank NCBI with the number MH538139.1.

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**Abstract 5551**

**Rapid diagnostic test: Identification of Candida spp. directly from the blood culture bottle using short-term subculture incubation and MALDI-TOF MS in a routine microbiology laboratory**

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**Abstract third-party references:** Hospital de Clínicas de Porto Alegre

**Background:** The development of rapid diagnostic assays for the identification of candida causing bloodstream infections is of utmost importance to reduce morbidity and mortality. Rapid diagnostic tests of pathogens is critical to guarantee adequate therapy for infections. In this study, we evaluated a rapid modified Candida spp. identification from positive blood cultures based on a short-time culture incubation to reduce the turnaround time in bloodstream infection diagnostics in a routine microbiology laboratory.

**Materials/methods:** All hemocultures flagged as positive by bacT/ALERT®, Gram staining positive to yeast of patients admitted at a tertiary hospital in southern of Brazil were included [March to November 2019]. Rapid identification was performed as follow: five drops of blood culture were transferred to the center of a Sabouraud agar and then incubated (35 °C for ut to 4-5h). Growth on the plate was placed onto a spot according to the manufacturer’s instructions for analyses using VITEK MS® system database v3.0 [bioMérieux, France]. Results were compared with standard identification from the subculture in solid medium after 24 hours. A minimum confidence level of 80% has been set for identification criteria.

**Results:** A total of 112 samples were tested: 40 (35.7%) Candida albicans, 2 (1.8%) Candida dubliniensis, 3 (2.7%) Candida krusei, 44 (39.3%) Candida parapsilosis Complex and 23 (20.5%) Candida tropicalis. The percentages of total correct identification of the isolates tested at species level using the rapid protocol were 94.64% [106] samples. Only 6 samples were not identified by this methodology, 1 C. albicans and 5 C. parapsilosis complex. The Vitek MS system was not able to identify closely related species belonging to C. parapsilosis Complex.

**Conclusions:** Current technologies employed in routine diagnostics are based culture growth, which constitutes the actual gold standard. Although those methods are precise and sensitive, they are rather slow. Rapid identification directly from the blood culture bottle using rapid culture is feasible and easy to perform within the laboratory routine. Identification by the rapid method showed a high degree of accuracy. The marked reduction in time to results may have significant implications for patient care.

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Abstract 5552

Missed opportunities for an early HIV diagnosis

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Background: The World Health Organisation has set out the goal of 90-90-90 in order to control the HIV pandemic. Individuals with indicator conditions (IC) are not always offered testing, suggesting a missed opportunity for an early diagnosis.

Materials/methods: HIV infection dates were inferred by molecular clock analysis using a Bayesian method. Patients’ files were reviewed in order to identify healthcare contacts, where there would be an IC for HIV testing prior to HIV diagnosis.

Results: Among the study population, 82.7% (206/235) were male, 46.8% (110/235) were reported MSM, 41.3% (97/235) PWID, and 10.2% (24/235) heterosexuals. Regarding their diagnosis status, 54% (127/235) were late presenters, and 29.4% (69/235) had advanced disease.

A total of 178 healthcare contacts were recorded in 124 patients (52.7%) between their infection date and the HIV diagnosis date. The most frequent, included mononucleosis-like syndrome (35/178, 19.7%), unexplained weight loss (17/178, 9.6%), sexually transmitted infections (17/178, 9.6%) and a diagnosis of hepatitis B and/or C (13/178, 7.3%). AIDS defining conditions were 24/178 (13.5%). Only 60.4% of people with indication for testing were diagnosed within 1 month of their first healthcare contact.

Our population was divided in 3 groups, i) those diagnosed with preemptive testing (PT) (N=111), ii) individuals with medical indication and proper testing (MIPT) (N=75) and iii) people with indication but no testing (MINT) (N=49).

The median time interval from infection to diagnosis was much shorter for the PT group (230 days, IQR:77-542) than the MIPT group (487 days, IQR:215-827) and the MINT group (680 days, IQR:361-1527) [p<0.001].The median CD4 at diagnosis was 409cells/µl (IQR:226-610), 310cells/µl (IQR:126-480) and 283cells/µl (IQR:135-485) [p=0.039], for the 3 groups respectively.

People in the PT group were less likely to present with advanced disease [24/111, 21.6% vs 27/75, 36% vs 18/49, 36.7%, p=0.046].

Conclusions: Our study shows that preemptive and IC-guided HIV testing can facilitate early diagnosis of HIV. This is one of the few studies that used a combination of clinical and molecular methods to provide evidence about the benefits of different testing strategies to combat late diagnosis.

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Effectiveness of bacteriophage-antibiotic combinations for daptomycin-resistant Enterococcus faecium harbouring LiaS and LiaR substitutions

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Background: Enterococcus faecium (E.fcm) infections are difficult to eradicate and there is a growing concern regarding the increased prevalence of daptomycin (DAP)-nonsusceptible (DNS) strains. It has been shown that alterations in liaFSR (three-component regulatory system) are crucial mediators of DNS in enterococci. Given the rising occurrence of DNS E.fcm, there is an urgent necessity of novel therapies. Obligately lytic bacteriophages [phages] are viruses that infect bacteria, replicate within the cell, then lyse the cell to release their progeny to reinitiate the infection cycle. Positive interactions have been described with phage-antibiotic combinations; however, no study has evaluated phage-antibiotic combinations against DNS E.fcm strains, and limited studies have analyzed membrane vesicle (MV) formation [virulence mechanism] with phage-antibiotic combinations. The objective of this study was to determine the ability of combinations of phage plus DAP alone and in combination with DAP plus beta-lactams to improve bacterial killing and/or alter resistance development in DNS E.fcm.

Materials/methods: Clinical strain E.fcm R497 (with substitutions in liaFSR) was evaluated. Due to DAP’s calcium-dependency, Mueller-Hinton broth II (Difco, Detroit, MI) supplemented with 50 mg/L calcium was utilized for susceptibility testing and time-kill analyses (TKA). Minimum inhibitory concentration [MIC] testing was performed and 24h TKAs were evaluated at 0.5x MIC or biologic free peak concentration [whichever was lower]. Phage ATCC 19950-B1 was utilized at ~105 PFU/mL. Synergy (≥ 2-log10 CFU/mL kill compared to the most effective agent alone at 24 hours) and bactericidal activity (≥ 3-log10 CFU/mL reduction at 24 hours compared to the starting inoculum) were evaluated in TKAs. MV experiments and evaluation of antibiotic resistance development were performed as previously described.

Results: R497 exhibited elevated MICs to all antimicrobials evaluated [DAP=16 mg/L, ampicillin [AMP]=128 mg/L, ertapenem [ERT]=>64 mg/L]. The combinations of DAP-AMP and DAP-ERT failed to demonstrate bactericidal or synergistic effects [exception: synergy observed with DAP-AMP]. In contrast, the addition of phage to DAP-AMP and DAP-ERT exhibited bactericidal and synergistic effects (figure 1). There were no significant differences in MV formation and no emergence of antibiotic resistance was observed.

Conclusions: Based on these encouraging results, further research is needed to evaluate phage-antibiotic combinations in DNS E.fcm strains.

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Atelerix algirus as host of Salmonella species in Tenerife, Spain
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¹University of La Laguna, Instituto Universitario de Enfermedades Tropicales y Salud Pública de Canarias, San Cristóbal de La Laguna, Spain

Abstract third-party references: by ProID2017010092, Gobierno de Canarias, FEDER

Background: The Algerian hedgehog, Atelerix algirus, is an invasive species in the Canary Island, Spain. Nowadays, it seems to have colonized the islands of Fuerteventura, Lanzarote, Gran Canaria, Tenerife, and La Palma. There is not much information available about A. algirus biodiversity impact on the Canary Islands, and only few studies had been carried out studying the zoonotic pathogens that it could be hosting around the world. Besides, wild hedgehogs are often kept as pets in Canaries, especially by children. Because of the lack of knowledge about the possible pathogens that A. algirus could be hosting, the aim of this study was to analyse the presence of species of Salmonella in faeces of A. algirus.

Materials/methods: Two different types of samples were collected: fresh faeces from living specimens (36) and faeces from the intestine of dead animals (2). All samples and their provenance were provided by La Tahonilla, a wildlife recovery center of Excmo. Cabildo Insular Tenerife. Samples were analysed by FilmArray gastrointestinal panel (Biomerieux).

Results: Salmonella sp. were found in 26 of the 38 samples analysed (68.42%), in nearly every area in which this study was performed, not finding any difference in the prevalence between warm and cold areas.

Conclusions: The high prevalence of Salmonella sp. present in wild hedgehogs in Canaries, could implies a high risk of transmission, not only to other wildlife animals, but to humans, as these animals are often kept as pets by children, the most severe affected by gastrointestinal diseases. Another factor to take into consideration is that hedgehogs present a behavior named anting or anointing, which consist in moistening their spines with saliva. The fact that hedgehogs showed high prevalence of Salmonella sp. could imply a risk for humans to get this bacterium only by touching these animals. The present results could be of help to competent entities to take control measurements in order to prevent the transmission of this causative agent of diarrhea. [Funded by ProID2017010092, Gobierno de Canarias, FEDER].

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Abstract 5556

**Appropriateness of antibiotic recommendations within infectious diseases guidelines for patients with a penicillin allergy: a systematic review**

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**Background:** Clinical practice guidelines are used by clinicians to assist in the management of patients with infectious diseases (ID) and include antibiotic recommendations for patients allergic to penicillin. Modern investigations have established that cross-reactivity between penicillin, cephalosporins, and carbapenems is primarily based on side-chains, not the shared beta-lactam ring. These data indicate that cephalosporins with dissimilar side chains and carbapenems can safely be used in patients with penicillin allergies. The objective of this systematic review is to describe penicillin allergy recommendations and assess the appropriateness based risk of cross-reactivity.

**Materials/methods:** Current guidelines written and/or endorsed by American Academy of Pediatrics, Centers for Disease Control and Prevention, Infectious Diseases Society of America, and Pediatric Infectious Diseases Society that included antibacterial recommendations were included in the analysis. The primary outcomes were the frequency in which ID guidelines recommend non-beta-lactams for patients allergic to penicillin and the risk of cross-reactivity between penicillin and first-line beta-lactams.

**Results:** Twenty-eight guidelines were included, resulting in 560 antibacterial recommendations. Beta-lactams were identified as first-line treatment for 413 (74%) recommendations. Penicillins were included in first-line options in 174 (31%) recommendations, cephalosporins in 184 (33%), and carbapenems in 61 (11%) recommendations. Of the 413 beta-lactam recommendations, there were 261 (63%) alternative antibiotic recommendations: 188 (72%) of those recommendations were specific for patients with penicillin allergies and 73 (28%) included alternative antibiotic recommendations not specific for patients with penicillin allergies. Non-beta-lactams were recommended in 202/261 (77%) treatment recommendations. The risk of cross-reactivity between penicillin and first-line beta-lactams was less low (less than 2%) for 235/413 (57%) recommendations, medium (2 – 20%) for 14/413 (3%) recommendations, and high (greater than 20%) for 164/413 (40%) recommendations.

**Conclusions:** ID guidelines recommend non-beta-lactams for patients with penicillin allergies in 77% of the recommendations. This results in the increase use of less effective and/or more toxic antibiotics than beta-lactams. These ID guidelines should be updated and include recommendations for cephalosporins with dissimilar side chains or carbapenems for patients allergic to penicillin.

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Antifungal susceptibility patterns among clinical isolates of *Aspergillus fumigatus* from paediatric cystic fibrosis patients in Greece: a laboratory-based study with focus on azole resistance

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1Clinical Microbiology Laboratory, “Attikon” University General Hospital, Medical School, National and Kapodistrian University of Athens, Athens, Greece; 2Microbiology Department, “Aghia Sophia” Children’s Hospital, Athens, Greece; 3Department of Medical Microbiology and Infectious Diseases, Erasmus University Medical Center, Rotterdam, Netherlands

**Background:** Allergic bronchopulmonary aspergillosis is estimated to occur in ~18% of cystic fibrosis (CF) patients in Greece [Armstead 2014]. *Aspergillus fumigatus* species complex (SC) is the predominant mould recovered from respiratory secretions of these patients. The prevalence of azole-resistant *A. fumigatus* (AR-Af) in CF patients varies greatly between centres and may reach 9% [Seufert 2018]. Data on Greek clinical isolates are lacking. We therefore investigated the occurrence of AR-Af in Greek paediatric CF patients.

**Materials/methods:** A total of 55 *A. fumigatus* SC strains recovered from sputum samples of 37 paediatric CF patients (14 male-23 female) during 2008-2009 (32 isolates-21 patients) and 2017-2019 (23 isolates-16 patients) were retrospectively tested. Isolates were macro-/microscopically identified to SC level. *A. fumigatus sensu stricto* (SS) were presumptively identified based on growth at 48°C. *In vitro* susceptibility testing of *A. fumigatus* SC strains to amphotericin B (AMB), itraconazole (ITC), voriconazole (VRC), posaconazole (POS), isavuconazole (ISA), anidulafungin (AFG), caspofungin (CAS) and micafungin (MFG) was performed according to EUCAST E.DEF9.3.1. Azole resistance was also tested with the agar dilution method (EUCAST E.Def10.1) and gradient concentration strips (MTS).

**Results:** All isolates grew at 48°C indicating that they belonged to *A. fumigatus* SS. Antifungal susceptibility patterns among all strains are summarized in Table. In total, all isolates were AMB-susceptible and exhibited echinocandin wild-type phenotypes. POS was the most potent azole in *in vitro*, followed by ITC, ISA and VRC. Overall, 2/55 (3.6%) pan-AR-Af SS (ITC, VRC, ISA, POS MIC >8, 4, 8, 1 mg/L, respectively) were detected. The pan-AR-Af phenotype was also found with the agar dilution method (visible growth on azole-containing plates) and MTS (ITC, VRC, ISA, POS MIC >32, 2, 4, 0.75-1 mg/L, respectively). Particularly, these isolates were recovered from subsequent specimens (August/December 2018) of 1/37 (2.7%) 16-year-old male patient without prior azole exposure. Confirmatory molecular identification of the pan-AR-Af isolates and detection of specific mutations in the cyp51A associated with azole resistance are under investigation.

**Conclusions:** This is the first study to document the presence of AR-Af SS in Greek CF patients emphasizing the importance of antifungal susceptibility testing of *A. fumigatus*. Further surveillance multicentre studies are required to estimate the exact prevalence of AR-Af.

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Abstract 5559

**Increasing frequency of OXA-48-producing Enterobacterales worldwide and activity of ceftazidime-avibactam, meropenem-vaborbactam and comparators against these isolates**

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**Abstract third-party references:** This study was performed by JMI Laboratories and supported by Pfizer, Inc., which included funding for services related to preparing this abstract.

**Background:** OXA-48 are oxacillinases with weak carbapenemase activity that poorly hydrolyze cephalosporins. Isolates producing these enzymes usually harbour other resistance mechanisms that may increase the MICs for $\beta$-lactam agents. We describe the occurrence, additional $\beta$-lactam resistance mechanisms and activity of ceftazidime-avibactam, meropenem-vaborbactam and other antimicrobials against 319 OXA-48-like-producing isolates collected in a 3-year surveillance period.

**Materials/methods:** Among 55,162 Enterobacterales isolates collected during 2016 to 2018, 319 carbapenem-resistant isolates carried genes encoding OXA-48-like enzymes. All isolates were susceptibility tested for ceftazidime-avibactam and comparator agents using reference broth microdilution methods. Meropenem-vaborbactam was tested using lyophilized broth microdilution panels (ThermoFisher). Analysis of $\beta$-lactam resistance mechanisms and MLST was performed in silico using whole genome sequencing data.

**Results:** OXA-48-like-producing isolates increased from 0.5% (80/18,656) in 2016 to 0.8% (150/18,808) in 2018. Isolates were mainly recovered in Europe and adjacent countries (Russia, Turkey and Belarus) and 286 were *K. pneumoniae* (plus 6 species). *K. pneumoniae* isolates belonged to 47 sequence types (STs) with ST395, ST23 and ST11 being the most common (93, 31 and 27 isolates, respectively. All these common STs were detected in Russia. A total of 266 isolates carried *bla*_{OXA-48} and 5 variants of this gene were detected (*bla*_{OXA-163}, *bla*_{OXA-181}, *bla*_{OXA-232}, *bla*_{OXA-244}, *bla*_{OXA-370}). All but 3 isolates carried additional $\beta$-lactamases and 248 isolates carried CTX-M enzymes (229 CTX-M-15) alone or with acquired cephalosporinases, OXA-1 or other $\beta$-lactamase genes. OmpC/OmpK36 was disrupted in 264 isolates and 206 had disrupted OmpF/OmpK35 and these 2 porins were interrupted in 181 isolates. All isolates tested were susceptible to ceftazidime-avibactam and 36.7%/45.5% were susceptible to meropenem-vaborbactam applying CLSI/EUCAST breakpoints. Other $\beta$-lactams were active against 7.5%-21.6% of these isolates and aminoglycosides were active against 14.7% to 51.4%. Tigecycline and colistin were the most active comparators against these isolates inhibiting 95.6%/81.7% at US FDA/EUCAST susceptible breakpoints.

**Conclusions:** The rates of OXA-48-like-producing isolates almost doubled in the 3-years of this investigation, with most isolates being detected in Russia and Turkey. These isolates have multiple $\beta$-lactam resistance mechanisms. OXA-48-like-producing isolates were resistant to most agents tested, but among $\beta$-lactams, ceftazidime-avibactam was active against all isolates tested.

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Abstract 5563

**Intestinal colonisation with extended-spectrum beta-lactamase-producing Escherichia coli after international trips in travellers attending a travel clinic in Rio de Janeiro**

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**Background:** Travel is an important factor for acquisition of colonization by extended-spectrum beta-lactamase (ESBL) producing microorganisms. Risk factors for acquisition of these bacteria include destination region, usage of antimicrobial agents, and occurrence of diarrhea during travel. The aim of this study was to determine the frequency of acquisition of ESBL-producing *Escherichia coli* colonization by travelers attended at the travel medicine center of Universidade Federal do Rio de Janeiro.

**Materials/methods:** Travelers over 18 years of age attended between 2015 and 2018 were invited to participate in the study. Subjects answered a questionnaire and were oriented to collect an anal stool specimen with a cotton swab before travel and upon one week after return. Stool samples were stored into skim-milk, tryptone, glucose and glycerin media. Cultures in Mac-Conkey agar containing 2 microg/mL ceftriaxone were used for ESBL-producing testing. Identification of isolates as *E. coli* was performed by MALDI-TOF. ESBL enzymes were identified by PCR and sequencing. Antimicrobial susceptibility tests (CLSI, 2018), phylogenetic grouping and random amplification of polymorphic DNA (RAPD) were performed for one isolate pre and other isolate post-travel per participant.

**Results:** 153 travelers were interviewed; 65% were female and 143 provided the swab on return. Prior to the trip, ESBL production was observed in 7% (10/153) of the isolates. Among the 143 participants, 29 (20%) returned from the trip with ESBL-producing *E. coli*. All ESBL types isolated were CTX-M: *blaCTX-M15* (18), *blaCTX-M14* (4), *blaCTX-M55* (3), *blaCTX-M2* (2), *blaCTX-M8* (1) e *blaCTX-M27* (1). The highest frequency of acquisition was in the Southeast Asia (50%) (p=0.003). Tourism travel was related to a higher rate of colonization of ESBL producing *E. coli* (p=0.020). Most isolates belonged to phylogroups A or C, followed by B1 and B2. RAPD typing of multidrug resistant isolates revealed that isolates from each subject belonged to a different RAPD type. Isolates showed high resistance frequencies to gentamicin (9%), ampicillin (44%) and trimethoprim-sulfamethoxazole (38%) after return.

**Conclusions:** These data show that travelers departing to international trips from Brazil acquire resistant bacteria in high frequencies, similar to what is observed in travelers from developed countries.

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Abstract 5565

Antimicrobial activity of cefepime in combination with taniborbactam (formerly VNRX-5133) against clinical isolates of Enterobacterales from Europe collected from 2018-2019 surveillance

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Background: Taniborbactam is a novel cyclic boronate-based broad-spectrum β-lactamase inhibitor with potent and selective direct inhibitory activity against both serine- and metallo-β-lactamases (Ambler Classes A, B, C and D). Taniborbactam greatly enhances the activity of cefepime against many difficult to treat organisms, including cephalosporin- and carbapenem-resistant Enterobacterales and Pseudomonas aeruginosa. The activity of the investigational combination cefepime-taniborbactam (FTB) and comparator agents was evaluated against clinical isolates of Enterobacterales from Europe during a 2018-2019 surveillance study.

Materials/methods: MICs of cefepime with taniborbactam fixed at 4 mg/L and comparators were determined following CLSI M07-A11 guidelines against 2,977 Enterobacterales. Isolates were from community and hospital infections collected from 113 sites in 24 European countries in 2018-2019. Resistant phenotypes were based on 2019 EUCAST breakpoints v9.0. A provisional susceptible breakpoint of ≤8 mg/L for FTB was considered for comparative purposes. A set of 198 Enterobacterales with meropenem MIC ≥4 mg/L (n=95) or with cefepime/ceftazidime MIC ≥2 mg/L (n=103) was evaluated for the presence of MBL, KPC, ESBL, and OXA-48 group genes via PCR and sequencing. Three isolates with FTB MIC values of 16 mg/L were interrogated by WGS.

Results: FTB showed potent in vitro activity against all Enterobacterales, with MIC90 values of 0.06/0.25 mg/L and >99% inhibited at the provisional susceptible breakpoint of ≤8 mg/L. FTB maintained activity against MBL-, KPC-, OXA-48 group, and ESBL-positive isolates (MIC90 range, 1 to 8 mg/L; 93.3% to 100% of MIC values of ≤8 mg/L).

Conclusions: Taniborbactam significantly restored the in vitro activity of cefepime against Enterobacterales, including isolates nonsusceptible to recently-approved BL/BLI combinations and expressing serine and metallo-β-lactamases. These findings support the continued development of FTB as a potential new treatment option for challenging infections due to resistant Gram negative pathogens.

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**Serum concentrations of intravenously administered posaconazole in critically ill patients**

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**Background:** Posaconazole is mainly used for prophylaxis and salvage therapy of mold infections in hematological patients and stem cell transplant recipients. To improve bioavailability compared to oral solution in 2016 an intravenous formulation was introduced. Up to now very limited data on the serum concentration of posaconazole in critically ill patients on intensive care units (ICU) are available.

**Materials/methods:** An opportunity to determine posaconazole concentrations (PC) in serum from ICU patients after intravenous application of the azole has been provided to German clinical centers. PC have been determined by HPLC assay. As part of the therapeutic drug monitoring (TDM) information of dosage, time point of first and most recent application, organ impairments, and laboratory values have been requested. All PC of patients receiving a dose of 300 mg daily have been analyzed retrospectively in a pseudonymized databank.

**Results:** 59 PC have been determined from 32 patients (19 female, median age 52 years, range 17-72 years, median body weight 75 kg, median BMI 25.1, range 16.0 – 36.7). Median PC from all 59 samples was 816 ng/mL, mean 1005 ng/mL, range 45 to 4468 ng/mL (figure). 15 PC were below 500 ng/mL and one above 3750 ng/mL. Taking into account only the first sample of each patient median PC was 1129 ng/mL, mean 857.5 ng/mL, range 82 to 4468. Using the average PC per patient the results respectively were 846.0 ng/mL, 1128.9 ng/mL and 82 to 4468 ng/mL. No association of PC with age, BMI or bodyweight have been detected.

**Conclusions:** The majority of patients had sufficient PC. As the PC in this study were lower than those published previously in non-ICU patients, it seems reasonable to use posaconazole TDM in ICU patients. Further investigations are needed to analyze factors having influence on PC in critically ill patients.

![Figure: Posaconazole serum concentrations in 59 samples from ICU patients.](image)

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Abstract 5567

**Outcome of Clostridioides difficile infection in patients that are PCR positive: comparison of toxin positive with toxin negative cases**

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**Background:** Optimal algorithms for the laboratory diagnosis of Clostridioides difficile infection (CDI) remain somewhat controversial. Molecular detection of the toxin gene[s] is sensitive but lacks clinical specificity. Conversely, assays that detect free toxin are specific but lack sensitivity. The most appropriate management at population level for patients with diarrhoea who test positive for the toxin gene only remains unclear. Management of 100 patients with toxin gene positive stool samples was assessed.

**Materials/methods:** In our hospital stool samples are tested on all adult patients with diarrhoea (type 5 stool or above). Specimens are processed using the Serosep EntericBio realtime® C. difficile assay for the detection of the C. difficile toxin B gene. Positive samples are subsequently tested for the presence of toxin using an EIA toxin detection test (Abbott tox A/B Quik Chek®). Clinicians are informed of the EntericBio result only. Management is determined at ward level by clinical parameters. Detailed analysis of the presentation and management of 100 randomly selected patients from a 12 month period was performed.

**Results:** 77 patients were toxin negative, 23 toxin positive. Mean CT values were 31.17 (24.81-35.98), Median 31.59. Of the PCR positive, toxin negative cases 31 had subsequent positive tests [range 1-8, 11 > one subsequent positive] and 27 had subsequent negative tests [range 1-8, 12 > one subsequent negative, 14 had subsequent positive tests]. Ribotype data below (excluding 13 not isolated, 15 not available). Data on treatment, stool frequency, stool consistency, response and severity assessment is also presented.

**Conclusions:** The optimal management of diarrhoea in patients who are C. difficile toxin gene positive, but free toxin negative is not well defined. We present data on the clinical parameters and management of a subset of these patients based on clinical assessment and without access to the free toxin result to further inform this debate.

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Abstract 5568

**Spread of metallo-β-lactamases among distinct species of Pseudomonas putida group in Brazil**

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**Background:** PpG species are usually ubiquitous and rarely involved in human infections. However, these strains might act as a reservoir of antibiotic resistance determinants, which may be transferred to clinical isolates and vice-versa. Herein, we report the emergence of carbapenem-resistant PpG carrying distinct MβL encoding genes causing human infections in Brazil.

**Materials/methods:** A total of 12 non-duplicated carbapenem-resistant Pseudomonas spp. isolates initially identified as *P. putida* by Phoenix BD® automated system were recovered from different clinical specimens in two Brazilian hospitals located in the city of São Paulo, Brazil, between May/2010 and October/2019. The identification at species level was confirmed using MALDI-TOF MS. Minimal inhibitory concentrations (MICs) of nine antimicrobials were determined by EUCAST broth microdilution. The detection of carbapenemase encoding genes was performed by PCR followed by sequencing. Genetic relationship within species was determined by ERIC-PCR.

**Results:** Most isolates were identified as *P. monteilii* (n=7), followed by *P. putida* (n=3), *P. graminis* (n=1), and *P. plecoglossicida* (n=1). They were recovered from blood (n=6), sputum (n=1), peritoneal fluid (n=2), and urine (n=3). All isolates were resistant to meropenem (MICs varying from 32 to >128 mg/L), ceftazidime (MICs varying from 16 to >128 mg/L), and aztreonam (MICs varying from 16 to >128 mg/L). In addition, most PpG isolates (n=10) were resistant to imipenem (MICs varying from 4 to >128 mg/L), piperacillin/tazobactam (n=9, MICs varying from 2 to >128 mg/L), and ciprofloxacin (n=8, MICs varying from 1 to >128 mg/L). In opposite, all isolates were susceptible to amikacin and polymyxin B (MIC90, 8 and 0.5 mg/L, respectively). MβL encoding genes were found in all PpG isolates, as follows: *bla*<sub>VIM-2</sub>-like (n=4), *bla*<sub>IMP-16</sub>-like (n=3), *bla*<sub>IMP-34</sub>-like (n=2), and *bla*<sub>IMP</sub>-like (n=1). Preliminary sequencing results showed that one *P. monteilii* carried a novel putative carbapenemase. Additionally, one *P. putida* isolate harbored both *bla*<sub>MP13</sub>-like and *bla*<sub>VIM-2</sub>-like genes. Interestingly, no predominant clone among the MβL-producing PpG isolates was detected.

**Conclusions:** This is the first report of MβL encoding genes among distinct PpG species causing infections in Brazil. We demonstrated that these environmental species can also be pathogenic and act as reservoirs for further spread of antimicrobial resistance determinants.

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Abstract 5571

The variability of the lymphocyte populations in the cerebrospinal fluid of patients with tick-borne encephalitis
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Abstract third-party references: Medical University in Białystok, Poland, National Science Centre, Poland, grant UMO-2018/31/B/NZ6/02744

Background: The clinical presentation and outcome of tick-borne encephalitis (TBE) is highly variable, with no validated prognostic markers. Lymphocytes infiltrating central nervous system (CNS) are probably crucially involved both in the control of TBE virus infection and in the immune-mediated tissue pathology. However, the pathogenetic role and a potential prognostic significance of particular lymphocyte subsets remains unclear. To constrain it better, we have analyzed abundances of blood and CSF lymphoid cell populations in TBE patients stratified according to a clinical presentation and severity.

Materials/methods: We have studied paired blood and CSF samples from 50 patients in the early neurologic phase of TBE (30 with uncomplicated meningitis, 18 with mild to moderately severe meningoencephalitis and 2 with myelitis), 20 meningitis controls with non-TBE aseptic meningitis and 11 healthy controls (blood only). TCD3+, TCD3+CD4+, TCD3+CD8+, double-positive TCD3+CD4+CD8+, CD19+ B lymphocytes and CD16/56+ NK cells were labeled with fluorochrome-stained monoclonal antibodies and counted cytometrically. The data were analyzed with non-parametric tests, p<0.05 considered significant.

Results: Blood: Compared to controls, TBE patients had decreased total lymphocyte, TCD3+, TCD3+CD4+ and TCD3+CD8+, marginally decreased NK and not altered B lymphocyte counts. Cell counts did not associate with the TBE clinical presentation. CSF: Compared to aseptic meningitis, TBE patients had lower counts of all the studied populations except B cells. Lymphocytes B were more abundant in meningoencephalitis/myelitis than in meningitis. The higher TCD3+, TCD4+ and TCD8+ counts associated with the altered consciousness, but not with the other symptoms of encephalitis (focal neurologic deficits, cerebellar syndrome). However, two myelitis patients had exceptionally high proportion of both TCD8+ and B lymphocytes. The minor double-positive TCD4+CD8+ population associated negatively with clinical severity and was relatively more abundant in meningitis than in meningoencephalitis/myelitis.

Conclusions: The distinct CSF lymphoid cell populations associate differently with the clinical presentation of TBE, suggesting their distinct pathogenetic roles and offering a potential of distinguishing TBE phenotypes based on the intrathecal immune response and associated clinical features. Higher counts of B, TCD4+ and TCD8+ lymphocytes may associate with overlapping but distinct spectra of CNS manifestations, while a higher fraction of double-positive T cells associates with uncomplicated meningitis.

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Effectiveness of ceftazidime-avibactam in a tertiary hospital of Spain

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Background: Ceftazidime-avibactam (CAZAVI) is a broad spectrum antimicrobial for the treatment of gram-negative multi-drug-resistant bacilli infections. Its activity against OXA-type and KPC carbapenemases is particularly relevant. The aim of our study was to evaluate the effectiveness of the treatment in the infections caused by this type of microorganisms.

Materials/methods: Between June 2018 and October 2019 patients treated with CAZAVI in the Cruces University Hospital (Basque Country, Spain) were analysed. This is a 900 bed tertiary hospital, covering a health area of 300,000 inhabitants. Demographic, clinical and microbiological data were analyzed for each patient.

Results: During the study period, 14 patients received treatment with CAZAVI, 11 males and 3 females with a median age of 63.5 years. There were four cases of septicaemia, 3 urinary tract infections, 3 abdominal syndromes, 3 respiratory infections and CAZAVI was only used empirically in other case of non-specific febrile syndrome but after previous positive colonization cultures. Treatment was directed against OXA-48 producing K. pneumoniae in 9 patients, KPC producing enterobacteria and other multi-resistant microorganisms in 2 each one and ceftazidime susceptible P. aeruginosa in other one. One patient suffered 2 episodes and was treated in both with CAZAVI. The median number of days of treatment was 5. The evolution was favourable in 11 patients while 3 died. In 6 patients microbiological eradication was achieved in subsequent cultures, while in 6 not and in 2 was unknown due to lack of subsequent cultures. In one deceased patient, treatment was directed towards a multidrug resistant A. baumannii. Of the other 2 deceased patients, one suffered a cholecystitis by K. pneumoniae producing OXA-48 that was microbiologically eradicated and the other one, a septicaemia by E. coli KPC + CIT-type plasmidic AmpC with unknown eradication. Both were terminally ill and died for underlying diseases.

Conclusions: The evolution of the patients treated with CAZAVI was favourable in 78% of the cases. The deceased patients were patients with multiple comorbidities and their death was due to other causes than infectious. Ceftazidime-avibactam was shown to be an effective treatment for infections produced by microorganisms harbouring carbapenemases type OXA-48 and KPC.

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Abstract 5573

**ESBL- and pAmpC-producing *Escherichia coli* in imported broiler breeding birds for the Swedish broiler production**

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**Background:** Extended-spectrum beta-lactamases (ESBL) and plasmid mediated AmpC (pAmpC) producing *E. coli* is commonly described in the European broiler production, including in countries i.e. Sweden that are regarded as favorable countries regarding the antibiotic resistance situation. In Sweden use of antibiotics in broilers production is very limited, and extended spectrum cephalosporins are not used at all. Thus, selection due to usage was unlikely. Instead it was hypothesized that the bacteria could have been introduced from imported breeding birds and spread through the production pyramid. This theory was proven correct in a study following imports and their prodigy in 2010 to 2011. As a results SVA has since 2010 monitored all imports of breeding birds for the occurrence of ESBL- and pAmpC-producing *E. coli*.

**Materials/methods:** Samples of paper linings from shipments of breeding animals was first pre-enriched in either MacConkey broth supplemented with 1 mg/L cefotaxime or buffered peptone water. From the enrichment 10 µl was plated on MacConkey Agar with 1µg/mL cefotaxime, suspected isolates were than confirmed with PCR.

**Results:** Of 107 shipments in the period 2010 to 2018, 40% of the shipments were shown to be positive for either ESBL- or pAmpC-producing *E. coli*. In addition, the proportion of positive shipment decreased over the years and in 2018 all shipments were negative [Figure 1.]. The ESBL genes detected were blaCMY-2-gene group, blaCTX-M-1 -gene group and sporadically the blaSHV-group.

**Conclusions:** Due to the potential risk of transfer of ESBL- and pAmpC-producing *E. coli* from broilers directly or via food to humans, it is important to monitor and understand the occurrence of these bacteria in broilers. We could show that these bacteria were present in imported breading birds for the Swedish broiler production on arrival to Sweden and that the proportion of positive shipments decreased over the years.

![Figure 1. Percent of shipments of imported breeding animals positive for ESBL/pAmpC-producing E. coli from August 2010 to 2018.](image)

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Abstract 5575

A multi-omics approach to understanding the aetiology of Q fever fatigue syndrome
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Background: Q fever fatigue syndrome (QFS) is characterised by a state of prolonged fatigue following 20% of acute Q fever infections that has major health-related consequences. However, the aetiology of QFS remains unclear. In order to understand this, we compared the gut microbiome, blood metabolome, and inflammatory proteome of QFS with those of chronic fatigue syndrome (CFS) patients and healthy controls.

Materials/methods: The study population consisted of 31 QFS patients, 50 CFS patients, and 50 healthy controls. All subjects were matched for age (± 10 years), gender, and general geographical region. The gut microbiome composition was assessed by Metagenomic sequencing using the Illumina HiSeq platform. For inflammatory proteome and metabolome, a total of 92 circulating inflammatory markers and 1607 metabolites were measured using Proximity Extension Essay and a high-throughput non-targeted metabolomics approach.

Results: Significant differences are documented in microbiome taxonomy when comparing QFS and CFS patients to healthy controls, reflected by upregulation of pathways like urate biosynthesis/inosine 5'-phosphate degradation (P = 1.32x10^-30 and 8.94x10^-57) and CMP-3-deoxy-D-manno-octulosonate biosynthesis I (P = 3.37x10^-23 and 5.27x10^-34). When comparing QFS patients to CFS patients, differences are less significant, reflected by upregulation of pathways like L-lysine biosynthesis III and VI (P = 8.93x10^-5 and 2.12x10^-4). Blood metabolite profiles show significant differences when comparing QFS and CFS patients to healthy controls, reflected by upregulation of pathways like sphingolipid (P = 0.008 and 6.25x10^-4) and glycerophospholipid (P = 0.036 and 0.028) metabolism. No significant differences were found when comparing QFS to CFS patients. Inflammatory markers 4E-BP1 (P = 9.60x10^-16 and 1.41x10^-7) and MMP-1 (P = 7.09x10^-9 and 3.51x10^-9) are significantly more expressed in both QFS and CFS patients compared to healthy controls.

Conclusions: We show that; QFS and CFS patients have similar profiles in gut microbiome taxonomy and blood metabolite composition, QFS patients have more of an inflammatory profile compared to both CFS patients and healthy controls, and 4E-BP1 and MMP-1 have potential to differentiate QFS and CFS patients from healthy controls.

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Antimicrobial activity of cefepime in combination with taniborbactam (formerly VNRX-5133) against a European 2018-2019 surveillance collection of Pseudomonas aeruginosa

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Background: Taniborbactam is a novel cyclic boronate-based broad-spectrum β-lactamase inhibitor with potent and selective direct inhibitory activity against both serine- and metallo-β-lactamases (Ambler Classes A, B, C, and D). Taniborbactam greatly enhances the activity of cefepime against many difficult to treat organisms, including cephalosporin- and carbapenem-resistant Enterobacteriales and Pseudomonas aeruginosa. In this study, we evaluated the in vitro activity of the investigational combination cefepime-taniborbactam and comparator agents against clinical isolates of P. aeruginosa collected in Europe during 2018-2019 surveillance.

Materials/methods: MICs of cefepime with taniborbactam fixed at 4 mg/L (FTB) and comparators were determined following CLSI M07-A11 guidelines against 676 P. aeruginosa from community and hospital infections collected from 86 sites in 23 countries in Europe in 2018-2019. Resistant phenotypes were based on 2019 EUCAST breakpoints v9.0. As FTB breakpoints have not yet been established, a provisional susceptible breakpoint of ≤8 mg/L was considered for comparative purposes. The presence of metallo-β-lactamase genes was assessed via PCR and Sanger sequencing for 95 randomly selected isolates with meropenem MIC ≥28 mg/L and 45 isolates with cefepime or ceftazidime MIC ≥16 mg/L, and via WGS for 18 isolates exhibiting FTB MIC values ≥16 mg/L.

Results: FTB demonstrated potent in vitro activity (MIC50/90, 2/8 mg/L; 96.9% inhibited at ≤8 mg/L) against P. aeruginosa isolates from Europe. Provisional susceptibility rates to FTB ranged from 75.0% vs ceftolozane-tazobactam nonsusceptible (NS) isolates to 90.1% vs meropenem NS isolates compared to 0 to 72.8% susceptible for comparators against the NS subsets (Table). Against the 22 strains with acquired β-lactamases identified, FTB MICs were ≤8 mg/L (n=13), 16 mg/L (n=7) and >32 mg/L (n=2; both IMP producers).

Conclusions: Cefepime in combination with taniborbactam demonstrated potent in vitro activity against P. aeruginosa from Europe with different phenotypic resistance profiles, including nonsusceptibility to cefepime, meropenem, and piperacillin/tazobactam, and to the recently introduced protected β-lactam/β-lactamase inhibitors ceftazidime-avibactam, cefotazidime-tazobactam, and meropenem-vaborbactam. These findings support the continued development of FTB as a potential new treatment option for challenging infections due to resistant Gram negative pathogens.

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Abstract 5578

Comparison of bacterial recovery of stored sonication fluid cultures using liquid broth and solid media obtained from orthopaedic implant-associated infections

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Background: Sonication of explanted hardware during surgery has shown superior results as microbiological diagnostic tool in orthopedic implant-associated infections (OIAI) when compared to periprosthetic tissue cultures. In addition, sessile microorganisms seem to grow easily and faster on liquid media compared to solid agar plates. Notwithstanding, contamination on liquid media may be a source of false-positive results. We aimed at investigating the usefulness of the thioglycollate (TG) and brain heart infusion (BHI) broth compared to solid media (5% sheep blood agar and MacConkey agar) for the microbial recovery of stored sonication fluid samples of implant-associated infections.

Materials/methods: This study analyzed sonication fluid samples stored at -80°C, which were obtained from retrieved prosthesis, plates and screws of 426 patients with OIAI, between 2014 and 2018. Diagnosis of OIAI was based upon standard criteria as previously published. Briefly, implants were packed into sterilized solid polyethylene containers and covered with Ringer’s solution, sonicated for 5 minutes at a frequency of 40±2 kHz and power density 0.22±0.04 W/cm², followed by 30 seconds of vortexing. Stored sonication fluid was defrosted at room temperature and 15-20 µL plated onto aerobic plates, TG and BHI, and incubated aerobically at 35°C in 5% CO2 for 4 days. The microorganisms isolated were identified according to standard method. Statistical analysis was performed using McNemar’s test for related proportions.

Results: Sonication fluid cultures yielded 63.4% (n= 270/426) of pathogen detection. Subsequently, 162 positive sonication samples were plated on agar and 146 on broth (TG and BHI). Identification of pathogens using agar plaques and broth (TG and BHI) resulted in 41.3% (n= 67/162) and 66.4% (n= 97/146) of positivity, respectively (p<0.0001). Identification of pathogens using TG or BHI broth resulted in no statistical significance, in which microorganisms were recovered by BHI and TG in 60.8% (n=59/97) and 39.1% (n= 38/97), respectively (p=0.11).

Conclusions: We highlight that the recovery of subcultured samples in liquid broth contributed to the identification of the microorganism. Lastly, it is important to emphasize that TG broth is an enriched medium, given that, contaminants can grow as well occurring false-positive diagnostic.

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In vitro susceptibility of carbapenem-resistant Enterobacteriaceae from the Arabian Peninsula to ceftazidime-avibactam, aztreonam-avibactam and other rescue antibiotics

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Background: The aim of the study was to assess susceptibility of carbapenem resistant Enterobacterales (CRE) from the Arabian Peninsula to potential rescue drugs, and to relate the data to various mechanisms of carbapenem resistance.

Materials/methods: Altogether 1192 non-repeat CRE isolated in 2009-2017 from 33 hospitals in 5 countries of the Arabian Peninsula were tested. Minimum inhibitory concentration (MIC) of 14 antibiotics including ceftazidime-avibactam and aztreonam-avibactam was determined by broth microdilution, and of fosfomycin and tigecycline by agar dilution. Common carbapenemase and 16S methylase genes were detected by PCR. Clonality of the strains was assessed by PFGE.

Results: The highest rate of susceptibility was detected to aztreonam-avibactam (95.5%) followed by colistin (79.8%), fosfomycin (71.8%) and tigecycline (59.9%). Aminoglycoside susceptibility was affected by the frequent production of a 16S methylase (44.2% of isolates), most commonly armA and rmtF. Susceptibility to ceftazidime-avibactam was impacted by the high rate of MBL producers (46.3% of all isolates). Ceftazidime-avibactam susceptibility rate of the non-MBL producers was 98.9%. While the majority (93.4%) of carbapenemase non-producing strains exhibited a meropenem MIC value <16 mg/L, this was comparatively rare (27.8%) among carbapenemase producers. With considerable variations between countries, 12.4% of the strains expressed both NDM and OXA-48-like carbapenemases, and these exhibited the lowest rate of susceptibilities. The aztreonam-avibactam resistance was not related to any carbapenem resistance mechanism, and although the majority of the 54 isolates were E. coli (n=41), they did not exhibit clustering by PFGE.

Conclusions: Based on the in vitro susceptibility rates, of the currently available options to treat CRE infection in the Arabian Peninsula, colistin, tigecycline and co-administration of ceftazidime-avibactam with aztreonam appear to be the most effective. In the light of the relatively high rate of fosfomycin susceptibility, it is desirable to have parenteral fosfomycin licensed in the region. A notable concern is the presence of non-clonal CRE isolates, in which avibactam does not lower the aztreonam MIC below the clinical breakpoint, potentially hindering the efficacy of co-administered ceftazidime-avibactam and aztreonam as a rescue therapy.

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Abstract 5580

Increased burden of invasive pneumococcal disease caused by non-vaccine serotypes in individuals with underlying diseases: a population-based case-control study

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Background: The impact of introducing pneumococcal conjugate vaccines (PCV) in the childhood vaccination program on invasive pneumococcal disease (IPD) in individuals with co-morbidities is insufficiently understood. In this nation-wide study we investigated the risk of serotype-specific IPD in individuals with co-morbidities, and the effect of co-morbidities on the IPD incidence after PCV introduction in Sweden in 2009.

Materials/methods: A case-control study was performed during 2006-15, including all IPD cases in Sweden, and randomly selected controls from the general population, matched on age, sex and region. It is mandatory to report IPD to the Public Health Agency of Sweden where serotyping of isolates is performed. Data on co-morbidities was obtained from the Patient and Pharmaceutical Registers that contain information on all hospital visits and prescriptions. Co-morbidities were defined as immunocompetent chronic medical conditions (CMC), and immunocompromising conditions (IC). Incidences and risks were analyzed for certain serotypes, and according to serotypes included in the vaccines: PCV13, non-PCV13, PPV23-non-PCV13, and non-vaccine serotypes (NVTs).

Results: Totally 14096 IPD cases and 137289 controls were included. Preliminary analyses show an increase of co-morbidities both among cases and controls when 2006-7 (pre-vaccine) was compared to 2014-15 (post-vaccine). The absolute increase of the IPD incidence caused by non-PCV13, PPV23-non-PCV13 and NVTs, was higher in individuals with IC and CMC, than in those without co-morbidities. The odds ratios (OR) for IPD caused by non-PCV13, and particularly NVTs, compared to PCV13 serotypes, were higher for individuals with CMC and IC. Five serotypes [16F, 15C, 19F, 35F and 23A], of which four are not included in PCV13 or PPV23, conferred the highest risks with ORs between 4 and 5 in individuals with CMC and >10 for those with IC. The mortality due to non-PCV13 serotypes increased from the pre- to the post-vaccine period in individuals with IC and CMC, while it remained stable for those without co-morbidities.

Conclusions: We observed an association between PCV childhood immunization and an expansion of NVTs that preferentially cause IPD in individuals with underlying disease, in particular those with IC. These results have implications for development of new vaccines and immunization strategies.

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The trouble with gentamicin: a realist evaluation exploring two distinct protocols for prescribing gentamicin in hospital settings

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Background: Gentamicin is one of the most frequently prescribed aminoglycosides in UK hospitals, but it is challenging to prescribe and the evidence basis for prescribing it is limited. Consequently, each hospital in the UK has developed their own prescribing protocol.

We used a realist evaluation approach to explore two distinct protocols for prescribing gentamicin in hospital settings, to understand the mechanisms they trigger and the clinical outcomes they achieve.

Materials/methods: The project was conducted in three phases: initial programme theory (IPT) generation; testing; and refinement of the IPT.

We collected empirical data using a mixed-methods approach. The qualitative component involved semi-structured interviews of healthcare professionals' experiences of prescribing gentamicin according to the existing protocols in their institution [Site 1, a more traditional, complex protocol; Site 2 a newer, simplified protocol]. The quantitative component included prospectively auditing the accuracy of 100 gentamicin prescribing episodes.

We developed the IPT from analysis of the gentamicin prescribing protocols. We detailed the 'intended' process of prescribing, identifying possible key contexts, mechanisms and outcomes in this process. We then tested and refined these theories during the interviews. Qualitative and quantitative data were analysed together to support developing theories.

Results: The mean accuracy of gentamicin prescribing at Site 1 was 65.67% and 78.79% at Site 2 (p<0.01). Eight patients developed an acute kidney injury. Of these, seven had received an accurate dose of gentamicin.

Thirty participants were interviewed. From respondents we identified key contexts [prescriptiveness of protocol; clinician experience; availability of patient information] that influenced their ability to prescribe, and triggered hidden mechanisms [uncertainty; fear; confidence; frustration] which can lead to both the intended outcome (adherence to the prescribing protocol), and unintended outcomes [intentional deviation from protocol; unintentional non-adherence; unnecessary gentamicin levels]. The audit data supported our suggested mechanisms, contexts and outcomes. For example, participants frequently reported concerns about nephrotoxicity and were aware that this could lead to cautious prescribing. According to audit data, under-dosing occurred at 24% at Site 1, 12% at Site 2.

Conclusions: A simplified prescribing protocol for gentamicin is better accepted by prescribers, leads to better adherence to protocol and more accurate prescribing.

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Evaluation of a quantitative multiplex PCR panel for the diagnosis of pneumonia: how do we optimise utilisation?

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Background: Guidelines for the management of adults with hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) were recently published by IDSA and ATS. For patients with suspected infections, the recommendations include empiric therapy against Staphylococcus aureus (SA) and Pseudomonas aeruginosa (PA). While antimicrobial de-escalation can occur when susceptibility results are available 48 hours after specimen collection, this is often a missed opportunity.

Materials/methods: We chose to evaluate a recently FDA-approved quantitative multiplex PCR panel designed to aid in the diagnosis of pneumonia in an effort to determine the potential impact on the recommendations of this guideline. A total of 126 BALs and mini-BALs submitted for routine bacteriologic culture were tested using the FilmArray Pneumonia Panel (BioFire, Salt Lake City, UT), a multiplex PCR panel that includes 18 bacteria (15 of which are quantitated as copies/ml), 7 antimicrobial resistance markers and 8 viruses. Pneumonia Panel (PP) results were compared to quantitative and semi-quantitative cultures. Out-patient (N = 29) and in-patient (N = 97) results were analyzed separately.

Results: Of the 97 in-patient specimens, 34 (35%) were categorized as positive (>10^4 CFU/ml) for at least one bacterial pathogen by either PP or culture. For 23 of these 34 (67%), PP and culture were concordant. For discordants, 8/11 cultures grew organisms that are not on the PP panel and 3/11 PP were positive for PA and cultures were negative. PA and/or SA were detected in 15 of 34 (44%) positive samples. Sixty-three specimens were PP negative and were ultimately finalized as "No growth" or "Mixed Commensal Microbiota".

Conclusions: Based on this analysis, we determined that utilization of the PP could have a positive impact on antimicrobial management of patients suspected to have HAP or VAP. Targeted therapy for patients with PA and/or SA could have been initiated for 44% and antimicrobial avoidance could have been considered for 65% of patients being evaluated. In conclusion, we believe the PP is an excellent adjunct to other aspects of clinical care and diagnostic testing.

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Abstract 5584

Routine use of MALDI-TOF MS for identification of non-tuberculous mycobacteria species in the clinical laboratory
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Background: Currently, there are 199 different mycobacterial species described and the isolation of nontuberculous mycobacteria (NTM) is increasing in clinical laboratories. It is important for patient management to reach species level identification, but the commercial molecular methods used to identify them are limited to a certain number of species. The MALDI-TOF mass spectrometry system has proved to be faster and cheaper, and it could be an alternative for mycobacteria identification. The aim of this study was to evaluate the routine use of MALDI-TOF for identification of NTM isolates from clinical samples.

Materials/methods: A prospective study of all NTM isolated in our geographical area (Costa de Ponent, Barcelona) was carried out during two years (2018-2019). The identification to species level was performed as follows: a) MALDI-TOF Biotyper system (Bruker Daltonics); b) PCR-reverse hybridization (GenoType CM/AS, Hain Lifescience); c) Sequencing of partial 16S rRNA gene in case of discrepancy among the previous methods. The protein extraction procedure for MALDI-TOF was carried out by heat inactivation, acetonitrile, formic acid and sonication. A score cut-off ≥1.7 was used as correct species identification.

Results: A total of 274 isolates of NTM were identified during the period of the study. The MALDI-TOF identified 250 (91.2%) isolates with a score ≥1.7 (26 different species). The PCR-reverse hybridization identified 262 (95.6%) isolates (16 different species). Among the isolates that did not reach score ≥1.7: a) 2 1/24 were slow-growing mycobacteria, and b) 1 7/24 were processed from liquid media. Three (1.1%) isolates that were not recognized neither by MALDI-TOF nor PCR-reverse hybridization were identified by gene sequencing. The results provided by MALDI-TOF were obtained between 0-4 days after culture positivity. The PCR-reverse hybridization required to batch the samples, so it was performed once a week.

Conclusions: All the NTM species with a score ≥1.7 by MALDI-TOF were accurately identified. Although the number of isolates identified by mass spectrometry was slightly lower than PCR-reverse hybridization, it reached a higher important number of different NTM species. Thus, the first method of choice for rapid, accurate and diverse NTM identification could be MALDI-TOF, followed by other molecular methods.

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Neuro-inflammation in patients with chronic and Q fever fatigue syndrome

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Background: The pathophysiology of chronic fatigue syndrome (CFS) and Q fever fatigue syndrome (QFS) remains elusive. Increasing evidence suggests that neuroinflammation plays a role. Neuroinflammation is characterised by microglia and astrocyte activation, which in turn is associated with increased expression of translocator protein (TSPO). This study investigated the presence of neuroinflammation in CFS patients and QFS patients compared with healthy controls, using Positron Emission Tomography (PET) with the TSPO ligand [11C]-PK11195.

Materials/methods: The study population consisted of CFS patients (n = 9), QFS patients (n = 10), and healthy controls (n = 9). All subjects were matched for age (± 5 years), gender and geographical region (south-eastern part of the Netherlands). All subjects were between 18 and 59 years of age and did not use any medication (including doxycycline), other than paracetamol or oral contraceptives, and were not vaccinated in the last six months. None of the subjects reported substance abuse in the past 3 months or showed signs of underlying psychiatric disease, i.e., depression, bipolar disorders, anxiety, schizophrenia, psychosis, or eating disorders, on Mini-International Neuropsychiatric Interview (MINI). All subjects underwent a [11C]-PK11195 PET scan and the [11C]-PK11195 distribution volume ratio (DVR) was calculated using the cerebellum as a reference region.

Results: The DVR was found to be highest in the brainstem for all groups (1.15 ± 0.05). For all other examined brain regions the DVR ranged between 0.83 and 1.2. No statistically significant differences were found for CFS patients when compared to healthy controls, although for the right temporal cortex, right parietal cortex, and left and right occipital cortex a 1.9 to 2.8% increase in DVR was found. A statistically significant higher DVR (P < 0.05) was found in the right parietal cortex (0.98 ± 0.04) of QFS patients when compared to healthy controls (0.93 ± 0.03).

Conclusions: This study revealed a statistically significant increase in [11C]-PK11195 DVR in the right parietal cortex of QFS patients, indicating the presence of neuroinflammation. Patients with CFS tended to show a higher [11C]-PK11195 DVR in cortical regions, but these differences were not statistically significant.

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Innovative procedures for micro-elimination of hepatitis C virus infection in a high-risk population of undocumented migrants and low-income refugees

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Background: Because of the intermediate HCV endemicity in immigrant populations and the high efficacy of DAA therapy, programs should be undertaken to eradicate the infection in this difficult-to-manage setting. The aim of this study was to evaluate an innovative model to eliminate HCV infection in this population.

Materials/methods: A prospective, multicenter, collaborative study, based on the long-term cooperation between five first-level clinical points and two corresponding third-level units of Infectious Diseases (ID) was performed in Campania, Southern Italy. A screening to identify the subjects with HCV infection, free of charge and without bureaucratic procedures, was proposed to all undocumented migrants and low-income refugees prospectively observed by a physician and a cultural mediator at one of the first-level clinical centers from June 2018 to March 2019. All migrants received correct information and illustrated brochures on transmission and prevention of HCV infection, related diseases and available treatments. All anti-HCV positive subjects were addressed at one of the two ID units for further clinical investigation including HCV-RNA determination and, if positive, HCV-genotyping (GT). HCV-RNA positive patients were treated with sofosbuvir plus velpatasvir+ribavirin for 12 weeks and followed up for 12 weeks after treatment withdrawal.

Results: Of the 3,401 migrants observed, 3,286 [96.6%] accepted to be screened. They were young [median age 27 years], predominantly male [83.3%] and came mainly from Northern Africa [4%], Sub-Saharan Africa [67.1%], Eastern Europe [9.3%], and Indo-Pakistan region [16.4%]. Of the 3,286 enrolled subjects, 180 [5.4%] resulted anti-HCV positive. The Figure shows the HCV-cure cascade. All the 180 anti-HCV-positive subjects were linked to care at 3rd level center and tested for HCV-RNA, and 48 [26.6%] resulted HCV-RNA positive. Of these, 40 [83.3%] started DAA regimen [14 with GT 1b, 21 with 1a, 18 with 3, 4 with 4 and 2 with 2]: 38 completed the follow-up with a SVR rate of 100% and 2 are still pending. No subject had adverse neither was drop-out.

Conclusions: This innovative procedures for micro-elimination of HCV infection seems to be effective in undocumented migrants and low-income refugees with rates of diagnosis, linkage to care and cure in line with the WHO goals.

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Abstract 5601

Change of antimicrobial susceptibility testing guidelines from CLSI to BRCAST: impact of breakpoint change on the susceptibility of clinical isolates in a tertiary care hospital in Brazil

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Background: The Brazilian Ministry of Health appointed the use of Brazilian Committee for Antimicrobial Susceptibility Testing (BRCAST) standards as mandatory in all clinical laboratories in Brazil from 2020. However, the actual effect of the guideline changes on cumulative hospital antibiograms is unknown, even though local cumulative antibiograms are important for guiding empirical antibiotic therapy. We set out to compare antibiotic susceptibility interpreted by the two guidelines to determine whether adoption of BRCAST guidelines would affect our institution’s susceptibility patterns.

Materials/methods: Antibiotic susceptibilities of non-duplicate isolates collected within a 2 month period (October to November 2019). The Kirby-bauer method was used for TSA determination. We reviewed inhibition zone diameters of various antibiotics routinely reported for Enterobacteriaceae, Staphylococcus aureus, Coagulase-Negative Staphylococcus (CoNS) and Pseudomonas aeruginosa at the Microbiology Laboratory - Hospital de Clínicas de Porto Alegre. The inhibition zone diameters were then interpreted using both CLSI 2019 and BRCAST 9.0 2019 breakpoints and classified as resistant, intermediate or susceptible. We compared the susceptibility rate between the CLSI and BRCAST categorizations.

Results: A total of 226 susceptibility data from 153 Enterobacteriaceae (105 E. coli, 35. K. pneumoniae and 13 Enterobacter spp.), 27 S. aureus, 23 CoNS and 23 P. aeruginosa clinical isolates were included. The majority of species/drug combinations showed no differences in susceptibility rates comparing CLSI 2019 and BRCAST 9.0 2019, 72% vs 71.8%, respectively. However, in some gram-negative bacilli, decreased susceptibility rates were observed when comparing CLSI 2019 with BRCAST 9.0 2019 within E.coli / cefepime, 92% [CLSI] vs. 87% [BRCAST]; K.pneumoniae / cefepime, 51% [CLSI] vs. 49% [BRCAST]; P.aeruginosa / cefepime 86% [CLSI] vs. 79% [BRCAST].

Conclusions: The results show comparable antibiotic susceptibility patterns between CLSI and BRCAST breakpoints. The change of AST guidelines led to a decrease of susceptibility rates in clinical isolates for defined species/drug combinations. Given that BRCAST guidelines are freely available, it makes it easier for laboratories in resource poor settings to have an updated and readily available reference for interpreting antibiotic susceptibilities.

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A leak in compliance with ventilation system maintenance instructions resulted in an aspergillosis outbreak

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Abstract 5603

**Background:** Invasive aspergillosis (IA) is an important cause of morbidity and mortality in patients with hematologic malignancies. Here, we shared our experience for an aspergillosis outbreak in an oncology hospital in November 2017.

**Materials/methods:** Detection of four consecutive patients with IA who were hospitalized in the same ward triggered an outbreak investigation. A case was defined as any patient with clinical symptoms that could be related to IA after at least 1 week of hospitalization and *Aspergillus* spp isolation from culture. Possible causes of the outbreak were questioned. Samples for fungal culture were taken from the ventilation system outlets in the patient rooms.

**Results:** Although there were no cases that matched with the case definition in October, four cases were detected in November. All patients with IA had neutrophil count < 500 mm³, *Aspergillus fumigatus* or *Aspergillus flavus* were isolated from respiratory samples of three patients and sinus biopsy culture of one patient. Three patients were diagnosed as probable pulmonary IA and one patient was diagnosed as *Aspergillus* sinusitis according to EORTC/MSG definitions for invasive mold diseases.

The investigation revealed that the filters of the ventilation system were changed in all patient rooms without compliance with the institutional instructions for maintenance and repair for air conditioning and ventilation system. Patients were kept in their rooms without any air protection during the filter change and all further steps such as, use of hepafiltered cleaner, cleaning and disinfection of the room and change of curtains and sheets were missed. *Aspergillus* spp (*Aspergillus fumigatus, Aspergillus niger, Aspergillus spp*), *Paecilomyces* spp, *Chrysonilia* spp and unspecified mold growth were detected in environment cultures. N95 masks were recommended for all the neutropenic patients in the ward and they were quickly transferred to other wards. New patient admissions were stopped. After then, the air conditioning filters were changed according to the instructions, ventilation system and the rooms were cleaned and disinfected. After the intervention, no fungal infection (pneumonia or sinusitis) was detected in the first quarter of 2018 (Figure 1).

**Conclusions:** Any leak for infection control precautions can lead to severe consequences. Continuous education and surveillance are crucial.

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Abstract 5611

Role of multidrug-resistant bacteria on nosocomial pneumonia mortality
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Background: Nosocomial pneumonia is a leading cause of infections in the hospital setting. In recent years, an increased incidence of multidrug-resistant bacteria (MDR) has been described as causative pathogens of different respiratory tract infections. The presence of MDR is associated with poor clinical outcomes, including increased mortality.

Materials/methods: Descriptive and retrospective study of 738 patients diagnosed with nosocomial pneumonia between Jan 2012 and December 2017 at a single center. Diagnosis was based on the identification of a pneumonia 48 hours or more after admission and not present at admission. In-hospital mortality was established as the outcome variable. Both univariable and multivariable analysis was performed using logistic regression to assess the differences between survivors and non-survivor groups, adjusting for demographic and clinical variables. MDR was defined as non-susceptibility to at least one agent in three or more antimicrobial categories.

Results: 738 patients were selected, of which 565 cases (76.6%) were associated with ward hospitalization and 173 (23.3%) with mechanical ventilation; 59.2% male, mean age 71 years (SD ±17); median hospitalization days prior to diagnosis 10 days (IQR 25-75); Median Charlson comorbidity index 6 points (IQR 4-8); 32% previous stay at ICU. In 303 patients there was microbiological identification of a pathogen: 69 blood cultures (9.3%), 161 sputum cultures (21.8%) and 111 (15%) bronchoaspirate samples; 71.6% were monomicrobial and 28.4% polymicrobial; in 173 cases (57.1%) gram-negative bacteria were isolated. In 91 cases (30%), MDR were identified, the most frequent were Pseudomonas (12%), Klebsiella (13%) and Acinetobacter (9%). 216 patients (29.3%) died during admission, of whom 38 (17.6%) presented MDR isolations. In multivariate analysis, identification of MDR (OR 1.75 [95%CI, 1.05-2.79], p=0.031), Charlson comorbidity score (OR 1.24 [95%CI, 1.17-1.32], p<0.01), the use of vasoactive drugs (OR 3.48 [95%CI, 2.11-5.72], p<0.01); and the use of antifungals on empirical treatment (OR 2.40 [95%CI 1.09-5.72], p=0.29) were independently associated with mortality.

Conclusions: The identification of MDR in patients with nosocomial pneumonia is associated with higher mortality. Empirical therapy for nosocomial pneumonia must include adequate antibiotic coverage for MDR, based on local susceptibility patterns.

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Increasing importance of *Enterococcus faecium* as an aetiological agent of healthcare-associated bloodstream infections

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**Background:** *Enterococcus faecium* is an important etiological agent of healthcare-associated infections (HAI). It causes both localised and systemic infections. Enterococci are characterised by natural resistance to cephalosporins, isoxazolyl penicillins and linkosamides, as well as low concentrations of aminoglycosides. Of particular clinical importance is an acquired resistance of enterococci to glycopeptides and oxazolidinones. The aim of the study was to assess the trend in the change of epidemiology of bloodstream infections (BSI) caused by *E. faecium* in 2015–2018 in a university-affiliated hospital (1050 beds).

**Materials/methods:** Analysis comprised the results of blood culture (n=68709). Only non-repetitive, clinically significant isolates of bacteria cultured from samples of peripheral blood were included in the study (n=10723). Blood samples were monitored in the Bactec FX system (Becton Dickinson). Bacterial isolates were identified using MALDI-TOF MS analyser (Bruker). Antimicrobial susceptibility was evaluated by disk-diffusion technique, according to the EUCAST recommendations, as well as with the use of antibiotic gradient strips (E-test, bio-Merieux).

**Results:** In the analysed period, the percentage of BSI episodes caused by *E. faecium* was 5.56%, 8.30%, 11.39%, and 7.18%, respectively [an increasing trend]. Simultaneously, a decrease in the rate of infections caused by *Staphylococcus aureus* was recorded (15.08%, 11.30%, 9.61% and 11.26%, respectively). No significant changes were noted in the frequency of BSI episodes caused by predominant Gram-negative rods – *E. coli* (14.29%, 16.25%, 16.90% and 15.01%, respectively) and *K. pneumoniae* (13.29%, 9.57%, 13.35% and 10.77%, respectively). In the analysed period, a steady increase was observed in the percentage of VRE strains causing BSI – from 42.86% in 2015 to 59.46% in 2018. Since 2016, *E. faecium* strains resistant to linezolid have emerged.

**Conclusions:** 1. *E. faecium* infections should be monitored closely due to an increase in the frequency of HAI BSI of this etiology. 2. An increase in the rate of *E. faecium* HAI BSI may be linked to a high percentage of glycopeptide-resistant strains and an emergence of linezolid-resistant isolates. 3. An emergence of linezolid-resistant strains of *E. faecium* denotes depletion of therapeutic possibilities in treatment of BSI caused by *E. faecium* VRE strains.

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European and national *Clostridioides difficile* infection surveillance

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Abstract third-party references: On behalf of the COMBACTE-CDI consortium

Background: In 2018, the "Combatting Bacterial Resistance in Europe – *Clostridioides difficile* Infections (COMBACTE-CDI) project" was initiated that aims to assess the epidemiology and clinical impact of CDI across Europe. A specific work package was developed to analyse and compare CDI surveillance practices per country.

Materials/methods: In each of the 12 participating countries, several laboratories/hospitals, that perform diagnostic testing of faecal samples from both in-patients and community patients, were recruited and requested to send all diarrheal samples from two selected days in 2018. Each centre and their associated community practices, that had sent samples, were requested to complete a web-based questionnaire on surveillance practices.

Results: Here we present data from 105 hospital/hospital-based laboratories facilities that responded. Of these, 13 (12.4%) mentioned participation in international surveillance. Five sites in five countries participated in the CDI surveillance of the European Centre for Disease Prevention and Control, and others referred to temporary studies. Participation in national surveillance was reported from 11 countries by at least one hospital/laboratory (figure). On local site level, 44.8% participated in national surveillance. Inclusion criteria and content however, varied between and within countries. National CDI surveillance programmes of five countries focussed only on hospital-diagnosed or -acquired cases. In three countries both hospital- and community-acquired cases were recorded and the remaining countries provided varying answers. Cases were included in national surveillance either when there was a combination of a positive test and clinical characteristics (44.7%) or when there was a positive test, irrespective of clinical characteristics (55.3%). A combination of a positive test and symptoms was required for inclusion in at least one hospital/laboratory in the majority of countries (8/12). Furthermore, surveillance programmes differed in inclusion requirements regarding recurrences and age. Case-based data, other than gender and age, and hospital-based data were only reported in some programmes.

Figure: Participation in national CDI surveillance.

Conclusions: National CDI surveillance has been established in at least one hospital/laboratory in 11/12 participating countries. The overall focus in national surveillance schemes is on hospital-diagnosed CDI, but there is considerable variation in inclusion criteria, required positive tests and reported case- and hospital-based data between and within countries.

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Mycoplasma genitalium infections can comprise mixtures of both quinolone-susceptible and quinolone-resistant strains

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Background: Mycoplasma genitalium is an important sexually-transmitted infection that has recently been added to the CDC antimicrobial resistant threats “watch list” as it has rapidly become resistant to mainstay treatments, including macrolides and quinolones, over the past decade. In Australia, despite changes to treatment guidelines for M. genitalium, treatment failure remains common and may occur even where patient samples are shown via Sanger sequencing to harbor only wild-type (susceptible) strains.

Materials/methods: Suspecting that some patients may potentially harbor mixtures of both susceptible and resistant strains, which may be missed by Sanger sequencing, we developed and applied a suite of molecular assays to detect both wild-type sequences and resistance mutations. Here, we focused on quinolone resistance mutations that occur at amino acid positions 83 and 87 of the parC gene in M. genitalium and have been previously associated with quinolone resistance/susceptibility. We specifically included technologies that can readily identify mixtures of susceptible/resistant nucleotides sequences, including both allele-specific PCR and amplicon deep sequencing. These results were compared to Sanger sequencing.

Results: A total of 433 M. genitalium-positive samples were screened. For the majority of samples (n = 412), only a single allele, either wild-type (n = 354) or mutant (n = 58), was identified using all methods. However, 21 (4.8%) samples were shown via allele-specific PCR and/or deep sequencing to harbor mixtures, with the most common mixtures being wildtype S83 and mutant S83I. Notably, only 4 of these mixtures were identified by Sanger sequencing, even where the chromatographs were further scrutinized for additional peaks.

Conclusions: Our data show that M. genitalium infections can often comprise a mixture of both quinolone-susceptible and quinolone-resistant strains, and that such mixtures will typically be missed using “gold standard” Sanger sequencing. These findings highlight the complex nature of antibiotic resistance in M. genitalium, and have obvious implications for the selection of appropriate antimicrobial treatments to improve patient-directed therapy and minimize treatment failure for M. genitalium infections.

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Abstract 5619

**Research priorities to increase vaccination coverage (EU Joint Action on Vaccination)**
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**Background:** The EU Joint Action on Vaccination was launched with the aim to increase vaccine coverage in Europe. Filling evidence gaps to allow the design of effective strategies and approaches towards this goal is of key importance. We therefore propose a prioritization process to identify research priorities towards generating and synthesizing needed evidence to increase vaccine coverage.

**Materials/methods:** We used a multi-criteria decision analysis (MCDA) method inspired by the Child Health and Nutrition Research Initiative developed by Rudan et al. This quantitative methodology follows a series of steps including different groups of experts and relevant stakeholders. The first step consists in identifying key research questions through a broad consultation. In parallel, a first group of experts is tasked to select criteria for prioritization research questions, taking into consideration the ultimate goal of the exercise. Another group of experts is then requested to assess a weight to each of the criteria, using pair-wise comparisons. The final step consists to gather experts who will assess each research question against the weighted criteria. This evaluation leads to assigning a score to each individual research question, which can then be ranked in order of priority.

**Results:** We focused our work on four pre-selected pilot vaccines (pertussis, measles containing combination vaccines, influenza and HPV). The consultation generated 110 questions, which were secondarily sorted and re-worded to obtain 30 questions to be ranked. Criteria for setting priorities are the following: accessibility, answerability, deliverability, disease prevalence/incidence, effectiveness, equity, generalization, and territory. The final list of ranked research topics will be defined – using weighted criteria - during a face-to-face meeting in Paris in early 2020.

**Conclusions:** With the great diversity of possible topics, in a context of limited resources, prioritizing research questions becomes crucial. We have developed a transparent, evidence-based rigorous process applied to defined key research questions to generate evidence towards the design of strategies to increase vaccine coverage. Results will be disseminated broadly and submitted to the EC for funding in the context of The Horizon Europe Program. Following thorough evaluation of the methodology, it will be adapted as needed and generalized all types of vaccines.

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Whole genome sequence-based country-wide study reveals a high ongoing transmission of multidrug-resistant Mycobacterium tuberculosis in southern Brazil

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Background: The Mycobacterium tuberculosis (M.tb) is the pathogen responsible for tuberculosis (TB) that remains as the major death cause from a single infectious agent worldwide. The knowledge about molecular characteristics of different M.tb strains enables more effective surveillance and control measures. In this way, whole genome sequencing (WGS) provides high-throughput and resolutive data. We are carrying on a WGS-based evaluation of the M.tb strain diversity, drug-resistance and ongoing transmission across Brazil. M.tb strains from different Brazilian States were already sequenced and here we show the preliminary results.

Materials/methods: Here we are carry on a WGS-based evaluation of the M.tb strain diversity, drug-resistance and ongoing transmission in different Brazilian States. We used a 5 SNPs cut-off to delineate genomic clusters and in addition searched for possible epidemiological-links (epi-links) for recent TB transmission substantiation.

Results: The main results regarding the population-based study conducted in Rio Grande do Sul State including 325 drug-resistant M.tb isolates, indicated a high rate of multidrug-resistant (MDR) M.tb recent transmission. Of the 325 clinical isolates, 189 were grouped in 32 genomic clusters. In total, 27 epi-links were identified involving 91 patients, where 62 were patients in community epi-links, 29 in prison establishments and two household contacts. Among the isolates from the 183 MDR-TB patients 131 (71.58%) were grouped into genomic clusters, this number has decreased for the patients with INH-monoresistant TB (39.83%) and with poly-resistant TB (47.36%).

Conclusions: Our preliminary results put in evidence a scenario involving a high transmission of multiple phylogenetically distinctive clades of MDR M.tb strains in Southern Brazil, stressing the need for measures in order to quickly TB diagnosis and contacts tracing.

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Abstract 5626

The effect of intestinal alkaline phosphatase and physical activity on the course of experimental colitis in obese mice

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Background: Inflammatory bowel diseases (IBDs) are chronic inflammatory disorders of the colon and small intestine, commonly described as Crohn disease and ulcerative colitis. Even though most of IBD's patients are underweight, the ratio of intraabdominal fat is greater than in healthy individuals. Visceral fat constitutes the major source of pro-inflammatory cytokines. Intestinal alkaline phosphatase (IAP) is an important apical brush border enzyme acting through dephosphorylating of bacterial lipopolysaccharide released from cells walls during stressful events. However, whether IAP administration combined with exercise known to exerts the intestinal anti-inflammatory effect, can improve the healing of experimental colitis and the alterations in microbiota during the course of healing of colitis remains unknown.

Materials/methods: We determined the effect of IAP and physical activity on the course of experimental colitis in obese mice. Animals fed high-fat-diet (HFD) were randomly assigned to exercise group maintained on in-cage running wheels for 8-weeks. Then mice were administered i.g. with IAP for 2-weeks followed by intrarectal administration of 2,4,6-trinitrobenzenesulfonic acid (TNBS). Disease activity index (DAI) and the colonic blood flow (CBF) were determined. The composition of intestinal microbiota was examined by Next-Generation Sequencing (NGS). The effect of physical activity was assessed by Grip-strength test. The intensity of oxidative stress was examined by determination of factors involved in radical genesis.

Results: HFD delayed healing of colitis as manifested by increase of DAI and fall in CBF. In contrast, IAP administration and physical exercise reduced DAI, oxidative stress (MDA, SOD, GSH) and increased GBF in mice with colitis. In HFD mice, the combination of IAP with exercise favored intestinal colonization of Faecalibacterium, Helicobacter, Alistipes and reduced Clostridium, Bacteroides, Desulfovibrio, Parasutterella.

Conclusions: Combination of IAP and exercise accelerates healing of colonic mucosal damage in mice model of colitis via mechanism involving the attenuation of oxidative stress markers and enhancement of CBF. The alteration of bacterial composition was observed in obese mice and the high load of bacteria with the loss of their diversity were reversed when IAP was combined with physical exercise. These experimental results may be recommended as complementary non-pharmacological treatment of intestinal disorders when confirmed in human IBD.

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Abstract 5627


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Background: The prevalence of Invasive Candida Infections (ICI) has significantly increased in recent years, and candidemia has still a mortality rate up to 40%. Our objective was to evaluate the appropriateness of antifungals (AF) first-line treatment, adaptation after documentation, and time to adaptation.

Materials/methods: Patients with at least one blood culture positive for yeasts and a systemic AF treatment between January 2014 and December 2018 were included. Epidemiology, susceptibility, patients’ data and treatments were collected from computerized medical records and Mycology Laboratories. Deaths were attributed to ICI when there was no other cause and no negative blood culture control.

Results: 151 patients were included, 70 females and 81 males. Candida albicans was isolated in 47% of patients. No resistance for the 4 tested AF (amphotericin B, caspofungin, voriconazole and fluconazole) was observed for C. albicans and C. parapsilosis. Patients were hospitalized in ICU (33%), gastroenterology (17%), surgery (12%), infectious diseases department (8%), but also in geriatric units (12%) and other departments not used to treat those severe patients. Thirty-two percent of patients died within 3 months after candidemia. The delay between blood culture and first-line treatment was 2.3 days. Delays were shorter among the deceased patients (1.7 days vs 2.5 days among alive patients). First-line treatment was caspofungin (67%), fluconazole (28%), voriconazole (n = 3), micafungin (n = 2) or amphotericin B (n = 1). Time between documentation and treatment adaptation was 3.2 days, and time between susceptibility results and treatment streamlining was 1.8 days. Seventy-nine percent of AF treatments was appropriate, inappropriate in 17 patients (16% inappropriate in deceased patients vs 9% among alive patients), and 14 patients were lost. The probability of survival was worse at 90 days if treatment was inappropriate (p = 0.56).

Conclusions: This work underlined the importance to treat invasive Candida infections quickly, but with an appropriate drug. A systematic monitoring of candidemia by an antifungal stewardship team could improve management and clinical outcome of these severe patients, with invasive Candida infections, hospitalized in many departments apart from ICU.

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Abstract 5628

Preliminary results for the evaluation of the impact of syndromic lower respiratory tract panel on antimicrobial management and infection control

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Background: Diagnosis of lower respiratory tract infections, hospital-acquired pneumonia (HAP) or community-associated pneumonia (CAP) in patients remains an important and challenging problem associated with significant morbidity, mortality, and cost. Syndromic lower respiratory tract infection panel (Biofire LRTI Panel) may shorten the time to apply the targeted antimicrobial treatment in patients with pneumonia and provide rapid application of isolation measures.

The aim of this study was to investigate the impact of Biofire LRTI Panel on targeted antimicrobial therapy and management of infection control in patients diagnosed with community-acquired pneumonia (CAP) or early hospital-acquired pneumonia (HAP) whom are planned to be hospitalized and treated in intensive care unit (ICU).

Materials/methods: Between October 2018 and September 2019, >18 years old patients admitted to Marmara University Pendik Training and Research Hospital, and planned to be hospitalized with the diagnosis of CAP or early HAP were chosen. Patients excreted sputa with <10 squamous epithelial cells, > 25 PNL in each high-power field at microscopic examination were included. Bacterial culture and syndromic lower respiratory tract infection panel (Film Array LRTI Panel, RUO version, BioFire Diagnostics, USA) performed simultaneously on sputum samples. Results were blind evaluated by two infectious diseases specialists for the decision of treatment change and application of infection control measures. Decision of antibiotic change, time to optimal antimicrobial change, bacterial culture result, Biofire LRTI panel result and applied infection control measures were recorded for each patient.

Results: Forty patients were met the inclusion criteria and evaluated. Biofire LRTI Panel detected at least one pathogen in 31 patients (77.5%), among these, 29 had bacterial, 15 had bacterial and viral, and 2 had viral pathogens. No pathogen could be detected in 9 patients (22.5%). Sputum cultures were positive only in 14/40 (35%) patients. Antibiotic change was decided in 20 patients and infection control measures were applied in 21 patients (Table 1 & 2).

Conclusions: Biofire LRTI Panel provides faster access to optimal antimicrobial treatment and high rate of antibiotic de-escalation in patients diagnosed with CAP and early HAP, and also contributes to the rapid implementation of infection control measures.

Table 1. Performance of Biofire LRTI Panel in comparison with bacterial culture.

<table>
<thead>
<tr>
<th>Biofire LRTI Panel</th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial culture</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>14</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Negative</td>
<td>15</td>
<td>11</td>
<td>26</td>
</tr>
<tr>
<td>Total</td>
<td>29</td>
<td>11</td>
<td>40</td>
</tr>
</tbody>
</table>

Table 2. Impact of Biofire LRTI Panel on optimal antimicrobial therapy and infection control.

<table>
<thead>
<tr>
<th>Decision according to Biofire LRTI Panel result</th>
<th>#patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antimicrobial change</td>
<td></td>
</tr>
<tr>
<td>De-escalation</td>
<td>9 (45)</td>
</tr>
<tr>
<td>Escalation</td>
<td>7 (35)</td>
</tr>
<tr>
<td>Targeted antiviral therapy</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Stop antimicrobial treatment</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Application of infection control measures</td>
<td>21 (52.2)</td>
</tr>
<tr>
<td>Droplet isolation precautions</td>
<td>13 (62)</td>
</tr>
<tr>
<td>Contact isolation precautions</td>
<td>8 (38)</td>
</tr>
</tbody>
</table>

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Abstract 5629

Quality of life and its determinants among pulmonary tuberculosis patients taking direct observation therapy in Kabul, Afghanistan

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Background: Afghanistan faces a high burden of tuberculosis (TB) among the global, according to the World Health Organization (WHO). An estimated 60,000 new cases arise yearly, and the treatment success rate is only 49 percent on average in the country. Literature extensively supports that TB significantly destroys the quality of life (QoL) of the patients. Direct Observation Therapy (DOT) was introduced by WHO to enhance the effectiveness of treatment. This program uses sputum negativity and weight gain as prognostic indicators but does not consider health related QoL. The purpose of this study was to assess the QoL among Pulmonary Tuberculosis (PTB) patients of > 18 years of age, taking the DOT therapy.

Materials/methods: An analytical cross-sectional study was conducted to answer the study questions. Through convenient sampling, 302 PTB patients (age >18 years) were selected from National Tuberculosis Center Sanatorium, Kabul Afghanistan for interviewing, based on the WHOQoL-BREF tool.

Results: This study estimated the mean score of QoL as 25.61 among the participants. The participants showed that environmental (23+15.03) and physical (24.4 + 13.3) domains were most affected after PTB. The study presented 36.8% associated factors that affect the QoL of PTB patients independently in the multivariate regression. Among the participants, the ones who were satisfied with the DOT therapy (p=0.003) and had good knowledge about the disease (p=0.01) possessed good QoL. Whereas, participants who were on the intensive phase of Category-2 (p=<0.001), had kidney disorders (p=0.03), intensive cough which hindered prayers (p=<0.001), nausea initiating pain (β=9.0, p= 0.02), lost their significant other in the last one year (p=0.002), and facing financial difficulties (p=0.01) had poor QoL. Moreover, stigmatization stood out as the biggest problem for the PTB patients in the society, especially when it affected the relationship with siblings (p=0.001), and other kept a distance (p=0.001).

Conclusions: This study showed a very poor QoL among adult PTB patients in Kabul Afghanistan. Cough, pain stigmatization, knowledge related to disease, financial difficulties, parent’s support, and loss of significant other were significantly associated with QoL among PTB patients. Broad interventions are needed to address the problems of the PTB sufferers.

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Abstract 5630

**Surveillance of circulating carbapenemase genes with automated molecular system (BD Max) at a healthcare centre in Buenos Aires, Argentina**

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**Background:** Carbapenemase-producing Enterobacteriaceae (CPE) represent an increasing public health problem. Early detection of patient colonization at healthcare facilities can help the implementation of appropriate infection control measures. Predominant documented carbapenemase enzymes are KPC, OXA, NDM, VIM and IMP type. Our objectives were: 1- To evaluate the prevalence of CPE in rectal swabs from patients in critical areas of our institution; 2- Evaluate the prevalence of carbapenemase gene types. 3- Evaluate the turnaround time to results report with implementation of a molecular methodology (in comparison to manual methods).

**Materials/methods:** Prospective descriptive study, period 01/2018-05/2019. Rectal swabs samples were obtained from patients with any of the following criteria: 1) patients referred from another healthcare institution with ≥6 days of hospitalization; 2) hospital admission in the previous 30 days; 3) history of CPE colonization or infection in the last 30 to 90 days. Samples were processed with BD MAX™ System and Check-Direct CPE Screen for BD MAX™ molecular methodology (MM) according to the manufacturer’s recommendations.

**Results:** From a total of 2461 samples, 768 (31%) were. The frequency of carbapenemase gene detection in our center was: 330 for blaKPC (13.4%), 194 for blaOXA-48 (7.9%), 160 for blaVIM (6.5%) and 84 for blaNDM (3.4%). The turn-around time for results reporting was reduced from 48 to 3 hours.

**Conclusions:** The use of MM for detection of CPE colonization, provides a considerable shorter turn-around time, enabling same day screening and reporting of newly admitted patients. CPE screening results delivered in just a few hours, could improve the clinical management of colonized/infected patients reducing the possibility of resistance spreading.

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Treating nocardiosis with cotrimoxazole monotherapy in solid organ transplant recipients: real-life data from a multi-centre retrospective study

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Background: Nocardiosis is a rare but life-threatening opportunistic infection. Despite the fact that solid organ transplant (SOT) recipients with nocardiosis have a one-year mortality rate around 10-20%, their therapeutic management is still a matter of debate. Our aim was to report our real-life experience with cotrimoxazole (trimethoprim-sulfamethoxazole, SXT) monotherapy in SOT recipients with nocardiosis.

Materials/methods: We analysed data from a previously published retrospective multicentre European study. In the current study, we included all patients who received SXT and less than 5 days of combination with another antibiotic in the first 15 days post-diagnosis (cohort A). To assess effectiveness, we focused on the subset of patients who received at least 30 days of SXT monotherapy (cohort B). A standardized clinical form was sent to each investigator to collect additional data. Acute kidney injury (AKI) was defined according to the KDIGO classification: increase in serum creatinine by ≥ 0.3 mg/dl (≥ 26mmol/l) within 48 h; or increase in serum creatinine to ≥ 1.5 times baseline.

Results: Thirty-one patients were included. Transplanted organs were mostly kidney (20/31, 65%) and heart (5/31, 16%). Among them, 11/31 (36%) had a disseminated infection and 4/31 (13%) had a brain abscess; most had lung or pleural involvement (26/31, 84%). SXT was discontinued in one-third of the cases due to toxicity (10/31, 32%). Treatment was interrupted because of isolated hematological toxicity (n=3), isolated AKI (n=3), combination of AKI/hepatitis, AKI/hyperkalemia, AKI/leucopenia, diarrhea/hepatitis (n=1 for each). Regarding effectiveness, we focused on the 24/31 (77%) patients who received at least 30 days of single-drug regimen with SXT (cohort B). Among these 24 patients, four had late (> 30 days) drug discontinuation, one experienced treatment failure (likely due to a lack of adherence) and 19/24 (79%) completed treatment with SXT monotherapy. Clinical outcome was favourable in all these 19 patients, despite the facts that 8/19 (42%) had a disseminated infection and 2/19 (11%) had a brain abscess.

Conclusions: SXT monotherapy was an effective option in SOT recipients with Nocardia infection but treatment was interrupted in around 1/3 of the cases, mostly because of AKI or hematological toxicity.

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Abstract 5636

Evaluation of Bacillus anthracis agar-based susceptibility testing by Etest for ciprofloxacin, levofloxacin, doxycycline and tetracycline

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Background: Following exposure to Bacillus anthracis, the causative agent of anthrax, antimicrobial susceptibility testing (AST) results are crucial to guide antibiotic treatment. Broth microdilution (BMD) is the reference method for AST with B. anthracis, but requires specialized expertise for MIC endpoint determination and can be resource-intensive. The Etest method is a simple and cost-effective AST alternative. Here, the utility of the Etest method was evaluated for B. anthracis using strains from the CDC collection; Etest MICs for ciprofloxacin (CIP), levofloxacin (LVX), doxycycline (DOX), and tetracycline (TET) were compared to MICs generated by BMD.

Materials/methods: Twenty-five genetically and geographically diverse B. anthracis strains including four naturally occurring penicillin-resistant strains were included in this study. Additionally, four avirulent (ΔpXO2) strains were included as fluoroquinolone and tetracycline non-susceptible controls. All B. anthracis strains were tested in triplicate. For BMD, in-house prepared, 96-well panels containing Mueller-Hinton broth with increasing concentrations of CIP, LVX, DOX and TET, were inoculated following CLSI guidelines. The Etest method was performed concurrently. All MIC endpoints were visually interpreted by three readers.

Results:

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>No. of MIC results with log dilution differences for Etest and BMD methods</th>
<th>% EA</th>
<th>MIC50 (µg/mL) (Etest/BMD)</th>
<th>MIC90 (µg/mL) (Etest/BMD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>CIP</td>
<td>6</td>
<td>196</td>
<td>23</td>
<td>2</td>
</tr>
<tr>
<td>LVX</td>
<td>1</td>
<td>120</td>
<td>102</td>
<td>2</td>
</tr>
<tr>
<td>DOX</td>
<td>1</td>
<td>224</td>
<td>100</td>
<td>1</td>
</tr>
<tr>
<td>TET</td>
<td>3</td>
<td>138</td>
<td>84</td>
<td>100</td>
</tr>
<tr>
<td>Control strains</td>
<td>5</td>
<td>23</td>
<td>8</td>
<td>100</td>
</tr>
<tr>
<td>CIP</td>
<td>3</td>
<td>19</td>
<td>14</td>
<td>100</td>
</tr>
<tr>
<td>LVX</td>
<td>3</td>
<td>19</td>
<td>14</td>
<td>100</td>
</tr>
<tr>
<td>DOX</td>
<td>3</td>
<td>34</td>
<td>2</td>
<td>100</td>
</tr>
<tr>
<td>TET</td>
<td>36</td>
<td>100</td>
<td>1</td>
<td>1/&gt;4</td>
</tr>
</tbody>
</table>

The 25 wild-type B. anthracis study strains were susceptible to CIP, LVX, DOX and TET by Etest and BMD. Essential agreement (EA) was >99% for all strains tested, and categorical agreement was 100%. MIC50 and MIC90 values of both the wild-type and control strains were similar for both methods.

Conclusions: Etest showed a high-level of agreement compared to the conventional BMD reference method for all drugs tested. Etest is a suitable AST method for determining B. anthracis susceptibility to CIP, LVX, DOX and TET.

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Risk factors for carbapenem-resistant Enterobacteriaceae acquisition among kidney transplant recipients
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1Clinical Hospital, Infection Control Service, São Paulo, Brazil, 2Clinical Hospital, Infectious Diseases Department, São Paulo, Brazil, 3Clinical Hospital, Kidney Transplant Service, São Paulo, Brazil

Background: Carbapenem-resistant Enterobacteriaceae (CRE) infections have a high mortality rate among solid organ transplant patients. However, there are few studies about risks for CRE-acquisition among kidney transplant recipients (KTR).

The goal of this study was to identify risk factors for CRE-acquisition among KTR and risk factors for CRE-infection among CRE-colonized KTR.

Materials/methods: We performed a case-control study. Case was defined as any KTR that had CRE-acquisition identified from January 2010 to January 2019. We chose two controls per case, selected among KTR hospitalized in the same period of the case. We also analyzed the risk factors for CRE-infection within 90-days of first positive CRE-culture, among CRE-colonized KTR. In this retrospective cohort, we analyzed only the first infection episode per patient. Infections criteria used were those outlined by NHSN. All patients were followed until death, graft lost or end of follow-up. We included variables related to recipient, KT-procedure and post-KT intercurrences. Variables were recorded until first CRE-culture for cases and until discharge for controls. Statistical analysis was performed by chi-square, Fisher Test and Mann-Whitney test when appropriate and binary logistic regression for multivariate analysis.

Results: During study period we identified 332 CRE-colonized patients, in 271 (81.6%) the first culture was a surveillance culture. The most common CRE was K. pneumoniae (91.9%). The median time from KT to CRE identification was 41.5 days, 11 (3.1%) KTR was submitted to KT colonized by CRE. Risk factors for CRE acquisition were: diabetic nephropathy (p<0.03), delay of graft function (p<0.001), acute cellular rejection in previous 6 mouths (p<0.001), ureteral stent (P 0.001), increased age at CRE identification (p<0.01), and previous carbapenem use (p<0.08). 108 (32.5%) KTR developed CRE-infection and 53 (16.0%) had bacteremic infection. The most common site of infection was urinary tract infection, 59 (54.6%). Risk factors for infection among CRE-colonized patients were: previous carbapenem use (0.02), platelets count under 105/µL at CRE-acquisition (p<0.01), lymphocytes count under 1500/mm3 at CRE acquisition (p<0.01), and polymyxin-resistant strain (P0.003).

Conclusions: In conclusion, the proportion of CRE-colonized KTR that develop infection is high. KTR have risk factors for CRE acquisition and infection that are unique for this population.

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Abstract 5640

Comparison of three rapid diagnostic blood culture identification panels for Gram-negative bloodstream infections
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Background: To best manage bloodstream infections, rapid diagnostic testing (RDT) has become critical in improving patient outcomes. The primary objective of this study was to assess and compare three gram-negative rapid diagnostic blood culture panels.

Materials/methods: Retrospective study from 8/2018 to 11/2019 at the University of Maryland Medical Center. Positive blood cultures from each patient were tested for gram-negatives using Verigene® Blood Culture, BioFire® Blood Culture Identification panel (BCID), and the new BioFire® Blood Culture Identification Panel 2 (BCID2; Research-Use-Only) panels were compared to each other against standard culture identification with VITEK®MS and antibiotic susceptibility testing using VITEK®2.

Results: 103 positive gram-negative blood cultures were used in this study. P. multocida (2), Burkholderia spp (1), P. laetus (1), P. intermedia (1), Achromobacter (2), P. pseudoalcaligenes (1) and Psychrobacter (1) were not on any of the panels so they were excluded. The Verigene® panel does not include B. fragilis (1), and S. marcescens (10) so they were excluded (82/103 included). Among included organisms, Verigene® failed to identify 1 K. pneumoniae for an overall positive agreement of 99% (81/82). BCID panel also does not include S. maltophilia (1), B. fragilis (1), Citrobacter (1) and A. junii (1) so those were excluded (90/103 included). BCID misidentified 3 E. coli, 2 E. cloacae complex, 1 Acinetobacter spp., 2 Proteus spp., 1 K. oxytoca, 2 S. marcescens, and 1 K. pneumoniae for 87% (78/90) overall positive agreement. BCID2 (RUO) had a positive agreement of 96% (89/93) misidentification of 2 E. coli, 1 S. maltophilia, and 1 E. cloacae complex. Citrobacter (1) samples were not included in BCID2 analysis as it is not on the panel (93/103 included). Verigene® and BCID2 identified the 6 CTX-M. CTX-M was not on the BCID panel and, therefore was not detected.

Conclusions: Verigene® and BCID2 have high percent positive agreements. BCID2 is an improvement on BCID as it has increased positive agreement and the panel includes more organisms. BCID2 has the most extensive gram-negative panel of the three. Local epidemiology of bloodstream infections should be considered when laboratories are determining optimal use of rapid detection testing.

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Seroprevalence of hepatitis E virus among blood donors in the Qassim Region, Saudi Arabia

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Background: Hepatitis E virus (HEV), belonging to the Orthohepevirus genus in the family Hepeviridae, causes liver diseases in humans. HEV is now recognized as a major public health issue, causing over 20 million infections every year worldwide and accounting for approximately 70,000 deaths. Fecal-oral transmission is considered the main route of HEV transmission, but other transmission routes have been suggested. In particular, blood transfusion transmission has become one of the main routes, especially in some low-income countries in Asia. In this study, we estimated the HEV seroprevalence among blood donors in Qassim Region, Saudi Arabia. This is to evaluate whether the HEV routine screening would be considered as a routine screening of blood donations in Saudi Arabia in the future.

Materials/methods: Serum samples (n = 1,078) were collected from volunteer blood donors from January to April 2019 and tested for the presence of anti-HEV IgG and IgM by indirect enzyme-linked immunosorbent assays. Samples were tested in duplicate and samples yielding borderline results were retested in duplicate to confirm the initial results. Only IgG-positive samples were tested for the presence of anti-HEV IgM.

Results: The study was composed of 1,002 men (93%) and 76 women (7%). The number of Saudi donors was 924 (85.7%) and non-Saudi donors were 154 (14.7%). Overall, the seroprevalences of anti-HEV IgG and IgM among blood donors were 5.7% and 1.3%, respectively. Additionally, the seropositive rates of anti-HEV IgG and IgM were significantly higher in non-Saudi donors (22.1% and 7.8%) than in Saudi donors (3% and 0.2%). The seroprevalence of anti-HEV IgG increased with age; however, there was no correlation between gender and anti-HEV IgG and/or IgM.

Conclusions: The seroprevalence of HEV among blood donors in the Qassim Region was lower than previous estimates for other regions of the country. This low HEV seroprevalence might be related to the sensitivity and/or specificity of the commercial ELISA; therefore, further investigation is needed. These results extend our understanding of the distribution of HEV in Saudi Arabia, providing a basis for the development of screening strategies.

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Audit on HIV quality of care to new patients in a level 4 teaching Hospital

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Background: HIV has become a complex, chronic condition requiring a comprehensive, multifaceted care approach. Recognising this, the HIV Medical Association has developed criteria to benchmark the quality of care provided to HIV patients.1 St. James’s Hospital has the largest HIV positive patient cohort in Ireland, with 2,535 patients attending the clinic at the of the Department of GU Medicine and Infectious Diseases (GUIDe) in 2018.

Materials/methods: We performed a retrospective analysis of all new patients attending GUIDe in 2018. Data was collected using the Electronic Patient Record System (EPR).

Results: There were 260 new patients attending the clinic in 2018. Data analysis is currently ongoing. 86% were retained in care and 94% had a CD4 count >200. 98% were prescribed ART with 98% achieving virological suppression [VL<40 or not detected]. Where appropriate, 100% of patients were prescribed PCP prophylaxis. Chlamydia and Gonorrhoea screening was performed on initial presentation in 68% of the cohort with 0% testing positive. 61% of patients were screened for injection drug use, while 100% were screened for risky sexual behaviour. 100% of patients were screened for syphilis on first clinic review with 40% testing positive on initial antibody screening. 96% of patients were screened for Hepatitis B using core antibody testing with 2% testing positive. 36% of patients had prior Hepatitis B immunity defined as surface antibody positive > 10 IU/ml. 14% received no hepatitis B Immunisation, 26% completed 3 doses hepatitis B vaccination. Hepatitis C screening was performed in 100% of patients. 95% of patients were given at least 1 dose of the influenza vaccine, with 45% achieving yearly immunization, 95% of these in the influenza window (October – April). Regarding TB screening, 60% of patients had a chest X Ray and 6% were investigated with quantiferon testing.

Conclusions: This audit outlines the strengths of the HIV care provided at the GUIDe clinic, largely complying with the HIVMA standards of care. Additionally, it raises clinically important areas where further educating care providers could improve the uptake of screening and vaccination.

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Abstract 5645

Descriptive analysis of carbapenemase genes in Acinetobacter baumannii in the Antibiotic Resistance Laboratory Network: United States, 2017–2019

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Background: Acinetobacter baumannii is an opportunistic pathogen often associated with multidrug resistance, outbreaks of healthcare-associated infections, and severe outcomes for patients who are infected. Carbapenemases are enzymes that confer resistance to carbapenems and other beta-lactam drugs. Plasmid-mediated carbapenemase determinants, including Ambler Class A (bla\textsubscript{KPC}), Class B (bla\textsubscript{NDM}, bla\textsubscript{VIM}, bla\textsubscript{IMP}) and Class D (bla\textsubscript{OXA23-LIKE}, bla\textsubscript{OXA48-LIKE}, bla\textsubscript{OXA58-LIKE}) are of particular public health concern because they can spread easily. Carbapenem-resistant Acinetobacter baumannii (CRAB) is not a reportable condition to Public Health Departments in most states in the United States; therefore in 2017, the U.S. Centers for Disease Control and Prevention (CDC) initiated sentinel CRAB surveillance. We describe the distribution of carbapenemases among CRAB in the Antibiotic Resistance Laboratory Network from 2017 through 2019.

Materials/methods: Beginning in 2017, sentinel clinical laboratories from 42 of 50 states submitted all CRAB isolates to AR Lab Network regional public health laboratories for organism identification and PCR detection of Class A and B carbapenemase genes (bla\textsubscript{KPC}, bla\textsubscript{NDM}, bla\textsubscript{VIM}, and bla\textsubscript{IMP}). In 2019, the Network laboratories started testing isolates for the presence of Class D oxacillinase genes (bla\textsubscript{OXA23}, bla\textsubscript{OXA48-LIKE}, bla\textsubscript{OXA58-LIKE}). Testing results were submitted to CDC at least monthly.

Results: From January 2017 through October 2019, regional laboratories tested 3,595 sentinel CRAB isolates; Class A or B carbapenemase genes were detected in 21 (0.58%) of these (10 bla\textsubscript{KPC}, 11 bla\textsubscript{NDM}). From January through September 2019, 6 of 7 regional labs also tested 1,116 CRAB isolates for the presence of Class D carbapenemase genes; the percentage of Class D-positive CRAB was much higher (median of 68%) and varied by geographic region.

Conclusions: Class A and Class B carbapenemases among Acinetobacter baumannii appears to be rare whereas Class D carbapenemases appear to be much more common in the United States and vary by geographic region. Healthcare facilities and public health officials should respond aggressively to any carbapenemase-producing Acinetobacter baumannii detected in order to prevent their spread.

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Prevalence and molecular characterisation of methicillin-susceptible Staphylococcus aureus carrying Panton-Valentine leucocidin gene isolated from patients with invasive infections and nasal carriers

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Background: Staphylococcus aureus causes a wide range of infections. Panton-Valentine Leucocidin (PVL) is an important virulence factor mainly present in community-acquired methicillin-resistant S. aureus (CA-MRSA). CA-MRSA is commonly associated with rapidly progressive skin and soft tissue infections, especially USA 300 clonal lineage. However, PVL-positive [PVL (+)] methicillin-susceptible S. aureus (MSSA) have also been described both in carriers and in infections, with variable prevalence. Some of these strains have Spa types related to USA 300, such as t008 and t024. Our aim was to describe the prevalence and Spa types of PVL (+) MSSA isolated from invasive infections and nasal carriers in Santiago, Chile.

Materials/methods: 142 isolates of MSSA were included: 95 from invasive infections [tissue, blood, normally sterile sites] treated at Clínica Alemana de Santiago and 47 from nasal carriers [University of Chile healthcare students]. Endpoint PCR was used for detection of PVL and mecA genes in all strains. Spa type of PVL (+) MSSA and a representative sample of PVL-negative strains were determined by sequencing. Sequence analysis and Spa type was performed using DnaGear Software and Ridom database, available at: https://www.SpaServer.ridom.de/. Antimicrobial susceptibility phenotype was determined by disk diffusion (CLSI M100, 2019).

Results: 10.5% [10/95] of MSSA clinical isolates was PVL (+) versus none in carriers. Eight Spa types were found in PVL (+) MSSA strains [2 t318 and 1 of each of the following: t4908, t1164, t088, t2409, t330, t012, t5160]. One strain had a new combination of repetitions, so no known Spa type could be assigned. Seventeen Spa types were found in PVL (-) MSSA strains [19/23]. Spa type t008 and t068 were the most prevalent [2 strains of each]. MSSA clinical strains showed higher antimicrobial resistance than isolates from carriers: ciprofloxacin 3.16% vs. 2.13%; erythromycin 32.63% vs. 25.53%; clindamycin 24.21 vs. 8.51%, respectively. No strain was resistant to trimethoprim-sulfamethoxazole.

Conclusions: the PVL gene is present in MSSA clinical isolates but not in nasal carriers. Spa types related to USA 300 clonal lineage were found in 2 PVL (-) MSSA strains. Macrolide and clindamycin resistance is common in clinical strains.

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Direct-acting antiviral based treatment for HCV-infected persons who inject drugs: a multi-centre real-life study

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Background: The treatment of HCV in high-risk population, such as people who inject drugs (PWID), is essential to reduce the spread of infection worldwide. In the present study we aimed to evaluate the factors associated with virological response in a cohort of HCV infected PWID treated with DAAs.

Materials/methods: We conducted a multicentre retrospective cohort study enrolling all HCV infected subjects who reported a former or recent injection of illicit drugs, for which HCV-RNA loads at 12 weeks after end of treatment were available. The primary outcome evaluated was the SVR12 rate; the epidemiological, clinical and virological characteristics associated with the viral response were analysed. A logistic regression analysis was applied to identify independent predictors of virological failure.

Results: During the study period, 551 PWID treated with DAAs were enrolled; the mean age was 47.15 ± 8.5 and 485 (88%) were male; 181 (32.8%) patients presented a genotype 1a, 115 (20.87%) a genotype 1b, and 177 (33.0%) a genotype 3; 113 (20.36%) showed a staging of fibrosis according to Metavir score of 3, while 161 (29.45%) had a cirrhosis; 120 (21.77%) and 388 (70.41%) were treated with a DAA regimen of second and third generation, respectively. Only 13 subjects (2.35%) showed a positive HCV-RNA at 12 weeks after EOT, 6 of which had dropped out before the scheduled duration of therapy. No epidemiological and virological characteristic were associated with treatment failure. Patients F3-F4 showed a lower rate of SVR12 compared to patients with less advanced fibrosis (95.8 vs 99.23%, p=0.03); as expected, subjects treated with first or second generation DAAs presented a higher treatment failure than those treated with a third generation regimen (SVR12: 93.3 vs 98.9%, p=0.002). At the multivariate analysis, the treatment with a first or second generation DAA resulted the only factor independently associated with treatment failure (OR: 10.9, 95%CI 2.39-42.61; p=0.002).

Conclusions: The treatment with DAAs led to a high SVR12 rate (97.65%) among a large cohort of HCV-infected PWID. Systematic screening and treatment with highly effective third generation regimens will make the elimination of HCV in this setting a feasible goal.

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Abstract 5656

Analysis of treatment failures of haematogenous prosthetic joint infections: new infections occur more often than infection persists or relapses

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Background: The optimal management of haematogenous periprosthetic joint infection (hPJI) is controversial. While guidelines recommend debridement and implant retention (DAIR) for acute hPJI, some authors advocate prosthesis removal due to poor outcome with DAIR. We investigated the treatment outcome of hPJI according to surgical procedure and failure type.

Materials/methods: Consecutive patients with hPJI treated at our institution between 2010 and 2017 were included and followed-up for infection occurrence. Infection failure was stratified into persistence/relapse of infection (defined as infection with the same or no pathogen or infection-related death) or new infection (defined as infection caused by a new pathogen). The probability of persistence/relapse-free and infection-free (overall) survival was estimated using the Kaplan-Meier survival method.

Results: Of 106 patients with hPJI, follow-up was available for 94 patients, involving hip (n=50), knee (n=42), shoulder (n=1) and elbow (n=1) prostheses. At the time of diagnosis the following pathogens were isolated: Staphylococcus aureus (n=34), Streptococcus spp. (n=30), Enterococcus faecalis (n=13), Enterobacteriaceae (n=9), coagulase-negative staphylococci (n=6), Clostridium innocuum (n=1) and no pathogen (n=1). DAIR was performed in 38 (40%), prosthesis exchange or permanent removal in 56 (59%) and no surgery in 2 episodes (2%). At 48-month follow-up (Figure), infection relapse occurred in 14 patients (15%) (including 11 with same or no identified pathogen and 3 infection-related deaths) and new infection in 19 patients (20%). Consequently, the persistence/relapse-free survival was 85% and the overall infection-free survival 65%. New infections occurred more often after prosthesis exchange/removal compared to DAIR (13 vs. 6 failures), whereas infection persistence/relapses were similar in both surgical groups (6 vs. 7 failures, one without surgery). Among 33 failures, 17 (52%) were another hPJI, caused by same (n=6) or new pathogen (n=11). The type of surgical treatment, causative pathogen or CRIME80-Score had no impact on the treatment outcome.

Conclusions: The persistence/relapse-free survival after treatment of hPJI was high (85%), irrespective of the surgical treatment. However, new infections occurred in additional 20% of treated patients in the following 4 years, reducing the overall success to 65%. About half infection failures were again hematogenous, mainly caused by a new pathogen, suggesting a general predisposition for hPJI.

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Characterisation of carbapenemase-producing Enterobacterales isolates with phenotypic and genotypic methods in southern Hungary

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Background: Infections caused by carbapenem-resistant Enterobacterales (CRE) are serious issues in clinical practice, leaving physicians with few treatment options available. For infection control and public health purposes, the differentiation of carbapenemase-producers (CP-CRE) is essential, because these resistance determinants are readily transferable. The aim of our study was to characterise carbapenemase-producing strains in a low-prevalence setting in Hungary, through the use of various phenotypic and genotypic methods.

Materials/methods: Fifty strains obtained between 2014 and 2017 were included in the study from the culture collection of the Institute of Clinical Microbiology (University of Szeged). Inclusion of these strains was based on the screening criteria recommended by ESCMID (meropenem disk diameter <28 mm). The following phenotypic methods were used: modified cloverleaf (Hodge) test (MHT), modified carbapenem inactivation method (mCIM) and chromID CARBA SMART agar (bioMérieux). The presence of carbapenemase- and extended spectrum beta-lactamase (ESBL) encoding genes were detected using PCR, followed by sequencing. Production of AmpC-β-lactamases was verified using AmpC Detection Disk Set (Mast Diagnostics). Susceptibility of the strains to colistin (broth microdilution, Merlin Diagnostika) and fosfomycin (E-test, Liofilchem) was also determined.

Results: Carbapenemase genes were detected in 18 isolates (2 blaNDM, 6 blaOXA-48-like and 10 blaVIM), nine of these isolates were carbapenemase/ESBL (mainly blaCTX-M) co-producers. 12 isolates were inducible AmpC β-lactamase-producers, while in 5 isolates, none of the above could be verified. Sensitivities/specificities of the modified Hodge-test, CARBA SMART agar and mCIM test were 85.7%/80%, 95%/100% and 100%/100%, respectively. All tested isolates were susceptible to colistin (MIC range: 0.5-1 mg/L), while 37 out of 50 isolates were resistant to fosfomycin.

Conclusions: The diversity of carbapenemase enzymes and their co-occurrence with other resistance mechanisms affecting susceptibility to β-lactam antibiotics (AmpC, ESBLs, porin loss) often makes detection of these resistance-determinants difficult for routine diagnostic laboratories. Based on our results, the use of modified Hodge-test is not recommended due to its poor specificity, while chromogenic media (easy to use) and mCIM (panels can be prepared in-house) offer viable options for the detection and confirmation of carbapenemase-producing Enterobacterales for routine laboratories.

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Abstracts 2020

Abstract 5661

Linezolid treatment for methicillin-sensitive Staphylococcus aureus bacteraemia
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Background: Standard care for Methicillin-Sensitive Staphylococcus aureus bacteraemia is currently a minimum of 14 days of intravenous flucloxacillin or an equivalent antibiotic. Pharmacokinetic data show that linezolid is very well absorbed orally, and recent data suggest that linezolid can be an effective oral agent in the treatment of Methillin-Resistant Staphylococcus aureus and Methillin-Sensitive Staphylococcus aureus bacteraemia.

Materials/methods: We conducted a retrospective cohort study of adult patients who were treated with oral Linezolid for Staphylococcus aureus bacteraemia between August and October 2019 in an outpatient setting in a tertiary care hospital. Outcomes were safety data, inflammatory markers, clinical need to switch to other agents and recurrence of bacteraemia.

Results: Fifteen adult patients were included of the 3-month period. The leading sources of bacteraemia were including discitis, osteomyelitis, wound infections and cellulitis. Of the 15 patients, 13 were started on linezolid, and two started with intravenous flucloxacillin but were then switched to oral linezolid. All the patients were followed up weekly in the OPAT clinic and had blood test monitoring on all their follow up visits. There were no drug related events leading to discontinuation of linezolid observed. All the patients responded to the oral linezolid monotherapy as suggested by the clinical and biochemical improvement, and no recurrence of bacteraemia occurred after cessation of therapy. The duration of linezolid ranged from 2-5 weeks depending on the source of infection.

Conclusions: Treatment of Methillin-Sensitive Staphylococcus aureus bacteraemia with oral linezolid was found to be effective and safe in all 15 patients. Additionally, oral linezolid treatment enabled patients to continue treatment for Methillin-Sensitive Staphylococcus aureus bacteraemia without the need to stay in hospital. Oral linezolid therapy could serve as a cost-effective treatment for Methillin-Sensitive Staphylococcus aureus bacteraemia.

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Abstract 5662

**Reporting of interferon gamma release assay results close to cut-off value**

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Abstract third-party references: Abstract submitted on behalf of European TB Reference Laboratory network (ERLTB-Net-2) funded by ECDC

**Background:** Detection and treatment of latent tuberculosis infection (LTBI) can reduce the risk of developing active tuberculosis (TB) thus contributing to elimination of TB. Interferon gamma release assays (IGRA) are widely used for detection of LTBI. Several reports have shown high rates of conversion and reversion in results close to the clinical decision cut-off value, and determination of uncertainty as well as use of a borderline zone has been suggested to reduce an impact of test variability on diagnostic and clinical management of patients.

**Materials/methods:** To better understand practices in reporting IGRA results and identify potential areas for improvement, we conducted a survey within the ECDC European Reference Laboratory Network for TB (ERLTB-Net-2) using structured questionnaire.

**Results:** Responses were received from 16 National TB reference laboratories (NRLs) offering IGRA testing using QFT-plus (Qiagen) as part of their routine laboratory services, response rate was 100%. Four NRLs reported qualitative IGRA results, 11 qualitative results with numerical values, one quantitative plus qualitative for specific cases.

Six laboratories do not report results close to the cut-off value as equivocal and/or indeterminate within an uncertainty range. Ten NRLs have policies on reporting equivocal and/or indeterminate results based on either pre-defined ranges, or use specific methodologies to determine ranges for reporting results as equivocal.

When asked about special provisions for reporting of results close to the clinical decision cut-off value, seven laboratories responded that they report them as positive or negative following Manufacturer’s instructions. Six laboratories ask customers for another specimen. Two laboratories repeat the test and report the second result. One NRL suggests interpreting the results based on clinical history. In total, seven laboratories do not repeat tests with results close to a cut-off value, nine do.

**Conclusions:** Practices of reporting of IGRA results close to the clinical decision cut-off value differ significantly among NRLs, a finding that calls for further attention. Harmonization of reporting results close to cut-off value could be beneficial for patient management. A phase II study potentially involving collection of data on repeat testing is currently in the pipeline. Consent to participate has been obtained from 14 European NRLs.

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An interoperable informatics application for the work-flow improvement of an antimicrobial stewardship programme in a tertiary hospital

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Background: Hospital antimicrobial stewardship programs are aimed to reduce inappropriate use of these drugs by optimizing treatments (molecule, dose, route of administration and therapy duration) in order to improve patient outcomes and reduce antimicrobial resistances. Informatics technology in these programs are essential since can speed up the prescription revision, the interventions in the clinical records and help to measure the antimicrobial consumption, the number of interventions and their acceptation rate. The aim of this study was to develop an interoperable informatics application for the work-flow improvement of an antimicrobial stewardship program.

Materials/methods: A database interoperable with the patient clinical records was designed and evaluated in a tertiary hospital in northern Spain during a one-year period (November 2018 to November 2019). This application is capable of automatically update treatments, culture results (including antimicrobial susceptibility data) as well as patient information such as location in the hospital, somatometry and analytical results; being all this information filterable, facilitating the antimicrobial prescription revision. Interventions were classified in the application as: multidrug-resistant microorganism control, antimicrobial de-esacalation and escalation, dose adjustment, duration of therapy, sequential therapy, restricted antimicrobials control, antimicrobial prophylaxis duration, adherence to empirical therapy guidelines and therapeutic drug monitoring.

Results: A total of 6452 antimicrobial regimens from patients admitted in the hospital were reviewed by the antimicrobial stewardship team during the study period by using this application. These revisions led to 3325 interventions in the patient clinical records with a grade of acceptation among the patient’s responsible physicians of 75%. A reduction of 3% and 8% of days of therapy (DOTs) in antibiotics and antifungals were achieved, respectively; with an antimicrobial direct costs reduction of 13.7% (306015 euro) with respect to the same previous year-period.

Conclusions: Our application allowed to streamline the prescription revision by the antimicrobial stewardship team, leading to a high number of interventions with a high rate of acceptance, which resulted on an improvement in the global data of antimicrobial consumption. Further analysis of the impact in patient length of stay, infection outcomes and mortality is required, but our application seems to be a promising useful tool for antimicrobial stewardship programs.

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Abstract 5664

An OXA-48 variant hydrolysing carbapenems, expanded-spectrum cephalosporins and aztreonam: welcome OXA-793

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Background: The spread of carbapenemase-producing Enterobacteriaceae (CPE) has become a major public health concern. Among these CPEs, OXA-48-producing Enterobacteriaceae have now widely disseminated throughout European countries. OXA-48 confers high-level resistance to penicillins, including temocillin and hydrolyzes carbapenems at a low level, but spares expanded-spectrum cephalosporins (ESC). Since the first identification of OXA-48, different variants have been reported, differing by few amino acid substitutions or deletions mostly in the region of the β5-β6 loop. Whereas some OXA-48-variants have similar hydrolytic activities to OXA-48, others, such as OXA-405 do not hydrolyze carbapenems but ESCs instead. Here, we have characterized a novel OXA-48 variant, named OXA-793, able to hydrolyze both ESCs and carbapenems.

Materials/methods: Multidrug-resistant K. pneumoniae strain 163G4 was isolated in France in 2018. Whole genome sequencing using an Illumina MiSeq platform was performed. OXA-793 was cloned in pTOPO and expressed in Escherichia coli Top10. Disc diffusion and MIC determinations were used to study antibiotic susceptibility. Plasmid reconstruction, characterization and mating-out assay were performed. Steady state kinetic parameters of the purified enzymes were determined and compared to those of OXA-48

Results: OXA-793 conferred resistance to expanded-spectrum cephalosporins and aztreonam, as well as carbapenems. OXA-793 differed from OXA-48 by a amino acid deletion (Ile215 and Glu216) in the β5-β6 loop. The substrate specificity was confirmed by steady state kinetic parameters of the purified enzyme, which exhibited high catalytic efficiencies for all the β-lactams including cephalosporins (broad and expanded-spectrum) aztreonam and carbapenems but no activity against temocillin. The blaOXA-793 gene was located on a conjugative ca. 60-kb plasmid identical to the prototype IncL blaOXA-48 -carrying plasmid.

Conclusions: OXA-793 is the second description of an OXA-48-like β-lactamase capable of hydrolyzing ESCs and carbapenems at the same time. The presence of blaOXA-793 gene on the highly conjugative IncL plasmid increases the risk of dissemination of this new variant. Finally, as temocillin resistance is currently used for OXA-48 detection, OXA-793 may go undetected and thus spread silently.

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Abstract 5665

Take care of the cents and the euros look after themselves? Antimicrobial activity of European money

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Background: Money is a frequently touched surface and it is supposed that money might be involved in pathogen transmission. Due to copper fractions of >75% in euro and cent coins loose change is assumed to have antimicrobial activity. Antimicrobial activity of solid surfaces are often investigated by the unrealistic ISO 22 196. In this study we investigated the antimicrobial activity of european coins and banknotes under realistic conditions using a touch transfer assay [Knobloch, PlosOne, 2016] modelling the dry contamination by skin contact.

Materials/methods: For the touch transfer assay primary contaminated surface (PCS) were prepared with Enterococcus faecium ATCC 6057 or Staphylococcus aureus ATCC 6538 dried on the surface of ceramic tiles. Uptake of bacteria from the PCS was performed with moistened sterile cotton gloves. With the contaminated gloves bacteria were transferred to 5 cent, 50 cent and 1 euro coins as well as 5 Euro banknotes by touching the surface. Ceramic tiles were used as control surface in the touch transfer assay. Quantitative culture of the SCS was performed immediately [T0] as well as after 24 h storage.

Results: In independent experiments using E. faecium (n=4) and S. aureus (n=5) variable numbers of transferred bacteria were observed on the different surfaces. Similar transfer rates were observed for the ceramic tile (control) and banknotes. The smaller surface of the 5 cent coin resulted in a lower amount of transferred bacteria compared to 50 cent and 1 euro coins. All copper containing coins displayed a detectable antimicrobial activity. Reduction rates (log10) on 5 cent, 50 cent and 1 euro were calculated with 1.9, 2.1 and 2.3 for S. aureus as well as 1.5, 2.0 and 1.9 for E. faecium, respectively. In contrast, the decrease of bacteria after 24 h on the banknote was similar compared to the control.

Conclusions: In contrast to a 5 euro banknote, copper containing coins display a detectable antimicrobial activity. However, in most experiments bacteria were not completely eliminated from the coins. Therefore, even coins might act as vectors for the transmission of microbes.

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Impact of antibiotic stewardship programme on the most utilised antibiotics’ utilisation and financial expenditure in 57,357 Children Cancer Hospital Egypt inpatient setting

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Abstract third-party references: 57357 Children Cancer Hospital Egypt, Dr Lobna Shalaby - Head of the Infectious Disease Unit

Background: Antibiotic Stewardship program (ASP) was designed and implemented to reduce the misuse and abuse of antibiotics, and to reduce the overall bacterial resistance patterns in our hospital, 57357 Children Cancer Hospital Egypt. In order to evaluate the effectiveness of the program, and justify the costs involved in implementing it, a monthly outcome measures were set.

Aim of this study: to measure the effect of ASP on cost, and utilization of the high volume antibiotics in our hospital, CCHE, in 2019 after implementation of ASP against the same drugs at the same period of time in 2018, before implementation of ASP.

Materials/methods: This is a retrospective study, analyzing the cost per patient, defined daily dose (DDD) and days of therapy (DOT) per 1000 patient days; from January till September before and after implementation of the ASP for the most utilized antibiotics in our hospital. Drugs under study are, amikacin, liposomal amphotericin b, vancomycin and voriconazole. The entire population administering these antibiotics in the inpatient setting was included with exclusion of the outpatient, emergency and daycare setting.

Results:

<table>
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<th>Antibiotic</th>
<th>Average DOT per 1000 patient days Before ASP</th>
<th>Average DOT per 1000 patient days After ASP</th>
<th>Average DDD per 1000 patient days Before ASP</th>
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<th>Average Cost per patient before ASP in EGP</th>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>voriconazole</td>
<td>57</td>
<td>38</td>
<td>53</td>
<td>37</td>
<td>10609</td>
<td>10158</td>
</tr>
<tr>
<td></td>
<td>(33.3% decrease)</td>
<td>(30.2% decrease)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: ASP initiatives were associated with an observed reduction in stewardship-focused antibiotic utilization. Significant decreases in antimicrobial expenditures were also observed. These observed outcomes were related to the implementation of our hospital-designed-ASP; mainly focusing on infectious disease pharmacists and infectious disease physicians’ rounds, and ensuring the implementation of our local fever & neutropenia guidelines.

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Molecular characterisation of multiresistant *Mycobacterium tuberculosis* strains circulating in the state of Santa Catarina, Brazil from 2013 to 2017

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**Background:** Santa Catarina State, a high-income state in southern Brazil, with a TB incidence rate of 22.5 per 100,000 population. However, some regions have higher rates than the national average (>33.5/100,000 population). Previous studies conducted in Santa Catarina State showed predominance of the LAM lineage circulating strains, including the MDR isolates. Molecular epidemiology study is essential to understand the transmission dynamics of multidrug-resistant (MDR) isolates in the state. MDR phenotype is characterized by simultaneous resistance to rifampicin and isoniazid.

**Materials/methods:** The samples were culture in liquid medium (MGIT-BD, USA) and reisolated in Ogaw-Kudoh medium. DNA were extracted by CTAB. DST testes were made by critical concentrations. The study included all MDR isolates from Santa Catarina State during the evaluated period (2013-2017), corresponding to 63 isolates of *Mycobacterium tuberculosis*. Molecular epidemiology was characterized by the combined analysis of spoligotyping and MIRU.

**Results:** The 63 isolates were classified into 14 SITs, 13 sublineages and four lineages, and three isolates had unknown profile and one isolate Orphan profile (sublineage T2). The LAM lineage was the most prevalent (75%), followed by the T superfamily (14%), Harleem (5%) and EAI (2%). With 71% of isolates integrating 4 SITs (2263, 42,106 and 73), all corresponding to the LAM lineage (LAM9, LAM7 and LAM5). The LAM9 sublineage was responsible for 52% of isolates. The dendrogram constructed by the combined analysis of MIRU and spoligotyping identified nine clusters (100% similarity) and 13 Recent Infection Group (GIR) (90-99% similarity). The largest cluster consisted of 18 isolates from SIT2263 (LAM9), the second largest consisting of eight isolates from SIT106 (LAM7). The largest GIRs consisted of nine isolates of the LAM9 sublineage and one with 31 isolates of LAM9 and one T1, corresponding to 52.3% of the total isolates (33/63).

**Conclusions:** The isolates classification maintained similar proportions during the five years studied. The work was fundamental to determine the epidemiological profiles of multidrug-resistant *Mycobacterium tuberculosis* in Santa Catarina State, identifying the LAM lineage as the main family and as sublineages LAM9 (SIT2263 and SIT42) and LAM7 (SIT106).

**Figure1:** Spoligotyping result for the 63 MDR isolates, grouped by families and subfamilies

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Abstract 5675

Is Mycobacterium lentiflavum “the new” Mycobacterium avium?

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Background: Mycobacterium lentiflavum is a slow-growing nontuberculous mycobacteria (NTM) that has been increasing gradually during the last years. Its pathogenic role is controverted, and as Mycobacterium avium complex (MAC) it has been isolated from respiratory samples and from lymph nodes specially from children.

Materials/methods: retrospective study from 2009 to 2019 in a universitary hospital in the community of Madrid, Spain. All samples for micobacteria diagnosis were included. Microbiological diagnosis was carried out by an automated culture (MGIT™ 960 system, Becton Dickinson). Bacterial identification was obtained by mass spectrometry (MALDI-TOF) or DNA studies.

Results: a total of 3338 samples were positive for micobacteria (2751 NTM): 53.73% MAC and 13.34% M. abscessus were the most prevalent micobacteria. Mycobacterium lentiflavum was isolated from 230 samples (8.36% total NTM isolates) from 173 patients: 40.46% female, median age 63.12 years, 50 (28.90%) suffering bronchiectasis and 11 (6.35%) cystic fibrosis. The respiratory tract was the main origin of M. lentiflavum isolates (198, 86.09%), following by lymph nodes (28, 12.17%). All the positive lymph nodes came from children except one from an adult. 22 patients (12.71%) had two or more M. lentiflavum isolates: the principal origin was respiratory tract (21 patients, 95.45%), M. lentiflavum was the only microorganism isolated from 12 patients (54.54%). During the period, an increase in the number of isolates and the M. lentiflavum-NTM proportion is observed (Graph 1): from 5 isolates (2.67% NTM) in 2009 to 19 (9.6% NTM) in 2019.

Conclusions: the high frequency of isolation, the isolation from more than one sample and the absence of other microorganism in the cultures, support this NTM as causative agent of infection not only in pediatric population, but also in adults. Moreover, during this ten years’ period a continuous rise of isolation is noted, even displacing MAC as the main micobacteria isolated from lymph nodes in paediatric population, therefore new studies that clarify its pathogenic role are necessary to improve the correct management of these patients.

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Occurrence and predictors of nephrotoxicity in adult patients treated with intravenous colistin: a cohort study
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Background: Colistin has been increasingly used due to the emergence of multidrug resistant bacteria. Nephrotoxicity is its most important side effect. Our aim was to determine the prevalence and risk factors associated with nephrotoxicity in patients treated with colistin.

Materials/methods: Retrospective cohort study of adult patients treated with at least 48h of intravenous (IV) colistin in a single tertiary care hospital from 2015 to 2018. Nephrotoxicity was defined according to RIFLE criteria. The adequacy of dosage was classified according to the International Consensus Guidelines. The association of independent variables with nephrotoxicity was evaluated using logistic regression.

Results: The prevalence of nephrotoxicity in our cohort was 41.07% (69/168) and it led to treatment interruption in 6 patients (3.57%). Five patients (7.25%) needed dialysis, 52 (75.36%) classified as Failure, 5 (7.25%) as Injury and 7 (10.14%) as Risk. Sixty-two patients (36.9%) received an insufficient dose of colistin. These patients were less likely to develop renal toxicity (OR 0.07; IC95% 0.01 - 0.56; p=0.01). The occurrence of nephrotoxicity was adjusted for dosage of colistin. Older age (OR 1.03; IC95% 1.00 - 1.06; p=0.03), duration of treatment (OR 1.08; IC95% 1.03 - 1.14; p=0.02) and colistin use in the preceding month (OR 10.86; IC95% 1.31 - 90.31; p=0.03) were identified as risk factors for nephrotoxicity. In 36 (23.38%) patients the kidney injury had not reversed on discharge home. The overall 30-day mortality was 41 (24.40%).

Conclusions: The prevalence of nephrotoxicity in our cohort was high and similar to other studies, although more than one third of patients were treated with suboptimal dose. Most kidney injury was severe and long-lasting. There are settings when colistin is the only therapeutic option but its use is greatly limited by toxicity. Better tolerated antibiotics should be used whenever possible, especially in high risk patients.

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Abstract 5681

Usefulness of human cytomegalovirus (HCMV)-specific immunological monitoring in the management of HCMV infection in lung transplant recipients

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Background: We evaluated the usefulness of immunologic monitoring in LTRs for predicting the onset of HCMV DNAemia after stopping antiviral prophylaxis post-transplant and to individuate possible markers predictive of the risk for HCMV infections using both aspecific and HCMV-specific immunological monitoring.

Materials/methods: In this prospective cohort study were enrolled 63 consecutive LTRs between February 2017 and December 2018 and monitored for at least six months post-transplant. Antiviral prophylaxis was based on donor (D) and recipient (R) serology. The virological and immunological monitoring was established at time 0, 1 and each three months after transplant. Immunological monitoring was performed using two commercially-available tests QuantiFERON and ELISpot.

Results: The median age was 35 years [IQR 25-51] at time of transplant, 58.7% were male and 61.9% LTRs came from cystic fibrosis.

At 120 days post-transplant, the CD4+ T-cell count was significantly higher in the group of patients with undetectable HCMV DNAemia in comparison to those with detectable HCMV DNAemia post-transplant (p=0.0124). The cumulative incidence of HCMV DNAemia events was significantly higher in the group of patients with CD4+ T-cell count lower than 650 cells/µl (89.2%) than respect to patients with CD4+ T-cell count higher than 650 cells/µl (28.6%; p<0.0001).

We observed an excellent agreement between ELISpot and serology status at transplant (kappa 0.93) while lower agreement between QuantiFERON and serology status (kappa 0.63). On 696 assays performed during the follow up of LTRs, the agreement between ELISpot and QuantiFERON was moderate (kappa of 0.54). 14/49 patients R+ showed persistent negative QuantiFERON assay despite the presence of detectable immunity measured by ELISpot. 28.6% of R+ LTRs showed persistent negative QuantiFERON in presence of positive ELISpot during all the period of follow-up.

Analyzing IE1-specific T-cell response at pre-transplant, we observed a statistical trend of significance (p=0.0505) for the prediction of HCMV reactivation in HCMV-seropositive patients.

Conclusions: ELISpot resulted most sensible that QuantiFERON to detect the HCMV-specific T-cell response in LTRs. CD4+ T-cell count measured at 120 days post-transplant and IE1-specific T-cell response could represent predictive markers to identifying LTRs at risk of HCMV infection and to adjust the period of prophylaxis.

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**Abstract 5684**

**Increase of *Escherichia coli* with reduced susceptibility to cefepime and OXA-1 compatible phenotype in urinary tract infections along the years**

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**Background:** *E. coli* isolates with reduced susceptibility or resistance to amoxicillin-clavulanate (AMC), piperacillin-tazobactam (PTZ) and cefepime (CEF) (OXA-1-beta-lactamase compatible phenotype) are emerging in the last years. The aim of this study was to quantify the number of *E. coli* isolates with this OXA-1 compatible phenotype from 2015 to 2019 from clinical samples and to analyze the antibiotic susceptibility patterns and patient’s characteristics.

**Materials/methods:** From January 2015 to October 2019, 31085 non duplicate *E. coli* from various clinical specimens were obtained (first isolate per patient). Antimicrobial susceptibility testing was determined by MicroScan WalkAway (Beckman Coulter) and Eucast criteria were applied. *E. coli* isolates (excluding ESBL and AMPC) in which the MIC of AMC was ≥16 mg/L, PTZ ≥16 mg/L, and CEF ≥2 mg/L were considered compatible with an OXA-1-beta lactamase. Cefuroxime (30 µg) disk diffusion test was performed in a selection of isolates. Microbiological and clinical data were recorded.

**Results:** A total of 224 patients presented an *E. coli* with OXA-1 compatible phenotype (28 in 2015, 29 in 2016, 35 in 2017, 75 in 2018 and 57 until October 2019), mainly isolated from urine samples (85%); 83% were outpatients, 73% women, and 52% ≥65 years. The percentages of susceptibility (S) were: 20.5% cefuroxime, 98% cefixime, 78% cefotaxime, 96% ceftazidime, 98% aztreonam, 100% carbapenems, 53% ciprofloxacin, 72% gentamicin, 65% tobramycin, 90% amikacin, 58.5% trimethoprim-sulfamethoxazole, 97% nitrofurantoin, and 96% fosfomycin. In 34 isolates cefuroxime susceptible by the Microscan WalkAway system a cefuroxime disk diffusion test was performed, that resulted resistant in 32 (94%) of the 34 isolates.

**Conclusions:** The number of *E. coli* isolates with OXA-1 compatible phenotype has gradually increased in recent years (especially from 2018) mainly associated with urinary tract infections (UTI) in outpatient women. Reduced susceptibility has been found for cefuroxime (with false susceptible results from the MicroScan WalkAway system), cefotaxime, gentamicin, tobramycin, ciprofloxacin and trimethoprim-sulfamethoxazole, that added to the resistance profile to amoxicillin-clavulanate, piperacillin-tazobactam and cefepime may result in multidrug-resistant isolates with limited treatment options. Fosfomycin and nitrofurantoin remain a good treatment option for uncomplicated UTI.

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Kaposi sarcoma herpes virus infection in solid organ transplant recipients
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Background: HHV8/KSHV causes neoplastic and non-neoplastic diseases in SOT (solid organ transplant). At ISMETT (Mediterranean Institute for Transplantation and Advanced Specialized Therapies) a prospective study on liver donors and recipients published in 2011 showed that 50% of mismatch recipients (D+/R-) developed a primary HHV8 infection, 50% with fatal outcome. In 2016 we described the first case of KICS (KSHV Inflammatory Cytokine Syndrome) in an HIV-negative SOT recipient, successfully treated.

We aimed to describe epidemiology and incidence of infection and disease HHV8-related in different risk-groups of SOT population: mismatch (D+/R-), patients HHV8Ab-positive pre-transplant, seronegative patients.

Materials/methods: Donors and recipients were screened for HHV8-Ab at transplant time. We performed infectious, dermatological and virologic follow-up with different timing according to the risk category, in order to identify infection or treat associated disease.

Results: We found an overall HHV8-seroprevalence of 6.3% in our population of donors and recipients [January 2012-March 2019]. Among 27 mismatch recipients (1 heart, 1 lung, 5 kidney, 20 liver), 12 liver recipients presented HHV8 transmission (44.4%), intended as seroconversion or detectable viremia. (Table 1)

Of note, 6 patients (22%) developed a KICS-like syndrome after SOT: two patients had fatal outcome. Both happened before strict clinical and virologic monitoring took place.

Among 76 positive recipients before SOT, four patients (5.3%) developed HHV8-disease: three cutaneous Kaposi Sarcoma and one visceral Kaposi Sarcoma with fatal outcome. One patient presented a de novo HHV8 infection after transplant with KICS syndrome.

HHV8-related mortality in risk-patients [mismatch and positive recipients, n=103] was 2.9%.

Mismatch liver recipients represent a high-risk group

Conclusions: Considered the possible serious complications, SOT patients must be strictly followed-up for HHV8 infection/ reactivation. Knowledge about HHV8 related disease in SOT need to be improved.

Table 1. HHV8 transmission in mismatch recipients

<table>
<thead>
<tr>
<th>Type of transplant</th>
<th>N.</th>
<th>Transmission</th>
<th>Seroconversion (only HHV8-Ab positive)</th>
<th>Detectable viremia (positive HHV8-DNA)</th>
<th>Disease HHV8-related</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>1</td>
<td>0; (-)</td>
<td>0; (-)</td>
<td>0; (-)</td>
<td>0; (-)</td>
</tr>
<tr>
<td>Lung</td>
<td>1</td>
<td>0; (-)</td>
<td>0; (-)</td>
<td>0; (-)</td>
<td>0; (-)</td>
</tr>
<tr>
<td>Kidney</td>
<td>5</td>
<td>0; (-)</td>
<td>0; (-)</td>
<td>0; (-)</td>
<td>0; (-)</td>
</tr>
<tr>
<td>Liver</td>
<td>20</td>
<td>12; (60)</td>
<td>2/12; (17)</td>
<td>10/12; (63)</td>
<td>6/12; (50)</td>
</tr>
</tbody>
</table>

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Abstract 5686

The effectiveness of antibiotic prophylaxis in the prevention of respiratory tract infections in antibody-deficient patients: a single-centre cohort study

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Background: Antibiotic prophylaxis has become an integral part of the management of antibody deficient patients, but very few studies have been attempted to define its role. In an era of therapeutic immunoglobulin shortage and rising antimicrobial resistance (AMR), the need to clarify this role has become even more critical.

Materials/methods: In a tertiary immunology referral centre in England (UK), we retrospectively analysed the hospital Immunology database to identify adult antibody deficient patients who had received antibiotic prophylaxis to prevent lower respiratory tract infection (LRTI) over the past 15 years. Primary outcome was to assess the impact on hospital admissions and sputum culture positivity. Secondary outcome was to assess the emergence of AMR and adverse drug reactions.

Results: One hundred and five patients were identified with a cumulative monitoring period of 870 years (mean 3.9 years). There was a significant reduction in infection-related hospital admissions by almost 50% [53/year vs 27/year] and positive sputum cultures were reduced by a third [1.61/year vs 1.05/year] [Figure 1]. Although 10% of patients reported antibiotic related side effects, diarrhoea (n=4) and genital thrush (n=3) being the most common, none of them developed Clostridium difficile infection. Overall, emergence of secondary AMR to the corresponding antibiotic the patient was receiving at the time occurred in 15 patients (14%). This was mainly against macrolides and there was evidence of cross resistance across different agents in the same class. In terms of risk of colonisation with multi-drug resistant organisms (MDRO), there were 8 patients with extended-spectrum Beta-lactamase (ESBL) producing Enterobacteriaceae, 5 patients with Methicillin-resistant Staphylococcus aureus (MRSA) and a single case of vancomycin resistant Enterococcus (VRE). The annual cost of the top three agents Cotrimoxazole, Azithromycin and Amoxicillin were £56, £120 and £32 respectively. They are significantly lower than the cost of a single day of hospitalisation in a publicly funded National Health Service (NHS) in England.

Conclusions: Overall, antibiotic prophylaxis is effective in antibody deficient patients. Taking into account the cost and scarcity of immunoglobulin and hospital beds in the NHS, our study shows the cost effectiveness of antibiotic prophylaxis in this patient population.

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Possibilities of implementation of lactobacilli’s antagonistic properties for Clostridioides difficile growth suppression

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Background: Colon-derived Lactobacillus strains could be divided into groups with high, intermediate, low and absent antagonistic activity (AA). Lactobacilli’s antagonistic properties are promising for prevention and treatment of nosocomial multiresistant infection

Materials/methods: We isolated 30 Lactobacillus spp. strains, 3 Yersinia spp. strains and 150 C. difficile strains from the patients’ colon biotope. All C. difficile strains caused clinically relevant antibiotic-associated diarrhea, 28 strains were toxin B positive, 116 strains were toxin (A+B) positive and 6 strains were toxin-negative. We also used Lactobacillus plantarum 38 strain from “Lactobacterin dry” probiotic [Microgen, Russia] and Helicobacter pylori NCTC 11639, Campylobacter jejuni NCTC 11635, Salmonella enterica serovar typhimurium 3542 reference strains. Lactobacilli’s AA was quantified by measurement of growth suppression zone of the culture of interest: > 30 mm – high, 20 – 30 mm – intermediate, 5 – 20 mm – low, ≤ 5 mm – absent.

Results: Lactobacillus spp. content in 30 faeces samples varied from 10³ to 10⁶ CFU / g. 10⁶ - 10⁸ CFU / g Lactobacilli multiplicity was characterized by high [38,9%], intermediate [11,1%] and low [11,1%] AA. AA-absent strains [38,9%] had very heterogeneous multiplicity [10³ - 10⁸ CFU / g]. None of the Lactobacillus strains have shown high level of AA against Salmonella enterica serovar typhimurium 3542. We revealed high AA against Helicobacter pylori NCTC 11639 in 17 [55,6%] Lactobacillus strains and low AA only in 8 [26,3%]; this parameter was coordinated with AA against Campylobacter jejuni NCTC 11635 and Yersinia spp. strains. Lactobacillus plantarum 38 reference strain has shown monotonous high AA against all clinically relevant microorganisms except toxin-producing C. difficile. Luminal-derived Lactobacilli of the patients have shown high and intermediate AA against toxin-negative and toxin B positive C. difficile while having low or absent AA against (A+B) positive C. difficile.

Conclusions: Lactobacilli’s AA evaluation is perspective for fighting nosocomial infection caused by resistant microorganisms; particularly the use of Lactobacillus autostrains could suppress the growth of toxigenic C. difficile strains.

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Abstract 5692

Systematic review of Legionella amelioration systems in healthcare facilities
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Background: Contaminated water systems have been the source of healthcare-associated Legionella infections. We conducted a systematic literature review to assess the effect of mitigation systems on Legionella contamination of healthcare facilities’ water systems.

Materials/methods: We searched reference lists, MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, and clinicaltrials.gov using the key terms legionnaires, legionella, water, hospitals, and healthcare facilities to identify articles published through 7/10/2017 pertaining to Legionella amelioration methods. We included studies that provided information on amelioration methods for Legionella in hospital water systems and cultured water samples for Legionella for > 1 year after implementation of the system. We excluded articles that: were not in English, addressed only Legionella infections, provided inadequate information, or provided aggregate data from > 1 facility.

One investigator screened titles, abstracts, and manuscripts. Two investigators independently abstracted data. They resolved disagreements by reviewing the papers together.

Results: 62 articles published between 1975-2017 met inclusion criteria. 72 hospitals were located in: the United States (34), Europe (28), Canada (5), and Asia (5). 52% of hospitals used > 1 amelioration system during their study periods.

<table>
<thead>
<tr>
<th>Amelioration system</th>
<th>Maintained 0%+ cultures</th>
<th>Median 0%; some + cultures</th>
<th>Achieved but did not maintain 0%+ cultures; no follow up information</th>
<th>Achieved 0%+ cultures</th>
<th>Did not achieve 0%+ cultures</th>
<th>≥ 1 Clinical cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heat and Flush (6)</td>
<td>1 (16.7%)</td>
<td>0</td>
<td>1 (16.7%)</td>
<td>0</td>
<td>4/6 (66.7%)</td>
<td>5 [100% of those reporting]</td>
</tr>
<tr>
<td>Hyperchlorination (36)</td>
<td>1 (2.8%)</td>
<td>0</td>
<td>4 (11.1%)</td>
<td>0</td>
<td>31 (49.2%)</td>
<td>15 [48.4% of those reporting]</td>
</tr>
<tr>
<td>Copper/silver (34)</td>
<td>1 (2.9%)</td>
<td>3 (8.8%)</td>
<td>5 (14.7%)</td>
<td>12 (35.3%)</td>
<td>13 (38.2%)</td>
<td>3 (8.8%)</td>
</tr>
<tr>
<td>Chlorine dioxide (11)</td>
<td>0</td>
<td>1 (9.1%)</td>
<td>0</td>
<td>2 (18.2%)</td>
<td>8 (72.7%)</td>
<td>1 (9.1%)</td>
</tr>
<tr>
<td>Monochloramine (5)</td>
<td>1 (20%)</td>
<td>0</td>
<td>2 (40%)</td>
<td>0</td>
<td>2 (40%)</td>
<td>0</td>
</tr>
<tr>
<td>Ultraviolet light (n = 6; 1 new; 5 existing hospitals)</td>
<td>1 (100%) of new; 0 existing</td>
<td>0</td>
<td>1/5 (20% of existing)</td>
<td>0</td>
<td>4 (80% of existing)</td>
<td>Not clear</td>
</tr>
</tbody>
</table>

Conclusions: Amelioration systems varied in their ability to suppress Legionella growth and prevent infections. Very few hospitals maintained a rate of 0% positive Legionella surveillance cultures once Legionella was identified in the water system.

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Abstract 5695

Implementing rapid susceptibility testing directly from positive blood cultures in the routine laboratory workflow for sepsis

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Background: Early diagnosis and treatment of bloodstream infections decreases mortality rate of sepsis. Timely reporting of susceptibility results of bacteria isolated from blood cultures (BC) is crucial for promptly administering an appropriate antimicrobial treatment, improving patients’ outcome and possibly conferring cost savings. The aim of this study was the evaluation of the performance of light scattering technology Alfred60®T (Alifax, Italy) for rapid (in a few hours) susceptibility testing directly from positive BC and its applicability in routine use.

Materials/methods: We evaluated 156 significant episodes of bacteraemias produced by 77 Gram-negative and 77 Gram-positive bacteria. Only monomicrobial according to Gram stain BC were included. The antimicrobials tested were chosen among ciprofloxacin, gentamicin, meropenem, piperacillin-tazobactam and colistin for Gram-negative and cefoxitin, vancomycin, linezolid and daptomycin for Gram-positive bacteria. Alfred60®T provided qualitative results in terms of clinical category (SIR). Concordance assessment was performed in comparison with the routine method Vitek2 (bioMérieux, France) except for colistin which was compared with the automated broth microdilution system MICRONAUT-S (Merlin, Germany). Discrepancies were resolved with MICRONAUT-S or E-test (bioMérieux, France). Interpretation of clinical categories (SIR) was determined according to EUCAST recommendations.

Results: Total turnaround time for a complete Alfred60®T result was 6-6.5h. Out of 587 (320 for Gram-negative and 267 for Gram-positive) susceptibility determinations, 94.73% (95.62% for Gram-negative and 93.64% for Gram positive) showed categorical agreement (CA) with the routine method and this percentage increased to 95.41 (96.56 and 94.02 respectively) after discrepancy analysis. CA for most antimicrobials was above 90% except for daptomycin for Gram-positive (86.4%). There were 0.68% very major errors, 3.23% major errors and 1.36% minor errors. It should be pointed out that very major errors were reported only for cefoxitin in Staphylococci.

Conclusions: The evaluated method Alfred60®T was easy to use, provided rapid and reliable results given in a few hours after BC positivity compared to the 48 h required in the conventional method on isolated colonies. Implementing this technology in routine workflow for critically ill patients allows clinicians to optimize adjusted therapy with potential clinical benefit and impact on the antibiotic stewardship.

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Abstract 5697

In vitro activity of imipenem/relebactam among Gram-negative clinical isolates in two Spanish tertiary hospitals
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Background: According to WHO objectives, carbapenem resistant Enterobacteriaceae, carbapenem resistant Pseudomonas aeruginosa and carbapenem resistant Acinetobacter baumanii, are considered "priority pathogens" to promote research and development of new antimicrobials. Imipenem/relebactam is a new combination which attempts to recover imipenem activity between resistant strains. In our study we tested 192 strains to imipenem and imipenem/relebactam and compared the minimum inhibitory concentrations obtained.

Materials/methods: Imipenem/relebactam was tested against 192 strains previously characterized (49 E.coli imipenem susceptible which carry different extend spectrum betalactamases [ESBL] or AmpC betalactamases, 50 carbapenem resistant Enterobacteriacea by different carbapenemases [19 KPC, 19 OXA-48, 11 VIM and 1 NDM], 50 A.baumanii and 43 imipenem resistant P.aeruginosa [23 of them carbapenemases carrier; 19 VIM and 4 KPC]. Minimum inhibitory concentrations [MIC] were obtained by standard broth microdilution method following the CLSI guidance.

Results: All E.coli imipenem susceptible were also susceptible to imipenem/relebactam, and in 28/49 strains MICs were reduced one to two folds, with a MIC90 of 0.125 mg/L. Focusing on the carbapenem resistant Enterobacteriacea group, the greatest MIC reduction was obtained among KPC carriers (≥ 5 fold in most cases). In 10 of the 19 OXA-48 carrying strains, MIC was reduced to 8 mg/L or below, where 9 of these 10 strains were BLEE carriers too. The 12 strains carrying class B carbapenemase obtained MIC equal to or greater than 16 mg/L. There were no changes in MIC50 and MIC90 for A.baumanii strains. For P.aeruginosa strains without carbapenemases, MIC was reduced 1 to 5 folds, it was reduced 4 folds for the 4 KPC carriers and there was no reduction or one fold reduction for the VIM strains.

Conclusions: In our study imipenem/relebactam showed a great activity against KPC carriers. Activity against OXA-48 strains seemed to be related to the activity against ESBL. The small differences found in the MICs obtained against class B carbapenemases carriers do not cause any improvement. There was also no recovery in the activity against A.baumanii. For P.aeruginosa this combination showed a good activity except to class B carbapenemases carriers.

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Abstract 5702

An audit of community-acquired pneumonia antimicrobial compliance using a mobile audience response system (ARS) care bundle in an Irish hospital

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Background: Hospitalisations with community acquired pneumonia (CAP) are often not managed in accordance with antimicrobial guidelines. The aim of this study was to assess if guideline driven antimicrobial prescribing for CAP can be improved using an intervention bundle. Secondary measures assessed were duration of iv antibiotics and total antibiotic duration, length of stay, mortality, improving uptake of appropriate investigations and documentation of CURB65.

Materials/methods: A retrospective cohort of hospitalised CAP patients from August -September 2018 was compared with a post intervention prospective cohort from May-June 2019. Intervention bundle included a mobile audience response system (ARS) session, promotion of the antimicrobial app, development of a physical card with local guidelines and incorporating CURB65 into the unscheduled admission hospital proforma. Local guidelines are in keeping with BTS CAP guidelines1.

Results: 69 patients were included in the study (37 retrospective, 32 prospective). Overall compliance with local CAP guidelines improved from 21% to 62.5% (p<.001). No difference in initial intravenous antibiotic duration was seen 4.1 vs 4.2 days (p=0.73), total antibiotic duration was significantly shorter in the post intervention group, 9.4 vs 7.3 days (p=.01). No difference in length of stay or mortality was seen between the groups. Documentation of CURB65 improved from 5.6% to 46.9% (p<.01). Uptake of streptococcal urinary antigen improved from 18.9% to 40.6% (p=.024).

Conclusions: A simple cost-effective quality improvement bundle featuring a mobile ARS can significantly increase appropriate antimicrobial prescribing and shorten total length of antibiotics.

<table>
<thead>
<tr>
<th>GUIDELINE</th>
<th>CURB65</th>
<th>amoxicillin</th>
<th>Co-amoxiclav</th>
<th>piperacillin-tazobactam</th>
<th>cefuroxime</th>
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</tr>
</tbody>
</table>

Table 1: Blue boxes represent number of inappropriate prescriptions for a given CURB65 score as per second column. The first column represents correct beta-lactam/lactamase choice (non-pen allergic)


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Comparison of two molecular methods for the diagnosis of sexually-transmitted pathogens

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Background: Rising sexually transmitted infections (STI) is a major concern worldwide. Molecular methods offer rapid and sensitive diagnosis method. The aim of this study is to compare two different PCR assay to detect STI-causing pathogens.

Materials/methods: We performed a prospective observational study between 20/09/2019-15/11/2019 including routine clinical care samples received from patients with suspected STI (urethral, endocervical/vaginal, rectal swabs and urines). Samples were submitted in parallel into two commercially available PCR methods: Allplex™ STI Essential Assay (Seegene) and Alinity m STI Assay (Abbott). Allplex assay requires a previous step of sample pre-treatment and DNA extraction before the amplification step. By contrast, Alinity can analyze directly the samples in the same recipient in which they are collected and includes a combined extraction-amplification method.

Results: Out of 833 samples included, 156 (18.7%) showed positive results, 138 (16.6%) in both assays. Allplex assay detected 139 (16.7%) positive samples and Alinity assay 155 (18.6%) samples, 17 (2.0%) samples were positive only by Alinity assay. By microorganism, Alinity detected 79/79 (100.0%) Chlamydia trachomatis, 29/29 (100.0%) Neisseria gonorrhoeae, 31/31 (100.0%) Mycoplasma genitalium and 16/17 (91.7%) Trichomonas vaginalis and Allplex 74/79 (93.7%), 26/29 (89.7%), 23/31 (74.2%) and 16/17 (91.7%), respectively. Alinity assay detected 5/12 (41.7%) coinfections not detected by Allplex, the cycle threshold (Cts) of the microorganisms detected only by Alinity were all more than 35.0. The average Cts of Alinity assay were 24.4 for C. trachomatis, 24.1 for N. gonorrhoeae, 26.9 for M. genitalium and 17.1 for T. vaginalis, and for Allplex 24.9, 24.8, 30.3 and 22.3, respectively. The differences between average Cts for Alinity and Allplex were significant (p=0.05) for C. trachomatis, M. genitalium and T. vaginalis.

Conclusions:
- Alinity detected 2.0% STI-causing microorganism more than Allplex assay
- Alinity assay detected 100% C. trachomatis and N. gonorrhoeae vs 93.7% and 89.7% for Allplex, differences were remarkable for M. genitalium (100.0% vs 74.2%)
- Alinity had lower average Cts by microorganism than Allplex assay
- Alinity assay is less time-consuming and easier to perform than Allplex

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Diagnostic test characteristics of radiographic keywords in the diagnosis of bacterial pneumonia
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Background: Noninfectious syndromes mimicking bacterial pneumonia lead to unnecessary antibiotic use in hospitalized patients. Reliable tools to aid in ruling out bacterial pneumonia could help stewardship programs de-escalate or discontinue antibiotics. The purpose of this study was to assess the diagnostic test characteristics of the presence or absence of pre-specified keywords in radiology reports of chest imaging studies to rule out pneumonia in patients who were treated for pneumonia.

Materials/methods: Retrospective cohort study of adult hospitalized patients between 2008-2017 with presumptive pneumonia (defined as positive respiratory cultures and continuous receipt of ≥ 5 days of new antibiotics) who achieved clinical cure. All clinical data and imaging were independently reviewed by blinded Infectious Diseases physicians to validate the diagnosis of pneumonia, based on formal IDSA/ATS criteria with the additional requirement that a more likely alternative diagnosis was not suspected. Subjects were grouped into those with pre-specified keywords [infection, pneumonia, consolidation, opacity[ies], opacification, infiltrate[s], airspace] in the radiologist interpretation of chest imaging obtained within 48 hours of pneumonia diagnosis and those without pre-specified keywords present. Select clinical criteria measured at the time of presumptive pneumonia diagnosis were abstracted from the medical record.

Results: Of 705 cases reviewed, 242 cases [34.3%] were deemed to not be pneumonia, and 463 [65.7%] cases were consistent with a diagnosis of pneumonia. Pre-specified keywords in chest imaging were present in 640 (90.8%) cases, including 450 patients [97.2%] with a confirmed diagnosis of pneumonia and 190 [78.5%] patients without pneumonia (p<0.01). The absence of keywords had a sensitivity of 97.2% and a negative predictive value (NPV) of 80.0% for the diagnosis of pneumonia. The absence of keywords, when combined with different clinical criteria, augmented the NPV (Figure 1).

Conclusions: Among patients with positive sputum cultures who received antibiotics for treatment of suspected pneumonia, the absence of specific radiographic keywords was associated with a low likelihood of true pneumonia, particularly when combined with certain clinical criteria. The absence of radiographic keywords can be used to target patients for further assessment by stewardship personnel where de-escalation or discontinuation opportunities are likely.

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Abstract 5705

Direct-acting antivirals-based treatment for HIV/hepatitis C virus co-infected patients: analysis of factors of virological sustained response in a real-life study

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Abstract 5705

Background: Coinfection with HCV is common in HIV seropositive subjects. It is well known that both viruses can alter glucose tolerance, lipids metabolism and renal function. However, data from real-life studies evaluating the virological outcome of regimens based on all-oral direct acting antiviral agents (DAAs). The aim of this study was to identify the factors associated with the viral response of the treatment with DAAs in a cohort of HIV/HCV coinfected patients.

Materials/methods: We conducted a multicenter retrospective cohort study enrolling all HIV/HCV coinfected patients treated with DAAs in one of the nine participating centers [8 in Campania, 1 in Apulia], for which HCV-RNA loads at 12 weeks after EOT were available. The outcome evaluated was the SVR12 rate; the epidemiological, clinical and virological characteristics associated with the viral response were analysed.

Results: During the study period, 243 HCV-RNA-positive PLWHIV treated with DAAs, with a median post-treatment follow-up of 48 weeks [range 12-144] were enrolled. The median age of patients was 52; 77.8% were males; 64.2% were injection drug users. At the enrolment the mean CD4+ cell count was 629.9 (+322.4) and 91.3% of patients had a HCV-RNA load <50 cps/mL; 39.3% were infected with HCV genotype 1a and 32.5% with genotype 3. A cirrhosis was present in 36.6% of subjects; 17 (7.0%), 110 (45%) and 116 (47.7%) were treated with first, second and third generation DAAs, respectively. The SVR12 was registered in 233 (95.9%) patients; no difference in sex and age distribution, risk factors, virological and immunological features, cardiovascular, metabolic, renal or psychiatric comorbidities, stage of liver disease and treatment received was observed between SVR and non-SVR patients.

Conclusions: The treatment with DAAs led to a high SVR12 rate in our cohort of HIV/HCV coinfected subjects, irrespective of epidemiological, clinical or virological characteristics.

All p values >0.05

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CD377, a novel antiviral Fc-conjugate, demonstrates a lower resistance potential than baloxavir and oseltamivir against pandemic influenza A(H1N1)
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Background: AVCs (antiviral Fc-conjugates) developed by Cidara Therapeutics are novel, long-acting immunotherapeutic conjugates of potent antivirals and the Fc domain of human IgG1. CD377 is an AVC development candidate for the prevention and treatment of seasonal influenza, comprising a neuraminidase-targeting small molecule conjugated to IgG1 Fc. CD377 was designed to provide broad-spectrum coverage of influenza A and B, including drug-resistant strains. Herein, the resistance potential of this agent was assessed by in vitro serial passage in comparison to standard of care agents baloxavir and oseltamivir.

Materials/methods: Serial passage was conducted in Madin-Darby canine kidney (MDCK) cells infected at an MOI of 0.01 with A/California/07/09 H1N1 pdm. Selecting agent concentrations were optimized as required for maximum virus inhibition, while maintaining sufficient virus for subsequent passages [CD377 - 4 nM, baloxavir - 4 nM, oseltamivir - 200 nM]. A PBS no-drug control group was also included. Following the addition of drugs, cells were incubated for 24 hours. Next, viral supernatants were collected and used to quantify viral titer by plaque assay. Finally, freshly seeded cells were re-infected in the presence of compounds. The process was repeated for 10 passages.

Results: Over the course of 10 passages, A/California/07/2009 H1N1 pdm did not show any increase in viral titer in the presence of CD377 [Fig. 1]. In contrast, viral titers in the baloxavir and oseltamivir selection groups increased to levels similar to those observed in the PBS control after passages 6 and 8, respectively, indicating reductions in susceptibility.

Figure 1. Viral titers for A/California/07/2009 passaged in MDCK cells with sub-inhibitory concentrations of CD377, baloxavir, or oseltamivir

Conclusions: CD377 demonstrated a low resistance potential as compared to baloxavir and oseltamivir in serial passage with a pandemic H1N1 influenza strain. Follow-up studies on plaque-purified viruses from each passage group will characterize any changes in genotype, phenotype, or fitness. Future serial passage studies will investigate the resistance profile of CD377 against other clinically relevant influenza strain types, such as H3N2 and B.

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Abstract 5709

Analyzing the public health impact of human immunodeficiency virus and tuberculosis co-infections in Brazil

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Background: Tuberculosis (TB) is the biggest cause of death amongst persons living with Human Immunodeficiency Virus (HIV) in the world and the greatest global risk factor for acquiring TB is a prior HIV infection. Brazil is the largest Latin American country and the WHO ranks Brazil amongst the top 30 countries globally with the highest burden from this dual epidemic. The prevalence of TB/HIV is thought to be around 20%. The objective of this review was to show the effects of the HIV/TB co-infection on the public health system of Brazil in terms of both economic and social impact.

Materials/methods: The two main databases used to analyze papers for this review were: Pubmed and Web of Science.

Results: The results of our review showed that patients with a TB/HIV co-infection presented a far greater economic burden to the Brazilian public health system compared to other related conditions. Compared to those with a HIV/AIDS infection, mean total costs were shown to be at least 3 times higher. Reasons for this increased cost included: patients with TB/HIV presenting with more advanced conditions than those with HIV/AIDS and TB/HIV patients being more treated with more expensive medications in general. Various papers also showed that patients with TB tended to have higher have higher rates of lifestyle vulnerability [such as drug and alcohol dependency] compared to sole HIV/AIDS sufferers. Pertinently, patients with well controlled or latent TB/HIV infection had far lower treatment costs compared to other related groups. Frequently mentioned risk factors for developing a HIV/TB included: homelessness, alcohol or drug use, lower socioeconomic or educational status.

Conclusions: The results of this review highlight the great burden the TB/HIV co-infection is placing upon the Brazilian public health system. It shows the need for increased collaborative TB/HIV activities such as more thorough TB and HIV screening programs within Brazil. It also emphasizes the need for prompt TB treatment in HIV/TB sufferers due to associated improved health outcomes for the patient and decreased economic burdens for the public health system in Brazil.

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Abstract 5711

Incidence of ventilator-associated pneumonia in children intubated in paediatric intensive care unit
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Background: Ventilator-associated pneumonia (VAP) is the second most common nosocomial infection diagnosed in mechanically ventilated patients. A great variability exists regarding the incidence of VAP in the pediatric population and previous studies found incidences ranging from 0.6 to 41 episodes per 1000 ventilation-days. In addition to the estimation of VAP incidence, our study is the first to use a survival analysis to study risk factors. We aimed to study VAP incidence in our French pediatric intensive care unit (PICU) and risk factors.

Materials/methods: We performed a single-center retrospective study in the PICU of Grenoble-Alpes university hospital. All patients <18 years admitted to the PICU supported by invasive mechanical ventilation for more than 48 hours between January 2013 and December 2018, were included. Patients with aplasia or bacterial community-acquired pneumonia were excluded. VAP definition of the Centers for Disease Control and prevention was used. A survival analysis adjusted on duration of mechanical ventilation was used to study risk factors of VAP.

Results: Among 1092 mechanically ventilated patients during the study period, 355 patients were included [median age 18 months, interquartile range [IQR]: [2-84], 62% were boys]. A total of 39 children [11%] developed a VAP and among them, 22 children [56%] had a bacteriological confirmation. Overall, the incidence rate of VAP was 15.5 per 1000 ventilation days. Median delay between admission and VAP was 6 days [3-11]. The most performed microbiological sampling was semi-quantitative culture of tracheal suction [n=36, 92%]. The main organism identified were Haemophilus influenzae [7/26] and Staphylococcus aureus [5/26]. The age group 2-6 years was the most at risk of VAP [Hazard Ratio [HR] 2.66, 95%Confidence Interval [CI] 1.26-5.62]. Patients admitted for non-bacteriological respiratory disease were 76% [HR 0.24, 95%CI 0.05-0.99] less likely to have VAP before 15 days of ventilation. Median duration of mechanical ventilation was significantly longer for VAP patients in comparison to patients without VAP [14 vs 5 days].

Conclusions: VAP are common in PICU. Risk factors identified in our study were considered as inherent to the patient but the establishment of a prevention protocol may reduce this high rate.

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Twenty-seven years of chromoblastomycosis in Martinique

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Background: Chromoblastomycosis (CBM) is an endemic but neglected fungal infection that prevails in regions with tropical and subtropical climates. It is caused by a variety of dematiaceous fungi, which gain entry into the skin via traumatic implantation. CBM is prevalent throughout the Caribbean region including Martinique island, where its incidence has never been described.

Materials/methods: We performed an observational retrospective study including all the cases of CBM diagnosed at the University Hospital of Martinique between 1993 and 2019, whose infection was proved by the presence of muriform cells in direct examination of skin smears and the etiologic agent identified by culture.

Results: A total of 19 patients (18 males and 1 female) were enrolled in this study. Cases were distributed throughout Martinique regardless of rainfall intensity (Fig.1). None of them had travelled to another CBM endemic area. The mean age at diagnosis was 71 years. The time elapsed between the onset of symptoms and consultation was highly variable, ranging from 3 months to 40 years. Patients had lesions of mild to moderate severity, localized in exposed parts of the body. Miscellaneous clinical presentations were observed, the most frequent being verrucous or nodular. The most common initial topography was the lower limbs (55%). Fonsecaea pedrosoi was involved in 17 of the 19 cases, while Cladophialaphora carrionii and Fonsecaea monophora were responsible for the remaining two cases, respectively. The various treatments used, whether surgical or by antifungal chemotherapy, never lead to complete healing, but significant improvements were noted for some cases.

Conclusions: This study confirms CBM endemicity in Martinique, where F. pedrosoi seems to be the best adapted species. Although relatively rare, several factors such as slow and insidious evolution, variability in clinical presentation, as well as global ignorance suggest that the burden of CBM remains under-estimated. Moreover, failure of antifungal therapy (mainly due to poor medication adherence) and relapse remain a substantial issue. Improved prevention and medical management and follow-up of the infected patients seems mandatory, in order to avoid complications and the appearance of new cases in the next future.

Figure 1. Distribution of chromoblastomycosis cases in Martinique (1993-2019)

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Impact of applying mucosal barrier injury laboratory-confirmed bloodstream infection criteria in patients with solid tumours and haematologic malignancies

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Background: The Centers for Disease Control (CDC) has defined criteria for Mucosa Barrier Injury Laboratory-Confirmed Bloodstream (MBI-LCBI), excluding from Central Line-Associated Bloodstream Infections (CLABSI) rates the cases whose source is probably the translocation of the gastrointestinal tract. The aim of this study was to evaluate the impact of using the MBI-LCBI criterion on the CLABSI rate in patients with solid tumors and hematologic malignancies.

Materials/methods: Retrospective cohort study at a university cancer hospital. Revised CLABSI from 2015 to 2017, and reclassified as MBI-LCBI and Catheter-Related Bloodstream Infections (CRBSI) according to the criteria of the CDC and the American Society for Infectious Diseases, respectively. Outcomes Evaluated: CLABSI rate considering or not MBI-LCBI, MBI-LCBI rate and proportion of CRBSI among those classified as MBI-LCBI. Rates were compared between patients with solid tumors or hematologic malignancies.

Results: 339 CLABSI were detected in the period, 51 (15.0%) classified as MBI-LCBI, and among the last, 10 (19.6%) met criteria for CRBSI. In patients with solid tumors, the CLABSI rate dropped from 2.67 to 2.60 after MBI-LCBI withdrawal, and none of them was CRBSI. In the population with hematologic malignancy, the rate of CLABSI dropped from 9.61 to 5.57 after removal of the MBI-LCBI, and among these, 22% were CRBSI. In the ICU, in patients with solid tumors, the CLABSI rate dropped from 2.47 to 2.35 after MBI-LCBI removal, and among them, none was CRBSI; In the population with hematologic malignancy, the rate of CLABSI dropped from 34.21 to 26.37 after removal of the MBI-LCBI, and among these, 27% were CRBSI.

Conclusions: The use of MBI-LCBI criteria significantly decreased the rate of CLABSI in individuals with hematologic neoplasia, but not in those with solid tumors, regardless of the hospitalization unit. However, a significant proportion of cases classified as MBI-LCBI were actually CRBSI. Use of the combined criteria can measure the risks associated with greater accuracy.

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**Abstract 5721**

**Molecular epidemiology of methicillin-resistant *Staphylococcus aureus* infections during 7 years in a regional hospital in Israel**

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**Background:** Molecular characterization of Methicillin-resistant *S. aureus* (MRSA) is useful for surveillance studies and infection control decisions. In Israel, several hospital- and community-based studies emphasized the importance of community-associated (CA)-MRSA strains in both settings, although clonal repertoire differs between hospitals and geographic locations. We studied the molecular epidemiology of MRSA infections in a single, regional, medium-sized hospital during 2012-2019.

**Materials/methods:** Healthcare-associated (HcA)-MRSA was defined when isolate was taken >72 hours from admission, or on admission in case the patient had a history of hospitalization or facility residency in the previous year. All other infections were defined as CA. MRSA were determined by the presence of *mecA/C* gene. The presence of LukS/F-PV (PVL toxin) and *SCCmec* type were determined by PCR. *spa* types were assigned by the BioNumerics 7.6.3 software.

**Results:** During 7 years, we analyzed 166 clinical MRSA: 115 (69%) bloodstream, 42 (25%) wounds/abscesses and 9 (5%) anterior nares screening isolates. 145 (87%) isolates were HcA and only 21 (13%) were CA. Common *spa* types (73%) were t002, t032, t008, t001 and t065. 67/145 (46%) were from *spa* types related to *SCCmec*-IV. t032 (EMRSA-15) was CA in only 1 case, while it was the second most common among the HcA isolates. The *lukS/PV* gene was found in 7 isolates, 4 were CA and 4 were bloodstream isolates. Of the HcA isolates, 65 were acquired in our hospital. The dominant hospital *spa* types were t002 (n=23), t032 (n=13) and t001 (n=6). There were no temporal fluctuations of types over the course of time and no association between types and specific wards. 80 isolates were imported from long-term care facilities. There were no differences in the demographics or outcomes of patients with CA- or HcA-MRSA infections. Most isolates (95%) were sensitive to trimethoprim/Sulfamethoxazole, 47% to clindamycin/erythromycin and 60% to mupirocin.

**Conclusions:** The MRSA population in this longitudinal study was stable and consisted mainly of molecular lineages widespread in Europe. The most common MRSA isolates in this cohort, mostly bloodstream infections, were acquired in the healthcare setting. High level mupirocin resistance, within-hospital acquisition, as well as import of new cases are among the challenges and targets for infection control.

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Abstract 5724

**Time to positivity for mycobacterial culture as a measurement of bacillary load in clinical practice**

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**Background:** The bacillary load of Mycobacterium tuberculosis (Mtb) may be estimated in the BACTEC 960 MGIT (MGIT) by the time to positivity (TTP) which is automatically recorded but rarely reported. TTP-analyses are increasingly used in early bactericidal activity (EBA) studies of new drugs. The aim of this study was to evaluate the potential use of including TTP-analysis in clinical practice.

**Materials/methods:** TTP in MGIT was recorded in consecutive clinical isolates from tuberculosis (TB) patients in South-East Sweden during 2016-2018. The shortest TTP registered at diagnosis was compared to smear microscopy and PCR-results as well as to sedimentation rate-levels, chest X-ray and body mass index (BMI). Reproducibility of TTP was analyzed comparing the variability between three individual sputum samples from the same patient. Additionally, a standard curve was developed by comparing TTP to CFU-counts on Middlebrook 7H10 medium. In a subset of patients (n=7), TTP was analyzed repeatedly during the first two months of treatment.

**Results:** Overall, TTP was distributed between 3-31 days (n=51) where 23.5% patients had a TTP within one week, 41% patients between 1-2 weeks, 29.5% between 2-3 weeks and 6% after three weeks. Among high-grade, smear positive patients and those with a strongly positive PCR (Ct<33), 89% and 78% respectively had a TTP of less than one week. Patients with TTP <one week had more extensive lung involvement (>one lung lobe involved) compared to patients with TTP>one week. When three samples were obtained at diagnosis, 82% (29/35) and 60% had TTP levels within ±7 and 2 days respectively. There was a linear correlation between CFU counts and TTP levels where a TTP of one week corresponded to 37250 CFUs. A pilot study showed a steady and significant prolongation of TTP during treatment for patients with drug susceptible TB on first line treatment (median delta TTP: 16 hours/day for week 0-1).

**Conclusions:** In conclusion, we explored the potential use of TTP in routine clinical practice. The data show that TTP is strongly linked to the bacillary load and may be an important surrogate marker for clinical improvement during treatment of use both in routine practice and clinical trials.

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Tricyclic boronates inhibit carbapenemases
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**Background:** The rapid increase of the prevalence of \(\beta\)Lactamases (BLAs) and the emergence of new-variants in carbapenem-resistant bacteria (CRE) menace the antimicrobial effectiveness of last resort carbapenems. It is particularly worrying that carbapenemases that only showed weak activity in the past have evolved to improve their catalytic efficiency. To prevent the detrimental action of carbapenemases in public health, the search of pan \(\beta\)Lactamase inhibitors is fundamental. Cyclic boronates appeared to be one the few compounds that could inhibit several serine-\(\beta\)-lactamases (SBLs) but more interestingly metallo-\(\beta\)-lactamases (MBLs). Meropenemvaborbactam was the first combination of a carbapenem and a boronate based \(\beta\)Lactamase inhibitor. Others, such as VNRX-5133 has proved to have good *in vitro* and *in vivo* properties. However, none of the bicyclic boronates demonstrate to be as potent as avibactam against the clinically relevant class D \(\beta\)Lactamases. Therefore, we have aimed to have a mechanistic insight of the structure-function relationship of novel tricyclic boronate derivatives against SBLs and MBLs carbapenemases.

**Materials/methods:**

**Inhibition assays:** tricyclic boronate (TB1, TB2, TB3) were screened against a panel of SBLs and MBLs. FC5 was used as the reporter substrate.

**Minimal Inhibitory Concentration (MIC):** meropenem and cefepime were tested alone and in combination with TB versus NDM-1 and OXA-48 producing strains (NCTC 13443, NCTC 13442). **Crystallography:** NDM-5 and OXA-10 were crystallized by sitting drop vapor diffusion. Crystals were cryoprotected and diffraction data was collected at Diamond Light Source. The structure was solved by molecular replacement and iterative refinement in PHENIX.

**Results:** TB2 derivative showed to have the widest range of activity in the series, being more effective against the clinically relevant \(\beta\)Lactamases NDM-1, VIM-2, and IMP-1 when compared to Lcaptopril. Structural studies confirm the mode of binding of the boron atom of TB2 which is comparable to the mode of binding observed for VNRX-5133 and NDM-1 and OXA-10. The \(\beta\)Lactamase inhibitory activity of APC-434 tested in bacterial cells, restores meropenem activity in the *Klebsiella pneumoniae* OXA-48 carrier and proves to be at least 3-fold better than vaborbactam.

**Conclusions:** Structural studies and biochemical characterization demonstrate the potential of tricyclic boronates to design pan-\(\beta\)-Lactamase inhibitors.

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**Abstract 5729**

**Investigation of antibiotic susceptibilities, clonal relationships and carbapenems resistance mechanisms of *Serratia marcescens* obtained between 2011 and 2019 in a university hospital**

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**Background:** *Serratia marcescens* can cause an opportunistic infection in several sites, especially in immunocompromised patients. Additionally, *S. marcescens* species may harbor multidrug resistance mechanisms that can complicate treatment decisions. In this study, antibiotic resistance rates, resistance to carbapenems and clonal relationships of carbapenems resistant isolates of *Serratia marcescens* from various clinical specimens of inpatients were investigated.

**Materials/methods:** We investigated 84 *S. marcescens* isolates from various clinical specimens in clinical bacteriology laboratory between 2011-2019. MALDI-TOF MS was used for bacterial identification. Susceptibilities of ceftriaxone, ceftazidime, meropenem, amikacin, gentamicin, tigecycline and ciprofloxacin were studied by microdilution method and the results were evaluated according to EUCAST standards. ATTC Escherichia coli 25922 was used as control isolate. In meropenem resistant *Serratia marcescens* isolates (*n* = 10), KPC, NDM-1, IMP, VIM, SPM, AIM, OXA-48, GES and SME-1 type carbapenemases were investigated by PCR and clonal relationships were evaluated by PFGE method. To investigate the activity of efflux pumps in meropenem resistant *S. marcescens* isolates, MICs of meropenem in the presence of efflux pump inhibitors Phe-Arg β-naphthylamide dihydrochloride (PAβN) (Sigma) or carbonyl-cyanide-m-chlorophenylhydrazone (CCCP) (Sigma) were determined. At least four fold reduction in the presence of CCCP and PAβN compared to MIC determined by microdilution was considered significant for the presence of active pump.

**Results:** The MICs of the 84 isolates to 7 antimicrobial agents are shown in Table 1. Genotyping of β-lactamases revealed that *bla-OXA-48* was presence in only one isolate. A greater than or equal to fourfold decrease in MIC of meropenem when tested in combination with either efflux pump inhibitors PAβN or CCCP, was shown in one and three of the *S. marcescens* isolates, respectively. Eight pulsotypes were detected by PFGE. The number of clusters was determined as three and the number of strains in each cluster varied between 1-3 (Figure-1).

**Conclusions:** In *S. marcescens* isolates, it was observed that the resistance to carbapenems was due to different mechanisms. Meropenem resistant isolates belong to three different clones. Other mechanisms such as porine loss and overexpression of AmpC may be found in isolates whose resistance mechanism can not be determined.

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Abstracts 2020

Abstract 5730

Epidemiological study of main enteropathogens causing infectious gastroenteritis in a Madrid tertiary hospital

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Background: acute infectious gastroenteritis (GE) is one of the most chief complaints in our health system. The aim of this study was to characterise the epidemiological distribution and prevalence of main enteropathogens causing GE in our area and to analyse the possible association between these agents with sex, age and its seasonality in order to gain insight about our risk population and infectious patterns.

Materials/methods: a retrospective cohort study with all positive stool culture analysed between April 2018 and September 2019 in a tertiary hospital was performed. Positive samples were defined as the isolation of species from the genus Aeromonas, Campylobacter, Salmonella, Shigella, Yersinia and Vibrio. Microbiological data was recovered and statistically analysed by means of the Chi Square distribution.

Results: during the study period, enteropathogens were detected in 282 stool cultures (6.35% of positivity). Median age was 46 years and 66% were male. Isolated species were Campylobacter jejuni (108) and coli (22), Salmonella enterica group (68), Aeromonas spp. (40), Yersinia spp. (25), Shigella spp (17) and Vibrio parahaemolyticus (2). There was a statistically significant relationship between age and the isolation of Aeromonas [which was mainly isolated in adults over 50 years old, p<0.001], and Campylobacter, Salmonella, Yersinia and Shigella [which were most isolated in patients under 50 years old, p<0.0001]. Moreover, a statistically significant association was found between sex and the isolation of Campylobacter [which was more prevalent among men, p<0.05] and Shigella [which was more prevalent among women, p<0.05]. No statistically significant differences were found about the rest of enteropathogens with age or sex. Furthermore, seasonal variations in the isolation of three of these enteropathogens were observed: Campylobacter was most prevalent during the summer-spring period, Salmonella during the summer and Shigella during the autumn-winter period (p<0.01).

Conclusions: According to these results, the isolation of the main enteropathogens is strongly associated with sex, age and seasonality, in line with previous reports. The sex distribution of Campylobacter in men and Shigella in women requires further studies.

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Abstract 5731

Serodiagnosis of Lyme disease: cheese and chalk or peas in a pod?
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Background: Serological testing for Lyme disease (LD) varies across the world. Recently, United States Food and Drug Administration (FDA) cleared several serologic assays with new indications for use, allowing for an EIA rather than western immunoblot assay as the second test in a LD testing algorithm. Current UK NICE guidelines (2018) have raised a question mark over the ELISA based screening tests for LD. In Bristol (South-West England), we have some of the highest rates of Lyme serology positivity in the UK. However, the demographics of LD across the region are not clear, and the sensitivity and specificity of local screening tests are not well established. We aimed to look at the epidemiology of our local Lyme ELISA results as compared to the National reference laboratory.

Materials/methods: We recorded basic demographics of patients tested, then evaluated our local Diasorin Liaison XL® analyser ELISA IgM (OspC and VlsE) and IgG (VlsE only) assay for LD in terms of positivity; compared with the National reference laboratory’s screening C6EIA and confirmatory Immunoblots for the whole of 2017. In general, any positive local result for IgG or IgM was sent to the reference laboratory. Full analysis of the epidemiology of test results was performed.

Results: A total of 3131 tests were performed on 2803 patients by our local EIA. 74% of these were from primary care. Median age was 48.5 years (range 0.6 – 95) and 57% were from females. Our ELISA showed 93.4%, 2.1% and 4.5%; 89.8%, 1.8% and 8.4% respectively for negative, equivocal and positive against IgG and IgM. Comparative results with the reference C6EIA and immunoblots are shown below (Figure 1). Of the 328 repeat tests performed, 22(6.7%) and 37(11.3%) seroconverted for IgG and IgM respectively during 2017.

Conclusions: Local epidemiology of Lyme disease is complex in South-West England. We have a reasonably high positivity rate on screening tests, especially IgM. A significant number of positive IgM and IgG results locally were not ultimately confirmed by the reference lab, leading to some difficulty in patient management. Scientifically robust tests/algorithms are urgently needed for the diagnosis of LD.

Figure 1.

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Ceftriaxone penetration into epithelial lining fluid: are dosing regimens sufficient for severe community-acquired pneumonia?

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Abstract third-party references: FIS [PI15/00506], ISCIII, Madrid, Spain, SEPAR [064/2015 and 086/2018], Madrid, Spain, BITRECS, IDIBAPS, Barcelona, Spain, La Marató Foundation of TV3, Barcelona, Spain

Background: Ceftriaxone (CRO), a third-generation cephalosporin with a broad-spectrum, is commonly administered for the empirical or pathogen-directed therapy of numerous infections, such as community-acquired pneumonia (CAP). Despite being a frequently used antibiotic, no data are available on CRO epithelial lining fluid (ELF) penetration.

Materials/methods: In six pigs (33.2±2.2 kg) with severe pneumococcal pneumonia, pharmacokinetics of CRO were assessed. Animals were allocated to intravenously received: 50 mg/kg, 100 mg/kg, or 150 mg/kg of CRO as 1-h infusion. Sequentially, plasma and bronchoalveolar lavage (BAL) fluids were collected to quantify CRO concentrations at 1, 2, 4, 6, 8, 12, and 24h after the dose in each pig. Protein binding was assessed in duplicate at 1 and 2h. Urea correction was used to calculate ELF values. CRO plasma and ELF concentrations were fitted to a two-compartment model. A 5,000 subject Monte Carlo simulation was performed for each dose to define the ELF penetration [area under the curve in ELF (AUCELF) / free AUCplasma] and the percentage of free time above the minimum inhibitory concentration (fT>MIC) for MIC of 2 mg/L.

Results: 41 plasma and 31 BAL samples were fitted adequately by the model. The model parameters (mean ± standard deviation) for CRO pharmacokinetics were volume of central compartment, 9.54±4.36 L; clearance, 4.47±1.36 L/h; and volume of peripheral compartment, 34.77±18.16 L. The resulting simulated free AUC0-24h and %fT>MIC of 50 mg/kg dose achieved similar human exposures in plasma (2g q24h)1. The median [interquartile range] ELF AUC0-24h was 36.8 [30.6-45.1], 73.5 [62.2-90.2], 111.3 [91.8-135.3] mg·h/L for 50, 100 and 150 mg/kg doses, respectively. The overall penetration ratio was 8.4 [7.8-9.7] %. For MIC of 2 mg/L, 50, 100 and 150 mg/kg doses achieved 25.8 [21.3-31.7], 37.1 [29.6-46.3], and 43.3 [34.2-54.2] % ELF fT>MIC, respectively.

Conclusions: Our data indicate that CRO penetration into ELF achieved 8.4% in a swine model. At MIC of 2 mg/L, the percentage ELF fT>MIC ranged from 25.8 to 43.3, depending on the dose. Future studies assessing the bactericidal activity of these regimens against common pathogens of severe CAP are needed.


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Abstract 5734

The effects of antibiotic cycling and mixing on acquisition of antibiotic-resistant bacteria in the intensive care unit: a post-hoc analysis of a prospective cluster-randomised crossover study


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Background: Antibiotics exert selective pressure for antibiotic resistant bacteria (ARB). Cyclic rotation of empiric antibiotic treatment strategies diversifies antibiotic selective pressure, but different strategies [antibiotic cycling and mixing] failed to change unit-wide prevalence of ARB carriage in an international cluster-randomized crossover study (Lancet ID 2018, PMID: 29396000). However, unit-wide and individual risks can differ due to what is called an "ecological fallacy". The aim of this post-hoc analysis was to assess carriage acquisition risks of Gram-negative ARB in individual patients between cycling and mixing treatment strategies.

Materials/methods: This was a nested-cohort in a cluster-randomized crossover study with 8,267 inclusions from 7 ICUs in 5 countries. The study compared two 9-month antibiotic rotation strategies: cycling (changing first-line empiric therapy for Gram-negative bacteria every other 6-weeks), to mixing (change of antibiotic type every other empiric antibiotic course). Rotated antibiotics were 3rd or 4th generation cephalosporins, piperacillin-tazobactam and carbapenems in randomized order.

For this analysis ARB was defined as Enterobacterales species with reduced susceptibility to: 3rd- or 4th generation cephalosporins or piperacillin-tazobactam, and Acinetobacter species and Pseudomonas aeruginosa with reduced susceptibility for piperacillin-tazobactam or carbapenems. Patients were selected with >1 clinical culture, of which the first had to be negative for ARB and without carriage with ARB in the first 2 days of admission. Primary endpoint was acquisition of ARB. Interventions were compared using bivariate testing and mixed effects logistic regression modelling.

Results: For this analysis 3,944 (48%) admissions were eligible with 21,662 clinical cultures. Incidences of acquisition with ARB were 3.8% (n=137) and 3.5% (n=145) during cycling and mixing, respectively (p-value 0.56), yielding an adjusted odds ratios (aOR) 0.98 (95% CI 0.74 till 1.29) for acquisition during mixing.

Conclusions: Individual patients’ risk of acquiring infection or carriage with Gram-negative ARB was comparable during cycling and mixing. Adjusted analysis, showed no difference between interventions. These findings substantiate the lack of effect of cycling and mixing on the epidemiology of Gram-negative ARB in ICU.

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Lineage CC398 among methicillin-susceptible and methicillin-resistant *Staphylococcus aureus* isolates of blood cultures. A multi-centre study in Spanish hospitals

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Background: *Staphylococcus aureus* (SA) of lineage CC398 is causing human infections in Europe. In Spain, the prevalence of Livestock-Associated (LA) methicillin-resistant SA (MRSA)-CC398 at hospital level was closely related to pig-farming density, tetracycline-resistance (TET\textsuperscript{R}) being a phenotypic marker of this clone. Methicillin-susceptible SA (MSSA)-CC398 was reported as an emerging cause of invasive infections, mainly in France; however, data and epidemiological characteristics are still scarce. Our work aimed to determine the prevalence of MSSA-CC398 and LA-MRSA-CC398 among blood culture SA isolated from patients in Spanish hospitals located in regions with different pig-farming density and to analyse the antimicrobial resistance pheno/genotype, the virulence factors and the molecular characteristics of CC398 isolates.

Materials/methods: A total of 951 SA isolates was recovered from patients’ blood cultures during 2018-2019 in 17 Spanish hospitals located in regions with different pig-farming densities \([\text{in } 10^3 \text{ pigs/km}^2]\) \(\text{[Low Pig Density: 0-10; Medium Pig Density: 11-60; High Pig Density (HPD): } >160]\). The isolates were subjected to antimicrobial susceptibility test: MSSA (\(n=706\)) and MRSA (\(n=245; 18 \text{TET}^{\text{R}}-\text{MRSA}\)). All MSSA and TET\textsuperscript{R}-MRSA isolates were further characterized. CC398 lineage identification, spa\textsuperscript{-}typing, antimicrobial resistance genes and human immune evasion cluster (IEC) genes detection were performed by PCR/sequencing. Moreover, \textit{eta}, \textit{etb} and \textit{lukF/lukS-PV} genes were screened by PCR.

Results: The prevalence of MSSA-CC398 was 5.2% respect to MSSA and 3.9% to SA \((n=37\text{ isolates})\). The prevalence of MRSA-CC398 was 0.4% respect to SA and 22.2% to TET\textsuperscript{R}-MRSA \((n=4\text{ isolates})\). Among MSSA-CC398, six spa-types were recorded (predominant: t571, 43.2% and t1451, 35.1%). All, but three MSSA-CC398 isolates \((t011\text{ and } t1451)\), were IEC-negative. Resistance to erythromycin/clindamycin-inducible, mediated by \textit{erm}(T) gene, was detected in 72.9% of MSSA-CC398. Three isolates harboured the \textit{eta} gene. No correlation of MSSA-CC398 and pig density was evidenced. On the other hand, all 4 MRSA-CC398 isolates were detected in HPD regions, and were \textit{spa-t011} or \textit{t034}, and IEC-negative.

Conclusions: LA-MRSA-CC398, infrequent in blood culture samples, is related to HPD regions. On the other hand, MSSA-CC398 \((\text{mostly } t571\text{ and } t1451)\), is not associated with HPD and seems to be an emerging human-adapted clone \((5.2\%/\text{MSSA})\). The \textit{erm}(T) gene, associated with erythromycin/clindamycin-inducible resistance, could be a MSSA-CC398 marker.

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Abstract 5738

Prevalence of antibiotic resistance in skin infections among migrants compared to Danish-born patients

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Background: Skin infections are one of the most common infections among patients in primary and secondary care. Previous studies have documented a high prevalence of MRSA and multi-resistant gram-negative bacteria infections among refugees and asylum seekers admitted to hospital care. However, little is known about pathogen causes of skin infections and resistance patterns among migrants, in comparisons to Danish-born patients. The aim of the study is to address this gap in the literature.

Materials/methods: The study is a register-based cohort study building on a cohort of more than 80,000 migrants (≥ 18 years) and a Danish comparison group. Migrants, who obtained residence in Denmark from 1.1.1993 – 31.12.2015, were included. The migrant cohort and the comparison group were merged with clinical data extracted through a microbiology database covering the hospitals in the Copenhagen Capital Region. All patients with positive skin cultures from 1.1.2000 – 31.12.2016 were identified. Descriptive analyses and multivariate regression analysis was used when comparing migrants and Danish-born regarding differences in resistance patterns.

Results: Our dataset compromises 39,589 individuals, respectively 34,865 Danish-born and 4,724 migrants, with positive first skin swab samples. Migrants were further categorized as refugees (n=1,712) or family reunified migrants (n=3,012). Staphylococcus aureus was the most prevalent pathogen for skin infections found in both groups; constituting 58.9 % among migrants and 63.7 % among Danish-born individuals. Yet, fewer refugees (OR 0·87, 95% CI: 0·78-0·96) and family-reunified patients (OR 0·80, 95% CI: 0·74-0·86) had infections due to Staphylococcus aureus compared to Danish-born individuals. Significantly more refugees (OR 1·56, 95% CI: 1·34-1·82) and family-reunited migrant patients (OR 1·50, 95% CI: 1·33-1·69) compared to Danish-born patients had gram-negative bacteria infections. Especially Pseudomonas aeruginosa (OR 1·35, 95% CI: 1·16-1·54) were more prevalent among migrants. The regression analysis has been adjusted for age, sex, socioeconomic status and co-morbidities. The analyses for antibiotic susceptibility will follow and is currently preliminary.

Conclusions: In order to prevent the increase of antibiotic resistance among patients with skin infections, it is important to identify persons at increased risk. Our finding can contribute to developing guidelines to improve future treatment and prevention of antibiotic resistance in patients.

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Abstract 5740

Measurement of influenza antibodies in a cohort of vaccinated patients admitted to a cardiac intensive care unit: are they clinically relevant?


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Background: As part of a prospective study that we are carrying out to determine the usefulness of systematic influenza screening in patients who require admission to a Cardiac intensive care unit (C-ICU), we decided to assess whether the presence of antibodies against influenza could be related to the risk of having a flu episode during C-ICU admission or to its severity.

Materials/methods: Multicentric (5 centres), prospective cohort, including Flu vaccinated patients admitted to a C-ICU during the last two Flu seasons. Influenza was diagnosed using Xpert® Flu/RSV assay. Serum IgG screening against Flu A and Flu B was performed by a chemiluminescence technique (VIRCLIA/Vircell®). In case of positivity, IgG titres were determined by indirect immunofluorescence (Vircell®). Clinical data were registered.

Results: 526 patients were admitted to the 5 coronary ICUs during the last two influenza seasons. Overall, 235 (44.7%) had been vaccinated, from which 179 agreed to participate in the study. Influenza PCR was positive in 14/179 (7.8%) recruited vaccinated patients (11 Flu A and 3 Flu B). A positive IgG against influenza was only detected on admission in 92 patients (51.4%) (87 for Flu A, 75 for Flu B and 74 for both). The distribution of IgG titres were as follows: ≤128: 16 (17.4%), 256: 41 (44.6%), 512: 35 (38.0%), 1024: 32 (34.8%), ≥2048: 22 (23.9%). The titres were higher for Flu B than for Flu A (IgG ≥2048: 27.8% vs 2.8%). Conditions related to non-production of influenza antibodies despite vaccination were: transplantation (6.9% vs 0%, p=0.01) and immunosuppression (9.2% vs 2.3%, p=0.05). The presence of antibodies did not correlate with whether influenza developed during the stay in the C-ICU (5/92-5.5% in patients with antibodies vs 8/87-9.2% without antibodies), nor with its severity, nor with the rate of associated complications.

Conclusions: Only half of the influenza vaccinated patients admitted to a C-ICU in different hospitals during the last two Flu seasons developed antibodies. No antibodies production was mostly related to transplant and immunosuppressed patients. No correlation was found between a specific titre and the presence of influenza, its severity or related complications.

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Abstract 5741

A cross-sectional survey of the perceived workload of UK infection specialists related to Lyme disease

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Background: Anecdotally, there is a perception from UK infection specialists that they are predominantly consulted on Lyme disease (LD) in relation to patients with long-standing, non-specific symptoms. However, no formal description of this perception exists. The project’s aim was to describe UK infection specialists’ perceptions in relation to consultations concerning LD.

Materials/methods: An electronic cross-sectional survey was distributed to members of the British Infection Association’s ‘e-list’. This is an open forum for infection clinicians. Respondents answered questions relating to demographics, and LD-related queries received. This included questions on the format their consultations took, patient’s symptoms, number of consultations per year, and confidence in dealing with these consultations.

Results: 82 specialists responded to at least one survey question. The most common grade was consultant (68/79, 86%), with remaining respondents at specialty-trainee level. South-West England (24/80, 30%) and North England (20/80, 25%) regions predominated. The other endemic areas in the UK - South-East England and Scotland - made up 15% and 5% of respondents, respectively. Phone advice (65% 146/226) was the most common interaction, involving discussions around diagnostic testing and management for confirmed LD. In relation to how patients presented, non-specific long-standing symptoms, or asymptomatic tick-bites were most common. In relation to numbers of consultations per year, proportions were relatively evenly split between those for possible early LD, and those relating to long-standing symptoms. Respondents were more confident in dealing with queries relating to possible early LD [highest proportion - 32% (25/79) graded their confidence as 9 out of 10], than those relating to long-standing symptoms [highest proportion – 24% (19/79) graded their confidence as 5 out of 10].

Conclusions: The management of typical confirmed Lyme borreliosis was not perceived as a problem. In contrast to anecdotal perceptions, UK infection specialists’ workload in relation to LD appears to be relatively evenly split between queries relating to early possible LD, and those relating to long-standing symptoms. However, they were more confident in dealing with the former, highlighting an area to target in future UK LD-related training and education. Further guidance and research around long-standing medically-unexplained symptoms and any relationship to borreliosis would be helpful.

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Profile of neurological manifestations related to varicella zoster virus reactivation

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Background: Varicella-zoster virus (VZV) is neurotropic. In about 20% of patients with an history of VZV primary infection, VZV reactivates later in life producing herpes zoster with potential neurological manifestations. Our aim was to describe neurological complications related to VZV reactivation.

Materials/methods: All patients from the Toulouse University Hospital between 2010 and 2019 with CNS manifestations and a positive PCR for VZV in the CSF were analysed. Patients with primary VZV infection were excluded. Risk factors for severe manifestations and death were investigated by uni- and multivariate analyses.

Results: 55 patients with CNS manifestations related to VZV reactivation were included. Mean age was 50.5 ± 20.5 years, 21/55 (38 %) were immunocompromised, 35/55 (65%) displayed shingles. None were vaccinated against shingles. CSF analysis showed 253 ± 200 leucocytes/mm³, 1.36 ± 0.7 g/L of proteins, and normal glucose level. 28/55 (51%) had meningitis while 29/55 (49%) had meningoencephalitis. Patients with meningoencephalitis were significantly older (62.9 ± 23 years) than those with meningitis (38.5 ± 22 years, p<0.001), and had lower CSF pleiocytosis (167 ± 183 versus 340 ± 339 leucocytes/mm³, p=0.049) while proportion of patients having zoster, trigeminal zoster, being immunocompromised, and biochemical CSF profile, did not differ between the two groups. All received acyclovir at a mean dose of 30 ± 5 mg/kg/day for a mean duration of 21 ± 7 days. Four patients died, all in the meningoencephalitis group, including 2 immunocompromised patients and 2 elderly patients. Of note, 6 patients in the meningoencephalitis group did not display CSF pleiocytosis, including 4 immunocompromised patients and 2 elderly patients, leading to delayed acyclovir initiation that may have participate to death in 1 patient and severe neurological sequelae's in 2. Within 12 months after the VZV reactivation, 1 patient relapsed from VZV infection and 2 developed strokes related to post-VZV cerebral vasculitis requiring steroids.

Conclusions: The burden of neurological complications related to VZV reactivation among elderly and immunocompromised patients is significant. In those populations, the absence of CSF pleiocytosis doesn’t exclude the diagnosis. The recombinant zoster vaccine may help to reduce in the future this burden.

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Prevalence of infections in the risk for infection in immunosuppression outpatient consultation: a retrospective analysis between 2014-2018

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Background: With the growing usage of immunosuppressive therapies, clinicians face the challenge of having to prevent/treat infections in the immunosuppressed population. It is important to study which factors are associated with infections in order to define strategies to minimize their impact. The aim of this study was to identify types and risk factors associated with infections affecting patients referred to the risk for infection in immunosuppressive/immunomodulatory therapies outpatient consultation, which is targeted for patients with autoimmune diseases, cancer or transplanted hosts.

Materials/methods: A retrospective analysis was conducted which included patients followed in our risk for infection in immunosuppression/immunomodulatory outpatient consultation between May 2014 and December 2018. Data was collected regarding epidemiologic, clinical and therapeutic information. Infectious events were only considered in the analysis if they occurred between the diagnosis of the underlying disease and December 2018. Statistical analysis was performed using IBM SPSS.

Results: 758 patients were included, mostly female (51%). 94% were referred to this consultation being diagnosed with an autoimmune/inflammatory disease and 52% had severe immunosuppression at first consultation. 283 infectious events were registered in 182 patients (24%; n=758): 42 (14.8%) were considered opportunistic and 241 (85.2%) were non-opportunistic. 60 (8%) patients had more than one infectious event and 17 (3%) had three or more events. The most prevalent aetiology was bacterial (65,3%). The most common non-opportunistic infections were urinary tract infections (52 episodes, accounting for 21.6%) and upper respiratory infections (31 episodes, accounting for 12.9%). 24% of the opportunistic infections were caused by mycobacterium tuberculosis and 17% were cytomegalovirus reactivations. TNF-alfa inhibitors were associated only with the occurrence of opportunistic infections (p < 0,05). There was no association between corticotherapy and the occurrence of infection (p>0,05). Age (OR 1,153), systemic lupus erythematosus (OR 3,403) and being transplanted (OR 9,184) were independent factors associated with the occurrence of opportunistic infections (p < 0,05).

Conclusions: In our population, age and the underlying disease were considered relevant risk factors for the occurrence of infection, as described in the literature. Despite what would be expected, corticotherapy alone or in association was not associated with the occurrence of an infectious event.

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Abstract 5746

Emergence and spread of plasmid carrying blaIMP and mcr-9 in Enterobacteriaceae isolated from hospitalised patients in West London from 2016 to 2019

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Background: The emergence of carbapenemase-producing Enterobacteriaceae (CPE) infections drives the use of colistin, with colistin resistance a major concern for public health systems worldwide. The plasmid-located mcr-9 was first reported in May 2019 with subsequent studies confirming the co-harboring of beta-lactamase (bla) genes and mcr-9 from hospitalised patients. Here, we describe the genomic epidemiology of blaIMP and mcr-9 CPE from a diagnostic laboratory.

Materials/methods: Loop-mediated isothermal amplification was used to examine the prevalence of mcr-9 amongst 47 blaIMP CPE isolates circulating between 2016-2019 in a London acute hospital group. Colistin susceptibility testing was performed by broth microdilution (Micronaut) according to EUCAST guidelines and we also adapted the MALDIxin test for phenotypic resistance to colistin. These isolates were then characterized by WGS (Illumina NextSeq 500). An in-house bioinformatic pipeline was developed to improve the resolution in plasmid phylogeny using long-read sequences (MinION) as reference plasmids.

Results: WGS confirmed blaIMP in 47 CPE isolates, Enterobacter cloacae was the most common species (n=18) followed by Klebsiella pneumoniae (n=9). Four isolates were from clinical samples (a skin biopsy, 2 urines and a nasopharyngeal aspirate), the rest screening isolates. 40 out of 47 blaIMP carrying CPE isolates harboured mcr-9 and all of these were co-located on an IncHI2 plasmid. 11 of the blaIMP isolates were non-susceptible to colistin (MIC 2 to >64). WGS analysis revealed that 10 co-harboured blaIMP and mcr-9, and, of these, 4 had novel chromosomal point mutations at pmrA, pmrB, PhoP or PhoQ, which are associated with colistin non-susceptibility. 5 of the isolates without chromosomal point mutations (all with colistin MIC 2) were susceptible on Micronaut re-testing.

Conclusions: 85% of the blaIMP CPE isolates in this study encoded for the recently described mcr-9 gene. Genomic analysis found that the two genes were co-located on IncHI2 plasmid. However, only 15% of mcr-9 carrying isolates were consistently phenotypically resistant to colistin, highlighting phenotypic detection difficulties and questions regarding the gene’s impact on resistance. This work shows that WGS can be used to detect plasmid spread in real-time, to help direct hospital resources and focus interventions to mitigate spread.

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Abstract 5751

**Prospective evaluation of septic shock patients in a tertiary care educational university hospital: a series of 739 cases**

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**Background:** Herein, we aimed to evaluate the septic shock (SS) cases in terms of mortality and affecting variables for outcomes in a tertiary-care educational university hospital.

**Materials/methods:** Patients who had SS (sepsis+hypotension+adrenergic agent) and consulted by Infectious Diseases consultants between December 2013 and October 2019 in our center were followed up prospectively. Arterial lactate level of >2 mg/dL criterion was added as an including criteria for SS according to 3rd International Sepsis and Septic Shock Consensus Statement after 23rd Feb 2016. Statistical analysis was performed via Chi square test and a p value <0.05 was considered significant.

**Results:** There were a total of 739 patients (mean age 65.55 ± 15.16 years and 42.89% female). 393 (53.17%) patients in community-acquired (CASS), 346 (46.82%) patients in nosocomial SS (NSS-developed after 48-72 h of hospitalization) group fulfilled the study criteria. Mean CRP, leukocyte count and procalcitonin levels were 17.35 ± 12.23 mg/dl, 16806 ± 22102/mm³ and 24.81 ± 33.74 µg/l, respectively. Arterial lactate level was available in 634 cases (mean:5.44 ± 4.56 mg/dl). The most common infection sites were pneumonia [n:401] followed by intraabdominal infection [n:188] and urinary tract infection [n:174]. Microbiological etiology was elucidated in 338 cases. The most common pathogens were 101 E.coli (76 ESBL+), 66 Klebsiella spp. (42 carbapenem-resistant), 65 yeasts and 38 Acinetobacter spp (35 carbapenem-resistant). In 115 out of 338 cases, >1 pathogen were isolated. Mortality on day 30 was 66,98% (495/739) and significantly higher (144/188-76.5% vs 351/551 - 63.7%, p=0.0016) in the intraabdominal infection SS subgroup vs others. Mortality was lower in SS with elucidated microbiological etiology [176/338-52% vs 319/401-79.5%] (p<0.0001). Among 236 patients qSOFA score was equal to 3 points and mortality rate at day 30 was significantly higher than qSOFA 1 or 2 [p:0.00001] (185/236-78,3 (qsofa3) vs 235/366-64,2% (qsofa2) vs 75/137-54,7% (qsofa1). One month mortality was 65,3% [257/393] in CASS, 68,7% [238/346] NSS (p:0.347).

**Conclusions:** SS patients have different properties in terms of infection source and it seems to be possible that qSOFA score >2 for sepsis screening seems to define the cases associated with poor outcome. Determining the etiology is important in terms of survival.

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Abstract 5753

An eight years-long experience of Nocardia spp. infection in Italy: does immunosuppression matter?

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Background: Nocardia spp. have always been considered a pathogen of the immunocompromised patient. Recently, evidences have highlighted its role as pathogen also in the immunocompetent subject. We reviewed all the cases of Nocardia spp. infections in our center to assess the role of immunosuppression in the disease.

Materials/methods: We retrospectively collected clinical and microbiological data of all the patients with a diagnosis of nocardiosis hospitalized at the IRCCS San Matteo Hospital Foundation of Pavia, Northern Italy, between 01/01/2012 and 30/09/2019. Patients were divided among three groups: typical immunocompromised, atypical immunocompromised and immunocompetent.

Results: Overall, we identified 53 patients with an infection caused by Nocardia spp. The median age at diagnosis was 66.7 years and men were the majority (28, 52.8%). Thirty-two patients (60.4%) were immunocompromised: 17 (53.2%) typical and 15 (46.8%) atypical immunocompromised. The two most common conditions associated with the infection were chronic lung disease (41.5%) and high dosage of immunosuppressive drugs (33.9%). The lung was the most common site of infection, being involved in 47 patients (88.8%). Among the 5 different Nocardia species identified in 27 patients, Nocardia abscessus (16, 59.2%) was the most frequently isolated, followed by Nocardia farcinica (6, 22.2%).

Conclusions: In our series the most frequent risk factor was chronic lung disease. Less than half of the patients had classic immunosuppressive risk factors. A remarkable prevalence of nocardiosis in immunocompetent and atypical immunosuppressed patients was observed, thereby stressing the importance of always suspecting this infection particularly in the presence of known chronic pulmonary disease.

<table>
<thead>
<tr>
<th>Species</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nocardia abscessus</td>
<td>16</td>
<td>59.2</td>
</tr>
<tr>
<td>Nocardia farcinica</td>
<td>6</td>
<td>22.2</td>
</tr>
<tr>
<td>Nocardia wallacei</td>
<td>1</td>
<td>3.7</td>
</tr>
<tr>
<td>Nocardia brasiliensis</td>
<td>1</td>
<td>3.7</td>
</tr>
<tr>
<td>Nocardia nova</td>
<td>1</td>
<td>3.7</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>27</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 1 Microbiological species of Nocardia identified with relative frequencies (n=27) and Antimicrobial susceptibilities of the isolated Nocardia spp. [Number of sensitive specimens/total number of tested specimens] [TMP/SMX: Trimethoprim/sulfamethoxazole].

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Abstract 5756

**Independent risk factors associated to inappropriate antibiotic prescription in the emergency department**

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**Abstract third-party references:** On behalf of the Infectious Disease Group of the Emergency Medicine Spanish Society

**Background:** inappropriate antibiotic treatment is frequent in the Emergency Departments (ED) and it could be associated with an increase in the mortality in shock septic patients, or with an increase of the cost in non-severe patients. The aim of this study was to describe the individual risk factors associated with inappropriate antibiotic treatment in the ED.

**Materials/methods:** national, retrospective cohort study including all patients attended for an infectious disease in 54 Spanish ED during 2017, in whom a microbiological isolation was available from a culture obtained during their attention in the ED. Demographic, clinical, type of bacterial isolation and first treatment prescribed in the ED were collected. A multivariable analysis was done to recognise the independent risk factors associated with inappropriate antibiotic prescription in the ED.

**Results:** during the study period, 5,460 bacteria were isolated from samples obtained in the ED. The mean age of patients was 70.5 years (standard deviation [SD] 18.3), and 2,846 (52.1%) were males. Patients with inappropriate treatment were 1,082 (19.8%). Regarding mortality, 507 (9.3%) patients died, 330 (7.9%) in the group of appropriate treatment and 147 (13.6%) in patients with inappropriate antibiotic treatment (p<0.001). The independent risk factors associated with inappropriate treatment have been described in the Table 1.

**Conclusions:** one in five patients had inappropriate treatment in the ED. Several factors has been identify as independent associated factors.

**Table 1. Multivariate analysis to predict inappropriate treatment**

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>OR (CI 95%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>1.200</td>
<td>1.001-1.439</td>
<td>0.049</td>
</tr>
<tr>
<td>Hemiplegia</td>
<td>1.742</td>
<td>1.086-2.793</td>
<td>0.021</td>
</tr>
<tr>
<td>Moderate to severe chronic kidney disease</td>
<td>1.247</td>
<td>1.021 – 1.522</td>
<td>0.031</td>
</tr>
<tr>
<td>Indwelling urinary catheter</td>
<td>1.986</td>
<td>1.274 – 3.096</td>
<td>0.002</td>
</tr>
<tr>
<td>Residence in a long term centre</td>
<td>1.934</td>
<td>1.561 – 2.397</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Colonisation by ESBL-producing Enterobacteriaceae</td>
<td>1.547</td>
<td>1.042 – 2.294</td>
<td>0.030</td>
</tr>
<tr>
<td>Antibiotic treatment in the previous week</td>
<td>1.373</td>
<td>1.116 – 1.689</td>
<td>0.003</td>
</tr>
<tr>
<td>Antibiotic treatment in the previous 3 months</td>
<td>1.347</td>
<td>1.132 – 1.603</td>
<td>0.001</td>
</tr>
</tbody>
</table>

OR: odds ratio; CI: confidence interval; ESBL: extended spectrum betalactamases

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Abstracts 2020

Abstract 5758

**CREATE: Carbapenem-Resistant Enterobacteriaceae: Animal Testing and Epidemiology. A plan for veterinary medicine**

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**Background:** The emergence of carbapenem resistant *Enterobacteriaceae* (CRE) in companion animal veterinary medicine was inevitable – and yet we are completely unprepared. In April 2019, passive surveillance identified the blaNDM-5 gene in a carbapenem-resistant *E. coli* isolated from a dog at a veterinary teaching hospital (VTH) in Philadelphia, USA. A retrospective review of hospital records showed, that from July 2018 through June 2019, CR-*E. coli* was isolated from 15 animals (14 dogs, 1 cat). The outbreak response showed that: there were no validated microbiology methods for the detection of colonized or infected animals; no veterinary specific infection prevention recommendations on how to deal with CRE colonized, or infected, animals in veterinary healthcare facilities and there were no antimicrobial stewardship guidelines for the treatment of animals with CRE.

**Materials/methods:** A crisis management team (CMT) was formed. Representatives from the VTH leadership, the Diagnostic Laboratory, the Infectious Disease Committee (IDC) and the Antimicrobial Stewardship Committee (ASC) addressed Infection Prevention (IP), Facilities and stewardship issues. A literature review was performed to determine if a sensitive, screening and/or culture method was available to comply with recommendations to conduct point prevalence testing and colonization screening of animals at the facility.

**Results:** Limited literature existed on the prevalence of CRE in companion animals. Recommendations to deal with CRE infections were targeted to human healthcare settings. A plan was initiated, known as CREATE (Carbapenem-Resistant Enterobacteriaceae: Animal Testing and Epidemiology). The Diagnostic Laboratory developed a testing strategy to rapidly screen animals for CRE colonization: with selective culture confirmation to obtain isolates. Methods were validated and tested with weekly point prevalence surveys, and a period prevalence survey. The IDC revised the Infection Control Manual and the ASC developed guidelines for consultation.

**Conclusions:** Veterinary hospitals must prepare for the emergence of CRE in companion animals, now that spill over from human medicine has occurred. CREATE a Plan defines validated lab methods that can be standardized across the veterinary community to enable rapid colonization screening of animals and determine the molecular mechanism of resistance. IP and stewardship guidelines are defined and there is a strong recommendation to enhance global veterinary surveillance efforts.

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Abstract 5760

Mucosal barrier injury laboratory-confirmed bloodstream infection in oncology patients: descriptive analysis of epidemiological and laboratorial data

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Background: In 2013 the Centers for Disease Control (CDC) defined the criteria for infection of serious diseases associated with Mucosal Barrier Injury Laboratory-Confirmed Bloodstream Infection (MBI-LCBI), cases whose source is probably the translation of the gastrointestinal tract. The aim of this study was to describe the epidemiological and laboratory data of MBI-LCBI in cancer patients.

Materials/methods: Retrospective cohort study conducted in a large cancer hospital. Central Line-Associated Bloodstream Infections (CLABSI) were reviewed from 2015 to 2017, and those that met the CDC criteria were reclassified as MBI-LCBI. Collected epidemiological data - gender, age, underlying disease; and laboratory - microbiological.

Results: 339 CLABSI were detected in the period, 51 (15.0%) classified as MBI-LCBI - 6 (11.8%) in patients with solid tumors, and 45 (88.2%) in patients with hematologic neoplasms. Twenty-six (51.0%) were male, mean age 46.88 years (22-69 years). Thirty-five (68.5%) of the oncologic diagnoses were Leukemia. All patients had neutropenia. Sixty-two microorganisms were isolated in blood cultures (Table).

<table>
<thead>
<tr>
<th>Isolated microorganisms</th>
<th>TOTAL N = 62</th>
<th>Solid tumors N = 7</th>
<th>Hematologic malignancies N = 55</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N / %</td>
<td>MR / %</td>
<td>N / %</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>29 / 46,9</td>
<td>22 / 75,9</td>
<td>2 / 28,6</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>10 / 16,1</td>
<td>8 / 80,0</td>
<td>2 / 28,6</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>8 / 12,9</td>
<td>1 / 12,5</td>
<td>0 / 0</td>
</tr>
<tr>
<td>Candida spp.</td>
<td>7 / 11,3</td>
<td>- / -</td>
<td>3 / 42,8</td>
</tr>
<tr>
<td>Streptococcus grupo viridans</td>
<td>3 / 4,8</td>
<td>0 / 0</td>
<td>0 / 0</td>
</tr>
<tr>
<td>Streptococcus salivarius</td>
<td>2 / 3,2</td>
<td>0 / 0</td>
<td>0 / 0</td>
</tr>
</tbody>
</table>

Conclusions: Most cases of MBI-LCBI occurred in patients with hematologic malignancies. Gram-negative bacilli were the most identified microorganisms.

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Abstract 5762

Contribution of high risk clones *Pseudomonas aeruginosa* ST111 and ST235 in the spread of VIM-2 carbapenemase in a Greek Hospital

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**Background:** Carbapenem-resistant *Pseudomonas aeruginosa* isolates are currently a serious problem in the management of health-care associated infections. The aim of this study was to examine the molecular characteristics of carbapenem-resistant *P. aeruginosa* detected in a Greek hospital, during 2018.

**Materials/methods:** A total of 120 *P. aeruginosa*, isolated in 2018, from patients treated in University Hospital of Larissa (UHL) (Greece) were included in this study. Identification to species level and susceptibility testing against various antimicrobial agents was performed by the automated system Vitek 2. All *P. aeruginosa* isolates were typed by PFGE and MLST. Additionally, all isolates were tested for carbapenemase production by a modified Hodge test with a meropenem disk. Carbapenemases were detected phenotypically and by PCR. The metallo-β-lactamase (MβL)-encoding integrons were amplified and sequenced.

For 4 isolates representing different STs, bacterial genomes were sequenced using the Illumina MiSeq platform. Annotation and analysis were performed using software available on the Internet.

**Results:** A total of 50 (41.6%) out of 120 *P. aeruginosa* isolates were MHT positive. The population structure of the carbapenemase-producing isolates studied by MLST was classified into 7 sequence types (STs). The international clone ST111 was the most prevalent, accounting for 30 isolates. Fourteen of the isolates were distributed in the pandemic ST235. The remaining six isolates belonged to distinct STs. The majority of the carbapenemase-producing *P. aeruginosa* isolates (n=48; 96%) produced the VIM-2 MβL, while two isolates produced VIM-4. No other carbapenemase-encoding genes, *bla*<sub>OXA-48</sub>, *bla*<sub>KPC</sub>, *bla*<sub>NDM</sub> and *bla*<sub>IMP</sub>, were found. Three different class I integrons were identified: two structures coding for VIM-2 (*aacA29a*<sub>1</sub>|*bla*<sub>VIM-2</sub>, and *bla*<sub>oxa-10</sub>|*aacA4</sub>||*bla*<sub>VIM-2</sub>|*sma-2*), and one for VIM-4 (*bla*<sub>VIM-4</sub>|-*fbr*<sub>7</sub>|*arr-7</sub>|-*aacA4</sub>|-*bla*<sub>PSE-1</sub>*). In selected isolates, S1 profiling and Illumina sequencing showed that MβL-encoding integrons were integrated into their chromosomes.

**Conclusions:** VIM producers comprised 642% of the carbapenem-resistant *P. aeruginosa* recovered in UHL during 2018. Most (88%) of the VIM producers belonged to the internationally-distributed clones of ST111 and ST235, which produced VIM-2 or VIM-4 enzymes. Therefore, recognition of carbapenemase-producing *P. aeruginosa* hyper-epidemic clones by molecular tools represents an important step towards tracing transmission routes, developing targeted control and prevention strategies, and monitoring their effectiveness.

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Abstract 5763

Optimisation of culture protocol for the recovery of fungal pathogens from expectorated sputum of cystic fibrosis patients

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Background: The role that fungi play in patients with Cystic Fibrosis (CF) is not well characterized, largely due to a lack of standardized laboratory guidelines for the optimal recovery of fungi in respiratory tract of CF patients. We previously reported use of selective fungal culture media increased rates of detection of fungi in CF cultures. In this study, we attempted to further determine the impact of incubation temperature of culture media and pre-treatment of expectorated sputum with a mucolytic agent on CF fungal cultures.

Materials/methods: 400 prospective CF expectorated sputa samples were simultaneously tested by two protocols: 1) the current protocol included inoculating sputa on the following media: MacConkey, CNA, blood, chocolate with and without bacitracin, Burkholderia cepacia selective, Mannitol salt & Sabouraud dextrose with Gentamicin (SABG), and incubated at 37°C for 3 days. 2) the study protocol including Phase I [P I] and Phase II [P II]. In P I, 200 sputa were inoculated on SABG, Inhibitory mold with Gentamicin (IMAG) and Brain heart infusion with Gentamicin (BHIG) and incubated at 30°C and 37°C, respectively. In P II, 200 CF sputa were pre-treated with and without a DTT free mucolytic agent, Liquilizer® (Metasystems Group, Inc) followed by repeating the P I protocol (excluding BHIG). All culture plates were observed for seven days.

Results: Total growth rate for the current protocol was 22% (88/400), for P I 38% (76/200), for P II 43% (85/200) using a combination of SABG and IMAG at 30°C and 37°C. The study protocol was statistically better than the current protocol (p<0.05). Pre-treatment of sputa with Liquilizer® did not significantly enhance the yield of fungal organisms. The most common fungal pathogens recovered were Aspergillus (56%), Exophiala (12%), Scedosporium (9%), Trichosporon (6%) and Rasamsonia (5%). The rate of recovery of these fungi was not significantly affected by temperature and media; however, extended incubation time increased the quantity of fungi recovered.

Conclusions: A combination of SABG and IMAG inoculated at both 30°C and 37°C along with a prolonged incubation of 7 days' time produced the maximum isolation of fungal pathogens, 87% (139/159).

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**Abstract 5764**

**Clostridioides difficile infection is associated with persistent high level of innate immune response**

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**Background:** The expression of CD11b (member of the beta-integrins) and CD64 (Fc receptor for IgG) on neutrophils increases in the presence of bacterial components. While their expression has been studied during neonatal sepsis, little is known during Clostridioides difficile infection (CDI). The aim of the study was to investigate the dynamic changes of CD64 and CD11b expression on neutrophils and monocytes before and after CDI-specific treatment.

**Materials/methods:** Patients with CDI and, as a control group, 7 healthy donors (HD) matched for age and sex were enrolled in the study. For each subject, whole blood samples were collected before (T0) and at the end (T1) of CDI-specific treatment. Identification and expression of CD64 and CD11b on peripheral blood neutrophils and monocytes were evaluated by flow cytometry and expressed as percentage or median fluorescence intensity (MFI), as appropriate.

**Results:** Twelve patients (median age 78 years) with CDI were included in the study, with 4/12 (30%) having a severe CDI. As for the 60-day outcome, 5/12 (41.6%) had a recurrence and 1/12 (8.3%) developed a nosocomial bloodstream infection. At T0, neutrophils and intermediate monocyte percentages were significantly higher than HD (p=0.007; p=0.01, respectively) as well as the CD64 MFI on neutrophils and monocytes (p=0.007 and p=0.04, respectively). Overall, CD64 MFI on neutrophils and monocytes showed a reduction from T0 to T1, especially on intermediate monocytes (p=0.04). Of note, at T1 values of CD11b and CD64 remained significantly higher than that observed in HD. Stratifying patients according to the development of recurrence or not (R+ and R- groups, respectively), a significant reduction of CD64 and CD11b MFI on neutrophils and monocytes from T0 to T1 in R- subjects was observed (p=0.03, p=0.03 for CD64; p=0.01 and p=0.01 for CD11b, respectively) whereas in R+ these biomarkers remained persistently high (Figure 1).

**Conclusions:** CDI is associated with a high level of innate immune response which lowers at the end of CDI-specific therapy, however without reaching values comparable to HD. Persistent high level of CD64 and CD11b expression on neutrophils and monocytes might have a role on the development of CDI recurrence.

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Abstract 5770

Prescribing in paediatric inpatients in England, 2016: factors associated with prescribing “watch” and “reserve” antibiotics

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Background: In England, 89% of antibiotics for human use are prescribed in primary care. Of these, approximately a third are for children younger than 15 years. There is little published information on paediatric antimicrobial prescribing in English hospitals; our objective was to describe inpatient paediatric antimicrobial use in order to inform future stewardship interventions.

Materials/methods: Data collected from the 2016 national healthcare-associated infection and antimicrobial usage point prevalence survey, conducted in accordance with the European Centre for Disease Prevention and Control protocol, was analysed. The dataset was restricted to paediatric inpatients, either recorded as admitted to a paediatric specialty or aged less than 16 years old. Healthy neonates were excluded from the analysis. Descriptive statistics were prepared and logistic regression was performed to identify factors associated with prescribing “Watch” and “Reserve” antibiotics as defined in the World Health Organization’s AWaRe categories.

Results: Of 3465 paediatric patients hospitalised in 87 Trusts, 1865 (53.8%) were less than 12 months old and 1649 (47.7%) were female. There were 247 (7.1%) admissions to paediatric intensive care units (PICU) and 455 (13.3%) to neonatal intensive care units (NICU). One thousand four hundred and forty-five (41.7%) patients received at least one antibiotic or antifungal agent. Of 2330 prescriptions, the most common agents were gentamicin (277, 11.9%), benzylpenicillin (255, 10.9%), and amoxicillin-clavulanate (219, 9.4%). The most common indications were community-associated infection (979, 42.0%), healthcare-associated infection (615, 26.4%), and medical prophylaxis (325, 13.9%). Age 12 months or older, admission to PICU, and the presence of a healthcare-associated infection were predictors of “Watch”/“Reserve” antibiotic prescribing (odds ratio OR 1.27, 95% confidence interval CI 1.22-1.33; OR 1.21, CI 1.13-1.30; OR 1.09, CI 1.03-1.15, respectively).

Conclusions: These findings highlight possible areas where national stewardship interventions could focus, such as in paediatric intensive care units. Further work is required to assess the appropriateness of antibiotics prescribed in these areas and target interventions aimed at optimising antibiotic prescribing. In addition, efforts aimed at reducing healthcare-associated infections may help decrease prescribing of “Watch”/“Reserve” antibiotics. The creation of a national paediatric antimicrobial stewardship network may support the implementation of these interventions.

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Double carbapenem therapy for isolated pneumonia in carbapenem-resistant *Klebsiella* spp. and *Acinetobacter* spp.

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**Background:** Herein, we aimed to describe the outcomes of patients with carbapenem-resistant (*CR*) *Klebsiella* spp and *Acinetobacter* spp pneumonia who received ertapenem containing double carbapenem therapy (*ECDCT*), retrospectively.

**Materials/methods:** (>18 years old) patients with culture-proven *Klebsiella* spp and *Acinetobacter* spp carbapenem-resistant pneumonia (clinical+radiographic findings+lower respiratory tract culture) treated with ECDCT between August 2016-October 2019 were included in the study. Patients with other concomitant CR infections in other foci were excluded. Bacterial identification was performed via MALDI-TOF MS [BioMerieux, France] and antimicrobial susceptibility testing of the isolates was performed via the VITEK 2 system [bioMérieux]. Resistance to imipenem, ertapenem, and meropenem was tested by E-test [bioMérieux]. The results were interpreted according to the EUCAST criteria. Ertapenem dosage was adjusted as creatinine clearance as >30 1 gr/day (12 cases); <30 0.5 gr/day (2 cases) while meropenem dosage was 3x1 gr/day when creatinine clearance >50 (9 cases), 2x1gr/day when 10-50 (5 cases).

**Results:** Fourteen cases (8 female-67.71 +/- 11.30 years- eight *Klebsiella* spp. six *Acinetobacter* spp.) fulfilled study criteria. Ten cases had a history of antibiotic usage in the previous one-month period. Two cases had concomitant fungal urinary tract infection and two cases had concomitant bacteraemia. All isolates were resistant to meropenem and ertapenem with the MIC levels ≥ 16 and ≥8 μg/ml, respectively. Ten isolates were resistant to gentamycin and thirteen isolates were also resistant to ciprofloxacin. Three isolates were found to be sensitive (MIC ≤ 2 μg/ml) and three isolates were intermittently sensitive (MIC=4 μg/ml) to tigecycline. All cases were treated with ECDCT while eleven were combined with colistin and eight were combined with tigecycline. The mean duration of ECDCT was 18.07 +/- 7.11 days. Microbiological eradication was observed in 4 of 8 (50%) *Klebsiella* spp. cases and in 2 of 6 *Acinetobacter* spp cases (33%) [p=0.627 via Fisher Exact test]. Overall one-month survival rates (with one relapse) were 35.7% (5/14), 3/8 in *Klebsiella* spp. and 2/6 in *Acinetobacter* spp. (p=1 via Fisher Exact test).

**Conclusions:** Although the number of cases is low and uncontrolled, ECDCT containing therapy resulted in relatively unsuccessful outcomes in CR *Klebsiella* spp and *Acinetobacter* spp pneumonia.

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Antibiotic consumption in 417 nursing homes: results from a pilot survey

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Background: Point prevalence surveys (PPS) in French nursing homes (NH) highlighted frequent use of broad-spectrum antibiotics such as ceftriaxone and fluoroquinolones. Easier than PPS, continuous monitoring of antibiotics dispensed by pharmacies, with feedback to prescribers, could help in improving prescribing practices. Antibiotic consumption was described in 417 NH in 2018.

Materials/methods: The standardized methodology and webtool (ConsoRes) provided by the national project for surveillance and prevention of antimicrobial resistance in hospitals (SPARES) were used to collect antibacterials for systemic use (J01class, WHO Anatomical Therapeutic Chemical classification, ATC-DDD system, 2019 version), oral imidazole derivatives and fidaxomicin dispensed in 2018 by the internal pharmacy for residents in voluntarily participating nursing homes. Consumption was expressed in number of defined daily doses (DDD) per 1 000 resident-days (RD).

Results: Among 417 participating nursing homes, 5 were independent, 15 were part of private clinics, 12 part of psychiatric centres, 27 part of long-term care or rehabilitation centres and 358 were part of public hospitals. Antibiotic use ranged from 31 DDD/1000 RD in independent nursing homes to 41 in nursing homes belonging to long-term care or rehabilitation centres. Most used antibiotics were co-amoxiclav (33%); amoxicillin (28%), ceftriaxone (7%). Ofloxacine accounted for 44% of fluoroquinolones. Nitrofurantoin use accounted for 5.3% of antibiotics in NH belonging to psychiatric centres whereas it represented 0.7% to 3% in other types of NH. No relationship between consumption and the size of the NH was observed.

Conclusions: When expressed in number of DDD/1000 RD, the three most used antibiotics were not the same than reported in PPS where number of treatments or resident treated are measured. In the lastest, the most used antibiotic was ceftriaxone (in 13% of residents). As continuous monitoring of antibiotic prescriptions from individual electronic records is not yet available in French nursing homes, retrospective surveillance of dispensed antibiotics expressed in number of DDD/1000 RD through a national network allowing benchmarking could be useful to raise awareness among prescribers. Adjustment for risk factors (patient dependency) could be used to improve reliance of benchmarking.

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Background: For non-tuberculous mycobacteria (NTM), minimum inhibitory concentration (MIC) distributions of wild-type isolates have not been systematically evaluated and epidemiological cut-off values (ECOFF) not determined. Evidence-based clinical breakpoints for NTM do not exist and should be defined from ECOFFs, clinical outcome and pharmacokinetic/pharmacodynamic (PK/PD) data, as for other bacteria. Currently, the Clinical and Laboratory Standards Institute (CLSI) recommend using broth microdilution (BMD) in cation adjusted Mueller Hinton broth (CAMHB) for AST of most NTM. We collected MIC distributions for major clinically relevant NTM using BMD as a first step towards determining EUCAST ECOFFs.

Materials/methods: MIC distributions in CAMHB for the major NTM drugs were gathered from six laboratories for M. abscessus (MAB; M. abscessus subsp. abscessus, massiliense and bolletii) and M. avium complex (MAC; M. avium and M. intracellulare) along with quality control (QC) strains. Species identification was made by line probe assays and/or gene sequence-analysis. ECOFFs were analyzed according to the EUCAST guidelines.

Results: For M. avium, M. intracellulare and MAB, MICs from 1240, 409 and 656 isolates were analyzed. Clarithromycin wild-type MIC ranges were 0.25-16 (mode 2) mg/L and 0.12-8 (mode 2) mg/L for M. avium and M. intracellulare respectively with corresponding ECOFFs at 16 and 8 mg/L. Amikacin MIC wild-type ranges were 2-64 (mode 16) mg/L and ECOFFs 64 mg/L for all three species. Reproducibility for QC strains were within ±one MIC dilution for all drugs and within CLSI targets. MIC-distributions and tentative ECOFFs for subspecies and other drugs such as imipenem and tigecycline (MAB), rifamycins and ethambutol (MAC) as well as moxifloxacin, linezolid and sulfamethoxazole (MAB and MAC) are under analysis.

Conclusions: As a first step towards evidence-based clinical breakpoints for NTM, tentative ECOFFs were defined for MAC and MAB. Based on the results and internal work, a detailed reference protocol for NTM AST is expected from the EUCAST subcommittee for antituberculosis drug susceptibility testing (AMST) during 2020 which will then be used to set clinical breakpoints using the EUCAST procedure.

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Antibiotic use indicators: which and how? Pilot study of 3 indicators in French hospitals

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Background: Antibiotic consumption is monitored to assess selection pressure on bacteria. In addition to the overall amount of antibiotics, the nature of the antibiotic plays a role in selection and dissemination of resistant bacteria. This is why indicators based on the proportion of specific antibiotics among the total quantity of antibiotics may be developed, building upon lists of specific antibiotics from national or international organisations. In France, the national medicines agency established a list of 51 critical antibiotics. In the United Kingdom, 23 narrow-spectrum antibiotics were used to define an index adapted from the WHO AWaRe index (AWaRe-UK). An indicator representing the percentage of broad-spectrum antibiotics is used by ECDC for the hospital sector. In this context, we studied the usefulness of these indicators for comparisons of hospitals involved in the surveillance network managed by the national mission for surveillance and prevention of antimicrobial resistance (SPARES).

Materials/methods: The three indicators (one based on the French medicines agency list, ANSM; AWaRe-UK; ECDC) were calculated for 1622 hospitals that provided data on antibiotic use in 2017: 560 public non-teaching hospitals, 452 private clinics, 389 rehabilitation centres, 127 psychiatric centres, 49 university hospitals, 20 long term care hospitals, 20 cancer centres and 5 military hospitals. For each indicator, hospital ranks were compared using Spearman test among hospitals of the same type.

Results: Comparison of ranks differed according to hospital types. The ANSM and AWaRe-UK indicators were significantly linked for all types of hospitals (Rs 0.74 to 0.89) except for cancer centres. ECDC indicator resulted in different ranking or in similar ranking than the two others but with a weaker correlation Rs 0.32 to 0.52 with ANSM; Rs 0.39 to 0.53 with AWaRe-UK – except university hospitals (0.75) and cancer centres (0.71).

Conclusions: As indicators to better express antibiotic use and its relationship with antimicrobial resistance are being developed, this pilot study underlined the utility of complementary indicators that provide different information for hospital benchmarking. In addition to ECDC indicator, an index based on “virtuous antibiotics” for first-line prescription could be used, adapted from the AWaRe-UK to fit to the national hospital context.

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Short-term prognosis and factors associated with acute kidney injury in imported severe malaria: results of a multi-centre retrospective study

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Background: Acute kidney injury (AKI) is a well recognized complication of severe malaria (SM) in endemic areas and its prevalence can reach 40% of adult patients. Few data are available on AKI in imported SM. This study aimed to determine the prevalence, the prognosis and associated factors of AKI in this setting.

Materials/methods: We conducted a multicentre retrospective study in four intensive care units between January 1, 2000 and December 31, 2016. All consecutive patients with SM were included. AKI was defined using the KDIGO classification: increase in serum creatinine by ≥ 0.3 mg/dl (≥ 26mmol/l) within 48 h, or increase in serum creatinine to ≥ 1.5 times baseline. The reference serum creatinine (SCr) was estimated for each patient according to age and ethnicity. The evolution of renal function was assessed from the last SCr available for each patient. A logistic regression was used to compare the groups with and without AKI.

Results: One hundred and twenty-nine patients were included, Forty-two (32.6%) had AKI at presentation (mean age 46.9 (standard deviation 2.3), 31/42 (74%) males): 17/42 (40%) stage 1, 13/42 (31%) stage 2 and 12/42 (29%) stage 3. None had prior chronic renal failure. A worsening of AKI was seen in 6 patients during their hospital stay: 1 patient with KDIGO1 and 4 patients with KDIGO-2 evolved to KDIGO-3. 1 patient with KDIGO 1 developed KDIGO 2. The average time from ICU admission to the maximum serum creatinine value was 2.9 days (0.9). Among the 42 patients, 22 (52%) needed renal replacement therapy.

Higher age (p<0.01), shock (p=0.02), respiratory distress (p=0.03), higher leukocytes count (p<0.01) and coexisting bacterial infection (p=0.01) were associated with AKI at presentation.

The average follow-up was 45 (12.4) days and data were available for 38 patients. Among them, 30/38 (79%) patients had recovered a SCr at +/- 50% of the reference value and only 23/38 (61%) had a SCr at +/- 5% of the reference value.

Conclusions: SM patients with AKI portend unsatisfactory short-term renal outcomes and deserve a careful and longer follow-up, especially under nephrology care.

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Abstracts 2020

Abstract 5785

Phage-antibiogram
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Background: Bacteriophage (phage) therapy is re-emerging a century after it began and is widely considered to be the solution to antibiotic resistance. Phages have been championed as ideal personalised medicines in the critically ill due to their specificity at species and strain level. Thus, measuring the bacteria host range plays an important role in utilizing the phages as antimicrobials. Here we designed a high-throughput, liquid assay to simultaneously and efficiently detect host range and phage-antibiotic synergy. This has the potential to inform adjuvant phage therapy in critically ill patients in a timely manner.

Materials/methods: The 96-wells microtiter plates were prepared on Eppendorf epMotion 5075 liquid handling robot for high throughput testing containing LB broth, target bacterial isolates, gradient dilutions of phage [s] across rows and fixed concentrations of antibiotics [1/2 - 1/4 MIC]. Lytic phages against clinical isolates of Klebsiella pneumoniae and Escherichia coli belonging to virulent ST and capsular types were included in this study. Standard plaque assay for host range was done in parallel for comparison. Representative antibiotics from each drug class were investigated for synergy effect with phages, biological replicates were used. The plates were incubated at 37°C for 18 hours with orbital shaking in SpectraMax iD5 microplate reader with bacterial kinetics monitored every 30 minutes.

Results: The automated plate assay correctly determined the phage virulence in majority of cases in comparison to the plaque assay (>96% agreement). The plaque assay tended to overestimate phage host range. The advantage of using this platform was continuous monitoring of bacterial growth and the rise of bacterial resistance over continued phage exposure. Phage combination with imipenem and ciprofloxacin exhibited synergistic activity among the Klebsiella pneumoniae phages tested and significantly delayed the appearance of resistant mutants (P value=<0.05).

Conclusions: Parallel experiments indicated that this high throughput liquid assay is reproducible and comparable to the standard reference plaque assay to determine phage virulence determination. The results inform synergistic activity between phages and different antimicrobial drugs. Thus, this system can potentially assist with clinical decisions at the bedside, especially where phage therapy is being used with best established antibiotic therapy in refractory infections.

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Phenotypical and molecular characterisation of non-lactose fermenting Escherichia coli isolated from outpatients with urinary tract infection in a private health centre in Santiago, Chile

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Abstract 5787

Phenotypical and molecular characterisation of non-lactose fermenting Escherichia coli isolated from outpatients with urinary tract infection in a private health centre in Santiago, Chile

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Background: Isolation of non-lactose-fermenting E. coli (NLF-E. coli) is increasing, especially sequence type (ST) 1193. It is more resistant to fluoroquinolones, gentamicin and trimethoprim –sulfamethoxazole than lactose-fermenting E. coli. Data about this clonal group is lacking in Chile. The aim of this study was to determine the prevalence, antimicrobial resistance (AM) patterns (phenotype/genotype), virotype, phylotype, sequence and clonal relationship of NLF-E. coli isolated from urine samples of outpatients with urinary tract infection (UTI).

Materials/methods: 96 isolates of E.coli from urine samples of outpatients with UTI, studied in a private health center in Santiago, Chile, between August-December 2017, were included (1 isolate/patient). NLF-E. coli was detected by phenotypic tests. AM susceptibility testing was performed by agar diffusion. ESBL was confirmed by double disk method and blaCTX-M PCR. Virulence genes were detected by multiplex PCR (kpsMTII, feoB, iutA, fimH, hlyA, cfn1 and sat). Quadruplex PCR was used to establish phylotype (chuA, arpA, yjaA, ytsPE4C2). MLST was used for detection of clonality. Sequence type was performed using the MLST. Clonal relationship was investigated by generating a Minimum Spanning Tree (MST), through the Phyloviz 2.0 software. STs of 23 NLF-E. coli and 62 UPEC were analyzed using http://enterobase.warwick.ac.uk/species/ecoli/search_strains.

Results: The prevalence of NLF-E. coli was 26% [25/96]. It showed higher rates of AM resistance than lactose-fermenting E.coli for ciprofloxacin: 68% versus 12% (p = 0.00) and trimethoprim-sulfamethoxazole: 48% vs. 17% [p = 0.0028]. 12% [3/25] produced CTX-M-15 ESBL. Mutations in S83L and D87N were present in the QRDR zone of the gyrA gene in 10 ciprofloxacin-resistant NLF-E. coli studied. Phylotype B2 was the most common (92%). Frequency of virulence factors was: fimH (100%), feoB (92%), sat (80%), kpsMTII and iutA (76% each), cfn (68% and hlyA (16%). ST1193 (54%) was the most prevalent, belonged to phylotype B2, was 100% resistant to ciprofloxacin and showed low ESBL production (7.7%).14 strains belonged to clonal complex (CC) 14.

Conclusions: The prevalence of NLF-E. coli isolated from outpatients with UTI was 26%. ST1193 was the most frequent ST, belonged to phylotype B, was related to CC14 and highly resistant to fluoroquinolones.

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Abstract 5788

**Antiviral treatment in severe influenza pneumonitis**

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**Background:** Severe influenza is under-recognized and not always timely treated with anti-viral agent, even though the role of antiviral agents is not documented. We want to define whether antiviral treatment may improve the outcome of severe influenza pneumonitis.

**Materials/methods:** We started to enhance our awareness of severe influenza at Linkou Chang Gung Memorial Hospital upon the 2009 novel H1N1 pandemic. Since then, all bronchoscopic bronchoalveolar lavage (BAL) samples in intensive care units (ICUs) were tested for influenza by PCR. There were 82 adult ICU patients with severe pneumonitis and PCR positive BAL samples from 2009 to 2019. Nineteen cases of APACHE 3 predicted extreme high and low mortality were excluded. Demographic and clinical data were collected for the other 63 patients. Outcome measurements were compared between those with and without timely treatment (within 3 days of symptoms onset), those with and without empiric treatment, those with treatment before and after BAL examination, and those of the first and the second halves of the 10 years study period.

**Results:** Co-morbidities and disease severity are matched between the comparison groups. Survival rates were higher for patients treated within 3 days after symptoms onset [89% (16/18) vs 51% (23/45), p=0.005], for patients empirically treated before definitive laboratory diagnosis [79% (22/28) vs 49% (17/35), p=0.015], and for patients treated before BAL exams [75% (30/40) vs 39% (9/23), p=0.005]. The survival rate was also slightly higher for the patients of the second half of the 10 years study period, although not statistically significant [66% (21/32) vs 52% (16/31), p=0.098]. There was no difference in other outcome measurements.

**Conclusions:** Early, timely, even empiric treatment before definitive laboratory diagnosis, especially without delay until invasive bronchoscopy conferred a significant survival benefit. The patients of the second 5 years of the 10 years study period were with higher disease awareness. They came to medical attention earlier and as a result, they get earlier treatment. In conclusion, it is prudent advice to encourage empiric antiviral treatment for patients with possible severe respiratory tract infection with influenza.

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Implementation of a smartphone application intervention to increase linkage to and engagement with HIV care among people with tuberculosis and substance use in Irkutsk, Siberia

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Abstract third-party references: Supported by the National Institutes of Health and the Russian Foundation for Basic Research

Background: Fueled by injected heroin use, Irkutsk, Siberia faces a high prevalence of co-infection with human immunodeficiency virus (HIV) and drug-resistant tuberculosis (TB). Treatment for co-infection in this context tends to consist of cumbersome multi-drug regimens delivered in separate care settings, which along with associated stigma and social isolation poses considerable barriers to engagement in care for people living with HIV (PLWH) and TB.

Materials/methods: The Irkutsk HIV/AIDS Centre and Irkutsk Regional Tuberculosis Referral Hospital partnered to implement a smartphone app-based intervention called MOCT (Russian for 'Bridge') for a co-infected cohort developed for the local language and cultural context. The app includes daily medication and appointment reminders, educational resources, and peer and provider messaging. The cohort was trained on MOCT use and initiated on antiretroviral therapy. Participants were surveyed on medication adherence, visit attendance and perspectives on the app, and usage was compared to other commercial health apps.

Results: This cohort (N=52) had a high proportion of history of intravenous drug use (IVDU) (60%), alcohol use (81%) and hepatitis C infection (42%). Patients using the MOCT app reported a high medication adherence ('I take medications as prescribed most days') at 6 months (27/29 for both HIV and TB meds). Surveys thus far also indicate that patients remained engaged in HIV care at 6 months (27/28 patients attended at least one visit, 25/26 patients refilled meds at least once). Comparing retention in care scale scores [1-10 points] at baseline and 6 months, we observe an increase by 2.07 points [p=0.001] in patients’ self-scoring of their likelihood of contacting the HIV clinic with questions [N=27]. The cohort demonstrated a higher mean response rate to daily queries over 6 months (49.5%) compared to popular commercial mobile apps (4-20%).

Conclusions: A language and cultural context adapted app was associated with excellent engagement in care among a cohort of people using substances and at considerable risk for lack of engagement, as well as improved patient self-efficacy in terms of likelihood of reaching out to providers, with high rates of app usage over time.

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Abstract 5793

**Efficacy of CD377, a novel antiviral Fc-conjugate against seasonal influenza in lethal mouse models**

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**Background:** Cidara’s AVCs (antiviral Fc-conjugates) are novel, immunotherapeutic conjugates of potent, antiviral agents with the Fc domain of human IgG1. CD377 is an AVC development candidate for prevention and treatment of influenza that has demonstrated broad anti-neuraminidase activity in both enzymatic and cell-based assays, and the ability to engage the immune system through its Fc domain. These attributes, coupled with an exceptional PK profile, underscore the potential of CD377 for the long-term prevention of seasonal influenza.

**Materials/methods:** Efficacy studies were conducted in female BALB/c mice lethally challenged intranasally at 3x the LD95 with influenza A virus [H1N1, H3N2] and influenza B [Victoria, Yamagata lineages]. CD377 was administered as a single dose subcutaneously (SC) at various concentrations 2 hours after viral challenge. Body weights (BW) and health scores were monitored daily, with 20% BW loss recorded as a mortality.

**Results:** In mice challenged with a lethal dose of a pandemic H1N1 strain [A/California/07/09], a single dose of CD377 (0.1 to 3 mg/kg) administered 2 hours post-challenge was fully protective (P=0.0026 relative to vehicle). This result was accompanied by only a transient drop in BW that was greatest on Day 4 before full recovery to starting BW by Day 9. In a similar study against a mouse-adapted H3N2 subtype [A/Hong Kong/1/68], a single dose of CD377 at 0.3 mg/kg was fully protective (P=0.0025).

The activity of CD377 was also evaluated against both lineages of influenza B. Against influenza B/Malaysia/8/34 (Victoria), a single CD377 dose of 0.1 mg/kg was fully protective (P=0.0027) while the Fc-only control dosed at 1 mg/kg was not (P=0.3173), as expected. Against the Yamagata lineage [B/Florida/4/06], CD377 demonstrated even greater potency, achieving full protection from lethal challenge at 0.03 mg/kg (P=0.0023).

**Conclusions:** CD377 was protective against lethal challenge with several seasonal influenza subtypes at single doses of 0.3 mg/kg or less. The exceptional PK profile of CD377 combined with its ability to engage the immune system highlight its potential for use as a long-term preventative against seasonal influenza.

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Clonal expansion of extended-spectrum β-lactamase-producing Escherichia coli ST131 in bloodstream infections of Ecuadorian patients from 2009 to 2018

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Background: Escherichia coli-St131 (E. coli-ST131) clone has emerged rapidly worldwide until it became an important extra-intestinal pathogen. The aim of this study was to determine, in a collection of E. coli strains from 2009 to 2018, the sequence type (ST), the phylogenetic groups and the blaCTX-M genes in ESBL-E. coli strains collected from bloodstream infections.

Materials/methods: From the collection of E. coli strains, 147 were E. coli-ESBL. During this period, a total of 509 E. coli (147/509; 28.8%) were isolated from bloodstream infections and processed in the Bactec 9120 system and bacterial identification in Vitek2. Demographic data was obtained from Whonet software. The genes for β-lactamases, and phylogroup analysis were determined by conventional PCR and sequencing. The sequence type was determined by MLST analysis (CH type).

Results: The rates of ESBL-positive strains ranged from 9.4% in 2008, and increased to 27.9% in 2018, with the highest rate of 40% in 2015. The blaCTX-M-15 gene was the most frequent (88/147; 60%) among the strains carrying blaCTX-M during all the analyzed years, followed by blaCTX-M-27 (8/147; 5.44%) and blaCTX-M-55 (7/147; 4.76%). Phylogroup B2 was the most prevalent (102/147; 69.38%), followed by phylogroup A (18/147; 12.24%). E. coli-ST131 first appeared in 2010; this strain did not carry a blaCTX-M15 gene, but a variant of the CTX-M-25 group. Before the appearance of E. coli-ST131 in 2010, the blaCTX-M-15 gene was found in E. coli-ST88 belonging to the phylogroup F (2009).

Conclusions: The presence of clone E. coli ST131 was not evidenced before 2009 in this study. A higher prevalence of the ST131 clone together with blaCTX-M-15 was observed throughout these 10 years, which could indicate that this clone is responsible for the dissemination of blaCTX-M-15. The persistence of this clone in the 10 years period demonstrates its presence in Latin America and Ecuador has not escape to the emergence of ST131 outbreak clone.

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Evaluation of large urban-rural outpatient antibiotic stewardship programme

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Background: Judicious prescribing of antibiotics is necessary in addressing the crisis of emerging antibiotic resistance and reducing adverse events. Nearly half of antibiotic prescriptions in the outpatient setting are inappropriate. Data outlining the misuse of antibiotics in the outpatient setting provide compelling evidence of the need for more rational use of antimicrobial agents beyond hospital settings. To evaluate the effect of a behaviorally enhanced quality improvement (QI) intervention to reduce inappropriate antibiotic prescribing for viral URI in the ambulatory care clinics an Outpatient Antibiotic Stewardship program was implemented.

Materials/methods: The program was implemented in January 2018 at five pilot sites. Interventions included identification of a site champion, educational sessions, sharing of clinic and individual provider data, and patient and provider educational materials. In addition, pre-clinic huddles and resident education sessions for internal medicine resident physicians were conducted with a display of public commitment to prescribe antibiotics appropriately. The primary outcome was defined as the provider-level antibiotic prescribing rate for acute URI, defined as patient visits with antibiotic-nonresponsive diagnoses without concomitant diagnostic codes to support antibiotic prescribing.

Results: 116,122 antibiotic prescriptions were dispensed from April 2017 through December 2018 compared to the period from April to December 2017 where 9,129 fewer prescriptions were ordered. Inappropriate antibiotic prescribing for viral URI for ambulatory clinic encounters (n=>45,000 visits/month) declined from 14.3% to 7.6%. Academic hospital-based sites showed little seasonality trends and no statistically significant decrease in prescription rates (p=0.5176). On the other hand, community-based sites showed strong seasonal fluctuations and a statistically significant decrease in prescription rates after intervention (p=0.000189).

Conclusions: A multifaceted behaviorally enhanced QI intervention to reduce inappropriate prescribing for URI in ambulatory care encounters at a large integrated health system was successful in reducing both inappropriate prescriptions for presumed viral URI as well as total antibiotic use. Findings suggest that implementing leadership roles, education sessions, and low-resource behavioral nudging together can decrease excessive use of antibiotics by physicians. A Hawthorne effect may be an important component of these interventions. Future studies are needed in order to determine the optimal combination of behavioral interventions that are cost-effective in outpatient settings.

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Abstract 5800

Clonal diversity of uropathogenic Escherichia coli strains from Zimbabwe

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Background: Extra-intestinal pathogenic Escherichia coli (ExPEC) is a common cause of community and hospital-acquired urinary tract and bloodstream infections (BSIs) globally. Limited information is available on the real burden of the pathogenic ExPEC and the population structure of such isolates in Zimbabwe. A study was designed to characterise E. coli from urinary tract infections (UTIs) that were collected and stored at the National Microbiology Reference Laboratory (NMRL) in Zimbabwe from 10 One Health participating centres during 2017 to 2019.

Materials/methods: A total of 823 non-repetitive UTI E. coli isolates were referred to NMRL, 110 isolates were randomly selected for this study. The Kirby Bauer method was used for antimicrobial susceptibility testing and interpretation as per CLSI guidelines. Extended spectrum beta-lactamase (ESBL) production was tested in all ceftazidime/cefepime resistant isolates, while the presence of carbapenemases was determined using the modified carbapenem inactivation method (mCIM) in meropenem resistant isolates as per CLSI guidelines. Sequence types (STs) and fimH types were determined using a published 7-single nucleotide polymorphism quantitative PCR.

Results: The overall non-susceptibility rates were as follows: ampicillin (102/110; 92.7%), trimethoprim-sulfamethoxazole (95/110;86.4%), ceftriaxone (95/110;77.2%), ciprofloxacin (100/110;90.9%), tetracycline (99/110;89.9%), nalidixic (102/110; 92.8%), ceftazidime (77/110;70%), cefepime (46/110;41.9%), meropenem (10/110; 9%). Extended spectrum beta-lactamase production was confirmed in 84 isolates, while 14 isolates harbored a carbapenemase. Five dominant sequence types (STs) were identified and included ST10 (38), ST131 (12); with different fimH types, ST58 (6), ST73 (4) and ST95 (3). Other STs that were detected included ST88 (2), ST69 (1), ST14 (1), while seaptypes 770 (31), 61 (7), 701 (4) and 660 (1) could not be converted to STs and require sequencing. Most isolates belonging to ST58, ST95 and ST73 had susceptible profiles. The ST131 and ST10 isolates displayed ESBL positive and carbapenem resistant phenotypes.

Conclusions: The population structure of ExPEC causing UTIs in Zimbabwe is dominated by clone(s) ST10 displaying ESBL and carbapenem resistance. Two-thirds of the isolates were multidrug resistant (MDR) and belonged to several STs/septatypes. Our results indicate that targeting specific STs [e.g. ST10, ST131 and ST58] through control programmes will substantially decrease antimicrobial resistance of cephalosporins and fluoroquinolones among ExPEC.

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Disease prevention not decolonisation: a cohort study for faecal microbiota transplantation for patients colonised with multidrug-resistant organisms

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Abstract third-party references: BRC NIHR Gut Health Theme

Background: Faecal Microbiota Transplantation (FMT) is widely utilised for the treatment of recurrent Clostridioides difficile infection. Use for eradication of multidrug-resistant organisms (MDROs) in the intestine has been described, with intestinal decolonisation rates from 37.5% to 87.5%, in heterogeneous studies with few looking at prevention of infection. We perform FMT via naso-gastric tube using donor stool prepared anaerobically, using prevention of MDRO invasive disease as an endpoint.

Materials/methods: MDRO colonisation was defined as carbapenemase-producing Enterobacteriaceae (CPE), vancomycin resistant Enterococci (VRE) or extended-spectrum beta lactamase Enterobacteriaceae (ESBL) isolated on rectal screening. Patients considered were colonised with at least one MDRO (Group 1) and who were at risk of invasive MDRO disease or patients who had recurrent MDRO-mediated invasive disease (Group 2). Clinical outcomes were analysed for six months pre and post-FMT by Wilcoxon ranked pairs, for non-parametric data.

Results: FMT was performed on 20 patients. Figure 1 describes the outcomes. In Group 1, all 11 patients had an underlying haematological disorder. Six had a MDRO bloodstream infection (BSI) pre-FMT. Eight underwent a stem cell transplant post-FMT. All patients had shorter inpatient stays (P=0.002) and fewer days on carbapenems compared to the preceding six months (P=0.00167). In Group 2, all nine patients had recurrent ESBL UTIs. Four patients were co-infected with C. difficile and five patients had a previous renal transplant. There was a reduction in frequency of MDRO UTIs post-FMT (P=0.0078). Across both groups there was a reduction in invasive BSIs for both MDRO BSIs (P=0.0469) and all BSIs (P=0.0283). Forty one percent of patients lost detection of colonising MDRO on stool culture post-FMT within 6 months.

Conclusions: Despite lack of complete decolonisation, concordant with published literature, patient outcomes post FMT were significantly improved in this study. The mechanism of FMT has not fully been established; therefore, improvement of colonisation resistance to invasive disease by manipulating microbiota composition, lowering the carriage of the pathogen (disinfection <10^5 CFU) or improvement of gut barrier functionality in at risk groups appears to be a more important factor independent of full intestinal eradication of MDRO in terms of patient outcome.

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Abstract 5806

**Gastrointestinal colonisation by vancomycin-resistant enterococci and carbapenem-resistant Gram-negative bacteria in an endemic setting: prevalence, risk factors, and outcomes**

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**Background:** Acquisition and gastrointestinal colonization by vancomycin-resistant enterococci (VRE) and carbapenem-resistant Gram-negative bacteria (CRGN) constitutes a major public health concern as it may be followed by clinical infection development or lead to intra-hospital dissemination. Detection of carriers and implementation of infection control measures are essential in every hospital. In this study we determined the point prevalence of VRE and CRGN in the fecal flora of the inpatients of a tertiary university hospital in Greece, we identified risk factors for colonization and examined the impact of colonization on hospital outcomes.

**Materials/methods:** A point prevalence study of VRE/CRGN rectal colonization of inpatients was conducted on March 2018. Specimens were selectively cultured for VRE/CRGN, microorganisms were biochemically identified, submitted to antibiotic susceptibility testing and tested for carbapenemase production. Data on potential risk factors and hospital outcomes were collected at the time of culture and until hospital discharge. Multivariable logistic and linear regression models were used adjusting for confounders.

**Results:** 491 patients were enrolled in the study. Of them, 64 (13.0%) carried VRE, 40 (8.2%) CRGN and 10 patients (2.1%) were carrying both VRE and CRGN. VRE colonization was independently associated with age over 65 years (adjusted OR: 2.4 [95%CI: 1.3, 4.5]) and length of stay (LOS) before rectal sampling (OR: 1.1 [95%CI: 1.0, 1.1]). Carrying a CRGN was associated with 11 days increase of LOS after rectal sampling (β-coef: 11.4 [95%CI: 1.6, 21.2]), with 3.5-fold increased risk of acquiring a resistant pathogen after rectal swabbing (RR: 3.5 [95%CI 1.2, 9.9]) and with 8-fold increased risk of mortality (RR: 6.1 [95%CI: 2.1, 17.9]), after adjusting for sex, age and comorbidity index.

**Conclusions:** High prevalence rates were found for VRE and CRGN colonization among the inpatients of our hospital. Prolonged hospitalization and age were independent risk factors for VRE colonization, while CRGN carriage was associated with increased risk of acquiring a resistant pathogen, prolonged hospital stay and increased mortality.

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Simulated exposures of oritavancin in vitro PK/PD models select for MRSA with reduced susceptibility to oritavancin but minimal cross-resistance or seesaw effect with other antimicrobials

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Background: Oritavancin is a long-acting lipoglycopeptide with activity against Gram positive bacteria including MRSA. The long elimination half-life (~10 days) allows for once weekly or single dose treatments but could prolong the mutant selection window, increasing the risk of resistance. The objective of this study was to evaluate the capacity of average post-distributional pharmacokinetic exposures of oritavancin to select for cross-resistance to vancomycin and daptomycin and cross-susceptibility to β-lactams i.e. the "seesaw effect" among clinical strains of MRSA.

Materials/methods: Using a well-described in vitro PK/PD model we simulated average post-distributional, free-drug exposures of oritavancin 1200mg IV once (fCmax 11.2 μg/mL, β-elimination t½ 240h) against 4 strains of clinical MRSA. Pharmacodynamic samples were taken at 0h, 8h, and 24h, and then daily for 672h. Samples were serially diluted in cold sterile saline and spiral-diluted onto tryptic soy agar for colony enumeration or TSA enriched with oritavancin and polysorbate 80. Surviving colonies were subjected to repeat MIC testing against oritavancin, vancomycin, daptomycin and a panel of β-lactams to investigate the seesaw effect as well as whole genome sequencing.

Results: Oritavancin was bactericidal against all strains for at least 48h but as long as 408h before regrowth of less susceptible subpopulations. Isolates with reduced susceptibility to oritavancin were detected as early as 120h but increased above the susceptibility breakpoint of 0.25mg/L in all models by 672h. Vancomycin and daptomycin MICs increased by 2-8-fold but did not exceed the susceptibility breakpoints in most isolates. β-lactam MICs were largely unchanged among the recovered isolates with reduced oritavancin susceptibility. Many mutations were observed among resistant isolates including walK, saeS, and apt, but the most commonly mutated gene was purR, with over 10 unique variants identified.

Conclusions: These observations suggest that oritavancin is less likely than dalbavancin to select for cross resistance to other important classes of agents. It is unclear why oritavancin does not seem to select for cross resistance but is likely related to differences in the mechanisms of action and the different genotypes that were selected for, especially the many purR mutations relative to the genes more commonly implicated in glycopeptide resistance.

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Abstract 5826

Retrospective analysis of intravenous fosfomycin use at Florence University Hospital, Italy: clinical and microbiological analysis

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Background: Intravenous fosfomycin may be used as last-resort therapy of infections caused by multidrug-resistant pathogens. We conducted a retrospective analysis of intravenous fosfomycin use at Careggi University Hospital in Florence (Italy) evaluating clinical indication, efficacy, antimicrobial susceptibility and safety.

Materials/methods: Retrospective observational study of adult patients who received at least a single dose of intravenous fosfomycin between January 2016 to July 2019 at a single hospital in Florence, Italy. Fosfomycin susceptibility was tested by reference agar dilution method according to ISO 20776-1,2006 and results interpreted according to EUCAST clinical breakpoints (v. 9.0 2019).

Results: 54 patients were included, 37 (68.5%) were male, median age 48 years (IQR=37-67). Indications were pulmonary exacerbations of Cystic Fibrosis (CF) (26, 42.6%); other indications were for treatment of infections in non-CF patients (28, 45.9%). Among non-CF infections, urinary tract infections (UTI) (13, 46.4%) and pneumonia (7, 25%, including 2 cases of hospital-acquired pneumonia and 5 cases of ventilator-associated pneumonia) were the most common types of infections. Carbapenem-resistant Klebsiella pneumoniae (CR-KP) (12, 44.4%) and Pseudomonas aeruginosa (9, 33.3%) were the most frequently treated pathogens. Antimicrobial susceptibility testing was performed on 20 isolates (74%). 41.6% of CR-KP were resistant, all Pseudomonas aeruginosa isolates presented MIC ≤ 128 mg/L (interpreted as susceptible for the purposes of this study). Combination therapy was prevalent (n=24, 85.7%) with tigecycline (7, 29.1%), ceftazidime/avibactam (6, 25%) and carbapenems (6, 25%) administered concomitantly. High dose fosfomycin (24 g/day) was used in 28.6% of cases. Doses adjusted for renal insufficiency were required in 46.4% of patients. Renal toxicity was reported in 3.6% of cases and electrolytes disorders in 21.4% of cases, neither resulting in fosfomycin discontinuation. Clinical success and mortality rates were 50% and 21.4%, respectively. Assessing outcomes according to microbiological susceptibility, clinical cure was achieved in 54% of patients with susceptible pathogens and 43% of resistant ones.

Conclusions: In this case series, intravenous fosfomycin had good in vitro activity against resistant Gram-negative pathogens mostly used in combination. Intravenous fosfomycin was safe. Fosfomycin was used primarily as salvage therapy for infections where there were few other treatment options.

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Abstract 5830

**Cytomegalovirus in intensive care unit immunocompetent patients: mortality and clinical aspects**

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**Background:** A controversial point nowadays is whether to treat or not the critically ill patient who has Cytomegalovirus (CMV) replication, since there are different opinions and no consensus about whether treatment generates a benefit in prognosis. In Costa Rica, the CMV seroprevalence is around 90%. The aim of this study is to evaluate the clinical characteristics of CMV infection in the immunocompetent population of the medical and neurointensive care units and to determine the intensive care unit (ICU) and 30-day mortality.

**Materials/methods:** An observational, descriptive and retrospective cohort was undertaken in Costa Rica´s Mexico Hospital, from April 2019 to October 2019. No sample calculation was performed, since all the patients meeting the inclusion criteria during this period of time were included. The quantitative real-time PCR detection of CMV DNA was detected using Qiagen Artus PCR Kits. All patients with viral load above 1000 copies/mL (3.2 log10 IU/mL) received antiviral therapy.

**Results:** A total of 37 patients were included. Pneumonia (29.7%), neurosurgical procedure (24.3%) and Diabetes mellitus II (24.3%) were the most frequent comorbidities. The mean SOFA score was 8 and the APACHE II score of 19. The incidence of CMV viremia was 16% (n=6) and the mean age was 47.9 years old. The mean viral load at which treatment was initiated was 9217 copies/mL (4.18 log 10 UI/mL). The clinical features associated with positive viremia were the use of steroids (p=0,011, 95% CI), diagnosis of sepsis or septic shock at admission (p = 0,003, 95% CI), Pa/FiO2 ratio of 120 (p <0,001) and ICU length stay of 51,7 days (p<0,001). There was no statistical difference in ICU (p=0,74) and 30-day mortality (p=0,66) between the patients with or without CMV replication.

**Conclusions:** Despite the presence or not of viral replication, the mortality was not different between both groups. One possible cause is that the treatment with ganciclovir equalized the outcome of this patients. Further studies are needed to compare patients with and without treatment.

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Abstract 5831

Safety and efficacy of triazole use for prophylaxis and treatment of invasive fungal diseases in patients receiving gilteritinib, a novel tyrosine kinase inhibitor for the treatment of acute leukaemias

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Background: Gilteritinib is a novel selective oral tyrosine kinase inhibitor approved for the treatment of relapsed or refractory acute myeloid leukemia with FMS-like tyrosine kinase 3 (FLT3) mutation. Because gilteritinib is primarily metabolized via CYP3A, concomitant use of gilteritinib with strong CYP3A inducers or inhibitors is not recommended. Pharmacokinetic analyses have shown that itraconazole and fluconazole increased gilteritinib’s Cmax and area under the curve when administered concomitantly. We sought to evaluate the safety and efficacy of concomitant gilteritinib and triazole therapy in patients with hematological malignancies.

Materials/methods: We included all patients with acute leukemia who received ≥1 dose of gilteritinib with or without triazole therapy at Brigham and Women’s Hospital and Dana-Farber Cancer Institute between 28Nov2018 – 27Nov2019. The primary outcome was the number of patients who experienced any potential gilteritinib-related adverse events in the concomitant gilteritinib and triazole group compared with the gilteritinib group. Secondary outcomes include clinical outcomes of gilteritinib therapy, incidence of gilteritinib discontinuation, and 90-day mortality.

Results: Twenty-seven patients were included in the study. Twenty patients (74%) had a history of allogeneic hematopoietic-cell transplantation. The median starting dose of gilteritinib was 120 mg/day with a median duration of 135 days (IQR, 71-225). Fifteen patients (55.5%) received concomitant triazole therapy with fluconazole (8), isavuconazole (5), posaconazole (1), or voriconazole (1). Nine patients (33%) received triazole therapy for treatment of suspected or confirmed pulmonary or sinus IFD, or mucosal candidiasis, and 6 patients (22%) for antifungal prophylaxis in the setting of concurrent graft-versus-host disease. Median time of concomitant gilteritinib and triazole therapy was 72 days (IQR, 14-171). Two patients (13.3%) who received concomitant gilteritinib and triazole therapy had their gilteritinib dose reduced due to initiating triazole therapy or renal impairment. The number of patients who experienced any gilteritinib-associated adverse events [100% vs 75%; p=0.08] and 90-day mortality [26.7% vs. 8.3%, p=0.34], in the gilteritinib-triazole group was numerically higher compared to the gilteritinib group, likely due to baseline comorbidities.

Conclusions: This preliminary analysis suggests that concomitant gilteritinib and triazole therapy is feasible without routine dose reductions when required for clinical care and not associated with clinically-meaningful increase in adverse outcomes.

<table>
<thead>
<tr>
<th>Concomitant gilteritinib and triazole therapy (n=15)</th>
<th>Gilteritinib alone (n=12)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients who experienced any gilteritinib-related adverse events</td>
<td>15 (100)</td>
<td>9 (75)</td>
</tr>
<tr>
<td>- Liver injury</td>
<td>4 (26.7)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>- Fatigue/malaise</td>
<td>8 (53.3)</td>
<td>5 (41.7)</td>
</tr>
<tr>
<td>- Gastrointestinal side effects</td>
<td>5 (33.3)</td>
<td>3 (25)</td>
</tr>
<tr>
<td>- Abnormal CK</td>
<td>5 (33.3)</td>
<td>3 (25)</td>
</tr>
<tr>
<td>- Febrile neutropenia</td>
<td>5 (33.3)</td>
<td>3 (25)</td>
</tr>
<tr>
<td>- Fever</td>
<td>5 (33.3)</td>
<td>3 (25)</td>
</tr>
<tr>
<td>- Abnormal LFT</td>
<td>8 (53.3)</td>
<td>5 (41.7)</td>
</tr>
<tr>
<td>- Myelosuppression</td>
<td>2 (13.3)</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>- Rash</td>
<td>2 (13.3)</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>- Other adverse events</td>
<td>8 (53.3)</td>
<td>4 (33.3)</td>
</tr>
<tr>
<td>90-day mortality</td>
<td>4 (26.7)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>- Death due to IFD</td>
<td>2 (13.3)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>- Death due to leukemia</td>
<td>1 (6.7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Discontinuation of gilteritinib due to side effects</td>
<td>3 (20)</td>
<td>5 (41.7)</td>
</tr>
<tr>
<td>Gilteritinib dose reduction</td>
<td>2 (13.3)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>- Due to triazole interaction</td>
<td>1 (6.7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>- Renal impairment</td>
<td>1 (6.7)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>- Adverse events</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Clinical outcomes of gilteritinib</td>
<td>1 (6.7)</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>- CR</td>
<td>5 (33.3)</td>
<td>4 (33.3)</td>
</tr>
<tr>
<td>- ICR</td>
<td>6 (40)</td>
<td>4 (33.3)</td>
</tr>
<tr>
<td>- Disease progression</td>
<td>3 (20)</td>
<td>6 (50)</td>
</tr>
<tr>
<td>- Not assessed</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Data expressed as n (%) 
CR (complete remission) 
ICR (complete remission with incomplete hematologic recovery)

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Impact of different antimicrobial exposures on the gut microbiome and resistome characterised by metagenomic sequencing

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Background: Selection of antimicrobials is guided in part by perceived differences in the extent to which they disrupt the gut microbiome and select for antimicrobial resistance. However, there is a lack of clinical data quantifying this disruption and comparing different antimicrobials. Comparative data could promote stewardship by focussing prescribing on less disruptive antimicrobials.

Materials/methods: Single stool samples were collected from healthy volunteers and patients at Oxford University Hospitals, UK, and data on antimicrobial exposure from electronic records. Metagenomic sequencing was performed with Illumina HiSeq at 3.5 million reads/sample. MetaPhlAn2 was used for taxonomic classification. Resistance gene detection was performed with ARIBA using the CARD database.

We considered associations with Shannon diversity in multivariable regression models. The proportion of the past week in which patients received each antimicrobial was used as the primary exposure, simultaneously for each antimicrobial received by >5 participants, adjusting for age, sex, participant type, and measures of comorbidity and acute illness. We also considered log relative abundance of specific taxa and classes of resistance genes.

Results: Data were available from 225 participants; 33 (15%) healthy volunteers and 192 (85%) inpatients. 119 (53%) had received antibiotics in the past week.

Exposure to several antibiotics was associated with substantially lower diversity, including piperacillin-tazobactam (-1.7 if received continuously for the last week, [95%CI -2.2 to -1.2], p<0.001), meropenem (-1.1, [-1.7 to -0.5], p<0.001), intravenous co-amoxiclav (-1.3, [-2.2 to -0.3], p=0.008), oral co-amoxiclav (-0.7, [-1.1 to -0.2], p=0.004), and oral ciprofloxacin (0.9, [1.9 to 0.0], p=0.05).

In contrast, antibiotics associated with minimal changes in diversity included doxycycline (+0.5, [-0.5 to 1.5], p=0.4) and gentamicin (+0.1, [-0.7 to 0.9], p=0.8). No antifungal or antiviral was associated with a significant change in diversity.

Meropenem, piperacillin-tazobactam and ceftriaxone significantly increased the relative abundance of Enterococcus faecium, and also the vanA glycopeptide resistance gene, but decreased Enterobacteriaceae (as did ciprofloxacin).

Conclusions: Our data provide simultaneous quantification of gut microbiome disruption by many different antimicrobials in the same study. The disruptive effect of some broad-spectrum beta-lactams contrasts markedly with several less disruptive antimicrobials. Larger studies using this approach would allow accurate comparison between even the more disruptive antimicrobials, and could greatly aid stewardship.

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Abstract 5834

Evaluation of antimicrobial susceptibility testing assays for ceftazidime-avibactam and ceftolozane-tazobactam with Gram-negative bacteria directly from positive blood culture on the Pheno system

Niels Oppermann¹, Anyangatia Ndobegang¹, Aaron Sikorski¹, Aimee Taku¹, Dulini Gamage¹, Christina Chantell¹, Romney Humphries*¹

¹Accelerate Diagnostics, Inc., Tucson, United States

Background: New antibiotics recently FDA-approved for multidrug-resistant organisms include: ceftolozane-tazobactam (C/T), a compound with activity against multidrug-resistant *Pseudomonas aeruginosa* and ceftazidime-avibactam (CZA), a beta-lactam/beta-lactamase inhibitor compound with activity against class A and D carbapenemase-producing organisms. AST performance for these compounds with Enterobacterales and *P. aeruginosa* directly from positive blood culture (PBC) was evaluated using the Accelerate Pheno™ system, compared to broth microdilution (BMD).

Materials/methods: 294 clinical isolates (100 *P. aeruginosa*, 82 *Klebsiella* spp., 56 *E. coli*, 24 *Citrobacter* spp., 15 *Proteus* spp. and 3 *S. marcescens*) were tested with CZA and C/T. Aliquots of BD BACTEC™ Standard Aerobic media containing healthy donor blood were seeded with 10-100 bacterial cells and incubated until positivity. PBC aliquots were run using the Accelerate PhenoTest™ BC kit on the Accelerate Pheno™ system according to manufacturer instructions for use and results compared to BMD. Only samples with valid results from both methods were included in analysis. Essential agreement (EA), categorical agreement (CA), very major error (VME) and major error (ME) rates were calculated using EUCAST 2019 breakpoints.

Results: EA/CA for all antimicrobial/organism combinations were >90%. CZA had 1 VME and 6 ME. CZA does not have an intermediate range with *P. aeruginosa* and Enterobacterales, and 3 of 6 CZA ME were in EA. For C/T, there were 2 VME and 2 ME.

Conclusions: Results demonstrate the tests for CZA and C/T on the Accelerate PhenoTest™ BC kit are good. A limitation of this study is only 27 CZA-resistant organisms were tested. Further work will evaluate a larger number of resistant isolates.

<table>
<thead>
<tr>
<th></th>
<th>Ceftazidime-Avibactam</th>
<th></th>
<th>Ceftolozane-Tazobactam</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Enterics</td>
<td><em>P. aeruginosa</em></td>
<td>Overall</td>
<td>Enterics</td>
</tr>
<tr>
<td><strong>n</strong></td>
<td>186</td>
<td>86</td>
<td>272</td>
<td>175</td>
</tr>
<tr>
<td><strong>EA</strong> (99.6%)</td>
<td>185</td>
<td>83 (96.5%)</td>
<td>268 (98.6%)</td>
<td>173</td>
</tr>
<tr>
<td><strong>CA</strong> (96.9%)</td>
<td>184</td>
<td>81 (94.2%)</td>
<td>265 (97.4%)</td>
<td>173</td>
</tr>
<tr>
<td><strong>VME</strong> (7.7%)</td>
<td>1</td>
<td>0</td>
<td>1 (3.7%)</td>
<td>2</td>
</tr>
<tr>
<td><strong>ME</strong> (0.5%)</td>
<td>5</td>
<td>5 (6.9%)</td>
<td>6 (2.4%)</td>
<td>0</td>
</tr>
<tr>
<td><strong>S</strong></td>
<td>173</td>
<td>72</td>
<td>245</td>
<td>102</td>
</tr>
<tr>
<td><strong>R</strong></td>
<td>13</td>
<td>14</td>
<td>27</td>
<td>73</td>
</tr>
</tbody>
</table>

Presenter email address: rhumphries@axdx.com
**Abstract 5835**

**Two antibiotics are better than one: using functional genomics to elucidate mechanisms of action in combination therapy**

Geraldine Sullivan*, Ram Maharjan, Natasha Delgado, Amy Cain

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**Background:** Antimicrobial resistance is a serious threat, with the 2014 O’Neill Report on antimicrobial resistance stating resistance-associated deaths worldwide are expected to rise to 10 million by 2050. The use of combinations of antibiotics in clinical and agricultural settings has been shown empirically to be effective, yet their precise mechanisms of action remain elusive. One of the most commonly used antibiotic combinations is trimethoprim and sulfamethoxazole (co-trimoxazole), first marketed in 1974. Despite its ubiquity in clinical settings, the mechanisms underlying its efficacy require further elucidation to improve treatment outcomes and predict trends in resistance to combination therapy. This project aims to identify genes responsible for synergistic antibiotic combinations, using *E. coli* as a model organism.

**Materials/methods:** Minimum and fractional inhibitory concentrations (MICs and FICs) were determined following the Clinical and Laboratory Standards Institute guidelines for antimicrobial susceptibility testing. The functional genomics technique TraDIS (transposon directed insertion-site sequencing) was used in *E. coli* K12 MG1655 to identify all genes that convey altered fitness in the presence of antibiotics individually or in combination at sub-inhibitory concentrations (¼ MIC/FIC).

**Results:** A dense library of random *E. coli* mutants was constructed using a Tn5 transposon yielding 340,000 unique mutants (1 insertion site per 13 bp). Challenges against the mutant library identified genes involved in survival under antibiotic stress. These included expected resistance genes (e.g. efflux pumps *acrAB/tolC*), as well as novel resistance modifiers. Genes with increased insertions, i.e. sensitivity genes and negative regulators, such as *aroK* and the sulfurtransferase complex *tusBCD*, helped identify novel interaction pathways (e.g. amino acid synthesis pathways). Confirming the roles of these genes with the KEIO collection knockouts allowed us to validate key findings in an *in vivo* context.

**Conclusions:** These genes can be used to finally understand mechanisms of action of an important antibiotic combination therapy, ultimately helping to improve treatment with antibiotic combination and also mitigating adverse side effects.

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Abstract 5836

**Evaluation of the clinical economic efficacy of the antibiotic therapy of inpatients with community-acquired pneumonia**

Anna V. Demchuk*, Yuriy Mostovoy

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**Background:** The economic evaluation of effectiveness of antibiotic treatment community-acquired pneumonia (CAP) has great importance. In routine medical practice, antibacterial therapy does not always meet the guidelines, which can lead to failure in the treatment of CAP and increase its cost. We analyzed the clinical and economic efficacy of antibiotic combinations, most commonly administered to patients with CAP, according to their compliance with guidelines.

**Materials/methods:** The observational study of 438 inpatients with CAP (male 231 (48.6%), mean age 56.1±1.79) was performed. Most of patients (399 (91.1%)) had moderate severe CAP and 39 (8.9%) – severe CAP. We assessed CAP outcome (recovery – success, without recovery - failure), compared direct cost, cost-effectiveness index (CE), incremental coefficient for recommended by guidelines and not recommended antimicrobial therapy.

**Results:** Adherence to the recommendations was accompanied by significantly higher efficacy compared to not recommended antibiotics (74.2% [132 patients out of 178] versus 73.5% [191 patients out of 260], p = 0.013). Combination of ceftriaxone or co-amoxicillin with clarithromycin was most advantageous clinically and economically (CE were lowest - UAH 25.13 % and UAH 28.90 %, respectively). Levofloxacin were economically least profitable (CE - 32.24 UAH %). In the case of severe CAP, the combination of meropenem, levofloxacin and amikacin (CE ratio of 44.36 UAH %) was at 1.5 times most economical than levofloxacin with beta-lactams [64.69 UAH %]. Non-compliant antibiotic therapy was characterized by using ceftriaxone with levofloxacin for patients with moderate severe CAP (CE 25.31 UAH %). Incorrect using amikacin, combinations of levofloxacin + ceftriaxone + amikacin or macrolide for patients with moderate severe CAP resulted in clinical failure in 7 (63.6%) patients and 12 (44.4%) patients, respectively, and the highest economic cost – (amikacin - 59.56 UAH %, combination of 3 antibiot-ics - 70.39 UAH %). The incremental coefficient was 409.31 UAH of the additional cost of treatment recommended in national guidelines compared to the non-recommended one.

**Conclusions:** The CE analysis of the recommended and non-recommended antibiotic regimens confirmed the higher clinical and economic feasibility of choosing the appropriate to guidelines therapy.

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Septic shock and age are risk factors for mortality in bacteraemia by multidrug-resistant pathogens in a Brazilian cohort of critical patients

Luciana Campos¹, Camila Rizek², Marina Farrel Côrtes², Sânia Santos², Ana Paula Marchi², Katia Gonçalves¹, Silvia Figueiredo Costa*²

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Background: multidrug-resistant bacteria (MDR) is an established public health threat and bloodstream infection by these agents is associated with high mortality. We aim to identify the risk factors for mortality in patients with MDR organisms bacteraemia hospitalized in an Intensive Care Unit (ICU) in a Brazilian trauma reference hospital during an 18 month period.

Materials/methods: in this observational cohort study, during the period of May 2017 to August 2018, all patients admitted in the ICU with the first episode of bacteraemia by the following MDR organisms - carbapenem resistant Gram negative bacteria, methicillin resistant *S.aureus* (MRSA) and vancomycin resistant enterococcus - had clinical and demographic data collected in order to investigate if any of these measurements were associated with death. Data were compared among the patients who survived and died and variables with p < 0.05 were analyzed in a logistic regression model using stepwise forward to identify risk factors for death. The isolates of *K.pneumoniae* e MRSA were investigated for carbapenemase production and presence of mec gene, respectively.

Results: 1528 fulfilled the inclusion criteria; 66 patients had bacteraemia by a MDR pathogen and 77.27% died during hospitalization. Age, systemic hypertension, quick SOFA score, Pitt bacteremia score and septic shock were associated with mortality. Trauma and bacteraemia by MRSA showed a tendency to be protective factors and were not associated with mortality. In the multivariate analysis, age (OR 1.08 CI95% 1.0 – 1.16; p 0.03) and septic shock (OR 27.82 CI95% 2.36 – 326.9; p 0.0082) remained independently associated with death. Prescription of antibiotics with in vitro activity against these agents in less than 24 hours was not associated with survival. We identified 71 isolates: 26 (36.82%) *K.pneumoniae* and 27 (40%) MRSA. 83.8% of *K.pneumoniae* strains were positive for KPC and all MRSA carried mecA gene.

Conclusions: age and septic shock were independent risk factors for mortality in patients with bacteremia by MDR organisms in a Brazilian ICU with a very high mortality where the predominant agents were *S.aureus* and *K.pneumoniae*. The better outcome of bacteremia by MRSA could be explained by the existence of an effective available treatment.

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Evaluation of a culture surveillance application for the detection of methicillin-resistant Staphylococcus aureus in the clinical setting

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Abstract third-party references: Becton Dickinson and Company

Background: The currently available BD Kiestra™ platform offers a modular approach to automating the clinical microbiology laboratory, including specimen processing, plate inoculation, streaking, image acquisition, and automated analysis of images by a suite of imaging applications. The aim of this study was to demonstrate the performance of the BD BBL™ CHROMagar™ Surveillance Application (CSA) for the detection of growth and colony color for Methicillin-Resistant Staphylococcus aureus (MRSA) on chromogenic media.

Materials/methods: Six hundred and thirty nine (639) isolates from de-identified, remnant anterior nares specimens from NorthShore University HealthSystem were processed on BD BBL™ CHROMagar™ MRSA II (CHROM MRSA) plates for detection of growth and color associated with the presence of MRSA. Plates were imaged using the BD Kiestra™ ReadA Compact and Optis™ imaging software. All 18-24 hour images were manually reviewed by two microbiologists for growth and presence of color consistent with MRSA. For discrepant results, a third reader served as an arbitrator. BD CSA algorithm results were determined for growth versus no growth, and presence or absence of color consistent with MRSA for comparison to manual image reading results.

Results: Of the 639 samples, 37.8% (n=242) were growth positive with an observed MRSA prevalence of 94.6% (n=229). The application demonstrated a 95% [0.934 – 0.966] accuracy for growth detection with a positive predictive accuracy rate of 99.2% [0.979 – 1.000]. The MRSA CSA was able to detect color consistent with MRSA for 98.7% (n=228) of the growth positive samples, demonstrating a positive predictive accuracy rate of 99.6% [0.986 – 1.000].

Conclusions: The MRSA CSA can help differentiate between growth positive and negative CHROM MRSA plates, with capabilities to further discriminate plates with growth consistent with the presence of MRSA. Typically, approximately 80% of MRSA surveillance samples will be growth negative in the clinical setting. The MRSA CSA may help streamline workflows in the clinical laboratory, automatically segregating growth negative cultures, preventing laboratorians from spending time screening negative cultures, and enabling microbiologists to focus on tasks that require their expertise.

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Impact of rapid antimicrobial susceptibility testing on antimicrobial stewardship and clinical outcomes of patients with Gram-negative rod bloodstream infection

Catherine Hogan*1,2, Bertrand Ebunji1,3, Nancy Watz2, Kristopher Kapphahn4, Joseph Rigdon4, Emily Mui5, Lina Meng5, William Alegria2, Marisa Holubar5,6, Stan Deresinski5,6, Niaz Banaei1,2,6

1Department of Pathology, Stanford University School of Medicine, Stanford, United States, 2Clinical Microbiology Laboratory, Stanford Health Care, Stanford, United States, 3Meharry Medical College, Nashville, United States, 4Quantitative Sciences Unit, Stanford University School of Medicine, Stanford, United States, 5Department of Quality, Patient Safety and Effectiveness, Stanford University School of Medicine, Stanford, United States, 6Division of Infectious Diseases and Geographic Medicine, Department of Medicine, Stanford University School of Medicine, Stanford, United States

Background: Clinical justification for rapid antimicrobial susceptibility testing (AST) in patients with Gram-negative rod (GNR) bacteremia is compelling; however, supporting empirical evidence is sparse. We investigated the impact of rapid AST for GNR bacteremia on initiation of appropriate antimicrobial therapy, de-escalation of antibiotics, and patient outcomes in a real-world clinical setting.

Materials/methods: We performed a before and after quasi-experimental study from February 2018 to July 2019 at a tertiary hospital to assess the clinical impact of the continuous implementation of the direct VITEK®2 AST method for GNR bacteremia coupled with real-time, electronic isolate-specific de-escalation comments, and antibiotic stewardship program (ASP) intervention during regular working hours. The primary outcome was time from positive blood culture Gram stain to appropriate antibiotic escalation or de-escalation (hazard ratio 1.41; 95% CI 1.07-1.87; p=0.01), with median times of 46.0 (IQR 32.4-64.6) vs 31.8 hours (IQR 23.3-54.9). There was no significant difference in median time to oral antibiotic step-down (56.2 vs 49.3 hours), hospital length-of-stay (96.1 vs 115.2 hours), 30-day all-cause mortality (7.1 vs 4.8%), 7-day acute kidney injury incidence (17.3 vs 13.1%) and 30-day C. difficile infection (2.1 vs 1.8%).

Conclusions: Rapid AST in GNR bacteremia led to improved stewardship measures but did not impact LOS and other clinical patient outcomes. These results highlight that other variables in addition to the timing of AST result contribute to clinical outcomes and warrant further investigation to identify interventions that justify rapid AST implementation.

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Abstract 5851

Outcomes of scaling down vancomycin-resistant Enterococcus surveillance in a tertiary hospital in Singapore
Isaac Low1, Emily Xier Yeo2, Hwang Ching Chan1, Revathi Sridhar1, Dale A. Fisher1,3, Natasha Bagdasarian*1,3

1National University Hospital, Singapore, Singapore, 2Alexandra Hospital, Singapore, Singapore, 3National University of Singapore, Singapore, Singapore

Abstract third-party references: National University Hospital [Singapore]

Background: Infection prevention priorities at National University Hospital, a 1200-bed hospital in Singapore, were re-evaluated due to a growing issue with gram-negative resistance, in the face of relatively stable Vancomycin-resistant Enterococcus (VRE), and Methicillin-resistant staphylococcus aureus rates. This led to a scaling down of active surveillance measures for VRE starting in 2017. This study aims to assess the impact of reducing these VRE surveillance measures.

Materials/methods: A retrospective review was conducted using surveillance data collected between January 2015 and September 2019. The data was divided into three periods: “pre-transition” (January 2015 to December 2016), “transition” (January 2017 till March 2018), and “post-transition” (April 2018 to September 2019). During the transition period, the hospital VRE surveillance policy was amended – contact tracing ceased, and screening criteria were revised. Epidemiological analysis was conducted to compare trends in positive screens and infections. An audit in September 2019 was done to assess compliance to revised surveillance policies.

Results: 233 VRE cases pre- and post-transition were analyzed. After scaling down surveillance measures, the average number of screening samples per month reduced from 359 to 172, but rate of VRE carriers detected through screening increased from 9.29 per 1,000 screens to 18.2 per 1,000 screens. An audit on September 2019 on a sample of 53 hospital-wide VRE screens showed that 12 (22%) screens were inappropriate. There was an increase in VRE infections in the post-transition period: 34 cases pre-transition to 44 post-transition cases post-transition, or from 0.46 to 0.79 cases per 10,000 patient days, rate ratio (RR) 1.70 (95% Confidence Interval (CI) 1.06 to 2.74). However, hospital onset VRE bacteremia remained essentially unchanged: 6 pre-transition cases versus 5 post-transition cases, or 0.08 versus 0.09 per 10,000 patient days, RR 1.09 (CI 0.26 to 4.30).

Conclusions: Scaling down VRE surveillance has improved VRE screening efficiency, though this could be further improved with better compliance to revised screening practices. While no significant increase in VRE bacteremia incidence was noted, further follow up will be required to ensure that rates of VRE infection remain stable after scaling down of VRE surveillance practices.

Presenter email address: natasha_bagdasarian@nuhs.edu.sg
**Evaluation of an investigation-use-only prototype of the BIOFIRE FILMARRAY Blood Culture Identification 2 (BCID2) panel for detection of bacteria, yeast, and antimicrobial resistance markers from positive blood cultures**

Alexandra Vasilakopoulou, Aikaterini Tarpatzi, Sophia Vourli, Paraskevas Tsilikis, Yang Lu, Kristen Holmberg, Usha Spaulding, Kerrin Koch, Alexandra Alvanidi, Nikoletta Koumasi, Spyros Pournaras

1Athens Medical School/Attikon University Hospital, Clinical Microbiology Laboratory, Athens, Greece, 2BioFire Diagnostics LLC, Salt Lake, UT, United States

**Background:** Bacteremia and candidaemia are important causes of mortality in the hospital. Rapid identification of pathogens and resistance genes from positive blood cultures (PBCs) can help in the early selection of appropriate antimicrobial therapy. The Investigation-Use-Only (IUO) BioFire FilmArray Blood Culture Identification 2 (BCID2) Panel (BioFire, Salt Lake City, UT) simultaneously detects 33 pathogens and 10 resistance genes in approximately one hour. The performance of the BCID2 Panel during a prospective evaluation study is compared to standard of care (SoC), as well as to independent PCR comparator assay (compPCR) results.

**Materials/methods:** Eighty-four aerobic and anaerobic de-identified PBCs from 84 patients with at least one gram-negative bacterium or fungus detected by Gram stain were tested using the BCID2 Panel. SoC included culture, standard biochemical identification and antimicrobial susceptibility testing (AST) of pathogens. Aliquots of residual PBCs and isolates were frozen for compPCR testing and discrepancy resolution. Sensitivity/positive percent agreement (PPA) and specificity/negative percent agreement (NPA) were determined for each BCID2 Panel analyte as compared to SoC.

**Results:** The BioFire BCID2 Panel results matched SoC results in 162/171 detections. The nine results that were initially categorized as false-positives were favorably resolved by compPCR as true-positives. Sensitivity/PPA and specificity/NPA of the BCID2 Panel with SoC identification methods were 97.9% and 99.8%, respectively. Twelve out of 13 Candida were identified by the BCID2 Panel (5 Candida albicans, 4 Candida parapsilosis, 2 Candida krusei, 1 Candida tropicalis) while only 1 case of Candida lusitaniae remained unidentified since it is not included in the panel's analytes. Six Enterobacterales species that exhibited resistance to 3rd generation cephalosporins by SoC, were correctly detected as CTX-M positive by the BCID2 Panel. Furthermore, eight Enterobacterales species resistant to carbapenems tested positive for carbapenemase genes (4 KPC, 3 VIM, 1 NDM) by the BCID2 Panel.

**Conclusions:** The BCID2 Panel with its new expanded menu has exhibited high sensitivity and specificity for pathogen identification. Consequently, the BioFire BCID2 Panel is expected to provide rapid and accurate results for key pathogens, as well as important antimicrobial resistance genes. Data presented are from assays that have not been cleared or approved for diagnostic use.

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Clinical impact of metagenomics next-generation sequencing in patients with suspected central nervous system infection: a real-world study

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Background: Previous studies have already shown metagenomics next generation sequencing (mNGS) can enhance pathogen identification in central nervous system (CNS) infection. However, it has not been assessed yet whether mNGS results convinced the clinical practitioners and had impact on clinical decisions in real world.

Materials/methods: We conducted two prospective cohorts of patients with suspected CNS infection at admission, to investigate the impact of the mNGS on diagnosis, management and clinical outcomes. In the mNGS-assisted cohort, a total of 220 patients had their CSF specimens tested in parallel by mNGS and culture, and also other diagnostic tests decided by practitioners. The mNGS results were provided to clinical practitioners in 72 hours, and the results of culture or other laboratory tests were also provided as soon as they came out. In the control cohort, a total of 86 patients had CSF specimens tested in exclusively conventional diagnostic assays, and the patients included were 1:2 paired with NGS-assisted cohort in diagnosis. No intervention was given to either cohorts. Medical records were reviewed retrospectively to collect information including the final diagnosis, initial regimen selection and adjustment, length of stays and clinical outcomes.

Results: Within 81 mNGS positive results, 57 (70.4%) detected pathogens were considered as culprits of CNS infections. All these patients had their diagnosis supported or guided by mNGS results, but only about 1/3 (24, 29.6%) had therapy adjustment guided by mNGS. Within 139 mNGS negative results, 44 (31.7%) supported final diagnosis as non-infection CNS disorders. Only 12 (8.6%) had therapy adjustment based on the negative mNGS results. Compared with the control cohort, the mNGS-assisted cohort showed a shorter median length of stays (18 days vs 23 days, P<0.001), but the mortality was similar (P =0.93).

Conclusions: For suspected CNS infection cases, positive results of mNGS were frequently considered meaningful and had significant impact on diagnosis in practice, but negative results of mNGS were less relied on. The impact on therapy adjustment was limited. The mNGS results contributed to a shorter length of stay, but had no significant impact on patient outcomes.

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Abstract: The role of HPV/STI coinfection in development of CIN is largely a research challenge. The data that our population presents a high prevalence of UU and HR HPV coinfection, especially in women between 26 and 35 years, require further examination.

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A case of sepsis from a novel pathogen: Haematospirillum jordaniae

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Background: We report a case of sepsis from leg cellulitis caused by a novel pathogen Haematospirillum jordaniae

Materials/methods: A 69-year-old Caucasian man was admitted for progressive right leg swelling, pain, and erythema of seven-day duration. Four days before the onset of symptoms, he reported cleaning grass standing in brackish water at a lake. On arrival, he had fever, tachycardia, hypotension and was diagnosed to have sepsis from right leg cellulitis. No open wound or drainage was evident. Laboratory data showed leukocytosis. Blood cultures were drawn, and empiric intravenous vancomycin was initiated. At 48 hours, blood cultures showed no growth, and the antibiotic regimen was de-escalated to intravenous ceftriaxone. The patient continued to improve clinically with this therapy. On hospital day four, the blood cultures unexpectedly returned positive for a slow-growing gram-negative bacterium. The isolate could not be identified by hospital day six and, therefore, was sent to the reference laboratory (LabCorp, Burlington, NC, USA). The patient was discharged before the identification of the isolate, on oral ciprofloxacin and cefadroxil. Genetic sequencing of 16S rRNA identified the strain as Haematospirillum jordaniae. Antibiotic susceptibilities of the organism are shown in Table 1.

Results: Haematospirillum jordaniae, is a novel human pathogen, recognized as a new bacterial genus and species in 2016 by the Centers for Disease Control (CDC). So far, 15 human infections with H. jordaniae have been reported in the literature, with our patient being the 16th case. H. jordaniae is a gram-negative spiral-shaped aerobe in the family of Rhodospirillaceae. It’s a common environmental microbe rarely implicated as a human pathogen, as in our patient. There are concerns that slow-growing gram-negative rods identified in blood culture could be potential bioterrorism agents.

Conclusions: Haematospirillum jordaniae is a novel organism with pathogenic potential. Physicians should be aware of this organism and the need for genetic sequencing to identify this pathogen.

Table 1: Antibiotic susceptibilities of Haematospirillum jordaniae.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC (ug/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>≤ 4</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>&gt; 16</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>16</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>2</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>≤ 1</td>
</tr>
<tr>
<td>Meropenem</td>
<td>4</td>
</tr>
<tr>
<td>Piperacillin- Tazobactam</td>
<td>≤ 8</td>
</tr>
<tr>
<td>Trimethoprim- Sulfas</td>
<td>≤ 2 /38</td>
</tr>
<tr>
<td>Ticarcillin/Clavulanate</td>
<td>≤ 8</td>
</tr>
</tbody>
</table>

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Comparing *Klebsiella pneumoniae* isolates from invasive infections versus carriage in Vietnam: genotypes and capsule types

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**Background:** *Klebsiella pneumoniae* (Kp) is an important cause of community-acquired blood stream infections in Asian countries. This study aims to compare the population structure and capsule types of Kp isolates from patients and healthy people in northern Vietnam.

**Materials/methods:** We characterized Kp isolates from patients with invasive Kp infection admitted to the National Hospital of Tropical Diseases, Vietnam between 2007 and 2011. We included 93 isolates from patients and 110 isolates from throat swabs from healthy volunteers living in the referral area of the hospital. We determined the sequence types by multi-locus sequence typing (MLST) and capsule typing by PCR. Susceptibility testing to antibiotics was performed by disk diffusion.

**Results:** The population structure of Kp in our study population was diverse. CG23 (63/203; 30%) was the most common clone in both invasive and carriage isolates (28/93, 30.1% versus 35/110, 31.8%, p=0.791). CG65 was significantly higher in invasive isolates (17/93, 18.3%, versus 6/110, 5.5%, p=0.004). In both invasive and carriage isolates, the most common capsule types were: K1 (39/203, 19.2%, mainly ST23) and K2 (29/203, 14.3%, multiple STs: ST65, ST86, ST380). We also detected 11 invasive isolates with capsule type K64, which had not been reported before. The resistance to Trimethoprim/Sulfamethoxazole (SXT) was 14.3%, to ciprofloxacin 3.4%, and imipenem 0.5%. We identified 15 (5.4%) ESBL – producing Kp, which included 11 invasive isolates.

**Conclusions:** In general, the population structure of Kp in our study population was diverse, with a remarkably high frequency of clone CG23 in carriage. Capsule type 64 is possibly a novel virulent capsule type but requires confirmation.

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Abstract 5869

**Does herd immunity from conjugate vaccines alter the epidemiology of invasive pneumococcal disease in adults?**

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**Abstract third-party references:** Toronto Invasive Bacterial Diseases Network

**Background:** There are many factors that affect the presentation and severity of pneumococcal disease. Several studies in the pre-conjugate vaccine era demonstrated that organism characteristics, including serotype, are associated with variability in disease presentation and severity. We undertook an analysis of population based surveillance for invasive pneumococcal disease (IPD) to assess whether herd immunity from PCVs will change the presentation and severity of IPD in adults.

**Materials/methods:** The Toronto Invasive Bacterial Diseases Network has performed population-based surveillance for IPD in Toronto and Peel region (pop’n 4.5M) since 1995. All sterile site isolates of *S. pneumoniae* are reported to a central study laboratory, isolates are serotyped, and clinical and vaccination data are collected via patient and physician interview and chart review. Population data are obtained from Statistics Canada. Backwards stepwise logistic regression assessed patient characteristics, illness features, and isolate factors associated with clinical presentation and case fatality.

**Results:** Between 1995 and 2018, 8815 episodes of IPD were identified in adults. Patients infected with PCV10not7 serotypes were younger, more likely male and without underlying illness. Patients with infections due to non-vaccine types were more likely to be immunocompromised. Case fatality in IPD declined from 177/754 in 1995/6 to 113/554 in 2017/8; OR 0.67, 95%CI0.51-0.86, P<.0001 and in all serotype groups (Figure). In multivariable models adjusted for host factors, relative to infections caused by PCV7 serotypes, those caused by PCV10not7 were less likely to be fatal (OR 0.65, 95%CI 0.46-0.91); those caused by PCV13not10 were more likely to be fatal (OR 1.6, 95%CI 1.3-1.9). Bacteremic pneumonia as a proportion of presentations is highest in IPD due to PCV10not7 and PCV13not10 serotypes (85% and 83%, respectively), and lowest in IPD due to non-vaccine serotypes and PCV20not15 (59% and 68%, P<.0001). Meningitis is least common in IPD due to PCV10not7 serotypes (2.6%), and highest in cases due to non-vaccine types and PCV20not15 (9.0% and 8.0%, respectively, P<.0001).

**Conclusions:** In our population, herd immunity from PCVs will result in a higher proportion of adult IPD occurring in immunocompromised cases, and a shift from bacteremic pneumonia to bacteremia without focus and meningitis.

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**Abstract 5873**

**A novel plasmid-mediated RND family efflux pump confers tigecycline resistance in Klebsiella pneumoniae**

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**Background:** Colistin and tigecycline are considered the last-resort antimicrobials, especially for treating infections involving multidrug-resistant *K. pneumoniae*. To date, the plasmid-mediated colistin resistance gene (*mcr*) has spread to a global scale, while it remains unclear the machnisms of tigecycline resistance in *K. pneumoniae* except for the recently reported *tet(X3)* and *tet(X4)*.

**Materials/methods:** A total of 14 tigecycline-resistant *K. pneumoniae* with unknown resistance mechanisms were identified by screening of 199 tigecycline-resistant *K. pneumoniae*. Whole genome sequencing and bioinformatics analysis were performed to investigate the unknown resistance mechanisms. Transconjugants experiment was utilized to test the transferrability of the novel tigecycline resistant plasmid.

**Results:** A novel plasmid-mediated tigecycline resistance gene, an RND family efflux pump pmexAB-oprY, which has never been reported in *K. pneumoniae* was identified. This pump was found to be co-existed with other resistance genes such as *mcr* and *blaNDM*. Interestingly, *pmexAB-oprY* co-existed with *mcr-8* in the same plasmid were identified in 4 strains. Importantly, the plasmid co-harboring *pmexAB-oprY* and *mcr-8* was able to transfer to the recipient strains, leading to a significant increase in the resistance to colistin and tigecycline. Bioinformatics analysis suggested that the *pmexAB-oprY* efflux pump was transferred to *Klebsiella pneumoniae* by *tnS393*.

**Conclusions:** Our findings revealed a novel mechanism in tigecycline-resistant *K. pneumoniae*, highlighting an urgent need for global efforts to control the spread of these resistant genes.

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Impact of safety alerts and warnings on fluoroquinolone and alternative antibiotic use in Colombian outpatient care
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Background: Fluoroquinolones have been associated to several adverse drug effects and have been the object of various FDA warnings and an EMA suspension and restriction report. In Colombia FDA warnings are widely spread among healthcare personnel.

Materials/methods: The objective of this study was to evaluate the impact of FDA and EMA warnings in the outpatient fluoroquinolone use and on the use of alternative antibiotics. Information about dispensation of outpatient antibiotics from 2015-2019 pertaining 3 Colombian public health insurance companies was obtained. Variables collected were: number of formulas, number of patients, DDD (defined daily doses) dispensed and number of patients insured. DHD (DDD/100,000 inhabitants/day) were calculated. Antibiotics were categorized in groups and using monthly data the trends were analyzed. Annual averages were calculated and variability was assessed for fluoroquinolone and alternative outpatient antibiotics.

Results: Figure 1 shows the antibiotic use during the study period. Fluoroquinolone use decreased during the study period while alternative antibiotics had non significant variations. Annual average variability showed a 20% decrease in fluoroquinolone dispensation while the other antibiotics remained stable. However when antibiotic groups were analyzed separately urinary agents, cotrimoxazole and cephalosporins had an upward trend while tetracyclines, macrolides and aminoglycosides dispensation decreased. Penicillin/B lactamse inhibitor combinations increased alongside fluoroquinolone decrease but then the trend reverted.

Conclusions: Safety alerts are a warning system that allows changes in prescription trends as new evidence emerges about drug use. Several warnings regarding fluoroquinolones were edited during the study period and a downward trend in the use of this antibiotic is clear. Alternative outpatient antibiotics surprisingly showed no increase, perhaps owing to antibiotic stewardship that has had an impact in overall antibiotic use, though the use of several groups of antibiotics, particularly those with indication for UTI, increased associated to a decrease in fluoroquinolone use. Warnings and restrictions edited by international agencies seem to have an impact in the use of fluoroquinolones in outpatient care in Colombia.

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Abstract 5878

Characterising the incidence and outcomes of endogenous endophthalmitis in hospitalised patients with Staphylococcus aureus bacteraemia

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Abstract third-party references: The Ohio State University Wexner Medical Center

Background: Staphylococcus aureus bacteraemia (SAB) is a leading cause of morbidity and mortality in the United States with metastatic disease such as endocarditis and septic joint commonly reported. Ocular spread may occur in select circumstances, with recent literature describing Staphylococcus aureus as a major pathogen in cases of bacterial endogenous endophthalmitis (BEE). Given the need for directed therapeutic intervention and serious disease-related complications, this study sought to describe the incidence of SAB BEE and clinical outcomes in affected patients.

Materials/methods: This retrospective descriptive study included patients aged 18-89 years hospitalized with SAB at an academic medical center from November 1, 2011 to August 30, 2019. Prisoners were excluded due to protected status. Individuals with Ophthalmology service consults during a SAB-related admission underwent chart review to elucidate patient demographics, infection characteristics, ocular findings, and medical and surgical therapies provided. The primary outcome of this study was to determine the percentage of BEE cases in the entire SAB population.

Results: During the study time period, 2435 patients with SAB met inclusion criteria with 182 (7.5%) patient encounters paired with Ophthalmology service consultation. An infectious concern was listed as the reason for consult in 60.4% (n=110) of cases, with 21.4% (n=39) for concomitant fungemia as part of a care bundle. Twenty patients were given a diagnosis of BEE representing 11.0% of consults and 0.82% of the SAB population. The BEE cohort was predominately male (85%) with a median age of 51 years (IQR 36-60). Common comorbidities included diabetes mellitus (35%, n=7) and substance abuse disorder (25%, n=5). Median time to Ophthalmology service evaluation following presentation was 1 day (IQR 0-1.5). The primary source of SAB was endocarditis (30%, n=6). Vitreous and/or aqueous cultures were collected on all patients with organism growth in 25% (n=5). All patients received intravitreal and systemic antimicrobials. Five patients underwent vitrectomy and one patient required enucleation.

Conclusions: The incidence of BEE was low in a large cohort of hospitalized patients with SAB (0.82%). Larger studies evaluating BEE in all patients who present with SAB are required to further characterize the impact of this condition.

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Evaluation of in vitro activity of new polymyxin B analog SPR206 against clinical multidrug-, colistin- and tigecycline-resistant Gram-negative bacilli

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Background: SPR206 is a novel polymyxin analog that is active against multi-drug-resistant Gram-negative pathogens such as A. baumannii, P. aeruginosa and Enterobacteriaceae. The aim of the study was to assess activity of SPR206 against a diverse collection of isolates collected in China in 2016-17.

Materials/methods: A contemporaneous (2016-2017) collection of 200 drug-sensitive and multidrug-resistant (MDR), including carbapenem-resistant, tigecycline-resistant, and colistin-resistant clinical isolates of A. baumannii, P. aeruginosa, K. pneumoniae, E. coli, E. cloacae, and S. maltophilia were obtained from 50 centers across China. Isolates were derived from respiratory tract, urine, and blood samples, and purposely selected on a basis of phenotypes, genotypes, and specimen origins. MICs of SPR206 and other antimicrobials were determined and interpreted in accordance with CLSI.

Results: Except for colistin-resistant isolates, SPR206 displayed potent, broad spectrum antimicrobial activity against the Gram-negative clinical isolates tested. All colistin-resistant strains were also resistant to SPR206, with MIC\text{50/90} of 16/128 mg/L vs. 8/128 mg/L for SPR206 and colistin, respectively. SPR206 demonstrated potent activity against colistin-susceptible OXA-producing A. baumannii (MIC\text{50} 0.064/0.125 mg/L), NDM-producing Enterobacteriaceae (MIC\text{50} 0.125/0.25 mg/L), and KPC-2-producing Enterobacteriaceae (MIC\text{50} 0.125/0.5 mg/L). Indeed, SPR206 was the most potent agent assessed, exhibiting 2- to 4-fold greater potency than colistin and polymyxin B against A. baumannii, P. aeruginosa, and Enterobacteriaceae and 16- to 32-fold lower (MIC\text{50/90} 0.064/0.125 mg/L) than tigecycline (MIC\text{50} 2/2 mg/L) for tigecycline-susceptible carbapenem-resistant A. baumannii.

Conclusions: SPR206 showed potent in vitro activity against MDR (carbapenem-resistant and tigecycline-resistant) and non-MDR clinical isolates. Additionally, SPR206 exhibited in vitro antimicrobial activity comparable to or better than colistin and polymyxin B, with MIC\text{50/90} consistently 2- to 4-fold lower. These promising in vitro data suggest SPR206 could be an effective option for multidrug-resistant Gram-negative infections.

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Risk factors for *Clostridioides difficile* infection among hospitalised patients in Brazilian centres: a multi-centre prospective study

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**Abstract third-party references:** Pfizer and bioMerieux

**Background:** *Clostridioides difficile* infection (CDI) is the leading cause of health care-associated diarrhea worldwide. However, risk factors for CDI are not fully understood in Brazil.

**Materials/methods:** Prospective, multicenter study that evaluated the prevalence and risk factors for healthcare associated CDI in 5 Brazilian hospitals. Hospitalized patients >18 years with diarrhea (> 3 soft stools /24 hours) were included. All the samples were tested for glutamate dehydrogenase (GDH) and toxins A and B, using a rapid membrane enzyme immunoassay (*C. difficile Quick Chek Complete*), and for of toxin B gene (*tcdB*), binary toxin gene (*cdtA*), and deletion of 117 nucleotides in the *tcdC* gene, using the real-time polymerase chain reaction (PCR) kit (*Xpert C. difficile test, Cepheid*). Culture was also performed, and the identification was confirmed by matrix-assisted laser desorption/ionization mass spectroscopy (MALDI-TOF/MS). We performed whole genome sequencing (WGS) of the isolates. CDI case was defined as a positive ELISA test for toxins A and B or a positive PCR.

**Results:** From April 2018 to June 2019, 377 samples from 361 patients were included. The overall CDI prevalence was 15%. 94% of CDI patients received antibiotics in the past 3 months. Ceftriaxone, meropenem, vancomycin, piperacillin-tazobactam, ciprofloxacin and clindamycin were the most frequently used antimicrobials. Risk factors for CDI, by univariate analysis, was previous use of ceftriaxone (RR, 2.07; 95% CI, 1.14-3.78), meropenem (RR, 3.41; 95% CI, 1.83-6.35) and onset of diarrhea before hospitalization (RR, 4.38; 95% CI, 1.69-11.2). HIV infection (RR, 0.14; 95% CI, 0.01-1.04) and lung disease (RR, 1.12; 95% CI, 0.01-0.95) were factors of protection. Multivariate analysis identified as independent risk factors for CDI: age (OR, 1.01; 95% CI, 1.00-1.038) and previous use of meropenem (OR, 4.9, 95% CI, 2, 45-10.09). CDI patients had more mucus in stool (OR, 3.2; 95% CI, 1.36-7.57) and left shift with > 20% of rods (OR, 4.07; 95% CI, 1.37-12.04). The classical hypervirulent strains ST1/RT027 and ST11/RT078 were not identified in our cases.

**Conclusions:** The prevalence of CDI is 15% in our study. Independent risk factors associated with CDI in our study were age and previous use of meropenem.

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Population pharmacokinetics of cefazolin in paediatric patients undergoing cardiac surgery

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Background: Limited data exist regarding pharmacokinetics of cefazolin in children undergoing cardiac surgery. This study aimed to describe the population pharmacokinetics of unbound cefazolin concentrations and assess the appropriateness of doses recommended for paediatric patients undergoing cardiac surgery.

Materials/methods: In a prospective observational study, paediatric (<16 years) patients undergoing cardiopulmonary bypass and receiving a 50 mg/kg bolus dose of prophylactic cefazolin, followed by 3-hourly intra-operative 25 mg/kg doses and 8-hourly post-operative 25 mg/kg doses received in the paediatric intensive care unit (PICU) were enrolled. Fourteen serial plasma samples were collected peri and post-operatively and used for measurement of unbound cefazolin concentrations by LC-MS/MS. A non-parametric population pharmacokinetic analysis was performed using Pmetrics® in R, with subsequent Monte-Carlo dosing simulations (n=1000) to estimate the probability of target attainment of 90% time above MIC (fT>MIC). The fractional target attainment (FTA) was estimated based on the EUCAST MIC distribution for Staphylococcus aureus.

Results: Sixty-six patients, including 23 neonates (25 female) with median (IQR) weight 6.2 (3.5 – 16.2) kg, albumin concentration 30 (22-47) g/L and serum creatinine 35.6 (30-97) µmol/L, were enrolled. A two-compartment model adequately described the concentration-time data for unbound cefazolin. Mean (SD) parameter estimates for cefazolin clearance 3.7 (2.2) L/h and 4.7 (3.3) L/h; Vc 6.2 (3.8) L and 7.2 (4.3) L for during surgery and while in the paediatric intensive care unit (PICU), respectively. The dose described in the protocol failed to achieve the 90% fT>MIC target (for MICs <2 mg/L) for FTA for patients <45 kg for up to 30 h after the commencement of surgery. Simulations found all patients receiving a 50 mg/kg bolus dose of prophylactic cefazolin, followed by 3-hourly intra-operative 25 mg/kg doses and 6-hourly post-operative 50 mg/kg doses received in the PICU were adequate to achieve 90% fT>MIC exposure for all patient weight ranges.

Conclusions: A 50 mg/kg bolus dose of prophylactic cefazolin, followed by 3-hourly intra-operative 25 mg/kg doses and 6-hourly post-operative 50 mg/kg doses is appropriate for achievement of target exposures for paediatric patients undergoing cardiopulmonary bypass.

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Abstracts 2020

Abstract 5894

**Delayed diagnosis and increased length of stay in patients requiring hospitalisation with influenza who present without fever**

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**Background:** Case definitions for influenza-like illness typically include fever. However, many patients who require hospitalisation with influenza will present without fever as part of their clinical syndrome. While the recently updated Infectious Diseases Society of America guidelines for seasonal influenza no longer require fever as part of their testing algorithm, the impact of fever or lack of fever on clinical decision-making and patient outcomes has not been studied.

**Materials/methods:** We conducted a retrospective review of adult patients admitted to our tertiary health service with laboratory-confirmed influenza within 72 hours of arrival between April 2016 and June 2019 who had been recruited as part of local influenza surveillance. Demographic and symptom data were linked to hospital database extracts containing patient comorbidities, diagnoses, and emergency department (ED) observations. Data were analysed using Pearson’s Chi-squared test, Wilcoxon rank-sum test, and multivariate logistic regression.

**Results:** Of 578 patients meeting inclusion criteria, 359 (62.1%) had fever, defined as a temperature greater than or equal to 37.8°Celsius, while in the ED.

Patients without fever had lower rates of testing for influenza in the ED (64.8% vs 77.2%, p = 0.002) and increased hospital length of stay (median 2.4 days, IQR 1.3 - 4.5) compared to those with fever (median 1.9 days, IQR 1.0-4.0).

Fever was less likely in individuals with age greater than 65 years (adjusted [a] OR: 0.37, 95% CI [0.25, 0.54]), a non-respiratory presentation (aOR: 0.44, 95% CI [0.25 - 0.76]), Influenza B infection (aOR: 0.45, 95% CI [0.29,0.72]), symptom duration of greater than two days (aOR: 0.53, 95% CI [0.36, 0.78]), chronic lung disease (aOR: 0.55, 95%CI [0.37, 0.81]), and female sex (aOR: 0.68, 95% CI [0.47, 0.98]).

Patients without fever were less likely to receive antiviral treatment (55.7% vs 65.6%, p=0.02) and more likely die in hospital (3.2% vs 0.6%, p=0.03) although the difference in mortality was not significant after adjustment for age and comorbidities.

**Conclusions:** Using case definitions including fever to identify patients with influenza in the hospital setting may lead to delays in diagnosis and poorer outcomes including lower rates of antiviral treatment and longer length of stay.

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Quantitative detection of bacterial resistance by meropenem hydrolysis using MALDI-TOF MS

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Background: Carbapenem resistant bacteria (CRB) are considered the main problem, by the World Health Organization, regarding antimicrobial resistance. As the main resistance mechanism of CRB in Brazil is carbapenemase production, such as KPC and NDM, the development of rapid methods to detect these determinants of resistance is necessary. The aim of this study was to develop a quantitative methodology to rapidly detect bacterial resistance to meropenem by MALDI-TOF/MS among Klebsiella pneumoniae.

Materials/methods: Thirty-three isolates carrying blaKPC or blaNDM gene and 25 isolates without carbapenemase genes were evaluated. Detection of carbapenemase genes was performed by High Resolution Melting-PCR. Meropenem minimum inhibitory concentration (MIC) was determined for all isolates. The hydrolysis test was performed as follows: a 1 µL loopful of bacteria was suspended in a meropenem solution (1 mg/mL); the suspension was incubated at 37°C for 2 hours, centrifuged and the supernatant (1 µL) was spotted onto a MALDI-TOF/MS target plate; the spot was dried and overlaid with 1 µL of HCCA matrix. Spectra were obtained by a Microflex LT mass spectrometer (Bruker Daltonics) and peak analysis was performed using flexAnalysis 3.4. Intensities of the peaks at 384 m/z (intact meropenem molecule) and at 401 m/z (matrix) were compared to evaluate meropenem hydrolysis. Hydrolysis index (HI) was calculated as follows: HI = (Peak intensity 384 Test / Peak intensity 401 Test) / (Peak intensity 384 Control / Peak intensity 401 Control). HI close to zero indicates maximum hydrolysis; HI close to 1 indicates minimum hydrolysis. Escherichia coli ATCC 25922 was used as control (HI = 1).

Results: Twenty-three isolates were positive for blaKPC (KPC) and 10 for blaNDM (NDM) with MICs varying from 16 to >1 28 µg/mL; 12 isolates negative for carbapenemase genes had MICs ≤0.5 µg/mL (NegS) and 13 had MICs from 4 to 16 µg/mL (NegNS). All isolates with carbapenemase genes presented a HI <0.5 and the isolates without carbapenemase genes (NegS and NegNS) presented a HI >0.5 (Figure 1).

Conclusions: These preliminary results indicate that this technique is a promising quantitative method to detect meropenem resistance due to carbapenemase production.

Figure 1. Hydrolysis index of isolates according to carbapenemase presence and MIC.

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**Abstract 5897**

**Hepatitis B virus epidemiology among chronic kidney disease patients under haemodialysis**

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**Background:** Hepatitis B virus (HBV) can be transmitted through the parenteral route and the group of patients with chronic kidney disease (CKD) undergoing hemodialysis (HD) treatment is more vulnerable to infection due to increased exposure to invasive procedures. The objective of this study was to evaluate the prevalence of HBV infection markers in serum samples from patients with CKD in HD from the Southeast region of Brazil.

**Materials/methods:** A total of 644 patients with CKD underwent regular HD in dialysis units located in Rio de Janeiro State were recruited from 2013 to 2017. Samples were tested for HBsAg, anti-HBs and anti-HBc using commercial immunoenzymatic assays. HBsAg reactive or anti-HBc isolated samples were subjected to Semi-Nested PCR for HBV surface/polymerase gene amplification and nucleotide sequencing to determine genotypes and resistance to antivirals.

**Results:** Mean age was 50.3 ± 15.2 years and most of them was male (346/644). The prevalence of current infection (HBsAg +), previous contact (anti-HBc +), immunity for hepatitis B (anti-HBs +), and susceptibility to HBV (anti-HBc- / anti-HBs- / HBsAg-) were 5.9%, 36.0%, 57.3%, 34.3%, respectively. HBV DNA was detected in 36.8% (14/38) of the HBsAg reactive individuals indicating infection with active replication. Anti-HBc isolated was found in 18 individuals, where 6 had HBV DNA indicating 0.94% prevalence of occult HBV infection (OBI). We found a higher prevalence of genotype A (76.4%) followed by genotype D (23.5%) regardless of infection characteristic (current infection or OBI). Isolates of HBV were phylogenetically close to isolates from hemodialysis patients of Brazil, as well as some strains from the same unit had homology above 90%. All subjects in the study did not present resistance mutations to lamivudine, tenofovir, entecavir, adefovir and telbivudine.

**Conclusions:** We found high prevalence of HBV infection and low number of individuals immune to infection indicating the need for vaccination in this group. There was a higher prevalence of genotype A and the presence of closely related strains in the same dialysis unit, which reinforces the need for laboratory monitoring for hepatitis B among hemodialysis patients.

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The DECISIVE study: defining beta-lactam concentration in intensive care unit patients - pharmacokinetics of cefepime, meropenem and piperacillin in critically ill patients across Malaysian intensive care units

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Abstract third-party references: Supported by Malaysian Fundamental Research Grant Scheme [FRGS16-048-0547], Supported by Australian National Health & Medical Research Council (NHMRC) REDUCE - Centre of Research Excellence (CRE)

Background: Critically ill patients often demonstrate extreme physiological changes. Conventional antibiotic dosing may lead to sub-therapeutic exposure and therapeutic failure.

Materials/methods: This is a preliminary report from the DECISIVE Study, a prospective, multi-centre pharmacokinetic (PK) study aiming to describe the PK of seven beta-lactam antibiotics and the pharmacokinetic/pharmacodynamic (PK/PD) target attainment of critically ill patients across three Malaysian ICUs. Serial blood samples were collected across seven predetermined time-points. Two PK/PD targets were tested; achieving trough concentrations of 1xECOFF (conventional target) and 4xECOFF (aggressive target) of Pseudomonas aeruginosa. PK parameters were estimated using non-compartmental method. Univariate and multivariate analyses were applied.

Results: Ninety-five patients were included; 51 received piperacillin/tazobactam, 33 received meropenem and 11 received cefepime. The median 24-hour antibiotic dose for piperacillin/tazobactam was 18.0 g [9.0-18.0], 3.0 g [2.0-4.0] for meropenem, and 6.0 g [2.0-6.0] for cefepime. The median age was 56.5 years, body mass index was 23.2 kg/m², serum albumin was 24.0 g/L, and the estimated Cockcroft-Gault creatinine clearance (CLcr) was 65.2 mL/min. The median APACHE II and SOFA scores on admission were 14.0 and 6.0, respectively. Twenty-four patients (25.3%) underwent surgery 24 hours prior to study inclusion. Beta-lactam concentrations were highly-variable with coefficient of variation of ≥65%. The volume of distribution (Vd) and clearance (CL) of piperacillin were 0.42 L/kg [0.13-0.93] and 0.18 L/hr/kg [0.01-0.47], 0.37 L/kg [0.17-0.84] and 0.14 L/hr/kg [0.04-0.57] for meropenem, and 0.37 L/kg [0.16-0.67] and 0.11 L/hr/kg [0.03-0.39] for cefepime, respectively. Older age was significantly associated with increasing Vd and CLcr, and higher CLcr was significantly associated with faster CL, for all beta-lactam antibiotics. Additionally, higher serum albumin and recent surgery were significantly associated with higher CL of piperacillin and meropenem. Eighty-two (86.3%) and 55 (57.9%) patients achieved the conventional and aggressive PK/PD targets, respectively, and they tend to be older, with slower CLcr and receiving continuous infusion. Based on the most parsimonious logistic regression model, higher CLcr and intermittent infusion were significant predictors of sub-optimal target attainment for both PK/PD targets. The 30-day mortality was 33.7%.

Conclusions: Beta-lactam antibiotic concentrations were highly-variable in the ICU leading to variable PK/PD target attainment in this patient cohort.

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Abstract 5907

Standardization of a pncA gene complementation in Mycobacterium tuberculosis pncA-knockout: tool for the study of the relationship between mutations in pncA and phenotypic parameters

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Background: Mutations in the pncA gene, which encode pyrazinamidase, are the major cause of resistance to pyrazinamide (PZA), but there are alternative mechanisms that also promote resistance. The objective of the study was to standardize the pncA gene complementation in Mycobacterium tuberculosis H37Rv pncA-knockout to evaluate the effect of mutations in the pncA, in a scenario controlled by the genetic variability of clinical isolates.

Materials/methods: Strains complemented with pncA genes wild type and mutant were generated through the pNIT-1 expression system to evaluate pyrazinoic acid (POA) production through quantitative Wayne test, pncA gene expression level and PZA susceptibility under non-induced and induced conditions. Also, these parameters were evaluated to the clinical isolates where we identified the mutations D49N, H51R, G78C, and F94L.

Results: The pNIT-pncA expression system restored the susceptible phenotype of the pncA-knockout strain. The basal expression levels of wild type and mutants pncA were constant and similar to that H37Rv strain. The pncA wild type complemented strain, non-induced, showed POA production and Minimum Inhibitory Concentration of PZA similar to H37Rv (0.6 uM and 100 ug/mL, respectively). Although the overexpression of pncA wild type in the complemented strain, that was nine times greater than H37Rv strain, and it promoted higher production of POA than H37Rv strain (3 uM), the susceptibility was same. By contrast, the mutant pncA complemented strains non-induced did not produce POA, but in the induced condition the F94L and G78C complemented strains produced POA (0.8 and 1.4 uM, respectively); however, they were lowest than pncA wild type complemented strain-induced. Additionally, these strains were resistant in both conditions. The clinical isolates with the respective mutations were resistant (>1000 ug/mL), and no produced POA, except the clinical isolate with F94L mutation (0.5 uM).

Conclusions: The complementation of the pncA-knockout strain with the pncA wild type, through pNIT expression system, allowed the restoration of the susceptible phenotype, and the D49N, H51R, G78C and F94L mutations in the complemented strains really conferred resistance to PZA, and we verified that the overexpression of these mutants allowed to verify the total or partial loss their enzymatic function of the mutant pyrazinamidase.

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Abstract 5914

**A simple cleaning intervention to prevent transmission of carbapenemase-producing Enterobacterales from hospital sinks**

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**Background:** A prolonged outbreak of carbapenemase-producing *Serratia marcescens* (CPSM) was identified in our quaternary healthcare centre over a two-year period from 2015-2017. A reservoir of IMP-4-producing *S. marcescens* in sink drains of clinical hand basins (CHB) was implicated in propagating transmission, supported by evidence from whole-genome sequencing (WGS). We assessed the impact of manual bioburden reduction intervention on further transmission of CPSM.

**Materials/methods:** Environmental sampling of frequently touched wet and dry areas around CPSM clinical cases was undertaken to identify potential reservoirs and transmission pathways. After identifying CHB as a source of CPSM, a widespread annual CHB cleaning intervention involving manual scrubbing of sink drains and the proximal pipes was implemented, with pre- and post-intervention point prevalence surveys (PPS) of CHB drains performed to assess for CPSM colonisation. Surveillance for subsequent transmission was conducted through weekly screening of patients and annual screening of CHB in transmission areas, and six-monthly whole-hospital PPS of patients. All CPSM isolates were assessed by WGS.

**Results:** A total of six patients were newly identified with CPSM from 2015-2017 (4.3 transmission events per 100,000 surveillance bed days [SBD]; 95% CI 1.6–9.4). All clinical CPSM isolates were linked to CHB isolates by WGS. The CHB cleaning intervention resulted in a reduction in CHB colonisation with CPSM in transmission areas from 72% colonisation to 28% (ARR 0.44; 95% CI 0.25–0.63). A single further clinical case of CPSM linked to the CHB isolates was detected over two years of surveillance from 2017-2019 following the implementation of the annual CHB cleaning program (0.7 transmissions per 100,000 SBD; 95% CI 0.0–3.9). No transmission events occurred as a direct result of the cleaning intervention.

**Conclusions:** A simple intervention targeted at reducing the biological burden of CPSM in CHB drains at regular intervals was effective in preventing transmission of carbapenemase-producing Enterobacterales from the hospital environment to patients over a prolonged period of intensive surveillance. This highlights the importance of detailed cleaning for controlling the spread of multidrug-resistant organisms from healthcare environments.

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Detection of high rates of HIV-seropositivity in urban university hospital emergency department
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**Background:** With the ongoing public health impact of undetected human immunodeficiency virus (HIV), routine universal screening of HIV in the emergency department may identify populations who are not getting tested in other settings. The objectives of this analysis were to evaluate opt-out HIV screening and determine the number of new and known HIV-positive individuals out-of-care at an academic emergency department in Sacramento, California.

**Materials/methods:** From November 27, 2018 through October 31, 2019, electronic medical record (EMR) based HIV screening was implemented in a quaternary care emergency department in Northern California. EMR best practice alerts (BPA) were developed based on a combination of local and CDC guidelines and screening for persons aged 18-64 years (excluding persons with a confirmatory HIV+ test in their medical record) was implemented using a 4th generation HIV antigen/antibody assay. Upon notification of a positive test result through EMR, a patient navigator is responsible for coordinating an in-person notification/counseling and linking patients to receive medical follow-up.

**Results:** Over a period of 11 months, 14,068 individuals were tested for HIV, resulting in 22 (22%) new HIV diagnoses, of whom 17 (77%) were successfully linked to care. Universal screening also identified 23 out-of-care for >12-months HIV+ individuals of whom 14 (61%) were successfully relinked to care. Testing initiated either by physician on the basis of perceived HIV risk behaviors and/or clinical manifestation or through the screening program yielded an HIV seroprevalence of 0.9% with 29 percent self-reported history of intravenous drug use (IVDU).

**Conclusions:** The emergency department (ED) has unfortunately become the primary medical provider for HIV-at-risk populations. ED setting has been demonstrated to be effective for HIV screening. One of the major commonly identified risk factors for HIV is men having sex with other men (MSM), but with the rising opioid epidemic IVOD has been noted to contribute to an increase of new HIV infections thus contributing to the epidemic of viral hepatitis. Screening based on commonly known risk factors, such as MSM, captures missed opportunities to identify HIV-seropositive patients. The high seroprevalence in northern California is uncommon and indicates that HIV-1 infection is widespread in this population.

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Heuristic identification of carbapenemase-encoding plasmids by short-read sequencing data: validation by ONT long-read hybrid assembly of a large Singaporean carbapenem-resistant Enterobacteriaceae collection

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Background: Alike the previous rapid global spread of extended-spectrum β-lactamases (ESBLs), transmission of carbapenem resistance across Enterobacteriaceae strains is facilitated by horizontal-gene-transmission of carbapenemase-encoding plasmids. Plasmid structures are difficult to resolve by short-read sequencing – a recent study benchmarking short-read plasmid analysis tools suggested that the resolution of large plasmids of >50kbp in size remains a challenge (Arredondo-Alonso et al., 2017). Long-read sequencing (e.g. PacBio and Oxford Nanopore Technologies (ONT)) is able to address the difficulty in plasmid assembly but is currently not as widely available as short-read sequencing within clinical/research institutions. Our study presents a heuristic short-read pipeline for plasmid identification based on the existing Plasmidseeker tool (Roosaare et al., 2018).

Materials/methods: We tested our pipeline on MiSeq short-read sequence data for 1251 Singaporean CPE isolates, of which ~700 have been sequenced using ONT. Best-match plasmid identities were assigned from carbapenemase-specific reference plasmid databases, based on query identity of the carbapenemase-bearing short-read assembly contig (qcov), and isolate kmer coverage of the reference plasmid (kcov). Plasmid predictions were validated against ONT hybrid assemblies based on sequence and replicon/antimicrobial resistance (AMR) gene profile similarity, and plasmid-matching rules were fine-tuned accordingly.

Results: Best-match carbapenemase-encoding plasmid identities were assigned for 487/541 (90.0%) blaNDM, 500/535 (93.5%) blaKPC and 60/150 (40%) OXA-48-family isolates. Preliminary validation of blaNDM plasmid calls indicate 391/409 (95.6%) are in agreement with actual structures based on a Mash distance threshold of 0.01; replicon and AMR gene profiles were also largely concordant. Difficulties in distinguishing between similar reference structures were observed and addressed by clustering reference plasmids based on kmer similarity. The blaNDM plasmid pNDM-ECS01 (n=305) and a novel 71,861bp blaKPC plasmid (n=344) were predominant in our dataset.

Conclusions: While our short-read pipeline does not produce the exact plasmid structures and is highly dependent on the coverage of existing databases, it is nonetheless able to assign best-match identities that are functionally representative of the actual isolate plasmids, allowing the epidemiological tracing of specific plasmid structures and their associated AMR genes. Coverage gaps in the pipeline will be addressed with the increasing availability of novel complete plasmid structures through long-read assembly.

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Abstract 5918

**Epidemiology of Neisseria gonorrhoeae antimicrobial resistance and evaluation of alternative antibiotics**

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**Background:** Development of resistance in *Neisseria gonorrhoeae* to ceftriaxone monotherapy or ceftriaxone plus azithromycin dual therapy is a global public health concern, alternative clinically approved antimicrobials are urgently needed for future alternative therapies. Resistance against ceftriaxone is related to mosaic penA alleles. In addition, penicillinase-producing *N. gonorrhoeae* (PPNG) expressing the TEM-135 β-lactamase variant are alarming as this variant requires only a single amino acid substitution to develop into an extended-spectrum β-lactamase (ESBL). In this study, we analyzed the trend in antimicrobial susceptibility of clinical isolates from Hangzhou, China, over the period 2015-2017 to previous and current antimicrobial therapies and to several alternative clinically approved antimicrobials.

**Materials/methods:** The antimicrobial susceptibility of in total 379 clinical isolates was determined by the agar dilution method. Phylogenetic and clustering analysis was determined using porB and tbpB sequences. PPNG isolates were investigated by nitrocefin test and representative isolates were investigated by qPCR, western blot analysis and in vivo β-lactamase activity assays.

**Results:** Ceftriaxone resistance, decreased susceptibility to ceftriaxone and azithromycin resistance were observed in 3%, 17% and 21% of the isolates and resistance levels to ceftriaxone and azithromycin increased over the study period. Phylogenetic and cluster analysis showed the emergence and expansion in 2017 of a clonally related cluster containing strains with high abundance of decreased susceptibility to ceftriaxone, which was related to the presence of the mosaic penA allele X. Screening of alternative antimicrobials identified tigecycline and ertapenem as antibiotics with excellent activity and limited cross-resistance with previously used antibiotics. Finally, PPNG isolates consisted of three major clusters, and isolates of the Asian plasmid/blaTEM-135 cluster showed the highest penicillin resistance and β-lactamase activity, which was explained by higher blaTEM gene expression and higher TEM stability.

**Conclusions:** Resistance levels to ceftriaxone, which was related to presence of the mosaic penA allele X, were rising over the study period. Furthermore, we identified tigecycline and ertapenem as possible alternative clinically approved antimicrobials for future therapies. Finally, we showed that the blaTEM-135 gene is commonly present on the Asian plasmid in PPNG isolates from Hangzhou, posing major treat to the development of ESBLs in *N. gonorrhoeae*.

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Abstract 5926

Analysis of outcomes by geographic region of enrolment in STRIVE, the phase II of rezafungin for the treatment of candidemia and invasive candidiasis

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Background: Rezafungin is a novel echinocandin in Phase 3 development. STRIVE (NCT02734862) is the global, Phase 2 trial of rezafungin once-weekly for treatment of candidemia and/or IC versus standard of care. Results of STRIVE were evaluated by geographic region to assess for differences in the complete trial population.

Materials/methods: Data were stratified by region of enrollment (EU vs North America [NA]) and analysed for differences in patient demographics and baseline characteristics, treatment patterns, and efficacy outcomes.

Results: Patients enrolled in EU (N=131) were older than in NA (N=76) (mean, 64 vs 52 years, respectively) and were predominantly male (61.1%) and White (93.1%). The NA population was 50% male and comprised 23.7% Black or African-American patients. On average, NA patients weighed more and had higher BMI (+2.3 kg/m²).

The same leading Candida species were isolated at baseline in both regions but with differing distribution. Candida albicans comprised 44% of EU isolates, and proportions of Candida parapsilosis, Candida glabrata, and Candida tropicalis were similar (13-18%). In NA, C. albicans accounted for 52% of isolates, followed by 25% C. glabrata and 7% each for C. parapsilosis and C. tropicalis.

In both regions, 55% of patients received 8-14 days of IV treatment; 27% of EU patients received >14 days versus 18% in NA. Fewer patients in EU were switched to oral step-down (24.4% vs 42.7% NA). The NA population had a higher proportion of patients with IC (26.3% vs 17.6% EU).

Outcomes were comparable between regions except for higher rates of overall success in EU patients treated with rezafungin 400 mg in Week 1 followed by 200 mg once weekly, compared with the NA cohort (Table).

Conclusions: The Phase 2 STRIVE trial demonstrated few differences by region in demographic and baseline characteristics. The EU population was slightly older, and NA patients were generally heavier. Non-albicans species were predominant in the EU and comprised almost half of the NA isolates. Efficacy by region showed no consistent trends, although interpretation of efficacy-related differences are limited by group size. Results of this analysis may inform future evaluation of data from the rezafungin clinical trial program.

<table>
<thead>
<tr>
<th>Geographic Region of Enrollment</th>
<th>Overall Response - Success at Day 14, % (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rezafungin 400mg Wk1/400mg QWk</td>
</tr>
<tr>
<td>Europe</td>
<td>60.4 (32/53)</td>
</tr>
<tr>
<td>North America</td>
<td>60.9 (14/23)</td>
</tr>
</tbody>
</table>

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Influence of biofilm formation on clinical outcome and their associated genetic virulence factors in *Klebsiella pneumoniae* bloodstream infections in India

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**Background:** *Klebsiella pneumoniae* is one of the leading causes of nosocomial infections. Carbapenem-resistant (CR) *K. pneumoniae* are on the rise in India. The biofilm forming ability of *K. pneumoniae* further complicates the patient management. There is still a knowledge gap on association of biofilm formation with patient outcome and carbapenem susceptibility, which is investigated in the present study.

**Materials/methods:** *K. pneumoniae* isolates from patients with blood stream infections admitted in critical care units with catheters were included. *K. pneumoniae* (n = 18) were tested for antimicrobial susceptibility as recommended by CLSI 2019 and subjected to 96-well titre plate biofilm formation assay. Based on optical density at 570 nm isolates were graded as strong, moderate and weak biofilm formers. Strong biofilm formers were subjected to whole genome sequencing with IonTorrent PGM. Core genome phylogeny using Roary and RaxML, and association of known biofilm virulence genes with other virulence genes by cytoscape network modelling were performed. Biofilm formation was compared for their association with the carbapenem susceptibility and outcome of the patients. Statistical significance, correlations and graphical representation were performed using SPSS v23.0 and Prism v8.2.0.

**Results:** Infections by stronger biofilm forming pathogen significantly (P<0.05) resulted in fewer ‘average days alive’ for the patient (4.43), in comparison to moderate (4.63) and weak biofilm formers (5.66). Among the strong, moderate and weak biofilm formers, 100%, 75% and 66% were carbapenem resistant respectively, thereby showing a positive correlation. Gene network model revealed close association of biofilm genes allS, iutA and rmpA2 with other genetic virulence factors. These genes might significantly contribute to the biofilm mechanism. Further analysis, also revealed association of CR gene, *bla*NDM with biofilm factors.

**Conclusions:** Biofilm forming ability of clinical *K. pneumoniae* isolates had a significant association with the morbidity/mortality. The strong biofilm formation significantly reduced the number of days alive for the patient (5.66 to 4.43). These results highlight the importance of biofilm testing, especially for nosocomial pathogens which are difficult to clear in vivo. As *K. pneumoniae* nosocomial infections require additional treatment which might effectively help in improving the patient outcome.
Abstracts 2020

**A M R genes and plasmids**

Figure 1:
A) Depicting biofilm formation efficiency of *K. pneumoniae* from bloodstream infections (left Y axis), and length of hospital stay from the date of admission (right Y axis). L1 depicts the cut off for weak biofilm formers, and L2 the cut off for moderate and strong biofilm formers, respectively.

B) Core phylogeny of *K. pneumoniae* depicting distinct AMR genes and plasmid profile for the two separate clones.

C) Comparison of strong biofilm study *K. pneumoniae* with known global-carbapenem resistant clones. Showing match between Indian and global resistant isolates.

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Abstract 5935

Clinical implementation of routine whole genome sequencing for hospital infection control of multidrug-resistant pathogens

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Background: Every year ~200,000 Australians experience a healthcare-associated infection (HAI). The impact is exacerbated by increasing rates of antibiotic resistance. There is limited capacity in clinical laboratories to routinely track pathogens causing HAI in real-time or to detect cross-transmission events. We established a pre-emptive whole-genome sequencing (WGS)-based surveillance program to identify clustering of clinically relevant multi-drug resistant (MDR) bacteria, suggesting in-hospital transmission, before outbreaks can become established.

Materials/methods: We prospectively collected methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant enterococci (VRE), carbapenem-resistant Acinetobacter baumannii (CRAB), extended-spectrum beta-lactamase (ESBL) and carbapenemase-producing Enterobacterales (CPE) isolated from sterile sites or screening specimens across three tertiary referral hospitals (2 adult, 1 paediatric). Whole genome sequencing (Illumina NextSeq) was used to determine in silico multi-locus sequence typing (MSLT) and resistance gene profiling via a bespoke genomic analysis pipeline. Putative transmission events were identified by comparison of core genome single nucleotide variants (SNVs). Combined with automated transfer of clinical meta-data from the laboratory information system, the genomic analyses were collated into hospital- and pathogen-specific reports and distributed to infection control teams at least monthly.

Results: Over two years (November 2017 to November 2019) more than 1700 MDR isolates were sequenced. This included MDR gram-negative bacilli (n=142 CPE, n=868 ESBL and n=27 other), MRSA (n=477) and VRE (n=249). Core genome SNV data identified that 21% of isolates formed 51 distinct clusters that were not identifiable using traditional surveillance techniques. Of 51 clusters, 18 were contained to one of three target hospitals suggesting ongoing transmission within the clinical environment. One cluster was related to a previous outbreak of CRAB, thought to have been resolved, prompting a targeted engineering response preventing further transmission. The remaining 33 clusters represented inter-hospital transmission events or strains circulating in the community acquired prior to hospital admission. In one hospital, diversity of non-multi-resistant MRSA strains and the lack of hospital transmission enabled changes to infection control policy. The effectiveness of this policy change will be assessed prospectively by ongoing WGS.

Conclusions: Implementation of routine WGS for MDR pathogens in clinical laboratories is feasible and reveals previously unknown transmission events, which can enable targeted infection control responses.

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Abstract 5939

An agent-based simulation of hand hygiene and contact precautions for the control of Clostridioides difficile in an intensive care unit setting

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Abstract third-party references: US Centers for Disease Control and Prevention

Background: Clostridium difficile (CD) is one of the most common nosocomial infections. Strict adherence to hand hygiene (HH) and contact precautions (CP) by healthcare providers (HCP) is believed to be critical to controlling CD spread, particularly in hospital intensive care units (ICUs).

Materials/methods: We collected data from two ICUs (cardiovascular and medical/surgical) over several weeks each, using wireless sensors to track HCP movements, patient and room object interactions, and HH adherence, and daily microbiological cultures of patients, objects, and HCP hands. We then used these data to design and parameterize a high-fidelity agent-based simulation of nosocomial CD transmission in a single 20-bed ICU. The model was calibrated against local and published data and validated internally and externally.

Scenarios exploring the full range of HCP HH compliance were simulated 100 times each over a one-year period. Additional scenarios were performed exploring HH compliance based on the intensity of the HCP room visit, defined by the combination of time spent near the patient and number of patient/object touches per visit. Scenarios employing universal CP were also explored. Model output was expressed as CD infections per 10,000 patient-days (PD).

Results: When overall HH adherence was dropped below base-case values established from data collection, CD acquisition and infection rates increased rapidly; alternatively, raising HH adherence brought relatively little return (Figure). Interestingly, raising HH for visits of low intensity (no near-patient time/no touches) had the most pronounced effect, likely because these are the most frequent HCP visits. Implementing universal contact precautions (CP), without changing HH adherence from baseline, had a moderate impact on outcomes (mean 8.4 vs. 14.5 CD infections/10,000 PD).

Conclusions: Our model results suggest that, although typical overall HH rates may seem suboptimal, improving them may have a limited impact on CD infection rates, even when improvement is focused on high-intensity visits. At the same time, universal CP can have a moderate but incomplete effect on CD infections. This highly granular simulation can be used to explore the costs and benefits of infection control strategies otherwise difficult to assess in real-world settings, providing valuable input for targeting specific interventions to control CD transmission.

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**Bacteriological study of kidney stones**

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**Background:** Urolithiasis remains a significant cause of morbidity and mortality due to the high rate of recurrent urinary tract infections and the progressive deterioration of renal function. Although the pathophysiological mechanisms underlying the formation of kidney stones (KS) are not yet fully understood, some studies indicate the possible involvement of bacteria in this process.

**Materials/methods:** Prospective study of KS surgically extracted by nephrolithotomy over a 1-year period [from 1 November 2018 to 31 October 2019]. The chemical composition of KS was obtained by infrared spectroscopy. After 18 to 24 hours of incubation in 5 mL of thioglycolate broth, the bacteriological study of previously macerated KS was done by a quantitative sub-culture in blood agar and MacConkey agar [cutoff ≥ 10^5 CFU/mL]. Bacterial identification was performed by MALDI-TOF mass spectrometry.

**Results:** 75 KS from individuals with a mean age of 52 years were studied, 43% [n=32] belonging to males and 57% [n=43] to females. The chemical composition of KS included calcium oxalate, calcium phosphate, uric acid, magnesium ammonium phosphate [struvite], apatite and cystine, and most had a mixed composition. The bacteriological study of KS was sterile in 40% [n=30] and revealed bacterial growth above the cutoff in 60% [n=45], 45% [n=34] demonstrating a monomicrobial culture and 15% [n=11] a polymicrobial culture. In decreasing order of prevalence, the isolates were Enterobacterales, Staphylococcus spp. [mostly coagulase-negative staphylococci], Enterococcus spp., Pseudomonas aeruginosa and Streptococcus spp. [all viridans group streptococci].

**Conclusions:** The bacteriological study of KS allowed the isolation of well-recognized pathogens in a significant proportion of cases, particularly *Escherichia coli* and urease-producing bacteria [such as *Staphylococcus* spp., *Klebsiella* spp., *Proteus* spp. and *Pseudomonas* spp.]. Since these can survive in the interstices of KS [where antimicrobial agents have poor penetration], the bacteriological study of KS seems to provide valuable information that is representative of the renal pelvis; thus, it is possible to initiate targeted antimicrobial therapy for urinary tract sterilization and for prevention of recurrence or re-growth of residual KS after initial removal and treatment of postoperative infections.

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A rare case of paragonimiasis infected by Paragonimus ohirai
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Background: Paragonimiasis is a zoonotic disease caused by lung flukes of the genus Paragonimus. Humans usually acquire infection via consumption of undercooked or raw freshwater crab or crayfish. More than 50 species of Paragonimus have been described and the best known is P. westermani. The P. ohirai is phylogenetically distinct from the well-known P. westermani. It is known from Japan, Korea and China with very occasional human infections reports. Here we report a rare case of P. ohirai infection simultaneously affecting pulmonary, hand and chest wall.

Case report: A 17-year-old girl from Zhejiang Province, China, presented with right chest pain and dry cough for 2 months. She was a high school student, and denied a history of hemoptysis, fevers, appetite suppression, or weight loss. There were no unusual food or animal exposures. The biological examination showed a hypereosinophilia (8,890 cells/mm3) and a raised C-reactive protein and ESR. The IgE was normal. Chest computed tomography (CT) revealed multiple migratory pulmonary infiltrates, cavities and pleural effusion. Sputa for mycobacterial, T-SPOT. TB, serology for Cryptococcus, all were negative. In the course of disease, she developed subcutaneous swellings in left index finger. She received a surgical drainage of left index finger and antibiotics treatment, but the chest CT showed no improvement. Even worse she presented with subcutaneous swelling in left palm and right chest wall, then she was referred to our hospital. We performed lung and chest wall biopsies, and the anatomopathology revealed large amounts of eosinophils. We could not observe characteristic parasite eggs in stool, sputum, bronchoalvelolar lavage fluid, lung tissue or chest wall tissue. The antibodies against P. westermani was negative. However, polymerase chain reaction (PCR) on the chest wall tissue was positive for P. ohirai. The girl received 4 course of praziquantel therapy, with rapid resolution of symptomatology and a decrease of eosinophil count. A follow-up chest CT at 2 months after treatment revealed normal.

Conclusions: To date, P. ohirai has not been observed in human infections, and this is the first report of Paragonimiasis infected by Paragonimus ohirai. PCR might be a useful tool for species diagnosis of Paragonimiasis.

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Abstract 5943

Coproduction of mcr-9 and KPC-2 by archived clinical Enterobacter spp. strains from Colombia
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Background: Members of the Enterobacter cloacae complex (ECC) have gained major clinical significance in the last decade, becoming difficult-to-treat nosocomial pathogens due to the increasing presence of bla_{KPC}. Polymyxins are important “last-line” antibiotics to treat infections caused by carbapenem-resistant Enterobacteriaceae (CRE), especially in KPC-endemic countries like Colombia. We report the first clinical set of carbapenem resistant Enterobacter spp. isolates (CRE) coharboring bla_{KPC-2} and the mobile resistance colistin gene mcr-9 from Colombia.

Materials/methods: A total of 67 ECC isolates carrying bla_{KPC} were obtained from an archived library of clinical samples collected between 2007 and 2017 in 7 Colombian cities. Paired-end Illumina whole genome sequencing (WGS) and de novo assembly was performed for all isolates. Species confirmation, resistome and plasmid typing, were obtained from the assemblies. For the 5 isolates where mcr-9 was identified, polymixin B (PolB) antimicrobial susceptibility testing was performed using the broth macrodilution method and long read WGS (Oxford Nanopore MinION) was carried out to identify the elements harboring bla_{KPC} and mcr-9.

Results: The mcr-9 harboring isolates were collected from 3 different cities; 3/5 were identified as E. asburiae, and 2/5 E. hormaechei (subsp. xiangfangensis and subsp. hoffmannii, respectively). All isolates carried bla_{KPC-2} in plasmids of different sizes and replicon types. For E. asburiae isolates mcr-9 was chromosomally encoded, and their PolB MIC was ≥ 8 mg/L; while E. hormaechei isolates harbored mcr-9 in multi-replicon plasmids and displayed low PolB MICs (0.25 and 0.125 mg/L; Table 1). Analysis of the genetic context of mcr-9 revealed that this gene was flanked by insertion sequences from the IS5 and IS481 families followed downstream by wbuC (encoding a putative enzyme of the cupin superfamily), the qseBC [two-component system], and an ATPase gene.

Conclusions: This study highlights the increased likelihood of a wide, sometimes silent dissemination of the newly identified mobile colistin resistance gene mcr-9 among ECC. Mobile genetic elements play a key role in mobilization, by aiding it to insert not only into plasmids, but also into the chromosome. Further surveillance is urgently needed to understand the prevalence and dissemination of mcr-9, especially taking into account its inducible nature.

Table 1. Summary of isolates included in the study.

<table>
<thead>
<tr>
<th>Isolation Year</th>
<th>City</th>
<th>Species</th>
<th>Source</th>
<th>mcr-9 Location</th>
<th>PoIB MIC (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>Bogota</td>
<td>E. asburiae</td>
<td>Urinary tract</td>
<td>Chromosome</td>
<td>8</td>
</tr>
<tr>
<td>2009</td>
<td>Cali</td>
<td>E. asburiae</td>
<td>Blood</td>
<td>Chromosome</td>
<td>&gt;8</td>
</tr>
<tr>
<td>2009</td>
<td>Cali</td>
<td>E. asburiae</td>
<td>GI tract</td>
<td>Chromosome</td>
<td>&gt;8</td>
</tr>
<tr>
<td>2009</td>
<td>Medellín</td>
<td>E. hormaechei subsp. xiangfangensis</td>
<td>Urinary tract</td>
<td>Plasmid</td>
<td>0.25</td>
</tr>
<tr>
<td>2016</td>
<td>Bogota</td>
<td>E. hormaechei subsp. hoffmannii</td>
<td>Blood</td>
<td>Plasmid</td>
<td>0.125</td>
</tr>
</tbody>
</table>

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Abstract 5944

**Do DNA based NAAT tests lead to over diagnosis of Chlamydia trachomatis infections?**

Alison Todd*1,2, Wilhelmina Huston1, Nicole Lima1,2

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Abstract third-party references: University of Technology, Sydney, SpeeDx Pty Ltd, University of New South Wales

**Background:** Since NAATs are so sensitive and specific, reliance on DNA detection alone may overestimate infectivity and lead to overtreatment of CT. Further, both DNA and RNA can remain detectable after pathogens are dead. VITA RT-PCR is a novel method which determines viability by quantifying the ratio of RNA to DNA thus using transcriptional vigour of the pathogens as a surrogate “index of life”.

**Materials/methods:** A cohort of 20 asymptomatic MSM, who tested positive for rectal CT DNA using the Roche cobas CT/NG test, provided self-collected rectal specimens upon return visits to the clinic at (i) commencement of 7 days of doxycycline treatment, (ii) conclusion of treatment, and (iii) 4 weeks post treatment. Samples were assessed for viable CT by VITA and culture; and CT DNA was detected by an in-house PCR (and cobas CT/NG at the final visit). VITA results were reported as Alive/Viable (RNA>DNA; Index>2), Dead (DNA only; Index<2) or Negative (No RNA or DNA).

**Results:**

(i) VITA indicated 35% of patients did not have viable CT infections (6 negative/1 dead). Of samples deemed “alive” by VITA, 61.5% grew in culture, whereas no negative/dead samples grew.

(ii) No samples were viable by VITA (PCR confirmed DNA in 1 dead sample)

(iii) No samples were viable by VITA (PCR & cobas test confirmed DNA in 1 dead sample).

Overall, DNA detection by VITA was 94% and 100% concordant with PCR and the cobas test respectively.

**Conclusions:** This pilot study indicated up to 35% of the 20 patients did not have viable CT at visit (i) and may therefore have received unnecessary doxycycline treatment. Since the cobas CT/NG had detected CT DNA ≤6 days previously, it is hypothesised the test may have detected residual DNA associated with dead CT from infections in the process of self-clearing at the time of diagnosis, or between then and visit (i); or may detect DNA associated with CT exposure which did not result in infection. Support for the hypothesis includes studies showing pre-treatment samples where 18-20% had cleared, or where 17-24% where found to be non-viable by V-PCR or RNA analysis respectively.

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Clonality of regional *Candida auris* isolates identified by whole genome sequencing

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**Background:** *Candida auris* is a novel emerging fungal species capable of both antifungal resistance and person-to-person transmission. Research into the epidemiology and genotypic characteristics of *Candida auris* is limited.

**Materials/methods:** 16 *Candida auris* isolates from Northwestern Memorial Hospital (NMH) and ACL Laboratories (ACL) in Chicago, Illinois from 2017 to 2019 and 10 international isolates from the Centers of Disease Control and Prevention (CDC) were obtained. Antifungal susceptibility testing and whole-genome sequencing (WGS) were performed. Nanopore-long read sequencing was obtained on one NMH sample with the remainder of strains aligned to this reference.

**Results:** 26 samples were collected and underwent WGS. A maximum of 35 single-nucleotide variants (SNV) were present between any two non-CDC strains. NMH and ACL isolates were not genomically distinct. All isolates differed from the nearest genomic clade, South America, by 185 – 204 SNVs. Amongst regional strains, fluconazole minimum inhibitory concentrations ranged from 2 to 256 µg/mL. Phylogenetic trees of all sequenced isolates, and isolates compared to the closest clade, are shown in Figure 1.

**Conclusions:** There is high genomic similarity between local *Candida auris* strains in spite of varying antifungal resistance patterns. No grouping patterns were observed when comparing NMH to ACL strains. Regional isolates appear distinct from previously identified clades but are most closely related to the South American clade. Further study is needed to clarify this evolutionary pattern.

Figure 1: Phylogenetic tree of NMH clinical (purple), NMH environmental (green), and ACL (red) isolates when compared to the South American clade (black).

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Perceptions of general practitioners on antimicrobial stewardship: a nation-wide survey in Australia

Sajal Saha*1, David Kong2, Karin Thursky1, Danielle Mazza1

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Background: Establishing antimicrobial stewardship (AMS) programs in general practice is central to optimise antimicrobial prescribing in primary care. To date, the views of Australian general practitioners (GPs) on the national antimicrobial resistance strategies, uptake of AMS strategies when prescribing antimicrobials and GP-pharmacist collaboration to improve AMS remains unknown. This evidence gap hinders the development of models for implementing AMS strategies by improved GP-pharmacist collaboration in primary care. This study explored GPs’ AMS awareness and practices and attitudes towards GP-pharmacist collaborative approaches to optimising AMS in Australia.

Materials/methods: Across Australia, 3000 GPs derived from AMPCo database using a stratified random sampling method were invited to participate in a paper-based survey with two reminders between January to May 2019. Outcomes included awareness of AMS, uptake of evidence-based AMS strategies, attitudes towards GP-pharmacist collaboration and future AMS improvement strategies. Descriptive statistics and regression analysis were performed.

Results: Responses from 386 GPs (16.8%) were included for analysis. Participants were familiar with the term AMS (68.9%) and positively perceived the objectives of AMS: reduction of inappropriate antimicrobials use (61.7%) and treatment costs (70.8%). The most frequently used AMS strategies were Antibiotics Therapeutic Guidelines (TG) (83%) and delayed prescribing strategy (72%). Point of care testing (18.4%), patient leaflets (20.2%), peer prescribing reports (15.5%) and audit-feedback (9.8%) were poorly utilised. GPs who completed antimicrobial prescribing courses showed greatest awareness of AMS (p<0.002) and better uptake of AMS strategies (p=0.000). GPs were receptive to pharmacists’ recommendations on the choice (55%), and dose (63%) of antimicrobials. More than 60% of GPs would support a policy fostering GP-pharmacist collaboration. Most GPs were willing to be trained on AMS (72%), supported integration of electronic TG with prescribing software (87.3%) and a policy that would limit the prescribing of selected antimicrobials (74.4%).

Conclusions: GPs in Australia are aware of AMS but shows poor uptake of some evidence-based AMS strategies when prescribing antimicrobials. The majority of GPs hold positive attitudes towards GP-pharmacist collaboration to furthering AMS. GPs’ poor adoptions of AMS strategies and feasibility of GP-pharmacist collaborative AMS strategies can be further investigated to optimally design effective AMS strategies in Australian primary care.

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Abstract 5948

Induction of erythromycin resistance in *Bordetella* sp. confirmed by whole genome sequencing

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**Background:** *Bordetella pertussis*, the etiological agent of whooping cough, is highly infectious and re-merging globally despite widespread vaccination. The recommended antibiotics for treatment of *B. pertussis* infections and post-exposure prophylaxis are macrolides, Erythromycin and Azithromycin. However, mutations have occurred in the 23S rRNA gene resulting in macrolide resistance. While still uncommon, macrolide-resistant *B. pertussis* have been reported in Europe and Asia. The mechanism of resistance was identified as an A-to-G transition SNP mutation at position 2037 according to the *B. pertussis* Tohama I 23S rRNA gene.

The target sequence IS481 for routine clinical diagnosis has been found in both *Bordetella holmesii* and *B. pertussis* genomes. *B. holmesii* is often the main cause of false-positive results when screening symptomatic patients for Pertussis with routine PCR methods. Previous studies have shown that *B. holmesii* infections range from 0-32% of nasopharyngeal samples from patients with pertussis-like illnesses. Given the causative agent of Pertussis-like illnesses can be caused by other *Bordetella* sp. we aimed to examine the development of macrolide resistance in *B. pertussis*, *B. holmesii*, *Bordetella parapertussis*.

**Materials/methods:** To generate resistance in four *B. pertussis*, three *B. holmesii* and three *Bordetella parapertussis* strains, these isolates were grown on CBA or HBA media with an Erythromycin E-test or disc for 15 weeks and subcultured every 3-4 days. Passaged isolates were sequenced on an Illumina NextSeq500 every 4 weeks. Long reads were obtained using Nanopore MinION.

**Results:** *B. parapertussis* isolates developed resistance (>256 µg/mL) within three to seven weeks. *B. holmesii* isolates took six to twelve weeks to develop resistance (>256 µg/mL), from an initial MIC ranging from 0.047-0.25 µg/mL. However, following 15 weeks, *B. pertussis* MIC fluctuated between 0.032 to 0.38 µg/mL and did not gain resistance. Sequencing results revealed mutations in the 23S rRNA gene in *B. holmesii*. However, sequencing of *B. parapertussis* did not resolve any differences between susceptible and resistant strains.

**Conclusions:** This study was able to demonstrate a potential resistance mechanism for *B. holmesii*. Although *B. parapertussis* developed a resistant phenotype on subculture, no mechanism was found. Fortunately, a resistant *B. pertussis* phenotype could not be induced by this method.

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Abstract 5956

**In vitro activity of cefepime-taniborbactam (VNRX-5133) against genetically-diverse, largely multidrug-resistant, *Pseudomonas aeruginosa* clinical isolates**

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**Background:** Cefepime-taniborbactam is in phase 3 clinical development. Taniborbactam (VNRX-5133) is a cyclic boronate β-lactamase inhibitor that inhibits Ambler class A, B, C, and D β-lactamases. Our objective was to assess the in vitro activity of cefepime-taniborbactam against *Pseudomonas aeruginosa* clinical isolates, including those resistant to ceftazidime-avibactam and ceftolozane-tazobactam.

**Materials/methods:** Aztreonam, ceftazidime, ceftazidime-avibactam, ceftolozane-tazobactam, imipenem, and piperacillin-tazobactam minimum inhibitory concentrations (MICs) were determined in triplicate by broth microdilution. Cefepime was tested alone and with a fixed concentration of taniborbactam (4µg/mL). All isolates underwent whole-genome sequencing (Illumina).

**Results:** 100 *P. aeruginosa* isolates representing 58 different sequence types (ST) were tested; ST241 (*n*=7), ST129 (*n*=6), ST244 (*n*=6), and ST348 (*n*=6) were most common. All isolates harbored *bla*OXA-50. Other β-lactamase genes included *bla*OXA-2 (*n*=11), *bla*ORB (*n*=4), *bla*QMB (*n*=3), and *bla*VIM-2, *bla*OXA-10, *bla*VIM-1 (*n*=1 each). Thirty-two unique Pseudomonas-derived cephalosporinase (PDC) variants were identified, including PDC-338 (*n*=13), PDC-382 (*n*=10), and PDC-51 (*n*=8). MICs are shown in the Table. 74% of isolates were MDR (R to ≥3 agents) or XDR (R to ≥1 agent from all classes), including 29 isolates non-susceptible (NS) to ceftazidime-avibactam and/or ceftolozane-tazobactam. 70% of isolates were R to cefepime (MIC≥16µg/mL). Following the addition of taniborbactam, R rates were reduced to 27%; the median MIC fold-change was 2 (range: 0–32). 69% and 45% of MDR/XDR or isolates NS to ceftazidime-avibactam or ceftolozane-tazobactam were susceptible to cefepime-taniborbactam, respectively. In subsequent experiments we evaluated serial isolates from 24 patients who developed R to ceftolozane-tazobactam. Baseline (*n*=27) and post-exposure (*n*=40) isolates exhibited median ceftolozane-tazobactam MICs of 2 and 64µg/mL, respectively. Corresponding median MICs of ceftazidime-avibactam were 4 and 64µg/mL, demonstrating cross-resistance (median 16-fold MIC increase). Median cefepime-taniborbactam MICs increased 4-fold post-exposure (from 8 to 32µg/mL), however, 20% retained susceptibility.

**Conclusions:** Against a challenging largely MDR/XDR collection of *P. aeruginosa* clinical isolates, cefepime-taniborbactam demonstrated similar in vitro activity to ceftazidime-avibactam and ceftolozane-tazobactam. Importantly, the combination retained susceptibility against some isolates NS to ceftazidime-avibactam and ceftolozane-tazobactam. These data support the potential role for cefepime-taniborbactam against MDR *P. aeruginosa* infections, for which therapeutic options remain limited and the emergence of resistance to other novel agents has been documented.

**Table. Antimicrobial MICs (µg/mL) against 100 *P. aeruginosa* clinical isolates**

<table>
<thead>
<tr>
<th>Agent</th>
<th>MIC range</th>
<th>MIC50</th>
<th>MIC50</th>
<th>%S†</th>
<th>%I*</th>
<th>%R*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aztreonam</td>
<td>0.5 - &gt;128</td>
<td>32</td>
<td>128</td>
<td>16</td>
<td>20</td>
<td>64</td>
</tr>
<tr>
<td>Cefepime</td>
<td>1 - &gt;256</td>
<td>16</td>
<td>64</td>
<td>30</td>
<td>30</td>
<td>40</td>
</tr>
<tr>
<td>Cefepime-taniborbactam</td>
<td>1 - &gt;64</td>
<td>8</td>
<td>32</td>
<td>73</td>
<td>13</td>
<td>14</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>1 - &gt;62</td>
<td>32</td>
<td>128</td>
<td>33</td>
<td>12</td>
<td>55</td>
</tr>
<tr>
<td>Ceftazidime-avibactam</td>
<td>1 - &gt;256</td>
<td>4</td>
<td>32</td>
<td>81</td>
<td>19</td>
<td>55</td>
</tr>
<tr>
<td>Ceftolozane-tazobactam</td>
<td>0.5 - &gt;64</td>
<td>2</td>
<td>16</td>
<td>77</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Imipenem</td>
<td>0.5 - &gt;32</td>
<td>2</td>
<td>32</td>
<td>50</td>
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<td>41</td>
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<tr>
<td>Piperacillin-tazobactam</td>
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*Based on CLSI breakpoints; cefepime breakpoints were applied to cefepime-taniborbactam

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Evaluation of a liquid chromatography and tandem mass spectrometry-based Carba detection method using the Acrion system for clinical isolates expressing multiple carbapenemases

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Background: Carbapenem resistance among Gram negative bacteria is a significant health threat due to the nature of carbapenems being considered antibiotics of last resort. Within this broad group are carbapenemase-producing organisms [CPOs], which distinguish themselves by actively expressing enzymes to inhibit carbapenems. Successful therapy is frequently dependent on identifying those specific mechanisms. In the majority of CPOs, a single carbapenemase is expressed, such that the challenge is to determine which carbapenemase is produced, and to respond accordingly, however, in recent years there has been an increase in CPOs that produce more than a single carbapenemase, leading to multiple, sometimes synergistic combinations of resistance. Having the ability to identify the full extent of carbapenemases expressed by a single isolate is critical for both successful therapy and epidemiological surveillance.

We present a method herein that offers the ability to detect multiple carbapenemases of the "big five", KPC, NDM, OXA-48-like, VIM and IMP, from within a single isolate and using high resolution mass spectrometry.

Materials/methods: Samples are prepared in an automated fashion following harvesting of cell colonies from culture. Cells are mechanically lysed, proteins are extracted from supernatant following centrifugation, and subjected to a short chromatographic separation with subsequent electrospray ionization and mass spectrometric analysis.

Results: Isolates of Enterobacteriales and Pseudomonas aeruginosa were evaluated for the presence of multiple carbapenemases. To date, we were able to detect combinations of KPC/OXA-48-like (2 strains), KPC/NDM (1 strain), NDM/OXA-48-like (2 strains) based on strain availability. These resistances were identified by leveraging tandem mass spectrometry to fragment intact carbapenemase proteins and detecting diagnostic fragments produced, each fragment having a specific mass-to-charge (m/z) and charge state and being produced from a specific intact protein m/z. Multiple carbapenemases are constantly sought for the majority of the method by alternating between different m/z, each corresponding to different intact carbapenemases.

Conclusions: We present a method that offers automation from sample preparation all the way to results. Following the use of liquid chromatography for sample simplification, the use of tandem mass spectrometry allows for multiple targets to be probed in rapid succession, allowing for detection of multiple carbapenemases in a single method.

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Phenotype or genotype: association between mortality and minimum inhibitory concentration or beta-lactamase genes for patients with ceftriaxone non-susceptible *Escherichia coli* or Klebsiella spp. treated with piperacillin/tazobactam compared with meropenem.

Andrew Henderson1,2, David L. Paterson3, Mark Chatfield4, Paul Tambyah5, David Lye6,7, Partha Pratim De8, Raymond Tzer-Pin Lin9, Ka Lip Chew10, Yin Mo11,12,13, Tao Hong Lee11,12,13, Mesut Yilmaz14,15, Rumeya Lakmaki, Thamer Alenazi16,17, Yaseen Arabi18,19,20, Marco Falcone20, Matteo Bassetti20,21, Elida Righi20,21, Benjamin Rogers20,21,22, Souha S. Kanji23, Hasan Bhally23, Jonathan Iredell23,24, Marc Mendelson23, Tom Bouley23, David Looke24, Naomi Runnegar25,26, Spiros Miyakis27,28,30,31, Genevieve Walls32,33, Mohammed Al Khamis34, Ahmed Zikri35, Amy Crowe36, Paul Ingram36,37, Nick Daneman38, Paul Griffin39,40, Eugene Athan41, Leah Roberts42, Scott Beaton42, Anton Peleg43,44, Kyra Cottrell42, Michelle Bauer42, Khin Chaw45,46,47, Graeme Robert Nimmo48,49, Tiffany Harris-Brown49, Patrick Harris1,2.

**Background:** This study aims to assess the association of piperacillin/tazobactam and meropenem minimum inhibitory concentration (MIC) and beta-lactamase resistance genes with mortality from patients with ceftriaxone non-susceptible *E. coli* and *Klebsiella* spp. bloodstream infections.

**Materials/methods:** Blood culture isolates from patients enrolled in the MERINO trial were tested by broth microdilution, Vitek 2, disk diffusion and whole genome sequencing at a central laboratory. Classification and regression tree (CART) was performed to determine the optimal MIC cut point for 30-day mortality based upon broth microdilution. Multivariate logistic regression was performed to account for confounders. Absolute risk increase for 30-day mortality between treatment groups was calculated for the primary analysis (PA) and the microbiologic assessable (MA) populations.
Results: 320 isolates from 379 enrolled patients were available with susceptibility to piperacillin/tazobactam 94% and meropenem 100% by broth microdilution. Very major error, major error and minor error for piperacillin/tazobactam were 67%, 5% and 17% for Vitek 2 and 44%, 1% and 13% for disk diffusion. The piperacillin/tazobactam non-susceptible breakpoint (MIC > 16 mg/L) best predicted 30-day mortality after accounting for confounders (odds ratio 2.0, 95% CI 1.3 – 3.4). The absolute risk increase for 30-day mortality for patients treated with piperacillin/tazobactam compared with meropenem was 9% (95% CI 3% – 15%) and 8% (95% CI 2% – 15%) for the original PA population and the post-hoc MA populations, which reduced to 5% (95% CI 1% – 10%) after excluding strains with piperacillin/tazobactam MIC values > 16 mg/L. ESBL and OXA co-harbouring strains showed a higher absolute risk increase for patients treated with piperacillin/tazobactam compared to ESBLs only (14%, 95% CI 2% – 28% vs 5%, 95% CI -3% – 14%).

Conclusions: 30-day mortality was significantly higher for patients treated with piperacillin/tazobactam with MICs > 16 mg/L. After excluding non-susceptible strains, 30-day mortality difference was less pronounced for piperacillin/tazobactam. Poor reliability in susceptibility testing performance for piperacillin/tazobactam and mortality differences from the MERINO trial suggest that meropenem remains a preferred choice for definitive treatment of ceftriaxone non-susceptible *E. coli* and *Klebsiella*.

*PTZ MIC >16mg/L excluded;^PTZ MIC >16mg/L EUCAST or >64mg/L CLSI excluded; PTZ – piperacillin/tazobactam; MER - meropenem

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<th>Sub/Population</th>
<th>PTZ *</th>
<th>PTZ/MER Non-susceptible Breakpoint</th>
<th>PTZ/MER Non-susceptible Breakpoint (excluding PTZ MIC &gt; 16 mg/L)</th>
<th>PTZ/MER EUCAST Resistant Breakpoint</th>
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<td>132</td>
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| Susceptible strains* |        |                           |                                                           |                                   |                                   |
| PTZ/MER Non-susceptible Breakpoint | 13 | 134 | 6 | 149 | 5 (1, 11) |
| PTZ/MER Non-susceptible Breakpoint (excluding PTZ MIC > 16 mg/L) | 11 | 116 | 6 | 119 | 4 (1, 11) |

| Susceptible and Intermediate strains* |        |                           |                                                           |                                   |                                   |
| PTZ/MER EUCAST Resistant Breakpoint | 15   | 134 | 6 | 149 | 5 (1, 11) |
| PTZ/MER CLSI Resistant Breakpoint | 15   | 138 | 6 | 150 | 7 (1, 13) |

| Genotype |        |                           |                                                           |                                   |                                   |
| ESBL   | 9   | 78 | 5 | 83 | 9 (3, 14) |
| AmpC (Acquired) | 7   | 59 | 1 | 62 | 14 (2, 28) |
| De repressed AmpC | 0   | 15 | 0 | 13 |                           |
| ESBL/AmpC | 0   | 2   | 0 | 1 |                           |
| ESBL/AmpC/OXA | 1   | 1   | 0 | 1 |                           |
| OXA   | 0   | 0   | 0 | 1 |                           |
| No ESBL/AmpC/OXA | 1   | 0   | 0 | 2 |                           |

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In vitro susceptibility of multidrug-resistant *Pseudomonas aeruginosa* following treatment-emergent resistance to ceftolozane-tazobactam

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**Background:** Multidrug-resistant (MDR) *Pseudomonas aeruginosa* is a major public health threat. Treatment with ceftolozane-tazobactam improves patient outcomes compared to salvage therapy; however, resistance has emerged in ~15% of patients following courses ranging from 7 to 53 days. Our objective was to study the *in vitro* activity of other β-lactams agents in the setting of ceftolozane-tazobactam resistance to evaluate cross-resistance or collateral sensitivity.

**Materials/methods:** Serial isolates from 15 patients in whom ceftolozane-tazobactam resistance emerged were selected for analysis. Minimum inhibitory concentrations (MICs) were determined by standard broth microdilution in triplicated and interpreted by CLSI breakpoints. Mechanisms of resistance were explored through whole-genome sequence (WGS) analysis.

**Results:** 20 baseline and 23 post-treatment isolates were included. The median baseline ceftolozane-tazobactam MIC was 1.5 µg/mL (range: <0.25 – 8 µg/mL). 75%, 55%, 50%, and 15% of baseline isolates were resistant to imipenem, piperacillin-tazobactam, ceftazidime, and ceftazidime-avibactam respectively. Following a median 20 (range: 4-52) days of therapy, the median post-treatment ceftolozane-tazobactam MIC was 128 µg/mL (range: 8 – >256 µg/mL). Resistance was predominantly associated with mutations in AmpC. 45%, 40%, 90%, and 65% of post-treatment isolates were resistant to imipenem, piperacillin-tazobactam, ceftazidime, and ceftazidime-avibactam [Figure]. The corresponding MIC fold-changes were -8, -2, 6, and 16, respectively. Median imipenem-relebactam MICs did not change before or after treatment with ceftolozane-tazobactam (median = 2 µg/mL for both) and 83% were classified as susceptible (MIC ≤ 2).

**Conclusions:** Our findings show that resistance to ceftolozane-tazobactam impacts the susceptibility of other β-lactams. Cross-resistance was evident between ceftolozane-tazobactam and ceftazidime-avibactam [median 16-fold MIC increase]. On balance, imipenem and piperacillin-tazobactam MICs were decreased suggesting that AmpC mutations alter the substrate profile of the enzyme. Importantly, imipenem-relebactam MICs were unchanged providing evidence that the agent may be a reasonable therapeutic option in the setting of ceftolozane-tazobactam resistance.

**Figure 1:** Distribution of β-lactam MICs against baseline and post-treatment isolates. The red bar denotes the median. As MICs increased for ceftolozane-tazobactam, median MICs increased for ceftazidime and ceftazidime-avibactam, decreased for imipenem and piperacillin-tazobactam, and were unchanged for imipenem-relebactam.

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The diagnostic accuracy of cryptococcal antigen detection in serum and cerebrospinal fluid in HIV patients with suspected cryptococcal meningitis: systematic review and meta-analysis

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Background: Delayed diagnosis of HIV-associated cryptococcal meningitis (CM) is a major determinant of poor outcome. Cryptococcus spp. characterised by a capsular polysaccharide known as cryptococcal antigen (CrAg), detectable as a biomarker of infection could ensue timely institution of induction antifungal therapy.

Materials/methods: To determine the diagnostic accuracy of CrAg, we searched MEDLINE, EMBASE, and Web of Science (1981 – 2019) for studies comparing CrAg detection in blood (serum or plasma) or cerebrospinal fluid (CSF) to Indian ink staining and fungal culture of CSF in HIV-positive adults with symptoms suggestive of CM. CrAg detection was with either latex agglutination, enzyme-linked immunosorbent assay or by lateral flow assay. We used quality assessment of diagnostic accuracy studies (QUADAS-2) to evaluate risk of bias (RoB) and concerns about applicability of included studies. Through random-effects meta-analysis, we obtained summary estimates of the prevalence of serum CrAg positivity, prevalence of confirmed CM as well as the sensitivity and specificity of serum and CSF CrAg and agreement between CSF CrAg and CSF culture in diagnosing CM.

Results: We included eleven studies from eight countries on 3600 participants, 5 of which were judged at low RoB. The summary prevalence of serum CrAg was 63% (95%CI: 45 – 81) and of confirmed CM was 43% (95%CI: 26 – 59). Summary sensitivity and specificity of serum CrAg detection were 97% (95%CI: 87 – 100) and 92.6% (95%CI: 89 – 98), respectively. Summary sensitivity and specificity of CSF CrAg detection were 98.8% (95%CI: 96.2 – 99.6) and 99.3% (95%CI: 96.7 – 99.8), respectively. There was very high agreement between CSF CrAg and CSF culture at 98% (95%CI: 97 – 99) in classifying patients with and without CM.

Conclusions: In HIV-positive adults with symptoms suggestive of CM, negative serum CrAg may rule-out CM while positive serum CrAg should prompt lumbar puncture (LP) for CM confirmation. If LP is not feasible, symptomatic serum CrAg positive patients should be considered for induction antifungal therapy. In settings where LP is feasible, patients who present with a first episode of symptoms suspicious of CM, CrAg detection in CSF is diagnostic.

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Abstract 5969

The epidome: a species-specific approach to quantify population dynamics and heterogeneity of Staphylococcus epidermidis colonisation and infection in primary samples

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Background: Staphylococcus epidermidis has gained attention as an increasingly important multidrug-resistant nosocomial pathogen in infections related to foreign body infections. Identification of S. epidermidis as an invasive agent is not trivial, and recent research suggests that heterogeneity is a common phenomenon in both carriage and infection. To elucidate clonality of S. epidermidis communities, we developed the “Epidome” assay, a culture-independent method based on targeted-sequencing of S. epidermidis-specific targets that provide information on quantity and diversity of S. epidermidis from primary samples.

Materials/methods: Based on >850 S. epidermidis genomes, core genes from representatives of all major lineages were parsed for highly conserved and variable regions suitable as PCR targets. These amplicon targets were evaluated for their ability to discriminate the entire population before designing primers for best candidates. For validation, DNA from S. epidermidis representing 15 sequence types and from 49 other common skin commensals, including 25 Staphylococcal species, were used for laboratory validation. Even and staggered genomic mock communities were subjected to a duplex PCR before applying paired-end Illumina sequencing. In addition, a qPCR probe was designed and validated for quantification of total genomic copies of S. epidermidis. Application of the method was demonstrated on human samples collected by ESwab from skin and nose of healthy carriers to investigate heterogenicity.

Results: No single target sufficiently differentiated the S. epidermidis population, so two targets (493/521-bp) were selected and optimized in a duplex PCR. The qPCR probe for one of the S. epidermidis gene targets revealed a sensitivity of ~100 S. epidermidis/μL template. Applying next-generation sequencing revealed a high level of reproducibility on even- and staggered-mock communities that allowed reliable differentiation of the S. epidermidis population. The primary samples from nares and skin showed high levels of S. epidermidis heterogeneity.

Conclusions: The Epidome approach provides information on S. epidermidis quantity and diversity well beyond species-level in primary samples. Our targeted sequencing method allows rapid differentiation and identification of clinically important nosocomial lineages in samples with low abundance. The method can be useful for investigating clonality of S. epidermidis communities, population dynamics and temporal stability or niche selection due to antimicrobials.

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Meropenem versus piperacillin-tazobactam for definitive treatment of bloodstream infections caused by AmpC beta-lactamase-producing Enterobacter spp., Citrobacter freundii, Morganella morganii, Providencia spp., or Serratia marcescens: a pilot multi-centre randomised controlled trial (MERINO-2)

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Abstract third-party references: University of Queensland Centre for Clinical Research

Background: Enterobacter spp., Klebsiella aerogenes, Citrobacter freundii, Morganella morganii, Providencia spp., and Serratia marcescens possess chromosomally encoded AmpC beta-lactamases that may hydrolyse third-generation cephalosporins [3GC]. Whether piperacillin-tazobactam is effective carbapenem-sparing therapy for bloodstream infection (BSI) caused by these organisms is uncertain. We undertook a pilot randomised controlled trial (RCT) (ACTRN12614001211651; NCT02437045) to assess feasibility and inform the design of a larger definitive trial.

Materials/methods: We enrolled adult patients from 7 sites in Australia and Singapore with BSI caused by chromosomal AmpC beta-lactamase producers. Participants were randomized within 72 hours of initial blood culture collection 1:1 to piperacillin-tazobactam 4.5g 6-hourly or meropenem 1g 8-hourly for a minimum of 3 days. Treating clinicians were not blinded to treatment allocation. The primary outcome was a composite of death within 30 days post randomisation; or clinical failure at day 5 post-randomisation; or microbiological failure on days 3-5; or microbiological relapse from day 5 to 30.

Results: Interim results are presented here. Between July 2015 and May 2019 a total of 56 patients were enrolled, from 575 screened. Of these, 50 were randomized appropriately, received at least one dose of study drug and were included in the primary analysis population (piperacillin-tazobactam=26; meropenem=24). No patients were lost to follow-up. The mean age was 65.0 years [range 19-93], 26% were female and 78% of BSI were healthcare-associated. The most common source was line-related [24%], biliary [20%] or urinary tract [18%]. A total of 10/26 [38.5%] met the composite primary outcome in the piperacillin-tazobactam group, and 5/24 [20.8%] in the meropenem group [P=0.174]. Only 1 death occurred in a patient randomised to meropenem. There were 4 microbiological failures, all occurring in patients randomised to piperacillin-tazobactam, of which two demonstrated emergent resistance. Recruitment will continue until 31 Dec 2019 to a maximum of 100 patients. Final outcome results will be available for presentation at ECCMID.

Conclusions: This is the first RCT to specifically compare treatment options for BSI caused by Gram-negative species with chromosomally encoded AmpC beta-lactamases. The results of this pilot trial will help inform larger definitive trials to define carbapenem-sparing options for these infections.

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Impact of the Spanish Bacteraemia Zero project on central line-associated bloodstream infection rates

Sulamita Carvalho Brugger*1,2, Montserrat Vallverdú1,2, Mar Miralbés1,2, Begoña Balsera1,2, Silvia Rodriguez1,2, Silvia Iglesias1,2, Jesús Caballero1,2

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Background: Central line associated bloodstream infection (CLABSI) is an important cause of hospital-acquired infection associated with morbidity, mortality and cost, and one of the most common infections acquired in ICU. In 2009 was launched in Spain the Bacteriemia Zero (BZ) project, based on specific measures related to the insertion and management of central venous catheter (CVC), and on other measures to promote a daily safety culture on ICU. This work aims to describe the impact of CLABSI rates after the implementation of BZ project in a Spanish ICU and the CLABSI etiology in our unity.

Materials/methods: Descriptive retrospective study, based on data from ENVIN-HELICS database, from an 18-bed polyvalent ICU. We analyzed CLABSI rates in the last 19 years, divided in 2 periods: P1 before BZ implementation, from January 2001 to July 2009; and P2, from August 2009 to October 2019, after BZ implementation. The difference between rates in the 2 periods was analyzed with Fisher’s exact test (signification with p<0.01).

Results: In P1 99 CLABSI were recorded, for 26449 days of stay, while in P2 there were 79 CLABSI for 57630 days of stay. The rates for P1/P2 were 3.7/4.17 for 1000 days of stay, 4.92/1.79 for 1000 days with CVC and 3.73/1.4 CLABSI for 1000 catheters days (CVC + arterial catheter). This is a reduction of 60.97%, 64.23% and 62.46%, respectively. The distribution by microorganisms was, in both periods: Staphylococcus epidermidis 34.0%/38.9%, methicillin-sensitive Staphylococcus aureus 10.7%/13.0%, methicillin-resistant Staphylococcus aureus 2.9%/1.2%, Acinetobacter baumannii 7.8%/1.3% (p<0.001), Pseudomonas aeruginosa 6.8%/7.8%, other gram-negative bacilli 23.3%/14.3%, Enterococcus 6.8%/6.5%, Candida spp 8.7%/9.1%, and other microorganisms 8.7%/8.8%. In 2018, there were just 2 cases of CLABSI in our unit (0.41/1000 days of stay), and 4 cases in 2019 until October.

Conclusions: Starting from a CLABSI rate superior than the one recommended by the quality standard, after the implementation of BZ project there was a significantly reduction on CLABSI in our unity, bigger than 60%, reaching values below the Spanish rates. The microbiological etiology was similar in both periods, except for the almost disappearance of A baumannii.

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Abstract 5985

Antimicrobial stewardship opportunities at discharge: current prescribing at Boston Medical Centre
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Background: Most antimicrobial stewardship interventions target inpatient prescribing; however, the majority of individual treatment courses are completed following hospital discharge. Additionally, data suggests antibiotics prescribed during this transition of care are often inappropriate. The objective of this study was to assess the appropriateness of antimicrobials prescribed upon hospital discharge at Boston Medical Center in order to guide future stewardship opportunities at the institution.

Materials/methods: Data on antimicrobials prescribed at discharge were collected between August 4th to 17th, 2019. Discharge antibiotics were assessed for overall appropriateness, defined as a composite of appropriateness of drug choice, dose, and duration. Antibiotic indication, inpatient, outpatient, and total days of therapy were collected and excess antibiotic days were calculated. Excluded prescriptions were those sent from the emergency department, or those from the observation or pediatric care teams.

Results: A total of 203 patients were included with 250 unique prescriptions. Overall appropriateness (as a composite of drug choice, dose, and duration) was only 40.4% (101/250). The most common antibiotics prescribed were cefpodoxime (14%), trimethoprim-sulfamethoxazole (12.8%), and amoxicillin-clavulanate (10.8%). Drug choice was appropriate in 85.6% (214/250) of prescriptions, however for urinary tract infections and community-acquired pneumonia only 62.2% (28/45) and 69.2% (18/26) were appropriate, respectively. The drug with the highest inappropriate selection was cefpodoxime at 54.3% (19/35), followed by levofloxacin at 35% (7/20). Overall, doses were prescribed appropriately in 97.6% of cases (244/250); however the duration of therapy was appropriate in only 48.0% of prescriptions (120/250), resulting in an average excess duration of 3.6 days. Inpatient and outpatient days of therapy were 5.0 and 10.9 days, respectively, for a total average days of therapy of 15.9 days.

Conclusions: Antibiotics at discharge are an important area of focus for antimicrobial stewardship interventions. Shortening durations of therapy remains the largest target, followed by appropriate antimicrobial selection, specifically for urinary tract infections and community-acquired pneumonia. This data highlights a significant need for antimicrobial stewardship interventions on prescribing upon hospital discharge with a focus on drug selection and duration.

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Abstract 5987

**C-reactive protein patterns by age, sex and pathogen in patients with Gram-negative bacteraemia**

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**Background:** C-reactive protein (CRP) levels have been reported to differ by sex and age in healthy volunteers, but acute-phase patterns have been poorly characterized in patients with bloodstream infections. We explored differences in CRP kinetics by age, sex, and infecting pathogen.

**Materials/methods:** The multicenter non-inferiority PIRATE trial (NCT03101072) randomized 504 adult patients with gram-negative bacteraemia to an individualized/CRP-guided duration, 7 days, or 14 days of antibiotic therapy. Patients with complicated infections and/or non-fermenting bacteria were excluded. Per local practice, CRP levels were drawn daily from onset of illness until a descent from peak was documented; in the individualized arm, antibiotic therapy was discontinued when CRP levels decreased by 75%. Plasma CRP concentrations are measured via immunoturbidimetry.

**Results:** Among 498 patients with CRP data, median age was 79 years (IQR 68-86); 304 (61%) were women. Median peak CRP was 164 mg/l (IQR 105-247) and occurred median 1 day after bacteremia (IQR 0-2). While peak concentrations did not differ between men and women (median 164 mg/l for both), the very elderly (≥85 years, n=154) trended toward lower values (median 151 mg/l [IQR 104-216] versus 167 mg/l [IQR 103-262], ns), and experienced a significantly slower CRP descent thereafter (odds ratio for CRP>50% of peak by day 5: 1.78 [95% CI 1.21-2.63]). Patients with *Escherichia coli* infections (370/498, 74%) had significantly higher peak values (median 174 mg/l [IQR 117-251] versus 167 mg/l [IQR 103-262], ns), and experienced a significantly more rapid CRP descent (OR for descent by ≥50% by day 5: 1.98 [95%CI 1.31-2.98]). Patients with other Enterobacteriaceae followed the same pattern, with the notable exception of *Klebsiella* spp.: these (81/498, 16%) had significantly lower peak CRP values (median 118 mg/l [IQR 78-191] versus 174 mg/l [IQR 114-253], P=.0002) that declined significantly more slowly (OR for CRP>50% of peak by day 5: 2.00 [95% CI 1.22-3.29]).

**Conclusions:** The very elderly trend toward lower peak CRP concentrations and have significantly slower return to normal levels. Patients with *E. coli* infections have significantly higher peak CRP values and significantly more rapid CRP descent, while those with *Klebsiella* infections have significantly lower peak CRP values and significantly slower descent.

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Abstract 5989

**Rapid identification of positive blood culture, short-incubation subcultures by MALDI-TOF MS comparing pre-conditioned and non-conditioned culture media adapted to laboratory automation**

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**Background:** Rapid identification methods, including short incubation subcultures utilising MALDI-TOF-MS, have been developed to decrease positive blood culture (posBC) turnaround times. Short-incubation subcultures often utilize pre-conditioned media but there are no reports comparing pre-conditioned and non-conditioned media. This study assessed early MALDI-TOF-MS identification of posBC isolates from pre-conditioned agar (CO₂-35°C) and non-conditioned media (room-temperature) used for short-incubation MALDI-TOF-MS methods, that were adapted to a laboratory automation system.

**Materials/methods:** One drop of neat posBC was inoculated manually onto each of two CBA pre-conditioned agar (CO₂-35°C minimum 4 hrs), and incubated (pCBA-S, in standard CO₂-35°C incubator; pCBA-K in CO₂-35°C automated laboratory incubator [BD-Kiestra-WCA, first inoculation protocol]). Similarly, a third CBA agar (CBA-K, room-temperature) was inoculated and incubated in CO₂-35°C BD-Kiestra-WCA incubator. MALDI-TOF-MS (4 wells each with 0.5 µl formic acid [BioMerieux]) was performed from all short-incubation CBA, if any visible growth was present on any these CBA (checked at 2, 3 and/or 4 hrs). Results of all short-incubation methods were compared to MALDI-TOF-MS identification at 18-24 hrs from standard subcultures. All MALDI-TOF-MS testing was performed on Vitek MS [BioMerieux].

**Results:** A total of 110 posBC bottles from 83 patients were assessed, and of these 106/110 (96.4%) were mono-microbial. Gram-positive bacteria (GP) were isolated from 53/110 (48.2%) posBC, and Gram-negative bacteria (GN) from 52/110 (47.3%) posBC. After 4 hrs incubation, the concordance rates (compared to MALDI-TOF-MS from standard cultures, 24h) for identification were similar for all short-incubation CBA. Early GP identification rates were 40/53 (75.5%), 40/53 (75.5%), 41/53 (77.4%) for pCBA-S, pCBA-K and CBA-K respectively. Similarly GN rates were 52/52 (100%), 50/52 (96.2%), 51/52 (98.1%). Yeast were isolated from 5/110 (4.5%) but none were identified from any short-incubation CBA. There were no differences in yield between different genera for conditioned and non-conditioned plates.

**Conclusions:** Concordance rates for early identification of GP and GN using MALDI-TOF MS on posBC isolates from all short-incubation cultures were high. Pre-conditioning media did not improve concordance and routine use may not be required. Short-incubation culture can be adapted to laboratory automated systems, streamlining workflow whilst maintaining reduced turnaround times.

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Metagenomics analysis of novel viruses in dromedaries from the Middle East
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Background: Viruses in dromedary camels have been extensively studied over the past decades since the emergence of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) outbreak in the Arabian Peninsula and its surroundings. They are known as carriers of many viral pathogens, however, fundamental aspects of other novel infectious virus communities in dromedaries remains poorly described.

Materials/methods: Next generation sequencing (NGS) has made metagenomics a gold standard in microbiome studies and it had become the main tool for virus discovery. Camels at Middle East were regularly checked for MERS-CoV since its outbreak and these upper respiratory samples were cultured intensively as there might be potential unidentified viruses that can cause disease in humans. Those with high cytopathic effect (CPE), which is not typical to MERS-CoV were collected for further investigation. The cultured samples were extracted and sequenced on an Illumina HiSeq platform. Reads were filtered, assembled and aligned from short fragments of contigs with DIAMOND. They were annotated and then analysed with MetagenomeAnalyzer (MEGAN) producing metagenomics tree as belonging to the virus groups or other undefined viruses. Contigs matched to groups of viral families especially those previously unknown to dromedaries were selected for further studies.

Results: Cellular organisms were often the most abundance group. In this study, we had successfully obtained complete genome of Avian avulavirus infecting dromedary which is not common and non-occurrence in camels but is a common disease in bird species. Investigation shows that these viruses are lethal to dromedaries. The host of infection belong to the Family of Paramyxoviridae which consist of 6 genes in the order 5’-N-P-M-F-HN-L-3’. Currently, there is no evidence on how does the virus transmits to dromedaries, it is likely that the routes of transmission were through the droppings, sharing of foods and water and also mix farming.

Conclusions: Overall, our studies provide insights that cross transmission among camels and other animals (in this context not only mammalian) are possible, highlighting the importance of in depth studies in camels as a secondary host. Understanding the cross transmission of diseases from other animals presents the basis towards developing a better management strategies in camel farming.

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Metagenomic sequencing to identify environmental reservoirs of carbapenem-resistant Acinetobacter baumannii associated with clinical outbreaks

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Abstract 6000

Background: Metagenomics is an emerging technology that has wide-ranging potential for use in clinical and public health settings for outbreak management, pathogen detection and for antimicrobial resistance gene surveillance. Metagenomics bypasses the cultivation bottleneck by directly sequencing the DNA of all organisms within a sample, allowing for relatively unbiased pathogen detection and resolution of the resident microbial community. However, questions over detection sensitivity and cost have seen the technology remain largely under-utilised in clinical research. Here we report the use of metagenomics sequencing to identify environmental reservoirs of pathogenic bacteria associated with an ongoing carbapenem-resistant Acinetobacter baumannii (Cr-Ab) outbreak in a burns unit.

Materials/methods: Environmental swabs and water samples were collected from the ICU and Burns ward of a single hospital and subjected to traditional culturing methods and shotgun metagenomic sequencing. Sequence read data for all samples were screened against a database of complete bacterial genomes, seeded with the complete genomes of a representative outbreak strain. Positive metagenomics samples were confirmed by culture and isolate sequencing.

Results: Over a four-month period a total of 54 environmental swabs and water samples were collected from areas of presumed high bacterial load (e.g. floor drains, plumbing, burns bath drains). Of 54 environmental samples only two were culture positive for A. baumannii, while five were positive for A. baumannii based on preliminary analysis of the metagenomic sequencing data. Culturing and metagenomics where only concordant in one case indicating that high sequencing depth (~5 gigabase pairs) is required to reliably discriminate specific species from the background population. Enrichment of metagenomic samples by filtering for A. baumannii sequence reads enabled strain level sequence typing by MLST profiling and phylogenetic analysis. Targeted cleaning of plumbing and decommissioning of contaminated burns baths resulted in no new positive cases being reported.

Conclusions: Here we demonstrate the feasibility of using metagenomic sequencing for targeted surveillance during an active outbreak. The identification of the outbreak strain in the plumbing enabled a precision infection control response resulting in resolution of the outbreak and cost savings which offset sequencing costs.

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Co-infection with Mycoplasma or Ureaplasma spp. among HIV-positive men who have sex with men in Taiwan

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Abstract 6004

Background: Mycoplasma and Ureaplasma spp. have recently been recognized as pathogens causing urethritis and infertility. However, the data on coinfection with Mycoplasma and Ureaplasma spp. are limited among HIV-positive patients. We aimed to evaluate the prevalence of and associated factors with mycoplasmal and ureaplasmal coinfection among at-risk HIV-positive patients.

Materials/methods: From May to November 2019, we prospectively included HIV-positive men who have sex with men (MSM) with a history of sexually transmitted infections (STIs) or symptoms suggestive of STI. Urine and rectal specimens were collected and tested for Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG), Trichomonas vaginalis (TV), Mycoplasma genitalium (MG), Mycoplasma hominis (MH), Ureaplasma urealyticum (UU), Ureaplasma parvum (UP) with the use of multiplex real-time PCR assay.

Results: During the 6-month study period, 114 HIV-positive MSM (median age, 37 years) were included. All patients had been receiving combination antiretroviral therapy (cART) with a median CD4 count of 623 cells/µL and 85.1% having achieved plasma HIV RNA load <20 copies/mL. Among 26 patients having symptoms at screening, only 7 (26.9%) had symptoms suggestive of proctitis and 2 (7.7%) had urethritis. The prevalences of CT, NG, TV, MG, MH, UU, and UP infections among the 114 patients were 50.0% (n=57), 20.2% (23), 0%, 11.4% (13), 15.8% (18), 39.4% (45), and 5.3% (6), respectively. The prevalences of MG, MH, UU, and UP infections were even higher among patients coinfected with CT and/or NG (15.6%, 23.4%, 51.6%, and 4.7%, respectively) than that without (6.0%, 6.0%, 24.0%, and 6.0%, respectively). More than half of Mycoplasma and Ureaplasma spp. were detected from rectal swab specimens: 71.4% for MG, 85.0% for MH, 54.5% for UU, and 83.3% for UP. The factors associated with acquisition of UU were concurrent gonorrheal (adjusted odds ratio [AOR], 3.19; 95% CI, 1.11-9.20) and anal sex in 6 months (AOR, 2.89; 95% CI, 1.11-7.48).

Conclusions: Rectal mycoplasmal and ureaplasmal coinfections were common among at-risk HIV-positive MSM. The high rate of UU positivity and association with gonorrhea support the use of multiplex testing for detection of concurrent, multiple STIs.

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**Adherence to routine monitoring guidelines for people living with HIV is poorer in higher-volume outpatient settings: when more is not better!**

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**Background:** Potent antiretroviral therapy (ART) has transformed HIV from a fatal disease to a manageable chronic condition. Treatment goals for people living with HIV (PLHIV) have shifted from achieving durable viral suppression to person-centred healthy aging. Regular monitoring of biochemical parameters and vaccination uptake are essential components of care for PLHIV, but adherence to monitoring guidelines in our institution are currently unknown.

**Materials/methods:** A cross-sectional study of PLHIV who were initiated on ART between Jan 2012 – Dec 2015, and followed-up in the general Infectious Diseases clinic, was conducted. Adherence to monitoring for cardiovascular health, bone health, vaccination uptake, and renal disease, over the time period of June 2017- June 2019, was assessed. Optimal monitoring frequency was defined as per 2019 DHHS Guidelines. Correlation between patient and/or physician characteristics with adherence to monitoring were evaluated. Additional correlations were made after differentiating high- and low-volume physicians by median number of PLHIV seen per physician.

**Results:** A total of 163 PLHIV were recruited, of which, 91.4% were male; 53.4% were employed, 14.1% had social issues. 89.6% were compliant to ART and 68.7% were virologically suppressed. 42.9% received recommended vaccinations; 63.2% underwent bone health screening, and 55.2% underwent regular cardiovascular screening. Of those on a tenofovir-containing regimen (71.2%), 28.4% (33/116) had regular renal function monitoring. PLHIV followed up with lower-volume physicians had significantly higher cardiovascular screening rates (71.9% vs 51.1%, p=0.047) compared to higher-volume physicians. Vaccination frequency (56.3% vs. 39.7%, p=0.112) and bone health screening (68.8% vs 61.8%, p=0.543) were comparable in both groups. On multivariate analysis, being on followup with higher-volume physicians was independently associated with poorer compliance to metabolic screening (aOR=2.55, 95%CI=1.01-6.64). Other factors independently associated with poorer compliance to metabolic screening included current employment; being on a tenofovir-containing regimen, and physician seniority.

**Conclusions:** Surprisingly, PLHIV followed up by higher-volume physicians in the outpatient setting tended to have lower rates of regular cardiovascular screening, despite greater presumed physician familiarity with PLHIV care. Creating streamlined pathways for PLHIV care may improve physician adherence to regular monitoring of biochemical parameters and vaccination uptake.

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Abstract 6009

**Efficacy of CD377, a novel antiviral Fc-conjugate, against influenza A(H1N1) in a lethal mouse model of Severe Combined Immunodeficiency (SCID)**

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**Background:** Cidara’s AVCs (antiviral Fc-conjugates) are novel, immunotherapeutic conjugates of potent, antiviral agents with the Fc domain of human IgG1. These long-acting AVCs directly inhibit viral replication while simultaneously engaging the immune system. CD377 is an AVC development candidate being evaluated for seasonal and pandemic influenza, including in immune-deficient populations who are unable to benefit from vaccination. We evaluated CD377 in SCID mice to determine the impact of compromised immune status on its efficacy.

**Materials/methods:** Efficacy was evaluated in female BALB/c or BALB/c scid mice challenged intranasally with 3x the LD95 of influenza A/Puerto Rico/8/1934 (H1N1) [3E2 or 2E2 pfu/mouse respectively]. Mice were treated with a single subcutaneous dose of CD377 (between 0.01 and 10 mg/kg) two hours after viral challenge. The SCID study included baloxavir as comparator, at 3 or 10 mg/kg, bid x 1 day. Body weights (BW) were monitored daily for 14 or 28 days, with 20% BW loss recorded as mortality.

**Results:** In a benchmark study with immune-competent mice, CD377 was protective at 0.1 mg/kg (P=0.0031 relative to vehicle) accompanied by a transient drop in BW of less than 7%. Full recovery to starting BW was observed by study end (Day 14). Groups treated with vehicle or Fc-only control fully succumbed to infection by Day 6.

In a similar study with immune-compromised scid mice challenged with the same virus, CD377 dosed at 0.1 mg/kg was fully protective for 21 days. At 0.3 mg/kg, mice were fully protected for the entire study (28 days) (P=0.0020). In contrast, mice treated with 6 mg/kg [total dose] of baloxavir were only protected until Day 13, reaching 40% mortality by study end on Day 28. The potency of CD377 was further supported by BW data; scid mice treated at 0.3 mg/kg demonstrated only a transient BW drop of <3% [Day 4].

**Conclusions:** CD377 demonstrated robust efficacy in immune-competent and severely immunodeficient mouse infection models. The dose necessary to protect lethally challenged mice from both studies for 14 days was equivalent. This result supports further development of CD377 as a novel antiviral for prevention against influenza, including high-risk patients with immunodeficiencies.

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Abstract 6013

Effect of the capsule exchange between serotype K1 and K20 *Klebsiella pneumoniae* on serum killing, neutrophil phagocytosis and mice lethality

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**Background:** Capsular polysaccharide (CPS, K-antigen) of *Klebsiella pneumoniae* (Kp) is one of the major factors for hypervirulence. In this study, we investigate the effect of capsule exchange between serotype K1 and K20 Kp on serum killing, neutrophil phagocytosis and mice lethality.

**Materials/methods:** Capsule exchange strains between serotype K1 and K20 (K1∆K1cps::K20cps and K20∆K20cps::K1cps) and cps knockout strains (K1∆cps_{wzx-gnd} and K20∆cps_{wbaP-gnd}) were constructed to perform the experiment of serum killing, neutrophil phagocytosis and mice lethality.

**Results:** Capsular type of K1 and K20 ∆K20cps were confirmed as K1 whilst K20 and K1∆K1cps::K20cps were typed as K20. Neither K1∆cps nor K20∆cps had agglutination with K1-antiserum/K20-antiserum. The thickness and form of the capsule of the cps exchange strains shown in electron microscopy (EM) resemble to the type of cps it received. No capsule was found in K1∆cps and K20∆cps. Except the parental K20 strain, the parental K1 and the switched cps clones of K1 and K20 had shown hypermucoviscous (hmv) phenotype in the string test. In serum killing experiment, K1, K1∆cps and K1∆K1cps::K20cps were serum resistant (grade 5-6) whilst K20, K20∆cps and K20∆K20cps::K1cps were serum sensitive (grade 1-2). With the presence of the lipopolysaccharide (LPS), changing capsular type in Kp did not affect much in serum susceptibility. In neutrophil phagocytosis, K1, K20 and K1∆K1cps::K20cps were phagocytic resistant whilst K20∆K20cps::K1cps, both cps knockout strains were phagocytic susceptible. K1∆K1cps::K20cps would not alter its phagocytic susceptibility. Vice versa, K20∆K20cps::K1cps would turn from phagocytic resistant to sensitive. Likewise, LD_{50} of K1∆K1cps::K20cps [5.4x10^{1} CFU] in mice lethality was comparable to that of K1 [5.0x(10^{1}-10^{2}) CFU]. K20∆K20cps::K1cps [LD_{50}=3.1x10^{4} CFU] was attenuated when compared to K20 [LD_{50}=6.1 x (10^{3}-10^{4}) CFU]. LD_{50} of both cps knockout strains were higher than 10^{6} CFU. Under K1 genetic backbone, K1 could support K20 CPS expression and hence the virulence of K1∆K1cps::K20cps would keep. However, with K20 genetic backbone, K20 was unable to fully support K1 CPS expression resulting to the decline in virulence of K20∆K20cps::K1cps.

**Conclusions:** Switching capsular type in Kp could affect CPS expression, but retain its serum susceptibility. Effect on phagocytosis or mice lethality would depend on the genetic backbone of the recipient Kp.

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Abstract 6019

**The effectiveness of two rapid identification technologies in Gram-negative bacteraemia without antimicrobial stewardship interventions**

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**Background:** Rapid diagnostic technologies provide faster organism identification with subsequent antimicrobial susceptibilities, which would improve antimicrobial therapy selection or optimization. This quality improvement study consists of four parts: 1) no rapid diagnostic technologies (nRDT) 2) implementation of Verigene (VG) 3) implementation of Accelerate Pheno (AP), 4) AP with antimicrobial stewardship (ASP) intervention. The study aim is to compare the first three phases prior to implementing the last phase utilizing RDT with ASP interventions.

**Materials/methods:** We evaluated the first 100 cases of gram-negative bacteraemia (GNB) in the baseline period (2016) and intervention period (VG:2018, AP:2019) using quasi-experimental design. The subjects were divided into three groups based on the method of gram-negative organism identification: no RDT (nRDT), Verigene (VG), and Accelerate Pheno (AP). Vitek-2 was used for antimicrobial susceptibility testing. Inclusion criteria were patients with the first incidence of GNB and age ≥18-years-old. Patients with a hospital length of stay <2 days or those with GNB caused by organisms not detectible by either VG or AP were excluded. Study outcome measures include all-cause hospital mortality, length of hospitalization after positive blood culture (LOS), time to effective antibiotics, time to clinical stability, and incidence of VG/AP misidentification/detection failure. Electronic medical records were reviewed for patient specific factors and desired outcomes data.

**Results:** The study included 222 subjects (nRDT, n=67; VG, n=86; AP, n=69). All-cause mortality differed between groups, (nRDT, n=2(3%); VG, n=11(13%); AP, n=2(3%), p=0.02). LOS were similar between groups, (mean days±SD, nRDT, 6.1±6.9; VG, 6.5±5.8; AP, 7.6±10.9, p=0.64). Time to effective antibiotics was shortest in the AP group, (mean hours±SD nRDT, 5.5±8.8; VG, 5.2±13 ; AP, 3.6±9.3, p<0.001). Achievement of clinical stability were similar (nRDT, n=58(87%); VG, n=73(85%); AP, n=57(83%), p=0.81). A difference was detected in the time to clinical stability (mean days±SD nRDT, 1.9±2.8; VG, 4.4±8; AP, 1.6±2.2, p=0.004). Incidence rates of misidentification/detection failure were similar, (VG, n=2(2%); AP, n=6(9%), p=0.14).

**Conclusions:** We found outcome differences including, mortality, time to effective antibiotics, and time to clinical stability between the groups. Further evaluations of RDT with ASP interventions is needed to determine if further optimization RDT can be achieved.

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Adequacy of antibiotic treatment in patients with negative blood cultures: identifying a novel target for antimicrobial stewardship (NOBACT study)

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Background: There are scarce data about patients with negative blood culture (NBC) and how often they receive inadequate antimicrobial treatment. The objective of this study was to characterize the inadequacy of antibiotic treatment in patients with NBC with the aim of evaluating this as an easy-to-detect population that may be a good target for antimicrobial stewardship (AS) interventions.

Materials/methods: A multicenter, prospective cohort study conducted in 3 tertiary hospitals with active AS programmes in Spain, from October 2018 to July 2019 was performed. The features of randomly selected patients with NBC were collected. Adequacy of antibiotic treatment on day 2 was evaluated according to local guidelines. Chi-squared or Fisher, and Mann-Whitney U tests were used for comparisons.

Results: 499 patients were included. Antibiotic treatment on day 2 was considered inadequate in 204 (40%) of cases, due to insufficient coverage in 84 (41.2% of inadequate ones), too broad coverage in 76 (37.6%), unnecessary treatment in 34 (16.7%) and other causes in 10 (4.9%). There were no significant differences between patients with inadequate and adequate treatment in terms of demographics, underlying conditions, type of acquisition, suspected infection site or severity. Among patients with inadequate treatment, only 4% had undergone a specific AS intervention according to the local programmes. Overall, 30-day mortality was 19% (N=16) and 6.7% (N=8) among patients with insufficient (N=84) and sufficient coverage (N=120), respectively (OR, 3.29; 95% CI: 1.34-8.11).

Conclusions: Patients with NBC often received inadequate antimicrobial treatment, which may have clinical relevance, and had not been captured by other AS interventions. Therefore, this population may be a convenient and novel target for AS activities. No specific features of the patients were associated with inadequate treatment.

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Abstract 6025

Aetiology and outcome of children hospitalised for acute respiratory tract infections in Europe: findings from a multi-country combined case-control and cohort study

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Abstract third-party references: on behalf of the PED-MERMAIDS Study Group

Background: Recently, major aetiology and outcome studies on paediatric acute respiratory tract infections (ARI) have been reported from LMICs. In contrast, studies using standardised protocols across Europe are lacking.

Materials/methods: The EU-funded Paediatric Multi-centre EuRopean study of MAjor Infectious Disease Syndromes (PED-MERMAIDS) enrolled children under 5 years hospitalised for ARI and well controls across 11 EU countries. Information on symptoms, course of disease and clinical management was collected prospectively. Admission day nasopharyngeal swabs were analysed for influenza, parainfluenza, rhinovirus, coronavirus, metapneumovirus, bocavirus, respiratory syncytial virus (RSV), parechovirus, enterovirus and adenovirus and Streptococcus pneumoniae (Sp), Haemophilus influenzae, Mycoplasma pneumoniae, Chlamydia pneumoniae and Staphylococcus aureus.

Results: 353 ARI children, median age 1.13 years (IQR:0.44-2.56) and 352 controls, median age 1.76 years (IQR:0.96-3.73) were enrolled over 2½ years. Swabs were analysed from 327 ARI children and 302 controls. No potential pathogen was detected in 4.6% of ARI, only bacteria in 10.9%, only viruses in 33.9% and both bacterial and viral potential pathogens in 51.4%. Codetection of multiple (up to 4) viruses occurred in 31.2% of ARI and codetection of multiple bacteria in 16.9%. The most commonly detected pathogens are listed in table 1. Respiratory pathogens were detected in 62.8% of controls. Of the frequently detected pathogens, only RSV and influenza were strongly associated with hospitalisation for ARI (table 1). The population attributable fractions (PAF) were 33.6% for RSV and 18.0% for Sp.

Table 1:

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>cases(%)</th>
<th>controls(%)</th>
<th>OR(95%-CI)</th>
<th>Only pathogen detected in ARI(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSV</td>
<td>115[35.2]</td>
<td>7[2.3]</td>
<td>22.9[10.4-59.1]</td>
<td>31[27.0]</td>
</tr>
<tr>
<td>S.aureus</td>
<td>63[19.3]</td>
<td>83[27.5]</td>
<td>0.6[0.4-0.9]</td>
<td>6[9.5]</td>
</tr>
<tr>
<td>Influenzavirus</td>
<td>33[10.1]</td>
<td>6[1.0]</td>
<td>5.5[2.2-16.4]</td>
<td>13[39.9]</td>
</tr>
<tr>
<td>others</td>
<td>&lt;10%</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

OR: odds ratio, 95%-CI: 95%-confidence interval; *% of detected in cases

209 ARI children (60.6%) received antibiotics, but this was not associated with detection of bacterial pathogens in study samples (OR=0.78, 95%-CI:0.48-1.28). Length of stay in hospital ranged between 0 and 49 days (median 3, IQR:2-5) and no child in the study died after admission for ARI.

Conclusions: Similarly to LMIC studies, RSV had the highest PAF for ARI hospitalisation in Europe, but with considerably lower mortality.

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**Abstracts 2020**

**Abstract 6026**

**Resistome analysis of new bacterial species isolated at the Institut Hospitalo-Universitaire Méditerranée**

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**Background:** The discovery of new bacterial species is always a source of curiosity and new input for the scientific community. The era of high throughput sequencing and the subsequent easy access to the bacterial genomes open up a new field of research. In this work, we are exploring antibiotic resistance in new bacterial species isolated at the Institut hospitalo-universitaire méditerranée infection.

**Materials/methods:** The work included 352 new bacterial species including 78 actinobacteria, 45 bacteroidites, 213 firmicutes, 2 fusobacteria, 14 proteobacteria. The bioinformatic analysis was performed by the ARG-ANNOT software. Genes showing low similarity results with available sequences in ARG-ANNOT database are analysed using the blast program against the NCBI database. Bacteria with potential novel resistance genes were selected for in vitro antibiotic sensitivity tests.

**Results:** Of the 352 analyzed genomes, 261 bacteria had at least one resistance gene showing a minimum of 30% identity and coverage. The sequences identity exceeded 70% in only 188 bacteria. When the antibiotic sensitivity was tested, 44 of the predicted resistance genes showed a resistance profile in vitro. Five out of these 44 genes appear to be novel resistance genes with no significant similar sequences in the NCBI database. Among these, three genes encoding for fosfomycin resistance were found in Bacillus genus, one gene encoding for tobramycin resistance was found in Paenibacillus genus and one gene encoding for clindamycin was found in Enterococcus genus.

**Conclusions:** The results obtained during this work are mainly based on a bioinformatic approach. The new sequences encoding for potential resistance can be added to ARG-ANNOT database to strengthen our ability to identify genes involved in antibiotic resistance. Further in vitro experiments, like complementation cloning are needed to validate the resistance activity.

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Epidemiological and clinical characteristics among HIV adults with invasive fungal infections in north-eastern Mexico

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1Hospital Universitario Dr. José Eleuterio González, Monterrey, Mexico

Background: HIV-infected patients are at great risk of developing invasive fungal infections (IFIs), most of them AIDS-defining illnesses. Despite antiretroviral treatment, IFIs contribute to high mortality in this population. We aimed to evaluate the clinical characteristics (viral load, CD4+ cell counts and previous antiretroviral treatment) of IFIs among HIV-infected patients in North-eastern Mexico.

Materials/methods: We conducted a retrospective study including HIV-infected adults with suspected or confirmed IFI who were hospitalized from 2013 to 2019 in Hospital Universitario “Dr. José Eleuterio González” in Monterrey, México. Viral load, CD4+ cells count, the number of patients on antiretroviral therapy and intrahospital mortality were assessed.

Results: A total of 149 patients were included. The mean age was 39.8 years (±10.8) and 77.2% (n=115) were men. 98% (n=147) were born in Northeastern México. 20.1% (n=30) were already on antiretroviral therapy, with NNRTI as regimen base in 65.4% (n=17) of the cases. The median viral load was 152,000 copies/mL (IQR 2,620-350,000), and only 7.4% (n=6) of patients with available viral load were undetectable (<50 copies/mL). 81.8% of the patients had less than 200 CD4+ cells/µL. The most frequent fungal infection was Pneumocystis jirovecii pneumonia in 67.8% (n=101) of the cases, diagnosis was primarily made by clinical characteristics (20.8% [n=21] had P. jirovecii identification in bronchoalveolar lavage). Cryptocococcal meningitis was diagnosed in 21.5% (n=32) patients, 31 of 32 had positive CSF Indian ink stain, 11 of 32 had positive CSF culture and 1 of 32 had a positive PCR test. A higher incidence of histoplasmosis was noted with 8 of 10 cases seen in the last year in a non-endemic area, all of them with disseminated disease. Intrahospital mortality was 27.5% (n=41), and length of stay was a median of 10.5 days (IQR 6–19).

Conclusions: Although most IFIs are considered opportunistic infections in HIV-infected adults, 16.8% (n=13) had CD4+ cell counts higher than 200 cells/µL and 7.4% (n=6) had undetectable viral loads. Interesting data was found with the number of cases of histoplasmosis vs coccidioidomycosis despite epidemiological reports in Northeastern México. Intrahospital mortality remains high in our studied population making an argument for improving the diagnostic approach.

Presenter email address: gloria.m.aguirre@gmail.com
Abstract 6032

**Gram-negative screening the neonatal unit: can we predict bloodstream infections?**

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1University Hospitals Birmingham, Birmingham Heartlands Hospital, Birmingham, United Kingdom, 2Sandwell and West Birmingham Hospitals, Black Country Pathology Services, Birmingham, United Kingdom

**Background:** Gram-negative bacilli (GNB) account for 20-40% of cases of neonatal sepsis. Routine screening for colonisation with antimicrobial-resistant GNB is standard practice in many neonatal units (NNUs), however evidence supporting a positive impact on clinical care is lacking.

We aimed to assess whether the causative organism in GNB blood-stream infection (GNB BSI) could be predicted from prior colonisation screening results, and to calculate the number needed to screen in order to pre-emptively optimise antimicrobial treatment choice.

**Materials/methods:** Rectal and umbilical swabs were performed on admission to NNU and weekly thereafter as standard care. Retrospective search of four years of laboratory records from 2015-2019 for all neonatal screening samples and all clinical isolates was performed. Case notes were reviewed for babies with GNB BSI.

**Results:** 2835 neonates were screened, of which 1267 (45%) were found to be colonised with at least one GNB. There were 10 (0.4%) babies who developed GNB BSI, of whom six had a preceding colonisation screen that yielded the same species, with a median time difference of 11.5 days (range: 3-27). Of these, in one case ESBL-producing E coli was isolated on screening and consequently empiric antibiotic therapy with meropenem was used to treat them for suspected sepsis, prior to confirmation of the BSI. In this case blood cultures were taken on the day that the screening result became available.

**Conclusions:** In our NNU, GNB colonisation was very common (45%), but GNB BSI was rare (0.4%). We found only six GNB BSI cases preceded by proven colonisation with the same organism species, with significant treatment impact in only one case. The number needed to screen to pre-emptively optimise treatment was therefore 2835. These results suggest that colonisation screening may be of limited usefulness in guiding antimicrobial choice in suspected neonatal BSI, although rising carbapenem usage and antibiotic administration prior to blood culture sampling may be confounding factors. Other potential benefits, such as guiding infection prevention, and harms, such as over-use of broad spectrum antimicrobials, were not explored in this study but merit further work.

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Partnering with bedside nurses: questionnaire-based approach during an outbreak of carbapenem-resistant Acinetobacter baumannii in two separate intensive care units

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Background: Although bedside nurses are essential participants in the infection control, there are limited studies to understand their attitudes, practices, and barriers regarding infection control measures. This study aimed to assess attitudes and barriers to hospital infection prevention and control policies among intensive care unit (ICU) nurses.

Materials/methods: Carbapenem-resistant Acinetobacter baumannii (CRAB) was endemic in the two adult ICUs comprising 38 beds (19 in medical; 19 in surgical ICU) before 2019. A change in the clinical manifestation of CRAB infection was noted during the first 14 weeks of 2019 with 8 CRAB bacteremia episodes (5 in medical; 3 in surgical ICU). Following the ICU outbreak, aggressive infection control interventions were instituted. Despite reinforced infection control, CRAB has resurged, predominantly in medical ICU (Figure 1). An anonymous survey consisting of 30 questions, including 13 questions about compliance with infection control measures (point 1: do not consider, to 5: always perform), was administered to both ICUs.

Results: Thirty-two nurses (16 from each ICU) responded to the survey. Characteristics of responders were comparable between ICUs (Table 1). Surgical ICU nurses tended to perform infection control procedures more perfectly (p=0.15). Overall rate of 5-points responses (always perform) for the 13 questions on infection control procedures was significantly higher in surgical ICU than in medical ICU (82% vs. 69%, p=0.002). The scores for leader nurses regarding infection control in surgical ICUs were also higher (10 vs. 8, p=0.02), and the scores for physicians showed lower values than those of nurses in both ICUs. Although half of nurses thought that environmental cleaning was the most effective strategy, the rate of 5-points responses for daily surface cleaning and terminal cleaning was suboptimal (63% and 72%). Shortage of staff (28%) was the top-cited factor contributing to spread of infection.

Conclusions: CRAB outbreak is difficult to terminate and requires understanding the behaviors of bedside nurses. During the predominant resurgence of CRAB in medical ICU, we observed better compliance of nurses and better insights of leader nurses for infection control policies in surgical ICU than medical ICU. Infection preventionists should make more effort to partner with nurses for effective infection control.
Abstracts 2020

Figure 1. Incidence rate of *Acinetobacter baumannii* infection and colonization cases in two ICUs. VHP, vaporized hydrogen peroxide

<table>
<thead>
<tr>
<th>Table 1. Characteristics of subjects and responses by units.</th>
<th>Total (N=32)</th>
<th>MICU (n=16)</th>
<th>SICU (n=16)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median (IQR)</td>
<td>26 (25-28)</td>
<td>26 (25-30)</td>
<td>26 (25-28)</td>
<td>0.66</td>
</tr>
<tr>
<td>Man (%)</td>
<td>6 (19)</td>
<td>4 (27)</td>
<td>2 (13)</td>
<td>0.33</td>
</tr>
<tr>
<td>No. of years worked, median (IQR)</td>
<td>2 (1-5)</td>
<td>2 (1-8)</td>
<td>3 (2-3)</td>
<td>0.38</td>
</tr>
<tr>
<td>No. of years worked in ICU, median (IQR)</td>
<td>2 (1-5)</td>
<td>2 (1-5)</td>
<td>3 (2-3)</td>
<td>0.58</td>
</tr>
<tr>
<td>Nurse-to-patient ratio, median</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>0.58</td>
</tr>
<tr>
<td>Personnel points earned from 13 questions on infection control procedures, median (IQR)</td>
<td>62 (57-65)</td>
<td>60 (56-65)</td>
<td>64 (58-65)</td>
<td>0.17</td>
</tr>
<tr>
<td>No. of questions on infection control procedures with ‘5 points (always perform)’ responses, median (IQR)</td>
<td>10 (8-13)</td>
<td>10 (8-13)</td>
<td>13 (9-13)</td>
<td>0.15</td>
</tr>
<tr>
<td>Total No. of questions on infection control procedures with ‘5 points (always perform)’ responses (%)</td>
<td>3154 (76)</td>
<td>3144 (208)</td>
<td>3217 (82)</td>
<td>0.002</td>
</tr>
<tr>
<td>Knowledge, attitude, and practices of co-workers regarding multidrug-resistant organisms, median (IQR)</td>
<td>8 (8-9)</td>
<td>8 (7-9)</td>
<td>9 (8-9)</td>
<td>0.6</td>
</tr>
<tr>
<td>Knowledge, attitude, and practices of charge nurses and unit managers regarding multidrug-resistant organisms, median (IQR)</td>
<td>9 (7-10)</td>
<td>8 (5-9)</td>
<td>10 (8-10)</td>
<td>0.02</td>
</tr>
<tr>
<td>Knowledge, attitude, and practices of physicians regarding multidrug-resistant organisms, median (IQR)</td>
<td>6 (4-9)</td>
<td>6 (4-7)</td>
<td>7 (5-9)</td>
<td>0.29</td>
</tr>
</tbody>
</table>

IQR, interquartile range.
* Each question used a 5-point scale: 1: do not consider; 2: rarely; 3: often; 4: usually; 5: always perform.
* Each question used a 10-point scale.

Presenter email address: sleepju@naver.com
Abstract 6037

Environmental epidemiological survey of carbapenem-resistant Klebsiella pneumoniae in 5 intensive care unit
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Background: Carbapenem-resistant Klebsiella pneumonia (CRKP) is one of the nosocomial infection pathogens in hospital intensive care units (ICU), causing 26%-44% attributable death. The hospital environment, especially high-touch surfaces, is considered as potential reservoir for CRKP transmission.

Materials/methods: Chromogenic medium [mSuper CARBA] was used to sample in high frequency contact surface, common area surface, tank wall and drainage hole in five surgical ICU, and 24-hour positive culture were identified by MALDI-TOF Mass Spectrometer. Double disk diffusion test was used to detect phenotype, EDTA was used to detect metalloproteinase synergistically, and PCR was used to detect KPC and NDM resistance genes.

Results: The isolation of CRKP from high frequency contact surface (1/66), common area surface (1/89), or workers’ clothes (1/24) was rare. However, contamination of CRKP in drainage hole (25/29) was common. The phenotypic identification of carbapenemase showed that 5 strains produced class A enzyme, 11 strains produced class B metalloproteinase. PCR results confirmed that 2 strains produced KPC resistance gene and 3 strains produced NDM resistance gene.

Conclusions: CRKP contamination in high frequency contact surface is low, but high in drainage hole. The phenotypic identification of carbapenemase and PCR results indicated that CRKP may not be endemic by transmission in ICU.

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**Abstract 6039**

**Coverage of influenza vaccination in patients over 64 years hospitalised for severe acute respiratory infection according to their chronic diseases**

Latorre Millán Miriam1, Amparo Larrauri2, Alin Manuel Gherasim2, Clara Mazagatos2, Nieves Martínez Cameo1, María Pilar Hernández1, Yolanda Gracia1, Silvia Pina1, Vanessa Guerrero1, Antonio Rezusta1, Ana María Milagro Beamonte1

1Miguel Servet University Hospital, Aragon Health Research Institute (IIS Aragon), Zaragoza, Spain, 2National Epidemiology Center, Carlos III Health Institute, Madrid, Spain

Abstract third-party references: Miguel Servet University Hospital (Microbiology and Parasitology Service), Zaragoza, Spain. National Center for Epidemiology (Carlos III Health Institute), Madrid, Spain. Research group on infections difficult to diagnose and treat (Aragon Health Research Institute).

**Background:** The flu vaccination is the most appropriate protection measure for patients over 64 years old and people with chronic diseases. Knowledge of the coverage of influenza vaccination and the presence of influenza in patients over 64 years with chronic pathologies can provide useful information for their clinical management.

**Materials/methods:** Data of the patients included by the Miguel Servet University Hospital in the European IMOVE+ study, during the 2016/17, 2017/18, and 2018/19 seasons, were analyzed. Patients older than 64 years hospitalized with symptoms of Severe Acute Respiratory Infection (SARI), not institutionalized, provided a sample of pharyngeal smear in which the presence of influenza was detected by PCR-RT. The frequency of distribution of their most frequent chronic pathologies was studied according to the influenza vaccination status and diagnosis, using the chi-square test ($\chi^2$) adjusted by Monte-Carlo methods.

**Results:** 1314 patients with SARI were recruited, of which 57.45% were vaccinated. Compared to those not vaccinated, a higher proportion of respiratory disease presence and a lower one of morbid obesity was observed in those vaccinated patients (both $p<0.05$). No significant differences were found for these comparisons between those diagnosed with flu.

<table>
<thead>
<tr>
<th></th>
<th>Unvaccinated</th>
<th>Vaccinated</th>
<th>$\chi^2$</th>
<th>$p$</th>
<th>Unvaccinated</th>
<th>Vaccinated</th>
<th>$\chi^2$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n 557)</td>
<td>(n 752)</td>
<td></td>
<td></td>
<td>Flu + (n 234)</td>
<td>Flu + (n 237)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>462 (83.1%)</td>
<td>639 (85.0%)</td>
<td>0.848</td>
<td>0.357</td>
<td>193 (82.8%)</td>
<td>199 (84.0%)</td>
<td>0.109</td>
<td>0.741</td>
</tr>
<tr>
<td>Rheumatology</td>
<td>301 (54.0%)</td>
<td>420 (55.9%)</td>
<td>0.460</td>
<td>0.498</td>
<td>118 (50.4%)</td>
<td>118 (50.0%)</td>
<td>0.009</td>
<td>0.926</td>
</tr>
<tr>
<td>Respiratory</td>
<td>276 (49.6%)</td>
<td>416 (55.2%)</td>
<td>4.166</td>
<td><strong>0.041</strong></td>
<td>114 (48.7%)</td>
<td>123 (51.9%)</td>
<td>0.477</td>
<td>0.490</td>
</tr>
<tr>
<td>Anemia</td>
<td>188 (33.8%)</td>
<td>283 (37.6%)</td>
<td>2.024</td>
<td>0.155</td>
<td>81 (34.6%)</td>
<td>79 (33.3%)</td>
<td>0.086</td>
<td>0.769</td>
</tr>
<tr>
<td>Diabetes</td>
<td>184 (33.1%)</td>
<td>248 (32.9%)</td>
<td>0.004</td>
<td>0.952</td>
<td>86 (36.8%)</td>
<td>81 (34.2%)</td>
<td>0.341</td>
<td>0.559</td>
</tr>
<tr>
<td>Renal</td>
<td>163 (29.3%)</td>
<td>236 (31.4%)</td>
<td>0.670</td>
<td>0.413</td>
<td>69 (29.5%)</td>
<td>73 (30.9%)</td>
<td>0.116</td>
<td>0.733</td>
</tr>
<tr>
<td>Cancer</td>
<td>148 (26.6%)</td>
<td>182 (24.2%)</td>
<td>0.990</td>
<td></td>
<td>55 (23.5%)</td>
<td>63 (26.6%)</td>
<td>0.594</td>
<td>0.441</td>
</tr>
<tr>
<td>Liver</td>
<td>110 (19.7%)</td>
<td>149 (19.8%)</td>
<td>0.001</td>
<td>0.980</td>
<td>42 (18.0%)</td>
<td>41 (17.4%)</td>
<td>0.034</td>
<td>0.853</td>
</tr>
<tr>
<td>Morbid obesity</td>
<td>27 (4.9%)</td>
<td>18 (2.4%)</td>
<td>5.906</td>
<td><strong>0.015</strong></td>
<td>14 (6.1%)</td>
<td>8 (3.4%)</td>
<td>1.883</td>
<td>0.170</td>
</tr>
</tbody>
</table>

**Conclusions:** A significant proportion of patients hospitalized with influenza older than 64 years who had chronic pathology were not vaccinated, reinforcing the importance of influenza vaccination.

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Complete genome sequencing of extended-spectrum beta-lactamase (ESBL) producing Escherichia coli isolated from dairy cattle in Japan

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Background: Beta-Lactam antimicrobials are used worldwide in both human and veterinary medicine due to their little reported side effects and broad spectrum activity. The plasmid-mediated Extended-Spectrum Beta-Lactamase (ESBL) genes, which can confer resistance to third-generation cephalosporins, have been observed in isolates derived from livestock animals. Here, we present the complete genome sequence of ESBL-producing E. coli isolated from dairy cattle in Japan assembled using a combination of short- and long-read sequencing techniques.

Materials/methods: Ceftiofur resistant E. coli previously isolated from bovine feces: strain TC7-1, was used. Bacterial DNA was extracted using chemical and enzymatic lysis methods. ESBL genes were identified by PCR. The short- and long-read sequencing were performed using Illumina Miseq platform and Oxford Nanopore Technologies MinION platform, respectively. The long-read sequences were corrected with short-read sequences using LoRDEC v0.9 and assembled using Canu v1.7. The final assemble was annotated using Prokka. The plasmids and specific genes were identified with the bioinformatic pipeline of the Center for Genomic Epidemiology (CGE).

Results: The complete genome of TC7-1 comprises a 4,711,313 bp chromosome with 4,427 coding sequences. CGE revealed that TC7-1 belongs to the multilocus sequence type ST10 and harbors genes (wzy and filC) specific for O28ac/O42:H37 serotype. According to PlasmidFinder and ResFinder, TC7-1 contains a self-transmissible plasmid carrying the antimicrobial resistance (AMR) genes including blaCTX-M-2 and sul1. The incompatibility groups of AMR genes encoding plasmid of TC7-1 was IncN.

Conclusions: The first complete genome sequence of ESBL-producing E. coli, TC7-1, which includes IncN plasmid carrying blaCTX-M-2 isolated from livestock animal in Japan was obtained. A previous study reported that blaCTX-M-2 has been detected in E. coli isolated from humans in Japan. Further investigations are planned using the other two ESBL-producing E. coli isolated from livestock animals, which contains plasmids belonging to several Inc groups, to determine the genetic differences of ESBL-producing E. coli between human and animal origins.

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Hospital related factors associated with multidrug-resistant organism acquisition: a multilevel case control study
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1Aga Khan University, Karachi, Pakistan, 2The Indus Hospital, Karachi, Pakistan

Background: Antimicrobial resistance was recently declared a major global problem by World Health Organization. Such alarming rates of prevalence and transmission pose a public health problem as there are extreme limitations in the choice of antibiotics for treating patients with these infections. Association of modifiable hospital-related factors such as average ward/unit length of stay, understaffing and bed occupancy rates to multidrug-resistant organism acquisition remains unexplored. We aimed to determine the association of hospital-related factors with multidrug-resistant organism acquisition.

Materials/methods: We conducted a case-control study (1:2 ratio) at a tertiary care center in Karachi, Pakistan. Cases included patients with culture-proven multidrug-resistant organism after more than three days of hospitalization, while controls did not have a multidrug-resistant organism in any culture specimen. Data was collected on a structured proforma from hospital records for patient demographics and clinical data including admission diagnosis, type of infection and exposure to invasive devices. Ward/unit length of stay was the main hospital factor, defined as number of patient days per monthly number of patients in ward unit. Other hospital ward related risk factors included bed occupancy rate, 24 hour nurse to patient ratios and hand hygiene compliance. Multilevel logistic regression was performed to assess the individual and joint effects of patient- and hospital-related variables.

Results: 154 cases and 302 controls were included in the analysis. The odds of acquiring multidrug-resistant organism increased with the length of stay (OR 1.50, 95%CI 1.04-2.17) controlling for other factors. Among the patient related factors, MDRO acquisition was associated with presence of nasogastric tube, (OR 4.31, 95%CI 2.44-7.91), use of (OR 10.07, 95%CI 5.19-19.53), use of glycopeptide (OR 3.06, 95%CI 1.61-5.83), use of beta lactam/beta lactam inhibitor (OR 2.60, 95%CI 1.46-4.63) and central nervous system disease on admission (OR 3.75, 95%CI 1.65-8.51). MDRO acquisition decreased with increased hand hygiene compliance rate (OR 0.96, 95%CI 0.92 – 0.99). The intra class correlation was 0.94.

Conclusions: In conclusion, average length of stay in an individual ward is a modifiable hospital-related risk factor for multidrug-resistant organism acquisition. Moreover, it is also associated with empiric use of broad spectrum antibiotics whereas hand hygiene compliance is protective.

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Evaluation of cystic echinococcosis prevalence in an endemic region of Kazakhstan

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1Asfendiyarov Kazakh National Medical University, Almaty, Kazakhstan, 2University of Pavia, Clinical, Surgical, Diagnostic and Pediatric Sciences, Pavia, Italy, 3Kazakh Institute of Oncology and Radiology, Almaty, Kazakhstan, 4Syzganov National Scientific Centre of Surgery, Almaty, Kazakhstan, 5Texas A&M University, College Station, United States, 6IRCCS San Matteo Hospital Foundation, Unit of Infectious Diseases, Pavia, Italy, 7Royal Tropical Institute, Amsterdam, Netherlands

Abstract 6044

Background: Human cystic echinococcosis (CE) is a zoonotic infection caused by the cestode, Echinococcus granulosus. CE is believed to be endemic in Central Asia. We present findings from an ultrasound-based survey to estimate the prevalence of CE in the Turkistan region, where an incidence of 10.5/100,000 population was previously reported based on surgical records.

Materials/methods: The survey was carried out in October 2019 in six villages chosen following reported cases of surgically treated CE. Inhabitants 5 to 90 years of age were invited to undergo a free abdominal ultrasound to screen for CE cysts. All identified cysts were staged according to the World Health Organization-Informal Working Group on Echinococcosis (WHO-IWGE) classification. During the survey, information was also collected on individuals who had been previously diagnosed and surgically treated for CE.

Results: Of the 22,206 inhabitants, 2,252 (9.8%) underwent ultrasound screening (62.7% female). Twenty-two (0.97%) patients had CE, with a combined total of 33 cysts: 25 (73.5%) inactive (14 CE4, 11 CE5) and 8 (23.5%) active/transitional (2 CE1, 1 CE2, 3 CE3a, 2 CE3b). One additional patient had a post-surgical cavity. Of the 2,252 evaluated individuals, 68 (3.0%) reported prior surgical treatment for CE: 45 with hepatic cysts, 12 with lung cysts, and 5 with cysts in more than one location. Thirty-four (50.0%) patients were treated surgically in the last five years. In the same time period, the official surveillance system recorded 36 cases in the Turkistan region. In 25 patients, prophylaxis with albendazole was either not used or expert recommendations on dosing regimen and duration were not followed. Of the 22 current CE cases, 5 (22.5%) were under 18 years of age. Of the 68 patients who previously underwent surgical treatment for CE, 18 (26.5%) were under 18 years of age at the time of their surgery.

Conclusions: CE is endemic in the study area and the presence of active cysts suggests ongoing E. granulosus transmission. The large number of surgical patients suggests an underestimation of disease burden by the current surveillance system. Further studies on local CE epidemiology and the implementation of expert treatment recommendations are needed.

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Simplification of direct MALDI-TOF MS identification from positive blood culture broth

Jessica Brotto¹, Elizabeth Grabsch¹, Kyra Chua*², Marcel Leroi²

¹RMIT University Bundoora Campus East, Mill Park, Australia, ²Austin Health, Heidelberg, Australia

Abstract: Rapid identification of positive blood culture (posBC) isolates has the potential to improve patient treatment and outcomes. Utilisation of Matrix-assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS) is well established for rapid identification of positive blood culture (posBC) isolates, but may have significant impact on laboratory workflow. A previously reported simple direct method using saponin-lysis has potential to reduce blood culture turn-around times (TAT). We evaluated MALDI-TOF MS identification for saponin-lysis and pre-warmed short incubation chocolate blood agar (pCBA) methods, and compared these results to the reference standard of MALDI-TOF at 24 hours.

Materials/methods: PosBC broths were subcultured on pCBA (manually), and standard culture media (automated BD Kiestra system). As previously described, 1 ml of posBC broth was added to 200 µl 5% saponin, vortexed for 1 minute at its maximum setting, centrifuged for 1 minute (13000 rpm) and the pellet resuspended in 1 ml deionised water, and the suspension was re-centrifuged. The final spun pellet was spotted onto 4 target wells [each with 0.5 µl 70% formic acid (in-house)]. MALDI-TOF (4 wells each with 0.5 µl formic acid [BioMerieux]) was performed from pCBA when visible growth was present [checked at 2, 3 and/or 4 hours]. Results of both early identification methods were compared to MALDI-TOF identification at 18-24 hours. All MALDI-TOF testing was performed on Vitek MS (Biomerieux).

Results: Overall, 227 mono-microbial and 20 poly-microbial posBC were analysed. In the mono-microbial posBC group, saponin-lysis was concordant with 24-hour MALDI-TOF in 92/158 (58%) Gram-Positive (GP) and 49/58 (85%) Gram-Negative (GN) culture samples. pCBA concordance rates were 85/158 (54%) and 45/58 (78%) for GP and GN posBC respectively. 2/227 (2.2%) of isolates were misidentified using saponin-lysis, and none with pCBA. Labour time for saponin-lysis method was 7.4 min compared to 4.5 min for pCBA. Notably, results using the saponin-lysis method were available 2-4 (median 4) hours earlier.

Conclusions: Our study confirmed that saponin-lysis provides acceptable rates of identification for GP posBC, and high rates for GN posBC. Saponin-lysis and pCBA identification rates were comparable but saponin-lysis was more rapid, with expected benefits in patient management and anti-microbial stewardship.

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Abstract 6054

**Characterisation of phage obtained from methicillin-resistant Staphylococcus aureus**

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**Background:** Antimicrobial resistance is increasing despite new treatments being employed. Bacteriophages (phages) are one of the most promising alternatives to antibiotics for clinical use. Phage therapy is the use of lytic phages to treat pathogenic bacterial infections. However, there are limitations for the use of lytic phages, such as, rapid toxin release by the lytic action of phages, and difficulty in dose determination in clinical situations. Therefore, the use of recombinant phages has gained importance. In this study, we investigated small size lysogenic phage that can be easily manipulated.

**Materials/methods:** Previously, we isolated 23 temperate phages of 27 MRSAs isolated from the hospital. One of 23 phages is much smaller than the others. We characterized the small phage after cutting with a restriction enzyme and cloning into pBSK vector. The primer walking sequencing method was followed to complete the whole sequence of the phage. Obtained sequences were investigated by using the NCBI Blast program.

**Results:** The phage genome is around 20 kb in size and contains 41 ORFs. The phage contains genes related to tail, DNA packaging, and head structure, lysis, and DNA metabolism. The gene map of the phage is given in the figure (below). In addition to the genome size, sequence results indicate that the phage is more similar to the family of Podoviridae. The members of the Podoviridae family are characterized by a small genome and short noncontractile tail. When sequences were investigated by using the NCBI BLAST program, 41.4% of the ORFs were found to encode a protein, with 43.9% could not be identified, and the remaining 6 (14.6%) were evaluated as a hypothetical protein. In a study in which Pelletier et al. studied genomes and proteins belonging to 27 staphylococcal phages; 2170 ORFs were examined, 35% of them could be found for protein equivalent, 44% of these genes were matched with none of the proteins. The results of the study are close to our scientific results.

**Conclusions:** Here we described a new phage obtained from MRSA. Due to its small size, we assume that it will be useable for the genetic engineering of phages.

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Abstract 6056

**Basophil activation test use for identification of fungal sensitisation in severe asthma patients**

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**Background:** Identification of fungal sensitization is important for the diagnosis of allergic bronchopulmonary aspergillosis (ABPA). Recently, much attention has been paid to in vitro methods, the advantage of which is patient safety, specificity and the possibility of standardization. To study the possibility of using the basophil activation test (BAT) with Aspergillus fumigatus allergen using flow cytometry for identification of fungal sensitization in asthma patients.

**Materials/methods:** In prospective study included 76 severe asthma patients with median age 36 years (23 – 78). All patients underwent skin tests with six fungal allergens, determination of total IgE, specific serum IgE to fungal, domestic and epidermal allergens level (by enzyme immunoassay) and BAT by flow cytometry (Allergenicity kit, Beckman Coulter, USA). For basophil stimulation were used allergens A. fumigatus (AlcorBio, Russia). ABPA diagnosis was made according R. Agarwal et al (2013) criteria.

**Results:** Severe asthma with fungal sensitization (SAFS) was detected in 17 patients, severe asthma without fungal sensitization (SAwFS) - 39, ABPA – 20.

The amount of activated basophils A. fumigatus allergen in patients with ABPA was 81.9 (53.1-93.0) %.

The stimulation index (IS) in patients with ABPA was significantly higher 21.6 (18.0-32.2) compared with patients with SAFS and SAwFS: 4.4 (1.9-16.3) and 1.0 (0.8-1.4), p = 0.001, p = 0.000, respectively.

To evaluate the diagnostic value of IP in the detection of fungal sensitization, a ROC analysis was performed. The area under the curve (AUC) was 0.94, the sensitivity and specificity was 86.1% and 89.7%, (p<0.0001). The optimal cut-off value for IP was 2.55.

Among all patients with fungal sensitization, a direct correlation was found between IgE and the percentage and absolute number of eosinophils (r = 0.42, r = 0.46, p < 0.05), the level of sIgE to A. fumigatus (r = 0.47, p < 0.05), the percentage of basophils activated by the allergen A. fumigatus (r = 0.41, p < 0.05) and IP (r = 0.41, p < 0.05), as well as the inverse correlation with FVC (r = -0.35, p < 0.05).

**Conclusions:** Basophil activation test is a promising method for the laboratory diagnosis of fungal sensitization.

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Abstract 6057

**Development of an antimicrobial stewardship programme for post-acute and long-term care centre by the use of telemedicine**

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Abstract third-party references: On behalf PROA-PSMAR group

**Background:** Post-acute care (PAC) and long-term care (LTC) facilities represent important areas of antibiotic consumption. Our objective was to develop an interdisciplinary AMS program in a PAC-LTC setting.

**Materials/methods:** Prospective study was conducted in a 148-bed PAC-LTC center linked to a tertiary-level university hospital (January-October 2019). AMS-team was composed of a geriatrician and pharmacist from the PAC-LTC setting and an Infectious Diseases (ID) physician from the tertiary-level hospital. Previous years [2017-2018], formal AMS training was given to geriatrician. All patients under antimicrobial therapy admitted in the Post-Acute Unit (70 beds) were detected by the pharmacist through computer-generated data. Pharmacist and geriatrician reviewed and optimized these prescriptions. When complex patients, ID physician electronically reviewed them and made recommendations.

**Results:** 221 patients under antimicrobial therapy were evaluated by the AMS-team: 121 (54.8%) female, age 83 (IQR 73-88); 103 (46.6%) had prior surgery and 43 (19.5%) indwelling urinary catheter. Median Barthel index at admission and discharge were 33 (IQR 21-47) and 69 (IQR 31-88), respectively. Source of infection were: urinary 74 (33.5%), respiratory 63 (28.5%), soft tissue 34 (15.4%), bone 31 (14.0%), abdominal 6 (2.7%), catheter 3 (1.4%), unknown/others 10 (4.5%). Main microorganisms isolated were: *Enterobacteriaceae* 70 (31.7%), *Pseudomonas aeruginosa* 16 (7.2%), *Enterococcus* 13 (6%), *Staphylococcus aureus* 8 (3.6%), *Streptococcus* 4 (1.8%), others 11 (5.0%) and 17 (7.7%) polymicrobial. 17 (7.7%) had negative cultures and 65 (27.4%) not available. Regarding MDR profile, 13/70 (18.6%) *Enterobacteriaceae* were extended-spectrum-beta-lactamase (ESBL) carrying isolates and 2/70 (2.9%) had an acquired AmpC beta-lactamase. 8/16 (50%) *P. aeruginosa* isolates were XDR and 6/8 (75%) S. aureus MRSA. Main antibiotics used: 68 (30.8%) amoxicillin-clavulanate, 60 (27.1%) fluoroquinolones, 30 (13.6%) antipseudomonal-penicillins, 28 (12.7%) carbapenems and 25 (11.3%) cephalosporins. 63/221 (28.5%) were subsequently evaluated by the ID physician who made recommendations regarding: 48/63 (76.2%) duration (including stop unnecessary treatments), 31/63 (49.2%) antibiotic choice, 13/63 (20.6%) de-escalation, 6/63 (9.5%) intravenous-to-oral switch therapy and 5/63 (7.8%) dose adjustment.

**Conclusions:** The implementation of an interdisciplinary antimicrobial stewardship program in Post-Acute and Long-Term care facilities may be an effective intervention to improve antimicrobial use in these facilities. Telemedicine infectious diseases consultations may be useful in this setting.

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Abstract 6058

Evaluation of the performance of Vitek MS and Bruker MS on the identification of *Candida haemulonii* species complex

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**Background:** To evaluate the results of original identification, Vitek MS and Bruker MS identification of *Candida haemulonii* species complex collected from National China Hospital Invasive Fungal Surveillance Net (CHIF-NET) 2010-2015.

**Materials/methods:** A total of 40 *Candida haemulonii* and five *Candida duobushaemulonii* were collected from all hospitals in China as part of CHIF-NET 2010-2015. The original identification results were evaluated by setting the review results as “gold-standard”, and the performances of Vitek MS and Bruker MS matrix assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS) in the identification of the *C. haemulonii* species complex were observed.

**Results:** As compared with the molecular identification, the accurate rate of original identification of *C. haemulonii* was 47.5%, while 15% of the strains were mistakenly identified as *Kodamaea ohmeri* and *Cryptococcus neoformans* by CHROMagar chromogenic media, ATB Rapid ID32C, API 20C or Vitek 2 Compact system; *C. duobushaemulonii* could not be identified by using routine identification methods. As for the identification of the *C. haemulonii*, the accurate rate of the Vitek MS IVD2.0 and Bruker MS DB 5989 were 100% and 57.5%, respectively. There were no reference spectra for *C. duobushaemulonii* in the Vitek MS IVD 2.0 database, so it could not be identified by Vitek MS IVD 2.0 and misidentified all *C. duobushaemulonii* as *C. haemulonii* with confidence value >90%. There were no reference spectra for *C. haemulonii* complex in the Vitek MS RUO database, so this complex could not be identified by Vitek MS RUO. 20% of *C. duobushaemulonii* were identified correctly to species level by Bruker MS DB 5989. After complementation with the “in-house” database, all of the remaining isolates were correctly identified to species level (score >2.00).

**Conclusions:** This is the first study to evaluate the performances of Vitek MS and Bruker MS in the identification of *C. haemulonii* species complex in China. MALDI-TOF MS can provide rapid and accurate identification but is reliant on a robust mass spectra database. The performance of MALDI-TOF may be improved by adding mass spectral profiles (MSPs) into the current databases.

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Direct-acting antivirals failure in HCV genotype 3: virological features and efficacy of re-treatment

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Abstract

Background: direct-acting antivirals (DAA)-regimens are associated with failure in about 5% of the cases. The failure was associated with the emergence of resistance associated substitutions (RASs) within the viral quasispecies. This real-life study characterized the virological patterns in genotype 3 patients failing to DAA and evaluated the efficacy of retreatment.

Materials/methods: all the consecutive 51 HCV patients genotype 3 failed to DAA observed at the laboratory of infectious diseases of University of Campania, Naples were enrolled. All the patients were treated according to HCV genotype, international guidelines and local availability. Sanger sequencing of NS3, NS5A and NS5B was performed at failure by home-made protocols.

Results: Patients enrolled were mainly males (88,2%) with median age of 55 years (range, 31-80). HCV RNA, IU/ml median value was 1,0 x 10^6 (range, 1,3x10^3-2,2x10^7), 56,8% of patients had a diagnosis of cirrhosis, 80,4% were relapse, 19,6% were non responder.

Out of the 51 patients enrolled, 26 (51%) were re-treated. Table 2 shows the epidemiological, clinical and virological characteristics of the 26 retreated patients. At failure, 61,5% of patients presented one RAS and 19,2 % had 2 or more RAS. At retreatment 84,6% obtained SVR and 15,4% were relapse. In table 3 we analyze the SVR prevalence according to previous/latest DAA regimens, RASs distribution and Resistance-Guided Therapy (RGT). Patients retreated with the latest DAA regimen most frequently obtained SVR than patients retreated with previous generation of DAA (94,4% vs 62,5%, p<0.05). Patients with SVR most frequently had RGT (77% vs 25%, p<0.05).

Conclusions: The prevalence of RASs was high in our real-life population. Failed patients have at least one RAS in one HCV region. The latest DAA regimen more frequently obtained SVR despite previous regimen. Patients with RGT more frequently obtain SVR. NS3, NS5A and NS5B sequencing seems mandatory in the choice of re-treatment DAA.

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Abstract 6063

How long do patients with undiagnosed Chlamydia infection remain test positive? A lesson from the Finnish new variant of Chlamydia trachomatis

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Background: The Finnish new variant of Chlamydia trachomatis (Fi-nvCT) is characterized by a mutation (C1515T) in its 23S rRNA gene. Until its discovery in the spring of 2019, this variant caused false-negative test results in Aptima Combo 2 screening test (AC2). Since June, Hologic recommends reflex testing for negative/equivocal samples with relative light units (RLUs) ≥15 by a test with an alternative target, and ECDC recommends recalls of patients who may have received false negative results, with an initial look-back period of six months.

In southern Finland about 8% of chlamydia cases have been missed because of Fi-nvCT. The look-back period was set at six months prior to the earliest confirmed case, i.e. January 2018. Based on data collected in three Finnish laboratories using AC2, we expected that during this period, up to 96% of samples with RLUs ≥20 would have been positive for CT by Aptima CT.

Materials/methods: Probable false-negative samples were traced from the instrument and laboratory data. 101 patients (71 females and 30 males) were invited to give a new specimen.

Results: By the end of October, 49 (69% of invited) females and 24 (65%) males have been retested. Of them, 31 (42 %) have been positive for CT, all variant-type (AC2 RLU 11-52 and ACT≈6000). Results according to the interval between the samples are shown in the table. Clinical data on symptomatic treatments are pending.

<table>
<thead>
<tr>
<th>Interval between samples</th>
<th>≤6 months</th>
<th>7-12 months</th>
<th>&gt;12 months</th>
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<tr>
<td>Result of sample 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Females</td>
<td>CT pos</td>
<td>CT neg</td>
<td>CT pos</td>
<td>CT neg</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>14</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Males</td>
<td>CT pos</td>
<td>CT neg</td>
<td>CT pos</td>
<td>CT neg</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>8</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>All</td>
<td>CT pos</td>
<td>CT neg</td>
<td>CT pos</td>
<td>CT neg</td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>24</td>
<td>10</td>
<td>9</td>
</tr>
</tbody>
</table>

Conclusions: Our results suggest that a 6 to 12-mo look-back period may be feasible. However, among all patients diagnosed with Fi-nvCT in 2019, the earliest samples with AC2 RLU≥20 date 24 and 36 months prior to the diagnostic one in a female and a male patient, respectively.

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Presence and distribution of fungal species and dermatophytes in nail and skin samples

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Background: Cube Dx’s test hybcell Fungi DNA xB detects 6 fungal genera and 33 species by amplifying 28S DNA followed by the proprietary compact sequencing process. The limit of detection of this test is about 20 CFU/sample. This study examines the abundance of other (potential pathogenic) fungal species besides dermatophytes in healthy and patients’ skin samples.

Materials/methods: In total 192 skin and nail samples were analysed in this study, thereof 172 clinical dermatological samples from patients and 20 samples from individuals without signs of disease (healthy controls). Samples were lysed and total DNA was isolated using the automated MagnaPure96 system (Roche Diagnostics). All samples have been verified for dermatophytes with a lab-developed test using real-time PCR and melting point analysis (Unilabs AB). The relative frequencies of tested fungal species in patient samples and samples from healthy individuals were calculated and are shown in the illustration below.

Results: Of the clinical samples 34% were positive for dermatophytes by the conventional lab method. In the hybcell Fungi DNA positive samples could be identified by Tm peaks > 89°C. Some species were only detected in the patient group: Trichophyton spp., some Aspergillus species, Candida tropicalis, Zygosaccharomyces rouxii, Pichia kudriavzevii and Cryptococcus neoformans. Most others were found in both groups at similar ratios, but in different combinations for individual samples. Two fungal species exhibited exceptional patterns: Saccharomyces cerevisiae was identified in all samples of healthy individuals and in about 80% of patient samples, whereas Candida albicans was positive in more than 60% of patient samples but in only about 15% of samples from healthy individuals.

Conclusions: Trichophyton spp., Aspergillus spp., Candida tropicalis, Zygosaccharomyces rouxii, Pichia kudriavzevii and Cryptococcus neoformans were only found among the clinical samples, as expected. No difference in abundance was observed for most non-dermatophyte fungal species in nail and skin samples of patients and healthy individuals. These species were detected at individual ratios in all samples and should be regarded as normal flora of human skin and nails. Further investigation and inclusion of more samples is necessary to validate initial results.

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Abstract 6069

Comparison of clinical spectrum and outcomes of patients with extremely drug-resistant Salmonella enterica with multidrug-resistant strains

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Background: With the emergence of the Extensively Drug Resistant (XDR) strain of Salmonella Enterica, due to the H58 haplotype mutation identified in 2016 in Hyderabad Pakistan, there is a growing threat of complicated Enteric fever. Statistics from Sindh from November’ 2016 to July’ 2019 have reported 14297 cases of Enteric fever, of which 9822 were XDR, making the treatment challenging and leaving only carbapenems and azithromycin as the last resort.

Materials/methods: A retrospective chart review of culture positive Salmonella Typhi, in all age groups, was conducted, at the Indus Hospital Karachi from 1st July’ 2017 to 31st December’ 2018, capturing details of demographics, clinical features, treatment, complications and outcomes.

Results: 1518 Enteric fever patients were included in the study, 1341 pediatric and 177 adults. 50.5% [n=767] were XDR, 46.6% [n=707] Multi Drug Resistant (MDR) and 2.9% [n=44] Drug Sensitive (DS) enteric. 264 (17.4%) required admission (233 pediatric and 41 adults); 177 of which were XDR, 79 MDR and 8 DS. Definite outcomes are known for only 34.1% [n=517] patients, while 60.8% [n=923] were lost to follow or left against medical advice and 5.1% [n=78] were referred out due to non-availability of bed. Of the known outcomes, 33.7% [n=511] were cured, while 0.4% [n=6] died. In XDR cases, 37.2% [n=108] were cured on monotherapy, while 62.8% [n=182] were cured on multiple drugs. In MDR 59.1% [n=91] were cured on monotherapy, while 40.9% [n=63] were cured on multidrug therapy. Whereas, in DS, 50% [n=6] cases were cured on either of the regimens. Curiously, 4 cases of XDR Salmonella were cured with ceftriaxone monotherapy.

Conclusions: Due to shift of Salmonella Enterica towards the XDR strain, treating patients is delayed and sometimes unaffordable, especially in a resource limited country, leading to increasing morbidity and mortality. Further swift action and research needs to be undertaken to tackle this rapidly spreading disaster.

<table>
<thead>
<tr>
<th>Complications</th>
<th>XDR</th>
<th>MDR</th>
<th>DS</th>
</tr>
</thead>
<tbody>
<tr>
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<td>24</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Acute abdomen</td>
<td>83</td>
<td>27</td>
<td>1</td>
</tr>
<tr>
<td>PR bleeding</td>
<td>9</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Metastatic abscess</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>CNS manifestations</td>
<td>13</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>6</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Septic arthritis</td>
<td>2</td>
<td>0</td>
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</tr>
<tr>
<td>Death</td>
<td>4</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

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Comparative genomics of global linezolid-resistant Enterococcus faecalis strains unveils a chromosomal hotspot for optrA acquisition

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Abstract third-party references: The work was supported by UID/MULTI/04378/2019 with funding from FCT/MCTES through national funds.

Background: Linezolid-resistant Enterococcus faecalis (LREfs) carrying optrA are increasingly reported globally from multiple sources, but we still lack a comprehensive analysis of human and animal optrA-LREfs strains. We aimed to compare the genomic content of publicly available optrA-Efs genomes to give insights about the pathogenic potential of circulating clones and optrA mobilization.

Materials/methods: We investigated the phylogenetic structure, genetic content [ABR/virulence/prophages/plasmidome] and optrA-containing platforms of 28 publicly available optrA-positive E. faecalis genomes from different hosts in 7 countries through CGE tools [http://www.genomicepidemiology.org]. In house databases with 57 virulence and 391 plasmid-replication genes were tested using MyDbFinder-CGE. PHASTER identified the presence of prophages. Genomic data for 23S rDNA and rplC/rplD/rpIV mutations were compared to Efs-V583 (Geneious-Prime BLASTN). optrA-platforms were compared (Geneious;Easy-fig-v2.2.2;VectorNTI-advance-v11) and gene functions annotated [eggNOG4.5.1,http://eggnogdb.embl.de/#/app/home].

Results: Our analysis showed a diversity of clones and adaptive gene sequences related to a wide range of genera, mainly but not exclusive from Firmicutes. Epidemiologically unrelated clones [ST476-like and ST21-like] obtained from human clinical and animal hosts in different continents over 5 years [2012-2017] were phylogenetically related [3-122 SNPs difference]. optrA was located on the chromosome within a Tn6674-like element [n=9] or on medium-size plasmids [30-60 kb; n=14] belonging to main plasmid families [RepA_N/Inc18/Rep_3]. In most cases, the immediate gene vicinity of optrA was identical in chromosomal [Tn6674] and plasmid [impB-fexA-optrA] backbones. Tn6674 was always inserted in the same ∆radC integration site and embedded in a 32 kb chromosomal platform common to diverse strains [patients/healthy-humans/animals] in Europe/Africa/Asia during 2012-2018 (Figure). This platform is conserved among hundreds of Efs genomes and proposed as a chromosomal hotspot for optrA integration.

Conclusions: The finding of optrA in strains enriched in different adaptive traits and sharing common genetic backgrounds across different hosts/countries suggests the occurrence of common and independent genetic events occurring in distant regions, and might explain the easy de novo generation of optrA-positive strains. It also highlights the relevance of genomic studies exploring the dissemination and reservoirs of optrA at a global and One Health scales in order to anticipate a dramatic increase of optrA carriage and spread, with a serious impact in linezolid’s efficacy.
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Species distribution and antifungal susceptibility of yeast bloodstream isolates in adult patients at three university hospitals in South Korea

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Abstract third-party references: The authors wish to acknowledge the financial support of the Catholic Medical Center Research Foundation made in the program year of 2017.

Background: Echinocandin antifungals are the agents of choice for the treatment of invasive candidiasis. Widespread echinocandin usage has been accompanied by reports of emerging drug resistance among clinical Candida isolates.

Materials/methods: In a prospective multicenter study, we analyzed 106 of bloodstream isolates identified by yeast from three university hospitals in South Korea. For the molecular identification of yeast isolates, we performed an internal transcribed spacer (ITS 1 & 4 regions) PCR, sequencing, and blast searching. The alignment of their sequences was performed by clustal omega method, and phylogenetic analysis was performed using the Maximum Likelihood method based on the Tamura-Nei model of MEGA7. Also, we sequenced and analyzed hot spot regions (HS1 & HS2) mutation of the β-(1,3)-D-glucan synthase for the correlation of echinocandin susceptibility in C. albicans and C. tropicalis isolates.

Results: The sequencing analysis of ITS showed that C. albicans, C. parapsilosis, C. glabrata, and C. tropicalis isolates were prevalent in the yeast bloodstream infections. In addition, Clavispora lusitaniae, Cyberlindnera fabianii, Kodamaea ohmeri, Meyerozyma guilliermondii, Pichia kudriavzevii, Saccharomyces cerevisiae, and Wickerhamomyces anomalus were identified. The genetic distance in non-candida yeasts arranged from 0.00 to 0.25, and the phylogenetic analysis exhibited four of major clades diverged from that of major Candida species (C. albicans, C. parapsilosis, and C. tropicalis) except for C. glabrata. In the analysis of HS regions, there were no mutations (641-FLTLSRD-G-649 & 1357-DWIRRTYL-1364) in C. albicans and C. tropicalis isolates except for a few silent mutations of HS1 (5 isolates in C. albicans).

Conclusions: Rare yeast species accounted for about 10% of yeast bloodstream isolates. Despite the increased use of echinocandin antifungals, echinocandin resistance among C. albicans and C. tropicalis was still low among bloodstream isolates in South Korea.

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Estimation of the prevalence of the plasmid-encoded septicolysin gene in carbapenem-resistant Acinetobacter baumannii

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Abstract 6082

Background: Septicolysin is a member of the thiol-activated cytolysin family, a prominent group of bacterial toxins. The cytolysin mechanism of action is the formation of pores in the cell membrane, resulting in the lysis of host cells. The role of cytolysins in the pathogenesis of infections by a number of Gram-positive pathogens is well described. However, the prevalence of septicolysin in Gram-negatives such as A. baumannii is unknown. Recently, fatal clinical cases involving carbapenem-resistant A. baumannii (CRAB) harboring a plasmidic septicolysin gene were reported in Israel. In this study, we aimed (1) to compare the prevalence of the septicolysin gene in CRAB isolated from blood in 2019 vs. previous years; and (2) to evaluate the relationship between clonality and septicolysin gene prevalence.

Methods/Results: The sample consisted of 49 randomly selected CRAB blood isolates from 3 hospitals and one post-acute care facility in 2019 and 106 CRAB blood isolates from 1 hospital in 2008-2011, all in Israel. Septicolysin gene presence was detected by PCR; primers were designed using a core genome alignment analysis of three septicolysin-positive CRAB genomes. PCR products were sequenced to confirm septicolysin gene presence. CRAB clonality was determined by sequencing of the blaOXA-LIKE gene. Periods were compared using a test of proportions or a chi-square test.

Results: The septicolysin gene was detected in 95.9% [47/49] of the specimens from 2019 and in 79.2% [84/106] of the specimens from 2008-2011, representing a 17% increase (P=0.01) The distribution of variants among the 2019 isolates was oxa-66 53.1% [26/49], oxa-71 44.9% [22/49], and oxa-94 2.0% [1/49]. The distribution of variants among the older isolates was oxa-66 64.2% [68/106], oxa-71 16.0% [17/106], and blaOXA-LIKE 19.8% [21/106] (P<0.001). Comparing the earlier period to 2019, the prevalence of the septicolysin gene among oxa-66-type variants increased nonsignificantly from 86.8% [59/68] to 96.2% [25/26] (P=0.19). The presence of septicolysin among the oxa-71-type variants increased markedly from 41.2% [7/17] to 100.0% [22/22] (P<0.001).

Conclusions: The plasmidic septicolysin gene appears to have played a role in the spread of a hypervirulent CRAB clone.

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Abstract 6085

Faecal carriage of carbapenem-resistant *Acinetobacter baumannii*: comparison to clinical isolates from the same period

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Abstract third-party references: Bence Balázs, Zoltán Tóth, Fruzsina Nagy were supported by New National Excellence Pro- gram of the Ministry for Innovation and Technology (UNKP-19-3-1.), Gábor Kardos was supported by Bolyai Scholarship of the Hungarian Academy of Sciences

Background: Increasing incidence of *Acinetobacter baumannii* was documented in a tertiary-care hospital between 2010-2014, with increasing prevalence of carbapenem resistance mediated by *bla*\(^\text{OXA-23}\) carbapenemase. The dominant carbapenem resistant strain (ST2) was replaced by *bla*\(^\text{OXA-72}\) carriers (ST636; ST492) in 2015 among clinical isolates, as confirmed by whole genome sequencing. We investigated the prevalence of *A. baumannii* in faecal samples of inpatients in this high-incidence setting, and characterised faecal and clinical isolates collected between January and April 2017.

Materials/methods: Identification of *A. baumannii* faecal isolates was carried out by Microflex MALDI-TOF-MS. *A. baumannii* were not detected from any other samples of the patients. Susceptibility of isolates was determined by disk-diffusion method, according to EUCAST guidelines; carbapenemases were sought for by PCR. Whole genomes of 16 faecal isolates from 2017, 2018 and 2019 were sequenced by Illumina MiSeq; resistome and MLST types were determined. Time-kill assays were performed with meropenem, imipenem (16 and 128-1024 mg/L) and colistin (2-32 mg/L) and killing rates (k) were calculated.

Results: Twenty-four non-duplicate *A. baumannii* isolates were found in the examined period out of 2042 faecal samples (1.18%), contrasting previous years, when only one isolate was found in 4285 samples collected between February 2011 and February 2013 (0.02%). The prevalence of carbapenem resistance was lower among faecal than among clinical isolates (33.3% vs. 95.4%). The occurrence of *bla*\(^\text{OXA-72}\) was similar (70.8 % vs. 76.9% respectively), while *bla*\(^\text{OXA-23}\) occurred in 3.1% of clinical isolates and was completely lacking in faecal isolates. Among faecal isolates only the ST636 and ST492 have been detected; the ST2 and ST49, previously dominant in clinical isolates, were absent. Against carbapenem resistant faecal isolates, meropenem was bactericidal only at ≥256 mg/L against ST492, but against ST636 even 1024 mg/L remained ineffective. Imipenem at ≥256 mg/L and colistin at ≥2 mg/L were bactericidal against both Sfs.

Conclusions: The prevalence of the *bla*\(^\text{OXA-72}\) gene in faecal isolates, the absence of *bla*\(^\text{OXA-23}\) gene and the ST pattern suggests that the microbiota of the patients may serve as a source of the new, but not for the previously dominant strains.

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Abstract 6088

**Improving culture of Neisseria gonorrhoeae, by immediate plating and incubation at a venereology clinic**

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**Background:** Culture of *Neisseria gonorrhoeae* is necessary for surveillance of antimicrobial resistance. Total culture success rate of *N. gonorrhoeae* was 20% in 2014 at the Department of Microbiology, Oslo University Hospital, Norway. We hypothesized that immediate plating and incubation of patient samples would significantly improve culture rates of *N. gonorrhoeae*.

**Materials/methods:** From May 2016 to October 2017, a quality improvement study was performed at the Venereology Clinic of Oslo University Hospital. For 684 consecutive PCR positive samples of *N. gonorrhoeae* two samples were taken for culture:

1) Immediate culture involved plating of material from the site of infection directly on pre-warmed CLAT plates (selective enriched chocolate agar plates containing colistin, lincomycin, amphotericin B, and trimethoprim) and immediate incubation at 35°C, 5% CO₂, in moist atmosphere, for 48 hours. Plates were then transported to the Department of Microbiology for identification and antimicrobial susceptibility testing.

2) Standard culture involved transport of swabs (Puritan Liquid) to the Department of Microbiology for plating according to the routine procedure.

Culture success rate of immediate versus standard routine was compared.

**Results:** Overall culture rate was 59% during the study period. The immediate culture success rate was 55.6% (95% CI; [51.8 - 59.3]) versus the standard culture success rate 39.3% (95% CI; [35.7 - 43.0]). Culture results of PCR positive samples, immediate culture versus standard culture according to sample site are shown in table 1.

**Conclusions:** The total culture success rate was significantly improved when samples were plated and incubated immediately at the Venereology Clinic. We recommend immediate plating and incubation of samples from patients with gonorrhoea to optimize culture rates of *N. gonorrhoeae*

Table 1

<table>
<thead>
<tr>
<th>Culture result</th>
<th>Immediate culture / Standard culture</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n [% per sample site]</td>
</tr>
<tr>
<td></td>
<td>positive/positive</td>
</tr>
<tr>
<td>Anus*</td>
<td>92 [41.3%]</td>
</tr>
<tr>
<td>Pharynx*</td>
<td>11 [4.55%]</td>
</tr>
<tr>
<td>Urethra*</td>
<td>133 [68.2%]</td>
</tr>
<tr>
<td>Cervix/Vagina</td>
<td>9 [37.5%]</td>
</tr>
<tr>
<td>All sample sites*</td>
<td>245 [35.8%]</td>
</tr>
</tbody>
</table>

*P<0.05, significant difference in culture rate (McNemar’s test).

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Abstract 6090

**Benchmarking blood culture turnaround times in an automated laboratory, at a tertiary teaching hospital**

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**Background:** Blood cultures (BCs) detect blood-borne bacteria/fungi that may be causing an infection with serious and life threatening implications. Rapid and accurate (BC) results are essential in providing best patient outcomes and reducing hospital-associated costs. Positive-blood culture turnaround times (BC-TATs) for Austin Pathology Microbiology Laboratory (AuPath-Micro) were compared against recently published benchmarks for microbiology laboratories [with/without automated systems] for reporting; Gram stain (GS), organism identification (Org-ID) and antibiotic susceptibility testing (AST).

**Materials/methods:** AuPath-Micro utilises advanced technology to standardise specimen/culture processing and improve workload efficiency. Technology/automation includes Bactec-FX BC-System (BD), Kiestra-Work Cell Automation (BD), MALDI-TOF mass spectrometry (Vitek MS, Biomerieux) identification and automated antimicrobial-susceptibility (Vitek2-XL Biomerieux). BCs collected January-February 2019 from Austin Health patients (N=7838 bottles, 3976 requests, 1391 patients; 508/7838 [6.5%] positive) were reviewed. Detailed analysis of all first positive bottles (n=220, 184 patients) was performed, as these results have the most impact on patient management and are given highest priority.

**Results:** The median [Interquartile Range [IQR]] BC-TATs [hours from BC collection] to GS, preliminary results for Org-ID and AST were 21.1 [14.9-31.2], 24.2 [19.2-32.4] and 36.0 [32.9-43.4], respectively. Similarly, final-results for Org-ID and AST reporting were 35.3 [27.1-46.6] and 49.4 [40.3-65.3]. Respective benchmark results [in hours] for automated and non-automated laboratories were GS 19.2 [14.6-28.3], 19.2 [15.4-25.9]; final Org-ID 36.0 [22.3-43.7], 43.4 [32.2-59.0]; final AST 60.0 [45.4-73.0], 65.0 [59.0-71.8]. Unlike AuPath-Micro, both laboratories reported GS results 24/7. GS BC-TATs during AuPath-Micro business hours [BH] were 18.7 [13.4-26.6] and after hours [AH] 23.3 [19.0-37.7]. During BH AuPath-Micro reported BC-GS TATs 0.5hrs earlier than the benchmark. Facilitated by Kiestra-Automation and standardised incubation, final Org-ID and AST are set up where possible using 6hr subcultures from positive-BCs, potentially explaining rapid BC-TAT.

**Conclusions:** Measuring TATs against benchmarks is an important quality exercise that assists in optimising workflow and reporting in clinical laboratories. Method development and monitoring of BC-TATs will ensure that improvements in reporting of BC results are ongoing.

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Abstract 6093

**Carbapenem-resistant Enterobacteriaceae: a 7-year surveillance at Keimyung University Dongsan Hospital and changes after moving to a new location**

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**Background:** Carbapenem-resistant Enterobacteriaceae (CRE) is increasing within healthcare facilities and causing an important concern for health care and infection control globally. We described the epidemiologic and genetic characteristics of CRE isolated from patients at a tertiary care university hospital in 7 years, and compared any changes after moving to a new location.

**Materials/methods:** All CRE isolates were collected from patients between Oct 2012 and Oct 2019. The hospital was moved to a new location (10 km apart) on Apr 2019. The isolates were identified by automated identification system, subsequently confirmed by matrix-associated laser desorption ionization-time of flight mass spectrometry and antimicrobial susceptibility tests then, multiplex real-time PCR was used for identifying the types of carbapenemase of CRE.

**Results:** A total of 379 non-duplicated CRE were isolated: 241 isolates between Oct 2012 and Mar 2019 before moving, and 138 isolates during 7 months after moving. Carbapenemase producing CRE (CPE) was accounted 72.6% (275/379) in total, and the prevalence has increased significantly from 0% (0/2) in 2012 to 81.1% (150/185) in 2019. The comparisons of CPE prevalence before and after moving were 68.9% (166/241) and 79.0% (109/138), respectively. The types of carbapenemase-encoding genes were blaKPC 88.4% (243/275), blaNDM 4.7%, blaNDM with blaOX4-48 like 3.6%, blaOX4-48 like 1.8%, blaVIM 1.1%, and blaKPC with blaOX4-48 like 0.4%. The CPE with blaKPC genes was increased from 1.4% in 2017 to 94.0% in 2018 and was 94.5% after moving. The most common CRE species were in the order of *Klebsiella pneumoniae*, *Escherichia coli*, *Enterobacter cloacae* and *E. aerogenes*. Most common specimen type was sputum followed by urine and stool.

**Conclusions:** The incidence of CRE has risen significantly at this hospital since 2018 which was correlated with the overall incidence within Korea and continued its high prevalence even after moving to new place. While knowing new hospital started with newly admitted patients from emergency room and outpatient clinic, it may be worthwhile to evaluate the reason for this trend. Monitoring of hospital environment and enforced education for CRE could be important applications in infection control and prevention of unrecognized dissemination of CRE in the new hospital.

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Abstract 6094

Evaluation of a Point-of-Care molecular system for rapid detection of toxigenic *Clostridioides difficile* in paediatric patients: impact on diagnostic yield and time to result

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Abstract third-party references: Supported by Roche Diagnostics

**Background:** *Clostridioides difficile* is the main etiological cause of bacterial infectious diarrhoea in hospitalised patients. The standard microbiological diagnostic algorithm for detecting toxigenic *C. difficile* in our hospital is based on a two-step procedure that includes use of an enzyme immunoassay (EIA) targeting antigen glutamate dehydrogenase (GDH), enterotoxin-A, and Cytotoxin-B, followed by a point-of-care PCR targeting toxigenic *C. difficile*. This easy algorithm requires re-testing EIA GDH-positive and toxin-negative samples by PCR to distinguish toxigenic vs. non-toxigenic strains. As a consequence, time to result (TAT) of algorithm implementation may range from minutes to > 1 hour. cobas® Liat® Cdiff is a new single-step automated system for molecular detection of toxigenic *C. difficile* in 20 minutes. Our objective was to evaluate diagnostic yield of Liat compared to our two-step standard microbiological diagnostic algorithm.

**Materials/methods:** Prospective study including fresh stool samples collected from patients between 2 and 18 years of age suspected of toxigenic *C. difficile* infection attended in Hospital Sant Joan de Deu (Barcelona, Spain) during the period December 2018 - August 2019. Liat performance was compared with performance by the Cdiff quik check complete® EIA (TAT~30 minutes) combined with targeted Xpert® *C. difficile* PCR (TAT~47 minutes) in EIA GDH-positive and toxin-negative samples.

**Results:** A total of 122 stool samples were collected from 91 patients [mean age, 8 years] during the study period. Liat identified 24 (19.7%) positive samples. The EIA yielded 97 (79.5%) GDH- and toxin-negative results, 11 (9%) GDH- and toxin-positive results, and 14 (11.5%) GDH-positive and toxin-negative results, of which 11 (78.6%) were confirmed as positive for the toxin by PCR. Overall GDH- and toxin-positive samples by the standard algorithm were 22 (18.0%). There were 2 results positive by Liat and GDH- and toxin-negative by EIA: one result was confirmed as positive by PCR after re-testing the sample while another was confirmed as positive by the standard algorithm after testing a second stool sample from the patient 3 weeks later.

**Conclusions:** cobas® Liat® Cdiff, a rapid system for detection of toxigenic *C. difficile*, increased diagnostic yield in paediatric patients compared to a two-step standard microbiological diagnostic algorithm.

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Prevalence and genetic diversity of *Blastocystis* in asymptomatic and symptomatic individuals from Puducherry, India

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**Background:** *Blastocystis*, an intestinal parasite, consists of 17 subtypes (ST), of which nine are capable of inhabiting humans. *Blastocystis* pathogenicity is controversial as it harbours both symptomatic and asymptomatic individuals. In India, molecular studies on *Blastocystis* are meagre. Hence, large scale molecular epidemiological studies are required to unveil genetic diversity and pathogenicity of *Blastocystis*.

**Materials/methods:** In this cross-sectional analytical study, a total of 752 stool samples (379 male; 373 female) were collected from asymptomatic (group I, n=384) and symptomatic (group II, n=368) individuals. Group II was subcategorized based on the specific clinical presentations: diarrhoea (n=152), inflammatory bowel disorder (IBD, n=83), dysentery (n=75), irritable bowel syndrome (n=31), and colorectal cancer (n=27). 18SSU rDNA was targeted in PCR for the detection and sub-typing of *Blastocystis*. 83 representative samples were sequenced and phylogenetic analysis was performed using MEGA 7 software. The subtypes and allele types were determined using [http://www.pubmlst.org/Blastocystis](http://www.pubmlst.org/Blastocystis) database. Fisher’s exact test was employed for the comparison between the groups. At 95% CI, p-value < 0.05 was considered statistically significant.

**Results:** Asymptomatic individuals had higher occurrence of *Blastocystis* (n=135; 33.7%) compared to the symptomatic patients (n=117; 31%) but statistically insignificant (p=0.33). Within-group II, patients having diarrhoea had the highest detection rate of *Blastocystis* (n=57; 37.1%) and the least in patients having IBD (n=18; 21.6%). A Comparison between subgroup IBD and asymptomatic group yielded statistically significant results (p=0.016). Out of the 252 samples positive for *Blastocystis*, ST1 (n=79), ST2 (n=23), ST3 (n=145), and ST1+ST3 mixed infections (n=5) were identified. ST3 was predominant subtype in both groups. Sequenced samples were deposited in NCBI GenBank (Accession. No. MK719604-MK719686). Allele 31, 34, and 36 of ST3, allele 9 and 11 of ST2 and allele 4 and 80 of ST1 were detected. The phylogenetic tree showed no distinct segregation of sequences of symptomatic and asymptomatic isolates.

**Conclusions:** This study largely contributes to *Blastocystis* molecular epidemiology in India. For the first time, ST2 was identified from India. However, the existence of all three subtypes in both symptomatic and asymptomatic individuals infers that inter-subtype variation may not be a reliable marker to assess the pathogenicity of *Blastocystis*.

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**Abstract 6104**

**Short- and long-term outcomes of infective endocarditis admission in adults: a population-based registry study in Finland**

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**Background:** Infective endocarditis (IE) is a disease associated with high mortality. However, data of factors associated to length of stay (LOS) in hospital due to IE is scarce. In addition, long-term mortality of more than one year is inadequately known. In this large population-based study we investigated age and sex differences, temporal trends, and factors affecting the LOS due to IE and in-hospital, 1-year, 5-year and 10-year mortality of IE.

**Materials/methods:** Data of patients (≥18 years of age) admitted to hospital due to IE in Finland during 2005-2014 were collected retrospectively from the nationwide obligatory registries.

**Results:** We included 2166 patients in our study. Of the patients 67.8% were men. The mean age of the patients was 60.7 years (SD 18.2, range 18-97). The median LOS was 20.0 days (20.0 days in men and 18.0 in women, p=0.015). In the youngest patients (18-39 years) the median LOS was significantly longer than in the oldest patients (24.0 vs. 16.0 days, p=0.014). Patients with Charlson Comorbidity Index (CCI) score of 0 had significantly longer LOS compared to the patients with CCI score of ≥1 (p=0.008). The in-hospital mortality was 10%. The 1-year mortality was 22.7%, 5-year and 10-year mortality 37.5% and 48.5%. The 5-year and 10-year mortality was higher in women (HR 1.18, p=0.034; HR 1.18, p=0.021). Both the in-hospital and long-term mortality increased significantly with aging and comorbidity burden. Both the mortality and LOS remained stable over the study period and no seasonal variation was found.

**Conclusions:** Men had longer hospital stays due to IE compared to women. The youngest patients had the longest admissions. The 5- and 10-year mortality was higher in women. No seasonal variation was found in the LOS or mortality of IE. The mortality of IE or LOS did not change over time.

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Abstract 6106

**Diagnosis of deep cutaneous mycoses in kidney transplant recipients by clinical metagenomics approach**

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¹Necker, Paris, France, ²Hôpital Henri-Mondor Ap-Hp, Créteil, France

**Background:** Deep cutaneous mycoses in transplant recipients are infections frequently caused by fungal invasion of the skin and subcutaneous tissue frequently arising after traumatic inoculation. They often involved rare or emerging opportunistic fungal pathogens originated from soil, yielding the species identification difficult. Clinical Metagenomics (CMg) could be a comprehensive method for pan-pathogen detection and particularly accurate identification of fungi from clinical samples. However, fungal infections have been little explored by these techniques because of incomplete genetic knowledge and the low percentage of genome informativeness for its identification. We propose in this study to validate the CMg on a cohort of kidney transplant patients, presenting a subcutaneous fungal infection.

**Materials/methods:** Biopsies of 13 kidney transplant patients with fungal subcutaneous infection characterized by conventional mycology techniques (microscopy, culture, mass spectrometry, molecular biology) were tested by CMg. An ISO 15189 accredited CMg pan-pathogens technics routinely used was performed with specific pan-pathogen extraction, DNA/RNA library prep followed by sequencing with NextSeq500 (Illumina) and analysed with MetaMIC software. An algorithm including informative fungal genes was developed to allow accurate species identification.

**Results:** Based on DNA, only 7/13 patients could be diagnosed positive while 13/13 patients were screened with a correct identification to the genus from the RNA including dematiaceous molds (n = 6), hyphomycetes (n = 3), dermatophyte (n = 2), and Mucorales (n = 2). Among these 13 patients, 9 were identified to the species level with a high confidence. Fungal loads could be established and showed a median of 1.93 log higher with RNA compared to DNA explaining the difference in sensitivity between the two markers.

**Conclusions:** Metagenomics using unbiased RNA sequencing improves the efficiency of CMg method to identify fungal pathogens even from cutaneous biopsies which are a difficult matrix because of the low fungal genetic materials compared with human. We were able to show that under extreme conditions, CMg had the ability to establish a reliable fungal identification, confirming its pan-pathogenic spectrum. Moreover, this accredited routinely used technic demonstrates that it can be perfectly adapted in complex cases of infection involving rare pathogens.

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Abstract 6107

Epidemiological changes in bloodstream infection in southern Spain during the last ten years: results from the PROBAC study

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Background: During the last decade, some changes in the epidemiology of invasive infections have been reported; however, specific studies with patient-level data are scarce. The aim of this study is to describe and evaluate the epidemiologic changes in bloodstream infections (BSI) during the last decade in Andalusia, Spain.

Materials/methods: Data from two prospective cohorts of BSI in adults with the same methodology performed ten years apart in 11 hospitals (8 tertiary and 3 community) in Andalusia, Spain were compared; the 2006/2007 cohort was performed between October 2006 and March 2007, and the 2016/2017 cohort between October 2016 and March 2016. Population-based incidence rates were calculated and extrapolated for 1 year. Relative risk ratios were calculated between the 2 periods. Multivariate analyses were performed by logistic regression.

Results: Overall, 1,262 episodes of BSI were included, 563 (44.6%) in 2006/2007 and 699 (55.3%) in 2016/2017. Incidence was 91 and 113 cases per 100,000 population-year in 2006/2007 and 2016/2017, respectively. The incidence increased for community (15 and 35 in 2006/2007 and 2016/2017, respectively) and healthcare-associated episodes (21 and 30), and was reduced for nosocomial ones (53 and 47). Similar changes were seen for incidence rates based on admissions. Multivariate models selected the following changes in patients’ features in 2016/2017, after controlling for type of acquisition: higher age (OR=1.02,95%CI:1.01-1.03), lower urinary catheter (OR=0.37,95%CI:0.26-0.48) and lower Pitt score (OR=0.76,95%CI:0.71-0.82). Crude comparisons in aetiology showed an increase in Gram negative organisms (51.5% in 2006/2007 vs 58.8% in 2016/2017, RR=1.14,95%CI:1.03-1.26), and specifically in Klebsiella and Proteus spp.; and a reduction in Gram positives (45.6% vs 35.8%, RR=0.78,95%CI:0.69-0.90), specifically in coagulase-negative staphylococci. The proportion of methicillin-resistance among S. aureus decreased from 32% to 15.3%, and of ESBL-producers among Enterobacterales from 15.1% to 11.2%. There were no cases of carbapenemase producers in 2006/2007 and one in 2016/2017. Adjusted estimations considering patients’ features and exposure to procedures showed a reduction in coagulase-negative staphylococci (OR=0.47,95%CI:0.32-0.69); and an increase in Proteus spp. (OR=3.12,95%CI:1.18-8.23) and Candida spp. (OR=3.01,95%CI:1.03-8.86).

Conclusions: We found relevant epidemiological changes in BSI in our area, including rates, frequency of acquisition types, changes in patient's profiles and in aetiologic agents.

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Healthcare-associated bacteraemic urinary tract infections: results of the prospective multi-centre ITUBRAS-2 project

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Abstract third-party references: On behalf of ITUBRAS-2 study group, GEIH/GEMARA groups of the Spanish Society of Infectious Diseases and Clinical Microbiology (SEIMC), Supported by MSD

Background: The ITUBRAS-2 project is a Spanish prospective multicenter study of bacteraemic urinary tract infections (BUTI). The aim of this study was to compare community-onset healthcare-associated (CO-HCA) with hospital-acquired (HA) BUTI.

Materials/methods: A multicenter cohort observational study was conducted at 12 Spanish hospitals. All consecutive CO-HCA-BUTI and HA-BUTI episodes were prospectively included [September 2017-April 2019]. Susceptibility results were interpreted according to 2019 EUCAST criteria. MDR profile was defined as non-susceptibility to ≥1 agent in ≥3 antimicrobial categories and XDR profile as resistance to ≥1 agent in all but ≤2 antimicrobial categories

Results: 445 episodes were included: 224 CO-HCA-BUTI and 221 HA-BUTI. Regarding CO-HCA-BUTI group, Friedman criteria were: 146 (65%) prior hospitalization, 71 (32%) receiving specialized ambulatory care, 93 (42%) indwelling urinary devices, 50 (22%) residency in long-term care facility, 21 (9%) receiving chemotherapy, 4 (2%) haemodialysis and 4 (2%) day-hospital patients.

Table 1 summarizes main differences between groups.

Causative microorganisms isolated in the cohort were: 221 (50%) *Escherichia coli* (68% MDR), 103 (23%) *Klebsiella spp.* (46% MDR, 5% XDR), 64 (14%) other *Enterobacteriaceae* (39% MDR, 3% XDR), 38 (9%) *Pseudomonas aeruginosa* (29% MDR, 18% XDR) and 22 (5%) *Enterococcus spp.* (32% MDR).

<table>
<thead>
<tr>
<th>CO-HCA-BUTI (n=224), n(%)</th>
<th>HA-BUTI (n=221),n(%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, m [IQR]; years</td>
<td>77 (69-83)</td>
<td>71 (62-78)</td>
</tr>
<tr>
<td>Charlson, m [SD]; points</td>
<td>6.7 (2.86)</td>
<td>6.03 (3.02)</td>
</tr>
<tr>
<td>Prior antibiotic</td>
<td>164 (73)</td>
<td>152 (69)</td>
</tr>
<tr>
<td>Pitt score, m [SD]; points</td>
<td>1.66 (1.94)</td>
<td>1.24 (1.69)</td>
</tr>
<tr>
<td>Septic shock</td>
<td>36 (16.8)</td>
<td>23 (11.1)</td>
</tr>
<tr>
<td>MDR bacteria</td>
<td>120 (56.9)</td>
<td>104 (51.5)</td>
</tr>
<tr>
<td>Appropriate empirical treatment</td>
<td>181 (81.9)</td>
<td>164 (78.9)</td>
</tr>
<tr>
<td>Clinical cure</td>
<td>121 (54.0)</td>
<td>145 (67.4)</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>18 (8)</td>
<td>16 (7.4)</td>
</tr>
</tbody>
</table>

Clinical cure was independently associated with HA-BUTI [OR 1.88; 95%CI 1.23-2.85]. In an adjusted logistic regression analysis, Charlson Comorbidity Index [OR 1.26; 95%CI 1.021-1.55] and being immunosuppressed [OR 7.05; 95% 1.56-31.83] were identified as independent risk factors for mortality.

Conclusions: A worrying high rates of MDR were observed in healthcare-associated BUTI in our country, higher than 50% in both CO-HCA and hospital-acquired infections. Although no differences were observed in mortality, patients with CO-HCA-BUTI presented a worse clinical cure than hospital-acquired BUTI.

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Abstract 6110

**Persister response of Klebsiella pneumoniae to colistin exposure**

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**Background:** Persister cells are responsible for chronic recurrent infections. During antibiotic therapy small population of bacteria, known as persisters, can survive and become a source of relapsing resistant infections. Our aim was to investigate the response of starvation induced and colistin induced K. pneumoniae persister cells to colistin exposure.

**Materials/methods:** One carbapenem resistant, colistin susceptible clinical K. pneumoniae isolate (K1251) was studied. Two types of persister cells were generated with starvation of cultures [16 hours of incubation] and colistin stress [10XMIC, 1 hour]. Wild type cells were used as control group for the experiment. Time kill assay was performed with exposure of 10XMIC colistin and at time points of 0th, 1st, 2nd, 4th, 6th and 24th hours colony counts (CFU/ml) were determined. Meanwhile, cells were examined for viability with resazurin assay and NPN assay was performed for membrane integrity of the cells.

**Results:** In time kill assays, 10XMIC colistin did not cause growth inhibition on both general persister (log10 cfu/ml 7.25; 7.0; 6.90; 6.85; 7.19 at 0th, 1st, 2nd, 4th, 6th, respectively) and colistin persister (log10 cfu/ml 3.26; 1.99; 2.27; 1.96; 2.88 at 0th, 1st, 2nd, 4th, 6th, respectively) cells in 6 hours. However, in wild type cells 4-log decrease in colony counts was detected within one hour (log10 cfu/ml 7.50; 3.31 at 0th, 1st, respectively). In resazurin assay, viability of the both types of persister cells was constant until 6th hour of experiment. In NPN [1-N-phenyl-naphthylamine] uptake assay, membrane integrity was less than growth control in colistin induced persister cells however increased membrane integrity was found in general persister cells.

**Conclusions:** K. pneumoniae persister cells may have different types of phenotypic response to colistin stress depending on their triggering factors. General and colistin induced persister cells resist to high concentration of colistin however only colistin induced persister cells lose their membrane permeability.

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Secular trends in the epidemiology and clinical characteristics of *Enterococcus faecalis* infective endocarditis in a referral centre (2007-2018)

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**Background:** Recent studies suggest that *Enterococcus faecalis* infective endocarditis (EFIE) is more frequent than expected. The aim of this study was to analyze the epidemiological and clinical changes of EFIE between 2007 and 2018 in a referral centre for IE.

**Materials/methods:** First, all definitive IE episodes treated in our centre during the study period were registered prospectively. The Mantel-Haenszel (MH) trend test was used to verify trends in the percentage of aetiologies over time.

Second, definite EFIE episodes were divided into three 4-years periods. The clinical differences between periods were studied using $\chi^2$ or Fisher exact test for qualitative variables, and Kruskal-Wallis for continuous variables.

Third, we collected retrospectively all episodes of *E. faecalis* monomicrobial bacteraemia diagnosed in our centre between 2010 and 2018, the number of echocardiograms performed in that patients and the number of definite EFIE diagnosed. The MH trend test was used to verify trends in the percentage of echocardiograms performed and EFIE diagnosed over time.

**Results:** Between 2007 and 2018, 648 definite IE episodes were treated in our centre. We detected an increase in the percentage of EFIE (from 15% in 2007 to 25.3% in 2018, $P=0.038$), currently being the first cause of IE.

We studied 108 episodes of definite EFIE (2007-2010 n=30, 2011-2014 n=22, 2015-2018 n=56). Patients from the last period were older (median 70.9 vs 66.5 vs 76.3 years, $P=0.015$), abdominal origin was established more frequently (20% vs 13.6% vs 42.9%, $P=0.014$), they had less indication of surgery (63.3% vs 54.6% vs 32.1%, $P=0.014$), and a non-statistically significant lower in-hospital mortality (30% vs 18.2% vs 12.5%, $P=0.139$).

There was an increase in the percentage of echocardiograms performed in *E. faecalis* monomicrobial bacteraemias between 2010 and 2018 [30% in 2010, 51.2% in 2018, $P=0.014$], as well as in the percentage of definite EFIE diagnosed [15% in 2010, 32.6% in 2018, $P=0.004$].

**Conclusions:** *E. faecalis* is a frequent and increasing cause of IE. Its greater diagnosis seems to be linked to an increase in the percentage of echocardiograms performed. The multiple factors that justify changes in the clinical characteristics of EFIE should be thoroughly studied.

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Abstract 6113

**Mutations variability of KPC-3 carbapenemase related to ceftazidime/avibactam resistance found in Klebsiella pneumoniae strains isolated in Verona, Italy**

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**Background:** Avibactam is a non-β-lactam β-lactamase inhibitor, active against KPC enzyme, approved, in combination with ceftazidime. Ceftazidime-avibactam (CZA) resistance is an emerging threat. Porins mutations, efflux overexpression usually accounts for resistance in clinical isolates. Recent reports showed the involvement of KPC mutations in the CZA resistance.

This study focused on the analysis of KPC sequence of KPC producers *Klebsiella pneumoniae* resistant to CZA, isolated from purulent specimens.

**Materials/methods:** 9 KPC producer *K. pneumoniae* resistant to CZA were studied. Antimicrobial susceptibility was performed by broth micro dilution with a fixed concentration of avibactam of 4 mg/L. Phenotypic determination of carbapenemase production was based on Carba NP test and immune-chromatographic Carba5 test. Molecular characterization of carbapenemase genes (*blaKPC*, *blaVIM* and *blaIMP*, *blaNDM*) and ESBL genes (*blaCTX-M*, *blaTEM*, and *blaSHV*) was performed through PCR. Bioinformatics analyses were performed by Illumina sequencing to determine genetic mutations.

**Results:** All 9 strains confirmed CZA resistance and amplification of *blaKPC* gene. Eight out of 9 strains showed KPC production by immune assay.

Two strains showed the same deletion of 6 nucleotides in position 498-503, corresponding a deletion of a glutamic acid and leucine in position 167 and 168. The amino-acid in position 167 is involved in the proton acceptor active site.

One strain showed the mutation D179Y bringing to KPC-31 variant, known to be responsible for CZA resistance. The amino acids 163-179 in KPC include the omega-loop involved in the proton acceptor active site.

One strain showed the mutation T243M, mutation that is comprise in the region close to the hinge-loop that surrounds the active site of KPC.

All isolates showing deletion/mutation in the *blaKPC* gene had no carbapenems hydrolysis activity, presented low carbapenems MICs. The strain harboring KPC-31 confirmed also a negative immune-chromatographic assay.

5 strains had a KPC-3 variant without mutations, all of them harbor *blaSHV* and *blaCTX-M1* group.

**Conclusions:** We confirmed the variability of mutations, responsible for CZA resistance, affecting KPC-3 variant.

We found three different mutations in 9 strains.

Point mutations seems to drive the emergence of CZA resistance, probably related to drug exposition.

Further investigation on the ESBL genes is needed.

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The appropriateness of prescribing antimicrobials in an infectious emergency outpatient department

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Abstract 6116

Background: Overuse of antibiotics has contributed significantly to antimicrobial resistance, and antimicrobial stewardship is among important measures to reduce its spread. Despite up-to-date guidelines, adherence is questionable and should be regularly assessed. We aimed to assess the rationality of antibiotic prescription and adherence to recommendations at our infectious emergency outpatient department.

Materials/methods: In this retrospective study, antibiotics prescribed to adult patients in the outpatient department were analysed. Recorded prescription parameters - suitability of drug choice, prescription correctness, and overall rationality, including right diagnosis, drug suitability, prescription correctness and concomitant diseases - were assessed for adherence to local recommendations by an experienced infectious disease specialist.

Results: 896 patients were included in the period from January 1st and October 31st 2018. There were 452 (50.4%) males and 444 (49.6%) females, with a mean age of 59 ± 20.6 years. We included outpatients with new antimicrobial prescription (first or changed from another antimicrobial). Co-amoxicillin was most frequently prescribed (n=224; 25.0%), followed by doxycycline (n=139; 15.5%) and ciprofloxacin (n=110; 12.3%). Overall, the diagnosis was correct in 692 (77.8%) cases, antibiotic suitable in 721 (80.5%) cases, and prescription correct in 629 (70.2%) cases. Prescription was most often incorrect due to wrong or unspecified duration, as observed in 220 (24.6%) cases. Significant differences were observed for drug suitability with regards to patient age (p=0.042), (more errors made in younger patients), organ system affected (p<0.001) (the most errors in respiratory infections), and antibiotic class (p<0.001) (the most errors when prescribing moxifloxacin and azithromycin). No association was observed between doctors’ gender and drug suitability (p=0.074), prescription correctness (p=0.628) or overall rationality (p=0.693), while differences were observed for levels of specialization with regards to prescription correctness (p<0.001), but not drug suitability (p=0.704) or rationality (p=0.248). Overall, in 467 (52.1%) cases, at least one prescription parameter was flawed.

Conclusions: Despite it being previously pointed out, antibiotics are still often not prescribed rationally. Certain broad-spectrum antibiotics are overprescribed, with drug choice even more questionable in certain age groups of patients or organ systems affected.

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Abstract 6117

Combinations activity of azidothymidine and colistin against colistin-resistant *Klebsiella pneumoniae* in a murine model of urinary tract infection

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**Background:** Repurposing drugs or using combinations are attractive approaches to identify critically required therapies to treat MDR infections. We showed previously that azidothymidine (AZT) and colistin acted synergistically *in vitro* and *in vivo*. In this study, the therapeutic effect of azidothymidine with colistimethate sodium (CMS) was tested in a murine model of *K. pneumoniae* urinary tract infection (UTI).

**Materials/methods:** Female C3H/HeN mice were pre-conditioned by 5% glucose in drinking water from day -5. On day 0, mice were infected with *K. pneumoniae* B817, a recent MDR colistin resistant clinical isolate (MIC 16µg/mL), by transurethral administration into bladders. Treatment was initiated 24h post infection with CMS (3, 10 and 30mg/kg/dose), AZT (3, 15, 75mg/kg/dose) or 3 and 10mg/kg/dose CMS in combination with 3, 15 or 75 mg/kg/dose AZT. All treatments were intravenous and continued q8h for 9 doses. Mice were euthanized 96h post infection and bacterial burden quantified in urine, bladder and kidneys.

**Results:** We had shown previously that AZT and CMS acted synergistically against *K. pneumoniae* B817 *in vitro*. The murine UTI model maintained a robust infection over 96h with bacterial burden >4.8 log10 CFU/g in urine, bladder and kidney.

Monotherapy with CMS at 3, 10 and 30mg/kg showed a dose dependent reduction in burden in all tissues and urine. AZT monotherapy at 3, 15 and 75mg/kg was also dose dependent in reduction of bacterial counts in urine and bladder, but no clear dose response was seen in the kidneys.

Significant additional reductions in burden were achieved when the two drugs were dosed concomitantly. Combination treatment with CMS at 3mg/kg or 10mg/kg plus AZT at a dose range of 3, 15 and 75mg/kg showed a reduction in bacterial burden in urine and kidneys when compared monotherapy treatment. However, this additional effect was not observed in bladder.

**Conclusions:** When tested in a murine model of UTI with the colistin resistant strain *K. pneumoniae* B817, combinations of CMS and AZT achieved efficacy superior to single agents as measured in kidney and urine burden. These results support continued investigation of combination treatment with AZT and colistin for the treatment of MDR Gram-negative infections.

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Abstract 6119

**Diagnostic value of the IMMY Aspergillus LFA on bronchoalveolar lavage fluid of intensive care patients**

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**Background:** The diagnosis of invasive pulmonary aspergillosis (IPA) is challenging, especially in the intensive care unit (ICU) setting, where clinical symptoms as well as imaging are mostly aspecific. Recently, Aspergillus lateral flow tests were developed to decrease the time to diagnosis of IPA. Several studies evaluated the value of these new tests in the hematology population. We aimed to evaluate the value of a new lateral flow test for Aspergillus in ICU patients.

**Materials/methods:** Using left-over bronchoalveolar lavage fluid (BALf) from patients previously admitted to the ICU of a university hospital, we studied the performance of the sōna Aspergillus galactomannan lateral flow assay (LFA, IMMY, Norman, Oklahoma, USA). Patients included were >18 years of which BALf stored at ≤ -20°C was available. The Platelia™ Aspergillus EIA test was used to measure galactomannan. Based on the result of the fungal culture and galactomannan, the patients were classified according to 2 frequently used definitions: the EORTC-MSG criteria and the modified AspICU criteria (=AspICU criteria in which galactomannan is incorporated as well). For each case of IPA, we aimed to include 2 aspergillus negative controls. BALf was tested with the LFA according to the manufacturer’s instruction. The LFA was read out visually and with a digital reader by researchers blinded to the clinical diagnosis and IPA classification.

**Results:** Seventy-two patients were included of which 14 had probable or proven IPA according to the EORTC/MSG definitions, 24 had IPA according to the modified AspICU criteria and 48 served as IPA negative controls. Depending on the definitions used, sensitivities and specificities varied between 0.79 and 0.86 (table 1). The area under the ROC curve of the LFA was 0.85.

**Conclusions:** In ICU patients, the IMMY LFA performed well on BALf and can be used as a rapid screening test while waiting for culture results and conventional galactomannan results.

<table>
<thead>
<tr>
<th>Classification</th>
<th>Cases / Controls</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case = EORTC/MSG Proven/probable</td>
<td>14 / 28</td>
<td>0.86 [0.52 – 0.98]</td>
<td>0.82 [0.63 – 0.94]</td>
</tr>
<tr>
<td>Case = Modified AspICU Proven/probable/putative</td>
<td>24 / 48</td>
<td>0.83 [0.63 – 0.95]</td>
<td>0.79 [0.65 – 0.90]</td>
</tr>
</tbody>
</table>

Table 1. Diagnostic performance of digital readout of the LFA including their 95% confidence intervals

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Abstract 6120

Comprehensive analysis of evolutionary dynamics of circulating strains and immunopathogenesis and co-infections of human metapneumovirus associated acute lower respiratory tract infections in children

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Background: The study explored the role of circulating genotypes, evolutionary dynamics, co-infections, viral load and host cytokines in hMPV mediated ALRTI.

Materials/methods: Npas of 349 children were collected between the year 2013-2017. Samples positive for hMPV PCR were subjected for viral load estimation by Real Time PCR and co-infections by FTD Respiratory 21. IL-17A, IFN-Ɣ, TNF-α, IL-10, IL-6, MMP-9 and TIMP-1 levels in NPA samples were determined by CBA and ELISA. The viral load and cytokine levels were correlated with the WHO specified criteria for ALRTI severity. 'F' gene region of hMPV(n=12) was sequenced for phylodynamics analysis and potential N-glycosylation and O-glycosylation sites prediction.

Results: hMPV positivity was 6.59% (23/349). Twelve hMPV strains were analyzed and classified as hMPV A (n=8) and B (n=4) which contained 98% nucleic acid identity. The hMPV-A strains (n=8) phylogenetically belonged to hMPV A2a cluster whereas hMPV-B strains (n=4) belonged to lineage B1. The global time scaled evolutionary rate of hMPV A and B strains were 3.52X10-4 substitutions/site/year and 6.67X10-4 substitutions/site/year respectively. The potential O and N glycosylation sites in F gene were conserved among reference and test strains and without any variation in both hMPV A and B strains. hMPV A strains revealed two non-synonymous amino acid mutations. R82K mutation was seen to be conserved among all the strains and A185D mutation was seen in 7 strains and 1 strain contained A185N mutation. Only one strain of hMPV B contained R189K mutation in comparison to hMPV B reference strains. In 50% (11/22) of the infections hMPV was the sole pathogen. RSV was the most common virus (n=5) present along with hMPV followed by Rhinovirus (n=3) and Human Bocavirus (n=3). The Concentration of TNF, IL-6 and IL-10 levels in hMPV infected patients were significantly higher in severe ALRTI patients. The concentrations of TNF, IL-6, IL10, MMP-9 were (29.5±6.5 vs 5436.7±4473.7), (3432.3±1952.2 vs 15365.9±6013.9), (62.47±32.6 vs 290.2±135.3) and (33.9±33.02ng/ml and 1058.7±349.3ng/ml) in ALRTI and severe ALRTI patients respectively.

Conclusions: This study highlights the phylodynamics of circulating hMPV strains in Indian subcontinent where Th2 cytokine bias has been observed towards disease severity of ALRTI in Children.

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Abstract 6121

**Impact of the D26N amino acid substitution in the RND-type efflux regulator AdeR on antimicrobial susceptibility of Acinetobacter baumannii**

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**Background:** The Acinetobacter baumannii RND efflux pump AdeABC is regulated by the 2-component regulator AdeRS. In previous studies the AdeR amino acid substitution D26N was supposed to increase AdeABC expression, since it was found frequently in tigecycline resistant isolates [1]. The objective of this study was to determine the impact of the AdeR amino acid substitution D26N, identified in the tigecycline resistant clinical isolate MB-R112, on the antimicrobial resistance phenotype of A. baumannii.

**Materials/methods:** Deletion of adeRS in A. baumannii ATCC 17978 and complementation with adeRS of ATCC 19606 and MB-R112 was done by markerless mutagenesis. D26N substitution in AdeR19606 was achieved by site directed mutagenesis. Minimal inhibitory concentrations (MICs) for azithromycin (AZI), ciprofloxacin (CIP), gentamicin (GEN) meropenem (MEM), tetracycline (TET), and tigecycline (TGC) were determined by agar dilution. AdeRS of MB-R112 was aligned to A. baumannii reference strains for detection of additional amino acid substitutions.

**Results:** Introduction of the amino acid substitution D26N in AdeR19606 increased the MIC for AZI, CIP, GEN, and TET by one dilution step. Complementation with adeRSMB-R112 had a more noticeably effect by increasing the MIC fourfold for CIP, eightfold for TET and TGC, and 16-fold for AZI and GEN (Table 1). Analysis of the AdeRS amino acid sequences did not reveal unique amino acid substitutions in MB-R112 beyond D26N.

**Conclusions:** This study shows that the D26N amino acid substitution in AdeR does have an impact on antimicrobial susceptibility in A. baumannii. However, the single amino acid substitution had less impact than introduction of the entire adeRSMB-R112 construct, although it did not contain another unique substitution. Therefore, we hypothesise that accumulation of mutations in AdeRS, we assumed as silent, may actually facilitate AdeABC expression.


### Table 1. Antimicrobial susceptibility testing of ATCC 17978 adeRS mutants.

<table>
<thead>
<tr>
<th>Antimicrobial</th>
<th>ATCC 17978::adeRS19606</th>
<th>ATCC 17978::adeR[D26N]S19606</th>
<th>ATCC 17978::adeRSMB-R112</th>
</tr>
</thead>
<tbody>
<tr>
<td>AZI</td>
<td>4</td>
<td>8</td>
<td>32</td>
</tr>
<tr>
<td>CIP</td>
<td>0,25</td>
<td>0,5</td>
<td>1</td>
</tr>
<tr>
<td>GEN</td>
<td>1</td>
<td>2</td>
<td>16</td>
</tr>
<tr>
<td>MEM</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>TET</td>
<td>2</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>TGC</td>
<td>0,5</td>
<td>0,5</td>
<td>2</td>
</tr>
</tbody>
</table>

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**Evaluation of the carbapenem inactivation method (CIM) as a predictor for carbapenemase-producing Gram-negative bacteria**

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**Background:** The CIM test is now widely used to phenotypically detect carbapenemases in Gram negative bacteria due to its greater sensitivity compared to commercial methods. The specificity of the assay and its performance in specific genera are less well characterised. The aim of this study was to evaluate the specificity of the CIM for the detection of carbapenemase producing Gram-negative bacteria.

**Materials/methods:** A total of 37 clinical and screening isolates that had reduced meropenem susceptibilities were assessed.

Three variations of the CIM test were assessed;

1) The first described method by Van der Zwaluw et al (oCIM)

2) A modification of the Van der Zwaluw et al method that included a prolonged incubation of the meropenem disk in the bacterial suspension (aCIM)

3) The modified CIM described in the 27th edition of the CLSI (mCLSI)

The Blue-Carba test was performed as previously described. A multiplex PCR to detect a panel of carbapenemase genes was performed by the Microbiological Diagnostic Unit Public Health Laboratory.

**Results:** There were 9 isolates that were CIM negative, Blue-Carba negative and carbapenemase genes not detected.

0 of the 18 isolates that contained various carbapenemase genes, all yielded a positive CIM result. The three isolates that demonstrated a negative Blue-Carba result contained blaOXA genes.

10 isolates (8 Enterobacter cloacae complex, 1 Morganella morganii and 1 Citrobacter amalonaticus) yielded a positive CIM result using both oCIM and aCIM methodology, however no resistance genes were detected via molecular methods. These were considered false positive CIM tests.

7/9 isolates, all Enterobacter cloacae complex, that were considered false positives were susceptible to non-β-lactam agents. In contrast, all of the carbapenemase producing Gram negative bacteria had multi-drug resistance except one isolate with isolated ciprofloxacin resistance.

**Conclusions:** The increased inoculum used in the oCIM and aCIM increased the sensitivity for the detection of carbapenemases in Acinetobacter species, which may be due to lower expression of these genes. However, this increased sensitivity is at the expense of reduced specificity in Enterobacterales, specifically Enterobacter species. The absence of multidrug-resistance may flag the possibility of a false positive oCIM and aCIM result.

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Collateral treatment effects in *Pseudomonas aeruginosa* on antibiotic susceptibility and virulence mechanisms

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**Background:** *P. aeruginosa* causes serious nosocomial infections and rapidly develops resistance against most antibiotics. This development of resistance has collateral effects that change the susceptibilities to other antibiotic. We treated PAO1 reference strains with ciprofloxacin and imipenem, and studied the collateral effects on antibiotic susceptibilities and genetic modifications.

**Materials/methods:** The PAO1 reference strains (MI and DTU) were treated with either ciprofloxacin (Cip) [0.05-256 µg/ml] or imipenem (Imi) [0.5-128 µg/ml], for 20 passages. Passages performed in 24-well plates contained three 2-step dilutions of antibiotics. Antibiotic concentrations were increased maximum 4-fold between passages. Minimal inhibitory concentration (MIC) testing was done for Cip, Imi, tobramycin (Tob), ceftazidime (Cef), and azithromycin (Azm) with E-tests (bioMérieux) and colistin (Col) with MIC-Strips Colistin (Merlin). The final passages were plated on a 4-fold dilution of the passages’ antibiotic concentration before sequencing 2×250bp PE, (MiSeq, Illumina). Parental strains were sequenced using Pacbio Sequel (PacificBio Sciences). Analysis was done using in-house developed pipeline BacPipe v.1.2.6 and CLC Genomics Workbench 9.5.1 (CLCbio, Qiagen).

**Results:** In the Cip-treated populations (>256-fold MIC increase) mutations were found in *gyrA, gyrB, parC* and *parE* (fluoroquinolone targets) and in *nfxB* and the *nfxB* binding site (MexCD-OprJ regulator). Increased efflux accounted for increased resistance against Azm (>32-fold MIC increase), a substrate of the MexCD-OprJ efflux pump. Cip treatment also resulted in increased susceptibility to Tob (4- to 6-fold MIC decrease) and Imi (< 2-fold MIC decrease) due to increased outermembrane permeability caused by the increased MexCD-OprJ expression. In the Imi-treated populations (>32-fold MIC increase), mutations were found in *oprD* (encoding an outer-membrane porin) (figure c). Both Cip- and Imi-treated populations showed mutations in lipopolysaccharide (LPS) synthesis genes of which, *tagO* (initiates O-polysaccharide synthesis) showed a G229 deletion leading to a frameshift (figures c and d).

**Conclusions:** Cip and Imi treatments increased susceptibilities to tobramycin. Prolonged and increasing exposure to ciprofloxacin and imipenem led to novel alterations in genes involved in synthesis of LPS, a major virulence factor of *P. aeruginosa*, that could lead to a potential lack of O-antigen and impact the organisms’ ability to cause infection.

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Abstract 6128

Evaluation of ceftolozane-tazobactam disk diffusion testing of *Pseudomonas aeruginosa* in a multi-centre UK study

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**Background:** *Pseudomonas aeruginosa* (PAER) is an important pathogen in healthcare associated infections, including nosocomial pneumonia, urinary tract (UTI) and bloodstream infections. It is adept at developing antimicrobial resistance, which impacts treatment options and patient outcomes. Ceftolozane/tazobactam (C/T) is an anti-pseudomonal cephalosporin combined with an established inhibitor licensed for complicated intra-abdominal infections, hospital & ventilator acquired pneumonia, complicated UTI and acute pyelonephritis. Susceptibility testing should be accurate, especially for drugs not tested routinely. We have evaluated locally performed disk diffusion (DD) on 6 antimicrobials including C/T against broth microdilution (BMD).

**Materials/methods:** Clinically significant PAER, from Cystic Fibrosis (CF) & non-CF, were tested locally at 14 laboratories in the UK as part of the INVICTUS study. EUCAST DD was performed on C/T (MAST), piperacillin/tazobactam (TZP), ceftazidime (CAZ), aztreonam (ATM), imipenem (IMI) & meropenem (MEM). Triplicate DD tests were performed at a reference laboratory on a percentage of isolates as part of quality Control (QC) as well as BMD on 159 non-CF isolates. Categorical agreement (CA), Major Errors (ME) and Very Major Errors (VME) were calculated.

**Results:** CA were C/T (79%), PT (85%), CAZ (86%), ATM (91%), IMI (90%) & MER (81%). ME, where DD result was resistant (R) but BMD susceptible (S), for C/T DD were 18.9% (n=30), whilst VME were 2.5%. Of the 30 ME, 9 were re-tested, 6 confirmed S results whilst 3 had zone diameters near the DD breakpoint. ME & VME for TZP, CAZ, ATM, IMI & MEM were 0%, 1 2.6%, 5.9%, 5.7% & 1.9% and 1 2%, 1.9%, 3.8%, 4.4% & 0% respectively. MEM also had 17% minor errors (mE). Five PAER exhibited TZP DD results in the area of technical uncertainty (ATU), 4 with R MIC results and 1 with S.

**Figure 1:** Ceftolozane/tazobactam histogram of local DD zone diameters versus MIC

**Conclusions:** Categorical agreement was lowest for C/T at 79% with high levels of MEs, suggesting high rates of false resistance in local laboratories with DD (Figure 1). However, CA improved upon re-testing of some isolates in the reference laboratory. CA was also low for TZP, CAZ and MEM. TZP showed a high VME rate.

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Metagenomic analyses of antibiotic resistance genes in gut microbiome of healthy people in Korea: high carriage rate of blaCTX-M, blaCMY-2 and plasmid-mediated quinolone resistance genes

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Abstract third-party references: This research was supported by a fund [2017N-ER5407-00] by Research of Korea Centers for Disease Control and Prevention.

Background: To characterize carriage of antibiotic resistance genes (ARGs) in gut microbiome of healthy people.

Materials/methods: We investigated fecal carriage of ARGs in gut microbiome in healthy Koreans by using whole metagenome sequences and targeted metagenomics approach. Sixty-one Koreans aged 30 to 59 without underlying diseases were included.

Results: The median age was 46 and 47.5% were female. Eighteen (29.5%) carried blaCTX-M or plasmid-mediated AmpC or both alleles in their gut: blaCTX-M 23% (14/61), blaCMY2 13.1% (8/61) and blaDHA 3% (2/61). None carried plasmid-mediated carbapenemase alleles. Regarding plasmid-mediated quinolone resistance (PMQR) alleles, 36 (59%) carried PMQR, and 30 of 36 (83%) harbored 2-4 PMQR alleles: qnrB 44.3% (27/61), qnrD 4.9% (3/61), qnrS 47.5% (29/61), and aac(6’)-ib-cr 13.1% (8/61), respectively.

Based on ARGs abundance in gut microbiome, 61 people were categorized into high, medium, and low ARGs, and characteristics of people in each group were analyzed; high ARG group [relative abundance of ARGs ≥ 120 gene per million] were found to have visited hospitals more often \( (p = 0.039) \), particularly for upper respiratory tract infections \( (p = 0.047) \), and carry more blaCTX-M \( (p \text{ for trend}=0.008) \) than other groups. Presence of CTX-M alleles correlated with abundance of most ARG groups such as \( \beta \)-lactam, aminoglycoside, macrolide in gut resistome \( (p =0.006, p =0.034, p =0.009, \text{ respectively}) \). Unlike blaCTX-M, PMQR alleles existed irrelevant to abundance of ARGs \( (p \text{ for trend}=0.176) \). PMQR and blaCMY2 existed in association with individual PMQR alleles.

Conclusions: Fecal carriage of PMQR alleles were broad and multiplex, which might indicate a frequent exposure during daily life.

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Diagnosis of invasive pneumococcal disease in children by using a classification method based on nasopharyngeal microbiota signatures

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**Background:** Streptococcus pneumoniae is a pathobiont that colonizes children's nasopharynx asymptomatically and has the potential to cause Invasive Pneumococcal Disease (IPD). IPD microbiological diagnosis is based on isolation/DNA detection of pneumococcus in sterile body fluids but this approach is invasive and yields limited sensitivity. This study aims to evaluate the utility of non-invasive nasopharyngeal microbiota for children IPD diagnosis.

**Materials/methods:** Prospective double-case-control study including all IPD cases <18 years pre-exposed <24h to antibiotics attending Hospital Sant Joan de Déu (Barcelona, Spain) during 2014-2018, paired by age/sex/seasonality with at least 2 healthy controls (HC) and 1 control with upper viral respiratory infection (UVRI). Nasopharyngeal DNA pneumococcal detection/quantification/serotyping (different multiplex real-time PCRs), DNA/RNA viral detection (Allplex-Respiratory-Panel, See gene) and microbiota characterization by sequencing V3-V4 region from 16S rRNA (Miseq, Illumina) was performed. Results were used for building a case-control classification model with Random Forest.

**Results:** A total of 140 children were selected (IPD=27, HC=65, UVRI=48). Viral RNA/DNA was detected in 100% of UVRI, 81.5% of IPD and 60.0% of HC (p-value=0.081). Pneumococcal DNA was detected in 100% of IPD, 61.5% of HC and 52.1% of UVRI (p-value<0.001). PCV13 serotypes (IPD=51.8%, HC=6.1%, UVRI=16.0%; p-value<0.001) and invasive serotypes (IPD=51.8%, HC=12.5%, UVRI=16.0%; p-value<0.001) were more prevalent in IPD. Independently of case-control grouping, viral infection was associated to decreased Shannon diversity (p-value=0.012) and a trend for richness (Observed species, p-value=0.065). When stratified by viral detection, cases presented lower richness than HC among viral-positive samples (Observed species, p-value=0.022). Beta-diversity showed an evident separation between viral-positive IPD, viral-negative IPD, viral-positive HC, viral-negative HC and UVRI groups (Adonis p-value=0.002), more notably between viral-negative HC and viral-positive IPD. This separation was confirmed by hierarchical cluster analysis. Deep insight at microbiota patterns with LEfSe revealed specific bacterial-biomarkers: Neisseria-Streptococcus pneumoniae in IPD, Dolosigranulum-pigrum-Gemella in HC and Moraxella in UVRI. Random forest model demonstrated high performance in distinguishing cases-controls, with AUCs of 0.87 for IPD-HC (accuracy=0.79 [95% CI: 0.54-0.94]) and 0.92 for IPD-UVRI (accuracy=0.88 [95% CI: 0.69-0.97]).

**Conclusions:** Integrated analysis from viral DNA/RNA detection, pneumococcus detection/quantification/characterization and microbiota composition of nasopharyngeal samples is a promising tool for easy non-invasive IPD diagnosis in children.

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Abstract 6135

**Lensless imaging for non-destructive and label-free identification directly on agar**

Inès Zamoun1, Alexis Maire1,2, Patrick Schiavone1, Pierre R. Marcoux3, Tonatiuh Yescas González6, Emmanuel Picard2, Marc Zelsmann1, Emmanuel Hadji2, David Peyrade1

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**Background:** The pursuit of non-invasive and non-destructive identification methods has raised an increasing interest for label-free optical techniques, e.g. vibrational spectroscopies (infrared and Raman), elastic light scattering and lensless imaging. Among these technologies, elastic scattering and lensless imaging can be performed directly on agar plates, making them particularly compatible with the growing need for automated methods. Both techniques use a coherent or partially coherent light source to illuminate the Petri dish. Resulting scatterograms are then processed by pattern recognition algorithms, resulting in identification. Contrary to elastic scattering, lensless imaging can provide the simultaneous identification of several colonies.

**Materials/methods:** We report here the very first example of identification down to species with a widefield lensless imaging device, namely 22.3mm x 14.9mm (pixel size 4.335µm). Considering this large field of view, several hundreds of colonies can be analysed simultaneously. A partially coherent green light emitting diode (main wavelength 523nm) illuminated different microbial cultures growing on tryptic soy agar at 36°C. Cultures of Gram-positive, Gram-negative and yeast reference strains were imaged every 10 minutes, for 22 to 23 h of incubation. An example image of *E. coli* culture is given at 14h of incubation. For the automatic analysis of scatterograms, classical machine learning algorithms (i.e. Support-Vector Machine), as well as some deep learning models (i.e. Convolutional Neural Network), were developed.

**Results:** Deep learning algorithms, as well as classical machine learning, were investigated for the analysis of the collected database (5 reference strains). Six convolutional neural network models were assessed including transfer learning models such as VGG16, MobileNet etc., with up to 2000 samples (i.e. images of colonies) per species. The algorithms yielded unambiguous identification of the five species, with at least 98% accuracy.

**Conclusions:** This very first database paves the way towards a future imaging device for the simultaneous identification of all the isolated colonies on a 90mm Petri dish. Furthermore, as culture growth is being recorded in situ, the technique is capable of identification during the early stages of incubation. An extended database, including clinical isolates, will soon be collected.

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Abstract 6140

Differentiation of Blastocystis subtypes by PCR and Sanger sequencing versus NGS-based total ribosomal DNA analysis

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Background: Blastocystis may be the most common intestinal parasite in the world, infecting both human and a vast variety of non-human hosts. Based on SSU rDNA analysis, at least 17 subtypes of Blastocystis (arguably separate species/genera) are known, of which at least nine have been found in humans. State-of-the-art differentiation of Blastocystis subtypes relies on ‘barcoding’ (PCR and Sanger sequencing); however, novel technology may prove better subtype resolution and ease the identification of subtypes in mixed subtype infections. In this study, we compared barcoding with ILLUMINA-based sequencing and differentiation of ribosomal genes amplified by broad-specificity eukaryotic primers.

Materials/methods: We used 51 stool samples from symptomatic and asymptomatic individuals living in periurban communities from Arequipa, Peru. All DNAs were extracted by the Stool DNA Isolation kit (Norgen) and processed by i) state-of-the-art barcoding (PCR using the primers BhRDr and RD5 and Sanger sequencing), and ii) a microbiome assay using amplicon-based sequencing of total nuclear ribosomal genes, automated data clean-up and annotation to genus/species level by the in-house software BION. Sequences obtained by Sanger sequencing were edited manually and BLASTed against a curated Blastocystis database to gain information on subtype. Blastocystis-specific sequences identified by BION were clustered and consensus sequences for each cluster were BLASTed against the NCBI Database. Subtype identification as called by the two methods was compared.

Results: By barcoding, an unambiguous and single-peak DNA sequence reflecting a single subtype was observed in 77% of the samples. By the microbiome assay, subtype results were available for 96% of the samples. The results of the microbiome assay were in accordance with those obtained by barcoding, and the microbiome assay moreover allowed resolution of mixed subtype carriage in those samples where DNA sequence traces obtained by Sanger sequencing were ambiguous.

Conclusions: Based on Sanger sequencing, barcoding produced unambiguous results for 77% of the samples, possibly giving the DNA sequence of the most predominant subtype. Meanwhile the microbiome assay was able to subtype 96% of the samples and moreover enabled the detection and differentiation of mixed Blastocystis subtype infection. The microbiome assay therefore appears to be a useful supplement or alternative to barcoding.

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Intracellular persistence of uropathogenic Escherichia coli is undetectable in urinary bladders from mecillinam-treated pigs

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Background: Type-1 pili dependent invasion of bladder epithelial cells by uropathogenic Escherichia coli (UPEC) is suggested to serve as reservoirs for recurrent urinary tract infections (rUTI). However, the intracellular pathogenic cascade has only been observed in murine models, and its relevance for human rUTI has been a subject of debate and remains to be demonstrated. To provide a missing link between mice and humans, the aim of this study was to investigate the influence of type-1 pili on experimentally induced cystitis in pigs, and whether UPEC survives conventional antibiotic treatment by invading the bladder epithelium of this animal.

Materials/methods: The study was based on a recently developed porcine model of cystitis. Pigs were inoculated with the reference cystitis strain, UTI89, in different concentrations; 10^8 CFU/ml, 10^6 CFU/ml, 10^4 CFU/ml, and 10^2 CFU/ml (4 pigs in each group). Another group (n = 4) was inoculated with the type-1 pili deficient mutant UTI89ΔfimH in a concentration of 10^2 CFU/ml. In a separate experiment, six pigs were subjected to a three-day peroral treatment with the extracellular drug, mecillinam, to investigate if intracellular UPEC could survive antibiotic treatment in vivo. Regular urine and blood samples and clinical parameters were collected to monitor the infection. Whole bladders were removed and analyzed for the presence of intracellular UPEC using ex vivo gentamicin protection assays.

Results: Successful bladder colonization was achieved by all pigs infected with UTI89, however only 25% (1 of 4) of pigs became colonized upon inoculation with UTI89ΔfimH. Intracellular bacteria were present in low numbers in whole bladders following 14 days of persistent bacteriuria, however, no viable UPEC were detectable in the bladders of mecillinam-treated pigs.

Conclusions: Type-1 pili is non-essential but highly advantageous for UPEC to surpass initial bottlenecks during acute UTI in pigs. Also, UPEC is capable of invading the bladder epithelium of pigs, however, they fail to survive conventional antibiotic treatment in vivo suggesting that intracellular colonization does not serve as reservoirs of rUTI.

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Abstract 6144

Gliotoxin, a new candidate against methicillin-resistant Staphylococcus aureus showing synergistic effect with classical antimicrobial drugs in Caenorhabditis elegans infection model

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Background: Multidrug-resistant bacteria such as methicillin-resistant Staphylococcus aureus (MRSA) is among the major causes of hospital-acquired and community infections, and pose a challenge to the human health care system. Therefore, it is important to find new drugs that show activity against these bacteria, both in monotherapy and in combination with other antimicrobial drugs. Gliotoxin is a mycotoxin produced by Aspergillus fumigatus and other fungi of the Aspergillus genus. Some evidence suggests that gliotoxin shows antimicrobial activity, especially against S. aureus.

This work aims to evaluate the antibiotic efficacy of gliotoxin as monotherapy or in combination with other therapeutic against MRSA in vitro and in vivo using a C. elegans infection model.

Materials/methods: MRSA ATCC700699 sensitivity against gliotoxin was analysed by different methods: disc diffusion, time-mortality curves, microdilution assays. The synergistic effects of gliotoxin with others anti-staphylococcal drugs (vancomycin, fusidic acid and linezolid) were tested by a checkerboard assay.

Transformed synchronized C. elegans L4 worms were infected with MRSA. The culture was supplemented separately with gliotoxin, vancomycin or its combination to different concentrations. The survival rate of C. elegans was scored manually every 12h for 4 days.

Results: Sensitivity analysis of MRSA against gliotoxin showed that gliotoxin has a potent antimicrobial activity (MIC = 2 µg/ml). In addition, synergistic activity was observed, when the gliotoxin was combined with vancomycin and fusidic acid, using checkerboard and time-kill assays. This synergistic effect was confirmed by CalcuSyn software (CI = 0.15 for 1 µg/ml of gliotoxin combined with 2 µg/ml of vancomycin).

The in vivo study of S. aureus infection in a C. elegans model showed that combined treatment of vancomycin with gliotoxin increased 70% in survival rate of the MRSA-infected worms.

Conclusions: Our results suggest that gliotoxin is effective against MRSA strains indicating their potential use as a new drug against MRSA infections.

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Abstract 6145

Hepatitis B and hepatitis D virus infection in immigrants living in south Italy: epidemiological and virological characteristics

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Background: in several European countries, there has been an increase in migration from countries with a high prevalence of HBV. In Italy epidemiological data relating to HBV and HDV infection in the migrant population are scanty. Aim of our study was to investigate the demographic and virological characteristics of HBV and HDV infection in a cohort of migrants living in Southern Italy.

Materials/methods: Between January 2012 and december 2018 all the migrants attending to one of the 5 first-level centers, 2 in Naples, 2 in Caserta and 1 in Foggia were tested for HBV. Data for demographic characteristics and risk factors for HBV infection were collected. All HBsAg positive subjects were tested for HDV. HBV genotype was evaluated in viremic subjects. For all HDV positive subjects was performed HDVRNA.

Results: 3184 subjects were tested; the 243 (7.6%) HBsAg positive subjects had median age of 26 (range 15-55) years and 227 (94%) were males; 214 (88%) came from Sub-Saharan Africa, 3 (1.2%) from North Africa, 17 (7%) from Eastern Europe, 8 (3.2%) from IndoPakistan area, one from South America (table 1); 8 of 243 subjects (3.2%) were HDVAb positive. Table 2 shows the characteristics of the 243 HBsAg positive patients enrolled and stratified according HDV serostatus.

We found that HDVAb negative subjects lived in Italy for a longer period (p = 0.001) compared to HDVAb positive patients. No variables independently associated with HDVAb positivity were identified (table 3). HBV-DNA levels were similar in the two groups. The HBV genotype was available for 90 samples in the group of HDVAb negative patients; genotype A was present in 17%, C in 3%, D in 12% and E in 69%. HDV-RNA was performed for all HDV Ab positive patients but only one patients (12.5%) was found HDV-RNA positive genotype-1. None of the patients was aware of their HBV or HDV serostatus.

Conclusions: In this study we found a high prevalence of HBV and HDV in a cohort of migrants living in our geographical area. This data suggests the need to adopt a universal screening and vaccination strategy for HBV in this vulnerable category.

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Novodiag CarbaR+ assay for the detection of carbapenemase-producing bacteria

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Abstract 6146

Background: Carbapenemase-producing Gram-negatives organisms (CPOs) represent a global concern for public health. The rapid implementation of infection control measures at the hospital requires easy, efficient and reliable detection tools of carbapenemase positive isolates.

Materials/methods: The NOVOdiag® CarbaR+ is a fully automated random access, multiplex nucleic acid based diagnostic test for the detection carbapenemases and mcr-1 genes on bacterial culture or fecal swabs in eNAT™ tubes. It is based on real-time PCR and microarray hybridisation with detection by contact fluorescence imaging and evanescent excitation all performed within a single cartridge. The CarbaR+ cartridge targets 9 carbapenemase encoding genes including blaKPC, blaNDM, blaVIM, blaIMP, blaOXA-48-like, the Acinetobacter OXA-carbapenemase genes including blaOXA-23-like, blaOXA-24-like, blaOXA-58-like, the chromosomally-encoded blaOXA-51-like genes with upstream inserted ISAb1 and the plasmid-mediated colistin resistance gene mcr-1. 201 cultured colonies of Gram-negatives organisms (61 Pseudomonas, 60 Acinetobacter and 80 Enterobacterales) with characterized β-lactamase content and 80 clinical rectal swabs collected from hospitalized high-risk patients for CPE colonization were tested.

Results: Globally, the NOVOdiag® CarbaR+ assay detected carbapenemase and MCR-1 encoding genes with a 98.8 % Sensitivity (Ss) and 99.7 % of Specificity (Sp). When breaking down these results by main bacterial species, a 100% Ss and Sp was obtained for Pseudomonas spp.; 96.7 % Ss and 99.4 % Sp for Acinetobacter sp.; 100 % Ss and 99.7 % Sp for Enterobacterales. On clinical fecal swabs 97.8 % Ss and 98.6 % Sp were correctly identified, when using culture as gold standard. 1 swab with E. coli OXA-181 was not detected (FN), and 1 NDM/OXA-48 PCR positive swab from a patient formerly known as OXA-48 carrier could not be confirmed by culture, and was considered FP.

Conclusions: The Novodiag® CarbaR+ is an easy to use sample in-answer out technology. The instrument is random access with results obtained in 80 minutes. The test allows the detection of the most frequently encountered carbapenemases and their variants among Enterobacteriales and non-fermenters but unfortunately excluding GES carbapenemases. Performance directly on fecal swab are very good but further evaluation on a larger number of clinical samples and from countries with different CPEs than those encountered in France.

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Extensively drug-resistant Klebsiella pneumoniae ST383 co-harbouring OXA-48 and NDM-5 outbreak at a tertiary care centre in Lebanon

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Background: Carbapenem-resistant Enterobacteriaceae (CRE) are a heterogenous group of MDR organisms harboring multiple different mechanisms of resistance. In November 2017, we accepted two patients transferred for management of gunshot wounds who had no major risk factors for MDR carriage. However, screening admission cultures grew extensively drug resistant Klebsiella pneumoniae (XDR-Kp). Shortly later, multiple cases of XDR-Kp were identified with a similar profile of resistance. This prompted an outbreak investigation.

Materials/methods: The outbreak investigation occurred at Saint George Hospital, a 333-bed tertiary care center in Lebanon. The two index cases grew XDR-Kp found to be resistant to cephalosporins, quinolones, aminoglycosides, carbapenems, colistin, and susceptible to tigecycline. All cultures growing XDR-Kp with this susceptibility profile from any clinical specimen in the period November 2017 - June 2018 were extracted from the laboratory electronic database. Charts of these patients were reviewed for clinical data including outcome, infection control measures, and antibiotic use. A subset of five isolates from the index cases were further identified with MALDI-TOF MS and genotypic analysis with PCR and MLST.

Results: A total of 25 cases were identified. The isolates overall came from sputum, urine, surgical wounds, and blood. Despite this extensive resistance profile, none of the patients experienced any related severe sepsis. Crude mortality rate at 30 days was 12% (3/25). Two deaths were due to non-infectious complications and one was due to a polymicrobial bacteremia. In light of the few therapeutic options available, a special effort was made to distinguish colonization from infection. Strict infection control practices were enforced.

The five isolates were co-harboring OXA-48 and NDM-5 carbapenemase genes and were part of the ST383 clone. The last identified case of this clone was in June 2018.

Conclusions: Our outbreak combines an unexpected high-level of resistance mediated by two notorious mechanisms of resistance coupled with a relatively benign clinical presentation. Infection control measures may have helped in containing this clonal spreading. Efficient diagnostic efforts eliminated the need for unnecessary therapy and was helpful when faced with a lack of therapeutic options. High level antimicrobial resistance should be tackled by deep investigation rather than empirical broad-spectrum combinations.

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Abstract 6149

Catheter-associated bloodstream infections: Empirical antibiotic recommendations based on microbiological data

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Background: Central line and peripheral venous catheter-associated bloodstream infections (CA-BSIs) increase patient morbidity, length of stay, and hospital costs. Every hospital should have its own policy to control and prevent CA-BSIs. The collection of microbiological data in a CA-BSI register improves knowledge of the local epidemiology and allows for recommendations to be made regarding prevention and empirical antibiotic therapy.

Materials/methods: We collected microbiological data (microorganisms, susceptibility profiles), in addition to clinical data, from the CA-BSI register of Son Llàtzer Hospital, a 350-bed university hospital in Majorca (Spain), for the period from August 2015 to June 2019.

Results: 212 episodes of CA-BSIs were identified; 115 (54.2%) were peripheral venous catheter-associated bloodstream infections (PVC-BSIs) and 97 (45.8%) were central line-associated bloodstream infections (CLA-BSIs). The incidence rate was 0.26/1000 patient-days for PVC-BSIs and 0.24/1000 patient-days for CLA-BSIs. All PVC-BSIs and 59/97 CLA-BSIs occurred in non-intensive care units.

A polymicrobial aetiology was found in 19 cases. Gram-negative (GN) rods were isolated in 109 (47.2%) cases (86 Enterobacteriaceae and 22 non-fermentative), gram-positive (GP) rods in 112 (48.5%), and yeasts in 10 (4.3%). GN rods were more frequently isolated in PVC-BSIs than in CLA-BSIs (55.2% vs 37.7%), and yeasts were found in all CLA-BSIs.

GN susceptibility rates of 78% to cefotaxime (only Enterobacteriaceae), 80% to piperacillin/tazobactam, and 96.1% to meropenem were found. Among the GN microorganisms, 12 were ESBL producers (6 from CLA-BSIs and 6 from PVC-BSIs), 3 CAmpCs producers, and 2 Pseudomonas XDR non-carbapenemase-producing.

Among Staphylococcus aureus isolates, methicillin resistance was present in 8/51 (16.7%) isolates, 4 from CLA-BSIs and 4 from PVC-BSIs. Vancomycin MIC was ≤1 µg/mL in all cases. Candida spp. was identified in 10 cases (C. albicans in 7 cases and C. glabrata in 3 cases), and no resistance to echinocandins was found.

Conclusions: The incidence rate of CA-BSIs is high in our institution. GN bacteria were isolated more frequently than GP bacteria in PVC-BSIs. Based on the local epidemiology, when a CA-BSI is suspected, antimicrobial therapy should be initiated with a bactericidal agent active against S. aureus and CoNS, and GN coverage with piperacillin/tazobactam or in selected cases meropenem should be mandatory.

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Abstract 6151

Whole genome sequencing and phenotypic characterisation of non-typeable Haemophilus influenzae in Hong Kong: 2000-2016

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Background: Non-typeable H. Influenzae (NTHi) is increasingly recognized to play an important role in respiratory tract infections. Increasing reports of ampicillin- and β-lactamase-negative ampicillin-resistance are also noted. We aimed to study the epidemiology and characteristics of NTHi from a collection of archived Haemophilus influenzae (HI) strains from Hong Kong using whole genome sequencing. We also examined the antibiotic susceptibilities of these isolates to characterize genetic determinants of resistance phenotypes.

Materials/methods: 391 non-duplicate isolates of HI archived from carriage and respiratory diseases of children and adults were whole genome sequenced using NextSeq (Illumina) 2 x 150bp paired-end read chemistry. These included 231 isolates from NPAs of children’s carriage, 132 from sputa of adults with pneumonia/COPD and 26 from blood/body fluids saved during 2000-2016. Sequence Types (STs) were identified using ‘mlst’ (https://github.com/tseemann/mlst) and population structure analysed using PopPUNK. Minimum inhibitory concentrations (MICs) of ampicillin, amoxicillin-clavulanate, cefuroxime, cefotaxime, imipenem, azithromycin, tetracycline, doxycycline, minocycline and ciprofloxacin were determined according to CLSI (2019).

Results: Three serotypeable strains were identified based on in silico analysis of capsular loci – one each of serotypes A, B and F. From the remaining 388 NTHi, 86 known STs were identified. In addition, 32 novel STs comprising known allele sequences and six fuculose kinase (fucK) isolates were found. The remaining 32 isolates had novel STs defined by new allele sequences. The most common ST was 107 (8.0%; n=25) followed by ST12 (6.4%; n=20) and ST159 (6.0%; n=19). Preliminary analysis revealed a population structure contained within six clusters. Overall, 27% (n=104/385) of NTHI were ampicillin-resistant (MIC ≥4.0, MIC50/90 0.5/16 mg/L), 1% (4/385) amoxcillin/clavulanate-resistant (MIC≥4/2mg/L), 5.7% (22/385) cefuroxime-nonsusceptible (MIC≥8.0 mg/L), 7% (28/385) tetracycline NS (MIC≥4 mg/L). No statistical difference in percentage of ampicillin resistance between sputa vs NPA isolates (p>0.3) were obtained. Single isolates were resistant to cefotaxime, azithromycin, and imipenem. All isolates were susceptible to ciprofloxacin.

Conclusions: This represents the first in-depth analysis of NTHi from Hong Kong. The population epidemiology is diverse based on ST but can be defined within a minimal number of genome-level clusters. A moderate rate of ampicillin-resistance (27%) was observed and resistance to amoxicillin-clavulanate remains low (1%).

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Effects of mutations in the hepatitis B virus genome on viral loads testing

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Background: Disease management of patients with chronic infection of hepatitis B virus (HBV) is largely dependent on HBV viral load (VL) monitoring. Many commercial tests were developed in recent years to test VLs, based on real time PCR or TMA (transcription-mediated amplification) technology: e.g. Xpert® HBV Viral Load and COBAS HBV Test are based on RTPCR, while Aptima™ HBV Quant Assay of Hologic is based on TMA technology. The tests also use different target-genes for amplification: while the first two amplify the precore/core region Aptima is directed to amplify the S/polymerase region. Aim: Comparing the 3 methods for HBV-DNA-monitoring.

Materials/methods: 36 sera were tested for HBV-VL by 3 kits: Xpert® HBV Viral Load, COBAS HBV, and Aptima™ HBV Quant Assay of Hologic. In 2 cases the precore/core region of HBV was amplified using specific primers, and the amplicons were analyzed further.

Results: In most cases there was a good agreement between the three methods. Out of 36 patients that were tested only two exhibited dramatic variations between COBAS/Genexpert VLs and the Aptima results (5562 IU/mL by the Panther vs. <20 by Roche, and 3825 IU/mL by the Panther vs. <20 by Roche). Further investigations have shown a deletion in the precore/core region in the genome of HBV that was isolated from these two patients. This deletion probably contributed to decrease VLs when the patients were tested by a method that is based on amplification of precore/core region.

Conclusions: Health care providers should be aware of deletions and sequence variation of HBV genome that accumulates during chronic infection with HBV. Depending on the circumstances, in certain cases, testing patients for HBV VLs by more than one method should be recommended.

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Chronic pluripathological patients in over 64 years old with flu or serious acute respiratory infection, according to flu vaccination status

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Abstract third-party references: National Center for Epidemiology (Carlos III Health Institute), Madrid, Spain, Miguel Servet University Hospital (Microbiology and Parasitology Service), Zaragoza, Spain., Research group on infections difficult to diagnose and treat (Aragon Health Research Institute).

Background: Influenza virus infections should be considered in all older adults with risk factors, as they may be associated with higher mortality. Knowledge of the distribution of chronic diseases present in these patients can help in their clinical management.

Materials/methods: Data of the patients included by the Miguel Servet University Hospital (HUMS) in the European IMOVE+ study, during the 2016/17, 2017/18, and 2018/19 seasons, were analyzed. Patients older than 64 years hospitalized with symptoms of Severe Acute Respiratory Infection (SARI), not institutionalized, provided a sample of pharyngeal smear in which the presence of influenza was detected by PCR-RT. The number of the most frequent chronic pathologies was studied according to the influenza vaccination status and diagnosis, using the chi-square test ($\chi^2$) adjusted by Monte-Carlo methods.

Results: Among the three studied seasons, 1314 patients with SARI were recruited, of which 35.9% were diagnosed of flu, and 94.2% were considered pluripathological patients according to OMS definition. More than three quarters of them had three or more chronic diseases, and approximately a third had five or more. No significant differences were found when comparing the number of diseases according to the vaccination status, neither in the presence of flu.

<table>
<thead>
<tr>
<th>Number of Diseases</th>
<th>Unvaccinated (n=557)</th>
<th>Vaccinated (n=752)</th>
<th>$\chi^2$</th>
<th>p</th>
<th>Unvaccinated Flu+ (n=234)</th>
<th>Vaccinated Flu+ (n=237)</th>
<th>$\chi^2$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>7 (1.3%)</td>
<td>6 (0.8%)</td>
<td>9.941</td>
<td>0.450</td>
<td>3 (1.3%)</td>
<td>2 (0.9%)</td>
<td>9.775</td>
<td>0.369</td>
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<tr>
<td>1</td>
<td>34 (6.2%)</td>
<td>29 (3.9%)</td>
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<td></td>
<td>21 (9.2%)</td>
<td>14 (6.0%)</td>
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<tr>
<td>2</td>
<td>72 (13.1%)</td>
<td>95 (12.8%)</td>
<td></td>
<td></td>
<td>29 (12.7%)</td>
<td>37 (15.7%)</td>
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<tr>
<td>3</td>
<td>134 (24.5%)</td>
<td>188 (25.3%)</td>
<td></td>
<td></td>
<td>556 (24.6%)</td>
<td>54 (23.0%)</td>
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<tr>
<td>4</td>
<td>123 (22.4%)</td>
<td>184 (24.8%)</td>
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<td></td>
<td>50 (21.9%)</td>
<td>58 (24.7%)</td>
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<td>5</td>
<td>92 (16.8%)</td>
<td>129 (17.4%)</td>
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<td></td>
<td>36 (15.8%)</td>
<td>37 (15.7%)</td>
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<tr>
<td>6</td>
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<td>76 (10.2%)</td>
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<td>22 (9.6%)</td>
<td>22 (9.4%)</td>
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<tr>
<td>$\geq$7</td>
<td>30 (5.5%)</td>
<td>36 (4.8%)</td>
<td></td>
<td></td>
<td>11 (4.8%)</td>
<td>11 (4.7%)</td>
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</tbody>
</table>

Conclusions: There is a high number of pluripathological patients over 64 years unvaccinated for the flu who needed hospital admission for SARI [with or without flu]. This should be taken into account in clinical practice, especially during epidemic periods of influenza, and reinforce the importance of vaccination in this population.

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Performance of a commercially available LAMP assay and RDT for diagnosing *Plasmodium falciparum* malaria at very low parasitemias in a controlled human malaria infection trial

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**Background:** Malaria is the most common imported tropical infection in European travellers with short-term exposure, with roughly 1500 infections annually in the UK. Current UK guidelines for diagnosis recommend thick and thin film microscopy and state that a rapid diagnostic test (RDT) alone cannot be used to exclude malaria. The accuracy of microscopy is dependent on operator experience and RDTs have variable performance with reduced sensitivity at low parasitaemias. Nucleic acid amplification techniques, in particular loop-mediated isothermal amplification (LAMP), have been developed to try to improve sensitivity compared with traditional microscopy or RDTs. Performance of RDTs and LAMP assays at low parasitaemias is typically assessed by diluting blood samples with a known parasite density. Controlled human malaria infection (CHMI) provides an opportunity to assess these diagnostics with serial, undiluted clinical samples with very low parasitaemias compared with qPCR.

**Materials/methods:** Eleven participants took part in a *P. falciparum* CHMI trial in which infection was administered intravenously. Participants were monitored twice daily for symptoms, with blood taken to assess parasitaemia by qPCR at each visit. Participants were treated once they had a parasitaemia of >5000 parasites/mL if symptomatic, or >10,000 parasites/mL if asymptomatic. Based on previous data and qPCR results, we assessed blood samples from day 6 post-CHMI (C+6) for malaria positivity using the Carestart™ Malaria (Pan) RDT and from C+4 using the illumigene Malaria® LAMP assay.

**Results:** Daily samples were tested for the eleven participants until the pre-defined qPCR thresholds for treatment were reached. LAMP assay positivity in relation to parasitaemia by qPCR (parasites/mL) in serial samples from malaria-infected individuals is shown in the attached figure.

**Conclusions:** To our knowledge, this is the first time the illumigene Malaria® assay has been assessed using serial samples from infected individuals at very low parasitaemias. Our data show that assay is 100% sensitive at the published detection limit of 2 parasites/µL in this setting, and reliably detected *P. falciparum* at parasitaemias well below this, although LAMP remains less sensitive than qPCR. This supports its use as a method for excluding malaria in returning travellers, although it has limitations for diagnosis.

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Phenotypic and molecular investigation of ST11 NDM-1-producing Klebsiella pneumoniae isolates persisting between 2015 and 2018 in a Bulgarian hospital

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Background: A surveillance was conducted in “Tsaritsa Yoanna” University Hospital, Sofia, Bulgaria, between August 2015 and January 2018 to estimate the burden of carbapenem-resistant (CR) Gram-negative pathogens in the hospital.

Materials/methods: During the surveillance period (Aug2015-Jan2018), samples from high-risk wards (i.e. ICU, surgery and haematology) were plated also on selective media for detection of carbapenems (BD BBL CHROMagarTM CPE). Identification and antimicrobial susceptibility testing (AST) were performed by VITEK and conventional methods. Double disk synergy test IMP/MER-EDTA and CarbaNP test were conducted. AST of isolates resistant to carbapenems was (re-)confirmed with gradient MIC testing method and interpreted according to EUCAST guidelines. All CR isolates were sent for whole-genome sequencing (WGS). Identification was reconfirmed by MALDI-TOF. Genomic DNA was extracted using MasterPureTM DNA Purification Kit and sequenced via 2×250b PE sequencing (Miseq, Illumina). Comparative genome analysis was performed using in-house developed pipeline BacPipe v.1.2.6. wg/cgMLST scheme was generated and compared using chewBBACA and visualized in PHYLOViZ.

Results: A total of 21,151 samples were processed and 533 Klebsiella pneumoniae isolates were identified throughout the surveillance period. We detected 30 CR K. pneumoniae and 1 CR E. coli isolates. All CR K. pneumoniae isolates had MICs of imipenem and meropenem >32 mg/L, except one which showed MICs of 2 and 4, respectively. The MICs for both carbapenems in E. coli was 32. The isolates were also resistant to gentamicin, amikacin, piperacillin/tazobactam and ciprofloxacin. WGS analysis showed that all 31 isolates carried \( \text{bla}_{\text{NDM-1}} \) in combination with other beta-lactamases such as \( \text{bla}_{\text{CMY-4}} \), \( \text{bla}_{\text{CTX-M-3}} \) or \( \text{bla}_{\text{CTX-M-15}} \) and \( \text{bla}_{\text{SHV-11}} \). Majority of the K. pneumoniae isolates were ST11 (n=29, 96.7%). The E. coli isolate was ST101. The wg/cgMLST comparison indicated that a single clone was circulating within the surveillance period and that it evolved slightly (23 allelic loci differences) (Figure).

Conclusions: We could highlight the spread of a persisting NDM-1-producing ST11 K. pneumoniae clone in our hospital. This clone and the ST101 E. coli have already been reported in Bulgaria and their dissemination is causing local outbreaks in several hospitals. This is a worrisome trend which demands robust infection control measures and concerted action at a national level.

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The rates of antimicrobial resistance in leprosy are higher among cases diagnosed in France than in those diagnosed in African countries [WHO sentinel surveillance network]

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Background: Since leprosy is still a prevalent infectious disease with 210 000 new cases in 2018, WHO new strategy recommends monitoring resistance rates in new and retreated cases. As Mycobacterium leprae doesn’t grow in vitro, studying its antimicrobial resistance can be done either phenotypically by using the mouse footpad model, which requires qualified persons and is time consuming, or genotypically by detecting mutations in the genes involved in resistance. Our laboratory is mandated for leprosy as National Reference Center in France and as supranational for African countries.

Materials/methods: M. leprae strains from patients diagnosed in France [Metropolitan and overseas territories] between 2001 and 2019 and in 7 endemic African countries between 2009 and 2019 were screened for resistance genotypes using the GenotypeLepraeDR® kit [Hain Lifescience] and confirmed by PCR sequencing in case of mutations.

Results: We studied 240 cases [from 206 new cases and 34 relapses] diagnosed in France, and 374 [316 new cases, 48 relapses, 10 unknown] diagnosed in African countries. Molecular detection of resistance showed that the resistance rate was 6.9% in cases diagnosed in France whereas it was 3.2% in cases from African countries. In France and African countries, there were 13 and 9 strains resistant to dapsone, 3 and 1 strains resistant to rifampicin, and 2 and 2 strains resistant to fluoroquinolones, respectively. No multiresistance was detected. Mutations conferring resistance were the following [France cohort, African cohort]: P55L [6 and 6], T53R [0 and 2], T53A [1, 1], T53I [4, 0] in folP1 for dapsone, S456L [2, 1] and S456F [1, 0] in rpoB for rifampicin, and A91V [2, 2] in gyrA for fluoroquinolones. The resistance rate was significantly different between primary and secondary resistance [4.8% vs. 23.5%, p<0.001] for cases diagnosed in France. On the contrary, there was no secondary resistance in African countries, but 3.8% primary resistance.

Conclusions: antimicrobial resistance rates for leprosy were significantly higher in cases diagnosed in France than in African countries. This might be explained by a specific WHO programmatic organization in African countries contrary to France and/or by the lower use of antimicrobials in Africa.

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**Abstract 6168**

**HHV-6A infection and systemic sclerosis: clues of a possible association**

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**Background:** Systemic sclerosis (SSc) is a very severe autoimmune disease characterized by vasculopathy and fibrosis of the connective tissues, which is often fatal. Its etiology remains unknown, and several infectious agents, including human herpesvirus 6 [HHV-6], have been suggested as possible triggering factors, although direct association between infection and SSc is still missing. Since HHV-6 infection/reactivation has been associated to many autoimmune conditions, including thyroid disease that is often present in SSc, the aim of our study was to investigate such possible association.

**Materials/methods:** Twenty-six SSc patients were analyzed for the presence of HHV-6 in tissues and blood by a specifically designed digital droplet PCR allowing the distinction between 6A and 6B species. Anti-HHV6 humoral and cellular immune responses were also analyzed respectively by ELISA and Fluorospot assays. HLA-G plasma levels, and KIR typing were also analyzed. Furthermore, as endothelial cells (EC) have a main role in the disease pathogenesis and are a target for HHV-6 infection, we analyzed by quantitative real-time PCR microarray the expression of pro-fibrotic factors in HHV-6 infected EC.

**Results:** HHV-6A was detected at the skin level in all available SSc biopsies, whereas no control skin samples harboured the virus. HHV-6B was detected at the blood level in 80.7% of SSc patients (vs 40% of controls). Increased virus loads were associated with disease severity and poor natural killer (NK) response against the virus, particularly in subjects exhibiting a KIR2 phenotype. SSc patients also displayed a higher frequency and titer of antibodies directed against the HHV-6 U94 product. SSc patients also displayed a higher frequency and titer of antibodies directed against the virus, particularly in subjects exhibiting a KIR2 phenotype. HLA-G plasma levels were significantly higher in HHV-6/KIR2 positive SSc patients, and in vitro HHV-6 infection-induced pro-fibrosis factors expression in EC, supporting its role in the development of the fibrosing process

**Conclusions:** Our data suggest an association between virus infection/reactivation and disease, opening the way to future studies to understand the mechanisms by which HHV-6 might contribute to the multifactorial pathogenesis of SSc.

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Abstract 6173

Novel qPCR demonstrates azole-resistant TR34/L98H and TR46/Y121F/T289A Aspergillus fumigatus, in air spore-samplings around Danish agricultural fields

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Background: Azole-resistant (AR) Aspergillus fumigatus is increasing worldwide and arise through medical and environmental azole use. Environmentally driven AR today accounts for the majority of AR cases in Denmark. We developed a novel Taqman qPCR for detection of the two dominating environmental AR mechanisms (TR34/L98H and TR46/Y121F/T289A) and applied the assay on spore-trap samples from air.

Materials/methods: Primers and probes were designed specifically for the promotor of cyp51A in A. fumigatus based on in-silico analysis covering >800 cyp51A Genbank sequences including >200 sequences from 44 Aspergillus non-fumigatus species. Three probes was included specific for A. fumigatus, TR34 and since 2018 also TR46. Sensitivity was evaluated by 10-fold dilution series of normalized DNA concentrations and by CFU experiments with spore suspensions subjected to bead-beating and Nuclisens easyMag (biomérieux, Denmark) DNA extraction. Environmental air-sampling was performed using Burkhard spore collectors, with tape-strips corresponding to 24-hour samplings. Three sampling-periods were included, 2012-2014 (N=512), 2016 (N=645) and 2018 (N=439), collected across Denmark. DNA was extracted from tape as previously described (Duvivier et al. 2013).

Results: Based on DNA quantification and CFU experiments, the limit of detection (LOD) was estimated to 50 fg (<20 copies) and 50-200 CFU/mL, respectively with no differences between the three probes (A. fumigatus, TR34 and TR46). A. fumigatus cyp51A was detected in 47 (9%), 87 (13.5%) and 122 (28%) samples in 2012-2014, 2016 and 2018, respectively. Increased detection rate may be correlated to improved DNA processing and continuous optimisation of the PCR assay. Two samples with TR34 were discovered in 2016, four TR34 in 2018 but none in 2012-2014 (Table).

<table>
<thead>
<tr>
<th>Sampling period</th>
<th>AR-PCR positive sampling sites</th>
<th>Detected A. fumigatus (cyp51A) / total number of samples (%)</th>
<th>Detected TR34 (%)</th>
<th>Dates of detection</th>
<th>Detected TR46 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012-2014 total</td>
<td>47 / 512 (9.2)</td>
<td>0 (0)</td>
<td>NA</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>2016 total</td>
<td>87 / 645 (13.5)</td>
<td>2 (2.3)</td>
<td>See below</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>Gadsor 1</td>
<td>17 / 80 (21.3)</td>
<td>1 (5.0)</td>
<td>05.07.2018</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>Flakkebjerg 1</td>
<td>20 / 160 (12.5)</td>
<td>1 (5.0)</td>
<td>25.09.2019</td>
<td>ND</td>
<td></td>
</tr>
<tr>
<td>2018 total</td>
<td>122 / 439 (27.8)</td>
<td>4 (3.3)</td>
<td>See below</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Flakkebjerg 1</td>
<td>60 / 222 (27.0)</td>
<td>1 (1.2)</td>
<td>10.06.2018</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>

AR: Azole resistance, NA: Not available, ND: Not done

Conclusions: Environmental AR A. fumigatus was detected in 2016 and 2018 despite low content of A. fumigatus on tape samples. This is probably underrepresented as the AR spores constitute a minority among total A. fumigatus spores and thus potentially often below LOD. Although, this assay (single-copy gene target) displays lower sensitivity than diagnostic Aspergillus PCRs (multi-copy gene target) and lack extensive specificity testing, the assay offers a novel method for direct detection of TR34 and TR46 in clinical samples and for screening of environmentally driven azole resistance in complex specimens.

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Abstract 6174

**Change of gut microbiome and resistome of the patients with *Clostridioides difficile* infection and those with chronic obstructive pulmonary diseases compared with healthy population**

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**Abstract third-party references:** This research was supported by a fund [2017N-ER5407-00] by Research of Korea Centers for Disease Control and Prevention. This research was supported by the National Research Foundation of Korea [NRF] grant funded by the Korea government [MSIT] [No. 2015R1C1A1A01055646].

**Background:** The aim of this study is to investigate the change of gut microbiome and resistome in the patients with different exposure to antibiotics

**Materials/methods:** As for models of different antibiotic exposure, we selected 3 groups of people; healthy person without exposure to antibiotics within 2 months, chronic obstructive pulmonary disease patients [COPD] as people with frequent but subacute exposure to antibiotics, and Clostridioides difficile infection patients [CDI] who had dysbiosis caused by antibiotics. Whole metagenome sequences and targeted metagenomics approaches were performed.

**Results:** A total 61 healthy, 16 COPD, and 26 CDI patients were enrolled. Median days of antibiotic use within 2 months were 0, 8, and 12.5 days respectively (p < 0.001 by Kruskal Wallis). Median days of antibiotic-free within 2 months were 60, 39, and 0 days respectively (p < 0.001 by Kruskal Wallis). Bifidobacterium was the most prevalent genus in healthy gut microbiome and Ruminococcus in COPD and Enterococcus in CDI with statistical significance (p value by Kruskal Wallis < 0.001, each). Person who were exposed to antibiotics showed a positive correlation with abundance of Enterococcus (rho 0.773, p <0.001) and negative correlation with Faecalibacterium (rho -0.722, p <0.001), Bifidobacterium (rho -0.579, p <0.001), and Ruminococcus (rho -0.555, p <0.001).

Relative abundance of antibiotic resistance genes [ARGs] showed a significant difference between the groups [median 100 GPM in healthy vs 138 GPM in COPD vs 384 GPM in CDI with p < 0.001 by Kruskal Wallis]. Aminoglycoside was the most abundant ARGs [median 16.1 GPM in healthy, 21.7 GPM in COPD, and 70 GPM in CDI with p < 0.001 by Kruskal Wallis] and followed by beta-lactam [median 9.9 GPM in healthy, 20.6 GPM in COPD, and 50.8 GPM in CDI with p < 0.001 by Kruskal Wallis] and polymyxin (figure).

**Conclusions:** The bacterial composition of gut microbiome and resistome differed according to different antibiotic exposure.

![Figure. The abundance of antibiotic resistance genes according to the use of antibiotics](quidam76@hanyang.ac.kr)
Renal manifestations of severe fever with thrombocytopenia syndrome

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Background: Severe fever with thrombocytopenia syndrome (SFTS) is a tick-borne hemorrhagic fever caused by the SFTS virus (SFTSV), a newly discovered phlebovirus of family Phenuiviridae, which was previously classified as family Bunyaviridae. SFTS is characterized by high fever, leukopenia, and thrombocytopenia and often leads to multiorgan dysfunction, including kidneys. However, there are limited data on renal involvement of SFTS. We thus investigated the frequency and characteristics of kidney involvement of SFTS.

Materials/methods: All the PCR-confirmed SFTS patients who were admitted to Asan Medical Center, a tertiary hospital, Seoul, South Korea, between January 2013 and October 2018 were retrospectively enrolled. Patients with a history of previous urologic or chronic kidney disease were excluded. Proteinuria was defined as urinary albumin greater than two plus in dipstick urine test, and hematuria was defined as urinary blood greater than two plus in dipstick test and/or accompanying microscopic hematuria [≥5 red blood cells per high-power field].

Results: Of a total 43 patients with SFTS, 13 (30%) experienced acute kidney injury during the hospitalization. Proteinuria and hematuria were observed at 74% (32/43) and 79% (34/43), respectively. Both proteinuria and hematuria occurred at median 7.5 days (range, 2-13 days) after symptoms onset and lasted for 4 days (range, 1-21 days) and 4 days (range, 1-23 days), respectively. According to the degree of the proteinuria or hematuria, patients who had renal manifestation showed significantly higher frequency of septic shock or ICU admission than who did not (Table 1). Increased creatinine level, proteinuria, and hematuria were observed to be transient and fully recovered during the follow-up.

Conclusions: Reversible renal involvement was commonly observed among the patients with SFTS. The level of proteinuria and hematuria may reflect the severity of the viral illness. Regular monitoring of kidney function test with urinalysis is warranted in the management of SFTS patients.

Table 1. Clinical characteristics of patients with SFTS according to proteinuria or hematuria.

<table>
<thead>
<tr>
<th></th>
<th>Proteinuria ≥ (+++)</th>
<th>Proteinuria ≥ (+++)</th>
<th>Hematuria ≥ (+)</th>
<th>Hematuria ≥ (+++)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes (n=32)</td>
<td>No (n=11)</td>
<td>Yes (n=22)</td>
<td>No (n=21)</td>
</tr>
<tr>
<td>Septic shock</td>
<td>16 (50.0)</td>
<td>2 (18.2)</td>
<td>13 (59.1)</td>
<td>5 (23.8)</td>
</tr>
<tr>
<td>ICU admission</td>
<td>15 (46.9)</td>
<td>1 (9.1)</td>
<td>11 (50.0)</td>
<td>5 (23.8)</td>
</tr>
<tr>
<td>Mortality</td>
<td>6 (18.8)</td>
<td>1 (9.1)</td>
<td>3 (13.6)</td>
<td>4 (19.0)</td>
</tr>
</tbody>
</table>

Data are No (%), unless otherwise specified.

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Abstract 6177

Comparison of in vivo pathogenicity of four Candida auris clades in a neutropenic bloodstream infection murine model

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Abstract third-party references: Bence Balázs, Zoltán Tóth, Fruzsina Nagy were supported by New National Excellence Program of the Ministry for Innovation and Technology (ÚNKP-19-3.1.)

Background: Candida auris is an emerging worldwide concern and while many studies focus on virulence and pathomechanisms of this peculiar fungus, data are scarce regarding the behaviour of different C. auris lineages in mammalian hosts.

Materials/methods: Different isolates of the four prevalent C. auris clades (South Asian/Indian n=5, South African n=5, South American/Israeli n=5 and Japanese/Korean n=4) were compared to assess their virulence in a mammalian host using a neutropenic murine bloodstream infection model (10 animals/group). The infecting dose was 10^7 CFU/mice. Primary endpoint was mortality 21 days postinfection. Fungal tissue burden and histopathological examination were also performed two and six days postinfection (five animals at each time point) of relevant organs (kidney, heart, liver, spleen) using a similar infection protocol with two C. auris isolates of each clade chosen based on lethality experiments.

Results: Highest overall mortality at day 21 was observed for the South American/Israeli clade (96%, range 90%-100%), followed by South-Asian/Indian isolates (80%, range 50%-100%), while infection with Japanese/Korean and South-African isolates resulted in significantly lower cumulative lethality (44% and 45%, ranges 30-70% and 0-90%, respectively; Figure 1.). Survival differed significantly among isolates of all clades except the Japanese/Korean clade.

The highest fungal burden at day six was also found with the South American clade in all examined organs, while it was comparable for the other three tested clades. Fungal tissue burden varied with South Asian/Indian and South African clade isolates, but not in case of the South American or Japanese/Korean clades. Histopathological examination revealed a surprisingly high myocardial fungal burden with all lineages, which is less common for other clinically relevant Candida species.

Conclusions: Hereby we present the first comparison on the in vivo virulence of the four worldwide distributed C. auris lineages in a mammalian host. High fungal burden in the myocardium is notable. Isolates of the same clade showed differences in virulence in mice, but a markedly higher virulence of the South American/Israeli clade was clearly demonstrated.

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Population structure of extended spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae from anthropogenic environment and food in five European cities

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Background: ESBL-producing E. coli (ESBL-Ec) and K. pneumoniae (ESBL-Kp) have been widely isolated from humans, anthropogenic environment (AE), and food. The circulation of these isolates between the different sources is not well-understood and could differ between countries. Here, we compare the population structure of ESBL-Ec and ESBL-Kp in AE and food from five European cities.

Materials/methods: 1329 samples were collected between April 2017 and November 2019 in France, Switzerland, Spain, Germany, and The Netherlands. U-bends of long-term care facilities (LTCF) were sampled twice. LTCF sewers, water inflow of wastewater treatment plants (WWTPs), and river downstream from WWTPs were sampled 8 times over 32 weeks. Food samples were collected in supermarkets and LTCF kitchens. 328 ESBL-producing Enterobacteriaceae were retrieved: 266 ESBL-Ec (168 from AE and 98 from food) and 62 ESBL-Kp (49 from AE and 13 from food), of which genomes were sequenced using Illumina NextSeq. Sequence types (STs) and blaESBL were identified in silico.

Results: The predominant STs and the prevalent ESBL genes depending of their origins are shown in Table 1. ST131 ESBL-Ec was only found in the AE. Half (48.8%) of isolates retrieved in AE harbored blaCTX-M-15 while only 12.2% of food-isolated strains carried this gene. One third (28.6%) of the food-isolated strains harbored blaCTX-M-1 against 12.2% for AE-isolated strains. ST10 clade was in similar proportion in both AE- and food-isolated strains but harbor different blaESBL (blaCTX-M-15 or blaSHV-12, respectively). blaCTX-M-15 was overrepresented in ESBL-Kp (77.4%), with comparable proportions in food- and AE-isolated strains. ST405 and ST307 isolates were specifically retrieved in Spain while ST233 were found only in France.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>E. coli</th>
<th>K. pneumoniae</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>STs</td>
<td>blaESBL</td>
</tr>
<tr>
<td>AE</td>
<td>ST131 (22.7%)</td>
<td>blaCTX-M-15 (48.8%)</td>
</tr>
<tr>
<td></td>
<td>ST110 (9.3%)</td>
<td>blaCTX-M-27 (14%)</td>
</tr>
<tr>
<td></td>
<td>ST38 (6.4%)</td>
<td>blaCTX-M-12 (12.2%)</td>
</tr>
<tr>
<td>Food</td>
<td>ST10 (10.2%)</td>
<td>blaSHV-12 (32.6%)</td>
</tr>
<tr>
<td></td>
<td>ST155 (9.2%)</td>
<td>blaCTX-M-4 (28.6%)</td>
</tr>
<tr>
<td></td>
<td>ST69 (8.2%)</td>
<td>blaCTX-M-65 (12.2%)</td>
</tr>
</tbody>
</table>

Conclusions: Our results suggest that the population structure of ESBL-Ec retrieved from AE differs from foodborne ESBL-Ec for the European cities studied. In contrast, ESBL-Kp population seems to be structured by geography.

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Abstract 6183

Characterisation of *Pseudomonas aeruginosa* isolates co-harbouring IMP-18 and VIM-2 metallo-beta-lactamases from Peru

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**Background:** Antimicrobial resistance is increasing worldwide, including the Americas. *Pseudomonas aeruginosa* (PA) is a major pathogen responsible of nosocomial infections, especially in immunosuppressed patients. Carbapenem-resistance (CR) due to production of carbapenemases is an increasing problem in PA. VIM and IMP are the most frequent Metallo-β-lactamases (MBL) identified in PA. In Peru, molecular characterizations of CR in PA are very rare. The aim of the study was to characterize PA isolates co-expressing IMP and VIM MBLs.

**Materials/methods:** 81 non-duplicate carbapenem non-susceptible PA were collected from clinical specimen: blood (29), urine (21) and bronchial and tracheal secretions (31) of patients hospitalized at the National Institute of Neoplastic Diseases (INEN) of Peru from January to December 2017. Bacterial identification and antimicrobial susceptibility testing were performed using the Phoenix system (BD Diagnostics, Sparks, MD). Disc diffusion antibiograms were also performed. NG-test Carba 5 was used to detect the 5 main carbapenemases. Carbapenemase genes were sought by PCR and WGS.

**Results:** Out of the 81 PA of this study, 52 (64%) were carbapenemase producers: 34 (42%) were harboring *bla*<sub>IMP</sub> gene, 4 (5%) *bla*<sub>VIM</sub> gene and 14 (17%) *bla*<sub>IMP</sub> and *bla*<sub>VIM</sub> genes together. All PA isolates co-expressing *bla*<sub>IMP</sub> and *bla*<sub>VIM</sub> genes were resistant to all tested antibiotics except aztreonam and colistin. WGS revealed that the IMP-producers corresponded to IMP-74-producing ST357 or IMP-16-producing ST176 PA, while the co-producers corresponded to IMP-18-VIM-2 ST111 PA. The *bla*<sub>IMP-18</sub> and *bla*<sub>VIM-2</sub> genes were present on two different integrons, suggesting the acquisition of *bla*<sub>IMP-18</sub> gene by the VIM-2 producing ST111 PA. Despite repeated attempts, no plasmids could be evidenced in these isolates. NG-test Carba 5 was positive to all strains except PA with IMP-18, nevertheless, those could be detected with the second version of NG-test Carba 5v2.

**Conclusions:** To the best of our knowledge this is the first report of PA co-harboring VIM-2 and IMP-18 MBLs in Peru. Our results show that these isolates were highly resistant to most antimicrobials, except to colistin and aztreonam. Preliminary results revealed that the co-MBL producing isolates belong to single clone, while for the IMP producers, several unrelated clones were detected.

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The Insertion Sequence (IS) disruption of mgrB gene is critical for colistin susceptibility testing efficiency of Sensititre in carbapenem-resistant *Klebsiella pneumoniae*

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Background: The broth microdilution (BMD) method is currently the recommended technique for antimicrobial susceptibility testing of colistin by both EUCAST and CLSI. In routine microbiology laboratories, BMD method is often not implementable. Sensititre (EURGNCOL, SensititreTM, Thermo Fisher) are considered as an alternative method. The aim of the study was to evaluate the performance of Sensititre for antimicrobial susceptibility testing of colistin in *Klebsiella pneumoniae* and to find molecular mechanisms of discordant results.

Materials/methods: A total of 210 carbapenem resistant *K. pneumoniae* clinical isolates were included in this study. The colistin minimum inhibitory concentration (MIC) were determined by both BMD according to the recommendations of EUCAST and Sensititre EURGNCOL according to the manufacturer’s instructions. In colistin resistant isolates, the *mgrB* gene was amplified by PCR and sequenced by Sanger sequencing to determine truncation, insertions and mutations in the gene. Carbapenamase genes were examined by PCR.

Results: In total of 210 *K. pneumoniae*, OXA-48 was found in 187 (89%), NDM-1 was in 30 (14.28%), KPC-2 was in 9 (4.28), both OXA-48 and NDM-1 was in 24 (11.42) isolates. In BMD method, 144 (68%) isolates were resistant to colistin however 66 (31.3%) were found to be resistant to colistin by Sensititre. All colistin resistant isolates (144) had alterations in *mgrB* gene. The IS disruption in *mgrB* gene was detected in 38 (26.38%), point mutations and intragenic deletions were found in 106 (73.6%) isolates. Sensititre revealed false-resistant results in two isolates (0.95% major errors, ME) and 54 false-susceptible results (25.71% very major errors, VME) were detected. Among the 54 isolates with ME, 52 (96.3%) had no IS in *mgrB* gene.

Conclusions: The mechanism of *mgrB* disruption affects the efficiency of Sensititre in colistin susceptibility testing of carbapenem resistant *K. pneumoniae*.

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Abstract 6185

**Impact of the Spanish Neumonía Zero project on ventilator-associated pneumonia rates**

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**Background:** Ventilator associated pneumonia (VAP) is the most common healthcare associated infection in intensive care. It is associated with increased morbidity, mortality, length of stay and costs. The Spanish Neumonía Zero project (NZ) is a multifactor intervention proposal based on the application of evidence based interventions in patients receiving mechanical ventilation (MV) to prevent VAP and reduce its incidence in the ICUs. This work aims to describe the impact of VAP rates after the implementation of NZ in a Spanish ICU and the VAP etiology in our unity.

**Materials/methods:** Retrospective descriptive study, based on data from ENVIN-HELICS database, from an 18-bed polyvalent ICU. We analyzed VAP rates in the last 19 years, divided in 2 periods: P1 before NZ implementation, from January 2001 to March 2011; and P2, from April 2011 to October 2019, after NZ implementation. The difference between rates was analyzed with Fisher´ s exact test (signification with p<0,01).

**Results:** In P1 258 VAP were recorded, for 37351 days of stay and 25706 days of VM, while in P2 there were 87 VAP for 47330 days of stay and 25473 days with MV. The rates for P1/P2 were 6,91/1,84 for 1000 days of stay and 10,04/3,41 for 1000 days with MV. This is a reduction of 73.4% and 66% respectively (p<0,01). The distribution by microorganisms was, in both periods: Acinetobacter baumannii 25,2%/8%(p<0,01); Pseudomonas aeruginosa 19,4%/19,3%; methicillin-sensitive Staphylococcus aureus 13,6%/13,8%; methicillin-resistant Staphylococcus aureus 4,3%/2,3%; Escherichia coli 6,6%/2,3%; Klebsiella spp 5,4%/5,7%; Candida spp 1,9%/1,15%; Aspergillus 0,77%/0; Haemophilus influenza 3,1%/0; Enterobacter 5,8%/5,7%; Streptococcus pneumonia 2,7%/1,1%; other gram-negative 7,7%/10,3%; other gram-positive 1,9%/2,3%. On the last 12 months there was a rate of 4,1 VAP/1000 days of MV, against 10,8/1000 on the same period 10 years ago.

**Conclusions:** Starting from a VAP rate superior that the one recommended by the quality standard, after the implementation of NZ project there was a significantly reduction on VAP in our unity, bigger than 65%, reaching values below the Spanish rates. The microbiology was similar in both periods, except for A. baumannii.

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The risk of microbial contamination associated with nine different needle-free connectors
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Background: Needle-free connectors (NFCs) are widely used in clinical practice, and they can significantly reduce the incidence of catheter-related bloodstream infection (CRBSI) in critically ill patients. However, no study ascertain whether surface undulations of NFCs is a key factor for microbial decontamination, and subsequently allow microorganisms to enter the fluid pathway.

Materials/methods: The cap surface of 9 commercially available NFCs were inoculated with *Staphylococcus aureus* (*S. aureus*) for 15 seconds, cleaned for 30 seconds with a 70% (v/v) isopropyl alcohol wipe, and allowed to dry for 30 seconds. Syringes were used to activate each NFC and to flush with 10 ml aseptic saline, and all saline flushes were collected and pooled in a sterile filter cup to collect any *S. Aureus*. Then, the filter papers were aseptically transferred to blood agar plates with incubation for 48 hours at 37 °C.

Results: The standard NFC with decontamination had associated negative culture, while median log10 CFU counts in the standard NFC without decontamination after inoculation with *S. aureus* were 3.2, 2.8, 3.3, 3.5 on days 1 to 4, respectively. *S. aureus* isolated from 9 commercially available NFCs after decontamination for 15 seconds with 70% (v/v) isopropyl alcohol wipe at day 1 to day 4 is shown in table 1.

Conclusions: This finding suggested that there may be differences in the risk of internal microbial contamination with different surface undulations and even 15 seconds of decontamination may not eradicate microorganisms from these devices.

<table>
<thead>
<tr>
<th>Day</th>
<th>Brand A</th>
<th>Brand B</th>
<th>Brand C</th>
<th>Brand D</th>
<th>Brand E</th>
<th>Brand F</th>
<th>Brand G</th>
<th>Brand H</th>
<th>Brand I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1</td>
<td>1</td>
<td>6</td>
<td>0</td>
<td>9</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Day 2</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>10</td>
<td>7</td>
<td>7</td>
<td>7</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Day 3</td>
<td>1</td>
<td>4</td>
<td>0</td>
<td>10</td>
<td>6</td>
<td>8</td>
<td>6</td>
<td>5</td>
<td>—</td>
</tr>
<tr>
<td>Day 4</td>
<td>3</td>
<td>6</td>
<td>0</td>
<td>10</td>
<td>8</td>
<td>6</td>
<td>6</td>
<td>3</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td>27.5%</td>
<td>55%</td>
<td>0%</td>
<td>97.5%</td>
<td>60%</td>
<td>57.5%</td>
<td>55%</td>
<td>42.5%</td>
<td>45%</td>
</tr>
</tbody>
</table>

Presenter email address: fengzhihuanxing@126.com
Abstract 6187

**Susceptibility to bacteriophage K, biofilm formation, presence of ica operon and adhesins among staphylococci**

Maria Plet (=), Foteini Gkartziou, Nikolaos Giormezis, Fevronia Kolonitsiou, Iris Spiliopoulou

1University of Patras, Department of Microbiology, School of Medicine, Patras, Greece, 2University of Patras, National Reference Centre for Staphylococci, School of Medicine, Patras, Greece, 3Institute of Chemical Engineering Sciences, FORTH/ICE-HT, Patras, Greece

**Background:** Staphylococci, mainly *Staphylococcus aureus* and *S. epidermidis*, are frequent etiologic agents of hospital infections. Among the virulent factors implicated, are the adhesion mechanisms used by the bacteria to anchor to the surface of various materials. Of importance is the production of an intercellular polysaccharide adhesin encoded by the ica operon, and biofilm formation. Due to the increasing antimicrobial resistance, there is a resurgence of interest into bacteriophages. In this study, *S. aureus* and *S. epidermidis* were tested in terms of phage and antimicrobial resistance, biofilm formation, ica and adhesins' genes carriage.

**Materials/methods:** In total, 179 staphylococci (106 *S. aureus* and 73 *S. epidermidis*) recovered from patients with staphylococcal infections, were identified at species level by Vitek 2 Advanced Expert System (bioMerieux, France). Biofilm formation was performed by the microtiter dish assay method. Antimicrobial resistance was tested by the disk diffusion and a gradient method, according to EUCAST guidelines. Susceptibility to bacteriophage K (ATCC19685-B1) was tested using two concentrations of phage suspensions (10⁴ and 10⁶ pfu/ml) on agar plates. The presence of ica operon and adhesins' genes [aap, fnbA in *S. aureus* and atlE, fbE in *S. epidermidis*] was investigated by PCRs.

**Results:** Among 179 strains, 64 (35.8%) produced biofilm (35 *S. aureus* and 29 *S. epidermidis*), whereas 70 (39.1%) were methicillin-resistant (10/106 *S. aureus* and 54/73 *S. epidermidis*). Statistically significant difference was observed for ica operon and both adhesins genes carriage in biofilm-positive *S. epidermidis* strains and for aap among *S. aureus*, as compared to biofilm negative ones (p<0.05, Figure 1). Susceptibility to phage K was detected in 83 strains: 64/106 *S. aureus* (60.4%) and 19/73 *S. epidermidis* (22%). Carriage of fnbA in *S. aureus* was positively associated with phage K susceptibility (97% vs 90.5%), whereas, both adhesins in *S. epidermidis* were more often found in phage K-resistant strains.

**Conclusions:** In our hospital, methicillin-resistant staphylococci are a major cause of infections. Phage susceptibility is more frequent in *S. aureus* and biofilm-negative strains. Methicillin resistance is observed more frequently in biofilm-positive strains that carry the ica operon and adhesins genes as compared to biofilm negative ones, enhancing their virulence capacity.

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Abstract 6191

**Direct MALDI-TOF MS identification from positive blood cultures: rapid Sepsityper**
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**Background:** The rapid identification of the causative agent of sepsis plays a key role for the adoption of an appropriate antibiotic therapy, and hence is crucial for the patients’ clinical outcome.

In this study, we evaluate the implementation into the routine workflow of the Rapid Sepsityper kit for the rapid bacterial identification by MALDI-TOF MS directly from positive blood culture bottles.

**Materials/methods:** From February 2018 to October 2019, a total of 5,271 routine positive blood cultures samples underwent direct MALDI identification by Rapid Sepsityper (Bruker Daltonik).

The bacterial pellet extracted from 1 ml of positive blood culture by the lysis/centrifugation Sepsityper protocol was spotted directly onto the MALDI target for the species identification.

For 1,648 samples, the same pellet was then used to set up the antibiotic susceptibility testing by Microscan WalkAway (Beckman Coulter) broth microdilution panels.

**Results:** Overall, the Rapid Sepsityper enabled the direct identification of 4,493/5,060 (88.7%) monomicrobial samples. It showed a very good performance for enterobacteria, non-fermenting gram-negative rods, staphylococci and enterococci. The missed identifications were restricted mainly to a few groups of microorganisms (streptococci, corynebacteria, Bacteroides spp. and yeasts).

Among the polymicrobial samples, in 68/211 samples both species were identified, in 76/211 only one species, in 65 samples none of them.

Susceptibility testing was successful for 2489/2648 samples (94%) (for 159 samples the growth in the panel was insufficient).

**Conclusions:** The Rapid Sepsityper proved to be a reliable and robust method for the bacterial identification directly from positive blood cultures, with an excellent efficacy (near to 100%) for the most clinically relevant causative agents of sepsis (enterobacteria, S. aureus, enterococci). It delivered a result in a very short time (around 1 h for a batch of 10-15 samples).

Further, the same bacterial pellet used for the MALDI identification proved to be suitable to set up the antibiotic susceptibility testing, simplifying and speeding up the routine workflow and the time-to-report.

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Abstract 6192

**Uncovering cryptic clusters of Group B streptococcal infant disease in the UK and Ireland through genomic analysis**

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**Background:** A recent systematic review of hospital outbreaks of invasive group B streptococcal (iGBS; *Streptococcus agalactiae*) disease identified 30 documented outbreaks worldwide since 1966. Whilst this suggests that these are rare events, prolonged serial intervals between cases pointed to likely under-recognition. To assess the frequency of infant iGBS clusters in the UK and Ireland, whole genome sequencing (WGS) data from isolates collected during a period of enhanced surveillance were analysed alongside epidemiological data.

**Materials/methods:** Potentially linked (<10 single nucleotide polymorphisms, SNP) iGBS cases from infants with early (<7 days of life) or late-onset (7 - 90 days) disease were identified from WGS (HiSeq 2500 platform, Illumina) data from clinical sterile site isolates between April 2014 and April 2015. We assessed accompanying time/place data to determine an appropriate SNP threshold for clustered cases. Data for cases in England were augmented through linkage to national hospital admission data to determine admission/discharge timelines and identify hospital transfers of cases.

**Results:** Through analysis of sequences of 753 iGBS isolates, coupled with time/place information, we adopted ≤5 SNP differences as cut-off to define likely clusters. We identified 7 clusters comprising 16 cases over the 13-month period consistent with intra-hospital horizontal transmission. Of these, 15 were late-onset cases (of 192 late-onset cases with sequenced isolates) and one an early-onset index case. Six clusters were pairs and one cluster involved 4 infants. Serial intervals between cases ranged from 0 to 59 days (median 12 days). In one cluster, the iGBS infections were diagnosed by two different hospitals, the second infant being readmitted to a different hospital to their place of birth. Only 3 of the 7 clusters had been previously identified.

**Conclusions:** Our study identified that approximately 1 in 12 late-onset infant GBS cases formed part of a hospital cluster and most clusters were previously unrecognised. Routine submission of iGBS isolates to the national reference laboratory is essential to identify potential clusters, ensuring timely investigation and confirmation through genomic analysis.

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Severity of chronic diseases in patients over 64 years old with flu or serious acute respiratory infection, according to flu vaccination status

Latorre Millán Miriam*1, Amparo Larrauri2, Alín Manuel Gherasim3, Clara Mazagatos4, Nieves Martínez Cameo1, Mª Pilar Hernández1, Yolanda Gracia1, Vanessa Guerrero1, Ana Martínez-Sapiña1, Antonio Rezusta1, Ana María Milagro Beamonte1

1Miguel Servet University Hospital, Aragon Health Research Institute (IIS Aragon), Zaragoza, Spain, 2National Epidemiology Center, Carlos III Health Institute, Madrid, Spain

Abstract third-party references: Miguel Servet University Hospital (Microbiology and Parasitology Service), Zaragoza, Spain. Research group on infections difficult to diagnose and treat (Aragon Health Research Institute). National Epidemiology Center (Carlos III Health Institute), Madrid, Spain.

Background: Influenza virus infections should be considered in all older adults with risk factors, as they may be associated with higher mortality. Knowledge of the distribution of chronic diseases present in these patients can help in their management in clinical practice.

Materials/methods: Data of the patients included by the Miguel Servet University Hospital (HUMS) in the European IMOVE+ study, during the 2016/17, 2017/18, and 2018/19 seasons, were analyzed. Patients older than 64 years hospitalized with symptoms of Severe Acute Respiratory Infection (SARI), not institutionalized, provided a sample of pharyngeal smear in which the presence of influenza was detected by PCR-RT. The severity of their chronic diseases was studied as the number of their related previous hospitalizations in the last year, according to the flu vaccination status and diagnosis, using the chi-square test \( \chi^2 \) adjusted by Monte-Carlo methods.

Results: Among the three studied seasons, 1,314 patients with SARI were recruited, of which 424 were unvaccinated, and 35.9% were diagnosed of flu. Approximately, a half of them had some hospitalization related to their chronic diseases in the last year, and more than a quarter had two or more. No significant differences were found when comparing the number of previous hospitalizations according to the vaccination status, regardless of the presence of flu.

<table>
<thead>
<tr>
<th>Severity</th>
<th>Unvaccinated (n=557)</th>
<th>Vaccinated (n=752)</th>
<th>( \chi^2 )</th>
<th>p</th>
<th>Unvaccinated Flu+ (n=234)</th>
<th>Vaccinated Flu+ (n=237)</th>
<th>( \chi^2 )</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>299 (53.8%)</td>
<td>383 (51%)</td>
<td>7487</td>
<td>0.609</td>
<td>132 (56.7%)</td>
<td>123 (51.9%)</td>
<td>7.191</td>
<td>0.409</td>
</tr>
<tr>
<td>1</td>
<td>129 (23.2%)</td>
<td>192 (25.6%)</td>
<td></td>
<td></td>
<td>54 (23.2%)</td>
<td>60 (25.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>70 (12.6%)</td>
<td>87 (11.6%)</td>
<td></td>
<td></td>
<td>22 (9.4%)</td>
<td>33 (13.9%)</td>
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<tr>
<td>3</td>
<td>24 (4.3%)</td>
<td>47 (6.3%)</td>
<td></td>
<td></td>
<td>10 (4.3%)</td>
<td>10 (4.2%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>14 (2.5%)</td>
<td>23 (3.1%)</td>
<td></td>
<td></td>
<td>6 (2.6%)</td>
<td>5 (2.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>8 (1.4%)</td>
<td>10 (1.3%)</td>
<td></td>
<td></td>
<td>5 (2.1%)</td>
<td>3 (1.3%)</td>
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<tr>
<td>6</td>
<td>7 (1.3%)</td>
<td>5 (0.7%)</td>
<td></td>
<td></td>
<td>4 (1.7%)</td>
<td>1 (0.4%)</td>
<td></td>
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</tr>
<tr>
<td>7</td>
<td>4 (0.7%)</td>
<td>2 (0.3%)</td>
<td></td>
<td></td>
<td>0 (0.0%)</td>
<td>2 (0.8%)</td>
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</tbody>
</table>

Conclusions: There is a high proportion of patients over 64 years unvaccinated for the flu between those who needed a hospitalization for SARI [with or without flu] and had some previous hospitalizations for their chronic diseases in the same year. This reinforce the importance of highlighting vaccination in this population.

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Abstract 6194

Rapid phenotypic susceptibility testing of *Neisseria gonorrhoeae* using Graver-Wade medium, broth microdilution, and the flow cytometry-assisted susceptibility test (FAST)

Malgorzata Kopczyk¹, Teagan Paton¹, Kieran Mulroney², Timothy Inglis¹,², Christine Carson*¹,²

¹PathWest Laboratory Medicine WA, Perth, Australia, ²The University of Western Australia, Perth, Australia

**Background:** Gonococci are immensely challenging to existing antimicrobial susceptibility test (AST) regimes. No international reference AST method for *Neisseria gonorrhoeae* exists. Improved methods would better support gonorrhoea treatment recommendations. The fastidious physiology of gonococci complicates AST development. We demonstrate use of Graver-Wade (GW) broth medium in both a broth-microdilution (BMD) assay and a Flow Cytometry-Assisted Susceptibility Test (FAST) application for rapid susceptibility profiling of *N. gonorrhoeae*.

**Materials/methods:** 24 isolates of *N. gonorrhoeae* were tested by BMD and FAST using GW medium in Sensititre™ HPB1 plates. The range of antimicrobial agents on the plate was not ideal for gonococci but included ceftriaxone, penicillin, tetracycline and agents from other drug classes used to treat gonorrhoea. Isolates selected for inclusion had a range of ceftriaxone, penicillin and tetracycline MICs previously determined by agar-dilution (AD) method. Overnight cultures in GW broth were adjusted to approximately $5 \times 10^5$ cfu/ml in GW broth and inoculated into HPB1 plates using a Sensititre™ auto-inoculator. Plates were incubated at 35°C with 5% CO$_2$; 18-24 h for the BMD, 5 hours for FAST. At 5 h, FAST plates were diluted 1:2 with a staining buffer containing 5 µM SYTO® 9, and read using an Attune™ NxT flow cytometer with an autosampler. Flow data were analysed using bespoke software to predict MIC and susceptibility in ≤ 6 hours from antimicrobial plate inoculation.

**Results:** Concordance between AD and BMD results was 90% (penicillin), 96% (tetracycline), and 100% (ceftriaxone). Across 18 antimicrobials tested, essential agreement between FAST and BMD was 91.44%. Categoric agreement for ceftriaxone, penicillin and tetracycline was 100%, 79.17% and 75%, respectively. Using the EUCAST v9.0 breakpoints, 11 errors were present. For penicillin, 5 minor errors overestimated resistance of the discordant isolates, while for tetracycline, 6 minor errors underestimated resistance. The flow cytometry data suggested transition of cells to a quiescent state during measurement on the autosampler stage may be influencing results.

**Conclusions:** Graver-Wade medium should be reconsidered as a fully defined, liquid culture medium suitable for gonococcal ASTs. FAST results using GW broth are encouraging but would likely benefit from better control of the antimicrobial challenge and measurement conditions.

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Comparative inflammatory cytokines gene expression in culture of human macrophages infected with Leishmania tropica and Leishmania major parasites

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Background: Human cutaneous leishmaniasis is mainly caused by two species Leishmania tropica and L. major in Old World. The type of skin lesion, its duration, severity and appearance is different between Anthropogetic Cutaneous Leishmaniasis [ACL] due to L. tropica and Zoonotic CL [ZCL] due to L. major. Since Pro- and anti-inflammatory cytokines significantly contribute in severity and outcome of CL lesion, this experiment aimed to compare the gene expression changes of these cytokines in culture of human macrophages infected with L. major and L. tropica parasites.

Materials/methods: Peripheral blood mononuclear cells were isolated from a healthy individual without the history of CL from non-endemic region and macrophages were prepared by culture of adherent monocytes in 6well flat-bottomed plates for 6 days in 37°C incubator with 5% CO2. Macrophages (3x10⁵/well) were stimulated with either live L. major or live L. tropica promastigotes (Parasite:MQ ratio of 10:1) or unstimulated. At three time points T1=4, T2=10 and T3=24 hours after stimulation, RNAs were extracted and gene expression of TNF, IL-1B, IL-6, TGF-B, and IL-10 were measured by relative real-time RT-PCR method using ∆∆Ct calculation.

Results: Significant upregulation of TNF, TGF-B and IL-1B genes was shown in stimulated macrophages. The expression of IL1B in macrophages stimulated with L. major was significantly higher than that of L. tropica. In L. tropica stimulated macrophages the expression of TNF was 93.05 fold higher in T2=10 hr compared to T1=4 hr and significantly decreased after 24 hr. In L. major stimulated macrophages the expression of TGF-B was 213.78 fold higher in T2=10 hr compared to T1=4 and significantly decreased after 24 hr, but in L. tropica stimulated macrophages TGF-B expression was significantly higher in T3=24 hr culture.

Conclusions: This study suggested alterations in pro-inflammatory cytokine IL1B and anti-inflammatory cytokine TGF-B associated with L. major vs. L. tropica infection in vitro. Changes in pro- and anti-inflammatory cytokines seems to play a role in differences occur between severity/appearance of ACL and ZCL lesions.

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**Abstract 6205**

**Hypervirulent Klebsiella pneumoniae bloodstream infections in adults: results from a retrospective study in a French intensive care unit**

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**Background:** Hypervirulent variants of Klebsiella pneumoniae (hvKp) have been initially reported in the Asian Pacific Rim in 1986. Although reports of invasive infections due to hvKp in Western countries is increasing, European data remain limited. The objective of our study was to describe hvKp bacteremia prevalence in intensive care unit (ICU) patients of a French university hospital.

**Materials/methods:** We retrospectively screened all K. pneumoniae bloodstream infections in adult ICU patients between January 2016 and June 2019. Clinical features were collected from hospitalization reports. The hypermucoviscous phenotype was defined by a positive string-test (ST). We performed a multiplex PCR detecting K1/K2 capsular genotypes and genes encoding for the following virulence-related factors: regulator of mucoid phenotype (rmpA), aerobactin receptor-encoding gene (iutA), enterobactin (entB) and yersiniabactin (ybtS), allantoin metabolism (allS), and type-3 fimbriae (mrkD). Isolates positive for the rmpA gene were defined as hypervirulent.

**Results:** A total of 53 non-redundant K. pneumoniae isolates was collected. Prevalence of hvKp was of 13% (7/53), mainly belonging to K1/K2 serotypes (5/7, 71%), all harboring iutA, mrkD and entB virulence genes. Classical K. pneumoniae (cKp), i.e. non hypermucoviscous, strains, were mainly non-K1/K2 (44/46, 96%, p<0.001) and iutA-negative (45/46, 98%, p<0.001). All hvKp strains displayed a wild-type susceptibility profile to antibiotics. Compared to molecular hvKp definition, the ST had a sensitivity and a specificity of 86% and 94%, respectively. Bacteremic patients with hvKp were all males and seem younger than patients with cKp (mean age 53 vs. 64 yrs). None of them was Asian and no recent travel to endemic countries was reported. The portal of entry in hvKp bacteraemia was the respiratory tract in 5/7 cases including community-acquired pneumonia (n=3) and aspiration pneumonia (n=1). Although not statistically significant, mortality was higher in the hvKp group (57% vs. 39%).

**Conclusions:** Our study confirms the burden of hvKp invasive infections in Europe in patients without usual associated risk factors (travels to Asia and Asian ethnicity). The prevalence might be underestimated by the ST performances and a consensus definition of hypervirulence must be established, together with guidelines for the management of patients suffering from hvKp infections.

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**Abstract 6210**

**Gut microbiota of healthy volunteers with or without stool carriage of Klebsiella pneumoniae in an area with invasive Klebsiella pneumoniae syndrome**

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**Background:** Invasive Klebsiella pneumoniae syndrome (IKS) is an important endemic disease in Taiwan. Intestinal carriage of certain clones causing IKS in asymptomatic adults has been demonstrated. Data comparing healthy adults and children with or without stool KP carriage was rarely reported.

**Materials/methods:** Healthy volunteers without antibiotic exposure within three months were recruited from medical staff and their family in a Taiwanese medical center. Stool samples were sent for gut microbiota analysis. The gut microbiota was analyzed using amplification of the V4 hypervariable regions of the 16sRNA followed by high-throughput sequence. Rectal swab was sent for *K. pneumoniae* culture and identification by MALDI-TOF method.

**Results:** A total of 55 adults (Age: 23.13-72.14, 45.97) and 20 children (Age: 0.09-5.81, 2.29) were enrolled. 29 adults and 6 children had positive rectal swab of *K. pneumoniae*. Children had lower diversity compared with adults with higher relative abundance of *Streptococci* and *Bifidobacterium* spp. The relative abundance of *Klebsiella* spp. were (1.56E-02, 0.00E+00-3.06E-01) among adults and (6.74E-03, 0.00E+00-4.33E-02) among children. Relative abundance of *Klebsiella* was significantly higher in personnel with positive rectal swab (*p*<0.0001, analyzed with linear discriminant analysis effect size). Interestingly, rectal swab positive for *Klebsiella* is strongly negatively correlated with *Enterobacter* spp. (*p*<0.0001). Difference in the relative abundance of the three major intestinal genus including *Bacteroides*, *Prevotella* and *Bifidobacterium* was also noted among *Klebsiella* carrier and non-carrier. However, there is no known demographic factors correlated to positive rectal swab positive for *Klebsiella*.

**Conclusions:** *Klebsiella* species could be found in early days of life. Competition of *Klebsiella* spp. and *Enterobacter* spp. might occur.

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Abstract 6212

Outbreaks of multidrug-resistant *Klebsiella pneumoniae* in neonatal intensive care units in Ghana: a case for improved surveillance and infection control

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**Background:** Hospital outbreaks are rarely reported from sub-Saharan Africa. Using whole genome sequencing we describe two outbreaks involving carbapenemase- and ESBL-producing *Klebsiella pneumoniae*, respectively, in two neonatal intensive care units (NICUs) in Ghana.

**Materials/methods:** Two outbreaks were detected during a hand hygiene intervention programme at the NICUs of the Korle-Bu Teaching Hospital (KBTH) and 37 Military Hospital (37MH) in Ghana between September 2017 and March 2019. We conducted surveillance of bloodstream infections, screened neonates for carriage of multi-drug resistant Gram-negative bacteria and sampled for bacterial contamination of the environment. We sequenced the genomes of all sampled carbapenemase-producing *K. pneumoniae* from KBTH. Likewise we sequenced 10 ESBL positive *K. pneumoniae* randomly selected from 126 positive blood cultures with growth of this organism at 37MH. Genome sequences were analysed for antibiotic resistance genes, presence of plasmids, multi-locus sequence typing and single nucleotide polymorphisms (SNPs).

**Results:** Twenty-nine carbapenemase-producing *K. pneumoniae* were isolated from KBTH, 18 from external carriage, 8 from bloodstream infections and 3 from the environment. All were multi-drug resistant with reduced susceptibility to carbapenems but susceptible to colistin. Carbapenemase production was mediated by *bla-oxa-1*81. Ninety-seven percent (28/29) of the isolates belonged to ST 17 and *in silico* defined capsular type KL25. The 28 ST 17 isolates differed by 0-32 SNPs in their core genome suggesting they constitute a clonal outbreak. Plasmid incompatibility groups IncX3, F1B[Mar], O1, ColKP3 were present in all the isolates. At 37MH all 10 *K. pneumoniae* isolates were multi-drug resistant but susceptible to amikacin, meropenem and tigecycline. ESBL production was mediated by *bla-CTX-M-15*. Nine of the isolates (90%) belonged to ST 25, and *in silico* defined capsular type KL2. Core genome phylogeny revealed that they belonged to an outbreak with a maximum SNP distance of 7 across the tree. None of these outbreak strains carried plasmids.

**Conclusions:** We documented two outbreaks of MDR *K. pneumoniae* from two NICUs in Ghana over a 19-month period. Improved clinical microbiology services, enhanced surveillance and access to newer molecular diagnostic tools is likely to improve outbreak detection and control in sub-Saharan African hospitals.

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Abstract 6217

The microbiome of nasal samples from an all-age, healthy, UK cohort reveals the epidemiology of potentially protective bacterial genera

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Background: Respiratory infections remain significant contributors to global morbidity and mortality yet there is increasing evidence that certain microbiota compositions are beneficial to health. Carriage of Corynebacterium and Dolosigranulum sp. predict the absence of Staphylococcus aureus carriage, and a decrease in carriage of both Streptococcus pneumoniae and Haemophilus influenzae leading to reduced incidence of acute otitis media. These interactions suggest that the modification of the microbiome may be beneficial, however significant fundamental knowledge gaps remain.

Materials/methods: Nasal self-swabs (n=471) were collected from individuals attending general practitioners (GP) practices from the South-East (UK) hub of the Wessex Primary Care Research Network between May to August 2012 and February to April 2013. DNA was extracted from 200µL STGG-stored swab contents and the 16S rRNA gene was amplified using V4 primers 515FB and 806RB. Sequencing was done on a MiSeq (Illumina, UK) with 2 × 300bp paired-end V3 chemistry. Microbiome analysis was done using the R package Phyloseq v1.29.0. Sample metadata included bacterial culture, age, antibiotic usage, recent respiratory infection and vaccination status.

Results: Nasal microbiome profiles were dominated by Proteobacteria, Firmicutes and Actinobacteria. The richness and evenness of the microbiota compositions sampled during winter months was significantly lower than spring (p = 0.022) and summer (p = 0.034). No clustering based on participant age was observed. No age-related differences in the relative abundance Corynebacterium sp. were observed. In contrast, the relative abundance of Alloiococcus sp. (also commonly referred to as Dolosigranulum sp.) was significantly higher in both children less than five years old and adults (18 to 65) compared to children and adolescents between the ages of 5 and 18. The prevalence of both genera was significantly higher in respiratory samples that were culture negative for Staphylococcus aureus. In all cases the culture of a pathobiont (H. influenzae, S. pneumoniae or Moraxella catarrhalis) was associated with a higher prevalence of each of Corynebacterium sp. and Alloiococcus sp.

Conclusions: The prevalence of Corynebacterium and Alloiococcus sp. exhibit different epidemiological prevalence across age-groups. The central posit that the presence of Corynebacterium and Alloiococcus sp. predicts lower prevalence’s of pathobiont colonisation requires further examination.

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Multi-centre whole genome sequencing bioinformatic outbreak analysis proficiency test conducted in The Netherlands

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Abstract third-party references: SIG Bioinformatics in Medical Microbiology NL Consortium

Background: The introduction of Whole-genome sequencing (WGS) for outbreak detection, made other methods to analyse outbreaks almost deprecated. Nevertheless, the reproducibility and comparability of WGS based outbreak analysis among different centres using distinct analysis tools, has not been fully explored. Furthermore, centres that are performing these complicated outbreak analyses need external validation of their methods in order to meet health care standards. To accommodate these issues, the SIG Bioinformatics consortium has setup a Multi-centre proficiency test.

Materials/methods: 40 paired-end Illumina Klebsiella pneumoniae and Enterococcus faecium sequence read sets were obtained from the Sequence Read Archive. To the best of our knowledge, no publicly available outbreak analysis was conducted previously on these samples. These samples together with standardized result forms were distributed to 16 centres in the Netherlands via a secure data share. Centres were asked to perform WGS Outbreak analysis and report the detected outbreak clusters as they would report to their own Infection and Prevention Control. Additionally, centres were asked to specify their methodology and outbreak cluster definitions. Results were reported back and uploaded to a secure data share. The reported outbreak clusters were reconstructed per centre and compared to each other by using pairwise distances and multidimensional scaling.

Results: 13 out of 16 (81.25%) centres participated in this proficiency test and reported outbreak clusters for both the K. pneumoniae and the E. faecium dataset. A majority voting strategy was employed to assess performance of each centre. Preliminary analysis reveals only small variations in the reported clusters. Furthermore, some similarity in methodology among centres was observed, 8/13 used Ridom SeqSphere+, 4/10 a fully custom approach and 1/13 BioNumerics.

Conclusions: This proficiency test is the first step to EQA/proficiency testing and validation of WGS based outbreak analysis and gives us clear insights inside the variability in outcome and methodology. Furthermore, the analysis strategy used in this proficiency test can be adopted by WGS outbreak analysis proficiency tests in the future. The study demonstrates that even though a wide variety in methodology is employed for WGS based outbreak surveillance, similar clusters are defined, demonstrating harmonisation of methodology is not essential.

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Typing of *Salmonella enterica* by Fourier-transform infrared spectroscopy

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**Background:** *Salmonella enterica* is one of the leading causes of foodborne diseases worldwide and represents a major public health burden. Differentiation of *S. enterica* at intra-species level is crucial, for epidemiological investigations and to control foodborne outbreaks, as well as from the clinical point of view (identification of typhoid/non-typhoid serovars). Several methods are currently used for this purpose (serotyping, phage typing, molecular methods), but they all are laborious and cost-intensive.

In this study, we investigated the discriminatory power of the Fourier Transform Infrared Spectroscopy for *S. enterica* typing, in comparison with classical serotyping methods based on somatic and flagellar antigens.

**Materials/methods:** A total of 148 well characterized clinical, foodborne, veterinary and environmental *S. enterica* isolates, belonging to 19 different serogroups, were analysed by the IR Biotyper system (IRBT - Bruker Daltonik). This dataset includes also 24 *S. Typhi* isolates.

Infrared absorption spectra were acquired in transmission mode from a bacterial suspension in water/ethanol, placed in three technical replicates on a silicon sample plate, and let air dry.

Using the IRBT software, spectra relation within a wavenumber range from 1300 to 800 nm was analysed applying hierarchical cluster analysis (HCA) with Euclidean metric and single linkage.

**Results:** Congruence of IR Biotyper HCA and O-serogroups was evaluated with adjusted Wallace algorithm, indicating that IRBT can predict the O serogroup with 95% accuracy.

The 19 different serogroups were clustered separately at a threshold of 0.20. In addition, at a lower threshold, further intra-serogroup clustering was possible for some serotypes, in particular the separation of *S. Typhi* from the other 0:9 serotypes was observed.

**Conclusions:** IR Biotyper enabled an accurate discrimination of *Salmonella enterica* isolates at serogroup level, and in some cases also at serotype level, the most clinically relevant of which is the reliable discrimination of *S. Typhi* from other 0:9 serovars.

This technique has the capability to be a reliable, fast, high throughput and low-cost alternative typing methodology, suitable for implementation into routine microbiology laboratories for both diagnostics and epidemiological investigations.

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The REAnimation Low Immune Status Markers study: phenotypic and functional alterations of adaptive immune response in critically ill patients

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Background: Immune response to sepsis is complex and dynamic. Several alterations of the adaptive immune response have been already described and some even observed in other severe injuries like trauma. However, the comprehensive description of phenotypic and functional immune alterations development overtime in a large cohort of patients has never been done. In addition, it is not known whether these alterations depend on the type of injury (infectious vs sterile) and if they are associated with an increased risk of deleterious outcomes.

Materials/methods: A prospective longitudinal, single-center observational study was set up in Edouard Herriot Hospital (Lyon, France) between December 2015 and March 2018. A total of 354 ICU patients suffering from sepsis, severe trauma or after major surgery, and 175 healthy volunteers were enrolled. Blood specimens were collected once for volunteers and three times for patients during the first week of ICU stay. The adaptive response was measured by concomitantly assessing cellular phenotypes (circulating lymphocyte subpopulations) and functions (proliferation, cytokine production), and mRNA levels (CD3D, CD127, PD-1) with standardized tests.

Results: Injury-induced adaptive immune profile was similar in the 3 groups of patients and characterized by a major decrease in the number of circulating effector cells affecting every lymphocyte sub-populations except for regulatory T cells. Remaining circulating T cells were dysfunctional as illustrated by their decreased effector responses ex vivo. Intensity of these injury-induced alterations was maximal at D1 and decreased overtime. The persistence at the end of the first week after injury of profound lymphocyte alterations measured by the decreased CD3D mRNA level was associated with an increased risk of death and an increased risk of secondary infections independently of exposure to invasive devices.

Conclusions: Our results show that the adaptive immune response induced after injury is not dependent on the type of injury and is characterized by major alterations of T cell number and functions that are present from D1 in patients. When persisting, they are associated with deleterious outcomes in accordance with the development of delayed injury-acquired immunodeficiency. Our data support the rational for an immune intervention to restore functional immune response in these patients.

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The Red Flag Sepsis Screening tool and Sepsis Six. defining the New Zealand Red Flag Sepsis population and introducing the change

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**Background:** The Red Flag Sepsis (RFS) Screening Tool and Sepsis Six resuscitation bundle were first introduced in the UK. Although bundle adherence is associated with superior clinical outcomes, concerns have been raised that protocolisation could lead to antibiotic overuse. We collected clinical and microbiologic data whilst implementing the RFS tools at a tertiary academic medical centre in New Zealand.

**Materials/methods:** A whole-of-system multi-disciplinary quality improvement initiative (the "Sepsis Ready Program") was launched in August 2018. Impact on time to delivery of each bundle component was assessed through retrospective chart review targeting randomly selected adult, non-palliative, sepsis patients identified using a published coding algorithm. Clinical, demographic and microbiological information were collected to describe the key features of RFS.

**Results:** Bundle adherence (excluding urine output measurement) was assessed preintervention and at two time periods post-intervention. Adherence increased from 50% at baseline (n=40) to 76% post intervention (n=42) and was maintained at 65% in the final period (n=43). The time to administration of bolus fluid improved from a median of 50mins (IQR 15-85) at base-line to 15mins (IQR 0-25). Median time to first doctor review reduced from 35mins (IQR 4-74mins) to 15mins (IQR 0-35mins).

224 pathway-eligible patients with at least one red flag were reviewed. Māori were over-represented in the 15-64 year age group and under-represented in older age groups. 164 patients [73%] had two or more Red Flags. 53 [24%] died within 30 days and of these, 11 [21%] died within the first 24 hours. At least one set of blood cultures were submitted in 199 cases, of which 91 cases [46%] were demonstrated to have significant bacteraemia. Predominant organisms were *Escherichia coli* (32.6%), β haemolytic streptococci (22%), and *Staphylococcus aureus* [including MRSA] (10%).

**Conclusions:** This study supports the use of the RFS Screening Tool to target urgent intervention to patients with a high probability of bacteraemia and poor outcomes. A multidisciplinary approach to sepsis education and awareness based around the concept of Red Flag Sepsis is associated with improvements in the administration of sepsis care. Frequent sepsis presentations amongst Māori demonstrates health inequity in New Zealand.

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Outcomes of candidaemia caused by biofilm-forming isolates in haematological patients
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Background: The goal of this study was to evaluate the etiology, risk factors, outcome of candidemia caused by biofilm-forming Candida (BFC) spp.

Materials/methods: The prospective study was conducted in 2006-2017. Only the first episode of candidemia was included. Mortality was estimated within 30 day of the onset of candidemia.

Results: A total of 75 patients with candidemia were enrolled, of them 34 (45%) were infected by BFC isolates (C.krusei-24%, C.tropicalis-21%, C.parapsilosis-18%, C.albicans-14%, C.lusitaniae-9%, C.guilliermondii-6%, C.pelliculosa-6%, C.kefyr-3%) and 41 (55%) non-BFC isolates (C.albicans-51%, C.parapsilosis-22%, C.guilliermondii-15%, C.tropicalis-5%, C.glabrata-5%, C.krusei-2%). Overall, biofilm production was most frequently observed for C.krusei (24% vs 2%, p=0.01), C.tropicalis (21% vs 5%, p=0.04), more young patients (42 years vs 50 years, p=0.04). Biofilm production by C.albicans was less frequent (14% vs 51%, p=0.001).

The 34 patients with BFC were more likely to have candidemia caused by Candida non-albicans than 41 patients with non-BFC (85% vs 49%, OR 6.09, p=0.001), persistence of Candida spp in blood (44% vs 15%, OR 5.47, p=0.01), septic shock (44% vs 29%, OR 1.91, p=0.03). Other characteristics were comparable. Central venous catheter (CVC) had 97% patients in each group. For treatment of candidemia with BFC and non-BFC were administered echinocandins 47% and 37%, azoles 9% and 19%, amphotericin B 20% and 34%, accordingly. Antifungal therapy was not used in 2 (6%) patients with BFC and in 4 (10%) patients with non-BFC.

The 30 days survival was lower in patients with candidemia caused by BFC than non-BFC (49.5% vs 62.3%, p=0.2) (Fig.a). Survival was comparable in patients treated by echinocandins (74%) (Fig.b) and differed in amphotericin B therapy. All patients with BFC treated with amphotericin B died (Fig.c). Cure rates were higher in patients with BFC treated by echinocandin as 1st line therapy (81% vs 28%, p=0.002) and CVC has been removed (62% vs 0%, p=0.01).

Conclusions: Candidemia caused by BFC is associated with Candida non-albicans, persistence in blood, septic shock and with increased mortality especially in patients treated with amphotericin B. Better outcomes were seen for patients with BFC who received echinocandin therapy and CVC has been removed.

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Abstract 6226

Investigation of Candida parapsilosis outbreaks by microsatellite genotyping and emergence of clonal antifungal drug-resistant strains in a multi-centre surveillance in China

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Background: Candida parapsilosis is an important species causing invasive candidiasis in China. Our study aims to conduct a national multicenter study of the molecular epidemiology and susceptibility profiles of C. parapsilosis.

Materials/methods: Non-duplicate C. parapsilosis isolates were collected from 10 hospitals across China in the CHIF-NET program 2016-17. C. parapsilosis isolates were genotyped using four highly polymorphic microsatellite markers, and susceptibility profiles were determined using Sensititre YeastOne™ Y010.

Results: A total of 319 C. parapsilosis from separate patients with invasive candidiasis were studied; 49.2%, 33.2%, and 10.3% isolates were from patients in surgical departments, intensive care units (ICUs) and neonatal ICUs, respectively. C. parapsilosis showed good susceptibility to nine antifungals. Microsatellite analysis identified 122 microsatellite (MT) types for 319 isolates. There were four major MT types prevalent in three hospitals: MT48, MT95, MT29, and MT42. There were four MT types (84 isolates) involved in outbreak in hospital H01 and one MT type (38 isolates) prevalent in hospital H10, mainly affecting surgical departments and ICUs. MT42 was prevalent in hospital H06 (all 22 patients were from NICU). Of 16 fluconazole-resistant isolates, seven from hospital H02 shared the same genotype MT70, and three from hospital H04 shared genotype MT47. For 37 5-flucytosine non-WT isolates, 29 isolates from hospital H01 hospital were of genotype MT48.

Conclusions: The present study, the first to conduct a nationwide molecular epidemiology study of C. parapsilosis in China, identified several unrecognized outbreak cases including antifungal resistant isolates. The findings provided important data for Candida infection control in China.

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Prevalence of virulence factors in colonising and infecting Klebsiella pneumoniae isolates obtained from a German multi-centre surveillance study

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Background: Virulence enables Klebsiella pneumoniae (Kpn) to overcome physical and chemical barriers, and evade host defenses. Cases of hypervirulent strains causing severe infections have been reported [1]. The objective of this study was to compare the prevalence of virulence factors in third-generation cephalosporin-resistant (3GCR) and carbapenem-resistant (CR) Kpn isolated from rectal swabs of patients obtained on hospital admission and from those with bloodstream infections (BSI) in Germany.

Materials/methods: Isolates were obtained from rectal swabs upon hospital admission (n=71), or from BSI (n=64) between 2016 and 2018 from 6 German university hospitals and selected using chromID ESBL (bioMérieux) and MAST CHROMAgar mSuperCARBA (Mast Diagnostica). Whole-genome sequencing was performed by Illumina MiSeq. Assembled genomes were used for MLST to identify sequence types (ST) associated with high-risk clones (HiR). Genes encoding for virulence factors; type I fimbriae (adherence), type 3 fimbriae (biofilm formation), siderophores (iron acquisition), and colibactin (toxin) were identified using BacWGSTdb [2]. Capsular locus types (KL) were assigned using Kaptive Web [3].

Results: We identified 54 KL-types, which varied between colonizing and invasive isolates. In both cohorts KL107 was the most prevalent and was mainly associated with HiR ST307 and ST17. KL2, which is common in hypervirulent isolates, was often found in isolates belonging to HiR ST14. The same pattern of virulence factors like type I fimbriae and type 3 fimbriae was found in colonizing and BSI isolates. Colibactin encoding genes were only detected in two colonizing isolates. The hypervirulence associated capsular polysaccharide synthesis activator rmpA was found in a single BSI isolate, which further harboured genes coding for the siderophore aerobactin and belonged to HiR ST17.

Conclusions: In this study, we found that KL107 was the most common capsular type and correlated with HiR. However, KL-types were diverse in colonizing and BSI isolates. In terms of virulence factors contributing to adherence, biofilm formation, iron acquisition and toxins, there was no difference between colonising and infecting isolates. In conclusion, our results indicate that hypervirulent genotypes are rare among these German K. pneumoniae clinical isolates.


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Abstract 6229

**Antimicrobial susceptibility of medically important Nocardia species in Korea**

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**Background:** *Nocardia* species is the most commonly recognized human pathogen of aerobic actinomycetes which are ubiquitous in the environment. There are often geographic differences in epidemiology and antimicrobial susceptibility by *Nocardia* species. This study first investigated species distribution and antimicrobial susceptibilities of medically important *Nocardia* species in Korea.

**Materials/methods:** From 2008 to 2019, clinical isolates of *Nocardia* species were consecutively collected in Asan Medical Center. Species identification was confirmed by 16S rRNA gene PCR sequencing and antimicrobial susceptibility was determined by Sensititre RAPMYCOI Plate (Thermo Scientific, Waltham, MA).

**Results:** A total of 43 isolates were collected, including 16 *N. farcinica* (37.2%), 11 *N. cyriacigeorgica* (25.6%), 3 *N. brasiliensis*, 3 *N. kroppenstedtii*, 3 *N. nova*, 2 *N. abscessus*, and 1 *N. concava*, *N. elegans*, *N. exalbida*, *N. pseudobrasiliensis* and *N. puris* respectively. While only one *N. farcinica* isolates had minimum inhibitory concentration (MIC) to trimethoprim-sulfamethoxazole of 4 μg/mL and five *N. farcinica* and all *N. kroppenstedtii* isolates had MIC of 2 μg/mL, all isolates of other than *N. farcinica* and *N. kroppenstedtii* had MIC of lower than 1 μg/mL. All *Nocardia* species were susceptible to amikacin and linezolid but frequently resistant to clarithromycin, doxycycline and minocycline, whereas *N. nova* and *N. pseudobrasiliensis* isolates were consistently susceptible to clarithromycin. A half of *N. farcinica* and all *N. kroppenstedtii* isolates were susceptible to fluoroquinolone but the other *Nocardia* species were resistant to ciprofloxacin. All *Nocardia* species except *N. abscessus* and *N. puris* showed various susceptibilities to β-lactams.

**Conclusions:** In Korea, *N. cyriacigeorgica* and *N. kroppenstedtii* are more prevalent than western countries. High prevalence of sulfonamide resistance-prone species, *N. farcinica* and *N. kroppenstedtii* raised the issue of species identification and antimicrobial susceptibility testing for all clinically relevant isolates.

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Abstract 6230

**Characterisation of the human gut microbiome in a high antibiotic use and resistance setting in Vietnam**

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**Background:** Repeated exposure to antibiotics may drive the microbiome into a steady-state that is different from the original one, particularly in a high antibiotic use and resistance setting like Vietnam. Here, we studied the microbiome and resistome in relation to recent antibiotic use and we compared the results with a low use and resistance Dutch cohort.

**Materials/methods:** We characterised the microbiome from 102 participants using 16S rRNA amplicon sequencing and obtained their antibiotic use history. We used Qiime2 and vegan R package to compare the diversity and differential abundance in a gradient of antibiotic exposure (<1 month, 1-4 months, and >4 months of no exposure) and in the presence of three ESBL genes (CTX-M-1, 2 and 9), assessed metagenomically.

**Results:** Among 102 participants 40 had used antibiotics, mostly cephalosporins (n=39), at least once in the past 4 months and 78% carried ESBL genes. Overall, we found a reduced richness and diversity when compared to a Dutch cohort in a low use and resistance background. Within the group of Vietnamese participants who used antibiotics, we observed a significantly reduced species richness (Chao1, p<0.05), but not diversity (Shannon). The microbiota, as measured using Bray-Curtis dissimilarity, were partially shaped by age group, antibiotic exposure, and the presence of ESBL genes [adonis2, total R² of 11%, p-values < 0.05]. In particular, we found a decrease in the abundance of Lachnospiraceae spp. among antibiotic users (ANCOM, W=168) and a higher abundance of the class of Bacillales and the Enterobacteriaceae family in CTX-M-2 carriers (n=18 vs 84, ANCOM, W=23 and W=395, respectively), but no different abundance across compositions with and without mcr-1 (n=84 vs 18).

**Conclusions:** We characterized the human gut microbiome in a rural community in Vietnam where antibiotic use and resistance are high. A reduced overall diversity and richness was observed compared to a low use and resistance setting, while richness was further reduced among antibiotic users. These perturbations may be caused by the high background use of antibiotics.

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Screening research of antibacterial potential of selected released-active forms of antibodies

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Background: Products based on released-active forms of antibodies (RAF Abs) are a fundamentally new approach to treating a number of diseases. Their safety and efficacy are supported by preclinical and clinical data making them an attractive tool for further application. A growing resistance of bacterial strains is one of the most important medical problems worldwide. Considerable attention in this field is devoted to the products whose mechanism of action is aimed at enhancing host immunity. Thus, the purpose of the study was to conduct screening research and examine antibacterial properties of several RAF Abs targeted at a variety of molecules involved in the host immune response to bacteria.

Materials/methods: Nonlethal infection with Neisseria meningitidis A-208 was chosen as a screening model. Before infection, outbred mice (n=10/group) were randomised for treatment with the test samples (11 groups) or distilled water used as a control. The examined substances targeted at either host immune molecules (RAF Abs to MHC II, AIM2, TRL7, etc.) or pathogen (RAF Abs to beta-lactamase, VacA, etc.) were given 5 days before and 10 days after infection via drinking bowls in a 1:1 ratio. The survival rate was recorded during 10 days after contamination; colony-forming units (CFU) circulating in blood were assessed in acute phase, 24h after bacterial challenge.

Results: Administration of RAF Abs to MHC class II resulted in a statistically significant reduction in bacterial load compared to the control group. Survival rate for this group and a group of the animals treated with water equaled 100%. However, as for the other tested substances, mortality was still observed. Nevertheless, our findings indicate that eight molecules were ineffective, one possessed a moderate activity and the other two were the most effective ones suggesting their protective role in disease progression.

Conclusions: The study results have shown that out of all tested substances RAF Abs to MHC class II was the most efficient and thus seems to be a worthy candidate for further preclinical investigation as antibacterial agents. However, additional experiments are essential to validate this proposal.

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Evolutionary insights into carbapenem-resistant and sensitive Acinetobacter baumannii isolates from India

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Background: Carbapenem resistance Acinetobacter baumannii is a major nosocomial pathogen which is widely studied at the global level. However, comprehensive whole genome investigation of A. baumannii from India is lacking. Prevalence of carbapenemases, their allelic diversity in context of genome diversity amongst carbapenem resistant/sensitive A. baumannii (CRAB/CSAB) will be of utmost evolutionary importance. Since, India have highest usage of antimicrobials and heavy patient load, allelic variations of these beta-lactamases will be significant. In the present study, we carried out whole genome comparative studies of CRAB/CSAB isolates.

Materials/methods: Thirty A. baumannii isolates (one isolate per patient) were collected from blood, body fluid or CSF during 2013 to 2016 in Indian tertiary care unit. Carbapenem sensitivity for imipenem, meropenem and doripenem was performed by Kirby Bauer Disk diffusion method. Whole genome sequencing was carried out using Illumina MiSeq platform with pair-end sequencing. Reads were error corrected and assembled using SPAdes v3.13.0 and annotated using NCBI-PGAP pipeline. Multilocus sequence typing (MLST) was performed using PubMLST database (https://pubmlst.org/). Resistome of the strains was fetched by ABRicate v0.9.8 (https://github.com/tseemann/abricate).

Results: Out of thirty isolates, twelve were CSAB and remaining eighteen were CRAB. Clonal complexes and sequence types were confirmed with whole genome level recombination analysis. Interestingly, 10/18 CRABs were forming a distinct clonal complex with one of the CSABs as its closest ancestor. At the same time significantly enriched and differential resistome was found for CRAB/CSAB isolates. Among carbapenemases, class C and D were present in all the CRAB/CSAB isolates while, class A and B carbapenemases were present only in CRAB. Three out of four groups of class D, blaOXA-51 family, blaOXA-23 and blaOXA-58 were present in CRAB/CSAB. Genomic investigation of carbapenemase alleles reveals multiple novel allele amongst the set of isolates. Further, resistome of CRABs was enriched for sulfonamide and aminoglycoside resistance. Comparative genomic analysis of these isolates to investigate genomic differences and correlations among CRAB/CSAB is being analysed.

Conclusions: Systematic genome wide association studies are allowing us to uncover critical knowledge related to emergence, evolution and spread of CRAB/CSAB isolates both at regional and global level.

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Phenotypic susceptibility testing for vancomycin-resistant enterococci in less than 4 hours using the flow cytometry-assisted susceptibility test

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Background: Enterococci are commensal flora of the gastro-intestinal tract. The rise of vancomycin resistance has increased the necessity for rapid vancomycin susceptibility testing for nosocomial infections caused by enterococci. The intrinsic ability of enterococci to acquire and/or evolve new forms of vancomycin resistance underscores the need for phenotypic testing. We present the use of the Flow Cytometry-Assisted Susceptibility Test (FAST) to rapidly assess antimicrobial susceptibility in enterococci.

Materials/methods: 21 Enterococcus faecalis and 5 E. faecium were tested by FAST and broth microdilution (BMD) against 18 antimicrobials using Sensititre™ GPN3F plates. Isolates deliberately represented a diverse range of vancomycin MICs, including two PCR-confirmed vanA positive and 3 vanB positive isolates. Three colonies from blood agar purity plates were inoculated into trypticase soya broth overnight. Bacterial suspensions were standardised to 0.5 McFarland using a Sensititre™ nephelometer and inoculated into paired Sensititre™ plates using a Sensititre™ auto-inoculator module. Both plates were incubated at 35°C. One plate was incubated for 18-24 h followed by visual recording of MIC results. The other plate was incubated for 3 hours after which well contents were diluted 1:4 with a staining buffer containing 5 µM SYTO® 9 and read using an Attune™ NxT flow cytometer with an autosampler. Data were analysed using bespoke software to predict MIC and susceptibility in ≤ 4 hours from antimicrobial plate inoculation.

Results: Across all 18 drugs tested, there was 95.34% essential agreement between FAST and BMD. There was 98.40% categoric agreement for the 8 agents with breakpoints. Three minor errors were reported for quinupristin/dalfopristin. For vancomycin, all vanA and vanB isolates were reported as resistant. Remaining isolates were reported as susceptible with one exception: a single isolate of E. faecalis demonstrated a vancomycin MIC > 128 mg/L [both by FAST and BMD across multiple replicates]. Investigative molecular testing found no known vancomycin resistance mechanisms in this isolate.

Conclusions: FAST can provide phenotypic AST results for enterococci in ≤ 4 hours with excellent accuracy. The correct prediction of MIC and susceptibility for the vancomycin-resistant E. faecalis isolate with no known resistance mechanism underscores the need for phenotypic AST to capture all resistant isolates.

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**Abstract 6236**

**Characterisation of vaginal microbiota in pregnant women with preterm prelabor rupture of the foetal membranes**

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**Background:** Preterm prelabor rupture of the fetal membranes (PPROM) is a leading cause of preterm birth and is associated with high morbi-mortality. Vaginal dysbiosis can cause PPROM by activation of the local immune system. Moreover, one third of PPROM cases are associated with microbial invasion of the amniotic cavity (MIAC) and/or intraamniotic inflammation. The purpose of this study was to characterize and compare the vaginal microbiome in patients with PPROM with and without MIAC.

**Materials/methods:** One hundred pregnant women with PPROM were included and categorized into 2 groups according to amniotic fluid (AF) analysis: patients with MIAC [positive amniotic fluid culture and/or detection of microbial 16S ribosomal RNA] and Non-MIAC group. The AF concentration of IL-6 was assessed by enzyme-linked immunoassay (Biosource; Invitrogen, Carlsbad, CA). Vaginal swabs from these patients were collected. DNA was extracted (PureLink™ Microbiome, Invitrogen) and a 16S rRNA sequencing library was constructed (Nextera XT, Illumina) targeting the V3 and V4 hypervariable regions. Sequencing was performed on a MiSeq platform. Bioinformatics and statistical analyses were performed using QIIME2 and R version 3.4.2 software.

**Results:** A total of 28 women presented MIAC, being *Ureaplasma* spp. the microorganism most frequently isolated (N=15). We did not find significant differences regarding alpha-diversity between groups. The compositional analysis at the genus level, revealed that *Atopobium* spp., *Gardnerella* spp., *Streptococcus* spp., and *Ureaplasma* spp. were overrepresented in the MIAC group, whereas *Lactobacillus* spp. were underrepresented (Fig 1). A low-rank approximation analysis (biplot) revealed that the family Lactobacillaceae was associated with gestational age and was inversely related with microbial diversity (Faith PD), presence of inflammation [IL-6], presence of MIAC, and relative abundance of the family Mycoplasmataceae [which includes *Ureaplasma* spp].

**Conclusions:** Changes in the vaginal microbiota correlate with clinical and biological phenotypes and may provide new insights into the pathophysiology of PPROM. Further studies will be required to establish the potential role of the vaginal microbiome to predict the outcome in patients with PPROM.

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**Figure 1. Differences in genus relative abundance between MIAC and Non-MIAC group.**

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Stable mutants and persisters variants are involved in heteroresistance to colistin in wild-type *Klebsiella pneumoniae* of clinical origin

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**Background:** Heteroresistance (HR) can be defined as the presence of bacterial subpopulations with various susceptibilities to an antibiotic within an isolate. This can be related to the emergence of persisters (organisms can survive the lethal action of antibiotics without a minimum inhibitory concentration [MIC] change) or the selection of stable mutants (stable increment of MIC). The objective of this study is to evaluate if clinical isolates of *K. pneumoniae* with a wild-type (Wt) phenotype (resistant only to aminopenicillins; susceptible to colistin), express HR to colistin.

**Materials/methods:** Ten Wt clinical strains isolated from different patients were evaluated. MICs of colistin were determined by standardized broth microdilution (BMD; CLSI-EUCAST). The activity of colistin was also tested with gradient strips, using different inocula \(10^8\) and \(10^{10}\) UFC/mL, incubating plates at 35 °C for 7 days to evaluate the emergence of colonies within the inhibition zone. The minimum bactericidal concentration (MBC) was determined by subculturing supra-MIC wells in BMD on colistin-free agar plates. Colistin HR was determined by population-analysis-profiling (PAP), performing bacterial counts on media with increasing concentrations of colistin (up to 64 mg/L). Up to 8 colonies were selected from PAP plates; bacteria were subcultured twice in antibiotic-free medium and BMD were again subsequently performed.

**Results:** All isolates were susceptible (BMD) to colistin (MICs: 0.125 and 0.25 mg/L). MBC values were one dilution step higher than the MIC. MICs of colistin with gradient strips ranged 0.094 to 0.125 mg/L \(10^8\) and 0.094 to 0.25 mg/L \(10^{10}\). No colonies observed in the inhibition zones in any isolate. PAP indicated that all strains contained colistin-heteroresistant subpopulations with colonies growing up to 32 (1 isolate) or 64 mg/L (9 isolates). In all isolates, the organisms growing in supra-MICs were stable mutants (MIC: 16-128 mg/L). Additionally, in 6 of the 10 isolates some colonies from plates containing only 1-2 mg/L of colistin were persisters.

**Conclusions:** Wt *K. pneumoniae* contain colistin heteroresistant subpopulations. HR is more frequently related to the selection of stable mutants, but it is also related to the emergence of persisters at low supra-MIC of colistin.

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Evidence of high prevalence, transmission rate and persistence of *Escherichia coli* ST131-Rx among residents of nursing homes in south Spain (JPI-ST131TS project)

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**Background:** A sublineage of the *E. coli* ST131 clone, which carries mutations in *gyrA* and *parC* (subclone H30-R), has been found as a dominant ExPEC strain. Our aim was to study the prevalence of this lineage and transmission dynamics among nursing home (NH) residents.

**Materials/methods:** Rectal swabs were collected from 2 NH, A and B (55 individuals in NH-A and 31 in NH-B) in Sevilla during 10-month-period (two 3-month cohorts with a 4-month separation-period). Eight samples (S1-S8) per individual were taken (baseline and 1, 4 and 12 weeks later in each cohort). Sampling of sinks and bathroom surfaces were also carried out. Bath sharing among residents was 100% and 45% (14/31) in NH-A and NH-B, respectively. Samples were inoculated on UTI-agar (Oxoid®) with 2 mg/L ciprofloxacin after a a enrichment step. Up to three morphologically different colonies of *E. coli* were selected per plate for ST131 screening by PCR. Isolates with <2 bands of difference with *XbaI*-PFGE were considered the same pulsotype.

**Results:** Fifty (58%) individuals were found to be colonized by ST131 FQR at any time: 28 (33%) at S1, 28 (33%) at S2, 24 (28%) at S3, 28 (33%) at S4, 21 (24%) at S5, 21 (24%) at S6, 13 (15%) at S7 and 9 (10%) at S8. Twenty-two negative individuals (26%) became colonized and 12 (24%) positive individuals acquired a new pulsotype at any time of study. Among the positives individuals, 4 (5%) were colonized by the same pulsotype during the 10-month study period, and 13 (23%) during the first 3-month cohort. Eight clusters in NH-A (79% of positive cases) and 7 in NH-B (88% of positive cases) were identified. At least two of the individuals from each cluster share the same bathroom in 6/8 clusters in NH-A and 1/7 clusters in NH-B. Twenty-two (15%) environmental samples (6 NH-A and 16 NH-B) were positive, and 15 (68%) isolates were identical to those of residents.

**Conclusions:** 1) Half of nursing homes residents in our area were found colonised by ST131 FQR *E. coli*. 2) A third remained colonized during the first 3-month period. 3) Bathroom-sharing seems to be a risk factor for cross-transmission among residents.

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Abstract 6241

Application of logistic regression model in the identification of potential HIV-1 drug resistance-associated mutations

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Background: Many software has been applied to predict HIV-1 drug resistance by detection of major drug-resistance associated genetic mutations, defined by in vivo clinical observation and in vitro cell culture-based experiments. In this study, the logistic regression model was designed to detect the presence of amino acid mutations which might not be recognized as major mutations, but its presence is significantly associated with drug resistance.

Materials/methods: A total of 6214 RT sequences (aa 1-250), 6200 protease sequences (aa 1-99), and 2563 integrase sequences (aa 1-288) from HIV-1 infected patients recruited at National Taiwan University Hospital between 2008 and 2019 were analyzed. Each sequence was encoded to a binary vector of corresponding features (independent variables in regression) where the corresponding a.a. is mutated or not compared with the HXB2 reference. The resistance level of the sequence (dependent variable) was labeled as 0, susceptible or potential low-level, and 1, low to high-level, based on the Stanford drug-resistance database regarding to protease inhibitors (PI), nucleoside RT Inhibitors (NRTI), or non-nucleoside RT inhibitors (nNRTI) and integrase inhibitors (INSTI). The logistic regression model is implemented by Python 3.6 scikit-learn package.

Results: After each logistic regression model fitting by thousands of samples in this study, we narrowed down the resistance-associated amino acid residues about ten. The amino acid residues and their related p values. For NRTI, all of the eight amino acid mutations were defined as the major mutations by the Stanford database, while for nNRTI and INSTI, only five and six of eight and eleven were the previously defined major mutations. For PI, only one of eight was not in previously defined major mutations. Nevertheless, the regression models generated great accuracy ranging from 0.64 to 0.94, in prediction of drug resistance as compared with the Stanford database.

Conclusions: The regression methods gave great prediction of drug resistance. It can identify the major mutations and also implicate the potential association of novel non-polymorphic mutations which have not been addressed before. The interaction between the major mutations and these non-polymorphic mutations will be investigated by further modeling analysis and in vitro characterization.

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Abstract 6243

The frequency and clinical implications of Epstein-Barr virus DNA in the cerebrospinal fluid of immunocompetent and immunodeficient patients diagnosed with meningoencephalitis

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Background: The role of Epstein-Barr (EBV) virus in central nervous system (CNS) infections and the clinical significance of EBV-DNA in the cerebrospinal fluid (CSF) are not fully understood. The aim of this study was to investigate clinical implications of positive CSF EBV-DNA PCR results in the context of the patients’ final diagnosis.

Materials/methods: From January 2008 to October 2019, a total of 54 CSF samples from 37 patients were positive for EBV DNA (of 646 samples tested). Clinical and laboratory data extracted from patient’s medical records were available for 31 patients that were included in our cohort. Data are presented as frequencies (%) and medians with interquartile ranges (IQR).

Results: Of the 31 patients included, 12 had advanced HIV infection (11 males, age 43.5, IQR 35-48.7 years) with low CD4+ counts (23, IQR 27-49) and HIV viral load of 372,500 (IQR 125,794-829,250 copies/mL). Clinical diagnoses in HIV-infected patients included: biopsy-proven primary CNS lymphoma (PCNSL, n=4; EBV DNA of 99,325 copies/mL, IQR 7,112-201,125), toxoplasmosis (n=3, including 1 suspected PCNSL; EBV DNA 226,500 copies/mL, IQR 174,750-226,500), cryptococcal meningitis (n=1), tuberculous meningitis (n=2) and 2 patients with HIV-encephalopathy (including 1 patient with CMV coinfection).

HIV-negative patient group included 4 children (2 with acute EBV infection and ME, 1 with entroviral ME and 1 with chronic EBV infection) and 15 adults (11 males; age 51, IQR 37-67). Of two solid-organ transplant recipients, one had invasive CNS aspergillosis (EBV DNA 5,700 copies/mL) and other EBV reactivation (EBV DNA 402,000 copies/mL). Among the remaining 13 immunocompetent adults, viral etiology was diagnosed in 5 (HSV-1=2, VZV=2, enterovirus=1), postinfectious ME in 3, neurotuberculosis in 1, PCNSL in 1 (EBV DNA 186,500 copies/mL). In 3 patients etiology remained unknown. Patients with viral ME had lower CSF EBV DNA (7,550 copies/mL, IQR 6550-8900) than patients with postinfectious ME (15,050 copies/mL, IQR 10675-21025) or unknown etiology (19,025 copies/mL, IQR 12712-254750).

Conclusions: While detection of EBV is associated with PCNLS and toxoplasmosis in HIV+ patients, in immunocompetent adults it is frequently associated with other infectious agents or postinfectious syndrome.

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A systems thinking methodology for evaluating interventions to optimise antibiotic use along the surgical pathway and minimise AMR

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Background: The integration of Antimicrobial stewardship (AMS) across the surgical pathway can optimize antimicrobial use for managing infectious complications like Surgical Site Infections (SSI) and thereby reduce Antimicrobial Resistance (AMR). Systems thinking (ST) is a holistic novel approach that accounts for health system behavior and utilizes quantitative as well as qualitative data to model the integration of AMS and interventions to reduce AMR. ST methodology utilizes system dynamic (SD) tool, a resource efficient method that can evaluate prospective interventions and assess the impact on incidence of performance indicators.

Materials/methods: Clinical and operational information on managing post-surgical infectious complications were collected. The ’cause-effect links’ generated using ST methodology that incorporate prospective interventions and elements of AMS influencing performance indicators would be converted into a quantitative SD model. Cultural and contextual factors would be integrated into the model as part of wider research inputs from ethnographic observations on antimicrobial prescriptions along surgical pathway and macrolevel policy analysis. The simulation of the model at the base line level and post inclusion of specific interventions would enable comparison of the effect on SSI and other performance indicators.

Results: The patient flow along surgical pathway was initially developed by mapping the requisite procedures, medical investigations, administrative requirements and relevant stake holders across the pre-surgical, surgical and post-surgical phases. Interventions selected for simulation are ensuring hand hygiene compliance to reduce SSI and recording right indication for antimicrobial prescription and feedback of audit data as part of AMS. Performance indicators identified to assess the impact of interventions span clinical, operational and economic domains for evaluating both implementation effectiveness and clinical effectiveness.

Conclusions: ST modeling would aid decision makers in optimizing and selecting the best interventions that could prove as effective solutions. ST is a potentially novel application in the field of evaluating interventions across surgical pathway for optimizing antimicrobial use and emerges promising in supporting clinical systems as ST is an evidence based decision making methodology.

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Molecular epidemiology of leptospirosis in Tahiti, French Polynesia, during the 13-year-time spanning from 2007 to 2019

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Background: Leptospirosis, caused by spirochetes of the genus Leptospira, is the zoonosis with the widest global distribution causing more than one million severe cases resulting in 60,000 deaths every year. Rodents have been considered to be the main animal reservoir, however, leptospirosis is ubiquitously present within the animal kingdom. This study describes the molecular epidemiology of leptospirosis in Tahiti, French Polynesia - a hotspot for this disease - in the 13 years-time span from 2007 to 2019.

Materials/methods: We collected in total 418 serum samples from patients diagnosed with leptospirosis at the Centre hospitalier in French Polynesia. Using a combination of traditional and nested PCR followed by Sanger sequencing, we determined the sequences for secY locus in 249 serum samples (60%). In addition, 16 Leptospira strains isolated from patient blood were fully characterized at species and serogroup levels and used as references for the association of different phylogenetic branches with respective serogroups. The secY sequences were compared with sequences from wild rats, farm pigs and domestic dogs from a previous study in French Polynesia (Guernier et al. 2017).

Results: The phylogenetic analyses divided our sample set into 18 genotypes clustering into 4 lineages. Lineage 2 (L. weilii associated with serogroup Mini) was found exclusively in human patients. Its source remained unknown. Lineage 3 (L. interrogans associated with serogroup Canicola) was correlated with its co-isolation from human patients and farm pigs (Sus scrofa, p-value=0), while lineage 1 (L. borgpetersenii associated with serogroup Ballum) was correlated with its co-isolation from rats (Rattus exulans and Rattus norvegicus, p-value=0). The most prevalent lineage 4 (L. interrogans) consisted of two central genotypes, 9 (associated with serogroup Icterohaemorrhagiae) and 10 (associated with serogroup Australis). Remarkably, genotype 9 predominated each year (2007-2019). The ability to survive in a wide host range (dogs, rats and pigs) might have facilitated its high prevalence and predominance over the 13 years period.

Conclusions: With this study we shed light on the population dynamics of leptospires circulating among patients in Tahiti during 2007 to 2019 and on the role potential animal reservoirs (pigs, rats and dogs) play in leptospirosis transmission to humans.

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**Abstract 6251**

**Bismethylgliotoxin is detected in serum from oncohaematological neutropaenic paediatric patients: presentation of two cases of probable IPA with negative galactomannan and positive bmGT**

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**Background:** Invasive pulmonary aspergillosis (IPA) is a leading cause of morbidity and mortality in immunocompromised oncohaematology pediatric patients. This is mainly due to the absence of optimal diagnostic modalities, which hamper early specific disease detection and treatment. Thus, diagnosis of IA is still challenging and constitutes a major problem during management of pediatric patients at risk of infection, where the number of studies validating different diagnosis biomarkers is more limited. In a previous study, we demonstrated the high diagnostic accuracy of bis(methyl)gliotoxin (bmGT) compared to GM for IPA diagnosis in adults. The objective of this study is to show bmGT suitability for IPA diagnosis in oncopediatric patients in comparison with GM, monitoring the course of bmGT concentration in serum during voriconazole treatment.

**Materials/methods:** The presence and concentration of bmGT and voriconazole in sequential serum series from 9 oncopediatric patients with febrile neutropenia (retrospective and prospective samples) were simultaneously quantified by High Performance Thin Layer Chromatography (HPTLC) and confirmed using LC/MS/MS by an independent lab.

**Results:** HPTLC allowed simultaneous sensitive detection of bmGT and voriconazole in serum and BAL of pediatric patients confirmed by LC/MS/MS. We present two patients [17 and 36 months]. In the phase of prolonged neutropenia, fever, hypoxemia and pulmonary infiltration compatible with Aspergillosis in high resolution CT are started. In one patient, bmGT was detected earlier than GM, allowing early initiation of treatment, with the voriconazole treatment the GM was negativized and the bmGT levels decreased. In the second patient, GM was negative and bmGT positive in serum and BAL, so treatment with voriconazole was started, then a decrease in bmGT values was detected coinciding with the patient clinical improvement.

**Conclusions:** The determination of bmGT in pediatric patients allowed the early diagnosis and effective treatment of two cases of IA, being a promising tool in neutropenic pediatric patients at risk of IPA. Identification of bmGT by HPTLC has been confirmed by LC/MS/MS indicating the presence of this biomarker during IPA in pediatric population. Analyses to establish the performance of serum bmGT detection together with beta-d-Glucan, PCR and IL8 to diagnose IPA in pediatric oncohaematological patients are ongoing.

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Abstract 6254

**Early empirical anidulafungin therapy reduces the prevalence of invasive candidiasis in critically ill sepsis patients: a retrospective study**

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**Background:** Invasive candidiasis (IC) in critically ill patients is a serious infection with high rate of mortality. Like empirical antibiotics, the use of antifungals empirically is not common in intensive care units (ICUs). The practice of anidulafungin empirically in critically ill patients is very limited worldwide. The objective of this study was to evaluate the clinical outcomes of empirical anidulafungin therapy in critically ill ICU patients with sepsis and/or septic shock.

**Materials/methods:** This retrospective case-control study was conducted on 149 (N) sepsis/septic shock ICU patients. The patients of 'empirical anidulafungin therapy (EAT)' group [case] (n = 77) found empirical anidulafungin in early hospitalization hours with standard dose. On the other hand, 'no empirical anidulafungin therapy (NEAT)' group's [control] patients (n = 72) received no empirical antifungal therapy including anidulafungin. The clinical outcome of empirical anidulafungin therapy was evaluated in terms of prevalence rate of IC, mortality rate and ICU leaving rate.

**Results:** Patients in EAT group received empirical anidulafungin and showed less incidences of IC (5.19%, n = 77) than that of NEAT group’s patients (29.17%, n = 72) with the relative risk of 0.175 (95% CI, 0.064-0.493, p value <0.05) and the risk difference (RD) rate was 24% (95% CI, 12.36%-35.58%) among the groups. The 30-day mortality rate in NEAT group was higher (19.44%, n = 72) than that of EAT group (10.39%, n = 77) (p value = 0.04). Within the first 10-ICU-days, patients in EAT group left ICU in higher rate (62.34%, n = 77) than that of NEAT group (54.17%, n = 72).

**Conclusions:** IC in critically ill patients is a life-threatening event. Sepsis patients with early empirical anidulafungin therapy showed better clinical outcome, lower mortality rate and higher ICU leaving rate within the first 10-ICU-days than the sepsis patients received no anidulafungin therapy empirically.

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Prevalence and antibiotic resistance of ESKAPE pathogens isolated in the emergency department of a tertiary care teaching hospital in Hungary: a 5-year retrospective survey

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Abstract

Background: Emergency departments (EDs) have a central role in the triage and early management of patients with potentially severe bacterial infections. ESKAPE pathogens are one of the key contributors to multidrug resistance and excess mortality worldwide. The purpose of this study was to characterize the epidemiology and susceptibility patterns of ESKAPE bacteria isolated in an ED of a tertiary-care teaching hospital in Hungary over a 5-year period.

Materials/methods: Data collection was carried out retrospectively by reviewing the microbiology record database of the Department of Clinical Microbiology (University of Szeged), corresponding to ESKAPE isolates. Only the first isolate per ED patient was analysed during the designated study period (2014.07.01-2019.07.01.). Bacterial identification was performed using MALDI-TOF MS (Bruker Daltonics). Antibiotic susceptibility-testing, phenotypic detection of resistance mechanisms and interpretation of drug resistance (MDR/XDR) categories were based on ESCMID/EUCAST standards. The classification of Gram-negative isolates into usual drug resistance (UDR) and difficult-to-treat resistance (DTR) categories were based on the criteria defined by Kadri et al.

Results: During the study period, the number of ED admissions was 39,146±477/year. Out of the 7681 individual isolates, 67.2% (n=5161) were ESKAPE bacteria. Most of the isolates originated from urine specimens [catheter-specimen: 30.6%, midstream: 15.0%], blood cultures (29.0%), wound samples (13.1%) and abscesses (4.2%). The distribution of ESKAPE bacteria and their classification into resistance categories is presented in Table 1.

Table 1. Prevalence and resistance characteristics of ESKAPE bacteria during study period

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Prevalence among ESKAPE (%)</th>
<th>UDR</th>
<th>MDR (%)</th>
<th>XDR</th>
<th>DTR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococcus spp.</td>
<td>9.2%</td>
<td>-</td>
<td>3.9%; VRE: 2.3%</td>
<td>0%</td>
<td>-</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>10.9%</td>
<td>-</td>
<td>19.6%; MRSA: 16.7%</td>
<td>0%</td>
<td>-</td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>1.1%</td>
<td>58.9%</td>
<td>39.2%</td>
<td>19.6%</td>
<td>19.6%</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>3.8%</td>
<td>38.5%</td>
<td>10.9%</td>
<td>4.7%</td>
<td>5.2%</td>
</tr>
<tr>
<td>Enterobacterales</td>
<td>75.0%</td>
<td>75.1%</td>
<td>28.2% [ESBL: 17.3%]</td>
<td>18.0%</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

Conclusions: EDs are essential components of the healthcare system, presenting as gateways for many patients to inpatient units; however, due to the significant flux of patients, they may also have pronounced roles in the emergence and spread of resistant bacterial strains. The number of MDR and XDR Gram-negative isolates (both Enterobacterales and non-fermenters) presents a worrisome therapeutic challenge to clinicians.

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Abstract 6260

An epidemiological description of Panton-Valentine-leukocidin-positive Staphylococcus aureus (PVL-SA) at ambulatory health units of the Rhine-Ruhr metropolitan region in North Rhine-Westphalia, Germany

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Background: Staphylococcus aureus (SA) is known to cause severe skin and soft tissue infections by producing the virulence factor Panton-Valentin-leukocidin (PVL). The prevalence of PVL-positive SA (PVL-SA) isolates differs in geographical regions. We determine the percentage of PVL-SA in skin swabs and analyse epidemiological variables of outpatients with PVL-SA from health centres of the Rhine-Ruhr region in North-Rhine-Westphalia, Germany.

Materials/methods: A retrospective study was performed to analyse the presence of PVL-SA in random skin specimens. We included patients with clinical manifestations in skin with the positive results of SA. Identification and susceptibility testing of SA-isolates were done using the VITEK 2-system (bioMérieux®, France). The presence of PVL was determined by in-house real-time PCR assay according to Pichon et al. [2012] by MVZ Dr. Eberhard & Partner Dortmund, Germany. Demographic and clinical characteristics of the patients were obtained from the patient records.

Results: 8355 SA in clinical samples were identified (5954 Methicillin-sensitive SA (MSSA) and 2401 Methicillin-resistant SA (MRSA)) from January 2017 to September 2019. Of these samples, the detection of PVL-SA was performed in 122 specimens (52.5% abscess swabs, 20.5% skin swabs, 15.6% wound/ ulcer swabs, 7.4% nose/throat swabs and 4% other samples) of 114 patients (36.9% women and 63.1% men). The PVL-SA-PCR was positive in 41.8% of all specimens analysed, which inferred a prevalence of 0.61% of all identified SA, 0.55% in MSSA and 0.75% in MRSA. 78.4% of positive PVL-SA were from men (p<0.05). The highest rate in total of PVL-positive results was detected in patients 16-47 years of age (58.8%). The mean age of the PVL-positive patients was 33 years. Of the swabs 66.7% (p<0.05) were PVL-SA-PCR positive abscesses. These came from mainly the axilla (20.6%), the leg (20.6%) or the head (14.7%).

Conclusions: Our study revealed that men were significant more often infected with PVL-SA. In the Rhine-Ruhr metropolitan region the highest rate of PVL-positive was found in patients 16-47 years of age and especially in swabs taken from abscesses. This analysis highlights sample types which are often PVL-SA positive and thereby informing laboratories on when to perform examination for PVL-SA.

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Abstract 6262

Development of a predictive score for Enterococcus spp. in biliary tract-related bloodstream infections: Results from the PROBAC study


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Abstract third-party references: Supported by Instituto de Salud Carlos III [PI16/01432], On behalf of PROBAC REIPI/GEIH-SEIMC/SAEI group.

Background: Enterococcus spp. represent the third cause of bloodstream infection from a biliary tract source (BT-BSI) following E. coli and Klebsiella spp. Several studies have demonstrated that enterococcal BT-BSI are related to inadequate antimicrobial treatment and worse outcome. Our aim is to investigate risk factors for enterococcal BSI in patient with biliary tract infections.

Materials/methods: PROBAC is a prospective multicentric cohort collecting patients with bloodstream-infection older than 14 years from 26 Spanish hospitals, between October 2016 and April 2017. Patients with BT-BSI were included in this analysis. Bivariate comparisons were done using Chi square or Fisher test for categorical variables and Mann-Whitney for continuous variables; independent predictors were identified by logistic regression. A score was developed, by providing weighted points to each variable; positive and negative predictive values (PPV, NPV) were calculated.

Results: 850 episodes of BT-BSI were included, 73 (8.5%) were due to Enterococcus spp., of which 50 (68%) were due to Enterococcus faecalis and (23) 32% due to Enterococcus faecium; in 51% of the cases, Enterococcus spp. were isolated in polymicrobial infection. In univariate analysis, the factors associated with Enterococcus spp. were [RR (95%CI)]: liver disease [2.23 (1.36-3.62)], moderate-severe chronic kidney disease [1.83 (1.01-3.32)], cancer [1.69 (1.09-2.63)], cholangiocarcinoma [5.35 (2.80-10.20)], immunosuppressive therapy [2.30 (1.29-4.05)], biliary prosthesis [2.23 (1.41-3.52)], hospital acquisition [3.59 (2.35-5.52)], previous surgery [2.35 (1.25-4.42)], upper gastrointestinal tract endoscopic procedure other than esophago-gastroduodenoscopy [1.69 (1.09-2.63)] and previous antimicrobial treatment [2.25 (1.45-3.73)]. By multivariate analysis, the variable associated with Enterococcus spp. were cholangiocarcinoma [5.47 (3.75-18.43)], moderate-severe CKD [2.71 (1.30-5.68)], biliary prosthesis [2.05 (1.11-3.83)] and hospital acquisition [3.57 (2.06-6.19)]. The AUC of the model was 0.73 [95% CI 0.66-0.79]. A score was developed, with 3, 1, 1 and 2 points for these variables, respectively. For a score ≥4, the PPV was 66.7%, and for a score <2, the NPV was 94.7%.

Conclusions: A moderately predictive score for enterococcal aetiology of BT-BSI was developed. A high punctuation in the score may be used to consider empirical coverage against these pathogens in patients with severe presentation of the infection. The score would need to be externally validated.

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Geodes Antibiotiques: restituting French antimicrobial consumption in the ambulatory sector using two indicators and an interactive website

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Background: In France, surveillance of antibiotic consumption in the ambulatory sector started in the early 2000s, based on pharmaceutical sales data. The indicators were expressed in defined daily doses (DDD) per 1000 inhabitants per day, as recommended by WHO. However, they were only available at national level and did not allow stratifying consumptions by age group or place of residence.

Materials/methods: We used data from the National Health Data System [i.e., all reimbursements to outpatients of drugs in the J01 ATC classes] in order to assess antibiotic consumption in the ambulatory sector from 2009 to 2018. We produced two annual indicators: the first one as the number of DDDs and the second one as the number of prescriptions, both expressed per 1 000 inhabitants per day. These indicators were broken down for eight age groups and by region or department.

Results: At national level, although overall antibiotic consumption expressed in number of DDD remained stable over the study period (22.5 DDD per 1 000 inhabitants per day in 2018), the number of prescriptions decreased by 15% (2.81 vs 2.38 per 1 000 inhabitants per day, in 2009 and 2018 respectively). This downward trend was particularly noticeable in children < 5 years old [-31%] but not in the elderly (> 65 years old). A switch of prescriptions from other beta-lactams (including cephalosporins; -54.5%) to broad-spectrum penicillins (including amoxicillin; +28.8%) mainly explains different trends for each indicator, as the DDD for amoxicillin remains lower than doses usually prescribed by French medical doctors. In addition, fluoroquinolone prescriptions decreased by 41.7% over the study period. Last, both indicators [numbers of DDD and prescriptions] reveal important variations in antibiotic consumption by region or department [map].

Conclusions: The prescription indicator is a very useful addition to the number of DDD in order to better monitor and understand antibiotic use in France. Particularly, it highlights trends that suggest changes in specific prescription behaviours. Both indicators are now publicly available through an interactive web site [https://geodes.santepubliquefrance.fr/] for better assessing and guiding antimicrobial stewardship actions.

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Abstract 6264

Preliminary data on initial antimicrobial regimen from a prospective cohort study of sepsis in hospitalised neonates: the NeoOBS study

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Abstract third-party references: on behalf of the NeoOBS Study

Background: NeoOBS is a prospective, multinational, multicentre, observational cohort study of the inpatient management of neonatal sepsis and was set up to collect high-quality observational data to inform future clinical trials. One important aim was to explore which antibiotics are routinely given empirically in neonatal sepsis internationally (standard of care) in order to define the comparators for trials to assess the efficacy of novel antibiotic regimens in areas with high endemic rates of antimicrobial resistance.

Materials/methods: Hospitalised infants aged <60 days [post-natal] with a primary diagnosis of sepsis were enrolled in 19 sites in 11 countries across Asia, Africa, Europe and South America. Antibiotics started within 24h of the blood culture being taken were classified based on coverage; associations with birth-weight, age, central line/indwelling catheter, and time of hospitalisation were estimated using multivariable logistic regression with site-level random effects.

Results: 1760 neonates enrolled between Aug 2018-Aug 2019 with known antimicrobial regimen were included in this analysis. Antibiotic regimens received fell into five broad groups: 1) 1st-line penicillin (mostly ampicillin) in 19% (73% also started gentamicin), 2) 3rd generation cephalosporin (mostly cefotaxime) in 15%, 3) antipseudomonal penicillin/cephalosporin/quinolone with incomplete ESBL coverage (mostly ceftazidime or piperacillin/tazobactam) in 32%, 4) ESBL-covering regimen (mainly meropenem) in 26%, and 5) carbapenem-resistant organism-covering regimen (mainly colistin) in 3% of participants; 4% started another regimen. In group-3, 63% also started amikacin (11.14% in the other groups). Regimen varied considerably between sites (Figure). In sites with at least 10% of neonates starting group-1 or group-2 regimens (8 sites, 828 neonates), these regimens were independently less frequently prescribed in neonates aged ≥7days [OR=0.17 [95% CI 0.11-0.27] p<0.001], with lower birth weight [OR 0.08 [0.03-0.21], 0.18 [0.10-0.32] and 0.44 [0.28-0.67] for birth-weight <1000g, 1000-1500g, ≥1500-2500g versus ≥2500g, respectively, p<0.001], with a central line/indwelling catheter [OR=0.15 [0.04-0.53] p=0.004], and not born in the recruiting hospital [OR=0.45 [0.25-0.78] p=0.005].

Conclusions: Initial antibacterial regimens vary widely across sites, and are associated with important patient characteristics. Further analyses will explore additional factors to better assess the impact of disease severity on choice of empiric regimen.

Figure:

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**Abstract 6267**

**Risk factors for colonisation with multiple species of extended-spectrum beta-lactamase producing Enterobacteriales: a case-case-control study**

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**Background:** Colonization with multiple species of extended-spectrum beta-lactamase producing Enterobacteriales (ESBL-PE) has been reported in up to 11% of carriers. Risk factors for colonization with ESBL-PE have been investigated in several studies, yet further information on patients at risk of colonization with multiple ESBL-PE species is lacking. We therefore investigated risk factors associated with multiple- rather than single-species ESBL-PE colonization.

**Materials/methods:** We performed a retrospective case-case-control study at the University Hospital Basel, Switzerland. Hospitalized patients colonized with multiple species of ESBL-PE between 01/2008 and 12/2018 were included in case group 1. Case group 2 consisted of hospitalized patients with ESBL-PE and an additional ESBL-PE species within a following hospitalization. Controls (i.e. patients with detection of only one species of ESBL-PE within different hospitalizations) were frequency-matched 1:3 to cases of the second group according to the time-period between isolate-dates to standardize duration of colonization. Risk factors differentiating these three groups were determined using conditional logistic regression analyses.

**Results:** 154 cases met eligibility criteria (67 in group 1, 22 in group 2, 65 in group 3). Univariable analysis revealed recent stay abroad (OR1 2.3, 95%CI3.49-43.37, p=0.000), hospitalization abroad (OR2 3.51, 95%CI3.03-182.21, p=0.003) and prior antibiotic exposure within the last three months (OR2.88, 95%CI1.42-5.84, p=0.003) to be associated with carriage of multiple ESBL-PE-species. Recent stay abroad (OR1 2.57, 95%CI3.48-45.45, p=0.000) and prior antibiotic exposure (OR2.96, 95%CI 1.37-6.41, p=0.006) independently predicted multiple species-ESBL-PE-colonization as determined by stepwise backward/forward regression and selection by Akaike information criterion. Admission from another acute-care facility was the only predictor of a shift of ESBL-PE species (OR6.02, 95%CI1.15-31.49, p=0.003) within the same patient. Analyses regarding genetic relatedness of respective strains, plasmids, and ESBL-genes are ongoing.

**Conclusions:** In addition to antibiotic selection pressure, acquisition of specific strains and/or plasmids of ESBL-PE in settings with differing ESBL-epidemiology may be associated with an increased likelihood of co-colonization with ESBL-PE, either by transmission of ESBL-encoding plasmids to colonizing non-ESBL-PE or by direct acquisition of multiple strains of ESBL-PE. These findings point to strain-related factors being the main drivers of co-colonization with different ESBL-PE and may support stratification of infection prevention and control measures according to ESBL-PE species/strains.

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Abstract 6268

**Comparative in vitro activities of eravacycline and various antibiotics against multidrug-resistant clinical strains of Acinetobacter baumannii isolated from intensive care units**

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**Background:** Acinetobacter baumannii is an opportunistic pathogen that often causes nosocomial infections. Increased antibiotic resistance including carbapenems and the absence of alternative antimicrobials have made the treatment of multidrug-resistant (MDR) A. baumannii infections difficult. On 27 August, 2018, FDA approved eravacycline is a synthetic tetracycline derivative antibiotic agent that has shown activity against Gram-positive and Gram-negative pathogens, including multidrug-resistant bacteria. The aim of the present study was to evaluate the in vitro activity eravacycline and various antibiotics against MDR Acinetobacter baumannii strains.

**Materials/methods:** The antimicrobial activities of eravacycline and various antibiotics were studied against 80 MDR A. baumannii strains isolated from an intensive care unit between 2018-2019. Minimum inhibitory concentration (MIC)s were determined by microdilution method according to CLSI.

**Results:** The in vitro activities of the studied antibiotics against 80 MDR A. baumannii strains are summarized in Table 1. Susceptibility testing demonstrated that the MIC ranges for tobramycin, levofloxacin, meropenem, cefepime, colistin, and eravacycline were 0.25- >256, 2- 256, 8- >256, 32- >256, <0.125- >256 and 0.25- 128 mg/l, respectively. Based on MIC results, 75% of the A. baumannii strains were resistant to tobramycin, although 20% of the tested isolates were resistant to colistin. Additionally, all of the studied isolates were resistant to meropenem, and cefepime. Versus comparator antibiotics, eravacycline showed the lowest MIC90 values against tested isolates.

**Conclusions:** Based on MIC90, eravacycline was the most potent antibiotic of those tested against MDR A. baumannii, including isolates that were resistant to meropenem or/and colistin. Eravacycline has been evaluated as a good treatment option against MDR A. baumannii isolates.

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>MIC range</th>
<th>MIC50</th>
<th>MIC90</th>
<th>S</th>
<th>I</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOB</td>
<td>0.25- &gt;256</td>
<td>128</td>
<td>&gt;256</td>
<td>19 (23.75)</td>
<td>1 (1.25)</td>
<td>60 (75)</td>
</tr>
<tr>
<td>LVX</td>
<td>2- 256</td>
<td>15</td>
<td>128</td>
<td>1 (1.25)</td>
<td>1 (1.25)</td>
<td>78 (97.5)</td>
</tr>
<tr>
<td>MEM</td>
<td>8- &gt;256</td>
<td>128</td>
<td>256</td>
<td>0, 0</td>
<td>0, 0</td>
<td>80 (100)</td>
</tr>
<tr>
<td>FEP</td>
<td>32- &gt;256</td>
<td>256</td>
<td>&gt;256</td>
<td>0, 0</td>
<td>0, 0</td>
<td>80 (100)</td>
</tr>
<tr>
<td>CL</td>
<td>&lt;0.125- &gt;256</td>
<td>0.5</td>
<td>32</td>
<td>64 (80)</td>
<td>0, 0</td>
<td>16 (20)</td>
</tr>
<tr>
<td>ERV*</td>
<td>0.25- 128</td>
<td>4</td>
<td>8</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*No breakpoints defined.

**Table 1:** In vitro antimicrobial activities eravacycline and various antibiotics.

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Abstract 6270

**A retrospective analysis of ceftriaxone-resistant *Neisseria gonorrhoeae* isolated in Japan nation-wide surveillance in 2013**

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**Background:** Reduced susceptibility to ceftriaxone of *Neisseria gonorrhoeae* is a public health concern in the world. In 2009, high-level ceftriaxone-resistant H041 emerged in Japan. Since then, we have paid attention to the clonal spreading of H041.

**Materials/methods:** To analyze the clonal spreading of H041, we used 55 gonococcal strains which were collected from 25 hospitals in Japan in 2013 by the levofloxacin surveillance group. This surveillance was funded from DAIICHI SANKYO COMPANY, LIMITED. Antimicrobial susceptibility testing (AST) was performed by the agar dilution method. Multilocus sequence typing (MLST) and full-length of penA sequence encoding penicillin-binding protein 2 were determined by the draft whole-genome sequencing (WGS). The penA which affected to reduced susceptibility to ceftriaxone was evaluated by the transformation of full-length penA PCR amplicon DNA and by the AST.

**Results:** Antimicrobial-resistance rate was 98% [54/55], 80% [44/55], and 2% [1/55] for benzylpenicillin, cefixime, and ceftriaxone, respectively. The only one ceftriaxone-resistant strain (TUM15748) showed the minimum inhibitory concentration (MIC) of 0.5 mg/L of ceftriaxone. The strain belonged to sequence type (ST) 7359 which was different ST from H041 strain. The other ST7359 strains (n=10) were susceptible to ceftriaxone. The amino acid sequence of TUM15748 PenA (encoded penA-TUM15748) was novel and consisted of two amino acid substitutions (A311V and T483S). By the transformation with penA-TUM15748, the ceftriaxone MIC of the transformant showed 30-fold higher than that of ceftriaxone-susceptible recipients (NG9807 and another ST7359 strain).

**Conclusions:** Although the H041 clone was not found, we found a ceftriaxone-resistant strain which was another genotype with H041 and had a novel penA in Japan in 2013.

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Evaluation of the combined use of galactomannan antigen and \textit{Aspergillus} DNA real-time PCR detection in laboratory diagnosis of invasive aspergillosis among haematological patients

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\textbf{Background:} Diagnosis of invasive aspergillosis (IA) still remains a critical issue among hematological patients. According to the guidelines released by the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EDRTC/MSG), the serological detection of galactomannan (GM) has been considered as the mycological diagnostic standard method. Nevertheless, \textit{Aspergillus} DNA detection has not been included in the guidelines, due to the lack of standardization and validation.

\textbf{Materials/methods:} In the current study the combined use of \textit{Aspergillus} GM and \textit{Aspergillus} DNA detection was evaluated as a useful practice for diagnosis of suspicious invasive IA. The study includes 1,041 samples by 454 patients with hematological malignancies (59 adults and 395 children) from five hematologic units of tertiary care Greek hospitals during 2012-2018. The measurements were made by GM immunoenzymatic method Platelia \textit{Aspergillus} (Bio-Rad, Hercules, CA) and PCR \textit{Aspergillus} (Standard Real-Time PCR detection kit for \textit{Aspergillus}, PrimerDesign). In the immunoenzymatic method, positive samples were considered those with a cut-off index $\geq 0.5$ and $\geq 1.0$ in serum and bronchoalveolar lavage (BAL), respectively.

\textbf{Results:} GM and PCR-\textit{Aspergillus} DNA investigation showed that 44 from 454 patients (9 from 59 adults and 35 from 395 children) were positive for IA. 17 patients (6 adults and 11 children) were found positive using both assays (GM+/PCR+), 2 adults and 16 children were positive by GM only (34 sera & 1 BAL), while 1 adult and 8 children were positive by PCR only (12 sera) (Table). The results’ agreement of GM+/PCR+ and GM-/PCR- were found in 427 patients and 993 samples (94% of the total patients and 95% of the total samples). Respectively, discrepant results were found in only 27 patients (48 samples; 4.6% of total), in which the positive result in any of the two methods was evaluated as true positive, in conjunction with the clinical and radiological findings.

\textbf{Conclusions:} Our findings indicate that the combination of GM-antigen and PCR-\textit{Aspergillus} DNA detection could be an important laboratory tool for the diagnosis of IA in conjunction with clinical, radiological and other laboratory findings of the patient.

\begin{table}[h]
\centering
\begin{tabular}{|c|c|c|c|c|c|c|c|}
\hline
\textbf{Results} & \textbf{Serum} & \textbf{BAL} & \textbf{Number of samples} & \textbf{Number of patients} & \textbf{Serum} & \textbf{BAL} & \textbf{Number of samples} & \textbf{Number of patients} \\
\hline
GM+/PCR+ & 3 & 7 & 10 & 6 & 35 & 7 & 42 & 11 \\
GM+/PCR- & 2 & 1 & 3 & 2 & 32 & - & 32 & 16 \\
GM-/PCR+ & 1 & - & 1 & 1 & 11 & 1 & 12 & 8 \\
GM-/PCR- & 53 & 8 & 61 & 50 & 862 & 18 & 880 & 360 \\
Totals & 59 & & & & 395 & & & 1,041 \\
\hline
\end{tabular}
\end{table}

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Abstract 6274

**Bacterial STI-testing in the private sector in France, 2006-2018**

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**Background:** Protective barrier methods, testing and efficient treatments are main strategies to control the transmission of bacterial sexually transmitted infections (STIs). This study aims to analyze the evolution of STIs testing in private laboratories in France by exploring health insurance reimbursement data.

**Materials/methods:** In France the national health insurance covers 95% of the population. This system contains data on healthcare reimbursements and socio-demographic information. Reimbursement data of the national health insurance enable to monitor the number of persons tested for syphilis, *Chlamydia trachomatis* (*Ct*) or gonococcal infections in private laboratories. National and regional testing rates were calculated per 1,000 inhabitants aged 15 and over, by age and sex. Trends were described since 2006 with a focus on the 2016-2018 period.

**Results:** In 2018, 2.1 million people (39 per 1,000 inhabitants) were tested for *Ct* (figure). The annual number of tests increased by 9% from 2016 to 2018. Nearly 1.6 million people were tested for gonorrhea, with a rate of 30 per 1,000 inhabitants and a sharp increase of 18% since 2016.

For these two STIs, testing rates are higher in populations aged 25 and over. However the testing activity was twice higher in 2018 compared to 2016 in younger people (men or women < 25 years).

In 2018, 1.8 million syphilis tests (33 per 1,000 population) were carried out, with a 14% decrease compared to 2017. Future data will enable further interpretation of this point. The testing rates of these STIs in 2018 were twice higher in most French overseas territories (French West Indies, Reunion Island and French Guiana) than those in mainland France.

**Conclusions:** The increase in the number of tests for *Ct* and gonococcal infections from 2006 to 2018 might result from a better testing offer by health professional following prevention campaigns. The reimbursement of combined *Ct* and gonorrhea tests and the systematic *Ct* screening for young women (< 25 years) extended to general practitioner since 2018 should improve testing in France. However, epidemics remained uncontrolled. Condom use, improvements of the testing offer and its diversification toward most exposed populations are crucial to prevent STIs transmission.

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Abstract 6275

WGS-based characterisation of clinical Pseudomonas aeruginosa isolates obtained from teaching and specialist hospitals in Lagos, Nigeria

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Background: Pseudomonas (P.) aeruginosa is one of the most frequently involved pathogens in serious infections of hospitalised patients. These infections are difficult to treat due to limited treatment options in particular when multidrug resistant (MDR) strains are encountered. Infections with MDR Paeruginosa have become a major concern of public health and infection control experts worldwide, emphasizing the need for detailed surveillance data on a global scale.

Materials/methods: In the present study, we obtained non-duplicate clinical P. aeruginosa isolates (n=124) from three large hospitals in Lagos, Nigeria. Identification was achieved by MALDI-TOF (Microflex LT, Bruker Daltonics, Germany), antimicrobial susceptibility was performed using the VITEK2 (bioMérieux SA, France) supplemented with E-Tests (bioMérieux SA, France), All 124 isolates were subjected to whole genome sequencing using a NextSeq instrument (Illumina, San Diego, USA).

Results: Overall 92 (74%) isolates were resistant to fluoroquinolones, 74 (60%) to piperacillin-tazobactam, 65 (62%) to ceftazidime or cefepime and 54 (44%) to carbapenems. Co-resistances to fluoroquinolones, piperacillin-tazobactam, cephalosporins and aminoglycosides were frequently observed in the carbapenem resistant strains.

In the 54 carbapenem resistant isolates a carbapenemase gene was detected in 53 (98%) of the strains, with blaNDM-1 (34=64%) and blaVIM-5 (11=21%) being the most prevalent ones.

Phylogenetic analysis revealed a broad diversity of the isolates, but also indicated clusters of closely related strains suggesting possible transmission events. Extraction of the multilocus sequence types (STs) revealed the presence of three important STs, namely ST773, ST2613 and ST233. Interestingly, the predominant ST encountered in our strain selection was ST773, which has been frequently reported from different areas around the world.

Conclusions: To the best of our knowledge, this is the first report of application of whole genome sequencing on a larger scale to understand resistance mechanism and epidemiology of clinical P. aeruginosa isolates obtained from Nigeria. The alarmingly high percentage of carbapenemase carrying isolates warrants further investigation. Long-read based analysis is currently being conducted to distinguish between plasmid and chromosomal location of the resistance genes and to elucidate the genetic environments of blaNDM-1 and blaVIM-5.

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Abstract 6276

Epidemiology of dengue, chikungunya, Zika and West Nile diseases from 2012 to 2019: data from an Italian regional reference centre

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Background: Arboviral infections represent an important public health problem. In the recent years many elements favoured their spreading. Increasing travels, emigrations from endemic zones, introduction of vectors at other latitudes, contributed to the onset of autochthonous infections. Many countries, including Italy, introduced surveillance programs in order to control and prevent these diseases. The aim of this study is to analyse epidemiological data of Dengue (DENV), Chikungunya (CHKV), Zika (ZIKV) and West Nile (WNV) infections diagnosed at the Laboratory of Clinical Microbiology, Virology and Bioemergencies, L. Sacco University Hospital, Milan.

Materials/methods: We searched for DENV, CHKV, ZIKV and WNV in 4091 samples of 1191 patients in 2012-2017, 4066 samples of 1132 patients in 2018-2019. For detection of IgM and IgG antibodies serum samples were used and the positive ones were confirmed by Plaque Neutralization test (PRNT). The presence of viral RNA was investigated in serum, urine, whole blood, liquor and saliva samples. Medical and epidemiological informations were collected in a data sheet. Data obtained in 2012-2017 have been compared with those from January 2018 to September 2019.

Results: Comparing 2012-2017 with 2018-2019, an increased number of cases of DENV (+153%: 27 vs 41.5), CHKV (+125%: 4.4 vs 5.5), WNV (+232%: 2.8 vs 6.5) and a decreased number of ZIKV cases (-11%: 5.6 vs 5) have been recorded. Positive patients in 2012-2017 came from: 49.5% South-East Asia, 30% Central America, 9.1% South America, 6.4% Europe, 5% Africa; while in 2018-2019 they were from: 54% South and East Asia, 23% Central America, 5% South America, 10% Europe, 4% Africa and 4% Oceania.

Conclusions: A remarkable increase in number of arboviral diseases in the recent years has been observed. South and East Asia, Central America (including Caribbean), can still be considered as the main endemic zones. According to data, a surveillance system proved to be essential. In fact, in order to control the spreading of the diseases, effective measures must be initiated as soon as possible.

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Abstract 6277

The global burden of sepsis in adults: updated systematic review and meta-analysis
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Abstract third-party references: World Health Organization

Background: Sepsis is a major global health threat, but its burden remains largely unknown, in particular in low- and middle-income-countries (LMIC). We investigated the global burden of sepsis in adults by updating and expanding a systematic review and meta-analysis [Fleischmann AJRCCM 2016].

Materials/methods: 13 electronic databases were searched for studies on the population-level sepsis incidence defined according to clinical criteria (sepsis-1, sepsis-2 or sepsis-3) or relevant ICD-codes. The search of the original systematic review was updated for studies published between 06/2016-02/2019 and complemented by a search targeting LMIC studies published between 01/1979-02/2019. We performed a random-effects meta-analysis with sepsis incidence and proportion of deaths among sepsis cases as outcomes. The model accounts for the potential heterogeneity in the outcomes across studies by the between-study standard deviation (τ).

Results: Our search yielded 4,746 results, of which 32 met the inclusion criteria. 25 studies contributed complete data and were pooled with the 38 studies of the original meta-analysis. The resulting 63 studies were from 4 WHO-regions and 22 countries (Fig. 1). 58/63 studies were from high-income-countries. We found a pooled incidence of 261.16 [95% CI, 199.01, 342.65, τ=0.653] hospital-treated sepsis and 196.83 [142.97, 270.92, τ=0.882] hospital-treated severe sepsis cases per 100,000 person-years. An estimated 22.7% [18.7%, 27.2%, τ=0.411] and 27.4% [24.1%, 30.9%, τ=0.597] sepsis and severe sepsis patients died, respectively. There was a higher incidence of both sepsis and severe sepsis incidence observed in the past decade (+22% and +68% compared to the overall time frame, respectively). Random-effects estimators for ICU-treated sepsis and severe sepsis were 46.88 [23.76, 92.44, τ=1.284] and 65.99 [47.32, 92.03, τ=0.682] per 100,000 person-years, respectively. An estimated 52.6% [34.5%, 70.1%, τ=0.333] of ICU-treated sepsis and 39.0% [32.5%, 45.8%, τ=0.331] of ICU-treated severe sepsis patients died until hospital discharge.

Conclusions: The burden of hospital-treated sepsis is high. Extrapolating the recent estimates on a global scale, we estimate 25 million global hospital-treated severe sepsis cases per year with 6.8 million patients dying from or with sepsis. Data on sepsis epidemiology is lacking from the vast majority of LMICs. Improved epidemiological sepsis surveillance is urgently needed.

Figure 1:

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Abstract 6278

Evaluation of the rapid antimicrobial susceptibility testing (RAST) from positively-flagged blood cultures

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Background: Antibiotic-resistant pathogens are of growing concern to public health. The disk diffusion method and VITEK2 automated drug sensitivity test currently used clinical microbiology laboratories both require 18-24 hours to obtain the results. Development of rapid antimicrobial susceptibility testing (RAST) is important for patient care and improving clinical outcomes.

Materials/methods: Microorganisms from 142 positively flagged blood culture bottles were directly identified by Bruker MALDI-TOF Biotyper using the saponin pretreatment methods. RAST recommended by the EUCAST (European Committee on Antimicrobial Susceptibility Testing) were performed for E. coli, K. pneumoniae, S. aureus, E. faecalis, E. faecium, P. aeruginosa. The results obtained by RAST were interpreted at 4, 6, and 8 hours and were compared with those analyzed by the routine AST method (VITEK 2).

Results:

Table 1. Accuracy (agreement) rates of RAST as compared with the results from VITEK 2 AST

<table>
<thead>
<tr>
<th>Organism (no. of isolates)</th>
<th>4 hours</th>
<th>6 hours</th>
<th>8 hours</th>
<th>VME</th>
<th>ME</th>
<th>MIE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia coli (50)</td>
<td>70</td>
<td>85</td>
<td>91</td>
<td>3</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Klebsiella pneumoniae (47)</td>
<td>83</td>
<td>88</td>
<td>90</td>
<td>1</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa (9)</td>
<td>-</td>
<td>85</td>
<td>93</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Staphylococcus aureus (17)</td>
<td>74</td>
<td>69</td>
<td>81</td>
<td>0</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Enterococcus faecalis (5)</td>
<td>47</td>
<td>53</td>
<td>67</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Enterococcus faecium (14)</td>
<td>67</td>
<td>69</td>
<td>69</td>
<td>1</td>
<td>1</td>
<td>9</td>
</tr>
</tbody>
</table>

Interpretation of RAST and VITEK 2 AST results to selected antimicrobial agents was based on the guidelines recommended by the EUCAST. The high MIEs of E. faecalis and E. faecium were due to fuzzy zone edges of vancomycin. VME, very major error; ME, major error, and MIE, minor error.

Conclusions: RAST were useful (>85% agreement) for early detection of susceptibilities at 8 hours for E. coli, K. pneumoniae, and P. aeruginosa. However, several isolates of these species exhibited VMEs. Using MALDI-TOF MS and RAST from positive blood cultures, the entire time for bacterial identification and AST was shortened from 36-48 hours to 4.5-8.5 hours. It is expected to effectively reduce patient mortality, shorten hospital stay, and reduce medical costs.

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Abstract 6280

Comparative evaluation of CHROMagar COL-APSE, MicroScan Walkaway, ComASP Colistin, and Colistin MAC test diagnostic efficiencies in detecting colistin-resistant Gram-negative bacteria

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Abstract third-party references: National Health Laboratory Service (NHLS) for their generous support in cash and kind, Department of Medical microbiology, University of Pretoria

Background: Colistin belongs to the polymyxin class of antimicrobials. Subsequent to its successful introduction however, its use was halted due to its side effects. Increasing antimicrobial resistance has led to the resurgence of colistin as the last-resort antimicrobial agent to treat multidrug-resistant (MDR) Gram-Negative Bacteria (GNB). Colistin resistance was reported after identification of a mobile colistin resistance (mcr-1) gene in E. coli isolates from patients, food and food-producing animals. To date, the mcr-1 gene and its variants have spread globally. Owing to the threat posed by colistin-resistant (COL-R) GNB, it is crucial that patients are quickly diagnosed and treated accordingly. However, this requires diagnostic assays that can rapidly and timeously detect COL-R GNB. Currently, only the Broth Microdilution (BMD) is the accepted colistin antimicrobial susceptibility (AST) testing technique for routine diagnostic laboratories.

Materials/methods: A total of 84 GNB were screened with the BMD to determine their colistin Minimum Inhibitory Concentrations (MICs). A multiplex PCR (M-PCR) was used to screen all isolates to detect the presence of the mcr-1 to mcr-5 genes. CHROMagar COL-APSE was challenged for the recovery and identification of COL-R organisms. The MicroScan® was challenged with all isolates to determine their colistin MICs and species taxon. The ComASP™Colistin, was also challenged with the isolates. A novel screening assay, the Colistin MAC Test (CMT) was used to identify mcr positive isolates.

Results: The M-PCR detected a single mcr-1 positive E. coli isolate. CHROMagar recovered 45% COL-S and 55% COL-R isolates with a sensitivity of 82.05% and specificity of 66.67%. The MicroScan® had a specificity and sensitivity of 92.31% and 76.92%. The ComASP™Colistin had a sensitivity and specificity of 100% and 88.89% respectively. The CMT detected one mcr-positive isolate. The MicroScan® was the most expensive at a cost (per sample tested) of R221.59, followed by CHROMagar COL-APSE, M-PCR, CMT and ComASP™Colistin at R119.33, R75.08, R20.12 and R2.64 respectively. CHROMagar was the easiest to perform, followed by ComASP™, M-PCR, MicroScan®, CMT AND BMD.

Conclusions: The ComASP™ Colistin was the best performing diagnostic test and is therefore recommended as a potential commercial BMD assay that can improve routine colistin AST in clinical laboratories.

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First European outbreak of eosinophilic meningitis in travellers returning from Cuba

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Background: Angiostrongyliasis caused by the rat lungworm Angiostrongylus cantonensis (AC) is endemic in Asia, the Pacific Islands and the Caribbean. Humans become infected by ingestion of larvae contained in raw or undercooked snails, prawns or contaminated vegetables. Infection can lead to eosinophilic meningitis with CNS involvement. We report the first imported outbreak in the European Union of eosinophilic meningitis caused by AC. Diagnosis of four cases was based on clinical symptoms and confirmed by serology.

Materials/methods: An 18-year-old woman (Case 1) and her sister aged 23 (Case 2) were admitted to the Emergency Department due to severe occipital and retro-orbicular headache and vomiting in the last 4 days. Two weeks earlier they had returned from a trip to Cuba. From asking for potentially exposures, the patients reported to have eaten raw freshwater prawns, salad and half-cocked pork (“ropa vieja”). Few days later, other members of the family developed similar symptoms and in addition intense conjunctivitis (Case 3) and paraesthesia/dysesthesia (Case 4). Clinical and analytical data suggested the diagnosis of eosinophilic meningitis.

Results: Laboratory tests displayed blood eosinophilia with normal acute phase parameters. CSF was collected from two patients (1, 3) and CSF examinations were consistent with aseptic meningitis: lymphocytic predominance with 18-36% eosinophils. Serum samples of three patients were collected during acute phase and convalescence phase for serological analysis. All samples were tested in the following tissue helminth serology: Trichinella, Toxocara, Fasciola, Filaria, Schistosoma and Strongyloides with ELISA, and Angiostrongylus spp. with EITB. The acute phase samples were additionally tested for Gnathostoma serology (EITB).

All serologies were negative except for the Angiostrongylus. The acute phase samples were all negative, while all convalescence phase samples were positive for specific IgG antibodies directed against the 31 kDa protein of A. cantonensis. In all cases seroconversion took place within three weeks after onset of symptoms. Patients were treated with systemic prednisolone.

Conclusions: These results show the importance of repeated testing for specific antibodies in patients with suspected angiostrongyliasis. AC infections should always be considered in cases of eosinophilic meningitis, even outside of endemic areas. Travel counseling is mandatory to avoid the infection.

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Abstract 6288

Using dried blood spots in drug dependency treatment centres to diagnose active hepatitis C infection
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Background: Patients attending drug dependency treatment centres (DDTC) have high prevalence of hepatitis C virus (HCV) active infection in Spain, as well as low connection with health system environment. If no new diagnostic and treatment strategies are implemented, eradication of this disease will not be possible. The purpose of this study was to evaluate the use of dried blood spots samples (DBS), obtained in DDTC, in hepatitis C diagnosis in a clinical microbiology laboratory in Tenerife, Spain.

Materials/methods: 254 DBS were collected and treated with different protocols in order to obtain an eluate to perform a serology to detect anti-hepatitis C virus antibodies (Alinity, Abbott Diagnostics), or to perform a rtPCR to measure the viral load (Cobas 6800, Roche Diagnostics). In the positive viral load cases, the patients were scheduled for a doctor appointment 1-2 weeks later, where plasma sample was obtained and treatment was started.

Results: Seventy-one DBS gave positive results in serology and quantitation, diagnosing an active infection. 183 were negative in the rtPCR, ten of them treatment controls, previously diagnosed by normal algorithms. Other five DBS were treatment controls, previously diagnosed also by DBS technique.

Correlation of the 71 positive results between DBS and normal detection of the antibodies were 97.18%, and 100% with viral load results. In DBS technique, viral loads were 2.24 log on average lower [International Units/mL], from the results obtained 1-2 weeks later in plasma in untreated patients.

Conclusions: DBS based techniques are very useful methods to detect active hepatitis C infection in these communities. Our results showed that amount of viral load should not be considered when performing DBS techniques, as it normally results in lower detection of HCV RNA. However, lower results of viral loads of DBS may be due to lower volume of blood used in blotting DBS as compared to plasma.

Further investigation and validation studies need to be performed to address these problems, as DBS techniques have showed promising results in detection of hepatitis C active infection, and could substantially improve worldwide screening, diagnosis and access to care.

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Predicting co-amoxiclav resistance in *Escherichia coli* bloodstream infections using machine learning methods and bacterial genome-wide association studies

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**Background:** Several methodologies have been developed to predict antimicrobial susceptibilities from whole genome sequencing (WGS) data. Levels of performance vary. However, predictions of beta-lactam/beta-lactamase inhibitor susceptibility in Enterobacteriaceae have proved challenging. This is partly driven by the modest reproducibility of laboratory phenotypes and differences in reference methodologies. We investigated if alternative approaches using machine learning (ML) could improve resistance prediction for co-amoxiclav in *Escherichia coli*.

**Materials/methods:** We investigated *E. coli* isolated from blood (January 2013-August 2015, Oxfordshire, UK). For each isolate, WGS was used to identify genetic features relevant to co-amoxiclav resistance and MICs were measured by microbroth dilution (BD Phoenix). Input genetic features were constructed both from presence/absence of known resistance elements (Resfinder database), and by creating agnostic patterns of k-mer presence/absence (using 31-mers) with bacterial genome-wide association studies for feature selection. We predicted susceptible/resistant phenotypes (using EUCAST breakpoints) using regularized logistic regression, support vector machines, and ensembles of decision trees (random forests, gradient boosting). For MICs we considered regularized multinomial logistic regression, generalization of regularized logistic regression for ordered outcomes (ordinal regression), regularized regression and ensembles of trees.

**Results:** Of 976 *E. coli* bloodstream infections, 36% were phenotypically co-amoxiclav resistant. For susceptible/resistant prediction the best-performing model, determined using cross-validation, included the 5561 most significant 31-mer patterns of presence/absence using L2-regularised logistic regression [accuracy 89%, sensitivity 88%, specificity 89%, AUC 96%].

The best-performing model for essential agreement (MIC within a doubling dilution) utilised ordinal regression with known co-amoxiclav resistance determinants and their DNA copy-number as input features [essential agreement 92%, accuracy 58%, sensitivity 74% and specificity 98% [sensitivity/specificity against the predicted binary phenotype]]. The same ML algorithm with the top 5088 31-mer presence/absence patterns had similar performance (Figure).

**Conclusions:** The largest improvement in performance was obtained through feature engineering (e.g. DNA copy-number, Figure); choice of ML algorithm further improved this. Agnostic 31-mers were able to achieve similar predictive performance as that obtained using known resistance gene databases, despite not accounting for copy-number, suggesting further improvement may be possible.

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Abstract 6292

Dealing with the current dengue viral fever outbreak: an experience from a tertiary care hospital in Karachi

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Background: Pakistan is currently facing its worst outbreak of Dengue Viral Fever (DVF) since 1994 with over 42,120 confirmed cases and 75 mortalities. In Sindh alone, 12,053 cases were confirmed and 33 deaths were reported. More than 90% cases of Sindh were recorded in Karachi, with heavy rainfall, hot, humid weather, overflowing sewage and garbage dumps being the perfect breeding ground for the mosquito vector. The Indus Hospital, located in Korangi, Karachi, deals with DVF cases all year round but received an enormous surge in cases over the past two months.

Materials/methods: A retrospective review of confirmed DVF cases of all age groups was conducted at The Indus Hospital Karachi from August till October 2019 capturing details of demographics, clinical features, investigations and outcomes.

Results: A total of 1,631 confirmed cases were reported during August to October 2019 (August: 211, September: 321 and October: 1289 cases respectively). Detailed analysis was performed on data from Oct-2019, out of which 79.3% (n=1,022) were diagnosed on positive Dengue NS1 antigen test and 21% (n=270) on positive Dengue IgM antibodies with 7.21% (n=93) of the latter showing concomitant IgG positivity. Fifty-three patients (4.1%) presenting with severe Dengue Fever were admitted and recovered uneventfully. Five (0.4%) patients presenting with Dengue Haemorrhagic Fever expired within hours of presentation to the Emergency Department. Demographics are shown in figure 1. Thirty-nine (3.13%) patients had platelets <20 x 10^9/L, lowest reported being 4 x 10^9/L. The lowest total leukocyte count was 1.13 x 10^9/L (mean±SD of 5.35±3.53 x 10^9/L). Haemoglobin ranged from 4 gm/dl- 20.1 gm/dl and highest haematocrit recorded was 60.1% (Mean± SD: 40±5.9%). Malaria and dengue co-infection was observed in 8 (0.62%) patients, one of which (with falciparum parasitic load of 16%) survived after prolonged ventilatory, haemodynamic and dialysis support.

Conclusions: In this 2019 outbreak, DVF has caused significant morbidity, overwhelming our resource limited hospital. Vector control in high burden areas and better preparedness at hospital level can help curtail future seasonal outbreaks.

Figure 1: Karachi dengue outbreak and patients characteristics [single center experience]

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Abstract 6294

Initial clinical features from preliminary analyses of a global multi-centre prospective observational cohort of sepsis in hospitalised neonates: the NeoOBS study

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Abstract third-party references: on behalf of the NeoOBS Study Team

Background: Neonatal sepsis is estimated to be responsible for 680,000 deaths per year, with an estimated 214,000 deaths attributable to antimicrobial resistance, demonstrating a need for new treatment strategies. However, the lack of a universally accepted and workable definition of neonatal sepsis, particularly for low-middle income countries (LMIC), undermines estimates and is a challenge for designing sepsis trials. This multi-country observational study is the largest to link clinical presentation, microbiology, response to antibiotic treatment and outcomes in LMIC settings.

Materials/methods: Hospitalised infants aged <60 days, with a primary diagnosis of sepsis, fulfilling at least 2 clinical or laboratory sepsis criteria (at least 1 clinical) were enrolled over 2018-19 in 19 sites in 11 countries across Asia, Africa, Europe and South America (up to 200 cases per site). Infants were included after a decision to treat with new antibiotics for a sepsis episode, and were excluded if an alternative primary diagnosis was suspected to be more likely.

Results: 1826 neonates for whom preliminary clinical data could be analysed were included. 43% are female, with median birth weight 2270g and postnatal age 6 days. The median number of clinical signs was 4, the most common being shown in figure 1. The frequency of most signs varied with birth weight and (post-natal) age. In particular, respiratory signs were more frequent at lower birth weights (54%<2500g vs 94%<1000g, P<0.001), younger age (78%<7d vs 57%>7d, P<0.001) and for inborn newborns who had remained in hospital since birth (OR=1.8, 95% CI 1.6-2.0, P<0.001 after adjustment for birth weight and age). The most common laboratory criteria was CRP, which was >10mg/L in 725 (62%) of 1,177 infants in whom it was measured (64% of total), and more commonly raised in infants >7d old (71% vs 51%, P<0.001).

Conclusions: In this preliminary analysis, infant factors such as birth weight and age were associated with different frequencies of common signs of sepsis, with implications for clinical sepsis definitions and neonatal sepsis trial design. Further analyses will explore how such factors influence the sensitivity and specificity of signs for prediction of culture positivity, response to therapy and outcomes.

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Abstract 6296

**Phenotypic and molecular characterisations of carbapenem-resistant *Acinetobacter baumannii* isolates collected within the EURECA study**

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**Abstract third-party references:** on behalf of the EURECA study team

**Background:** Carbapenem-resistant *Acinetobacter baumannii* (CRAB) isolates were collected from patients with sepsis from 50 European sites that participated in the EUropean prospective cohort study on Enterobacteriaceae showing REsistance to CArbapenems (EURECA) (May 2016 to November 2018).

**Materials/methods:** Local laboratories stored all *A. baumannii* blood isolates resistant to carbapenems (MIC ≥ 16 mg/L for imipenem or meropenem, and/or disc diffusion zone diameter ≤17 mm and/or ≤15 mm, respectively). Patients with CRAB bacteremia were enrolled into the study. The isolates were shipped to the central lab (University of Antwerp) for identification (MALDI-TOF) and phenotypic (disc diffusion) confirmation. In addition, MIC testing was performed by broth microdilution and interpreted by EUCAST guidelines. Genomic DNA was extracted using MasterPure™ DNA Purification Kit and sequenced via 2×250b PE sequencing (Miseq, Illumina). Comparative genome analysis was performed using an in-house developed pipeline (BacPipe v.1.2.6). Since *A. baumannii* isolates have a high genetic diversity, we performed a gene-by-gene approach-based allelic loci comparison using chewBBACA by generating a study-specific wg/cg MLST scheme and visualized it using PHYLOViZ.

**Results:** A total of 227 CRAB strains from 29 sites were collected. The identification and susceptibility testing results of almost all isolates (n=225; 99.1%) were confirmed at the central lab. Whole-genome sequencing data revealed 26 diverse ST-types according to the Oxford MLST scheme, the most common being ST195 (n=75; 33.2%). ST-type could not be assigned to 19 isolates (8.4%). Pasteur MLST scheme identified 12 different STs; the most prevalent was ST2 (n=153; 67.7%). A majority of the isolates harboured the *bla*OXA-23 (n=153; 67.7%), while the main oxacillinase in 70 isolates (30.1%) was *bla*OXA-72. The *bla*OXA-66 gene was present in 179 isolates (79.2%, usually in conjunction with *bla*OXA-23 (n=138; 61.1%). Four isolates from Serbia that had *bla*OXA-72 and *bla*OXA-66 also co-harboured *bla*NDM-1. Genetic relatedness based on cgMLST allelic loci distances showed that isolates were scattered in various clusters despite belonging to the same ST-type (Fig. 1).

**Conclusions:** Findings from the local labs were confirmed at an excellent rate which underlines the importance of training microbiology labs in clinical trials on anti-infectives. *bla*OXA-23 was the most predominant oxacillinase. The most common ST types were ST195/ST2.

![Fig. 1. Phylogenetic tree showing the clonal relatedness of Acinetobacter baumannii isolates within the EURECA study. Isolates from participating countries are shown in different colors.](image-url)

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Quantitative detection of human cytomegalovirus and Epstein-Barr virus using the real-time PCR STAT-NAT CMV and STAT-NAT EBV assays

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Background: Human Cytomegalovirus (HCMV) and Epstein-Barr virus (EBV) are two Herpesviridae family DNA viruses, widely spread in human population, with estimated seroprevalence up to 80% and above. Despite being generally asymptomatic in healthy subject, HCMV and EBV infection represents a leading cause of morbidity and mortality in non-immunocompetent subjects (i.e.: transplant recipients, newborns, children). Molecular methods demonstrated to be rapid, sensitive and reliable tools for viruses detection. The aim of this work was to evaluate the performance of new quantitative freeze-dried and ready-to-use Real-Time PCR assays (STAT-NAT CMV and STAT-NAT EBV) for HCMV and EBV DNA detection in human samples.

Materials/methods: Both assays were developed as ready-to-use lyophilized mix, combining viruses specific primers and probes, primers and probes for the detection of Internal Control (exogenous for HCMV, endogenous for EBV) and other reagents. In the present study, a total of 50 HCMV and 50 EBV whole-blood samples were extracted by means of QIAamp DSP Virus Spin Kit (QIAGEN) and then processed using CFX96 Real-Time PCR Detection System (Bio-Rad Laboratories, Inc.); results were compared to those previously obtained with the routine method used at L. Sacco Hospital (ASST FBF Sacco – Milan, Italy), CMV and EBV ELITe MGB® Kit (ELITechGroup).

Results: All samples were successfully amplified for both targets, as confirmed by ICs results. HCMV and EBV-DNA values were comparable with those obtained with ELITe MGB® Kits; in particular, a difference >0.5 Log was found in <5% of samples. From analytical studies the CMV test resulted in a LLoQ of 102 cps/rxn, a LoD of 30 cps/rxn and linearity range between 102 and 106 cps/rxn. Analytical studies of EBV showed a LLoQ of 101 cps/rxn, a LoD of 5 cps/rxn and linearity range between 101 and 107 cps/rxn. Cross-reactivity studies did not show evidences of spurious amplification.

Conclusions: These novel Real-Time PCR assays proved their effectiveness for detection and quantification of HCMV and EBV DNA in clinical samples. The high sensitivity and specificity, the ready-to-use setup and the possibility to storage at room temperature make these assays suitable for molecular monitoring in patients management.

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Abstract 6300

A high-throughput real-time liquid-based Caenorhabditis elegans model for assessing the virulence of clinical encapsulated multidrug-resistant Klebsiella pneumoniae isolates

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Background: MDR Klebsiella pneumoniae (Kpn) is an important pathogen responsible for life-threatening infections. There is an urgent need for a rapid in vivo model for virulence assessment of this pathogen. Caenorhabditis elegans nematode is a powerful model for studying host-pathogen interactions. The standard nematode killing assay (NKA) is an agar-based method performed with nematodes placed on a bacterial lawn and virulence is assessed by following nematode survival. This model is suitable for various pathogens but is inapplicable for highly mucoid encapsulated bacteria such as Kpn. We aimed to develop a high-throughput real-time nematode liquid-based killing assay (NLKA) that enables rapid virulence assessment of multiple MDR Kpn strains.

Materials/methods: NLKA experiments were performed in 96-multiwell plates with manual live/dead counting of nematodes [strain AL98] using an inverted-light microscope. Nematodes (L4 larvae) were inoculated (15-20 worms/well) into BM2 broth-containing wells (150µL) with the tested K. pneumoniae strain (~10^7 CFU/well). High throughput NLKA experiments were developed in 384-multiwell-plates (50µL medium) placed in an automated microscope imaging system (WiScan® Hermes, 7.5 min time-laps). Image analysis was performed using CellProfiler™. Escherichia coli strain OP50 was used as a non-virulent control strain. Survival curves and statistics were performed using Log-rank test (GraphPad-Prism).

Results: Agar-based NKA experiments are irrelevant for encapsulated Kpn strains. Therefore, NLKA experiments were carried out to enable a feasible nematode survival follow-up (Figure). Virulence assessment of eight ESBL-producing MDR Kpn strains on BM2 medium demonstrated their killing ability compared to E. coli OP50 (100% survival). LT50 values ranged from 4.75 to 6.0 hr ± 0.39 hr. An automated rapid NLKA experiment was developed and applied on KpnU95 UTI strain. Virulence was assessed on two growth media- BM2 and artificial urine. KpnU95 showed enhanced virulence when grown on artificial urine compared to BM2 (LT50 of 2.82 ± 0.25 hr and 3.37 ± 0.42 hr, respectively, p<0.05).

Conclusions: We present here a high-throughput real-time assay for comparative virulence assessment of highly encapsulated K. pneumoniae strains. This method allows the simultaneous screening of a high number of bacterial isolates and is highly valuable for comparative virulence assessment of mutants and host-pathogen in vivo studies of Klebsiella.

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Abstract 6301

The impact of medical drugs on the acquisition of ESBL-producing Enterobacterales: a matched case-control study

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Abstract third-party references: R-GNOSIS WP5 study group

Background: Little is known about the impact of non-antimicrobial agents on the selection of ESBL-producing Enterobacterales (ESBL-E). The aim of this study was to investigate medical drugs as potential risk factors for ESBL-E acquisition.

Materials/methods: We conducted a retrospective, exploratory, matched case-control study based on a larger trial in a 3000-bed University Hospital carried out between 2014 and 2016. Rectal surveillance cultures were obtained on admission and at least once before discharge to screen patients for ESBL-E carriage.

Patients with ward-acquired ESBL-E were matched one-to-one with Non-ESBL-E carriers. Matching was based on ward, number of rectal cultures, number of days at risk (ESBL-E free days), and Charlson Comorbidity Score (CCS). Medication prescription data were collected from paper charts and patient data management system and documented according to Anatomical Therapeutic Chemical Classification System (ATC). Multivariable conditional logistic regression was used to calculate independent risk factors for ESBL-E acquisition.

Results: In total, 232 cases and 232 controls from eight non-ICU wards were analyzed. Baseline characteristics such as patient age (median years 65; IQR 52-74), gender (Male 56.9%), number of samples (median 3; IQR 2-4), number of days from admission to first sample (median 2, IQR 1-2), number of days at risk (median 8; IQR 6-11), and CCS (median 4; IQR 2-6) were similar between cases and controls.

There was no difference between cases and controls with regard to the use of systemic antimicrobials, particularly fluoroquinolones (J01M) and third-generation cephalosporins (J01DD) in univariate analysis, all p>0.05.

Multivariable analysis showed that use of pantoprazole (proton pump inhibitor) and ipratropium bromide (anticholinergic agent) independently increased the chance to detect ESBL-E (OR 1.96; CI95% 1.19-3.23; P=0.047, and OR 16.36; CI95% 2.03-131.82; p<0.01, respectively), while bisacodyl (laxative) and citalopram (selective serotonine-reuptake inhibitor) decreased it (OR 0.13; CI95% 0.04-0.44; P<0.01, and OR 0.21; CI95% 0.06-0.75; P=0.026, respectively).

Conclusions: In a non-ICU-setting, medicinal agents other than antimicrobials were determined as independent risk factors for ESBL-E acquisition. Interestingly, substances with side effects favouring intestinal motility were determined as protective, while substances with constipating effects were risk factors. However, uncertainty was large as some drugs were prescribed to only few patients.

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Abstract 6303

Paediatric invasive pneumococcal disease in Portugal: dominance of serotype 3 and increase in serotype 8 four years after PCV13 inclusion in the national immunization plan

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Abstract third-party references: Portuguese Study Group of Invasive Pneumococcal Disease of the Paediatric Infectious Disease Society, Portuguese Group for the Study of Streptococcal Infections

Background: In Portugal, vaccination with pneumococcal conjugate vaccines (PCVs) of infants in the private sector led to significant decreases in the incidence of pediatric invasive pneumococcal disease (pIPD). We aimed to determine serotype distribution and antimicrobial susceptibility patterns of pneumococci causing IPD between July 2015 (when PCV13 was introduced in the National Immunization Plan - NIP) and June 2019 to determine the impact of PCV13 on pIPD.

Materials/methods: A total of 196 Streptococcus pneumoniae isolates recovered from pIPD cases in 62 hospitals in Portugal between July 2015 and June 2019 were characterized by serotyping and antimicrobial susceptibility testing. In 96 cases with culture-negative CSF or pleural fluid samples, real-time PCR identified and serotyped S. pneumoniae.

Results: Most pIPD cases were caused by serotypes not included in PCV13 (55%, n=161), with serotypes 8 (n=19), 10A (n=20), 15B/C (n=13), 15A (n=11) and 33F (n=9) being the most frequent. Among PCV13 serotypes, serotype 3 was the most frequent overall (27%, n=78) followed by serotypes 14 (5%, n=15) and 19A (4%, n=12). Other PCV13 serotypes detected included 19F (n=8), 6B (n=6), 1 (n=5), 23F (n=4) and 18C (n=3), together accounting for 9% of the cases. Comparing with the period prior to the inclusion of PCV13 in the NIP, PCV serotypes 1 and 7F showed significant decreases, while the opposite was true for serotypes 3, 8 and 33F. Susceptibility to penicillin and erythromycin was found in 75% of the isolates, while 10% were simultaneously resistant to erythromycin and penicillin non-susceptible (MIC>0.06 mg/L). Overall, 12% of the isolates were penicillin non-susceptible and 18% were resistant to erythromycin, mostly associated with serotypes 1, 19F, 33F and 6B.

Conclusions: Despite universal vaccination with PCV13 for more than 4 years, serotype 3 is still the dominant serotype in pIPD while other PCV13 serotypes decreased significantly, suggesting that vaccination is not equally effective against all serotypes. Furthermore, the increase of serotypes not included in PCV13 such as serotypes 8, 33F and, to a lesser extent, 10A and serogroup 15 is of concern because NVTs may begin to erode the benefits of vaccination.

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Abstract 6304

The epidemiology, genotypes, antifungal susceptibility of Trichosporon species, and impact of voriconazole therapy on outcome of Trichosporon fungaemia

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Background: Trichosporon species is an emergent opportunistic pathogen that might cause life-threatening invasive infections, and exhibit an intrinsic resistance to echinocandins. Very little is known regarding whether epidemiology, clinical characteristics and therapeutic management differences are associated with the clinical outcomes of Trichosporon fungaemia. The aim of this study was to determine the Trichosporon species distribution, genotypes, antifungal susceptibilities, and predictors of clinical outcomes of Trichosporon fungaemia.

Materials/methods: This was a multicenter, retrospective study enrolled patients with a positive culture for Trichosporon species between January 2010 to December 2018 identified from records of the microbiology laboratory at four medical centers in Taiwan. Isolates were identified to the species level by sequence analysis of the ribosomal DNA ITS region and IGS1 region. In vitro susceptibility against antifungal agents were determined by the Sensititre YeastOne panel.

Results: Among the enrolled 117 isolates, blood cultures (n=53) were the majority. Trichosporon asahii was the most frequently isolated species (72.6%), followed by T. dermatis, T. montevideense, and T. faecales. Of the 85 T. asahii isolates, genotype 1 was the most predominant (41.2%). Generally, T. asahii isolates had higher MIC geometric means value than non-asahii Trichosporon isolates. New azoles had good in vitro activity, and voriconazole was the most potent. After excluding 11 patients from fungemia analysis (2 with incomplete data, and 9 who died within the first 48 hours), the overall 14-day mortality was 54.8%. Kaplan-Meier plot revealed that patients with voriconazole treatment had a significantly better survival rate compared with those who did not (p=0.036). Compared with those without antifungal treatment, voriconazole was associated with better 14-day survival rate in cox regression model (odds ratio: 0.29, 95% confidence interval: 0.10-0.84, p = 0.22). In the multivariate analysis, SOFA score, septic shock, source control and voriconazole use were independent predictors of 14-day mortality.

Conclusions: Our study demonstrated that Trichosporon asahii was the most frequently isolated species, and the most predominant genotype of T. asahii is genotype 1. Among patients with Trichosporon fungaemia, T. asahii remains the main isolates. Voriconazole use is the optimal choice and predicts the positive outcome of 14-day mortality.

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Abstract 6305

Clinical and bacterial characteristics of paediatric invasive infections caused by Streptococcus pyogenes

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Background: In industrialized countries, Streptococcus pyogenes (Group A Streptococcus, GAS) is mostly associated with pediatric tonsillopharyngitis, but it may also cause severe invasive disease (iGAS), especially among infants and the elderly. This study aimed at performing a clinical, epidemiological and molecular characterization of pediatric iGAS in Portugal.

Materials/methods: During 2014-2018, the pediatric departments and microbiology laboratories of 36 hospitals throughout Portugal were asked to report all pediatric (<18 years) cases of iGAS and to submit the corresponding isolates. Relevant demographic and clinical data were recorded. The emm type and the presence of 11 superantigen (SAg) genes was determined for all available isolates.

Results: We identified 129 children with iGAS, with an average annual incidence of 1.45/100,000 (3.97/100,000 in patients <4 years old), 56% males, and a median age of 3 years (range 2 days-15 years). Clinical information was available for 118 cases. The most frequent diagnosis was bacteremia without focus (38%), osteoarticular infection (21%), skin/soft tissue infection (20%), and pneumonia (14%). STSS occurred in 13% of the patients. The case-fatality ratio was 5% (20% among STSS patients, p=0.027). Risk factors for mortality were diarrhea (p=0.042), higher cardiac rate at presentation (p=0.027), and STSS (p=0.040). Ninety non-duplicate isolates were available for molecular characterization, comprising 10 emm clusters, 14 emm types and 23 SAg profiles. Three emm types accounted for 66% of the isolates, namely emm1 (37%), emm3 (19%), and emm6 (10%). There were no significant associations between individual emm types or clusters and STSS or mortality.

Conclusions: The incidence of pediatric iGAS determined herein is lower than that reported in other European countries, but with a higher associated mortality. The most frequent lineages in this study are among the leading lineages causing iGAS in the general population in Portugal up to 2015, but with a higher prevalence of emm1 and emm3. The second most common emm type among all iGAS in 2010-2015 (emm89), accounted for only 3% of the pediatric isolates. Further studies are necessary to evaluate if these lineages have a different ability to cause iGAS in children and adults, or if their prevalence changed among all iGAS since 2016.

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Global multi-centre prospective observational cohort of sepsis in hospitalised neonates highlights complex case mix: the NeoOBS Study

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Abstract third-party references: on behalf of the NeoOBS study team

Background: Nearly half of global deaths in children under 5 years occur in neonates and sepsis is a major cause of neonatal mortality. Antimicrobial resistance is a significant challenge to reducing neonatal mortality. Understanding patient characteristics and current neonatal sepsis management in areas where the WHO recommended first-line ampicillin+gentamicin is not used due to resistance is key to designing future clinical trials of antibiotic regimens.

Materials/methods: A prospective longitudinal observation cohort study of infants with significant sepsis has been recruiting at 19 predominantly tertiary hospitals in 11 countries [5 WHO regions] since August 2018. Infants <60 days presenting with clinical sepsis, defined as the presence of at least two clinical or one clinical and one laboratory predefined signs are eligible. Daily clinical and antimicrobial data, as well as all routinely obtained laboratory and microbiology data, are collected for up to 28 days while the neonate is hospitalised and receiving antimicrobial treatment. Outcome data on day 28 is collected. Recruitment target is 2500-3000 babies. Here we describe patient characteristics of neonates with sepsis at global tertiary hospitals.

Results: 1853 neonates from 18/19 site included in this analysis; 57% [1047/1839] are male. The median postnatal age at enrolment is 6 days [IQR:2-15]. 46% [854/1841] of neonates are inborn and 54% [987/1841] are admitted from elsewhere (e.g. other hospital or community). The median gestational age is 36 weeks [IQR:30-39 weeks] and birth weight is 2272 grams [IQR:1295–3044 grams]. 51% [936/1837] of neonates were delivered by spontaneous vaginal birth and 46% [850/1837] were born via caesarean. Neonates with sepsis had a wide range of admission diagnoses including respiratory distress [56%, 1038/1853], prematurity [45%, 833/1853], low birth weight [41%, 757/1853] and infection [40%, 733/1853]. 8% [138/1808] have a congenital anomaly, of which heart [28%, 39/138] and gastrointestinal [23%, 31/138] are the most common systems affected. Comorbidities are summarised in table 1.

Conclusions: To our knowledge, this is the largest study of hospitalised neonates with sepsis to date. Hospitalised neonates with sepsis have a wide range of comorbidities at diagnosis. Future antimicrobial clinical trials will need to account for the variation and complexity of these patients.

Table 1. Baseline comorbidities of neonates with severe clinical sepsis.

<table>
<thead>
<tr>
<th>Baseline Comorbidities</th>
<th>Overall</th>
<th>Lung</th>
<th>Kidneys</th>
<th>Heart</th>
<th>Gastrointestinal</th>
<th>Brain and spinal cord</th>
<th>Musculoskeletal</th>
<th>Other</th>
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<td>Congenital Anomalies</td>
<td>7.6%</td>
<td>2.9%</td>
<td>8.7%</td>
<td>28.2%</td>
<td>22.5%</td>
<td>5.8%</td>
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<td>15.3%</td>
<td>9.9%</td>
<td>7.7%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Prematurity</td>
<td>45.0%</td>
<td>40.9%</td>
<td>39.6%</td>
<td>15.3%</td>
<td>9.9%</td>
<td>7.7%</td>
<td>5.5%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Birth weight</td>
<td>45.0%</td>
<td>40.9%</td>
<td>39.6%</td>
<td>15.3%</td>
<td>9.9%</td>
<td>7.7%</td>
<td>5.5%</td>
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</tr>
<tr>
<td>Other</td>
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<td>40.9%</td>
<td>39.6%</td>
<td>15.3%</td>
<td>9.9%</td>
<td>7.7%</td>
<td>5.5%</td>
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Abstract 6308

Optimised standard of care for Ebola virus disease patients in eastern Congo: a mandatory effort associated with specific therapies


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Abstract third-party references: INSERM, ALIMA

Background: The current Ebola outbreak in Democratic Republic of the Congo (DRC) has been reported since August 2018. The lethality rate for hospitalized patients remains high despite increasing access to vaccines, innovative treatments and patient management. We have been running the EVISTA cohort (Ebola Virus STAndard of care) on three Ebola Treatment Center (ETC) in eastern DRC.

Materials/methods: All patients admitted into participating sites with a positive Ebola RT-PCR were included in the study providing informed consent. Clinical and biological data, as well as information regarding supportive care were collected through medical records prospectively when possible, otherwise retrospectively.

Results: 835 Ebola confirmed patients were included, which represent almost one third of the total amount of cases diagnosed during this outbreak. All of them received specific treatment through investigational therapeutic evaluation efforts. Median age was 28 years [IQR 18,40], 57% female. The overall mortality was 45%, 81% occurred during the first 5 days of hospitalization (cf fig. 1). The median hospitalization duration was 2 days [IQR 1, 5] when outcome was death, and 17 days [IQR 14, 21] when patients were discharged. Among the 63 children (≤ 5 years old) included, mortality was 52%. The 8% of pregnant women experienced a 50% mortality rate. On the 186/835 (22%) previously vaccinated patients, median delay between vaccination and positive RT-PCR was 8 days [IQR 5,12]. Mortality amongst vaccinated participants was 31%. Descriptors for standard of care and clinical and biological issues are generated.

Conclusions: Even with the development of specific treatment, lethality during this outbreak remains quite high. This feature highlights the paramount for optimizing standard of supportive care efforts, especially resuscitation procedures. In the cohort, several patients were managed with an optimized level for intensive care (e.g., oxygen, vasoactive drugs, point-of-care ultrasound and vital parameter monitoring), which might contribute to the overall decrease of mortality in our ETCs and in comparison with reports from West Africa outbreak. This effort needs to be evaluated for evolving decision-making procedures, insofar specific drugs and vaccine will not be the only support for saving more lives.

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Role of the gut microbiota in the anastomotic leakage after colorectal surgery

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Abstract third-party references: Supported by the Spanish Network for Research in Infectious Diseases (REIPI) and Instituto de Salud Carlos III.

Background: Colorectal cancer is one of the most frequent oncologic processes with an incidence of 1.8 million new cases every year. Despite surgery is the selective treatment, it presents serious complications such as anastomotic leakage that leads to septic shock, multiple organ failure, and death. Factors that could predict this complication has not yet been described, however, several recently studies suggest that gut microbiota may be involved.

Materials/methods: A total of 108 patients diagnosed of colorectal cancer give their informed consent and contributed each one with a fecal sample and biopsies (proximal and distal tissue of the tumor) after surgical resection. Bacterial composition was determined by PCR amplification and sequencing of the V3-V4 region (16S rDNA) using a MiSeq platform (Illumina). Bioinformatics was performed using QIIME2. Differential abundance was assessed by LEfSe. The indexes for calculating the Alpha-diversity were Chao1, Shannon and Faith-phylogeny, while, for Beta-diversity were Bray-Curtis and UniFrac distances.

Results: Only 10 out of the 108 patients developed anastomotic leakage (10.8%). Microbiota analysis showed no statistical significance for Alpha-diversity in any of the samples, showing that gut microbiota near the tumor (both proximal and distal) and feces were equally diverse in patients with and without anastomotic leakage. Regarding Beta-diversity, Bray-Curtis index showed a statistical significance in the proximal (p=0.033) and distal (p=0.016) tissue between patients with and without anastomotic leakage. However, when phylogenetic distances were taken into account by Weighted and Unweighted UniFrac, no significant differences were found. LEfSE analysis (Figure 1) decipher that in proximal tissue there was an increase of Enterobacteriaceae in patients with anastomotic leakage. In distal tissue samples, also an Enterobacteriaceae enrichment was linked to anastomotic leakage, whereas Bifidobacterium and Faecalibacterium seems to protect from developing this complication. Microbiota from feces only showed an increase of Firmicutes in patients with no anastomotic leakage.

Conclusions: A particular microbiota profile, and probably the expression of particular virulence factors, may be related to the development of anastomotic leakage more in concrete with the presence of Enterobacteriaceae. Additionally, Bifidobacterium and Faecalibacterium may have a protective character probably related to their metabolism and the production of short chain fatty acids.

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Microbiological Point-of-Care analysis of endotracheal aspirate from intubated patients admitted to the intensive care unit

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Background: The paraclinical diagnosis of lower respiratory tract infection (LRTI) still relies heavily on culturing of respiratory tract samples, which are quite insensitive, hence resulting in false negative response. There is a growing market for commercially available multiplex polymerase chain reaction (PCR) assays promising fast turnaround time (TAT) and high sensitivity towards a variety of common pathogens, which may improve antibiotic stewardship. The purpose of this study was to assess the applicability of the FILMARRAY® Pneumonia Panel Plus (PP) in the clinical setting of an Intensive Care Unit (ICU).

Materials/methods: Tests were performed on undiluted specimens from mechanically ventilated patients at the ICU on the first day of intubation. The FILMARRAY® Pneumonia Panel Plus was used to test 76 endotracheal aspirate samples frozen in a biobank. Comparison with pathogen detection using conventional microbiological methods (CMM) was performed, and concordance rates between methods was assessed taking into account incomplete investigation by conventional methods. Evaluation on the usage of antibiotics was done retrospectively by a clinical microbiologist and an Intensive Care physician assessing a potential change in treatment based on FILMARRAY® results and patient status.

Results: In 42 (55.3%) samples PP and CMM are in full concordance. Additional findings by CMM were seen in 2 (2.6%) samples. Additional findings by PP were seen in 31 (40.7%) samples. Complete discrepancy between methods were seen in 1 (1.3%) sample. In 2 samples, PP detected methicillin resistant Staphylococcus Aureus, even though CMM showed methicillin sensitive Staphylococcus Aureus. By CMM, extended virus panel TAT was a median of 111.28h. TAT for culture and susceptibility a median 52.82h. PCR for atypical 40.04h. PP TAT was estimated 2h, making de-escalation possible in 35 (46.1%) patients, among these discontinuation of macrolide would have been possible in 24 (31.6%).

Conclusions: The FILMARRAY® Pneumonia Panel Plus may offer valuable information, however it detected several additional pathogens compared to conventional microbiological methods and the interpretation of results appears difficult in terms of disease causality and antibiotic resistance. The biggest impact may be on fast-delivered negative results, which resonated in the possible discontinuation of macrolide. Even though our study showed potential for the FILMARRAY® Pneumonia Panel Plus, further investigations on clinical effect should be performed prospectively.

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Abstract 6312

**Do bacterial growth conditions affect antibiotic resistance evolution?**

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**Background:** It is well known that sub-inhibitory levels of antibiotics are a selector for antibiotic resistance genes in bacterial species. However, it is unclear whether varying levels of sub-inhibitory concentrations have an effect on natural selection for resistance mutations. Different strengths of selection pressure could lead to a different spectrum of resistance mutants arising, with different effects on bacterial fitness [benefits and costs of the mutations]. This will affect how the bacterial population evolves during exposure to antibiotics, and when the antibiotic is removed. The effect of the growth medium on the resistance rate and costs and benefits is also not well established. These could also be very different in different environments. *In vitro* tests are regularly performed in standard laboratory media; however, it is unclear whether resistance rates would vary in a more clinically realistic model. We hypothesize that evolution in standard lab media such as Mueller Hinton Broth may lead to different resistance levels when compared with bacteria evolved in artificial cystic fibrosis sputum.

**Materials/methods:** We grew two species of pathogenic bacteria which infect the lungs of people with CF, in the presence of colistin in either Mueller Hinton broth or artificial sputum [ASM]. First, we assessed if there was a difference in the minimum inhibitory concentrations [MICs] between the different media used. Following this, the clinical isolates were evolved in the various media with increasing concentrations of antibiotic.

**Results:** Evolution in both MHB and ASM led to increases in MIC. Although isolates evolved in ASM survived at higher concentrations of antibiotic than those grown in MHB, the MIC for MHB was double that for ASM.

**Conclusions:** The data suggests that the growth conditions can have an effect on the resistance phenotype and potentially genotype of bacteria. Further tests will assess the effects of phenotypic tolerance and evolved, genetic resistance. Whole genome sequencing will be used to assess whether there are any differences in the mutations formed from the bacterial growth conditions.

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**Abstract 6313**

**A prolonged incubation time is not needed for cultures obtained from acute periprosthetic joint infections**

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**Background:** A prolonged incubation time (i.e. 10-14 days) is generally recommended for diagnosing periprosthetic joint infections (PJIs). However, in literature, no distinction is made between acute and chronic infections. In this study we investigated whether time to positivity differs between acute and chronic PJIs.

**Materials/methods:** All patients that underwent surgical debridement or revision of the prosthesis between November 2015 and February 2019 were retrospectively evaluated. Synovial fluid and an average of 5 periprosthetic tissue samples were obtained during surgery and the prosthetic implant and/or mobile components were sent for sonication. Sonication fluid and synovial fluid was incubated in blood culture bottles, while tissue cultures were directly incubated on culture plates and in fastingidious broth. All cultures were incubated for 9-14 days. Acute and chronic PJIs was diagnosed according to the criteria proposed by the Musculoskeletal Infection Society (MSIS).

**Results:** A total of 62 patients were analyzed, including 21 with an acute PJI (incl. 36 isolates) and 41 with a chronic PJI (incl. 52 isolates). In acute PJIs, all isolates grew within 4 days [Figure 1A], while this took 11 days for chronic PJIs [Figure 1B]. *Staphylococcus aureus*, Gram negative rods, enterococci and streptococci all grew within 2 days, while *Cutibacterium acnes*, Gram positive rods and coagulase negative staphylococci grew within 9 days. Sonication fluid incubated in blood culture bottles showed the highest culture yield and shortest time to positivity for chronic PJIs, but no difference was observed for acute PJIs [Figure 1C-D].

**Conclusions:** In contrast to cultures from chronic PJIs, acute PJIs do not need a prolonged incubation time and no clear time to positivity benefit is observed for sonication in this patient category. These results need to be confirmed in a larger cohort of patients.

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Genomic investigation of *Klebsiella pneumoniae* complex isolates recovered from pigs and humans in Thailand

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**Background:** *Klebsiella pneumoniae* complex members are common bacteria living in animal and human guts and in natural environments. Antibiotic-resistant *Klebsiella* species and hypervirulent *Klebsiella* species have been reported as the causative agent of human infections worldwide. Here, we report on the characterization of *K. pneumoniae* complex isolates from healthy pigs and humans in Thailand based on their antibiotic resistance, virulence, and genetic relatedness.

**Materials/methods:** *K. pneumoniae* complex species were isolated from rectal swabs of pigs (97-pooled samples) and human feces (134 humans) from 97 farms in Thailand by plating out on SCAI agar. Antibiotic susceptibility testing using disc diffusion (EUCAST) and Illumina whole-genome sequencing (WGS) were performed. Antibiotic resistance genes, virulence genes, and plasmids were extracted from WGS data. Genomic typing was assessed and compared with public core genome multi locus sequence typing (cgMLST) schemes.

**Results:** Among the 231 *K. pneumoniae* complex isolates, two mcr positive strains (ST290/mcr-1 and ST761-1LV/mcr-8) and one ESBL-producing strain (ST500/blaCTX-M-3) were isolated from pigs. MLSTs of our 231 strains showed high genetic diversity, comprising 175 different STs and 89 K-loci. However, some STs were shared between pigs and humans. ST111-2LV the most prevalent ST was found from both hosts suggesting the possibility of transmission between pigs and humans living in the same district area.

**Conclusions:** Our data demonstrate high genetic diversity and low level of ESBL and colistin resistance among *K. pneumoniae* complex isolates from pigs and humans in Thailand. ST111-2LV was found in both hosts in the same district area indicating zoonotic transmission of this particular ST.

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Clinical evaluation of FASTinov kits for ultra-rapid antimicrobial susceptibility testing directly from positive blood cultures

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Abstract third-party references: This project received funding from the H2020 FTI pilot 2016, project number 730713 "FAST-bact". A novel fast and automated test for antibiotic susceptibility testing for Gram positive and Gram negative bacteria.

Background: Bloodstream infections (BSI) remain a major public health concern with high rates of morbidity and mortality. Antimicrobial susceptibility testing (AST) of microorganisms causing BSIs is crucial for optimal antimicrobial therapy. Current conventional methods require sub-culture of positive blood cultures (BCs) to begin AST, taking nearly 2 days for definitive results. New approaches can reduce time-to-result avoiding this sub-culture but are still growth-based taking at least 6 hours to report. The objective of this work was to evaluate the clinical performance of the Fastinov\(^\circ\) kits (Porto, Portugal), an ultra-rapid AST assay performed directly on positive BCs, based on flow cytometry analysis.

Materials/methods: An internal validation was performed using spiked BC with bacteria with well-characterized resistance phenotypes. Two kits were evaluated, one for Gram-negative (Enterobacterales, Pseudomonas and Acinetobacter) and another for Gram positive (Staphylococcus and Enterococcus) organisms by testing primary drugs used to treat sepsis. In parallel a proof-of-concept in an external clinical environment was performed at Ramon y Cajal hospital in Madrid (Spain), using patients’ BC. A total of 480 positive BC (257 Gram-negative and 223 Gram-positive bacteria) were included with 98 patient samples (64 Gram-negative and 34 Gram-positive). After extracting microorganisms from positive BC, bacteria were incubated for 1 hour at 37ºC with antibiotics together with fluorescent probes followed by flow cytometric analysis with CytoFLEX (Beckman Coulter) platforms. Both CLSI and EUCAST criteria were followed and a dedicated software used to produce a report. The obtained phenotype, as well as ESBL detection and screening for the presence of AmpC and carbapenemases, were compared with reference methods and categorical agreement (CA), quantification and classification of errors determined.

Results: The overall CA for the FASTgramneg panel was 95.9% and 95.6% respectively for EUCAST and CLSI. The FASTgrampos panel CA was 98.4% and 98.2% respectively for EUCAST and CLSI. A maximum of 2/266 very major errors was found for FASTgrampos and 8/872 errors for FASTgramneg, mainly due to beta-lactam-beta-lactamase inhibitors combination.

Conclusions: FASTinov\(^\circ\) kits represent an alternative for direct ultra-rapid AST of Gram-negative and Gram-positive bacteria in bloodstream infections showing time-to-result <2 hours versus nearly 2 days with current methodology.

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Abstract 6320

**An updated analysis of the burden of fungal diseases in Uganda**

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**Background:** It is of utmost importance to monitor any change in the epidemiology of fungal diseases that may arise from a change in the number of the at-risk population or availability of local data. We sought to re-evaluate the incidence and prevalence of major fungal diseases in Uganda.

**Materials/methods:** Using the Leading International Fungal Education methodology, we reviewed published data on fungal diseases and drivers of fungal diseases in Uganda. Regional or global data were used where there is no Ugandan data.

**Results:** With a population of ~45 million, overall we estimate annual burden of severe fungal diseases at 981,680 cases (2.2% of the population), excluding cases of tinea capitis. Estimates for the annual incidence of HIV-related life-threatening fungal disease include cryptococcal meningitis (17,859 cases), Pneumocystis pneumonia (4,962 cases in adults and 2,888 cases in children), oral candidiasis (29,772), oesophageal candidiasis (79,924 cases), and invasive pulmonary aspergillosis (920 cases). We estimate 656,340 cases of recurrent vulvovaginal candidiasis and 6,084 cases of fungal keratitis annually. The overall prevalence of post-tuberculosis chronic pulmonary aspergillosis is 8,905 cases (annual incidence of 1,291 cases) and the burden of fungal asthma at 171,863 cases (allergic bronchopulmonary aspergillosis, 74,079 cases and severe asthma with fungal sensitisation, 97,784 cases). Candida peritonitis and candidaemia are estimated at the rate of 0.8/100,000 (343 annual incidence) and 5/100,000 (2,287 annual incidence), respectively. The neglected tropical fungal disease mycetoma is uncommon with an annual incidence rate of 0.3/100,000 (79 cases annually).

**Conclusions:** Fungal diseases affect a significant proportion of Ugandans every year. Tuberculosis and HIV remains the most important predisposition to fungal disease in this population. The burden of fungal diseases in Uganda has remained stable for the past five years, calling for accelerated preventive, diagnostic and therapeutic interventions for the management of these diseases.

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Investigation of skin microbiota reveals Mycobacterium ulcerans-Aspergillus sp. trans-kingdom communication

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Background: Mycobacterium ulcerans secretes a series of non-ribosomal-encoded toxins known as mycolactones that are responsible for causing a disabling ulceration of the skin and subcutaneous tissues named Buruli ulcer. The disease is the sole non-contagious mycobacteriosis among the three most common mycobacterial diseases in humans. Direct contact with contaminated wetlands is a risk factor for Buruli ulcer, responsible for M. ulcerans skin carriage before transcutaneous inoculation with this opportunistic pathogen.

Materials/methods: Initially, we used molecular biology to study the possibility of asymptomatic skin carrying of M. ulcerans in farmers in Burkina Faso using two IS2404 IS2606 insertion sequences and the Kr-b genes specific to M. ulcerans. In a second step, we analysed the bacterial and fungal skin microbiota in individuals exposed to M. ulcerans in Burkina Faso. Then, we cultured the skin microbiota of asymptomatic M. ulcerans carriers and negative control individuals, all living in the region of Sindou.

Results: We showed that M. ulcerans-specific DNA sequences were detected on the unbreached skin of 6/52 (11.5%) asymptomatic farmers living in Sindou versus 0/52 (0%) of those living in the non-endemic region of Tenkodogo. A total of 84 different bacterial and fungal species were isolated, 21 from M. ulcerans-negative skin samples, 31 from M. ulcerans-positive samples and 32 from both. More specifically, Actinobacteria, Aspergillus niger and Aspergillus flavus were significantly associated with M. ulcerans skin carriage. We further observed that in vitro, mycolactones induced spore germination of A. flavus, attracting the fungal network.

Conclusions: These unprecedented observations suggest that interactions with fungi may modulate the outcome of M. ulcerans skin carriage, opening new venues to the understanding of Buruli ulcer pathology, prophylaxis and treatment of this still neglected tropical infection.

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Abstract 6324

**Hepatic phaeohyphomycosis due to Pleurostoma hongkongensis, a novel species**

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**Background:** The genus *Pleurostoma* houses Phialaphora-like fungi which possess a creamy white-to-pale yellow colony appearance with no diffusible pigment and produce small-to-large, subspherical-to-allantoid conidia at the phialide tips. These fungi are mainly found in soil, woody plants, and sewage. Within this genus, *P. repens*, *P. richardsiae*, and *P. ootheca* have been reported to cause phaeohyphomycosis in humans. In this study, we isolated a novel dematiaceous mould pathogen, HKU44T, from a 65-year-old Chinese male patient. Preliminary morphological analysis and ITS sequencing showed that this fungus belonged to the genus *Pleurostoma* but its exact species identity could not be ascertained.

**Materials/methods:** The clinical history of the patient was reviewed. The colony and microscopic morphologies of strain HKU44T was examined for its phenotypic characteristics. The ITS, 18S rDNA, 28S rDNA, and β-tubulin gene of HKU44T, along with an additional 28 strains of the species *P. richardsiae*, *P. ochraceum*, *P. repens*, and *P. ootheca* were amplified by conventional PCR and sequenced. The DNA sequences were then compared with each other by pairwise alignment and the phylogenetic relationship of HKU44T and other *Pleurostoma* species were inferred using the maximum likelihood method.

**Results:** Histological examination of the abscess wall biopsy collected from the patient showed numerous fungal hyphae. HKU44T, the mold recovered from the abscess sample, exhibited typical phenotypes shared by *Pleurostoma* species, including hyaline-to-pale brown colonies as well as branched, septate hyphae and subspherical, hyaline-to-brown conidia. Pairwise alignment of the ITS sequence of HKU44T and those of the type strains of *P. richardsiae*, *P. ochraceum*, *P. repens*, and *P. ootheca* showed 87.32%, 86.49%, 88.57%, and 88.87% similarities, respectively. Phylogenetic trees of all the four DNA markers showed that HKU44T is phylogenetically distinct from all four *Pleurostoma* species, although it is most closely related to *P. ootheca* and *P. repens*. The results suggested that HKU44T is a novel species of the genus *Pleurostoma*, which we propose to name it *Pleurostoma hongkongensis* sp. nov.

**Conclusions:** A novel fungal pathogen, *Pleurostoma hongkongensis*, was discovered from the subhepatic abscess of a liver failure patient in Hong Kong, and this fungus is capable of causing invasive phaeohyphomycosis.

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Abstract 6326

**Evaluation of Genomera CDX system for influenza and respiratory syncytial virus infections**

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**Background:** Performances comparison [Concordances (κ), sensitivity (Se), specificity (Sp)] of RT-qPCR assays detecting major viral respiratory pathogens on the GenomEra®CDX system, using the GenomEra® FluA/B+RSV assay (Influenzavirus (IAV/IBV), or Respiratory Syncytial virus (RSV)) to our standard of care process (Allplex Respiratory; Seegene).

**Materials/methods:** Prospective assays on fresh samples (n = 299; 116 nasal swabs (NS), 129 combined nasal and throat swabs (NTS) and 54 nasopharyngeal aspirates (NPA)) collected for 2018 - 2019 winter season, from patients hospitalized in the University Hospital of Poitiers, France. Samples with discrepant results were tested with a 3rd method: a real time PCR method (Rgene, Biomérieux®). Our referential consider concordance of ≥2 molecular testing specific for a specific viral target (including the result of the third method if needed). Inclusivity, cross-reactivity and reproducibility testing were associated to analyses on clinical samples.

**Results:** Performances could be obtained for each viral target (no IBV-positive sample during the epidemics). On NS, Se, Sp, and κ were: i) 100%, 95% and 0.89 for IAV; ii) undetermined, 97%, and undetermined for IBV; iii) 100%, 100%, and 0.91 for RSV. On NTS, performances were: i) 100%, 99% and 0.96 for IAV; ii) undetermined, 98% and undetermined for IBV; iii) 95%, 100% and 0.92 for RSV. On NPA performances were: i) 86%, 100% and 0.91 for IAV; ii) undetermined, 100% and undetermined for IBV; iii) 97%, 100% and 0.92 for RSV.

**Conclusions:** With 1 false negative and 5 false positive (including one IBV) results, performances for Influenza detection are very good but remain perfectible. With 1 false negative result, performances for RSV detection are very impressive.

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Abstract 6327

Cutaneous lesions due to *Staphylococcus aureus* in inflammatory bowel disease patients undergoing anti-TNFα treatment: molecular characteristics and strains comparison in different niches

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**Background:** *Staphylococcus aureus* is a common inhabitant of the skin microflora and colonizes the nares and other human mucosa. This is also an opportunistic bacterium capable of causing a wide range of severe diseases when it gains access to underlying tissues. Among patients with inflammatory bowel disease (IBD), those treated with anti-TNFα therapy present frequently particular cutaneous lesions associating nasal and retroauricular fissures, alopecia and the presence of *S. aureus*. The aim of this study was to describe the molecular characteristics of *S. aureus* isolated from these skin lesions and at different body sites (anterior nares, post-auricular, umbilical and axillary, anal throat and mouth) in this population.

**Materials/methods:** IBD patients undergoing anti-TNFα therapy and presenting cutaneous lesions were included between January 2018 and June 2019 in Department of Dermatology in Montpellier University Hospital (France). “Control” patients with IBD treated with anti-TNFα therapy, but without any cutaneous wound were also included. A screening of *S. aureus* in the lesions and in different mucosa niches was performed. After identification by Maldi-tof (Vitek MS⁶), all the isolates were analyzed using DNA micro-arrays (Clondiag⁷) and MLST (https://pubmlst.org).

**Results:** Twenty-two IBD patients with cutaneous lesion and 42 controls were included. The IBD patients with lesions harbored a significantly higher *S. aureus* colonization rate (15, 68.2%) vs controls (10, 23.8%) (p<0.001). Among these patients, 13 had positive *S. aureus* cultures in cutaneous lesions samples (59.1%), with 12 co-colonized in anterior nares (92.3%). Eighteen isolates, including different morphotypes, were definitively collected. All of them were methicillin-sensitive and belonged to 9 different clonal complexes (CC), with a predominance of STS-MSSA (50%). Eleven out of 13 patients (84.6%) had similar clones in lesion and at least one niche (mainly the anterior nares).

**Conclusions:** The role of *S. aureus* nasal colonization in IBD patients with anti-TNFα medication seems particularly important in the development of cutaneous lesions. Screening of this nasal carriage before treatment could be considered.

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Latent tuberculosis infection among household contacts of pulmonary tuberculosis cases in Nairobi, Kenya

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Background: Tuberculosis (TB) is a major health problem in sub-Saharan Africa and other developing countries including Kenya, which is ranked among the top 30 countries with the highest burden TB. Household Contacts (HHCs) of Pulmonary Tuberculosis (PTB) patients have a higher risk of LTBI. However, its prevalence and risk factors among adults living with PTB patients are poorly documented in Kenya.

Materials/methods: An analytical cross-sectional study was conducted to establish the prevalence and risk factors of LTBI in a cohort of adult HHCs of active PTB patients who were seeking health care services in a per-urban public district hospital in the Kenyan capital, Nairobi. Informed consent was obtained. A structured questionnaire was used to capture socio-demographic data of the study participants and thereafter 3 blood samples collected by venipuncture from each HHCs directly into the blood collection tubes provided in the QuantiFERON®-TB Gold In-Tube kit (QFT-GIT) for Interferon-gamma release assays (IGRAs).

Results: A total of 166 PTB patients yielded 175 adult HHCs of whom 29.7% (52/125) were males and 70.3% (123/125) were females. A majority of HHCs (65.7% [115/175]) lived in a single-room house with the patient and (37.7% [66/175]) were in the age group 30-39-years. The overall prevalence of LTBI was 55.7%, peaking among spouses of the patients (70.0% [14/20]) and the 30-39 year age group (63.5% [42/66]). Potential risk factors for LTBI included cohabiting with a TB patient for 8 to 12 weeks [OR= 3.6 (0.70-18.5), p=0.107], being a spouse of the patient [OR=2.0 (0.72-5.47), p=0.173] and sharing a single room with the patient [OR=1.58 (0.84-2.97), p=0.158].

Conclusions: There is an increasing awareness of the problem LTBI poses to HHCs of PTB patients. In Kenya, however, data on LTBI is mainly anecdotal, which hinders its active management. Overall, it was evident that LTBI is a common yet neglected problem for HHCs, with factors such as age, relation to TB patients, and the length of time spent cohabiting with or caring for TB patients leading to repeated exposure and thus the risk of developing LTBI. The findings demonstrate the need for targeted contact-screening programs in high TB transmission settings.

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Abstract 6332

Integrated diagnosis by metagenomic and host transcriptomic of pulmonary infection in solid organ transplant patients

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Background: Pulmonary infection is a common complication after solid organ transplantation but diagnosis can be difficult because symptoms may be attenuated and the presence of microorganisms is sometimes difficult to interpret (infection, commensalism…). In this context, developing host-based exploration assays associated to broad spectrum micro-organisms detection methods may help to better understand, manage and treat infection/disease. Our aim is to evaluate a combined approach which allows both infection diagnosis by metagenomic and host transcriptomic profile determination in the same single assay in solid organ transplant (SOT) patients.

Materials/methods: Bronchoalveolar lavages were collected from 13 patients (12 lung and 1 heart transplant patients). Conventional bacterial and virological diagnostic methods were performed according to the standard recommendations. In parallel, accredited routine metagenomic next-generation sequencing MetaMIC (mNGS) was used and combined a DNA/RNA extraction protocol adapted for all types of pathogens and human, DNA/RNA libraries preparation with Nextera XT and Stranded Total RNA (Illumina), and sequencing on NextSeq500 (Illumina). Metagenomic and transcriptomic data were analysed using a dedicated software (MetaMIC). The first gave a final automatic report of presence of micro-organisms while the second provided a transcriptome profiling identifying over/underexpressed genes in different patients.

Results: Among the patients, 9/13 were considered infected by at least one micro-organism. Conventional microbiology and mNGS were fully concordant in 9 cases (4 negative and 5 positive) and partially discordant in 4 cases (2 Streptococcus pneumoniae found only by mNGS and 2 low viral load CMV found only by PCR). Transcriptomic analysis revealed a different host transcriptional signature in infected vs uninfected patients and between CMV DNA positive and CMV DNA negative patients. Ontology analysis with over/under expressed genes in infected patients revealed activated immunity pathways.

Conclusions: The mNGS technique has demonstrated its ability to explore both hosts and pathogens in a single analysis. Thus, it offers an unprecedented opportunity to explore the host-pathogen relationship, to better understand the physiopathology of infections, while allowing the detection of microorganisms. Integrating unbiased pathogen detection and host transcriptomic may be a promising alternative to pathogen-based diagnostics, in order to understand and manage infectious complications in SOT patients.

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Abstract 6336

**Effectiveness and cost-effectiveness of antimicrobial stewardship programmes in French acute care hospitals**

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**Background:** Multidrug resistant (MDR) infections represent a growing burden for patients and healthcare system. Antimicrobial stewardship programs have been implemented to improve antibiotic use to prevent the expansion of MDR. The objective of this study was to assess the effectiveness and cost-effectiveness of different antimicrobial stewardship (AMS) strategies in a hospital setting.

**Materials/methods:** We used a decision tree incorporating a Markov model to simulate the trajectory of patients admitted to hospital for a urinary tract infection. We evaluated three AMS strategies: Strategy 1 (S1) implemented on day 1, at admission, strategy 2 (S2) implemented on day 2 or 3, when antibiotic treatment is reassessed, while strategy 3 (S3) combined S1 and S2. These strategies were compared to a baseline scenario (BSL), with no ASP intervention. Effectiveness was assessed by the number of life-years (LY) gained. An incremental cost-effectiveness ratio (ICER) less than French annual gross domestic product per capita was considered cost-effective (30,100€).

**Results:** All AMS strategies were more expensive than the baseline scenario. S1 and S3 were associated with 310 LY gained when compared to BSL, while S2 did not lead to additional LY gained. S2 and S3 were dominated by S1: less effective and more expensive for S2; equally effective and more costly for S3. ICER comparing S1 to BSL was of 2169€/LY gained. Probabilistic sensitivity analyses indicated that 91% of the ICER comparing S1 to baseline were under 5000€/LY gained.

**Table 1: Cost-effectiveness analysis results**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Costs (undiscounted)</th>
<th>Costs (discounted)</th>
<th>Effectiveness (discounted)</th>
<th>Incremental costs (ΔC)*</th>
<th>Incremental effectiveness (ΔE)*</th>
<th>ICER**</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSL scenario</td>
<td>52 753 232 €</td>
<td>48 423 270 €</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Strategy 2</td>
<td>53 400 376 €</td>
<td>48 971 016 €</td>
<td>0</td>
<td>- €</td>
<td>0</td>
<td>(Dominated)</td>
</tr>
<tr>
<td>Strategy 1</td>
<td>53 490 443 €</td>
<td>49 095 714 €</td>
<td>310</td>
<td>672 444 €</td>
<td>310</td>
<td>2 169 €</td>
</tr>
<tr>
<td>Strategy 3</td>
<td>54 082 841 €</td>
<td>49 594 340 €</td>
<td>310</td>
<td>498 626 €</td>
<td>0</td>
<td>(Dominated)</td>
</tr>
</tbody>
</table>

*compared to the previous undominated strategy **compared to BSL

**Conclusions:** Implementing ASP in acute-care setting is effective and cost-effective, and investing in ASP interventions targeting patients at admission could be more efficient.

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Abstract 6339

Whole genome sequencing of bloodstream isolates of *Staphylococcus aureus* reveals prolonged transmission chains within neonatal intensive care units

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**Background:** *Staphylococcus aureus* is one of the commonest agents of nosocomial bacteremia. Outbreaks in neonatal intensive care units are frequent, typically identified if the organism is methicillin-resistant or produces unusual clinical syndromes. To identify potential transmission of this organism, we have completed whole genome sequencing (WGS) of bloodstream isolates of *S. aureus* from across Scotland.

**Materials/methods:** 1545 bloodstream isolates of *S. aureus* from across Scotland from the years 2015 to 2017 were collected, with complete coverage of isolates from the Greater Glasgow area. WGS using the Illumina platform was performed for all isolates. Single-nucleotide polymorphisms (SNPs) in the core genome were identified using SMALT and VarScan software. A threshold of 50 SNPs or fewer was used to identify highly related strains.

**Results:** We found 150 pairs of isolates with 50 or fewer pairwise SNP differences. Associated clinical data identified persistent transmission chains within neonatal intensive care units; we focused on those within areas where all bloodstream isolates had been collected within the time frame studied. In one unit over a 20-month period, we discovered 10 neonates with bloodstream *S. aureus* ST30 infection with fewer than 50 SNP differences. 9 of the isolates were methicillin sensitive; one isolate acquired methicillin resistance. For 8 of these infections the patients had overlapping hospital admissions but for 2 patients there was no overlap, and the sequential differences in SNPs could not be explained by simple transmission from patient to patient, strongly suggesting intermediate carriers of this strain or environmental contamination. None of these cases were flagged as possible outbreaks. Similar prolonged transmission chains of strains of methicillin-sensitive *S. aureus* were found in other neonatal intensive care units.

**Conclusions:** The high resolution of WGS allowed us to identify previously unsuspected transmission of *S. aureus* strains producing bloodstream infection within neonatal intensive care units within Scotland. Carriage by patients, carers and staff seem the most likely source, although environmental contamination cannot be excluded. Routine WGS of bloodstream isolates of *S. aureus* within neonatal intensive care units would allow early identification of similar transmission events and thus allow measures to prevent further transmission to be instituted.

**Circulation of ST30 in a hospital in Scotland between years 2015 and 2017**

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Abstracts 2020

Abstract 6342

**Evaluation of carbapenem-resistant *Enterobacteriaceae* treatment outcomes in a quaternary hospital in the United Arab Emirates**

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**Background:** Carbapenem-resistant *Enterobacteriaceae* (CRE) infections are on the rise and they’re internationally known to be among the major public health threats associated with high rates of mortality exceeding 50% in some reports. Current clinical evidence for treatment guidance and options and their possible outcomes are limited. This study aims to evaluate the efficacy of different treatment options for CRE infections.

**Materials/methods:** This study is an observational retrospective chart review study from January 2015 to December 2018 aiming to investigate the outcomes of different CRE therapy. This study was conducted at Cleveland Clinic Abu Dhabi, Abu Dhabi, UAE. Data of all adult patients with at least one culture positive for CRE infection were electronically extracted from January 2015 until December 2018. Ambulatory patients with CRE isolates were excluded from the data. Patient demographics, colonization with CRE, risk factors for CRE, as well as different antimicrobial regimens and their treatment outcomes were collected. Descriptive statistics were used to analyze the data.

**Results:** A total of 96 cases with CRE were included for the analysis. Twenty-seven outpatient isolates were excluded from the study. Sixty-nine cases were included for the final analysis. Colistin monotherapy was used in 28.9% (20/69). Seventy-one percent (49/69) of the patients received combination therapies with other antimicrobial agents such as colistin-carbapenem (9/49), colistin-ceftazidime/avibactam (14/49), colistin-tigecycline (12/49) and other regimens (14/49). Re-occurrence of infection within 2 weeks was observed in 23% (16/69) of all cases. The overall 30-day mortality was 50% (10/20) among the monotherapy treated patients and the among the patients who received combinations treatments mortality was up to 26.5% (13/49).

**Conclusions:** Over the past few years CRE infections significantly increased and it poses a threat to public health. There hasn’t been an ultimate guideline for the treatment of CRE Infections, but our study suggests that the combination antimicrobial therapies may be associated with lower mortality rates than monotherapy.

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Abstract 6348

**Probability of target attainment by conventional pharmacokinetic/pharmacodynamic targets is overestimated in obese patients receiving linezolid and meropenem**

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**Background:** Clinical pharmacokinetic/pharmacodynamic (PK/PD) targets represent a proxy for exposure at the infection site and are typically based on studies in non-obese patients. Due to lack of alternatives, they are often also employed in probability of target-attainment (PTA) analysis in various other populations, including the obese. Since drug penetration into the target-site might differ, it remains unclear if these targets are valid for obese patients. This analysis aimed at evaluating the adequacy of PK/PD targets in obese patients based on PTA analysis.

**Materials/methods:** Previously, two nonlinear mixed-effects PK models had been developed based on plasma and target-site data obtained via microdialysis from 15 obese (BMI mean±SD=49±11 kg/m\(^2\)) and 15 non-obese patients (BMI mean±SD=24±2 kg/m\(^2\)), receiving a standard 30-min infusion of 1000 mg meropenem and 600 mg linezolid before abdominal surgery [1,2]. Here, Monte-Carlo simulations were performed for concentration-time profiles in plasma and at target-site for obese and non-obese patients (n=1000, NONMEM version 7.4.3). PTA was calculated for the PK/PD targets "unbound concentrations exceed MIC=2 mg/L during 95% of dosing interval" (meropenem) and "AUC/MIC≥80 for MIC=4 mg/L" (linezolid) in plasma and target-site.

**Results:** In obese versus non-obese patients PTA increased for meropenem whereas PTA decreased for linezolid (Table 1). For both drugs, the difference in PTA between plasma and target-site was larger for obese compared to non-obese patients (relative reduction, meropenem: -65% versus -55%, linezolid: -97% versus -71%), reflecting population dependent differences in the relevant exposure at target-site.

**Conclusions:** The discrepancy between PTA in plasma and target-site for obese and non-obese patients indicated altered penetration into target-site and therefore inadequacy of conventional PK/PD targets in obese patients leading to overestimated PTA in plasma. Thus, there is the necessity to develop new targets for obese patients which can then be investigated in clinical studies.


**Table 1:** Probability of target-attainment in obese versus non-obese patients for meropenem and linezolid for the standard dosing regimens.

<table>
<thead>
<tr>
<th></th>
<th>Meropenem</th>
<th>Linezolid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Obese</td>
<td>Non-obese</td>
</tr>
<tr>
<td>Plasma</td>
<td>34%</td>
<td>22%</td>
</tr>
<tr>
<td>Target-site</td>
<td>12%</td>
<td>10%</td>
</tr>
</tbody>
</table>

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Abstract 6349

Exploring social links and networks of communication in relation to infection prevention and control and antibiotic stewardship across surgical specialties in South Africa

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Background: Cultural differences exist between medical and surgical specialties that determine antibiotic prescribing outcomes, which require contextually-fit interventions. We investigated communication and team dynamics in relation to antibiotic stewardship (AS) and infection prevention and control (IPC) across two surgical teams at a tertiary hospital.

Materials/methods: Data were collected between May to November 2019, by direct observations of ward rounds, and face-to-face interviews with ward round participants. Field notes from observations and the transcripts of interviews were analysed using a grounded theory approach. Additionally, graphs (sociograms) were drawn plotting the content and flow of communication and the social links between individual participants. Sociograms enabled data triangulation and validation, and were a powerful visual illustration giving participants a global view of interactions and team dynamics on ward rounds.

Results: 60 hours of observations, including 1024 individual patient discussions were gathered. Seven patients and 60 healthcare professionals were interviewed. Discussions about antibiotic prescriptions and IPC are inconsistent across specialties and depend on the leadership style of the consultant. Communication flow is mainly between the consultants and registrars, and seldom includes input from the nurse, or wider team members. Although consultants facilitate key decision-making, individual leadership styles determine how decisions are assigned to team members. Mapping the communication flow using sociograms (Fig 1) demonstrates that whereas AS (e.g. initiating an antibiotic) and IPC (e.g. removing indwelling lines) actions are verbalised between the consultants and registrars, little direct communication occurs with nurses who are responsible for activating or maintaining decisions. Similarly, patients often remain passive recipients of care with little details about decisions on AS and IPC communicated with them.

Conclusions: AS and IPC discussions on ward rounds occur predominantly between consultants and registrars with little interaction noted with patients and nurses. Nurses activate decisions made on ward rounds and the lack of directed communication may result in delayed or missed AS and/or IPC interventions. The sociograms identified positive examples of practice and engagement with the wider team which can be developed into a model of effective communication on ward rounds in relation to AS and IPC.

Figure: Sociogram mapping communication flow on consultant round

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Integrated molecular surveillance of carbapenem-resistant Enterobacterales in Germany

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Background: Carbapenem-resistant Enterobacterales (CRE) are an important cause of healthcare-associated infections. Although prevalence in Germany is low, case numbers significantly increased over the past years. CRE are notifiable and national guidelines recommend sending all isolates to the national reference centre (NRC) for analyses of resistance mechanisms. Enzyme-mediated resistance by carbapenemases is particularly worrisome. To control their spread, routes of transmission need to be identified. The Robert Koch-Institute (RKI) and the NRC are joining their efforts for an integrated molecular surveillance (IMS) of CRE in Germany by combining microbiological and epidemiological data with whole-genome sequencing (WGS) to improve identification of otherwise undetected outbreaks.

Materials/methods: All CRE cases have to be notified to local health authorities and pseudonymized patient data is forwarded to the RKI. Likewise, the NRC receives CRE isolates from diagnostic laboratories with pseudonymized patient information. In a suspected outbreak, an IMS approach was tested: Available data sources were screened to detect irregular upsurges of carbapenemases (local, temporal or both). WGS was performed for selected isolates followed by core genome multi locus sequence typing (cgMLST) and SNP analysis. If microbiological analyses indicated clonal spread, related isolates were matched with notified cases and responsible health authorities were contacted for outbreak investigations.

Results: The NRC detected an increase of OXA-244-producing Escherichia coli from 2017 (n=32) to 2019 (n=101). WGS analyses revealed that 59 isolates belonged to a cluster of closely related E. coli ST38 of which 39 were successfully matched with notified cases from ten federal states throughout Germany. No specific age group was affected (0-90 years). Exploratory questionnaires showed two possible common exposures: stay/family abroad and previous hospital admissions. Investigations are currently ongoing to identify specific circumstances of strain acquisitions and transmissions.

Conclusions: Our use case for IMS shows that a combined approach of microbiological technologies and epidemiological methodologies can be applied to identify otherwise unrecognizable relations between CRE cases. IMS is likely to detect more suspected outbreaks in the future as the detection algorithms will be automatized and analyses’ methodologies continue to improve. Detailed outbreak investigations, as for OXA-244, will help identifying potential sources and deciphering common transmission routes.

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Abstract 6351

**Polyphasic validation of a nisin-biogel aiming at the control of canine periodontal disease**

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³Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Lisboa, Portugal

**Background:** Periodontal disease (PD) is one of the most frequent inflammatory diseases in dogs. It results from a complex interaction between the polymicrobial biofilm in the dental surface (dental plaque), and consequent host inflammatory response. Previous work showed that nisin incorporated in a guar-gum biogel (nisin-biogel) can inhibit and eradicate pre-formed canine oral enterococcal-biofilms, being a promising alternative for canine PD control[1]. This project aimed to evaluate if (1) the nisin-biogel maintained its antimicrobial activity in a simulated oral environment; if (2) it kept its antimicrobial activity during a 24-month storage at different temperatures; and if (3) its application is safe towards eukaryotic cells.

**Materials/methods:** To achieve the first objective, a previously characterized collection of 20 canine oral enterococci was used in a spot-on-lawn assay, to evaluate the antimicrobial activity of nisin and nisin-biogel in the presence of canine saliva. Nisin and nisin-biogel were diluted in filtered saliva, collected from healthy dogs, achieving nisin concentrations of 12.5, 25, 50 and 100μg/mL.

To evaluate the influence of storage in the nisin-biogel antimicrobial activity, 62.5, 250 and 500μg/mL solutions were stored in different conditions (-20ºC, 4ºC, room temperature and 37ºC) during 1, 3, 6, 9, 12, 15, 18 and 24 months, after which a spot-on-lawn assay was performed.

Finally, a cytotoxicity assay, using a Vero cell line and a canine primary small intestinal fibroblast cell culture, was performed to evaluate nisin and nisin-biogel safety in eukaryotic cells[2].

**Results:** The presence of saliva didn’t inhibit nisin antimicrobial activity, but this activity was expressed at higher concentrations. Regarding the influence of storage, a significant reduction (p<0.05) in nisin’s antimicrobial activity towards the canine enterococci under study was observed at 37ºC, over the 24-month period, regarding all solutions tested. The cytotoxicity assay revealed absence of toxicity (cell viability higher that 90%) of the nisin and nisin-biogel solutions with concentrations lower than 200μg/mL.

**Conclusions:** Nisin-biogel kept its antimicrobial activity in a simulated oral environment and after 24h-month storage at freezing, refrigeration and room temperatures, being safe to be applied to eukaryotic cells. This work supports nisin-biogel as a promising compound for the control of canine PD.

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Results from the 2019 antimicrobial susceptibility testing External Quality Assessment (EQA) exercise organised for EARS-Net participants

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Background: The United Kingdom National External Quality Assessment Service (UK NEQAS) for Microbiology provides the annual external quality assessment (EQA) for antimicrobial susceptibility testing to the EARS-Net. The aim is to assess and monitor the comparability of results between laboratories and countries and thus justify the pooling and comparison of routinely collected antimicrobial susceptibility test data across Europe.

Materials/methods: An analysis was carried out on the performance of participants in the EQA exercise. Participation was invited from 954 laboratories in 30 countries. Six organisms were distributed: Acinetobacter baumannii complex, Klebsiella pneumoniae, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa and Streptococcus pneumoniae. Participants’ results for identification and antimicrobial susceptibility testing were collated and assessed.

Results: Eight hundred and eighty-five participants returned results. The level of performance with these EQA specimens was generally satisfactory, with >80% consensus [at the ‘S, I, R’ level] with the intended results of 88.5%. Poor performance was noted for an isolate of E. coli expressing discrepant resistance to third generation cephalosporins, for an isolate of K. pneumoniae expressing resistance to amoxicillin-clavulanate. Furthermore, difficulties were again seen with categorising resistance to benzylpenicillin, cefotaxime and ceftriaxone in an isolate of S. pneumoniae which expressed intermediate susceptibility to third generation cephalosporins. Two challenging bug-drug combinations from the 2017 and 2018 EQAs were distributed again in 2019. Specimen 5586 contained a strain of S. aureus resistant to beta-lactam agents, clindamycin, linezolid and tetracycline. Resistance to linezolid was correctly reported by 84.1% of participants, a significant improvement compared to 16.3% participants in the 2017 EQA. Specimen 5587 contained a strain of S. pneumoniae with intermediate susceptibility to cefotaxime. Only 59.3% of participants reported a susceptible result, but this was also an improvement compared to 65.7% when the same isolate was distributed in 2019.

Conclusions: The overall concordance between participating laboratories was satisfactory. However, difficulties arose where there was borderline susceptibility to the agents and there were several areas where discrepancies were found in susceptibility testing. There was an improvement in performance for some challenging bug-drug combinations.

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Abstract 6354

**Faecal microbiota transfer in real-life is more effective for recidivant *Clostridioides difficile* infection than for highly resistant bacteria decolonisation**

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**Abstract third-party references:** Groupe Français de Transplantation Fécale, GFTF

**Background:** Fecal microbiota transplantation (FMT) is effective in recurrent *Clostridioides difficile* infections (rICD) for which antibiotic therapy have shown limitations. New indications are discussed such as the decolonization of emerging highly resistant bacteria (eHRB).

**Materials/methods:** Demographics, rICD characteristics, treatments and FMT procedures for patient who received FMT produced in a TMF center between 2016 and 2019 were collected prospectively. Donor screening was performed according to GFTF guidelines including BLSE and eHRB screening in donor’s feces. The FMT was performed according to the recommendations in rICD cases or as compassionate in case of eHRB decolonization. The final end point for evaluation was at 90 days after FMT. All patients consent for FMT procedures and for data collection.

**Results:** During the study period 41 independent FMT were performed for 32 patients. rICD was the main indication (81%) followed by compassionate eHRB colonization (19%). Median age was 68.3 years old [min=19-max=90] and sex ratio [F/M] was 0.88. Forty percent of the patients were immunocompromised, due to chemotherapy (8/13) or immunosuppressive therapy (5/13). Patients were hospitalized in medicine departments, intensive care unit (25) or hematology department (6%). FMT was mostly performed for second relapse (81%) to 5 relapses (3%). They had received 1 FMT (88%), two (12%) or three (3%) independent FMT. FMT was administered through oral route using capsules (72%), upper way (gastrostomy or nasogastric tube (25%) and one per coloscopy (3%). All FMT were performed with anonym donor frozen feces following pre-FMT antibiotherapy (vancomycin (77%)). For eHRB decolonization no antibiotics were used. Bowel lavage using classic colic preparation was performed the day before FMT. rICD cure was obtained in 85% after a unique FMT. There was no difference in terms of route, pre-FMT antibiotic regimen, FMT route or immunocompromised status, respectively.

**Conclusions:** FMT is a highly effective therapy for rICD including in patients with numerous risk factors for ICD relapse. FMT was safe in our study with no side effects in particular no bacteremia, no death and no evidence for resistant bacteria transmission. In contrast in real life FMT for eHRB decolonization in compassionate use was not effective with 100% of failure.

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Comparative metabolomics of Pseudomonas aeruginosa in response to polymyxin B
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Background: P. aeruginosa is the most commonly cause of life-threatening lung infections. Polymyxins are last-line antibiotics which retain efficacy against this MDR pathogen. Despite their clinical utility, the exact antibacterial killing mechanism of polymyxins is not completely understood. Herein, for the first time, we employed untargeted metabolomics to decipher the mechanism(s) of action of polymyxin B against three P. aeruginosa strains.

Materials/methods: Two polymyxin-susceptible P. aeruginosa strains [PA01 and PA14] (polymyxin B MIC=2 mg/L) and one polymyxin-resistant strain the Liverpool epidemic strain LESB58 (polymyxin B MIC=16 mg/L) were grown in M9 minimal media and treated with polymyxin B: 2 mg/L for polymyxin-susceptible strains and 4 mg/L for polymyxin-resistant strain (n=4). Samples were collected at 15 and 60 min and processed through LC-MS. The significant cellular metabolites (≥1.0-log2-fold; P≤0.05; FDR≤0.1) were determined using multivariate and univariate analyses and reconstructed using IDEOM and KEGG Mapper to elucidate the perturbed metabolic pathways.

Results: In line with the putative mode of action of polymyxin B via disorganising the outer membrane, at 15 and 60 min the bacterial cell envelope biogenesis was markedly perturbed due to polymyxin B treatment particularly in P. aeruginosa PA01 and PA14. This is manifested by a marked decline (≥ -1.0 log2FC) in the complex interrelated pathways of amino and nucleotide sugar (e.g. N-acetyl-D-glucosamine 6P), peptidoglycan (e.g. L-Ala-γ-D-Glu-m-DAP-D-Ala) and lipopolysaccharide biosynthesis (e.g. 3-Deoxy-D-manno-octulosonate). In P. aeruginosa LESB58, only peptidoglycan biosynthesis (e.g. D-Alanyl-D-alanine) was significantly perturbed at 15 and 60 min (-0.98 log2-fold). Consequently, the abundance of the main precursors of bacterial membrane glycerophospholipids (e.g. sn-glycerol-3-phosphate) and fatty acids (e.g. palmitoleylCoA) underwent a considerable decreased (≥ -1.0 log2FC) following polymyxin B treatment in all tested strains. Furthermore, at 15 min and 60 min, polymyxin B caused significant changes in the cellular antioxidant network pool, TCA cycle and the downstream arginine pathway mainly in polymyxin-susceptible strains.

Conclusions: Our results indicated that the killing effect of polymyxin B was largely due to the inhibition of cell envelope biosynthesis, the cellular antioxidant network, TCA cycle and its downstream pathways. This study shed lights on key mechanistic information for optimisation of polymyxin B in clinical setting.

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Abstract 6356

Patterns of antimicrobial treatment of health-acquired infections in France
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Background: Monitoring the use of antimicrobial drugs within hospitalized patients is critical owing to the risk of resistance selection following exposure to broad-spectrum molecules. This study aims to describe the patterns of antimicrobial prescription for the most frequent health-acquired infections (HAI) in France, relating drugs selection and potentially resistant microorganisms.

Materials/methods: We used data from 2017 point-prevalence survey of HAI and antimicrobial use in France - a large nationally representative sample survey of hospitalized patients. We sought unambiguous correspondence between individual indications of antibiotic regimen and HAI sites to determine which molecules (individually or in combination) are directed towards which pathogen (by resistance profile).

Results: Of 75698 adult patients from 401 hospitals, 5.1% had an active HAI and 4.3% had a curative treatment for an HAI. The two most frequent therapeutic indications of treatment were lower respiratory tract (LRTI, 27.7%) and urinary tract infections (UTI, 18.4%) and could be matched with corresponding HAI sites. For LRTI, the most prescribed antimicrobial was amoxicillin-clavulanic acid (27.8%) and most frequently isolated pathogens were in equivalent proportions (~17%) Staphylococcus aureus, Pseudomonas aeruginosa and Escherichia coli. Methicillin-resistant Staphylococcus aureus LRTI were more likely treated by linezolid (see figure-A). For UTI, ofloxacin, ceftriaxone and amoxicillin (with or without clavulanic acid) were mostly prescribed (f13% each) and Escherichia coli predominantly isolated (52.0%). Extended-spectrum beta-lactamase-producing Escherichia coli UTI were more likely treated by fosfomycin, pivmecillinam, piperacillin-tazobactam or ertapenem (see figure-B). We estimated that f56% of LRTI/UTI were treated by broad-spectrum antimicrobials and f75% of prescriptions in absence of microbiological information ("empirical treatment") complied with national guidelines.

Conclusions: In this study, we provide a baseline of antimicrobial use in relation to microbiological information in patients with the most common HAI. Our results can serve to direct future effort of antimicrobial stewardship. Also, we leveraged a type of data that is available in many countries, notably in Europe where similar surveys have been conducted, and as such our work could be extended to a broader population.

Figure: Proportion of antimicrobial prescription according to pathogen resistance for MRSA LRTI (subfigure A) and ESBL-producing E. Coli UTI (subfigure B).

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Investigating the feasibility and clinical impact of a prospective genomics workflow for hospital infection control

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Abstract third-party references: Supported by Melbourne Genomics Health Alliance

Background: Multidrug-resistant organisms (MDROs) are associated with significant morbidity, mortality and costs in hospital patients, yet routine microbiological methods have limited ability to detect nosocomial MDRO transmission. This study aims to evaluate the feasibility and potential clinical impact of applying whole genome sequencing (WGS) of multiple MDROs, across multiple healthcare institutions, to characterise and detect transmission of MDROs in hospitals, and identify challenges for implementation.

Materials/methods: Prospective multi-centre study (8 university hospitals) conducted over 15 months (2 month pilot phase, 13 month implementation phase). Hospital inpatients with positive clinical or screening cultures for MDROs (MRSA, vanA VRE, ESBL Escherichia coli or Klebsiella pneumoniae) were included. Isolates were collected prospectively, underwent usual testing in hospital laboratory, then sequenced (Illumina NextSeq) in parallel. Core genome pairwise single nucleotide polymorphism (SNP) distances were used to infer phylogenetic relationships within same species/ST. Epidemiological information was assessed for pairs of patients with genomically related isolates (below specified SNP distance threshold) to assess likelihood of hospital MDRO transmission. Results were presented to hospitals in the implementation phase, and changes to infection control practices were monitored.

Results: 2285 isolates from 1873 patients were included (41% ESBL E. coli, 36% MRSA, 15% VRE, 8% ESBL K. pneumoniae); 63% of isolates were from clinical samples. Hospital transmission (isolates genomically and epidemiologically-related to another patient) was demonstrated for all MDRO species, including 33% of patients overall, most of which would not have been detected without genomics. This varied from 87% of patients with vanA VRE to 19% for MRSA. Genomic data influenced infection control practices, contributing to management of outbreaks, directing focused infection control interventions, and altering cleaning practices. Critical analysis of genomics workflows identified contributors to delays in turnaround times, including difficulties accessing digital patient data, delays in isolate transfer, and need for innovative data visualisation methods to report genomic data to hospitals.

Conclusions: Prospective genomic workflows offer unparalleled resolution for infection control MDRO surveillance, allowing hospitals to more effectively target their infection control interventions, and potentially decrease MDRO transmission. This study has identified some of the key challenges and inputs required for future implementation of this promising technology.

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Usefulness of reverse transcriptase nested polymerase chain reaction in clinical specimens for the diagnosis of haemorrhagic fever with renal syndrome

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Background: Hemorrhagic fever with renal syndrome (HFRS) is confirmed by Hantavirus isolation in serum, virus-specific immunoglobulin M antibody detection, or 4-fold increase in immunoglobulin G antibody titer in the acute and convalescent period, using immunofluorescence antibody assay (IFA). However, these tests are imperfect for early diagnosis. The aim of this study was to investigate the usefulness of the reverse transcriptase nested polymerase chain reaction (RT N-PCR) in HFRS diagnosis in clinical samples such as whole blood and urine.

Materials/methods: The clinical and laboratory data of 6 HFRS confirmed patients were collected from medical records, between May, 2016 and July, 2017, at the Chosun University Hospital, an 828-bed, University-affiliated, tertiary referral center in Gwangju, Korea. The 6 patients confirmed with HFRS using IFA and RT N-PCR from clinical specimens (whole blood, urine, saliva, sputum).

Results: The virus was detected in all 6 patients, using RT N-PCR targeting the early phase large segment of genus Hantaan virus. Importantly, the virus was identified in urine as well as blood, using RT N-PCR. Our data shows that the virus can be detected in the blood for over a month, which is long, and in urine for up to 3 or 4 weeks, but not in saliva.

Conclusions: We report 6 HFRS cases diagnosed using RT N-PCR targeting the L-segment, with whole blood and urine samples, but not in saliva. Hantaan virus RNA detection by RT N-PCR in whole blood and urine may be helpful in confirming rapid diagnosis in the early phase disease, and useful for routine HFRS diagnosis.

Fig. 1 Phylogenetic trees for hantaviruses based on the partial L-segment genome sequences (A) and the partial S-segment genome sequences (B)

(A) L seg 360bp  (B) S seg 454bp
### Table 1. Clinical characteristics of 4 HFRS patients

<table>
<thead>
<tr>
<th>Patient (Occupation)</th>
<th>Age</th>
<th>Sex</th>
<th>Time A (Days)</th>
<th>Time B (Days)</th>
<th>C3c</th>
<th>AST/ALT</th>
<th>Prothrombin</th>
<th>APACHE II</th>
<th>Proteinuria (Score/mortality)</th>
<th>Time D (Days)</th>
<th>Specimen type</th>
<th>L-iso</th>
<th>RT-PCR</th>
<th>S-iso</th>
<th>RT-PCR</th>
<th>IFA IgG</th>
<th>IFA IgM</th>
<th>Total lg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Farmer)</td>
<td>57M</td>
<td>M</td>
<td>0</td>
<td>7</td>
<td>0</td>
<td>69/24</td>
<td>49/38</td>
<td>77.6%</td>
<td>+/−</td>
<td>&gt;1:32</td>
<td>WB</td>
<td>+</td>
<td></td>
<td>−</td>
<td>&gt;1:28</td>
<td>&lt;1:16</td>
<td>&lt;1:40</td>
<td></td>
</tr>
<tr>
<td>2 (Migrant)</td>
<td>36F</td>
<td>F</td>
<td>5</td>
<td>23</td>
<td>14</td>
<td>246/51</td>
<td>78/345</td>
<td>28/63.9%</td>
<td>+/−</td>
<td>&gt;1:128</td>
<td>WB/Ur/Sl</td>
<td>+/−</td>
<td>−</td>
<td>+/−</td>
<td>&gt;1:29</td>
<td>&lt;1:16</td>
<td>&lt;1:40</td>
<td></td>
</tr>
<tr>
<td>3 (Employed)</td>
<td>45M</td>
<td>M</td>
<td>3</td>
<td>7</td>
<td>0</td>
<td>15/20</td>
<td>10/50</td>
<td>23/66%</td>
<td>+/−</td>
<td>1:32</td>
<td>WB</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>1:32</td>
<td>&lt;1:16</td>
<td>&lt;1:40</td>
<td></td>
</tr>
<tr>
<td>4 (Employed)</td>
<td>41M</td>
<td>M</td>
<td>5</td>
<td>9</td>
<td>0</td>
<td>046/17</td>
<td>11/20</td>
<td>77/03%</td>
<td>+/−</td>
<td>1:32</td>
<td>WB/Ur/Sl</td>
<td>+/−</td>
<td>−</td>
<td>+/−</td>
<td>1:32</td>
<td>&lt;1:16</td>
<td>&lt;1:40</td>
<td></td>
</tr>
<tr>
<td>5 (Farmer)</td>
<td>81M</td>
<td>M</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>202/17</td>
<td>10/84</td>
<td>23/69%</td>
<td>+/−</td>
<td>1:239</td>
<td>WB/Ur/Sl</td>
<td>+/−</td>
<td>+/−</td>
<td>+/−</td>
<td>1:32</td>
<td>&lt;1:16</td>
<td>&lt;1:40</td>
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<tr>
<td>6 (Manufacturer)</td>
<td>44M</td>
<td>M</td>
<td>21</td>
<td>10</td>
<td>0</td>
<td>74/21</td>
<td>13/53</td>
<td>68/67%</td>
<td>+/−</td>
<td>1:512</td>
<td>WB/Ur/Sl</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>1:512</td>
<td>&lt;1:16</td>
<td>&lt;1:40</td>
<td></td>
</tr>
</tbody>
</table>

**PCR:** polymerase chain reaction; **RT-N-PCR:** reverse transcriptase nested polymerase chain reaction; **IFA:** immunofluorescence antibody assay; **lG:** immunoglobulin G; **lM:** immunoglobulin M; WB:** whole blood; **Time A:** time between symptoms onset and hospital admission (days); **Time B:** total admission date (days); **Time C:** total admission date in intensive care unit (days); **Time D:** time between symptom onset and sampling of specimens (days); **lG:** immunoglobulin G; **lM:** not applicable

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Clinical benefits of Point-of-Care rapid molecular influenza test at a hospital emergency service

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Background: Early diagnosis of influenza should help physicians at the emergency service to decide if a patient with symptoms of respiratory tract infection needs isolation, can be cohorted, should be given antibiotics or oseltamivir. In our county there is access to influenza PCR once daily weekdays and a multiplex PCR that tests for several different respiratory tract viruses and some bacteria (run office hours weekdays and before midday at weekends).

In prospective trials commercially available rapid molecular point-of-care tests have been found to lower hospitalization frequency, decrease use of antibiotics, increase correct use of oseltamivir, shorten stay at emergency service and help sort which patients need isolation. Although common in Swedish hospitals there has been no local prospective evaluation. Therefore, this trial aims to evaluate potential benefits of having access to a rapid molecular point-of-care influenza test in the hospital emergency service, and to evaluate the performance of the test.

Materials/methods: In the spring of 2018 a rapid molecular point-of-care test for influenza was made available every other week in the hospital emergency service. Patients tested for respiratory tract viruses (influenza PCR, multiplex PCR or point-of-care test) were included to the test group (n=230) when point-of-care test was available, or to the control group (n=187) when it was not.

Results: There was a significantly lower frequency in the test group of:

- Antibiotic treatment (62.17% vs 74.87%, p<0.01)
- Multiplex PCR (34.35% vs 57.75%, p<0.00001).

There was no significant difference between the test group and the control group in:

- Hospitalization (72.17% vs 79.14%)
- Oseltamivir treatment (13.04% vs 12.30%)
- Stay at emergency service (4.45 vs 4.57 hours)
- Stay at hospital (6.16 vs 5.87 days)
- Time to antibiotics (8.23 vs 10.45 hours)
- Length of antibiotic course (9.30 vs 7.98 days)
- Time to oseltamivir (13.34 vs 8.42 hours)

The sensitivity and specificity of the point-of-care test was 91.7% and 99.0%, for influenza A and 95.5% and 98.5% for influenza B, respectively.

Conclusions: Preliminary results from this trial suggest that access to rapid molecular point-of-care influenza test in the hospital emergency service offers limited clinical benefit.

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**Abstract 6361**

**Q fever endocarditis among patients with culture-negative infective endocarditis in South Korea**  
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**Background:** Q fever is the common pathogen of culture-negative infective endocarditis (CNIE), but there are only limited reports in South Korea that Q fever is the cause of CNIE. We thus investigated the incidence of Q fever endocarditis in patients with suspected CNIE in South Korea by using Q fever PCR assay in blood and tissue valves as well as 0 fever serology.

**Materials/methods:** All adult patients with infective endocarditis classified by modified Duke criteria or with large vessel infection at clinical imaging enrolled from December 2016 through September 2019. Of them, the patients with positive for blood or valve tissue culture were excluded. Q fever endocarditis was defined as 1) positive Q fever PCR of a cardiac valve, or 2) positive Q fever PCR of the blood or single phase I IgG antibody titer ≥ 1:6400 with evidence of endocardial involvement. Q fever vascular infection was defined as meeting the same microbiological criteria as endocarditis with the evidence of the aneurysm or vascular graft infection. We performed serologic test by indirect immunofluorescence assay and PCR targeting the transposase gene insertion element IS1111a of C. burnetii for blood and cardiac valve tissue from the patients.

**Results:** Of the 115 patients with endocarditis and 7 patients with vascular infection, 16 patients with culture-negative endocarditis and vascular infection were included in this study. Of 16 patients, 6 (38%) had predisposing heart condition and 5 (36%) had valve surgery. PCR results from blood and heart valve tissue was positive in 3 and 2 patients, respectively. Four patients (25%, 95% confidence interval 7–52%) was diagnosed with definite Q fever endocarditis. None of these patients received treatment for C. burnetii, but 2 patients had been stable after cardiac valve surgery. One patient died due to the development of surgical site infection after five months from heart valve surgery and the other one died due to worsening underlying disease.

**Conclusions:** These data suggest that Q fever endocarditis in South Korea is probably underestimated and further studies are needed to examine the epidemiology and outcomes of Q fever endocarditis patients in South Korea.

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**Abstract 6367**

**Early Lyme borreliosis in patients with chronic inflammatory bowel disease**

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**Background:** Information on the course and outcome of Lyme borreliosis (LB) in patients with chronic inflammatory bowel disease (CIBD) is limited.

**Materials/methods:** The source of information for the present study was database on 14,891 patients, diagnosed with EM at our institution from 1993–2018. The data were obtained prospectively using a structured questionnaire. EM was defined according to modified CDC criteria. Symptoms that had newly developed or worsened since the onset of the EM and had no other known medical explanation were regarded as LB-associated constitutional symptoms. Pre-and post antibiotic treatment characteristics in patients with EM and underlying CIBD were assessed and compared with sex-, age-, and antibiotic therapy-matched immunocompetent individuals diagnosed with EM in the same year; for each patient with CIBD two immunocompetent patients were chosen.

**Results:** During 26-year period, 50 patients (33 with Crohn’s disease and 17 with ulcerative colitis) with typical EM were diagnosed. There were 29 females and 21 males, aged 48 (20–74) years; 37/50 (74%) patients were receiving immunosuppressive therapy (mesalazin-20, azathioprine-2, corticosteroids-2, biological drugs-2, combined treatment-11). 12/50 (24%) patients had signs/symptoms of disseminated LB (multiple EM-8; meningitis-1; pronounced LB-associated symptoms-3), and in 2 patients with multiple EM *Borrelia afzelii* was isolated from blood. In contrast, only 2/100 (2%) immunocompetent patients had indications of disseminated borrelial infection (multiple EM-1, solitary EM without constitutional symptoms but with spirochtemia-1). The difference was statistically significant (12/50, 24% vs. 2/100, 2%; p<0.0001). Treatment failure was found in 4/50 (8%) patients with CIBD (persistence of EM >2 months after antibiotic treatment-2, development of severe LB-associated constitutional symptoms during follow-up-2) and in 1/100 (1%) immunocompetent patients (persistence of EM >2 months after antibiotic treatment) (p=0.0425). All 5 patients recovered after re-treatment with an alternative antibiotic and had smooth subsequent clinical course during one year follow-up.

**Conclusions:** In contrast to immunocompetent patients with EM, patients with CIBD had more common signs/symptoms of disseminated LB and more frequently needed re-treatment because of treatment failure. However, identical antibiotic treatment approach for EM in patients with CIBD as used in immunocompetent patients, including re-treatment with alternative antibiotics, resulted in favourable outcome of LB.

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Yellow fever enquiries to a national telephone advice line regarding travellers who are pre-conception, pregnant or breastfeeding

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Background: NaTHNaC (The National Travel Health Network and Centre) was set up with the broad goal of protecting the health of UK travellers. It provides advice for healthcare professionals advising those with complex itineraries or specialist health needs. NaTHNaC’s telephone advice line receives numerous enquiries relating to yellow fever vaccine (YFV), which is contra-indicated in certain patient groups and should be used with caution in others, making advice regarding vaccination risk challenging.

Materials/methods: We performed a retrospective audit of all electronic records of telephone enquiries to NaTHNaC between January 2016 – September 2019 relating to pre-conception, pregnancy or breastfeeding and YFV. Data were collected on traveller demographics, travel destination, purpose of travel and trimester of pregnancy. The aim was to quantify the frequency of telephone calls to NaTHNaC for YFV advice, travel destination, and identify the training needs of callers.

Results: There were 2,104 telephone enquiries to NaTHNaC between January 2016 – September 2019. 8,996 (43%) were related to YFV administration. 514 (6%) calls related to YFV in peri-partum travellers as summarised in figure 1. The majority of enquiries were related to pregnancy 250/514 (51%), with the first trimester of pregnancy accounting for most calls at 132/250 enquiries (50%). 42% related to 2nd trimester travellers, and just 2% 3rd trimester travellers. 155/514 (30%) enquiries related to breastfeeding, 47/514 (8%) to pre-conception and 7/514 1% related to miscarriage.

416/514 (81%) of phone calls were from GP practices. The most popular travel destinations were in West Africa, with Nigeria making up 19% of calls and Ghana 17%. The commonest reason for travel was visiting friends and relatives (VFR) 351/482 (73%).

Conclusions: Enquiries relating to YFV make up almost half of the calls to NaTHNaC, with a significant proportion relating to peri-partum enquiries. The commonest reason for travel was VFR in West Africa in 1st trimester pregnancy. This highlights training needs for those providing travel advice and the importance of raising awareness in this patient group to improve vaccination outside the peri-partum period.

Figure 1: Telephone Enquiries to NaTHNaC related to YFV and pregnancy, pre-conception, breastfeeding and miscarriage from January 2016 – September 2019

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Abstract 6370

Protective role for cytomegalovirus-specific neutralising antibodies in kidney transplant recipients treated with T-cell-depleting agents

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Abstract third-party references: Supported by the Spanish Ministry of Science, Innovation and Universities, Instituto de Salud Carlos III [FIS] P17/00014.

Background: Induction therapy with lymphocyte-depleting agents such as antithymocyte globulin (ATG) increases the risk of cytomegalovirus (CMV) infection after kidney transplantation (KT). Most previous studies have analyzed the predictive value of CMV-specific cell-mediated immunity (CMV-CMI) in this population. The contribution of CMV-specific neutralizing antibodies blocking infection of epithelial cells (AbNEI) remains unclear.

Materials/methods: Prospective cohort study of 105 CMV-seropositive KT recipients that received induction therapy with ATG and valganciclovir prophylaxis for a median of 92 days [IQR: 90 - 114]. AbNEI titers were measured at baseline and post-transplant months 3 and 6 using microneutralization assays. Experiments were performed in duplicate for each patient. CMV-CMI was assessed at months 3 and 6 by means of the QuantiFERON-CMV® assay (Qiagen, Hilden, Germany) as per manufacturer’s instructions.

Results: One-year cumulative incidence of CMV infection and disease were 40.9% and 6.7%, respectively. All the episodes of disease occurred after discontinuation of prophylaxis. AbNEI titers increased from baseline through month 6 (geometric mean of 295.3 and 409.4; P-value for trend = 0.032). Patients with AbNEI titers ≥160 at baseline had lower incidence of CMV disease than those with titers <160 [3.5% [3/85] vs. 22.2% [4/18]; log-rank P-value = 0.003], with no differences in the occurrence of overall CMV infection. Similar differences in the subsequent incidence of CMV disease were observed for AbNEI titers ≥160 at months 3 (P-value = 0.006) and 6 (P-value = 0.038). Patients with baseline AbNEI titers above this threshold were more likely to exhibit a reactive QuantiFERON-CMV assay at months 3 [73.7% [56/76] vs. 33.3% [4/12]; P-value = 0.015] and 6 [81.4% [48/59] vs. 46.2% [6/13]; P-value = 0.014]. After adjusting for clinical covariates (including age and CMV-CMI) by Cox regression, baseline AbNEI titers ≥160 remained protective for the development of CMV disease (hazard ratio: 0.148; 95% confidence interval: 0.030 – 0.732; P-value = 0.019). No association was found between CMV disease and the results of the QuantiFERON-CMV assay.

Conclusions: High baseline AbNEI titers are protective against CMV disease among CMV-seropositive KT recipients receiving ATG induction, suggesting a role for humoral immunity independent of CMV-CMI in the setting of ATG-induced lymphodepletion.

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Molecular characterisation of *Escherichia coli* isolated from children admitted with bloodstream infection in Dar es Salaam, Tanzania

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**Background:** *Escherichia coli* is one of the leading bacterial causes of blood stream infection in children and antimicrobial resistance rates among *E. coli* is increasing worldwide. This study aimed to understand the molecular characteristics of clinical *E. coli* isolates identified between March 2017 and July 2018 from children admitted with fever in four hospitals of Dar es Salaam, Tanzania.

**Materials/methods:** A total of 28 *E. coli* were isolated from blood cultures drawn from 2226 children, and identified by MAL-DI-TOF. Whole genome sequencing of the 28 identified isolates were performed using an Illumina platform and the sequencing reads were assembled using SPAdes. Acquired antibiotic resistance genes present in the assembled genomes were identified using ResFinder, sequence type of each isolate was determined using Multilocus Sequence Type (MLST) and the plasmids were characterized using plasmid incompatibility groups (Inc) and pMLST-type (IncF).

**Results:** Extended Spectrum Beta-Lactamase (ESBL) genes were found in twelve of the 28 isolates (42.8%). *blaCTX-M* was present on the majority of isolates (10/12, 83.3%), of which nine and one were *blaCTX-M-15* and *blaCTX-M-27*, respectively. All 10 *blaCTX-M* carrying isolates also harboured either *blaOXA-1* and/or *blaTEM-1B*. The remaining two ESBL isolates carried *blaSHV-106* and *blaACT-16*. We did not identify any carbapenemase resistance genes present on any of the 28 isolates. However, resistant genes towards aminoglycosides e.g., *aac(3)-Ila*, fluoroquinolones e.g., *aac(6′)-Ib-cr/qnrS1*, sulphonamides e.g. sul1/sul2, trimethoprim e.g., *dfra17/dfrA8*, tetracyclines tet(A)/tetB, and chloramphenicol e.g. catA1/catB3 were detected. Among all 28 *E. coli* isolates, thirteen different sequence types (STs) were identified, ST1193 was the most common (n=4), followed by ST131 (n=2), ST617 (n=2), ST216 (n=2) and ST2141 (n=2). Other STs only occurred once, and seven isolates were found to be novel STs.

All the ten *blaCTX-M* carrying isolates contained an IncF plasmid replicon type and different IncF pMLST types were detected; F31:A4: B1 (n=3), F1:A2: B20 (n=2), F29: A: B10 (n=1) and F-: A1:B10 (n=4).

**Conclusions:** Our study shows high prevalence of ESBLs among *E. coli* isolated from children with blood stream infection in Dar es Salaam, Tanzania, with *blaCTX-M* being the most prominent. Diversity of the STs obtained showed that the strains are not clonally related.

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**Abstract 6373**

**Performance evaluation of a novel BKV Quant Assay in plasma and urine specimens**

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**Background:** BK virus (BKV) infection is linked to two major complications: BKV associated nephropathy (BKVAN) in kidney transplant patients and BKV associated hemorrhagic cystitis in hematopoietic stem cell transplant patients. Consequently, active screening of BKV replication in urine and blood combined with preemptive modulation of immunosuppression therapy are essential measures to prevent complications from BKV infections. The NeuMoDx BKV Quant Assay, developed by Sentinel Diagnostics, enables rapid quantitative detection of BKV in plasma and urine matrices to assist in monitoring BKV infections in such patients.

**Materials/methods:** Performance of the NeuMoDx BKV Quant Assay was characterized in urine (550µL) and two different input volumes (100 µL and 500 µL) of plasma. The performance of the NeuMoDx BKV Quant Assay were demonstrated across key analytical metrics including analytical sensitivity (LoD), linearity, precision, turnaround time, and specificity. Evaluation of the analytical sensitivity was performed using the 1st WHO International Standard for BKV, and the limits of quantitation (LLoQ/ULoQ) were determined using the TAE ≤ 1.0 criterion.

**Results:** Using an input specimen volume of 550µL, the NeuMoDx BKV Assay demonstrated a limit of detection (LoD) and lower limit of quantitation (LLoQ) of 60 IU/mL in plasma and an LoD/LLoQ of 100 IU/mL in urine. With lower specimen volume, 100µL, the NeuMoDx BKV Assay demonstrated a LoD/LLoQ of 350 IU/mL in plasma. The NeuMoDx BKV Quant Assay also showed excellent linearity across a ~8-log dynamic range with a ULoQ of 9 Log10 IU/mL. Excellent quantitative precision across 3 systems over 6 days, as well as quantitative equivalency across multiple reagent lots was demonstrated. Turaround time was ~60min and no cross-reactivity was observed against >20 relevant non-target pathogens tested. The test performed efficaciously in the presence of endogenous/exogenous interfering moieties. Finally, equivalent quantitative performance (equivalence slope >0.95 with absolute bias < 0.25 Log10 IU/mL) was demonstrated across 100µL and 550µL input specimen volumes of plasma.

**Conclusions:** The NeuMoDx BKV Quant Assay is well suited for implementing BKV viral load monitoring using plasma and urine specimens in normal and low specimen volume settings.

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Abstract 6374

New approach for determination of antimicrobial susceptibility to amoxicillin by an acoustic sensor-based on a slot mode

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Background: The use of antibiotics leads to a decrease of the number of deaths from infectious diseases. Traditional microbiological methods, based on inhibiting the growth of microorganisms in the presence of antibiotics, are characterized by high detection sensitivity, but require a long time. Therefore, the development of new technologies and methods for testing the activity of the antibiotic against bacteria is very relevant.

Materials/methods: The experiments were carried out using the developed acoustic sensor, consisting of two piezoelectric plates separated by an air gap. Using two interdigital transducers located on one of the plates, a piezoactive acoustic wave was excited and received. The second plate served as the bottom of a liquid container with a suspension of test cells. Excitation of the slot mode in such a structure led to the appearance of resonance absorption peaks in the frequency dependence of the insertion loss. The change in the frequency and depth of these peaks when an antibiotic was added to nonresistant/resistant cells was used as an informative analytical signal.

Results: For the first time, a rapid method was proposed for determining the susceptibility of Escherichia coli cells to antibiotics by the example of amoxicillin by the acoustic sensor. It has been established that an indicator of the activity of an antibiotic in relation to microbial cells is the difference between the recorded sensor signal for cell suspension without exposure to the antibiotic and after exposure. The depth and frequency of the peaks of resonant absorption in the frequency dependence of the insertion loss of sensor varied after adding an antibiotic with different concentrations (2-18 μg/ml) to the cells. A criterion for the sensitivity of E. coli cells to amoxicillin for using an acoustic sensor was established.

Conclusions: These results demonstrate the possibility of using a device with a slot mode in an acoustic delay line for determining the susceptibility of microbial cells to antibiotics. The advantages of this method are the ability to carry out the analysis directly in the liquid, the short time of the analysis (within 15 min) and the possibility of multiple use of the sensor.

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A multi-year decline of multidrug-resistant Escherichia coli in French nursing homes and primary care: are we on the good track?

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Abstract 6376

Background: Since 2012, a French national system surveys the antimicrobial resistance among Enterobacteriaceae in primary cares and nursing homes (NH). This study describes characteristics and temporal and geographical trends of multi-drug resistant Escherichia coli.

Materials/methods: From 1st January 2012 to 31st December 2018, antibiograms of E.coli isolated from urine samples were collected in a large network of laboratories across France. Administrative and microbiological data were downloaded by laboratories on an e-platform dedicated to the surveillance. Strains isolated from patients living at home or NH residents were included in the analysis. Hospitalised patients and screening samples were excluded. The multi-drug resistant E.coli rates were the number of third generation cephalosporins (3GC) resistant or/and extended spectrum beta-lactamase (ESBL) E.coli strains by divided by the total number of strains. Statistical analyses were performed using Student test or variance analysis as appropriate.

Results: The total number of E.coli antibiograms included varied from 94,164 in 2012 (147 laboratories) to 381,141 in 2018 (742 laboratories across 11 French regions). When accommodation was notified, 95.3% (n=32,710) of patients were living at home and 4.7% (n=1,598) were residents in NH in 2012 vs 96.1% (n=335,338) and 3.9% (n=13,720) in 2018, respectively. Among patients living at home, the proportion of E.coli resistant to 3GC was 3.0% in 2012, 4.2% in 2015, and 3.2% in 2018 (p<0.001), and the proportion of ESBL-E.coli was 2.3%, 3.7% and 2.8% (p<0.001), respectively. In 2018 in the same population, the proportion of ESBL-E.coli varied from 2.2% to 3.6% according to regions. Among residents living in NH, the proportion of E.coli resistant to 3GC was 8.0% in 2012, 11.1% in 2015 (p<0.01) and 8.6% in 2018 (p<0.001), and the proportion of ESBL-E.coli was 6.6%, 9.7% and 7.7% (p<0.001), respectively. In 2018 in NH, the proportion of ESBL-E.coli varied from 15.1% to 28.6% according to regions. (Figure)

Conclusions: This study suggests a multi-year decrease of multi-drug resistance among E.coli both in the French community and NH. An analysis of potential associations with results obtained from national hand hygiene and antibiotic consumption surveillances is ongoing. Figure: Temporal and geographical trends for ESBL-E.coli in NH and the community.

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**Abstract 6380**

**Household transmission of ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* after hospital discharge of an ESBL carrier**

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**Background:** Human-to-human transmission of ESBL-producing *Enterobacteriaceae* (ESBL-PE) may play an important role in their dissemination, especially within households. This study aimed to determine rates and dynamics of ESBL-PE acquisition and transmission in households after hospital discharge of an ESBL-PE index patient.

**Materials/methods:** We conducted a prospective, observational cohort study between Nov 2017 and Aug 2019 in 5 European cities. ESBL-PE-positive index patients and their household contacts were recruited at index patients’ hospital discharge (baseline). During 4-month follow-up, all participants were asked to provide personal information and 4 stool samples or rectal swabs (at baseline, 1 week, 2 & 4 months). ESBL-producing *E. coli* (ESBL-EC) and *K. pneumoniae* (ESBL-KP) were identified by conventional methods and MALDI-TOF. Genomes were obtained with Illumina NextSeq and phylogenetic trees were built per species by PopPUNK. Incidence rates of acquisition [new ESBL-PE detection in a previously negative household contact] and transmission [acquisition of a similar strain previously detected in another household member] were estimated at pheno- and genotypic level overall and per species.

**Results:** 71 index patients were enrolled carrying ESBL-EC (n=46), ESBL-KP (n=20) or both (n=5). 29/95 household contacts (31%) in 26 households were ESBL-PE positive at baseline and 18 participants (18%) in 16 households became positive during follow-up. Based on phenotypical assessment, the overall incidence rate of ESBL-PE acquisition was 1.9/100 participant-weeks at risk [ESBL-EC: 1.1; ESBL-KP: 0.6; RR 1.7, 95%CI 0.7-3.9] and the overall rate of transmission was 1.3 events/100 participant-weeks of follow-up [ESBL-EC: 1.3; ESBL-KP: 1.0; RR 1.3, 95%CI 0.5-4.0]. Transmission rates varied between 0.2 and 2.1 event/100 weeks across cities. ST131 [41%] and ST1537 [13%] were the most frequent sequence types in ESBL-EC and ESBL-KP, respectively. *blaCTX-M-15* was the predominant ESBL gene in both species [57-67%]. 67% of strains phenotypically suspected of transmission shared the same MLST and ESBL genes.

**Conclusions:** Half of the households had secondary ESBL-PE cases, with a third of family members already positive at baseline. Transmission rates were similar for ESBL-EC and ESBL-KP. Two thirds of putative ESBL-PE transmission events were associated with genetically related strains.

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Abstract 6381

Antimicrobial resistance surveillance in low- and middle-income countries: can we estimate resistance in bloodstream infections from other types of specimen?

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Background: Antimicrobial resistance (AMR) is a major global health threat. AMR surveillance is difficult in LMICs, where lack of laboratory capacity prevents routine patient-level antimicrobial susceptibility testing, and systematic invasive testing of individuals may not be feasible. Evaluation of AMR in non-invasive/colonisation samples may be of benefit in predicting AMR in invasive cases.

Materials/methods: We used data from Oxford University Hospitals, UK, 1998-2018, to investigate if AMR rates in Escherichia coli and Staphylococcus aureus isolates from blood could be predicted using only other types of specimen, more readily cultured in LMICs. We compared the proportion resistant in blood versus the proportion resistant in other sample types in each calendar year using time series cross-correlations, including all antibiotics for which both blood and non-sterile sites isolates were consistently tested between 1998-2018 (four for E. coli, six for S. aureus). We compared the proportion of resistant blood cultures versus the proportion of resistant other cultures across drug-years including an additional eight and ten antibiotics respectively, tested only after 2013, using four clinically relevant resistance thresholds (<5%, 5-10, 10-20%, >20%).

Results: 8080 E. coli bloodstream infections, 32207 E. coli urinary tract infections, 6926 S. aureus bloodstream infections and 11463 S. aureus non-sterile site cultures were included in the analyses. Trends over time in blood vs other specimens were strongly correlated [maximum cross-correlation 0.53-0.98 with strongest associations between proportions in the identical year for 8/10 bug-drug combinations]. Resistance prevalence was broadly congruent across drug-years for each species [Figure], particularly allowing for uncertainty in estimating proportions. 212/318 (67%) bug-drug-years had resistance prevalence in other sample types within ±5% of blood isolates, and 279/318 (88%) within ±10%. 218/318 (69%) bug-drug-years had the same resistance percentage threshold categorisation for both blood and other specimen types, 310/318 (97%) had either the same resistance categorisation or within ±1.

Conclusions: The rate of AMR in bloodstream infections and other less invasive infections are strongly related, implying the latter could be used as a surveillance tool for AMR in LMICs. These infection sites are easier to sample from and cheaper to carry out antimicrobial susceptibility testing on, and can provide evidence for decisions such as empiric antibiotic recommendations.

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**Abstract 6385**

**A mobilisable plasmid spreads the blaGES-6 carbapenemase gene among multidrug-resistant Enterobacter cloacae complex isolates**

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**Background:** The clinical relevance of *Enterobacter* spp. is highlighted by its inclusion in the ESKAPE group. Resistance gene spreading through mobile genetic elements is of key importance to this group. One of the most important resistance mechanisms is the production of enzymes that hydrolyze carbapenem antibiotics.

Here we aimed at determining the genetic context of the *blaGES-6* carbapenemase gene found in a collection of multidrug-resistant *E. cloacae* complex (Ecpx) isolates, and the possible way for its dissemination.

**Materials/methods:** Nine clinical isolates of GES-6-producing Ecpx were selected for whole genome sequencing with Illumina MySeq. Genome assembly and plasmid reconstruction were carried out by using PLACNETw. Plasmid genome comparisons were performed with BRIG. Plasmid DNA was extracted with GeneJet plasmid kit (ThermoFisher), digested with restriction enzymes *BstBI*, *HpiI* and *MluI* to remove all plasmids but that encoding *blaGES-6* (*pGES-6*), and transformed into *Escherichia coli* strain DH5α. DH5α (*pGES-6*) was tested for antimicrobial susceptibility with Vitek2 (BioMerieux) or gradient strips, following the EUCAST recommendations. DH5α (*pGES-6*) derivatives, containing different conjugative plasmids (*pOX38, R100-1, R751, R388*, and *R64drd11*), were used as donors in mating experiments to test for *pGES-6* transfer. *E. coli* UB1637 was used as a recipient. Matings were carried at 37°C onto solid surfaces during 1h. The conjugation frequency was expressed as the number of transconjugants per donor cell.

**Results:** The carbapenemase gene *blaGES-6* is the single gene cassette of a class 3 integron encoded in a plasmid (*pGES-6*), which is 8259 bp in size and identical in all isolates (Figure 1). Susceptibility testing of DH5α (*pGES-6*) showed a MIC increase for amoxicillin, amoxicillin-clavulanate, cefuroxime, cefoxitin, ceftazidime and imipenem, compared to the empty strain. *pGES-6* is a MOBQ mobilizable plasmid that can be transferred between *E. coli* strains by different conjugative plasmids. The IncP1β plasmid R751 was the most efficient helper of *pGES-6* (mobilization frequency: 0.18).

**Conclusions:** Plasmid *pGES-6* circulates among Ecpx, spreading the *blaGES-6* carbapenemase gene. Its ability to replicate and transfer into other enterobacteria, such as *E. coli*, makes Ecpx bearing *pGES-6* a potential source for *blaGES-6* dissemination.

![Figure 1. Genetic map of the pGES-6 plasmid.](image)

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Whole genome sequence analyses by a new easy-to-use software solution confirm a neonatal ward outbreak of MRSA CC22 being related to strains in the neighbouring region

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Background: Effective monitoring of hospital transmission of pathogens requires efficient and detailed characterization of the microorganisms. Core genome MLST (cgMLST) based on whole genome sequencing allows bacteria to be divided into clusters with a unique resolution. 1928 Diagnostics is a new online cgMLST based software solution, which can be used to characterize and cluster selected bacteria, including S. aureus, by infection control units without bioinformatic assistance. We used 1928 Diagnostics to retrospectively test a neonatal ward outbreak of MRSA CC22 in 2014 after transfer of patients from a hospital in a neighboring area.

Materials/methods: We analyzed isolates of MRSA CC22 from 1) individuals considered part of the outbreak, 2) individuals living in the region, collected over the preceding seven years, and 3) individuals from the neighboring area in the same year as the outbreak. Two isolates from the region were from the same patient. Raw sequence data (.fastq.gz files) was uploaded to 1928 Diagnostics (https://www.1928diagnostics.com/).

Data processed by 1928 Diagnostics was presented with MLST sequence type (ST) and antibiotic resistance genes profiles. A core genome MLST (cgMLST) based cluster tree showed isolates of potential relatedness. Definite core genome MLST cluster types were not assigned to individual isolates.

Results: Sequence data from ten outbreak isolates, ten isolates previously obtained from individuals in the region, and twenty-six isolates from individuals in neighboring region passed the quality control step and were identified as MRSA ST22. The isolates were all SCCmec type IV. Genes for PVL, TSST and ETS were not detected. blaZ and mecA genes were present in all isolates and ermC gene was detected in six isolates. Cluster analyses revealed that all supposed outbreak isolates were within one cluster and that five of the isolates from the neighboring area were in the same cluster (Figure).

Conclusions:

- Online whole genome sequence analyses by 1928 Diagnostics characterized the isolates and separated outbreak isolates from local non-outbreak isolates.
- The results are in accordance with introduction of the outbreak strain with patients transferred from a hospital in a neighboring area.
- 1928 may prove valuable to infection control units without bioinformatic expertise.

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Unexpected genetic diversity among KPC-producing Klebsiella pneumoniae in France

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Background: The worldwide spread of KPC-producing K. pneumoniae (KPC-Kp) isolates was reported to be due to the dissemination of one clonal complex, i.e. CG258 (including ST258 and ST512). However, recent epidemiological European study is not available. The aim of this study was to deeply characterize the epidemiology of KPC-producing K. pneumoniae circulating in France in 2018.

Materials/methods: During 2018, 1,259 isolates of carbapenem non-susceptible K. pneumoniae clinical isolates were received by the french NRC for carbapenem-resistance in Enterobacterales. Among this collection, 63 KPC producing K. pneumoniae were fully sequenced by Illumina’s technology and further analyzed. Resistomes, susceptibility testing and clonal relationship at a nationwide scale were determined.

Results: Among the 63 KPC-producing isolates, 16 different STs were identified including two main clones, representing 41% of all isolates. These two STs, ST147 and ST307, represented 19 and 22% respectively. Analysis of resistomes indicated that the main variant was bla_{KPC3} (73%). In addition, one isolate co-harboured bla_{KPC2} and bla_{NDM4} genes and one co-harboured bla_{KPC2} and bla_{VIM-1}. The bla_{KPC} genes were mostly carried by Tn_{4401a} and Tn_{4401d} structures and 4 new NTE [Non Tn_{4401} Element] were characterized. These structures were carried mostly by three types of plasmids being IncN ST15, pKPQIL-like and an Inc-FIA-family plasmid. Epidemiological investigations highlighted that the emergence of these non-CG258 KPC-Kp in France was linked to the dissemination of these clones from Portugal.

Conclusions: This study described the unexpected wide genetic diversity of KPC-producing K. pneumoniae in France. Thus, KPC-producing Kp epidemiology has changed in Europe, at least in several not endemic countries of the West Europe such as France and Portugal, where CG258 is not the most prevalent clone anymore.

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Abstract 6392

**Identification of Mycobacterium species with MALDI-TOF mass spectrometry**

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**Background:** The identification of *Mycobacterium* to species level is important since the genus *Mycobacterium* consists of non-pathogenic environmental species as well as pathogenic species causing serious diseases. Matrix-assisted laser desorption ionization–time of flight mass spectrometry (MALDI-TOF MS) is an inexpensive, reliable way of identifying microorganisms. The aim of this study was to evaluate MALDI-TOF MS method in identification of *Mycobacterium* species so that appropriate treatment can be given when indicated.

**Materials/methods:** A total of 36 clinical isolates (24 species) of nontuberculous mycobacteria (NTM), that were identified with hsp65 gene restriction enzyme analysis, were included in the study. The isolates were subcultured onto both MGIT broth and Lowenstein-Jensen media. Heat inactivation and MALDI-TOF MS (Bruker MALDI Biotyper) procedures were applied, as it is recommended by the manufacturer, to the mycobacteria that were grown on both MGIT and Lowenstein-Jensen media.

**Results:** Among 36 isolates, 31 of them (20 species) were identified correctly with MALDI-TOF MS. These species were *M. gordoa*, *M. elephantis*, *M. peregrinum*, *M. cosmeticum*, *M. simiae*, *M. engbaekii*, *M. phocaicum*, *M. avium*, *M. kansasii*, *M. chelonae*, *M. xenopi*, *M. arupense*, *M. nonchromogenicum*, *M. abscessus*, *M. intracellulare*, *M. mageritense*, *M. celeriflavum*, *M. fortuitum*, *M. neoaurum*, *M. europaeum*. Five isolates (4 species) were misidentified. *M. smegmatis*, *M. senuense*, *M. monocense*, and *M. porcinum* species were misidentified as *M. mageritense*, *M. avium/terrae complex*, *M. fortuitum*, *M. septicum* respectively. Same MALDI-TOF MS results were obtained from cultures of MGIT and LJ media.

**Conclusions:** MALDI-TOF MS is a correct, relatively rapid, inexpensive way of identification of *Mycobacterium* species. Although results of MALDI-TOF MS had a high concordance with the results of hsp65 gene restriction enzyme analysis, it should be kept in mind that some genetically close species can be misdiagnosed with MALDI-TOF MS.

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A study of virulence factors and antimicrobial resistance in Staphylococcus epidermidis isolates from ocular infections

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Background: Staphylococcus epidermidis is part of commensal flora of the conjunctiva. It is also the most common bacterial pathogen causing ocular infections. Ocular infections occur due to some breach in ocular defence mechanisms; of which endophthalmitis and keratitis are the most common and most dreaded infections due to their effect on patient’s vision. The extent and course of infection depends on virulence and antimicrobial susceptibility of the infecting strain. The study was planned to speciate coagulase negative staphylocci (CoNS) isolated from keratitis and endophthalmitis patients, and to study the virulence factors and resistance profile of the S. epidermidis isolates.

Materials/methods: Culture isolates of CoNS from 86 cases of keratitis and endophthalmitis, and 20 healthy controls were included in the study. Speciation of CoNS was done using conventional methods and Matrix Assisted Laser Desorption Ionisation – Time of Flight Mass Spectrometry (MALDI TOF MS).

S. epidermidis was the most common CoNS isolated. The virulence attributes determined were ability to cause hemolysis and biofilm formation; and production of protease, gelatinase, lipase and DNase enzymes. Resistance profile was studied using disc diffusion, e-test for minimum inhibitory concentration (MIC) of vancomycin and polymerase chain reaction (PCR) for mec A gene causing methicillin resistance.

Results: Most common CoNS isolated was S.epidermidis (n= 48, 56% in test and n=9, 45% in control groups) followed by S.hemolyticus.

Production of lipase enzyme (96% isolates), biofilm formation (81% isolates) and alpha-hemolysis (58% isolates) were the most important virulence factors. Methicillin resistance was found in 67% and 56% of isolates in test and control groups respectively. Macrolide and fluoroquinolone resistance was seen in 63% and 35% of isolates respectively. Vancomycin-resistance was not seen in any of the isolates; however ‘creeping MIC’ phenomenon was seen in five test isolates. PCR for mec A gene was found positive in 65% of test and 56% of control strains.

Conclusions: The study has elucidated important virulence factors and resistance profile of the most common ocular bacterial pathogen. Also, to the best of our knowledge this is the first study co-relating methicillin resistance with presence of mec A gene in S. epidermidis isolates from ocular infections.

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Epidemiology and differential diagnosis of chikungunya and O’nyong-nyong virus: many gaps of knowledge to be filled
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Abstract third-party references: On behalf of GloPID-R chikungunya, o’nyong-nyong and Mayaro virus Working Group

Background: In the last 15 years, chikungunya virus (CHIKV) has impacted human health globally, with local transmission reported in Asia, Africa, Americas, Pacific region and, transiently, in Europe. The recent occurrence of extensive CHIKV epidemics has highlighted the need for improved capacity for diagnosis and surveillance, especially when the co-circulation of closely related viruses increases the chance of misdiagnosis. In particular, o’nyong-nyong virus (ONNV) is phylogenetically close to CHIKV, it causes a similar clinical presentation and its geographic spread overlaps with CHIKV in Africa. Serological tests are hampered by massive cross-reactivity between CHIKV and ONNV; among available assays, virus neutralization test (VNT) is actually the gold standard to distinguish the two viruses in sero-epidemiological studies.

Materials/methods: The GloPID-R (Global Research Collaboration for Infectious Disease Preparedness) CHIKV Working Group investigated gaps of knowledge about the diagnosis and the epidemiology of these viruses and aimed to provide adapted recommendations for future research. Data from available scientific literature were combined with experts' experience.

Results: The experts established that to improve diagnosis of CHIKV and ONNV at the acute phase, both molecular and serological assays require further evaluation, standardized protocols, reference panels and international standards. Moreover, available seroprevalence data on CHIKV and ONNV distribution are largely affected by cross-reactivity and in areas of potential co-circulation both viruses should be tested with VNT. In a cross-sectional study performed in Mali in 2016, CHIKV ELISA seroprevalence mean value was 48%, reaching up to 65-69% in some regions. When retested with VNT, the large majority of CHIKV+ samples was in reality ONNV+. These results highlight that high-throughput assays that can distinguish among the two viruses are necessary to perform large-scale epidemiological studies of public health relevance.

Conclusions: Overlapping clinical presentations, wide geographic spread and cross-reactivity among CHIKV and ONNV highlight the need for laboratory supports to unambiguously identify etiological agents and to obtain strong epidemiological data. This is important to ensure an early detection of cases and to support a clinical and public health response. Considering the high risk of future CHIKV and ONNV outbreaks, a major effort should be done to fill the existing diagnostic gaps.

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Ceftolozane-tazobactam for the treatment of bloodstream infection due to *Pseudomonas aeruginosa* in neutropenic cancer patients: a real-life experience (ZENITH study)

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Abstract third-party references: On behalf of the ZENITH study group

**Background:** We aimed to assess the characteristics and outcomes of neutropenic cancer patients with *Pseudomonas aeruginosa* (PA) bloodstream infection (BSI) treated with ceftolozane-tazobactam.

**Materials/methods:** We performed a descriptive, multicenter, international, retrospective cohort study including onco-hematological neutropenic patients with BSI due to PA who received ceftolozane-tazobactam as empirical and/or definitive therapy across 13 centres from 4 countries (January 2016 - October 2019).

**Results:** We included 31 episodes of PA BSI, of which 90.3% and 41.9% were caused by multidrug-resistant (MDR) or extensively-resistant strains, respectively. All patients had a underlying hematological disease, most commonly myeloid leukaemia (61.3%). 32.3% of patients were allogeneic hematopoietic stem cell transplant recipients, and 76.7% had profound neutropenia (<0.1x10⁹/L). Two episodes were polymicrobial. Pneumonia was the most frequent source of BSI (25.8%), followed by catheter infection (19.4%). Septic shock at onset was present in 29% of patients. Inadequate empirical antibiotic therapy was administered to 41.9% of patients, mainly with meropenem or piperacillin/tazobactam monotherapy. Ceftolozane-tazobactam was administered empirically in 8 patients; 4 in combination with other drugs (aminoglycosides 3, and colistin 1) and 4 in monotherapy. Five of these 8 patients were known to be previously colonized by a MDRPA strain. Ceftolozane-tazobactam was used as definitive therapy in 30 patients; 14 in combination with other drugs (aminoglycosides 11, fosfomycin 1, ciprofloxacin 1, and colistin + fosfomycin 1) and 16 as monotherapy. The main reason for antibiotic change was the identification of a MDRPA strain. Three patients with susceptible PA BSI received ceftolozane-tazobactam due to septic shock in 2 cases, and as a carbapenem-sparing alternative in 1. In 4 patients, it was administered in extended infusion. Seven patients required ICU admission and 4 mechanical ventilation. Only one patient had persistent BSI after 48 hours of antibiotic treatment. Early [7-day] and overall [30-day] case-fatality rates were 3.3% and 16.1%, respectively. No related adverse events were observed.

**Conclusions:** In this real-life experience, ceftolozane-tazobactam was used in patients with BSI due to PA, mostly in patients with infection due to MDR strains and pneumonia. Ceftolozane-tazobactam appears to be safe and efficacious for the treatment of these extremely high-risk patients.

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Abstract 6399

**Post-exposure prophylaxis for high risk contacts of Ebola virus using immunotherapies with monoclonal antibodies in the eastern DRC: a compassionate use program**

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**Abstract third-party references:** ALIMA, INSERM

**Background:** The largest Ebola epidemic of the Democratic Republic of the Congo has been ongoing since August 2018, with an overall mortality rate of over 65%. New vaccines and specific immunotherapies implemented during this outbreak allowed starting post exposure prophylaxis (PEP) management for high risk viral contact. Considering the gap between vaccine administration and individual protectiveness, those specific therapeutics based on monoclonal antibodies were to be used. ALIMA (French medical NGO) health care workers (HCW) with high risk contact were managed with PEP using specific immune-therapeutics through compassionate use (MEURI, for monitored emergency use of investigational drugs).

**Materials/methods:** After being exposed to intermediate (Intact-skin-only contact) or high risk (broken skin contact) with an Ebola positive patient, participants provided consent through MEURI protocol. Ebola RT-PCR and clinical examination was performed at D0, then mAb114 or REGN-EB3 drug was injected once negative RT-PCR results were confirmed. Clinical follow-up was done by phone at D7. Subsequently, D14 evaluation was implemented for clinical status and Ebola RT-PCR as to confirm patient status for infection.

**Results:** 33 participants were included (31 adults (30 HCW), 2 babies). Median (IQR) age was 31 (25, 39) years old, 58% male. Vaccination status was known for 31/33 participants, and all adults (29/31) were vaccinated. Mean (SD) time between contact and administration was 2.2 (1.2) days. On the 18/33 (55%) on which the exact dates of vaccination were known, median (IQR) time between vaccine and PEP administration was 173 (19, 427) days. 70% received the mAb114. Report suggest that no participants developed Ebola at D14.

**Conclusions:** With specific treatments raising proof of efficacy, it is considered now unethical on a field carer perspective not to propose the best individual strategy to avoid developing Ebola when being exposed to high risk contact. While ALIMA has been the first NGO to propose this solution to his personal, extending the PEP outside compassionate use will be of higher interest for next outbreaks. Good quality studies are needed to answer important questions, in particular about interaction with vaccines, both treatments sharing the same target as the vaccine strategy currently used in the field.

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The interplay of resistance mechanisms associated with reduced susceptibility and resistance to imipenem and ceftazidime-avibactam in clinical *Pseudomonas aeruginosa* isolates from Switzerland

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**Background:** Increasing reports of multidrug resistance (MDR) in clinical *Pseudomonas aeruginosa* have led to a necessity for new antimicrobials. The beta-lactamase/inhibitor combination, ceftazidime-avibactam (CAZ-AVI), is indicated for use against MDR *P. aeruginosa* against a broad range of infection types and particularly those that are carbapenem resistant. This study sought to determine the mechanisms of CAZ-AVI and imipenem (IPM) resistance in clinical *P. aeruginosa* isolates obtained from Swiss hospitals

**Materials/methods:** Increasing reports of multidrug resistance (MDR) in clinical *Pseudomonas aeruginosa* have led to a necessity for new antimicrobials. The beta-lactamase/inhibitor combination, ceftazidime-avibactam (CAZ-AVI), is indicated for use against MDR *P. aeruginosa* against a broad range of infection types and particularly those that are carbapenem resistant. This study sought to determine the mechanisms of CAZ-AVI and imipenem (IPM) resistance in clinical *P. aeruginosa* isolates obtained from Swiss hospitals

**Results:** Fifteen STs were identified amongst the 15 isolates in this study. No carbapenemases were detected but one isolate harboured the ESBL *bla*<sub>PER-1</sub>. Seven isolates were CAZ-AVI-R with MICs ranging from 1-2 to 64 mg/L, and the remaining eight isolates had either low/wildtype MICs (n=6; 1-2 mg/L) or reduced susceptibility (n=2; 4-6 mg/L). Six isolates were IPM-R, four of which had mutations resulting in truncations of OprD, and the remaining six IMP-S isolates had intact *oprD* genes. Within CAZ-AVI-R isolates, and those with reduced susceptibility, mutations resulting in *ampC* derepression, OprD loss, *mexAB* overexpression and ESBL (*bla*<sub>PER-1</sub>) carriage were observed in various combinations. Within the six wildtype isolates no mutations were found that would affect any AMR genes of interest when compared to PAO1. Just one isolate, with a CAZ-AVI MIC of 12 mg/L, had none of these mechanisms at play and requires further investigation

**Conclusions:** This preliminary study highlights that CAZ-AVI-R in *P. aeruginosa* is multifactorial and could be caused by the interplay between different resistance mechanisms including ESBL carriage, increased efflux, loss of permeability and derepression of its intrinsic AmpC enzyme. IPM-R appears to be mainly due to OprD loss as previously reported. This area warrants further study to prevent the selection of CAZ-AVI-R and the risk of subsequent therapy failure

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Increasing trends of emerging extensively drug-resistant bacteria cases at Lyon University Hospital, 2015-2019

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Abstract 6403

Background: Emerging extensively drug-resistant (eXDR) bacteria is a growing public health concern. Infection control measures are essential to limit their spread among hospitalized patients. The objective was to describe the trends of eXDR bacteria cases between 2015 and 2019 at Lyon University hospitals.

Materials/methods: Incident eXDR bacteria cases, including carbapenemase-producing Enterobacteriaceae (CPE) and vancomycin-resistant Enterococcus faecium (VRE) were monitored prospectively from January 1, 2015 to June 30, 2019 at Lyon University hospitals (5,300 beds). The microbiology laboratory alerts the infection control teams for each new eXDR bacteria isolated. A case was a colonized or an infected patient diagnosed with an eXDR bacteria. An outbreak was at least 1 secondary case due to the same bacteria with the same resistance mechanism, in the same unit within an acceptable interval time. Molecular identification might not be part of the definition in the emergency context. Incidence was reported for 10,000 hospital days.

Results: Since 2015, 667 incident eXDR bacteria cases were diagnosed, among them 575 (86.2%) CPE and 92 (13.8%) VRE. The mean age was 67.3 years. Overall, 368 (55.2%) cases were detected in medical wards, 146 (21.9%) in surgery wards and 83 (12.4%) in intensive care units. Sixty four (69.6%) VRE cases developed vanA resistance and 28 (30.4%) vanB resistance. Among CPE cases, 384 (66.8%) developed OXA-48 resistance, 135 (23.5%) VIM, 50 (8.7%) NDM, 5 (0.9%) KPC and 1 (0.2%) IMI. Regarding CPE species, 147 (24.5%) were Citrobacter freundii, 128 (22.3%) Enterobacter cloacae, 112 (19.5%) Klebsiella pneumoniae and 97 (16.9%) Escherichia coli. A total of 563 (84.4%) eXDR cases were colonized against 104 (15.6%) infected; 59 outbreaks occurred during the study period generating 200 (30.0%) secondary cases. The incidence rate increased from 0.44/10 000 hospitalization days in 2015 to 2.39/10000 in 2019 (p=0.003). Figure 1 shows the epidemic curve of eXDR bacteria cases from 2015 to 2019.

Conclusions: From 2015 to 2019, the incidence of eXDR bacteria cases and outbreaks increased dramatically. Further studies are needed to understand/explore the dynamics of this trend. Current recommendations might be improved to help infection control units to better control the spread of eXDR bacteria.

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**Investigation of waterborne outbreaks due to drinking water consumption in Greece, 2004-2019 (1st semester): time to learn our lessons**

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**Background:** Waterborne outbreaks (WBOs) remain a public health concern as large numbers of people can be infected within a short time. We summarize Greek data on WBOs from January 2004 to June 2019 and the conducted investigations and identify points for improvement.

**Materials/methods:** WBOs are mandatorily notified in Greece. Data on outbreak characteristics (type, size, duration, demographics, hospitalization, outcome) and conducted investigations (epidemiological, laboratory, environmental) were analyzed.

**Results:** Overall, 33 WBOs were recorded (mean 2.1 outbreaks per year). Analytical epidemiological studies were conducted in seven (21%) and suggested tap water consumption as the probable vehicle of infection. Environmental investigation was performed in 23 (70%). Clinical specimens were tested in 24 (73%) and water samples in 14 outbreaks (42%).

The median number of cases per WBO was 54 (range: 2-1,640); eight had more than 200 recorded cases each with a total number of 4,892 cases (81% of total recorded cases); 56% of cases were women. Most WBOs (72%) affected more than one household and affected people from all age-groups. Clinical manifestations were compatible with gastrointestinal illness and 194 cases were hospitalized (7%). No deaths were recorded. Outbreaks’ duration ranged from 1 to 44 days.

Clinical samples were positive in 79.2% (19/24) of the outbreaks; *Salmonella* spp., *Norovirus*, *Shigella* spp., *Campylobacter* spp., and *Rotavirus* were isolated in 6 (31.6%), 6 (31.6%), 3 (15.8%), 2 (10.5%) and 2 (10.5%) outbreaks respectively and in one multiple pathogens (*Norovirus, Campylobacter jejuni*, and Enterohemorrhagic *Escherichia coli*, EHEC) were detected. Water samples tested positive in 35.7% (4/11) of the outbreaks investigated. In two outbreaks samples were collected after chlorination and consequently results were negative. Environmental investigation identified factors that led to water contamination, such as failures in water treatment and disinfection, in 17/33 (52%) WBOs.

**Conclusions:** WBOs, although rare in Greece, pose a significant public health burden due to their usually large size. Environmental investigation often fails to identify the contributing factors. An integrated plan is needed to ensure water safety based on WHO recommendations, water sample collection before water treatment and testing of samples for a wide spectrum of pathogens.

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**Abstract 6406**

**Outbreak of Arcobacter butzleri? An emerging enteropathogen**

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**Background:** Arcobacter butzleri, previously named Campylobacter butzleri, is a gram-negative rod oxidase positive, with microaerobic growth at an optimal temperature of 37ºC unlike the genus Campylobacter, which grow at 42ºC. A. butzleri was reported to be the fourth most common Campylobacter-like organism isolated from patients with diarrhea, which is usually watery in case of Arcobacter and bloody in case of Campylobacter.

The aim of this study was to characterize a potential outbreak of A. butzleri detected in a short period of time in the University Hospital Marqués de Valdecilla.

**Materials/methods:** Eight strains of A. butzleri were detected in our hospital in only two months (October-December 2018). Isolates were identified by MALDI-TOF MS Vitek-MS™ system and 16S ribosomal DNA sequencing.

Enterobacterial repetitive intergenic consensus-PCR (ERIC-PCR) and Pulsed Field Gel Electrophoresis (PFGE) with KpnI were carried out to assess clonal relationship.

Erythromycin (ERY), ciprofloxacin (CIP), imipenem (IPM), fixed 2:1 ratio amoxicillin-clavulanic acid (AMC) and tetracycline (TET) gradient strips (Etest) were used to determine susceptibility by agar diffusion. Susceptibility categories were defined according to EUCAST [CIP, ERY, TET] and PK-PD EUCAST breakpoints [IPM, AMC] for Campylobacter jejuni. Cefazoline [CFZ], used as internal control because of its intrinsic resistance, was assessed by disk-diffusion method.

**Results:** During the analyzed period 328 stool samples were collected and the following microorganisms were recovered: Campylobacter jejuni (34), Salmonella enterica (28), Aeromonas sp. (7), Campylobacter coli (6) and Yersinia enterocolitica (1). Analysis of ERIC-PCR and PFGE confirmed the lack of clonal relationship between strains. Antimicrobial susceptibility is shown in Table 1.

**Conclusions:** Eight A. butzleri isolates were collected in our hospital during a 2-month period, although clonal relationship was not confirmed.

A. butzleri is an emerging pathogen with increasing incidence, and may be underestimated mainly because of the unique growth temperature at 42°C of most of laboratory at the time to isolate Campylobacter spp.

Imipenem could be an alternative treatment for multidrug resistant Arcobacter.

**Table 1: Antimicrobial susceptibility testing for the eight strains of Arcobacter butzleri.**

<table>
<thead>
<tr>
<th>No. strain</th>
<th>MIC (µg/mL)</th>
<th>Halo diameter (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ERY</td>
<td>CIP</td>
</tr>
<tr>
<td>1</td>
<td>2 s</td>
<td>0.125 s</td>
</tr>
<tr>
<td>2</td>
<td>8 R</td>
<td>&gt;32 R</td>
</tr>
<tr>
<td>3</td>
<td>4 s</td>
<td>0.125 s</td>
</tr>
<tr>
<td>4</td>
<td>1 s</td>
<td>0.032 s</td>
</tr>
<tr>
<td>5</td>
<td>4 s</td>
<td>0.06 s</td>
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<tr>
<td>6</td>
<td>1 s</td>
<td>0.016 s</td>
</tr>
<tr>
<td>7</td>
<td>4 s</td>
<td>0.064 s</td>
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<td>8</td>
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**Molecular detection of cytomegalovirus in intestinal tissue**

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**Background:** Cytomegalovirus (CMV) re-activation can occur anywhere along the gastrointestinal tract, though it seems that this virus prefers the colonic mucosa when there are injuries or inflammation. The introduction of molecular techniques has led to an improvement in the diagnosis of CMV when compared to cell culture, but there is no cut-off of CMV viral load (CMV-VL) in order to distinguish latent infection from disease. The aim of the study is to describe the positive-CMV cases detected in intestinal tissue in our hospital.

**Materials/methods:** The study (2018-2019) included 64 patients in whom the presence of CMV in rectal and colonic biopsy samples was qualitatively determined (SmartCycler®, Cepheid). Those samples with positive detection were re-analyzed by CMV-VL (COBAS® AmpliPrep/TaqMan, Roche). In addition, clinical setting and pathological examinations were reviewed.

**Results:** CMV was detected in 10 patients (15.6%). The CMV-VL was positive in 6 of them (60.0%) (average: 14,882.7 IU/mL; range: 631-57,603 IU/mL). Seventy percent of the patients were men (average age: 46.6 years; range: 17-86 years). All of the patients had some immunosuppressive risk factor: 2 (20.0%) HIV-infection, 6 (60.0%) inflammatory bowel disease chronically treated with corticosteroids and/or immunomodulators, 1 (10.0%) bone marrow aplasia and 1 (10.0%) advanced age. Moderate to intense colonic or rectal inflammation was present in all of them. Blood CMV-VL was requested for 6 (60.0%) patients, which was negative in all of the cases. Furthermore, CMV was ruled out for 6 patients (60.0%) by immunohistochemistry exam, with negative result in all of them. Finally, valganciclovir was administered in 7 patients (70.0%). All episodes were resolved favorably.

**Conclusions:** All of the patients had some immunosuppressive risk factor. All positive-CMV patients presented a moderate-intense inflammation of the intestinal mucosa. PCR qualitative detection of CMV in biopsy samples is more sensitive than the quantitative technique. Antiviral treatment was required in 7 patients with clinical improvement in follow-up.

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Abstract 6409

Comparison of colistin-resistant Klebsiella pneumoniae strains in five Greek hospitals

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Background: Klebsiella pneumoniae causes severe hospital infections. In Greece, since 2008, isolation of multi-resistant strains that produce Klebsiella pneumoniae Carbapenemase (KPC) with resistance to all beta-lactamic antibiotics including carbapenemes, has been reported. Thus, polymyxins (polymyxin B and colistin) are the treatment of choice. Despite of their recent entry in clinical practice, resistance to polymyxins has already been developed.

Materials/methods: Molecular identification and comparison of 18 colistin resistant K.pneumoniae strains that were sent to the Central Laboratory of Public Health from five Greek hospitals during the period 01/01/2011 until 30/07/2012, was performed. The 18 K.pneumoniae strains were sent from two hospitals of Athens, one of Thessaloniki and two of Western Greece. Antimicrobial Susceptibility Test to colistin and meropenem was performed by the E-test method. The gene of blaKPC was detected with PCR. The strains were identified with the molecular method of PFGE (Pulsed Field Gel Electrophoresis) and the imprints were compared with the GelCompar2 system.

Results: All of the 18 strains were resistant to colistin and meropenem and all of them produced beta-lactamase KPC. After performing PFGE the strains were categorized in nine types/subtypes. The dendrogram revealed that there were three different dispersions in different hospitals and different time. These dispersions referred to 2 strains of subtype A1, 2 strains of subtype C and 8 strains of subtype A4. The rest of 6 strains revealed heterogeneity which corresponds to sporadic isolations.

Conclusions: In Greece, K.pneumoniae resistance to colistin is not clonal, but is due to the dispersion of sporadic resistant isolates that are probably created during antibiotic treatment.

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Usefulness of sputum for the identification of the viral aetiology in adults with community-acquired pneumonia

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Background: Despite the molecular approaches developed in diagnosis, the identification of the causative agent of community-acquired pneumonia (CAP) remains a challenge; thus, only in approximately 50% of the CAP a definitive diagnosis of the etiologic agent is reached. Our goal was to know the value of sputum in the diagnosis of the viral etiology of CAP in adults.

Materials/methods: Prospective cohort study of consecutive adult patients hospitalized with CAP. Blood, nasopharyngeal swabs and sputum were taken in the first 24 h after hospitalization. From these samples, DNA/RNA was extracted and viruses were identified by a multiplex PCR (Allplex, Seegene, Madrid, Spain). Viral loads in sputum and blood were quantified using commercial standard curves of complete viral genomes (Amplirun, Vircell, Granada, Spain). Bacterial identification was carried out by standard blood and representative sputum cultures. Demographics and clinical data of the patients were collected. Data were compared by chi-square or Mann Whitney U tests; a \( p < 0.05 \) was considered significant.

Results: Two hundred and fifty adult patients with CAP have been included (January 2018-September 2019): 58 (23.2%), 37 (14.8%), and 34 (13.6%) with bacterial, viral, and mixed etiologies, respectively; in 121 (48.4%) patients an etiological diagnosis was not reached. Out of the 250 patients, 4 (1.7%, n=241) showed viremia (5.5x10^4 to 1.2x10^7 copies/ml). Fifty-seven (22.9%, n=249) and 28 (53.8%, n=52) had a virus detected in nasopharyngeal swabs and representative sputum, respectively. The mean viral loads in sputum ranged from 3.88x10^5 to 1.87x10^7 copies/ml. The most frequent viruses were rhinoviruses in 23 (9.2%) and influenza in 19 (7.6%) patients. Bacterial/virus co-infections were detected in 34 (13.6%) patients and virus-virus in 1 (0.4%). No differences were observed regarding hospital stays (5 [3.25-8] vs. 4.5 [4-5.75] days, \( p=0.58 \)) or mortality (6.3% vs. 1.1%, \( p=0.26 \)) between cases of bacterial and viral etiologies.

Conclusions: The frequency of viral etiology in hospitalized adults for CAP (mono- or co-infections) was 28.4%, with rhinovirus and influenza virus as the main etiologies. Viral detection and quantification in representative sputum is more sensitive than nasopharyngeal swabs for the etiological studies in viral CAP in adults. As expected, the frequency of viremia was low.

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Phylogenetic and geographical analyses of bat Coronaviruses
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Background: Coronaviruses (CoVs) are classified into four genera, namely Alphacoronavirus, Betacoronavirus, Gammacoronavirus and Deltacoronavirus. Similar to other single-stranded RNA viruses, CoVs possess a high tendency for recombination and high mutation rates. Hence, they have a broad host tropism. Notably, Alphacoronavirus and Betacoronavirus encompassing Rhinolophus bat coronavirus HKU2, Severe acute respiratory syndrome-related coronavirus, Middle East respiratory syndrome-related coronavirus, etc. are found in bats. As bats are capable of sustained flight and are globally distributed, it is important to study bat CoVs’ global epidemiology in order to understand CoVs evolution and their interspecies transmission pathways.

Materials/methods: Respiratory and alimentary samples of various bat species from different geographical locations were collected for viral RNA extraction. Extracted RNAs were then reverse transcribed and amplified by polymerase chain reaction for detection of CoVs and complete genome sequencing. The sequences obtained, together with those available in GenBank, were then used for phylogenetic analyses, recombination studies and geographical analyses.

Results: Only members of Alphacoronavirus and Betacoronavirus were found in bats. When analyzing the origins of different bat CoVs, it was revealed that both Alphacoronavirus and Betacoronavirus were globally distributed. However, members of Alphacoronavirus seems to be more prevalent, with a two-fold higher detection rate, and more widespread than members of Betacoronavirus. The distribution of CoVs was closely related to their hosts’ habitats as Merbecovirus which infected bats of the family Vespertilionidae possessing distinct and diverse habitats was more geographically widespread than Norbecovirus and Sarbecovirus. The higher the number of bat species with overlapping habitats there were, the more frequent coronaviral recombination events took place. Locations in which a high diversity of bats resided such as Yunnan Province in China were the regions with higher bat CoV diversity. More recombination events were observed in the bat CoV strains in these areas. Last but not least, a positive correlation between the diversity of CoVs and that of bats was indicated in Merbecovirus and Vespertilionidae.

Conclusions: A wide variety of bat CoVs belonging to Alphacoronavirus and Betacoronavirus were identified. Diversities, geographical distributions and habitats of bats were shown related to the diversity of CoVs through recombination studies and geographical analyses.

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Abstract 6413

Carbapenem-resistant *Acinetobacter baumannii* and its genotypic profile in a tertiary hospital South Sulawesi, Indonesia

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**Background:** *Acinetobacter baumannii* is one of the most important bacteria isolated from among hospitalized patients worldwide due to its high propensity to antibiotic resistance, including carbapenem antibiotics. Since surveillance report for this resistance from the eastern region of Indonesia is still not available, therefore, we aimed to determine the phenotypic prevalence and the molecular detection of carbapenemase genes among *A. baumannii* isolated at tertiary hospital in South Sulawesi Indonesia.

**Materials/methods:** Specimens from patients with signs of infection were collected for standard bacterial identification. Bacteria were identified to species level and antibiotic sensitivity test performed by an automated bacterial identification system. Isolated *A. baumannii* were subsequently extracted for DNA, and amplification of carbapenemase encoding gene by PCR was performed targeting bla-Oxa23, bla-Oxa51, Bla-NDM and Bla-IMP genes. In addition, gene sequencing was also performed.

**Results:** During eight months period, 106 *A. baumannii* were isolated. Majority of samples were sputum (62.3%), followed by pus (23.6%), urine (5.6%), and the rest; blood, bronchial lavage, body fluids, and ear exudates (8.5%). Among these isolates, phenotypically; 38 (35.8%) were resistant to carbapenem antibiotics. Further genotypic identification revealed 100%, 45.3%, 33.9%, and 11.3% of the isolates harboring the bla-Oxa51, bla-Oxa23, Bla-NDM, and Bla-IMP genes, respectively.

**Conclusions:** There is a high prevalence of carbapenem-resistant *A. baumannii* isolated in Tertiary Hospital of South Sulawesi within short period of time. Therefore, an extensive surveillance and preventative measures need to be implemented, immediately.

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Continuous genomic surveillance of the third generation cephalosporin-resistant Enterobacteriaceae circulating in intensive care units of a 1600 bed university hospital, France

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Background: Third generation cephalosporin resistant Enterobacteriaceae (C3G-E) are disseminating worldwide leading to increased mortality in intensive care units (ICU). The aim of this study was to determine C3G resistant-Escherichia coli (Ecol), Klebsiella pneumoniae (Kpn) and Enterobacter cloacae complex (ECC) clonal populations circulating in two ICU at the university hospital of Caen, France for nine months in 2019 using routine whole genome sequencing (WGS) analysis.

Materials/methods: The first C3G-E was collected from any clinical specimens or systematic faecal carriage screening. Identification was performed by mass-spectrometry (MALDI-TOF) and antimicrobial susceptibility testing by disk diffusion method according to the EUCAST guidelines. WGS was carried out on all Ecol, Kpn and ECC strains using NextSeq 500 platform. In silico sequence type (MLST) and antimicrobial resistance genes were searched. Core genome Multi locus Sequence Type (cgMLST) was realized using web-dedicated schemes for Kpn and Ecol and homemade scheme for ECC. Furthermore, mapping against genome references allowed single nucleotide polymorphisms approach for grouped cases investigation.

Results: For nine months, 126 patients were included (sex ratio M/F was 2, average age was 66 years old). Strains were isolated from rectal swabs (n=106, 84%), respiratory samples (n=9, 7%) and blood cultures (n=2, 2%). Ecol was the main species recovered (n=48, 38%), followed by ECC (n=40, 32%) and Kpn (n=38, 30%). CTX-M-15-producing C3G-E represented 66% of all strains. Ecol populations were diverse with 30 distinct ST with the ST131 (n=13, 27%) as the dominant one. Regarding the eleven ST ECC and Kpn populations found for each, ST66 and ST11 were the main ST for ECC (n=20, 50%; n=7, 18% respectively) and ST405 was major for Kpn (n=24, 63%). Furthermore, cgMLST and SNP analyses confirmed the homogenic ECC ST66 population and Kpn ST405 population (differed by 50 maximum SNP). Cross-transmissions between patient-to-patient and medical equipment contaminations have been revealed for ST114 and ST66 ECC and ST405 Kpn populations.

Conclusions: The diffusion of C3G-E into ICUs of our hospital was mainly clonal for ECC and Kpn whereas it was more diverse for Ecol. Implementation of systematic genomic surveillance could improve hygiene procedures by outbreaks, cross-transmissions and contaminated material detections.

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Abstract 6417

**High rate of microbiological clearance using intravenous fosfomycin combined regimens in infections caused by multidrug-resistant non-fermenting Gram-negative bacilli: clinical experience in an intensive care unit in Rome**

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**Background:** Infections due to MDR non-fermenting Gram-negative bacilli are characterized by a high mortality rate, and few therapeutic strategies. In this setting intravenous fosfomycin, thanks to synergistic activity with several antimicrobials could represent a feasible option for the treatment of these infections. We report our clinical experience in Intensive Care Unite (ICU) patients.

**Materials/methods:** A retrospective case-control study was designed, enrolling patients, from March 2018 until August 2019 admitted in ICU of “Cristo Re” General Hospital in Rome with infections caused by MDR *Pseudomonas aeruginosa* (MDR-PA) or *Acinetobacter baumannii*. Cases were defined as patients treated with fosfomycin combined regimens, controls were patients exposed to other regimens. All causes and infection-related mortality at 28 days and microbiological resolution (defined as a negative control at the end of treatment) were evaluated in both groups. Chi-square test was used to compare frequencies, t-test to compare means between groups.

**Results:** 41 patients were enrolled (24 pt with MDR-*Acinetobacter baumannii* and 17 with MDR-PA). 18 (43.8%) were male, with median age of 74 years (C.I 62.5-80.0). 18 pt (43.8%) showed septic shock at diagnosis. Most of infections detected were pneumonia (27 pts, 65.9%, HAP and VAP included), followed by BSIs (13 pts, 31.7%), UTIs (6 pts, 14.6%) and surgical infections (5 pts, 14.2%). Fosfomycin was used in 19 patients in combination with other antimicrobials. No differences in baseline characteristics were found between groups except for mean duration of treatment, significantly shorter for fosfomycin group (9.6 days vs 11.7 of controls p=0.03).

Any cause mortality was 36.8% and 45.5% in cases and controls respectively (p=0.58), but only 15.9% of patients treated with fosfomycin had an infection-related death (vs 22.7 of controls, p=0.57). Microbiological clearance was achieved in 84.7% of cases and 59.1% of controls (p=0.07). Moreover, a significant higher microbiological outcome was found for MDR-PA infections, in patients exposed to fosfomycin [100% vs 62.5% of controls p=0.04].

**Conclusions:** Our data show a high rate of microbiological success in treating MDR non-fermenting Gram-negative bacilli infections with intravenous fosfomycin based-regimens, especially in MDR-PA infected-patients. Furthermore better outcomes are achieved with a shorter duration of therapy.

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Efficacy of a carbapenem-sparing regimen for treating post-surgical intra-abdominal infections: a case-control study

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Background: Intra-abdominal infections (IAIs) are a common surgical complication that frequently leads to broad-spectrum and long-duration antibiotic therapy. The increasing prevalence of extended-spectrum beta-lactamases (ESBL) producing Enterobacterales raises concern about the choice of optimal antibiotic treatment. Objective of this study was to evaluate the clinical efficacy of a carbapenem-sparing empiric antibiotic therapy in post-surgical IAIs.

Materials/methods: We conducted a retrospective monocentric case-control study on patients diagnosed with localized post-surgical IAI admitted to Fondazione Policlinico IRCCS Gemelli in Rome, from January 2013 to December 2018. Patients with intra-parenchymal (i.e. liver or kidney) abscess, IBD or pancreatitis and patients who received empiric therapy different from carbapenem or piperacillin/tazobactam mono or combination therapy were excluded. We defined two groups: patients who received a carbapenem-based empiric antibiotic regimen (Carb-B) and those who received a carbapenem-sparing regimen with piperacillin/tazobactam (Carb-S). The primary outcome was adverse clinical outcome, defined as overall mortality and/or IAI relapse. Secondary outcomes were duration of therapy (DOT) and length of hospital stay (LOS). A multiple logistic regression analysis was performed to evaluate factors independently related to adverse clinical outcome.

Results: We included 265 patients, 113 in the Carb-B group and 152 in the Carb-S group. Patients in the two groups did not differ for sex, age, clinical severity at onset (SOFA score) and microbial etiology. The rate of adverse clinical outcomes was similar in the two groups: 21 (18.6%) in the Carb-B group and 22 (14.5%) in the Carb-S group, p=0.37. Median DOT (Carb-B: 20 days, IQR 14–28; Carb-S: 17 days, IQR 11–25; p=0.03) and median LOS (Carb-B: 19 days, IQR 12.5–37; Carb-S: 16 days, IQR 11–27; p=0.04) were significantly longer in the Carb-B group. At multiple logistic regression analysis, only SOFA score (OR 1.25, p=0.03) and Candida spp etiology (OR 3.19, p=0.01) were independently related to adverse clinical outcome, while receiving a Carb-B empiric antibiotic therapy had no impact on clinical outcome (OR 0.89, p=0.76).

Conclusions: A carbapenem-sparing empiric antibiotic treatment seems not to affect clinical outcome in patients with localized post-surgical IAI. These findings support the implementation of carbapenem-sparing hospital and local policies for treatment of post-surgical IAI.

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Abstract 6420

Infections in patients colonised with extended-spectrum beta-lactamase-producing Enterobacteriales: a retrospective cohort study

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Background: Patients colonized with extended-spectrum beta-lactamase-producing Enterobacteriales (ESBL-PE) have an increased risk of subsequent ESBL-PE infections compared to patients without prior ESBL-PE colonization. Concerns regarding this risk have led to a significant rise in carbapenem consumption. The likelihood of ESBL-PE versus non-ESBL-PE (nESBL-PE) infections in ESBL-PE colonized patients, however, is unclear. We investigated these relative proportions as well as relevant risk factors, as this knowledge may improve empiric antibiotic decision making for patients known to be colonized with ESBL-PE.

Materials/methods: We conducted a retrospective cohort study at the University Hospital Basel, Switzerland. Hospitalizations of patients with detection of ESBL-PE and at least one infection within the same hospitalization between 01/2016 and 12/2018 were included. The main outcome was the proportion of ESBL-PE and nESBL-PE infections. Secondary outcomes were risk factors differentiating patients with non-ESBL-PE-infections from patients with ESBL-PE-infections as determined by logistic regression analyses.

Results: 572 hospitalizations of patients colonized with ESBL-PE met eligibility criteria. Overall 684 infections occurred, of which 307 were caused by ESBL-PE (44.9%) and 377 were caused by non-ESBL-PE (55.1%). 8.2% of patients had ESBL-PE-infections as well as nESBL-PE-infections within the same hospitalization, yet most patients were affected either by only ESBL-PE-infections (44.4%) or nESBL-PE-infections (47.4%). 74.6% of ESBL-PE-infections occurred in the urinary tract whereas nESBL-PE-infections mostly affected the lower respiratory tract (42.7%). Non-ESBL-producing Escherichia coli was most frequently identified as causative bacterial pathogen in nESBL-PE-infections (16.4%). Multivariable analysis revealed dialysis to be associated with ESBL-PE-infections (OR 8.88, 95%CI 1.06-74.51, p=0.044), whereas age (OR 1.01, 95%CI 1.00-1.02, p=0.017), current ICU-stay (OR 0.58, 95%CI 0.33-0.95, p=0.033) travel abroad (OR 0.33, 95%CI 0.17-0.66, p=0.002), active immunosuppressive therapy (OR 0.42, 95%CI 0.28-0.64, p<0.001) were associated with nESBL-PE-infections. Overall mortality was higher and hospital stay longer in patients with nESBL-PE infections (OR 0.39, 95%CI 0.17-0.89, p=0.026 and OR 0.98, 95%CI 0.96-0.99, p<0.001).

Conclusions: In our cohort, ESBL-PE were not the causative pathogen in the majority of infections in hospitalized patients known to be colonized with ESBL-PE. Site of infection as well as patient-related exposures may be useful predictors of nESBL-PE infections in ESBL-PE carriers, potentially guiding empiric treatment recommendations aiming to restrict carbapenem consumption.

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**Abstract 6421**

**Beyond the minimal inhibitory concentration: novel pharmacokinetic/pharmacodynamic metrics quantify the exposure-effect relationship of levofloxacin against fluoroquinolone-resistant *Escherichia coli* based on *in vitro* infection models**

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**Background:** Dosing optimisation is crucial to tackle the challenge of antibiotic resistance and is mostly based on pharmacokinetic/pharmacodynamic (PK/PD) indices, linking PK metrics of an antibiotic to a pathogen’s minimal inhibitory concentration (MIC) [1]. However, their informative value is limited, because a dynamic component is lacking [2]. To derive novel PK/PD metrics, the exposure-effect relationship of levofloxacin (LEV) against *Escherichia coli* (Ec) was investigated utilising *in vitro* infection models (IVIM).

**Materials/methods:** Three LEV resistant clinical *E. coli* isolates (sequence type 58 (ST58), MIC=8 mg/L; ST88, MIC=2 mg/L; ST167, MIC=8 mg/L) with different *gyrA* and *parC* mutations were exposed to static LEV concentrations (n_total=35) and dynamic target site LEV concentration-time (C(t)) profiles (n_total=12). Bacterial concentrations over time were determined and the antibiotic effect was quantified as cumulative area between the growth control and the bacterial killing and regrowth curve, normalised to the cumulative area under the growth control curve. As dynamic exposure metric, the cumulative area under the LEV C(t) curve (cumAUC) was assessed. The exposure-effect relationship was analysed in R 3.6.0.

**Results:** An inhibition model, including the cumAUC50 as initial bacterial reduction parameter and cumAUCreg as a regrowth metric, best described the exposure-effect relationship under static and dynamic LEV exposure. Different model structures were compared by Akaike Information Criterion. Parameter values were precisely estimated and in accordance with observed time-kill behaviour. Lower cumAUC50 values represented a larger extent of initial bacterial reduction and lower cumAUCreg values described a more pronounced bacterial regrowth. Despite equal MIC, differences in exposure-effect relationship of ST58 and ST167 were captured in a 5-fold higher cumAUC50 for ST58 compared to ST167.

**Conclusions:** Beyond conventional PK/PD indices, our novel metrics characterised the differences in resistance and persistence mechanisms between the isolates. Different pre-existing genotypic resistance mechanisms resulted in increased cumAUC50 values. Additionally, differences in extent of phenotypic adaptation were represented by cumAUCreg estimates. The larger effect for continuously high concentrations in the static IVIM, compared to higher Cmax values in the dynamic IVIM, showed benefits of higher cumAUC values, which can be achieved by prolonging infusion times in the clinics.


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Abstract 6423

**Two in three final-year veterinary students demand improved education in rational antimicrobial use**

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**Background:** Education plays an essential role in the fight against antimicrobial resistance (AMR) in both human and veterinary medicine. Previous studies have shown that final year medical students in Europe are not satisfied with the quality of education on antibiotic use. PREPARE-VET was a joint initiative by the ESCMID study groups for veterinary microbiology (ESGVM) and antimicrobial stewardship (ESGAP) to evaluate the education of final year European veterinary students on AMR and antibiotic use.

**Materials/methods:** We invited all veterinary schools in 31 European countries to participate in a survey using the online platform SurveyMonkey®. Schools were enrolled in the study if at least 10% of their students participated in the survey. Only students that answered all questions were taken into account. The survey included questions addressing the students’ perception of quality of education on key topics related to AMR and antibiotic use as well as questions testing their knowledge and preparedness on these topics. All calculations and visualizations were performed in R.

**Results:** Thirty countries and 89 veterinary schools were included in the final analysis, accounting for 3423 students. Average participation was 45% (12-100%). Overall, 75% of the students demanded improved teaching on rational antibiotic use, of which approximately half also demanded improved teaching on general knowledge about antibiotics [see figure]. Indeed, we observed a strong lack of consensus in selecting treatment strategies towards some of the most common animal infections. For example, while Scandinavian students choose local antiseptic for treatment of canine superficial pyoderma, most students from other countries choose local antibiotics alone (31%) or combined with systemic therapy (22%). Moreover, less than half of the students knew the definition of ESBL, only 22% could recognize practices that minimize the emergence of AMR, and only one in four students was familiar with guidelines [national or international] for antibiotic use.

**Conclusions:** Veterinary students demand better education on AMR and antibiotic use. The lack of familiarity with common AMR threats, treatment guidelines, and treatment strategies that minimize AMR, calls for urgent harmonization and in-depth review of veterinary curricula in this field.

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Same-day diagnosis of severe pneumonia on intensive care using long-read whole gene 16S rRNA gene sequencing on single-sample flowcells

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Background: Nanopore sequencing allows real-time analysis, but has yet to be harnessed in clinical laboratories for rapid diagnosis. 16S rRNA whole gene sequencing improves discrimination compared to variable region assays. We investigated nanopore-based whole 16S rRNA gene sequencing (np16s) for same-day diagnosis of severe pneumonia in our ICU, the largest Severe Respiratory Failure service in the UK.

Materials/methods: A 2 phase study was conducted: (1) speciation accuracy and pipeline development; (2) performance on clinical samples. Phase 1: 167 clinically relevant species were tested (R9.4 flowcells/Guppy v2.0.5, Oxford Nanopore Technologies). Sequencing accuracy, reproducibility and limit of detection (LOD) were assessed. Multiple taxonomic classification tools, databases and read correctors were evaluated to construct a pipeline. Phase 2: 71 culture-positive and 26 culture-negative bronchoalveolar lavages were tested on novel single-sample flowcells (Flongle, ONT) using high accuracy basecalling (Guppy v3.0.6, ONT) and the Phase 1 pipeline. Analyses at 5 time-points across 16 hours were compared.

Results: Sequencing accuracy was 89% (Phase 1), 85% (Phase 2). The LOD was 55 genome copies per reaction, or 3 copies within a mixture; reproducibility was satisfactory. 140 (84%) isolates were speciated correctly. The only misclassified respiratory pathogen was Bordetella pertussis, identified as Bordetella spp. Read correction did not improve classification due to disparities between gene copies within the genome. Of 71 culture-positive BALs: 54 (76%) were concordant with culture; 12 failed quality control; 5 were discrepant including 4 misidentified Gram-negative bacteria. Of 26 culture-negative BAL: 10 had insufficient bacterial DNA for classification; 5 were positive with fastidious or easily-killed species (e.g. Mycoplasma pneumoniae); 3 contained mixed commensal organisms. Analysis at 1 hour of sequencing was equivalent to 16 hours, including composition of mixtures. A same-day automated workflow was approved for clinical service pilot commencing December 2019.

Conclusions: Np16S can be used for same-day diagnosis of severe pneumonia. New basecallers do not compensate for the reduction in sequencing accuracy from single-sample flowcells but classification remains adequate. Nanopore sequencing is sufficiently robust and consistent for routine use in a clinical diagnostic service, paving the way for the introduction of novel assays.

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A novel method for preparing structurally preserved toxoids of TcdA and TcdB from Clostridioides difficile
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Background: Clostridioides difficile is a Gram-positive, spore-forming and anaerobic bacterium and is the most common cause of healthcare-associated diarrhea in the western world. The disease results in tens of thousands of deaths annually, and carries an economic burden up to US$ 6.3 billion every year in the United States alone. Following intestinal colonization, C. difficile secretes the two cytotoxins, Toxin A (TcdA) and Toxin B (TcdB), which degrade the actin cytoskeleton in epithelial cells causing diarrhea, and may lead to pseudomembranous colitis and death.

Materials/methods: Metal-catalyzed oxidation (MCO) was used to irreversibly detoxify TcdA and TcdB, creating inactive toxoids. The cytotoxicity of the toxoids was tested on Vero cells, and the structural integrity studied using both far- and near-UV circular dichroism. Conservation of the immunogenic epitopes were assessed with an array of toxin-specific monoclonal antibodies in an indirect ELISA. Antibiotic-treated C57BL/6J mice were used to assess the immunogenic efficacy of the toxoids in a C. difficile challenge study.

Results: Here, we describe an efficient and safe method for preparing immunogenic and irreversible toxoids of TcdA and TcdB. We demonstrate that MCO using submillimolar concentration of an oxidant in combination with a pH-dependent conformational change, results in more than 6 log10 reductions in cytotoxicity of both toxoids relative to the native toxins. The toxoids are structurally similar to native toxins and highly recognized by monoclonal antibodies. Injection of the toxoids fully protected mice against disease symptoms and death following a C. difficile infection, and elicited substantial serum IgG responses against both toxins.

Conclusions: Using an optimized MCO method on TcdA and TcdB, we developed structurally intact and immunogenic toxoids, with highly conserved immunogenic epitopes. A vaccine comprising the toxoids were capable of fully protecting mice against C. difficile infection and inducing IgG antibodies against both toxins. This method is very suitable for the creation of safe toxin-based antigens and for future vaccine development should be considered as a potential replacement for cross-linking reagents.

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Abstract 6431

Polymerase chain reaction-based active surveillance of multidrug resistant pathogens in a paediatric intensive care unit: to screen or not to screen?

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Background: An increasing number of children at our institution with Multi-Drug Resistant (MDR) pathogens fostered by the limited information available on molecular surveillance, isolation, and clearance protocols, led us to delve into the rationale use of direct molecular screening of resistance genes into routine policies. Conventional culture methods take a few days, and their sensitivity and usefulness also need to be improved towards active surveillance as the use of the polymerase chain reaction (PCR).

Materials/methods: We carried out prospective admission and follow-up double surveillance comparing PCR and culture on 48 patients resided in the Pediatric Intensive Care Unit [PICU]. From February 2019 to October 2019 AllPlexTM Entero-DR assay [Seegene] which simultaneously detects eight antibiotic-resistance genes, including CPE (blaKPC, blaVIM, blaNDM, blaIMP and blaOXA-48), VRE (vanA, vanB) and ESBL (blaCTX-M) was performed directly on 207 swabs collected: 69 were from pharynx (33.3%), 68 nasal (32.8%), 64 rectal (30.9%) and 6 inguinal (2.9%).

Results: Among 207 samples, 21 (10.1%) from 10 patients were positive: 1 for a CPE type blaVIM-2 and 20 blaCTX-M (18 blaCTX-M 15 like, 2 blaCTX-M 14 like) all confirmed by sequencing. Furthermore, there was a tendency for younger age (< 15 months in 80%) although no differences were found on the basis of gender neither according to days of stay. 7 samples belonging to 4 patients were PCR-negative but culture-positive to microorganisms not targeted by the PCR (S. maltophilia, A. ursingii, S. multivorum, E. meningoseptica and C. amalonaticus). Overall, Positive Predictive Value of PCR was 100%.

Conclusions: Admission prompt surveillance identified a substantial proportion of MDR positive patients in our PICU gaining from 72 to 24 hours, although controlled comparative data were frequently lacking. Follow-up cultures drive out and patients cleared per protocol might enact more active routine programs that could reduce the prevalence of MDR and pre-emptive therapy. Resource limitations and uncertainty regarding the optimal approach may have kept many facilities to implement rigorous molecular screening programs that remain open to debate, enclosing a boarder amount of targets such as MRSA, S. maltophilia, P. aeruginosa MDR, A. baumannii, etc.

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Collateral responses to fluoroquinolone resistance in *Streptococcus pneumoniae*

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**Background:** *Streptococcus pneumoniae* is the major cause of community-acquired pneumonia and meningitis, responsible for high morbidity and mortality. Of increasing concern is the global dissemination of multi-resistant *S. pneumoniae* clones compromising treatment efficacy. A promising approach to address this problem is collateral sensitivity (CS) cycling. The aim of this study was to determine the CS and collateral resistance (CR) responses of fluoroquinolone-resistant *S. pneumoniae*.

**Materials/methods:** Eight isogenic fluoroquinolone-resistant *S. pneumoniae* R6/D39 mutants were selected at concentration of ciprofloxacin equal to EUCAST ECOFFs and were whole-genome-sequenced using Illumina MiSeq to identify resistance mechanisms and causal factors underlying CS/CR. In addition, nine *S. pneumoniae* R6/D39 transformants carrying clinically relevant *gyrA* and/or *parC* mutations were created. Minimal inhibitory concentrations (MICs) of 13 commonly used antibiotics were determined for each strain via broth microdilution. CS/CR was determined by comparing the MICs of resistant strains to the isogenic antibiotic-sensitive wild type strain.

**Results:** Although independently isolated resistant strains varied in their collateral responses, generated mutants exhibited extensive collateral sensitivity responses to penicillin (50% of the isolates), co-trimoxazole (62.5%) and several protein synthesis inhibiting antibiotics, mainly tetracycline (75%). CR responses were limited to daptomycin (50%). WGS analysis of mutant strains revealed the presence of the S79Y mutation in *parC* accompanied by mutations in different genetic loci in each spontaneous mutant, suggesting the pleiotropic effect of these secondary mutations on CS/CR phenotypes. Similar CS/CR responses were observed among isogenic transformant isolates exclusively carrying single or combination of mutations in *parC* (S79F, S79Y, D83N, D83Y and E85G) and *gyrA* (S81F) loci. Interestingly, double-mutants (*parC* and *gyrA*) exhibited differences in CS/CR responses and in some cases even in the intensity of responses compared to single mutants carrying identical mutations, suggesting epistatic effects influence collateral responses. In addition, nucleotide mutations resulting in different non-synonymous mutations at the same amino-acid caused distinct CS/CR responses.

**Conclusions:** Fluoroquinolone-resistant *S. pneumoniae* exhibit conserved CS responses to several antibiotics, especially tetracycline. Our data provide evidence that combination therapy based on CS responses may be a promising approach to eliminate *de novo* emergence of fluoroquinolone-resistance and/or treat *S. pneumoniae* infections.

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**Abstract 6434**

**Stepwise in vitro daptomycin resistance selection of Staphylococcus aureus: accumulation mutations and heteromutations**

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**Background:** Daptomycin (DAP) is one of the last-resort agents for treatment of MRSA infections. DAP resistance is rare, but frequently associated with heteroresistance or/and decreased susceptibility to vancomycin. In this study we followed genetic events during in vitro selection of DAP resistance in S. aureus of different genotypes.

**Materials/methods:** Five clinical MRSA strains and MSSA [ATCC29213] with initial MIC of DAP \(\leq 1\) mg/L were included in the study. Resistant mutants were selected during 40 passages in media with daptomycin. Whole genome sequencing was performed for derivative strains after 5, 20, and 40 passages. Hetero-mutations were calculated using Breseq as: the number of reads with mutational events in derivative strain in comparison with parental strain/number of reads in this point. Hetero-mutations were considered at a frequency of > 5% and < 91%.

**Results:** After 5-20 passages all derivative strains demonstrated MIC in range 132 mg/L due to mutations in \(mprF\), and at 20-40 passages level MIC increasing up to >64 mg/L due to additional mutations in \(cls2\). Mutation in \(pgsA\) and \(fabF\) were identified in two strains. In 3 of 5 stains mutations were identified in hypothetical protein \(YfhP\) which is localized in peptidoglycan biosynthesis locus. Distribution of hetero-mutations in the genomes was associated with the different genes of general metabolism (Table). Some hetero-mutations were eliminated during passages, other were converted to homologous (marked with * in the Table). In parallel passaging in antibiotic free media these mutations were not detected.

**Conclusions:** Main DAP resistance mechanisms are associated with mutations in \(mprF\), additional mutations in \(cls2\) promoted high level MIC. Mutations in potential gene \(yfhP\) can be regarded as new markers of DAP resistance. Detected hetero-mutations are a consequence of appearance a subset of a microbial population during resistance selection.

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Abstract 6435

Phase II clinical data showed that lower recurrence of *Clostridioides difficile* infection with ridinilazole is associated with minimal impact on the gut microbiota and bile acid composition

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**Background:** In 2019 the US CDC listed *Clostridioides difficile* as one of the five urgent public health threats. The key clinical challenge is high risk of recurrent *C. difficile* infection (rCDI), typically 25% after a first episode. CDI is generally associated with gut dysbiosis. Treatment of CDI with antibiotics can further damage the microbiota and increase the risk of recurrence. Ridinilazole (RDZ) is a novel targeted spectrum antibiotic under investigation to treat CDI and reduce rCDI. Phase 2 clinical data presented here review the effect of RDZ and vancomycin (VAN) therapy on rCDI, gut microbiota and bile acid (BA) composition.

**Materials/methods:** The Phase 2 clinical trial was a double-blind study of 100 patients randomized 1:1 for 10 days RDZ or VAN treatment. Stool samples were collected from baseline (BSL) up to 30 days post-end-of-treatment (EOT) and analysed for gut microbiota and BA composition using 16S rDNA sequencing and LC-MS², respectively.

**Results:** The Phase 2 clinical study showed a 60% reduction of the recurrence rate in the RDZ-treatment arm compared to VAN. Microbiota analysis at RDZ EOT showed a significant reduction of relative abundance of two Firmicutes families including *C. difficile* compared to BSL. At VAN EOT significant losses were observed in four Firmicutes families (often to below detection), in Actinobacteria (70% drop) and in Bacteroidetes (> 3 log decrease). These changes were associated with a 25-fold increase in Proteobacteria. RDZ had minimal impact on the microbiota-associated BA composition. In contrast, VAN EOT samples showed increased levels of conjugated primary BAs (100-fold) which can mediate *C. difficile* spore germination, and, decreased levels of secondary BAs (10-fold) which generally inhibit *C. difficile* growth. Secondary BAs result from the hydrolysis and transformation of conjugated BAs by the gut microbiota. Altogether these data correlate with the leading hypothesis that preserving the gut microbiota and its ability to transform BA can lower the rate of rCDI.

**Conclusions:** These data demonstrate that RDZ preserved both the gut microbiota and BA composition in CDI patients. This likely contributed to the lower rate of recurrence compared to VAN. RDZ is currently being evaluated in Phase 3 trials.

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Leukocytes apoptosis in pulmonary tuberculosis patients with different treatment schemes

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Background: Anti-tuberculosis (TB) immune response depends from activity of phagocytosis by blood cells, formation of specific antibodies and delayed-type hypersensitivity, all this processes are performed or depends from leukocytes. Thus, study of apoptosis process in TB patients has high practical and theoretical interest.

Materials/methods: The study was performed on 30 patients with pulmonary tuberculosis: 1 group – 12 patients treated by standart regimen with I line drugs; 2 group treated by individual regimen with I and II line drugs. Control group included 12 healthy donors. The study was performed by flow cytometry on a flow cytometer FACS Calibur with addition of markers CD45+, AnnexinV FITC detection KIT I, 7AAD.

Results: Analysis of state of cytoplasmic membranes of leukocytes in the blood of pulmonary TB patients of 1 and 2 groups showed that the proportion of live intact cells was 71.05± 3.66 % that is lower by 20.75 % from the results of control group. Comparative analysis of results between 1 and 2 groups showed significant differ between amount of alive cells that was not involved in apoptosis process. In 2 group the proportion of alive cells was lower by 12.9 % than in 1 group (p<0.05). In the same time, the proportion of leukocytes on the late of apoptosis/necrosis, that have deep damages of cell structure, was higher by more than 10 % than in 1 group (p<0.05). The differences between proportion of leukocytes on other stages of apoptosis were not significant (p≥0.05).

Conclusions: Our results suggest that treatment of pulmonary tuberculosis is accompanied with externalization of phosphatidylserine in the phospholipid leaflet of the plasma membrane of CD-45+ leukocytes. Significant difference between groups of patients in the proportion of absolutely alive leukocytes and cells on the late stage of apoptosis/necrosis can be a prove ment of higher activation of apoptosis process by individual treatment regimen that included I and II lines drugs, comparing with standart I line regimen. The obtained data allow us to recommend the study of influence of different antituberculosis drugs and regimens to apoptosis process of immune-competent cells to evaluate efficacy of pulmonary tuberculosis treatment.

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Can UF-5000 body fluid mode be an alternative for cerebrospinal fluid cell count?

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Background: Cellular analysis of cerebrospinal fluid (CSF) provides diagnostic information in meningitis or encephalitis. The aim of the study was to evaluate performance of UF-5000-BF (Sysmex Co., Kobe Japan) body fluid mode and compare the obtained results with cytometric analysis of CSF with optical counting as reference method.

Materials/methods: A total of 426 CSF samples from patients with suspected cases of central nervous system infection submitted to our clinical microbiology laboratory, were enrolled in the study. Specimens were counted with Thoma cell counting chamber and they were simultaneously analyzed with UF-5000 body fluid mode based on flow cytometry principle. The results were evaluated according to CLSI document H56-A. The manual white blood cell (WBC) counts were grouped into nine categories. The comparison of the manual method and the automated system according to these categories were determined with Pearson’s correlation coefficient.

Results: The study group consisted of 223 (52.3%) children and 203 (47.7%) adult patients. Of the 107 samples classified as positive (> 7 WBC/µL) in pediatric patients by manual counting, 90 were also determined as positive by UF-5000-BF. Sensitivity and specificity were 84.1% and 73.2%, respectively. In adults, 95 samples were counted as positive (>5 WBC/µL) by optical microscopy whereas 87 were analyzed as positive with UF-5000. Sensitivity and specificity were determined as 91.5% and 62.0%, respectively. The comparison between UF-5000 and light microscopy differentiation cell counts showed a Pearson’s correlation of 0.84 for WBC with p<0.0001 and results of UF-5000-BF displayed good agreement with light microscopy optical counting for WBC (Table 1).

Conclusions: The comparison between UF-5000-BF results and optical microscopy counts showed a good correlation for WBC. Particularly the performance of UF-5000-BF was very good at ≤20 cells/µL and 400 cells/µL. This result is meaningful for our laboratory, since WBC counts were detected in this range for 76% of the samples. Thus, UF-5000-BF can be rapid, effective and automated method for CSF samples in clinical microbiology laboratory.

Table 1: UF-5000-BF WBC counts corresponding to optical microscopy results

<table>
<thead>
<tr>
<th>Optical Microscopy Results</th>
<th>Category 1 (0 - 9 cell/µL)</th>
<th>Category 2 (10 - 19 cell/µL)</th>
<th>Category 3 (20 - 49 cell/µL)</th>
<th>Category 4 (50 - 99 cell/µL)</th>
<th>Category 5 (100 - 199 cell/µL)</th>
<th>Category 6 (200 - 399 cell/µL)</th>
<th>Category 7 (400 - 799 cell/µL)</th>
<th>Category 8 (≥ 800 cell/µL)</th>
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Co-occurrence of mcr and blaCTX-M genes in Escherichia coli from healthy pigs and humans in Thailand

Thongpan Leangapichart1, Rachel A. Hickman2, Kanonwan Lunha1, Jatesada Jiwakanon4, Sunpetch Angkititrakul4, Ulf Magnussen3, Josef Järhult2, Marianne Sunde1

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Background: The plasmid-mediated colistin resistance mcr-1 was initially described from China and have increasingly been reported in humans, animals and from the environment. Until now, bacteria harboring mcr, mainly mcr-1 and its family mcr-2 to -9, have been reported across the world. Moreover, coexistence of mcr with extended-spectrum beta-lactamase (ESBL), blaCTX-M genes has become an established and an increasing treat of horizontal gene transfer (HGT) mediated antibiotic resistance. Here, we investigate the presence of mcr and coexistence with blaCTX-M genes in Escherichia coli isolated from pig farms in Thailand.

Materials/methods: Rectal swabs were collected from 847 pigs (166-pooled samples) from 166 pig farms. Fecal samples were provided by from 159 farmers and 114 humans in proximity to farms but without direct contact with pigs. Isolation of multi-drug resistant (MDR) E. coli was done by use of selective methods. Minimum inhibitory concentrations and whole-genome sequencing (WGS) were performed for all isolates.

Results: Overall, 492 E. coli were isolated from 439 pooled-swab and fecal samples of which 33.7% (166/492) were mcr-positive. The predominant mcr genes were mcr-1 (109/166, 65.6%), mcr-3 (70/166, 42.1%), and mcr-9 (1/166, 0.6%). mcr-positive E. coli with blaCTX-M14 (54/103) and blaCTX-M55 (49/103) were detected among the isolates. Interestingly, coexistence of mcr-1, mcr-3, and a blaCTX-M gene was found in 15 isolates. WGS analysis of mcr-positive E. coli revealed high genomic diversity, comprising 64 sequence types (STs) and 24 new STs. A variety of plasmid backbones carrying mcr genes were identified including IncHI1, IncHI2, IncFI1, IncI2, IncP1, IncX1, and IncX4. Our results also indicate evidence of transmission of MDR bacteria between pigs and humans.

Conclusions: High prevalence of mcr-positive E. coli including the evidence of coexistence with blaCTX-M gene indicated high MDR bacteria in pig and human origins in Thailand. This study highlights the importance for more substantial monitoring which can aid in developing more appropriate antimicrobial stewardship. Also, there is a need to provide the knowledge of using antibiotics in both human and animal sectors.

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Phenotypic and genotypic comparison between *Escherichia coli* isolates causing recurrent and sporadic cystitis

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**Background:** *Escherichia coli* is by far the predominant agent of urinary tract infection. Half of women suffer from recurrent cystitis in the year following the index episode. However, their physiopathology is still poorly understood. Thus we aimed to analyse genomic and phenotypic markers associated with recurrent *E. coli* cystitis compared to sporadic ones.

**Materials/methods:** 343 *E. coli* prospectively collected over 18 months were analyzed; 124 from recurrent cystitis (49 patients with ≥2 episodes over 6 months) and 217 from sporadic cystitis. Genetic diversity was studied by Clermont phylo-typing and CH-typing (*fimH* and *fumC* sequencing). Afterwards, 80 isolates were selected: 43 from recurrent cystitis (9 patients, each with ≥4 episodes over 12 months) and 32 from sporadic cystitis (matched on CH-type). These isolates were further characterized by whole genome sequencing (wgs) by Illumina® technology, in silico MultiLocus Sequence Typing (MLST), analysis of the virulome (VirulenceFinder) and resistome (ResFinder, PointFinder), biofilm production measurement (crystal violet assay), antimicrobial susceptibility testing (disk diffusion method) and fitness (growth curve analysis).

**Results:** Phylotyping of the 343 isolates revealed that B2 was the most prevalent phylogroup (53%) followed by D (14%) and A (13%). 120 unique CH-types were identified with no specific lineage associated with recurrent or sporadic event. Despite this genetic diversity, half of the 49 patients with recurrent cystitis were infected at least 2 times with the same strain (identical phylogroup and CH-type). Interestingly, 100% of the 9 patients with ≥4 episodes in 12 months relapsed at least once with the same strain, consistent with MLST results. This must be confirmed by wg single nucleotide polymorphisms analysis. Comparative analysis of isolates from recurrent and sporadic cystitis has not shown significant differences in terms of virulome (genes involved in adhesion, iron capture or biofilm formation), biofilm production and fitness. Antibiotic resistance to amoxicillin, cotrimoxazole and ciprofloxacin was significantly more frequent in recurrent cystitis and correlated to resistome analysis.

**Conclusions:** Sporadic *E. coli* cystitis are due to a large diversity of strains. Recurrent ones mix episodes with unique strains and episodes with indistinguishable strains by classical typing methods. The reasons of such dual dynamic request further studies.

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Abstract 6442

**Personal experience and availability of surveillance data, diagnostics and therapeutics are the main drivers for treating carbapenem-resistant Gram-negative bacteria infections**

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¹University of Verona, Verona, Italy, ²Global Antibiotic R&D Partnership [GARDP], Geneve, Switzerland

**Background:** The GARDP COHERENCE survey aims at assessing prescription habits among clinicians who routinely treat infections due to carbapenem-resistant Gram-negative bacteria (CR-GNB) including *Acinetobacter*, Enterobacterales, *Pseudomonas* in adults and pediatric populations worldwide accounting for surveillance data, diagnostic and treatment availability.

**Materials/methods:** A 36-item anonymous web-based questionnaire was developed and validated by a multidisciplinary team. A core-expert group of 101 members from 70 countries facilitated the survey distribution through 50 international networks to prescribers via a SurveyMonkey link. Differences in responses across three main prescribers’ characteristics (geography, income and prescription frequency) were computed using Chi-square test with level of significance <0.05.

**Results:** In 10-week period, 1020 respondents from 95 countries and 687 hospitals completed the questionnaire. Twenty per cent (204) of respondents were from low and lower-middle income countries (LIC/LMIC), 14.4% (145) had experience in treating children or neonates. In 38% of the surveyed countries (33/95), clinicians could not rely on national/regional surveillance systems tracking carbapenem-resistance rates. Income status substantially affected the availability of diagnostics and therapeutics: 94% of LIC/LMIC countries had access solely to standard antimicrobial susceptibility tests, while molecular diagnostic tools were more frequent in HIC compared to LIC/LMIC. Molecules licensed in the last five years (ceftazidime-avibactam, meropenem-vaborbactam, plazomicin, eravacycline) were available only in 19 (20%) countries. Therapeutic schemes included 40 combinations in *Acinetobacter* up to 178 in Enterobacterales. In general, dual-antibiotic schemes were preferred over single and triple-antibiotic schemes, irrespective of sepsis source and bacterial species. The most prescribed dual-antibiotic scheme was carbapenem plus polymyxin. Empirc coverage for CR-GNB was mainly dictated by infection severity and less by epidemiological data and/or risk factors for CR-GNB acquisition. Eighty per cent of respondents prescribed combination therapy driven by the personal perception of higher clinical efficacy. In 62% of respondents, the choice of prescribing combination over monotherapy did not rely on evidence but on experts’ recommendation and personal experience.

**Conclusions:** The heterogeneity of prescription habits across the world seems to be mostly influenced by personal experience and unequal access to diagnostics and therapeutics. The development of guidelines for CR-GNB infections should consider these data when issuing recommendations targeting a global audience.

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**Abstract 6444**

**Persistence of serotype 19F and the importance of non-vaccine serotypes in paediatric non-invasive pneumococcal pneumonia in Portugal, 2015-2018**

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**Abstract third-party references:** Portuguese Group for the Study of Streptococcal Infections

**Background:** The introduction of pneumococcal conjugate vaccines (PCVs) into routine infant immunization programs led to significant changes in serotype distribution and antimicrobial susceptibility patterns of pneumococci causing IPD, but little is known about the epidemiology of non-invasive pneumococcal pneumonia (NIPP) in children. Given this, we aimed to characterize the pneumococcal population causing NIPP in children (<18 years) in Portugal from 2015 to 2018, after the inclusion of PCV13 in the National Immunization Plan, by serotyping and antimicrobial susceptibility testing.

**Materials/methods:** A total of 190 *Streptococcus pneumoniae* isolates recovered from sputum, bronchial secretions or bronchoalveolar lavage of pediatric patients in 62 hospitals in Portugal between January 2015 and December 2018 were characterized by serotyping and antimicrobial susceptibility testing.

**Results:** The majority of the NIPP cases were caused by serotypes not included in PCV13 (70%), with serotypes 11A (n=23), 23B (n=17) and 21 (n=9) being the most frequent. Among PCV13 serotypes, serotype 19F was the most frequent (n=19) followed by serotypes 3 (n=15) and 19A (n=10). Other PCV serotypes detected included 14 (n=7), 23F (n=2) and 4, 6A, 6B and 18C (n=1 each). In the same time period, the proportion of cases caused by PCV13 serotypes was significantly lower in NIPP than in IPD (30% vs 45%, p<0.001). 56% of the isolates were susceptible to penicillin and erythromycin, while 15% of the isolates were simultaneously resistant to erythromycin and penicillin non-susceptible (MIC>0.06 mg/L). Overall, 21% of the isolates were penicillin non-susceptible and resistance to erythromycin was expressed by 23% of the isolates, mostly associated with serotypes 14, 19A and 19F. When considering the current non-meningitis breakpoints, no strain would be resistant to penicillin.

**Conclusions:** Despite the use of PCV7 >15 years, serotype 19F is still an important serotype in pediatric NIPP in Portugal. In recent years, pediatric NIPP was mostly caused by non-vaccine serotypes in contrast to the dominance of PCV13 serotypes in IPD, suggesting different effects of vaccination on these two presentations. Continued pediatric NIPP surveillance is crucial to understand the full effect of vaccination.

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Squamous cell carcinoma of the anus screening in people living with HIV: HPV genotyping is as important as cytology in anal cancer early diagnosis

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Background: Squamous cell carcinoma of the anus is one of the most common non-AIDS-defining malignancy among people living with HIV (PLWH). Our project aimed to evaluate the incidence of precancerous lesions in high-risk patients, in order to assess the best screening method.

Materials/methods: All MSM and women with history of CIN PLWH, aged >18, outpatients attending the Infectious Diseases Clinic have been offered to perform a first level screening including anal Pap test and HPV genotyping followed by high resolution anoscopy (HRA) in Pap test positives or high risk HPV (HRHPV) carriers.

Results: 87 Pap tests (41.5% of 209 enrolled) were positive for HPV-related lesions, 78 (37.3%) low grade squamous intra-epithelial lesions (LSIL) and 5 (2.4%) atypical squamous cells of undetermined significance (ASCUS) while high grade lesions (HSIL) were found in 4 patients (1.9%). 157 of 209 screened (75.1%) performed also HPV genotyping and 123 (58.8%) carried least one high risk HPV (HRHPV). 169 screened (80.8% of 209) had the indication for second level screening. Among 68 HRAs performed until today (51 in Pap test positive and 17 in HRHPV carriers with Pap test negative), 29 (42.6%) showed LSIL and 12 HSIL/CIS (17.6%). In 4 patients HSIL was diagnosed only thanks to a high-risk genotype. Statistical significance was only achieved in the univariate analysis by correlating the positive pap test alone as an indication for HRA with biopsy confirmation of LSIL even with anoscopic examination. HPV16 is the most frequently isolated genotype (38 cases, 24.4%). Of note is the high frequency of isolation of genotypes considered to be possible / probable high risk as HPV 53 which was the second most prevalent genotype (21%) followed by HPV 66 (15.9%) and HPV 70 (14%).

Conclusions: We can state that anal carcinoma screening including anal Pap test, HPV genotyping and second level surveillance with HRA is currently the most complete and reliable method. It is expected that with the expansion of the present study it will be possible to establish the sensitivity and specificity of the cytology and genotyping performed during the Pap test and even to modify the current screening protocol.

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Impact of recent vaccine schedule changes on pertussis epidemiology in France

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Background: Despite widespread acellular vaccine implementation, pertussis is resurgent in several parts of the world including Europe. In France, Santé publique France, with the support of the National Reference Center (NRC) of whooping cough and other bordetelloses, is responsible for pertussis surveillance and collaborates with 2 outpatient laboratories (Cerba and Biomnis) that ensure the biological diagnosis of outpatient pertussis cases throughout the country. In 2017 and 2018, an increase of nasopharyngeal samples positive for Bordetella spp. was observed, mainly in the 2-5 years group. The aim of this study was to assess the effect of the French immunization schedule modification in 2013 (from a 2/3/4 + 16-18 months to a 2/4 + 11 months doses schedule) on pertussis epidemiology.

Materials/methods: We analysed outpatient laboratory results from nasopharyngeal swabs from symptomatic patients between 2012 and 2018, tested for Bordetella spp using PCR targeting insertion sequences IS481. The data analysis was based on a Poisson regression model, in which all positive cases by year and age depended on the year, the age group, the vaccine effectiveness and duration of protection, and the size of each age group. Different models were tested, in which vaccine effectiveness and duration of protection could depend on the type of vaccine schedule.

Results: The number of pertussis cases increased in 2017 and 2018 (x 2.4 compared to 2014-2016), with an increase in the proportion of the 2-5 years [1% in 2017-2018 vs. 7% in 2014-2016]. The models supporting a rapid decrease of vaccine protection following vaccination with the new vaccine schedule gave the best fit to epidemiological data. The predicted age distribution of cases for 2019 using the best model showed good correlation (r=0.96, p<0.001) with the observed age distribution reported between January and September 2019.

Conclusions: The increase of pertussis cases observed in 2017-2018 in children born after 2013 and aged 2-5 years, and the larger proportion of this age group among all pertussis cases, could be explained by a short-lived protection induced by the novel vaccine schedule recommended in France since 2013. A preliminary analysis of 2019 data seems to confirm this finding.

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Elevated tolerance to disinfectants in a carbapenemase-producing Klebsiella pneumoniae isolate obtained from a duodenoscopy-associated outbreak

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Background: Nosocomial outbreaks of carbapenemase-producing Klebsiella (K.) pneumoniae (CPKP) have become a major concern in healthcare facilities worldwide. In some cases duodenoscopes have been identified as a source of transmission. In 2014 a duodenoscopy-associated outbreak affecting 13 patients occurred in a German hospital. We investigated the efficacy of disinfectants used for the reprocessing of duodenoscopes in inactivating the CPKP outbreak strain.

Materials/methods: Genetic relationship of CPKP isolates obtained from 13 patients and one duodenoscope was confirmed by PFGE. Antimicrobial susceptibility testing was performed. MLST type, resistance and virulence genes were extracted from whole genome sequencing (WGS) data.

The efficacy of different disinfectants was tested in suspension tests based on DIN EN 13727 comparing the CPKP outbreak strain with a K. pneumoniae reference strain (ATCC 13883). Efficacy of peracetic acid (PAA)-based disinfection was further assessed in a biofilm assay developed at Robert Koch-Institute. Successful disinfection was defined as a reduction of ≥ 5 log10 recoverable mean CFUs.

Results: The CPKP outbreak strain was resistant to fluoroquinolones, aminoglycosides, cephalosporins and carbapenems but sensitive to tigecycline and colistin. WGS analyses revealed a ST101 K. pneumoniae strain with genes encoding the carbapenemase OXA-48 and ESBL CTX-M-15. Furthermore, genes involved in iron uptake systems (ybt, kfu) and biofilm formation (mrk) were detected.

The suspension tests showed no difference between the outbreak and reference strain in terms of efficacy of disinfection by H2O2, glutaraldehyde and isopropanol. However, we found decreased susceptibility of the outbreak strain towards PAA. We further pursued this phenomenon by testing efficacy of PAA disinfection in biofilm. Here, 0.15% PAA, the concentration used in reprocessing of the duodenoscope from which the outbreak strain was obtained, was sufficient to achieve disinfection of the reference strain but not of the outbreak strain.

Conclusions: We report a CPKP strain of a major epidemic clonal lineage that exhibited enhanced tolerance to PAA-based disinfection, which was performed for reprocessing of duodenoscopes at the time of the outbreak. This phenomenon has probably contributed to the transmission of the outbreak strain. Tolerance against disinfectants might contribute to nosocomial spread of epidemic K. pneumoniae and needs to be further studied.

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Abstract 6453

Potential impact of removing metronidazole from the treatment armamentarium for mild acute Clostridioides difficile infections

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**Background:** The epidemiology of Clostridioides difficile infection (CDI) has rapidly evolved, with increasing rates of resistances, toxin production, and recurrences. This, in addition to limited clinical data, resulted IDSA guidelines, to recommend removing metronidazole from the treatment armamentarium, even for mild CDI. However, superiority of vancomycin over metronidazole specifically for mild CDI, has not been firmly established, and extensive use of vancomycin, might lead to detrimental outcomes, including possible emergence of vancomycin-resistant enterococci (VRE).

**Materials/methods:** We conducted a retrospective cohort analysis (2010-15) at Shamir (Assaf Harofeh) medical center, Israel. Adult patients with acute CDI (first and single episodes) per IDSA definitions were enrolled. CDI severity was determined based on established criteria. Cox and Logistic regressions were used to analyze post-CDI VRE rates (up to 18 months), and in a sub-analysis (using propensity score matched analysis), the efficacy of metronidazole vs. vancomycin for mild cases, respectively.

**Results:** 409 patients were enrolled during the 6-year study period (median age 78 years). There were 13 post-CDI VRE acquisitions, all among patients treated solely with vancomycin during their acute CDI. In a multivariable controlled analysis, independent predictors of post-CDI VRE acquisition were recent exposure to proton-pump inhibitors (aOR=6.6, p=0.04), severe level of sepsis at CDI onset (aOR=5.2, p < 0.001) and treatment with oral vancomycin [alone or in combination, aOR=6.7, p=0.03]. Of 164 patients with mild CDI, 131 received monotherapy. In univariable analysis among these patients, all clinical outcomes were favorable in the metronidazole group. After propensity score matched analyses, metronidazole remained non-inferior to vancomycin in all 16 morbidity and mortality outcomes that were captured and analyzed (e.g., mortality, length of stay, functional deterioration, re-hospitalizations, institutionalization).

**Conclusions:** The recent shift in CDI treatment recommendations, might lead to increased usage of oral vancomycin, also for mild cases. We showed a significant independent association between treatment with oral vancomycin and later acquisition of VRE, and non-inferiority of metronidazole for mild cases. in first episodes of mild acute CDI, metronidazole should still be considered a valid treatment option and vancomycin should be restricted and used judiciously.

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Molecular characterisation of carbapenemase-producing Enterobacterales (CPE) in London, UK

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Background: Whole-genome sequencing (WGS) was applied over 30 months to determine the pattern of high-risk globally-dominant clones amongst CPE isolates submitted by London laboratories to the national reference laboratory for investigation of carbapenem resistance.

Materials/methods: WGS was applied between 1st Jan ‘14 and 30th June ‘16 to the first confirmed CPE referred by London laboratories from each new patient. Additional isolates from a patient were included only if harbouring a different carbapenemase or of a different species. WGS was performed on an Illumina HiSeq 2500 and the data analysed using an in-house bioinformatics pipeline, which determined species identification, MLST profile and resistance gene content.

Results: WGS data were obtained for 927 isolates, and 96.3% (892) were of five species: Klebsiella pneumoniae (504, 54.4%), Escherichia coli (267, 28.8%), Enterobacter cloacae (47, 5.1%), Citrobacter freundii (42, 4.5%) and Klebsiella oxytoca (32, 3.5%). The most common sequence types (ST) identified in K. pneumoniae were ST14 (119), ST147 (56), ST231 (35), ST11 (30) and in E. coli ST38 (60), ST416 (27), ST405 (26), ST162 (22), ST131 (8). The most common carbapenemase detected was OXA-48 (248, 26.8%) followed by NDM-1 (247, 26.6%), OXA-181 (99, 10.7%), OXA-232 (65, 7.0%), and NDM-5 (64, 6.9%). Other minor mechanisms (<5%) included NDM-1+OXA2-32 (25, 2.7%), IMP-1 (23, 2.5%), VIM-4 (22, 2.4%), NDM-7 (21, 2.3%), GES-5 (19, 2.0%) and KPC-2 (17, 1.8%). Most CPE were detected from rectal swabs or faecal samples (459, 49.5%), followed by urine (168, 18.1%), blood cultures (53, 5.7%) and wound swabs (52, 5.6%).

Multiple species/ST/carbapenemase mechanism combinations were detected:

K. pneumoniae ST14/NDM-1 was detected from four laboratories \{n=37\}, \{n=21\}, \{n=6\}, \{n=5\}.
K. pneumoniae ST147/NDM-1 from two laboratories \{n=9\}, \{n=7\}.
K. pneumoniae ST405/OXA-48 \{n=10\},
K. pneumoniae ST834/IMP-1 \{n=10\},
K. oxytoca ST13B/GES-5 \{n=14\},
E. coli ST38/OXA-48 from three laboratories \{n=13\}, \{n=6\}, \{n=5\}.
E. coli ST38/NDM-1 \{n=20\}.

Conclusions: K. pneumoniae ST14 and E. coli ST38 were the dominant clones associated with NDM-1 and/or OXA-48 carbapenemases. However, diverse combinations of species/ST/carbapenemase were detected in London over the 30-month period.

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Abstract 6455

mcr-8-mediated colistin resistance in a carbapenem-resistant Klebsiella pneumoniae isolate
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Background: During the last two years, resistance to polymyxin is increasingly reported in Gram negatives. In Gram negative bacteria, colistin resistance results mostly from addition[s] of cationic groups such as 4-amino-L-arabinose [L-Ara4N] and/or phosphoethanolamine [pETN] on the lipid A. These modifications could be chromosome- (mainly through mgrB alteration) or plasmid-encoded [mcr gene acquisition]. Here, we characterized the mechanism responsible for colistin resistance in a carbapenem-resistant K. pneumoniae isolate.

Materials/methods: Colistin susceptibility testing using broth microdilution, as recommended by EUCAST. Multiplex PCR was performed for the detection of mcr-1, -2, -3, -4 and -5. A recently described rapid [15 min] MALDI-TOF-based test [named MALDIXin test] was performed to detect modified lipid A responsible for colistin resistance. Whole genome sequencing (WGS) was performed using Illumina technology. ResFinder3.1 was used to identify acquired resistance determinants. Direct transfer of the colistin resistance gene mcr-B into E. coli J53 was attempted by liquid mating-out assays at 37°C. Selection was performed on agar plates supplemented with colistin (4 µg/ml) and sodium azide (100 µg/ml).

Results: A K. pneumoniae isolate with decreased susceptibility to carbapenems and resistant to colistin (MIC = 16 mg/L) was recovered from an immunocompromised patient with recent history of travel to Morocco. Carbapenemase production was excluded using Carba NP test and NG-test Carba5 immunochromatographic assay. Regarding colistin resistance, multiplex PCR for the detection of mcr-1, -2, -3, -4 and -5 remained negative. The MALDIXin test revealed the presence pETN-modified lipid A suggesting the production of an MCR-like enzyme. WGS data analysis revealed the presence of mcr-B gene. Transconjugants were obtained that harbored the ca. 130-kb plasmid carrying the mcr-B gene. This transconjugative E. coli J53 isolate was resistant to colistin with MIC at 8 mg/L but remain susceptible to all other antimicrobials. This self-conjugative plasmid does not carry other antimicrobial resistance genes.

Conclusions: This is the first report of MCR-B-producing K. pneumoniae clinical isolate that is not related to China.

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Genetic architecture of interspecies hybrids

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Background: Bacterial acquisition of foreign genetic material is closely associated with virulence and resistance to antibiotics. High frequency mechanisms of gene transfer are dedicated to promote the movement of mobile genetic elements such as plasmids and integrative conjugative elements. Chromosomal DNA can also be mobilised, for example when a conjugative plasmid is integrated into a chromosome. Intra-species chromosomal transfers have resulted in the creation of virulent and drug-resistant clinical isolates of *Klebsiella pneumoniae* and *Escherichia coli*. Classical experiments, mapping the repair of chromosomal mutations, have demonstrated Hfr-mediated intra- and inter-species conjugation involving *E. coli* and *Salmonella enterica* serovar Typhimurium. Very little is known about the genetic architecture and relative fitness of these hybrid strains.

Materials/methods: Using conjugation we created a set of *E. coli*-*Salmonella* hybrid strains. Hybrids were selected for the transfer of markers at different distances from the transfer origin. The relative growth fitness of hybrids was measured using Bioscreen and colony spot assays. Experimental evolution was used to address the rate and mechanisms of fitness cost amelioration. Whole genome sequencing was used to analyse the genetic architecture of the hybrids, before and after evolution.

Results: Almost all inter-species hybrids acquired a contiguous segment of donor chromosome replacing an equivalent region of recipient chromosome, with lengths ranging from ~100kb up to >4000kb. The length of acquired DNA did not correlate with relative fitness but most hybrids had reduced growth rate relative to the parental strains. Evolution to ameliorate fitness costs selected predominantly strains with mutations affecting global transcriptional regulators, and strains with increased mutation rates, suggesting that for low-fitness hybrids there is no simple path to high fitness. A very interesting observation is that several hybrid strains, in which 45% - 90% of the *Salmonella* chromosome was replaced with *E. coli* DNA, showed no reduction in growth fitness.

Conclusions: These data show that most *E. coli* – *Salmonella* hybrids suffer a severe reduction in fitness with no simple path to restore growth fitness. However, a significant fraction of hybrids retained parental levels of fitness suggesting that barriers to creating high-fitness inter-species hybrids may be significantly lower than generally appreciated.

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Faecal carriage of extended-spectrum beta-lactamase-producing members of order Enterobacterales among patients in Bulgarian hospitals

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Background: The fecal carriage of extended-spectrum β-lactamase/carbapenemase-producing Enterobacterales (ESBL/CPE) isolates remains an important risk factor for their dissemination and is poorly investigated in Bulgaria. The objective of this study was to determine the prevalence of ESBL/CPE fecal carriage in Bulgarian hospitalized patients.

Materials/methods: In total, 537 stool samples were collected from hospitalized patients in 6 hospitals in Bulgaria from December 2017 to December 2018. Species identification was done by MALDI-TOF mass spectrometry. ESBL selective agar was used for initial screening. Later the ESBL production was confirmed by the double-disc synergy test and the carbapenemase production - by the combined discs. The beta-lactamases were identified by PCR and sequencing. The disk diffusion method and MIC strips for tigecycline were used for antimicrobial susceptibility testing.

Results: Third generation cephalosporin resistant fecal carriage isolates were detected in 43.6 %: Escherichia coli (n=121), Klebsiella pneumoniae (n=66), Klebsiella oxytoca (n=7), K. michiganensis (n=3), Enterobacter cloacae complex (n=21), Citrobacter freundii complex (n=13) and Morganella morganii (n=3). Among all 537 collected isolates, PCR and sequencing identified 176 ESBL-producing isolates (32.8%). CPE fecal carriage was 2.6% (14 from 537). BlaCTX-M genes were identified in 99% of all ESBL-producing enterobacteria (n=176): blaCTX-M-1gr in 86.4% (152/176) and blaCTX-M-9gr in 11.9% (21/176). Only two isolates harboured blaSHV. The following blaESBL genes were found: blaCTX-M-15, blaCTX-M-3, blaCTX-M-1, blaCTX-M-9, blaCTX-M-14, blaCTX-M-27 and blaSHV. BlaKPC-2 and blaNDM-1 were detected in 3 and 11 isolates respectively. Twenty one AmpC hyperproducers and 13 plasmid mediated AmpC producers (7 DHA-1 and 6 from EBS family) were identified too. The susceptibility testing showed the following rates of resistance: cefotaxime(91.9%), amoxicillin/clavulanic acid(91.9%), ceftazidime(85%), cefepime(91.9%), cefoxitine(32.2%), meropenem(8.1%), imipenem(9.1%), piperacillin/tazobactam(71.8%), tobramycin(87.7%), gentamicin(56%), amikacin(47.9%), ciprofloxacin(67.1%), levofloxacin(60.7%), tigecycline(34.2%), trimetoprim/sulfamethoxazole(50%), chloramphenicol(21.4%). Only six colistin resistant isolates of K. pneumoniae was found.

Conclusions: The presented data showed a high rate of third generation cephalosporin resistant fecal carriage isolates. Most of these isolates carried ESBLs, while plasmid mediated AmpC enzymes were identified in single isolates only. The fecal carriage could be an important reservoir for various resistance determinants. The detection of carbapenemases producing fecal isolates clearly showed the need for strong infection control measures.

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Abstracts 2020

Abstract 6462

**Delayed haemolytic anaemia following artesunate treatment in a returning African traveller**

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**Background:** At our institution malaria is relatively uncommon with an average of 7 cases per year from 2014 to 2018. Nationally 59 cases were notified in Ireland in 2018. Over a 2 year period in our institution the majority of cases treated were *Plasmodium* (*P*) *Falciparum* (*n* = 10); five were treated as severe and received IV Artesunate followed by oral Artemether-Lumefantrine. We present the case of a patient with delayed haemolysis post IV Artesunate.

**Materials/methods:** Inpatient, outpatient medical records and laboratory results were reviewed.

**Results:** A 27 year old male presented to the Emergency Department with a 4 day history of fever, myalgia and headaches after returning to Ireland from a visit to Angola. He had not taken malaria chemoprophylaxis. His initial parasite count was 14%. He was diagnosed with severe *Plasmodium Falciparum* infection and admitted to the intensive care unit for monitoring. He was treated initially with IV Artesunate for 4 days followed by oral artemeter/lumefantrine for 3 days and was discharged after 7 days.

He was seen a week later in Infectious Diseases outpatient clinic where he had complained of dizziness, shortness of breath and palpitations. His haemoglobin (Hb) had decreased from 14.8g/dL to 9.8g/dL. He was admitted 5 days later with a Hb 8.0g/dL. Reticulocytes were elevated (11.7%), LDH was high (703IU/L) and haptoglobins were low (<0.24g/L) in keeping with a diagnosis of haemolytic anaemia. His folate level was low (4.0 µg/L) and was started on replacement therapy. He did not require blood transfusion. His haemoglobin improved and recovered within 9 days.

**Conclusions:** This case of delayed haemolytic anaemia highlights the importance of follow-up of patients treated with IV Artesunate. The pathophysiology of this syndrome is not fully understood but appears to occur with hyperparasitemia. It has been thought that it is the result of the splenic process of pitting - the normal removal of infected erythrocytes whose parasites have been killed by artemesunate. These once-infected erythrocytes have a decreased lifespan, leading to delayed onset haemolysis. Although the course of haemolysis was self-limiting we routinely follow these patients for 1 month post treatment for surveillance of this syndrome.

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Efficacy of ribavirin in post-exposure prophylaxis in Crimean-Congo haemorrhagic fever

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Abstract 6463

Background: Ribavirin is the only drug of choice for post-exposure prophylaxis (PEP) in Crimean Congo hemorrhagic fever (CCHF), however its usage is not absolutely recommended.

Materials/methods: In this study, we report the management of healthcare workers’ (HCW) exposure to one fatal CCHF patient. Exposures are grouped into 3 categories according to recently published meta-analysis. The high-risk group consisted of HCWs who were directly exposed to blood or body fluids. We also included HCWs who participated in CPR without wearing appropriate personal protective equipment (PPE) to the high-risk group. The moderate-risk group consisted of HCWs without a visible exposure to blood or body fluids but handled patient or performed physical examination without appropriate PPE. The low risk group consisted of HCWs who cared the patient when she had no bleeding but didn’t perform physical examination or participate in aerosol-producing procedures.

Results: At least 38 HCWs had contact with the index fatal patient. The patient was admitted to the emergency department, followed up in the internal medicine clinic (IMS) and intensive care unit (ICU). She had 1 CPR in IMS, 2 CPRs in ICU. Despite warnings about the suspicion of CCHF, physician who intubated did not wear mask or any other PPE, except gloves. During the ICU follow-up, she had severe bleeding. Two resuscitations of the patient in the ICU lasted approximately more than 1 hour. Physician who inserted femoral artery sheath and femoral catheter didn’t wear goggles and her gown was short-sleeved. An ICU nurse intervened her uterine prolapse due to severe bleeding with gloves but without a protective gown. None of the HCWs who had contact with the patient had appropriate PPE. Patient’s PCR and IgM were positive for CCHF. She died 48 hours after her admission. Among all known contacts, all HCWs in high and moderate risk groups (n=24) received PEP with ribavirin after within the 48 hours of the exposure. Non-severe side effect was observed in 3 (12.5%) HCWs. None of the HCWs developed nosocomial CCHF.

Conclusions: Ribavirin seems effective and well tolerated for nosocomial transmission of CCHF which has high mortality rate.

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Reconstruction of plasmids by shotgun sequencing of various environmental DNA: from hospital biofilms to wastewater treatment plants

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Background: Plasmids play important roles in microbial evolution and also in the spread of antibiotic resistance. Plasmid sequences are extensively studied from clinical isolates but rarely from the environment with a metagenomic approach focused on the plasmid fraction referred to as plasmidome. We defined a workflow for discriminating plasmids from chromosomic contaminants. This pipeline named PlasPredict was tested on 2 types of environment, hospital biofilm and waste water treatment plant (WWTP) receiving hospital and urban effluents, in terms of Mobile genetic elements (MGEs) involved in the transport of genetic information between genomes in different bacterial species

Materials/methods: PlasPredict pipeline: we benchmarked existing tools from assembling to the detection of the plasmids by reference-free methods (cBar and PlasFlow) and database-guided approaches. DNA extraction was optimized to enrich in plasmid DNA with conservation of large plasmids.

Results: From the WWTP assembly, 6.5 % of contigs were identified as chromosomes from the database approach [chromosomes and phylogenetic markers]. The detection of plasmid markers, circular sequences and whole plasmid sequences identified 2.16 % of contigs considered to be “true” plasmids corresponding to plasmids referenced in public databases. We also considered circular contigs to be plasmids. From the biofilm assembly, 21.27 % of contigs were identified as chromosomes and 7.02 % of contigs as plasmids. After PlasFlow treatment, 4.9 % of the remaining contigs were defined as chromosomes for WWTP and 9.3 % for biofilm. 5.4 % of the remaining contigs were defined as plasmids from WWTP and 17.1 % from biofilm. Concerning the biofilm, the reliability of the pipeline was confirmed by searching for plasmid markers such as MOB, MPF, OriT and rep sequences. A total of 9490 linear plasmids and 381 circular plasmids [size 1.4 kb to 235 kb] were reconstructed, with 2 of them already in databases. The sequences associated with antibiotic resistance mechanisms were mainly efflux pump [EmrE], ABC transporter and beta-lactamase-encoding genes.

Conclusions: This study highlights the major potential role of biofilms in hospital effluents as providers of resistance genes to urban effluents, adding new traits potentially generating dangerous multidrug-resistant pathogens and pose a hazard to environmental and public health.

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**Abstract 6468**

**Bacterial contamination of umbilical cord blood collected at Ankara University cord blood bank**

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**Background:** Cord blood (CB) is a unique graft source with the potential to be used as an alternative for bone marrow or hematopoietic stem cell transplantation. To make sure that full potential of a CB unit (CBU) is met, it is of crucial importance that every single unit is traced from donor to the recipient with very strict quality control measures. Microbial sterility is essential for the safety of the CB product. The aim of this particular study was to retrospectively analyze bacterial contamination rates in CBUs and the impact of delivery method on contamination frequencies.

**Materials/methods:** A total of 1653 CBUs collected in utero from consented maternal donors between June 2011 and October 2019 were enrolled in this study. BACTEC automated culture system was used to monitor bacterial growth. Ten individual units which were discarded due to microbial growth were thawed and re-cultured for the assessment of the impact of cryopreservation on bacterial growth.

**Results:** Microbial culture results of 1653 CBUs were evaluated to determine culture positivity and to specify contaminating microorganisms. Of the 1653 CBUs analyzed, 41 (2.5%) were found to be contaminated with 44 bacterial strains. Of those 41 units 68% were collected from cesarean section (C/S) and 32% from vaginal deliveries. Methicillin-susceptible coagulase-negative *Staphylococcus* (CoNS) was the most frequent microorganisms detected (12 out of 44 [27.3%]) followed by methicillin-resistant CoNS (10 out of 44 [22.7%]) (Figure 1). Most of the CoNS growth (91%) of was detected in CBUs collected from C/S (20/22). Post thaw analysis of 10 individual units revealed that 50% of formerly positive units were culture negative after cryopreservation. Three of the survivors were methicillin-susceptible CoNS, one was methicillin-resistant CoNS and the remainder was a member of *Actinomyces* genus.

**Conclusions:** A very low overall contamination rate (2.5%), mostly from CBUs collected from C/S, was determined in the CBUs investigated and the pre-dominant microorganism was found to be CoNS. Delivery method had a significant effect on contamination rates. Our results also indicated that some bacteria do survive after cryopreservation while some don’t, the precise mechanism being still unknown.

![Figure 1. Bacterial isolation rates of 41 contaminated CBUs](image)

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Abstract 6469

**In-host evolution of methicillin-resistant Staphylococcus aureus within individual carriers using core genome multi-locus sequence typing and single-nucleotide polymorphism analysis**

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**Background:** Methicillin-resistant *Staphylococcus aureus* (MRSA) colonize humans but also causes serious infections associated with poor outcome, which makes the pathogen highly topical in outbreak investigations. Intra-host evolution in carriers through mutations and recombination events are either best traced using whole-genome sequencing data where analysis are often performed using single nucleotide variants (SNV) presented as core genome multi-locus sequence typing (cgMLST) or single nucleotide polymorphisms (SNPs). In this study we aimed to evaluate the in-host evolution of MRSA in long term carriers as measured with cgMLST and SNP based analysis.

**Materials/methods:** MRSA isolates (n=94) from 20 individual long-term MRSA-carriers were collected from 2003 to 2019. The isolates were sequenced using Illumina Miseq (600-cycle). The sequence data were analyzed with two commercially available software; SeqSphere+ (Ridom GmbH) for cgMLST- and SNV-analysis, 1928D (1928 Diagnostics, Sweden) for cgMLST- and SNP-analysis but also using the bioinformatic tool NASP (https://github.com/TGenNorth/NASP) for a non-commercial, well validated, SNP-analysis. Calculations of mean, median and standard deviation were performed with Statistical software SPSS version 25.

**Results:** Three patients were excluded (n=13 isolates) due to an obvious change of MRSA strain during the follow up. For the remaining 17 patients the cgMLST analysis using SeqSphere+ showed a median of 4.1 (range 1.4-26) allele variants and a median of 1.4 (range 6-46) SNV/year. The cgMLST analysis by 1928D showed a median of 2.3 (range 0.6-20.3) allele variants/year and the SNP-analysis (including recombination events) showed a median of 112.5 (range 6.75-239.8) SNPs per individual/year. The NASP pipeline (excluding recombination events) results of the SNP-analysis showed a median of 5.5 (range 2.4-35.3) SNPs/year.

**Conclusions:** The estimated within host evolution for a MRSA isolate was less than 6 genetic changes per genome and year, according to the two cgMLST methods and the NASP SNP-based analysis used. However, using the 1928D SNP-analysis, which also includes recombination events, a much higher SNP variability was observed. These findings supports previous estimates and adds to the clinical utility of the tested bioinformatics tools.

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Abstract 6472

Development of LAMP-based multiplex real-time assay for rapid detection of genes of NDM, VIM, KPC and OXA-48 carbapenemase groups

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Background: Carbapenem resistance caused by acquired carbapenemases is a global public health concern and represents a serious problem for the treatment of related infection. Loop-mediated isothermal amplification (LAMP) can be used as a rapid and effective technique for detection of acquired antimicrobial resistance genes. The aim of this study was to develop a LAMP based assay for detection of genes encoding the most common for Enterobacterales spp carbapenemase of NDM, VIM, KPC and OXA-48-like groups.

Materials/methods: LAMP technique with real-time detection provided by fluorogenic loop primers (assimilating probes) was used to develop a new multiplex assay. The primer sets for target genes (VIM, KPC, NDM, OXA-48-like) were designed using PrimerExplorer V5 (Eiken Chemical Co., Ltd.). The LAMP reaction was performed at 65°C using CFX-96 instrument. The assay was validated using a panel of strains carrying the genes of the known carbapenemases (VIM-1, -2, -4, -10, NDM-1, -2, KPC-2, -3, OXA-48, -181, -244) on natural plasmids or recombinant vectors. Thirty-eight previously characterized clinical isolates of different Enterobacterales spp and Pseudomonas aeruginosa, 10 positive blood cultures with the same bacterial species and DNA extracted from 30 sputum samples from patients with nosocomial pneumonia were tested by the LAMP assay in comparison with commercial IVD real-time PCR assays «AmpliSens MBL-FL» and «AmpliSens KPC/OXA-48-FL» (CRIE, Russia).

Results: The assay composed of two multiplex real-time LAMP tests, was developed for detection of genes encoding four groups of carbapenemases. The first test allows the detection and discrimination of NDM and OXA-48-like carbapenemase genes and includes exogenous internal control (IC). The second test allows differential detection of VIM and KPC carbapenemase genes. Both LAMP-based tests produced correct results for strains carrying the known carbapenemase genes. The limit of detection corresponded to (1-4) x 10^3 copies per ml for all target gene groups. The LAMP based assay results for all tested clinical isolates, blood cultures and sputum samples were concordant with these produced by IVD real-time PCR assays.

Conclusions: The developed multiplex real-time LAMP assay allows the rapid and effective detection of VIM, KPC, NDM, OXA-48-like carbapenemase genes both in bacterial cultures and sputum.

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Abstract 6473

**Major changes detected in penicillin-binding proteins of vancomycin-resistant Enterococcus faecalis by sequencing and homology modeling**

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**Background:** Vancomycin-resistant enterococci (VRE) are currently one of the most common species that cause serious, hard to treat, hospital-acquired infections. Resistance to vancomycin is due to the change of the D-Alanine-D-Alanine group to D-Alanine-D-Lactate at the end of the pentapeptides forming cross-links of bacterial cell wall. Due to this change vancomycin can no longer bind to terminal dipeptide. The question of how penicillin-binding proteins (PBPs) bind D-Alanine-D-Lactate groups instead of D-Alanine-D-Alanine has not been studied until now. In this study, we have investigated possible changes in the PBPs of VRE for functioning properly with D-Ala-D-Lac group.

**Materials/methods:** We have studied the genes of PBPs of 3 clinical vancomycin resistant and 3 vancomycin susceptible (VSE) strains of Enterococcus faecalis. All the genes belonging to PBPs were amplified by PCR, sequenced by Sanger sequencing and compared to each other. The structural changes due to identified amino acid changes were evaluated by homology modeling using Swiss model portal for sequencing.

**Results:** The same amino acid changes which were identified in PBPs of VRE compared to VSE were present in all VRE strains investigated. It was identified 4 amino acid changes in PBP1B, 2 in PBP2A, and 5 in PBP3. Homology modeling of PBPs suggested that the changes were related to the active sites that bind to D-Ala-D-Lac which is also the binding site for beta-lactam antibiotics. We did not find any amino acid changes related to the catalytic region of PBP1A, PBP2B and PBP4.

**Conclusions:** We have identified significant changes related to the catalytic regions of PBP1B, 2A and 3 in VRE as we expected since the PBPs in VRE should use D-Ala-D-Lac instead of D-Ala-D-Ala for building cross links in the cell wall. These PBPs may have lower affinity to beta-lactam antibiotics creating further resistance to these drugs. Identification of these changes may give the opportunity to develop new beta-lactam drugs by redesigning there structure using homology modeling. The knowledge about the function of each PBP is quite limited. Further investigation about these, using large number of clinical strains is needed.

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Abstract 6474

Nanopore metagenomic sequencing of influenza virus directly from respiratory samples: diagnosis, drug resistance and nosocomial transmission

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Background: Influenza virus presents a significant public health challenge, causing seasonal epidemics and occasional pandemics. Nanopore metagenomic sequencing has the potential to be deployed for near-patient testing, providing rapid diagnosis of infection, rationalising antimicrobial therapy, and supporting interventions for infection and transmission control. This study aimed to evaluate the applicability of Nanopore sequencing as a routine laboratory test for influenza in clinical settings.

Materials/methods: We conducted Nanopore metagenomic sequencing for 180 respiratory samples from a UK hospital, including 90 influenza-positives and 90 influenza-negatives based on routine molecular diagnostic testing using Cepheid Xpress or BioFire FilmArray® Respiratory Panel. Samples were taken between October 2018 (first laboratory diagnosis of influenza from the hospital in the 2018/19 season) and February 2019, plus a putative clinical cluster on the ID ward. We investigated drug resistance, genetic diversity, and nosocomial transmission.

Results: Metagenomic sequencing was 83% (75/90) sensitive and 93% (84/90) specific for detection of influenza A viruses compared with the diagnostic standard. Viral reads were detected in all 58 samples with Ct≤31. HA subtype was determined for 59/75 (79%) samples (40 H1, 19 H3), and all samples with Ct≤27. 28/75 (37%) consensus sequences were assembled with genome coverage ≥70%. One H3N2 genome had the oseltamivir-resistant S331R mutation in the NA protein, potentially associated with the emergence of a distinct intra-subtype reassortant. Whole genome phylogeny refuted suspicions of a transmission cluster on the ID ward. It identified two other clusters that likely reflected nosocomial transmission of a dominant strain circulating in the community. We detected a range of other potentially pathogenic viruses and bacteria from the metagenome.

Conclusions: Nanopore metagenomic sequencing can detect the emergence of novel variants and drug resistance in influenza virus, providing timely insights for antimicrobial stewardship and vaccine design. Generation of full genomes can contribute to investigation and management of nosocomial outbreaks. While substantial work is still needed to refine the sequencing protocol and bioinformatic analysis, Nanopore metagenomic sequencing has the potential to become an applicable point-of-care test for infectious diseases in clinical settings.

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Optimisation of the MALDIxin test for the rapid identification of colistin resistance in *Klebsiella pneumoniae* using MALDI-TOF MS

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Background: With the dissemination of carbapenemase producers, a revival of colistin was observed for the treatment of infections caused by multidrug-resistant Gram-negatives. Unfortunately, the increasing usage of colistin led to the emergence of resistance. In *Klebsiella pneumoniae*, colistin resistance arises through addition of L-arabinose 4N (L-Ara4N) or phosphoethanolamine (pEtN) on the native lipid A. The underlying mechanisms involve numerous chromosome-encoded genes or the plasmid-encoded phosphoethanolamine transferase MCR. Currently, detection of colistin resistance is time consuming since it still relies on MIC determination by broth microdilution. Recently, a rapid diagnostic test based on MALDI-TOF detection of modified lipid A was developed (the MALDIxin test) and tested on *Escherichia coli* and *Acinetobacter baumannii*.

Objectives: Optimize the MALDIxin test for the rapid detection of colistin resistance in *Klebsiella pneumoniae*.

Materials/methods: This optimization consists on an additional mild-acid hydrolysis of 15 min in 1% acetic acid. The optimized method was tested on a collection of 81 clinical *K. pneumoniae* isolates including 49 colistin resistant strains among which 45 correspond to chromosome-encoded resistance, 3 MCR-related resistance and one isolate harbouring both mechanisms.

Results: The optimized method allowed the rapid (< 30 min) identification of L-Ara4N and pEtN modified lipid A of *K. pneumoniae* which are known to be the real triggers of polymyxin resistance. In the same time, it discriminates between chromosome-encoded and MCR-related polymyxin resistance.

Conclusions: The MALDIxin test has the potential to become an accurate tool for the rapid diagnostic of colistin resistance in clinically-relevant Gram negative bacteria.

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**Abstract 6477**

*Candida auris* species and lineage identification from plate and blood cultures applying Orbitrap ultra high-resolution mass spectrometry

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**Background:** Candidiasis, which includes both superficial and systemic infections, is the most common cause of fungal infection worldwide. Although *Candida albicans* remains the most frequently isolated species in the clinical setting, in some countries a dramatic shift to other species, such as *C. auris* is observed, emerging as a multidrug-resistant pathogen that can cause outbreaks of invasive infections. *C. auris* is identified in >35 countries, many of which have documented healthcare-associated spread. While many nosocomial outbreaks of *C. auris* have been reported worldwide (India, South Korea, Venezuela & Colombia, South Africa, Europe, USA and Middle East), the exact affiliation of a strain genotype to a lineage is highly time, cost and labor intensive and currently only possible by NGS research only (RUO) applications. It remains a pivotal element to clinical microbiology to develop cost-effective molecular epidemiological surveillance techniques beyond species identification, to track microbial spread and major clones circulating among global geographies, which are potentially prone to rapidly acquire resistances.

**Materials/methods:** High resolution mass spectrometry integrated in the Acrion™ system, was applied to protein extracts from *C. auris* strains originating from major outbreaks in East Asia, Central Asia, Africa, Europe, South America, Middle East and Arabian Peninsula. Strains were characterized using standard molecular barcodes and AFLP sequence typing. High resolution mass spectra were evaluated for the individual protein masses detected. Different identification approaches were compared.

**Results:** Applying the proposed rapid and easy workflow and benefiting from high resolution Orbitrap™ mass analyzer, accurate masses of multiple protein classes were detected. Across diverse strains of the *C. auris* complex the variation in the presence of proteins enabled searching for lineage specific protein masses that were used to delimit the tested entities.

**Conclusions:** The user friendly workflow with the high resolution database enabled rapid and accurate identification of *C. auris* species from plate and blood in Acrion™ system. Moreover lineage delimitation in a time-efficient manner is demonstrated for the first time using Orbitrap™ mass spectra, revealing equivalent typing-identification capabilities to NGS which is crucial for epidemiological tracking and dissemination prevention.

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In vitro activity of commonly used antimicrobial agents against clinical Gram-negative bacterial isolates from ATLAS Indian centres in 2018

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**Background:** Anti-microbial resistance is a huge concern in India while tackling gram negative organisms. ATLAS [Antimicrobial Testing Leadership and Surveillance], which is the integration of three surveillance programs (TEST, AWARE, INFORM), initiated in 2004, detects trends in multi-drug resistance longitudinally over time. This report analyses the susceptibility of gram negative nosocomial isolates from ATLAS to commonly used agents against MDR organisms.

**Materials/methods:** Non-duplicate clinical Gram negative nosocomial isolates (n= 788) were collected in 2018 from eight Indian tertiary care centers. Organisms were identified and susceptibility tested, by conventional methods. Susceptibility was confirmed at an IHMA (International Health Management Associates) laboratory using supplied broth microdilution panels [Microscan], according to CLSI guidelines, for all antibiotics. Selected isolates were screened for acquired beta-lactamase genes by PCR and sequencing. In-vitro activity of Cefoperazone sulbactam [C/S], piperacillin-tazobactam [P/T], ceftazidime-avibactam [C/A], meropenem, tigecycline, colistin and aztreonam was assessed for Enterobacteriaceae, Pseudomonas spp. and Acinetobacter spp. isolates from various clinical samples.

**Results:** Of the 788 gram negative isolates, 567 belonged to Enterobacteriaceae. Of the 221 non enterobacteriaceae, 66 belonged to Acinetobacter spp. and 151 to Pseudomonas spp.. Below is the in-vitro activity of the isolates to commonly used antibiotics against Gram negative organisms:

<table>
<thead>
<tr>
<th>Organisms</th>
<th>Percentage susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C/S</td>
</tr>
<tr>
<td>Enterobacteriaceae (n=567)</td>
<td>368 (65%)</td>
</tr>
<tr>
<td>Acinetobacter spp. (n=66)</td>
<td>15 (23%)</td>
</tr>
<tr>
<td>Pseudomonas spp. (n=151)</td>
<td>109 (72%)</td>
</tr>
</tbody>
</table>

Meropenem resistance was 23% in Enterobacteriaceae, 80% in Acinetobacter spp. and 27% in Pseudomonas spp. The susceptibility of Ceftazidime-Avibactam to Meropenem resistant Enterobacteriaceae and Meropenem resistant Pseudomonas spp. was 34% and 32% respectively.

**Conclusions:** Based on percentage susceptibility, C/S, P/T, C/A, meropenem and colistin exhibited good in-vitro activity against Enterobacteriaceae and Pseudomonas isolates. Tigecycline showed good susceptibility to Enterobacteriaceae. Higher resistance was seen among Acinetobacter spp. for which Colistin was the most active agent. Ceftazidime-avibactam may be a useful agent in meropenem resistant Enterobacteriaceae and Pseudomonas isolates.

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**Abstract 6480**

**Improving antibiotic prescribing for community-acquired pneumonia in resource-limited settings: pilot implementation of quality standards in a provincial hospital in northern Vietnam**

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**Background:** Despite the availability of evidence based Quality Standards [QS] in Vietnam for patients hospitalised with community-acquired pneumonia (CAP), there remains wide variation in care, providing opportunities for improvement. The pilot implementation of QS for CAP aims to test whether a co-designed improvement programme using PDSA methodology would result in better adherence to QS for CAP patients in a provincial hospital and better understanding of the barriers to QS adoption that could be applied to larger scale implementation.

**Materials/methods:** The QS implemented were designed to reduce unnecessary admissions and use of intravenous antibiotics and included CURB65 severity score documentation and use to guide hospital admission, timely diagnosis including early radiology, and in-patient antibiotic treatment review to limit the duration of intravenous antibiotic use. The implementation package was agreed during a staff workshop and included data collection on care quality, onsite updated-training to medical staff and tools to facilitate documentation in patient records. The piloted package was deployed in a 600-bed hospital in northern Vietnam over 10 months (from July 2018 to April 2019) following two iterations of the Plan-Do-Study-Act (PDSA) cycle methodology. In parallel we interviewed staff to understand factors that were inhibiting implementation.

**Results:** The pilot interventions resulted in limited change in QS adherence with improvements made only in CURB65 score documentation (68% versus 80% and 96%, p<0.05) and chest X-ray results available within 4 hours (39% versus 88% and 76%, p<0.05). We documented change barriers ranging from individual cultural to system blocks e.g. perceptions held by doctors regarding the evidence for CURB65, and lack of health insurance reimbursement for out-patient care, leading to over-admission and unnecessary longer intravenous antibiotic treatment.

**Conclusions:** Whilst specific solutions will differ by context, the dual approach of engendering local ownership of quality improvement activities whilst proactively understanding barriers to implementation of best practice to inform further improvement approaches will be applicable in other low and middle income countries (LMIC) s.

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Phylogenetic groups and virulence factors of uropathogenic Escherichia coli in pregnant and non-pregnant women in St. Petersburg, Russia

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Background: Uropathogenic Escherichia coli (UPEC) is responsible for a large majority of urinary tract infections (UTIs). UTIs are more prevalent in women, and in pregnancy can cause significant morbidity. Physiological changes in pregnancy are considered a major contributor to UTI-associated complications, and very little focus has been placed on the role of specific UPEC virulence factors. Molecular epidemiological studies are necessary for identifying UPEC traits predicting UTI severity, with identifying pregnant women with asymptomatic bacteriuria (ABU) who are at risk of developing pyelonephritis being of particular clinical relevance. This study aimed to determine the UPEC phylogenetic groups and virulence profiles in pregnant and non-pregnant women with different UTIs.

Materials/methods: UPEC strains were routinely isolated from women attending the D.O. Ott Research Institute of Obstetrics, Gynaecology and Reproductology from October 2017 to November 2019 for gynaecological and obstetrical care. E. coli phylogenetic groups and 15 genes encoding toxins (hly, cnf1, sat1), adhesins (papA, -EF, -C, focG, hra, fimH, afp), siderophores (fyu, iroN, iucD), invasin (ibeA), bacteriocin (usp) were determined using PCR assays (Clermont et al., 2013, Johnson & Stell, 2000; Yamamoto et al., 1995; Vila et al., 2002; Takahashi et al., 2006; Bingen-Bidois et al., 2002).

Results: In total, 73 UPEC strains were isolated from women aged 19-50 (median 31) years, 44 pregnant and 29 non-pregnant. ABU was diagnosed in 16 women (15 pregnant, one non-pregnant), cystitis in 23 women (4 pregnant, 19 non-pregnant), pyelonephritis in 34 women (25 pregnant, 9 non-pregnant). The distribution of the phylogenetic groups and virulence factors in pregnant women was similar to that in non-pregnant women, whereas significant differences were observed between UTIs (Table). Phylogenetic group A isolates were more frequent in pyelonephritis, and hlyA, cnf1, hra, iroN positive isolates – in cystitis, compared to the other UTIs. Group F isolates were more frequent in pregnant women with ABU compared to pyelonephritis.

Conclusions: The distribution of UPEC phylogenetic groups and virulence factors was mainly similar in pregnant and non-pregnant women, whereas significant differences were revealed between different UTIs. Cohort studies into UPEC traits in pregnant women are needed to identify predictors of UTI-associated pregnancy complications.

<table>
<thead>
<tr>
<th>Phylogenetic groups and virulence factors</th>
<th>Total (n=73)</th>
<th>Pregnant and non-pregnant women</th>
<th>Pregnant women</th>
<th>ABU (n=16)</th>
<th>Cystitis (n=23)</th>
<th>Pyelonephritis (n=34)</th>
<th>P value</th>
<th>ABU (n=15)</th>
<th>Pyelonephritis (n=25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>19 (14%)</td>
<td>2 (13%) 0 (0%) 6 (24%)</td>
<td>0.040</td>
<td>2 (13%)  6 (24%)</td>
<td>0.066</td>
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</tr>
<tr>
<td>B1</td>
<td>7 (10%)</td>
<td>1 (6%) 4 (17%) 2 (6%)</td>
<td>0.307</td>
<td>1 (7%)  2 (6%)</td>
<td>1.000</td>
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</tr>
<tr>
<td>B2</td>
<td>39 (53%)</td>
<td>7 (44%) 17 (74%) 15 (44%)</td>
<td>0.059</td>
<td>6 (40%) 11 (44%)</td>
<td>0.804</td>
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<tr>
<td>D</td>
<td>11 (15%)</td>
<td>3 (19%) 2 (9%) 6 (18%)</td>
<td>0.584</td>
<td>3 (20%) 6 (24%)</td>
<td>1.000</td>
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<tr>
<td>F</td>
<td>6 (8%)</td>
<td>3 (19%) 0 (0%) 3 (5%)</td>
<td>0.109</td>
<td>3 (20%) 0 (0%)</td>
<td>0.046</td>
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<tr>
<td>hlyA</td>
<td>21 (29%)</td>
<td>3 (19%) 12 (52%) 6 (18%)</td>
<td>0.011</td>
<td>3 (20%) 5 (20%)</td>
<td>1.000</td>
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<tr>
<td>cnf1</td>
<td>20 (27%)</td>
<td>3 (19%) 11 (48%) 6 (18%)</td>
<td>0.029</td>
<td>3 (20%) 4 (16%)</td>
<td>1.000</td>
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<tr>
<td>satI</td>
<td>22 (30%)</td>
<td>5 (31%) 5 (22%) 12 (36%)</td>
<td>0.546</td>
<td>4 (27%) 6 (32%)</td>
<td>1.000</td>
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<tr>
<td>papA</td>
<td>31 (42%)</td>
<td>8 (50%) 11 (48%) 12 (35%)</td>
<td>0.507</td>
<td>8 (53%) 6 (32%)</td>
<td>0.162</td>
<td></td>
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<tr>
<td>papEF</td>
<td>34 (47%)</td>
<td>8 (50%) 12 (50%) 14 (41%)</td>
<td>0.883</td>
<td>8 (53%) 10 (40%)</td>
<td>0.412</td>
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<tr>
<td>papG</td>
<td>32 (44%)</td>
<td>7 (44%) 12 (62%) 13 (38%)</td>
<td>0.582</td>
<td>7 (47%) 9 (30%)</td>
<td>0.605</td>
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<tr>
<td>focG</td>
<td>6 (11%)</td>
<td>2 (13%) 4 (17%) 2 (6%)</td>
<td>0.384</td>
<td>2 (13%) 1 (4%)</td>
<td>0.545</td>
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<tr>
<td>hra</td>
<td>24 (33%)</td>
<td>4 (25%) 13 (57%) 7 (21%)</td>
<td>0.014</td>
<td>4 (27%) 5 (20%)</td>
<td>0.705</td>
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<tr>
<td>fnmA</td>
<td>64 (88%)</td>
<td>15 (84%) 22 (96%) 27 (79%)</td>
<td>0.132</td>
<td>14 (83%) 19 (76%)</td>
<td>0.224</td>
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<tr>
<td>afp</td>
<td>1 (1%)</td>
<td>0 (0%) 1 (1%) 0 (0%)</td>
<td>0.332</td>
<td>-         -</td>
<td>-</td>
<td></td>
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<tr>
<td>fnfA</td>
<td>50 (68%)</td>
<td>13 (75%) 15 (75%) 20 (60%)</td>
<td>0.228</td>
<td>12 (80%) 16 (64%)</td>
<td>0.477</td>
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<tr>
<td>cnf2</td>
<td>35 (52%)</td>
<td>9 (56%) 17 (74%) 12 (35%)</td>
<td>0.015</td>
<td>8 (60%) 10 (40%)</td>
<td>0.720</td>
<td></td>
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</tr>
<tr>
<td>iucD</td>
<td>30 (41%)</td>
<td>5 (31%) 10 (43%) 15 (44%)</td>
<td>0.653</td>
<td>4 (27%) 10 (40%)</td>
<td>0.502</td>
<td></td>
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</tr>
<tr>
<td>ibeA</td>
<td>10 (14%)</td>
<td>0 (0%) 5 (22%) 5 (15%)</td>
<td>0.148</td>
<td>0 (0%) 5 (20%)</td>
<td>0.137</td>
<td></td>
<td></td>
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<tr>
<td>usp</td>
<td>45 (62%)</td>
<td>11 (65%) 16 (70%) 18 (53%)</td>
<td>0.360</td>
<td>10 (67%) 12 (48%)</td>
<td>0.251</td>
<td></td>
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</table>

ABU, asymptomatic bacteriuria; significant values are in bold letters (chi-square test or Fisher’s exact test)
Evidence from in vitro pharmacokinetic/pharmacodynamic studies on polymyxin-based combination therapies to treat infections due to carbapenem-resistant Gram-negative bacteria

Margherita Chiamenti1, Damiano Bragantini1, Luigia Scudeller2, Laura Piddock1, François Franceschi3, Sally Ellis3, Maurizio Sanguinetti4, Giulia Menchinelli4, Alessia Savoldi1, Elda Righi1, Evelina Tacconelli1

1University of Verona, Verona, Italy, 2IRCCS Ca’ Granda Ospedale Maggiore Policlinico di Milano Foundation, Milano, Italy, 3Global Antibiotic R&D Partnership (GARDP), Geneva, Switzerland, 4Università Cattolica del S. Cuore, Rome, Italy

Background: Poor-quality evidence from clinical trials supports the use of combination therapy (CoT) against carbapenem-resistant Gram-negative bacteria (CR-GNB). The objective of this systematic review and meta-analysis, performed within the GARDP COHERENCE project, was to assess the evidence on in vitro synergy of any CoT (old and new drugs) against CR-GNB in pharmacokinetic/pharmacodynamics (PK/PD) studies.

Materials/methods: Pre-clinical PK/PD studies targeting any CoT in CR-Acinetobacter baumannii (AB), CR-Klebsiella pneumoniae (KP), CR-Pseudomonas aeruginosa (PA) and other CR-Enterobacterales (Ent) were systematically searched in PubMed, Scopus, Web of Science and relevant conference proceedings from the inception until 12/2018 without language restriction. Synergism was defined as >2-log10 reduction in colony-forming unit for a CoT compared to that of the most active single agent; while antagonism as >2-log10 increase. The effect size was defined as pooled proportion (with 95%CI) of CoT showing synergy for each species (significance: p<0.05).

Results: Among 3754 records screened, 42 PK/PD studies reporting data on 100 bacterial isolates were included: 37 (37%) on KP, 35 (35%) on AB, 14 (14%) on PA and 14 (14%) on Ent. Twenty-one antibiotic agents belonging to 12 classes were combined in 41 different CoT (132 tests). Pooled data were available for 8 polymyxin-based CoT, accounting for 32 tests and 67 strains. Seven CoT showed synergism. Antagonism was not detected. In AB, colistin-based CoT showed significant synergism with rifampicin (0.99, 95%CI 0.92-1.06, three tests, six strains) and with tigecycline (0.64, 95%CI 0.32-0.96, two tests, eight strains); in KP, fosfomycin showed high synergism with polymyxinB (0.99, 95%CI 0.93-1.06, four tests, six strains) and colistin (0.67, 95%CI 0.40-0.95, five tests, 16 strains); in PA, colistin with doripenem showed significant synergism (0.66, 95%CI 0.23-1.09, six tests, eight strains). No PK/PD studies tested antibiotics approved in the last decade. High inter-studies heterogeneity was detected, associated with dosages and strains' differences.

Conclusions: To our knowledge this is the first systematic review and meta-analysis of PK/PD studies assessing the synergy of polymyxin-based CoT in CR-GNB. The evidence is limited and does not include any recently marketed drug. These results should be considered for the strategic research agenda for the assessment of CoT against CR-GNB.

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Abstracts 2020

Abstract 6483

**Validation of FASTmar kit, a flow cytometric assay for detection of main mechanisms of beta-lactams resistance directly from positive blood cultures**

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1FASTinov S.A., Porto, Portugal, 2Hospital Universitario Ramón y Cajal, Instituto Ramón y Cajal de Investigación Sanitaria (IRY-CIS), Servicio de Microbiologia, Madrid, Spain, 3Faculty of Pharmacy, University of Porto, Laboratory of Microbiology, Porto, Portugal, 4Faculty of Medicine, University of Porto, Division of Microbiology, Department of Pathology, Porto, Portugal

Abstract third-party references: This work received funding from the H2020 FTIPilot 2016 project nº 730713 ‘FAST-bact—A novel fast and automated test for antibiotic susceptibility testing for Gram positive and negative bacteria’.

**Background:** Detection of main mechanisms of resistance such as ESBL, AmpC and carbapenemases is recommended, not only to treat the patient accordingly but also for infection control. Most laboratories perform ESBL detection on Enterobacterales such as *Escherichia coli* and *Klebsiella* spp or *Proteus* spp but not on group II-Enterobacterales including *Enterobacter* spp, *Serratia* spp, *Citrobacter freundii*, *Morganella morganii*, *Providencia* spp or *Hafnia alvei*. AmpC are often underestimated and carbapenemases are usually identified using molecular assays targeting already described genes. FASTinov developed a rapid phenotypic method for detection of diverse class A, B, C and D beta-lactamases directly from positive blood cultures.

**Materials/methods:** Eighty-four blood cultures [80] were spiked with well characterized bacterial strains; 29 ESBL, 16 AmpC and/or 39 carbapenemases. When flagged positive, the microorganisms were extracted using a previously optimized protocol. Strains were either incubated with: i) serial concentrations of cefepime with and without clavulanic acid (for ESBL on group II-Enterobacterales); ii) serial concentrations of cefotaxime or ceftazidime with cloxacillin (for AmpC) and iii) serial concentrations of meropenem associated with different inhibitors [EDTA for metallo-carbapenemases and boronic acid for KPC] or considering susceptibility to temocillin for OXA-like 48 enzymes. After incubation of 1h together with a membrane potential probe, the cells were analyzed using CytoFLEX flow cytometer (Beckman Coulter). A dedicated software developed by FASTinov® gave automatically the result that was compared with phenotypic criteria according to EUCAST protocols. The proportion of agreement (PA) was calculated, as well as the sensitivity and specificity of the assay.

**Results:** Regarding ESBL detection, the PA was 90% with 100% specificity and 88% sensitivity (2 false negatives). For AmpC, the PA was 100% (100% sensitivity and specificity). Regarding carbapenemases the PA for KPC was 97.7% (100% specificity and 94% sensitivity) (1 false negative); the PA for metallo-beta-lactamases was 93% (100% specificity and 77% sensitivity) (3 false negatives); the PA for OXA-48-like was 100% (100% specificity and sensitivity).

**Conclusions:** A new, fast and accurate detection [time-to-results <2h] of main beta-lactams mechanisms of resistance on diverse Enterobacterales species is described showing an excellent correlation with the reference method with time-to-results of 2 days.

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Abstracts 2020

Abstract 6485

The PCV13 serotypes still account for a large fraction of invasive pneumococcal disease in adults three-years after PCV13 introduction in the paediatric vaccination schedule (Portugal: 2015-2018)

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1Universidade de Lisboa, Faculdade de Medicina, Lisboa, Portugal

Abstract third-party references: Portuguese Group for the Study of Streptococcal Infections

Background: In Portugal, the uptake of pneumococcal vaccines by the adult population (≥18 years) has been low, but changes in invasive pneumococcal disease (IPD) were detected, possibly by herd protection from the pediatric population. We aimed to determine serotype distribution and antimicrobial susceptibility patterns of pneumococci causing adult IPD between 2015 and 2018, after PCV13 introduction in the National Immunization Plan (NIP) for children.

Materials/methods: A total of 2135 Streptococcus pneumoniae isolates recovered from IPD cases in 62 hospitals in Portugal between January 2015 and December 2018 was characterized by serotyping and antimicrobial susceptibility testing. In one case, S. pneumoniae was identified and serotyped in a culture-negative CSF sample by real-time PCR.

Results: Most cases were caused by serotypes included in PPV23 (n= 1689, 79%) with serotypes found exclusively in this vaccine being among the most frequent – serotype 8 (n=408), 22F (n=143), 9N (n=94), 11A (n=73) and 20 (n=72). PCV13 serotypes represented 37% of the cases, with serotype 3 being the second most frequent overall (n=329), and serotypes 14 (n=137) and 19A (n=115) also ranking among the most frequent. All other PCV13 serotypes, except serotype 5, were also detected: 19F (n=53), 7F (n=40), 23F (n=29), 4 (n=27), 9V and 18C (n=13 each), 6B and 6A (n=10 each) and 1 (n=4). Comparing to the period prior to the inclusion of PCV13 in the NIP, PCV13 serotypes 1 and 7F showed significant decreases, while the opposite was true for serotype 8. Overall, 14% of the isolates were penicillin non-susceptible (MIC>0.06 mg/L) and 15% were resistant to erythromycin, mostly associated to serotypes 14, 19A and 19F. Simultaneous expression of erythromycin and penicillin non-susceptibility was found in 8% of the isolates and susceptibility to both these antimicrobials was found in 71% of the isolates.

Conclusions: The increase in proportion of IPD cases caused by serotype 8 and the resilience of serotype 3 and of other PCV13 serotypes, contribute to the dominance of isolates expressing PPV23 serotypes suggesting a potential role of more widespread vaccination in the prevention of adult pneumococcal invasive disease.

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Abstract 6486

Detection of colistin resistance in Pseudomonas and Acinetobacter by the ATB PSE EU strips

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**Background:** Colistin is a last line antibiotic for treating severe infections due to multi-resistant Gram negative bacilli. Disc-diffusion and gradient based methods do not allow reliable detection of colistin resistance for *Pseudomonas* spp. and *Acinetobacter* spp., only liquid methods seem to be satisfactory. The aim of the study is to evaluate the colistin test (COL) that is present in the ATB™ PSE EU strips. This test consists in one single well containing 2 mg/L of colistin sulfate in Mueller Hinton broth.

**Materials/methods:** The susceptibility of 69 isolates with known reference MICs by broth micro-dilution (BMD), comprising 38 *Pseudomonas aeruginosa*, 1 *Pseudomonas fluorescens* [9 S, 30 R] and 31 *Acinetobacter* spp. [8 S, 23 R], was determined by the COL test of the ATB™ PSE EU strip. Category agreement (CA), Major Errors (ME) and Very Major Errors (VME) were calculated following the EUCAST breakpoints [mg/L]: *Pseudomonas aeruginosa*: ≤2 [S] and >2 [R] with an area of technical uncertainty (ATU) at 4, *Acinetobacter*: ≤2 [S] and >2 [R].

**Results:** Results are summarized in the Table below. With this challenging panel (75% of R isolates), the colistin resistance detection by ATB™ PSE EU is good for *Acinetobacter*, and promising for *Pseudomonas*. Among the 6 isolates with a BMD MIC at 4 mg/L (R-ATU), 3 are S and 3 are R by ATB™ PSE EU.

**Conclusions:** This study shows that the ATB™ method has the potential to well detect colistin-resistant *Pseudomonas* and *Acinetobacter*, thus making possible the development of an ATB MIC test.

<table>
<thead>
<tr>
<th>Organism and Isolates number</th>
<th>CA (%)</th>
<th>ME (%)</th>
<th>VME (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Acinetobacter</em> spp</td>
<td>31</td>
<td>90</td>
<td>0</td>
</tr>
<tr>
<td><em>Pseudomonas</em> spp</td>
<td>39</td>
<td>82</td>
<td>0</td>
</tr>
<tr>
<td>Excluding 6 ATUs</td>
<td>33</td>
<td>91</td>
<td>0</td>
</tr>
</tbody>
</table>

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Molecular characterisation of blaNDM-1 from an Acinetobacter baumannii outbreak in a German university hospital

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**Background:** New-Delhi metallo-\(\beta\)-lactamase (NDM) producing *Acinetobacter baumannii* are associated with nosocomial outbreaks worldwide, however, in Germany these outbreaks are rare. The aim of this study was the molecular characterization of bla\textsubscript{NDM-1} from an *A. baumannii* outbreak in a university hospital in Germany.

**Materials/methods:** Between May and September 2019, ten *A. baumannii* isolates from nine patients and six environmental samples were collected from different wards in the clinic for internal medicine. Antimicrobial susceptibility testing was performed using Vitek2 and Etest (bioMérieux). Sequencing libraries were prepared using the Nextera XT kit for a 250bp paired-end sequencing run on a MiSeq (Illumina). Additionally, three isolates were sequenced using the MinION (Nanopore) platform. Hybrid- and non-hybrid methods were used for de novo genome assembly. The molecular epidemiology was investigated using the core-genome MLST (cgMLST) scheme from Ridom® SeqSphere+. The assembled genomes were used for 7-loci MLST (Pasteur) and resistome analysis.

**Results:** A total of 15 carbapenem-resistant *A. baumannii* isolates encoding both bla\textsubscript{NDM-1} and bla\textsubscript{OXA-23} were identified. One of the patients was found colonized with a carbapenem-resistant *A. baumannii* which harboured bla\textsubscript{OXA-23} and bla\textsubscript{NDM-1} and another carbapenem-resistant *A. baumannii* that was bla\textsubscript{OXA-23} positive but lacked bla\textsubscript{NDM-1}. All *A. baumannii* harboured the intrinsic bla\textsubscript{OXA-66} and were assigned as international clone (IC) 2 and ST570. By cgMLST analysis the isolates differed in less than 3 alleles indicating clonal transmission. Investigation of the bla\textsubscript{NDM-1} genetic environment using long-read sequencing revealed that it was encoded within a 19Kb Tn1\textsubscript{25} like transposon and was located in the chromosome upstream of IS\textsubscript{Aba14-aphA6} (Figure 1). This transposon was missing in the bla\textsubscript{NDM-1}-negative *A. baumannii* indicating its loss by a transposition event.

**Conclusions:** In this study we described the transmission of a bla\textsubscript{NDM-1} positive carbapenem-resistant *A. baumannii* in the clinic for internal medicine. One of these isolates lost bla\textsubscript{NDM-1} but remained carbapenem-resistant because of the presence of bla\textsubscript{OXA-23}. These results indicate that mobile genetic elements can lead to genetic variation within an outbreak and that the presence or absence of resistance genes should not be used to determine clonality.

**Figure 1.** Schematic diagram of the genetic environment of bla\textsubscript{NDM-1} in *A. baumannii* (19Kb).

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Study of the humoral response against adjuvanted and non-adjuvanted influenza vaccine in the elderly by age groups

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Background: Immune-senescence makes elderly people one of the main targets of seasonal influenza vaccination campaigns. Non-Adjuvanted influenza vaccines (NAIV) present limitations to reach desirable humoral responses in elderly. For improving these, adjuvanted influenza vaccines (ADIV) are used. The aim of this study is to compare the humoral response in elderly people

Materials/methods: A retrospective study was performed in 2,513 healthy individuals ≥65years vaccinated with NAIV and ADIV, recruited from 1990-2018. Of them, 1,018 were 65-74years, 1,003 were 75-84 and 492 were 85-94years old. Sera were obtained before and 28 days after vaccination. For analyzing antibodies titers, haemagglutination inhibition assay was performed at the National Influenza Centre of Valladolid(Spain) against classical-A(H1N1)(from 1990 till 2010), A(H1N1)pdm09(from 2010 till 2018), A(H3N2) and for both B/Yamagata and B/Victoria lineages. Statistical analysis was performed calculating Geometric Mean Titers increase induced by NAIV and ADIV. Differences were analyzed using Student-T test (α<0.05).

Results: A total of 1,467(58.37%) individuals were vaccinated with NAIV and 1,046(41.62%) with ADIV. GMTi was significantly higher using ADIV for A(H3N2) and classical-A(H1N1) among 75-84 and 85-94 years old respectively. Elderly among 65-74 showed significantly higher GMTi in NAIV for classical-A(H1N1)subtype. Results showed no significant differences between both vaccines for A(H1N1)pdm09subtype or B-lineages in any age groups. Results are shown in the following table.

<table>
<thead>
<tr>
<th>GMTi</th>
<th>NAIV 65-74</th>
<th>ADIV 65-74</th>
<th>p-value</th>
<th>NAIV75-84</th>
<th>ADIV75-84</th>
<th>p-value</th>
<th>NAIV85-94</th>
<th>ADIV85-94</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A(H1N1)pdm09</td>
<td>4,46</td>
<td>3,48</td>
<td>0,066</td>
<td>4,22</td>
<td>3,42</td>
<td>0,228</td>
<td>3,42</td>
<td>2,66</td>
<td>0,066</td>
</tr>
<tr>
<td>A(H1N1)</td>
<td>2,94</td>
<td>2,13</td>
<td>0,028</td>
<td>2,88</td>
<td>3,08</td>
<td>0,430</td>
<td>3,08</td>
<td>3,29</td>
<td>0,028</td>
</tr>
<tr>
<td>A(H3N2)</td>
<td>2,86</td>
<td>3,42</td>
<td>0,060</td>
<td>2,44</td>
<td>3,54</td>
<td>0,000</td>
<td>3,54</td>
<td>3,23</td>
<td>0,060</td>
</tr>
<tr>
<td>B/Yam</td>
<td>1,98</td>
<td>1,96</td>
<td>0,825</td>
<td>1,99</td>
<td>1,88</td>
<td>0,232</td>
<td>1,88</td>
<td>1,91</td>
<td>0,825</td>
</tr>
<tr>
<td>B/Vict</td>
<td>1,93</td>
<td>2,11</td>
<td>0,169</td>
<td>1,93</td>
<td>1,83</td>
<td>0,291</td>
<td>1,83</td>
<td>1,67</td>
<td>0,169</td>
</tr>
</tbody>
</table>

Conclusions: ADIV induced higher humoral responses against some influenza viruses as A(H3N2) and classical-A(H1N1) in 75-84 and 85-94 years respectively, while NAIV induced higher humoral response for classical-A(H1N1) subtype in 65-74 years. No differences were found for A(H1N1)pdm09 or B-lineages. ADIV is more useful than NAIV for inducing higher humoral responses in older groups, especially against A(H3N2) subtype which is the virus that present higher mortality among the elderly.

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Abstract 6494

**Discovery of convergent mutations associated with *Mycobacterium tuberculosis* clinical and microbiological characteristics**

Olga Lebedenko1, Mikhail Rotkevich1, Viatcheslav Zhuravlev2, Ekaterina Chernyaeva1, Peter Yablonsky1,3

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**Background:** Understanding of genetic mechanisms for *Mycobacterium tuberculosis* drug resistance is important to provide correct treatment plan. GWAS became well-established instrument for discovering genetic associations in many organisms, however it requires adaptation to bacterial genome analysis due to relatively strong population structure. The current study presents alternative algorithm convPhy based on detection of convergent mutations. Significantly, developed application can be expanded to identification genetic associations for any binary traits in evolutionary context

**Materials/methods:** The main goal of convPhy is detection of convergent mutations. convPhy assumes reconstruction phylogenetic tree, prediction ancestral genotype and phenotype. Phylogenetic tree branches lead to resistant or sensitive phenotype descendant labeled respectively. For each testing SNP sensitive and resistant branches are counted. Statistical significance is evaluated by permutation test. The source code of the project is available on github: https://github.com/OOLebedenko/convPhy. We validated conPhy on well characterized dataset PRJNA23585 consisting of 233 Indian *M. tuberculosis* isolates and applied to 71 pulmonary and 66 extrapulmonary Russian isolates PRJNA352769. Both datasets have experimentally determined drug susceptibility profile to rifampicin, isoniazid and ethambutol. Raw reads aligned on the reference genome H37Rv (NC_000962.3) with bwa mem 0.7.15-r1140. SNPs calling was performed with GATK ver. 4.0.1.2. SNPs were filtered by QD>30 and DP>20. Phylogenetic tree was constructed using RAxML with CTRCAT nucleotide substitution model, *M. canettii* (NC_015848.1) as outgroup and concatenated filtered SNPs as input.

**Results:** convPhy demonstrated high level of concordance with associations described in Indian validation SNPs set. In Russian isolates convPhy revealed association pathogen localization with mutations in PE/PPE genes, presumably participating in virulence. Moreover, convPhy detected mutation previously not associated with drug resistance in esxV, pks12, lppa, lppb, pknH, fadD19, glyA1, rpfA genes and cooperative interaction of single SNPs in isolates *M. tuberculosis* whose resistance to isoniazid and rifampicin are not explained by known mutations S315T katG and S450L rpoD.

**Conclusions:** convPhy seems promising tool for discovering resistance-related mutations in bacterial genome. The preference convPhy against previously described similar approaches is available source code with clear technical realization and module for detection interaction between single SNPs.

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Abstract 6495

Prospective study of breakthrough invasive fungal infections in haematologic patients in Spain

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Background: Breakthrough invasive fungal infections (BtIFI) are an emerging problem; however prospective epidemiological data are lacking. We aimed to describe the current epidemiology, treatment and outcomes of BtIFI in hematological patients in Spain.

Materials/methods: Prospective descriptive cohort study of all consecutive BtIFI diagnosed according to the revised EORTC criteria in 13 Spanish hospitals from September 2017 to July 2019 [22 months]. BtIFI was defined as any IFI occurring in patients with ≥5 days of antifungals within the last week. Antifungal susceptibility was tested in the Spanish National Center for Microbiology.

Results: 84 BtIFI were diagnosed: 25 [29.8%] proven, 36 [42.9%] probable and 21 [25%] possible. Most common underlying diseases were acute myeloid leukemia (44%) and hematopoietic stem cell transplantation (19%). Table 1 details the microbiological characteristics of the proven cases. Most frequent prior antifungals were posaconazole [31%], fluconazole [27.4%] and echinocandins [22.7%]; administered for primary prophylaxis [71.4%], secondary prophylaxis [10.7%] and preemptive therapy [6%]. Antifungal therapy was usually changed [84.5%], commonly to liposomal Amphotericin B [42.9%]. 100-day mortality was 51.2%.

Conclusions: Aspergillosis is still the most frequent cause of BtIFI but the appearance of rare fungi like Mucorales, Geotrichum or Fusarium and non-albicans Candida infections was evidenced. Most proven BtIFI were resistant to the prior antifungal administered. Mortality rate was high.

Table 1. Microbiological characteristics.

<table>
<thead>
<tr>
<th>Fungus</th>
<th>Proven (n=25)</th>
<th>Previous antifungal [S, R or NA]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspergillus</td>
<td>5</td>
<td>- A. niger: 3</td>
</tr>
<tr>
<td>Candida</td>
<td>13</td>
<td>- C. glabrata: 2</td>
</tr>
<tr>
<td>- C. guilliermondii: 2</td>
<td>Posaconazole (NA) and Anidulafungin (S)</td>
<td></td>
</tr>
<tr>
<td>- C. albicans: 3</td>
<td>Fluconazole (R), Vorneconazole (NA) and Fluconazole (NA)</td>
<td></td>
</tr>
<tr>
<td>- C. parapsilosis: 3</td>
<td>Posaconazole (S), Micafungin (NA) and Caspofungin (NA)</td>
<td></td>
</tr>
<tr>
<td>- C. tropicalis: 3</td>
<td>Micafungin (S)</td>
<td></td>
</tr>
<tr>
<td>- C. krusei: 1</td>
<td>Fluconazole (S) and Vorneconazole (NA)</td>
<td></td>
</tr>
<tr>
<td>- C. krusei: 1</td>
<td>Fluconazole (R) and Vorneconazole (NA)</td>
<td></td>
</tr>
<tr>
<td>Geotrichum spp.</td>
<td>2</td>
<td>Posaconazole (R) and Posaconazole (S)</td>
</tr>
<tr>
<td>Mucorales</td>
<td>4</td>
<td>- Lichtheimia spp.</td>
</tr>
<tr>
<td>- Conidiobolus spp.</td>
<td>Fluconazole (R)</td>
<td></td>
</tr>
<tr>
<td>- Rhizopus spp.</td>
<td>Fluconazole (R)</td>
<td></td>
</tr>
<tr>
<td>- Rizosporium spp.</td>
<td>Fluconazole (R)</td>
<td></td>
</tr>
<tr>
<td>Fusarium solani</td>
<td>1</td>
<td>Fluconazole (R)</td>
</tr>
</tbody>
</table>

Abbreviations: S= susceptible, R= resistant and NA= not available.

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Abstract 6497

**Innovative diagnosis strategy for pneumococcal infections in children using an immunochromatographic test in respiratory specimens**

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**Background:** Despite vaccination programs, *Streptococcus pneumoniae* remains among the main microorganisms involved in bacterial pneumonia, notably in terms of severity. The prognosis of pneumococcal infections is conditioned by the precocity of the diagnosis. This study evaluated the impact of a Rapid Diagnostic Test (RDT) targeting *S. pneumoniae* cell wall polysaccharide and performed directly in respiratory samples, on the strategy of diagnosis of pneumococcal respiratory infections in children.

**Materials/methods:** Upper-respiratory tract samples from 196 children consulting at hospital for respiratory infection were tested for *S. pneumoniae* using a newly-designed RDT (PneumoResp, Biospeedia), a semi-quantitative culture and two PCR assays. If positive on fluidized undiluted specimen, the RDT was repeated on 1:100-diluted sample. The clinical data analysis was conducted retrospectively.

**Results:** The RDT was highly specific when tested on non-*S. pneumoniae* strains. By comparison to culture and PCR assays, the RDT on undiluted secretions exhibited sensitivity (Se) and negative predictive value (NPV) over 98%.

<table>
<thead>
<tr>
<th>Microbiological tests</th>
<th>Number of positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Semi-quantitative culture</td>
<td></td>
</tr>
<tr>
<td>- 10⁷ CFU/ml</td>
<td>20 (10.2)</td>
</tr>
<tr>
<td>- ≥ 10⁸ CFU/ml</td>
<td>50 (25.5)</td>
</tr>
<tr>
<td>Positive PCR tests (ply and/or lytA)</td>
<td>169 (86.2)</td>
</tr>
<tr>
<td>- ply gene</td>
<td>167 (85.2)</td>
</tr>
<tr>
<td>- cycle threshold ≥ 22</td>
<td>104 (53.1)</td>
</tr>
<tr>
<td>- cycle threshold &lt; 22*</td>
<td>63 (32.1)</td>
</tr>
<tr>
<td>- lytA gene</td>
<td>123 (62.7)</td>
</tr>
<tr>
<td>- cycle threshold ≥ 23</td>
<td>91 (46.4)</td>
</tr>
<tr>
<td>- cycle threshold &lt; 23*</td>
<td>32 (16.3)</td>
</tr>
<tr>
<td>Positive PneumoResp RDT</td>
<td></td>
</tr>
<tr>
<td>- undiluted sample</td>
<td>133 (67.8)</td>
</tr>
<tr>
<td>- 1:100 diluted sample</td>
<td>76 (38.7)</td>
</tr>
</tbody>
</table>

* These thresholds were shown to correspond to approximately 10⁷ CFU/ml by qPCR.

By comparison to criteria of *S. pneumoniae* pneumonia combining typical symptoms, X-ray image and culture ≥ 10⁷ CFU/ml, the Se and NPV of RDT on diluted specimens were 100% in both cases.

**Conclusions:** In case of negative result, the excellent NPV of RDT on undiluted secretions allows excluding *S. pneumoniae* pneumonia at day 0 and orientates towards the search for another pathogen. In case of positive result, the excellent sensitivity of RDT on diluted secretions for the diagnosis of *S. pneumoniae* pneumonia allows proposing an anti-pneumococcal treatment at day 0.

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Abstracts 2020

Abstract 6499

**Polymicrobial species identification from positive blood cultures with high-resolution Orbitrap mass spectrometry**

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**Background:** Polymicrobial blood cultures occur due to co-infection, or as an incidence of skin contamination from blood sampling. Approximately 5-10% of positive blood cultures are polymicrobial and contain two or more species. Identification of all species present in polymicrobial blood cultures has remained challenging for diagnostic methods, as the ratio of different organisms can vary.

**Materials/methods:** Diagnostic protein markers were determined for seven common blood culture taxa including Enterococcus faecalis, E. faecium, Escherichia coli, Klebsiella pneumoniae, Staphylococcus aureus, S. epidermidis and Pseudomonas aeruginosa. Initially, monoculture protein profiles were measured with top-down data dependent acquisition (DDA) LC-MS2. Given the identified proteins, the potential markers were deduced by comparing predicted protein prevalence across strains of publicly available genomes [NCBI]. Preferred marker candidates displayed exclusivity to a clinical category, a high prevalence across strains of the targeted species, as well as a high propensity for detection with mass spectrometry [MS]. To test the approach and simulate polymicrobial cultures, seeded, positive blood culture of E. coli was mixed with corresponding blood cultures of S. epidermidis and E. faecalis. Microbial cells were enriched and lysed, and produced protein extracts were measured with targeted 2.5 min LC-MS2 method, using Acroion ProTrap™ columns and Orbitrap™ mass spectrometer. True microbe ratio in each sample was determined based on CFU in positive blood cultures and mixing ratio.

**Results:** The protein markers and corresponding species were identified based on diagnostic MS2 fragments. The approach to use targeted protein markers with a short LC-MS2 method for polymicrobial species identification was shown to be feasible, even with high mixing ratios (f1:100).

**Conclusions:** High-resolution targeted LC-MS2 is a promising method to identify species in polymicrobial blood culture samples, and can be utilised on a high-resolution MS platform such as Acroion™. Simultaneous detection of multiple species in one analysis facilitates diagnosis of bacteremia, and may have a significant impact to patient outcome.

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Abstract 6501

Impact of enteric viral co-infections on gastroenteritis among hospitalised children in Palermo, Italy, during a 10-year surveillance

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Background: Acute gastroenteritis is one of the most common illnesses in humans worldwide. Four viruses account most of the cases of childhood gastroenteritis: rotavirus, norovirus, adenovirus 40/41 and astrovirus. The recent availability of syndromic assays simultaneously detecting several pathogens allows to easily reveal co-infections.

The aim of this study was to investigate the extent and epidemiological features of concurrent rotavirus, norovirus, adenovirus and astrovirus infections in children hospitalized with acute gastroenteritis.

Materials/methods: A total of 4161 stools from children <5 years of age hospitalized in Palermo, Italy, from January 2008 to December 2018, collected for the sentinel surveillance activity of the Italian Study Group for Enteric Viruses (ISGEV; http://isgev.net), were investigated for the presence of rotavirus, norovirus, adenovirus and astrovirus.

Results: At least one enteric virus was detected in 55.5% of the patients, and the rate of co-infection was 4.06%, with a maximum of three different viruses being simultaneously detected. Rotavirus was the most prevalent virus in symptomatic children (24.8%) followed by norovirus (20.31%), adenovirus (7.4%) and astrovirus (2.84%). Astrovirus infections frequently also involved other enteric viruses (27.12% of co-infections), but rotavirus was most commonly detected in mixed infections, notably with norovirus G1P[8] (66.86%), astrovirus (10.06%) and adenovirus (4.73%). G1P[8] was the predominant rotavirus genotype found in co-infections (55.7%), followed by G9P[8] (14.7%) and G2P[4] (5.7%). Mixed infections involving more than one rotavirus genotype were seldom detected (6.5%). GIIP4 was the main norovirus genotype (41.3%) detected in co-infections, followed by GII.Pe (12.3%) and GII.P16 (15.2). In most cases, a significant difference in Ct values was observed among the co-infecting viruses, and rotavirus was generally detected at a lower Ct value compared to the concomitant norovirus or astrovirus (indicating 1 to >3 log higher viral load).

Conclusions: The systematic detection of four viruses allowed us to evaluate their involvement in co-infections. As detection of co-infections still represents a challenge for the diagnostic laboratory, further studies should be performed to understand if co-infection can increase the severity of enteric disease and the role of each pathogen involved.

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Clinical outcome of early central venous catheter removal in children with candidaemia: a retrospective multi-centre study

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¹Hopital Robert Debré, Paris, France; ²Hopital Armand Trousseau, Paris, France; ³Hopital Necker enfants malade, Paris, France

Background: Candida spp. is third leading organism of nosocomial bloodstream infection in pediatrics preceded by coagulase-negative staphyloccoci and Staphylococcus aureus. Vascular catheters are a risk factor of candidemia and its withdrawal is considered to be a standard. Pediatric specific data on the impact of central venous catheter (CVC) retention are limited.

Materials/methods: We have led a retrospective study in 2 pediatrics Parisians centers which aimed to study the impact of central venous catheter (CVC) retention beyond 72 hours in candidemia in children, between 2007 and 2017. We defined catheter-related bloodstream infection (CRBSI) according to IDSA definitions. The primary study outcome was clinical failure, defined as mortality within 30-days, persistent positive blood culture for ≥72 hours after the initiation of antifungal therapy, new sites of infection or relapse within 12 weeks.

Results: We included 93 patients. Median age was 4.4 years old. 58 patients (62.4%) benefited from a removal of CVC within 72h after the positive blood culture and 35 patients (37.6%) had conservative treatment of CVC. C. albicans, C. parapsilosis and C. tropicalis were the three most represented. 3 strains were resistant to fluconazole: 1 C. tropicalis, 1 C. krusei, et 1 C. haemulonii. None were resistant to echinocandins. 57 patients had criterion of clinical failure: 28/58 (48.3%) with removal CVC and 29/35 (82.9%) in conservative group (p=0.002). Mortality was 15 % : 7/58 (12%) in removal group, 7/35 (20%) in conservative group (p=0,46), 40 patients had persistent fungemia : 20/58 (34,5%) in removal, 20/35 (57%) in conservative group (p=0,054), 16 patients had new infection site : 6/58 (10,3%) in removal group, 10/35 (28,6%) in conservative group (p=0,048). Predictive factors of clinical failure were neutropenia (p=0,003), intensive care needed (p= 0,007) and retention of CVC (p=0.02).

Conclusions: Results of this pediatric cohort confirms guidelines for Candida CRBSI and reminded us the need to remove CVC as early as possible even if venous access is more complex in children. Maintained CVC seems to be associated with clinical failure.

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Abstract 6505

Comparison of antimycotic activity against clinical isolates of Candida albicans and Candida glabrata of originator and generics of voriconazole and anidulafungin

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Background: Concerns have been expressed about the interchangeability of innovator and generic antimycotics regarding their activity, stability and their susceptibility towards fungi.

Materials/methods: Activity of 2 different antimycotics was tested each with 1 originator and 2 generics. For voriconazole [fungistatic] the originator VFEND® from Pfizer and the two generics from Ratiopharm and Stada were used to test against 21 clinical isolates of Candida albicans (C. albicans) with reference strain ATCC-90028. For anidulafungin [fungicidal] the originator ECALTA® from Pfizer and the two generics from Stada and Pharmore were used and tested against 20 clinical isolates of Candida glabrata (C. glabrata) and reference strain ATCC-22019 Candida parapsilosis (C. parapsilosis). MIC testing was performed in triplicate for both settings in RPMI growth media in compliance with the EUCAST protocol for MIC testing of antifungal agents. Time Kill Curves (TKC) with concentrations above and below the respective MIC were performed for 1 representative clinical isolate and the corresponding ATCC-strain in Sabouraud broth (SAB). Samples were drawn at defined time points, and dilutions were plated on Sabouraud agar plates (SAG) to evaluate the CFU/mL. Stability testing of the antimycotics stored at 4°C and at room temperature over 24 hours was done with HPLC analysis.

Results: MIC results of clinical isolates and ATCC strains showed no significant difference in activity of generic and innovator antimycotic in all settings. The median MIC ratios of originator and generic [all combinations showed a ratio of 1] confirm the interchangeability of the drugs. Colony counts per mL in TKCs verify these findings as seen in figure 1 (a) and (b). HPLC analysis demonstrated stability of the tested antimycotics despite originator or generic.

Conclusions: This study showed that antimycotic activity of generics was identical to the originator for both settings with voriconazole and anidulafungin. Further, antimycotic stability within approved storing conditions could be confirmed. The present study demonstrates interchangeability of generic and originator antimycotic in-vitro potentially leading to broader public acceptance for generic antimycotics.

Figure 1: TKC of (a) voriconazol against C. albicans and (b) anidulafungin against C. glabrata tested with originators (O) from Pfizer (blue symbols), generics-1 (G1a and G1b) from Strada (red symbols), generic-2 (G2) from Ratiopharm and generic-3 (G3) from Pharmore (green symbols) with standard deviations over 72 and 24 hours, respectively are shown.

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Transglutaminase 2 inhibitors as a future intervention against non-tuberculous mycobacteria

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Background: Diseases caused by Non Tuberculous Mycobacteria (NTM) are on the rise worldwide, including immunocompetent adults. The current treatment against NTM infections is based on the combined use of antibiotics that are administered for 6-12 months. Despite these aggressive regimens, success rate barely exceed 50% due to the intrinsic and acquired NTM drug resistance. Host-directed therapies (HDTs) are emerging as a promising area of research and are opening new avenues in the treatment of mycobacterial infection. We recently demonstrated that genetic or pharmacological inhibition of transglutaminase 2 (TG2), a multifunctional ubiquitous enzyme that catalyses post-translational modifications of proteins in eukaryotic cells, results in the reduction of Mycobacterium tuberculosis replication in murine and human primary macrophages. In this study we aim to assess the anti-mycobacterial activity of the TG2 inhibitors cystamine and cysteamine against a panel of NTM.

Materials/methods: To test the potential activity of TG2-inhibitors, human monocyte-derived macrophages (THP-1) were infected with clinical isolates of NTM (Mycobacterium avium (MAV), Mycobacterium abscessus (Mabs), Mycobacterium intracellulare (MAI)) and then treated with antibiotics currently used in the standard therapy or with cystamine or cysteamine. We also evaluate cysteamine and cystamine activity in the human ex vivo model of granuloma-like structures (GLS).

Results: Intracellular CFUs were determined at day 2 and a significant reduction was observed following treatment with these inhibitors. Interestingly, when THP-1 cells were infected with the two colony variants of Mabs (Smooth and Rough), the treatment with cystamine and cysteamine turns out to have a superior antimicrobial response compared with the drug streptomycin and especially against the most virulent R variant of Mabs. The study in the GLS model further confirmed the ability of these drugs to restrict NTM replication (reduction of 1.2 log CFU for Mabs; ≈ 2 log CFU for MAV and 1.3 for MAI) and to reduce the size of GLS.

Conclusions: The antimicrobial activity of the TG2-inhibitors synergized with a standard drug as amikacin in human mono-ocyte-derived macrophages and in the GLSs model. Overall, the results of this study support the potential usefulness of the TG2-inhibitors cysteamine and cystamine as HDTs in NTM disease.

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Omitting the nightly dose of selective digestive tract decontamination provides equally effective decontamination of potential pathogenic bacteria: a cost reducing and sleep-promoting intervention

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Background: Selective digestive decontamination (SDD), targeting potential pathogenic microorganisms (PPMs), has been shown to prevent ICU-acquired infections and improve patient survival. SDD consists of application of non-absorbable antibiotics (colistin, tobramycin and amphotericin B) in the oropharyngeal cavity and the stomach, four times daily of which one dosage is at night, combined during the first four days with intravenous cefotaxim. Surveillance cultures are collected weekly to assess the effectiveness of decontamination. We aimed to demonstrate that omitting the nightly SDD dosage does not influence the effectiveness of decontamination.

Materials/methods: Retrospective equivalence study with a before-and-after design performed at a tertiary ICU that omitted the nightly dose of SDD three years earlier. We defined effective decontamination as the time-point at which surveillance cultures became negative for PPMs and remained so during the remainder of the ICU stay. Inclusion criteria were admission duration ≥72h and ≥2 surveillance cultures collected on different dates.

Results: In total 1958 ICU admission were included in the analysis, 1236 before (q.i.d.) and 722 after (t.i.d.) the change in SDD application frequency. Effective decontamination was achieved in 73.2% of the admission with q.i.d. versus 71.6% in t.i.d. SDD application (p-value = 0.4398). The proportion difference of effective decontamination between the two regimens was equivalent (-0.016, 99% CI: -0.07; 0.038). There was no significant difference in time to decontamination between the two regimens (log-rank test p-value = 0.55).

Conclusions: Omitting the nightly SDD dosage provided equally effective decontamination of PPMs. Sleep is essential for adequate immune, metabolic, and endocrine functioning. No formal cost analysis was performed but a 25% reduction of costs of the medication can be expected. These findings justify implementation of a t.i.d. SDD frequency as a cost reducing and sleep-promoting intervention.

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Clinical application of polyomavirus detection by metagenomic next-generation sequencing in urinary tract infection
Na Li1*, Bijie Hu1

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Background: Urinary tract polyomavirus replication is common, while the clinical significance of polyomavirus detection in the urine of patients with urinary tract infections remains elusive. We aimed to analyze the clinical value of polyomavirus detection in the urine by metagenomic next generation sequencing.

Materials/methods: Urine specimens were collected from 30 patients diagnosed with urinary tract infection in Zhongshan Hospital of Fudan University from September 2018 to October 2019. The random amplification, DNA nanoball, BGI-500 sequencing platform, and BWA were used for next generation sequencing and analysis of nucleic acid extracts from urine. The number of virus sequences in urine samples >100 was included in the study, and indexes of virus types, depth, coverage rate, abundance and reads number were observed.

Results: JC polyomavirus was detected in 26.7% (8/30) urine samples, with BK polyomavirus co-detected in one of them. 7 of the 8 patients were made a designation of complicated urinary tract infection, and only one of them had positive urine culture (Escherichia coli). All cases were immunocompromised patients, including rheumatic autoimmune diseases, tuberculosis, rheumatic heart disease, liver transplantation, T-lymphocyte tumor hyperplasia, and poorly controlled type 2 diabetes. The mean value of depth, coverage rate, relative abundance and stringently mapped reads number of JC polyomavirus were 40.2, 97.5%, 90.8% and 3464, respectively. Nucleic acid sequences of bacteria, fungi, other viruses and mycobacteria were also detected in some cases. There was a negative linear correlation between the RPM parameter (reads per megabyte of data) and the number of CD4+ T cells. In one case, the urinary irritation symptoms and urine test indexes were obviously improved after treatment with cidofovir, and the reads and RPM value of JC polyomavirus were significantly decreased during follow-up.

Conclusions: The possibility of infection should be considered upon JC polyomavirus detected in the urine of immunocompromised hosts. The metagenomic next generation sequencing is of great value in the diagnosis of viral urinary tract infection. Cidofovir may be effective in the treatment of urinary tract polyomavirus infection.

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Abstract 6510

Impact of infectious diseases consultation and appropriate empirical antibiotic therapy on mortality in patients with *Staphylococcus aureus* bloodstream infection: a two-year retrospective analysis

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**Background:** Guidelines on *Staphylococcus aureus* Bloodstream Infection (SA-BSI) recommend the implementation of bundles of interventions, including follow-up blood culture, echocardiography, source control, specific antibiotic therapy with appropriate length and Infectious Diseases consultation (ID-cons) to reduce mortality of SA-BSI. We aim to evaluate the adherence to the bundles for SA-BSI and the impact of ID-cons and empirical appropriate antibiotic therapy on in-hospital mortality.

**Materials/methods:** Two-years (2017-2018) analysis of all the SA-BSI diagnosed at San Paolo Hospital, Milan. Data on clinical characteristics, adherence to bundles of interventions and in-hospital mortality for any cause (by Kaplan-Meier) were collected. Factors associated with mortality were analyzed by uni- and multivariate Cox regression models adjusted for potential confounders.

**Results:** A total of 117 patients with SA-BSI diagnosed in 2017-18 were included; 41 (35%) were sustained by MRSA. Median age was 77 years (IQR:64-82); median Charlson score was 7 (5-10). 32.7% (38/117) of the SA-BSI were hospital-acquired and 51% were sepsis at onset; ID-cons was requested in 88 (79.2%) of cases. Overall adherence to the bundle protocol was 37.5%. High adherence was recorded for source control (72%); conversely, adherence to diagnostic work-up and to follow-up blood culture was 49% and 21%. Overall, 44% of the SA-BSI resulted complicated. Empirical antibiotic therapy was appropriate in 69.8% of the cases (86% MSSA vs 39% MRSA, p<0.0001). At survival analysis, the 30 days-probability of in hospital mortality was of 29% [95%CI 15.7-42.3], ID-cons was associated with a reduced 30 days-probability of mortality [ID-cons: 22%[95%CI 8-36] vs no ID-cons 52%[95%CI 28-75]; p=0.002] (Figure 1a). Similarly, appropriate empirical antibiotic therapy was associated with a reduced 30 days-probability of mortality [appropriate: 15%[95%CI 3-27] vs inappropriate 45%[95%CI 22-68]; p=0.002] (Fig. 1b). By multivariate analysis adjusted for MRSA, ID-cons (aHR 0.2, 95%CI 0.07-0.6. p=0.004) and appropriate empirical antibiotic therapy (aHR 0.1, 95%CI 0.02-0.4. p=0.006) were associated to a reduced risk, whereas high Charlson score (aHR 1.2, CI95% 1.0-1.4. p=0.03) and sepsis at onset (aHR 6.9, CI95% 1.7-28. p=0.007) were associated to increased risk of in-hospital mortality.

**Conclusions:** Our study confirms that ID-cons and appropriate empirical therapy result in a reduced SA-BSI-related in-hospital mortality.

![Figure 1. Kaplan-Meier curves for survival analysis: probability of in-hospital mortality with (A) and without (B) ID-cons (Fig 1a); probability of in-hospital mortality with (C) and without (D) appropriate empirical therapy (Fig 1b).](image)

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Evaluation of different commercial methods for fosfomycin susceptibility testing of Staphylococcus aureus

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Background: Recent studies demonstrated a good in vitro activity of fosfomycin against MRSA clinical isolates can cause a wide spectrum of diseases, including bacteremia, pneumonia, osteomyelitis, endocarditis, septic shock and other infectious diseases.

The clinical use of fosfomycin requires the in vitro testing of the drugs in order to be categorized correctly in the clinical reports. According to EUCAST, the only approved MIC method for testing the fosfomycin susceptibility is the agar dilution (AD) method, which is cumbersome and not routinely performed.

Our aim was to compare the AD reference method, Gradient test (GT) and a rapid AD commercial test for fosfomycin susceptibility against Staphylococcus aureus clinical isolates.

Materials/methods: Fosfomycin antimicrobial susceptibility testing was performed on 70 MRSA and n.10 MSSA clinical isolates, according to the GT and AD as described by the CLSI 2014. The gradient test was carried out on Mueller Hinton agar with strips containing fosfomycin and Glucose-6-Phosphate (Liofilchem, Roseto degli Abruzzi, Italy). The susceptibility testing by commercial AD method was performed as recommended by the manufacturer (Liofilchem, Roseto degli Abruzzi, Italy). The fosfomycin-resistance-related genes fosB, murA, glpT and uhpT were analyzed to explore the molecular mechanism of resistance.

Results: According to the selected breakpoints, fosfomycin, performed by AD reference method, inhibited 60% of the tested strains (n.49 MRSA and n.9 MSSA). fosB gene was detected in fosfomycin resistant strains with MICs >256 mg/L.

The results of the commercial AD method, compared with those obtained from the AD, used as reference method, demonstrated a Categorical agreement (CA) of 100% and an Essential agreement (EA) of 91%.

The comparison between GT and AD reference method showed a CA of 82,5% for all staphylococci tested.

Conclusions: The results obtained comparing the commercial AD method and AD reference method confirmed the feasibility to characterize fosfomycin susceptibility by Liofilchem panels, while the GT method was not suitable as an alternative to the AD. High-level resistance to fosfomycin was due to the presence of fosB gene.

In conclusion, the new commercial method was easy and rapid to use, resulting a valid alternative to the AD reference method in the routine laboratory.

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Clinical and epidemiological features of patients presenting with Crimean-Congo haemorrhagic fever at a tertiary care hospital in Karachi

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Background: Crimean Congo Haemorrhagic fever (CCHF) is a life threatening tick borne zoonotic infection caused by an arbovirus from the family Bunyaviridae. An increasing number of cases have been reported from Pakistan since 2007 and environmental changes such as movement of human and animal populations and increase in temperature and humidity have been identified as contributing factors. We describe the clinical and epidemiological features and laboratory findings of patients presenting with CCHF at a tertiary care hospital in Karachi.

Materials/methods: This retrospective observational study was conducted at Aga Khan University Hospital, Karachi. Medical records of all patients admitted with CCHF confirmed by PCR from 2000-2018 were reviewed.

Results: A total of 58 patients were admitted of which 89.7% were male. The mean age was 34.4 years. 41.4% had exposure to livestock and 12.8% had exposure to a patient with CCHF. The number of patients is higher in the months of May, July and August. Mean duration of symptoms from onset to hospitalization was 6.2 days. All patients had fever. The other common symptoms on presentation were bleeding (87.9%), vomiting (70.7%), headaches (65.5%) and myalgias (51.7%). A total of 41.4% of all cases were from Karachi and 39.7% were from Balochistan province. Almost all patients had thrombocytopenia and elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT). The mortality was 34.5%. As compared to survivors, non-survivors had a higher aPTT, ALT, AST and acute kidney injury. Shock and haemorrhage was seen in almost all patients who died.

Conclusions: Early diagnosis and management may lead to better outcomes. The population needs to be educated about the signs and symptoms of CCHF and mode of transmission to encourage them to seek early healthcare and prevent household exposures.

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Whole genome sequencing reveals differences between previously indistinguishable isolates of tobramycin resistant *Staphylococcus aureus*

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**Abstract third-party references:** Futurum - the Academy for Health and Care

**Background:** We have a collection of 250 tobramycin resistant *Staphylococcus aureus* (TRSA), spa type t084. The strains were collected from May 2012 until June 2019 from 140 neonates, hospitalized at the neonatal ward at Ryhov County hospital, Jönköping, Sweden.

In this study we used whole-genome sequencing (WGS) to clarify the similarity between a subset of the TRSA t084 strains.

**Materials/methods:** DNA was extracted from 21 TRSA isolates, using the EZ1 DNA Tissue kit on the EZ1 Advanced XL (Qiagen). Library preparation was performed using Nextera XT library prep kit (Illumina). Paired-end sequencing (2*250 cycles) was performed on a Miseq instrument (Illumina). Assembly and cluster analysis by core genome multilocus sequence typing (cg-MLST) based on 1861 genes was performed using SeqSphere (Ridom GmbH). The cluster alert difference was set to 24 allelic differences by default.

**Results:** Out of the 21 isolates, 19 passed quality control after WGS and cgMLST.

The isolates were divided into two distinct, but closely related, cluster types; 3008 and 18810. The majority of isolates (n=17) belonged to cluster type 3008. The remaining two isolates belonged to cluster type 18810. The two neonates with TRSA of cluster type 18810 were born at another hospital than Ryhov County hospital. They were culture positive immediately upon arrival at the neonatal ward at Ryhov County hospital and were therefore concluded to be colonized at the hospital where they were born.

**Conclusions:** WGS revealed two outbreaks among isolates that where considered indistinguishable in regards to the antibiotic susceptibility pattern combined with spa typing. This proves that WGS is more discriminatory than previous typing methods, even when they are combined.

The two neonates with the TRSA of cluster type 18810 were born and colonized at another hospital. It therefore seems as if cluster type 3008 is endemic to the neonatal ward at Ryhov County hospital.

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Genomic and structural protein characterisation of mutations conferring bedaquiline resistance in *Mycobacterium tuberculosis* clinical strains

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**Background:** The increasing incidence of multi- and extensively-drug resistant tuberculosis (MDR/XDR-TB) represents a global emergency. Many mutations conferring drug resistance have been characterized for first- and second-line drugs, and their detection offers a means of rapidly assessing drug susceptibility patterns to improve patient management. Mutations putatively involved in resistance to Bedaquiline (BDQ) were found in *atpE* and *Rv0678* genes. The aim of this work is to characterize mutations conferring BDQ resistance at genomic and structural protein levels and their association with strain phenotypes.

**Materials/methods:** A collection of *Mycobacterium tuberculosis* (*Mtb*) strains representing all different lineages and drug susceptibility profiles were included in the study: minimal inhibitory concentrations (MICs) of BDQ was determined by using microtiter plates. MIC values of resistant strains were confirmed by Bactec 960 MGIT system and resazurin microtiter assay as reference methods. For whole genome sequencing, paired-end libraries were prepared using Nextera XT-DNA Library Prep Kit and sequenced on NextSeq500. Data analysis was performed by MTBseq pipeline. Protein structure analyses were performed using Molecular Docking and Molecular Dynamics simulations.

**Results:** WGS analysis on these strains revealed the presence of previously uncharacterized non-synonymous mutations in the screened genomic loci. The analysis revealed the presence of non-synonymous mutations (80%), frameshift mutations (14%) and also synonymous mutation (6%) considering all BDQ genomic targets. Most of the resistance-conferring mutations on the on-target proteins are far from the drug binding site (> 10Å), implying allosteric effect in the resistance mechanism. Network analysis shown that the mutations in the off-target protein are involved in the resistance mechanism. Molecular dynamics simulations together with normal mode analysis shown that the long range mutations induce allosteric effect impairing the drug binding.

**Conclusions:** The comparison between the genotypic-structural protein and the phenotypic allowed to identify and discriminate SNPs correlated to DR phenotype from SNPs without any DR correlation. It is worth nothing that *Mtb* strains were isolated from patients never exposed to BDQ, confirming that resistance phenotypes are pre-existing in *Mtb* circulating strains. The structural protein analysis revealed that most of the mutations raised far from the binding site and few close to the binding site.

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Abstract 6527

Investigating the prevalence of ESBL-producing Escherichia coli in rooks (Corvus frugilegus) wintering in an urban area and comparing these isolates to contemporary human faecal and clinical isolates

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Background: During winter, Rooks (Corvus frugilegus) gather at a university clinic. Prevalence of ESBL-producing Escherichia coli was investigated in these birds and, in line with the One Health concept, compared them to contemporary human faecal and clinical isolates.

Materials/methods: During the winter of 2016-2017, cloacal swabs from 112 live-captured Rooks together with all 2455 contemporary human faecal samples sent for culture were examined for asymptomatic carriage of ESBL-producers. The isolates found were compared to 42 ESBL-producing E. coli from infections of contemporary inpatients. Resistance genes bla_SHV and bla_CTX-M were identified by sequencing. E. coli phylogroups and the ST131 clonal lineage were detected by PCR. Clonal relatedness was analyzed by pulse field gel electrophoresis.

Results: From Rook samples 43 (38%) and from human faecal samples 42 (2%) ESBL-producing E. coli were isolated. In Rook isolates the bla_CTX-M-55 was dominant (16/43) followed by bla_CTX-M-27 (13/43), while bla_CTX-M-15 was most prevalent in human clinical (18/42) and faecal isolates (20/42) followed by bla_CTX-M-27 (13/42 and 10/42, respectively). Of the isolates carried by birds and humans 56% and 68% belonged to commensal E. coli phylogroups (A, B1, C, E), respectively, while 74% of the clinical isolates belonged to phylogroup B2. Two, ten and 15 of Rook, human faecal and clinical isolates belonged to ST131 C1-M27 clade, while none, one and ten isolates belonged to ST131 C2 clade, respectively. Human clinical and faecal isolates clustered frequently together but Rook isolates tended to cluster separately. A cluster of ten human clinical and eight faecal isolates belonged to the ST131 pandemic clonal lineage; this cluster also contained the two Rook isolates from the ST131 C1-M27 clade. A small cluster consisted of three clinical, one faecal and one bird isolates; another cluster dominated by Rook isolates also contained one human faecal isolate.

Conclusions: Rooks are significant reservoirs of ESBL-producing E. coli and carry isolates of the pandemic clone ST131. However, ESBL genes and pulsotypes were shared infrequently between Rook- and human-derived isolates, suggesting that Rooks are important as reservoirs and potential long-distance vectors of resistant bacteria and resistance genes rather than as direct sources of human infections.

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Improvements in HIV-1 transmitted drug resistance surveillance in Ireland

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Background: HIV is of global public health concern and a priority European Centre for Disease Prevention and Control (ECDC) pathogen for molecular surveillance. This is imperative to reduce the risk of treatment failure at both an individual and population level. Trends in HIV transmitted drug resistance (TDR) can inform national treatment guidelines and contribute to Europe-wide surveillance.

Materials/methods: In 2017 and 2018, case-based, de-identified HIV epidemiological data on all newly notified HIV cases from the Computerised Infectious Diseases Reporting (CIDR) system were linked to antiviral resistance data generated by Sanger sequencing. Drug resistant mutations (DRM) were identified using the WHO 2009 surveillance DRM list for 2017, and the ECDC recommended DRM protocol for 2018.

Results: Sequencing was performed in 58% (n=283) of HIV diagnoses in 2017 and in 51% (n=266) in 2018. In the remainder, sequencing was not performed due to low viral load, a consequence of being on treatment at time of first diagnosis in Ireland. Of those sequenced, exposure to prior antiretroviral therapy could be determined for 73% in 2017 and 81% in 2018. TDR prevalence to any drug class was 8.6% in 2017 and 19.1% in 2018.

Non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance (7.5% & 15.5%) was significantly higher than nucleoside reverse transcriptase inhibitor (NRTI) resistance (1.1% & 2.1%) and protease inhibitor (PI) resistance (1.6% & 3.1%) for both study years. Integrase inhibitor (INI) resistance (1.6%) was identified by the ECDC protocol in 2018 only. TDR rates increased across all patient groups.

Conclusions: The increased TDR rate observed in 2018 was mainly due to changes in DRM identification, but requires close monitoring, as the introduction of next-generation sequencing and enhanced TDR surveillance may increase rates further. Comprehensive surveillance of TDR in HIV remains a public health priority in Ireland.

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Abstract 6532

**Comparison of native and a new recombinant fusion protein (AgB8/1+AgB8/2+Ag5) for serological diagnosis of cystic echinococcosis**

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**Background:** Cystic echinococcosis (CE) is one of the most common helminthic infections and is caused by larvae of the tapeworm *Echinococcus granulosus*. Diagnosis and monitoring CE is based on imaging and serologic methods. In our study, recombinant fusion protein (Ag5+AgB8/1+AgB8/2) consisting of AgB8/1, AgB8/2 and Ag5, all of which having a high sensitivity and specificity, was compared to cyst fluid using total Immunoglobulin G (IgG) ELISA test. Also, the usefulness of the recombinant fusion protein in the diagnosis and follow-up of CE patients was investigated.

**Materials/methods:** Two hundred fifty two patient sera belonging to 182 CE patients whose diagnoses were confirmed radiologically, serologically and/or surgically were tested. Together with 252 CE sera, 160 patient sera from individuals who received a positive clinical, serologic or parasitological diagnosis with regards to other parasitic infections such as alveolar echinococcosis (AE), fascioliasis, toxocariasis, toxoplasmosis, visceral leishmaniasis, and trichinellosis were also tested. Finally, 30 serum samples from healthy individuals were tested bringing the total number of tested serum samples to 442.

**Results:** The sensitivity of cyst fluid and recombinant antigen tested by ELISA were 86.5% and 29.3%, respectively, whereas, the specificity of cyst fluid and recombinant antigen were 82.6% and 94.2%, respectively. Cyst fluid ELISA showed low percentage of positivity in patients with inactive cyst stage (CE4-CE5). However, before treatment or in patients with post-operative relapse seropositivity was higher compared to those who were cured after treatment. In recombinant antigen ELISA no significant difference was found between cyst stages (P=0.085), however, significant difference was found between the presence of cyst in the liver and in other organs (P=0.030).

**Conclusions:** Fusion protein consists of promising antigens in the diagnosis and follow-up of CE patients, contrary to expectations, it was found to have low sensitivity and seropositivity rates. It was thought that studies using wider serum panel must be carried out to investigate the reasons of the low diagnostic performance of the antigen and to make necessary adjustments.

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Abstract 6535

**Biochemical description of seven putative novel species of the genus Yersinia identified by core-genome multilocus sequence typing (cgMLST)**

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**Background:** A phylogenetic analysis based on cgMLST of the genomes of 238 strains belonging to 18 Yersinia species performed by the French National Reference Laboratory evidenced seven putative novel Yersinia species being mainly derived from human stool samples (91.7%) besides veterinary (4.2%), environmental (1.4%), alimentary (0.7%) or undefined source of origin (2.0%): Y. frederiksenii 2 and 3, Y. kristensenii 2 and 3 as well as Y. new 2, 3 and 4 with the last two species clustering phylogenetically at the root of the Y. enterocolitica strains. We aimed in this study for a biochemical characterization of these species to better distinguish them phenotypically from the disease-causing Yersinia strains for a first estimation of their pathogenic potential.

**Materials/methods:** We performed O-serotyping and biochemical tests to obtain the phenotypical characteristics of the putative new Yersinia species. The results were compared to the characteristics of the already described Yersinia species. The significance of the observed biochemical patterns was tested via Fisher’s exact test. The strains of the putative novel species were highly variable in sample size: Yersinia new 2 (n=2), Y. new 3 (n=3), Y. new 4 (n=35), Y. frederiksenii 2 (n=11), Y. frederiksenii 3 (n=62), Y. kristensenii 2 (n=5), Y. kristensenii 3 (n=6).

**Results:** The new Y. kristensenii species showed differential characteristics in D-arabitol (p≤0.0109), indole (p≤0.0311), L-fucose (p≤0.0411), lipase (p≤0.0137), gluconate and 5-colo-gluconate (p=0.0049). Within the new Y. frederiksenii species lipase (p<0.0001) and citrate (p≤0.002) varied. Strains of Y. new 4 differed in Voges-Proskauer (p=0.0019), L-fucose (p=0.0183) and D-arabitol (p=0.0071). They were strongly associated with the O:10,34 serotype. Sample sizes of the species Y. new 2 and 3 were too low to determine significant characteristics. However, Y. new 2 was found to be negative for pyrazinamidase-activity which is usually associated with virulence in Yersinia.

**Conclusions:** Biochemical characteristics were successfully applied to discriminate the putative novel Yersinia species, as strong phenotypical associations were found. However, the low number of strains in some species requires larger studies. As a next step, the association of the species with epidemiological and clinical characteristics will be evaluated via descriptive analysis to further assess their pathogenic potential.

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Evaluation of a sub-culturing solution directly from manual blood cultures in low-resource settings

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**Background:** The Mini-Lab is a Médecins Sans Frontières project for the development of an all-in-one basic clinical bacteriology laboratory deployable in low-resource settings. In a previous laboratory evaluation study, the manual bi-phasic blood culture bottles (Autobio Diagnostics Co., Zhengzhou, China) chosen to be integrated in the Mini-Lab prototype for field-testing, showed insufficient growth on agar slant for downstream analyses; hence the need for a sub-culturing solution. The InTray® systems (Biomed Diagnostics Inc, OR, United States) were chosen for their ready-to-use compact format, the choice of media available and their 12 months shelf-life.

**Materials/methods:** Following a proof-of-concept study, the InTray® Müller-Hinton (MH) chocolate agar was chosen. In this study, this media was further tested against standard agar media (PolyViteX, bioMérieux) in two different settings: (1) In the clinical bacteriology laboratory of the Bicêtre Hospital (Paris), adult and paediatric blood culture bottles (BCBs) (BacT/ALERT, bioMerieux) were sub-cultured after positivity indicated by the automate and (2) at the Institute of Tropical Medicine in Antwerp, Belgium, Autobio bi-phasic and BacT/ALERT BCBs spiked with 2 mL of human blood (paediatric formulation) and clinical samples from low-resource settings (LRS) were sub-cultured after overnight incubation.

**Results:** Out of 70 BacT/ALERT positive BCBs sub-cultured (n=65 adults and n=5 paediatrics), InTray MH chocolate agar showed growth in 97% (n=68) with 100% agreement with standard media. Time to detection (TTD) was <20h in 97% of positives. When BCBs were spiked with LRS clinical samples (n=326), InTray MH chocolate agar showed growth in 96.6% and 99% (vs 100% of standard media) respectively, with a TTD of <24h in 100% of positives. In both settings suboptimal growth was observed when Streptococcus species were incubated in CO2 atmosphere. Presence of lawn (2-1%) as opposed to >10 isolated colonies (54%) on InTrays was probably due to condensation in the cassettes.

**Conclusions:** InTray MH chocolate agar is a valid sub-culturing solution, as it shows good performance after overnight incubation independently of type of BCB used. Elimination of condensation, optimization of the inoculation method, and incubation in air atmosphere to allow growth of most species were recommended.

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Accurate identification species of Enterobacter cloacae complex with Acrion system
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Background: E. cloacae complex is comprised of closely related Enterobacter asburiae, E. cloacae, E. hormaechei, E. kobei, E. ludwigii, and E. roggenkampii species. Discrimination of the species of the complex is challenging in clinical settings and requires molecular methods such as sequencing of the 16S rRNA, rpoB and hsp60 genes.

Species of the E. cloacae complex, especially E. cloacae, E. asburiae and E. hormaechei, are causing severe infections e.g. sepsis, pneumonia and urinary tract infections, in community and nosocomial outbreaks. Recently increase of prevalence of carbapenem resistance in E. cloacae complex species has been reported. Broad-spectrum antibiotic resistance, including the recent emergence of resistance to last-resort carbapenems, has led to increased interest in rapid and accurate identification and resistance detection in these species.

Materials/methods: Novel microbial diagnostic technique, Acrion™ system [Thermo Fisher Scientific] was applied to identification of E. cloacae complex species. Acrion identification and carbapenem resistance [CARBBA] detection is based on high resolution accurate mass spectrometry. Identification and CARBA resistance detection of the strains was compared with sequencing of seven house-keeping and blaKPC, blaNDM and blaOXA-48-like resistance genes as reference methods. The strains were recent clinical isolates or originated from culture collections. The strains were cultivated on agar media and as spiked blood cultures.

Results: Acrion Identification of species of E. cloacae complex from both positive blood cultures and agar media was accordance [96.9%] with the classification results based on sequencing of multiple genes. In addition, carbapenem resistance markers were correctly detected from E. cloacae and E. hormaechei strains. Both sequencing and Acrion showed that several strains from culture collections were originally misidentified, indicating the need for improved identification techniques for E. cloacae complex species.

Conclusions: The Acrion identified strains of E. cloacae complex, E. cloacae, E. asburiae, E. hormaechei, E. kobei, E. ludwigii, and E. roggenkampii correctly with high specificity from both positive blood cultures and isolated colonies. Carbapenem resistance was shown to be successful for the most common pathogens of the complex, E. cloacae and E. hormaechei. These results demonstrate accurate identification of E. cloacae complex species and carbapenem resistance detection with novel Acrion system.

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One-year surveillance report of carbapenem- and colistin-resistant Gram-negative bacteria within the MERCyCAT project

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Abstract third-party references: On behalf of the MERCyCAT study group

Background: This study aimed at performing a prospective study to evaluate the prevalence, epidemiology and dissemination of carbapenemase-producing and/or colistin-resistant GNB circulating in hospitals from Catalonia, Spain.

Materials/methods: The first GNB isolate/per patient was collected from 26 participating centers according to inclusion criteria: for Enterobacterales, MICs of >0.125 mg/L to meropenem and/or ertapenem and/or >1 mg/L imipenem, or disk inhibition zones of <25 mm to meropenem and/or ertapenem and/or <23 mm to imipenem; for A. baumannii, MICs of >2 mg/L to meropenem and >1 mg/L imipenem, or inhibition zones of <23 mm to meropenem and imipenem; for P. aeruginosa, MICs of >2 mg/L to meropenem and >4 mg/L imipenem, or inhibition zones of <24 mm to meropenem and <20 mm to imipenem. Species were identified by MALDI-TOF/MS, susceptibility was tested by disk diffusion and broth microdilution. Screening for carbapenemases and their genes was performed by mCIM method and PCR. Genetic relatedness was evaluated by PFGE and MLST.

Results: From January-2018 through May-2019, 118,041 isolates of GNB were reported, of which 0.67% and 0.19% were carbapenem- and colistin-resistant, respectively. E. coli isolates represented 60.8% of the total followed by K. pneumoniae and P. aeruginosa (13.3% and 9.7%), while A. baumannii constituted 0.16% of the total isolates. Among CarbR-isolates K. pneumoniae was predominant (53.6%) followed by P. aeruginosa (21%) and E. coli (11%). ColR-isolates were dominated by P. aeruginosa (46.9%) followed by E. coli (33.8%) and K. pneumoniae (14%). OXA-48 was the most abundant carbapenem-resistant gene (46.1%) and recovered in all hospitals mainly from K. pneumoniae. Among VIM-producers (16.9%) we distinguished the broad distribution of VIM-producing Enterobacterales, in terms of hospitals and species, and that of VIM-producing P. aeruginosa, more clonal and restricted to a few settings. KPC- and NDM-producers (16.7% and 3.5%) were associated with a few K. pneumoniae clones, causing small-sized outbreaks in one or two settings, and with sporadic cases of E. coli isolates due to horizontal-plasmid-transfer. Colistin-resistance was heterogeneous in its epidemiology and distribution.

Conclusions: Carbapenem and colistin resistance in Catalonia is still low but active surveillance should be continued to monitor the spread of major circulating clones.

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Unravelling HIV proviral latency by comparing HIV-1 and HIV-2 expression and reactivation with single round, double reporter constructs

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Abstract third-party references: Fonds Wetenschappelijk Onderzoek Vlaanderen

Background: Antiretroviral treatment does not cure HIV as the virus can persist in reservoirs of latently infected cells. Yet, the mechanisms governing proviral latency remain poorly understood. Like HIV-1, HIV-2 can cause AIDS but clinical data show slower disease progression and lower viremia, while the proviral DNA load is similar, suggesting HIV-2 may be more latent. By comparing HIV-1 and HIV-2 latency in vitro, we hope to learn more about the mechanisms governing HIV expression on a cellular level.

Materials/methods: The OGH double reporter construct contains an LTR driven eGFP gene and a constitutively active EF1a promoter, driving an mKO2 gene (Chavez et al., 2015), allowing detection of both silent and productively infected cells. We cloned the OGH cassette from the existing HIV-1 OGH construct, into an HIV-2 backbone. Next, we infected cell lines (SupT1, Jurkat) and primary cells (peripheral blood mononuclear cells and CD4+ T cells) with these single round HIV-1 and HIV-2 OGH viruses and measured reporter gene expression via flow cytometry, p24 levels in the supernatant and copy number via real-time quantitative PCR. Secondly, cells were treated with latency reactivating agents to measure reactivation.

Results: The fraction of latently infected cells was similar for HIV-1 and HIV-2. Yet HIV-2 median eGFP intensity was higher and over time, remaining HIV-2 expression was seen for higher eGFP intensities, where HIV-1 eGFP expression decreased uniformly. Upon reactivation with tumor necrosis factor alpha (TNFα), HIV-1 reactivated regardless of eGFP expression. HIV-2 was overall less sensitive to reactivation, and reactivated mostly at low eGFP intensity levels.

Conclusions: HIV-1 and HIV-2 have different expression and reactivation patterns. While HIV-2 is less sensitive to reactivation than HIV-1, median expression of eGFP was higher for HIV-2. Possible explanations for these differences include differences in the LTR promoter, Tat/TAR regulation, integration site selection and/or differences in toxicity. We continue to investigate the roles of each of these factors.

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Abstract 6544

Differences in nasopharyngeal microbiota composition according to the severity of human rhinovirus infection in the first 1000 days of life

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Background: Human Rhinovirus infection (HRVi) in early ages ranges from asymptomatic or mildly symptomatic infection to be often the only etiological agent in patients requiring advanced life support in intensive care units (ICU). The underlying determinants that contribute to the varying severity of HRVi are unknown. The objective of this study was to investigate the relationship between bacterial nasopharyngeal microbiota and the severity of HRVi in children <2 years old.

Materials/methods: Triple case-control study with patients <2 years old matched by gender and sex that were attended in Hospital Sant Joan de Déu (Barcelona, Spain) during the period 2014-2019. Cases (Group-A) were patients with severe lower respiratory tract infection (LRTI) associated with HRVi requiring admission to the ICU. A first control group (Group-B) included non-hospitalized patients with banal common cold symptomatology and confirmed HRVi. Healthy children with asymptomatic HRVi were the second control group (Group-C) and healthy children without HRVi were the third control group (Group-D). Nasopharyngeal aspirate samples were collected from participants and the variable V3-V4 region of 16S rRNA gene was analyzed using Illumina-Miseq. HRV was detected by a multiplex real-time PCR (AnyplexII-RV16, Seegene).

Results: Forty specimens from participants allocated to Group-A (n=9), Group-B (n=12), Group-C (n=8), and Group-D (n=11) were analyzed. No major differences between groups were observed in epidemiology variables. Richness values were also similar across groups. However, the diversity of Group-A was significantly lower to that of Group-D (p-value=0.012) and a trend for significance was observed when comparing Group-B vs. Group-D (p-value=0.07). Principal Coordinates Analysis showed a separation between the study groups (Adonis=0.009).

Analysis of the nasopharyngeal microbiota composition using LEfSe revealed that presence of Streptococcus pneumoniae was associated with Group-A, Moraxella genus with both Group-B and Group-C, and Dolosigranulum pigrum and Staphylococcus genus with Group-D. Additionally, all pairwise comparisons showed that Escherichia coli was associated with severe HRVi (Group-A).

Conclusions: The presence of HRV was associated with decreasing nasopharyngeal microbiota diversity. Patients with severe LRTI requiring admission to ICU were characterized by an increased abundance of Streptococcus pneumoniae and Escherichia coli. The absence of HRV was characterized by the presence of Dolosigranulum and Staphylococcus.

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Abstract 6551

Sexual behaviour and incidence of sexually-transmitted infections in high-risk men who have sex with men following pre-exposure prophylaxis commencement Sophocles-P4G demonstration study

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Background: Pre-exposure prophylaxis (PrEP) is an important tool to prevent HIV acquisition. Nevertheless, there is an aris-
ing concern that PrEP may result in a high burden of disease related to Sexually Transmitted Infections (STI). Our aim was to
determine the sexual behavior and the incidence of STIs among men who have sex with men (MSM) within the first 1 2 months
following commencement of PrEP.

Materials/methods: Sophocles-P4G, the first pilot PrEP study conducted in Athens, Greece, was designed to identify the
population at highest risk of HIV transmission among the MSM networks who would be eligible for receiving PrEP. Peer-driven
chain-referral was used to reach the population (Respondent-Driven Sampling). In total, 100 high-risk MSM were enrolled and
received daily PrEP for 12 months. Participants were scheduled for six visits every 1-3 months. Diagnosis for STI was based on
serology for syphilis, syndromic diagnosis and management for the other STIs. The number and type of sexual contacts during
PrEP was collected through daily diaries.

Results: From the 100 MSM participants with a mean age (SD) of 33.2 (9.3) years, 74 completed the 12-month study with a
discontinuation rate of 2.5 discontinuations per 100 person-months. At study entry, participants reported a median (25th, 75th)
of 13.3 (7.8, 21.0) sexual contacts per month and of 2.3 (0, 6.8) anal receptive sexual contacts without condom per month.
Sixty-seven per cent reported history of an STI. Following PrEP commencement, no change in the number of sexual contacts
(p=0.167), in the proportion of participants reporting sex without condoms (p=0.405), or in the number of receptive anal sexual
contacts without condom (p=0.935) was identified. During follow up, 36% experienced a new STI with an incidence rate (95% CI)
of 4.15 STIs per 100 person months (2.93, 5.87), while no HIV seroconversion was noted.

Conclusions: PrEP is a precious tool in reducing HIV new infections. Unsafe sex and the risk of STI were high, although no
change was observed during the 1-year PrEP period. These data underline the importance of routine STI screening and the need
of counselling to reduce high risk sexual behavior among PrEP users.

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Bone density, microarchitecture and tissue quality after 1 year of treatment with dolutegravir-abacavir-lamivudine

Jade Soldado1, Elisabet Lerma-Chipirraz1, Itziar Arrieta1, Alicia Gonzalez-Mena1, Ignacio Domingo1, Hernando Knobel1, Roberto Güerri Fernandez*1

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Background: People living with HIV (PLWHIV) suffer a decrease in Bone Mineral Density (BMD), a condition associated with antiretroviral treatment (ART) among other causes. There is little information about other components of bone strength.

Objective: To study the impact of Dolutegravir-Abacavir-Lamivudine-based therapy on bone health parameters—apart from BMD—in ART-naïve individuals with HIV after 48 weeks of treatment.

Materials/methods: Observational, prospective and analytical study of treatment-naïve patients with HIV undergoing a DTG-ABC-3TC-based regimen at 48-week follow-up. A Mann-Whitney U test was performed to evaluate changes in bone strength parameters (bone mineral density, bone microarchitecture and bone tissue quality measure).

Results: 20 naïve HIV individuals starting DTG-ABC-3TC were included. Three patients were withdrawn because of corticosteroid initiation. One individual was lost in the follow-up. After 48-weeks of treatment the median lumbar spine BMD showed a significant decrease from 1.013 g/cm² (IQR 0.964, 1.08) to 1.024 g/cm² (0.951, 1.065) (-2.25%, p=0.007) respectively as well as in femoral neck BMD from 0.835 g/cm² (0.797, 1.023) to 0.81 g/cm² (0.778, 1.006) (-4.1%, p=0.03). Bone microarchitecture, as measured by TBS, decreased from 1.359 (1.334, 1.371) to 1.321 (1.318, 1.329) (-2.5%, p=0.03). In contrast, bone quality measured by microindentation was significantly higher with respect to baseline [84 (82.75, 90) to 91.5 (87 , 94); +6.53%, p<0.001]. This result was indicative of improved bone material properties after the initiation of treatment (Figure 1). No significant changes were found in bone turnover markers. We did however find a significant decrease of -73% (p=0.02) in inflammation, as measured by an unspecified marker erythrocyte sedimentation rate (ESR). In addition, a positive significant correlation between CD4/CD8 ratio at baseline and changes in BMSi after 48 weeks of treatment was observed [Spearman's Rho=0.4974, p=0.04]

Conclusions: After a 48-week treatment with DTG-ABC-3TC-based ART, BMD and TBS decreased while bone tissue quality, as measured by microindentation, improved significantly. The state of the immune system—how balanced it is before infection, that is—seems to impact bone quality recovery. An overarching approach to assess bone toxicity in ART-treated patients is needed

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Flat lining of nine-year deaths rate throughout various carbapenem-resistant Gram-negative outbreaks at Saint George Hospital, Lebanon

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1Saint George Hospital, Infectious Disease Department, Antimicrobial Stewardship, Beirut, Lebanon, 2Aix-Marseille University, Marseille, France, 3Saint George University Hospital, Saint George University Hospital, Bayrut, Lebanon, 4Saint George Hospital, Pulmonary and Critical Care Department, Beirut, Lebanon

Background: Infamous reports attributing exceedingly high rates of mortality to antimicrobial resistance have been circulating for the past few years. Clear evidence is missing, probably due to the diverse consensus concerning attributable mortality and the difficulty of accurately gathering harmonious antimicrobial resistance data.

Materials/methods: We look at the rates of mortality and antimicrobial resistance from Jan 1, 2010 - Dec 31, 2018, at the 333-bed tertiary care center Saint George Hospital (SGH) in Beirut to understand the local and regional reality of the situation. We retrieved from our electronic antimicrobial stewardship database [ASP] the yearly number of: total deaths in the hospital and the Intensive Care Unit (ICU) - deduplicated top four isolated organisms resistant to carbapenems: Acinetobacter baumanii (Ab), Escherichia coli (Eco), Klebsiella pneumonia (Kp), and Pseudomonas aeruginosa (Pae) - Hospital (HD) and ICU (ID) Days. Rates were expressed as number/1000 days. Time series analysis (TSA) was used. No patient records accessed.

Results: A total of 642,564 HD, 27,307 ID and 2,886 isolates included throughout the study. No significant yearly variation in HD and ID. In 2010, we had 4.2 deaths/1000 HD, staying flat until 2018 at 4.4 deaths/1000 HD. The highest mortality reported in 2012 at 5.17 deaths/1000 HD [Figure 1]. No trend detected by TSA. Despite variations ranging from 34 deaths/1000 ID in 2010 dropping to 25 deaths/1000 ID in 2018, no significant trend was detected as well. Ab started at 0.74/1000 HD in 2010, peaked at 3.2/1000 HD in 2014-2015 during an outbreak and then significantly dropped to 0.98/1000 HD in 2018 after ASP implemented carbapenem sparing and colistin monotherapy strategies in 2016. As for Eco and Kp, both significantly trend upwards 2 and 3-fold starting 2016, reaching 0.48/1000 HD and 0.94/1000 HD, respectively. Pae had no signification variations throughout the study period, ranging from 1.44/1000 HD in 2010 to 1.78/1000 HD in 2018. No correlation between isolation densities of multidrug-resistant isolates and mortality by TSA.

Conclusions: The 9-year, flat death rate hospital wide and in the ICU, despite the witnessed multidrug-resistant outbreaks, and the lack of existing correlations indicate a so far independent relationship. Real-time factual data is needed to provide a balanced, solid ground and relieve the anxiety of antimicrobial resistance.
**Abstract 6554**

**Antimicrobial resistance among urinary Enterobacteriaceae from patient living in nursing homes**

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**Background:** Urinary tract infections are common problems in patient living in nursing home and important reason for consulting physicians, resulting in substantial financial burden to community. There are few data on resistance surveillance among these patients. So the PRIMO national reference center under the supervision of Public Health France follows the antimicrobial resistance of Enterobacteriaceae in nursing homes (NH). This surveillance is based on the e-tool MedQual-Ville, allowing the prospective collection of antibiotic patterns from strains isolated within a network of microbiology laboratories (ML).

**Materials/methods:** All the urinary Enterobacteriaceae strains isolated in these laboratories, from January 2018 to December 2018, were included in the investigation. All patients from private hospitals and emergency departments were excluded. Distribution of bacterial species and study of antibiotic resistance for fosfomycin (FOS), nitrofurantoine (NF), cotrimoxazole (SXT), mecillinam (MEC), 3rd generation cephalosporins (3GC). Exact Chi2 and Fischer tests were applied.

**Results:** In 2018, 421353 antibiograms performed on urinary Enterobacteriaceae strains were provided by the 742 ML across 11 French regions, of which 15896 (3.8%) were isolated from resident in NH. Escherichia coli was the majority bacterial species (86.3%, n=13720), followed by Klebsiella pneumoniae (9.2%, n=1459) and 1.9% of Enterobacter cloacae complex (n=304). Other Enterobacteriaceae isolates accounted for 2.6%. Less than 2.0% of E. coli strains were resistant to NF (1.0%) and FOS (1.8%). 10.6% of E. coli was resistant to MEC, 22.6% to SXT and 8.6% to 3GC. Klebsiella pneumoniae strains were significantly more resistant to antibiotics compared to E. coli strains (23.6% to NF, 19.1% to FOS, 41.3% to MEC, 19.8% to SXT and 21.2% to 3GC; p<0.001 for all antibiotics instead for SXT p=0.024). The overall proportion of ESBL-producing E. coli was 7.7%, significantly lower than for K. pneumoniae (18.8%, p<0.001).

**Conclusions:** The proportion of urinary strains resistant to 3GC isolated from resident living in nursing home was higher than urinary strains among primary care patients. For the French national survey PRIMO, it is planned to compare these results with those observed in medico social structures from 2019.

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Streptococcus pneumoniae: serotype distribution in adults with invasive disease after 8 years of systematic vaccination of children with PCV13

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1Hospital Arquitecto Marcide, Ferrol, Spain, 2Conselleria de Sanidade, Santiago de Compostela, Spain, 3Complexo Hospitalario Universitario da Coruña, A Coruña, Spain, 4Complexo Hospitalario Universitario de Santiago de Compostela, Santiago de Compostela, Spain, 5Hospital Universitario Álvaro Cunqueiro, Vigo, Spain, 6Complexo Hospitalario Universitario de Ourense, Ourense, Spain, 7Hospital Universitario Lucas Augusti, Lugo, Spain, 8Complexo Hospitalario Universitario de Pontevedra, Pontevedra, Spain, 9Hospital de Costa Burela, Burela, Spain, 10Hospital do Barco de Valdeorras, O Barco de Valdeorras, Spain, 11Hospital Comarcal de Monforte de Lemos, Monforte de Lemos, Spain, 12Hospital POVISA, Vigo, Spain

Background: Vaccination against Streptococcus pneumoniae with polysaccharidic 23-valent antipneumococcal vaccine (PPSV23) was authorized in 2000 in Galicia (Spain) for ≥65 years-old belonging to risk groups. In 2001 vaccination with antipneumococcal 7-valent conjugated vaccine (PCV7) was authorized for children in risk groups. In 2011, systematic vaccination in children with antipneumococcal 13-valent conjugated vaccine [PCV13] was established. The aim of this study is to analyze the behavior of PCV13 and PPSV23 serotypes through the study period.

Materials/methods: Every invasive pneumococcal disease (IPD)-causing isolate in adults was collected from sterile bodily fluids (2088 samples) between 2011 and 2018. Serotyping was performed by latex agglutination and Quellung reaction (Statens Serum Institut latex/antisera, Copenhagen, Denmark). Incidences were described in cases/100,000 inhabitants.

Results: IPD incidence has increased from 10.69 in 2011 to 15.55 in 2018. PCV13 incidence has decreased from 6.70 to 2.72, but non-PCV13/PPSV23 has increased from 1.83 to 8.43.

Regarding to PCV13/non-PCV7, serotype 3 has maintained its incidence, and serotypes 19A and 7F have decreased drastically. 1, 5 and 6A weren’t almost present from the beginning of the study. PCV7 were also less present, except 14 and 4, which decreased.

For PPSV23/non-PCV13, 12F, 9N and 22F have increased, and specially serotype 8, becoming the most prevalent in 2018 (29.72% of all cases). Data are shown in table below.

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</table>

Conclusions: After 8 years of systematic children vaccination with PCV13, IPD incidence in adults has increased, but PCV13-related IPD has decreased substantially.

There’s been an increase in the PPSV23 serotypes not included in PCV13, specially serotype 8, the most prevalent in 2018.

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Abstract 6556

**Saccharomyces cerevisiae fungaemia: a 10-year review in the CHU of Liege (Belgium)**

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**Background:** *Saccharomyces cerevisiae* is a yeast which has been used for decades mainly as probiotic in the medical field. For a long time, it was considered as safe and non-pathogenic but recently, the number of infections caused by this yeast has been rising particularly in immunocompromised patients. This study presents a review of cases of deep infection caused by *S. cerevisiae* during the last 10 years including the clinical relevance and therapeutic management.

**Materials/methods:** The systemic infections due to *Saccharomyces cerevisiae* that occurred at the University Hospital of Liege from January 2000 to January 2019 were reviewed by using the Glims laboratory database. The minimal inhibitory concentrations (MICs) obtained by microdilution with Sensititre YeastOne YO10 test (Trek, USA) was compared to the therapeutic management applied.

**Results:** During this period, from 2016 to 2019, 11 patients were diagnosed with fungemia due to *S. cerevisiae*. All the systemic infections occurred in patients presenting one or multiple risk factors: 4 out of 11 were oncologic patients upon chemotherapy, corticoids or radiotherapy, 3 were under Enterol® and 9 patients received broad-spectrum antibiotics prior to fungemia. Only 3 patients who were immunocompromised had multiple positive blood cultures (9, 5 and 3 respectively) contrary to the others, which had only one positive bottle. High MIC values were obtained for fluconazole (4-256 µg/mL), while MICs for amphotericin B were low (0.002-2 µg/mL). Among the 11 patients, 4 were treated with fluconazole, 2 with Amphotericin B and 5 only by catheter removal. All had a favorable outcome, except 2 oncologic patients who were under fluconazole (MIC = 8 µg/mL) and one who wasn’t treated due to her critical state.

**Conclusions:** The last 3 years, we noticed the emergence of blood infections caused by this yeast. They progressed into invasive conditions only in immunocompromised patients, who had been directly in contact with Enterol® or indirectly by caregivers. Therefore, it is necessary to limit the contact of fragile patients with probiotics containing the yeast. About the treatment, Amphotericin B seems to be the best option but due to its toxicity, fluconazole is preferably used, the outcome depending on the case.

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Background: Section Flavi within genus *Aspergillus* includes a large number of species that may behave as opportunistic pathogens in humans or animals and/or may produce mycotoxins. Morphological similarities between Flavi section members make precise identification difficult. In this study, we present data on antifungal susceptibility profile of molecularly characterized French clinical isolates of Flavi section.

Materials/methods: Sixty-one isolates, phenotypically identified as *A. flavus*, were included in the study. These clinical isolates were recovered over a 15-year period (2001-2015). For all isolates, specific identification was confirmed by sequencing a part of the β-tubulin and calmodulin genes. The isolates were first screened for their susceptibility to azoles antifungal agents by using 3-sectors agar plates containing itraconazole, voriconazole and a drug-free control. Susceptibility to 8 antifungal drugs was further determined by using EUCAST reference microdilution broth technique.

Results: Out of 61 isolates, molecular analysis of the partial β-tubulin and calmodulin sequences showed that 59 isolates were *A. flavus sensu stricto* and one isolate each was *A. parasiticus* and *A. nomius*. One isolate was azole-resistant by the screening test. The geometric mean MIC values (range) of amphotericin B, itraconazole, voriconazole, posaconazole, isavuconazole, caspofungin, micafungin, and anidulafungin were 3.32 (1-16), 0.36 (0.1-25-2), 1.02 (0.5-8), 0.4 (0.1-25-1), 1.26 (0.25-8), 0.066 (0.03-0.125), 0.016 (0.016-0.03), 0.017 (0.016-0.03) µg/mL for the *A. flavus sensu stricto*. For *A. parasiticus* and *A. nomius*, MICs were in the same range. Only one *A. flavus sensu stricto* isolate had voriconazole and isavuconazole MICs at 8 µg/mL.

Conclusions: Antifungal susceptibility to 8 drugs was determined on a large collection of clinical isolates belonging to *Aspergillus* Flavi section. Most of the isolates were identified as *A. flavus sensu stricto* and most of them were susceptible to antifungal drugs. Nevertheless, the occurrence of one resistant isolate highlights the need for susceptibility testing for any *Aspergillus* section.

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Abstract 6558

Monocyte progenitors are effector cells in mycobacterial infections
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Background: Mycobacterial tissue infections are characterized by formation of granulomas harboring a unique macrophage species, so-called multinucleated giant cells (MGC). The presence of MGC in the tissue has been associated with mycobacterial containment and immunocompetence. In order to identify cellular biomarkers for the immunological state in *M. tuberculosis* infections, we embarked on defining the hitherto unknown MGC progenitors.

Materials/methods: 1) An in vitro system for glycolipid-induced MGC formation to analyze MGC forming properties (transcriptome, metabolome, function) in macrophage progenitors isolated from mouse bone marrow; 2) Mouse models of *M. tuberculosis* lung infection and BCG liver granuloma; 3) Cell transfer in vivo.

Results: We found the common monocyte progenitor (cMoP) to have the highest potential to form MGC in response to mycobacterial glycolipids or whole mycobacteria. Moreover, mycobacteria induced robust formation of TNFα and nitric oxide in cMoP. Transcriptome analysis revealed a sustained synthesis and accumulation of cholesterol and fatty acid metabolism in cMoP undergoing transformation into MGC. Oxidation and depletion of cholesterol decreased MGC formation by >70%, but not cytokine formation in cMoP. Thus, the observed changes in lipid metabolism were a specific prerequisite for the MGC transformation program. In *M. tuberculosis* lung infection and in a BCG liver granuloma model, we identified a new c-kit-low cMoP descendent, which we denominated induced monocyte progenitor (iMoP), to circulate in the blood at significantly higher frequency (> 0.6% of CD45-pos. cells) than in controls (< 0.2%). By adoptive transfer we found iMoP to differentiate in vivo and preferentially localize to mycobacterial granulomas, i.e. > 75% of transferred cells reaching the liver were granuloma associated in BCG model.

Conclusions: A novel macrophage progenitor denominated iMoP circulates in the peripheral blood during mycobacterial infections and may seed MGC in the infected tissue. iMoPs exhibit a specific metabolic program that underlies their MGC forming properties. iMoPs are likely to contribute to mycobacterial immunity and may serve as cellular biomarkers in the future.

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Abstract 6560

MRSA from skin and soft tissue infections in Poland
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Background: The aim of this study was to examine the antimicrobial resistance and genetic diversity of Polish methicillin-resistant S. aureus (MRSA) from skin and soft tissue infections (SSTIs).

Materials/methods: 213 MRSA isolates, collected between 2013-2014 in 28 Polish hospitals were assigned to MLST-CC based on spa-typing and MLST analysis. MRSA, MLSB phenotypes and MICs of selected antimicrobials were determined according to the EUCAST guidelines. Presence of selected virulence and resistance genes was tested by PCR.

Results: Isolates were classified to 11 clonal complexes (CCs) with predominant, comprised over 80.0% of the isolates, CC59/ST338 (27.2%), CC5 (26.8%), CC30 (16.9%) and CC8 (12.2%). Amongst isolates, 62.0% were assigned to HA-MRSA and 32.0% to CA-MRSA. CA-MRSA isolates were significantly more predominant in children in comparison to older population (90.0% vs. 26.3%, p<0.0001). The PVL coding genes and ACME element were identified in CA-MRSA clones exclusively [pvl genes in ST338-V(5C2&5), ST8-IVa and ST30-IVc, while the ACME in ST8-IVa].

Only 7.0% isolates were susceptible to all antibiotics tested with the exception of β-lactams. Resistance in vitro to erythromycin, clindamycin, ciprofloxacin, tetracycline, doxycycline and gentamicin was found in 83.1%, 72.8%, 67.1%, 33.3%, 17.4% and 14.6% of isolates, respectively. Amongst erythromycin-resistant isolates, 87.6%, 9.0% and 3.4% represented cMLSb, iMLSb, and MSb phenotype, respectively. cMLSb phenotype was prevalent amongst isolates from CC30 (94.4%), CC5 (89.5%), and CC59/ST338 (84.4%).

Forty-six resistance profiles were identified. The most frequent OX-ERY-CLI-CIP (34.2%) comprised mainly CC5 (53.4%) and CC30 (39.7%) isolates, while the second ERY-CLI-CIP-SXT-TE-DK-MIN-GEN (8.9%) - exclusively CC59/ST338.

Resistance to erythromycin was mediated by single ermA gene (CC5, CC8, CCB/239 and CC30), ermC (CC1, CC8, CC22, CC45, CC97 and CC398), or both (CC30), and ermB gene (CC59). Tetracycline resistance was associated with tetK (69.0%), tetM (4.2%), tetL (2.8%) genes; both of the tetK and tetM genes (22.5%) were found mainly in CCB/239. All gentamicin resistant isolates carried aacA-aphD gene.

Conclusions: The present study revealed considerable heterogeneity of MRSA clones from SSTIs in Poland with predominance of ST338-V(5C2&5) clone. Different S. aureus clones causing SSTIs were associated with specific antimicrobial resistance and virulence gene profiles.

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**Abstract 6561**

**Investigation of increased prevalence of IMP carbapenemases by next-generation sequencing in Wales**  
Mandy Wootton*1, Massimo Mentasti1, Kerry Prime1, Swati Khan1, Kirsty Sands1, Joanne Watkins1, Sally Corden1, Thomas R. Connor2, Lim Jones3

1University Hospital of Wales, Specialist Antimicrobial Chemotherapy Unit, Public Health Wales, Cardiff, United Kingdom, 2Cardiff University, Cardiff, United Kingdom, 3University Hospital of Wales, Pathogen Genomics Unit, Public Health Wales, Cardiff, United Kingdom

**Background:** Carbapenemase producing Enterobacterales [CPE] cause serious infections and outbreaks which are increasingly difficult to treat. In Europe NDM/KPC/OXA-48 are the most common, whilst IMP/VIM are isolated less frequently. In Wales, 17 IMP producing CPE were isolated in five different hospitals between 2017-2019, compared to six between 2008-2016. The isolates were analysed by NGS to characterise resistance markers and sequence type (ST).

**Materials/methods:** DNA was extracted using eMAG (Biomerieux), libraries prepared using Nextera XT and sequenced using the V2 assay on the MiSeq sequencers (Illumina). Assemblies were run through Resfinder to determine resistance markers and MLST to establish the MLST.

**Results:** IMP-4 and IMP-70 were the two identified variants. At Hospital A, five *K. pneumoniae* ST20 were epidemiologically linked (EL). At hospital B, two *E. coli* ST224 were EL and also contained KPC-2. All isolates were resistant to ertapenem, while a significant number were susceptible to imipenem and meropenem (Table). In 3 other hospitals 2x and 1x ECL containing IMP-4 and 1x K/O with IMP-70 were found. A variety of other beta-lactamases (AmpC/ESBL), aminoglycoside modifying enzymes and in ST 20 *K. pneumoniae* isolates, a mcr-9 gene. These tested colistin susceptible, although inducible resistance (ICR) is associated with this gene, analysis did not suggest the putative regulatory genes needed for ICR were present.

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<th>IMP variant</th>
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<th>Meropenem</th>
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<td>744</td>
<td>IMP-70</td>
<td>0.75 (S)</td>
<td>0.75 (S)</td>
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**Conclusions:** IMP incidence have increased over the last 3yrs in Wales, however many isolates remain susceptible to IMI and MER. Only two IMP variants out of the 80+ so far described were identified. ST analysis showed spread of IMP+ CPE between different patients. KPC was also found in two EL isolates.

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Abstracts 2020

Abstract 6563

**Mycobacterium mucogenicum in hospital water: a potential source for human infection**

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**Background:** Non tuberculous mycobacteria (NTM) are a major cause of opportunistic infections. *Mycobacterium mucogenicum* is a rapidly growing mycobacteria, rarely but increasingly involved in infections, especially in immunocompromised patients.

The objectives of the study were to describe an outbreak of *M. mucogenicum* catheter-related bloodstream infections and investigate the potential environmental reservoir of this NTM.

**Materials/methods:** In 2018, patients diagnosed with NTM bacteremia by conventional bacteriological cultures (BACTEC™ FX, BD) were included. Identification was performed by mass spectrometry (Vitek MS, bioMérieux), 16S rRNA and rpoB genes sequencing. Clinical data were recorded from electronic clinical charts. Physicochemical and microbiology parameters were analyzed in the water of the hospital network during several sampling campaign. The presence of NTM was investigated by a membrane filtration (0.45 µm) followed by culture on Middlebrook 7H10 Agar.

**Results:** From Mars to November 2018, four patients were diagnosed with NTM catheter-related bloodstream infections. All patients were immunocompromised and hospitalized in the Oncology Unit. The species identified was *M. mucogenicum*. In this Unit, this NTM was also isolated from several water sources including tap water from sinks and showerheads in rooms patients (1-150 UFC/100 mL). However, *M. mucogenicum* was not found in the city water supplied to the hospital. Levels of chlorine in the water were intermittently low (<0.3 mg/l) and may have contributed towards bacterial growth. Corrective actions have been implemented: self-purging, UV and heat shock disinfection. No other cases have been identified since this period.

**Conclusions:** The cause of the *M. mucogenicum* outbreak seemed to be the water contamination of central venous catheter during bathing. Environmental survey and corrective actions allowed to control the outbreak. This study underlined the major role of the investigation of environmental sources, especially water supply, in NTM outbreaks.

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**Abstract 6565**

**Inhibition of metabolic signalling pathways controls inflammatory tissue destruction in tuberculosis**

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**Background:** Tuberculosis (TB) is a global infectious threat, complicated by rising drug resistance. The clinical manifestations of TB are due to severe inflammatory tissue destruction driven by pro-inflammatory cytokines and matrix metalloproteinase (MMP) enzymes. Patients also experience profound metabolic changes, notably weight loss. TB-infected macrophages demonstrate the Warburg effect, a metabolic shift from oxidative phosphorylation to aerobic glycolysis. However, little is known about metabolic control of inflammatory tissue damage in TB.

**Materials/methods:** Primary monocyte-derived macrophages (MDM) or normal human bronchial epithelial cells (NHBE) were pre-treated with specific metabolic inhibitors, or transfected with siRNA. Cells were then either infected with live, virulent *Mycobacterium tuberculosis* (*M.tb*) or stimulated with conditioned media from *M.tb*-infected monocytes (CoMTB). MMP and cytokine gene expression, secretion and activity were investigated by qPCR, ELISA, luminex, zymography, Western blot and confocal microscopy. Immunohistochemistry was performed on human TB lymph nodes.

**Results:** 2-deoxyglucose (2DG), a hexokinase inhibitor which impedes the rate-limiting step in glycolysis, decreased gene expression and secretion of the key collagenase, MMP-1. There was a 7-fold fall in MMP-1 secretion in CoMTB-stimulated NHBE (from 5852±1090 to 774±17 pg/ml; p<0.0001) and a 5-fold fall in *M.tb*-infected MDM (from 34733±2911 to 6709±506 pg/ml; p<0.0001). TB-enhanced expression of the transcription factor, HIF-1α, was attenuated by 2DG. 2DG decreased IL-1β secretion (p=0.0001), but increased TNF-α secretion (p=0.0012), in *M.tb*-infected MDM. Immunohistochemical staining of human TB lymph nodes demonstrated increased expression of hexokinase 2 within granulomas. Inhibition of the PI3-kinase-Akt-mTOR pathway enhanced MMP-1 and MMP-9 gene expression and secretion in CoMTB-stimulated NHBE. There was an associated functional increase in fluorescent collagen and gelatin degradation, confirmed by confocal microscopy. PI3 kinase-Akt-mTOR inhibition also increased IL1β and TNF-α secretion in *M.tb*-infected MDM. Inhibiting the metabolic regulator, AMPK, reduced MMP-1 gene expression and secretion, IL-1β and TNF-α secretion, and HIF-1α expression, in *M.tb*-infected MDM.

**Conclusions:** We show that glycolysis is an important modulator of MMP-1, pro-inflammatory cytokine and HIF-1α activity in TB. The PI3-kinase-Akt-mTOR axis and AMPK also have key regulatory roles. Metabolic pathways are potential targets for novel host-directed therapies in TB.

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**First outbreak of colistin-resistant OXA-23/NDM-1-producing *Acinetobacter baumannii* (France, 2019)**

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**Background:** Over the last decade, polymyxin resistance has been reported for a growing number of *Acinetobacter baumannii* strains worldwide. In this species, colistin resistance mainly results from mutations occurring in the pmrCAB operon, and that lead to the overproduction of phosphoethanolamine transferase PmrC and subsequent decrease in the net negative charge of the bacterial surface. The spread of XDR colistin- and carbapenem-resistant *A. baumannii* (CCRAB) strains in the European overseas territory of La Réunion Island (Indian Ocean) is reported here.

**Materials/methods:** Between April and August 2019, 7 clinical and 1 environmental CCRAB strains were isolated in the university hospital of La Réunion Island. Demographics, clinical data and diffusion dynamics of CCRAB cases were collected. Antibiotic susceptibilities were determined by broth microdilution or E-tests according to EUCAST recommendations. Whole genome sequencing (WGS) was performed to fully characterize the resistome of these isolates and the genetic context of *β*-lactamase-encoding genes. The selected strains were then compared to each other by cgMLST.

**Results:** The clinical CCRAB strains were recovered from 7 patients hospitalized in 3 different wards. Four patients were colonized and 3 infected (two resulting in death). The index case had been previously admitted to the hospital of Mayotte Island (The Comoros). The environmental strain was isolated from a chair in a nephrology room. An epidemiological link could be established for 6 patients who had stayed in two wards. All of the collected isolates displayed the same multidrug resistance profile, including carbapenems, colistin and aminoglycosides except tobramycin. They all produced the class D carbapenemase OXA-23, intrinsic class D *β*-lactamase OXA-69, and metallo-beta-lactamase NDM-1. Likely accounting for their resistance to colistin, a mutation (D82N) was detected in the response regulator PmrA of PmrAB two-component system. Genotyping experiments revealed that the 8 isolates belonged to the international clonal complex ST1 and were phylogenetically indistinguishable.

**Conclusions:** This study which relates the emergence and intra-hospital spread of an XDR *A. baumannii* emphasizes the need of strict application of prevention and control measures in institutions where the risk of imported XDR-bacteria is high.

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Nanopore metagenomic sequencing to investigate nosocomial transmission of human metapneumovirus from a unique genetic group among haematology patients in the United Kingdom

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Background: Human metapneumovirus (HMPV) infection causes a spectrum of respiratory tract disease, and is recognised as a significant pathogen in the context of immunocompromise. In Spring 2019, a group of patients under the care of the haematology unit in a UK teaching hospital were diagnosed with HMPV infection (BioFire FilmArray RP2), raising concerns of an outbreak. This study aimed to investigate whether nosocomial transmission occurred among these patients, and to elucidate genetic relationships between circulating strains in this setting.

Materials/methods: We conducted direct-from-sample Nanopore metagenomic sequencing of 25 respiratory samples submitted to the hospital’s microbiology laboratory. Samples came from 13 patients under the care of haematology over 20-days in Spring 2019 (two patients sampled twice), and ten patients elsewhere in the hospital between 2017-2019 to provide broader representation of sequence diversity in our patient population. We performed phylogenetic analyses for the complete genomes.

Results: We generated HMPV reads from 20/25 samples (sensitivity 80% versus routine diagnostic testing) and retrieved complete HMPV genomes from 15 samples. Consensus sequences from Nanopore data were identical to those generated by Illumina, and represented HMPV genomes from two distinct sublineages, A2b and B2. Sequences from 10/13 haematology patients formed a unique genetic group in the A2b sublineage, not previously reported in the UK. Among these, eight HMPV genomes formed a cluster (differing by ≤3 SNPs), likely reflecting nosocomial transmission, while two others were more distantly related and may represent independent introductions to the haematology unit. Two other A2b sequences from elsewhere in the hospital were >80 SNPs away from all other sequences; as were two B2 sequences from elsewhere in the hospital.

Conclusions: This study increases knowledge of UK HMPV lineages and demonstrates that Nanopore metagenomic sequencing can be used for HMPV detection, although more work is required to optimise sensitivity. Generation of full genome sequences can be used to support or rule out nosocomial transmission, contribute to improve infection prevention and control practices, and inform antimicrobial stewardship.

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Abstract 6570

Investigation of carbapenemases by RESIST-4 O.K.N.V immunochromatographic lateral flow assay in Enterobacteriaceae isolates

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Background: Carbapenem resistance in Enterobacteriaceae poses a significant threat to patients and healthcare systems. In the last years, several methods for detecting carbapenem resistance have become available. These methods include phenotypic-based methods that detect the activity of carbapenemase enzymes such as growth-based assays, immunochromatographic (IC) assays, and molecular-based methods. Here we evaluated the performance new immunochromatograph test, RESIST-4 O.K.N.V. test.

Materials/methods: One hundred and fifteen (115) carbapenem resistant Enterobacteriaceae isolates, isolated in 2016-2019 at Ege University Hospital Bacteriology, Laboratory of Medical Microbiology Department were studied. Escherichia coli ATTC 25922 and three carbapenem susceptible clinical isolates were included as negative control. VITEK MS and VITEK 2 Compact® automated systems were used for identification and antibiotic susceptibilities respectively. Minimum inhibitor concentration’s (MIC) of meropenem were determined by gradient test, according to EUCAST recommendations. The RESIST-4 O.K.N.V. test were used for detection of carbapenemase detection. The presence of blaOXA-48, blaVIM, blaNDM and blaKPC genes were also investigated by polymerase chain reaction (PCR) in the isolates.

Results: 90.8% of the isolates were identified as K. pneumoniae. At least one resistance gene was detected in all but one of the 115 resistant isolates included in the study. According to PCR results, co-existance of blaOXA-48 and blaNDM genes was the most common (41.17%) resistance mechanism. RESIST-4 O.K.N.V. test did not detect the presence of blaNDM in eleven (11) isolates which are already containing blaOXA-48.

Conclusions: Resist-4 O.K.N.V. stands out as a method that can be applied in the detection of carbapenemases on cultures. However, it should not be ignored that it can give false negative results in the detection of blaNDM.

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Abstract 6571

Routine use of genotype Genotype MTBDRsl assay on clinical samples in a high TB burden setting in South Africa: a descriptive analysis

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Abstract third-party references: University of KwaZulu Natal, National Health Laboratory Service

Background: Following WHO recommendations for the shortened multi-drug resistant TB (MDR) treatment regimen and use of the GenoType MTBDRsl Line Probe Assay (SL-LPA), the South African Department of Health developed a "DR-TB reflex" testing laboratory algorithm. The rationale for this algorithm is to identify those MDR or rifampicin-resistant TB patients who can be commenced on, and continue the shortened MDR-TB treatment regimen. This study aims to analyse the performance of the Genotype MTBDRsl in smear positive and negative samples; and describe common mutations detected in XDR isolates.

Materials/methods: We performed a retrospective data analysis of Genotype MTBDRsl results on 1841 MDR/Rif resistant clinical samples over 1 year (January – December 2018). DR-TB reflex testing comprises a panel of tests: Auramine-O smear, MGIT960 culture, Genotype MTBDRplus, Genotype MTBDRsl and where necessary phenotypic drug susceptibility testing. GenoType MTBDRsl assays were routinely performed on smear positive and negative samples.

Results: Of the 1841 clinical samples, 38% (701/1841) were smear negative and 62% (1172/1841) were smear positive. Of the smear negative samples, 67% (471/701) had inconclusive MTBDRsl results. 33% (230/701) showed good banding patterns with 25% (178/701) MDR TB diagnosed 5% (34/701) pre-XDR TB and 2% (18/701) XDR TB diagnosed.

For smear positive samples, 6% (77/1172) had inconclusive results. The remaining 93% (1095/1172) showed good banding patterns with 77% (930/1172) MDR TB diagnosed 12% (111/1172) pre-XDR TB diagnosed and 5% (54/1172) XDR TB diagnosed. Of the 72 XDR isolates, the commonest gyrA fluoroquinolone mutation pattern was an absent WT 2 with MUT 1 present; followed by absent WT 3, with MUT 3C present; indicating A90V and D94G respectively as the predominant mutations. The commonest rrs mutation was an absent WT 1 with MUT 1 present indicating A1401G as the commonest second line injectable drug mutation. No gyrB and eis mutations were detected.

Conclusions: Our data shows that the Genotype MTBDRsl performed sub optimally on smear negative samples with 67% having inconclusive results. gyrA and rrs gene mutations are the prevalent mutations observed. These findings question the routine use of Genotype MTBDRsl in smear negative samples in a high TB burden setting.

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Abstract 6577

**Epidemiology of serotypes of *Streptococcus pneumoniae* in patients older than 18-years in Russia**

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**Abstract third-party references:** MSD

**Background:** Introduction the PCV to the the National Immunization Program in Russia in 2014 and beginning of use of PPV in adults, could potentially change distribution of serotypes of *S. pneumoniae* in patients older than 18-years with non-invasive and invasive forms of pneumococcal infection in Russia.

**Materials/methods:** Collection of *S. pneumoniae* strains and identification was provided by the participating laboratory. Only clinical isolates that met the study criteria as defined by protocol, was stored and submitted to reference laboratory of the Institute of Antimicrobial Chemotherapy of Smolensk State Medical University (IAC, Smolensk). Re-identification of *S. pneumoniae* strains was initially carried out to the species level at the IAC laboratory using classic bacteriologic methods and MALDI Biotyper. Serotyping of *S. pneumoniae* was performed using Real-Time PCR.

**Results:** 192 consecutive non-duplicate strains of *S. pneumoniae* have been analyzed – 7 strains from middle ear fluid, 161 – from respiratory samples, and 24 – from blood samples and cerebrospinal fluid. The most common serotypes of *S. pneumoniae* were: 3 (14.1%), 6AB (9.9%), 19F (9.4%), 14 (5.7%), 9NL (5.7%), 23F (5.2%), 11AD (3.6%) and 15AF (3.6%), and 25% were nontypeable. Moreover, 14 and 19F serotypes were prevalent in patients with AOM and sinusitis - 28.7%. Causative for pneumonia were serotypes 3 (13.1%), 6AB (11.2%), 19F (9.3%), 14 and 9NL (5.6% each) and 23F (4.3%). IPD dominant serotype was 3 (25%), followed by 23F, 12F and 9NL (each 8.3%).

**Conclusions:** PCV13 immunization reduces an incidence of vaccine serotypes of *S. pneumoniae*, however there is an increase of non-vaccine serotypes circulation, which are covered by PPV-23.

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Possible horizontal transfer of enterococcal IS1216V-mediated composite transposon between enterococci and methicillin-resistant Staphylococcus aureus

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Background: Sequence type 59 (ST59), the dominant community-associated methicillin-resistant Staphylococcus aureus (MRSA) in Taiwan, is multiresistant to non-β-lactams due to the acquisition of MES, a highly composite transposon flanked by enterococcal insertion sequence IS1216V. Majority of ST59/staphylococcal cassette chromosome mec (SCCmec) IV MRSA acquires MES6272-2 encoding IS1216V-ermB [erythromycin resistance]-[aph(3’)-IIIa] [kanamycin resistance]-ΔaadE-[aacA-aphD] [gentamicin resistance]-IS1216V-IS1216V-cat [chloramphenicol resistance]-IS1216V-IS1216V. ST59/SCCmec V MRSA acquires MESPM1, encoding IS1216V-ermB-[aph(3’)-IIIa]-aadE [streptomycin resistance]-IS1216V-IS1216V-cat-IS1216V-IS1216V. Because the rearrangement of MES is mediated by enterococcal IS1216V, we hypothesize ST59 MRSA may acquire the transposon from enterococci.

Materials/methods: A total of 270 enterococcal species collected in Taiwan were analyzed. Presence of MES structures were screened by PCR. Sequences of the MES were determined by next-generation sequencing. Genetic relationships among the strains were explored by multilocus sequence typing and pulsed-field gel electrophoresis (PFGE). Horizontal gene transfer was tested by filter mating. Pheromone response was detected by clumping inducing assay.

Results: Two E. faecalis strains isolated in 1993 were found to carry MESPM1 structure; one E. faecium strain isolated in 2003 and ten E. faecium strains isolated in 2014 were found to carry MES6272-2-like structures. Both of the two E. faecalis strains were sequence type 64 (ST64), and had nearly identical PFGE patterns. The 11 E. faecium strains had four different pulsotypes but all belonged to clonal complex 17. Sequence analysis revealed that the MESPM1 in ST64 E. faecalis displayed 99.9% DNA sequence homology to that in ST59/SCCmec V MRSA; the MES6272-2-like structures in the E. faecium strains showed >99.7% identity in IS1216V-ermB-[aph(3’)-IIIa]-aadE-[aacA-aphD] cluster compared with that in ST59/SCCmec IV MRSA. The conjugative transfer ability of MES to E. faecalis JH2-2 was tested. MESPM1 in ST64 E. faecalis produced the highest frequency (3.7 x 10⁻²), probably due to pheromone-like response.

Conclusions: MESPM1 and MES6272-2-like structures were found in the enterococcal species isolated in Taiwan. The MESPM1 in ST64 E. faecalis showed 99% DNA similarity to that in ST59/SCCmec V MRSA, implying the highly composite transposon may undergo recombination in E. faecalis and spread to MRSA through the mediation of enterococcal IS1216V.

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Identification of microorganisms in polymicrobial blood culture bottles using short-term culture MALDI-TOF MS
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Background: Polymicrobial bloodstream infections (BSI) have been reported to comprise of 6-32% of all BSI incidents, and has double the mortality rate of monomicrobial sepsis. Since the prognosis of sepsis is correlated with the rapid administration of effective antimicrobial treatment, there is need for rapid identification methods for identification of microorganisms from polymicrobial blood cultures. Here, we assess the performance of short-term culture followed by MALDI-TOF MS in identifying microorganisms in polymicrobial blood cultures (BCs).

Materials/methods: Both simulated and clinical polymicrobial BCs were used for this study. Simulated samples were derived using two methods, either by inoculating known clinical isolates directly into new BC bottles and incubating in the BC system, or by mixing broth from two clinical monomicrobial BC bottles. Short-term culture followed by MALDI-TOF MS was performed by culturing broth directly from positive polymicrobial BC bottles for 6 hrs at 37 °C on four different agar plates ie. desoxycholate citrate agar, colistin nalidixin acid agar, cromogenic UTI agar, and cystine lactose without electrolytes agar. Aztreonam and linezolid antibiotic discs were used on blood agar. Observed growths from different plates and antibiotic inhibition zones were analyzed by MALDI-TOF MS. Samples were tested using short-term culture followed by MALDI-TOF MS and the results were compared to conventional culture-based methods.

Results: A total of 27 clinical samples and 112 simulated polymicrobial samples were analyzed. Short-term culture followed by MALDI-TOF MS identified at least one microorganism in almost all BC samples tested, and was able to identify all microorganisms in 84/124 (68%) and 3/15 (20%) of bottles that contained two or three microorganisms respectively. 229/292 (78%) of isolates that were identified by conventional methods were successfully identified by short-term culture followed by MALDI-TOF MS. Time to identification by short-term culture followed by MALDI-TOF MS took 7 hrs compared to 48-72 hrs by conventional methods.

Conclusions: Short-term culture followed by MALDI-TOF MS has high performance in rapid identification of microorganisms from polymicrobial BCs, and the method can be implemented in the clinical routine.

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Evaluation of a new automated Acrion system for rapid identification of microorganisms and detection of antimicrobial resistance markers directly from blood cultures in an Italian hospital

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Background: As a recent advance in bloodstream infection diagnostics, the Acrion™ system (ThermoFisher) provides a fully automated workflow for rapid detection of microorganisms and their critical antimicrobial resistance gene products [i.e. mecA product PBP2a] directly from positive blood culture (PBC) broths. The system combines liquid chromatography (LC) with high-resolution mass spectrometry (HRMS) for microbial protein analysis. We comparatively evaluated the Acrion™ system workflow and an in-house diagnostic workflow, where PBC broths were analyzed with the MALDI BioTyper® system (Bruker Daltonics) and/or FilmArray® blood culture ID panel (bioMérieux) for microorganism identification and with the eazyplex® MRSA assay (Amplex Diagnostics GmbH) for mecA gene detection.

Materials/methods: Using the two workflows, we separately tested broth aliquots from 218 (199 monomicrobial and 19 polymicrobial) PBCs that were consecutively (clinical, n = 195) or ad hoc (simulated, n = 36) obtained. Results by each workflow were compared with those of culture-based identification and antimicrobial susceptibility methods (here used as the reference method), and were reported as correct detections, misdetections or no detections, respectively. The time to results were calculated for each workflow.

Results: Of 199 monomicrobial PBCs, 190 (95.5%) yielded results by the Acrion™ system workflow that were concordant with those of the reference method, whereas there were 9 no detection results. In parallel, 192 (96.5%) of the 199 PBCs yielded results by the in-house diagnostic workflow that were concordant with those of the reference method, whereas 7 yielded misdetection results. The overall agreement between the workflows was 92.0%. Furthermore, the Acrion™ system detected at least one microorganism, whereas the in-house diagnostic workflow detected all the microorganisms, in the 19 polymicrobial PBCs. Interestingly, all the 7 mecA-positive Staphylococcus aureus were correctly detected, 2 Salmonella species were correctly identified as S. enterica and, ultimately, overall results by the Acrion™ system were available more shortly than those by the in-house diagnostic workflow.

Conclusions: The Acrion™ system is an easy, fast and reliable tool for the laboratory diagnosis of bloodstream infections and integrates multiple crucial tests into a single, effortless workflow.

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Laboratory capacity for the diagnosis of leishmaniasis in Greece, 2018: a national surveillance study
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Background: Leishmaniasis is a public health problem in many parts of the world. The most common forms of the disease are visceral (VL) and cutaneous (CL) leishmaniasis. Greece is endemic for zoonotic VL. Reported cases of anthroponotic CL are sporadic. The mean annual notification rate of domestic VL and CL cases was 0.49/100,000 and 0.05/100,000, respectively for the period 2004-2018. We evaluated the laboratory capacity of Greek hospitals to diagnose leishmaniasis, in order to explore areas for improvement.

Materials/methods: A structured questionnaire was dispatched to microbiological laboratories of all country’s public hospitals. Diagnostic methods used, typing capacity and collaboration with other laboratories for diagnosis of leishmaniasis were recorded. Data were analysed as a whole, by region and by method of testing, i.e. parasitological testing, which is the reference diagnostic method used for the disease, serological and molecular testing.

Results: Feedback was provided by 56 of 110 hospitals (response rate 51%); of these, 25 (45%) reported they had the capacity to diagnose the disease. Capacity varied among different regions of the country with hospitals in Attica [area of the capital of the country Athens] reporting the highest [52%] capacity overall.

Serology was performed by 16/56 (64%) hospitals, followed by parasitology (52%). PCR capacity was low (1 hospital). Three (12%) hospitals could type leishmania species, all located in Attica region; two of them reported capacity for typing L. donovani complex, one L. donovani donovani and one L. donovani infantum. No hospital could type L. tropica or other species.

Conclusions: There is suboptimal capacity to diagnose leishmaniasis in Greece with significant geographical variation. Future efforts should focus on enhancing diagnostic capacity preferably through the development of a network of specialised laboratories coordinated by a national reference lab, including the development of typing methods for the timely detection of new species that may emerge in Greece.

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The distribution, transmission and adaptation of Klebsiella species in multiple clinical and non-clinical settings

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Background: Species belonging to the genus Klebsiella, and in particular K. pneumoniae (Kp), are pathogens of increasing notoriety. Treatment options are limited by the spread of resistance to carbapenems (CRKP) and other antibiotics. K. pneumoniae and related species are ecological generalists and reside in multiple non-clinical and environmental sources. A “One-Health” perspective is therefore warranted to better understand the contribution of environmental reservoirs to the public health burden.

Materials/methods: Over 6,000 samples from hospitals, community carriage, farm, companion and wild animals, surfaces, soil and water were taken near the Italian city of Pavia from July 2017 to October 2018. 3510 Klebsiella colonies recovered from selective media were sequenced. Kleborate was used to confirm species, ST, and to assay for virulence and resistance genes. GWAS analysis was performed using Pyseer, and transmission events inferred using a bespoke clustering method.

Results: 1705 (48.6%) of the samples were K. pneumoniae, with the remaining samples corresponding to 15 other Klebsiella / Raoultella species (including at least two novel species). K. pneumoniae was enriched in human derived samples, Raoultella spp were dominant in soil and plants, and the K. oxytoca-like clade was marginally enriched in animals. No CRKP was detected outside of the hospital environment, but different classes of beta-lactamase genes were common in animals and in multiple Klebsiella species. Isolates from pigs were found to be associated with aerobactin, an important virulence factor. GWAS analysis pointed to a strong host adaptive role for genes conferring resistance to metals. Transmission for all species was predominantly inferred within, rather than between niches. Many Kp isolates recovered from hospital carriage and disease shared a high level of relatedness.

Conclusions: Although most Klebsiella species were observed in most settings, species distribution is not random. GWAS analysis points to a strong genetic component for host adaptation, and broadly supports the view that human and bovine Klebsiella strains represent distinct populations. Although most transmission occurs within a single setting, occasional transmission between hosts or environmental niches may still play a significant role in the emergence of new resistant or virulent strains over the long term.

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Study of the serological efficacy of influenza vaccine along 28 consecutive seasons
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Background: The classical serological criteria of the European Medicament Agency (EMA) for the evaluation of vaccine efficacy determine different parameters for analysis the efficacy in people below and >60 years. For 18-59 or >60 that encloses a sero-protection rate (SPR) ≥70%/60%, a seroconversion rate (SCR) ≥40%/30% and a geometric mean titre (GMT) increase between post and pre-vaccination serum samples ≥2.5/2.0 respectively. The aim of these study is to apply those criteria to analyze vaccine efficacy in population ranging from 15 to >95 years old.

Materials/methods: A retrospective study was performed in 4,008 individuals vaccinated against influenza recruited from 1990 until 2018. This population was divided by age groups [15-30,31-40,41-50,51-64,65-74,75-84,85-94 and ≥95 years old]. Sera were obtained before and 28 days after vaccination. For analyzing the antibodies titers in both sera, haemagglutination inhibition assay (HAI) was performed at the National Influenza Centre of Valladolid (Spain) against classical A(H1N1) [from 1990 till 2010], A(H1N1)pdm09 [from 2010 till 2018], A(H3N2) and for both influenza B/Yamagata and B/Victoria lineages. The analysis was performed calculating the Seroprotection Rate (SPR), Seroconversion Rate (SCR) and Geometric Mean Titers increase (GMTi). The current consensus was followed and a titre of 1:40 was considered as protective. Seroconversion was defined as a titre increase of at least four-fold between pre and post-vaccination sera. We applied those criteria considering 15-64 and ≥65 as the cut-off.

Results: Against A(H1N1)pdm09, the efficacy criteria were fulfilled in all age groups. For classical-A[H1N1] SCR criteria were not achieved in 15-30, 41-50 and ≥95. For A(H3N2) subtype SCR criteria were below 40% for all groups between 15 and 50 years. In the case of Influenza B viruses, no SCR criteria were achieved in either Victoria or Yamagata lineages, and GMTi only met the criteria for 31-40 in B/Yamagata and 31-40 and 65-74 in B/Victoria lineages. In all cases SPR was over 75%.

Conclusions: For A[H1N1]pdm09 and A[H3N2] subtypes, influenza vaccine showed great results fulfilling all EMA criteria in individuals >50 years old but not for younger individuals in the case of A[H3N2] subtype. B lineages have more difficulties to achieve the criteria proposed for most of the age groups.

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Abstract 6587

Trends in invasive pneumococcal disease in Italy, 2010-2018

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Background: In Italy, the 13-valent conjugate vaccine (PCV13) was used for children vaccination against pneumococcal diseases since 2010, and in 2017 it was introduced at national level for vaccination also in the elderly. Data regarding Invasive Pneumococcal Diseases (IPD) are collected through the nationwide surveillance system of invasive bacterial diseases (MIB).

Materials/methods: All IPD cases reported in the MIB surveillance in the period 2010-2018 were included in this analysis, mainly focusing on the two high-risk age classes, children <5 years and elderly ≥65 years. Total IPD incidence and serotype distribution were analyzed.

Results: During 2010-2018, an overall increasing IPD incidence was observed, from 1.4 cases in 2010 to 2.6 cases/100,000 inhabitants in 2018. The impact of PCV13 vaccination in children was more evident in the age <1 year, with an IPD incidence decreasing from 5.3 cases in 2010 to 3.5 cases/100,000 inhabitants in 2013. Starting from 2014, IPD incidence began to increase again, reaching 5.3 cases/100,000 inhabitants in 2018. PCV13 serotypes decreased from 83% in 2010 to 23% in 2018, while NVS became the most frequent cause of IPD in children during the last years. Among NVS, serotypes 10A, 12F, 8, 11A, 15B/C, 22F, 23B, and 24F are the most frequently reported. Regarding elderly ≥65 years, IPD incidence increased from 5.3 in 2010 to 6.7 cases/100,000 inhabitants in 2018. Although PCV13-related IPD decreased also in this age group due to herd protection, from 70% in 2010 to 31% in 2018, serotypes 3, 19A, and 14 still represent a frequent cause of IPD in the elderly. NVS IPD increased consistently, mainly due to serotypes 8 and 22F.

Conclusions: The overall IPD increasing trend observed during the study period is likely influenced by the progressive implementation in the sensitivity of the surveillance system. PCV13 immunization in children was effective in reducing PCV13-related IPD not only in vaccinated children but also in older unvaccinated individuals. NVS accounted for the majority of IPD cases in the last years under study, indicating the occurrence of a serotype replacement phenomenon. Continuous implementation of the IPD surveillance is warranted to better evaluate the overtime IPD epidemiology changes.

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Abstract 6589

Three-dimensional in vitro Staphylococcus aureus abscess communities are not affected by antibiotics or neutrophils

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Background: Staphylococcus aureus is a prominent pathogen in skin, soft tissue and bone-related infections where it can form staphylococcal abscess communities (SACs). Given the specificity of a number of virulence factors for human targets (e.g. leukocidins), working with human host cells should provide a more accurate estimation of pathogenicity. Advanced three-dimensional (3D) in vitro cell culture models enable the incorporation of human cells and can resemble structures observed in vivo. However, no in vitro models, 2 or 3 dimensional, for full grown SACs have been described in the literature to date. Generation of a 3D in vitro SACs model would enable studies into host cell-pathogen interactions, antibiotic tolerance, new drug targets and treatment efficacy.

Materials/methods: We developed a 3D in vitro model of SACs grown in a collagen gel supplemented with human plasma. Characterization of the model was done by transmission and scanning electron microscopy, and immunofluorescent stainings were preformed to determine whether the pseudocapsule around SACs consist of fibrin. Antibiotic tolerance of SACs was assessed with 100x the minimal inhibitory concentration (MIC) of gentamicin. Bacterial clearance of non-establised SACs and established SACs with or without pseudocapsule was determined by exposure to differentiated PLB neutrophil-like cells (dPLB) or primary neutrophils.

Results: The 3D in vitro SACs were on average 200 micrometers in diameter, consisted of 8 log10 CFUs and were surrounded by an inner and outer fibrin pseudocapsule. The in vitro grown SACs tolerated 100x the MIC of gentamicin for 24h and bacterial numbers did not significantly differ from control SACs (p=0.1000). dPLB neutrophil-like cells or primary neutrophils were unable to clear established in vitro SACs (p=0.1102 and p=0.8767, respectively). When the fibrin pseudocapsule was degraded by the enzyme plasmin, dPLB neutrophil-like cells or primary neutrophils caused a significant decrease in total CFU compared the SACs that did had a pseudocapsule (p=0.0333 and p=0.0272, respectively).

Conclusions: The 3D in vitro SACs were not affected by the antibiotic treatment nor neutrophils. The in vitro SACs model offers a tool for host-pathogen interaction and drug efficacy assessments, and is a valuable starting point for future research.

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Evolution of cutaneous bacterial microbiota of pressure ulcers in patients with spinal cord injury

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Background: Chronic wounds are naturally colonised by bacteria from the cutaneous microbiota. Very few data have described the evolution of the microbiota of pressure ulcers (PU) after management and the influence of bacteria species in the chronicity of the lesion. The aim of this study was to characterize the evolution of the cutaneous microbiota of PU in spinal cord injury (SCI) patients during wound management.

Materials/methods: Patients admitted in a French reeducation centre and harboring stage 3/4 PU were prospectively included between May 2015 to December 2016. PU tissular biopsies were performed at baseline (D0) and 28 days after (D28). The PU microbiota were analysed by a metagenomic approach using 16S rRNA gene-based sequencing analysis of the V3-V4 region and interpreted with the clinical evolution of PU.

Results: Twenty-four patients with 24 pelvic PU were included (15 males; median age: 62.5 years [31 -89]). Twelve PU were ischial [50.0%], 11 sacral [45.8%] and one trochanterial [4.2%]. Most of PU belonged to stage 3 [66.7%]. Analysis of the evolution of bacterial communities at D0 and D28 showed an increase of the Firmicutes phylum at D28 ([76.3% [D0] vs 94.7% [D28]]) and a decrease of the Proteobacteria phylum [22.7% [D0] vs 5.0% [D28]]. This evolution is observed whatever the clinical evolution of the PU [degradation/stagnation and improvement]. The main bacterial genera present at D0 were Staphylococcus [30.8% of Firmicutes], Anaerococcus [24.0% of Firmicutes], Streptococcus [21.4% of Firmicutes] and Escherichia [88.8% of Proteobacteria]. At D28, no evolution in bacterial genera could be noted. Interestingly, according to the clinical evolution, the association Anaerococcus and Finegoldia had a statistically higher relative abundance at D0 for wounds that have stagnated or deteriorated at 28 days [0.77% vs 4.98%, p=0.056 and 1.50% vs 53.89%, p=0.036 respectively]. Moreover, at D28, Proteus were significantly detected in these worsened wounds [0.00% vs 32.02%, p=0.001].

Conclusions: This study shows that the association of Anaerococcus/Finegoldia could be a prognostic tool of the wound evolution and Proteus a marker of wound degradation. The knowledge of skin microbiota could represent an interesting tool to manage PU.

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**Epidemiological and genomics insights into the first outbreak of an extensive drug-resistant NDM-1-producing *Klebsiella pneumoniae* in Portugal**

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**Background:** In Portugal, carbapenems resistant *Klebsiella pneumoniae* (Kp) rates increased ~80% since 2014, essentially by expansion of KPC-3-producing ST147 till very recently. Here, we provide epidemiological and comparative genomics analysis on the first noticed outbreak of an extensive drug-resistant NDM-1-producing Kp in hospitalized patients.

**Materials/methods:** NDM-producing Kp were detected by GeneXpert-CarbaR in rectal colonization screenings of seven patients (Nov 2018-Mar 2019), two of them simultaneously in infection sites (urine, bile). Bacterial identification/susceptibility testing were performed by standard methods and PCR/sequencing (carbapenemases). Fourier Transform Infrared (FTIR) spectroscopy was used to assess isolates’ relationships in less than 24h and support infection control. Whole genome sequencing (n=1) and available bioinformatics tools allowed characterization of antibiotic resistance and virulence genes, K/O-locus [KLEBORATE/BiGsdB/Center for Genomic Epidemiology] and phylogenetic analysis (SNP-based CSI-phylogeny).

**Results:** The index case is from a patient with no history of previous hospitalization or travel abroad, 5 cases were detected in contact screenings of patients hospitalized in the same unit/period of time, and the last one from a household resident with no epidemiological link. Reinforcement of carrier screening, cleaning/disinfection practices, patients’ cohort and antibiotic stewardship prevented new cases. All isolates were considered identical by FTIR and belonged to ST11 with KL105 capsular type, a lineage that had caused long-term outbreaks as a DHA-1 producer in our country [Ribeiro et al. IJAA 2019]. They were resistant to all antibiotics tested (n=21) except amikacin and colistin, and carried several resistance (*bla*\(_{\text{NDM-1}}, \text{bla}_{\text{CTX-M-15}}, \text{aac}, \text{aph}, \text{qpxAB}, \text{qnrB1}, \text{catB3}, \text{sul2}, \text{tetD}, \text{dfra14}\) and virulence (*fuyA-mkr-ybtS-entB-kfuBC-ureA-fimH-iutA*) genes. Comparative genomics revealed high relatedness with 29 ST11-KL105 NCBI genomes (120-300 SNPs) from multiple countries worldwide, including previous DHA-1-producing Portuguese strain, and typical *bla*\(_{\text{NDM-1}}\) backbones (\(\Delta\text{Tn125}\) identical to pNDM-MAR, IncHI1B plasmid). These data suggests wide dissemination of ST11-KL105 lineage carrying either DHA-1, CTX-M-3/-15, KPC-2/-3 and/or NDM-encoding plasmids.

**Conclusions:** FTIR is an extremely powerful tool to support surveillance and infection control. Data from the first outbreak of NDM-1-Kp in our country raises the alarm for the potential silent dissemination of NDM through unnoticed carriage, and the need to implement active surveillance for early recognition of colonization/infection by NDM-producers to prevent wide dissemination.

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Abstract 6593

A glance at the endothelial activation in complicated and uncomplicated malaria

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Background: Malaria is one of the major public health problems that cause millions of deaths each year across the world. The pathogenesis of malaria is complex. Even with greater understanding of pathogenesis and treatment available, complicated malaria still occur leading to increase in morbidity and mortality. We studied endothelium activation as one of the pathogenetic mechanism responsible for complications in malaria.

Materials/methods: In a case control study of 30 patients with vivax malaria, endothelial activation was studied in the form of measurement of VWF. The diagnosis of malaria was made by microscopy and/or Rapid Diagnostic tests. Nested PCR was performed for confirmation of microscopy and/or Rapid Diagnostic tests positive cases. The presenting symptoms, physical examination and investigations were noted as per protocol. Patients were classified into complicated and uncomplicated category according to WHO criteria. The levels of vwf were measured in citrated plasma of P. vivax malaria patients using the commercial ELISA and analyzed using the chi-square test. The patients were followed up till discharge/death.

Results: The median age of study participants was 31 years, ranged from 16 - 65 years with 21 (70%) being males. The presenting clinical features were fever (n=30), bodyache (n=30), vomiting (n=10), headache (n=30), abdominal pain (n=3), decreased urine output (n=2) and loose stool (n=1). 22 patients were diagnosed to have complicated malaria. Median hemoglobin in malaria patients was 11.8gm/dl (range 7.2 – 14.4 gm/dl) and median platelet count in complicated and uncomplicated malaria patients were 24000 (range 5000 – 57000), 36000 (range 18000 – 78000) respectively. Levels of VWF in healthy control ranged from 50-150% whereas 95 % of complicated and 77 % uncomplicated cases had levels of VWF ≥150%.

Conclusions: The outcome of our study indicates that the malaria parasite has the potential to activate the endothelium. Although increased VWF levels in malaria insights the alteration in coagulation, but couldn’t differentiate between the complicated and uncomplicated malaria. Therefore to define the role of VWF in malaria, further investigations with more sample size are required.

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**Abstract 6594**

**Methenamine: an audit of its use for recurrent UTIs in a large UK trust**

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**Background:** Patients with recurrent urinary tract infections (rUTI) present frequently to primary and secondary health care services. These patients commonly receive prophylactic antibiotics, driving antimicrobial resistance and reducing antimicrobial treatment options. Non-antibiotic prophylaxis has the potential to reduce these risks. There is evidence that methenamine hippurate (MH), a urinary antiseptic, has a role in rUTI prophylaxis, and has been approved for use in our trust since 2017. We retrospectively described the use of MH to ascertain efficacy and adherence to local protocol.

**Materials/methods:** A list of MH prescriptions from April 2017 to September 2018 at University College London Hospital was gained from pharmacy records. A total of 220 prescriptions were issued during this time. Of these, 100 patients were randomly chosen for analysis across different prescribers. Patients’ electronic records were reviewed and data inputted and analysed in Excel.

**Results:** Ninety-one percent of patients were female (median age =59). MH was prescribed by different specialties, mainly Urology, Neurology and Gynaecology. Renal tract abnormalities were absent in 59% patients. Prophylactic antibiotics were used in 61% of patients prior to starting MH. Bacteriuria was confirmed in 73% of patients - 23% of these isolates had significant resistance. Urine pH was measured in 31% patients prior to starting MH, with 13% undergoing urinary acidification with ascorbic acid.

MH was relatively well-tolerated with only 14% of patients reporting side effects and 17% discontinuing MH earlier than planned. Number of rUTI’s during treatment was documented in 63% of patients, with 25% reporting no UTIs during the initial 6 months’ therapy.

**Conclusions:** We describe MH use in rUTIs in a large UK tertiary hospital. MH appears to be widely used by different specialties in patients with evidence of rUTIs and prior use of prophylactic antibiotics. 25%of patients who were on MH therapy were free of rUTI for a minimum of 6 months, suggesting a reduction in antibiotic treatment prescriptions. Importantly, MH appears to be well-tolerated with minimal side effects. The impact of a new electronic prescribing protocol for MH and the effect that this has on recording of MH outcomes, including subsequent antibiotic prescriptions, will be shown.

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Detection rates of bacterial vaginosis and sexually-transmitted pathogens associated with genital discharge syndrome in the South-African private sector

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Background: Sexually transmitted infections (STIs) and bacterial vaginosis (BV) are associated with poor reproductive outcomes as well as increased transmission of HIV. In South-Africa, a high HIV prevalence setting, limited data are available regarding the prevalence of STIs and BV mainly due to the syndromic management of these conditions. We present the findings of a retrospective analysis of detection rates of pathogens responsible for the genital discharge syndrome amongst males and females as well as BV rates amongst females.

Materials/methods: The detection rates of Chlamydia trachomatis, Neisseria gonorrhoeae, Mycoplasma genitalium, Trichomonas vaginalis, Mycoplasma hominis, Ureaplasma urealyticum and Ureaplasma parvum using the Anyplex II STI-7 multiplex PCR (Seegene) as well as the BV rate determined using Nugent scores were calculated by retrospectively analyzing laboratory data for the period 1 February 2014 to 29 June 2019.

Results: A total of 11,413 specimens [urine and genital swabs] were available for analysis of multiplex PCR results and Nugent scores were available for 50,342 vaginal swabs. Detection rates were as follows amongst females (n=7082): C. trachomatis 5.2%, N. gonorrhoeae 1.5%, M. genitalium 1.9%, T. vaginalis 1.9%, M. hominis 16.9%, U. urealyticum 16.6% and U. parvum 42.8%. Sixty percent of the vaginal swabs submitted for microscopy had a Nugent score of 0-3 (normal); 31% of swabs had a Nugent score of 4-6 (indeterminate); and 9% of swabs had a Nugent score of 7-10 (BV). Detection rates were as follows amongst males (n=4331): C. trachomatis 10.2%, N. gonorrhoeae 6.3%, M. genitalium 4.2%, T. vaginalis 1%, M. hominis 5.3%, U. urealyticum 13.2% and U. parvum 13.2%.

Conclusions: High rates of C. trachomatis and N. gonorrhoeae were observed amongst males and females. Mycoplasma genitalium is an emerging pathogen with the potential for multi-drug resistance; the high rates observed especially amongst males is therefore concerning. The role of the Ureaplasma species and M. hominis in the genital discharge syndrome is unclear; however, the high rates observed in female patients indicate that symptomatic pregnant females should be screened and treated for these bacteria as they are associated with poor pregnancy outcomes.

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**Abstract 6597**

**Drugs repurposing: in vitro testing of licensed drugs to assess role against MDR/XDR-TB**

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**Background:** Carbapenems inhibit mycobacterial L,D-transpeptidases but they are inactivated by beta-lactamases. The addition of clavulanate improves carbapenem activity.

Clavulanate is available in the UK combined with amoxicillin whose addition to meropenem-clavulanate was synergistic against *Mycobacterium tuberculosis* (MTB). Unfortunately, meropenem requires IV administration 3 times a day. Ertapenem, faropenem and tebipenem have a better administration profiles. Faropenem showed good killing activity *ex vivo*. Tebipenem and ertapenem showed activity against multi-drug resistant (MDR) and extensively drug resistant (XDR) MTB isolates.

**Materials/methods:** Susceptibility was performed in microtiter plates in a final volume of 0.1 mL of Middlebrook-7H9. 8 concentrations of carbapenems (faropenem: 0.064 - 16 mg/L; ertapenem, meropenem and tebipenem: 0.125 – 32 mg/L) were tested combined with fixed concentrations of clavulanate (2.5 mg/L) and amoxicillin (2mg/L).

The plates were incubated at 37° CO₂ and read every 7 days. Susceptibility was interpreted when visible growth was seen in the growth control (GC) well.

**Results:** 82 fully susceptible, MDR and XDR MTB isolates were tested.

Faropenem/clavulanate minimal Inhibitory Concentration (MIC) 50 was 2 mg/L and the MIC90 was >16 mg/L. The addition of amoxicillin did not change these values. Meropenem/clavulanate MIC50 was 8 mg/L while the addition of amoxicillin produced a value of 4 mg/L; MIC90 was >32 mg/L. Tebipenem/clavulanate MIC50 was 2 mg/L and 1 mg/L after the addition of amoxicillin. Ertapenem showed MIC50 of 32 mg/L and MIC90 >32 mg/L with no changes after the addition of amoxicillin.

**Conclusions:** Meropenem, tebipenem and faropenem showed modest activity against some MTB strains. Resistant pattern was not associated with resistance to other drugs so being fully susceptible, MDR or XDR could not predict susceptibility to these drugs. Synergy, if present, was strain specific rather than a drug-combination phenomenon. Ertapenem testing remains a challenge as it degrades quickly.

Since these drugs are increasingly used, further research is required to determine ecological cut-offs, breakpoints and the best methodology for testing.

Information regarding clinical use and outcomes in humans is emerging, showing results suggestive of activity against MTB. However, the contribution of these beta-lactams to the outcome remains uncertain.

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Clinical evaluation of an investigational use only Aspergillus galactomannan lateral flow assay at a tertiary cancer care centre

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Background: Invasive Aspergillosis is the most common fungal infection in immunocompromised hosts, including oncology patients. Diagnosis is currently limited due in part to slow and/or insensitive methods. One method includes the detection of Aspergillus galactomannan (GM) antigen using an enzyme-linked immunosorbant assay (EIA). EIA can be time-consuming, laborious and requires batching for cost-effective testing, delaying results. The IMMY Aspergillus Galactomannan Lateral Flow Assay (GM LFA), is an immunochromatographic test that recently became commercially available for the rapid detection (30 minutes) of GM. In this study, we evaluated the accuracy of the IMMY Aspergillus GM LFA to the PLATELIA™ Aspergillus EIA Antigen assay (GM EIA).

Materials/methods: This was a single-center, retrospective study. All clinical samples (serum and Bronchoalveolar lavages (BAL)) received for testing by the GM EIA between March 2019 and August 2019 were included, except if remaining sample volume following testing by GM EIA was insufficient. Samples were stored at -20 °C prior to testing by the GM LFA. Performance characteristics including positive (PPA) and negative percent agreement (NPA) were calculated. Discrepant analysis was performed by review of patients medical records for evidence of fungal infections.

Results: 565 samples were collected for this evaluation, including 90 BAL and 475 serum samples. Overall, 10/565 and 541/565 samples were positive and negative respectively by both tests for a PPA of 100% (95% CI: 69.2-100%) and a NPA of 97.5 % (95% CI: 95.8-98.6%). PPA and NPA by specimen types were 100% (95% CI: 15.8-100%) and 93.2% (95% CI:85.8-97.5%) respectively for BAL and 100% (95% CI: 63.1-100%) and 98.3% (95% CI: 96.4-99.3%) respectively for serum. 11/14 discordant samples were collected from patients with supporting evidence of fungal infection (e.g. culture, BD glucans, histopathology).

Conclusions: In our oncology patients, the Aspergillus GM LFA outperformed the Aspergillus GM EIA for the detection of the galactomannan antigen. Furthermore, the simplicity and rapid time to results makes the Aspergillus GM LFA easy to implement in a wide range of laboratory settings. Further studies will determine the impact of additional positive samples detected by the Aspergillus GM LFA on patient outcomes.

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Mechanisms of resistance and virulence of azole-resistant *Aspergillus flavus* clinical isolates

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**Background:** Resistance to azole drugs is an emerging problem in *Aspergillus fumigatus* but has been rarely evaluated in *Aspergillus flavus*, the second most important species of *Aspergillus* in human and animal infections. Only few azole-resistant *A. flavus* isolates have been reported and the mechanism of resistance remains poorly understood. As in *A. fumigatus*, the resistance mechanism may be related to alteration in the *Cyp51* genes coding for 14-alpha-demethylase.

**Materials/methods:** Six clinical isolates morphologically identified as *A. flavus* and presumed to be azole-resistant by an agar screening test, were included. Partial sequencing of β-tubulin and calmodulin genes identified the isolates as *A. flavus sensu stricto*. Resistance was confirmed by EUCAST. The virulence was evaluated in a *Galleria mellonella* model for 2 resistant and 2 susceptible isolates. *Cyp 51C* was sequenced for all resistant isolates.

**Results:** Voriconazole MIC was 8 mg/l for 2 strains and itraconazole MIC of was 16 mg/l for 4 strains. There was a cross-resistance between voriconazole and isavuconazole and between itraconazole and posaconazole. The two resistant isolates tested in *G. mellonella* were less pathogenic than the susceptible isolates. Among the 6 resistant isolates, eight substitutions were detected in *Cyp 51C* (Table). All but one (S399I) of these substitutions were also present or have been previously reported in susceptible isolates.

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<th>Strains</th>
<th>MICs (mg/l)</th>
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**Conclusions:** The presence of *A. flavus* azole-resistant isolates in France is confirmed. Resistant isolates were less virulent than susceptible ones. Most of Cyp 51C substitutions were also present in susceptible strains. The role of Cyp 51C mutations in *A. flavus* azole-resistance in our isolates is unlikely and therefore, other mechanisms of resistance needs to be further evaluated.

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**Abstract 6601**

**Viral versus bacterial infection diagnosis: Affimer proteins as alternative molecular recognition reagents**

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**Background:** The lack of point-of-care diagnostic tools for infectious diseases leads to inappropriate prescribing of antimicrobial agents, which had been associated with the increasing prevalence of antimicrobial resistance (AMR). Therefore, robust platforms for clinicians to distinguish between viral and bacterial infections at point of care are vital. This will help reduce the inappropriate use of antibiotics and decrease the prevalence of AMR. Antibodies are the major molecular recognition reagents used in commercially available diagnostic kits. However, the inherent limitations of antibodies including cost, production time and batch-to-batch variation, directly impact the performance of antibody-based immunoassays. The sensitivity and specificity of such assays is critically dependent on the quality of the molecular recognition reagents used.

**Materials/methods:** Leeds has developed a non-antibody binding protein called Affimer type II. From phage display libraries, Affimer binders against >500 targets have been identified. Here, using phage display, the Affimer library was screened to identify sensitive and non-cross-reactive Affimer proteins against specific biomarkers of (i) bacterial infection (procalcitonin and CRP) (ii) viral infection (TRAIL and IP-10) and (iii) nosocomial infection such as *Clostridium difficile* (toxin A, toxin B and GDH). Selected Affimers were characterised for specificity, sensitivity, binding kinetics and thermostability. To test for improved sensitivity, performance of Affimers were compared with commercially available diagnostic kit.

**Results:** Phage display screening yielded high affinity and specific Affimers against all the targets tested. The Affimers were expressed in *E. coli*, with soluble protein yield as high as 250 mg/L. A combination of ELISA and SPR has shown that these Affimer proteins bind their targets with low nanomolar affinity. Affimer pairs that bind different epitopes on monomeric targets were identified and used as both capture and detection reagents in immunoassays. The pairs show high specificity and retained 96% of binding in complex matrices. These Affimer-based assays have shown increased sensitivity and specificity compared to current ELISA kits.

**Conclusions:** This study shows that Affimers are robust molecular reagents for the identification of high affinity and specific binders against the panel of targets tested. The selected Affimers have potential for use in point-of-care differential diagnostics for viral and bacterial infection.

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Abstract 6602

The natural history of gonorrhoea infection: an illustrative review

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Abstract third-party references: Funding: GlaxoSmithKline Biologicals SA

Background: Gonorrhoea is a sexually transmitted infection of the urogenital, pharyngeal or anorectal tract, or the eye. The natural history is complex and infection results in diverse clinical presentations and health outcomes in men, women and newborns, the scope of which is incompletely characterized in the literature. Traditional systematic literature searching based on broad search queries and multitudinous hits, may be too resource intensive to capture all related clinical and psychosocial outcomes. Using novel artificial intelligence-(AI)-assisted search methods we address this challenge, providing a single, evidence-based compendium of identified outcomes and a summary of related pathogenic processes.

Materials/methods: We combined traditional systematic review methodology using standard search engine technology with innovative AI Medline screening. The AI tool uses natural language pre-processing to screen abstracts for ‘topic-words’ associated with a query (‘gonorrhoea’), which are then weighted based on term and supporting-document frequency. Topic-words were screened independently by two reviewers for relevance to clinical and psychosocial gonorrhoea-related health outcomes, and key references selected according to an objective quality score. A systematic search of the literature combining pre-specified medical subject headings and keywords was also conducted to identify health outcomes and related key pathogenic processes (English, no time limit).

Results: Ninety-seven clinical conditions relating to Ng were first identified through a targeted search of works by seminal authors, websites of public health institutes (CDC, PHE/NHS and RKI) and gonorrhoea-related ICD9/10 and Read diagnostic codes. AI screening identified 18,289 Medline citations, of which 10,022 containing an abstract were included, incorporating 10,324 topic-words. Of 10,324 topic words manually screened, 230 outcome-related topic-words were selected, categorized by organ systems or outcomes and by quality score for supporting references (n=57 urogenital, n=20 anorectal, n=6 oropharyngeal, n=14 eye, n=26 psychosocial, n=25 coinfections, n=6 disseminated infection, n=2 antibiotic resistance, n=74 systemic/non-specific health domain). Pathogenic processes were summarized based on 35/101 full text articles reviewed.

Conclusions: Combining novel and traditional systematic search methodologies, we comprehensively identified evidence-based clinical and psychosocial health outcomes associated with gonorrhoea infection. This review informs clinicians, public health practitioners and policy makers, ultimately facilitating an evidence-based summary of the burden of gonorrhoea infection.

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Burden of viral infections among autologous stem cell transplant patients: a prospective longitudinal study

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Background: Hematopoietic stem cell transplantation remains the only curative treatment for many hematological disorders. Surrounding this immunosuppressive therapy, viral reactivations caused by herpesviruses, adenovirus, BK virus require particular attention to prevent organ damages. Despite some severe cases reported in autologous stem cell transplant (ASCT) patients, only few recommendations regarding the management of viral infections have been established so far. We aimed to investigate viral infections in patients who underwent ASCT in a large prospective longitudinal study.

Materials/methods: A systematic screening of plasma viral load, targeting 9 viruses at 11 time-points (from diagnosis to 90 days post transplantation), was performed on 477 samples from 48 patients (n=42 multiple myeloma, n=6 lymphoma) prospectively enrolled. Clinical criteria and hemogram values were collected. All patients received antiviral prophylaxis with valaciclovir.

Results: Of 4293 PCRs performed, 86 (2.0%) were positive corresponding to 75/477 (15.7%) samples. While sixteen patients (35%) had no virus detected during follow-up, most of positive samples (56%) were found after aplasia and 30 days after transplantation. Patients mainly presented CMV reactivation (59% of CMV seropositive patients). Overall, low viral loads (<3 log copies/mL) were found except for one patient with parvovirus B19 primary infection [11.85 log copies/mL], and for two patients with HHV6 [3.84 log copies/mL] and CMV [4.50 log copies/mL] clinical reactivations. For this latter patient, CMV was also the unique pathogen identified in the bronchoalveolar lavage collected during an interstitial pneumonia episode requiring 6 days of hospitalization. No specific reactivation was associated with clinical or biological criteria. Interestingly, no reactivation was found in multiple myeloma patients treated with daratumumab, a cd-38 monoclonal antibody for which an increase in viral reactivations was previously reported.

Conclusions: This is the largest prospective study reported so far describing viral detections during the whole follow-up of ASCT patients. We found a limited clinical impact of viral reactivations in these patients treated with valaciclovir, suggesting a potential benefit of administering an antiviral prophylaxis in all ASCT patients [even not yet recommended]. However, CMV testing should be systematically considered in case of infectious complications. This study might contribute to upgrade guidelines regarding ASCT patient management.

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Abstract 6610

Spectrophotometric detection of azole-resistant *Aspergillus fumigatus* clinical isolates with EUCAST broth microdilution method. Is it time for automating EUCAST antifungal susceptibility testing of *Aspergillus* spp.?

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**Background:** Timely detection of azole-resistant *Aspergillus* isolates is a significant challenge. EUCAST antifungal susceptibility testing of *Aspergillus* spp. requires visual inspection of microplates, which is time-consuming, subjective and requires experienced staff. We compared spectrophotometric and visual reading of EUCAST microplates for the detection azole resistant *A. fumigatus* in a large collection of isolates including resistant isolates with different mechanisms of resistance.

**Materials/methods:** The following *Aspergillus fumigatus* (n=181) were examined: 63 WT isolates, 60 isolates harboring TR34/L98H mutation and 58 harboring TR46/Y121F/T289A mutation. Susceptibility testing was performed following the EUCAST E.Def 9.3.1 methodology for amphotericin B, itraconazole, voriconazole, posaconazole and isavuconazole. The MICs of the isolates were determined after 48h of incubation visually and spectrophotometrically at 405 nm as the lowest concentration corresponding to 1, 3, 5, 10 or 15% OD increase above the conidia-free background OD. The essential agreement EA (±1 twofold dilution) and categorical agreement CA (based on the classification of the isolates as susceptible/intermediate/resistant using EUCAST breakpoints) were calculated. The best spectrophotometric endpoint (SPE) was chosen based on the highest CA and fewer very major (VME), major (ME) and minor errors (mE).

**Results:** The median (range) MICs of amphotericin B, itraconazole, voriconazole, posaconazole and isavuconazole were 0.5(0.25-1), 0.25(0.063-2), 0.25(0.125-1), 0.063(0.031-0.25) mg/l for WT, 0.5(0.25-2), >16(2->16), 4(2-16), 0.5(0.125-1), 8(2->16) mg/l for TR34/L98H and 0.5(0.125-4), 2(0.25->16), 16(0.5->16), 0.5(0.016-16), 32(0.5->16) mg/l for TR46/Y121F/T289A isolates. The best performing SPE was the 10% growth endpoint with EA 98%, 96%, 95%, 93% and 93% and CA 98%, 95%, 90%, 90% and 98% for amphotericin B, itraconazole, voriconazole, posaconazole and isavuconazole, respectively. The VME were 0% for all drugs except for itraconazole (1%). The ME and mE were 1-2% and 0-10%, respectively for all drugs.

**Conclusions:** Spectrophotometric reading of EUCAST microplates can be used for amphotericin B and azole antifungal susceptibility testing of *A. fumigatus* and particularly in detecting azole resistance. Spectrophotometric readings will lead to automation and increase objectivity of EUCAST E.Def 9.3.1 protocol.

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Abstract 6613

Definite prolonged antibiotic treatment in complicated prosthetic valve endocarditis with absolute contraindication to surgery: a single-centre retrospective analysis

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Background: Prosthetic valve endocarditis (PVE) is a serious complication after heart valve replacement. In case of complicated infections, Staphylococcus spp or peripheral embolism, the recommended treatment is the antibiotic therapy combined to surgery. Antibiotic therapy alone is not commonly recommended for complicated PVE. Here we retrospectively describe a case collection of patients with complicated PVE, conservatively treated with antibiotics because of the presence of absolute contraindication to surgery.

Materials/methods: We retrospectively collected complicated PVE cases diagnosed (according to Duke criteria) in our institution, between 2009 and 2017. Demographic data, antibiotic therapy, complications, radiologic and microbiologic findings were reported. All patients had an absolute contraindication to valve replacement and were treated with a definite prolonged antibiotic therapy (first intravenously and then orally). After antibiotic discontinuation, a one-year follow up was conducted.

Results: 28 patients (22 males, 78.5%) were included in the analysis. Median age at time of diagnosis was 72 (IQR: 65-76). In our cohort the prosthetic:biologic valve ratio was 1:1. Aortic valve was the most involved (17/28, 61%) and 21 patients (75%) had a late (> 1 year after surgery) PVE. Staphylococcus spp was responsible for infection in 11 patients (39.2%). A vegetation size of >10 mm was present in 8 patients (28.5%), a valvular abscess in 6 (21.4%) and 4 patients (14.2%) had a periprosthetic leak. Embolic phenomena were observed in 9 patients (39.1%). During hospitalization the median time of antibiotic treatment was 6 weeks (IQR: 5.75-7) whereas the median weeks for the outpatient antibiotic treatment (OPAT) were 24 (IQR: 10-24). After one year of follow up, 22 patients (78%) had no recurrence of infection.

Conclusions: In our study, we observed that a prolonged antibiotic treatment, together with a close follow-up, can be a valid option for those patients with complicated PVE, when surgery is contraindicated. A median of 30 weeks of treatment (6 intravenously and 24 orally) seems to reduce the recurrence of infections after one-year follow up. More studies on wider populations with longer follow up periods are needed to address the issue of definite conservative antibiotic treatment for complicated PVE.

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Abstract 6614

**Reference evaluation of two manual blood culture bottles for low-resource settings**

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**Background:** The Mini-lab is a Médecins Sans Frontières project for the development of an all-in-one basic clinical bacteriology laboratory deployable in low-resource settings (LRS). Blood cultures are considered priority specimens in this laboratory. An extensive evaluation of two “manual” (i.e., visually read) blood culture bottles (BCB) was done, in parallel to automated incubation of BCB (Bact/ALERT system, bioMérieux). In a previous pilot evaluation of five different manual BCB (n=112 for each BCB type), the Autobio Bi-State BCB (biphasic bottle – agar slant and broth) as well as the “manual” BacT/ALERT FA Plus/PF Plus BCB had shown the best performance.

**Materials/methods:** Both bottle types were further evaluated with a panel of 122 representative bacterial isolates from LRS comprising most clinically relevant bloodstream pathogens (16 bacterial species). Bottles were inoculated with spiked human blood in triplicate, both for pediatric and adult bottles and blood volumes. In total, 552 bottles of each type were inoculated, of which 354 in pediatric experiments and 198 in adult experiments. Bottles were visually inspected twice daily for signs of growth, such as turbidity and hemolysis. For BacT/ALERT bottles, color change of the CO₂ Indicator at the bottom of the bottle was also assessed. For the Autobio bottles, signs of growth on the agar slant as well as in the broth were recorded.

**Results:** The yield (% of inoculated bottles grown) of combined experiments was 95% for the automated BacT/ALERT incubation, 94% for Autobio bottles and 93% for manual BacT/ALERT bottles. Yield was lower in pediatric experiments (93%, 92% and 90% for automated BacT/ALERT, Autobio and manual BacT/ALERT BCB respectively) than in adult experiments (98%, 98% and 97%, respectively). Difference in yield between Autobio and manual BacT/ALERT bottles was not significant (p=0.07). All automated bottles showed growth after overnight incubation. For Autobio bottles, 91.3% showed growth after overnight incubation, versus 82.4% of manual BacT/ALERT bottles (p<0.001).

**Conclusions:** Yield of manual BCB was comparable to that of the automated bottles in our experiments. Autobio bottles showed similar yield but significantly faster growth than manual BacT/ALERT bottles. Visual signs of growth were more easily detectable in the Autobio bottles.

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Abstract 6615

Whole genome sequencing clarifies potential outbreak with extended-spectrum beta-lactamase-producing *Escherichia coli*

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**Background:** Between March and October 2019 we isolated Extended Spectrum Betalactamase (ESBL)-producing *Escherichia coli* from eight neonates in the neonatal ward at Ryhov County Hospital, Jönköping, Sweden. All of the neonates were colonized with ESBL-*E. coli*, none of the isolates were retrieved from clinical cultures.

By whole-genome sequencing (WGS) we clarified the similarity between the ESBL-*E. coli* isolates and used the information to elucidate whether transmission of bacteria between neonates had occurred or not.

**Materials/methods:** DNA was extracted from the eight ESBL-*E. coli* isolates, using the EZ1 DNA Tissue kit on the EZ1 Advanced XL (Qiagen). Library preparation was performed using Nextera XT library prep kit (Illumina). Paired-end sequencing (2*250 cycles) was performed on a Miseq instrument (Illumina). Assembly and cluster analysis by core genome multilocus sequence typing (cgMLST) based on 1602 genes was performed using SeqSphere (Ridom GmbH). The cluster alert distance was set to 10 allelic differences.

**Results:** The eight isolates were divided into five different clusters. Three of the clusters consisted of one isolate each. The remaining two clusters consisted of two and three isolates, respectively (Figure 1).

ESBL-*E. coli* isolates 1 and 2 were highly dissimilar although they were retrieved the same day.

Isolates 4, 5 and 6 were indistinguishable. Two of the isolates were collected from a pair of twins and the third isolate from a neonate cared for at the ward simultaneously as the twins.

The isolates from neonate 3 and 7 were indistinguishable. The neonates were not cared for simultaneously at the ward.

**Conclusions:** WGS shows that highly dissimilar ESBL-*E. coli* can be obtained from different patients simultaneously cared for in one ward. Epidemiological data alone indicated that transmission could have occurred.

The opposite is also shown by WGS, neonates with no overlap in hospitalization had the same type of ESBL-*E. coli*, indicating long survival in the environment and a possible delayed transmission.

In conclusion, WGS can be used both to rule out and detect bacterial transmission between patients in hospital care.

**Figure 1:** Minimum-spanning tree of the eight ESBL-*E. coli* isolates.

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Abstract 6616

**Designing and structure evaluation of uropathogenic *Escherichia coli* multi-epitope subunit vaccine**

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**Background:** Urinary tract infections (UTIs) are a severe public health problem and usually caused by UPEC. According to the increasing rate of antibiotic resistance, precaution strategies such as vaccination can be useful for UTI management. Immunoinformatics methods overcome the problems of traditional vaccinology such as high cost, time duration, and accuracy and has been applied successfully in vaccine design.

**Materials/methods:** To design a novel multiepitope subunit vaccine against UTI, FdeC, Hma, UpaB were selected. Different online tools such as IEDB, ABCpred, Net MHCI and Net MHCII were used to predict Bcell linear epitopes and T cell epitopes. Some physicochemical characteristics of the vaccine constructs were investigated by ProtParam tools and solubility was checked by the ccSOL omics server. Third structure of our designed constructs were modeled by I-Tasser and molecular docking was done by patchdock server using HLA alleles and GM1. Antigenicity and allergenicity of selected construct were evaluated by VaxiJen and AlgPred server respectively.

**Results:** In this study two constructs were designed: a construct which contains Bcell epitopes and a construct contains Tcell epitopes. According to the performed analysis, constructs which had best physicochemical characteristics and best c-score in I-tasser results were selected. Docking results of selected constructs with related receptors were desirable and constructs were found to be non-allergen.

**Conclusions:** Since humoral and cellular immunity are required for effective protection against UTI, we designed two constructs containing B-cell and T-cell epitopes and CTB as a build-in adjuvant. Computational analysis showed that our construct could induce effective immune responses. This study could be useful in achieving an ideal epitope based vaccine against UTI.

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Abstract 6617

Understanding the pathogenicity of Scedosporium species, the emerging cystic fibrosis pathogens
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Background: Scedosporium species are ubiquitous saprophytic hyaline filamentous fungi, which are commonly associated with anthropogenic habitats. As opportunistic human pathogens, these species are capable to cause a wide spectrum of infections (e.g., they are the second most frequently isolated filamentous fungi from the sputum of patients with cystic fibrosis), while known to be resistant against numerous clinically used antifungal drugs. The incidence of clinically relevant species does not reflect their environmental distribution, moreover, some species has not been associated with clinical samples at all. These observations suggest, that the different Scedosporium species might possess unique properties (e.g., a specific set of virulence factors) allowing them to colonize distinct environmental niches. These virulence factors might serve as novel targets for antifungal strategies.

Materials/methods: We investigate host-pathogen interactions using in vitro and in vivo model systems in order to compare the pathogenic potential of Scedosporium apiospermum, S. boydii, S. aurantiacum, S. angustum, S. dehoogii, S. ellipsoideum, S. minutisporum, S. fuscosporeum and S. desertorum. To reveal differences in the killing potential of macrophages against various Scedosporium species and to describe the immune cell damaging capacity of these fungi, cytotoxicity and imaging flow cytometry-based phagocytosis assays are performed. Alternative invertebrate infection models are also applied in order to compare the in vivo pathogenic potential of scedosporia.

Results: Our preliminary observations suggest some fundamental differences between the volatile sulfur and nitrogen metabolism of S. aurantiacum and other Scedosporium species (e.g., S. apiospermum and S. boydii). As sulfur metabolism has been previously associated with the virulence of other filamentous fungi, we assume that the observed metabolic differences is reflected in the virulence properties of scedosporia as well. Additionally, we observed significant differences in the in vitro and in vivo pathogenic potential of the tested species. The results of this ongoing project may reveal novel aspects of the background of pathogenicity mechanisms (e.g., virulence factors) and the main risk factors for the emergence and spread of scedosporia in our immediate environment.

Conclusions: This comprehensive study facilitates the understanding of the pathogenicity of filamentous fungi through the investigation of the emerging pathogenic Scedosporium genus.

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A study comparing the performance of an eravacycline Oxoid antimicrobial susceptibility testing disc against an FDA-cleared predicate device

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Abstract third-party references: Tetraphase Pharmaceuticals, 480 Arsenal St Ste 110, Watertown, USA, Thermo Fisher Scientific, Wade Road, Basingstoke, RG24 8PW, IHMA Europe Sarl, Rte de l'Ile-ai-Bois 1A, Switzerland

Background: An evaluation was designed to determine the accuracy and reproducibility of the new eravacycline Oxoid Antimicrobial Susceptibility Testing disc against the FDA cleared eravacycline disc from Hardy Diagnostics (the predicate device). Eravacycline is a synthetic halogenated tetracycline antibiotic from tetraphase and is indicated for the treatment of complicated intra-abdominal infections (cIAI) caused by the following susceptible microorganisms: Escherichia coli, Klebsiella pneumoniae, Citrobacter freundii, Enterobacter cloacae, Klebsiella oxytoca, Enterococcus faecalis, Enterococcus faecium, Staphylococcus aureus, Streptococcus anginosis group, Clostridium perfringens, Bacteroides species and Porabacteroides distasonis, in patients 18 or older.

Materials/methods: Two lots of investigational use only Oxoid eravacycline disks provided by Thermo Fisher were tested with 375 (300 clinical + 75 challenge) isolates using Clinical and Laboratory Standards Institute (CLSI) M02-A13 (2018) method with Mueller Hinton agar (Oxoid MHA). One lot of Hardy eravacycline disks were tested alongside as a predicate device. Quality Control (QC) was carried out daily as per CLSI M02-A13 and M100-S29 documents using American Type Culture Collection (ATCC) strains.

Results: When compared with the predicate device, five minor errors were observed (four challenge isolates, one clinical isolate) with categorical agreement of 98.67%. Reproducibility was calculated as the percent of results which were within plus or minus 3 mm of the modal value. All data was shown to be 100% reproducible both within-reader and between-reader. QC results were within range 100% of the time for each batch and each reader.

Conclusions: The results show that the Oxoid eravacycline disc demonstrates an equivalent level of performance compared to the predicate device. The high level of agreement obtained by the Oxoid eravacycline disc suggests this is an acceptable method for susceptibility testing of eravacycline.

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Abstract 6623

Relatedness of European Clostridioides difficile strains from humans, food and animals by whole genome sequencing, ribotyping and toxinotyping; results from COMBACTE-CDI

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Abstract third-party references: on behalf of the COMBACTE-CDI consortium

Background: Previous data from human-derived Clostridium difficile (CD) strains indicates country-specific clustering for some but not all ribotypes. COMBACTE-CDI provides the opportunity to explore this further with the addition of food/animal strains

Materials/methods: On two days, all diarrhoeal samples (regardless of tests requested, n=3163) from 119 sites in 12 European countries, were CD cultured at the coordinating laboratory (positive=287). Contemporaneous CD isolates were collected from animals (n=126) and food (n=67) in the same countries. All isolates underwent PCR-ribotyping, toxinotyping, and whole genome sequencing (WGS); dendrograms were constructed in BIOMÉRIEUX EPISEQ® CS using wgMLST with 95% cut-off and virulome compared between strains.

Results: Using WGS, isolates clustered by ribotype and toxinotype, although matches were not exact. Some ribotypes had within-country clustering (027, 181) while others did not (002, 015, 014, 020). Similarity threshold was increased to 99% to analyse highly-related ribotype 078 and 126 strains, demonstrating five distinct clusters with no within-country clustering for human isolates; animal and food isolates did cluster by country (Figure 1). Analysis highlighted one UK 027 isolate, clustered within 027 isolates from Poland; one 181 isolate from UK clustered within 181 isolates from Romania; one 018 isolate from an Italian community patient clustered next to an isolate from an Italian hospital patient. Virulome analysis on EPISEQ® CS aligned with toxinotyping, with two discrepancies (PaLoc not detected by EPISEQ® CS). Both parts of the binary toxin genes were present in all isolates from ribotypes 027, 181, 078 and 126; however several ribotypes only had cdtB (015, 001 and 005). All isolates from ribotypes 078 and 126 were deficient in fliA, which was ubiquitous in almost all other ribotypes.

Conclusions: There was not an exact match between WGS and ribotype, probably because these are two distinct typing schemes examining different parts of the genome. Previous data on strains that show within-country clustering was confirmed, while in contrast to previous data there was some country-specific clustering of 078 and 126 strains, however this was for food or animal source isolates only. EPISEQ® CS analysis highlighted potential transmission events for further investigation, and differences in virulence factors between ribotypes.

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Abstracts 2020

Abstract 6624

**Species distribution and antifungal susceptibility profile of the emerging yeast pathogen Blastobotrys**

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**Background:** The genus *Blastobotrys* (order Saccharomycetales) consists of a group of uncommon, fluconazole-resistant yeasts. Although infrequently cultured from clinical samples, these fungi can be isolated from cystic fibrosis patients or those with chronic bronchitis and have been associated with respiratory deterioration. However, many clinical laboratories do not routinely identify yeasts in respiratory specimens, and antifungal susceptibility profiles against this genus is not well-understood. Our objective was to evaluate the species distribution and antifungal susceptibility profile of clinically available agents and the novel inositol acyltransferase inhibitor manogepix against *Blastobotrys* isolates in the U.S.

**Materials/methods:** A panel of 22 clinical *Blastobotrys* isolates, mostly respiratory isolates comprised of 14 human and 8 animal specimens, received by the Fungus Testing Laboratory at the UT Health Science Center San Antonio for identification and antifungal susceptibility testing were included. Identification was determined by DNA sequencing and phylogenetic analysis of ITS rDNA region and LSU gene. *In vitro* susceptibility against 20 isolates was performed by the CLSI M27 broth microdilution method.

**Results:** Of the 22 *Blastobotrys* isolates, the majority (n=21) were identified as *B. raffinosifermentans*, while one was identified as *B. adeninivorans*. Of the clinically available antifungals the most potent activity was observed with micafungin (range ≤0.015 - 0.5 mg/L, GM MIC 0.268 mg/L), isavuconazole (0.06-8 mg/L, 0.287 mg/L), and amphotericin (0.25- 1 mg/L, 0.448 mg/L). The other extended-spectrum azoles (i.e., voriconazole, posaconazole, and itraconazole) also demonstrated activity although the GM MICs were at least 2 dilutions higher than that of isavuconazole (GM MIC range 0.896 - 1.04 mg/L; p <0.01 for each comparison vs. isavuconazole). Manogepix also demonstrated potent in vitro activity (range ≤0.015 - 0.03 mg/L; GM MIC 0.016 mg/L). In contrast, limited activity was observed with fluconazole (16 - >64 mg/L, 46.1 mg/L).

**Conclusions:** Of the clinical isolates tested, *B. raffinosifermentans* was the most prevalent species, which was cultured from both human and animal specimens. Potent *in vitro* activity was observed with the investigational agent manogepix and the clinically available antifungals micafungin, isavuconazole, and amphotericin B. Further studies are warranted in order to determine the clinical implications of these findings.

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Does vaccines need a gender perspective? Influenza says yes!

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Background: In the era of gender equality there are studies showing different responses to infectious diseases based on gender. This has been related to hormones and their impact on the immune system. The aim of this study is to compare the humoral response to influenza vaccination in men and women

Materials/methods: A retrospective study was performed in 2,077 individuals vaccinated with influenza vaccine recruited from 1990 till 2018. Population of study was divided by gender and age (14-64 and ≥65 years old). Serum samples were obtained before and 28 days after vaccination. For analyzing the antibodies titer in both sera, haemaglutination inhibition assay (HAI) was performed at the National Influenza Centre of Valladolid (Spain) against classical A(H1N1) (from 1990 till 2010), A[H1N1]pdm09 (from 2010 till 2018), A(H3N2) and for both influenza B/Yamagata and B/Victoria lineages. The statistical analysis was performed calculating the Geometric Mean Titters increase (GMTi) and the Seroconversion Rate (SCR). Differences by age and sex were analyzed using Student-T and chi-square tests (p<0.05).

Results: HAI was performed in 966(46.5%) men and in 1,111(53.5%) women. GMTi was significantly higher in women (14-64 years) for classical A(H1N1) (p=0.019) while GMTi were significantly higher in women ≥65 for both classical A(H1N1) (p=0.004) and A[H1N1]pdm09 (p=0.001) subtypes. The SCR was significantly higher in women ≥65 for both classical A(H1N1) (p=0.005) subtype and A[H1N1]pdm09 (p=0.001) subtypes but also for B/Victoria lineage (p=0.039). No other statistical significances were found. Values of GMTi and SCR are shown in the following table.

<table>
<thead>
<tr>
<th></th>
<th>GMTI Women(14-64)</th>
<th>GMTI Men(14-64)</th>
<th>GMTI Women≥65</th>
<th>GMTI Men≥65</th>
<th>SCR Women(14-64)</th>
<th>SCR Men(14-64)</th>
<th>SCR Women≥65</th>
<th>SCR Men≥65</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1pdm09</td>
<td>3.64</td>
<td>3.79</td>
<td>3.82</td>
<td>2.97</td>
<td>46.74</td>
<td>52.36</td>
<td>41.97</td>
<td>41.97</td>
</tr>
<tr>
<td>A/H1N1</td>
<td>3.23</td>
<td>2.92</td>
<td>2.11</td>
<td>3.14</td>
<td>37.36</td>
<td>40.59</td>
<td>30.12</td>
<td>30.12</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>2.01</td>
<td>3.39</td>
<td>1.91</td>
<td>1.77</td>
<td>24.11</td>
<td>24.62</td>
<td>21.03</td>
<td>21.03</td>
</tr>
<tr>
<td>B(Yam)</td>
<td>2.24</td>
<td>2.24</td>
<td>1.90</td>
<td>1.83</td>
<td>28.35</td>
<td>26.61</td>
<td>18.94</td>
<td>18.94</td>
</tr>
</tbody>
</table>

Conclusions: Our results showed that women experience higher humoral responses after influenza vaccination specially in the elderly against some influenza viruses as classical A(H1N1) and A[H1N1]pdm09 subtypes. These results confirm that there are biological differences between men and women affecting the humoral response induced by vaccination.

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**Abstract 6626**

**Association between first episode Clostridioides difficile infection management and recurrence in a tertiary hospital**

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**Background:** Inadequacy of treatment to guidelines and specific risk factors (advanced age, duration of hospitalization, exposure to antibiotics, underlying diseases and comorbidities, cancer chemotherapy, immunosuppression, gastrointestinal surgery, tube feeding, proton pump inhibitor [PPI]) are associated with recurrent cases of CDI (rCDI). The aim of the study was to analyze factors associated with recurrence in our health area.

**Materials/methods:** Between 2010 and 2018, patients >2 years old with unexplained and new-onset ≥3 loose stools in 24 h were included. Microbiological diagnosis of toxigenic strains was confirmed by EIA (C. diff Quik Chek®) or PCR (Xpert® C. difficile). Recurrence was defined as a relapse of CDI symptoms within 2-8 weeks of successful treatment of the initial episode. Clinical and microbiological risk factors associated with recurrence, as well as adjusted treatment to guidelines (IDSA 2010-2018, ESCMID 2014) were analyzed. Chi-square or Fisher and U-Mann Whitney were performed to investigate association between variables. Odds ratio and 95% confidence intervals [CIs] were calculated.

**Results:** 273 patients were included. Mean age was 64.90 year old, and 153 (56%) were women. Higher mortality rates were not found in recurrent patients. Clinical and microbiological risk factors significantly associated with recurrence, are shown in Table 1.

**Table 1. Variables analysed in patients with rCDI**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non recurrence (n/total (%))</th>
<th>Recurrence (n/total (%))</th>
<th>p-value</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aged &gt;65</td>
<td>139/244 (57%)</td>
<td>23/29 (79%)</td>
<td>0.021</td>
<td>2.896</td>
</tr>
<tr>
<td>Severe initial episode</td>
<td>52/244 (21%)</td>
<td>13/29 (45%)</td>
<td>0.005</td>
<td>3.000</td>
</tr>
<tr>
<td>Adjusted treatment¹</td>
<td>171/242 (71%)</td>
<td>12/29 (41%)</td>
<td>0.001</td>
<td>0.293</td>
</tr>
<tr>
<td>PPIs</td>
<td>133/244 (55%)</td>
<td>24/29 (83%)</td>
<td>0.004</td>
<td>4.006</td>
</tr>
<tr>
<td>Comorbidity (Charison)</td>
<td>149/244 (61%)</td>
<td>27/29 (93%)</td>
<td>0.001</td>
<td>8.607</td>
</tr>
<tr>
<td>Binary toxin</td>
<td>41/195 (21%)</td>
<td>7/23 (30%)</td>
<td>0.303</td>
<td>1.843</td>
</tr>
<tr>
<td>Ct² toxin B</td>
<td>194 (24,95) (22,8,28,4)</td>
<td>23 (22,9) (22,2,25,70)</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>n(median)(interquartile range)</td>
<td>30 (23,7) (22,2,28,1)</td>
<td>7 (22,9) (20,8,23,2)</td>
<td>0.178</td>
<td></td>
</tr>
</tbody>
</table>

¹IDSA 2010-2018, ESCMID 2014

²Ct: cycle thresholds.

**Conclusions:** Although finding association between some of the clinical and microbiological variables, our sample size wasn’t enough to achieve a robust recurrence predictor score. However, it seems that in the future these factors will be included in recurrence prediction algorithms. Furthermore, distribution of current guidelines would minimize the prevalence of recurrence.

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The population structure of extended-spectrum beta-lactamase-producing Enterobacteriaceae in households following hospital discharge and long-term care facilities is species dependent: MODERN-studies from 5 European countries (2017-2019)

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Background: Limited evidence is available on how the molecular population structure of extended spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-PE) differs between European countries, and to which extent transmission dynamics depend on bacterial species. Here we describe the molecular results of the MODERN-studies performed in 5 European countries between 2017 and 2019.

Materials/methods: In total, 728 ESBL-PE (Escherichia coli and Klebsiella pneumoniae) isolates were prospectively collected in two observational cohort studies. Firstly, isolates from 83 residents and 12 employees from six Long Term Care Facilities (LTCF). Secondly, isolates collected from 112 household members from 71 households. The first isolate of a specific sequence type (ST) per study participant was selected to prevent dependency between longitudinal measurements. This led to a selection of 201 E. coli and 89 K. pneumoniae isolates (127 from Spain, 59 from Switzerland, 38 from France, 44 from Germany, and 22 from the Netherlands) whose genomes were sequenced with Illumina NextSeq. Neighbour joining trees were constructed using PopPUNK.

Results: In total, 84 unique STs were found. For E. coli, ST131 predominated in 41% (n=82) of isolates, followed by ST10 in 12% (n=24), and ST38 with 4% (n=8) of isolates, following a similar pattern for all countries. In contrast, K. pneumoniae showed distinct clustering based on geographical origin, with ST405 and ST307 predominating in Spain, ST1537 in Switzerland, and ST405 in France. Fourteen unique blaESBL were detected, 9 genes from the blaCTX-M family, in 92% of isolates, and 5 genes from the blaSHV family, in 10% of isolates. For both species, blaCTX-M-15 was the most frequent (62% of all isolates). Phylogeny (figure 1) revealed clustering of K. pneumoniae isolates based on epidemiological setting (LTCF [in red and green] versus households [in blue]), while for E. coli a more heterogeneous pattern was seen.

Conclusions: In the MODERN-studies performed in six LTCFs and 71 households in 5 European countries, ESBL-producing E. coli has a similar ST distribution, while ESBL-producing K. pneumoniae demonstrates clustering based on geography and epidemiological setting. ESBL gene content shows a limited diversity, with large overlap between K. pneumoniae and E. coli, with a relatively even distribution across countries.
Figure 1. Core genome Neighbour Joining Trees for ESBL *E. coli* (left), and ESBL *K. pneumoniae* (right).

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Abstract 6631

Interactive access to current regional and national antimicrobial resistance data: the INFECT framework
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Background: Empirical antimicrobial therapy is a vital and widely applied concept in clinical medicine that relies on the availability of local antimicrobial resistance data and evidence-based guidelines. To support the availability of such data, we initiated the open-source project INFECT (INterface For Empirical antimicrobial Chemotherapy), aimed at informing and assisting clinicians with empirical antimicrobial treatments.

Materials/methods: NFECT is a web application that works with all major internet browsers, and a stand-alone mobile app. As data source for INFECT we used anonymized susceptibility test data from the Swiss Center for Antibiotic Resistance (anresis.ch). Each month, INFECT imports resistance information of the past 12 months, which is aggregated and shown in a substance-by-organism matrix. The matrix can be filtered by multiple characteristics. In order to handle the heavy computational load of combining filters, we have introduced a real-time data analytics service (RDA) that distributes load to multiple servers. To enhance the clinical usability of INFECT, we have developed an additional guideline module that combines third-party empirical antimicrobial treatment guidelines (e.g., Swiss national treatment guidelines) with the regional resistance data.

Results: Overall, by processing anresis.ch data our "INFECT by anresis.ch" web application now handles approximately 2 million antimicrobial resistance test results, from eight representative regions of Switzerland. Data can be filtered by users according to microbial (e.g., Gram stain), antimicrobial (e.g., substance class) or population (e.g., region, age) properties. Susceptibility is displayed as percentage in a coloured circle, with the circle colour showing the proportion of susceptibles while the circle size represents sample size (Figure). With RDA, aggregations for filters take only ~200ms. The additional guideline module provides a further diagnosis filter, which highlights expected pathogens and the guideline's recommended substances for the respective diagnosis.

Conclusions: With the INFECT framework it is now possible to routinely assist empirical antimicrobial therapies with state-of-the-art information technology using the latest epidemiological data and third party guidelines. Due to its flexible modular design, INFECT may be adjusted to other data sources, or extended with further modules as needed. The Swiss application "INFECT by anresis.ch" is available on infect.info and as mobile app for iOS and Android.

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Abstract 6634

Diagnostic yield of pharyngeal, axillary, inguinal and rectal swab samples for multidrug-resistant Gram-negative detection in intensive care patients

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Background: Colonization screening of multidrug-resistant microorganisms has been implemented in intensive care units (ICU) to prevent outbreaks and nosocomial infections. Multidrug-resistant Gram-negative bacteria (MDR-GNB) can be isolated from skin, respiratory and intestinal mucosa. Our aim is to assess pharyngeal (PSS), axillary (ASS), inguinal (ISS) and rectal (RSS) swab samples for recovering MDR-GNB in ICU patients at La Paz-Cantoblanco-Carlos III University Hospital (Madrid, Spain).

Materials/methods: Colonization screening was performed obtaining RSS, ISS, ASS and PSS on the same day, from January 2015 to December 2018. Samples were cultured on MacConkey agar supplemented with 4 mg/L of cefotaxime and/or CHROMID® CARBA SMART. Gram-negative isolates were identified using MALDI-TOF. Phenotypical and molecular methods were performed for bacterial resistance characterization.

Results: We analyzed 396 screening (1,584 samples) from 259 adult patients admitted to the burn ICU and post-operative ICU. MDR-GNB were isolated in 18% (72/396) of screening: 86% (62/72) from RSS, 55% (40/72) from ISS, 20% (15/72) from ASS and 19% (14/72) from PSS. The resistance mechanisms detected were: 46% extended-spectrum beta-lactamase (ESBL), 22% VIM, 14% OXA 48, 1% OXA 48+VIM producers and 17% MDR Acinetobacter baumannii. The isolates were 65% Klebsiella spp., 17% Acinetobacter baumannii, 14% Enterobacter spp., and 4% Serratia marcescens. Cumulative percentages of positive MDR-GNB are shown in table 1.

<table>
<thead>
<tr>
<th>MDR Acinetobacter baumannii (12)</th>
<th>GNB ESBL, VIM and/or OXA-48 producers (60)</th>
<th>Total MDR-GNB (72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RSS+ISS+ASS+PSS</td>
<td>100% (12)</td>
<td>100% (72)</td>
</tr>
<tr>
<td>RSS+ISS+PSS</td>
<td>100% (12)</td>
<td>100% (72)</td>
</tr>
<tr>
<td>RSS+ISS</td>
<td>93% (12)</td>
<td>95% (57)</td>
</tr>
<tr>
<td>RSS+PSS</td>
<td>100% (12)</td>
<td>88% (53)</td>
</tr>
<tr>
<td>RSS</td>
<td>83% (10)</td>
<td>86% (52)</td>
</tr>
<tr>
<td>ISS+PSS</td>
<td>58% (7)</td>
<td>70% (42)</td>
</tr>
<tr>
<td>ISS</td>
<td>25% (3)</td>
<td>61% (37)</td>
</tr>
<tr>
<td>ASS</td>
<td>8% (1)</td>
<td>23% (14)</td>
</tr>
<tr>
<td>PSS</td>
<td>41% (5)</td>
<td>15% (9)</td>
</tr>
</tbody>
</table>

Table 1: Yield of swab samples for recovering MDR-GNB.

Conclusions: RSS was the best sample for recovering MDR-GNB and, to a lesser extent, ISS for GNB ESBL/carbapenemase producers and PSS for MDR Acinetobacter baumannii. ASS did not contribute to the recovery of any MDR-GNB compared to other swabbed sites. Therefore, ASS cultures are not advisable for MDR-GNB colonization screening in ICU patients.

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An outbreak of Ralstonia pickettii bloodstream infection among paediatric leukaemia patients

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Background: Ralstonia pickettii is a non-fermentative Gram-negative bacillus and an opportunistic pathogen in both hospital settings and environment. It is waterborne and can survive in any kind of water sources and contaminate intravenous drugs and solutions used in hospitals. Herein an outbreak of Ralstonia pickettii related to contaminated saline infusion is reported.

Materials/methods: An outbreak occurred in Pediatric Hematology and Oncology Unit between 28.08.19-13.09.2019. Eleven leukemia patients affected by the outbreak were included. All these cases had a central venous catheter. They had minimum one positive blood culture for R. pickettii. Environmental samples such as tap water, saline, hand soap, total parenteral nutrition fluids were collected to find out the source of outbreak. Automated BactAlert 3D blood culture system (bioMerieux/France) was used for incubation of blood culture bottles. Bacterial identification and antibiotic susceptibility were performed with Vitek MS and Vitek 2 system (bioMerieux/France) respectively. Pulse Field Gel Electrophoresis (PFGE) was performed for all isolates.

Results: Eleven patients, seven of which were male and 4 were female and the median age was 6.5 years had positive cultures. All R. pickettii isolates were susceptible to ceftazidime, ciprofloxacin, imipenem, meropenem and resistant to aztreonam, cefepime, gentamicin, amikacin and piperacillin tazobactam. Four, 3, 2 and 2 cases were treated with meropenem, piperacillin tazobactam, cefepime and ciprofloxacin respectively. R. pickettii was also isolated in saline solution culture. PFGE showed that R. pickettii clones of saline solution and blood cultures were identical. The outbreak lasted in two weeks, and was controlled due to ending of usage and collecting back the saline solutions from the same manufactured batch.

Conclusions: A highly unusual outbreak of R. pickettii bloodstream infections occurred among 11 patients with leukemia. All of the clinical isolates were suggesting a sole source due to the identical PFGE pattern. To our knowledge, this is the first outbreak reported in pediatric leukemia patients. It’s important that clinicians and microbiology laboratory should be aware of the possibility of contamination of intravascular solutions with R. pickettii and infection control practices should involve sampling of these fluids directly, so further contamination and new cases can be prevented.

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Abstract 6638

Antimicrobial stewardship in Cambodia: the importance of antimicrobial point prevalence survey and lessons learned from the field

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Abstract third-party references: Diagnostic Microbiology Development Program, Defense Threat Reduction Agency

Background: Antimicrobial resistance in Cambodia is a significant concern with antimicrobial misuse a major driver. Diagnostic Microbiology Development Program works alongside physicians, nurses, microbiology staff, pharmacists and hospital management in provincial hospitals to improve rational prescribing through development and appropriate use of diagnostic bacteriology laboratories and antimicrobial stewardship (AMS) programs.

Materials/methods: Diagnostic bacteriology was established in Siem Reap Referral Hospital (SRRH) in June 2014. From December 2016-February 2017, SRRH undertook a hospital wide antimicrobial point-prevalence survey (PPS+). The tool (PPS+) also included information on use of microbiology laboratory, antibiotics prescribed prior to the survey, percentage of correct prescriptions and other parameters. Simultaneously, measurement of WHO standard defined daily doses (DDD) were calculated. Post survey, an AMS committee was established and three major interventions were developed and implemented. These were: surgical prophylaxis, restricted empirical treatment in emergency and directed treatment in all wards. A follow up survey was repeated 2 years later.

Results: A reduction in antimicrobial prescribing and an increase in microbiology specimen requests was observed. There was also a significant decrease in antimicrobial consumption during that period, which was reflected in an overall decrease in DDD.

<table>
<thead>
<tr>
<th>No. patients</th>
<th>2017</th>
<th>2019</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N Denominator</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Receiving antimicrobials day of survey (Excluding TB ward)</td>
<td>161</td>
<td>199</td>
</tr>
<tr>
<td>Receiving antimicrobials day of survey (Including TB ward, excluding TB medications)</td>
<td>161</td>
<td>211</td>
</tr>
<tr>
<td>Microbiology testing performed</td>
<td>21</td>
<td>161</td>
</tr>
</tbody>
</table>

Conclusions: Implementing an AMS program in a low-middle income country requires a systematic approach with effective management and multidisciplinary healthcare staff engagement. The PPS+ was key to providing data to healthcare staff, which was used as a learning tool as well as a powerful instrument for promoting engagement with these staff when proposing interventions for quality improvement. The interventions required engagement and training of healthcare staff, local guideline development, logistics, monitoring and feedback for these positive results.

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Assessment of the performance of the Vaginosis kit Aptima BV on Panther system from vaginal samples during a 3-month period at Nantes university hospital

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Background: In France, Bacterial vaginosis (BV) affects 20% of women. This pathology, benign for non-pregnant women, manifests increased concentrations of Gardnerella vaginalis, Mobiluncus sp and Atopobium vaginae paired with decreased level of Lactobacillus bacteria.

Over a three-month period, we gauged the impact of the Aptima BV kit on Panther for the detection of BV. The experiment was conducted using vaginal samples (VS), taken from non-pregnant women, above 18.

Materials/methods: From June to August 2019, vaginal samples (VS) were tested with the Aptima BV kit using Transcription Mediated Amplifications (TMA) to detect bacteria associated with BV, namely Gardnerella vaginalis and Atopobium vaginae with reduction of Lactobacillus sp. Results were compared to the Nugent score (more or less culture). A Nugent score (NS) of 3 or less was considered BV negative whereas a score of 7 or more was considered BV positive.

Results: 454 VS were included. 30 VS were excluded due to technical problems. 181 VS had a NS below 3, of which 171 with a negative test (94.5%). 47 samples showed a score between 4 and 6, 28 with a negative score (59.6%). Finally 49 samples displayed a score higher than 7. Among these, 45 with a positive test (91.8%).

After performing a curve analysis, among 91 VS, with various bacteria (excluding vaginal flora), the PCR results correspond to culture results in 84.6% of the cases. The correlation indexes are 94.3% and 71.4% respectively for VS with insufficient bacterial density (35 VS) and predominance of yeasts (21 VS). Sensitivity, specificity, positive and negative predictive value were 91.8%, 94.5%, 81.8%, 97.7% respectively.

Conclusions: Results provided by this new kit show a 90.4% correlation with NS and culture, excluding intermediary scores. This outcome demonstrates the analytical performance of this kit.

Among other benefits, this system would allow for faster analysis times (3h on average) and could provide a bacteriological help in the interpretation of intermediary NS, depending on the medical institution where it is used.

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Abstract 6641

Varicella zoster virus seroepidemiology in Caribbean Netherlands: implications for vaccine policy
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Background: In Caribbean Netherlands [CN], infection with varicella-zoster virus (VZV) is reported regularly in adolescents and adults. Among them, disease more often runs a severe course, including increased risk of complications such as pneumonia and encephalitis. Hence, the aim of this seroepidemiological study was to obtain insight into VZV susceptibility and its determinants in the general island populations of CN.

Materials/methods: In this cross-sectional population-based study, participants from Bonaire, St. Eustatius and Saba (n=1,829, aged 0-90 years, randomly selected via five age strata from the population registry) donated a blood sample and completed a health-related questionnaire, including characteristics possibly related to VZV disease. VZV-specific IgG antibodies were determined using a bead-based multiplex immunoassay. Risk factors for VZV seronegativity were analyzed using a logistic regression model.

Results: Overall seroprevalence in CN was 78% and did not differ between sexes. Estimates were lowest on St. Eustatius (73%) and highest on Bonaire and Saba (both 79%). Between different ethnic backgrounds, lowest overall seroprevalence was seen among people from the [former] Dutch overseas territories (71%), followed by Latin America and other non-Western countries (88%) and highest in those from Western countries (95%). Among people from the [former] Dutch overseas territories, seropositivity increased gradually with age, with 60% and 75% at ages 10 and 30 years, respectively, and ranging between 75-90% thereafter. Moreover, higher odds for seronegativity were seen among persons who were born in CN or resided there since early childhood as well as being a single-person household. Furthermore, the positive predictive value of self-reported history of VZV disease in this population appeared to be high (92%).

Conclusions: VZV susceptibility is relatively high among adolescents and adults in CN, in particular among those originating from the [former] Dutch overseas territories. This susceptibility pattern and the occurrence of severe varicella reflects the epidemiology on islands in tropical regions. These results ask for a swift consideration of routine varicella vaccination among islands populations – including a possible catch-up campaign in those susceptible – to reduce the burden of disease from VZV infection.

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Investigating the contribution of the RND-type efflux pump AdeABC in tolerance to chlorhexidine digluconate in Acinetobacter baumannii ATCC 19606

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Background: The RND-type efflux pump AdeABC in Acinetobacter baumannii is regulated by the two-component system AdeRS [1]. We have previously shown that A. baumannii ATCC 19606 adeRS knockout (∆adeRS) does not express adeABC and reveals increased susceptibility to various antibiotics. Furthermore, overexpression of RND-type efflux pumps contributes to triclosan resistance in Acinetobacter baumannii [2]. In Klebsiella pneumoniae, efflux pumps mediate resistance to chlorhexidine digluconate (CHX), an antiseptic used for wound and pre-operative skin disinfection, mouthwash and hand washing [3]. In this study, we have investigated the contribution of AdeABC to CHX tolerance in A. baumannii.

Materials/methods: ∆adeRS was produced through a markerless deletion. Minimal inhibitory concentrations for CHX of 19606 wild-type (wt) and ∆adeRS were determined by microbroth dilution in Mueller-Hinton broth. For a time-kill assay, bacterial strains were grown in Luria-Bertani medium until mid-log phase. CHX was added to a final concentration of 16 mg/L. 1 mL samples were taken before CHX addition and after 30, 60 and 180 minutes of CHX exposure. Cells were pelleted and washed with 0.9% sterile saline solution. CFUs were counted from appropriate dilutions on Mueller-Hinton plates after 24h-incubation at 37°C.

Results: Deletion of adeRS produces a four-fold decrease in the MIC for CHX (wt: MIC: 16 mg/L; ∆adeRS: MIC: 4 mg/L). In the time-kill assay, CFUs of 19606 ∆adeRS decrease under CHX exposure until reaching 1% of the initial amount after 180 min. CFUs of 19606 wt show an initial decrease, but begin increasing after 30 min until reaching 270% of the initial amount of CFUs after 180 min [Figure 1].

Conclusions: This study suggests that adeABC expression may enable A. baumannii ATCC 19606 to survive chlorhexidine digluconate exposure. Therefore, addressing efflux pump regulators could be a possibility to increase disinfectant susceptibility and impair persistence of A. baumannii in the hospital environment.


Figure 1. Time-kill curves with chlorhexidine digluconate (16 mg/L)

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Abstract 6643

**Local anti-Pseudomonas IgY therapy prevents pyelonephritis in a novel murine experimental Pseudomonas aeruginosa urinary tract infection model**

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**Background:** Previously, gargling egg yolk antibodies (IgY) targeting *Pseudomonas aeruginosa* (PA) reduced chronic infections in patients with cystic fibrosis. Spinal cord injured (SPI) patients are in risk of recurrent and chronic urinary tract infections (UTIs), due to intermittent catheterization. The chronic UTIs indicates biofilm growth and risk of developing antibiotic resistance. Therefore, our aim was to investigate the effect of IgY in a UTI model in mice.

**Materials/methods:** Female BALB/c mice (n=50) and PA PAO1 were used for the experiments. Firstly, 15 mice received 5x 10^6 CFU and 18 mice received 2.5x 10^7 CFU PA in the bladder through a temporarily inserted urethral catheter. Mice were sacrificed at day 1, 6, 9 or 13 after infection. In the second experiment 27 mice were injected with 5x 10^7 CFU PA in the bladder, and randomized in to three IgY intervention groups and one control group. IgY 10% was administered through a temporarily inserted catheter at day 0, 1 or 3, and all mice were sacrificed at day 7 after infection. Experiments were evaluated by means of quantitative bacteriology in the urine, the bladder and the kidneys.

**Results:** In general, quantitative bacteriology was non-statistically increased in the urine, bladder and kidneys in the high as compared to the low infectious dose group. However, there were more mice with a positive urinary (6 vs. 2, day 6, p<0.05, and 7 vs. 3, day 9, p<0.025), bladder (4 vs. 0, day 6, p<0.005) and kidney culture (4 vs. 0, day 6, p<0.005) in the 2.5x 10^7 CFU group. There was no significant difference between the IgY intervention and the control group regarding quantitative PA. However, in the control group 5 out of 7 mice (71.4%) had PA in the kidneys, compared to 5 out of 20 mice (25%) in the three intervention groups pooled (p≤0.03).

**Conclusions:** This study indicates that topical anti- *Pseudomonas* IgY have a preventive effect regarding ascending PA pyelonephritis. In SPI patients using intermittent catheterization, adjunctive IgY therapy seems a promising antibiotic reducing strategy. Accordingly, similar strategy may be attractive in a selected group of patients with urinary catheters.

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Characterisation of a cfr gene variant in multidrug-resistant (MDR) livestock-associated methicillin-resistant Staphylococcus aureus (LA-MRSA), isolated from Italian pig herds

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Background: Linezolid belongs to the oxazolidinone family, an antibiotic class classified among Highest Priority Critically Important (HPCIA) for humans. Gram-positive microorganisms, as methicillin-resistant Staphylococcus aureus (MRSA) can develop resistance to linezolid by several mechanisms, including the acquisition of the plasmid-borne cfr gene. cfr encodes a methyltransferase mediating multidrug resistance (MDR) towards phenicols, lincosamides, oxazolidinones, pleuromutilins, streptogramin A and 16-membered macrolides.

Materials/methods: Three cfr-positive Livestock-Associated (LA)-MRSA, with two of them belonging to Clonal Complex (CC)1 and one to CC398, detected in different Italian pig herds (2008-2011), in the frame of the EMIDA-ERANET project (acronym “LA_MRSA”), were retrospectively in-depth characterized by WGS (Illumina technology). Isolates were previously tested for their antimicrobial susceptibility by broth microdilution, using a panel of drugs recommended by EFSA. Results were interpreted according to EUCAST epidemiological cut-offs. Regarding WGS analysis, de novo assembled scaffolds were analysed with different bioinformatic tools to detect accessory resistance genes and plasmid replicons (https://cge.cbs.dtu.dk/services/). Presence of cfr mutations was investigated by mapping reads to the reference sequence AM408573 (S. warneri) and “variant calling” was performed using bwa mem v0.7.12, samtools v1.7 and IGV 2.0.1.

Results: The three LA-MRSA were phenotypically MDR, displaying a common resistance pattern to beta-lactams, amphenicols, fluoroquinolones and tetracyclines. 2/3 isolates were also macrolide (erythromycin), lincosamide (clindamycin) and pleuromutilin (tiamulin) resistant. All isolates tested cfr-positive, but just one CC1 LA-MRSA was phenotypically linezolid-resistant. Apart from this exception (Table 1), MDR phenotypes were confirmed by their genetic background. Variant calling analysis indicated that both linezolid-susceptible isolates presented a cfr gene with a single T nucleotide deletion (position 384), whereas linezolid-resistant LA-MRSA harboured a cfr sequence identical to the reference one. This mutation causes a reading frame-shift and consequently a truncated protein.

Conclusions: This study describes for the first time CC1 and CC398 LA-MRSA presenting different cfr variants and linezolid-resistant phenotypes. Considering its potential transmissibility of cfr and increasingly isolation in animal productions in Europe, these preliminary results have significant Public Health implications and backdate cfr presence in LA-MRSA from Italian pigs at least to 2008. Further studies are needed to better understand cfr characteristics and their relationships to different resistance patterns.

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Abstract 6645

**The impact of delayed analysis of positive blood cultures on the performance of short-term culture followed by MALDI-TOF MS**

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**Abstract third-party references:** On behalf of Alexander Johnsson.

**Background:** Rapid identification of bacteria is crucial for early appropriate antimicrobial treatment in sepsis patients. Transport time of blood culture (BC) bottles to the laboratories has been one of the major problems causing unnecessary delay in total turnaround time. Therefore, many central laboratories establish so called satellite BC systems and place them in clinics and other hospitals. BC bottles can therefore be incubated right after sampling. However, the positive BC bottles still need to be transported to the clinical microbiology laboratory for analysis. The aim of this study was to investigate how delayed analysis of positive BC bottles would affect the short-term culture followed by Maldi-ToF MS method.

**Materials/methods:** To simulate the effect of transportation and delayed analysis of BC bottles, 51 positive blood culture bottles were left to incubate for 0, 2, 4 and 24 hours at room temperature (RT). After each time-interval, a 2-4-hour short-term culture followed by Maldi-ToF MS was performed. In addition, 257 prospective clinical positive blood culture bottles were analysed with the same method after a 24 h incubation at RT.

**Results:** In the simulated samples, all (120/120) Gram-negative bacteria (GNB) and 77/84 (92%) Gram-positive bacteria (GPB) were accurately identified at species level after a 2-hour short-term culture, regardless of the duration of simulated transport time. In the clinical samples, 100/116 (86%) GNB and 44/141 (31%) GPB were accurately identified at species-level after a 2-hour short-term culture. When the contaminants were excluded, 39/71 (56%) of the GPB could be identified after 2h. After a 4-hour short-term culture, 112/116 (96%) of GNB and 107/141 (76%) GPB were accurately identified at species-level. Of the clinically relevant GPB, 68/71 (96%) were identified at species-level after 4 h.

**Conclusions:** Short-term culture followed by Maldi-ToF can provide fast and accurate results for identification of clinically relevant bacteria, despite long transportation times from satellite laboratories. The method can be used for identification of microorganisms from positive blood cultures transported from satellite BC systems.

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First report of colistin resistance in *Salmonella* spp. isolated from fresh minced meats and poultry faeces from primary production phase in Bosnia and Herzegovina

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Background: Colistin has been used in animal production plants in several countries for therapeutic, prophylactic and growth promotion purposes. Colistin is clearly associates with selection of resistant strains in livestock which can spread from animals to humans by direct contact, or indirectly, by the food chain.

Materials/methods: Thirty-two *Salmonella* spp. strains were isolated. Food samples and poultry faeces in primary production phase were analysed according to Rulebook which is in accordance with the International Standards (EN ISO 6579-1:2018) and Manual for Reporting 2018 - Data on antimicrobial resistance Decision 2013/652/EU. The isolates were identified by colony morphology, standard biochemical and serological tests. Antimicrobial sensitivity testing was carried out using disk-diffusion and minimal inhibitory concentration (MIC).

Results: Among 32 *Salmonella* spp. strains, seven were isolated from food samples – fresh minced meats from the markets, and 25 from the poultry faeces. Using agar dilution method test, seven (21.9%) *Salmonella enteritidis* strains were resistant to colistin, two (out of 7; 28.6%) from fresh minced meats and five (out of 7; 71.4%) from poultry faeces. MICs values for seven colistin-resistant isolates were in the range 4 to 8 µg/mL. Six isolates (out of seven) were resistant to cefazolin (85.0%) and one isolate were resistant to ciprofloxacin and nalidixic acid with the MIC values of 0.25 and ≥128 µg/mL.

Conclusions: In food animals, colistin is frequently used as oral medication for prevention and treatment of gastrointestinal tract infection. There is need for careful monitoring of colistin usage in animal husbandry, as well as to seek for alternative, effective, less expensive antibiotics, competitive with colistin in the treatment of animal gastrointestinal infections. Considering the importance of colistin usage in control of animal infections, and large use of this drug in animal production, colistin-resistance prevalence in *Salmonella* spp. of animal origin have to be monitored more closely. Detection mcr genes should be introduced as well.

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Mitigating the fitness costs of carbapenemase-encoding clinical plasmids in Escherichia coli: Piggy-backing on environmental adaptation

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Background: Acquisition of carbapenemase-encoding plasmids limits treatment options for Gram-negative infections. Resistance plasmids often decrease bacterial fitness in unselective environments, but adaptive processes may mitigate such plasmid cost. Investigating the mechanisms improving plasmid-host relationships is thus crucial for understanding the selection and spread of antibiotic resistance in clinical isolates.

Materials/methods: Two plasmids encoding carbapenem-resistance (bla\_NDM-1 and bla\_VIM-1) were respectively transferred from Klebsiella pneumoniae and Escherichia coli into a ST537 E. coli uropathogenic isolate. Plasmid-carrying and -free strains were evolved for ~300 generations in four parallels each in antibiotic-free medium. Evolved populations were whole genome sequenced and plasmid-cost was measured in head-to-head competitions for ancestral, evolved clones and knockout mutants.

Results: An initial fitness cost of 5% was observed for both plasmids. These costs were fully, and partially mitigated after experimental evolution in ST537 E. coli hosts harbouring bla\_VIM-1 and bla\_NDM-1 encoding plasmids, respectively. Independently of plasmid carriage, all evolved populations displayed chromosomal mutations in the same genes: crp, cpdA, arcA and arcB, previously associated with environmental adaptation. The bla\_VIM-1 plasmid still imposed a cost in parental and ΔarcA Keio collection E. coli strains but not on the ΔcpdA strain.

Conclusions: Mutations in global transcriptional regulators mitigate fitness costs of carbapenemase-encoding plasmids, suggesting that niche-adaptation can affect the plasmid-host potential of E. coli lineages. Our findings provide an explanatory frame-work for understanding why certain E. coli lineages appear to be predisposed to the acquisition of specific antibiotic resistance determinants and plasmid backbones.

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Toxigenic Corynebacterium ulcerans isolated from an Italian hunter

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Background: Corynebacterium ulcerans (C. ulcerans) has become an emerging pathogen today. In many European countries, cases of respiratory diphtheria and systemic infections have been increasing in recent years. Here we report the clinical course of a man affected by C. ulcerans diphtheritis with confirmed production of diphtheria toxin.

Case report: In late December 2018 a 65 year-old Italian man had been complaining of dysphonia, pharyngeal pain and mild fever for 5 days; symptoms worsened over a few hours with the onset of dyspnea and inspiratory retraction. He was a hunter and owned three dogs: one had died two days before and another one had cutaneous ulcerations; all dogs were subjected to swabs, that resulted negative for C. ulcerans. The patient was transported to the intensive care unit (ICU) of a tertiary care centre in Italy [Brescia]. Blood exams showed neutrophilic leukocytosis (24500 cell/μL, 93.5%). An arterial blood gas analysis was performed and revealed PO2 57 mmHg. Chest radiography was negative. Massive white and yellowish exudate (pseudomembrane) was observed in tracheal lumen through the bronchoscope. CT scan of the neck showed pharyngeal and soft palate edema, so the patient underwent surgical tracheostomy. Suspecting respiratory diphtheria infection, penicillin was administered and pseudomembranes were removed as much as possible. Vaccination history of the patient was unknown. Cultural exam of pseudomembranes revealed a toxin-producing strain of C. ulcerans. Diphtheria antitoxin (100,000 IU) was administered and in the following days the patient presented respiratory improvement. One week after he complained an acute chest pain with elevated troponin levels and progression of renal failure: cardiovascular magnetic resonance revealed an acute myopericarditis. Two months after, a progressive neuromuscular weakness developed and a diagnosis of polyneuropathy was done. After one month of intensive care the patient was discharged from the ICU.

Conclusions: Polyneuropathy, myocarditis and renal failure are well described complications caused by exotoxin-producing strains of Corynebacterium. In fact, diphtheria toxin is the major virulence factor of toxigenic C. ulcerans strains. This case report supports the idea that pathogenicity of corynebacteria is a multifactorial process; early diagnosis is essential for management and implementation of control measures.

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Abstract 6652

**Predictive value of sepsis scores for in-hospital mortality in patients with left-sided infective endocarditis**

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**Background:** Unlike other bacterial infectious diseases, death related to infectious endocarditis (IE) are likely to be associated to non-septic conditions, such as heart failure or embolization. However, pilot studies have suggested that sepsis scores have good accuracy in IE Patients. The aim of our study was to evaluate the accuracy

**Materials/methods:** We prospectively enrolled 517 patients diagnosed with left-sided IE from 2010 to 2019 admitted to a tertiary cardiology hospital. Inclusion criteria were age > 18 years and “possible” or “definite” IE according to Modified Duke Criteria. Patients in use of intravenous antibiotics for more than 3 days before enrollment were excluded. Univariate and multivariate analysis were performed to test association between clinical and laboratory results and in-hospital mortality. The sepsis scores evaluated were: SIRS, severe sepsis, qSOFA and SOFA. Receiver operating characteristic curves (ROC) were constructed to assess the accuracy of sepsis scores for prediction of in-hospital mortality.

**Results:** Patients included had median age of 57 years (range 18 to 87), 65% were male, 435 (84%) had pre-existing heart valve disease, and the overall mortality was 28%. Microorganisms most frequently isolated were: Streptococcus spp. (36%), Enterococcus spp. (10%) and S. aureus (9%). After multivariate analysis variables evaluated at admission that were associated with in-hospital death were: heart failure NYHA III/IV (aOR 2.37, CI95% 1.497-3.751, p<0.001) embolism (aOR 1.91, CI95% 1.091-3.324, p=0.022), diabetes mellitus (aOR 2.45, CI95% 1.490-4.345, p=0.001), low hemoglobin level (aOR 0.860, CI95% 0.773-0.956, p=0.005) and SOFA≥2 (aOR 3.26, CI 95% 2.056-5.137, p<0.001). The accuracy for sepsis scores to predict in-hospital mortality were: qSOFA (ROC 0.601, CI95% 0.522-0.681) and SOFA (ROC 0.699, CI95% 0.602-0.756). A sub-group analysis in patients with and without pre-existing valve disease for SOFA showed ROC curve of 0.627(CI95% 0.563-0.690) and 0.775(CI95% 0.594-0.956), respectively.

**Conclusions:** Overall, qSOFA and SOFA at admission presented low accuracy to predict in-hospital death in patients with IE. However, SOFA≥2 could be a useful predictor for mortality in patients with IE without preexistent valvar disease.

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Role of TAC1 orthologs in Candida auris azole resistance

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Background: Candida auris has emerged as a novel yeast pathogen in all continents with ability to cause nosocomial outbreaks and to develop antifungal resistance. Acquired azole resistance is a hallmark of most C. auris isolates. Mutations in hotspots of the azole target gene ERG11 have been associated with azole resistance in C. auris. However, other non-ERG11-related mechanisms of resistance to azoles may be involved, such as overexpression of drug transporters including ABC-transporters Cdr1 and Cdr2. Indeed, overexpression of CDR1 has been observed in some azole-resistant C. auris isolates. In C. albicans, CDR1 expression is controlled by the transcription factor Tac1 and azole resistance has been linked to gain-of-function mutations in TAC1. In this work, we investigated in C. auris the role of the TAC1 ortholog in azole resistance.

Materials/methods: Two putative TAC1 orthologs of C. auris were identified by nBLAST with C. albicans (30% homology). Deletion of these two TAC1 orthologs was performed by Crispr-CAS9 in an azole-resistant C. auris isolate (South American clade) not carrying ERG11 mutations. We also complemented a TAC1-deleted C. albicans mutant by the two TAC1 C. auris orthologs. Susceptibility to azole drugs (fluconazole, voriconazole) was tested by microbroth dilution method (CLSI protocol) and spotting assay. CDR genes expression in C. auris was analyzed by real-time reverse transcription PCR (RT-PCR).

Results: Deletion of both putative TAC1 genes in C. auris resulted in modest decrease of resistance to both fluconazole and voriconazole. Expression of CDR1 and CDR2 in the TAC1-deleted mutant was similar to the parental wild-type strain under basal conditions and after induction by fluconazole. Complementation of C. albicans-TAC1 by the two C. auris-TAC1 orthologs did not restore wild-type phenotype in C. albicans.

Conclusions: This work suggests that, contrarily to observations in C. albicans, the C. auris TAC1 orthologs have only a modest role in azole resistance of this C. auris isolate. Other azole resistance mechanisms should be involved and deserve further investigations.

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Abstract 6662

Emerging piperacillin-tazobactam resistance in Indian hospital settings
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Background: Resistance to beta-lactam antibiotics is effectively tackled by the use of beta-lactam/beta-lactamase inhibitor combinations. However, there is increasing evidence for emergence of resistance against one of the promising combination, piperacillin/tazobactum (TZP) worldwide. Recent report showed hyperproduction of blaTEM-1 causing resistance to piperacillin/tazobactam in Escherichia coli (Hansen et al., Zhou et al., 2019). Gram negative bacteria P. aeruginosa and A. baumannii have been reported to show resistance to TZP in India in similar studies (Anuradha et al., 2007). Here we present comprehensive TZP non-susceptibility data over three years.

Materials/methods: Antimicrobial susceptibility data from about 18674 isolates was collected from 2016-2019 through the AMR surveillance network of Indian Council of Medical Research (ICMR) from 20 tertiary care hospitals across the country. Antibiotic sensitivity and phenotypic assays of resistance are carried out as per the standard protocols of Bacteriology SOP of ICMR. MIC/DD data of the isolates is entered into the iAMRSN data management portal developed by ICMR and analyzed location-wise or specimen-wise through the data analysis system. Data from Gram negative organisms A. baumanii, K. pneumoniae, P. aeruginosa and E. coli that showed increasing resistance to TZP are given here.

Results: Our data showed high percentage of TZP non-susceptibility in gram-negative bacteria especially in ICUs. A. baumanii showed highest percentage non-susceptibility in ICU [92%] followed by K. pneumoniae [73%] and E. coli [55%]. The trend of percentage non-susceptibility showed was significant increase in A. baumanii [72-83%], from 2016-2018, which is of great concern [Fig 1].

A. baumanii showed higher non-susceptibility in isolates from lower respiratory tract (LRT) specimen, deep & superficial infections and cerebrospinal fluid (CSF) specimen, while K. pneumoniae showed higher non-susceptibility in isolates from CSF and blood. Region-wise analysis of data revealed that percentage non-susceptibility in A. baumanii [86-92%] and K. pneumoniae [72-78] was consistently high in Northern part of the country.

Conclusions: Increasing prevalence of piperacillin/tazobactam resistance in Indian hospital settings warrant implementation of better stewardship efforts in rational use of TZP. Antibiotic use and resistance rate was correlated in a retrospective observational study (Cusini et al., 2018) for TZP in E. coli emphasizing need for urgent interventions to optimize antibiotic prescribing.

Figure 1: Trend of Piperacillin-tazobactum Non-susceptibility

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Detection rates of the bacterial causes of gastroenteritis using a multiplex molecular assay in the South-African private sector

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Background: Infectious diarrhea remains a significant cause of morbidity and mortality globally. Many of the bacterial pathogens implicated in the causation of acute infectious diarrhea are fastidious in nature and stool cultures are positive in only about 2-4% of cases, consequently multiplex molecular panels are emerging as useful diagnostic tools.

Materials/methods: A 5 year retrospective analysis was performed on clinical stool specimens submitted for bacterial gastroenteritis multiplex PCR testing (BD MAX™ Enteric Bacterial Panel, Becton Dickinson, United States) performed at Ampath private laboratories, South Africa. Where available, stool culture results were compared to that of PCR.

Results: Of the 1498 stool specimens submitted for PCR testing, 305 (20%) tested positive for a pathogen. Campylobacter was the most commonly identified (42%), followed by Salmonella (24%), Shigella/Enteroinvasive E. coli (21%), Shiga toxin-producing E. coli (9%), Enterotoxigenic E. coli (5%), and Yersinia enterocolitica (4%). Of the positive samples, 223 (73%) were submitted for culture. An additional 54 (57%) Campylobacter spp., 16 (30%) Salmonella spp., 36 (78%) Shigella spp./EIEC, and seven (78%) Yersinia enterocolitica were detected by PCR. None of the 21 PCR positive STEC isolates were identified by culture. Campylobacter species were cultured from 41 specimens (34 Campylobacter jejuni, six Campylobacter coli, and one Campylobacter species). Of the campylobacters isolated, 39% were susceptible to ciprofloxacin, 97% to erythromycin, and 46.3% to tetracycline. Non-typhoidal Salmonella were cultured from 37 specimens with 97.3% susceptible to ampicillin and ceftriaxone and 100% susceptible to ciprofloxacin and cotrimoxazole. Shigella species were cultured from 10 specimens PCR positive for the ipaH gene of which 50% were susceptible to ampicillin, 30% to cotrimoxazole and all were susceptible to ceftriaxone and ciprofloxacin.

Conclusions: Multiplex molecular panels are valuable tools for the identification of stool pathogens, many of which remain undetected by culture. Drawbacks include cost, lack of susceptibility data and species level identification. Azithromycin remains a valuable treatment option for the empiric management of diarrhoea due to Campylobacter species. Ciprofloxacin and ceftriaxone remain good empiric choices for the management of disease due to Salmonella and Shigella species. Use of multiplex molecular panels should be limited to patients with severe disease.

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Abstract 6666

Genetic characterisation of multidrug-resistant *Klebsiella pneumoniae* harbouring colistin resistance gene *mcr-1* from North India

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**Background:** Multi drug resistant (MDR) *Klebsiella pneumoniae* accounts for a significant proportion of nosocomial infections. Colistin is considered as the drug of last resort for treatment of infections caused by MDR *K. pneumoniae*. The emergence of plasmid encoded mobile colistin resistance (*mcr-1*) gene has breached the barrier. Moreover, association of *mcr-1* gene with other resistance markers is a matter of concern. Here we report genetic characterisation of nineteen *mcr-1* producing *K. pneumoniae* isolates.

**Materials/methods:** The study investigated 19 *mcr-1* harbouring *K. pneumoniae* recovered from patients. Minimum inhibitory concentration was determined using broth microdilution method. The presence of various resistance markers and virulence factors were detected by PCR. Pulsed field gel electrophoresis (PFGE) and MLST was done to analyse the genetic relatedness among *mcr-1* producers. Conjugation assay was performed for Strains harboring *mcr-1* and *bla*$_{NDM}$. S1-nuclease-PFGE followed by Southern blotting was done to determine their genetic location.

**Results:** Among 19 *mcr* isolates; *bla*$_{NDM}$ was present in five isolates, all the strains harboured multiple resistance traits. Virulence factors were also present in all isolates. Diverse PFGE profiles were found among *mcr* producers and MLST revealed presence of eight unique STs. Conjugation assays showed that *mcr-1* and *bla*$_{NDM}$ containing plasmid could be transferred into *Escherichia coli* J53. S1-PFGE revealed that strains carried multiple plasmids, Southern blot showed that *mcr-1* and *bla*$_{NDM}$ gene were present on plasmid and chromosome simultaneously or alone.

**Conclusions:** Co-occurrence of *mcr-1* with *bla*$_{NDM}$ and other resistance genes in *K. pneumoniae* indicates towards evolution of multi-drug resistance to an extent where no treatment options are available against infections caused by such organisms.

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Evaluation of various stool collection devices for gut microbiome analysis

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Background: Various stool collection devices are available in the market. However, it is necessary to evaluate their user friendliness for customers and effectiveness for the use in lab. Currently there is no such comparative data available for choice of tools, which can guide customers towards better understanding of available devices. Hence, at Phylo bioscience we decided to evaluate three different stool collection devices for their ability of preserving microbial DNA and analyze relative abundance of microbial copy numbers.

Materials/methods: Three different collection vials were used for evaluation, 1: TOTAL-FIX stool collection vial (Medical Chemical Corporation (MCC), CA, USA), 2: C&S Stool Transport Vials (Meridian bioscience, USA), 3: µb-eNAT (Copan Italia, Brescia, Italy). Stool sample was donated by six anonymous volunteers by using these 3 collection devices. Volunteers were asked to score the user friendliness of each device. Samples were stored at room temperature for 24hr. DNA extraction was carried out by using KingFisher Flex DNA extraction instrument based on magnetic beads technology. DNA quantification was performed by using Qubit fluorometer. Extracted DNA were normalized for 1 nano gram per micro liter and were further analyzed for selected gut microbes. By using quantitative real time PCR (qRT-PCR) following bacterial targets were analyzed Bifidobacterium spp., Eubacterium spp, Bacteroides spp., Bacteroides vulgatus, Bacteroides ovatus, Bacteroides uniformis, Bacteroides thetaiotaomicron, Bacteroides dorei and endogenous control.

Results: The µb-eNAT stool collection device received better average score for user friendliness. As per the volunteer’s comments, the collection device uses a swab and low volume of preservation media which makes it easy to handle and less risky. qRT-PCR results for various bacterial targets did not show any significant deference between all three devices, figure shows result from one donor out of six.

Conclusions: Microbial copy number did not show any significant difference between devices, however µb-eNAT had better user friendliness score. Additional time points at room temperature should be accessed for the further evaluation of the devices.

![Graph showing comparative abundance of microbial gene copy numbers in various stool collection devices by qRT-PCR](image)

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Abstract 6669

**Yersinia enterocolitica-associated diarrhoea: descriptive epidemiology in a low-prevalence setting (Barcelona, Spain) from January 2016 to October 2019**

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**Background:** *Yersinia enterocolitica* is widespread in nature and its infection in humans is mostly considered as a zoonotic disease. Reservoirs range from mammals, avian and cold-blooded species, but most of the human pathogenic serogroups, principally O:3 and O:9, are recovered from porcine sources. The main objective is to describe the epidemiology of *Yersinia enterocolitica* diarrhea diagnosed in the Microbiology Laboratory of the Vall d’Hebron University Hospital in Barcelona in a 4-year period.

**Materials/methods:** From January 2016 to October 2019, all stool samples asking for bacterial diarrheal etiology were included. Conventional culture with selective plates, included CIN agar, was conducted. Combined biochemical and mass spectrometry methods were applied to species level identification. Specific anti-sera were used to serogroup investigation. Demographics (age, sex), travel report, seasonality and co-infection with other pathogens were registered.

**Results:** During the study period, 55,463 stool cultured samples were included and 47 *Yersinia enterocolitica* isolates were recovered from 46 patients [24 male and 22 female; median age 6.5 years old (range 0.5-79). Most cases [61%] occurred in patients aged ≤ 10 years old. Global frequency of isolation was 0.85 ‰. An increased frequency was observed: from 0.59 ‰ in 2016 to 1.49 ‰ in the 2019 period. Serogroup O:3 was the most frequent [65.2%] during all the study period. Minority serogroups [O:5, 6.4%; O:8, 4.3%] were only isolated in 2019. Most of the isolations [76%] occurred in spring and summer seasons. Six [13%] presented co-infection with other diarrheal pathogens: *Campylobacter jejuni* (2/6), *Salmonella typhimurium* (2/6) and *Dientamoeba fragilis* (2/6). Detailed data are shown in the table. Non previous travel history was reported.

**Conclusions:** *Yersinia enterocolitica* is a low prevalence diarrheal agent in our setting involving 0.85 ‰ of stool samples cultured. Nevertheless, increment prevalence was observed in the study period: in 2019 was 2.5 folds than 2016. According to the literature, *Yersinia enterocolitica* infection was more frequent in children and infants and serogroup O:3 was the most prevalent. Contrary to previously described, no serogroup O:9 was detected but we found more incidences in spring and summer seasons than in the coldest ones. No travel-related episode was detected.

<table>
<thead>
<tr>
<th>Period</th>
<th>Stool samples</th>
<th><em>Y. enterocolitica</em> positive cultures, Number (%)</th>
<th><em>Y. enterocolitica</em> serogroups (number)</th>
<th>Number of patients with <em>Y. enterocolitica</em> isolation</th>
<th>Age (years old, median range)</th>
<th>Gender (Male/Female)</th>
<th>Seasonality, number</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>13477</td>
<td>8 (0.59)</td>
<td>O:3 (6) Non-typable (2)</td>
<td>8</td>
<td>6.5 (6.0-44)</td>
<td>4/4</td>
<td>Winter 3 Spring 4 Summer 0 Autumn 1</td>
</tr>
<tr>
<td>2017</td>
<td>13780</td>
<td>8 (0.56)</td>
<td>O:3 (5) Non-typable (1) Not determined (2)</td>
<td>8</td>
<td>5.5 (1-60)</td>
<td>5/3</td>
<td>Winter 1 Spring 4 Summer 3 Autumn</td>
</tr>
<tr>
<td>2018</td>
<td>14793</td>
<td>11 (0.74)</td>
<td>O:3 (8) Non-typable (2) Not determined (1)</td>
<td>11</td>
<td>5 (0.8-72)</td>
<td>5/6</td>
<td>Winter 1 Spring 5 Summer 5 Autumn 0</td>
</tr>
<tr>
<td>2019 (until October)</td>
<td>13413</td>
<td>20 (1.49)</td>
<td>O:3 (11) O:5 (3) O:9 (2) Non-typable (2) Not determined (1)</td>
<td>19</td>
<td>25 (0.5-79)</td>
<td>10/9</td>
<td>Winter 1 Spring 7 Summer 7 Autumn 4</td>
</tr>
<tr>
<td>Total</td>
<td>55463</td>
<td>47 (0.85)</td>
<td>O:3 (30) O:5 (3) O:8 (2) Non-typable (7) Not determined (4)</td>
<td>48</td>
<td>6.5 (0.5-79)</td>
<td>24/22</td>
<td>Winter 6 Spring 20 Summer 15 Autumn 5</td>
</tr>
</tbody>
</table>

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Abstract 6672

**Rapid MALDI-TOF MS-based pneumococci confirmation by a standardised semi-automated workflow**

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**Background:** Rapid and reliable differentiation of the clinically important pneumococci from other Streptococcus mitis group streptococci (SMGS) using the proven bile solubility test (BST) remains challenging for routine laboratories. MALDI-TOF mass spectrometry (MS) may allow a standardized rapid workflow with easy and objective result interpretation. In this multi-center study, we investigated the performance of a standardized and (semi-) automated MALDI-TOF MS-based direct-on-target BST using a novel tool set available for rapid routine microbiological applications.

**Materials/methods:** Overnight plate culture colonies of in total 21 S. pneumoniae isolates belonging to 7 distinct serotypes (3, 6B, 8, 9V, 19A, 19F and 23F) and 9 non-S. pneumoniae isolates (3 S. mitis, 3 S. oralis, 3 S. pseudopneumoniae) as controls were suspended in water. 1-µL aliquots were transferred to a MALDI Biotarget96 (Bruker Daltonik), dried and subsequently subjected to direct-on-target bile acid lysis by adding 4 µL of a 7.5% sodium deoxycholate solution followed by incubation at 35 °C for 60 minutes under controlled humidity conditions using a dedicated incubation chamber prototype. For growth controls, 4 µL water were added before incubation. Liquid removal of supernatant and subsequent washing step was performed using a dedicated liquid removal stamp prototype. Analysis was performed using the MALDI Biotyper® (Bruker Daltonik) and a dedicated software prototype. To test for robustness and reproducibility of the workflow, the bacterial isolate panel was tested at two different sites.

**Results:** 100% sensitivity and 100% specificity were obtained at both test sites for classification of the tested pneumococci and other SMGS with 60 minutes incubation. All tested S. pneumoniae serotypes were correctly confirmed as pneumococci using this rapid and easy to handle method.

**Conclusions:** Using dedicated semi-automated hardware tools, software and standardized workflows allows the application of a rapid and accurate MALDI-TOF MS based BST in routine laboratory environments with minimal hands-on time providing an objective and traceable evaluation.

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Identifying the drivers of multidrug-resistant *Klebsiella pneumoniae* at a European level

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**Background:** Beta-lactam- and in particular carbapenem-resistant Enterobacteriaceae represent a major public health threat. Despite variation in resistance rates both across geographical settings and over time, there is only limited understanding of the underlying drivers: while antibiotic consumption is a primary driver of resistance, countries with similar consumption can have different resistance rates. Improved understanding of other possible drivers such as consumption structure, particular hospital vs. community, can aid in combatting this public health threat.

**Materials/methods:** We developed a transmission model of cephalosporin- and carbapenem-resistant *Klebsiella pneumoniae* based on antibiotic consumption and demographic data from eleven European countries and fit the model to resistance rates for *Klebsiella pneumoniae* across countries. The impact of consumption structure and nosocomial transmission on resistance was then assessed in counterfactual analyses.

**Results:** Based on reported consumption data, the model could simultaneously fit the prevalence of extended-spectrum beta-lactamase-producing and carbapenem-resistant *Klebsiella pneumoniae* (ESBL and CRK) across eleven European countries over eleven years (Figure). The model fits suggest thus that hospital transmission rates and consumption patterns can explain the large between-country variability of resistance. Based on this fit, a counterfactual analysis suggested that reducing nosocomial transmission and antibiotic consumption in the hospital would have the strongest impact on ESBL and CRK prevalence. Community antibiotic consumption also affected ESBL prevalence, but the relative impact was weaker than nosocomial consumption. Finally, we used the model to estimate a moderate fitness cost of CRK and ESBL at the population level.

**Conclusions:** Our study highlights the disproportionate role of antibiotic consumption in the hospital and of nosocomial transmission for resistance in gram-negative bacteria at a European level. This indicates that infection control and antibiotic stewardship measures should play a major role in limiting resistance even at the national or regional level.

![Figure: Model fit of ESBL and CRK. The model was fitted to the data of the annual prevalence of resistance in *Klebsiella pneumoniae* reported by ECDC from 2005 to 2015. Circles represent the reported data and solid and dotted lines represent the fit with variable between-country and uniform hospital transmission rates respectively.](image)

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Within-patient evolution of a clinical isolate of *Escherichia coli* uncovers an IS26-linked amplification of *bla*TEM-1 leading to piperacillin-tazobactam resistance

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**Background:** The emergence of invasive strains of *Escherichia coli* resistant to Piperacillin/tazobactam (TZP), but susceptible to carbapenems and cephalosporins has been identified in the Royal Liverpool University Hospital, Liverpool, UK. We sought to understand this mechanism of resistance to TZP, initially focussing on isolates obtained from individual patients to identify within-patient evolution of resistance.

**Materials/methods:** We identified 5 instances where two *E. coli* isolates had been obtained from the same patient, with TZP resistance detected only at the second point of isolation, post-antibiotic treatment. Potential clonality of these paired isolates was assessed using RFLP and confirmed with whole genome sequencing, using hybrid assembly of Oxford Nanopore long-reads and Illumina short-reads with Unicycler. Hyperproduction of beta-lactamase and efflux pumps was determined using a nitrocefin-based assay and the efflux inhibitor phenylalanine-arginine β-naphthylamide, respectively. All remaining 21 isolates with this resistance phenotype identified between 2016 and 2017 were sequenced in order to confirm the prevalence of the identified mechanism, and describe involved sequence types and genetic resistance profiles.

**Results:** Only one pair of *E. coli* isolates were confirmed to be clonal. The resistant isolate (MIC 64/4µg/ml) did not have increased efflux, or beta-lactamase promoter region mutations, but was found to hyperproduce *bla*TEM-1. Hybrid assembly of both isolates revealed an 11Kb resistance module present in the susceptible isolate was excised from the genome between two IS26 flanked repeat regions, forming a circular translocatable unit (TU) containing multiple resistance genes. This TU was amplified in the resistant isolate to a copy number of 8.5, likely due to multiple IS26 mediated re-insertion and excision events into the chromosome, increasing the copy number of all resistance genes present on the TU including *bla*TEM-1 and *bla*OXA-1. Sequencing of the remaining isolates revealed increased *bla*TEM-1 copy number in 50%, ranging from 5 to 210 copies. This increase was associated with IS26 in 70% of occurrences.

**Conclusions:** This study underlines the role of IS26 mediated amplification of beta-lactamase genes as a mechanism for overcoming beta-lactamase inhibitors, and highlights the importance of gene copy number and expression levels when inferring susceptibility to beta-lactam/beta-lactamase inhibitor combinations from genomic data.

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**Bordetella pertussis in the Netherlands, 2015-2019: a sharp increase in prn-deficient isolates**

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**Background:** In the Netherlands, pertussis notifications resurged since 1996, likely due to strain adaptation. We apply molecular methods to characterize *B. pertussis* clinical isolates with emphasis to vaccine antigens. Here, we report on the surveillance data from 2015 to 2019.

**Materials/methods:** All *B. pertussis* samples were cultured and suspected colonies were subjected to MALDI-TOF MS and phenotypical tests for species confirmation, followed by whole genome sequencing (WGS). The resulting data were used for identifying the pertussis toxin (*ptxA, ptxP*), fimbriae (*Fim3*) and pertactin (*Prn*) genotypes. Furthermore, core-genome MLST, using an in-house scheme consisting of 3,180 genes, was used to infer genetic relationships between the isolates.

**Results:** WGS revealed that 99% of all our 223 *B. pertussis* isolates that have been collected the past 5 years had a *ptxA1* and *ptxP3* genotype. A minimum spanning tree (MST) based on cgMLST, showed limited variation within the Dutch *B. pertussis* population with an average distance of 5 genes between two neighbouring isolates (range 0–56 genes). There was no clustering in the MST based on year of isolation or age, but there was a clear distinction between fim3-1 (39%) and fim3-2 (60%) isolates with a higher genetic diversity among fim3-1 isolates. The majority of isolates were prn-2, but no prn allele could be determined in 12% of the isolates isolated between 2015-2017. In 2018 and 2019, a sharp increase of Prn-deficient isolates was observed (24% of all), caused by multiple changes including inversion of ~22 kb in the promotor, IS481 element in the prn-gene, and the insertion of a stop codon.

**Conclusions:** The current Dutch *B. pertussis* population represents a homogenous group dominated by isolates that harbour *ptxP3* and *prn-2* as genotypes. In 2018-2019, a sharp increase in prn-deficiency strains was observed.

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Abstract 6678

**Early syphilis infection: a clinical case**
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**Background:** Serology is the most widely used approach for the diagnosis of Syphilis. Often discrepant results are obtained in practice using different methods of analysis. The purpose of this work is to present a clinical case of a proven very early syphilitic infection to highlight the benefits of newer generations of automated treponemal screening tests for the disease.

**Materials/methods:** used are: The first analytical step is automated enzyme-linked immunosorbent assay [ELISA/Gemini/Biokit] or chemiluminescent immunoassay [CLIA/LiaisonXL/DiaSorin]. If a positive result is obtained, the second confirmatory step is the T. pallidum hemagglutination test [TPHA/Biotec]. In case of ambiguous results, T.Pallidum IgG/IgM immunoblot test/Mikrogen is used for confirmation.

**Results:** A 46 years old man, who has been tested 7 times for syphilis and other STIs [HIV, HSV2, chlamydia] in the period 02.2017-06.2019. His results have always been negative. On 12.08.2019, the following results were obtained in syphilis test: ELISA 1.002 OD [c.off 0.250], CLIA 11.0 Index [c.off 1.0], TPHA 1:20. ELISA and CLIA results are positive and TPHA is negative. This required immunoblot confirmation. The results are: Immunoblot IgG negative and IgM positive. This is a very early syphilitic infection, where tests with higher recognition sensitivity [ELISA, CLIA] are positive earlier. A positive Immunoblot IgM strongly confirms the early phase of the infection. The VDRL [Veneral Disease Research Laboratory] test is positive (+++). The patient reports a risk contact in the middle of July 2019. A course of treatment with Benzathine penicillin G has been conducted. Control tests on 01.10.2019: ELISA 1.880 OD, CLIA 22.5 Index, TPHA 1:40, Immunoblot IgG positive, VDRL (++) show specific dynamics with increasing treponemal values tests and a decrease in the non-treponemal values resulting from the therapy.

**Conclusions:** The following clinical case confirms the data in the literature for higher sensitivity of ELISA and CLIA in the diagnosis of early syphilis compared to TPHA.

The use of Immunoblot IgM/IgG in difficult to interpret cases, with ambiguous results from the various methods used, can aid diagnostics by eliminating false positive results due to the high specificity of this method.

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Abstract 6680

**Changing epidemiology of Clostridiodes difficile infection in a French university hospital**

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**Background:** *C. difficile* infection (CDI) weighs heavily on healthcare system due to increased incidence, morbidity and mortality, as well as costs. CDI is mainly considered as a health-care associated (HCA) after exposure to broad-spectrum antibiotics. However, CDI has been reported outside health care institutions in people previously thought to be at low risk. The objective of this study was to compare characteristics of CDI cases regarding the infection presumed acquired in the community or in the hospital.

**Materials/methods:** Between November 2006 and October 2019, a prospective surveillance study of CDI was conducted in a 900-bed French university hospital. National and European definitions of CDI case, relapses and origin of acquisition were applied. Standardized questionnaire was used for data collection.

**Results:** A total of 1000 (=1031 episodes) patients were included with a mean incidence rate of 2.1 per 1000 hospital-stays. Most of episodes were HCA (76.7%). The remaining cases were community-acquired (CA) (17.8%) or indeterminate origin (5.5%). The mean age of patients was 59.8 and 67.7 years for CA and HCA cases respectively (P<0.001) and 31.3% of CA patients were ≤45 years (P<0.001). In CA cases, women were more prevalent (59.8% vs 49.4% in HCA-CDI, P=0.01). CA-CDI group had lower rate of recent antimicrobial exposure (40.9% vs 79.3%, P<0.001), antivirals (1.1% vs 6.8%, P<0.001) proton pomp inhibitor (39.5% vs 61.6%, P<0.001) and gastrointestinal surgery (2.3% vs 7.8%, P=0.008). Fever (>38°C), abdominal pain and ileus were significantly more frequent in CA cases (36.7% vs 26.3%; 45.5% vs 24.0% and 4.4% vs 1.2% respectively). Pseudomembranous colitis and admission in intensive care unit were more frequent in CA cases (7.7% vs 4.6%, P=0.06; 6.6% vs 1.7%, P<0.001 respectively). However, death was more frequent in HCA-CDI (11.4% vs 6.6%, P<0.001). The detection of free toxins A&B was similar between CA and HCA cases (P=0.85).

**Conclusions:** We found that approximately 20% of all CDI cases were CA with 60% of them not exposed to antimicrobial or proton pomp inhibitor drugs. Monitoring and active surveillance of CDI is needed to improve our understanding of the changing epidemiology of the disease.

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Pan-pathogen microbiological diagnosis by accredited routine clinical metagenomics: one-year experience

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Background: Clinical metagenomics (CMg) is a high-throughput sequencing technique dedicated to the etiological diagnosis of infectious diseases, regardless of the nature of the pathogen involved (bacteria, viruses, fungi, parasites). This technique has been implemented in 2018 at the Henri Mondor University hospital as part of routine diagnosis for "undiagnosed" suspected infections and accredited according to the ISO15189 standard in 2019.

Materials/methods: All of the CMg prescriptions prospectively received during year 2019 in the laboratory and validated by the biologists have been included in this retrospective analysis. The clinical indications and type of sample were collected. Samples have been processed by our in-house MetaMIC protocol including pre-extraction by bead-beating, QiaSymphony extraction, DNA and RNA library preparation (Illumina), NextSeq500 sequencing (Illumina) and MetaMIC software analysis. Results were interpreted in the light of the clinical context by a multidisciplinary microbiologist and clinician group.

Results: 208 CMg prescriptions have been received between January and November 2019. The clinical indications for CMg prescriptions included suspicions of: central nervous system infections (40%; 85/208), disseminated infections (25%; 51/208), hepatitis (9%; 18/208), pneumonia (7%; 14/208), cardiovascular infections (6%; 13/208), soft and skin tissue infections (5%; 11/208), bone and joint infections (4%; 8/208) and genitourinary infections (4%; 8/208) (Figure 1). The samples were found positive in 33% of cases (69/208), of which 65% (45/69) contained bacteria, 55% (38/69) contained a virus and 13% (9/69) contained a fungus. In total, 47 of the 69 positive cases (23% of the 208 tests) were considered to be clinically relevant by providing the final diagnosis of infection. CMg was particularly relevant in cases of decapitated infections, or with infrequent, difficult-to-detect or thus far unknown microorganisms.

Conclusions: In this study, prescriptions for CMg sent to the laboratory generally corresponded to situations of suspected infection with failure of usual techniques to detect an infectious agent. CMg identified this agent with excellent performance in a substantial proportion of cases, especially those with rare infections and/or unusual situations. Thus, CMg appears as a promising second-line option for the diagnosis of infectious diseases.

Figure 1: total number of samples analyzed by CMg.

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In vitro susceptibility of fosfomycin in Aerococcus spp. isolated from urine samples

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Background: The introduction of matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) in routine microbiology laboratories has led to an increased isolation of Aerococcus urinae and Aerococcus sanguinicola from human urine. Both these species have been reported to cause urinary tract infections (UTIs), being isolated from urinary cultures in only 0.2–0.8% of cultures sent to different laboratories.

The EUCAST established species-specific clinical breakpoints for aerococci in 2017 for penicillins, carbapenems, vancomycin, quinolones and nitrofurantoin. Fosfomycin, despite being the first-line empirical treatment option for uncomplicated UTIs in Europe, has no clinical breakpoint yet. The aim of this study was to evaluate the in vitro activity of fosfomycin against the Aerococcus spp. strains recovered from urine samples throughout this year.

Materials/methods: 51 nonduplicate isolates [37 A. urinae, 14 A. sanguinicola] collected from urine samples between January 2019 and November 2019 at the Clinical Microbiology Laboratory of the University Hospital Basurto (Bilbao) were analyzed. Species identification was obtained by using MALDI-TOF MS (Bruker Daltonics). Minimum inhibitory concentrations (MICs) of fosfomycin were determined by Liofilchem® MIC Test Strips using a McFarland 0.5 inoculum on BD Mueller Hinton agar plates with 5% sheep blood and incubated at 35±1°C in 5% CO₂ for 16-20 hours. MICs were interpreted using EUCAST 2019 breakpoints established for Staphylococcus spp., as there is no fosfomycin breakpoint in related bacteria such as viridans group streptococci.

Results: MIC distributions are shown in Figure 1.

According to EUCAST criteria for Staphylococcus spp., 31 A. urinae (83.8%) would be categorized as susceptible (MIC₅₀ =16 mg/L, MIC₉₀ =64 mg/L), whereas only 42.8% (6 isolates) of A. sanguinicola would be susceptible (MIC₅₀ =64 mg/L, MIC₉₀ =256 mg/L).

Conclusions:
- Our results indicate that fosfomycin demonstrates a good in vitro activity against A. urinae, in contrast to A. sanguinicola.
- Further multicentre surveillance studies should be carried out to better define the susceptibility of Aerococcus spp. clinical isolates to fosfomycin and for establishing an EUCAST breakpoint.
- In order to clarify if the in vitro results are applicable to the in vivo situation, clinical trials investigating the efficacy of fosfomycin in uncomplicated UTI due to Aerococcus spp. are needed.

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Abstract 6688

**Endemic situation regarding OXA-48-producing *Klebsiella pneumoniae* in north-west Spain**

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**Background:** *Klebsiella pneumoniae* belongs to **Enterobacterales** family being considered one of the most relevant pathogen causing important disseminated infections. Emergence of plasmid-encoded carbapenemases along with the ability to spread and persist in clinical and community setting could favor the current epidemiology of carbapenem-resistant *K. pneumoniae*. In 2013, an OXA-48-producing *K. pneumoniae* (OXA-48-kp) was isolated from 23 patients admitted to a hospital in A Coruña, Spain. This strain spread rapidly causing a large outbreak that has persisted to date. In this work, we report microbiological and clinical details of this outbreak.

**Materials/methods:** MALDI-TOF MS (Bruker) was used for isolate identification. MIC determination was performed in MicroScan WalkAway (Siemens HealthCare Diagnostics Inc.). The detection of carbapenemase was performed by Xpert® Carba-R Kit (Cepheid) and home-made PCR. Molecular typing was performed in 50 representative isolates by SpeI-PFGE and MLST (Multi Locus Sequence Type) analysis. Whole Genome sequencing (Miseq, Illumina) was performed in a representative epidemic clone. The resistome and virulome were analyzed using ResFinder (Center for Genomic Epidemiology) and VFDB (Virulence Factors Database), respectively.

**Results:** During the 6-year study, 5340 *K. pneumoniae* non-duplicate isolates were detected in clinical and/or colonization samples. A total of 682 harbored OXA-48 carbapenemase. From 462 patients tested we found that 431 (93.3%) were intestinal-ly colonized by OXA-48-kp. The urinary tract was the most common source for OXA-48-kp isolation. Forty-six isolates were recovered from blood samples. Most of cases (62.6%) were nosocomially acquired. Colistin, gentamycin and tigecycline were the most active antibiotics. Susceptibility to fosfomycin and meropenem was 66.6% and 67.5%, respectively. Most isolates (86%) belonged to ST-15. We detected additional resistance genes against aminoglycoside and fluoroquinolones (aac(6’)-Ib-cr), and betalactams (blaCTX-M-15), together with adherence-related virulence factors including a novel fimbriae system. Virulence factors involved in iron acquisition, secretion systems and capsule production were also detected.

**Conclusions:**

1) The colonization rates by OXA48-producing *Klebsiella pneumoniae* in this study are alarming, which makes difficult to control the outbreak promoting an endemic situation beyond the hospital environment.

2) Convergence of resistance and virulence determinants, particularly adherence-related virulence factors, could be favoring the progression of outbreak despite intensive intervention controls.

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Abstract 6690

Impaired membrane integrity as a marker for colistin susceptibility: a flow cytometry method for rapid AST in Pseudomonas aeruginosa and Acinetobacter spp.

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Background: Colistin constitutes an important last resort therapeutic for multi-drug resistant Pseudomonas aeruginosa and Acinetobacter species, which, in a global perspective, are common hard-to-treat agents in nosocomial infections. However, antimicrobial susceptibility testing for colistin remains cumbersome and broth microdilution (BMD) is still the only accepted method for determination of the minimal inhibitory concentration [MIC]. In this study we could within 2.5 hours, distinguish between wild type (WT) isolates and isolates with reduced susceptibility to colistin by detecting impaired membrane integrity using flow cytometry analysis.

Materials/methods: A collection of Pseudomonas aeruginosa (n=28) and Acinetobacter species (n=22, including 16 A. baumannii) with colistin MICs between 0.5-16 mg/L was assembled. Bacterial suspensions were inoculated in Mueller-Hinton broth and, after a pre-incubation step, dispensed in the wells of a microtiterplate containing freeze-dried colistin (0.06-64 mg/L). After 30 minutes, a fluorescent dye (YoPro-1 (Thermo Fisher Scientific)) for detection of impaired membrane integrity was added, followed by flow cytometry (Attune NXT) analysis. Non-linear regression analysis with the fraction of membrane-compromised cells as a function of colistin concentration was performed, and the colistin concentration required for 70% of maximum effect (EC70) was calculated.

Results: The colistin concentration needed to achieve 70% of maximum cellular effect (EC70 median [quartile range]) of the susceptible (MIC≤2) Pseudomonas strains was significantly lower (0.8 [0.2-0.5]) mg/L as compared with 16.6 [5.2-30.3] mg/L in the resistant (MIC>2) population. The corresponding figures for Acinetobacter were 0.4 [0.2-0.4] and 2.9 [1.1-7.0] mg/L. In one Pseudomonas and two Acinetobacter the estimated EC70 misclassified resistant isolates (MIC 4 mg/L) as susceptible. However, the epidemiological cut-off (ECOFF) for Pseudomonas is 4 mg/L, and it is possible that this isolate actually should belong to the WT population. For the two discrepant Acinetobacter isolates re-analysis resulted in MICs of 2 mg/L (susceptible according to EUCAST breakpoints) implying a correct classification by flow cytometry analysis.

Conclusions: Rapid detection of compromised membrane integrity after colistin exposure can be achieved by flow cytometry. Estimation of EC70 could be used as a cut-off to distinguish between WT and non-WT isolates for both P. aeruginosa and Acinetobacter spp.

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An ex vivo pig lung model demonstrates potential to distinguish key aspects of chronic and acute infection in the cystic fibrosis lung.

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Background: Robust laboratory models of chronic infections are needed to investigate determinants of chronic pathology and antimicrobial susceptibility in a complex in vivo environment. We previously described an ex vivo pig lung model (EVPL) of cystic fibrosis that demonstrates the influence of host tissue interaction and biofilm structure on growth and persistence of Pseudomonas aeruginosa infection. Here we present developments suggesting the model recapitulates important aspects of chronic S. aureus or P. aeruginosa infection including antibiotic tolerance and regulation of virulence factor production. The model has potential as a tool to investigate the switch from acute, antibiotic susceptible to chronic, antibiotic tolerant infection in the CF lung.

Materials/methods: Using an established EVPL model (pig bronchiole sections plus artificial CF sputum, ASM), growth of bacteria and antibiotic susceptibility was monitored over periods up to 48h. Lung-associated biofilms and/or bacteria growing in surrounding ASM were exposed to antibiotic solutions and viable cell numbers and virulence factor production quantified in treated and untreated model infections.

Results: S. aureus may adopt a silent persister phenotype in the EVPL: After 48h incubation, CF isolates of S. aureus tolerated clinically relevant levels of linezolid (12µl/ml), hemolysin production was down regulated and production of AIPs under agr regulation was not detectable. We also monitored the emergence of antibiotic tolerance in P. aeruginosa; clinical isolates showed tolerance to several antibiotics. They survived colistin concentrations that exceed MIC (planktonic culture in ASM) and in vitro MBEC (Calgary device with ASM), due in part to reduced penetration into biofilm. Some isolates also developed tolerance to meropenem following 8 H incubation in the EVPL, well before biofilm is established, suggesting that altered cell physiology also plays a role in tolerance. Meropenem tolerance correlated with an increase in pyoverdine production.

Conclusions: EPVL is a potentially important model to study key aspects of chronic or persistent infections in the CF lung and provides a more clinically relevant environment than standard in vitro models of infection for assessing virulence and antibiotic tolerance.

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Abstract 6694

**Prospective, non-interventional, multi-centre clinical study of the T2Resistance system for detection resistance genes in bacterial bloodstream infections: an interim analysis**

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**Background:** The incidence of blood stream infections (BSIs) caused by multi-drug resistant organisms (MDROs) is growing at an unprecedented pace. BSIs caused by MDROs are associated with high attributable mortality and increased healthcare costs. Rapid and reliable direct-from-blood pathogen identification remains an unmet healthcare need that may guide early-targeted therapy. The T2Resistance Panel provides direct-from-blood identification of resistance genes in both Gram-positive and Gram-negative pathogens within 3 to 5 hours of sample collection: \( \text{bla} \text{KPC}, \text{bla} \text{OXA}, \text{bla} \text{NDM}, \text{bla} \text{VIM}, \text{bla} \text{IMP}, \text{bla} \text{CTXM-14}, \text{bla} \text{C-TXM-15}, \text{bla} \text{CMY}, \text{bla} \text{DHA}, \text{vanA/B} \) and \( \text{mecA/C} \). The main objective of this study is to evaluate the diagnostic accuracy of T2Resistance in patients with BSIs in comparison to standard methods of blood culture diagnosis and to determine if T2Resistance results would impact treatment decisions in the enrolled patient population.

**Materials/methods:** This is a prospective, non-interventional, multicenter clinical study conducted in whole blood samples (4mL) that were collected in K2 or K3 EDTA tubes and analyzed using the T2Resistance and T2Bacteria panels and compared to standard pathogen phenotypic, and genotypic detection methods including direct from positive blood culture species identification via matrix-assisted laser desorption/ionization time-of flight mass spectrometry – MALDI-TOF.

**Results:** Among the 13 cases enrolled to date and of the 7 blood cultures that were positive, five cases demonstrated 100% concordance between the T2Resistance system and conventional methods. Results from the other two cases are pending blood culture results. The median time (range) to identification of resistance genes via T2Resistance was 3.7 h (3.5 – 8.8 h) versus 98 h (16 - 233 h) by conventional microbiological methods shown to be significant (p<0.001). The resistance genes identified by the T2Resistance system were NDM, VIM, CTX, KPC, AmpC, and MecA/C.

**Conclusions:** An interim analysis of the data from a prospective, multicenter clinical study of the T2Resistance system for detection of resistance genes in bacterial blood stream infections demonstrates a high concordance with the results of conventional microbiological methods but with results available in real time to physicians within 4 to 9 hours from the time of processing blood cultures.

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Oral vancomycin prophylaxis for primary and secondary prevention of *Clostridioides difficile* infection in patients treated with systemic antibiotic therapy: a systematic review and meta-analysis

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**Background:** There is an increasing interest in the role of oral vancomycin prophylaxis (OVP) to prevent *Clostridioides difficile* infection (CDI).

**Materials/methods:** A systematic review and meta-analysis was performed. The search was run up to 30 September 2019 through MEDLINE and Embase to include full-text studies comparing the use of OVP with no intervention in adult patients exposed to systemic antibiotics. Main outcome was CDI occurrence (first episode or relapse). Risk ratio (RR) estimates with 95% Confidence Interval (CI) were computed using random effects model. Sensitivity, subgroup analyses and meta-regression were carried out as appropriate. Statistical analysis was performed with RevMan (v 5.3) and Comprehensive Meta-analysis (v 3).

**Results:** Ten studies were selected: 4 addressing primary and 6 secondary prevention. All studies but one (a randomized controlled trial) were observational and retrospective, in different populations (elderly, solid organ transplantation, hematology). Overall, 2809 patients were included (2816 observations). Follow-up ranged from 30 days/in-hospital to 1 year. OVP regimens varied from 125 mg once-daily to 125 mg each 6 hours, from 2 up to 80 days, in parallel with antibiotic exposure. OVP was associated with a significant decrease in CDI risk (RR 0.29; 95% CI, 0.13-0.63), but heterogeneity was high ($I^2$ = 78%). Significant interaction ($p = 0.02$) existed between the subtotal estimates for the two main subgroups, primary (RR 0.09; 95% CI, 0.03-0.31; $I^2$ 0%) and secondary prophylaxis (RR 0.49; 95% CI, 0.24-0.99; $I^2$ 76%). In the latter, adjusted analysis (3 studies) showed a non-significant difference between OVP and control (aRR 0.66, 95% CI 0.36-1.22, $I^2$ = 70%). Meta-regression demonstrated decrease of CDI risk as OVP duration (days, mean) increases: slope coefficient was $-0.1546$ ($p < 0.001$), explaining a high portion of between-study variance ($R^2$ analog 82%). Only 4 studies reported infections/new colonization by vancomycin-resistant *Enterococcus spp.*, without differences between OVP and control.

**Conclusions:** OVP seems promising in decreasing CDI risk in patients receiving systemic antibiotic therapy, especially for primary prevention in selected populations. Nevertheless, caution is needed since current evidence relies mainly on observational studies, prone to bias and with high heterogeneity regarding OVP schedules, follow-up, baseline features of patients.

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Epidemiology and treatment outcome of Neisseria gonorrhoeae infections

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Background: Infection due to Neisseria gonorrhoeae is increasing in incidence worldwide. In Australia, resistance to recommended antimicrobials remains relatively uncommon. The aim of this study was to describe the epidemiologic distribution, choice of treatment and clinical outcomes of N. gonorrhoeae episodes over a 10 year period at a large metropolitan sexual health service.

Materials/methods: A retrospective cohort study from a prospective clinical database of all patients presenting to the Princess Alexandra Hospital Sexual Health (PASH) service over a ten-year period from January 1st 2008 to 31st of December 2017 with N. gonorrhoeae infection was performed. Patient characteristics and demographics were collected along with treatment choice, test of cure (TOC) and antimicrobial susceptibility testing results.

Results: Of the 36,212 tests performed during the period, N. gonorrhoeae was identified in 803 (2.2%) specimens from 621 individual cases. Of the 621 cases, 469 (75.5%) occurred in patients with attributable symptoms. Infection was predominantly identified in male patients between the age of 20-29 (n = 554, 89.2%), with 504 (91%) of male patients identifying as men who have sex with men (MSM). TOC was performed for 421 (67.8%) of those treated and was positive in 25 (6%) cases. Treatment choice or reduced susceptibility to ceftriaxone or resistance to azithromycin were not associated with a positive TOC. Overall rates of susceptibility to these agents remained high in the cohort. The highest rate of positive TOC was seen from cervical infections (18% of cervical infections treated).

Conclusions: N. gonorrhoeae infection during the 10-year period was predominantly identified in males with MSM history, however female patients with cervical infections had a higher positive TOC which may reflect treatment failure, non-viable DNA or reinfection. Further surveillance of gonorrhoea infection with additional molecular methods may help to shed light on transmission and persistent or recurrent infection.

Test of cure results by patient demographics and anatomical site of infection

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<th>Positive test of cure</th>
<th>Negative test of cure</th>
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<tr>
<td></td>
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<td>(%)</td>
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<table>
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<th>Positive test of cure</th>
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<td></td>
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<td>(%)</td>
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Abstract 6701

The clinical impact of extended blood culture incubation time

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Background: When suspecting endocarditis, it is still common practice in most Dutch hospitals to prolong incubation of blood cultures to ten or 14 days in order to increase the chance of finding fastidious bacteria that are able to cause endocarditis. However, recent literature questions the added value of incubation longer than five days with modern blood culture methods. In this study, we evaluated whether prolonged incubation led to clinical consequences, in terms of both benefit and harm to the patient.

Materials/methods: We analysed all blood cultures that became positive between five and ten days and were cultured in the microbiology laboratory of the Groene Hart Ziekenhuis in The Netherlands between November 14th 2014 and April 30th 2019. Medical records were used to determine the clinical consequences of the blood cultures. Furthermore, we randomly (using randomizer.org) selected 36 culture sets (two aerobic, two anaerobic) from the year 2018 (three per month) that did not grow any bacteria after ten days (i.e. negative) and searched the medical records to determine if these cultures had clinical consequences.

Results: From November 14th 2014 till April 30th 2019, 65697 blood cultures were processed of which 2353 were incubated for ten days and from the latter 188 became positive (8,0%). Only five of those positive blood cultures, from three different patients, became positive after five days (2,7%). Clinical record analysis of these three patients showed that one patient suffered from consequences of the positive culture, as blood cultures were repeated. No treatment changes were made based on these five positive blood cultures.

In 36 culture sets that were negative after incubating ten days, one had clinical consequences, as intravenous antibiotic treatment was continued until the end of the incubation period.

Conclusions: In accordance with previous studies, there was no benefit from prolonged incubation of blood cultures in our hospital. More importantly, prolonged incubation may even be harmful to patients, as it may lead to extra blood cultures or even prolonged antibiotic therapy. Our study supports that unnecessary diagnostics are a serious problem in current medicine and diagnostic tools and their relevance should constantly be re-evaluated.

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Abstract 6702

Reference-setting evaluation of MicroScan panels for identification of bloodstream pathogens in low-resource settings

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Background: The Mini-Lab is a Médecins Sans Frontières project for the development of an all-in-one basic clinical bacteriology laboratory deployable in low-resource settings, where bacterial identification is challenging. The MicroScan identifications panels by Beckman-Coulter were selected, based on target product profiles and market analysis. Their advantage consists in including all tests into one panel, ease of use and long shelf-life.

Materials/methods: The PID3 panels (reference B1017-221) for Gram-positive organisms, NID2 panels (reference B1017-27) for Gram-negative organisms and HNID panels for Neisseria and Haemophilus species (reference B1012-10B) were assessed with a broad selection of common bloodstream pathogens, originating from low-resource settings. In total, 151 Gram-positive isolates (representing 28 species), 180 Gram-negative isolates (20 species), 12 Neisseria and 13 Haemophilus influenzae isolates were tested. Among the species tested, 13 species (35 isolates) were not registered in the MicroScan database; they included mainly Gram-positive rods (Bacillus and Corynebacterium spp.) and Streptococcus suis, endemic to Asian regions. All panels were read visually using the manufacturer’s instructions. The MicroScan autoSCAN-4 reader was used in addition to visual reading for 42% of isolates tested.

Results: Of Gram-negative species registered in the MicroScan database, 89% (153/172) of isolates were correctly identified up to species level. Of Gram-positive species registered, 76% (94/124) of isolated were identified correctly up to species level. Among fastidious species, performance was better for Haemophilus species (85%) than Neisseria species (33%). As expected, species not registered in the database were not identified correctly; moreover 12 Gram-positive (comprising Bacillus spp. and S. suis) and 4 Gram-negative (Burkholderia thailandensis) isolates were incorrectly identified and generated high probability scores (> 80%). Among the isolates with both visual and autoSCAN-4 reading, agreement between readings was 72%, with automated and visual reading leading to correct identifications in 64% versus 68% respectively. Testing of Gram-positive isolates on Gram-negative panels and vice versa resulted in misidentification (with occasionally high probability scores) of 65% of tested isolates.

Conclusions: Performance of the MicroScan PID3 and NID2 panels for isolates from LRS was lower than previously described in high-resource settings. The HNID panel showed low performance for Neisseria.

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Restriction modification systems affect the ability of Escherichia coli ST73 to acquire plasmids

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Background: The spread of antibiotic resistance is frequently linked to the dissemination of multi-drug resistant high-risk clones and specific plasmid backbones. Yet, some clones display worldwide success despite being susceptible to virtually all antibiotics. Such is the case of Escherichia coli sequence type (ST) 73, a dominant ExPEC (Extraintestinal Pathogenic E. coli) lineage that is generally regarded as antibiotic-susceptible and plasmid-free. We aimed to understand the determinants responsible for this behavior of ST73.

Materials/methods: We transferred a clinical blaNDM-1 plasmid into 2 genetically diverse clinical E. coli strains representing 14 different STs, concomitantly measuring its conjugative efficiency. Transconjugants were propagated for ~300 generations to assess plasmid maintenance. Growth rates of transconjugants and isogenic plasmid-free strains were determined to evaluate the effect of the plasmid on host fitness. We downloaded all E. coli genomes belonging to the experimentally tested STs from GenBank and mined them for the presence of plasmids, restriction modification systems and CRISPRs.

Results: The plasmid transferred with lower efficiency to ST73 strains, where it also imposed higher fitness costs. The plasmid was maintained in most strains for 300 generations and its stability did not differ between ST73 and non-ST73 strains. Analysis of E. coli genomes belonging to the studied STs revealed lower frequency of plasmids in ST73 genomes than in other STs. ST73 genomes are often devoid of CRISPR, but exhibit changes in their restriction-modification repertoire. Specifically, such genomes tend to encode type III restriction-modification systems more frequently than other STs.

Conclusions: A plasmid encoding resistance to last resort antibiotics was fairly stable and did not impose detectable fitness cost in several genetic backgrounds. Additionally, ST73 strains exhibit a weaker ability to acquire plasmids than other STs. We suggest that type III restriction-modification systems may pose a barrier to plasmid acquisition in ST73. Our experimental data combined with an extensive bioinformatic approach may explain, at least in part, why molecular epidemiology studies suggest that ST73 is less associated with antibiotic resistance determinants.

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Abstract 6708

Mapping the roles and responsibilities for infection prevention and antibiotic prescribing along the surgical pathway in India and South Africa: case studies

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Background: The surgical pathway remains a hard to reach, but critical target for antibiotic stewardship (AS) globally. There is a need to develop contextually appropriate AS interventions, targeting the surgical pathway in different resource settings. We aimed to characterise the roles and responsibilities of various stakeholders for infection prevention and control (IPC) and AS along the surgical pathway, in two academic institutions in South Africa (SA) and India.

Materials/methods: Between July 2018 and August 2019, we conducted an ethnographic study across cardiac and thoracic (CTS) and gastrointestinal surgical teams utilizing non-participant observations, face-to-face interviews, and in-depth case-studies including patient and healthcare provider narratives on infection management and antibiotic prescribing along the surgical pathway. Data were analysed using an inductive-deductive approach, applying thematic framework informed by existing evidence.

Results: Over 100 hours of observations comprising shadowing of healthcare staff, attendance to meetings, and observation of ward activities and ward rounds were conducted. Across both sites, 14 patient SA) and 11 3 healthcare professional) interviews, and 5 case studies were recorded. These highlighted the multiple steps in IPC and antibiotic prescribing, and the implicit roles and responsibilities of different healthcare professionals involved in IPC and AS, along the surgical pathway. Despite available policies and guidelines on IPC, the patient case-studies highlighted the vulnerability to infections in settings where there are high patient numbers, low staff numbers and surgery with high risk for infection. The environment and resources, including the availability and level of training of staff, the nature of patient illness and level of demand, and the limited infrastructure, all present significant challenges for IPC.

Conclusions: Identifying the implicit existing roles in IPC and AS is critical, as historically most AS interventions target junior doctors, by-passing the existing roles of the wider range of healthcare professionals. In mapping the existing implicit roles along the surgical pathway in relation to IPC and AS, this study provides opportunities for using existing resources, including the workforce, to develop sustainable and context-sensitive interventions.

Figure 1: Roles and Responsibilities in relation to antibiotic prescribing and infection prevention and control

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Abstract 6709

**Cefepime 2g plus enmetazobactam 0.5g administered IV q8h achieves high probability of target attainment in patients with complicated urinary tract infections**

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**Background:** Enmetazobactam is a novel penicillanic acid sulfone β-lactamase inhibitor targeting extended-spectrum β-lactamases, the principal mechanism causing resistance to 3rd-generation cephalosporins (3GC) in Enterobacterales. The combination of enmetazobactam with cefepime is currently being investigated in a Phase 3 trial of patients with complicated urinary tract infections (cUTI) or acute pyelonephritis (AP). This study determined the joint probability of target attainment (PTA) of cefepime-enmetazobactam in adult cUTI/AP patients with varying degrees of renal function.

**Materials/methods:** Pharmacokinetic-pharmacodynamic (PK-PD) targets were 60% of the dosing interval during which free cefepime was above the minimal inhibitory concentration (ft > MIC), and 45% of the dosing interval during which free enmetazobactam was above a threshold concentration (ft > CT) of 2 mg/L. Population PK models for cefepime and enmetazobactam were established from cUTI/AP patients, healthy volunteers, and subjects with varying degrees of renal function. Monte-Carlo simulations (n = 4000 per group) were done accounting for between-patient variability and joint PTAs were defined as the fraction of simulated individuals who attained both targets. Covariate effects on probability of target attainment were predicted to assess if any of the statistically significant covariates require dose adjustments.

**Results:** The cefepime-enmetazobactam MIC distribution of 7168 recent clinical isolates of Enterobacterales was plotted as a histogram and overlaid with joint cefepime-enmetazobactam PTAs [Figure]. Glomerular filtration rate was identified as a covariate requiring dosing adjustment. A dose of cefepime 2 g enmetazobactam 0.5 g administered q8h as 2h IV infusion achieved high PTAs (≥98.3%) in patients with normal renal function or mild renal impairment up to a cefepime-enmetazobactam MIC of 8 mg/L. Half the dose administered q8h, q12h, and q24h achieved PTAs > 99% in patients with moderate and severe renal impairment, and end-stage renal disease, respectively.

**Conclusions:** High PTAs are achieved across the cefepime-enmetazobactam MIC distribution for Enterobacterales. Comparable pharmacokinetic properties of cefepime and enmetazobactam facilitate dosing-adjustment in patients with varying degrees of renal impairment. Cefepime-enmetazobactam may prove to be an important empiric, carbapenem-sparing therapy for the treatment of serious Gram-negative infections in settings where ESBLs are endemic.

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Evaluation of plasma lipocalin-2 as a biomarker of community-acquired pneumonia

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Background: Community-acquired pneumonia (CAP) is an infection of the respiratory tract associated with high morbimortality. Although the classical presentation of pneumonia typically includes symptoms like cough, sputum production, dyspnea, fever and pleuritic pain, in many cases these symptoms are absent, particularly in elderly patients with other underlying conditions. In this context, a rapid and more specific diagnosis is critical to accelerate treatment and improve prognosis of CAP. We evaluated the use of lipocalin-2 (LCN2), a well-characterised neutrophil-secreted protein, as a potential biomarker of CAP.

Materials/methods: A total of 130 patients with CAP were included in the study and classified into two groups: 71 bacterial infections (including 34 co-infections with virus); and 59 non-bacterial infections (17 viral and 42 with unknown etiology). Clinical (respiratory rate, heart rate, oxygen saturation, presence of symptoms and CURB-65, among others) and laboratory parameters (leukocytes, PCR, urea and creatinine, among others) were collected. LCN2 in plasma was determined using a modified enzyme immunoassay coupled with chemiluminescence (Architect). Statistical analyses were performed using RStudio (R version 3.4.0).

Results: The median (IQR) concentration of LCN2 was 122 ng/mL (62.6-192.6) in the bacterial group and 89.7 ng/mL (59.8-130.5) in the non-bacterial group \( p=0.03 \) (Fig1A). In patients with pneumococcal CAP there was a strong direct correlation between LCN2 concentration and pathogen copies/mL detected in blood \( R = 0.74 \), \( p=0.005 \) (Fig1B). Moreover, we observed a strong correlation between LCN2 concentration and CURB-65 index \( R = 0.37 \), \( p<0.001 \) (Fig1C).

Conclusions: LCN-2 could be a useful biomarker to identify bacterial CAP, allowing more responsible use of antibiotics. It could also play an important role in the discrimination between colonization and infection by \textit{S. pneumoniae}. Moreover, LCN2 concentration could be used as a complementary test to determine the severity of patients with CAP. Studies with a larger number of patients are necessary to corroborate the results obtained.

Figure 1. Lipocalin-2 concentration in plasma according to etiological group \( A \) and CURB index \( B \) and Spearman correlation between lipocalin-2 concentration and number of copies/mL of \textit{S. pneumoniae} target detected by PCR \( C \).

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Abstract 6712

Quality of documentation on antibiotic treatment in medical records: evaluation of the long-term impact of an antimicrobial stewardship intervention

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Background: In 2016, the antimicrobial stewardship team (AST) of the University Hospital of Liège, Belgium published a prospective, uncontrolled, interrupted time series study demonstrating the successful implementation of a combined intervention strategy from the AST to improve the quality of documentation on antibiotic therapy in the computerized medical records between 2012 and 2014. Since 2016, the AST repeated a point prevalence surveys (PPS) twice a year about that topic.

Materials/methods: We aimed to evaluate if the impact of the interventions remained stable over time on the documentation rate of 3 quality indicators: (1) the indication (2) the antibiotics prescribed and (3) the expected duration or review date, with a goal of achieving 90% compliance on each indicator. Using the PPS approach, a clinical pharmacist and physician, both from the AST, identified patients receiving one or more antibacterial agents from the Medication Administration Record (MAR). Patients seen in the outpatients or dialysis department or the emergency room, and those who underwent a specific medical intervention or surgery the same day were excluded.

Results: From 2016-2019, six PPS were performed. Overall 4691 patient MARs were reviewed from a total of 34 wards: 1118 (23.8%) took one or more antibiotics, 84.9% for the treatment of an infection, which was slightly lower than previous results (26-28% and 82-83%, respectively). The medical records of 949 patients receiving antibiotics for infection were carefully reviewed and analyzed. On average, 90.4% (vs 90.3% in comparison with our previous results) had an indication documented; 95.1% (vs 95.6%) had documentation of the antibiotics prescribed; and 65.2% (vs 67.7%) had a duration or review date documented.

Conclusions: In our institution, the quality of documentation on antibiotic therapy remained stable over a 5 years period of time, with 90% or more compliance on average for two quality indicators: the indication and the antibiotics prescribed, but less than 70% for duration or review date. This last point should be analyzed and new interventions should be considered to reach 90% compliance for this quality indicator.

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A comparative study to assess the prevalence and risk factors for *Clostridioides difficile* infection in patients with and without inflammatory bowel disease in a tertiary care hospital in northern India

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**Background:** The incidence of *Clostridiodes difficile* infection (CDI) is high among patients with inflammatory bowel disease (IBD) and is responsible for increased morbidity and mortality. In this study, we aim to describe the prevalence and risk factors in patients with IBD as compared to diseased controls (diarrhoea due to causes other than IBD).

**Materials/methods:** This study was conducted between June 2017 to June 2019 in a tertiary care hospital. Cases and controls were diarrhoeal patients with IBD and without IBD respectively. History was taken on a predesigned proforma. Stool samples were processed for routine microscopy and staining for opportunistic parasites. For *C. difficile* diagnosis, Glutamate dehydrogenase (GDH) assay and toxin detection by enzyme linked immunoassay (ELISA), culture and PCR were done. A diagnosis of CDI was made if both ELISA and PCR were positive. Statistical analysis was done using SPSS software version 21.0 (SPSS Inc., Chicago, IL, USA). Study was approved by institutional Ethical committee.

**Results:** A total of 160 cases and 108 age and gender matched control patients were included in IBD group and non-IBD group respectively. Six of 160 (3.8%) and none of controls had CDI (p value = 0.04). In IBD, 136/160 (85%) and 24/160 (15%) patients had ulcerative colitis (UC) and Crohn’s disease (CD) respectively. Only UC patients had CDI, all of which had active disease (3 mild and 3 severe UC), i.e. 6/73 (8.2%) compared to patients in remission (n=63, p value = 0.02). Exposure to levofloxacin (p < 0.001), cephalosporins (p = 0.03), proton pump inhibitors (PPI, p < 0.001) and infliximab (p = 0.02) were found significant risk factors. Using PCR as gold standard, the sensitivity and specificity of GDH ELISA and ELISA for toxins were 100%; 96.8% and 85.7%; 100% respectively.

**Conclusions:** This is first prospective study from India estimating *C. difficile* prevalence among IBD patients and showed prevalence of 3.8% which is lower than that reported from West. Exposure to antibiotics like fluoroquinolones and cephalosporins as well as PPI use are important risk factors for CDI development. An IBD flare and CDI have similar presentations therefore an early diagnosis is important.

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Abstract 6715

**Cefotaxime-resistance in *Escherichia coli* strains isolated from poultry faeces in primary production phase**

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**Abstract third-party references:** Ministry of Agriculture, Forestry and Water Management in Zenica-Doboj Canton

**Background:** Antimicrobial resistance is a serious public health problem worldwide. There is increasing evidence that animals constitute a reservoir of antimicrobial resistance. The aim of this study was to investigate the prevalence of cefotaxime-resistance in *Escherichia coli* strains isolated from poultry feces in primary production phase in Zenica-Doboj Canton, Bosnia and Herzegovina.

**Materials/methods:** Between September and October 2019, 108 fecal samples (cloacal swabs) were obtained from 25 different poultry farms of Zenica-Doboj Canton. The swabs were subcultured on MacConkey agar supplemented with cefotaxime (2 g/L). Antibiotic susceptibility was determined using the disk-diffusion method. Phenotypic detection of extended spectrum beta-lactamases (ESBL) and AmpC production was performed using double disk synergy and the phenyl-boronic acid test, respectively.

**Results:** Among 108 swabs, 75 (69.4%) were positive on *E. coli*, of which 27 (36.0%) were cefotaxime-resistant. All cefotaxime-resistant *E. coli* isolates were positive in phenotypic test for ESBLs and five (out of 27; 18.5%) were positive on AmpC beta-lactamase production. More than 70% of cefotaxime-resistant isolates were resistant to cephalosporins 1st, 2nd, 3rd and 4th generation, and more than 30% of isolates were resistant to fluoroquinolones. Low prevalence of resistance was observed for aminoglycosides and sulphamethoxazole-trimethoprim. There was no isolates resistant to imipenem, meropenem and colistin. Twelve (44.4%) of the cefotaxime-resistant isolates were multi-resistant [more than three classes of antibiotics].

**Conclusions:** The wide production of chicken meat and consequently a presence of their fecal waste likely have to an impact on an increase of development of antibiotic resistance. Poultry production systems represent a hotspot for development of antimicrobial resistance, possibly mediated by extensive use of antibiotics in production plants. Also, it is very important to develop national surveillance system of resistance in order to prevent a possibility of emergency and spread of multiple resistant strains between animals, as well as between animals and people.

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Identifying nosocomial transmission of influenza and associated deaths: a prospective, observational study

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Abstract 6717

**Background:** The extent and burden of disease from nosocomial transmission of influenza is not well defined. Nosocomial transmission is of particular importance as hospitalised patients are often at risk of complications and death due to existing comorbidities. This study seeks to identify the burden of influenza in our hospital, as well as the extent of nosocomial transmission, and associated morbidity/mortality outcomes.

**Materials/methods:** Adult patients admitted to our hospital with a laboratory diagnosis of influenza were enrolled in the prospective study (Dec to March). Inpatients who shared a bay with a laboratory-confirmed case of influenza were defined as contact. Contacts were followed up for 5 days, to monitor for signs and symptoms of influenza. Those contacts who became symptomatic were tested for influenza. Demographic, co-morbidity and outcome data (mortality, HDU/ITU admission) was collated for both cases and contacts.

**Results:** We enrolled 405 influenza cases during our study period, representing 95% of those eligible by the inclusion criteria.

360 cases were community-associated cases (diagnosed <48 hours of hospital attendance), with 39/363 (11%) admitted to HDU/ITU and 11/363 (3%) deaths. 45 cases were diagnosed >48 hours after admission and designated hospital-associated. In this group there was a significantly higher mortality (7/45, 15%) and admissions to HDU/ITU (14/45, 30%) (p<0.001).

We identified 298 contacts from 73 cases, of which 23 acquired influenza (8% attack rate). In this influenza-positive contact group there were 5 deaths (28%) and 6 (26%) admissions to HDU/ITU. This was significantly greater than for influenza-negative contacts (275/298), in which there were 11/275 (4%) deaths (p=0.001) and 20/275 (7%) admissions to HDU/ITU (p=0.003).

Multivariate analysis including factors like age, ward, co-morbidity and length of stay suggests that influenza acquisition in hospitalised contacts is a major risk factor for death.

**Conclusions:** Hospital-associated influenza carries greater morbidity and mortality, compared to community-acquired influenza. A large number of contacts were identified suggesting suboptimal clinical suspicion and infection control response. The high rate of influenza acquisition in contacts and the poor outcomes highlight the need for improved strategies to prevent nosocomial transmission. Whole genome sequencing is underway and may be able to corroborate our epidemiological data.

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Abstract 6718

**Epidemiology of carbapenem resistance genes in clinical isolates in South India**

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**Background:** The most clinically important carbapenemase genes are molecular class A (KPC type), Amber class B (NDM, VIM and IMP types) and class D (OXA-48 like). After the first discovery of NDM-1 in India and epidemiological studies that followed, indicated that the Indian subcontinent and Balkan region are reservoirs of NDM-1 producing bacteria and Turkey and surrounding Mediterranean basin is the reservoir of OXA-48-like producing bacteria. Both NDM and OXA-48 are carried on plasmids and other mobile genetic elements and have potential to spread rapidly. The objective of this study was to understand the epidemiology of carbapenem resistance genes in clinical isolates in a tertiary care hospital settings in South India.

**Materials/methods:** We studied 112 clinical isolates from blood (108), endotracheal secretions (1), urine (1), sputum (1), perigraft abscess (1) for the presence of carbapenamases by molecular and phenotypic testing over one year. Blood cultures from sepsis patients growing gram negative bacilli and isolates from above samples were subjected to Gene Xpert Carba (Cepheid) to look for the presence of KPC, Oxa-48, NDM, VIM and IMP. Disk diffusion and MIC’s for carbapenems were also determined simultaneously.

**Results:** Of the 108 blood culture isolates, phenotypic cabapenem resistance was found in 22 (21.3%) cases. This correlated with our hospital antibiogram pattern. Of the 23 isolates showing carbapenemase resistance, 11 had OXA-48, 4 had NDM and 5 isolates had both OXA-48 and NDM. One isolate from urine had Oxa-48. Two isolates that were carbapenem sensitive possessed both OXA-48 and NDM. In two phenotypically carbapenem resistant isolates, no carbapenemase genes could be detected suggesting other mechanisms of resistance. Oxa-48 was the most common carbapenamase in our study followed by joint presence of OXA-48 and NDM (Figure 1).

**Conclusions:** Our data indicates that OXA-48 carbapenemase gene is rapidly spreading in India overtaking NDM. Co-presence of NDM and OXA-8 possibly suggests acquisition of OXA-48 plasmids by isolates possessing NDM plasmids. This study also brings to relevance that ceftazidime avibactam can be used as a colistin sparing agent when presence of Oxa-48 is confirmed in clinical isolates.

**Percentage prevalence of carbapenemase resistance genes in clinical isolates**

![Pie chart showing percentage prevalence of carbapenemase resistance genes](image)

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Abstract 6720

**Longitudinal large-scale survey on blaCTX-M faecal carriage in children from Bolivian Guaraní indigenous communities**

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**Background:** CTX-M extended-spectrum beta-lactamases represent a huge challenge to healthcare. Community fecal carriage of CTX-M-producing enterobacteria has dramatically increased worldwide over the last two decades, with resource-limited countries being the most affected settings for reasons related to poverty and poor sanitation. Here we reported on a recent rapid increase of bla-CTX-M fecal carriage in healthy children from Bolivian Guaraní indigenous communities.

**Materials/methods:** School-aged children from four communities (Ivamirapinta and San Antonio del Parapetí, Santa Cruz Department; Chimeo and Tarairí, Tarija Department) were enrolled in 2016 (n=194) and 2019 (n=215). Of these, 23 were found to be included in both surveys. Stool samples (stored in fecal swab (Copan, Brescia, Italy) until processed) were plated as a first step onto MacConkey Agar (MCA), and then onto MCA plus cefotaxime 2 µg/ml (MCA-CTX). The bacterial growth on MCA-CTX was used as the template for the detection of group 1, 2, 8/25 and 9 blaCTX-M variants by mRT-PCR.

**Results:** Growth onto MCA-CTX was obtained with 318/409 stool samples (170/194, 2016; 148/215, 2019). Overall, a relevant increase of bla-CTX-M fecal carriage was observed in the study period (19.6%, 2016; 40.9%, 2019). Nonetheless, a discordant trend was observed in Tarairí, where prevalence of bla-CTX-M fecal carriage lowered from 41.5% in 2016 to 16.3% in 2019. Group 1 bla-CTX-M variants were found to have a major epidemiological impact (14.9%, 2016; 25.8% 2019, \(p < 0.05\)), and were the main responsible for the decreasing trend observed in Tarairí (31.7%, 2016; 7%, 2019, \(p < 0.01\)). Group 9 variants increased from 4.6% in 2016 to 14% in 2019 (\(p < 0.01\)), and group 8/25 variants appeared 2019 (3.7%, \(p < 0.05\)). Interestingly, no group 2 variants was detected. In 17 (N=4, 2016; N=13, 2019) samples (4.2%; 1%, 2016; 3.2%, 2019), the presence of bla-CTX-M variants of diverse groups was observed. Data from the 23 children enrolled in both surveys, did not suggest long-term colonization by CTX-M-producing enterobacteria.

**Conclusions:** High prevalence and rapid spread of CTX-M-producing enterobacteria were observed in the study setting, which encourages further studies to unravel the strains features and dissemination dynamics.

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Prevalence of positive serology for Trypanosoma cruzi in a sample population of migrants from El Salvador and Honduras living in the Metropolitan Area of Milan (MAM)

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Background: Studies on Chagas Disease (CD) among Latin Americans living in Europe Union (EU) calculated a pool seroprevalence of Trypanosoma cruzi (TC) of 4.2%. MAM is home to the largest Italian El Salvador Community. The aim of this study is to improve data in previous surveys about TC seroprevalence in Central American migrants living in MAM, especially El Salvador and Honduras.

Materials/methods: 385 migrants from Central America Area (CAA) (El Salvador, Honduras and Dominican Republic) were enlisted by OSF outpatient clinic (OSF) by interview. A serum sample was collected by all subjects enlisted and assayed by two serological methods (EIA Lisado Weiner - Effegiemme Italy; EIA Recombinant Weiner - Effegiemme Italy). Samples with discordant results were tested by Western Blot Method (WB) (LDBio - Effegiemme Italy). All subjects positive for at least two tests were attended to University Clinic (DIBIC) for clinical assessment.

Results: 9 subjects were positive for at least one assay (1 M, 8 F). Five were confirmed positives by WB and went for clinical examination. All positives were 2.3% of the sample population and all ones were Salvadorians. All patients with confirmed serology by WB were asymptomatic and their clinical assessment and follow up is in progress.

Conclusions: These preliminary results confirm seroprevalence for TC in El Salvador community dwelling in MAM. The screening is still in progress and so the clinical assessment and follow up of the patients seropositive for TC.

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Variation in strain types of extended spectrum beta-lactamase-producing Enterobacteriaceae in long-term care facilities: a multi-centre, prospective cohort study


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Abstract third-party references: This research project receives support from the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) under the funding reference 01KI1 701 resources of Bundesministerium für Bildung und Forschung.

Background: While transmission of ESBL-producing Enterobacteriaceae (ESBL-PE) has been extensively studied in hospitals, prospective collected data in long term-care facilities (LTCF) are scarce and usually limited to single center studies.

Materials/methods: A longitudinal observational study was carried out in six LTCFs in four European countries. In a 34-week study period residents and staff were screened or provided stool samples for detection of ESBL-producing Escherichia coli (ESBL-EC) and Klebsiella pneumoniae (ESBL-KP) at eight defined time points. Individual, clinical and epidemiological data were collected at each point prevalence survey (PPS). Residents had a daily diary to note relevant risk factors for ESBL-PE acquisition. Environmental surfaces of the LTCF living areas were screened at two time points. ESBL production was detected using selective media and confirmed phenotypically by double disc synergy tests. blaESBL determinants were identified using Whole Genome Sequencing (WGS). Continuous carriage was defined as at least 7 out of 8 samples positive.

Results: 300 residents were enrolled, 1958 rectal swabs or stool samples and 707 surface samples were analyzed. ESBL-KP and/or ESBL-EC were isolated from 83 residents (27%) in 294 samples (15%). Prevalence at first PPS varied substantially among residents ranging from no cases to 41%. Dominant sequence type was ESBL-EC ST131 (34%), dominant ESBL gene blaCTX-M-15. Continuous ESBL carriage occurred in 15 residents (17.9%): 3 (20%) had a change in species (EC/KP), 1 (6.7%) had a change both in species and sequence type (within EC), 2 (13.3%) had a change in sequence type, and 1 (6.7%) had 5 different EC sequence types in 7 samples. Among 35 transient carriers, 15 (42.8%) had a change in species and/or sequence type. 6 (17.1%) had a change in species (EC/KP), 5 (14.3%) had a change both in species and sequence type, and 4 (11.4%) had a change in sequence type. Environmental screening was positive only from the center with highest prevalence (15/146).

Conclusions: Variation in prevalence and diversity of strains among the LTCFs was extremely high. Contamination of surface samples was limited. Transmission in LTCFs seems complex and linked to multiple patient’ risk factors which require consideration before starting infection control interventions.

Duration and sampling schedule of the 4 European study centres

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**Abstract 6726**

**Colonisation and infection with carbapenemase-producing Enterobacteriaceae (CPE) in high-risk patients in a private hospital setting in Istanbul, Turkey**

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**Background:** Infections associated with carbapenemase-producing Enterobacteriaceae (CPE) is getting a growing problem worldwide. An important risk factor of nosocomial infections is colonization.

**Materials/methods:** The study was done in a private foundation hospital specialized in the field of hematology/oncology and accepting international patients from July 2014 to September 2019. High risk patients according to the algorithm were screened at admission for CPE to attempt preemptive isolation. All rectal swabs were inoculated in ChromID CARBA agar (Biomerieux, France), identified by Vitek2 compact automated system (Biomerieux, France). The CPE positive colonies were tested with CarbaNP simultaneously. Genotypic characterization of CPE was done by real-PCR for blaVIM, blaIMP, blaNDM-1, blaKPC, and blaOXA-48 genes.

**Results:** A total of 849 patients were screened for CPE with rectal swabs. Of these 65 patients were positive (7.5%). Geographical distribution of patients were 420 from Turkey, 158 from North Africa, 117 from Eastern Europe, 97 from former Soviet Union countries, 66 from Middle East countries (Table1). From CPE positive patients, 9 patients (13.8%) were infected with CPE and 6 (66.6%) of them died. The patients who were infected had mostly hematologic cancer as underlying disease. Two of these infections were pneumonia and 7 were bloodstream infection. All the deceased patients had sepsis. In infected patients; the pathogens were mostly *Klebsiella pneumoniae*, one was *Enterobacter cloacae*. Only in one there was colistin resistance. Even if four of them had colistin in their empirical therapy, all of them died.

**Conclusions:** The rate of 7.5 % CPE colonization is high. Therefore, it is worthy to screen patients at admission for preemptive isolation and determining empirical treatment. However, even if colistin was included in empirical therapy and 66% of patients were died of sepsis. In conclusion, we should make attention to infection control measures and we need new antibiotics which are effective for CPE.

<table>
<thead>
<tr>
<th>Region</th>
<th>Number of screened patients</th>
<th>CPE (+)</th>
<th>Ratio of CPE colonization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turkey</td>
<td>420</td>
<td>25</td>
<td>5.9%</td>
</tr>
<tr>
<td>North Africa</td>
<td>158</td>
<td>13</td>
<td>8.2%</td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>117</td>
<td>5</td>
<td>4.2%</td>
</tr>
<tr>
<td>Former Soviet Countries</td>
<td>97</td>
<td>8</td>
<td>8.2%</td>
</tr>
<tr>
<td>Middle East</td>
<td>66</td>
<td>14</td>
<td>21.2%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>859</strong></td>
<td><strong>66</strong></td>
<td><strong>7.5%</strong></td>
</tr>
</tbody>
</table>

Table1: Geographical distribution of CPE screening

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Abstract 6727

**Does trichomonas hurt? A five-year comprehensive full-region study**
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Trichomonas vaginalis (TVG) is the etiological agent of trichomoniasis, the most prevalent non-viral sexually transmitted disease worldwide and a widespread, global health concern. The relatively mild symptoms have historically led to this disease being under diagnosed, and under researched. However, growing evidence that TVG infections are associated with high morbidity in both men and women, has increased the efforts to diagnose and treat patients harbouring this parasite. In this study, we aimed to assess this burden of disease.

Between 1 May 2012 and 31 January 2017, we routinely screened all patients for TVG where any STD diagnostics were requested by a GP, gynaecologist or social health care service in the region. All samples were tested using real-time PCR. The patient catchment area covered the whole of Friesland, one of the twelve provinces of the Netherlands, comprising ~645,000 inhabitants. All requesters were asked to supply clinical information about their patients.

In total, 47,735 patients were screened, of which 69% was female. The median age was 27 (IQR: 22-38). Out of 67,774 samples, 540 (0.8%) were positive for TVG, with a median cycle threshold (Ct) of 22.47 (IQR: 18.33-29.15). As a comparison, 9.7% tests were positive for Chlamydia trachomatis (CTR) and 1.4% was positive for Neisseria gonorrhoeae (NGO). Compliance of the supply of clinical information was 87%. TVG was found in both women (489/540, 91%) and men (51/540, 9.4%), although the median DNA load was almost 300 times higher in women (Ct 21.6) then in men (Ct 29.8). In women, presence of vaginal discharge and/or irritation was predictive only for presence of TVG and, opposingly, predictive for absence of both CTR and NGO.

To our knowledge this is the first full-region approach to study on the prevalence of TVG in relation to clinical complaints. Although our study results corroborate previous findings in the Netherlands, they contrast the high prevalences seen worldwide. Vaginal discharge appeared to be predictive for presence of TVG, and this reason for clinical burden is probably easily overlooked by physicians. Additional, in-depth analyses will be necessary to further specify how TVG infections are associated with other disease states.

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Abstract 6728

Predictors of mortality in invasive pneumococcal disease: a meta-analysis

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Background: Invasive pneumococcal disease (IPD) is responsible for life-threatening invasive infections such as bacteremia, meningitis and sepsis. Several risk factors have been identified that predict IPD-related mortality in some potential risk groups. However, mortality-related risk factors have not yet been systematically identified among all patient groups with IPD. In this meta-analysis, we aimed to determine the risk factors for mortality in IPD.

Materials/methods: We conducted a systemic literature search to January 2019 in MEDLINE/PubMed, ISI Web of Science and Cochrane Central Register of Controlled Trials databases. After reviewing 2514 potentially relevant records, remaining 190 articles were included in the analysis. The study protocol was registered in PROSPERO (CRD42019120189). Summary estimates were evaluated as odds ratios (OR) with 95% confidence intervals (CI) by using random-effects model. The main outcome measure included death within 30 days after diagnosis of IPD.

Results: Male sex (OR: 1.12), age ≥45 years (OR: 0.97), alcohol abuse (OR: 1.82), previous tuberculosis (OR: 2.33), severe sepsis (OR: 3.12), septic shock (OR: 8.6), hospital acquired infection (OR: 2.17), acute respiratory failure (OR: 2.56), mechanical ventilation (OR: 5.21), altered mental status (OR: 2.69), coma/convulsion (OR: 4.28), admission to the internal care unit (OR: 7.02), multilobar infiltrate or effusion (OR: 2.79), Pitt bacteremia score ≥4 (OR: 5.59), Pneumonia Severity Index ≥4 (OR: 2.68), solid organ malignancy (OR: 2.13), underlying clinical conditions (OR: 2.5), immunocompromising conditions (OR: 1.43), diabetes (OR: 1.2), chronic cardiovascular disease (OR: 2.27), chronic kidney disease (OR: 1.99), chronic liver disease (OR: 2.25), neurological disease (OR: 2.14), Charlson Comorbidity Index ≥2 and ≥3 (OR: 1.95 and 2.5), dialysis (OR: 7.35), serotype 3 (OR: 1.84), serotype 6B (OR: 1.3), serotype 9N (OR: 1.38), serotype 10A (OR: 1.57), serotype 11A (OR: 2.44), serotype 16F (OR: 1.94), serotype 17F (OR: 1.37), serotype 19 and 19F (OR: 1.81), serotype 22F (OR: 1.2), serotype 23A (OR: 1.33), serotype 23F (OR: 1.37), serotype 31 (OR: 2.59), serotype 35F (OR: 1.94), penicillin resistant (OR: 1.27), previous antibiotic use (OR: 1.6), inappropriate initial antimicrobial therapy (OR: 1.95) and vancomycin use (OR: 2.09) were found as predictors of 30-day mortality in IPD.

Conclusions: The results of this meta-analysis highlight the most important variables in determining outcome of IPD. Understanding the risk factors for mortality in IPD will help to define the potential pneumococcal vaccine benefits and treatment schedules with increased coverage that might target risk factors associated with higher mortality.

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Migration and outbreaks of vaccine-preventable disease in Europe: a systematic analysis (1990-2019)

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Background: Migrant populations (defined as foreign-born) in the EU/EEA may be one of several under-immunised populations associated with outbreaks of vaccine-preventable diseases (VPDs). We synthesised existing EU/EEA data to explore whether migrants are involved in outbreaks and which particular subpopulations are at increased risk.

Materials/methods: We did both a systematic review (PROSPERO CRD42019157473; Medline, EMBASE, and Global Health January 1990 to October 2019) adhering to PRISMA guidelines, and a temporal analysis to map published reports of migrant-related outbreaks against data from the ECDC’s Surveillance Atlas of Infectious Disease. Studies on VPD outbreaks (measles, mumps, rubella, diphtheria, pertussis, polio, hepatitis A, N meningitidis, and H influenzae) in migrants residing in the EU/EEA and Switzerland were included.

Results: 54 studies were included, reporting on 55 VPD outbreaks across 13 EU/EEA countries, of which 96.4% (n=53) occurred since January 2000. Measles had the highest number of reports of outbreaks involving migrants (n=2; 5043 cases), followed by varicella (n=10; 595 cases), hepatitis A (n=8; 1082 cases), diphtheria (n=5; 35 cases), rubella (n=4; 512 cases), mumps, N meningitidis, polio (all n=2; 147, 7 and 15 cases, respectively), and pertussis (n=1; 10 cases). 21 (40%) of outbreaks were reported from camps or shelters for asylum seekers and refugees (mainly varicella or measles). Of 27 outbreaks where the index case was defined and reported, 20 (74.1%) were migrants, including 9 (33.3%) from Eastern Europe and 6 (22.2%) from Africa. When mapped against the ECDC timeline of measles outbreaks, migrant-related outbreak studies coincide with Europe-wide peaks in measles incidence, particularly in 2006, 2010, and 2017/2018 (shown in Figure 1).

Conclusions: Migrants represent one key group involved in VPD outbreaks in Europe, with refugees and asylum seekers residing in shelters or camps particularly at risk. Measles accounted for 38% of all reported outbreaks. Regional targets for elimination and control of vaccine-preventable diseases will not be met if we don’t better engage migrant populations in vaccination, alongside other under-immunised groups. Improved data collection is crucial to understanding the complex relationship between migration and occurrence of VPD outbreaks to inform policy decisions on the most effective strategies to prevent future outbreaks.

Figure 1. Published reports of outbreaks of measles involving migrants, mapped against the ECDC Surveillance Atlas of Infectious Disease timeline of all European measles outbreaks (1999-2018).

*Migrant-related outbreaks are marked as orange circles with the relevant reference.

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Abstract 6730

**Application of MALDI-TOF MS for identification of helminths in clinical samples**

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**Background:** Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry is the standard diagnostic technique for identification of bacteria, mycobacteria and fungi. Preliminary data suggest that MALDI-TOF might also be used for helminths. At present, their identification is mainly based on microscopy, but exact species differentiation cannot always be achieved. Hence, we evaluated the capacity of MALDI-TOF MS to identify helminths from clinical samples, and analysed the influence of different sample storage conditions.

**Materials/methods:** All experiments were carried out with a MALDI-TOF mass spectrometer (Bruker Daltonics), using the software Maldi Biotyper Compass Explorer\(^2\) and FlexAnalysis\(^2\). We analysed proglottids of *Taenia saginata* stemming from two different patients and one serum sample from a patient with active *Schistosoma mansoni* infection. The acquired raw MALDI spectra were tested with a commercially available database for bacteria and fungi as well as a previously developed in-house database for helminths. Log-score values (LSVs) of ≥2.00 were considered as reliable species identification. Additionally, proglottids of *T. saginata* were placed in tubes containing different fixatives (water, 0.45% sodium chloride, 70% ethanol, and formalin), and spectral profiles were visualized after 12 weeks.

**Results:** When employing our in-house database for helminths, the two new *T. saginata* samples and the *S. mansoni* serum specimen were correctly identified with average LSVs of 2.04, 2.10 and 2.21, respectively. In contrast, no identification was achieved with the commercially available database. The quality of acquired spectra was best if ethanol or sodium chloride solution were used as fixatives, whereas formalin-preserved samples did not yield any spectra [Figure].

**Conclusions:** MALDI-TOF MS can be employed to identify helminths in different sample types. Further research and database validation is needed to confirm its potential as diagnostic tool for parasitic pathogens. Formalin-fixed specimens cannot be subjected to MALDI-TOF analysis.

**Figure:** MALDI-TOF mass spectrometry profile of *Taenia saginata* proglottids in different fixatives after a storage period of 12 weeks. A decrease of the peak intensity at 3827 m/z and at 7065 m/z for samples stored in water (first row) as compared to ethanol (second row) can be observed. Third row: 0.45% sodium chloride. Fourth row: formalin.

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Abstract 6733

Examining the modified Duke criteria in infective endocarditis: a comparison of outcomes for ‘typical’ and ‘atypical’ bacteria

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Background: The 2000 modified Duke criteria remain the most often used internationally for the stratification of infective endocarditis (IE) as definite, possible or rejected. This study aimed to assess the sensitivity of the modified Duke criteria in IE and compare clinical outcomes between different infections and patient populations.

Materials/methods: This retrospective cohort review included all patients diagnosed with IE between 2016 and 2018 at a tertiary centre for Infectious Diseases, Cardiology and Cardiothoracic Surgery in London, UK. Detailed demographic, clinical, microbiology, imaging, management and outcome data were extracted from electronic health records and analysed in Excel. Modified Duke criteria was noted for each patient.

Results: 129 patients met the inclusion criteria, of whom 109 (85.8%) had positive blood cultures. 91 (70.5%) were male; median age was 67 (IQR: 51-76). Modified Duke criteria identified 81 (62.8%) cases as definite, 43 (33.3%) as possible and missed five (3.9%) of our cohort. 24/109 (22.0%) were infected with an ‘atypical’ organism, as per the modified Duke criteria; 20/129 (15.5%) were culture negative. The most common ‘atypical’ organisms were coagulase negative staphylococcus (six patients), group B streptococcus (five), and Streptococcus pneumoniae (two). When compared with ‘typical’ infections, ‘atypical’ infections led to lower mortality rates (31.8% vs 20.0%) but longer admissions (mean 32 versus 46 days). Staphylococcus aureus had the highest mortality rate (41.9%) of all infections. Intravenous drug users (IVDUs) had a better inpatient survival rate than non-IVDUs (75.0% vs 63.3%), despite fewer patients undergoing surgery (25.0% vs 34.9%).

Conclusions: Our study showed that in a large cohort of patients with IE, the modified Duke criteria showed a high sensitivity. However, an unexpectedly high proportion of infections did not fall into the ‘typical’ category as defined by these criteria; the largest groups were coagulase negative staphylococcus and group B streptococcus, which are both increasingly reported in the literature as causes of IE. The outcomes for ‘typical’ and ‘atypical’ bacteria differed in terms of mortality, which was lower in the ‘atypical’ group. 15.5% of patients were culture negative, supporting the need for improved diagnostics.

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Characterisation of *Staphylococcus aureus* isolates collected from children with respiratory tract infections in Tangier, Morocco

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**Background:** Data concerning the molecular epidemiology of *S. aureus* infections in Morocco, particularly methicillin-resistant *S. aureus* (MRSA), are very limited. The aim of the study was to perform the molecular characterization of *S. aureus* isolates recovered in respiratory specimens of children hospitalized in the Mohammed V Hospital in Tangier, Morocco.

**Materials/methods:** A total of 97 *S. aureus* isolates collected from respiratory tract infections between 2013 and 2014, were retrospectively identified and analyzed. Information was retrieved from the database of the bacteriology laboratory and through the medical record review. The antimicrobial susceptibility phenotypes were determined by disk diffusion according to EUCAST 2016. The presence of mecA (encoding PBP2a and methicillin resistance), lukS/F-PV (encoding PVL toxin), and tst (encoding TSST-1 toxin) genes were determined by PCR for all isolates. To describe the clonality of MRSA, genotyping was performed using Alere StaphType DNA microarray (Alere Technologies GmbH, Jena, Germany). Statistical analyses were performed using SPSS statistics version 20.0 software; p-values of ≤0.05 were interpreted as statistically significant.

**Results:** Susceptibility testing of the 97 investigated *S. aureus* isolates resulted in 89 (91.75%), methicillin susceptible *S. aureus* (MSSA) and eight (8.25%) MRSA isolates. All *S. aureus* isolates were found to be susceptible to rifampicin, pristinamycin, and vancomycin. The lukS/F-PV and tst genes were found respectively in 22 (22.7%) and 25 (25.7%) isolates. Of note, the lukS/F-PV genes were not detected in MRSA. The most prevalent MRSA genotype was the CC22-IV (UK-MRSA-15 / Middle Eastern variant; n=3) harbouring tst, egc genes followed by CC5-MRSAV+SCCfus (n=2), harbouring seb, egc, and three singletons belonging to CC88-MRSA-IV, CC5-MRSA-V, CC5-MRSA-IV Pediatric clone.

**Conclusions:** This study provides, for the first time, data on the genetic background of *S. aureus* isolates involved in respiratory infections among children in Tangier. Our results highlight the high prevalence of PVL+ MSSA as well as the high prevalence of MRSA in respiratory tract specimen in children.

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Antibiotic resistance in *Staphylococcus pseudintermedius* associated with skin and soft tissue infections in dogs and cats

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**Background:** Antimicrobial resistance in staphylococci causing skin and soft tissue infections (SSTIs) in companion animals is a growing public health concern. In this study we characterized a collection of *S. pseudintermedius* causing SSTIs in pets to document their phenotypic and genotypic profile towards antibiotics.

**Materials/methods:** The collection comprised 163 *S. pseudintermedius* associated with SSTIs in dogs and cats, collected between 2014 and 2018 at two veterinary laboratories in Lisbon (Portugal). Identification was confirmed by species-specific *spsJ* PCR approach and the susceptibility profile determined by Kirby-Bauer. The results were interpreted according to the VET08 CLSI guidelines or other, when necessary. Resistance determinants were screened for all isolates (*blaZ* and *mecA* genes) or for those showing a resistance phenotype (e.g. *erm*, *tet*, *aadD*, *vga*(C), *dfrA*(S1), *aph3-IIIa*).

**Results:** Among the 163 *S. pseudintermedius* tested, 136 (83.4%) were resistant to penicillin, all of which carried the *blaZ* gene. Methicillin resistance (MRSP) was detected in 52 isolates (31.9%), 51 of which carried *mecA* and 48 showed a multidrug resistance (MDR) phenotype. In general, multidrug resistance was detected in 77 isolates (47%) and the most common pattern was resistance to beta-lactams, aminoglycosides, macrolides and lincosamides. Resistance to aminoglycosides (39.3%) and macrolides/lincosamides (37.4%) was mostly associated with carriage of *aph3-IIIa* and *erm*(B) genes, respectively. Resistance to tetracyclines was found in 55.2% of the isolates, mostly related to *tet(M)* gene. We also detected resistance to trimethoprim-sulfamethoxazole (30.7%), fluoroquinolones (25.8%), chloramphenicol (14.7%) and fusidic acid (4.9%). No resistance was observed for linezolid, tigecycline or quinupristin-dalfopristin.

**Conclusions:** This ongoing study revealed a high frequency of MDR and MRSP strains and, in comparison with previous studies, an increasing trend of antibiotic-resistant *S. pseudintermedius* associated with SSTIs in pets. The close contact between these animals and humans may be a possible source for transmission of antibiotic resistant staphylococci, reinforcing the need of a One Health perspective in their study. These results also highlight relevant therapeutic limitations for the treatment of SSTIs in pets, which already include critically important antibiotics.

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Abstract 6738

Diagnosing disseminated histoplasmosis in an AIDS patient: the role of bone marrow evaluation
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Background: Histoplasmosis (HP) is a micosis caused by a dimorphic fungus *Histoplasma capsulatum*. HP represents a HIV-defining condition and in AIDS patients the pathogen can invade the bloodstream and spread to other organs and tissues leading to progressive disseminated histoplasmosis (PDH), a fatal disease in untreated patients. There are multiple methods for the diagnosis of histoplasmosis including histopathology/cytology and cultures, specific fungal stains, antigen detection, serological tests and molecular biology tests. The gold standard for identification of the pathogen is the culture demonstrating the thermal dimorphism of the fungus.

Materials/methods: A 52 year old male with HIV-1 infection (CDC-C3, CD4+: 4.5%, 27 cel/μl, HIV-RNA: 5640000 copies/mL) and a recent trip to Brasil, was admitted in the ICU with a diagnosis of *Pneumocystis jirovecii* pneumonia (under co-trimoxazole treatment) and haemophagocytic lymphohistiocytosis. A bone marrow (BM) aspirate, BM cultures (on Columbia blood agar, Sabouraud dextrose agar (SDA), SDA with gentamicin/chloramphenicol, SDA with cicloheximide incubated at two temperatures-25ºC and 35ºC), and BM PCR were requested.

Results: Stained May-Grunwald-Giemsa films revealed numerous yeast-like bodies inside and outside macrophages with morphology suggestive of *Histoplasma spp.* After 7 days the cultures revealed: at 35ºC- growth of white, smooth, creamy and yeast-like colonies and microscopic examination of a lactophenol blue mount preparation showed round to oval, small, budding, and thin-walled yeast-like cells. At 25ºC- growth of velvety/cottony white colonies with yellow reverse and a lactophenol blue mount preparation showed hyphae hialine and septate, with short conidiophores. Macroconidia were large, round, one-celled, hyaline, thick-walled and tuberculate. The isolate was identified as *Histoplasma capsulatum* based on its morphological features growth. Molecular results (bone marrow PCR) confirmed the microbiological diagnosis- *Histoplasma capsulatum*. Despite the diagnosis, due to several comorbidities the patient died 24 hours after the marrow morphology report.

Conclusions: PDH carries a poor prognosis, especially when the diagnosis is delayed. Giving its rarity in non endemic areas it poses a real challenge but should be always considered, specially in AIDS patients. In our case the prompt diagnosis was possible through direct microscopy and culture (for PDH cases the sensitivity of bone marrow culture is 75%).

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Efficacy and safety of tedizolid in difficult-to-treat osteoarticular infections: results of a multi-centre experience

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Background: Linezolid is widely used against Gram-positive osteoarticular infections (OAsI) but has limitations in particular scenarios. Tedizolid, a newer oxazolidinone drug, present a higher in vitro activity and less drug-interaction and toxicity. We aimed to describe our experience using tedizolid in difficult-to-treat OAsIs.

Materials/methods: Multicenter retrospective study (3 Spanish referral centers). Cases with OAI (prosthetic joint infections -PJIs-, osteoarthritis, and diabetic foot infections -DFIs-) receiving Tedizolid (200mg/d) for at least 7 days, were included (January 2017-March 2019). Failure: reappearance of signs of infection after treatment, absence of improving or suppressive treatment.

Results: 51 patients were enrolled (59% women), mean age was 65±14.3. Mean adjusted Charlson Index was 4.9±3.4.

27 (53%) cases presented with osteoarthritis, 17 (33%) with PJIs, and 9 (18%) with DFIs. 30 cases (59%) had device-related infection (DRI). 39.2% (n=20) were polymicrobial infections (55% combining Gram-positive bacteria). Most frequent isolates were coagulase-negative staphylococci (36%, n=26) followed by Staphylococcus aureus (29%, n=21 with 48% of MRSA), and Enterococcus faecium (n=4, 6%).

Potential interaction was main reason for tedizolid treatment (n=32, 63%) followed by cytopenia (n=28, 55%), and toxicity or failure with previous treatment (n=11). 24% cases received rifampin concomitantly.

Median days of treatment was 29 (IQR 15-44). Adverse events were scarce (vomits, n=2) and did not require discontinuation. Hemoglobin value and platelet count (overall cohort) stayed stable along treatment (from 110.3g/L to 120g/L, p=0.03 and 242x10⁶/mL to 239x10⁶/mL, p=0.88 respectively); cases with anemia or thrombocytopenia initially (n=28) did not worsen with treatment (from 94.7g/L to 107.7g/L, p=0.001 and 72x10⁶/mL to 218x10⁶/mL, p=0.001, respectively).

41 (80.4%) underwent surgery; 33% of DRI cases were managed with implant retention. Three cases [6%] were not evaluated due to non-related death after 30 days of infection. Median follow-up was 371 days (IQR 177-644) with a cure rate of 81.3% (n=39) and 4.2% of improvement while 7 cases (14.6%) failed (4 DRI).

Conclusions: Tedizolid proved safety in patients receiving anti-depressants and having relevant cytopenia. High efficacy of tedizolid alone and in combination with rifampicin was observed in difficult-to-treat OAsIs and DFIs. Tedizolid seems to be a suitable alternative for OAsIs while waiting for further experiences in this setting.

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Whole genome sequencing in an outbreak of Serratia marcescens in a neonatal intensive care unit of a tertiary care centre in Italy

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Background: Many outbreaks due to Serratia marcescens [S. marcescens] among hospitalised neonates have been described. In neonatal intensive care units, colonized or infected newborns are the main potential reservoir of S. marcescens, particularly in the gastrointestinal tract. The objective of this outbreak report was to establish the clonal relationships between different isolates of S. Marcescens and identify the source, using whole genome sequencing (WGS).

Materials/methods: In late July 2018 three neonates hospitalised in the neonatal intensive care unit (NICU) of a tertiary care centre in Italy (Brescia), were found to be colonised/infected with S. marcescens. It was considered a possible outbreak and an investigation was started with extensive environmental sampling. Ten patient isolates and two environmental samples positive for S. marcescens underwent WGS, using Illumina Miseq instrument. After alignment, cores of Single Nucleotide Polymorphisms (SNPs) were identified using GATK BestPractice to define genetic clusters with a minimum distance of 5 SNPs. Diffusion of bacterial strains was then analyzed using R Outbreaker2 package and presence of resistance genes was investigated using SRST2 software.

Results: Ten neonates were colonised with S. marcescens; 3 of these had invasive infection due to S. marcescens and 2 neonates had a localized infection (a conjunctivitis and an urinary tract infection). Of 353 environmental samples collected over the study period, S. marcescens was only isolated from the soap dispenser, sink in the lactaction room and soap in the kitchen of NICU. Clinical and environmental samples were closely related with an average of 4.8 SNPs (minimum: 1; maximum: 8); thus they belonged to a unique cluster (Figure 1).

Conclusions: Genotyping confirmed that our outbreak has been caused by a single clone of S. marcescens. The main source were the colonized/infected neonates; transmission was due to the hands of health care workers and parents; while liquid soap resulted ongoing reservoir. We believe that ample evidence is available to support the benefits of integrating WGS into outbreak investigations.

Figure 1 Heatmap of the SNP distances between the 12 isolates of S. marcescens. Heatmap color indicates the number of SNPs between isolates [red corresponds to 0 SNPs, white to 8 SNPs].

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Manipulation of raw pig meat is a risk for transmission of carbapenem-resistant *Pseudomonas fluorescens* to humans in the community

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Abstract third-party references: Project financed by FCT (reference PTDC/CVT-CVT/29510/2017)

**Background:** Carbapenem-resistant gram-negative bacteria (CRGNB) such as *Enterobacter*, *Klebsiella*, *Serratia*, and *Pseudomonas* species became one of the main causes of nosocomial infections worldwide, and colonize persons in the community. Although carbapenems are not used in animal farming, CRGNB have been reported in production animals. However, the prevalence of the different gram-negative bacterial species in production animals and the occurrence of transmission to humans through the food production chain are unknown.

**Materials/methods:** To determine the prevalence of carbapenem-resistant *Pseudomonas* spp. (CRP) and the potential of transmission to humans in pig production chain, we have sampled live pigs (ear and rectum) at slaughterhouse entrance, workers, equipment, raw and cooked meat and hands of human consumers before and after meat manipulation (*n*=90 samples) in Portugal (2019). Samples were screened for presumptive CRP by culturing in selective media with and without 4mg/L of meropenem; up to 5 colonies per sample (*n*=201) were selected for confirmation of carbapenem-resistance through growth in different meropenem concentrations (2, 4, 8 and 16 mg/L). Forty-six CRP isolates, collected from all sampling sites, were selected for species identification by sequencing an internal fragment of *rpoB*.

**Results:** Carbapenem resistant *Pseudomonas* spp. were detected in 46% (41/90) of the samples. Notably, the raw pig meat samples had the highest load of CRP (average: 1.19x10⁵ CFU). No resistant isolates were detected in pig rectum and equipment samples. A total of 60% (6/10) of the human consumers became colonized with CRP only after manipulation of the pig raw meat. The most frequent CRP species were *P. fluorescens* (74%, 34/46 isolates; 23%, 21/90 samples) followed by *P. aeruginosa* (13%, 6/46 isolates; 2%, 2/90 samples). *P. fluorescens* was detected in all sampling sites, whereas *P. aeruginosa* was only detected in the pig ear.

**Conclusions:** The pig food processing chain is a large reservoir for carbapenem-resistant *P. fluorescens*. Manipulation of raw pig meat constitutes a risk of transmission of carbapenem-resistant *P. fluorescens* to humans in the community and might aid in the spread into healthcare settings. Also, foodborne carbapenem-resistant *P. fluorescens* can be a reservoir of carbapenemase resistance genes to other more pathogenic species like *P. aeruginosa*.

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Abstract 6753

Activity of cefiderocol and comparator antibiotics on an Italian multi-centre collection of carbapenem-resistant Gram-negative clinical isolates

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Background: The recent worldwide spread of carbapenem-resistant Gram-negative pathogens underlined the need for novel antimicrobial therapies. Cefiderocol (Shionogi & Co) is a siderophore cephalosporin recently approved by FDA against complicated urinary tract infections caused by Gram-negative pathogens with limited treatment options. No data are available about the activity of cefiderocol against carbapenem-resistant clinical isolates in Italy. The aim of this work was to evaluate the in vitro activity of cefiderocol and comparator antibiotics against carbapenem-resistant Gram-negative isolates prospectively collected from four Italian hospitals (Lecco, Florence, Rome, Potenza).

Materials/methods: Non-duplicate carbapenem-resistant clinical isolates (surveillance samples excluded) of Enterobacteriales and Gram-negative non-fermenters (Pseudomonas aeruginosa, Acinetobacter baumannii and Stenotrophomonas maltophilia) were included in a period of 5 months during 2018. The most common carbapenemases were detected by Real-Time PCR. The susceptibility testing of cefiderocol and comparators (including ceftazidime/avibactam, ceftolozane/tazobactam, amikacin, gentamicin, tigecycline, colistin and trimethoprim/sulfamethoxazole) was performed using frozen broth microdilution plates with iron-depleted Mueller-Hinton broth for cefiderocol. MICs of cefiderocol and comparators were interpreted according to CLSI (29th ed; susceptibility ≤4 mg/L) and EUCAST (v 9.0) clinical breakpoints, respectively.

Results: Among the 234 isolates collected, 159 were confirmed as producers of acquired carbapenemases by molecular methods, including 87 KPC-producing Enterobacteriales, one VIM-producing Enterobacter cloacae, one VIM-producing Citrobacter spp, five VIM-producing P. aeruginosa, five GES-producing P. aeruginosa, one NDM-producing K. pneumoniae, one NDM-producing E. coli, 49 OXA-23-producing A. baumannii, 8 OXA-23- and ISAb1-OXA-51-coproducing A. baumannii and one NDM-producing A. baumannii. Excellent activity of cefiderocol was observed with all tested isolates. In particular, 99.1% of all isolates [N=232/234] exhibited MIC≤4 mg/L, including 98.9% of KPC producers and 90.0% of metallo-β-lactamase producers. Among Enterobacteriales, the cefiderocol MIC₅₀ and MIC₉₀ [2 and 4 mg/L, respectively] were lower than those of comparators, except for colistin and tigecycline. Moreover, non-fermenters, P. aeruginosa and S. maltophilia especially, had lower MIC values for cefiderocol than Enterobacteriales isolates. The highest MIC of cefiderocol was 8 mg/L, corresponding to an intermediate susceptibility, observed in a KPC-producing K. pneumoniae and a NDM-producing A. baumannii.

Conclusions: Cefiderocol showed a potent activity in vitro against multidrug-resistant Gram-negative bacteria, including carbapenemase producers of all classes.

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Abstract 6754

**Recurrent community-acquired bacterial meningitis in adults**
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**Background:** Recurrent episodes of bacterial meningitis episodes have been described in 5% of cases and was previously associated with a relatively favorable prognosis. Due to changes in population and epidemiology of bacterial meningitis risk factors and clinical characteristics may have changed. It is unclear whether this is done and if vaccine failures occur.

**Materials/methods:** We analyzed adult patients with recurrent episodes of bacterial meningitis from a prospective nationwide cohort study of community-acquired bacterial meningitis.

**Results:** We identified 143 recurrent episodes of community-acquired bacterial meningitis (5%) out of 2264 episodes in 123 patients. The median age was 57 years and 57 episodes (46%) occurred in men. The median duration between a first episode and the current episode was 5 years. For 78 of 122 patients [64%] the current episode was a second episode, 30 patients [25%] had between 1 and 5 previous episodes, 3 patients [3%] had 5 to 10 episodes, 1 patient had more than 10 recurrent episodes. Predisposing factors were identified in 86 of 123 patients [70%], and most commonly consisted of extra-meningeal foci of infections [45/123 [37%]] and cerebrospinal fluid leakage [36/122 patients [30%]]. The most common causative agents were Streptococcus pneumoniae in 80 patients [65%] and Haemophilus influenzae in 16 patients [13%]. The outcome was unfavorable [Glasgow outcome scale score <5] in 22 patients with recurrent bacterial meningitis [18%] versus 806 patients [40%] for non-recurrent meningitis patients [P<0.001]. Five patients [4%] died compared with 363 patients [18%, P<0.001].

**Conclusions:** Recurrent meningitis frequently occurs due to predisposing factors, most commonly extra-meningeal foci of infection and CSF leakage. Recurrent episodes are predominantly caused by S. pneumoniae and H. influenzae and the disease course is less severe with a lower mortality rate compared with non-recurrent bacterial meningitis patients.

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Evaluation of STANDARD E TB-Feron ELISA for the diagnosis of latent tuberculosis infection in healthcare workers

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Background: Laboratory diagnosis of latent tuberculosis infection (LTBI) is mainly performed with interferon-gamma release assays (IGRAs). We compared the performance of a new ELISA-based IGRA, STANDARD E TB-Feron ELISA (TBF; SD Biosensor, Gyeonggi-do, Republic of Korea), and a widely used assay, QuantiFERON-TB Gold In-Tube (QFT-GIT; Qiagen, Hilden, Germany), in a population of 425 healthcare workers (HCWs).

Materials/methods: All HCWs were screened with both assays per the manufacturers’ protocols and in a “cross-manner,” where tube sets from one assay were used with the alternative ELISA. Results were compared both qualitatively and quantitatively.

Results: TBF and QFT-GIT identified 11.3% (48/425) and 12.9% (55/425) positive samples, respectively. TBF demonstrated 81.6% positive and 97.4% negative percentage agreement with QFT-GIT, with a Cohen’s kappa value of 0.78 (strong agreement). Discordant results were detected in 20 subjects (4.3%): 13 samples (65.0%) were TBF(-)/QFT-GIT(+), 6 (30.0%) were TBF(+)/QFT-GIT(-), and one provided TBF/QFT-GIT indeterminate/negative results. We observed a statistical significant degree of correlation between interferon-gamma reactivity between both assays ($r_s=0.551$, $P<0.01$) and between standard assays and cross-manner tests ($r_s$ ranging from 0.449 to 0.816, $P<0.01$ for all combinations). Cross-manner tests also revealed that the ELISA kit of TBF provided higher TB antigen and nil values than ELISA of QFT-GIT under the same conditions ($P<0.01$), although these differences disappeared in the TB antigen minus nil value.

Conclusions: TBF showed a comparable and acceptable clinical performance in detecting LTBI comparing to QFT-GIT. TBF represents a useful alternative tool of ELISA-based IGRA, especially in large-scale LTBI screening in HCWs.

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Rapid simultaneous detection of TB and first line drugs gene mutations onto direct paediatric samples
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Background: The great challenges in diagnosing childhood TB are: low burden bacterial load, lack of sign and symptoms and high prevalence of Extrapulmonary TB.

Despite the incredible advances in the field of technological innovations, a major bottleneck in controlling tuberculosis is still the Turn-Around-Time to obtain a TB laboratory confirmed diagnosis. On the other hands, in the last few years we are witnessing the evidence of multidrug and extremely resistant TB strains pan-spread. Rifampicin resistance is mostly due to mutations in an 8bp "hot-spot" region of the rpoB-gene, while isoniazid resistance is due to mutations of several genes as catalase-peroxidase-

Materials/methods: we evaluated a new real-timePCR combined with automated platform [MDR/MTB-ELiTé-InGenius] able to perform simultaneous DNA extraction, detection of MTB and rifampicin-isoniazid resistance direct onto various samples. The DNA extraction is based on magnetic-beads technology and heat treatment using a low sample volume, while the RT-PCR amplification is performed independently. Within one session, one-to-12 samples are processed.

In order to evaluate robustness of MDR/MTB-PCR and platform feasibility, we selected a list of 12 well-known frozen positive samples [NAT and/or culture confirmed].

Afterwards, we tested 62 pediatric routine samples [51 patients] examined with PCR/ cultures/DST.

Results: A broad spectrum of samples was investigated: biopsy(4), gastric aspirate(19), sputum(16), BAL(22), exudate(1). No cross-reaction with non-tuberculous mycobacteria (5) was observed, 27 patients received a diagnosis other-than-TB, while 19 patients were TB positive.

Conclusions: Despite a low DNA Mycobacterial load in pediatric samples, the new assay MDR/MTB-ELiTé-InGenius could be a valid support for a rapid TB and drug-resistance detection.

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Abstract 6757

Potential coverage of invasive pneumococcal disease by current and next generation of anti-pneumococcal vaccines in children and adults in Spain

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Background: Introduction of pneumococcal conjugate vaccines (PCVs) has shown a marked reduction in the disease caused by vaccine serotypes in children providing herd protection to the elderly group. However, the emergence of non-vaccine serotypes is of great concern worldwide. The main goal of this study was to evaluate the serotype distribution of invasive pneumococcal disease (IPD) by age group in Spain to assess the potential coverage of the different pneumococcal vaccines.

Materials/methods: This study includes national laboratory data from IPD cases affecting pediatric and adult population for the last 10 years corresponding to the period 2009 to 2018. We show the potential coverage by age group of the different PCVs (PCV13, PCV15, PCV20) and also by the 23-valent polysaccharide vaccine (PPV23) comparing the years 2009 (pre-PCV13 period in private market) vs 2015 (pre-PCV13 in pediatric vaccination calendar) vs 2018 (late period).

Results: A total of 22978 laboratory-confirmed IPD cases were included in the study. In 2009, just the year before the introduction of PCV13 in the private market for the pediatric population, the coverage rates of IPD cases by PCV13, PCV15 and PCV20 in children under 5 years old were 78%, 80% and 86% respectively. In adults aged 65 years or older the coverage by PCV13, PCV15, PCV20 and PPV23 were 65%, 70%, 80% and 78% respectively. In 2015 coverages for children under 5 years old were 30%, 39% and 59% for PCV13, PCV15 and PCV20 respectively whereas for adults aged 65 years or older were 35%, 43%, 63% and 69% for PCV13, PCV15, PCV20 and PPV23 respectively. In the late period 2018, the potential coverages for PCV13, PCV15 and PCV20 in children under 5 years old were 24%, 33% and 53% respectively and for adults aged 65 years or older were 29%, 37%, 62% and 68% for PCV13, PCV15, PCV20 and PPV23 respectively (Figure 1).

Conclusions: The two new PCVs could provide additional increased coverage in the late period 2018 in Spain, with PCV15 and PCV20 potentially protecting against 33% or 53% of IPD pediatric cases respectively whereas in adults the coverage would be 37% or 62% respectively.

Figure 1: Potential coverage of IPD cases by pneumococcal conjugate vaccines in children and adults in the year 2018 in Spain

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Prediction Model for carbapenemase-producing Enterobacterales colonisation upon admission to hospital in an endemic geographic area

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Background: Carbapenemase producing Enterobacterales (CPE) have been established as important nosocomial pathogens worldwide. These organisms are sustained in healthcare facilities by continuous influx of already colonized patients. The timely detection of CPE carriers by active surveillance cultures is considered pivotal in controlling CPE. Universal screening, however, is unfeasible in resource-limited settings. We aimed to develop a prediction score to identify patients upon admission to the hospital who are at greater risk for colonization.

Materials/methods: The study was conducted between January 2014 and December 2015 in a tertiary-care 500-bed hospital located in a CPE endemic area, Athens, Greece. Rectal swabs were obtained from consecutive patients upon admission, periodically at different departments and inoculated on McConkey agar No.3 plates containing 0.5 mg/L meropenem. After incubation for 48 hours, all isolated enterobacterales were examined for the presence of \( \text{bla}_{\text{VIM}}, \text{bla}_{\text{KPC}}, \text{bla}_{\text{NDM}}, \text{bla}_{\text{OXA-48}} \) by PCR using specific primers. Relevant demographic and epidemiologic information were collected in a pre-designed form. Logistic regression analysis was used to identify factors associated with increased risk for CPE carriage. A points score was developed and the area under the Receiver Operating Curve (AUROC) was estimated to assess its discriminative ability. The predictive performance of the model was validated in a different cohort that took place in the same hospital between May and October 2016.

Results: Among 2199 patients examined, 95 (4.3%) were CPE carriers. Eight predictors were identified: Karnofsky score, prior hospitalization in previous six months, duration of prior hospitalization (\( \geq 10 < 10 \) days), stay in a long-term health care facility, history of \( \geq 2 \) different interventional procedures, known CPE colonization or infection, renal replacement therapy, and diabetes with complications. The developed points score to predict CPE risk ranged between 0 and 79 points with a corresponding risk estimate of 0% to 83.6% and an AUROC of 0.83. The AUROC of the score in the validation cohort of 1506 patients was 0.84.

Conclusions: This study provides useful information to help us limit the pre-active infection control measures and the active surveillance cultures to high-risk patients in CPE endemic areas and resource-limited settings.

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Abstract 6759

Features and outcomes of biliary tract-related bloodstream infections in patients with biliary prosthesis: results from the PROBAC study

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Abstract third-party references: Supported by Instituto de Salud Carlos III (PI16/01 432), On behalf of PROBAC REIPI/GEIH-SEIMC/SAEI group

Background: Biliary prosthesis (BP) is a well-recognized risk factor for biliary tract-associat ed bloodstream infections (BT-BSI). However, there are scarce data comparing BT-BSI with and without BP. Our aim is to provide information about BT-BSI in patients with BP.

Materials/methods: Patients with BT-BSI were selected from the PROBAC cohort, a prospective multicenter cohort collecting patients aged >14 years with BSI from 26 Spanish hospitals, between October 2016 and April 2017. Variable associated with BP were investigated through a bivariate analysis. Multivariate analysis using logistic regression was performed to estimate the adjusted risk of 30-day mortality associated to BP.

Results: We analyzed 850 episodes of BT-BSI; 153 (18%) were associated with BP. Beyond the reasons for having a BP, the variables associated with BP were younger age [70 years (IQR 59-84) vs 77 (IQR 67-84); p<0.01], moderate-severe liver disease [RR=2.34; 95%CI=1.64-3.44; p<0.001], and immunosuppressive therapy [RR=3.26; 95%CI=2.08-5.19; p<0.01]. Escherichia coli was the most frequent etiology in both groups but was less frequent in BP [56.9% vs 68.9%; RR=0.82; 95%CI: 0.71-0.96; p<0.01], while the following were more frequent: Enterococcus faecalis [9.2% vs 5%; RR=1.82; 95%CI: 1.00-3.30; p=0.05] and Escherichia (6.5% vs 2%; RR=3.26; 95%CI: 1.47-7.19; p<0.01). Pseudomonas aeruginosa [5.9% vs 1.4%; RR=4.10; 95%CI: 1.69-9.90; p<0.01] and polymicrobial BSI [22.9% vs 15.1%; RR=1.52; 95%CI: 1.08-2.13; p=0.02]. No difference in ESBL distribution was noted; carbapenem-resistance in Gram negatives was 3.1% and 1.1% [RR 2.83; 95%CI: 0.84-9.52; p=0.09]. Active empirical therapy was administered to 71.2% and 76.3% [RR=0.93; 95%CI:0.84-1.04; p=0.186]. BP was associated with worse outcomes in crude analyses: higher 30-day mortality [24.2% vs 13.1%; RR=1.85; 95%CI: 1.32-2.60; p<0.01], recurrence [RR=2.13; 95%CI: 1.15-3.91; p<0.01], persistent bacteremia [RR=3.65; 95%CI: 1.46-9.09; p<0.01] and secondary infection of endovascular or joint devices [RR=4.54; 95%CI: 1.33-15.65; p<0.01]. The risk of mortality adjusted by age, Charlson index, presentation with septic shock and inadequate empirical therapy was higher in patients with BP [OR=2.28; 95%CI: 1.45-3.58; p<0.01].

Conclusions: Our results highlight that BT-BSI in patients with BP was associated with specific pathogens and higher risk of death. Specific preventive and therapeutic strategies for BT-BSI must be investigated in these patients.

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Differentiation of phenotypic and genotypic characteristics of uropathogenic *Escherichia coli* isolates in acute and recurrent phases of urinary tract infection

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**Background:** Urinary tract infection (UTI) is one of the most common infections worldwide, and uropathogenic *Escherichia coli* (UPECs) are the main causative pathogens. However, their characteristics may vary depend on the phase (acute or recurrent) of UTI.

This study was conducted to evaluate any probable differences between UPEC isolates in acute and recurrent phases of UTI in the same patient.

**Materials/methods:** The urine samples of patients suffering from UTI in two referral hospitals of Tehran, Iran were collected and the patients were under supervision for any probable recurrence during 6 months. The isolates were subjected for differential cultures to select *E. coli* strains. Then, phyl- and sero-grouping, antibiotic susceptibility test, biofilm formation assay, was performed, and the genes responsible for antibiotic resistance, biofilm formation and iron transferring were detected.

**Results:** Sixty isolates (one isolate from each phase) were selected from 30 patients (16 females, 14 males) at different ages. In two-third of patients, phylogroups of the *E. coli* isolates were identical in the acute and recurrent phases, 70% of them were B2/B2. Similarly, in 70% of the patients, serogroups of the isolates were alike in both phases, 85.7% of them have O25/O25 pattern. The isolates with O15 serotype were significantly seen more in recurrent phase. All of the isolates form biofilm. However, only one-third of them showed equal biofilm intensity in both phases (mostly weak/weak). The isolates with strong biofilm ability were mainly detected in recurrent phase. When comparing antibiotic resistance pattern of the isolates in two different phases, the isolates from Imam hospital had more antibiotics in common to be resistant to than the ones from Loghman hospital. Likewise, the isolates in Imam hospital had more antibiotic resistance, biofilm-related and iron transfer genes in common than the ones in Loghman hospital. Interestingly, distribution of two resistance genes, *sul1* and *qnrA*, was more predominant in Imam and Loghman hospitals respectively.

**Conclusions:** Although it seems that UPEC isolates that are responsible for acute or recurrent phases of UTI may belong to common phylo- or sero-groups, but they show different resistance and virulence characteristics. These characteristics may vary from hospital to hospital.

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Abstract 6762

Pyogenic spinal infections in a tertiary care centre: trends in the last decade
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Background: The incidence of pyogenic spinal infections is increasing in the last 20 years. The aim of the study was to compare two subgroups of patients treated for two consecutive five-year periods at the Department of infectious diseases of a tertiary care centre and to identify possible trends.

Materials/methods: A retrospective observational study carried out in 2010-2019 enrolled 137 adult patients with pyogenic spondylitis, discitis and facet joint infections. Recorded parameters included demographics, chronic comorbidities, time to diagnosis, radiological work-up, anatomical level of spinal infection, etiological agent, complications, treatment and outcomes. The periods 2010-2014 and 2015-2019 were evaluated and compared.

Results: In 2010-2014 and 2015-2019, there were 57 vs. 80 patients enrolled, median age 66 years. The proportion of patients with comorbidities increased (64 vs. 75%) as well as median time to diagnosis (9 vs. 14 days). Diagnosis was made using MRI in 81 vs. 59% and CT in 16 vs. 35%. Epidural abscess developed in 53 vs 48%, paravertebral abscess or empyema in 61 vs. 51% of patients. The pathogen was identified in 82 vs. 69% of patients, mainly by blood culture in both periods (72 vs. 58%). Staphylococcus aureus was the most common pathogen isolated in 54 vs. 48%; Gram-positive bacteria in total caused 70 vs. 59% of cases. Forty-two vs. 35% of patients were treated surgically. The median length of hospital stay was similar in both periods (46 vs. 42 days) as well as the median length of antibiotic treatment (58 vs. 52 days). Sixty-five vs. 73% recovered with no or mild sequelae, 14 vs. 6% with severe sequelae, and 21 vs. 20% of patients died.

Conclusions: When comparing the two periods, we observed an increasing incidence, chronic comorbidities and time to diagnosis, but also better outcomes. An adverse finding is a decreasing proportion of identified aetiology, probably due to early initiation of antibiotic therapy and the absence of CT-guided disc biopsy. Despite the decline in identified Gram-positive aetiology, which can be partly explained by a decrease in the proportion of overall identified aetiology, Gram-positives remain the major pathogens and empirical therapy should target it.

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Abstract 6764

**A proof-of-concept evaluation of biphasic blood culture bottles for low-resource settings**

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**Background:** The Mini-lab is a Médecins Sans Frontières project for the development of an all-in-one clinical bacteriology laboratory deployable in low-resource settings. Blood cultures are priority specimens in this laboratory. Since automated blood culture systems are not yet feasible in these settings, biphasic "manual" blood culture bottles (BCB) were selected. They consist of a broth and an agar slant; the agar slant assists in recognizing growth and performing subcultures.

**Materials/methods:** Three biphasic BCB types (Zhuhai Encode Bi-State BCB, CD Rich Double Phase BCB and Autobio Bi-State BCB) were evaluated alongside visual reading of BacT/ALERT FA Plus and BacT/ALERT PF Plus (bioMérieux) BCB and a monophasic manual BCB (Hemo-aerobic culturing bottle and Hemo-aerobic culturing pediatric bottle, Liofilchem). They were inoculated with human blood spiked with ATCC strains representing 8 common bloodstream pathogens. For adult cultures, 10 ml blood per bottle (containing 1-10 colony forming units (CFU)/ml) was inoculated; for pediatric cultures, the volume was 2 ml (containing 2-25 CFU/ml).

**Results:** The yield (% of inoculated BCB grown) was 97.3% (109/112) for Autobio BCB, 89.3% (100/112) for CD Rich BCB (p=0.016 compared to Autobio), 84.8% (94/112) for Zhuhai Encode BCB (p=0.001), 95.5% (107/112) for Liofilchem BCB (p=0.47) and 100% (58/58) for manual BacT/ALERT BCB (p=0.21). More than 95% of grown bottles showed signs of growth within 48 hours of incubation, with similar results for all BCB types. Growth was more frequently observed in broth (91.7%) than on the agar slant (87.8%; n=336; p=0.006). First sign of growth was observed only in the broth in 51.0%, only on agar slant in 1.3% and in broth and agar slant simultaneously in 47.7% of grown biphasic BCB (n=304). At the moment of growth, only 6.3% – 10.1% of biphasic BCB showed sufficient bacterial growth on the agar slant to do further testing. Sufficient bacterial growth on the agar slant increased to 56.9 – 70% of grown biphasic BCB by the end of the 7 day incubation period.

**Conclusions:** Compared to a monophasic BCB, biphasic BCB had similar yield and speed of detection. The agar slant did not allow earlier detection and had insufficient growth to replace subculture.

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Abstract 6768

**Stool multiplex PCR for Shiga toxin-producing *Escherichia coli* sufficiently equals with culture for clinical diagnosis and follow-up**

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**Background:** STEC causes potentially severe gastrointestinal infections. Due to its public health importance, control measures are required, and carriers may need to refrain from work or day care when the spread risk to vulnerable people is high. We evaluated the usefulness of direct stool multiplex PCR compared to parallel stool culture for primary STEC diagnostics and for follow-up in order to update the national guidelines for STEC monitoring.

**Materials/methods:** At Helsinki and Uusimaa Hospital District, Finland, we identified 236 STEC PCR positive cases in 2016-2017. We included their follow-up samples, altogether 858 samples with stool PCR and corresponding culture. All STEC PCR positive samples were inoculated on non-selective BD™ CHROMagar™ Orientation agar plates (ORI). Culture positivity was confirmed from ORI culture sweeps by PCR.

**Results:** 211 (89%) of the cases were culture positive in their primary sample. Of all primary and follow-up samples 499 were PCR positive and of these 450 (90%) were culture positive. Ten cases (8%) had one PCR positive but culture negative ("intermediate") sample in between the culture positive and PCR negative sample(s), and one case (0.8%) had two such "intermediate" samples in between the culture positive and PCR negative samples. For 13 cases (10%), the initial sample was PCR positive, culture negative, followed by PCR negative samples. The remaining 15 cases (12%) had fluctuation of PCR and/or culture positivity in their follow-up samples. 89 cases were followed for at least three consecutive PCR negative samples. 2 cases (2%) had culture positive sample(s) after two consecutive PCR negative samples.

**Conclusions:** PCR is adequate for STEC diagnostics and follow-up in a clinical laboratory. When non-selective methodology is used, the vast majority of PCR positive samples (90%) are also culture positive. Furthermore, only two cases (2%) in our material had positive samples followed by two consecutive PCR negative samples. Consequently, to demonstrate the clearance from STEC infection, we consider two PCR negative follow-up samples sufficient. The Finnish national guidelines for STEC monitoring have recently been updated accordingly.

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Background: *Streptococcus pneumoniae* is the most common pathogen causing community-acquired bacterial meningitis. We evaluated the impact of the implementation of adjunctive dexamethasone treatment in 2002 and the 7-valent and 10-valent pneumococcal conjugate vaccines (PCVs) in 2006 and 2011 on the clinical outcome and cause of death in pneumococcal meningitis.

Materials/methods: We included adult patients (≥16 years of age) with community-acquired pneumococcal meningitis from two large nationwide prospective cohort studies in the Netherlands (1998-2002, 2006-2018). Patients were identified by the surveillance of the Netherlands Reference Laboratory for Bacterial Meningitis or were notified by the treating physician. Deaths were categorized independently by two physicians as neurologic or systemic. Missing data were imputed for logistic multivariable models to assess prognostic factors for death and unfavorable outcome.

Results: A total of 1816 episodes in 1783 patients were included (median age 62 [IQR 51,70], 902 episodes in males [50%], 1739 CSF culture positive episodes [96%]). The classic triad of fever, neck stiffness, and altered mental status was present in half of episodes. 11 of 336 (3%) patients in the 1998-2002 cohort and 117 of 1437 patients (82%) in the 2006-2018 cohort received adjunctive dexamethasone. Clinical outcome at discharge was unfavorable (Glasgow Outcome Scale score <5) in 772 of 1816 episodes (43%), with death occurring in 363 episodes (20%). Adjuvant dexamethasone led to a lower death rate (175/585 [30%] vs. 178/1188 [15%], p<0.001), both due to neurologic (15% vs. 9%) and systemic causes of death (15% vs. 6%). Mortality among patients not treated with dexamethasone was similar in the 1998-2002 and 2006-2018 cohort (32% vs. 28%). Age ≥75 years, immunocompromising condition, higher heart rate, lower Glasgow Coma Scale score, cranial nerve palsy, CSF white cells <1,000/µL, CSF:blood glucose ratio <0.23, C-reactive protein >200mg/L, and thrombocytes <75,000 units/L were associated with death and unfavorable outcome. Particular serotypes were associated with clinical outcome adjusted for dexamethasone use and age (Figure 1).

Conclusions: Pneumococcal meningitis is still associated with high mortality and morbidity rates. Implementation of PCVs has not affected clinical outcome.
Effectiveness of monitoring colonisation by multidrug-resistant bacteria in polytrauma patients: 7 years of experience

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Background: Patients with polytrauma need prolonged hospitalization and intensive care, which are risk factors for nosocomial infection. A recent increase of these infections due to Multidrug-resistant bacteria (MDR) involves application of surveillance procedures.

Monitoring colonization is performed by Active Surveillance Cultures (ASC) with fecal, nasal and pharyngeal swab (Copan).

Aim of the study is the evaluation of effectiveness of ASC for prevention and control of infections by MDR.

Materials/methods: We analyzed 1011 patients with Major Trauma, evaluated with Injury Severity Score (ISS) >15 admitted in Emergency Room of GOM Niguarda in a period of 7 years.

Each patient is monitored with ASC at hospitalization time and, if negative, every 7 days.

We considered hospitalization and intensive care duration, mortality; we also evaluated colonization, infections and sepsis due to MDR.

Results: 867 (85.8%) patients resulted permanently negative (ASC-), while 144 (14.2%) resulted positive during hospitalization (ASC+).

ASC+ presented major clinical severity at entry than ASC-, in terms of ISS and visceral lesions (p<0.05). ASC+ needed a longer hospitalization (35 days) than ASC- (20 days) (p<0.001), and longer stay in Intensive Care Unit, 20 days respect 7 days (p<0.001). Infections due to MDR were most frequent in ASC+ (68.1% versus 11.2%, p<0.001).

There were 40 cases of sepsis, 7/867 (0.81%) ASC- patients, and 33/144 (22.9%) ASC+ (p<0.001), mainly caused by Acinetobacter baumannii MDR and Meticillin-resistant Staphylococcus aureus. In ASC+, 32/33 sepsis were caused by the same MDR that were previously isolated in surveillance culture.

Mortality rate in ASC- was 10.9% vs 6.3% in ASC+ (p=0.056), the former mostly in the first days of hospitalization.

Conclusions: Surveillance allows to evaluate risk of MDR-infection of each patient during hospitalization period. In addition, a positive surveillance test provides information to set up a targeted therapy in case of MDR-driven infections, with important consequences on clinical outcome, including a trend in decreased mortality in ASC+ despite a higher rate of sepsis.

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Clinical characteristics, aetiology and risk factors for mortality of neutropenic patients with bloodstream infection presenting with septic shock

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Background: We aimed to describe the clinical characteristics and aetiology of bloodstream infections (BSI) in febrile neutropenic patients presenting with septic shock and analyze risk factors for mortality.

Materials/methods: All consecutive episodes of BSI in neutropenic patients were prospectively collected in two university hospitals [2010-2019]. Patients with septic shock, defined as hypotension requiring vasopressors despite adequate volume resuscitation, were compared with those without shock. Factors associated with 30-day mortality in patients with septic shock were assessed using univariate and logistic multivariate models.

Results: Out of 1563 BSI episodes, 257 (16.4%) presented with septic shock. The most frequent baseline diseases were acute leukaemia (45.2%), non-Hodgkin lymphoma (17.1%), and solid neoplasia (15.2%). Haematopoietic stem cell transplantation was undergone by 25.5% of patients. Patients presenting with septic shock were older (p=0.026), and had solid neoplasms (p<0.001) and other comorbidities (p=0.025) more frequently. Corticosteroid therapy, urinary catheter, and non-nosocomial acquisition (p<0.001 for all) were also more frequent. Pulmonary (p<0.001), abdominal (p=0.001) and urinary (p=0.027) sources of BSI were more common among patients with septic shock, whereas catheter and mucositis-related episodes (p<0.001 and p=0.001) were less frequent. Regarding aetiology, episodes with septic shock were more commonly caused by E. coli, K. pneumoniae and P. aeruginosa (p<0.001 for all), and less commonly by Enterococcus spp. and coagulase-negative Staphylococci (p<0.001 for both). Multidrug-resistant (MDR) Gram-negative bacilli (GNB) were the causative agents of septic shock in 15.2% of cases. 30-day mortality was higher among patients presenting with septic shock (54.9% vs 15.2%, p<0.001). Table 1 shows the independent risk factors for mortality in patients with septic shock.

Conclusions: Clinical and microbiological characteristics of neutropenic patients with shock are differential. Avoiding inappropriate empirical antibiotic treatment in those patients with GNB-BSI is the only modifiable factor in decreasing mortality.

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Adjusted OR (95% CI)</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Orotracheal intubation requirement</td>
<td>7.370 (3.538-15.351)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Gram-negative bacilli BSI receiving inappropriate empirical antibiotic treatment</td>
<td>3.473 (1.076-11.203)</td>
<td>0.037</td>
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</tbody>
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Abstracts 2020

Abstract 6779

Clinical characteristics and outcomes of respiratory syncytial virus infection among hospitalised adult patients: risk factors of intensive care unit hospitalisation and 30-day mortality

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Background: Respiratory syncytial virus (RSV) can cause intensive care unit (ICU) hospitalization with significant morbidity among the susceptible populations. However, clinical burden of this infection may vary in adult risk groups. This study aimed to investigate risk factors to RSV-related ICU hospitalization and outcomes among hospitalized adult patients.

Materials/methods: A retrospective cohort study was conducted in a university hospital in South Korea from March 2013 to February 2019. Subjects included hospitalized adult patients (≥19 years) diagnosed with RSV infection by RT-PCR. The RSV-associated events (pneumonia, aggravation of chronic co-morbid illness, ICU admission, etc.) were defined as those episodes occurred within prior and after 2 weeks of the RSV detection.

Results: A total of 272 adults with RSV infection were enrolled. The median age was 72. The subjects were categorized into ICU (54/272, 19.9%) and non-ICU (218/272, 80.1%) hospitalization groups. There were no significant differences in terms of age, sex, nursing facility residency, types of RSV infection, and co-infection with other respiratory virus between two groups, while more patients with immunocompromised conditions (IC) were in the non-ICU group (35.5% vs. 13.2%, P=0.002). In contrast, presence of chronic kidney disease (≥stage 3) (28.3% vs. 14.2%, P=0.014), RSV-associated heart failure (25.9% vs. 11.9%, P=0.009), and RSV-associated pneumonia (33.3% vs. 17.4%, P=0.010) were more common in the ICU group. In a multiple logistic analysis, RSV-associated pneumonia [odds ratio (OR) 2.73, 95% confidence interval (CI) 1.31-5.69], RSV-associated heart failure (OR 2.46, 95%CI 1.10-5.50) and septic shock (OR 50.0, 95%CI 5.16-446.90) were significant risk factors for ICU hospitalization, while the presence of IC (OR 0.38, 95%CI 0.15-0.94) was inversely associated with ICU hospitalization. Thirty-day mortality was 6.3% (17/272). In a Cox regression model, chronic kidney disease (≥stage 3) [hazard ratio (HR) 4.66, 95%CI 1.73-12.54], nursing facility residency [HR 8.15, 95%CI 2.21-30.06], and ICU hospitalization [HR 7.96, 95%CI 2.96-27.79] showed higher risk of 30-day mortality.

Conclusions: This study indicates that patients with chronic kidney disease and cardiac disease may be vulnerable to high clinical severity from RSV infection and need to be considered for prompt recognition and preventive measures for RSV infection.

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Abstract 6781

**Rapid, reproducible resistance analysis for all: the AMR package for R**

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**Background:** Antimicrobial resistance (AMR) is threatening healthcare on multiple levels worldwide, thus AMR surveillance is indispensable. However, analysis of antimicrobial resistance (AMR) is challenging due to the rapidly increasing amount of data, while microbiological laboratory systems are not equipped for thorough (epidemiological) data analysis. Smart analysis tools and scientifically reliable reference data are lacking, leaving analysts and clinicians with restricted and non-reproducible methods. To overcome this, we present a free and open-source software solution enabling a new standardised way of working with (anti-)microbial resistance.

**Materials/methods:** We developed the ‘AMR’ package in the increasingly popular statistical software R. By incorporating evidence-based methods and reliable reference data, the ‘AMR’ package is intended to simplify, facilitate, and automate AMR data cleaning, enhancing, and analysing. The software was tested by health care professionals of seven different public health institutes from three different countries.

**Results:** With intelligent rules, microbiological data can be transformed to valid, reproducible output within milliseconds. Antimicrobial resistance (rates) can be calculated, predicted, and plotted with integrated regression models, to which end empiric antimicrobial treatment could also be evaluated. The package can identify first isolates, apply EUCAST rules, and determine the presence of MDRs automatically based on different national and international guidelines. On top, the package contains the complete taxonomic tree of ~70,000 microorganisms and all names, tradenames, and defined daily doses (DDDs) of ~550 antimicrobial agents as reference data.

**Conclusions:** Being downloaded ~25,000 times from 74 countries since its release online last year (figure 1), the ‘AMR’ package is routinely used by epidemiologists and data scientists in many different microbiological laboratory institutes and universities worldwide. In organisations or countries with very limited resources this free and open-source package could also overcome a financial limitation that would otherwise hinder antimicrobial resistance analysis in these settings. Our new standard for clean and reproducible antimicrobial resistance data analysis can therefore empower epidemiological analyses to continuously enable surveillance in any setting.

Figure 1. World map showing all 74 countries (in blue) where the AMR package was downloaded from since its release last year.

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Abstract 6784

**Genome analysis of mecC-harbouring methicillin-resistant *Staphylococcus aureus* and methicillin-sensitive *Staphylococcus aureus* CC130 strains from different origins**

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**Abstract third-party references:** Supported by project SAF3016_76571 R of the AEI of Spain and FEDER of EU

**Background:** Methicillin-resistant *Staphylococcus aureus* (MRSA) CC130 has been associated with the unusual mecC gene, and never so far with mecA gene. In this work, the molecular characteristics of MRSA and methicillin-susceptible *S. aureus* (MSSA) isolates of lineage CC130, from different origins, were analyzed by whole-genome-sequencing.

**Materials/methods:** Eighteen CC130 isolates (13 MRSA and 5 MSSA) from different origins (domestic ruminant and wild animals, human and environment) and with different sequence types (ST130, ST1945, ST1583, ST3061, ST1581, ST1571, ST700) were sequenced (Illumina HiSeq-2000) and analyzed using bioinformatics tools.

**Results:** All 13 MRSA-CC130 contained the mecC, blaZ-SSCMecXI, arsB, and arsC genes (SSCMecXI) and no other resistance genes were detected; contrarily, MSSA-CC130 harbored tet(K) (n=2) and blaZ (n=1) genes. All CC130 strains carried the virulence genes lukED, hlgAB, hlgCB, edinB, splA/B, and aur. The three ST700 strains carried sec, sel, lukMF, and tst-like genes. etD2 gene was present in all the strains, but in ST700. Six MRSA-mecC strains was immune-evasion-cluster (IEC) positive (type-E). The pan-genome study showed a high similarity in core genome, with 2318 genes shared by all strains, but 29 unique genes in MRSA (mainly SCCmecXI-related), and 21 unique genes in MSSA (mainly bacteriophage-related). No unique genes in IEC-positive versus IEC-negative strains were found (except for bacteriophage φ3 related-genes) and hlb gene was also truncated in 3 IEC-negative strains. The vwbp gene was found in four MSSA strains (domestic ruminants and red deer). Three MSSA among CC130 strains presented rep genes: rep1, rep2, rep3, and rep4. Phage analysis showed 12 different intact prophages, with an average of 2±2 prophage regions-genome; four MSSA strains (small ruminants and red deer) showed a scn-like gene. The 5 MSSA strains grouped separately in a phylogenic three from MRSA stains, and those of ST700 were really distant to all the others.

**Conclusions:** Differences between MSSA and MRSA CC130 were detected. The etD2 gene could be a genetic marker of CC130 lineage (MSSA and MRSA), except in ST700, what reinforce the idea of this lineage outside of CC130. The presence of IEC system in some of the MRSA-mecC from animals open questions about the mecC origin.

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Predictors of 30-day mortality rate in patients with *Pseudomonas aeruginosa* bacteraemia

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**Background:** *Pseudomonas aeruginosa* is a major cause of morbidity and mortality among nosocomial pathogens. The CDC reports a serious threat level for multidrug-resistant *Pseudomonas aeruginosa*. UW Health is an academic medical center that is unique in testing ceftolozane-tazobactam susceptibilities on *Pseudomonas aeruginosa* routinely. The purpose of this study is to determine factors contributing to the 30-day mortality rate in *Pseudomonas aeruginosa* primary bacteremia.

**Materials/methods:** A retrospective chart review included patients less than 90 years old with a blood culture positive for *Pseudomonas aeruginosa* at UW Health. Data collection included patient's baseline characteristics, chronic conditions, antibiotic regimen, susceptibilities, and outcome. Statistical analysis was performed using Fischer's exact test, T-test, and Mann-Whitney U tests as appropriate, followed by a logistic regression using STATA with a p value cut point of p<0.02.

**Results:** Eighty-four patients were included. The 30-day mortality rate was 26% (22/84). Of these mortality cases, they remained susceptible to anti-pseudomonal beta-lactams include meropenem, piperacillin-tazobactam, and cefepime. Logistic regression demonstrated higher PITT bacteremia scores increased mortality rate (OR 2.841, p = 0.016, 95% CI (1.218 – 6.625)) and CKD indicated decreased 30-day mortality rate (OR 0.026, p = 0.082, (0.0004 – 1.5902)).

**Conclusions:** This study helps to identify patients with bacteremia that are at high risk for mortality. These factors can help identify patients at greater risk for a poor outcome and may need optimization of treatment to enhance outcomes.

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Abstract 6788

Emergence of resistance in Gram-negative bacteria and correlation with antibiotic use in 52 Swiss intensive care units

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Abstract third-party references: Supported by project SAF3016_76571_R of the AEI of Spain and FEDER of EU

Background: Intensive care units (ICUs) constitute a high-risk setting for antimicrobial resistance (AMR). Besides horizontal dissemination of resistant pathogens, antibiotic (AB) selection pressure is considered a main driver of the AMR epidemic. We aimed to assess temporal trends regarding resistant Gram-negative bacteria in Swiss ICUs and to correlate resistance data with institutional AB use.

Materials/methods: We analyzed data on AMR and AB use sent to the Swiss Centre for Antibiotic Resistance ANRESIS from 2009 to 2018. The following pathogens were analyzed: extended-spectrum cephalosporin-resistant Escherichia coli (ESCR-EC) and Klebsiella spp. (ESCR-K), carbapenem-resistant Enterobacteriales (CRE) and Pseudomonas aeruginosa (CRPA). AMR (one sample per species/patient/year) was expressed as % of all isolates; the use of systemic AB was calculated as defined daily doses (DDD) per 100 beddays (BD). On the institutional level (only ICUs contributing data for at least 3 years), we correlated AMR (median proportion of resistant pathogens) and the use of the following pre-specified antibiotic substances/classes (median DDD/100 BD): quinolones, 3rd/4th generation cephalosporins, piperacillin/tazobactam, and carbapenems. Temporal trends and correlations were analyzed using linear regression.

Results: Among 52 institutions (20 ICUs from French/Italian- and 32 from German-speaking parts), we observed a significant increase of ESCR-EC from 8% to 16% (P < .001) among a total of 11,817 E. coli isolates and of ESCR-K from 7% to 13% (P < .001; n=6,313) between 2009 and 2018. CRE increased from 1% to 6% (P=.007; n=19,665), and CRPA remained stable over time at 26% (P=.72; n=4,774). Trends were similar between geographic regions. For the correlation analysis, we included 24 ICUs. Quinolone use correlated with CRE (P=.01) and CRPA rates (P=.04); carbapenem use correlated with CRPA only (P=.03) (Figure). Use of 3rd/4th generation cephalosporins and piperacillin/tazobactam were not associated with AMR.

Conclusions: In Swiss ICUs, resistant Gram-negative pathogens have been steadily increasing over the last decade. Correlation between AB use and AMR was weak, except for carbapenem-resistant bacteria. Antibiotic stewardship programs are most promising if aimed at reducing the use of quinolones and carbapenems in this setting.

Figure

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Abstract 6790

**Long-term effect of dietary preferences and nutritional regimes on intestinal microbiota diversity and composition**

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**Background:** Long term effects of certain diet types on human gut microbiota is crucial for a better understanding how common dietary interventions modulate the microbiome. However, high variability of dietary effects and the technical difficulties of designing large cohorts of this sort constitutes a significant obstacle for wide-ranging studies. For this reason, we have investigated the modulatory effect of diet on a largest open-source datasets available, the American Gut Project data and reported the significant variations that might be undetectable or overlooked in small-cohort studies.

**Materials/methods:** After gathering the 16S rRNA sequencing gut microbiota data of around 16,000 participants in American Gut Project, the taxonomic profiles were obtained at genus level using QIIME pipeline. The metadata of the corresponding samples indicating the diet regime of a participant (i.e. omnivore, vegetarian, vegan, raw food diet, FODMAP diet, paleo diet, low grain-low processed food diet) were matched. Alpha diversities and genera relative abundances of each specific group were compared using Mann-Whitney U-test.

**Results:** Omnivores, dieters excluding raw sugar, dieters preferring low-processed food appeared to have significantly diverse microbiota; while vegetarians, vegans, raw food dieters, dieters excluding diary, low-grain dieters had significantly less diverse microbiota. Omnivores, vegetarians, vegans, paleo dieters, dieters excluding refined sugars, dieters excluding diary, dieters preferring low-processed food all had specific taxa significantly altered. Remaining diet populations did not have significant differences compared to the rest.

**Conclusions:** The analyses we conducted reveal that restrictions on animal products and grains might narrow the microbiome. In terms of high diversity and abundant beneficial taxa, cutting on raw sugar and processed food consumption while following a regular omnivore diet appears to be beneficial on gut microbiota.

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Abstract 6791

Pharmacokinetics and pharmacodynamics of dalbavancin in the clinical setting

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Background: Dalbavancin is a potent lipoglycopeptide active against Gram+ bacteria with a favorable pharmacokinetic/pharmacodynamic [PK/PD] and safety profile, suitable for numerous challenging infections. Dalbavancin has been approved for ABSSSIs, but its range of application and the relative posology is still debated. Nowadays, little is known about its PK/PD profile in the real-life.

Materials/methods: A clinical and PK/PD study is ongoing on patients receiving one (group 1) or two 1500 mg doses (group 2) of Dalbavancin in 2 centers in Italy. Given informed consent, plasma Dalbavancin concentrations were measured through a LC-MS/MS analytical Kit (CoQuaLab) at the end of infusion, after one hour and then weekly. AUCs, Volume of Distribution (Vd) and half-lives (t1/2) were calculated through Kinetica® (Thermo) software in the two groups. AUC/MIC and the estimated T>MIC were calculated according to reported MIC for susceptible microorganisms. Results are expressed as median (IQR).

Results: Twelve patients were enrolled: age 62.5 (52.5-76); 3 ABSSSIs, 1 IE, 6 osteoarticular and 2 intravascular device infections. Microorganisms were Oxacillin-Resistant in 50% of cases. Reasons for treating with Dalbavancin were simplification (33%) or failure (66%) to previous regimens There were no adverse events. Nine patients (75%) had favorable outcome. Nine patients belonged to group 1 and three to group 2. Median plasma concentrations were 233.627 mg/L (2 10.004-425.645) at peak, 70.765 mg/L (30.953-109.020) at week 1 and 5.635 mg/L (5.313-5.957) at week 1 2. Vd was 9.3 L (7.6-12.3), while t1/2 was 240 h (222-259) in group 1 and 542 h (535-550) in group 2. AUCs were 55958 mg*h/L (41918-69998) for group 1 and 136948 mg*h/L (128138-145758) for group 2. AUC/MIC and T>MIC were 447667 mg*h/L (335345-559990) and 116 days (111-121) in group 1, 1095584 mg*h/L (1025104-1166064) and 261 days (258-265) in group 2, respectively.

Conclusions: This is among the first evaluations of Dalbavancin PK/PD profile in a real-life clinical setting. From a theoretical PK/PD perspective, our data support a potential longer antibiotic activity than previously considered both for single or double 1500 mg dose administration, with T>MIC estimated up to 3 and 8 months, respectively. These data deserve further clinical evaluation in a larger sample.

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Abstract 6793

Prevalence and quantity of parvovirus B19 DNA among blood donors

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Background: Parvovirus B19 causes a range of diseases and morbidity in humans and is transmissible by transfusion of blood, blood components and plasma derivatives. This study aimed to investigate the prevalence and quantity of parvovirus B19 DNA and seropositivity in Turkish blood donors by using an in-house quantitative polymerase chain reaction method and ELISA respectively.

Materials/methods: Totally 1053 samples were collected from March to July 2016 at a blood bank for detection of Parvovirus B19 DNA and serological status of blood donors. Viral genomic DNA extraction from sera was performed by using viral nucleic acid extraction kit. Testing of the presence of viral DNA was performed by a quantitative real-time PCR with a 10^7 copies/ml detection limit. The primers and probe sequences targeting minor capsid protein VP1 gene of PB19. Enzyme Immune Assay for qualitative determination of IgM and IgG antibodies to Parvovirus B19 in human sera was performed for all DNA positive and randomly selected 267 (95% CI; 5% margin of error) PB19 DNA negative samples. The differences of Ig G serological status within different age groups and the differences of both parvovirus IgM and parvovirus IgG serological status within different age groups were analyzed statistically.

Results: Age distribution of donors was between 18-64; mean age was 27 and median was 23. Among the 1053 samples, 5 (0.47%) had PB19 DNA. All PB19 DNA positive donations had both B19 IgM and IgG antibodies. The DNA level for positive donations were between 0.9x10^2 to 3.1x10^4 copies/ml. IgG and IgM were present in 59.9% (160/267) and 0.74% (2/267) among the healthy donors without PB19 DNA. Two donors with positive results for IgM were also positive for IgG and negative for PB19 DNA.

Conclusions: Detected DNA concentration was less than 10^5 copies/ml. The presence of IgM in low level PB19 DNA positive donors may indicate that there might be a risk in transmission of PB19 to particularly immunosuppressed recipients. The clinical follow-up of blood donation with low level of PB19DNA should be considered to answer the questions about blood safety.

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Abstract 6794

**Chemotherapies for acute lymphoblastic leukaemia may have a long-term impact on bacterial gut microbiota**

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**Background:** The microbiota appears to play an important role in the fate of children with leukaemia, both in terms of response to anticanceral chemotherapy and infectious complications. Little is known about chemotherapies effects on the children microbiota with acute lymphoblastic leukaemia (ALL). Here, we describe the impact of anticanceral chemotherapy on 8 children's gut 16S microbiota.

**Materials/methods:** Stools from 8 patients with ALL were studied at different times of their management: one sample before chemotherapy (P1) and two after (P2 and P3). In total, 24 stools were analyzed. Amplicon libraries were prepared using QIAseq 16S/ITS Screening Panel kit (Qiagen®). Data generated by V2V3 region were analyzed using CLC Genomics Workbench 12 (Qiagen®) pipelines. All patients received antibiotics at some point during management.

**Results:** A significant decrease of α-diversity (Shannon index p=0.0078) between P1 and P3 was observed while no significant differences were found between P1 and P2. Similarly, β-diversity did not vary significantly between P1 and P2 but decreased from P1 to P3 (p=0.035). Microbiota before chemotherapy showed a majority of Clostridia and Actinobacteria that decreased over time. In turn, relative abundances of gamma-proteobacteria and Bacilli increased during management (Figure 1). Among the bacterial genera whose relative abundance has decreased, we can cite Faecalibacterium (p=0.008), Ruminococcus (p=0.016) and Ruminococcus torques group (p=0.008).

**Conclusions:** Our results suggest that all chemotherapies do not have a drastic effect on gut microbiota. However, a cumulative effect of several cycles of chemotherapy probably associated with antibiotic use may be responsible for the dysbiosis observed.

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Moraxella keratitis: investigating emerging pathogenicity through clinical and microbiological findings and whole genome sequencing for virulence determinants

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Background: Keratitis is an infection of the cornea. The most prevalent causative organisms are Staphylococcus aureus, Pseudomonas aeruginosa and Streptococcus pneumoniae. In recent years, there are increasing reports of Moraxella keratitis. In a tertiary hospital in Dublin, Ireland, specialising in ophthalmic care, Moraxella species are now the second most frequent organism implicated in keratitis after S. aureus.

Materials/methods: Fifty-two Moraxella isolates were collected from corneal scraping specimens from 2013 to 2018. Clinical findings, treatment and outcome data were extracted from medical records. Isolates were speciated by MALDI-TOF mass spectrometry. Antimicrobial susceptibility testing was performed by gradient testing for chloramphenicol, ciprofloxacin, ceftazadime, cefuroxime and gentamicin and interpreted using EUCAST guidelines. A non-specific assay to determine biofilm formation was used to investigate the potential for Moraxella to adhere to inert surfaces. Whole genome sequencing, followed by BLASTp analysis determined other potential virulence factors.

Results: The patients’ mean age was 65 years. The majority had systemic and/or ocular risk factors although none wore contact lenses. This infection led to blindness in one third of patients and 22% required surgical intervention including corneal grafting, transplantation and evisceration. The most prevalent organisms were M. lacunata (n=25) and M. nonliquefaciens (n=21) followed by M. osloensis (n=4) and M. catarrhalis (n=2). Antibiotic resistance was uncommon. The difference in biofilm formation ability was statistically significant (p ≤ 0.0001, 95% CI: 0.04-0.57) between M. lacunata, where 88% formed biofilms and M. nonliquefaciens, where 88% were non-biofilm producers. Biofilm formation does not appear to contribute to keratitis. BLASTp analysis of the genomes detected proteins involved in construction of the Type IV Pili system, degradative enzymes, toxins and antimicrobial efflux pumps.

Conclusions: Moraxella may cause opportunistic infection, however it is frequently associated with a poor outcome in keratitis. All but two isolates were found to be non-catarrhalis. The majority of isolates were susceptible to most, if not all, topical antibiotics tested. Biofilm formation was not a contributory factor to disease. The detection of other virulence factors appears to contribute to Moraxella’s pathogenicity in keratitis, although research on the functionality of the genes is required to fully determine the significance of these findings.

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Indwelling time of peripherally inserted central catheters and incidence of bloodstream infections in haematology patients: a cohort study

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Background: A recurring dilemma in clinical practice is whether we should routinely replace central venous catheters (CVCs) to prevent Central Line Associated Bloodstream Infections (CLABSI), or wait and see if one occurs. In haematology patients, peripherally inserted central catheters (PICCs) are frequently used to provide long-term venous access. Previous studies have shown that bacterial colonization of intravascular catheters increases with prolonged use, leading to increasing risk of infection with longer indwelling time. This suggests that routine replacement of PICCs may prevent CLABSI. We aimed to assess whether longer PICC indwelling time increases risk of CLABSI and thus address whether scheduled PICC replacement could aid in preventing CLABSI in haematology patients.

Materials/methods: Multicentre retrospective cohort study among haematology patients receiving PICCs between 2013-2015. Occurrence of CLABSI based on Centers for Disease Control definitions was assessed. We calculated cumulative incidence and hazard of CLABSI and determined risk factors. The cumulative hazard function was assumed to follow a Weibull distribution. As the curve showed a change in slope after 28 days, cumulative hazard was estimated separately for the period up to and after 28 days of PICC indwelling time.

Results: 455 PICCs were placed in 370 patients, comprising 19063 catheter days. Median indwelling time was 26 days (range 0-385) and CLABSI incidence was 4.0 per 1000 catheter days. Aplastic anaemia was associated with increased risk of CLABSI, patients undergoing autologous stem cell transplantation were less likely to develop CLABSI (Panel A & B). For the first 28 days, the estimated cumulative hazard function showed an increasing cumulative hazard over time (estimated shape parameter 1.8), but a constant hazard with indwelling time thereafter (estimated shape parameter 1) (Panel C).

Conclusions: Our study shows that risk of CLABSI increases during the first 28 days after PICC-placement, but does not appear to increase with indwelling time thereafter. Routine replacement of PICCs therefore is unlikely to prevent CLABSI in this population.

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Analysis and characterisation of rmtB-bearing plasmids disseminated in various species of Enterobacterales isolated from clinical specimens of hospitalised patients in Greece

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Background: Methylation of 16S ribosomal RNA has emerged as a new mechanism of resistance against aminoglycosides among gram-negative pathogens. The aim of this study was to characterize rmtB-bearing plasmids from various genera of Enterobacterales isolated from hospitalized patients in Greece.

Materials/methods: Single-patient, clinical isolates of Providencia stuartii (n=31), Klebsiella pneumoniae (n=41), Proteus mirabilis (n=6) and Escherichia coli (n=2) all harboring rmtB, consecutively collected during 2015-2016 in five tertiary-care hospitals in Athens, were studied. ESBL and carbapenemase production was confirmed by PCR. Transferability of rmtB was investigated by transformation with at least one strain of each species/PFGE clone. Representative rmtB-carrying plasmids (based on donor/β-lactamase content detected by PCR/susceptibility testing) were selected for complete sequencing.

Results: All rmtB-bearing isolates were carbapenemase-producers. P. stuartii, P. mirabilis and E. coli produced VIM-type carbapenemases. K. pneumoniae produced mainly KPC-carbapenemases (n=34, 82.9%), but also OXA-48 (n=3, 7.3%), KPC- and VIM- (n=3, 7.3%), or only VIM-type (n=1, 2.4%) enzymes. In all cases other β-lactamases were also detected. Analysis of TOP10 transformants showed two groups of similar IncA/C plasmids, one harboring rmtB, bla_VEB, bla_OXA-10 and bla_TEM, and the second co-harboring bla_VEB and bla_SHV. The second group was detected in all VIM-producers except for four P. mirabilis, which carried a plasmid of the first group (Table). Sequencing revealed that these plasmids were multireplicons [IncA/C and IncR]. In all plasmids, rmtB-1 was located downstream of a Tn3-like transposon, and bla_VEB-1 was the first gene cassette of a class 1 integron followed by aadB, arr2, cmIa1, bla_OXA-10 and aadA1 gene cassettes, with an IS1999 located upstream of bla_VEB-1. bla_VIM-1 occurred as the first cassette of a class I integron along with the aacA7, dfrA1, and aadA1, similar to Ine541, the integron structure harboring bla_VIM-1 in K. pneumoniae previously reported in Greece.

Conclusions: A multireplicon [IncA/C and IncR] plasmid co-harboring rmtB1 and bla_VIM-1 along with other ESBL genes is responsible for the dissemination of rmtB in clinical isolates of Enterobacterales in Greece. Another similar multireplicon plasmid, lacking bla_OXA-10 and bla_SHV-5 is disseminated among KPC- or OXA-48 producing K. pneumoniae isolates. The co-dissemination of these genes poses a public health threat.

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Abstract 6803

Frequency and severity of potential drug-drug interactions before, during and after an antifungal stewardship pilot project

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Background: Antifungal agents may lead to significant drug-drug interactions, which potentially impede the success of antifungal therapy or cause adverse or diminished clinical effects of concomitant drugs. After piloting an antifungal stewardship (AFS) project, we aimed to test the long-lasting effects on the awareness of potential drug-drug interactions of antifungal agents after termination of the project.

Materials/methods: AFS measures (medical training, pocket card with internal guidelines, daily pharmaceutical counselling on wards) were introduced for six months on two wards (68 beds) in the department of haematology/oncology in a German tertiary care centre. Frequency and severity of potential drug-drug interactions of antifungal agents with concomitant therapy was retrospectively analyzed before (phase I: 01-06/2016), during (phase II: 01-06/2017) and six months after termination of the AFS project (phase III: 01-06/2018). Severe and moderate potential drug-drug interactions were identified using the interaction databases Lexicomp® Stockley’s®, AiDklinik® and German SmPC (summary of product characteristics).

Results: We analyzed 104 patients (171 antifungal prescriptions; phase I), 103 patients (145 antifungal prescriptions; phase II) and 116 patients (166 antifungal prescriptions; phase III), respectively. Patients received on average 14 (phase I) and 13 (phase II and phase III) medications in addition to the antifungal agent. The number of patients with moderate and severe potential drug-drug interactions decreased from 22% (26 drug-drug interactions; moderate: 15, severe: 10) to 11% (13 drug-drug interactions; moderate: 9, severe: 4) during the AFS period, whereas an increase to 21% (36 drug-drug interactions; moderate: 27, severe: 9) was observed six months after the AFS project. Most common potential severe drug-drug interactions concerned the azol antifungal agents posaconazole and voriconazole, which were co-administrated with for example vinca alkaloids, statins (atorvastatin, simvastatin), apixaban and quetiapine.

Conclusions: Our data show that the implementation of AFS measures did not have sustained effects on frequency of potential severe and moderate drug-drug interactions after termination of the project. To obtain long-lasting effects regarding optimal quality of antifungal treatment, the implementation of AFS programmes in routine care is desirable. A precise evaluation of prescriptions regarding drug-drug interactions by a clinical pharmacist will reduce drug-related problems and ensure safe antifungal therapy.

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**Abstract 6805**

**Trends in antimicrobial use in Brazilian hospitals: 2017 and 2018 point prevalence surveys**

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**Background:** Although antimicrobial (AMC) stewardship is recommended by Brazilian government, data regarding prescription practices in Brazilian hospitals are scarce. This study aims to describe two point prevalence surveys on AMC consumption among 27 hospitals in Brazil.

**Materials/methods:** 27 Brazilian hospitals conducted the Global Point Prevalence Survey of AMC Consumption and Resistance (Global-PPS) in 2017 and / or 2018. A web-based program was used for data-entry of details on AMC prescriptions. The Global-PPS was developed by the University of Antwerp and funded by bioMérieux. Reporting one-day prevalence of AMC use and resistance in 2017 and 2018 are presented as risk ratios. The main outcomes are total AMC use and stratification of use for the classes separately, only carbapenems showed a decrease (10.2% to 8.6%, p=0.04). In 86 ICUs, 331 (60.0%) and 375 (52.4%) were on AMC treatment, in 2017 and 2018, respectively (p=0.03). Significant decrease of total AMC use was observed in four out of five most prescribed AMC: ceftriaxone (9.4% to 7.8%, p=0.03), meropenem (9.3% to 7.8%, p=0.04), vancomycin (7.6% to 5.6%, p=0.001), pipercillin-tazobactam (7% to 5.8%, p=0.07) and cefazolin (6.3% to 5.1%, p=0.05). Overall prevalence of MDRO infection was not different [5.6% to 5.8%, p=0.4]. Overall prevalence of AMC use to treat Gram negative MDRO decreased significantly (15.8% to 13.4%, p=0.01) although analyzing the classes separately, only carbapenems showed a decrease (10.2% to 8.6%, p=0.04). There was no significant change in prescriptions for Gram positive MDRO (10.7% to 9.3%, p=0.07). The most frequent diagnosis were pneumonia [16-18%], intra-abdominal sepsis [7-8%], skin and soft tissue infection [5-7%] and urinary tract infection [5-6%]. In 2018, there were significantly less AMC prescriptions for healthcare-acquired infections [HAI] [40.3% to 36.8%, p=0.02].

**Conclusions:** Although there was significant decrease in overall AMC use, especially for treatment of HAI, the prevalence of AMC prescribing among surveyed Brazilian hospitals remained high. These data may be helpful for further stewardship interventions and repetitive PPS to monitor their effects.

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Abstract 6807

**Activity of imipenem-relebactam and meropenem-vaborbactam against ceftazidime-avibactam-resistant Klebsiella pneumoniae isolates producing KPC carbapenemases**

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**Background:** Ceftazidime-avibactam (CZA) is an effective new treatment, against KPC-producing Klebsiella pneumoniae. Resistance to CZA, although rare, has been reported, magnifying the problem of limited treatment options. Vaborbactam and relebactam, two other β-lactamase inhibitors are developed in combination with meropenem and imipenem respectively. Our objective was to determine their activity against 10 CZA-resistant K. pneumoniae isolates producing KPC carbapenemases.

**Materials/methods:** A total of 9 CZA-resistant K. pneumoniae isolates producing KPC, collected in 2018-2019, were tested for susceptibility by broth microdilution and MIC Test Strips and interpreted per EUCAST criteria. Strain KP-90 isolated in 2016, producing KPC-23 was also included. Isolates underwent whole-genome sequencing for the determination of MLST-type and resistance genes.

**Results:** MICs of CZA ranged from 16 to >256mg/L (MIC₅₀ / MIC₉₀; 64/128), with ceftazidime MICs being ≥1024mg/L in all cases. Nine isolates were resistant to carbapenems and the addition of relebactam or vaborbactam to imipenem (I/R) and meropenem (M/V), respectively, decreased resistance from 90% to 0%. I/R MICs ranged from 0.125 to 4mg/L (MIC₅₀ / MIC₉₀; 0.5/1), and M/V from 0.125 to 4mg/L (MIC₅₀ / MIC₉₀; 0.25/2). Isolates were resistant to all other antibiotics except colistin for which 40% were susceptible. The isolate that was susceptible to both imipenem (MIC 0.5mg/L) and meropenem (MIC 2mg/L) harbored the *bla*KPC-3 and belonged to ST39 and was isolated from rectal swab of a patient previously treated with CZA. Isolates resistant to carbapenems harbored the *bla*KPC-23 (n=1) or the *bla*KPC-2 (n=8) and were isolated from clinical or surveillance cultures of patients not exposed to CZA. KPC-23 isolate belonged to ST258, one of the KPC-2- to ST39 and the rest seven KPC-2-producers to ST147. Isolates of ST147 exhibited a truncated OmpK35_v1 (*1 73) and OmpK36_v3, which have been previously associated with ST147 K. pneumoniae isolates from Greece. ST39 isolates had an intact OmpK35 and an OmpK36_v3 variant, while ST258 isolate exhibited a truncated OmpK35_v1 (*89) and an OmpK36_v1 characteristic of this clone.

**Conclusions:** As emergence of ceftazidime-avibactam resistance is increasingly recognized, meropenem-vaborbactam and imipenem-relebactam, the two novel combinations already approved by FDA, may provide clinicians with an alternative option for the treatment of serious infections caused by KPC-producing Enterobacterales, including CZA-resistant isolates.

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Professional exposure to brucellosis and Q-fever in veterinarians in Bosnia and Herzegovina

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Background: Veterinarians are the most exposed demographic and professional group for acquiring brucellosis and Q fever. The aim of this study is to determine seroprevalence on brucellosis and Q fever in veterinarians in Bosnia and Herzegovina (B&H), to determine and quantify professional risk factors for acquiring diseases and to define required protective measures.

Materials/methods: Two groups of subjects were analysed and randomised by gender, age and socio-demographic characteristics. Examined group consisted of 180 veterinarians and 100 voluntary blood donors were used as a control group. Subjects' sera were tested on presence of antibodies on brucellosis (Rose Bengal test) and Q fever (ELISA). Considering the nature of their work, veterinarians were divided into two subgroups – terrain and office workers. They were also classified by numerous socio-demographic and professional data (regional presence, age, years of service and usage of standard safety measures in working environment) which were provided through questionnaire.

Results: Seroprevalence of brucellosis and Q fever in veterinarians was 12.2% (p=0.010) and 35.6% (p<0.001), respectively, while seroprevalence in the control group was 3.0% and 15.0%, respectively. Significantly more veterinarians who are seropositive on brucellosis (90.9%, p<0.001) and Q fever (93.8%, p<0.001) are male. They all do terrain work and are involved in vaccination of ruminants. Veterinarians which were seropositive on brucellosis and Q fever wore gloves most of the time (95.4% and 89.1%, respectively) and usually did not wear goggles (36.4% and 28.1%, respectively) and mask (54.5% and 43.7%, respectively) as safety work equipment. There was no statistical significance in seroprevalence of brucellosis and Q fever in veterinarians considering age groups and residence. Double infections were noted in seven terrain veterinarians.

Conclusions: The seroprevalence of brucellosis and Q fever in veterinarians in B&H is significantly higher compared to general population. Having in mind that all veterinarians positive on brucellosis were involved in vaccination, this study emphasised how important is to wear safety equipment for prevention of infectious diseases in professionally exposed workers. It is important to encourage further epidemiological and epizootiological studies emphasising the importance of interaction between veterinary and medical vocation and their contribution for public health.

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Abstract 6810

**Diagnosis and sampling of human papilloma virus in men**

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**Abstract third-party references:** On behalf of Prof. Angelika Stary, Pilzambulatorium

**Background:** Recently it has been demonstrated that human papillomavirus (HPV) infections in men are highly prevalent, with up to 50% of men acquiring an HPV infection at least once in their lifetime. Unfortunately, male HPV testing has a high failure rate as there is no validated male sampling device currently available. The main reason for failure often is an insufficient amount of human cell material. Aim of this study was to evaluate 3 different sample collection devices in a smaller cohort in order to find a suitable collection device for HPV testing in men.

**Materials/methods:** For the preliminary evaluation of the optimal collection device, duplicate specimens from 79 male patients were collected. Three different collection devices have been compared; a brush from the PapilloCheck® Collection Kit (Greiner Bio-One GmbH), the FLOQSwabs® 552C (Copan Italia Spa) and the FLOQSwabs® 5E046S (Copan Italia Spa). Penile, perigenital and anorectal specimens were tested for HPV at the Outpatient’s Centre for Diagnosis of Infectious Venereodermatological diseases by using the PapilloCheck®, a microarray-based assay which allows the detection and identification of 18 high risk (hr) and 6 low risk (lr) HPV genotypes.

**Results:** Out of 79 samples collected with the brush, 49 were collected in parallel with the FLOQSwabs® 552C and 30 with the FLOQSwabs® 5E046S, respectively, and subsequently tested in duplicates. The brush produced 27.8% invalid results. Compared to that, 10.2% of samples collected with the FLOQSwabs® 552C were invalid. The best results so far were achieved with the FLOQSwabs® 5E046S displaying only 6.3% invalid test results. The results of high and low risk HPV types using different collection devices will be presented.

**Conclusions:** Due to its flocked swabs comprising of Nylon® fibers that are arranged in a perpendicular fashion, the FLOQSwabs® had a very low failure rate compared to the brush. These data are being further investigated with a larger cohort, which hopefully pave the way for a successful implementation of one of these swabs as HPV collection device for men.

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Efficient long-term storage of mycobacteria using conventional laboratory reagents

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Abstract 6811

Background: Common procedures for long-term preservation of mycobacteria frequently use skim milk as a cryopreservative. Achieving methods verification according to ISO 15189 requirements for procedures including unstandardized reagents could be difficult. The aim of the study was to validate a simple protocol using only standardized reagents for long-term preservation of both *M. tuberculosis* and non-tuberculous mycobacteria (NTM).

Materials/methods: 9 strains were selected: *M. tuberculosis* (n=3), *M. kansasii* (n=3), *M. chelonae* (n=1), *M. avium* (n=1) and *M. abscessus* (n=1). For each strain, a 0.5 McF suspension was prepared in a cryopreservative medium composed of 7H9 broth, OADC (10% vol.) and glycerol (10% vol.); suspensions were aliquoted in two series of tubes, allowing comparison of two different cooling rate protocols: a "rapid" cooling (aliquotes directly placed at -80 °C), and a "slow" cooling (aliquotes placed in insulated aluminum blocks at room temperature, and closed devices placed overnight at -80 °C before transferring tubes in standard cryoboxes). Aliquots were then respectively stored at -80 °C for 1 day, 3 months, 1 year, 2 years and 3 years, and the viable count of bacteria for each duration was compared to the initial count before freezing.

Results: The cooling rate had no impact on the strain viability, as the evolutive profiles were similar for both "rapid" and "slow" cooling procedures. With a few exceptions, viable count of strains were always lower after freezing compared to T0, with a progressive loss of viability increasing with the duration of freezing. However, even after 3 years of storage at -80 °C, ≥10^4 CFU/mL were recovered for each strain.

Conclusions: Using easy to control reagents commonly used for mycobacterial cultures (7H9 broth and OADC) supplemented with glycerol, our cryopreservative media allows efficient long-term storage of both *M. tuberculosis* and NTM. The cooling rate has no impact on the recovery rate: once the strain is suspended in the media, cryotubes can be directly stored in -80 °C using standard cryoboxes.

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An unusual case of recurrent lymphocytic meningitis
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Background: Recurrent lymphocytic meningitis is uncommon and requires detailed assessment to ascertain the cause. Risk factors including ethnicity and travel history is important to guide investigations along with multidisciplinary input to achieve a timely diagnosis.


Results: A 36 year old gentleman with no significant past medical history presented to his general practitioner with two days of headache. He was originally from South Africa who and moved to the UK in 2004. On examination, he had no other signs of meningeal irritation and no focal neurology. He subsequently presented to the accident and emergency department with worsening headache and vomiting. CT Head scan showed multiple cystic lesions with calcification likely to be neurocysticercosis. Magnetic Resonance Imaging confirmed CT findings but the lesions were considered to be inactive calcified lesions. A lumbar puncture showed his cerebrospinal fluid (CSF) had a lymphocytosis with high protein and a normal glucose. Despite negative viral PCR results he was treated conservatively for presumed viral meningitis and discharged. He presented on two further occasions 4 and 7 months later. On each admission his CSF had similar microscopy and biochemistry. TB and fungal cultures were done on the second admission and these were negative.

The diagnosis was clinched on his third admission on referral to the infectious diseases team. The imaging was reviewed with a neuro-radiologist and it was felt that the frontal lobe lesion had an enhancing wall and associated leptomeningeal enhancement indicating active disease. Specialist parasitology laboratory input was sought. The CSF Cysticercosis Immunoblot and ELISA were strongly positive as was the serum Cysticercosis Immunoblot suggesting antigen leak from this active frontal lesion was leading to his recurrent lymphocytic meningitis. The patient was successfully treated with Albendazole and Praziquantel.

Conclusions: This case highlights the difficulties with diagnosis of rare conditions in the absence of appropriate specialist input and the importance of multidisciplinary input. The specialist neuro-radiology and specialist parasitology laboratory input was key to clinching the diagnosis. Treatment for neurocysticercosis is not always required unless the lesions are active, as was clearly warranted in this case.

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Evaluation of total and excess treatment duration for community-acquired pneumonia: experience from a tertiary centre in the UK

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Background: Multiple randomized studies demonstrate non-inferior outcomes with shorter compared to longer durations of antibiotic therapy for a range of indications including community-acquired pneumonia (CAP). Despite national recommendations based on this evidence, clinical practice is often associated with longer courses, which carry an increased risk of harm. We evaluated total and excess durations of antibiotic treatment in patients with suspected community-acquired pneumonia (CAP) at Cambridge University Hospital (CUH).

Materials/methods: This was a retrospective single-centre cohort evaluation of all adult patients admitted with suspected CAP from 1st of September 2018 to 30th of June 2019. Patients were identified from electronic prescribing data and CURB-65 scores were calculated using a previously validated algorithm using the hospital electronic patient data records. Patients receiving less than 4 days total duration of therapy, those with underlying lung disease, those treated for multiple indications and those with a hospital discharge in the preceding 10 days were excluded. Records were deduplicated to only include the first episode. Excess days of treatment were calculated by subtracting the shortest recommended duration based on CURB-65 score (5 days for low scores (0-1) and 7 days for high scores (2-5)) from the actual duration.

Results: 1436 patients were included in the analysis [median age 78 (interquartile range (IQR) 61-87), 53% female]. Median total length of treatment was 8 days (IQR 7-10) and did not differ significantly between low and high CURB-65 scores. Only 577/1436 (40%) of patients received recommended durations of treatment. Patients with low CURB-65 scores were more likely to exceed recommended durations of treatment compared to those with high CURB-65 scores {470/577 (81%) vs. 389/859 (45%) respectively, p<0.001}. The median excess duration of treatment was 2 days (IQR 0-4), accounting for 3651 total excess days, 2056 (56%) of which were received on hospital discharge.

Conclusions: Antibiotic courses exceed recommended durations for most patients treated for suspected CAP in our hospital. Increased education is required to optimize course lengths for CAP, focusing on appropriate use of CURB-65 stratification and accurate calculation of discharge course lengths.

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Epidemic of carbapenem-resistant *Klebsiella pneumoniae* in a tertiary referral hospital for an annual surveillance in China

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**Background:** The nosocomial dissemination of carbapenem-resistant *Klebsiella pneumoniae* (CRKP) troubled the treatment of infectious diseases worldwide. The clonal CRKP isolates outbreak is a major problem in lots of hospitals of mainland China.

**Materials/methods:** An annual surveillance of CRKP was performed in a tertiary referral hospital that holds 2400 beds. Antimicrobial susceptibility testing against meropenem, imipenem and ertapenem and their MICs were determined by disk diffusion method. Next-generation high-throughput sequencing was applied for all non-duplicated isolates by using Illumina platform. Multiple locus sequence type (MLST), core genome- (cg-) MLST, and resistance genes of each strain was elucidated based on their assembly sequence data.

**Results:** A total of 281 non-duplicated CRKP isolates were collected in 2017. Most of CRKP isolates showed high resistant level against carbapenem and MIC90 to meropenem is >128 mg/L. The main source of isolates encompassed sputum (51, 18.1%), blood (46, 16.4%), drainage fluid (35, 12.5%), and urine (35, 12.5%). We found that Intensive Care Unit (ICU) is the most epidemic department, followed by department of general surgery, contributed 82/281 (29.2%) and 62 (22.1%) of CRKP isolates, respectively. This result suggested an ICU-centered nosocomial transmission route. The ST11 (237/281, 84.3%) and its derivative ST4496 (18/281, 6.4%) were the predominant clones that spread in the hospital. Moreover, carbapenemase-producing was found to be responsible for 98.9% (278/281) of CRKP isolates carbapenem-resistance, including the dominant type KPC-2 (274, 97.5%) and NDM-1 (3, 1.1%), IMP-4 (1, 0.4%). All ST11 isolates but one harbored bla\_KPC-2 gene.

**Conclusions:** A KPC-2-producing ST11-CRKP clone was emerged and spread widely in a typical tertiary referral hospital in China. The ICU is becoming a center of dissemination of multidrug resistant bacteria and posed a big challenge in hospital infection control. Therefore, public health efforts should focus on genomic pathogen surveillance, identifying the high-risk clones and their expansion early.

![Minimum spanning tree of all CRKP isolates base on cgMLST typing](image)

The nodes under a grey shadow represent a cluster of close lineages with the gene number difference less than 15. The red nodes are ST11-CRKP isolates.

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Mapping a nosocomial outbreak of measles, coinciding with a period of sustained transmission in south London in 2018

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Background: We describe an outbreak affecting two large London hospitals over 8 weeks in 2018 infecting patients, staff and visitors. We map spread to the community within suburban London, with a secondary case also identified internationally. Immediately prior to this outbreak there were only sporadic cases of measles in South London. This sustained outbreak is a reminder that measles can spread easily and quickly within unvaccinated groups and in high risk settings.

Materials/methods: Patients were identified retrospectively based on hospital case logs and laboratory results from 2018. Clinical information was obtained from medical notes, infection control correspondence and supplementary data held by Public Health England (PHE). Cases were defined as per PHE guidelines.

Results: This outbreak involved 34 measles positive cases, primarily young adults, with age range 14 days to 54 years. 19/34 (56%) cases were male.

Measles was confirmed by either measles RNA or IgM in 28/34. 2/34 represented reinfections. 4/34 were epidemiologically confirmed cases.

19/34 had an unknown vaccination status, and 3/34 had received two doses of vaccine. Remaining cases (12/34) were either unimmunised, ineligible due to age under 12 months or suboptimally vaccinated.

Outbreak investigation showed that members of an undervaccinated community (Travellers) spent time on-site after visiting hours due to inclement weather. An individual infected an unvaccinated worker of the on-site, 24/7 retail shop, who propagated the infection to other members of staff. The company who managed this shop did not have a robust occupational health policy to ensure vaccination of employees working on healthcare premises.

Conclusions: Our investigation suggests multiple factors contributed to the outbreak, including under-vaccinated communities, deficiencies in occupational health policy, adverse weather conditions affecting human behaviour, and lack of resources in the local community. We show that transmission occurred within the hospital via unvaccinated retail shop employees managed by a third party, who currently fall outside the scope of hospital occupational health policies. Emerging from this, one practice point is to expand occupational health policies so that evidence of protection against infectious diseases is recommended to all non-clinical employees on the hospital site.

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Can FT-IR spectroscopy reasonably type Saprochaete clavata isolates? A comparison with whole genome sequencing and MALDI-TOF MS approaches for outbreaks’ investigation

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Background: Nowadays an efficient outbreaks surveillance relies not only on the rapid identification of the pathogen but also on the characterization below species level by diverse typing methods.

The FT-IR technology, recently introduced in this landscape, analyzes absorption bands due to the stretching vibrations of specific functional groups, resulting in different spectroscopic fingerprints depending on the differences existing in the biochemical composition of microorganisms.

The objective of the present study was to evaluate the potentiality of FT-IR spectroscopy in the subtyping of six isolates of the yeast S. clavata, collected from single patients’ episodes of candidemia occurred in an Italian hematological ward, and compared with the cluster analysis obtained by WGS and MALDI-TOF protein fingerprint.

Materials/methods: For all the isolates, four replicates’ profiles were obtained on a IR Biotyper system [Bruker Daltonics] running the IR Biotyper software and distance was evaluated using the Euclidean average linkage method.

For WGS analysis whole single nucleotide polymorphisms [SNPs] within each genome was performed and phylogenetic analysis was inferred by SNPrelate and Ape/Phangorn.

Finally, after the generation of the main spectrum profiles by mass spectrometry, the isolates relatedness was inferred by MALDI-TOF hierarchical cluster analysis.

The congruence of the FT-IR spectroscopy clustering was compared to those of WGS and MALDI-TOF mass spectrometry.

Results: WGS analysis showed that the six isolates belonged to the same clade with one isolate harbouring a higher number of mutations with respect to the remaining ones, interestingly this isolate clustered in a separate branch in the dendrogram obtained by the FT-IR spectra. The remaining isolates showed a very high clonality being grouped together basing on each of the three methods applied, including the MALDI-TOF MSP dendrogram.

Conclusions: FT-IR spectroscopy tool thanks to its easiness of use could be reasonably applied to the implementation of infection control measures, nonetheless, additional analysis including a higher number of isolates, will allow further evaluation of the discriminatory power of this subtyping method as screening technology for outbreaks’ investigation purposes.

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Abstract 6822

**Molecular cpn60-targeted PCR sequencing to assess the diagnostic characteristics of the Nugent Score diagnosis of bacterial vaginosis in reproductive age Kenyan women**

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Abstract third-party references: KAVI-ICR Team

**Background:** The Nugent score (NS) is the gold standard microbiologic test to diagnose bacterial vaginosis (BV), but its performance in detecting abnormal vaginal microbiota is unclear. Analysis of the vaginal microbiome using cpn60-targeted sequencing, which characterizes Gardnerella vaginalis subtypes, improves upon 16S rRNA-sequencing. We compared the NS to the results of cpn60-sequencing.

**Materials/methods:** A cohort of non-pregnant reproductive age Kenyan women using contraception were followed in the KAVI-VZV-001 clinical trial [ClinicalTrials.gov identifier NCT02514018]. Over 48 weeks, monthly vaginal swabs were collected to determine NS, and for cpn60-sequencing. Bacterial sequencing reads were converted to proportions of each species per sample. Samples comprised by more than 80% bacteria species known to be BV-associated were considered to have ‘Molecular-BV’.

**Results:** A total of 362 samples were collected and included in the analysis. The NS was positive (NS ≥7) for a total 34 (9.4%) samples, and 81 (22.2%) were intermediate (NS 4-6). Multiple definitions of Molecular-BV were examined, such as BV-associated bacteria comprising 50% or 80% of the vaginal flora, but were not significantly different in relation to the NS. The 80% Molecular-BV definition was detected in 103 (28.5%) samples, and is compared to all NS thresholds in Table 1. The current NS interpretation (positive if ≥7) resulted in a sensitivity of 33%, specificity of 100%, and accuracy of 79%. If intermediate Nugent Scores (NS 4-6), were interpreted as positive the sensitivity was 66%, specificity was 95%, and accuracy was 85%.

**Table 1: Test characteristics of the Nugent score (NS) at all diagnostic thresholds compared against Molecular-BV.**

<table>
<thead>
<tr>
<th>Positive NS Threshold</th>
<th>NS True Positives</th>
<th>NS True Negatives</th>
<th>NS False Negative</th>
<th>NS False Positive</th>
<th>Sen.</th>
<th>Spec.</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>88</td>
<td>206</td>
<td>15</td>
<td>53</td>
<td>85.4%</td>
<td>79.5%</td>
<td>79.0%</td>
</tr>
<tr>
<td>2</td>
<td>84</td>
<td>226</td>
<td>19</td>
<td>33</td>
<td>81.6%</td>
<td>87.3%</td>
<td>83.4%</td>
</tr>
<tr>
<td>3</td>
<td>78</td>
<td>239</td>
<td>25</td>
<td>20</td>
<td>75.7%</td>
<td>92.3%</td>
<td>85.4%</td>
</tr>
<tr>
<td>4</td>
<td>68</td>
<td>246</td>
<td>35</td>
<td>13</td>
<td>66.0%</td>
<td>95.0%</td>
<td>84.5%</td>
</tr>
<tr>
<td>5</td>
<td>62</td>
<td>252</td>
<td>41</td>
<td>7</td>
<td>60.2%</td>
<td>97.3%</td>
<td>84.5%</td>
</tr>
<tr>
<td>6</td>
<td>47</td>
<td>255</td>
<td>56</td>
<td>4</td>
<td>45.6%</td>
<td>98.5%</td>
<td>81.2%</td>
</tr>
<tr>
<td>7</td>
<td>34</td>
<td>259</td>
<td>69</td>
<td>0</td>
<td>33.0%</td>
<td>100.0%</td>
<td>78.7%</td>
</tr>
<tr>
<td>8</td>
<td>22</td>
<td>259</td>
<td>81</td>
<td>0</td>
<td>21.4%</td>
<td>100.0%</td>
<td>75.4%</td>
</tr>
<tr>
<td>9</td>
<td>11</td>
<td>259</td>
<td>92</td>
<td>0</td>
<td>10.7%</td>
<td>100.0%</td>
<td>72.4%</td>
</tr>
</tbody>
</table>

Molecular-BV: Microbiota comprised by more than 80% with bacteria of species reported in the literature to predominate in bacterial vaginosis; determined by cpn60-sequencing.

**Conclusions:** In a population of reproductive age women, the NS is highly specific but very insensitive for detecting vaginal microbiomes abundant in bacteria associated with BV, determined by cpn60-sequencing. The clinical diagnosis of BV requires correlation with symptoms; however, our results suggest the utility of the NS in research settings could be improved by using lower thresholds. The current threshold is insensitive, and lower thresholds do not yield excessive false positives.

No current standard exists for the molecular determination of BV. Our study describes a method for defining Molecular-BV using cpn60-sequencing. Further work is needed to correlate this molecular definition with clinical outcomes, and replicate these results in other populations.

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Performance of two commercial multiplex PCR assays on the detection the aetiologies of sexually-transmitted infections in men who have sex with men
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Background: Data on the etiologies associated with sexually transmitted infections (STI) in men who have sex with men (MSM) in Taiwan are lacking. This study aimed to investigate the etiologies of STI from the urine and rectal swab samples of MSM in Taiwan.

Materials/methods: Two commercial multiplex PCR assays, including BD Max CT/GC/TV panel (Chlamydia trachomatis [CT], Neisseria gonorrhoeae [GC], and Trichomonas vaginalis [TV]) and Seegene STI panel 1 (N. gonorrhoeae [NG], Mycoplasma genitalium [MG], Mycoplasma hominis [MH], Ureaplasma urealyticum [UU], Ureaplasma parvum [UP], TV) were evaluated for HIV-positive adults and HIV-negative adults receiving pre-exposure prophylaxis (PrEP) for HIV infection in 2019. During the first period, urine and rectal swab samples from 91 patients were evaluated by both BD Max CT/GC/TV panel and the Seegene STI panel 1. During the second period, urine and rectal swab samples from 170 patients were evaluated initially by the BD Max CT/GC/TV panel and the Seegene STI panel 1 was applied only to patients (n=50) with positive results by the BD Max CT/GC/TV panel.

Results: Identical results for CT, GC (NG), and TV were found by the both methods during the two periods. For the first period evaluation, the positive rates of CT, GC (NG), MG, MH, and UU were 4.3%, 0%, 4.3%, 2.2%, and 12.1%, respectively for urine samples (n=91) and 16.4%, 6.5%, 9.9%, 13.2%, and 21.9%, respectively for rectal swab samples (n=91). TV and UP were not detected for all samples. During the second period, BD MAX was positive (≥ one of the CT, GC, TV tests) in 50 patients. The positive rates of CT, GC were 4.1%, 0.6% for urine and 22.3%, 10% for rental swab samples. TV were not detected for all samples collected. As for the Seege STI panel 1 results, positive rates of MG, MH, UU and UP were 6%, 4%, 26% and 0% for urine, and 10%, 26%, 38% and 6% for rental swab samples.

Conclusions: Using the multiplex PCR assays, high rates of etiologies associated with STIs were found in MSM. The positive detection rates were higher in rectal swabs than those from urine samples.

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Abstract 6828

**An outbreak of carbapenem-resistant Serratia marcescens carrying blaKPC in an intensive care unit between 2010 and 2013: which is the role of environment?**

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**Background:** Healthcare associated infection is a major problem worldwide especially due to the emergence of multidrug-resistant pathogens, such as Serratia marcescens (Sm). Although, the environment has been associated with outbreak by Sm in hospital settings, its role on maintenance of endemic infections needs better investigation.

Thus, the aim of this study was to investigate the role of carbapenem-resistant Sm carrying KPC environmental isolates on the maintenance of Sm outbreak that occurred in our hospital.

**Materials/methods:** A Sm outbreak occurred between 2010 and 2013 in the bone marrow transplanted (BMT) patients and in the intensive care unit (ICU) of Hospital das Clínicas-São Paulo. A weekly surveillance swab culture was stablished to identify colonized patients and the hospital environment (HE). A total of 63 Sm isolates were analyzed. 20 clinical and 3 environmental isolates were sequenced using illumina technology. The resistome was analyzed using CGE and BLAST. The phylogenomic analysis was performed using BEAST and included 33 other Sm genomes available in NCBI (n=57).

**Results:** Sm was isolated in 63 patients and in two sinks in room 4151. The unit was then blocked for complete ICU emptying and terminal cleaning. At the end of 2013 it was decided to change the taps of room 4151. The bioinformatics analysis revealed the presence of genes related to quinolone, rifampicin, trimethoprim, tetracycline, sulphonamide, beta-lactam, phenicol and aminoglycoside resistance in most of the genomes. 82.6% (19/23) of the genomes carried kpc gene including the HE isolates. Bayesian analysis showed that HE isolates from this work grouped closely to most of the clinical isolates and apart from other environmental isolates. Most of the genomes grouped together with other genomes from different places in USA. The 4 kpc-negative isolates grouped in other cluster together with USA isolates and 1 isolate from Mexico.

**Conclusions:** Hospital environment can be an important source of nosocomial pathogens as Sm. The Bayesian tree suggests that clinical isolates contaminated the HE and this environment became a reservoir of multidrug-resistant Sm. These data highlight the importance of cleaning practices specially in HE and brings more insights to better understand this poorly studied emerging pathogen.

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Heroes and villains: the dynamics of antibiotic-uropathogens interactions during recurrent urinary tract infections management

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Abstract third-party references: Supported by European and French Association of urology (EAU and AFU)

Background: Urinary tract infections (UTI) are a growing public health problem, with high recurrence rates and increased antimicrobial resistance complicating clinical management. Uropathogenic Escherichia coli (UPEC) is associated with between 60-80% of UTI cases.

Materials/methods: Here we describe the analysis of UPEC clinical isolates from the clinical trial AnTIC. AnTIC was an open-label, randomised clinical trial that compared antibiotic prophylaxis versus no prophylactic treatment to manage recurrent UTIs in clean intermittent self-catheterised patients.

Results: A key outcome of AnTIC was that rUTI frequency was lower among prophylactic patients. Our analysis argues that prophylaxis correlates with stable UPEC colonisation, when UPEC was isolated. This suggests a commensal-like role in preventing more pathogenic strains/species from colonising the urinary tract.

To investigate the evolution of antimicrobial resistance (AMR), we performed whole-genome sequencing on UPEC isolates from 20 ANtic patients that acquired multi-drug resistant (MDR) UPEC during the trial. Phylogenetic analysis revealed that nine patients retained the same strain, arguing that in these cases MDR evolved rather than incidences of new MDR strain infections.

Conclusions: Our data provides a unique insight into the dynamics of microbial colonisation during antibiotic use for a specific UTI at-risk group. Our analysis is therefore a foundation to develop alternative strategies to manage UTI risk in clean intermittent self-catheterised patients.

AnTIC microbiological analysis

Acute antibiotics and trimethoprim prophylaxis promoted E. coli colonisation

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Abstracts 2020

Abstract 6831

**Pandrug-resistant Ralstonia mannitolilytica isolates from a cystic fibrosis patient after lung transplantation**

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**Background:** Patients with cystic fibrosis (CF) are more prone to pulmonary infections with a wide range of bacteria. *Ralstonia mannitolilytica* (Rm) is an opportunistic pathogen that is becoming more common in CF infections. Little is known about antimicrobial resistance and virulence traits of Rm. The aim of this study was the phenotypic and genotypic characterisation of 16 pandrug-resistant Rm isolates from a CF patient.

**Materials/methods:** Sixteen consecutive Rm isolates recovered from blood, thoracic wounds and respiratory (including lung biopsy) samples of a CF patient after a bilateral lung transplantation were identified by MALDI-TOF. MICs of aztreonam, piperacillin-tazobactam, ticarcillin-clavulanate, ceftazidime, ceftazidime-avibactam, imipenem, meropenem, doripenem, gentamicin, tobramycin, amikacin, netilmicin, ciprofloxacin, levofloxacin, minocycline, tetracycline, colistin, trimethoprim-sulfamethoxazole, chloramphenicol, fosfomycin and cefiderocol were determined by broth microdilution, except for ceftazidime-avibactam and ceftolozane-tazobactam that were performed by Etest. EUCAST and/or CLSI breakpoints were applied accordingly. The Etest synergy test was performed by the MIC:MIC ratio method (Pankey et al., 2013) using combinations of meropenem, minocycline, fosfomycin and trimethoprim-sulfamethoxazole. The isolates were investigated for their antimicrobial resistant and virulence profiles by Whole-Genome Sequencing (WGS) on an Illumina MiSeq platform.

**Results:** Antimicrobial susceptibility test demonstrated that all the isolates were pandrug-resistant, as they were non-susceptible to all agents in all antimicrobial classes, including beta-lactam combination agents ceftazidime-avibactam and ceftolozane-tazobactam, and cefiderocol. Synergy was observed only for the meropenem-minocycline combination (ΣFIC=0.5). The rest of antibiotic combinations showed a ΣFIC between 1.4, considered indifferent. WGS analysis showed between 8 and 179 SNPs differences among the isolates, indicating a clonal evolution. The pan-genome was composed of 4401 core genes out of 47,488 total genes. All the isolates harboured the *bla*OXA-443 and *bla*OXA-60 genes. Two copies of *hcp* and *vgrG* genes were found, indicating the presence of a type VI secretion system (T6SS), a major virulence factor in several Gram-negative pathogens.

**Conclusions:** To the best of our knowledge this is the first report of pandrug-resistant *R. mannitolilytica* isolates from a lung transplant patient with CF. The occurrence of pandrug-resistant bacteria, including those resistant to cefiderocol, a last resort antibiotic, represents a new challenge for treatment of chronic infections such as the case of CF.

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Phylogenetic and resistome analysis of human and animal Acinetobacter baumannii ST25 isolates

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Background: Acinetobacter baumannii ST25 is an emerging lineage disseminating globally. In France, ST25 isolates producing OXA-23 have been found also in animals. To investigate a possible epidemiological link among human and animal isolates and strengthen the knowledge of this epidemic lineage, we analyzed the genetic relationships and the resistome of 32 ST25 isolates sampled during the same study period in humans and animals in France.

Materials/methods: Isolates collected during 2011-2018 from animals (dogs, n = 9; cats, n = 12; horses, n = 5; and ferret, n = 1) through the Resapath (ANSES-Lyon), and from humans (n = 5) by the Reference Center for Antimicrobial Resistance in Acinetobacter spp. (University Hospital of Besançon), were sequenced using the Illumina technology. The phylogenetic and resistome analysis were conducted using pyMLST (https://github.com/bvalot/pyMLST) and ResFinder 3.2 (https://cge.cbs.dtu.dk/services/ResFinder). The genetic elements harboring antimicrobial resistance genes were investigated by chromosome walking PCR and Southern Blot.

Results: The phylogenetic analysis, including all the genomes belonging to ST25 available from NCBI, generated five groups including one constituted by the genomes of the current study together with ten from NCBI. In this group, two subgroups [I, II] comprised 19 out of 32 isolates of this study, which harbored the blaOXA-23 gene on the chromosome, mostly on an AbaR4 island. The subgroup I comprised exclusively human isolates (n = 3), the second (II) included isolates from humans (n=2), dogs (n=5), and cats (n=9). The remaining isolates generated a third subgroup (III). All the isolates harbored one plasmid sizing according to the phylogenetic subgroup: 200, 150, and 250 Kbp in subgroup I, II and III, respectively. Most of the plasmids harbored two acetylases encoding genes and a genetic island containing the genes sul2, strA-strB and tetB.

Conclusions: The OXA-23 producers from animals demonstrated clonal relation to some human isolates. A transmission or a common source of contagion for humans and animals with carbapenem-resistant A. baumannii cannot be excluded. The plasmid content of the ST25 isolates of this study seems to be clonally expanded and the presence of the resistance island might favor the selection and persistence of these isolates among animals.

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Abstract 6835

High accuracy identification of ten common blood culture isolates by Acrion system

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Background: Direct pathogen identification from blood culture specimen has remained to be challenging with current mass spectrometry (MS) methods due to low recovery of microbial cells, interfering blood components and/or low sensitivity of the methods. Novel MS-based system Acrion (Thermo Fisher Scientific) utilizes a standardized, automated sample preparation that decreases human errors and increases the robustness of identification direct from blood culture.

Materials/methods: Ten bacterial isolates representing common blood culture pathogens were seeded into blood culture bottles with human blood and incubated until positive signalling. An aliquot [100-200 µl] of positive blood culture was placed into Acrion for automated sample preparation and species identification against the Acrion blood culture database. Results were compared against reference data acquired from reference collection or sequencing.

Results: The ten common blood culture pathogens were successfully identified from positive blood culture samples including Escherichia coli (20/20), Staphylococcus aureus (19/20), S. epidermidis (18/20), Klebsiella pneumoniae (22/22), Enterobacter aerogenes (20/20), Enterococcus faecalis (20/20), Bacteroides fragilis (20/20), Pseudomonas aeruginosa (20/20), Streptococcus pneumoniae (16/18) and Proteus mirabilis (20/20). Overall sensitivity for detection was 97.5% (195/200). The sensitivity of detection for gram negative bacteria was 100% (122/122) and for gram positive bacteria 93.6% (73/78). Positive identification results were in agreement with previously acquired sequencing data and demonstrate the resolving power of the high-resolution MS identification applied in Acrion.

Conclusions: Acrion System demonstrates high accuracy comparable to sequencing methods for the ten commonly met blood culture organisms. The automated sample preparation used in Acrion provides significant time savings for clinical laboratories and reduces human errors during sample handling.

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Fungal disease burden: an underestimated health challenge in Cote d'Ivoire

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Background: Due to limited access to more powerful diagnostic tools, there are few data on the burden of fungal infections in Cote d'ivoire, despite a high HIV and TB burden and many cutaneous diseases. Here we estimate the burden of serious fungal infections in this sub-Saharan country.

Materials/methods: National demographics were used to perform a PubMed search and retrieve all published articles on fungal infections in Cote d'Ivoire and countries bordering West Africa. When no data existed, risk populations were used to estimate frequencies of fungal infections, using previously described methodology by LIFE (www.LIFE-Worldwide.org).

Results: The population of Cote d'Ivoire is around 24 millions; 37% are children, and 9% are >65 years. Tinea capitis in children is common, measured at 13.9% in the last epidemiological study [2013]. Considering the prevalence of HIV infection (2.7% of the population, a total of ~500,000) and a hospital incidence of 6% of cryptococcosis, it is estimated that 3726 patients per year develop cryptococcosis. For pneumocystosis, it is suggested that 6023 new cases occur each year with the prevalence of 14.1% in paediatric HIV infection. An estimated 156 new cases of chronic pulmonary aspergillosis occur after pulmonary tuberculosis [a 5 year prevalence of 4938 cases (20.3/100,000)]. Allergic bronchopulmonary aspergillosis (ABPA) and severe asthma with fungal sensitisation (SAFS) were estimated in 104/100,000 and 151/100,000 respectively, in 1,100,000 adult asthmatics. Vulvovaginal candidiasis (VVC) is common and recurrent VVC affects ~6% of women in their fertile years - 407,000 women. An unknown number develop candidaemia and invasive aspergillosis. There are no incidence data on fungal keratitis, histoplasmosis and chromoblastomycosis, although some cases of mycetoma and histoplasmosis have been reported.

Conclusions: The present study indicates that around to 6.8% (1.6 million) of the population is affected by a serious fungal infection, predominantly tinea capitis in children and rVVC in women. These data should be used to inform epidemiological studies, diagnostic needs and therapeutic strategies in Cote d'Ivoire.

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Background: Recently, the development of Multiple Sclerosis (MS) is associated with the influence intestinal microbiota. Supposed, it to be related to the capacity of bacteria to stimulate the differentiation of Th17 cells or regulatory T cells (Lee, 2010; Kosiewicz, 2011). Therefore, it is important to understand which bacteria dominate under various disorders and how they affect immune cells and microbial community members. Lack of Akkermansia muciniphila in the intestine is associated with metabolic diseases, but its excess is associated with autoimmune pathology. It was shown that the content of A. muciniphila increases in patients with MS (Jangi, 2016) and it had proinflammatory effect (Cekanaviciute, 2017). However, there is no evidence of direct relationship between A. muciniphila and MS.

The aim of study was to investigate the association of A. muciniphila level in gut microbiota with MS course and immune cells subpopulations.

Materials/methods: 110 stool samples from MS patients with disease duration 12.2±0.9 years and 30 healthy people were analyzed. Gut microbiome was determined by the Illumina / Solexa sequencing method and by real-time PCR. Immune cell phenotypes were determined by flow cytofluorimetry.

Results: Among MS patients, there were 3 groups, in accordance with the A. muciniphila level: similarly to the healthy people group (32.3%), increased up to 20-30% (40.3%), and content less than 0.1% (27.4%). Although there was no correlation between the level of A. muciniphila and severity of MS score (EDSS), the higher content of A. muciniphila was observed in patients with EDSS>3.5 or in progressive course of MS. The most unfavorable MS course was observed in patients when, high A. muciniphila level was combined with the presence of Euryarchaeota, increased content of Actinobacteria and reduced content of phylums Proteobacteria (<1%) and Bacteroides (<4%) in gut microbiome. The presence of A. muciniphila in the intestinal microbiota was accompanied by redistribution subpopulations of Th17, Th1 / Th22 and pre-GC cells in blood.

Conclusions: The negative effect of a high level of A. muciniphila on the course of MS is manifested in a certain surrounding microbial environment, and can be mediated by redistribution of Th17 subpopulations and B cells.

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Infections due to multidrug-resistant bacteria among Swiss solid organ transplant recipients between 2012 and 2017

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**Background:** Solid organ transplant (SOT) recipients are at particular risk for infections caused by multi-drug resistant (MDR) bacteria. We describe temporal trends, risk factors and outcome for such infections among SOT recipients in Switzerland.

**Materials/methods:** We extracted data on proven infections due to Enterobacterales and Staphylococcus aureus between 2012 and 2017 from the Swiss Transplant Cohort Study (STCS), a prospective cohort including all Swiss SOT recipients. Temporal trends were described for episodes caused by extended-spectrum beta-lactamase (ESBL)-producing Enterobacterales and methicillin-resistant S. aureus (MRSA). Chart review was performed i) for patients infected with ESBL-producing or extended-spectrum cephalosporin (ESC)-resistant Enterobacterales [used as a proxy for ESBL-production] between 2012 and 2016, and ii) for a selection of patients infected with non-ESBL and ESC-susceptible Enterobacterales from the same time period. Factors associated with ESBL-Enterobacterales infection and with unfavourable 30-day outcome (death, relapse of infection, and graft loss) were assessed using logistic regression.

**Results:** We identified 1400 episodes due to Enterobacterales and 160 episodes caused by S. aureus. ESBL-production was 14% among Enterobacterales in 2012 and increased to 19% in 2017 (P-value for trend 0.10); MRSA rates remained stable over time (mean 9%; P-value 0.45). Among 155 patients undergoing chart review, 112 (72%) were kidney transplant recipients; 73 (47%) were infected with ESBL isolates (72% urinary tract infections). Prior antibiotic treatment within the last 3 months was the only independent risk factors for ESBL-Enterobacterales infection (OR 3.5, 95% CI 1.6-8.2). Patients infected with ESBL-Enterobacterales were more likely to have involvement of an infectious disease specialist (OR 2.6, 95% CI 1.3-5.0), and less likely to receive adequate empiric treatment (OR 0.2, 95% CI 0.1-0.6). Unfavourable 30-day outcome - mostly (82%) relapse - was more common among patients with ESBL (44% vs 20%, P-value 0.002). This association remained significant in multivariable analysis after correction for important co-variables (OR 3.4, 95% CI 1.5-8.1) (Figure).

**Conclusions:** ESBL-Enterobacteraeae are less common among Swiss SOT recipients compared to patients from other European countries. Given the potentially unfavourable impact of resistance on patient outcome, further efforts are needed to protect this vulnerable patient population from colonization and infection with resistant pathogens.

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Abstract 6842

Human-like miRNA detection of bacterial origin in human gut microbiome

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Background: MicroRNA (miRNA) are small noncoding regulatory RNA fragments of about 19-25 nucleotides in length. Whether bacterial miRNAs harbored in human microbiome affect human cells is a new and important research interest. The miRNA structure and the multiplicity of potential targets make experimental detection difficult and economically unfavorable. The aim of this study is to determine the presence of structures similar to human miRNA in human intestinal microbiota by developing an in silico approach mining the gut metagenomes.

Materials/methods: Pre-miRNAs, which constitute the structure of 1917 human miRNAs in Mirbase, all of which have experimentally proven to be miRNAs, were identified and used as a training set. A miRNA detector based on sequence features was developed. Several classification methods (Random forests, Support Vector Machines, Gradient boosted trees, k-Nearest Neighbors) have been experimented for the miRNA classification process and Gradient-Boosted Trees (GBT) gave the best accuracy value. A threshold of detection (0.98) was determined for a moderately sensitive, yet highly specific detector. Whole metagenome sequencing data from human feces from a cirrhosis cohort was scanned for human-like miRNA precursors of 70-110 nucleotides, which govern the secondary structure of miRNAs. The microbial contigs exceeding the threshold value were located and the species harboring that loci were determined using Kraken2 microbial taxonomic assignment method.

Results: 1141 different microbial species were found to contain human-like miRNA sequences. The number of putative miRNA for each species between the groups were tested statistically. *Streptococcus pluranimalium* (p=0.043), *Bacillus spp.* (p=0.036), *Limnochorda pilosa* (p=0.048), *Cellulophaga lytica* (p=0.024) were found to harbor differential number of putative sequences [Student’s t-test]

Conclusions: The study suggests that human gut microbiome contains abundant number of sequences resembling human miRNA, showing up in a broad biodiversity spectrum. In the context of disease, certain species exhibit variation in the putative miRNA sequences they harbor. Experimental validations should be carried out revealing to what extent these sequences are expressed and if they function in regulating human gene expression. In case of such validations, a new dimension in host-microbiome interactions will be in question, as well as a practical opportunity in the detection/treatment of disease with novel potential biomarkers.

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Abstract 6844

**Current treatment pathways for Clostridioides difficile infection in Europe**

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Abstract third-party references: On behalf of the COMBACTE-CDI consortium.

**Background:** The aim of this study is to report on the current *C. difficile* infection (CDI) treatment pathways in Europe, showing the differences between European countries and comparing the adherence to the most recent international CDI guidelines.

**Materials/methods:** In 2018, in the framework of the European COMBACTE-CDI project, a questionnaire on the awareness and observance of any European or local CDI treatment guidelines and on CDI treatment pathways was sent to the participating sites from 12 different European countries.

**Results:** One-hundred fifty-five European facilities participated in the survey, including hospitals or hospital-based laboratory facilities, general practitioners, long-term healthcare facilities, private laboratories and residential care facilities. Overall, 63% (98/155) of all the participating sites reported awareness of any European CDI treatment guidelines and the majority (78/83, 94%) of these sites declared that they followed them. Italy, Romania and the Netherlands were the countries where awareness was lowest i.e. 27/55 (49%), 3/8 (38%) and 1/6 (17%), respectively. In different settings, residential care facilities and general practitioners had lower awareness than hospitals (50% and 26%, respectively, versus 75%). Eighty one% (106/131) of the participants declared that they stratified via severity criteria for the treatment of a primary case of CDI. For treating a mild/moderate primary case of CDI, 76/155 (49%), 49/155 (32%), 12/155 (8%) reported using metronidazole, vancomycin and fidaxomicin, respectively whereas for severe primary CDI, 29/155 (18.7%), 113/155 (72.9%), 20/155 (12.9%) used metronidazole, vancomycin and fidaxomicin, respectively. Antimicrobials other than vancomycin, metronidazole or fidaxomicin were used by 1.9% of the sites, mostly by residential care facilities and hospitals in Romania and the UK. For the treatment of recurrent cases of CDI, antimicrobials different from vancomycin, metronidazole or fidaxomicin were used in 10% (15/155) of cases.

**Conclusions:** The results of the European survey on CDI treatment shows that awareness of European CDI treatment varied according with different geographical areas and settings, thus a strategy to improve awareness needs to be developed. Interestingly, the use of “other” antimicrobials tends to increase when the treatment of recurrent CDI cases is considered, perhaps suggesting a lack of trust in conventional CDI antimicrobials in this patient population.

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Background: The EUCAST rapid antimicrobial susceptibility testing (RAST) method, available to clinical laboratories since November 2018, lists breakpoints for seven common bloodstream infection pathogens. Acinetobacter baumannii is another important sepsis pathogen, especially in Southern Europe. This organism is often resistant to multiple agents. We aimed to evaluate the RAST method for A. baumannii.

Materials/methods: Blood culture (BC) bottles, BACTEC™ Plus Aerobic (BD), were inoculated with susceptible and resistant isolates of altogether 48 A. baumannii (Table). The EUCAST RAST method was performed on positive BC bottles for eight clinically relevant antimicrobial agents using Mueller-Hinton agar from two manufacturers (BBL/BD and Oxoid/Thermo Fisher Scientific) and Oxoid antimicrobial disks. Broth microdilution was performed according to ISO 20776-1 on custom Sensititre panels (Thermo Scientific) and used as a reference. MICs were interpreted according to EUCAST breakpoints v. 9.0 (2019). RAST breakpoints were set to correctly categorise as many isolates as possible and avoid false susceptible results.

Results: All inhibition zones could be read after 6 and 8h and all but one after 4h incubation (Table). Breakpoints were determined for all antimicrobials tested, but for amikacin at 4h only a resistant breakpoint was set. As for other pathogens in RAST, an Area of technical Uncertainty (ATU) was defined for all agents and reading times. With the proposed breakpoints 24, 4 and 3% of the inhibition zones were in the ATU after 4, 6 and 8h, respectively. One false susceptible result occurred with trimethoprim-sulfamethoxazole at 4h and four false resistant results occurred at 4h (n=3) and 8h (n=1) for different agents.

Conclusions: The EUCAST RAST method can be implemented for A. baumannii and breakpoints based on this study have been published on the EUCAST website. All but one zone diameters could be comfortably read after 4h. Seventy-five per cent of results after 4h could be categorised as S or R. Results read after 6 and 8h were only rarely (≤4 %) in the ATU. With the suggested breakpoints the number of errors was low when tested on a collection of both susceptible and resistant isolates.

Table. Theoretical and actual number of tests, the proportion of tests which could be read and interpreted after 4, 6 and 8 h, and the categorical errors with RAST at each reading time for 48 isolates of A. baumannii.

<table>
<thead>
<tr>
<th>Incubation time</th>
<th>4h</th>
<th>6h</th>
<th>8h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of tests (n)</td>
<td>768</td>
<td>768</td>
<td>768</td>
</tr>
<tr>
<td>Completed tests</td>
<td>765</td>
<td>765</td>
<td>765</td>
</tr>
<tr>
<td>Readable zones (% of completed tests)</td>
<td>764 (99.9)</td>
<td>765 (100)</td>
<td>765 (100)</td>
</tr>
<tr>
<td>Not interpreted to S or R (ATU)</td>
<td>24</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Interpreted to S or I</td>
<td>35</td>
<td>48</td>
<td>48</td>
</tr>
<tr>
<td>Interpreted to R</td>
<td>41</td>
<td>48</td>
<td>49</td>
</tr>
<tr>
<td>Errors calculated on the total number of zones interpreted to S or R (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mE</td>
<td>0.3</td>
<td>0.4</td>
<td>0.6</td>
</tr>
<tr>
<td>ME</td>
<td>0.5</td>
<td>0</td>
<td>0.1</td>
</tr>
<tr>
<td>VME</td>
<td>0.2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total errors:</td>
<td>1.0</td>
<td>0.4</td>
<td>0.7</td>
</tr>
</tbody>
</table>

mE (minor Error) = Categorised as susceptible (S) or resistant (R) with RAST when susceptible with increased exposure (I) with standard method.
ME (Major Error) = False resistant.
VME (Very Major Error) = False susceptible.

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**Abstract 6846**

**Acinetobacter baumannii and Klebsiella pneumoniae: intelligent design of phage cocktails against multidrug-resistant pathogens**

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**Background:** Multidrug-resistant Klebsiella pneumoniae and Acinetobacter baumannii are emerging as a cause of mortality worldwide. As such the need for alternative therapies are in high demand. Bacteriophages provide one potential mean to control the proliferation of pathogens that are insensitive to conventional antimicrobials. Yet, bacteria have developed multitude of ways to become resistant to phages, thus calling for efficient phage cocktail design.

**Materials/methods:** In this study, we investigated the response of K. pneumoniae and A. baumannii clinical isolates to various phages. Bacteria were exposed to multiple phages in different set-ups and the emerging phage-resistant pheno- and genotypes were determined.

**Results:** We show that the surviving K. pneumoniae exposed to multiple phages have severely impaired growth ability. Interestingly, K. pneumoniae strains harboring a CRISPR-system appears to respond to phage-selection via genomic mutations whereas closely related CRISPR-free strains become resistant by assuming only an alternative phenotype. Respectively, when phage selection is abolished, it takes significantly more time for genomic mutations to revert back into the wild-type (and likely pathogenic) form in comparison to exclusively phenotypic changes that readily return to their original form. We also demonstrate that phage isolation against first-line phage resistant phenotypes can help construct more efficient phage-cocktails.

In A. baumannii, exposure to first-line phages repeatedly select for a phenotype that is sensitive only to second-line phages. By combining first-line and second-line phages, the cocktail induces selection for less-fit and hence probably less-virulent pathogens.

**Conclusions:** Including phage isolation against first-line phage resistant K. pneumoniae and A. baumannii phenotypes can help develop antimicrobial formulations that may be more robust in reducing the pathogenicity in any surviving bacteria. Such evolution-predicting cocktails may improve the outcome of therapy trials and therefore help pave the way for adopting phages as emergency antimicrobials.

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Epidemiology, risk factors and outcomes of infections caused by carbapenem-resistant Gram-negative bacteria in paediatric intensive care unit

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Background: Infections caused by gram-negative resistant bacteria have increased worldwide but there are few available data for the pediatric population. For these reasons, the objectives of our study were to describe the epidemiology, risk factors and outcomes associated to infections due to CR-GN in PICU.

Materials/methods: We performed a retrospective observational study at the PICU of a large Italian Hospital from 2017 to 2019. We enrolled patients under 18 years of age with an infection due to GN, we divided them in two groups according to the sensitivity of isolates to carbapenems and we compared them to assess risk factors and outcomes.

Results: We enrolled 65 patients, 32 presented a CR-GN infection due to: A. baumannii (16; 50%), S. maltophilia (3; 9.4%), P. aeruginosa (11; 34.4%), K. Pneumoniae (2; 6.2%). All isolates were MDR, 13 (39.4%) isolates were sensitive to fluoroquinolones, 12 (36.4%) to aminoglycosides, 28 (84.8%) to colistin, 5 isolates were sensitive to tigecycline and 5 to piperacillin/tazobactam. Lower respiratory tract infections were the most frequent infections (20; 62.5%). At the univariate analysis we identified the following risk factors for CR-GN infection: age ≥ 24 months (p = 0.004), central venous catheter (p = 0.029), urinary catheter (p = 0.024), nasogastric tube (p = 0.001), orotracheal intubation (p = 0.042), mechanical ventilation (p = 0.042), corticosteroids use in the previous 30 days (p = 0.048) and at the time of infection (p = 0.040), antibiotic therapy in the previous 30 days (p = 0.002), in particular, carbapenems and glycopeptides (p = 0.011 and p = 0.047 respectively); length of stay in PICU before the infection (p <0.001); rectal colonization by carbapenemase-producing microorganism (p = 0.026); Candida spp. Infection in the previous 30 days (p = 0.010). We did not observe deaths, but the length of hospitalization was significantly longer in the group of patients who had a CR-GN infection (p <0.001).

Conclusions: Antimicrobial resistance is an emerging problem even in the pediatric population. Optimization of antibiotics use and an improvement in the management of medical devices could be a strategy to try to prevent CR-GN infections in children.

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Abstract 6849

Knowledge, attitude, and practice of Visiting Friends or Relatives (VFR) travellers towards prevention of malaria

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Background: An average of 900 cases of malaria are reported yearly in Germany, with around 95% of cases occurring in travelers returning from Sub-Saharan Africa. People who travel to foreign countries in order to visit friends or relatives (VFR) make up almost half of those cases. However, no systematic survey of VFR on their knowledge, attitude, and practice (KAP) towards prevention of malaria has been conducted in Germany so far.

Materials/methods: We are conducting a questionnaire-based survey in VFR living in Hamburg, Germany with the aim to study issues in malaria prevention, chemoprophylaxis and non-drug preventive measures.

Results: At the time of this preliminary analysis a total of 32 VFR could be included in our study. The male:female ratio was 1.3:1 and the median age was 39 years (range: 20 - 67 years). Eight participants were second or third generation immigrants that were born in Germany, the rest were born in Western Africa and lived in Germany since a median of 15 years (range: 2 - 25 years). The individual risk to fall ill from Malaria when visiting their friends and relatives, was perceived as "low" or "not present in" 63% (n=20) of participants. A total of 56% (n=18) had sought medical advice prior to their last travel, 47% (n=15) had taken malaria chemoprophylaxis. Reasons not take chemoprophylaxis were low risk perception (n=6), no such recommendation by the medical practitioner (n=3), high cost of chemoprophylaxis (n=3) and doubt of effectiveness (n=1). While six patients did not adhere to any non-drug preventive measures, others used mosquito nets (n=7), skin-applied chemical repellents (n=11), window screening (n=11) and bright long clothes (n=3).

Conclusions: Among a substantial proportion of VFR travelers in Germany, a lack of perceived individual malaria risk appears to be the predominant reason for low rates of pretravel medical consultation and low uptake of chemoprophylaxis. This underlines the need for awareness-raising campaigns addressing the population of VFR in order to decrease rates of imported malaria.

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Rescue diagnosis of a cerebral nocardiosis by accredited clinical metagenomics: a case report

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Background: Nocardia spp. are environmental Gram-positive rods responsible for rare and severe opportunistic infections in immunocompromised patients. Growth conditions of this bacterium require specific media and long culture duration. Microbiological documentation is mandatory to confirm the bacteriological identification and adapt antibiotic treatment according to the susceptibility profile of the strain. This case describes the exploration of a cerebral nocardiosis by Clinical Metagenomics (CMg).

Materials/methods: A 66 years-old man, with no past medical history, was admitted in intensive care unit for febrile coma. Flu-like symptoms, including headache, fever, asthenia and neurological impairment began 10 days before. Computed tomography (CT) brain scan revealed an abscess with hydrocephaly. Cerebrospinal fluid (CSF) showed meningitis with 750 elements (76 % neutrophils), hyperproteinorachia and hypoglycorachia. Conventional microbiological procedures (standard, mycobacterial and fungal cultures, 16S rDNA PCR, multiplex PCR (Film Array®)) failed to identify any pathogen. For that reason, the sample was submitted to CMg. Briefly, a specific extraction combining mechanical and enzymatical step was performed before DNA and RNA library prep using Nextera and Total RNA kits (Illumina), and sequencing with NextSeq500 (Illumina). Bioinformatic analysis was performed using the MetaMIC software.

Results: From a total of 36'882'731 reads generated from the CSL sample, 7'862 matched to Nocardia cyriacygeorgica genome, which corresponds to a high ratio of positivity (2.1 3x10⁻⁴) for our CMg method. This result was confirmed by PCR by the French Observatory of Nocardiosis (Hospices Civils de Lyon). Administration of imipenem-cilastatin associated with trimethoprim-sulfamethoxazol allowed the recovery of the patient. A posterior exploration of immunodeficiency showed antibodies against GM-CSF, treated successfully with anti-CD20. Two years later, the patient was considered cured under trimethoprim-sulfamethoxazol prophylaxis.

Conclusions: CMg is a new method based on new generation sequencing, which allows the detection of pathogens whatever their nature (bacteria, viruses, fungi). In our case, CMg was able to identify N. cyriacygeorgica as responsible for a brain abscess, whereas all other methods available in our laboratory were negative. This diagnosis allowed the adaptation of the antimicrobial treatment and also leaded to the detection of an acquired immunodeficiency, the medical care of which was then made possible.

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Abstract 6853

Microbiology of tubo-ovarian abscess in a tertiary hospital in Spain
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Background: Tubo-ovarian abscess (TOA) is a purulent collection involving the fallopian tube and/or ovary. Our aim is to describe the TOA microbiological characteristics.

Materials/methods: We reviewed medical records and microbiological results from confirmed cases of tubo-ovarian or tubarian abscess between January 2008 and November 2019. The microbiological diagnosis was studied by routine bacteriological culture and Sexually Transmitted Infections (STI) PCR assay (STI Essencial Assay, Allplex®, Seegene).

Results: 47 abscess and 40 peritoneal fluids were cultured from 74 women and 57 (77%) were tested by STI-PCR. The mean age was 40.4 years (SD=12.4). 30 (40%) had an intrauterine contraceptive device in situ. The median white blood recount was 14,748/µL (SD=5,703) and the median C reactive protein 168.4 mg/L (SD=121.7). The abscess localization was bilateral in 36 (48.6%), 19 left (25.7%) and 19 right (25.7%). The routine culture was positive in 42 (56.8%) patients: 20 (47.6%) aerobic flora, 15 (35.7%) anaerobic flora and 6 (14.3%) aerobic + anaerobic flora. In 2 patients with TOA culture negative, we also considered bacteria isolated in blood culture (BC). The STI-PCR was positive in 11/57 (19.3%) TOA samples, 10 (90.9%) Chlamydia trachomatis and 1 (9.1%) Neisseria gonorrhoeae. In 4 patients with this PCR negative or not realized, we also considered C. trachomatis detected in related endocervix (3) and DIU-PCR (1). Taking all these results into consideration, 55 (74.3%) patients had microbiological isolates, of which 15 (27.3%) had sexually transmitted bacteria implicated. The flora was polymicrobial in 13/50 (26%) cases and only 4 (7.3%) had mixed ST-bacteria + anaerobic flora. Ampicillin+gentamicin+clindamycin was used empirically in 52/62 (84%) consulted patients. About surgical management, drainage/washout was carried out in 11 (14.9%) women and salpingo/oophorectomy in 63 (85.1%).

Table 1. TOA isolated microorganisms

<table>
<thead>
<tr>
<th>PCR assay</th>
<th>Routine Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexually transmitted bacteria</td>
<td>Aerobic bacteria  (30)</td>
</tr>
<tr>
<td>(15)</td>
<td>Anaerobic bacteria  (24)</td>
</tr>
<tr>
<td>C.trachomatis (14)</td>
<td>Escherichia coli (18, 1 E.coli BLEA)</td>
</tr>
<tr>
<td>N.gonorrhoea (1)</td>
<td>Streptococcus Anginosus group (4)</td>
</tr>
<tr>
<td></td>
<td>Streptococcus pneumoniae (2)</td>
</tr>
<tr>
<td></td>
<td>Haemophilus influenzae (1)</td>
</tr>
<tr>
<td></td>
<td>Streptococcus pyogenes (1)</td>
</tr>
<tr>
<td></td>
<td>Staphylococcus aureus (1)</td>
</tr>
<tr>
<td></td>
<td>Capnocytophaga spp (1)</td>
</tr>
<tr>
<td></td>
<td>Eikenella corrodens (1) (BC)</td>
</tr>
<tr>
<td></td>
<td>Mycobacterium tuberculosis (1)</td>
</tr>
<tr>
<td></td>
<td>Bacteroides spp (8)</td>
</tr>
<tr>
<td></td>
<td>Fusobacterium spp (4) (1BC)</td>
</tr>
<tr>
<td></td>
<td>Prevotella spp (4)</td>
</tr>
<tr>
<td></td>
<td>Peptostreptococcus spp (2)</td>
</tr>
<tr>
<td></td>
<td>Micromonas micra (2)</td>
</tr>
<tr>
<td></td>
<td>Lactobacillus spp (2)</td>
</tr>
<tr>
<td></td>
<td>Actinomyces israelii (1)</td>
</tr>
<tr>
<td></td>
<td>Gardnerella vaginalis (1)</td>
</tr>
</tbody>
</table>

Conclusions:

- It’s essential in TOA samples to ask not only for bacteriological culture but also for STI-PCR.
- Our study shows a high yield in the microbiological diagnosis of TOA samples with an important presence of STI (27.3%) and polymicrobial flora (26%).
- E.coli is the most common isolated pathogen (32.7%), followed by C.trachomatis (25.5%) and Bacteroides spp (14.5%).

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Abstract 6854

**Identification of microorganisms direct from signal positive blood culture using Acrion system**

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**Background:** Mass spectrometry (MS) has made a major impact in the field of clinical microbiology in recent years, but there is still a need for more rapid and accurate identification of microorganisms from positive blood culture. Direct detection is challenging and although several extraction protocols are commercially available, these are expensive, laborious and time consuming. A widely used method in clinical laboratories is to subculture positive blood cultures on solid medium and incubate for a few hours before identifying the isolate using MALDI-TOF. Not only does this delay the time to result, but identification can be of low discrimination between certain closely related species. Here we present a high resolution mass spectrometry device, Acrion™, that is able to rapidly identify microorganisms directly from positive blood cultures with high accuracy.

**Materials/methods:** A 1–2 mL aliquot of over 200 signal positive blood culture samples (BioMerieux Bactec) was removed and frozen within five hours of signal positivity. Each positive blood culture aliquot was thawed at room temperature and 150 µL sampled for Acrion™ analysis. All samples were subcultured onto solid media and incubated in appropriate conditions to evaluate growth. Identification was carried out using MALDI-TOF or DNA sequencing. Samples where there was no recovery of viable organisms or minimal growth were discarded from the analysis.

**Results:** Altogether, 161 positive blood culture samples representing 34 different bacterial and yeast species were included in the study. Acrion™ identified the correct microorganism with 95.03 % accuracy (153/161) directly from positive blood culture, with 123 Gram positive, 37 Gram negative and 1 yeast isolates tested (Table 1).

<table>
<thead>
<tr>
<th>Result</th>
<th>All</th>
<th>Gram positive</th>
<th>Gram negative</th>
<th>Yeast</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct ID</td>
<td>153</td>
<td>115</td>
<td>3?</td>
<td>1</td>
</tr>
<tr>
<td>No ID</td>
<td>?</td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Combined</td>
<td>161</td>
<td>123</td>
<td>3?</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 1. Performance results

**Conclusions:** Using high resolution mass spectrometry, Acrion™ enables rapid identification of microorganisms with high accuracy directly from positive blood culture. The system offers a diagnostic solution of complete automation with rapid and reliable results.

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Abstract 6855

Molecular epidemiology of *Achromobacter xylosoxidans* in the airways of cystic fibrosis patients: a longitudinal study

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**Background:** *Achromobacter xylosoxidans* are increasingly recognized in patients suffering from cystic fibrosis (CF). These pathogens are highly resistant to commonly used antibiotics due to intrinsic and acquired resistance mechanisms. Detection of these pathogens in the airways of CF patients is accompanied with an impaired pulmonary function. Here, we aimed to detect genomic clusters of *A. xylosoxidans* strains in different CF patients to elucidate genetic alterations of these pathogens over time.

**Materials/methods:** All *A. xylosoxidans* isolates from sputa of CF patients admitted to the University Hospital Münster were collected from 2006 to 2018, analyzed by whole genome sequencing and compared in a gene-by-gene approach (core genome multilocus sequence typing, cgMLST) using *A. xylosoxidans* NCTC 10807 (GenBank accession number NZ_LN831029.1) as a reference sequence. Genetic relation was displayed using the minimum-spanning tree algorithm, whereby close genetic relationship was assumed at 20 allele difference or less.

**Results:** In total, 131 *A. xylosoxidans* strains isolated from 24 patients were genetically analyzed resulting in 13 clusters of two to 14 close related genotypes, whereby one cluster harbors genotypes isolated from three different patients, indicating a possible transmission of this pathogen. All other clusters only harbor isolates derived from one and the same patient. In three patients, isolates showed a cluster of distantly related (21-350 alleles difference) genotypes. Ten isolates derived from one patient over time resulted in 2 different clusters of unrelated and distantly related genotypes.

**Conclusions:** In the majority of cases one *A. xylosoxidans* clone persist in the airway of CF patients and alters genetically over time. Transmissions of *A. xylosoxidans* from one patient to another are possible, making infections control approaches more important.

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Abstract 6857

Results of a Zika virus screening programme in asymptomatic pregnant women in Spain

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Background: Zika virus is a mosquito-borne flavivirus transmitted by Aedes. In Spain, a monitoring protocol was developed to detect the exposure to the virus in pregnant women who reside or have traveled to areas with active Zika virus transmission. Our objective was to evaluate the results of the screening programme in Asturias.

Materials/methods: A total of 229 pregnant patients (179 came from endemic zone and 50 traveled to those areas before pregnancy) were included in the study from 23/11/2017 to 10/10/2019 (medium age= 31.53 years, range 14-51). Zika immunoglobulin G (IgG) and immunoglobulin M (IgM) were analyzed by indirect chemiluminescent immunoassay (ZIKA VIRCLIA® MONOTEST, Vircell, Spain). Zika IgG positive samples were confirmed by plaque reduction neutralization test (PRNT) in the Spanish National Center for Microbiology (Madrid, Spain).

Dengue virus determination by indirect immunofluorescence was also performed to rule out other flaviviruses that could interfere with Zika result (Arbovirus Fever Mosaic 2, Euroimmun, Germany).

Results: Zika IgG were detected in 88 patients (medium age= 29.73 years, range 17-51). The most common origin countries were: Dominican Republic (12), Colombia (12), Brazil (10), Ecuador (9), Paraguay (7), Honduras (7), Venezuela (5), and Senegal (5). No pregnant woman who traveled to endemic zone presented antibodies against Zika. Three positive samples were confirmed by PRNT (probable cases), 53 were negative and 32 undetermined. In none of them Zika IgM was detected. Therefore there was a Zika probable cases incidence rate in the study of 1.31%.

All three patients with Zika infection also had dengue IgG positive, indicating previous contact with dengue and Zika. Two of them were from Dominican Republic and one from Senegal. No complications during pregnancy and newborn were observed.

Of those unconfirmed Zika cases, in 67 patients dengue IgG were detected (past dengue infection), 3 patients were negative for dengue and in 15 patients no data were available.

Conclusions: The study of Zika virus in pregnancy allowed detecting those with previous contact with the virus and subsequent pregnancy and newborn monitoring.

The percentage of positive IgG results that are confirmed with neutralization is low, which suggest the need to confirm these results.

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Development of a high-throughput single nucleotide polymorphism (SNP) typing assay for Klebsiella pneumoniae

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Background: Multilocus sequence typing (MLST) is currently widely used for describing the population structure of many bacterial species including Klebsiella pneumoniae (KPN), one of the top priority pathogens on the WHO list, and for defining 'high-risk' clones associated with specific virulence and/or resistance traits. However, MLST, performed by conventional Sanger sequencing or next-generation sequencing, is still costly and laborious for analysis on large sample collections. Here, we aimed to develop a high-throughput real-time-PCR-based SNP-typing assay for KPN.

Materials/methods: The informative SNPs for typing were selected from concatenated sequences of MLST loci: gapA, infB, mdh, pgI, phoE, rpoB, tonB (https://bigsdb.pasteur.fr/klebsiella/) to achieve the maximum Simpson's index of diversity (D) for all known sequence types (STs). Additionally, two virulence genes, clbA and rmpA, commonly present en bloc in hypervirulent strains were included. Allele-specific real-time PCR with universal fluorescence-energy-transfer-labelled primers was used to detect SNPs. For each SNP, allele-specific primers were designed to contain a locked nucleic acid (LNA) at the 3’ end to improve specificity of priming, and the 5’-tail sequences, to introduce priming sites for the universal fluorogenic primers. Automated SNP calling was performed by detecting fluorescence generated upon amplification from differentially-labelled universal primers. The assay was validated on a panel of control strains representing various STs and SNPs combinations, and was applied for genotyping 179 carbapenemase-producing (CP) isolates from diverse sources.

Results: A set of 22 SNPs from seven loci was selected that provided a D-value of 0.997 by testing in silico 2440 unique MLST profiles (excluding those of K. variicola, K. quasipneumoniae and Raoultella terrigena). The developed SNP-typing assay permitted accurate and unambiguous identification of nucleotide bases at all selected SNP positions with typability of 100% for control strains. All CP isolates were successfully typed with majority of them being assigned to international multiresistant clones: CG395 (46.4%), CG147 (14.0%), CG307 (8.4%), ST11 (4.5%), ST340 (3.9%), ST258 (0.6%), and some to hypervirulent clone CG23 (1.1%), which was further confirmed by sequencing.

Conclusions: We developed a rapid, reproducible and cost-effective SNP-typing assay suitable for large-scale surveillance studies of KPN.

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Abstract 6861

**Characteristics and outcome of acute viral encephalitis in an infectious disease unit**

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**Background:** The main causes of infectious encephalitis are viruses. We performed a retrospective study to analyse the characteristics of adult patients with viral encephalitis.

**Materials/methods:** From January 2002 to October 2019, a retrospective study was conducted including patients hospitalized for viral encephalitis. All demographic and clinical data, as well as those regarding patient outcome were recorded.

**Results:** 93 patients were included. There were 67 males (72 %) and 26 females (28 %) with a mean age of 52.4 years ± 19.2 years (range 27–82 years). 82 patients (88.1%) had altered mental status, 48 (51.6%) focal neurological symptoms, 35 (37.6%) impaired level of consciousness and 42 (45.1%) seizures. Blood tests found moderate C-reactive protein increase in 65 patients (mean 13 mg/l). An elevated white blood cell count was found in 34 patients (mean 12,500/mm3 cells). Hepatic cytolysis was found in 27 patients (29%). Cerebral spinal fluid tests showed increased leukocytes > 10/mm3 in 90 patients (mean: 137/mm3 cells), and a majority of lymphocytes in 87 (93.5%). Moderate hyperproteinorachia was observed in 43 patients (46.3%). Hypoglycorrachia was observed in 67 cases (72%). The viral agent was identified in 42 cases: Herpes simplex virus (n=24, 25.8%), West Nile virus (n=10, 10.7%), rubelle (n=4, 4.3%), Cytomegalovirus (n=2, 2.1%), varicella-zona virus and VIH in respectively one case. 80 patients (86%) received antiviral drugs: aciclovir for 79 patients (73.4%) and ganciclovir for 2 (2.1%). The mean duration of antiviral treatment was 15 days ± 3.2 days. The outcome was good for 80 patients. Four patients died from acute viral encephalitis. Altered level of consciousness were noted in 8 of them (8.6%). One patient had developed a brain abscess needing surgery.

**Conclusions:** Our study describes the main characteristics of viral encephalitis. In order to increase the likelihood of positive results for a specific virus, it is important to know the best approach to collecting samples and to choose the best identification technique for each virus. Further studies are required to investigate defective mechanisms of defense against pathogens that might be genetically determined.

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A publicly accessible database for *Clostridioides difficile* genome sequences supports tracing of transmission chains and epidemics

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**Background:** *Clostridioides difficile* (formerly called *Clostridium difficile*) is the primary infectious cause of antibiotic-associated diarrhea. Local transmissions and international outbreaks of this pathogen have been previously elucidated by bacterial whole-genome sequencing, but comparative genomic analyses at the global scale were hampered by the lack of specific bioinformatic tools.

**Materials/methods:** Here we introduce a publicly accessible database within EnteroBase (http://enterobase.warwick.ac.uk) that automatically retrieves and assembles *C. difficile* short-reads from the public domain, and calls alleles for core-genome multilocus sequence typing (cgMLST).

**Results:** EnteroBase currently contains 13,515 quality-controlled *C. difficile* genomes which have been assigned to hierarchical sets of single-linkage clusters by cgMLST distances. This hierarchical clustering is used to identify and name populations of *C. difficile* at all epidemiological levels, from recent transmission chains through to pandemic and endemic strains. Moreover, it puts newly collected isolates into phylogenetic and epidemiological context by identifying related strains among all previously published genome data. For example, HC2 clusters (i.e. chains of genomes with pairwise distances of up to two cgMLST alleles) were statistically associated with specific hospitals (\(p<10^{-4}\)) or single wards (\(p=0.01\)) within hospitals, indicating they represented local transmission clusters. In contrast, clustering at level HC150 was largely compatible with PCR ribotyping, thus enabling comparisons to earlier surveillance data.

**Conclusions:** EnteroBase enables contextual interpretation of a growing collection of assembled, quality-controlled *C. difficile* genome sequences and their associated metadata. Hierarchical clustering rapidly identifies database entries that are related at multiple levels of genetic distance, facilitating communication among researchers, clinicians and public-health officials who are combating disease caused by *C. difficile*.

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Community antibiotic prescribing for children in France from 2015 to 2017: a prospective national study
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Background: To assess recent community antibiotic prescribing for French children and identify areas of potential improvement.

Materials/methods: We analyzed 223,506 pediatric (<15 years) visits in a nationally representative sample of 680 French general practitioners (GPs) and 70 community pediatricians (IQVIA's EPPM database), between March 2015 and February 2017, excluding well-child visits. We calculated antibiotic prescription rates per 100 visits, separately for GPs and pediatricians. For respiratory tract infections (RTIs), we described broad-spectrum antibiotic use and duration of treatment. We used Poisson regression to identify factors associated with antibiotic prescribing.

Results: Overall, antibiotic prescriptions rates were 26.1 and 20.1 per 100 visits, for GPs and pediatricians, respectively ($p<0.0001$). RTIs accounted for more than 80% of antibiotic prescriptions by GPs and pediatricians, respectively. For RTIs, antibiotic prescription rates per 100 visits were: otitis, 66.5 and 79.8; pharyngitis, 67.9 and 54.4; sinusitis, 67.9 and 77.3; pneumonia, 80.0 and 99.2; bronchitis, 65.2 and 47.3; nasopharyngitis, 21.7 and 11.6; other presumed viral RTIs, 23.3 and 11.7, respectively. For RTIs, GPs prescribed more broad-spectrum antibiotics (49.9% vs. 35.6%, $p<0.001$) and antibiotic courses of similar duration (6.9 vs. 7.1 days, $p=0.21$). After adjustment for diagnosis and season, antibiotic prescription rates were significantly higher in older children (3-14 years vs. <3 years) and older GPs (≥50 years vs. <50 years).

Conclusions: Future antibiotic stewardship campaigns should target presumed viral RTIs (notably bronchitis and nasopharyngitis), broad-spectrum antibiotic use, children 3-14 years old, and GPs ≥50 years.

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Background: Inappropriate antibiotic use and antimicrobial resistance have posed huge threat to healthcare safety. However, there were few reports on antibiotic use and antimicrobial resistance in the provincial level in Mainland China. Therefore, this study aimed to describe current situation of antibiotic use and burden of antimicrobial resistance in Shaanxi province in 2017.

Materials/methods: 116 secondary and 45 tertiary hospitals voluntarily participated in the provincial surveillance project. All surveillance data (aggregated data) of antibiotic use and antimicrobial resistance from each hospital were submitted to local Ministry of Health for analysis. Two infection control specialists conducted the surveillance data validation.

Results: A hundred and sixty-one participating hospitals provided information about antibiotic use in 2,093,548 patients. A total of 950,138 (45.38%) received one or more antibiotics; 542,754 (25.93%) for treatment. Of those on antibiotics for therapeutic purposes, 247,875 (45.67%) had microbiology testing before receiving treatment. Among gram-negative bacteria, i.e. Enterobacteriaceae of 27,881 strains, Klebsiella pneumoniae of 18,256 strains, Pseudomonas aeruginosa of 14,553 strains, Acinetobacter baumannii of 11,788 strains, the proportions of carbapenem-resistant Acinetobacter baumannii (CRAB), carbapenem-resistant Pseudomonas aeruginosa (CRPA), carbapenem-resistant Klebsiella pneumoniae (CRKP), carbapenem-resistant Enterobacteriaceae (CRE) isolated from all samples were 51.32%, 13.76%, 7.09% and 1.80%, respectively. Among gram-positive bacteria, i.e. Staphylococcus aureus of 13,101 strains, Enterococci of 6,109 strains, the proportions of methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococci (VRE) isolated from all samples were 35.11% and 1.17%, respectively. Furthermore, the proportions of CRAB, CRPA, CRKP, CRE, MRSA, and VRE isolated from blood samples were 51.22%, 13.76%, 10.26%, 2.86%, 33.48%, and 1.17%, respectively.

Conclusions: Clinical antibiotics use in the northwestern China largely relied on empirical treatment. Antimicrobial resistance was still one major concern in view of the relatively high rate of antibiotic-resistant bacteria, not only from all samples but also from blood samples.

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Study of the relationship of infections of *Chlamydophila pneumoniae* and *Mycoplasma pneumoniae* with recurrent course of respiratory sarcoidosis

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**Background:** It was found that patients with respiratory sarcoidosis (RS) have elevated antibody titers (AB) to *Chlamydophila pneumoniae* (C.p.) and *Mycoplasma pneumoniae* (M.p.) more often than healthy people and patients with interstitial pneumonia. However, we did not find information about the impact of intracellular respiratory pathogens on the incidence of relapses RS.

**Materials/methods:** The prospective study of patients with newly diagnosed RS was performed. All patients underwent the paired blood serum study of the level of AB IgA and IgG to C.p. and M.p. using enzyme immunoassay initially and 2 weeks after. A positive increase in the AB titer was taken 2 or more times. We calculated the OR (95% CI) of the development of the recurrent course of RS taking into account each type of AB.

**Results:** 60 patients (55 men [91.7%] and 5 women [8.3%]) with morphologically confirmed RS were examined. The average age was 33.9±10.8 years. The stage II of RS was in 80% (48) of patient, stage I – in 18.3% (11), and generalized sarcoidosis - in 1.7% (1). Average follow-up was 24.6±10.8 months. Recurrent course of RS was observed in 7 patients (11.7%). Elevated AB titers were detected in 29 patients: isolated infections (either C.p. or M.p.), and combinations thereof. Signs of current infection were detected in 30% (20), transferred - in 35% (21). In patients with elevated titers of AB, no clinical manifestations of respiratory tract infection were observed. OR of recurrent course of RS was for AB IgA C.p. - 0.57 [95% CI 0.06-5.2], AB IgG C.p. - 1.72 [95% CI 0.13-4.5], AB IgA M.p. - 1.31 [95% CI 0.13 - 12.78], and AB IgG M.p. - 0.51 [95% CI 0.06-4.66]; p>0.05 for each parameter.

**Conclusions:** Elevated titers of AB to C.p. or M.p. can be detected in 48.3% of patients with RS, but these titers are not associated with the recurrent course of RS. Currently, there is no convincing data on the benefits of antibiotic therapy for the prevention of recurrent course of RS. Further studies explaining the relationship of C.p. and M.p. with RS are needed, including an assessment of immunological mechanisms.

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Abstract 6871

In vitro susceptibility of carbapenem-resistant Enterobacterales urinary isolates to nitroxoline and other oral urinary antibiotics

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Background: Nitroxoline is a recently re-introduced antibacterial agent to treat urinary infections. The aim of the study was to compare the in vitro efficacy of this drug to other orally administered urinary antibiotics against a collection of carbapenem resistant Enterobacterales (CRE) urinary isolates.

Materials/methods: MICs of nitroxoline, fosfomycin, nitrofurantoin, trimethoprim-sulfamethoxazole and ciprofloxacin for a collection of well-characterized CRE (n=222) isolated from urine in 5 hospitals in Kuwait (n=39) and 13 hospitals in the United Arab Emirates (n=183) were determined by broth microdilution. The collection comprised of OXA-48-like (n=75), VIM (n=5), NDM (n=80), KPC (n=3) producing, NDM and OXA-48-like (n=30) and NDM and VIM (n=2) co-producing isolates, as well as carbapenemase non-producing (n=27) strains, and it also included two previously characterized metallo-beta-lactamase producing pan-drug resistant Klebsiella pneumoniae. Susceptibility was interpreted using the EUCAST breakpoints for urinary Escherichia coli isolates.

Results: The MIC90/50 and susceptibility rates of the collection is shown in the Table.

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>MIC90</th>
<th>MIC50</th>
<th>Susceptibility rate %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>&gt;64</td>
<td>&gt;64</td>
<td>4.5</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>&gt;256</td>
<td>&gt;256</td>
<td>18.5</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>512</td>
<td>256</td>
<td>32.4</td>
</tr>
<tr>
<td>Fosfomycin</td>
<td>128</td>
<td>16</td>
<td>75.2</td>
</tr>
<tr>
<td>Nitroxoline</td>
<td>16</td>
<td>8</td>
<td>92.3</td>
</tr>
</tbody>
</table>

All E. coli (n=36) were susceptible to nitroxoline with 4/8 mg/L MIC50/90. Seventeen K. pneumoniae had MIC of nitroxoline >16 mg/L, nonetheless, the two pan-drug resistant K. pneumoniae exhibited nitroxoline MIC below the breakpoint (MIC 8 and 16 mg/L). Nitroxine MIC50/90 of K. pneumoniae (n=169) was 8/32 mg/L.

Conclusions: Of the five oral urinary antibiotics tested, nitroxoline exhibited by far the best in vitro efficacy against urinary CRE isolates. More than 90% of CRE (205/222), including two K. pneumoniae resistant to all other available antibiotics, would be classified as susceptible, if the current EUCAST susceptibility breakpoints for urinary E. coli were applied. Consequently, if clinically feasible, nitroxoline appears to be the best option for oral treatment of urinary tract infections caused by CRE.

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Is Lactobacillus crispatus a marker of cytolytic vaginosis in women under 45-years old?

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**Background:** Cytolytic vaginosis (CV) occurs due to overgrowth of lactobacilli, which causes a decrease in vaginal pH. In gram staining, abundant gram-positive bacilli (GPB) compatible with *Lactobacillus* and citolysis with bare cell nuclei are observed. Clinically it is often confused with vulvovaginal candidiasis. Some studies have postulated the possibility that *Lactobacillus crispatus* could be a marker of this pathology. The objective of this study was to identify *L. crispatus* as a marker of CV by MALDI-TOF identification directly from the culture of vaginal exudates.

**Materials/methods:** Gram stains of vaginal exudates from 38 symptomatic women were studied. If the staining showed cytolysis along with a significant amount of GPB compatible with *Lactobacillus*, the patients became part of the CV group. If Gram staining showed GPB without the presence of cytolysis, the patients became part of the “normal microbiota” (NM) group. In all samples, MALDI-TOF MS was used for identification directly from the culture. Vaginal pH data was not available. Patients older than 45 years old (who may be in menopause) and MALDI-TOF interpretations with a score lower than 1.7 were excluded.

**Results:** Of the 22 patients belonging to the CV group, 7 were excluded. Average age: 31.7 years old. MALDI-TOF identifications: *L. crispatus* 73.3% [n=11], *Lactobacillus jensenii* 20% [n=3], *Lactobacillus iners* 6.6% [n=1]. Of the 16 patients belonging to the NM group, 4 were excluded. Average age: 37.1 years old. MALDI-TOF identifications: *L. iners* 58.3% [n=7], *L. jensenii* 16.6% [n=2], *Lactobacillus gasseri* 16.6% [n=2], *L. crispatus* 8.3% [n=1]. *L. crispatus* was the microorganism most frequently identified in the CV group [p<0.001] and so was *L.iners* in the NM group [p<0.01]. There was no statistically significant difference between the groups with the other *Lactobacillus* species.

**Conclusions:** Diagnosing CV is crucial to avoid unnecessary antifungal treatments that will increase vaginal microbiota disorders. That is why it is important to identify factors that help diagnosing this pathology. One of them could be the abundant presence of *L. crispatus* in the culture in combination with a gram stain suggestive of CV. Further studies will be required studying the pH to help confirming the diagnosis of CV.

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Abstract 6876

**Evolution of multidrug-resistant organisms active surveillance strategy in a Portuguese acute care hospital, from 2015 to 2018**

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**Background:** Multidrug-resistant organisms (MDRO) are a worldwide public health concern. Infection control guidelines advocate a strategy based on two central cornerstones: patient contact isolation and active screening tests, in order to contain MDRO dissemination. We describe the evolution of methicillin-resistant *Staphylococcus aureus* (MRSA) and carbapenemase-producing *Enterobacteriaceae* (CPE) active surveillance strategy in a Portuguese 340 bed acute care hospital, between 2015 and 2018.

**Materials/methods:** MRSA screening, through nasal swab, and CPE screening, through rectal swab, was implemented using real-time PCR methodology. A selected population for screening was defined, namely, in patients to be admitted: (1) from other hospitals/nursing homes, (2) with history of hospitalization (in national or abroad units), (3) antibiotic exposure in the last 6 months, (4) in intensive and intermediate care; (5) with chronic wounds (local swab for MRSA screening) and (6) doing haemodialysis. Direct contacts of newly detected inpatients were subjected to MRSA/EPC screening too. Every patient with suspicion/confirmation of MRSA/EPC was treated in contact isolation. In 2017 MDRO risk assessment was implemented to all patients to be admitted.

**Results:** A total of 13046 MRSA and 5905 EPC screening tests were completed, with a continuous rise in this time interval. The percentage of MRSA positive tests declined from 2015 to 2017 (10.9% to 6.4%) but, during 2018, increased to 7.8% (P=0.022) [Image 1]. The evolution of EPC positive screening tests is rising since 2016: from 3.5% to 4.1% in 2017 and 5.4% in 2018 (P=0.032). Considering a density of incidence, EPC increased continuously these four years, from 0.05 to 1.28 cases per 1000 patient-days (P=0.454) and MRSA increased since 2017 (2.09 versus 2.35, P=0.021). In these four years, MRSA positive patients were 8.6 years older than those who had negative test (P<0.001) and, in case of EPC, this difference was 4.7 years (P<0.001).

**Conclusions:** A screening strategy to MRSA and EPC in an acute healthcare setting is described. There is a tendency to the increase of this MDRO’s, which has important infection control implications in their management. Continuous active surveillance is needed, with periodical revision of risk criteria for screening.

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Investigation of a hospital outbreak of multi-drug resistant *Klebsiella pneumoniae* ST307, including isolates producing OXA-244 carbapenemase


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Abstract third-party references: Public Health Wales

**Background:** Carbapenemase producing *Kp* are becoming increasingly common. Antibiotic treatment options are limited and invasive infections are associated with significant mortality. Patient screening for Carbapenemase Producing Enterobacterales (CPE) was commenced on a surgical ward in a Welsh Hospital following isolation of CPE from two patient’s clinical samples. An outbreak investigation followed during which further OXA-48-like producing *Kp* were identified from clinical and screening samples.

**Materials/methods:** Susceptibility testing was performed according to EUCAST methods. OXA-48-like producing isolate were identified using in house RT-PCR. For NGS DNA was extracted using the eMAG (Biomerieux), libraries prepared using Nextera XT and sequenced using the V2 assaag on MiSeq sequencers (Illumina). Read assemblies were performed using Spades and run through Restfinder and PubMLST. The relationships of the Welsh isolates were contextualized by comparison with a previously published international dataset of 50 ST307 genomes. Sequence mapping used the software Snippy, against strain 616 (Accession CP0026495). Following the removal of regions that were putatively identified as repeats or mobile elements, variant sites were identified and phylogenetic trees produced using IQTree.

**Results:** The investigation identified a complex outbreak dominated by *Kp* ST307 producing OXA-244, identified in nine patients at the time of writing. All isolates were MDR, including resistance to ertapenem and variable activity against meropenem. All isolates were sensitive to amikacin, colistin and cefazidime-avibactam. Further NGS analysis confirmed that these isolates were closely related, forming a single, distinct, cluster on the global ST307 phylogenetic tree. This was compatible with epidemiological findings and isolation of cases, basic infection control and enhanced cleaning halted onward spread. During investigation further MDR, OXA-negative *K. pneumoniae* were also identified from clinical samples. These were predominantly either ST307 or ST1788. The ST307, OXA-negative isolates showed varying degrees of core genome identity to the outbreak strain.

**Conclusions:** *Kp* ST307 is an emerging high risk clone associated with nosocomial spread of infection and multi-drug resistant phenotype. Increasing reports of this organism acquiring carbapenemase genes are a public health concern. NGS can act as a useful adjunct to epidemiological investigations in understanding and controlling outbreaks, and can enhance our understanding of the epidemiology of nosocomial pathogens.

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High prevalence of Lymphogranuloma venereum in men who have sex with men in Alicante, south-east Spain

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Abstract third-party references: Ortiz de la Tabla, V, Infante Urrios, A, Gázquez Gómez, G

Background: Lymphogranuloma venereum (LGV) is a sexually transmitted infection (STI) caused by L serovars of Chlamydia trachomatis (CT). In developed countries LGV is predominantly associated with rectal infection in HIV-positive MSM. Data on the prevalence of LGV in Europe are sparse and not all laboratories have the capacity to identify LGV serovars. Alicante is a holiday town in Southeast Spain that receives travelers from many European countries, which can contribute to dissemination of STI. Our aim was to evaluate LGV prevalence and describe clinical and demographic characteristics of patients infected by CT LGV and non-LGV.

Materials/methods: From January to December of 2018, all anorectal samples positives for CT using the Cobas 4800 Real-Time CT/NG PCR (Roche®) were tested for LGV serovars. A confirmation LGV/non-LGV in house real-time PCR was performed.

Results: A total of 321 anorectal samples were tested (314 exudates and 7 biopsies).

Overall CT and LGV positivity was 11.8% (38/321) and 4% (13/321), respectively. Among 38 CT positive specimens, LGV positivity was 34.2% (13/38). All CT positives patients were MSM, with an average age of 33 years. Compared to CT non-LGV, patients with LGV were more likely to have rectal mucopurulent or bloody discharge (84.6% vs 39%; p=0.011), tenesmus and/or rectal pain (61.5% vs 5.6%; p=0.001) and inguinal lymphadenopathy (23% vs 0%; p=0.034). Three LGV positive biopsies specimens were from patients with symptoms suggestive of inflammatory bowel disease. More than half of non-LGV patients did not have symptoms at diagnosis, whereas only a single LGV case was asymptomatic.

Conclusions: We found a high prevalence of CT and LGV in MSM. The rate of LGV found in non-HIV patients was higher than expected. Unlike CT non-LGV, most cases of LGV were symptomatic and presented clinically with non-specific proctocolitis. Public health strategies should include testing for LGV on all CT positive samples from MSM, independently of their HIV status.

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Assigning the plasmidome: a novel approach to compare plasmids independent of host and incompatibility type
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Background: Plasmids carry a large diversity of antimicrobial resistance genes and are hosted in numerous species. Plasmids are nowadays considered the main protagonists for AMR transmission and other virulence factors. Epidemic plasmids can cause outbreaks which often remain undetected. In general, plasmids are complicated entities usually defined by high sequence versatility, which hampers their surveillance. In Enterobacteriales, plasmids can be identified by their incompatibility (Inc) type. In this study, we aim for an unbiased comparison including all currently available plasmid sequences, proposing a method to characterize plasmid sequences independent of host species and Inc type.

Materials/methods: A total number of 97,000 plasmid sequences were obtained from NCBI (08-10-2019). Prokka was used for annotation and Roary was utilized to generate the gene presence/absence information for all plasmids using 85% identity as cut-off for gene sequence without splitting paralogues. A text-mining algorithm in python was used for extracting metadata from Genbank records. RGI based on CARD was used for identifying resistome and Plasmidfinder for defining Inc types. An algorithm based on python was used to concatenate the data and apply filters for comparison. We applied our approach to plasmids carrying mcr (1-10) genes.

Results: Functional genomics comparison among all currently available plasmids was possible. We observed that every Inc type carried a specific backbone of genes. Each backbone was different regarding number and type of genes for plasmids with different size and Inc type (e.g. IncX4, IncI2 and IncHI2). A particular IncX4 mcr-1-carrying plasmid was present in more than nine species. Also, we observed plasmids carrying multiple Inc types. Our approach enabled comparison of plasmids from species where Inc types are unidentified. We were able to describe the evolution of mcr-containing plasmids and their global distribution including hosts.

Conclusions: Here, we propose a comparative collective method for characterizing plasmids independent of species and Inc type and show its applicability for mcr gene epidemiology. This unbiased approach can be applied for any gene of interest. Defining the plasmidome will provide more insight into the plasmidal epidemiology and the AMR landscape, which may contribute to new AMR prevention policies in local and global context.

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Molecular epidemiology of carbapenemase-producing *Escherichia coli* in northern Spain studied by molecular typing techniques and next-generation sequencing

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**Background:** Carbapenemases have spread worldwide in *Enterobacteriaceae*, limiting the therapeutic options available to treat the infections they cause. These enzymes are becoming more frequent in *Escherichia coli*, and this is a cause of concern because of the importance of this species in hospitals and its potential role in the transmission of antimicrobial resistance in the community.

**Materials/methods:** In the present study, 42 clinical isolates of carbapenemase-producing *E. coli* recovered between March 2017 and March 2018 in four hospitals located in northern Spain, and primary care centers associated with them, were analyzed. Bacterial genomes were sequenced with Illumina in a HiSeq 1500 to generate 125 bp paired-end reads. Serotyping, MultiLocus Sequence typing (MLST), clonotyping, as well as identification of phylogenroups, resistance genes, virulence genes and their genetic context, were accomplished by PCR and bioinformatics analysis (SeqSero, MLST, ResFinder, CARD, ArgAnnot, pMLST and PLACNETw). A phylogenetic tree was constructed using RAxML, based on SNPs in the core genome.

**Results:** Forty isolates were positive for the *bla* <sup>OXA-48</sup> gene while the remaining two carried *bla* <sup>VIM</sup>. All of them were multidrug-resistant and 23.8% harbored genes encoding extended-spectrum-β-lactamases (*bla<sup>CTX-M-1</sup>, *bla<sup>CTX-M-15</sup>, *bla<sup>CTX-M-27</sup>, *bla<sup>CTX-M-55</sup>, *bla<sup>TEM-10</sup>, *bla<sup>TEM-30</sup>, *bla<sup>TEM-150</sup> and *bla<sup>SHV-102</sup>). A wide variety of determinants conferring important resistances, such as plasmid-mediated quinolone resistance (*qnrB2*, *qnrS1* and *qnrS2*) or fosfomycin resistance (*fosA7*) were also found. Isolates belonging to diverse phylogroups: A (10), B1 (12), B2 (14), C (4) and F (2), and sequence types (Figure 1). Three clonotypes were determined within the O25b:H4-B2-ST131 clonal group: CH40-22 (2), CH40-30 (7) and CH40-298 (1). Fifteen isolates conformed the ExPEC and another 15 the UPEC status. The phylogenetic tree based on SNPs correlated with the STs.

**Figure 1:** Phylogenetic tree of the carbapenemase-producing *Escherichia coli* genomes. The tree is based on the core genome SNPs (2,509,672 +/- 154 bp; 2,633 core CDS with 90% identity; 96% pairwise alignment coverage). Bootstrap support values of 1,000 replicates are shown at the nodes. The hospital of origin of the isolates is colored in red (Hospital Universitario Central de Asturias, HUCA), black (Hospital Universitario San Agustín, HUSA), green (Hospital Universitario Marqués de Valdecilla, HMV) and dark blue (Hospital Universitario de Cabueñes, HUCAB).

**Conclusions:** A wide variety of carbapenemase-producing *E. coli* strains are circulating in northern Spain. Some of them belong to high-risk international clones such as ST58, ST131, ST410, ST48, ST648 and ST1193, carrying other antimicrobial resistances of concern and with potentially spread capacity, hence representing a threat to patients both in hospitals and the community.

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Abstract 6884

A high-resolution whole genome multilocus sequence typing (wgMLST) scheme for easy and scalable detection of *Streptococcus pyogenes* outbreaks

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**Background:** *Streptococcus pyogenes* is an infrequent, but usually pathogenic, component of the skin microbiota. Many important human diseases, which can range from mild skin infections to life-threatening systemic diseases, can be caused by *S. pyogenes*. Some strains are toxigenic causing infections that may lead to the potentially life-threatening streptococcal toxic shock syndrome. Typing based on whole genome sequencing data could help in quickly characterizing these toxigenic strains for outbreak analysis.

**Materials/methods:** We developed a whole genome Multi Locus Sequence Typing (wgMLST) scheme starting from 304 publicly available, annotated genomes that represent the known diversity of *S. pyogenes*. The scheme was validated against 7 recent published outbreaks characterized by whole genome Single Nucleotide Polymorphism (wgSNP) (Athey et al. 2016, Beres et al. 2017, Chalker et al. 2017, Chochua et al. 2017, Cornick et al. 2017, Davies et al. 2014, Engelthaler et al. 2016). Alleles were identified in BioNumerics 7.6.3 starting both from the assembled genome, using a BLAST based approach with 80% similarity threshold, and the raw sequencing data, using a k-mer based approach.

**Results:** In total, 991 strains were analyzed in less than two days. Using the wgMLST results we were able to reach the same conclusions regarding the outbreaks as the original authors did based on wgSNP results. wgMLST has the advantage that is more scalable than wgSNP. That is, each newly analyzed strain can be easily and directly compared to previous strains without the need of comparing it to a common reference. As such, we compared all 991 strains in one analysis to investigate whether the outbreaks could be linked with each other. The included strains originated from 5 different countries: Canada, Hong Kong, UK, USA and Scotland. In a few cases strains originating from different countries differing less than 10 loci were found, indicating possible links between the outbreaks.

**Conclusions:** The *S. pyogenes* wgMLST scheme developed in BioNumerics proved to be a valid and powerful tool for easy and scalable outbreak analysis. It enables finding possible worldwide links between different, individually described outbreaks.

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Abstract 6888

**Role of PRAS40/mTOR/Akt in the intracellular development of Toxoplasma gondii tachyzoites**
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**Background:** *Toxoplasma gondii* is an obligate intracellular protozoan able to invade and proliferate in all nucleated cells. In immunocompromised patients they produce various diseases that can lead to death. The pathogenicity of this parasite depends directly on its ability to control cell proliferation through various biochemical signals. PRAS40 [Proline Rich Akt Sustrate 40 kDa] may be involved in the survivor of the parasite by activating mTOR pathway by phosphorylation.

**Materials/methods:** Tachyzoites extracted from peritoneal lavage of a murine BALB/c were used for Invasion experiments in 3T3 NIH cell cultures at different times: 0, 6, 12 and 18 hours. Some experiments included the use of mTOR inhibitors drugs [Torin-2] plus tachyzoites in the cultures using times: 6, 12 and 18 hours. We also have 2 control conditions using insulin, the cultures were stimulated for 15 minutes with insulin, and in one of them it was added Torin-2 for 30 minutes. The proteins were extracted and analyzed by poly acrylamide gel electrophoresis [PAGE] and Western Blot using antibodies for the proteins we were studying.

**Results:** It was found that the *Toxoplasma gondii* develop increases the phosphorylation of PRAS40 in cell cultures, especially in the incubated at 12 hours. This phosphorylation was observed dependent on mTOR and Akt.

**Conclusions:** Results from the study suggest that PRAS40 is involved in the intracellular development of *Toxoplasma gondii* Tachyzoites, apparently the pathway regulated by mTOR participates in this process, contributing to the arrest of the host cell division and providing stability to the intracellular niche to the parasit.

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Abstract 6892

**Evaluation of QIAseq 16S/ITS screening panel kit sequencing 6 regions to analyse 16S microbiota**

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**Background:** The advent of high throughput sequencing allows the study and the understanding of the bacterial microbiota. Most of the time, only one region of the 16S ribosomal RNA is sequenced and analyzed for the bacterial microbiota 16S study. Here, we evaluated the QIAseq 16S/ITS Screening Panel kit (Qiagen®) allowing the amplification and sequencing of six 16S rRNA regions: V1V2, V2V3, V3V4, V4V5, V5V7, V7V9.

**Materials/methods:** Stools from seven children with acute lymphoblastic leukaemia were studied at different times of their treatment: one sample before chemotherapy (P1) and two after (P2 and P3). In total 21 stools were analyzed. DNA extraction was performed by QIAamp DNA stool Mini (Qiagen®). Amplicon libraries were prepared using QIAseq 16S/ITS Screening Panel kit (Qiagen®) and sequencing was performed on MiSeq 2x300 bp V3 kit. Data were analyzed using CLC Genomics Workbench 12 (Qiagen®) pipelines.

**Results:** The number of reads obtained before trimming varied between 5,950,910 for V5V7 region and 2,491,512 for V3V4 region. After trimming, the remaining sequence percentages were 40% for V1V2 and only 26% for V3V4. The rarefaction curves were reached for all samples in all regions except for 2 samples in V2V3. The percentage of OTUs assigned to gender was comparable for all regions. In order to assess the microbiota composition and ensure that important families are not missed by any of the PCR primers, we compared the relative abundances of Lachnospiraceae, Enterococcaceae, Enterobacteriaceae and Bacteroidaceae. No significant differences between relative abundances were found and no significant families were missed. Finally, the choice of 16S rRNA regions does not seem to impact significantly the α-diversity of bacterial microbiota. However, the regions V3V4 and V4V5 had the lowest Shannon index (α-diversity).

**Conclusions:** Our study highlights that the use of 6 regions to analyze 16S microbiota may not be necessary. Few differences between regions were observed with slight differences in terms of diversity. In contrast, sequencing depth is crucial to have comprehensive data. V3V4 region was the least sequenced region suggesting that it may not be the best, with the primers used, to analyze 16S microbiota.

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**Abstract 6896**

**Rapid detection of colistin-resistant *Klebsiella pneumoniae* using colistin drop test**

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**Abstract third-party references:** This study is supported by Laboratory of Pathology and Molecular Biology (LPBM), Gonçalo Moniz Research Institute, Oswaldo Cruz Foundation, Salvador, Bahia, Brazil and Faculty of Pharmacy, Federal University of Bahia, Salvador, Bahia, Brazil.

**Background:** The emergence and spread of carbapenem and colistin-resistant *Klebsiella pneumoniae* (ColR-KP) is an important threat to global health. At the diagnostic level, the only approved susceptibility testing method for colistin is broth microdilution (BMD). However, manual BMD is time consuming and often unfeasible in the clinical laboratory. During an outbreak of ColR-KP in a Tertiary Hospital of Salvador, Bahia / Brazil, was used the colistin drop, a less complex methodological alternative, and the BMD. In addition, the mechanisms of carbapenemic and colistin resistance were also evaluated.

**Materials/methods:** Phenotypic detection of carbapenemase production was performed using the Modified Carbapenemic Inactivation Method (mCIM) and the EDTA-Modified Carbapenemic Inactivation Method (eCIM) according to the CLSI standardized methodology. The PCR reaction was performed for *bla*OXA-48-LIKE, *bla*GES, *bla*KPC, *bla*IMP, *bla*VIM, and *bla*NDM. The colistin drop test was compared with BMD results.

**Results:** Fifty-nine ColR-KP were evaluated. The mCIM test was positive in 54 (91.5%) and the eCIM in 51 (86.4%). Nine (17.7%) of the eCIM positive strains were *bla*NDM and none was IMP or VIM, suggesting the possibility of another metallo-β-lactamase, currently under investigation. Fifty-one (86.4%) *bla*KPC were identified. The mCIM/eCIM showed 1 false negative in which the *bla*NDM gene was detected. One *bla*GES was detected in a negative mCIM/eCIM strain.

The *mgrB* gene was evaluated in 58 samples, being detected mutation in 43 (74.2%) and non-detection of the gene in 4 (6.9%). In 11 (19%) stains the *mgrB* gene was detected unchanged suggesting another mechanism of resistance. The mcr-1 test was negative in all samples. Of the 57 samples submitted to the drop colistin test, correlation with BMD were 98.2%. The only divergent case was a strain with a MIC of 2 mcg/ml and a drop colistin test positive and no detection of *mgrB* gene which would justify the resistance.

**Conclusions:** The colistin drop test showed a good correlation with BMD but a limitation is the non-determination of the colistin MIC. Although *bla*KPC was detected in 86.4%, the eCIM test suggested the presence of an unidentified metallo-beta-lactamase. The main mechanism of colistin resistance detected was the mutation of the *mgrB* gene.

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Synthesis and antibacterial evaluation of 9-substituted palmatine analogues as a novel class of anti-
H. pylori agents targeting urease

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**Background:** Antibiotic-resistant *Helicobacter pylori (H. pylori)* was increasingly found in infected individuals, which resulted in treatment failure and required alternative therapeutic strategies. This research was mainly focused on discovering novel antibacterial candidates with unique scaffold for the treatment of infections arising from *H. pylori*.

**Materials/methods:** A library of 9-substituted palmatine derivatives constructed in our lab was screened for their anti-*H. pylori* potencies using phenotype screening assay. MICs of all prepared compounds were tested on seven *H. pylori* strains including standard strains and clinical isolates using agar dilution method according to Clinical and Laboratory Standards Institute (CLSI) guidelines. All prepared compounds were characterized by ¹H NMR, ¹³C NMR and ESI-HRMS.

**Results:** A series of new 9-substituted palmatine including ethers, amines and amides were synthesized and evaluated for their antibacterial effect. Among them, compounds HP-1 and PN-1 exhibited high potency against metronidazole-sensitive and resistant strains of *H. pylori* with MIC values of 2-8 μg/mL. Preliminary mechanism study indicated that compounds HP-1 and PN-1 significantly inhibited urease which neutralizes stomach acid in order to create a suitable pH environment that the bacterium requires to survive and colonize.

**Conclusions:** Therefore, we consider 9-substituted palmatine derivatives to be a novel class of anti- *H. pylori* agents worthy of further investigation.

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Clinical performance of the novel multiplex real-time PCR ResistancePlus MG FleXible: a cartridge-based assay for simultaneous detection of *Mycoplasma genitalium* and macrolide resistance

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**Background:** *Mycoplasma genitalium* (MG) has a disturbing capacity to develop antibiotic resistance and may soon become untreatable. The resistance-guided treatment strategy has demonstrated very good efficacy against MG and prolongs the utility of existing antibiotics by optimizing antimicrobial stewardship. The aim of this study was to evaluate the clinical performance of the novel molecular cartridge-based test ResistancePlus® MG FleXible (SpeeDx Pty Ltd, AU) on the GeneXpert Infinity-48s Platform (Cepheid, USA) for detection of MG and mutations conferring macrolide resistance.

**Materials/methods:** The ResistancePlus® MG FleXible test detects MG through the *mgpB* gene and the macrolide resistance-associated mutations A2058G, A2059G, A2058T and A2058C in the 23S rRNA gene. Between March 2019 and April 2019, a total of 146 samples [95 MG positive and 51 MG negative], were collected at the Vall d’Hebron University Hospital in Barcelona, Spain. Specimens consisted of 18 vaginal swabs, 32 endocervical swabs, 15 urethral swabs, 38 first-void urines and 43 rectal swabs. Results were compared to the Allplex™ STI Essential assay (Seegene, SK) for MG detection, while Sanger sequencing of the 23S rRNA gene was used for confirmation of macrolide resistance-associated mutations.

**Results:** Results are displayed in table 1. Only 63/90 ResistancePlus® MG FleXible positives were suitable for subsequent Sanger sequencing.

<table>
<thead>
<tr>
<th></th>
<th>Allplex STI Essential</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ResistancePlus MG FleXible</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 146)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MG positive</td>
<td>90</td>
<td>0</td>
<td>94.7 (88.7-98.3)</td>
</tr>
<tr>
<td>MG negative</td>
<td>5</td>
<td>51</td>
<td></td>
</tr>
<tr>
<td><strong>ResistancePlus MG FleXible</strong></td>
<td>Sanger sequencing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 90)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-mutant</td>
<td>33</td>
<td>2a</td>
<td>93.3 (77.9-99.2)</td>
</tr>
<tr>
<td>Mutant</td>
<td>0</td>
<td>28</td>
<td></td>
</tr>
</tbody>
</table>

*aThese were two rectal swabs reported as non-mutant by the ResistancePlus® MG FleXible assay but harbouring mutations A2059G and A2058G, respectively, according to Sanger sequencing.

**Conclusions:** The ResistancePlus® MG FleXible assay is a rapid, simple and accurate assay for simultaneous detection of MG and macrolide resistance. This novel test may facilitate the implementation of the resistance-guided therapy for MG in many clinical settings, significantly improving clinical management and limiting antibiotic resistance selection.

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A real-world review on QIDP designation: what lessons can we learn?
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Abstract third-party references: Decision Resources Group

Background: Antibiotic resistance is a global crisis that threatens public health. In response to increasing antibiotic resistance, numerous initiatives have been undertaken to accelerate antibiotic development by addressing the barriers associated with antibiotics innovation. One such initiative is the qualified infectious disease product (QIDP) designation, which grants priority review and market exclusivity, among other incentives, to certain antibiotics for a specific indication.

Materials/methods: This study assesses the impact of QIDP designation on development and approval timelines and evaluates the time to first patient and use across indications. We evaluated US patient-level data from a real-world, outpatient claims data repository as well as US hospital charge master data covering more than 350 hospitals across 37 states from April 2014 to June 2019. To evaluate the correlation between real-world use and QIDP-designated indications, we assessed the relative usage of drugs across indications. Antibiotic utilization date and off-label usage were evaluated for 9 novel antibiotics launched between 2012 to 2018 using relevant medical codes and evaluating their corresponding diagnosis.

Results: Despite all evaluated antibiotics being labeled as QIDP, review durations took an average of eight months, exceeding the FDA target goal of six months. Analysis of real-world data indicated, the first prescription occurred within three months following launch, frequently in the indication included in the FDA label. Generally, a higher antibiotic usage was noted for the QIDP designated indication, but exceptions occur. Similarly, off-label usage happened within two months of the first on-label use. First use in pediatric populations was more variable, ranging from one month (ceftolozane/tazobactam) up to 25 months (oritavancin).

Conclusions: Our study highlights limited impact of QIDP designation in expediting regulatory approval, suggesting it may not be as impactful as intended from a commercial and resource allocation perspective. Moreover, despite antibiotic stewardship measures, off-label use of antibiotics is common, and driven by needs for agents active against resistant pathogens, or with better safety/tolerability profiles or more convenient administration. We believe that along with QIDP, other initiatives like relaxation of government reimbursement policies and incentivizing innovation will together help accelerate future antibiotic drug development.

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Abstract 6902

Cure rate comparison between rifampicin mono-resistant and multidrug-resistant tuberculosis: a retrospective multi-centre study from 1990 to 2017

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Background: World Health Organization (WHO) recommended in 2016 that all cases of rifampicin-resistant tuberculosis (TB), regardless of isoniazid susceptibility, should have been managed as multidrug-resistant (MDR) TB. The current updated WHO guidelines recommend the administration of all-oral regimens, if feasible. The present study aims to assess treatment outcomes in rifampicin mono-resistant (RMR) and MDR-TB.

Materials/methods: An observational, retrospective, multi-centre study was conducted using data from two Italian TB reference hospitals. Patients admitted from 1st of January 1990 to 31st of December 2017 were consecutively recruited. Demographic, epidemiological, and clinical variables of RMR- and MDR-TB cases were statistically compared.

Results: A total of 301 patients were diagnosed with RMR- (73, 24.3%) or MDR-TB (228, 75.7%). Their median age was 33 years and they were mainly male (188, 62.4%); 44 (14.4%) were HIV co-infected and 276 (91.6%) showed a pulmonary TB. Extra-pulmonary TB was more prevalent in RMR-TB (37% vs. 11%; p<0.0001). Positive culture for Mycobacterium tuberculosis was obtained in 297/301 (98.7%) cases and DST was performed in all 297 cases. The majority of RMR-TB cases (37; 52.9%) were Italian, whereas patients from Eastern Europe (73; 35.1%) were mainly affected by MDR-TB. Co-infection with HIV (33.8% RMR VS. 9.0% MDR-TB; P <0.0001) and social exclusion (22.2% RMR VS. 7.9% MDR-TB; P= 0.0001) were more prevalent in patients with RMR-TB. The overall treatment success rate was 66.9% (56.2% in RMR- VS. 68.0% in MDR-TB; P= 0.027). A lower treatment success was observed in those socially excluded (e.g., homeless and intra-venous drug users; P= 0.044) and with HIV co-infection (P= 0.07). Treatment success was more prevalent in patients treated with fluoroquinolone-containing regimens (78.3%VS. 51.3%; P <0.001). Mortality rate was 7.1% and 4.3% in RMR- and MDR-TB, respectively (P= 0.352).

Conclusions: Regimens combined with appropriate management of comorbidities and socio-economic hardship may improve treatment outcomes. The role played by social and clinical factors should be further assessed in a larger sample, including a large number of vulnerable population groups.

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Abstract 6904

**Mass visitation of show caves as a threat to human health**

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**Background:** Karst caves have been an attraction since the Middle Ages, and some became a place of mass visitation. Tourists emit bioaerosols inside caves which give a detailed view on conditions and dynamics in the atmosphere, and estimate human impact. Human-borne microorganisms can also represent a threat to human and environmental health. Mass cave tourism can impact people visiting or working in caves as well as ecology of the underground ecosystem.

**Materials/methods:** Air was sampled from February 2017 to November 2018 along footpaths before and during tourist visits in Postojna Cave, Slovenia, which is visited by more than 750,000 tourists annually, and in Škocjan Caves, Slovenia, which attracts more than 150,000 tourists annually. 4.5m³ of air was sampled by Coriolis-Impinger (Bertin Technologies, France) into 10mL of saline. 0.2mL were inoculated onto nutrient and blood agar plates and incubated aerobically at 20°C and 37°C for seven and two days, respectively. Concentrations of airborne microbes were expressed in CFU/m³ and identified by MALDI-TOF MS (Bruker Daltonik, Germany).

**Results:** Tourists significantly increased concentration of airborne microbes above the background level. The highest microbial load was in August when microbial biomass exceeded 300CFU/m³ at all sampling sites. The highest value (1146CFU/m³) was in a smaller chamber in Postojna Cave in the section Vivarij. In the air, a mix of bacteria typically associated with humans and other natural habitats was identified before and during tourist visits at all sites. Several isolates belonged to clinically important genera: *Staphylococcus*, *Pseudomonas*, *Moraxella*, *Acinetobacter*, *Aerococcus* and *Bacillus*.

**Conclusions:** Tourists impact air in show caves in terms of quantity and quality of airborne particles. Despite large underground chambers and air movements, the air always contained representatives of human microbiome. In the peak season, the microbial loads exceeded the maximum recommended value of 300CFU/m³ for indoor environments. Constant presence of Risk-Group 2 microbes in the air should be further evaluated as cave natural conditions can prolong their viability and enhance their transmission on longer distances. Further investigations should also estimate the potential health risks in susceptible hosts visiting caves during the peak season when concentration of airborne microbes is significantly elevated.

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Abstract 6906

**Zooming into the CoNS group on a species level exposes high heterogenicity in prevalence and antibiotic resistance: an in-depth data analysis in the MALDI-TOF era**

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**Background:** For years, coagulase-negative Staphylococci (CoNS) were not considered a cause of systemic illness and were often regarded as contamination. Yet, recent literature shows that CoNS lead to septicemia and high mortality rates. Still, little is known about the prevalence and resistance of the 39 species of the CoNS group. Therefore, we aimed at filling this gap by performing a region-wide, comprehensive species-specific prevalence and antibiotic resistance analysis.

**Materials/methods:** In this retrospective study, we analysed all CoNS isolates from blood cultures of 9,121 patients from all 14 hospitals in the Northern Netherlands between 2013 and 2019. All isolates were determined to the species level using MALDI-TOF. Using the 'AMR' package written in the open-source software R, we applied EUCAST rules, corrected for first isolates and analysed resistance of the bug-drug combinations of all isolates.

**Results:** In total, we included 12,587 isolates for epidemiological analysis from 24 different CoNS species. The five most prevalent species spanned 98% of all species. No vancomycin resistance was found, but teicoplanin resistance is increasing over the years in most species. Furthermore, we defined 'CoNS sepsis' as having at least 3 positive blood cultures with the same species within 60 days. Following this definition, 8.2% of all patients suffered from CoNS sepsis. The relatively most common causal agent to this end was S. haemolyticus (584/459 patients, 12.6%), followed by S. lugdunensis (9/72 patients, 12.5%) and S. epidermidis (538/4,315 patients, 11.1%). S. haemolyticus showed the highest resistance in the CoNS group for almost all antibiotic classes. Additionally, significant differences were found in both prevalence and resistance between patient gender, age groups and types of hospital.

**Conclusions:** To the best of our knowledge, this is the first comprehensive analysis of the CoNS group in a region-wide approach, using solely MALDI-TOF for species identification. Although S. epidermidis and S. hominis were 8-10 times more prevalent than S. haemolyticus, the latter was associated with higher morbidity (CoNS sepsis rate) than S. epidermidis and S. hominis. This study highlights how large in-depth epidemiological analyses can generate new insights on the species level, that could help increase awareness and evaluate treatment options.

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Leishmaniasis in immunocompromised individuals without HIV: not so different. A comparative analysis of 60 patients

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Background: To evaluate the clinical characteristics and prognosis of leishmaniasis among immunocompetent (group1), immunocompromised without HIV (group2) and HIV-infected individuals (group3).

Materials/methods: We present an observational, retrospective study including all the patients with leishmaniasis who were attended in the Department of Health number 6 in Valencia, Spain from 2015 to June 2019. The records of the Microbiology Department were reviewed for identifying the patients. The variables were retrieved from the medical records. Median and IQR were calculated for quantitative variables and frequencies for qualitative variables. The t-test and chi-squared were applied.

Results: A total of 60 patients were included –see table-. Among group2: rheumatological and inflammatory bowel disease were the more frequent. Methotrexate, corticosteroids and anti-TNF were the more common treatments. Distribution of sex, age, visceral leishmaniasis (VL) and cutaneous (CL), atypical presentation and clinical cure is shown in table 1. In group 1, two patients died and 1 relapsed, in group 3 one patient died, and 1 patient relapsed in group 2. Time to diagnosis was 1[0.3-2.5] months for VL and 6[2-10] for CL for group 1 and 0.5[0-1.25] in VL and 4[2.75-8.5] in CL for group 2, differences were not significative. Bone marrow microscopy yielded diagnosis in a total of 17/26(65%) and PCR in 22/24(91%) of cases; skin biopsy microscopy was diagnostic in 9/27(33%) and PCR in 28/28(100%).

Conclusions: In our area, the Mediterranean Basin, half of the cases of leishmaniasis are seen among immunocompromised individuals without HIV. In this group, VL was more frequent than in the immunocompetent patients but we did not find more frequency of atypical presentations, longer time to diagnosis, less frequency of clinical cure or more relapses. Bone marrow and skin biopsy PCR was superior to microscopy examination for establishing the diagnosis in immunocompetent and immunocompromised without HIV patients.

<table>
<thead>
<tr>
<th></th>
<th>Non-Immunocompromised (n=31)</th>
<th>Immunocompromised without HIV (n=22)</th>
<th>HIV-infected (n=7)</th>
<th>p- value</th>
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</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>55%</td>
<td>50%</td>
<td>71%</td>
<td>p=0.005</td>
</tr>
<tr>
<td>AGED 0-16years</td>
<td>13/31(42%)</td>
<td>1/22(5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17-65years</td>
<td>8/31(26%)</td>
<td>15/22(68%)</td>
<td>7/7(100%)</td>
<td></td>
</tr>
<tr>
<td>&gt;65years</td>
<td>10/31(32%)</td>
<td>6/22(27%)</td>
<td></td>
<td>p=0.005</td>
</tr>
<tr>
<td>VISCERAL LEISHMANIASIS (VL)</td>
<td>10/31(32%)</td>
<td>11/22(50%)</td>
<td>7/7(100%)</td>
<td>p=0.005</td>
</tr>
<tr>
<td>CUTANEOUS LEISHMANIASIS (CL)</td>
<td>21/31(68%)</td>
<td>11/22(50%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VL classic presentation</td>
<td>80%</td>
<td>90%</td>
<td>29%</td>
<td></td>
</tr>
<tr>
<td>CL classic presentation</td>
<td>80%</td>
<td>80%</td>
<td></td>
<td>p=0.26</td>
</tr>
<tr>
<td>CLINICAL CURE</td>
<td>22/25(88%)</td>
<td>18/18(100%)</td>
<td>5/6(83%)</td>
<td></td>
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</tbody>
</table>

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Abstract 6908

Direct detection and identification of microorganisms from clinical urine specimens by high-resolution mass spectrometry

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Background: Rapid and accurate identification of microorganisms from urine specimens is important to ensure that clinicians can select appropriate antimicrobial treatment for patients having urinary tract infections (UTIs). Conventional methods for microbial identification often include a culturing step that delays the identification roughly by 24 h. Furthermore, daily number of urine specimens is usually relatively high in hospitals and increases need of manual work and resources. Direct method to detect and identify microorganisms and antibiotic resistance markers from urine samples would ease the workflow and decrease the workload of laboratory personnel.

Materials/methods: Twenty clinical urine specimens (10 positive, 10 negative) were received from a Finnish service laboratory. Five milliliters of each specimen was concentrated by centrifugation and the cell pellet was washed and finally extracted by chemical lysis and sonication. Extracted proteins were subjected to solid phase extraction (SPE) followed by liquid chromatography and electrospray ionization mass spectrometry (LC-ESI-MS). MS1 data was examined for deconvoluted masses (here: proteoform counts) and MS2 was utilized to identify the ten most abundant proteins in each sample. MS2 data was analyzed using ProSightPC software and database searches were performed against UniProtKB/SwissProt. Protein identifications were imported to ProteinCenter which clustered the homological proteins to single entry.

Results: Less than 20 proteoforms were detected in UTI negative specimens by MS1, whereas more than 100 proteoforms were present in 7/10 (70%) of UTI positive specimens. Viable cell counts from the samples revealed that in remaining 3/10 UTI positive specimen, bacterial cells were present in less than 10^6 CFU/ml. Half of the UTI positive samples got matches with proteins specific to bacterial species in MS2. Four out of ten matched only with human proteins, and from one sample, no species specific proteins were detected by MS2.

Conclusions: The results suggest that SPE-LC-ESI-MS is a feasible option for direct detection of microbes in UTI positive specimens as long as the sample preparation is optimized to recover enough material to the analysis. Once optimized, the method could readily be transferred to already existing high-resolution MS platform such as Acrion™ System.

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Abstract 6910

**Viral respiratory tract infections in children: epidemiology and impact of the implementation of a multiplex PCR**

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**Background:** Viral respiratory tract infections are very common during childhood. In addition to immunochromatographic and real-time PCR assays, we recently implemented a multiplex PCR assay allowing a rapid identification of numerous pathogens. We aimed to describe the epidemiology of respiratory pathogens and the impact of the viral results on antibiotic prescription.

**Materials/methods:** All patients under 18 years old attending to the paediatric emergency department and/or hospitalised in the general paediatric unit between March 1st 2018 and February 28th 2019, who were tested for a respiratory pathogen either by: influenza A/B or respiratory syncytial virus (RSV) immunochromatographic assays, or influenza A/B-RSV PCR assay (GeneXpert®), or multiplex PCR assay (Filmarray respiratory panel®) were retrospectively identified by the microbiology unit. Clinical, laboratory and imaging characteristics of the patients were further collected from medical files as well as antibiotic prescriptions. Proportion of antibiotic prescription and duration of treatment were compared between patients regarding the presence or absence of a viral pathogen.

**Results:** A total of 300 respiratory tests were performed among 234 patients during 272 episodes, distributed as 142 immunochromatographic tests (116 influenza A/B, 26 RSV, and 158 PCR assays (50 influenza A/B-RSV PCR assays, 108 multiplex PCR assays). The main clinical features of the patients were: age under 3 years old (n=192; 70.5%), fever (n=217; 79.7%), and dyspnea (n=169; 62.1%). The most frequently identified viruses were influenza A (n=72; 26.4%), rhinovirus/enterovirus (n=35; 12.9%), and RSV (n=30; 11%). Of note, 5/116 (4.3%) influenza and 1/26 (3.8%) RSV immunochromatographic assays showed false negative results. Overall, antibiotic prescription rate was significantly higher when the patient had a negative respiratory test (107/111=96.4% vs. 70/161=43.5%, p<0.001), whereas no significant difference was observed when only multiplex PCR assays results were considered (17/27=62.9% vs. 48/81=59.3%, p=0.66). Surprisingly, patients with asthma and neonates received more frequently an antibiotic treatment when a virus was found (53.3% vs. 0%, p<0.001; and 53.8% vs. 33.3%, p=0.004, respectively), whereas no significant difference was observed among immunocompromised and sickle cell disease patients.

**Conclusions:** Population of patients undertaking viral respiratory test should be better defined in order to limit antibiotic prescription.

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Abstract 6914

Transcripts to Identify Meningitis (TRIM) test: a novel and accurate host transcript based multiplex PCR assay to rule-out bacterial meningitis

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Background: Meningitis is a devastating disease. The key to patient management is distinguishing bacterial causes, which need immediate antibiotic treatment, from clinical mimics, e.g. viral meningitis, which do not. The gold-standard for diagnosis is lumbar puncture (LP), microscopy and culture of the cerebrospinal fluid (CSF). However, LP can be delayed, or microbiological results inconclusive. Consequently, patients can be treated with unnecessary antibiotics until bacterial meningitis is excluded. One solution is to develop a blood test to rule-out bacterial meningitis.

Materials/methods: Host transcript analysis was undertaken in five phases to identify transcript that accurately distinguished between blood samples from bacterial meningitis patients and clinical mimics (n=600). Transcripts were retained based on accuracy. Initially (1), gene-expression data of patients from multiple countries with bacterial or viral meningitis, viral encephalitis, meningism, or invasive bacterial disease with meningitis were analysed (n=180). Next (2), high performing transcripts were re-tested via quantitative RT-PCR among adult UK meningitis patient samples (n=81); (3) translated into a multiplex PCR assay (n=91 samples); (4) the multiplex re-tested/refined (n=72 samples). Finally (5), the TRIM assay (based on five host transcripts) was tested, blind to sample classification, on a further set of adult UK meningitis patients (n=176). Samples were confirmed bacterial meningitis or clinical mimics [confirmed viral meningitis or meningism]. Confirmed cases had meningitis symptoms, CSF pleocytosis and detection of pathogen in CSF or blood. Meningism cases had meningitis symptom but no CSF pleocytosis.

Results: TRIM assay accuracy for correctly diagnosing bacterial meningitis from mimics was 87% (153/176). Excluding samples collected after five days of intra-venous antibiotic provision, sensitivity was 100% ([Streptococcus pneumoniae, Neisseria meningitidis, Haemophilus influenzae]) and specificity 90% (135/150). Accuracy was 98% (64/65) distinguishing confirmed bacterial from viral meningitis cases.

Conclusions: TRIM is the first syndromic blood test focussing on meningitis diagnosis and translated from gene-expression data to multiplex PCR assay. It potentially offers a highly sensitive test to rule-out bacterial meningitis. It remains accurate among antibiotic exposed patients. Test use could help clinicians rationalise treatment, reduce in-patient stay, lower hospital costs and lessen risk of antimicrobial resistance. We are validating TRIM in a large (>700 patients) European study.

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Abstract 6916

Epidemiological and molecular characteristics of human parechovirus infection in children <6 months hospitalised with symptoms of sepsis-like illness: Milan 2015-2018

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Background: Human parechoviruses (HPeVs) are widespread pathogens belonging to the Picornaviridae family and currently divided into 19 genotypes. Although most HPeV infections cause self-limiting mild respiratory/gastrointestinal diseases, severe clinical manifestations, such as sepsis-like illness, have been reported, particularly in youngest children. The epidemiological and molecular characteristics of HPeV infections in children <6 months hospitalized with symptoms of sepsis-like illness were investigated.

Materials/methods: From January 1st, 2015, to December 31st, 2018, biological samples (cerebrospinal fluid samples and/or blood samples) were collected from 115 patients <6 months (median age: 20 days; inter quartile range: 32 days) hospitalized with symptoms of sepsis-like illness at a university and research hospital in Milan (Northern Italy). After extraction, HPeV RNA was detected by real-time RT-PCR (target 5'UTR) and a portion of HPeV VP3/VP1 junction (nt. 2159–2458) was sequenced for typing and molecular characterization.

Results: Overall, 13% (15/115) of patients with symptoms of sepsis-like illness tested HPeV-positive. Cumulatively, 14/15 (93.3%) HPeV cases were children <3 months and 10/15 (66.7%) children <1 month. 9/15 (60%) HPeV-positive cases were identified during the summertime (June-August). 10/15 (66.7%) HPeV-positive samples were molecularly characterized and all resulted HPeV type 3.

Conclusions: In this study, HPeV infection was identified in 13% of children <6 months with symptoms of sepsis-like illness. Almost all HPeV infections were identified in children <3 months during the summertime; all HPeV molecularly characterized were HPeV type 3 that is considered an emerging pathogen. Including HPeV molecular detection in routine diagnostic tests would allow estimating the burden of HPeV infection and improving clinical management of young patients.

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Background: The gold standard for pathogen detection in blood is the inoculation of blood culture (BC) bottles and subsequent identification of microbes using mass spectrometry (MS). Rapid identification of the causative pathogen, and possible inherent antibiotic resistances, is crucial for appropriate treatment of severe infections.

Rapid pathogen identification is hampered as: (1) certain bacterial species proliferate very slowly under BC conditions (e.g. Bacteroides spp., Propionibacterium acnes); (2) in mixed infections, faster proliferating species overgrow slower ones, which might then be missed; (3) treatment with antibiotics prior to blood draw prolongs/inhibits bacterial growth; (4) antibiotic resistances are determined by (time-consuming) plating.

This work compares pathogen identification from positive BC by state-of-the-art MS and Cube Dx' molecular test: LINA compact sequencing, which uses a diluted sample of BC directly in a PCR reaction. After the PCR pathogens are identified using Cube Dx' compact sequencing, covering 101 targets (bacterial-, resistance- and fungal genes).

Materials/methods: In total, 277 blinded BC samples (178 positive, 99 negative) were analysed at Unilabs by conventional culture and MS in parallel to LINA compact sequencing, respectively.

Results: Among the positive samples both methods identified identical bacterial species/genus in 166/178 cases (93%). Seventeen samples (~6%) yielded discordant results. In 3 cases compact sequencing did not report a bacterial species. Interestingly, in 4 positive samples, compact sequencing yielded a result whereas MS did not, and in 9 cases more than one species was detected – indicating that molecular diagnostics reveals mixed infections, even if one species might be predominant in culture. As an example, 3 samples contained bacteria of the Acinetobacter baumannii complex and Escherichia coli according to compact sequencing, where MS only detected E.coli.

Conclusions: Results for positive BC samples with LINA compact sequencing were obtained within 3 hours. LINA detected almost all positive blood cultures concordantly with current established methods resulting in a sensitivity of 98%. In addition, several mixed infections and slow growing bacteria were identified which were missed by MS, including Acinetobacter species which are highly relevant carriers of antibiotic resistance genes, resulting in a specificity of 88%.

<table>
<thead>
<tr>
<th>Culture</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>positive</td>
<td>166</td>
<td>13</td>
</tr>
<tr>
<td>negative</td>
<td>4</td>
<td>94</td>
</tr>
</tbody>
</table>

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Healthy carriage of colistin-, ESC- and carbapenem-resistant Enterobacterales in workers in Lebanese pastries

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Background: In Lebanon, resistance to Extended-Spectrum Cephalosporins (ESC) and carbapenems in Enterobacterales have been reported in humans in the community, but not mcr-1-mediated colistin-resistance. Those resistances have also been reported in animals, the environment or along the food chain in this country.

Materials/methods: A longitudinal study was performed on 84 healthy adults working in three major pastries in North-Lebanon. All workers were sampled twice at a 6 months’ interval (t0 and t6). Resistant Enterobacterales were isolated on media supplemented with ceftazidime, ertapenem, and colistin, and identified by MALDI-TOF. Antibiotic susceptibility was determined by disc diffusion. Resistance genes were characterized using PCR and sequencing. Characterization of the bacterial clones (PFGE, phylogroups) and plasmids (PBRT, S1-PFGE and Southern hybridization) is ongoing. Selected isolates will be subjected to NGS.

Results: 32 workers (38.1%) and 26 (37.1%), from the first and second sampling, respectively, were susceptible to colistin, ESC and carbapenem. ESBLs were detected in 26 workers (30.9%) and 39 (55.7%) from the first and second sampling, respectively. The carbapenemase OXA-48 was identified in 3 workers (3.6%) from the first sampling only. Finally, the mcr-1 gene was detected in 5 and 1 E. coli from workers from the first and second sampling, respectively. Continuous ESC-R carriage was observed in 31 workers even though the same resistant Enterobacterales was very rarely found over the two samplings, suggesting a transient acquisition/loss dynamic. Molecular characterization of the collected bacteria is ongoing.

Conclusions: We report the first longitudinal study on ESBL/AmpC-, carbapenemase- and mcr-1-producing Enterobacterales carriage in the community in Lebanon. A persistent and high proportion of workers carrying ESC-resistant Enterobacterales (30.9% at t0 and 55.7% at t6) was highlighted but the individual carriage was transient. We also showed incidental carbapenemase producers and the emergence of mcr-1-positive colistin in the community. Cross-transfers of resistant Enterobacterales within pastries, including to foodstuff, is plausible. This highlights the peremptory necessity to reevaluate effective antimicrobial stewardship, enhance national surveillance systems and promote public awareness programs in order to limit the spread of AMR in Lebanon in a One Health perspective.

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Abstract 6925

**ETEST Imipenem-relebactam for antimicrobial susceptibility testing of Enterobacteriaceae and Pseudomonas aeruginosa: performance results from a multi-centre study**

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**Background:** Imipenem/Relebactam (IPR), RECARBRIO brand name, is a combination of imipenem, a penem antibacterial, cilastatin, a renal dehydropeptidase inhibitor, and relebactam, a beta-lactamase inhibitor, indicated in patients 18 years of age and older with complicated urinary tract infections including pyelonephritis (cITU) or with complicated intra-abdominal infections (cIAI) caused by susceptible gram-negative bacteria. This study evaluated the performance of ETEST® IPR, a new gradient diffusion strip (FDA cleared but not yet CE marked) for determining antimicrobial susceptibility of Enterobacteriaceae and Pseudomonas aeruginosa as compared to CLSI M07 broth microdilution reference method (BMD).

**Materials/methods:** A population of 652 isolates including 477 Enterobacteriaceae (30 Citrobacter freundii, 103 Enterobacter cloacae/Enterobacter cloacae complex, 165 Escherichia coli, 30 Klebsiella aerogenes, 32 Klebsiella oxytoca and 117 Klebsiella pneumoniae) and 175 Pseudomonas aeruginosa were tested at 4 clinical trial sites, including one internal laboratory using ETEST® IPR and BMD. Results were analyzed in terms of essential (EA), category (CA) agreements, minor (mE), major (ME) and very major (VME) error rates using FDA breakpoints (Enterobacteriaceae: ≤1/4 (S), 2/4 (I) and ≥4/4 (R) µg/mL, Pseudomonas aeruginosa: ≤2/4 (S), 4/4 (I) and ≥8/4 (R) µg/mL).

**Results:** Results are summarized in Table 1. ETEST® IPR performance for Pseudomonas aeruginosa met FDA acceptance criteria for EA (≥90%), CA (≥90%), ME (≤3%) and VME (≤2%). For Enterobacteriaceae ETEST® IPR performances met FDA criteria for EA, CA and ME but not for VME with a rate of 2.3% (1/44). That percentage was only due to one Very Major Error with an E. coli isolate. Repeat testing of both ETEST® Imipenem/Relebactam and the reference method with this isolate showed acceptable category agreement between the two tests.

**Conclusions:** When compared to the reference method, results of this multicenter trial support the accuracy of ETEST® IPR for determining the MIC of Enterobacteriaceae and Pseudomonas aeruginosa in a clinical setting. As such, the new ETEST® IPR can be considered as substantially equivalent to BMD.

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>EA</th>
<th>CA</th>
<th>mE</th>
<th>ME</th>
<th>VME</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterobacteriaceae</td>
<td>95.8%</td>
<td>98.1%</td>
<td>1.7%</td>
<td>0.0%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>96.0%</td>
<td>96.0%</td>
<td>2.3%</td>
<td>2.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

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Abstract 6926

Towards an enhanced diagnosis of relapsing fevers by the use of dried blood spots

Emilie Talagrand-Reboul*, Pierre Boyer1, Antoine Grillon1, Cathy Bartel1, Lisa Baldinger2, Marine Engel2, Laurence Zilliox2, Benoît Jaulhac1,2, Nathalie Boulanger1,2

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Background: Relapsing fever borreliosis (RFB) are worldwide distributed vector-borne diseases. The biological diagnosis of RFB is hardly performed in some remote areas, mainly because the sampling and analysis of venous blood by microscopic examination or PCR require laboratory facilities. In the aim to enhance this diagnosis, we have evaluated the methodology of Dried blood spots (DBS).

Materials/methods: Firstly, one Balb/C mouse was infected with Borrelia duttonii CR2a by intraperitoneal injection and the spirochaetemia was followed by microscopic examination of Giemsa-stained blood smears. In parallel, capillary blood spots were directly made on Whatman MM3 paper. Blood was eluted and then submitted to a bacterial DNA extraction and, a pan-relapsing fever Borrelia real-time PCR was performed. Secondly, we applied the same method to human blood samples kept at -80°C, formerly tested negative (n=56) or positive for B. crocidurae (n=6) or B. hispanica (n=1). The DNA extractions were performed after 24h drying at +20°C-+30°C and 1-3 days later.

Results: In the mouse, we have observed a spirochaetemial peak 3-6 days post-infection, followed by a reversion of the bacterial load, and then a relapse at 9-10 days that was cleared on day 13. RF Borrelia DNA was successfully amplified from the DBS extracts during the course of mice bacteremia (2-6.10^7 spirochaetes/mL). For human blood samples, a total agreement was obtained between the DBS extraction and the whole blood direct extraction methods. The DBS-qPCR method reached a higher sensitivity (100%; CI95%=59-100%) than blood smear examination (50%; CI95%=18-88%). The results of qPCR were not different from 1-day or 14-day DBS. In all tested conditions, there was not inhibitory effect and no contamination between samples.

Conclusions: This study is the proof of concept for the diagnosis of RFB by the use of DBS. We showed that Borrelia DNA contained in the DBS retained its integrity after storage 14 days at +25°C, allowing a delay for transport to a laboratory. Given the simplicity of the preanalytical phase well adapted to tropical medicine, the DBS methodology may enhance the biological diagnosis of RFB, and, furthermore, may be associated with the malaria molecular diagnosis from DBS samples in some areas.

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Abstract 6927

**Increasing rates of antimicrobial resistance in *Escherichia coli* and *Klebsiella sp.* bacteraemia are not associated with a proportional increase in mortality**

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**Background:** Increasing antimicrobial resistance rates may lead to increased mortality as infections become harder to treat. At our large centre in London we reviewed all *Escherichia coli* and *Klebsiella sp.* bacteraemias over 18 years and examined the relationship of antimicrobial resistance to 30 day and 90 day all-cause mortality.

**Materials/methods:** Records of *E coli* and *Klebsiella sp.* bacteraemias were extracted from the laboratory database for the years 2001 to 2018. Records were de-duplicated to determine the number of individual bacteraemic episodes. A new positive blood culture more than 28 days since the last was classified as a new episode. Antimicrobial susceptibility results were analysed and isolates were classified as wild type (WT), resistant (R) or multiply-resistant (MDR).

**Results:** Over 18 years there were 3519 episodes of *E coli* bacteraemia of which 1106 (31%) were WT, 1647 (47%) were R and 766 (22%) were MDR. There were 1069 episodes of *Klebsiella sp.* bacteraemia of which 755 (71%) were WT, 68 (6%) were R and 246 (23%) were MDR. Annual rates of resistance increased for both organisms with a stronger trend in *E coli* compared to *Klebsiella sp.* *E.coli* bacteraemic episodes had a mean 30 day mortality of 1.7% compared to 2.1% for *Klebsiella sp.* and were 24% and 31% for 90 day mortality respectively. There was a small trend (approx. 5%) over the study period for reduction in 30 and 90 day mortality rates for *E coli* episodes whereas with *Klebsiella sp* there was a small trend for increasing mortality rates (approx. 2% for 30 day and 4% for 90 days).

**Conclusions:** Despite increasing rates of resistance in *E coli* and *Klebsiella sp.* bacteraemias there was no evidence of a proportional increase in mortality over an 18 year period and in fact mortality from *E coli* fell. This was surprising. There are many possible explanations including changing patient populations or changes in pathogenicity of the circulating organisms. At the same time, there have been advances in rapid diagnostic techniques, improved recognition and treatment of sepsis and following the introduction antimicrobial stewardship programmes better prophylactic, empirical and result-led antimicrobial usage.

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Abstracts 2020

Abstract 6929

Toscana virus: clinical and biological studies based on 864 cases

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Background: Toscana virus is an arbovirus transmitted by sand flies within the Mediterranean area where it can cause febrile illness and neuroinvasive infections during the seasonal circulation period of the vector. Although it is an important cause of meningitis and encephalitis, it remains neglected.

Materials/methods: We searched global web-based resources [PubMed, Google Scholar, Web of Science] to collect all the Toscana virus case reports have been published since now. After gathering all the data, irrelevant publications were discarded. A total of 72 publications including 864 case reports of Toscana virus infection were collected. All the collected data were put in order based on country, year, sex, clinical signs, clinical presentation, biological signs, onset of symptoms. Clinical signs have been grouped in categories for further analysis. Additionally, imported case reports were categorized and analyzed separately.

Results: Sex ratio is 1.85. Since 1985, 864 human cases [834 autochthonous and 30 imported] were reported from inhabitants of Mediterranean countries and travelers who visited the region. More than 80% of the patients show manifestations of fever, headache, neck rigidity, Kernig's sign and nausea. Ocular, gastro-intestinal and cutaneous manifestations were reported between 40-80% of the cases. The neurological and muscular manifestations were identified in 27.6% and 22.6% of the patients, respectively. Manifestations as testicular pain/tenderness, hepatomegaly, incontinence, orthostatic hypotension represent less than 1% of the cases. There is one lethal case recorded after Toscana virus infection, who is a German tourist returning from a 3 week trip to Tuscany, up to now.

Conclusions: Toscana virus is currently the most important phlebovirus for public health which is transmitted by sand flies. Since Toscana virus is a neglected virus most of the cases caused by Toscana virus remain unidentified. Defining the most common manifestations and the characterization of Toscana virus can help physician and engage them to prescribe laboratory documentation when facing unexplained febrile illness in patient living in or returning from Toscana virus endemic regions. The population in Mediterranean area are at risk of Toscana virus infection which requires the increase of the awareness and the knowledge.

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Abstract 6930

**Carbapenem-resistant *Acinetobacter baumannii* fitness in murine model is associated with 14-day mortality in humans**

**Abstract third-party references:** European Commission FP7 AIDA project [preserving old antibiotics for the future: assessment of clinical efficacy by a pharmacokinetic / pharmacodynamic approach to optimize effectiveness and reduce resistance for off-patent antibiotics], Grant Health-F3-2011-278348

**Background:** Mortality among patients with carbapenem-resistant *A. baumannii* (CRAB) infections is high. In the AIDA trial, 14-day mortality among patients with severe infections caused by CRAB was 37%. We examined whether *in vivo* bacterial fitness in a murine thigh infection model is associated with outcomes in patients with CRAB infections.

**Materials/methods:** Bacterial isolates were collected from patients in the AIDA trial with hospital-acquired pneumonia (HAP), bloodstream infection (BSI), or urinary tract infection caused by CRAB. We tested *in vivo* fitness of each CRAB strain using a neutropenic mouse thigh infection model. Fitness was defined based on the CFU count 24 hours after injection of an inoculum of 10^5 CFU per mouse, and was modeled as a binary variable [below vs. at or above the median]. The primary outcome was 14-day clinical failure, defined as failure to meet all criteria: alive; hemodynamically stable; improved or stable SOFA score; improved or stable oxygenation; and microbiological cure of BSI. The secondary outcome was 14-day all-cause mortality. We compared bacterial fitness and demographic and clinical variables between patients with and without clinical failure. We used backwards selection to build a multivariable logistic regression model of the association between fitness and clinical failure. We repeated this process for the 14-day mortality outcome.

**Results:** The sample included 266 patients with infection caused by CRAB. Bacterial fitness ranged from 5.23-10.08 logCFU/gram (median 8.78 logCFU/gram). High bacterial fitness was not significantly associated with the study primary outcome of clinical failure in bivariate or multivariable analysis that controlled for age, appropriate empiric therapy, and diabetes [OR 1.26, 95% CI: 0.66-2.39, p=0.48]. High fitness had a nearly significant association with 14-day mortality [OR 1.56, 95% CI: 0.95-2.57, p=0.08] in bivariate analysis, and was significantly associated with 14-day mortality when adjusting for age and Charlson score in the multivariable model [OR 1.82, 95% CI 1.07-3.09, p=0.03].

**Conclusions:** This study provides evidence that the CRAB fitness as measured in a murine infection model is an important determinant of CRAB infection 14-day mortality. Strain fitness may be an important factor to measure and control for in CRAB clinical trials.

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Abstract 6932

**Xpert MTB/RIF Ultra: multi-centre evaluation of result “TRACE” in tuberculosis diagnosis**

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**Background:** Xpert® MTB/RIF Ultra (Cepheid), an automated PCR for identification of **Mycobacterium tuberculosis** complex (Mtbc) and Rifampin (RIF) resistance [detection limit 11.8 UFC/mL], has higher sensitivity than Xpert® MTB/RIF [131 UFC/mL]. The improved sensitivity is also due to result “TRACE”, which corresponds to a lower detectable bacterial load.

According to the interpretation algorithm of GLI – Global Laboratory Initiative (WHO), the result “TRACE” should be considered as Positive in non-respiratory samples.

**Aim of this multicentric study was the correlation between result “TRACE” and diagnosis of Tuberculosis.**

**Materials/methods:** We analyzed 130 biological samples (92 respiratory, 38 non-respiratory) processed in 8 different Microbiology laboratories, which reported “TRACE” with Xpert® MTB/RIF Ultra.

For respiratory samples, explicative note “Mtbc genome detected at inferior limit of Sensitivity. New sample is required” was enclosed in the medical report.

For each biological sample with result “TRACE”, we recorded culture positivity for Mtbc or possible positivity for Mtbc in other samples, or anamnestic data of ongoing Tuberculosis therapy.

**Results:** Among 130 samples with result “TRACE”, 50 (38.5%) had positive culture for Mtbc (36 respiratory, 14 non-respiratory).

17 (13.1%) samples with negative culture belonged to patients with positive cultures for Mtbc in other clinical samples (7 respiratory, 10 non-respiratory) within three months.

31 (23.8%) samples with negative cultures belonged to patients with ongoing therapy for Tuberculosis diagnosis (21 respiratory, 10 non-respiratory).

32 (24.6%) samples with result TRACE had no microbiological or clinical confirmation of Tuberculosis (28 respiratory, 4 non-respiratory) for absent repetition of test on other samples.

Overall, result TRACE with Xpert MTB/RIF Ultra test for 98 (75.4%) of 130 examined samples is coherent with Tuberculosis diagnosis, while for 24.6% the diagnosis wasn’t confirmed or excluded for absence of second sample, as required by interpretative algorithm, and/or for lack of clinical information.

Regarding the different specimens, the concordance with Tuberculosis diagnosis was 69.5% for respiratory samples (64/92) and higher for non-respiratory samples: 89.5% (34/38).

**Conclusions:** Data show clinical relevance and reliability of reply “TRACE” in Tuberculosis diagnosis in respiratory samples and even more in non-respiratory samples, corroborating the indication of WHO-GLI to report as POSITIVE a result “TRACE” in non-respiratory samples.

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Evaluation of the EUCAST rapid antimicrobial susceptibility testing directly from positive blood cultures for *Escherichia coli* and *Staphylococcus aureus* in a routine laboratory

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**Background:** With increasing antibiotic resistance it is important with rapid and correct antimicrobial susceptibility testing results. The EUCAST method for rapid antimicrobial susceptibility testing (RAST) directly from positive blood cultures is now available on the EUCAST website. The aim of this study was to evaluate the performance of RAST for *Escherichia coli* and *Staphylococcus aureus* in our routine clinical laboratory.

**Materials/methods:** Clinical blood culture bottles inoculated with blood or other sterile body fluid between 1 August 2018 and 31 July 2019 were included in the study. Disk diffusion according to EUCAST RAST methodology was performed by routine staff on consecutive positive blood culture bottles [BACTEC Plus bottles, BD] with monocultures of *E. coli* (n=335) or *S. aureus* (n=196). Inhibition zones were read at one or several of the possible incubation times (4, 6 and 8h). Initially, inhibition zones were primarily read after 6h incubation but after 28 May 2019 the 4h reading was prioritised. EUCAST standard disk diffusion, interpreted according to EUCAST Breakpoint Tables version 9.0 (2019), was performed on all isolates and used as reference. Only one isolate per patient and sampling time was included in the analysis.

**Results:** More than 95% of all zones could be read after 4h incubation for both species (Table). Some isolates of *E. coli* and *S. aureus* were read at more than one reading time (8% and 7% respectively). ESBL-producing isolates (n=23) [resistant to cefotaxime and/or ceftazidime with standard methodology] were correctly categorised as such. All MRSA isolates (n=6) were either categorised as resistant (5/6) to cefoxitin or in the Area of Technical Uncertainty, ATU (1/6). The total number of errors was below 1.5% and there were no false susceptible results.

**Conclusions:** The EUCAST RAST method in a routine laboratory resulted in AST results after only 4h incubation for most of *E. coli* and *S. aureus* isolates. Error rates were low and there were no false susceptible results. Most of the isolates categorised in the ATU for *E. coli* were due to piperacillin-tazobactam and tobramycin and for *S. aureus* clindamycin (75% and 79% respectively).

**Table.** Theoretical and actual number of tests, the proportion of tests which could be read and interpreted after 4, 6 and 8 h, and the categorical errors with RAST at each reading time for *E. coli* and *S. aureus*.

For each table, data are presented as (letters relating to footnotes):

A. The theoretical number of tests = Total number of possible isolate-agent combinations.

B. Number of completed tests = Number of completed test after excluding missing data (e.g. disk dropped).

C. Readable zones = Number of tests with readable inhibition zones.

<table>
<thead>
<tr>
<th>Species</th>
<th>Antimicrobial agents</th>
<th>E. coli</th>
<th>S. aureus</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>E. coli</td>
<td>S. aureus</td>
<td></td>
</tr>
<tr>
<td>Incubation time</td>
<td>Piperacillin-tazobactam, cefotaxime, ceftazidime, meropenem, ciprofloxacin, gentamicin and tobramycin</td>
<td>Cefoxitin, norfloxacin, gentamicin, clindamycin</td>
<td></td>
</tr>
<tr>
<td>4h</td>
<td>6h</td>
<td>8h</td>
<td>4h</td>
</tr>
<tr>
<td>Number of isolates tested</td>
<td>138</td>
<td>223</td>
<td>4</td>
</tr>
<tr>
<td>Theoretical number of tests</td>
<td>959</td>
<td>1554</td>
<td>28</td>
</tr>
<tr>
<td>Completed tests</td>
<td>954</td>
<td>1552</td>
<td>28</td>
</tr>
<tr>
<td>Readable zones (% of completed tests)</td>
<td>935 (98)</td>
<td>1549 (100)</td>
<td>21 (75)</td>
</tr>
</tbody>
</table>

| Results calculated on readable zones (%) | |
| Not interpreted to S or R (ATU) | 17 | 11 | 10 | 8 | 10 | 0 |
| Interpreted to S | 79 | 83 | 90 | 91 | 87 | 100 |
| Interpreted to R | 4 | 6 | 0 | 1 | 4 | 0 |
| Errors | mE | 1.3 | 0.9 | 0 | 0 | 0 |
| ME | 0.1 | 0.5 | 0 | 0 | 0.8 | 0 |
| VME | 0 | 0 | 0 | 0 | 0 | 0 |
| Total errors | 1.4 | 1.4 | 0 | 0 | 0.8 | 0 |

mE (minor Error) = Categorised as susceptible (S) or resistant (R) with RAST when susceptible with increased exposure (I) with standard method.

ME (Major Error) = False resistant.

VME (Very Major Error) = False susceptible.

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Abstract 6936

**Comparison of Illumina and nanopore sequencing methodologies for whole genome sequencing of influenza A virus from clinical isolates**

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**Background:** Influenza A virus remains a major global threat; causing significant patient mortality and morbidity as well as costly closure of hospital wards primarily due to seasonal influenza infections. Point-of-care tests rapidly identify viral subtype but have limited utility in tracing virus transmission or drug resistance in a healthcare setting. Minimising the time from sampling and reporting potential linkage between clinical isolates can aid clinical decisions; can inform both local and public health measures as well as reduce preventable nosocomial infections. Here, we compare whole genome sequencing methodologies of influenza A virus in terms of cost, speed and sensitivity. Illumina and Oxford Nanopore Technologies (ONT) sequencing platforms were compared for both H1N1 and H3N2 influenza A viruses.

**Materials/methods:** Full-length influenza A virus amplification was achieved using a two reaction RT-PCR for 24 known positive clinical isolates covering a range of viral loads (11 H1N1 and 13 H3N2). For Illumina sequencing, the Nextera® XT DNA library preparation kit with 1ng DNA input per sample was used and the generated library run on a MiSeq (V2 500 cycles reagent kit) taking approximately 45 hours. Sequence analysis was performed using an in-house de novo assembly pipeline. For ONT sequencing, 1µg DNA input per sample was used and the library prepared using the Ligation Sequencing Kit and associated protocols for native barcoding. For sequencing, a MinION flow cell was used and run for a total of three hours, base calling using MinKnow or guppy (ONT) with an in-house pipeline used to perform reference-based genome assembly.

**Results:** Across all samples concordance between MiSeq and MinION sequenced genomes was exceptionally good, generating consensus genomes with almost complete sequence and read-depth agreement. Nine of the 11 H1N1 pairs of genomes were identical, remaining samples differing by one and two nucleotides respectively. For the H3N2 samples the results were similar: five were identical and eight differed by less than five nucleotides.

**Conclusions:** Illumina and ONT sequencing methodologies performed equally well for influenza A whole genome sequencing. Therefore, time to results and scalability should be the influencing factors when determining the most applicable sequencing platform.

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Abstracts 2020

Abstract 6938

**Oral Chagas disease outbreak in the Brazilian Amazon: first report of an outbreak related to patauà fruit**

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**Background:** Acute Chagas disease (ACD) has a distinct epidemiological profile in the Amazon Region, with cases and outbreaks related to the ingestion of *Trypanosoma cruzi* contaminated food. For most reported outbreaks, epidemiologic investigations point to nonvectored transmission, implicating juices from local fruits contaminated with triatomine faeces or secretions from infected mammals.

**Materials/methods:** Descriptive study and outbreak investigation of the first ACD outbreak related to the local fruit patauà (*Oenocarpus bataua*) in a rural area of the Brazilian Amazon in September 2019. Clinical evaluation, epidemiological, entomological and microbiological survey were performed. Relative Risk and Attack Rate were calculated. Confirmed, suspicious and exposed cases were defined according to established criteria.

**Results:** During the study period we detected 41 exposed people, 16 (39%) were diagnosed as ACD confirmed cases. All of them were diagnosed by direct visualization of parasite in thick drop. 8 of them were women (50%), the mean age was 36,8 ± 16,1 years. The Attack Rate in individuals exposed to patauà was 50% (25% in non exposed), lethality 0% (0/16), a calculated Relative Risk (RR) of 1.9 and a mean incubation time of 11.5 days (range 7 – 15 days). 16/16 patients (100%) had fever, 12/16 (75%) myalgias, 8/16 (50%) rash, 7/16 (38%) abdominal pain, 6/16 (38%) headache and 2/16 (13%) diarrhea, none presented acute miocardiopathy. All confirmed patients referred consumption of patauà juice prepared with inadequate hygienic measures. Serologies, PCR and direct parasitological study with thick drop was carried out to all individuals who had ingested patauà juice (n=41). 9 specimens of *Rhodnius robustus* and *Rhodnius pictipes* were captured during entomological survey in patauà palm trees, no domiciliary infestation was detected.

**Conclusions:**

- Oral transmission of *T. cruzi* involving the patauà fruit is the most likely hypothesis for acute chagas disease in these patients.

- To date, this is the first report of an acute Chagas disease outbreak associated with consumption of patauà.

- This study highlights the increasing incidence of oral ACD in the Amazon Region and the need to improve prevention and education campaigns at rural areas of this region focusing on hygienic and better harvesting methods.

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Abstract 6941

**Diagnostic evaluation of the new FluoroType MRSAfast assay for the detection of MRSA from clinical swab specimens**

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**Background:** Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are caused by a type of bacteria strains resistant to at least all beta-lactam antibiotics and are thus difficult to treat. By establishing screening measures for high-risk patients when admitted to hospital, MRSA carriers can be identified at an early stage. The new FluoroType MRSAfast VER 1.0 is a qualitative *in vitro* PCR test for fast detection of MRSA strains directly from clinical specimens including the methicillin resistance-mediating genes mecA and mecC.

**Materials/methods:** DNA extraction for PCR was performed with the SpheroLyse-Kit. The eluted DNAs were analyzed with the new FluoroType MRSAfast VER 1.0 on the FluoroCycler 12 and FluoroCycler XT and the FluoroType MRSA Ver 2.0 (Hain Lifescience). The swab was used for inoculation of BBL Trypticase soy broth bouillon (Becton Dickinson). The trypticase soy broth was incubated for 24 h and then used to inoculate selective culture and non-selective culture (CNA agar). Species identification by MALDI-TOF (MALDI Biotyper, Bruker Daltonics) was used to confirm appropriate selection of colonies prior to culture differentiation. Culture differentiation by GenoType MRSA VER 3.0 (Hain Lifescience) was performed from all positive cultures on selective and/or non-selective agar to confirm the presence or absence of MRSA and to allow the differentiation of mecA- or mecC-strains. MRSA history and additional culture results were also considered in results evaluation.

**Results:** 512 swabs were analysed. The inhibition rate of the MRSAfast assay was at least 0%. The sensitivity / specificity / positive predictive value / negative predictive value were 96.3% / 97.6% / 99.6% / 99.6% on the FluoroCycler 12 and 94.5% / 96.5% / 76.5% / 99.3% on the FluoroCycler XT compared to combined MRSA results.

**Conclusions:** The specifications resulting from the data in our FluoroType MRSAfast study are in line with the expectations of PCR-based tests for the screening of MRSA at risk patients to derive timely hygiene-relevant measures. The turnaround time is significantly reduced (approx. 1h for FluoroType MRSAfast PCR vs. 2h for FluoroType MRSA 2.0 PCR). This represents a clear advantage over the previous FluoroType MRSA Ver. 2.0 results in consistent performance in the test execution.

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Abstract 6942

**Gut microbiome characterisation in irritable bowel syndrome patients following faecal microbiota transplant: a case report study**

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**Background:** Irritable bowel syndrome (IBS) is a multifactorial digestive disorder affecting up to 11% of the adult population. Recent studies suggested the role of bacterial, viral and parasitic infections in triggering IBS, therefore targeting microbiota represents a promising approach in IBS patients. In this study we present the case of two patients with IBS that underwent fecal microbiota transplant (FMT): sequential studies of gut microbiome pre and post-transplant are performed.

**Materials/methods:** Microbial DNA was extracted from stool samples of seven healthy donors and two IBS patients eligible for FMT. NGS 16S metagenomics (pair-end amplicon sequencing) protocol was performed by using MiSeq platform (Illumina) and MiSeq reagent kit v.3 (600 cycles). Following FMT, longitudinal samples from IBS patients were collected (day 3, 10 and 28 post-transplant) and analyzed in the same manner. The bacterial microbiome diversity was primarily characterized at Family, Genus and Species levels using BaseSpace app from Illumina dedicated software. An extensive analysis was further performed by using QIIME and mothur tools.

**Results:** The donor for FMT was selected for high diversity of beneficial bacteria families. Both IBS patients had a good clinical outcome post- FMT, with slight differences. By analyzing the microbiome longitudinal data in IBS patients we observed that bacterial families considered beneficial (*Blautia, Faecalibacterium, Roseburia, Lahnospira*) were transmitted from the donor to the recipient, replacing other bacteria that are frequently associated with IBS (*Ruminococcus, Enterobacter, Pseudomonas*). For some bacteria families the effect was stable while in other cases it was transient (some disappeared at day 28 post-FMT). In one IBS patient we observed a few bacterial families not seen in donor microbiota or pre-FMT sample suggesting the role of other factors in shaping the gut microbiome.

**Conclusions:** Gut microbiome characterization by NGS coupled with bioinformatics analysis represents an important tool in personalized medicine for IBS patients useful by selecting the adequate FMT donors and monitoring the post-transplant effects. Clinical improvement was associated with stable transfer of bacterial populations.

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Utility of early kinetics of TTV DNA in stool for the prediction of intestinal graft versus host disease in the allogeneic haematopoietic stem cell transplantation setting

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Background: Intestinal acute Graft versus Host Disease (aIGvHD), is a frequent immune-related complication after allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT). Torque Tenovirus (TTV) DNA in plasma behaves as a surrogate marker for immune reconstitution in transplant recipients. Here, we assessed the potential value of TTV DNA quantitation in stool for predicting of aIGvHD in this setting.

Materials/methods: Retrospective, observational study including 86 undergoing allo-HSCT at two Hospitals in Valencia between July 2016 and July 2019. TTV DNA was quantified in plasma and stool specimens using a TaqMan real-time PCR targeting conserved UTR sequences. A standard curve was generated by spiking a TTV plasmid in stool samples at concentrations ranging from 10^6 copies to 10^3 copies/ml.

Results: Stool specimens obtained after transplant (median, 14 days; range, 6-23 days) were available from all patients. Baseline specimens were available from 71 patients. Fifteen patients had paired plasma samples. 31 (36%) patients had developed aIGvHD [III-IV] at a median of 43 days (15 to 178) after transplantation. TTV was undetectable in 24 (33.80%) and 36 (41.90%) of pre and post HSCT in stool samples, respectively, while only in 1 (6.66%) and 2 (1.33%) of plasma samples. No differences were found regarding baseline TTV levels between patients who either went on to develop aIGvHD or not [median 3.17 Log_{10} copies/ml [1 to 5.88] vs 2.57 [1 to 4.44], P=0.18]. TTV loads after allo-HSCT were lower in patients with aIGvHD [median <1 to 5.88] vs 2.49 [1 to 6.82], P=0.11. As for TTV kinetics, the majority of patients with aIGvHD [80.00%] had declining levels of TTV in stool [median of differences between post and pre HSCT TTV DNA of 3.93 Log_{10} [2.04 to 7.42], P=0.03] whereas most patients had decreasing TTV loads in plasma, regardless of the occurrence of aIGvHD. A correlation was found between TTV DNA load in plasma and stool samples obtained prior to but not after HSCT [\rho= 0.87, P<0.01].

Conclusions: Early kinetics of TTV DNA in stool samples may help to anticipate the occurrence of aIGvHD in Allo-HSCT patients.

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Invasive CNS aspergillosis in non-neutropenic patients: a review of nine cases from North India

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Background: Invasive aspergillosis involving the central nervous system (CNS) is a rare and difficult to manage entity with most of the available literature describing it in patients with malignancies or patients undergoing bone marrow transplant. We describe a series of nine patients with CNS aspergillosis from a tertiary care teaching institute in North India.

Materials/methods: All patients who had clinical and radiological features consistent with fungal CNS infection and showed the presence of septate hyphae on histopathology/microscopy and were either culture positive for Aspergillus spp. or had serum galactomannan positivity were diagnosed as CNS Aspergillosis. Clinical features, risk factors, diagnostic modalities, treatment details and outcome at last follow-up were recorded of all patients diagnosed with CNS aspergillosis.

Results: A total of nine patients with an average age of 38+/-12 years were diagnosed with CNS aspergillosis between July 2016 and June 2019. Four patients were known case of Type 2 Diabetes mellitus (DM), two patients were diagnosed with chronic granulomatous disease (CGD) on primary immunodeficiency work-up and one patient had a recent history of head injury. No risk factors were identified in three patients (Table 1). The median duration of symptoms at presentation at our hospital was six months (IQR-2-9 months). Four patients were diagnosed as sino-cerebral aspergillosis, two patients were diagnosed with skull-based osteomyelitis due to Aspergillus spp. and the rest of the three patients had isolated brain abscess. Culture was positive in three patients and serum galactomannan was positive in six patients. Extensive surgical debridement was done in three patients. All patients were treated with voriconazole therapy. All but one patient survived at the last follow-up. The average duration of last-follow up was 14 months (IQR-8-21.5 months). Two patients had complete resolution and voriconazole was stopped at the last follow-up and the rest of the patients were continued on voriconazole. Of the six patients who were continued on voriconazole, all but one had >50% radiological resolution on follow-up imaging.

Conclusions: Invasive aspergillosis should be suspected even in non-neutropenic patients with DM or CGD presenting with CNS manifestations.

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German multi-centre study on standardised in vitro testing of ceftazidime-avibactam against extensively drug-resistant clinical Pseudomonas aeruginosa isolates from 2017-2019

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Background: Multidrug resistance is an emerging healthcare issue, especially concerning gram-negative bacteria such as P. aeruginosa. Activity of ceftazidime-avibactam has been studied on P. aeruginosa with derepressed AmpC, ESBL- and metallo-β-lactamase-producing and efflux-based resistance mechanism. There is a lack of commercially available reliable standardised testing methods for ceftazidime-avibactam and reliability of gradient diffusion or disk diffusion test remains questionable.

Materials/methods: Minimum inhibitory concentrations (MIC) of 186 clinical extensively-drug-resistant (XDR, resistance to all but 2 sentinel agents of antimicrobial agent classes) P. aeruginosa isolates of three university hospitals in Germany from various sites of infection were determined according to EUCAST guidelines. MERLIN MICRONAUT-S microdilution test plates containing ceftazidime-avibactam (0.125/4-128/4 mg/L) and meropenem (0.0625-128 mg/L) were used. Test plates were provided by Pfizer Pharmaceuticals Inc.. Growth was assessed via photometric read-out using MICRONAUT6 software. P. aeruginosa ATCC strain 27853 was included as quality control in each run. In addition, Liofilchem® MIC Test Strip for ceftazidime-avibactam was conducted for comparison (173/186) and isolates were tested for presence of carbapenemase by PCR (130/186).

Results: Overall, for ceftazidime-avibactam MIC range was 0.25->128 mg/L, MIC90 was 32 mg/L and MIC50 was 8 mg/L. According to clinical EUCAST 9.0 breakpoints, 116 isolates were reported as susceptible and 70 isolates were reported as resistant in automated reading. Most, but not all VIM-positive (31/130) isolates showed elevated MICs (MIC range 0.25-64 mg/L, MIC90 32 mg/L, MIC50 16 mg/L) in vitro. MIC Test Strip for ceftazidime-avibactam generally showed higher MICs (MIC90 64 mg/L, MIC50 32 mg/L) with essential agreement of 58.38% (101/173) and categorical agreement of 70.52% (122/173).

Conclusions: Overall, 62.36% of clinical XDR-P. aeruginosa isolates were tested susceptible for ceftazidime-avibactam by semi-automated microdilution in vitro, though efficacy of ceftazidime-avibactam has shown to be variable with high inter-isolate variance. With semi-automated EUCAST microdilution via MERLIN MICRONAUT-S plates, testing is quick and standardised, yet delivers significantly differing results in comparison to gradient diffusion test. As Liofilchem® MIC test strips are reported to overestimate resistance for up to 20% of XDR-P. aeruginosa isolates, semi-automated microdilution may represent an alternative for MIC-determination of ceftazidime-avibactam for XDR-P. aeruginosa isolates in a clinical setting.

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Abstract 6946

Characterisation of *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* infections in Palestinian children older than 5 years of age

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**Background:** Worldwide, *M. pneumoniae* and *C. pneumoniae* are responsible for 3% to 43% of Community Acquired Pneumonia (CAP). *M. pneumoniae*; is the smallest self-replicating organism that belongs to a special class of bacteria called the “Mollificates” whereas *C. pneumoniae* is an intracellular bacterium that belongs to the family Chlamydiaceae. This study aimed at determining the epidemiology of *M. pneumoniae* and *C. pneumoniae* in Palestinian children. In addition, the types of antibiotics prescribed to the infected patients and macrolide resistance pattern of *M. pneumoniae* was also assessed.

**Materials/methods:** A retrospective study was conducted on 438 nasopharyngeal aspirates collected from hospitalized children older than 5 years of age between 2015-2018. All patients were hospitalized at Caritas Baby Hospital due to pneumonia. *M. pneumoniae* and *C. pneumoniae* detection relied on utilizing an in-house validated multiplex Real-Time Polymerase Chain Reaction (RT-PCR). All positive *M. pneumoniae* samples were screened for macrolides resistance by sequencing the 23S rRNA domain V at positions 2063, 2064 and 2617. Patient charts were reviewed to determine the type of antibiotic the patient received and comparisons were performed using the Chi-Squared test.

**Results:** Of the 438 NPA samples, 21 (4.8%) were positive for *M. pneumoniae*, while 6 (1.4%) were positive for *C. pneumoniae*. *M. pneumoniae* circulation was most prevalent in the spring season (P<0.001) mainly between the months of February and April, while *C. pneumoniae* had a sporadic months distribution. Overall, antibiotics were prescribed to 20 (74%) patients (P<0.001) of whom 12 (60%) received the macrolide azithromycin. In addition, 19 (70%) patients also received either a second or third generation cephalosporins. Sequence analysis of the *M. pneumoniae* 23S rRNA gene revealed that 3 (14%) patients’ isolates were mutated at position 2063 (A2063G) in domain V.

**Conclusions:** Similar to other parts of the World, *M. pneumoniae* and *C. pneumoniae* were prevalent in Palestinian children older than 5 years of age. Implementation of rapid detection techniques of *M. pneumoniae* and *C. pneumoniae* not only will help in proper prescription of macrolides, but will help in eliminating the usage of second or third generation cephalosporins used to manage patients respiratory infections.

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**Abstract 6951**

**In vitro activity of ceftaroline and ceftobiprole against Enterococcus faecalis recovered from infective endocarditis and/or bloodstream infections**

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**Background:** Enterococci are a major leading cause of infective endocarditis (IE) and a common cause of hospital-acquired bacteremia. Ceftaroline and ceftobiprole are two novel broad-spectrum cephalosporins with bactericidal activity against multidrug-resistant Gram-positive bacteria, including *Enterococcus faecalis*, and also against many Gram-negatives. However, there are not current clinical trials in which the use of these drugs has been investigated in the initial treatment of bacteremia or IE caused by *E. faecalis*.

The aim of this study was to evaluate the *in vitro* activity of ceftaroline and ceftobiprole against a collection of *E. faecalis* recovered from IE and bacteremia.

**Materials/methods:** All patients admitted to a tertiary hospital in Spain with the diagnosis of IE by *E. faecalis* between January 2015 and October 2018 were studied. The modified Duke criteria were applied for diagnosis. Also, we evaluated the patients with bacteremia by *E. faecalis* in a six-month period (March-December 2018). Bacterial isolates were recovered from blood and/or heart valve cultures which had been processed at the Clinical Microbiology Unit and identified by MALDI-TOF MS (Bruker Daltonik, Bremen, Germany) or by PCR amplification of the gene encoding 16S ribosomal RNA and subsequent sequencing. When bacterial growth was obtained, minimum inhibitory concentrations (MICs) of ceftaroline and ceftobiprole were determined by using E-test strips (Biomérieux, Marcy l’Étoile, France) and interpreted according to CLSI guidelines.

**Results:** 162 patients were diagnosed with IE during the study period. A total of 65 *E. faecalis* isolates (19 from IE and 46 from other source of bacteremia) were recovered and tested. Microbiological data, including MICs to ceftaroline and ceftobiprole are summarized in Figure 1.

**Conclusions:** Isolates recovered from IE and bacteremia confirm that ceftaroline and especially ceftobiprole have an excellent activity against *E. faecalis* (MIC₅₀ 0.75 and 0.5 µg/mL, respectively), despite the theoretical intrinsic resistance of this organism to cephalosporins. Our data confirm that, due to its broad spectrum, both of this antibacterial could be a good choice for the initial treatment of IE or bacteremia by *E. faecalis*, probably combined with ampicillin and replacing ceftriaxone (drug included in current IE guidelines), however further clinical experience is required.

**Figure 1:** *In vitro activity of ceftaroline and ceftobiprole against Enterococcus faecalis*

<table>
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<th>Infection</th>
<th>N</th>
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<th>MIC₅₀ (mg/L)</th>
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**Abstract 6953**

**Evolution of candidaemia epidemiology and outcomes over the last 10 years: a single-centre study**

Julien Battistolo*, Emmanouil Glampedakis, Lauro Damonti, Julien Poissy, Thierry Calandra, Jean-Luc Pagani, Philippe Eggimann, Pierre-Yves Bochud, Oscar Marchetti, Frederic Lamoth

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**Background:** Candidemia remains an important cause of morbidity and mortality in hospitals. Increased use of antifungal drugs has been associated with epidemiological changes of candidemia with a shift from *Candida albicans* to more resistant non-albicans Candida species. The management of candidemia has also evolved over the last decade with increased use of echinocandins exhibiting a broader spectrum and possibly better efficacy than fluconazole. The aim of this study was to analyze the evolution of the epidemiology and outcome of candidemia over the last decade in our institution.

**Materials/methods:** This was a single-center retrospective analysis comparing all candidemic episodes occurring in our hospital between 2004-2006 (period A) and 2014-2017 (period B). Data about characteristics of patients and infections, Candida species and antifungal susceptibility, antifungal treatment and outcome were collected.

**Results:** A total of 158 candidemic episodes were included (68 in period A and 90 in period B). During period B, candidemia occurred more frequently in the ICU (41% vs 19% p=0.003), in patients that were older (mean 68 vs 58 years old, p=0.006) and experienced more frequently mechanical ventilation (43% vs 25%, p=0.01) and septic shock (27% vs 7%, p=0.02) compared to period A. Mortality was significantly higher in period B (37% vs 18%, p=0.01). While most cases of period A (76%) were treated by fluconazole, caspofungin was the most frequent first-line antifungal therapy in period B (51%). There was no differences in the proportion of Candida spp. between the two periods with *C. albicans* remaining the predominant species (59% vs 56% in period A and B, respectively, p=0.74). Resistance rates to fluconazole and echinocandins remained low and stable over years.

**Conclusions:** Compared to historical cases (10 years apart), candidemia currently affects mainly ICU patients with severe underlying conditions and is associated with higher overall mortality rates. Despite increased echinocandin use, the Candida species distribution and susceptibility patterns remain unchanged in our institution.

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Molecular analysis of metronidazole-resistant Bacteroides strains from Kuwait

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Background: Metronidazole resistance is still a serious problem among anaerobic pathogens, especially in countries where antibiotics are misused. Its best described resistance mechanism is mediated by nim gene-insertion sequence (IS) element pairs which can be a matter of question, but most of the metronidazole-resistant clinical Bacteroides isolates do harbour them. Metronidazole resistance among Bacteroides strains is also a major concern along with the emergence of multidrug-resistant strains as well.

Materials/methods: 421 clinical Bacteroides strains were collected during 2006-2018 in Kuwait. Antibiotic susceptibilities were recorded by Etests and nim genes and IS elements were detected by PCR in metronidazole-resistant strains. Nim gene types were determined by nucleotide sequencing and the localization of the nim genes was determined by plasmid DNA isolation and Southern blotting. The genetic relatedness of the metronidazole-resistant Bacteroides strains was investigated by ERIC [Enterobacterial Repetitive Intergenic Consensus] PCR typing. Carbapenem resistance mechanisms were also analyzed using similar methods.

Results: Of the 421 Bacteroides isolates 12 proved to be metronidazole resistant (10 B. fragilis, 1 B. dorei and 1 B. thetaiotaomicron). All but one was nim gene-positive harbouring the nimE gene. Of these, 9 were activated by ISBf6 and 5.7, 8.3, ~10 and ~13 kb plasmids carried the nimE genes. Interestingly, 6 of the nim-positive strains were also cfiA-positive with 5 silent and with 1 phenotypic resistance. By means of ERIC PCR typing, the B. fragilis strains were not clonal.

Conclusions: The prevalence of metronidazole resistant Bacteroides strains is around 4% in Kuwait and it is mainly due to nimE gene and ISBf6-carrying plasmids that in our cases represented four molecular weight classes. Since most of the examined strains were also cfiA-positive therefore possible treatment options are severely restricted.

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Monitoring outpatient antibiotic utilisation using sales and reimbursement data: a population-based comparison in France, 2012-2017

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Background: To assess whether a retail sales database could be used to monitor antibiotic utilization in the outpatient setting.

Materials/methods: We extracted outpatient antibiotic retail sales data (IQVIA’s Xponent database) and individual reimbursement data from the National Health Insurance (SNDS database), France, 2012-2017. We compared monthly-aggregated estimates of antibiotic use (number of antibiotic prescriptions per 1000 inhabitants per day, PrID) and antibiotic consumption (number of DDDs per 1000 inhabitants per day, DID) between sales and reimbursement data. We used Pearson’s $r$ statistics and linear regression to study how well Xponent data correlated with SNDS data. Autoregressive integrated moving average transfer function models were used to assess the possibility of using Xponent data to predict SNDS values.

Results: We analyzed approximately 390 million antibiotic prescriptions, comprising nearly 3.5 billion DDDs. Overall, Xponent slightly overestimated SNDS data, by 1.4% in PrID (Figure) and 1.8% in DID on average, consistently across major ATC classes, individual antimicrobial agents, types of prescribers, and regions. There were 3.5% missing data on age in the Xponent database; Xponent slightly underestimated SNDS data when evaluating adult [-1.1% and -0.5% for PrID and DID, respectively] and children [-0.5% and -2.8% for PrID and DID, respectively] antibiotic utilization. Xponent and SNDS data were highly correlated, both for PrID ($r$ coefficient = 0.998, $p < 0.0001$) and DID ($r$ coefficient = 0.996, $p < 0.001$). Linear regression modeling confirmed the high degree of correlation between Xponent and SNDS data (slope = 0.973 and 0.976 for PrID and DID, respectively, both $p < 0.0001$). Transfer function modeling showed that Xponent data could predict SNDS values with low deviation (between 0 and -1.1%), and that there was no divergence between the two time series.

Conclusions: IQVIA’s Xponent retail sales data were highly consistent with reimbursement data and were able to accurately predict SNDS values. IQVIA’s Xponent database is suited for monitoring outpatient antibiotic utilization in France.

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Genomic surveillance of carbapenemase-producing Enterobacterales over 5 years reveals transmission clusters of clones and plasmids and extensive diversity of bacterial species encoding carbapenemases

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Background: Carbapenemase-producing Enterobacterales (CPE) are a major public health concern in Ireland. Screening for CPE is extensive and the number of cases, in particular of colonization, detected has increased progressively. The frequency of multispecies outbreaks remains poorly understood. Here, we sought to identify the transmission of CPE clones and plasmids circulating in Ireland using genomic surveillance. In addition, we investigate sharing of carbapenemase-encoding plasmids within and between species.

Materials/methods: We performed whole genome sequencing on all isolates received by the National CPE Reference Laboratory in Ireland between August 2012 and July 2017. We sequenced 782 CPE from 33 Irish hospitals (371 Klebsiella spp, 198 E. coli, 117 Enterobacter spp, 64 Citrobacter spp, 6 Serratia spp, 3 Raoultella spp, 1 Leclercia adecarboxylata, 1 Morganella morganii and 1 Providencia stuartii). Species and multi-locus sequences types (ST) were identified and genome comparisons were performed within each species. Carbapenemase genes were identified and mobile elements encoding carbapenemases were compared within and between species.

Results: High bacterial diversity was observed for the 766 isolates for which an ST could be defined (237 STs). blaOXA-48, blaKPC and blaNDM genes were detected in 490, 189 and 73 isolates, respectively (96% of isolates overall). blaOXA-48, blaKPC and blaNDM were observed in 26/33, 12/33 and 21/33 of the study hospitals, respectively. Genome analyses revealed both local and national clonal expansion (>5 isolates/ST from 1 or more hospitals) of carbapenemase producing Citrobacter spp, Enterobacter cloacae, Enterobacter hormaechei, E. coli, K. grimontii, K. pneumoniae, K. pneumoniae quasipneumoniae and K. oxytoca. Long-read sequencing identified a highly similar (99% identity) blaOXA-48 plasmid in 6 different bacterial species.

Conclusions: We characterised CPE isolated in Ireland from 2012-2017 using whole genome sequencing. This highlighted diversity in bacterial species encoding carbapenemases, and widespread dissemination of CPE clones. A highly similar blaOXA-48 plasmid was observed in different bacterial species. Additional analyses are underway to determine whether other carbapenemases are encoded on mobile elements that are disseminated within and between species and being transferred between hospitals.

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A model-based analysis identifies differences in phenotypic resistance between in vitro and in vivo: implications for translational medicine within tuberculosis

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Background: Proper characterization of drug effects on Mycobacterium tuberculosis relies on the characterization of phenotypically resistant bacteria to correctly establish exposure-response relationships. The aim of this work was to evaluate the potential difference in phenotypic resistance in in vitro compared to murine in vivo models using colony forming unit (CFU) data alone or CFU together with most probable number (MPN) data following resuscitation with culture supernatant.

Materials/methods: Predictions of in vitro and in vivo phenotypic resistance i.e. persisters, using the Multistate Tuberculosis Pharmacometric (MTP) model framework was evaluated based on bacterial cultures grown with and without drug exposure using CFU alone or CFU plus MPN data.

Results: Phenotypic resistance and total bacterial number in in vitro natural growth observations i.e. without drug, was well predicted by the MTP model using only CFU data. Capturing the murine in vivo total bacterial number and persisters during natural growth did however require re-estimation of model parameters using both the CFU and MPN observations implying that the ratio of persisters to total bacterial burden is different in vitro compared to murine in vivo. The evaluation of the in vitro rifampicin drug effect revealed that higher precision in the persister drug effect was seen using CFU and MPN compared to CFU alone although drug effects on the other bacterial populations were well predicted using only CFU data.

Conclusions: The ratio of persistent bacteria to total bacteria was predicted to be different between in vitro and murine in vivo. This difference could have implications for subsequent translational efforts in tuberculosis drug development

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Epidemiology and mortality of neonatal Group B streptococcal meningitis and sepsis in the Netherlands: a 30-year nationwide surveillance study

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Background: Group B streptococcus (GBS) is the most common cause of invasive neonatal disease. We assessed the molecular epidemiology, incidence and mortality of neonatal GBS sepsis and meningitis in the Netherlands over 30 years and compared strain characteristics of meningitis with sepsis cases.

Materials/methods: We performed this nationwide surveillance study with data from neonatal (0-3 months of age) invasive disease cases between 1987 to 2016, from the Netherlands Reference Laboratory for Bacterial Meningitis. Serotyping was performed by latex agglutination. Capsule- and multi locus sequence types were determined using whole genome sequence data. Outcome data was obtained through the Municipal Personal Records Database.

Results: 1396 episodes in 1386 patients were identified, of which 177 (13%) were cultured from CSF, 344 (25%) from CSF and blood, and 875 (63%) from blood only. For meningitis, mean annual incidence was 0.09 (95%CI 0.08-0.10) per 1000 live births and remained stable over time (b=0.009, p<0.001; Figure 1). However, the annual incidence of sepsis only cases increased during the observation period (b=0.009, p<0.001) from a mean incidence of 0.07 per 1000 live births in the first decade to 0.26 per 1000 live births from 2006-2016. Late onset disease was associated with meningitis (p<0.001). Serotype III (62%) and sequence type (ST) 17 (34%) predominated in both sepsis and meningitis. Serotype III was identified among 26 STs, mostly ST17 (54%) and ST19 (24%). ST17 was associated with late onset, even after correcting for serotype and meningitis (OR 1.7 95%CI 1.30-2.33). Incidence of ST17 increased in sepsis (b=0.003, p<0.001). ST17 also increased in meningitis (b=0.001, p=0.090), when ST19 concurrently declined (b=-0.001, p<0.001). Mortality rate was 8% (27/323) in meningitis cases and 6% (39/656) in sepsis cases (p=0.175). Serotype Ib was associated with mortality in neonatal meningitis (OR 8.78 95%CI 1.92-40.05) compared to serotype III, even after correcting for multiple testing.

Conclusions: Hypervirulent strain ST17 increased overall, resulting in an increase in incidence of sepsis. Due to declining rates of other STs the overall incidence of meningitis remained stable.
Abstract 6969

**Experience of 319 post-surgical abscesses: focus on empiric antifungal therapy**

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**Background:** Post-surgical abscesses are serious intra-abdominal infections (IAIs). Fungal etiology is less frequent than bacterial but associated with severe prognosis and difficult to establish due to inadequate sampling and polymicrobial cultures. Empiric antifungal therapy of IAIs must sometimes be considered, but guidelines in this regard are based on poor evidence. This work aimed to analyze the factors associated with the administration of empiric antifungal therapy in a real-life cohort of post-surgical IAIs and the impact of empiric antifungal therapy on patients’ outcome.

**Materials/methods:** We conducted a retrospective chart review in a tertiary level hospital in Italy for years 2013-2018. Adult patients with post-surgical abscesses who had been cared for by our ID consultation service were included. We excluded ICU and Hematology patients, intra-hepatic abscesses, extra-peritoneal collections and IBD cases. Empiric therapy was defined as administered within forty-eight hours from presentation. Freshly drawn percutaneous specimens or surgical specimens only were considered for etiology determination.

**Results:** Three-hundred nineteen post-surgical IAIs were retrieved (males 55.8%). Forty-six patients (14.4%) received empiric antifungal therapy (azoles 65.2%). *Candida* was isolated in 34 (10.7%) cases, all polymicrobial: 17 *C.albicans*, 10 *C.glabrata*, 2 *C.tropicalis*, 1 *C.incospicua*, 4 more than one species. One candidaemia by *C.tropicalis* was observed. Among 46 patients who received empirical antifungal therapy *Candida* was isolated in 11 cases, in 18 cases abdominal samples were not obtained, 15 had negative cultures 2 grew bacteria. On multivariate analysis, upper GI surgery, urgent surgery and re-intervention within 30 days were associated with empiric antifungal therapy. Pancreas or biliary tract surgery was associated with *Candida* isolation on univariate analysis. Among 34 fungal isolates, 11 patients received empiric antifungal therapy. Survival analysis showed an advantage against composite adverse outcome of death or IAI relapse when empiric therapy was administered (OR 0.11, p=0.05).

**Conclusions:** Criteria for empiric antifungal therapy administration in IAIs are not well-established and evidence from the literature is weak. Classic risk factors seem not to intercept all patients with *Candida* infection. Empiric therapy could provide an advantage in survival, thus better definition of criteria to guide empiric therapy should be defined through further studies.

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**Predictive value of a positive Pneumocystis jirovecii DNA result in the diagnosis of Pneumocystis jirovecii pneumonia in haematological patients**

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**Background:** *Pneumocystis jirovecii* (PJ) causes life-threatening pneumonia (PJP) in patients with underlying immunological disorders. Diagnosis of PJP relies on direct examination of bronchoalveolar fluid. Real-time PCR assays display increased sensitivity in comparison with microscopy; nevertheless, a positive PJ DNA PCR result in the absence of positive microscopy remains challenging, since because it may merely reflect carriage rather than infection.

**Materials/methods:** Retrospective, two-center study including 192 hematological patients (105 undergoing hematopoietic stem cell transplantation) who presented with clinical signs of pneumonia. All the respiratory tract specimens (BAL, sputa, and tracheal aspirates) were obtained and processed following routine procedures (including bacterial, fungus [extends galactomannan] and viruses examination). For PJ detection the RealCycler PJIR kit® (Progenie-Molecular, Spain) was used.

**Results:** The study included 219 episodes of pneumonia from 192 patients. In transplant patients (n=105, [allo-HSCT; n=86]), these episodes occurred at a median of 227 days after transplantation (0 to 3,231 days) and in non-transplant patients (n=87) at a median of 62 days after diagnosis (-8 to 5,326 days).

All specimens were negative by direct examination for PJ, while 27 displayed positive results by PCR (Bronchoalveolar lavage [BAL], n=18, sputa, n=7, and tracheal aspirate, n=2). Twenty-four out of these 27 patients were treated with Trimethoprim/Sulfamethoxazole. In twelve samples, PJP was the most probable diagnosis, of which 8 were non-transplant patients. Patients not undergoing anti-PJ prophylaxis were more likely to display a clinically significant PJ PCR result (P=0.04). Overall, higher serum levels of LDH was observed for patients with PJP (P=0.15). Corticosteroid use was equivalent across two groups.

Co-detection of other microorganisms was documented in 17 out of 27 specimens, mostly respiratory viruses, and was significantly lower (P=0.001) in patients with PJP when compared to those colonized by PJ. (OR= 0.02; 95%CI, 0.002-0.26).

When only considering BAL specimens, PCR C₅₇₃ were significantly lower in patients with PJP (median, 29.0 [26.4-34.7] vs. median 34.6 [30.0-41.0]; P=0.04).

**Conclusions:** Absence of co-detection of other microorganisms in respiratory specimens along with a low PJ PCR C₅₇₃ result may help to ascertain the clinical significance of PJ detection in hematological patients.

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Individuals at risk of developing rheumatoid arthritis possess a unique microbiome

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Background: Individuals with newly diagnosed rheumatoid arthritis (RA) have a distinct microbiome when compared with healthy controls. However, little is known as to when these microbiome perturbations begin or indeed if they predate the onset of arthritis. RA is now recognised as an endpoint of a disease continuum encompassing genetic risk and development of autoantibodies, which may occur years before symptoms develop. Using a prospective ‘at-risk’ cohort of individuals positive for Anti-Citrullinated Peptide Antibodies (ACPA) with musculoskeletal symptoms but without arthritis, we investigated for the presence of a gut dysbiosis before the onset of RA.

Materials/methods: The gut microbiomes of 25 ACPA positive individuals were compared with a publically available control population using 16S rRNA sequencing, matched for rRNA V4 amplification region, sequencing technique, and approximately for age, gender, diet and ethnicity. Median interval between sample collection and analysis was 9 months. Data were quality controlled and annotated (Cutadapt, QIIME, RDP). OTU files were imported in MEGAN for further analyses. R was used for graphics.

Results: There were significant differences \( p=0.01 \) at family level in gut microbiome of ACPA positive individuals when compared with the control population. Five individuals progressed to RA in between sample collection and analysis. This progressor population displayed decreased microbiome diversity (Shannon/Simpson) when compared with non-progressors. Clustering of the progressor samples was observed on a phylogenetic network created using a pair-wise similarity network (Goodall’s index).

Conclusions:
ACPA positive at-risk individuals have a distinct microbiome when compared with healthy controls. The presence of decreased diversity and clustering suggests that distinct taxa may be involved in the development of RA and warrants further investigation.

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Abstract 6975

Prevalence of fosfomycin resistance among Escherichia coli and Enterococcus faecalis isolates causing urinary tract infection in 34 primary care units in Brazil

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Background: Urinary tract infection (UTI) is one of the causes that often leads men and, specially, women to seek treatment at health units. Fosfomycin has been widely used in the treatment of lower uncomplicated UTI because of its excellent performance against Escherichia coli and Enterococcus faecalis. The aim of this study was to evaluate the prevalence of fosfomycin resistant Escherichia coli and Enterococcus faecalis strains recovered from patients attended at 34 primary care units in Brazil.

Materials/methods: We performed a retrospective study using the data obtained from laboratory records from January to September 2019. One sample by patients was including, and demographic variables such as age and gender were evaluated. The isolates were identified using BD Phoenix system and the susceptibility testing for fosfomycin were done by disk-diffusion technique using the breakpoints values according to CLSI standards.

Results: During the study period 39,958 urine cultures were performed at 34 primary care units (city of Sao Bernardo, Brazil). These samples were obtained by midstream technique and cultured at the clinical microbiology laboratory of the Health Center University ABC; a total of 6,676 (16.7%) urine cultures were positive and Escherichia coli and Enterococcus faecalis were isolated in 3,416 patients. The average age of these patients was 50.3 years (median 53 years) and 89.5% were female. Among these, 460 patients collected more than one urine sample. A total of 3,972 isolates were recovered being 3,478 (87.6%) E. coli and 494 (12.4%) E. faecalis. The fosfomycin resistance was observed in 45 isolates (1.1% E. coli and 1.4% E. faecalis). Resistant strains were observed in 44 patients with average 56.6 years old (median 64 years) and 79.5% occurred in women. Only one patient had 2 isolates resistant to fosfomycin in different episodes of UTI.

Conclusions: Fosfomycin resistance is still very uncommon among E. coli and E. faecalis causing UTI in patients attending at primary care units in patients. Thus, this drug can be used as a first choice of treatment for uncomplicated UTI in this setting. Strains resistant to fosfomycin were observed in cases of UTI mainly in women and in older patients.

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Characterisation of virulence in KPC-2-producing *Klebsiella pneumoniae* CG258 from an outbreak in high complexity hospital in Brazil

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**Background:** *Klebsiella pneumoniae* is an important opportunistic pathogen often associated with nosocomial infections. The capsular serotype, lipopolysaccharide, iron-scavenging systems, and fimbrial and non-fimbrial adhesins are some of the main factors implicated in the virulence of *K. pneumoniae* strains. In this study, we characterize through Whole Genome Sequencing (WGS) the capsular polysaccharide (CPS) and virulence characteristics in *Klebsiella pneumoniae* carbapenemase producing (KPC-KP) strains isolated from a Brazilian Hospital outbreak.

**Materials/methods:** A total of 11 KPC-KP isolates out of 88 isolates identified at a hospital in the city of São Paulo, Brazil were submitted to the WGS. This eleven isolates were assigned to clonal lineages by Pulsed Field Gel Electrophoresis (PFGE). Capsule typing genes (wzy sequencing and wzc), virulence factors of these strains were determined by biofilm formation, virulence genes including clpK, entB, ybtS, mrkD, ycfM, fimH, rmpA, ailS, iutA, kfu, wcaG, aerobactin, fecIRA, shiF, magA e pagO and Galleria Mellonella infection model.

**Results:** Four different STs were found among the 11 KPC-KP strains: 6 belonged to ST437; 3 to ST11; 1 to ST340 and 1 to ST101. Based on the DNA sequences of the wzy and wzc gene, these 11 strains were classified as capsular type K36 (n=5), all belonging to representatives of ST437; K161 (n=1) belonging to ST437; K64 (n=3) all representatives of the ST11 study; K107 (n=1) belonging to ST340, K17 (n=1) ST101. Biofilm formation was found in all isolates, and two ST437 isolates, one from blood culture and the other from the sternum secretion, showed a high adhesion to plaque. All 11 strains had the virulence genes entB, mrkD, ycfM, fimH followed by clpK in 10 strains, traT in 4, ybtS in 3, kfu in 1. The Galleria Mellonella infection model, showed that only 1 representative of ST11 killed 73.3% of the larvae within 24 h.

**Conclusions:** KPC-KP strains exhibited variability in traits associated with virulence. Therefore, the emergence of resistant KPC-KP strains associated with virulence factors in blaKPC-2 biofilm producing strains contributes to this pathogen causing infections, leading to its rapid expansion and persistence in the hospital environment.

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Abstract 6979

**Zika virus: a global health threat and current situation in Pakistan**

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**Background:** Zika virus (ZIKV) is an emerging mosquito borne virus, which belongs to the family flaviviridae. It was first reported from a sentinel rhesus monkey in a Ugandan forest in 1947. The first human case of ZIKV was identified in Central Java, Indonesia in 1977, since then there has been several reports of ZIKV spread in Asia, Africa and Latin America. This dissemination of ZIKV around the globe makes it a serious health concern and has been declared by WHO as a state of ‘international emergency’ in February 2016.

**Materials/methods:** A cross-sectional, observational study was performed to identify flavivirus other than dengue as cause of acute febrile illness (AFI) including ZIKV. Patients were recruited at basic health units and or district hospitals at five different sites of the Sindh region of Pakistan. Serum samples of patients tested negative for dengue virus infection (using Pan Bio Rapid Detection kit for NS1-antigen, InBios ELISA kit for IgM antibodies and real time PCR (RTPCR) were selected for ZIKV testing using InBios ELISA kit for IgM antibodies and RTPCR and PRNT testing.

Nine hundred and ninety-five (n=995) patients were recruited over period of one year (April 2015 to December 2016).

**Results:** Of 995 tested 521 (52.36%) were found to be negative for dengue using all tests mentioned above. These samples were also tested negative for West Nile Virus (WNV), Japanese Encephalitis Virus (JEV) IgM antibodies. These samples were then tested for Zika Virus IgM using InBios ZIKV Detect™ 2.0 IgM Capture ELISA kit, 5.72% (n=57) were positive for Zika Virus IgM, these samples were considered presumptively positive for ZIKV. Confirmatory PRNT tests and PCR testing is in process. This is the first ever report of ZIKV activity from Pakistan.

**Conclusions:** In this study, we would like to share the demographic and clinical details of patients confirmed positive cases for ZIKV based on PRNT result.

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Abstract 6982

**Determination of prevalence of *Chlamydia trachomatis* in pregnant women between 15 to 25 years old at Hospital Universitario La Paz, Madrid, Spain**

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**Background:** *Chlamydia trachomatis* is one of the most commonly reported sexually transmitted diseases, it mostly affects sexually active young women. The newly born infants of infected mothers could be infected when passing through the birth canal. The aim of this study is to know the prevalence of *C. trachomatis* in pregnant women aged between 15 and 24 years and to obtain data about vertical transmission.

**Materials/methods:** We collected urine samples from pregnant women between 15 and 24 years old who gave birth in Hospital Universitario La Paz (Madrid, Spain) before delivery or in the immediately postpartum period, in a period of 7 months from November 2018 to June 2019. We performed a nucleic acid amplification test by real time PCR multiplex (BD-Max, Becton Dickinson) which detects *C. trachomatis*, *Neisseria gonorrhoeae* and *Trichomonas vaginalis*. Urine and respiratory samples were collected from all the infants of infected women. Conjunctival samples were also collected from those newborn who presented conjunctivitis signs.

**Results:** We analized a total amount of 136 urine samples and 31 of them showed a positive result. *C. trachomatis* was detected in 25 patients (18.38 %), *N. gonorrhoeae* in 4 patients (2.94%) and *T. vaginalis* in 5 (3.67%). In three patients with a positive result for *C. trachomatis* a mixed infection was detected (2.20%), in one case with *N. gonorrhoeae* (0.73%) and on the other two with *T. vaginalis* (1.47%). To this moment a total of 20 infants have been studied out of the 31 mothers that tested positive. In the newly born group 5 patients received a positive test.

**Conclusions:** We observed that there is a high prevalence of *C. trachomatis* infection among the population we studied, and that there is also the risk to transmit the infection to the newborn. Although perinatal transmission have been investigated in few recent publications, in Europe some studies have shown that the prevalence of *oftalmia neonatorum* is around 15%. For all that we consider that it will be usefull to perform a screening test for this microorganisms in pregnant women between 15 and 24 years old.

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Influence of extracorporeal membrane oxygenation on the pharmacokinetics of ceftolozane/tazobactam

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Background: Extracorporeal Membrane Oxygenation (ECMO) is increasingly used in Intensive Care Unit and can modify drug pharmacokinetics and possibly lead to under-exposure associated with treatment failure. Ceftolozane/tazobactam is an antibiotic combination used for complicated infections in critically ill patients. Launched in 2015, sparse data are available on the influence of ECMO on its pharmacokinetics. The objective of the current study was to determine the influence of ECMO on the pharmacokinetics of ceftolozane-tazobactam.

Materials/methods: An ex vivo model (closed-loop ECMO circuits primed with human whole blood) was used to study adsorption during 8-hour interdose intervals over a 24-hour period (in all 3 ceftolozane/tazobactam injections) with 8 samples per interdose intervals. Two different dosages of ceftolozane/tazobactam injection were studied and a negative control (whole blood in a glass tube with one ceftolozane/tazobactam injection and adsorption study over 24 hours) was performed. An in vivo porcine model was developed with a 1-hour infusion of ceftolozane-tazobactam and concentration monitoring for 11 hours. Pigs undergoing ECMO were compared with a control group. Pharmacokinetic analysis of in vivo data (non-compartmental analysis using PK-solver and non-linear mixed effects modelling using MONOLIX®) was performed to determine the influence of ECMO.

Results: With the ex vivo model, concentrations ranged from 20 to 180 mg/l and from 10 to 75 mg/l for ceftolozane and tazobactam respectively. Height-hour variations in concentration ranged from -5.73% to 1.26% and from -12.95% to -2.89% for ceftolozane and tazobactam, respectively. The in vivo pharmacokinetic exploration showed that ECMO induces a significant decrease of 37% for tazobactam clearance without significant modification in the pharmacokinetics of ceftolozane, probably due to a small cohort size.

Conclusions: Considering that the influence of ECMO on the pharmacokinetics of ceftolozane and tazobactam is not clinically significant, normal ceftolozane and tazobactam dosing in ICU patients should be effective for patients undergoing ECMO.

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Genomic analysis of invasive Streptococcus pyogenes isolated in 2013 and 2018 from Hungary

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Background: Most of the severe invasive infections has been caused by several emm types of Streptococcus pyogenes (emm1, emm12, emm28, emm3, emm4 and emm89) in Europe. In 2005 emm1 was the prevalent type among invasive S. pyogenes isolates in Hungary. Since 2012 the number of invasive S. pyogenes cases among patients older than 25 years has steadily increased. The aim of the study was to perform genomic analysis of such isolates collected in 2013 and 2018 in order to compare their genetic background and relationships.

Materials/methods: We investigated 39 selected S. pyogenes isolates (14 from 2013, 25 from 2018) from invasive samples of patients older than 25 years originated from 13 Hungarian hospitals by whole genome sequencing on Illumina MiSeq. Clonal relationships were investigated by emm-typing and core genome (cg)MLST (SeqSphere+ [Ridom]). A bioinformatic pipeline was generated based on 60 genes associated with virulence and 18 genes associated with resistance. Antibiotic susceptibility tests were performed by gradient MIC tests and interpreted using EUCAST guidelines.

Results: Rates of antimicrobial resistance were: erythromycin 5.1%, clindamycin 2.6%, tetracycline 23.1% and levofloxacin 5.1%, which could be also predicted by resistome analysis. Thirteen emm types were detected, of these in 2013 emm28 (28.6%) and emm1, emm3, emm117 (each 14.3%), while in 2018 emm59 (24%), emm1 (20%), emm3 and emm81 (each 12%) were prevalent. The tetracycline resistance was significantly associated with emm59. According to cgMLST, all six emm59/ST172 isolates originated from six hospitals in 2018 could be assigned to one cluster, while clonal relationship between eight emm1/ST28 isolates was unlikely. Four minor clusters from different STs could be also observed. All isolates harboured genes encoding hyaluronic acid capsule (hasA-B-C), DNAse (spd), hyaluronidase (hyl), streptolysin O (slo), NADase (nga), exotoxin B and G, and adhesins (fbp54, lmb). Among the emm1/ST28 isolates 54-56% of investigated virulence factors could be detected, while among emm59/ST172 isolates only 37%. The most frequent emm-type/exotoxin-profile combinations were emm1/A-B-C-G-J-smeZ (20.5%) and emm59/B-G-J-smeZ (15.4%).

Conclusions: Our results suggested that the emm59/ST172 with tetracycline resistance appeared clonally in geographical distant parts of Hungary and became a prevalent type among invasive S. pyogenes population in 2018.

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Clinical outcomes in patients receiving high vs standard dose caspofungin in the treatment of Candida intravascular infections

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Background: Echinocandin antifungals are an important therapeutic option in the management of Candida infections. The 2016 Infectious Diseases Society of America Guidelines recommend high dose (HD) caspofungin (150 mg daily) for treatment of Candida intravascular infections (CINs), including endocarditis and implantable cardiac device infections. In vitro studies have shown reversal of fungal growth inhibition at high doses of echinocandins. Clinical implications of this paradoxical effect among Candida species is unknown. The aim of this study is to compare clinical outcomes associated with HD vs standard dose (SD) (50 mg) caspofungin therapy in patients with CINs.

Materials/methods: This was a single-center, retrospective cohort of inpatients with CINs from Jan 2012 to October 2018 who received caspofungin for a minimum of 48 hours. Data collected included baseline clinical characteristics, echinocandin dose received and adverse events (ADEs). Patients receiving HD vs SD caspofungin were compared. The primary outcome was treatment failure necessitating a change of antifungal therapy. Secondary outcomes included all-cause in-hospital and 90-day mortality and 90-day infection relapse. The Wilcoxon Rank Sum test, Pearson chi-squared test, and Fisher’s exact test were utilized as appropriate.

Results: There were 44 eligible patients with CINs, of which 28 (64%) received HD caspofungin and 16 (36%) received SD caspofungin. There were no significant differences in the baseline clinical characteristics. The most common indications were Candida endocarditis (36, 82%) and cardiac device infection (8, 18%). Candida albicans was the predominant species (15, 34%). The caspofungin dose did not affect time to microbiological clearance (p=0.91), with a median of 3 candidemia days in both groups. There was no difference in treatment failure with HD vs SD caspofungin therapy (29% vs 19%, p=0.72). All-cause in-hospital mortality (18% vs 13%, p=1.00) and 90-day mortality (11% vs 25%, p=0.24) were also similar. None of the patients had 90-day infection relapse. The most common ADE was hepatotoxicity, but there was no significant difference between the HD and SD caspofungin groups.

Conclusions: SD caspofungin therapy had similar outcomes and tolerability compared to HD caspofungin therapy for CINs. Further studies are warranted to evaluate the safety and efficacy of HD caspofungin.

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Dalbavancin use in the United Kingdom: a multi-centre, retrospective evaluation of real-world use of an extended dosing interval lipoglycopeptide

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Abstract 6994

Background: Dalbavancin is a lipoglycopeptide antibiotic, highly active against gram positive organisms with a prolonged half-life permitting an extended dosing interval. It is licenced for the treatment of acute bacterial skin and skin structure infection (ABSSSI) but data supporting use in other conditions are limited.

Materials/methods: a multicentre, service evaluation recording all use of dalbavancin in 10 UK centres.

Results: 269 patients received 409 doses of dalbavancin. Dalbavancin was well tolerated with 11 adverse effects recorded (4% of patients). One patient died within 72 hours of drug administration. The most common indications for dalbavancin were ABSSSI (45%), osteomyelitis/septic arthritis (21%), prosthetic joint and orthopaedic device related infection (12%), infective endocarditis (11%) and sepsis in people who inject drugs (PWID) (7%). The most common reasons for selecting dalbavancin were practical difficulties with OPAT (35%), PWID (26%), OPAT capacity (18%) and IV access difficulties (5%).

In 122 cases of ABSSSI, dalbavancin was administered after a median 1 day of antibiotic therapy (range 0-16). 75% received 1500mg and the remaining 25% received 1000mg of dalbavancin ± 500mg a week later. 4 patients (3%) with ABSSSI were readmitted to hospital and 10 patients (8%) received a further dose of dalbavancin after 2 weeks because of an ongoing need for IV antibiotics. 1 patient failed to respond.

Dalbavancin given for other indications was associated with greater duration of prior therapy (median 7 days, range 0-200). Bacteraemia was recorded in 63/147 (43%) of patients with 45 (31%) having Staphylococcus aureus bacteraemia (SAB). 41 patients including 12 with bacteraemia (9 SAB) received < 48 hours of treatment prior to receiving dalbavancin usually to treat osteoarticular infection (61%) or other deep-seated infections in PWID (24%). In this group, outcomes were generally favourable with 2/41 patients reported to have experienced treatment failure and 1/41 being readmitted to hospital with a presumed febrile reaction to dalbavancin. In 106 cases given > 48 hours of antibiotics prior to dalbavancin, 6 (5%) experienced treatment failure.

Conclusions: Dalbavancin was safe and well tolerated. In ABSSSI, dalbavancin was typically administered within 24-48 hours whereas in other infections, dalbavancin was usually given after initial treatment with alternative agents.

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Abstract 6997

Distinct augmenting contribution of hyperbaric oxygen therapy to neutrophil function and antibiotic efficacy against Staphylococcus aureus

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Background: Staphylococcus aureus (SA) is known to cause severe endovascular infections such as infective endocarditis (IE), in which it accounts for up to 40% of cases. As mortality rates are high, clinical management of left-sided SA IE remains challenging. Previously, we showed that hyperbaric oxygen therapy (HBOT) enhances the effect of tobramycin-treatment in a rat model of left-sided IE. Since the mechanism of HBOT is not clarified, the present in vitro study aimed at investigating the contributing anti-SA mechanisms of HBOT on direct bacterial killing, antibiotic potentiation and polymorphonuclear leukocyte (PMN) enhancement.

Materials/methods: SA (1.25x10⁷ CFU/mL) was exposed to isolated human PMNs (1.25x10⁶ PMN/mL from one healthy individual), tobramycin (0.007 µg/mL; MIC = 0.125 µg/mL) and ciprofloxacin (0.03 µg/mL; MIC = 0.25 µg/mL). HBOT was used in humanized exposure (100 % O₂, 2.8 bar, first 90 minutes of the assay). Bacterial survival and growth were observed after 4 hours by quantitative bacteriology and optical density (OD₆₀₀nm) measurements. For measuring PMN functionality, 100 µL whole blood was stimulated with 1.67 mM phorbol myristate acetate or 3x10¹⁰ CFU/mL SA and exposed to normoxic and normobaric conditions or HBOT for 40 minutes at 37 °C. Intracellular ROS-production was measured as mean fluorescence intensity by means of dihydrorhodamine analysis in a flow cytometer.

Results: We established an in vitro assay of SA infections and showed that HBOT exhibits significant direct anti-staphylococcal effects (32% killing, p=0.0002). Furthermore, HBOT increased the functionality of PMNs 18 % in general (p=0.0004) and 15 % in response to SA (n.s). Finally, HBOT showed an additive effect as 35 % additional killing to sub-MICs of tobramycin (p=0.006) and 57 % additional killing of ciprofloxacin (p=0.0001).

Conclusions: The present in vitro study provides evidence that HBOT has differential beneficial mechanisms mediating its anti-SA effects in infections. Despite the direct effect, it enhances the host-immune response and improves the oxygen-dependent antibiotic killing by tobramycin and ciprofloxacin. This observation can help to improve the clinical management of severe SA infections with adjunctive HBOT by augmenting the host immune response and optimizing the efficacy of antibiotic treatments.

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**Abstract 6998**

**Performance of the Accelerate Pheno system in a tertiary care hospital in Germany**

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**Abstract third-party references:** Accelerate Diagnostics

**Background:** The number of multidrug-resistant Gram-negative bloodstream infections (BSI) has dramatically increased the problems faced, when treating a hospitalized patient. In recent years, many attempts have been undertaken to enhance antibi-otic management and reduce the turnaround time for reporting of the antimicrobial susceptibility profile (AST) of the identified organism to improve clinical outcome for patients. The Accelerate Pheno System (ACC) provides ID and AST results in 7 hours, directly from positive blood culture. We aimed to evaluate the analytical performance of ACC for Gram-negative BSI in a tertiary care hospital.

**Materials/methods:** The ACC was implemented at the University Hospital of Eppendorf (Germany) and compared to Standard of care (SOC; Vitek2). Categorical agreement (CA, results with the same interpretation), rates of very major errors (VME, proportion of resistant isolates by SOC, tested susceptible by ACC), major errors (ME, susceptible isolates by SOC, resistant by ACC), minor errors (mE, intermediate isolates by SOC, resistant or susceptible by ACC) and area of technical uncertainty (ATU) were analyzed.

**Results:** 75 blood cultures with Gram-negative isolates as a causative agent were prospectively measured with the ACC. The most commonly identified organisms were *E. coli* (36), *K. pneumoniae* (8) and *Pseudomonas aeruginosa* (5). 938 AST results were available by the ACC. Overall CA was 98.3%. mE rate was 0.64%, ME rate was 0.1%, VME rate was 0.53% and 0.42% were in the ATU. In 10 cases of mono-microbial infections the ACC could not identify the causative bacterium. Four poly-microbial blood cultures were measured, of which two were correctly identified, in one case the ACC identified one of two organisms and failure to identify any organism occurred in one case. In 7/61 (11.5%) cases, the ACC correctly identified the causative organism, but failed to create an AST record.

**Conclusions:** ACC can help to quickly identify a causative organism of a BSI directly from the positive blood culture and perform a rapid AST, reducing the turnaround time. ACC should be initiated within 8 hours of blood culture positivity, therefore laboratories must consider workflows and integration into a structured antimicrobial stewardship program to ensure maximal benefit for the patients.

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Identification by proteomic (MALDI-TOF MS) of non-tuberculous mycobacteria from liquid medium in clinical practice

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Background: The use of MALDI-TOF MS for the identification of non-tuberculous mycobacteria (NTM) in solid medium has proven to be very useful and allow good discrimination at the species level. To reduce the response time we would need to be able to identify the NTM directly from the liquid medium. The objective of our study was to compare the results obtained by identifying the NTM with MALDI-TOF MS of liquid medium and those obtained by Genotype ® Mycobacterium CM / AS. (Hain Lifescience, Germany).

Materials/methods: From November 1, 2018 to March 31, 2019, we studied 31 cultures of positive clinical samples for NTM in Bactec Mycobacteria Growth indicator tubes (MGIT, Becton Dickinson), making the identification by MALDI-TOF MS from liquid medium. For the identification, we used the extraction procedure described by B. Rodriguez Sanchez, 2018, using the Mycobacteria library 4.0 database. The cultures were sent to the reference center of the Costa del Sol Hospital (Marbella) for the realization of reverse hybridization Genotype ® Mycobacterium CM / AS.

Results: We worked with 31 MGITs, of which 29 (93.5%) were correctly identified. In 27 samples, the results coincided with those obtained using Genotype® Mycobacterium CM / AS [M.chimaera intracellulare-group M. lentiflavum, M. mucogenicum phoacaicum group, M. chelonae, M. lentiflavum, M. fortuitum, M. avium and M. gordonae]. Two cases identified as M. canariasense / cosmeticum and M. elephantis, not being in the Genotype ® Mycobacterium CM / AS database, were sent to the National Center for Microbiology, where they confirmed the identification.

Of the 29 identifications made, 13 were obtained with a score > 2,000, 13 with a score between 2,000-1,700 and 3 with <1,700. In two samples, no protein peaks were obtained and identification was not possible.

Conclusions: MALDI-TOF MS is a useful technique for the rapid, reliable and cost-effective identification of non-tuberculous Mycobacteria from liquid medium, presenting a high concordance with the reference method. The spectrum of identified species is not very extensive, it would be necessary to increase the number of samples in order to evaluate the ability to identify other species.

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**Evaluation of the interactions of polymyxin B in combination with aztreonam, minocycline, meropenem and rifampicin against NDM- and OXA-48-like producing Escherichia coli**

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**Background:** The prevalence of infections with multidrug-resistant Gram-negative bacteria is steadily increasing. Combination therapy is used to enhance the efficacy of the available antibiotics. However, there is a paucity of data on which combinations are most effective, mechanisms of synergistic interactions and associations between the susceptibility to specific combinations and the presence of resistance genes. This study aimed to determine the in vitro effects of polymyxin B combinations against Escherichia coli producing NDM and OXA-48-like carbapenemases.

**Materials/methods:** Time-lapse microscopy was used to screen the antibacterial activity of polymyxin B in combination with aztreonam, meropenem, minocycline and rifampicin at multiple drug concentrations against 20 clinical isolates of NDM (n=13), OXA-48-like (n=5) and NDM and OXA-48-like-producing (n=2) E. coli. After 24 h the samples were spotted on agar with and without 4x MIC polymyxin B to assess resistant subpopulations. The strains were characterized by MIC determination according to EUCAST guidelines and whole genome sequencing to detect antibiotic resistance genes and genes involved in efflux.

**Results:** A synergistic and bactericidal effect was found with polymyxin B and minocycline against 11 of the 20 strains and with polymyxin B and rifampicin against 9 strains. Synergy was less frequently observed with combinations including aztreonam (3 of 20) and meropenem (2 of 20). Bacterial growth >2 log10 CFU/mL on 4x MIC polymyxin B was only detected in 3 of 1600 24-h samples, suggesting very little resistance development. In addition to the carbapenemases, all strains carried other β-lactamase genes, most commonly blaCTX-M-15 and blaTEM-1B. Tetracycline resistance genes were present in all but two strains. The tet(B) gene and a wild-type soxR gene were correlated with synergy of polymyxin B plus minocycline and no synergy was found for polymyxin B in combination with aztreonam or meropenem against any of the strains carrying blaCTX-M-15.

**Conclusions:** Combinations of polymyxin B and minocycline or rifampicin were most effective showing synergistic and bactericidal effects against approximately half of the tested NDM and OXA-48-like-producing E. coli. Potential associations between synergistic interactions and resistance genes were found, which could be of interest in the future search for promising combination therapies.

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Abstract 7005

Long-term impact of an antimicrobial stewardship programme implemented in a tertiary care Greek hospital on antibiotics consumption and on the incidence of carbapenem-resistant Gram-negative pathogens: an interrupted time-series analysis

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Background: During the last decade the prevalence of Carbapenem-resistant (CR) Gram-negative pathogens (GNP) has dramatically increased in Greek hospitals. Our aim was to evaluate the impact of an antibiotic stewardship program (ASP) implemented in a 535-bed tertiary-care hospital on the consumption of 3 classes of protected antibiotics (PrA, i.e. carbapenems, colistin, tigecycline) on the incidence of CR isolates of three major GNP: Klebsiella pneumoniae (KP), Pseudomonas aeruginosa (PA) and Acinetobacter baumannii (AB).

Materials/methods: A prospective audit with feedback ASP targeted specifically to three PrA was evaluated by comparing a pre-interventional period (PP) (January 2014-October 2016) to the interventional period (IP) (November 2016-September 2019). A total of 653 CR blood isolates belonging to the 3 GNP during the two study periods were included. The incidence rate of carbapenem-resistance was calculated as number of carbapenem-resistant isolates/1000 patient-days (PD). Antibiotic consumption was expressed as Defined Daily Doses (DDDs)/100 PD. Statistical analysis was performed using interrupted time-series models.

Results: A statistically significant reduction in the consumption of all 3 classes of PrA between PP and IP, was observed. The most significant decline was observed in carbapenem consumption with a change at intervention period of -10.3 DDD/100 PD (p<0.001; Figure 1A). Regarding the incidence rate of carbapenem-resistant GNP, a prominent reduction was observed among CR KP isolates, in which the increasing, but non-significant pre-intervention trend, turned to a significantly (p=0.042) decreasing trend after the intervention (Figure 1B). A less evident, not statistically significant decreasing trend was recorded in the incidence of CR PA and AB isolates. Both total in-hospital crude mortality and mean length of hospital stay, which were used as quality indicators, were not significantly affected.

Figure 1: Observed values and model predictions of (A) carbapenem consumption (DDD/100PD), (B) incidence in KP CR isolates/1000 patient-days. Solid lines represent predicted value from interrupted time-series analysis models

Conclusions: After almost three years of successful and safe implementation of an ASP program, in a hospital with high resistance rates, a decreasing trend in the incidence of CR GNP was recorded. This tendency was most apparent for CR KP isolates.

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Abstract 7006

**Genome wide mutations in a clinical Escherichia coli isolate with a DNA mismatch repair gene defect after exposure to remnants of a phagemid-containing Escherichia coli**

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**Background:** In a recent proof-of-concept study, we have shown that exposure of a clinical amoxicillin-susceptible *Escherichia coli* isolate to remnants of a disinfectant-treated *E.coli* K-12 strain, containing a pBluescript KS(-) phagemid, resulted in the development of amoxicillin resistance. The genomes of these isolates were screened for mutations and DNA mismatch repair (DMMR) gene defects.

**Materials/methods:** Short-read sequence data (Illumina) of the amoxicillin-susceptible *E.coli* isolate (EUR1) and twelve of its amoxicillin-resistant mutant isolates (EUR1M1 - EUR1M10, EUR1S1, EUR1S2) were analysed. De novo assembly was performed with CLC Genomics Workbench v11 (Qiagen), followed by whole-genome multilocus sequence typing (wgMLST) with Ridom SeqSphere+ v5.1.0 (Ridom). Twenty-eight DMMR genes were detected in and extracted from the genomes using BLAST v2.6.0. and Biopython v1.73. Extracted genes were translated with Biopython v1.73 and aligned against translated DMMR genes of 18 *E. coli* isolates with the same sequence type from a publicly available database (PREJB15226) using Vector NTI Advance 11 software (ThermoFisher Scientific). Assembled genomes were uploaded to the online bioinformatics tools ResFinder v3.2.0. and PointFinder v3.1.0 (CGE).

**Results:** The EUR1 isolate belonged to ST73. The number of wgMLST allele differences between the amoxicillin-susceptible and –resistant isolates ranged from 21 (0.59%) to 69 (1.96%) alleles. In total, 526 mutations were detected in 517 mutated alleles. Of those, 505 (96%) were transitions (96%), of which 294 (58%) were G:C>A:T transitions. Out of 517 mutated alleles, 56 alleles (11%) were mutated in more than one amoxicillin-resistant isolate. The EUR1 isolate harboured a MutL gene amino acid sequence that was different from the *E. coli* ST73 isolates from the publicly available database and lacked a vsr gene. This specific MutL sequence and vsr gene absence are known to be associated with a constitutive increased mutational phenotype. In contrast to the amoxicillin-susceptible isolate, all amoxicillin-resistant mutants harboured mutations in the promoter of the chromosomal AmpC (cAmpC) gene, associated with AmpC hyperproduction (Figure 1).

**Conclusions:** Exposure of an *E. coli* isolate with a MutL gene defect and no vsr gene to remnants of a phagemid-containing *E. coli* was associated with genome wide mutations, among which mutations in the cAmpC promoter that resulted in beta-lactam resistance.

**Figure 1 Mutations in cAmpC promoter/attenuator region of amoxicillin-susceptible and -resistant isolates.**

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Pleuromutilin resistance in methicillin-resistant *Staphylococcus aureus* at the human-animal interface, Denmark

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**Background:** Since 1979, pleuromutilins have been widely used in veterinary medicine and account for 10-15% of all antimicrobials used in the Danish pig production system. In Denmark, pleuromutilins have not yet been marketed for clinical use in humans, although they were recently approved in the EU and USA. In this study, we used whole-genome sequencing and bioinformatics analysis to evaluate the activity of pleuromutilins against: 1) livestock-associated methicillin-resistant *Staphylococcus aureus* clonal complex 398 (LA-MRSA CC398), which was present in 88% of Danish pig farms and accounted for 17% (256/1,478) of all human MRSA infections in 2018; 2) the predominant human-origin MRSA (HO-MRSA) clones circulating in Denmark.

**Materials/methods:** The study included 444 LA-MRSA CC398 isolates collected from pigs (n=288) and patients (n=156) and 726 HO-MRSA isolates representing CC5, CC6, CC8, CC22, CC30, and CC80. All 1,170 MRSA isolates were whole-genome sequenced and investigated for pleuromutilin resistance genes and amino acid substitutions in ribosomal protein L3.

**Results:** In total, 70% of the LA-MRSA CC398 isolates from pigs and 76% of the LA-MRSA CC398 isolates from patients were genotypically resistant to pleuromutilins, of which 94% and 88% carried *lsa* on mobile genetic elements, respectively. In comparison, only one of the 726 HO-MRSA isolates was genotypically resistant to pleuromutilins due to the presence of the *vga* gene. The plasmid-borne *cfr* gene conferring cross-resistance to pleuromutilins and linezolid was not detected in any of the isolates.

**Conclusions:** Our findings showed that pleuromutilin resistance is widespread in LA-MRSA CC398 isolates from pigs and humans, supporting that use of antimicrobials in animals can (co-)select for resistance in zoonotic bacteria. There is currently no evidence for transfer of *lsa* from LA-MRSA CC398 into HO-MRSA, but this might change if pleuromutilins become available for clinical use in humans. Thus, the applicability of pleuromutilins as anti-MRSA drugs will depend on the relative disease burden of LA-MRSA CC398 in a given area and the transferability of pleuromutilin resistance between LA-MRSA CC398 and HO-MRSA. The results highlight the usefulness of integrated surveillance of antimicrobial consumption and resistance at the human-animal interface when assessing the efficacy of antimicrobials in human and veterinary medicine.

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Abstracts 2020

Abstract 7009

The role of using the UBU (Urethritis Basic Unit) and the FVU (First-Void Urine) in the quick diagnosis and adjustment of treatment in urethritis

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Background: Urethritis is a common infection in men which can benefit from rapid diagnosis and selected treatment.

Materials/methods: Data from 100 patients with urethritis were collected in a prospective study conducted in a Sexually Transmitted Infections (STI) Clinic based in a Microbiology Laboratory. A urethral swab and a first-void urine (FVU) sample were taken from all patients. In most patients, a STI serology and in some of them, a pharynx, anal, glans or/and skin's lesions samples were also performed. While examining the patient, a small extension of Gram staining of the urethral swab was performed, which allowed viewing what we call UBU (Urethritis Basic Unit), which represents a picture of the state of the urethral mucosa, as well as flow cell cytometry counting from the FVU. Having this quick information in addition to clinical and epidemiological data, allowed treating patients with an accurate approach to the underlying cause of urethritis before leaving the STI Clinic. Additionally, traditional culture and PCR (STI, Seegene) were performed.

Results: The etiological diagnosis was established in 92/100 patients: 31 Chlamydia trachomatis (33.7%), 31 Neisseria gonorrhoeae (33.7%), 20 Ureaplasma urealyticum (21.7%), 14 Mycoplasma genitalium (15.2%), 4 Haemophilus influenzae (4.3%), 1 Haemophilus parainfluenzae (1%), 3 herpes simplex virus type 1 (3.2%), 1 herpes simplex virus type 2 (1%) and 2 adenovirus (2.2%). Discrepancies between urethra and urine leukocyte counting were found in 21 samples, finding <5 leukocytes/field in urethra's Gram staining and higher counting in FVU flow cytometry. All gonococcal urethritis were detected by microscopy observing gram-negative diplococcus in the urethral swab (and therefore, treated with intramuscular ceftriaxone). 39 patients suspected of infection with a non-gonococcal urethritis received 1 g. of azithromycin. There were 7 suspicions of viral urethritis and 6 were confirmed. Only one of the viral infections was initially treated with azithromycin because of polymorphonuclear predominance.

Conclusions: The proximity between a STI Clinic and a Microbiology laboratory, allows using quick techniques to optimize choosing a better treatment adjusted to etiological suspicion. The use of FVU allowed detecting urethritis which weren’t detected after microscopy observation of the urethra’s Gram staining following classic urethritis diagnosis criteria.

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Abstract 7011

**Evaluation of T2MR in a Greek university intensive care unit**

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**Background:** T2 Magnetic Resonance (T2MR) is a novel method of detecting ESKAPE pathogens in blood specimens. T2MR test is a fully automated procedure which amplifies microbial cell-associated DNA using a thermostable polymerase and target-precific primers and detects signals by amplicon-induced agglomeration of superparamagnetic particles and T2 magnetic resonance. We aim at evaluating the performance of this method in an ICU population.

**Materials/methods:** This is a prospective observational study that took place in a 35 bed university ICU were surveillance data report 40 % ESCAPE pathogens in BCs. Inclusion criteria were age >18 y.o., and clinical suspicion of a new bloodstream infection. Patients who were unsalvageable were excluded. A sample for T2MR and a blood culture (BC) sample were collected simultaneously from all patients. The T2MR test was run according to the manufacturer’s guidelines and the blood cultures were processed according to the hospital standard procedures.

**Results:** 26 patients were included in the study. The results of the T2MR and BCs are presented in the Table. In 20 cases the results of T2MR were in concordance with the BCs. In the remaining 6 cases, the BCs were negative while the T2 MR detected one or more ESKAPE pathogens. There were no false negative results. Mean time to culture positivity was 84 hours while mean time to T2MR result was 3.5 hours. The negative predictive value of T2MR was 100%

<table>
<thead>
<tr>
<th>T2MR</th>
<th>BC</th>
<th>Number of cases</th>
<th>ESKAPE organisms</th>
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<tr>
<td>-</td>
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<td>16</td>
<td></td>
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<tr>
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</tbody>
</table>

(+): ESKAPE pathogen detected  
(-): Escape pathogen not detected

**Conclusions:** T2MR detects more pathogens than BCs and provides a quicker detection time that could shorten the time to targeted therapy. The number of positive T2MR cases with negative BCs can be attributed to the high sensitivity of T2MR compared to the gold standard (BCs).

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Abstract 7018

Clinical evaluation of ChromaCode’s HDPCR tick-borne pathogen panel
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Abstract third-party references: ChromaCode Inc.

Background: The number of reported tick-borne illness cases in the US has been increasing steadily since the 1990s. In addition to carrying the causative agent of Lyme disease, Borrelia burgdorferi, the Ixodes scapularis tick can carry other pathogenic microorganisms including Anaplasma, Ehrlichia, Babesia, and other Borrelia species. These non-Lyme infections can present similarly with a range of severity from asymptomatic to an acute febrile, flu-like illness, occasionally resulting in fulminant multi-organ failure. While clinical guidelines dictate that Lyme disease is best diagnosed with serologic testing, acute illness with the remaining tick-borne pathogens is optimally detected from whole blood using nucleic acid amplification testing within the first few weeks of symptom onset.

Materials/methods: To address this need, we evaluated the HDPCR™ Tick-Borne Pathogen (TBP) Panel from ChromaCode (Carlsbad, CA). It is a qualitative assay which uses qPCR to detect nine pathogens that cause disease (Anaplasma phagocytophilum, Ehrlichia chaffeensis, Ehrlichia ewingii, Ehrlichia muris eauclairesis, Rickettsia spp., Babesia microti, Borrelia miyamotoi, and Groups #1 and #2 of Borrelia) in one reaction and uses cloud-based analysis software for reporting results. We compared the ChromaCode panel to our own laboratory-developed test (LDT) that uses qPCR to detect the four non-Lyme pathogens most likely to cause acute tick-borne illness in New England (A. phagocytophilum, E. chaffeensis, B. microti, and B. miyamotoi).

Results: One hundred and fifteen clinical samples were tested on the TBP panel. Seventy samples, which were obtained from either ARUP Laboratories, The Mayo Clinic, or the Dartmouth-Hitchcock Microbiology Laboratory, were positive for either A. phagocytophilum, E. chaffeensis, B. burgdorferi or B. microti. The remaining 45 samples were clinical samples containing other bacteria or viruses as well as samples taken from patients with no suspected tick-borne illness. There was 98.3% positive agreement in results between ChromaCode’s TBP panel and with our qPCR assay. The two discrepancies were in samples where the LDT detected A. phagocytophilum however the TBP panel reported a co-infection of Rickettsia spp. and E. muris eauclairesis in both samples.

Conclusions: The ChromaCode TBP panel was straightforward, easy to use, and the cloud-based analysis software made results easier to obtain than our LDT.

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Interplay between genetic disorders and gut microbial community: Rubinstein-Taybi syndrome as a model

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Background: Rubinstein-Taybi syndrome (RSTS) is a genetic disorder affecting 1 out of 125,000 newborns characterized by intellectual disability, skeletal and gastrointestinal anomalies and growth deficiency. RSTS is caused by mutations in the genes CREBBP, encoding for CBP protein, or EP300, encoding for p300 protein. As CBP and p300 are lysine acetyl-transferases, RSTS patients show an imbalance between histone acetylation and deacetylation. Preclinical studies have shown that histone deacetylase inhibitors (HDACi) may attenuate the chromatin impairment improving the phenotype. As microbial-derived short-chain fatty acids, especially butyrate, display HDACi activity, the aim of this study was to assess the endogenous level of butyrate and the relative abundance of butyrate-producing taxa in a RSTS cohort.

Materials/methods: We enrolled 23 RSTS patients and 16 healthy siblings (HC), as control group to minimize environmental factors having a well-recognized role on gut microbiota. We assessed dietary intake and performed gut microbiota analysis by next-generation sequencing using V3–V4 hypervariable 16S rRNA genomic region. Fecal SCFAs were quantified by gas chromatography. Exogenous HDACi effect on acetylation of lymphoblastoid cell lines (LCLs) derived from RSTS patients was assessed by Alpha LISA technology.

Results: The biodiversity of gut communities (alpha-diversity) was similar for all the assessed metrics (Observed species, chao1, Shannon index, PD-whole tree) between RSTS and HC. Conversely, a clear difference among HC and RSTS subjects was highlighted in beta-diversity analyses, as both unweighted and weighted Unifrac distances revealed a significant separation between groups (p=0.022 and p=0.013, respectively). We found several significant differences in taxa relative abundance between groups across all phylogenetic levels. In particular, RSTS were depleted in major butyrate-producing genera Faecalibacterium and Roseburia. Fecal SCFA concentrations were similar except for butyrate that was found reduced in RSTS. Sodium butyrate (HDACi) appeared to restore acetylation levels in RSTS LCLs.

Conclusions: Despite sharing diet habits and the environment, RSTS gut microbiota is depleted in major butyrate-producing taxa, resulting in a decreased butyrate production. Deepening our knowledge of RSTS gut microbiota alterations could offer new hints to explore strategies aimed at restoring a normal microbial community, and potentially improving some co-morbidities associated to RSTS, such as gastrointestinal discomfort.

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**Abstract 7024**

**Evolutionary trajectories of carbapenemase-producing Escherichia coli**

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**Background**: Carbapenem-resistant Enterobacteriaceae are considered by WHO as "critical" priority pathogens for which novel antibiotics are urgently needed. The dissemination of carbapenemase-producing Escherichia coli (CP-Ec) in the community is a major public health concern. However, the global molecular epidemiology of CP-Ec isolates remains largely unknown as well as factors contributing to the acquisition of carbapenemase genes.

**Materials/methods**: We first analyzed the whole-genome sequence and the evolution of the E. coli sequence type (ST) 410 and of its disseminated clade expressing the carbapenemase OXA-181. We reconstructed the phylogeny of 19 E. coli ST enriched in CP-Ec and corresponding to a total of 2026 non-redundant isolates. Using the EpiCs software, we determined the significance of the association between specific mutations and the acquisition of a carbapenemase gene and the most probable order of events. The impact of the identified mutations was assessed experimentally by genetic manipulations and phenotypic testing.

**Results**: In 13 of the studied STs, acquisition of carbapenemase genes occurred in multidrug resistant lineages characterized by a combination of mutations in ftsI encoding the penicillin binding protein 3 and in the porin genes ompC and ompF. Mutated ftsI genes and a specific ompC allele related to that from ST38 inducing reduced susceptibility to diverse β-lactams spread across the species by recombination. We showed that these mutations precede in most cases the acquisition of a carbapenemase gene. The ompC allele from ST38 might have contributed to the selection of CP-Ec disseminated lineages within this ST. On the other hand, in the pandemic ST131 lineage, CP-Ec were not associated with mutations in ompC or ftsI and show no signs of dissemination.

**Conclusions**: Lineages of CP-Ec have started to disseminate globally. However, their selection is a multistep process involving mutations, recombination, acquisition of antibiotic resistance genes and selection by β-lactams from diverse families. This process did not yet occur in the high-risk lineage ST131.


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**Abstract 7028**

**Reliable HCV genotyping and resistance associated substitutions identification by a new next-generation sequencing approach**

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**Background:** Hepatitis C virus (HCV) is an RNA virus causing 4 million of new infection worldwide. Liver disease and hepatocellular carcinoma can be consequences of chronic infection by HCV. The aim of World Health Organization (WHO) is the eradication of the virus by 2030. Pangenotypic Direct Antiviral Agents [DAA] were FDA approved in 2016 and increasingly used for all HCV genotypes treatment. High variability as well as strong mutation rate of HCV can lead to the appearance of Resistance Associated Substitutions [RASs]. Furthermore, different strains of HCV virus can co-exist in the same host originating a coinfected. Hence the importance to develop a single kit able to characterise all HCV strains and RASs.

**Materials/methods:** We developed a new NGS workflow for detection of both genotypes and RAS on HCV. V-Seq HCV system allows to identify genotypes 1-7 and to detect RASs for genotypes 1a and 1b by sequencing HCV regions 5UTR, CORE, NS3, NS5A and NS5B. RNA from 153 HCV positive samples were tested. All samples used for the validation were previously genotyped with a reference method. The validation was performed in AB ANALITICA and in Molecular Biology Unit of Venice Hospital. Diagnostic sensitivity/specificity, Limit of Detection (LoD) and precision were evaluated.

**Results:** All samples analysed were correctly genotyped with a median coverage of more than 90% (100X) on target regions. The diagnostic sensitivity and specificity were respectively 98% and 100% with a LoD of 200IU/mL for genotype 1-4 and 500IU/mL for genotype 5-6. The reproducibility was more than 95%. RASs identification, evaluated with proficiency testing samples, were concordant with the expected results. Coinfection and recombinant genotypes were correctly identified in the 100% of cases.

**Conclusions:** V-Seq HCV device is a powerful tool able to correctly recognize HCV genotypes, coinfections and recombinants, with the capability to identify samples at low viral load. The most important RASs described by the major international HCV guidelines were recognized by the kit. V-Seq HCV can improve the HCV treatment leading to a personalized medicine. Similar approach will be used for other pathogens such as CMV or HIV.

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Abstract 7031

Impact of the FilmArray Blood Culture Identification Panel (BCID) compared to VITEK-MS and the VITEK-2 ID/AST instrument in the diagnosis and management of bloodstream infections in a 24-hour laboratory setting

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Background: The rapid identification and reporting of blood-borne isolates allows physicians to promptly manage their patients with the most appropriate antimicrobial therapy, aimed at improving patient outcomes. Technologies, such as the FilmArray® Blood Culture Identification Panel (BCID), incorporate a multiplex PCR amplification and detection system allowing the identification of 24 pathogens and 3 antimicrobial resistance markers. We evaluated the BCID1 panel in a 24-hour laboratory prospectively against the Vitek-MS® and retrospectively against the Vitek-2® ID/AST instrument.

Materials/methods: Blood cultures identified as positive (BD Bactec®) were plated onto appropriate media and gram stained. Bottles with visible bacteria on gram stain were processed using the BCID1. Simultaneously, a direct, or, where necessary, re-processed identification after 6 hours of growth detection technique using the Vitek-MS® was performed. Technologists relayed the results to the wards in the first half of the study (268 patients), microbiologists discussed positive results with physicians in the second half of the study (265 patients).

Results: Five hundred thirty-three unique patients (blood cultures) were analyzed. Mean time to identification for the BCID-1 was 1.39 hours. In comparison, mean identification times for the Vitek-MS® and Vitek-2® were 1.7 - 10.4 hours (direct and indirect) and 25.5 hours respectively. The BCID-1 correctly identified 91% (485/533) of all isolates (8% of isolates not found in the BCID database). Vitek-MS® identified approximately 80% of gram negatives and 60% of gram positives by direct detection, the remaining isolates required a minimum of 6 hours growth prior to identification. Thirty-three percent of all blood-borne Staphylococci were methicillin resistant. The one-hour identification and detection of mecA by BCID-1 resulted in a statistically significant reduction in empiric vancomycin use during the study period. Compared to historic controls, physicians used less piperacillin-tazobactam and carbapenems empirically when results were discussed with a microbiologist. Twenty-eight percent of cultures were polymicrobial. The BCID-1 correctly identified all isolates in 86% (24/28) of cases including one case with 8 pathogens.

Conclusions: The BCID-1 is a rapid detection system that identified 91% of blood-borne pathogens an hour from detection. It is an effective tool in antimicrobial stewardship resulting in more appropriate managements of patients.

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**Abstract 7032**

**Rapid syndromic panel for the diagnosis of infectious meningitis and encephalitis: a systematic review and meta-analysis of accuracy**

Giulia Menchinelli*, Brunella Posteraro¹, Maurizio Sanguinetti², Teresa Spanu², Giulia De Angelis¹

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**Background:** Infectious meningitis and encephalitis are potentially life-threatening diseases, in which rapid identification of the responsible microorganism is imperative. Therefore, recent guidelines recommend the use of molecular tests for rapid detection of pathogens directly from cerebrospinal fluid (CSF). FilmArray® meningitis/encephalitis (ME) panel (BioMérieux) is a syndromic panel largely used in clinical laboratory practice for the direct detection of 14 pathogens (6 bacteria, 7 viruses and 1 yeast) in CSF samples. The aim of this study was to systematically review and summarize the literature evidence about the diagnostic accuracy of the FilmArray® ME panel.

**Materials/methods:** We searched PubMed up to November 1, 2019 to identify studies reporting on the diagnostic accuracy of the FilmArray® ME panel in comparison with conventional methods (i.e. based on microscopy, culture and/or PCR). Two reviewers independently selected articles, extracted data and performed a quality assessment. We generated a bivariate random-effects model to obtain pooled sensitivity and specificity estimates. The R software 3.6.0 (mada package) and Microsoft Excel software 1.30 were used for statistical analysis.

**Results:** We selected 23 articles from 567 search records, including 6931 CSF samples tested by the FilmArray® ME panel and conventional methods for 63,967 results in total. Overall pooled sensitivity and specificity were 84.9% (95% confidence interval [CI], 74.4–91.5) and 99.5% (95% CI, 98.9–99.8), respectively. Pooled sensitivity was higher for bacteria (91.6%; 95% CI, 86.4–94.9) than for virus (90.2%; 95% CI, 86.0–93.3) and Cryptococcus (52.4%; 95% CI, 28.1–75.7). By single targets, pooled sensitivities ranged from 72.5% (95% CI, 59.5–82.5) for herpes simplex virus 1 to 92.0% (95% CI, 87.3–95.1) for enterovirus. Pooled specificities were higher than 98.0% for all the targets. Additionally, cumulative positive predictive values ranged from 58.3% (95% CI, 51.5–64.7) for human herpesvirus 6 to 100% for both *Listeria monocytogenes* and paraechovirus.

**Conclusions:** Based on these findings, the FilmArray® ME panel is an accurate tool for the laboratory diagnosis of the most common aetiologic agents of meningitis/encephalitis worldwide.

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Evaluation of IP-10 as a potential biomarker for the diagnosis of latent tuberculosis infection in vulnerable populations at high risk of TB

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Background: HIV-infection and biologic drugs therapies increase the risk of progression to active tuberculosis (TB). Latent TB infection (LTBI) identification is needed to propose preventive therapy thus reducing TB reservoir. The QuantiFERON-TB Gold Plus (QFT-Plus) is a test for LTBI diagnosis, in which a new tube containing peptides stimulating both CD8- and CD4-T-cells has been added. Alternative biomarkers to interferon-γ (IFN-γ) as interferon-γ inducible protein 10 (IP-10) have been proposed. IP-10 evaluation in the QFT-Plus of LTBI subjects with HIV infection or with rheumatic disorders has never been performed. We aimed to evaluate IP-10 accuracy in QFT-Plus for LTBI diagnosis in these fragile populations.

Materials/methods: QFT-Plus was performed in 85 individuals: 13 HIV-infected, 16 co-infected TB-HIV and 22 co-infected LTBI-HIV; 34 LTBI subjects with rheumatic diseases (R-LTBI) were also included. IP-10 results were analyzed and compared to the IFN-γ-QFT-Plus. Active TB was defined by microbiological means, LTBI by a positive QFT or by radiological lesions suggestive of a previous TB exposure.

Results: TB-HIV and LTBI-HIV co-infected subjects were all positive to IFN-γ-QFT-Plus while only 2/34 R-LTBI subjects scored positive to IFN-γ-QFT-Plus. IP-10 levels are increased in TB1 and TB2 tubes in TB patients compared to TB-HIV co-infected and HIV-infected subjects only; moreover, IP-10 is significantly increased in TB1 and TB2 tubes in LTBI subjects compared to HIV-LTBI [p<0.0001] co-infected subjects and to R-LTBI [p=0.006] co-infected subjects and to R-LTBI [p>0.0001], with the lowest levels in this last population. Based on a previously identified IP-10 cut-off of 1174 pg/mL for TB1 and 928.8 pg/mL for TB2, 19/22 (86.4%) and 21/22 (95.5%) LTBI-HIV co-infected subjects scored positive to TB1 and TB2 respectively. Regarding R-LTBI, 17/34 (50.0%) and 18/34 (52.9%) subjects scored positive to IP-10 in TB1 and TB2 respectively. However, when R-LTBI were stratified based on the IFN-γ-QFT-Plus results, 3/13 (23.1%) subjects with a negative IFN-γ-QFT-Plus but showing radiological lung lesions associated with past TB exposure, scored positive to IP-10.

Conclusions: These results suggest that the IP-10 evaluation may be proposed as an alternative biomarker to IFN-γ in subjects scored QFT-negative, but at high risk of TB based on origin and/or reported exposure to M. tuberculosis.

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Evaluation of Biofire Filmarray Pneumonia for the detection of pathogen bacteria in respiratory infections

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Background: The objective of this study is to evaluate the usefulness of Biofire Filmarray Pneumonia Panel (BioMérieux, France) for detection of pathogenic bacteria in patients with community and nosocomial respiratory infections.

Materials/methods: From October-2018 to October-2019, we studied respiratory samples from 60 patients prospectively: 6 children and 54 adults. Only one sample per patient was included: 32 sputum, 20 BAS and 8 BAL. The results obtained with Biofire Filmarray Pneumonia Panel (BFP) were compared with those obtained in the conventional culture and Real Cycler® Molecular Progenie PCR (RCPM) for Legionella pneumophila and Mycoplasma pneumoniae/Chlamydia pneumoniae.

Results: Of the 60 samples processed, 23 samples obtained negative results with BFP, with no pathogen found in the culture. We detected a bacterial pathogen with BFP in 37 samples, some of them in coinfection: 10 H.influenzae, 8 S.pneumoniae, 6 P. aeruginosa, 4 S.aureus, 3 M.catarrhalis, 7 enterobacteria, 2 Legionella pneumophila, 2 Mycoplasma pneumoniae y 1 Chlamydia pneumoniae. In 16 of these cases, the same bacteria was detected in the culture (43.2%), with a difference of 1-2 logarithms less between the CFU isolated in the culture respect to the copies/ml in BFP. In the 21 samples with no pathogens isolated in culture, the following microorganisms were detected with BFP: 8 H.influenzae, 6 S.pneumoniae, 5 S.aureus, 3 P. aeruginosa, 3 K. pneumoniae, 2 M.catarrhalis, 1 K. oxytoca and 1 E. coli. 13 of these 21 samples corresponded to patients who had received antibiotic treatment in the previous 24 hours (61.9%). Legionella pneumophila was detected in two samples, the result of the culture, the RCPM and the detection of antigen in urine being negative. Mycoplasma pneumoniae was detected in two samples and Chlamydia pneumoniae in one sample, the three cases being confirmed by RCPM. There was no culture with pathogenic microorganisms not detected with BFP.

Conclusions: BFP panel seems to be a useful tool for the etiological diagnosis of respiratory infections, improving sensitivity and rapidity against the culture, especially in patients who have received previous antibiotic treatment. Correlation studies with culture counts are necessary to establish cut-off points in the quantification of BFP that allow us to manage this new tool.

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Efficiency of phototherapy as a non-conventional antimicrobial strategy against selected Gram-negative bacteria in planktonic and biofilm models

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Abstract third-party references: German University in Cairo

Background: Antibiotic resistance in bacteria has emerged as a critical and devastating problem that challenges modern healthcare system. Searching for alternative non-conventional antimicrobial agents is crucial nowadays. Photothermal therapy implementing gold nanoparticles as photosynthesizers is gaining attention as a new strategy for combating antibiotic resistance. Gold nanorods (GNRs), have several advantages including biocompatibility and superior capability of heat release due to their high surface plasmon resonance. The aim of the current study is to investigate the efficacy of GNRs coupled with laser irradiation against *P. aeruginosa*, *E. coli* and *S. typhi*, in planktonic and biofilm models.

Materials/methods: Gold nanorods were synthesized using seed-mediated method with an average aspect ratio of 3.43 (±0.21) and biofunctionalized by cross linking to a phage peptide that selectively binds to gram negative bacteria. The efficacy of gold nanorods at concentrations 10, 100, 500 and 1000uM against the selected bacteria, was investigated in planktonic and biofilm models by incubation for 90 minutes followed by near infrared (NIR) laser irradiation for 6 minutes at 500mW. The cytotoxicity of GNRs on mammalian fibroblasts was assessed by MTT assay. Transmission Electron Microscopy was also done to investigate the possible killing mechanism.

Results: Our results showed that gold nanorods coupled with laser irradiation significantly killed all the bacteria tested in both planktonic and biofilm model as compared to gold nanorods alone. Peptide tagged GNRs had significantly higher killing activity compared to untagged GNRs. No significant change in cellular viability was observed in irradiated fibroblasts. TEM showed accumulation of GNRs on bacterial cell surface, rupture of cell membrane and release of cytoplasmic content following irradiation.

Conclusions: The current study is one of very few which uses a peptide as a targeting agent on gold nanorods to photothermally kill bacteria. Gold nanorods coupled to NIR laser irradiation has shown promising results by being able to totally eliminate bacteria such as *P. aeruginosa*, *S. typhi* and *E. coli* in planktonic and biofilm model. This could offer an non-conventional antimicrobial agents alternative to the antibiotics to treat infections caused by antibiotics-resistant bacteria.

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Abstract 7039

**SynAST, a reliable in vitro synergy test as support for New Delhi metallo-beta-lactamase Klebsiella pneumoniae infection therapy**

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**Background:** New Delhi metallo-beta-lactamase producing *Klebsiella pneumoniae* (NDM-Kp) is increasingly reported in Europe and represents a clinical challenge because of limited available treatment options. Combination therapy with aztreonam plus extended-beta-lactamase, ESBL, inhibitor is required against NDM-Kp and new methods to demonstrate its efficacy are needed. The aim of this study is to propose a reliable and easy in vitro synergy test named SynAST.

**Materials/methods:** Twenty bloodstream isolates of NDM-Kp, co-expressing CTX-M bla1 ESBL, were tested by SynAST, a micro-dilution method adapted to a commercial plate (DKMGN, Thermo Fisher Scientific, MA, USA). Briefly, 100 µL of a 0.5 McFarland suspension was inoculated in 10 mL of cation adjusted Mueller-Hinton Broth; 200 µL of this suspension was added to the wells containing aztreonam obtaining a concentration range of 0.125-4 µg/mL. After aztreonam resuspension, 50 µL were distributed from these wells to those containing piperacillin/tazobactam, amoxicillin/clavulanate and ceftazidime/avibactam, with beta-lactamase inhibitor concentrations fixed at 4 µg/mL, 2 µg/mL and 4 µg/mL, respectively. Minimum inhibitory concentration (MIC) of aztreonam/ beta-lactamase inhibitor combinations was determined after an overnight incubation at 37°C. Clear wells were subcultured to obtain minimum bactericidal concentrations (MBC) values. We considered as synergistic those aztreonam/ ESBL-inhibitor combinations which reduced aztreonam MIC below EUCAST clinical breakpoint (1 µg/mL). SynAST results were confirmed by the validated gradient-test superposition method.

**Results:** All the strains were resistant to aztreonam (MIC > 32 µg/mL), piperacillin/ tazobactam, amoxicillin/ clavulanate and ceftazidime/ avibactam (MIC > 32, 64,16 µg/mL, respectively). The combination of aztreonam plus ceftazidine/ avibactam was synergistic [MIC and MBC of aztreonam were ≤0.125 µg/mL for 20/20 strains]. Also in presence of amoxicillin/ clavulanate MIC and MBC of aztreonam were reduced below the clinical breakpoint [0.25 µg/mL for 1/20 strain and ≤0.125 µg/mL for 19/20 strains]. No synergistic activity was observed when aztreonam was added to piperacillin/ tazobactam [MIC > 4 µg/mL for 20/20 strains].

**Conclusions:** SynAST can easily be used to test the synergism between aztreonam and beta-lactamases inhibitors; it also provides information about MBC values, clinically relevant in severe infections, especially in compromised patient. SynAST could support clinicians to select the most appropriate therapy for NDM-Kp infections.

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Abstract 7040

Single-locus-sequence-based typing of the mgpB gene reveals transmission dynamics in Mycoplasma genitalium

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Background: The sexually transmitted infection (STI) Mycoplasma genitalium (MG) is a major problem worldwide, especially after demonstrating a marked propensity to develop antimicrobial resistance. Since very few treatment options exist, clinicians face an important challenge in the management of the infection. In this scenario, little is known regarding the transmission dynamics of MG and the epidemiology of antimicrobial resistance.

Materials/methods: A total of 70 samples from 66 asymptomatically MG-infected individuals were prospectively collected at a point-of-care service for rapid STI screening in Barcelona, Spain, between October 2017 and January 2018, as part of a parent study. Of them, 57 from 54 participants were suitable for molecular epidemiology studies using the mgpB-based single-locus-sequence-based typing system. The genotypic profiles were complemented with information regarding gender/sexual conduct, infection site, HIV serostatus, and the presence of antibiotic resistance-associated mutations in the 23S rRNA and the parC genes, respectively.

Results: Overall, 32 different sequence types (STs) were described among the 54 infected individuals. None of the STs was identical with the reference ST_G37. The phylogenetic dendrogram is shown in figure 1. The major genotypic cluster 1 is mainly comprising infections occurring in women and heterosexual men (MSW) [11/17; 64.7%], while major cluster 2 is mostly grouping infections in men who have sex with men (MSM) and bisexual men (MSMBI) [31/37; 83.8%]; p < 0.001. This correlation between sexual behaviour and genotype is translated into the structuration of well-defined epidemiological clusters, and may suggest the presence of two independent sexual networks with little connectivity between them. Also, in accordance with other investigations, our study demonstrates the multiclonal feature of the emergence of antibiotic resistance in MG to both macrolides and fluoroquinolones.

Conclusions: The study provides further evidence regarding the transmission dynamics and the structure of sexual networks in MG infection. Furthermore, the investigation demonstrates the multiclonal selection and spread of antibiotic resistance in MG, and assesses the specific allodemic situation of macrolide resistance among MSM.

Figure 1. Abbreviations: MSM, men who have sex with men; MSMBI, bisexual men; MSW, men who have sex with women; HIV, Human Immunodeficiency Virus; ND, not determined; MXD, mixed genotypes.

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Abstract 7041

**Seroprevalence of Bordetella pertussis in Tunisian adults**

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**Background:** Pertussis, an infectious disease caused by *Bordetella Pertussis*, is still a public health problem in many countries despite high vaccination coverage rates. Its current reservoir is represented by adults with undiagnosed pertussis, with the risk of contamination of unvaccinated children, in whom pertussis can be serious or even fatal. In Tunisia, although pertussis vaccine is part of the vaccination schedule, the adult booster dose is not current. The purpose of this study was to estimate the seroprevalence of pertussis in Tunisian adults.

**Materials/methods:** It was an epidemiological, cross-sectional study conducted in adults recruited from the laboratory department of the military hospital of Tunis in marsh 2019 in whom we practiced a serological test for pertussis. We used the EUROLINE kit for a qualitative study of IgG antibodies against Pertussis toxin (PT) and Adenylate Cyclase toxin (ACT) antigens of *Bordetella pertussis* according to the manufacturer’s instructions.

PT: specific for *Bordetella Pertussis*, its antibodies (anti-PT) are detectable both after infection and vaccination.

ACT: secreted by *Bordetella Pertussis* and *Bordetella Parapertussis*, its antibodies can be an indication of a naturally acquired infection.

**Results:** A total of 200 adults [57.5% female; mean age 42.9±15.6 years] were enrolled. Seventy-seven point five percent were from urban area and 33.2% were smokers. None of the subjects had received pertussis vaccination in the last five years. More than half of the subjects (56.0%) reported a cough in the last 12 months, 90.2% of which lasted more than 14 days and required hospitalization in six cases. A total of 33 (16.5%) subjects were seropositive for anti-PT IgG. Only 12 (6.0%) adults were vaccinated. The prevalence of anti-ACT antibodies was 43.0% indicating a naturally acquired infection. We didn’t find any significant relationships between increased rates of seropositivity and age, sex or smokers.

**Conclusions:** Our study highlights the low prevalence of anti-PT antibodies in Tunisian adults, despite the fact that pertussis vaccination is part of the vaccination schedule. This requires a greater awareness of the need to introduce a booster dose for pertussis in adulthood, to confer immunization against it and prevent its transmission to vulnerable infants.

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Abstract 7042

Introduction and spread of the novel GII.P16 pandemic recombinant norovirus in Italy detected by a newly designed PCR primer pair

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Background: Noroviruses (NoVs) are a leading cause of acute gastroenteritis across all ages, causing 685 million cases/year. They are classified in 7 distinct genogroups (GI-GVII). Genogroups I, II and IV are able to infect humans and have been further divided in more than 30 genotypes based on polymerase (ORF1) and capsid protein (ORF2) sequences. New NoV genotypes combinations and variants continuously emerge resulting in epidemics and sometimes global pandemics.

Materials/methods: From January 2016 to December 2017, 251/1185 (21.2%) stool samples collected from children hospitalized with acute gastroenteritis at the “G. Di Cristina” Children’s Hospital in Palermo, Italy, were detected NoV-positive by Real-time PCR, targeting ORF1/ORF2 junction. NoV dual-typing was performed by sequencing two genomic portions, encompassing region A-B of ORF1 (pol) and regions C-D of ORF2 (cap), using JV12A/JV13B and COG2F/G2SKR primers, respectively. Concomitantly, ORF1 was amplified with new degenerate primers JV12Y/JV13RN, designed using a dataset of ORF1 sequences belonging to all NoV genotypes.

Results: With standard protocols pol genotyping was obtained for 56/251 (22.3%) NoV-positive samples. Lacking ORF1 fragment amplification, partial ORF2 genotyping was obtained for 47 GII.2 and 42 GII.4 strains. ORF2 phylogenetic analysis showed that these strains were strongly correlated to the new recombinant GII.P16_GII.2 and GII.P16_GII.4, spreading worldwide since 2016. When a wide panel of complete NoV ORF1 sequences was retrieved from GenBank and aligned with JV12A/JV13B primers sequences, GII.P16 sequences showed multiple nucleotide mismatches with the PCR primers used. Therefore, degenerate primers JV12Y/JV13RN were created. The use of JV12Y/JV13RN degenerate primers allowed to obtain the missing ORF1 sequences and to confirm the circulation of GII.P16_GII.2 and GII.P16_GII.4 recombinant strain in Palermo since September and December 2016, respectively.

Conclusions: From 2016, new recombinant NoV variants are spreading in Italy but an update of PCR protocols was necessary to amplify ORF1 diagnostic fragments of GII.P16 genotype strains. A continuous update of the methods used their detection is essential for molecular surveillance of NoVs, for monitoring emerging strains and to study the impact of NoV disease on public health.

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First vector-borne cases of Zika virus diseases in Europe: a seroprevalence survey
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Background: Zika virus (ZIKV) is a flavivirus in the family Flaviviridae, primarily transmitted to human by Aedes mosquitoes. ZIKV was responsible for major outbreaks of eruptive illness, neurological complications and adverse pregnancy and birth outcomes in 2016 in the Americas. In October 2019, the three first cases of vector-borne ZIKV disease acquired in Europe were detected in a neighbourhood in Hyères, southern France, with symptom onset within 8 consecutive days in the first half of August. Since the majority of ZIKV infections remain subclinical, several cases may have gone unnoticed. We conducted a seroprevalence study within 200m-radius around the focus, nearly the expected flight range of 90% of the local vector mosquito, to determine the extent of ZIKV transmission in Hyères.

Materials/methods: We collected capillary blood from all consenting inhabitants over 2 years old, and information on their medical and travel histories, and exposure to mosquito bites.

Laboratory tests are currently pending. Recent infections will be identified using IgM and IgG anti-ZIKV ELISA, followed, when positive, by neutralisation tests on serum against ZIKV, dengue virus 1–4 and West Nile virus. The prevalence estimator will be calculated using recent reference demographic data. Spatial clustering of Zika cases within the affected neighbourhood will be quantified at various distance ranging from 0 to 200m as the risk of two cases living with a distance range relative to two non-infected individuals living within the same distance. We will develop a statistical model to characterize the spread of ZIKV in this population and reconstruct the most likely transmission tree.

Results: We surveyed 60% (89/150) of the households of the study area and tested 67% (172/257) of the eligible inhabitants. Our study will provide an estimate of the prevalence of ZIKV infection in the affected population. The spatial analysis should contribute to assessing the distance over which infected mosquitoes spread ZIKV. We will estimate the proportion of subclinical cases and their contribution and place to the transmission tree.

Conclusions: This study should characterise the potential for ZIKV spread and outbreaks in temperate regions and to guide efficacious control interventions.

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Abstract 7045

**Analysis of the practices of the multidisciplinary consultation meeting on infectious endocarditis**

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**Background:** Infectious endocarditis is associated with a severe prognosis with a mortality rate of 30% at one year projection. The latest recommendations of European Society of Cardiology (ESC) in 2015 put the multidisciplinary consultation meeting (MCM) “infectious endocarditis” at the heart of endocarditis management.

**Materials/methods:** This unicentric retrospective study analyses the patient files presented at MCM and hospitalized or transferred to the Clermont-Ferrand University Hospital in 2017.

**Results:** One hundred and seventy-seven patients were included in this study and 35 excluded (of which 24 were hospitalized in peripheral hospitals only). MCM identified 98 patients with the diagnosis of endocarditis in which 20 had the mention of probable/possible endocarditis. After deliberation, seventy-nine patients did not ultimately have endocarditis. *Staphylococcus aureus* was the most frequent bacteria (27%) involved in the cases submitted. The main relevant characteristics of the 2 groups are described in table I. Concerning files analysis by MCM, review of the cardiac ultrasound confirmed the diagnosis of endocarditis for 7 patients and invalidated it for 10. The proposal for additional examen was made for 14 patients (64%). Their results confirmed the diagnosis of endocarditis for 13 patients and invalidated it for 9 patients. Only 96 patients presented (54%) had a brain imagery. Seventy-three patients with endocarditis (75%) had a post-hospitalisation consultation achieved by a cardiologist or an infectiologist in the hospital.

**Table I:** Main relevant characteristics of endocarditis and excluded endocarditis groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Endocarditis group (n=99)</th>
<th>Excluded endocarditis Group (n=77)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified Duke criteria (ESC)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Definite endocarditis</td>
<td>58 (59)</td>
<td>9 (12)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Probable endocarditis</td>
<td>36 (36)</td>
<td>48 (62)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Without enough criteria</td>
<td>4 (4)</td>
<td>22 (29)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Neurological injury imaging</td>
<td>42 (42)</td>
<td>8 (10)</td>
<td></td>
</tr>
<tr>
<td>At least one septic location</td>
<td>50 (51)</td>
<td>27 (35)</td>
<td>0.025</td>
</tr>
<tr>
<td>Mortality at 2 years (%)</td>
<td>16</td>
<td>30</td>
<td>0.118</td>
</tr>
</tbody>
</table>

**Conclusions:** This study shows that the expertise of the multidisciplinary team is required to adapt the modified Duke criteria by ESC for each patient. Moreover, clear quality control of MCM must be done to improve the management of infectious endocarditis.

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**Abstract 7046**

**T cell immunomonitoring of pulmonary tuberculosis treatment using mass cytometry: a multi-centre prospective study in high-burden countries**

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**Background:** Tuberculosis [TB] is the leading infectious cause of death in the world. It is caused by Mycobacterium tuberculosis [Mtb]. Low treatment adherence promotes the emergence of multi-drug resistant Mtb. Immunomonitoring of TB treatment is a promising prognostic option because signs of immune reversion are thought to occur earlier than signs of microbiological clearance. We are investigating blood-based immune biomarkers of TB treatment response in patients from high burden countries, using a putative mycobacterial recall antigen: recombinant Mtb heparin-binding hemagglutinin expressed in Mycobacterium smegmatis [rmsHBHA].

**Materials/methods:** We enrolled non-immunocompromised adults presenting with microbiologically confirmed pulmonary sensitive or resistant TB in Bangladesh, Georgia, Paraguay, Lebanon, and Madagascar. Patients were followed up after 2 months of treatment, at the end of therapy, and 2 months afterwards when possible. Sputum and blood samples were collected. After in vitro whole blood stimulation by rmsHBHA and conventional QuantiFERON-TB Plus antigens, plasma and white blood cells were separated, cryopreserved, and shipped to France. Plasmatic IFN-γ response to stimulation was assessed by ELISA. Leukocytes were analyzed by mass cytometry, and supervised and unsupervised analyses were performed. Immunological results were evaluated over the course of treatment and compared to clinical and microbiological data.

**Results:** Between December 2017 and October 2019, 172 patients were recruited. IFN-γ ELISAs were performed for 79 patients having finished treatment. A significant increase of IFN-γ response to rmsHBHA stimulation was observed during treatment (p<0.01). CyTOF analyses were performed for 11 patients. A significant increase in the overall proportion of rmsHBHA stimulated T-cells was observed after 6 months of treatment (p<0.01). In Mtb-specific CD4+ T-cells, a significant decrease in the proportion of CD40L+ and CD69+ cells was observed (p<0.05). Consistently, unsupervised analyses revealed a significant decrease in clusters of memory CD4+ cells (CCR7CD45RA+CD69CD40L–HLA-DR+) co-expressing CD69, CD38, CD40L, and HLA-DR.

![Plasmatic IFN-γ response to mycobacterial stimulation.](image)

T0: inclusion. T1: T0+ 2 months. T2: end of treatment (6 to 9 months).

Data are presented as median + interquartile range. Each grey dot represents a value for one patient. ****: p<0.001. *: p<0.01 (Friedman’s test with Wilcoxon-Nemenyi-McDonald-Thompson’s post-hoc test).
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Conclusions: rmsHBHA is a good recall antigen for in vitro T-cell activation testing, and a promising biomarker for prediction of successful TB treatment. The proportion of rmsHBHA-stimulated activated CD4+ T-cells decreased significantly over treatment course. In-depth investigations will be performed in parallel with NGS and pharmacokinetics data to uncover more exhaustive trends.

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Abstract 7047

**Dispersal of microbes to hospital surfaces following two hand drying methods: paper towels or a jet air dryer**

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**Background:** Hand drying is important to minimise microbial spread, noting pathogen survival on environmental surfaces and opportunities for transmission and spread. We investigated whether there are differences in extent of microbe transmission, according to hand drying method, beyond the toilet/washroom to the hospital environment.

**Materials/methods:** Four volunteers simulated contamination of hands/gloved hands using a bacteria-free preparation of bacteriophage (phage PR772; ATCC® BAA-769-B1) at 10⁷ pfu/ml. Hands were dried using either paper towels (PT) or a jet dryer (JD). Each volunteer wore an apron, to enable measurement of body/clothing contamination during drying. Hand drying was performed in a hospital public toilet and, after exiting, samples were collected from public and ward areas. Environmental/surface sites (n=11) were sampled following contact with hands or apron. Samples were analysed by real-time PCR targeting the P3 gene of phage PR772 (results expressed as copies/µl).

**Results:** Both JD and PT methods significantly (p<0.05) reduced phage contamination of hands (2.2 and 3.3 log₁₀ copies/µl, respectively, Figure). For 10/11 surfaces, significantly greater environmental contamination (p<0.05) was detected after JD versus PT use. All surfaces sampled following JD use showed phage contamination, compared with 6 surfaces after PT use. Average surface contamination following hand contact was >10-fold higher after JD versus PT use (4.1 vs 3.0 log₁₀ copies/µl). Phage dispersal to apron/clothing was 3.5 and 2.8 log₁₀ copies/µl with JD and PT, respectively. Phage transfer from body to environmental surfaces was detected only after JD use (average 3.2 log₁₀ copies/µl).

**Conclusions:** There are clear differences, according to hand drying method, in the residual microbial contamination of the subject’s hands and body. Crucially, these differences in contamination translate into significantly greater levels of microbe contamination after JD vs PT use from hands and body beyond the toilet/washroom. As public toilets are used by patients, visitors and staff, the hand drying method chosen has the potential to increase [JD] or reduce [PT] pathogen transmission in hospital settings.

**Figure:** Real-time PCR results for gene P3 of bacteriophage PR772 detection on environmental samples. Green bar represents 10⁷ pfu/ml stock solution used for hand contamination. Changes are presented as logarithms to achieve normal distribution.

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**Colistin hetero-resistant Klebsiella pneumoniae and Escherichia coli blood isolates**

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**Background:** The increase of multidrug-resistant Enterobacteriaceae led to increased use of colistin as a treatment of last resort. The emergence of colistin heteroresistance (HR) in Enterobacteriaceae may pose a threat to the prognosis of patients following colistin treatment.

In this study, we investigated the prevalence of colistin HR in *Klebsiella pneumoniae* and *Escherichia coli* blood isolates.

**Materials/methods:** A total of 301 *K. pneumoniae* and *E. coli* blood isolates recovered from hospitalized patients between January 2016-August 2018 were included in the study. In vitro antimicrobial susceptibility testing was performed using the broth microdilution method (BMD). Colistin HR was detected by population analysis profiles (PAP). For investigation of colistin HR, we selected the ones with colistin MICs ranging from 1 to 2 µg/ml (*n* = 111). Heteroresistance was considered if the antibiotic concentration exhibiting the highest inhibitory effects was at least 8-fold higher than the highest noninhibitory concentration.

**Results:** Of 301 *K. pneumoniae* and *E. coli* blood isolates, 60 isolates (20%) were found as resistant to colistin by BMD method. Among 301 blood isolates, 241 were detected susceptible to colistin by BMD. The MIC values of isolates were ≤0.06 (*n* = 1), 0.25 (*n* = 11), 0.5 (*n* = 118), 1 (*n* = 99) and 2 µg/ml (*n* = 12). The overall incidence of colistin heteroresistance was 21.2% (*n* = 64).

**Conclusions:** Despite its favorable bacterial killing, the high prevalence of colistin resistance and heteroresistance in *K. pneumoniae* and *E. coli* isolates found in this study. These results clearly demonstrate that heteroresistance could lead failure of this antibiotic in vivo.

For detection of HR, the gold standard is PAP analysis which is cumbersome and unsuitable for routine use in clinical laboratories. Therefore, the high incidence of colistin heteroresistance may raise concern about the choice of antimicrobial susceptibility testing methods to assess HR, as the prevalence of colistin-resistant isolates is widely underestimated.

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Effect of brincidofovir on adenovirus and cellular transcriptome profile

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Background: Brincidofovir, a lipidic conjugate of cidofovir, is currently used off-label for the treatment of severe human adenovirus (HAdV) infections. Its mechanism of action is the inhibition of DNA polymerase by DNA elongation termination. In order to determine whether brincidofovir present other mechanisms, the impact of brincidofovir on cellular and viral transcriptome was investigated by RNAseq.

Materials/methods: We tested four conditions: lung epithelial cells mock infected (A549), A549 cells infected with HAdV C5 (ADV), A549 cells infected with HAdV C5 and treated with brincidofovir (ADV+BCV), and A549 cells mock infected with brincidofovir treatment (BCV). Cellular mRNAs were extracted and sequenced on a NextSeq 72 hours after infection. The sequences were aligned on the human and adenovirus C5 genomes. Differentially expressed genes (DE) were selected (corrected p-value<0.05 and fold change>2) and then used in ontological analysis.

Results: The brincidofovir treatment decreased significantly the overall viral transcription (ADV+BCV vs ADV). However, after normalization with the number of viral reads aligned, brincidofovir treatment was associated with an overexpression of the HAdV early genes E1A and E4 and of the late gene L1 and with a decreased expression of several structural genes (L2 pV, L3 PVI, L4 100K and pVIII and L5 PVI) and of one early gene E3 12.5K. The most significant alterations of the cellular transcriptome were observed with brincidofovir treatment; 555 DE genes for ADVBCV vs ADV, 374 for BCV vs A549 and 113 for ADV vs A549. In non-infected cells, brincidofovir treatment showed a significant inhibition of the biological function “viral replication”, including 25 dysregulated genes. The putative upstream regulators of those genes are NOS2, the cytokine TNFSF10, the PI3K family and the STAT3 transcription regulator. A large overlap of DE genes (218) was found between ADVBCV vs ADV and BCV vs A549, suggesting that the profile of cellular expression after brincidofovir treatment was maintained even after HAdV infection.

Conclusions: Our results suggest indirect antiviral action of brincidofovir by interaction with cellular signalling pathways. Further research is needed to better understand the cellular interactome of brincidofovir and its importance in the treatment of viral infections.

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One Health in practice: longitudinal screening of antibiotic residues, antibiotic resistance genes and zoonotic bacteria in soils fertilised with pig manure

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Background: Fertilization with animal manure is one of the main routes responsible for the introduction of antibiotic residues, antibiotic resistance genes and zoonotic bacteria into the environment. In the context of One Health, it is not well known which contribution is exerted by the agricultural environment for the dissemination of antibiotic residues, antibiotic resistance genes and zoonotic pathogens.

Materials/methods: Five agricultural fields were sampled at five consecutive time points in Flanders (Belgium), starting before fertilization up to harvest. Quantification of antibiotic residues in manure and soil samples were performed through Liquid chromatography-mass spectrometry. The abundance of nine antibiotic resistance genes belonging to three antibiotic classes and the 16S rRNA gene were quantified using qPCR. Detection of Salmonella and Campylobacter and enumeration of E.coli was performed through standard bacteriological cultivation.

Results: Low concentrations of antibiotic residues could be observed in the soils until harvest. The antibiotic resistance genes studied were already present in the soil environment prior to fertilization but after fertilization with pig manure an increase in relative abundance was observed for most of them, followed by a decline back to background levels by harvest-time on all of the fields studied [see graph for tetM gene as example]. No apparent differences regarding the presence of antibiotic resistance genes in soils were observed between those fertilized with manure that either contained antibiotic residues or not. It seems that fertilization with animal manure directly adds resistance genes to the soil and that this mechanism may be more important than possible selective pressure in soil-dwelling bacteria exerted by antibiotic residues present in the manure. The results also indicate that zoonotic bacteria detected in the manure could be detected in the soil environment directly after fertilization, but not after one month.

Conclusions: To the best of our knowledge, the present study is the first to assess a multitude of antibiotic residues as well as resistance to several classes of antibiotics in pig manure and in fertilized soil over time. This is also the first study to report environmental resistance data for Flanders, Belgium, a region with an intensive pig industry.

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Abstract 7061

**Meningococcal disease-associated prophage-like elements are present in Neisseria gonorrhoeae and some commensal Neisseria sp.**

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**Background:** Neisseria sp. possess four clades of filamentous prophages, termed Nf1 to 4. A filamentous bacteriophage from the Nf1 clade termed Meningococcal Disease Associated phage (MDA φ) is associated with clonal complexes of Neisseria meningitidis that cause invasive meningococcal disease. Nf2, 3 and 4 clades of prophage are most closely associated with Neisseria gonorrhoeae. Recently we recovered an isolate of Neisseria gonorrhoeae (ExNg63) from a rare case of gonococcal meningitis, and found that it possessed a region with 90% similarity to Nf1 prophages, specifically the meningococcal MDA φ. This led to the hypothesis that the Nf1 prophage may be more widely distributed in amongst other Neisseria sp.

**Materials/methods:** A collection of 91 reference genomes representing 17 commensal Neisseria sp. and 44 closed genomes of N. meningitidis and 28 closed genomes of N. gonorrhoeae was interrogated for the presence of intact Nf prophage regions by NCBI Blast and by the annotation in the PubMLST database. Intact phage genomes were aligned using MAFFT alignment tool. Maximum likelihood phylogenetic trees were constructed using MEGA7 with 500 bootstrap replicates. hierBAPS was used to define genetic population groups of prophages using the aligned sequences. Bayesian Evolutionary Analysis by Sampling Trees (BEAST) v 1.8.3 was used to infer time measured phylogeny of a dated subset of forty one Nf1 sequences.

**Results:** 160 filamentous prophages were identified in the reference genome collection. Maximum likelihood phylogeny and population structure analysis using hierBAPS revealed Nf1-like prophages in N. gonorrhoeae, N. Lactamica, N. cinerea and N. polysaccharea. In N. gonorrhoeae, Nf1 prophages had a restricted distribution amongst a few sequence types, but notably was present in all representatives of ST1918. A timed phylogeny inferred that N. meningitidis was the donor of the Nf1 prophages in N. lactamica and N. gonorrhoeae.

**Conclusions:** Nf1 prophage is present in N. gonorrhoeae and some human commensal Neisseria sp. Further work is required to determine whether Nf1 prophages are active and can act as accessory colonization factors in these species.

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Short-term and long-term mortality rates among patients with bloodstream infections receiving appropriate antibiotic therapy: a multi-centre, prospective cohort study

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Abstract third-party references: Supported by the German Center for Infection Research (DZIF)

Background: Estimation of burden of bloodstream infections (BSIs) is limited by time of assessment (commonly in-hospital mortality) and lack of adjustment by appropriateness of antibiotic therapy. The aim of this study was to determine short-term and long-term survival patterns among patients with BSIs receiving appropriate empiric and targeted antibiotic therapy.

Materials/methods: BLOOMY.COM is a 24-month prospective cohort study conducted at 6 german universities hospitals. All adult patients with BSI caused by Staphylococcus aureus, Enterococcus spp., Escherichia coli, Klebsiella spp., Enterobacter spp., Pseudomonas aeruginosa, or Acinetobacter baumannii and receiving appropriate therapy were included. Appropriate therapy definition was based on sensitivity pattern of the isolate. Demographic, microbiological, and clinical data were collected at defined time points throughout hospitalization and at month-6 after discharge. Primary outcomes were crude short-term and long-term mortality at month-6. Risk analyses included age, gender, BMI, ICU stay, etiology, BSI focus, and mode of acquisition. Mortality rates were calculated per 1,000 patient-days (PD).

Results: The cohort included 2289 patients, 278.025 patient-days of follow-up. Patients were predominantly male [1432, 63%] with a median age of 68 (IQR:58-77). E. coli [799, 35%] and S. aureus [580, 25%] were the most common etiology. The mortality rate was 3.0 overall (95%CI 2.4-3.98)/1000 PD (risk:36.4%); 28.6 at day-3 (22.7-38.2)/1000PD (8.6%); 9.6 at day-14 (6.7-15.5)/1000PD; 4.9 at day-28 (3.4-7.7)/1000PD (6.1%); and 1.6 at month-6 (1.3-2.1)/1000PD (20.1%). 3-day mortality varied greatly by risk population and was highest in patients with ICU admission at BSI diagnosis (mortality rate: 86.0), respiratory focus (80.0), vancomycin-resistant enterococci (VRE) BSI (50.3). Patients with carbapenem-resistant Enterobacteriales BSI (5.5), VRE BSI (3.9), metastatic cancer (3.9), methicillin-resistant S. aureus (2.9), and BMI <20 kg/m2 (2.7) had the highest long-term mortality rate.

Conclusions: Assessment of burden of BSIs is complex and cannot be limited to in-hospital mortality. Results of this study might inform burden studies on the importance of accounting for focus of infection, etiology (both sensitive and resistant strains), and comorbidities to perform appropriate cost-effectiveness analyses and plan public health interventions. Kaplan-Meier-curves for mortality among BSI patients according to focus of infection: 

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Abstract 7069

**Impact of letermovir and associations of antivirals in vitro and in ex vivo first-trimester placenta model**

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**Background:** Human cytomegalovirus (HCMV) is the first cause of viral congenital disabilities. There is a lack of therapies available to pregnant women. Letermovir showed good efficacy and low toxicity in vitro and in CMV prophylaxis. We thus test this antiviral drug in a placenta model to assess toxicity and antiviral efficacy.

**Materials/methods:** We performed in triplicate toxicity and antiviral assays for efficacy (EC50) in various cell lines (MRC-5, ARPE-19, U373 and HUVECs) and in 1st trimester placental villi explants from CMV-seronegative women. Cytotoxicity (CC50) was checked using a range of concentrations from 0.5mM to 5µM, and a DMSO control. To evaluate placenta viability, we quantified β-HCG in explants supernatants at day 4, 7, 10 and 13-post treatment.

We infected placenta explants with fibroblastic or endotheliotropic strains: AD169, TB40E and VHLE (MOI of 1). After 5 days of infection, letermovir was added at concentrations of 0,4, 4, 6.1 and 40nM. We harvested explants at day 5 post-treatment and measured CMV viral load in villi by CMV/albumin quantification qPCR.

We associated LTV with different anti-HCMV compounds: Ganciclovir (GCV), Cidofovir (CDF), Foscarnet (FOS), Maribavir (MBV) and Aciclovir (ACV) and test the combinations in MRC-5, against AD169. Effect of combination [Synergism, additive or antagonism] was determined with Compusyn © software.

**Results:** LTV shows no toxicity in vitro at tested concentrations. EC50 was 0.92 nM against AD169 in MRC-5 cells, and 1.34 nM against TB40E in ARPE-19. In vitro associations, showed an additive effect with GCV, ACV and MBV, and a light synergy with CDF and FOS. The different associations showed no toxicity. We didn’t reach CC50 in treated placenta, neither in DMSO control placenta. Letermovir antiviral efficacy was dependent of placenta and viral strain: EC50 was 31 nM for AD169, 25 nM for TB40E and 11 nM for VHLE.

**Conclusions:** The good antiviral efficacy of low concentration of letermovir in placenta, although depending on viral strain is encouraging. Moreover, the molecule showed no significant toxicity at the tested concentrations. In vitro associations with conventional anti-HCMV therapies are promising for further trials in placental model, particularly for ACV which is well-tolerated during pregnancy.

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Public health impact of the introduction of a high dose quadrivalent inactivated influenza vaccine in France

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Background: Influenza epidemics are annually responsible for a substantial public health and economic burden especially in adults 65 years of age and older (seniors). The need for improved vaccines and higher coverage rate in this age group is a public health priority. A High Dose quadrivalent influenza vaccine (QIV HD) is currently being evaluated at EU level and should be approved in 2020 in France. The high-dose vaccine is supported by a substantial body of clinical and economic evidence demonstrating benefit over standard dose vaccines currently used in France. The objective of this study is to estimate the public health benefits associated with the introduction of QIV HD in France.

Materials/methods: A static decision tree model was used to compute influenza cases, general practitioner (GP) visits, hospitalizations, and deaths during one influenza season. The current situation – vaccination of seniors with QIV SD at 50% VCR was compared to two alternative scenarios: switching to QIV HD in seniors at the current VCR, switching to QIV HD in seniors and increasing VCR to the official target of 75%.

Results: Vaccinating seniors with QIV HD compared to QIV SD would prevent on average 57,208 influenza cases, 13,704 GP visits, 1,728 hospitalizations and 764 deaths each season compared to the current situation. Reaching a 75% VCR with QIV HD would prevent 204,012 influenza cases, 48,869 GP visits, 6,161 hospitalizations and 2,725 deaths each season compared to the current situation.

Conclusions: The introduction of QIV HD in France could have a substantial public health impact by maintaining the older adults healthy and active and relieving unnecessary clinical and socioeconomic burden from French healthcare systems.

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**Abstract 7075**

**Haemophilus influenzae/parainfluenzae as triggers of urethritis in men: risk factors and characteristics of this emerging problem**

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¹Hospital de La Princesa, Madrid, Spain

**Background:** Both *Haemophilus influenzae* and *Haemophilus parainfluenzae* are colonisers of the upper respiratory tract. Transmission of oropharyngeal commensal flora to the urethra via insertive oral sex is recognised as a mode of transmission of several pathogens including *Haemophilus spp.* The aim of this study was to describe the characteristics of the urethritis possibly caused by *H. influenzae/parainfluenzae*.

**Materials/methods:** A retrospective study with all positive urethral samples for *H. influenzae/parainfluenzae* isolated from adult men between January 2019 and September 2019 was performed. Those whose samples were requested from primary heath care centers (PHCCs) were excluded for the lack of enough information. The identification was made by MALDI-TOF and the antibiogram by disk diffusion.

**Results:** In that period the urethritis were: gonococcal 28% (n=136), non-gonococcal 72% (n=350). *H. influenzae/parainfluenzae* were isolated in 13.7% (n=67). Finally we studied 30 patients (not requested from PHCCs) of which 3 had *H. influenzae* and 27 had *H. parainfluenzae*. From these strains of *Haemophilus* we studied the resistance to the following antibiotics: amoxicillin-clavulanic acid (10.3%), cefotaxime (0%), levofloxacin (13.7%), cotrimoxazole (24.1%).

To elucidate how many of these 30 patients actually had *Haemophilus influenzae/parainfluenzae* urethritis, those with more than one isolation and those without the characteristic symptoms of urethritis were excluded. Therefore, we considered that only 15 patients actually had *Haemophilus* urethritis. From these patients (average age 34 years old), we found the following symptoms: urethral discharge 40% (n=12), dysuria 36.6% (n=11), erythema 16.6% (n=5), meatus inflammation 6.6% (n=2). We also studied the next data:

<table>
<thead>
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<th></th>
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<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSM</td>
<td>5</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Risky oral sex practices</td>
<td>5</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>HIV</td>
<td>4</td>
<td>11</td>
<td>0</td>
</tr>
</tbody>
</table>

Conclusions: According to our results, the most frequent symptoms in patients with *Haemophilus influenzae/parainfluenzae* urethritis are urethral discharge and dysuria. A high percentage of the strains in our environment are susceptible to cefotaxime. As such, we conclude that third generation cephalosporins are a good option as an empirical treatment. Non-safe oral sex practices and MSM could be risk factors for acquire this opportunistic pathogen. More studies with larger sample size are needed to link *Haemophilus spp.* with urethritis.

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Abstract 7077

Trends of antibiotic consumption in German hospitals from 2015-2018

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Background: The Antibiotic Consumption Surveillance (AVS)-system has been built up by the national public health institute in cooperation with the national reference center for surveillance of nosocomial infections in order to serve the hospitals in monitoring antimicrobial consumption and to support antibiotic stewardship activities. Trends in antibiotic consumption from the years 2015 to 2018 are presented.

Materials/methods: The calculation of antibiotic consumption values is based on the ATC (Anatomical Therapeutic Chemical)/DDD (Defined Daily Dose) method of WHO (ATC/DDD-version 2019). Target value is the antibiotic consumption density (CD) expressed in DDD per 100 patient days (PD). The data of systemically applied antibiotics (A07AA, J01, J04AB02, P01AB01) are presented as medians and interquartile range. The analysis results rely on the data submission of general acute care hospitals from the years 2015-2018 and represent sequential cross-sectional analyses. Trend analysis was performed by linear regression and a p-value of <0.05 was considered as significant.

Results: From 2015 to 2018 the number of participating hospitals increased from 103 to 209 hospitals. The median of total antibiotic consumption shows a decrease from 55.1 DDD/100 PD in 2015 to 51.2 DDD/100 PD in 2018. Analysis of the different antibiotic groups reveals a significant decline of the CD of cephalosporins from 17.4 DDD/100 PD to 12.1 DDD/100 PD, which is primarily due to a decrease of second generation cephalosporins while third generation cephalosporins remained nearly constant. A decrease can also be observed for macrolides, fluoroquinolones, imidazoles, sulfonamides/trimethoprim and glycopeptides. In contrast, the group of penicillins shows an increase from 14.0 DDD/100 PD to 16.2 DDD/100 PD which includes a rise of penicillins combined with beta-lactamase inhibitor as well as small-spectrum penicillins (Table 1). The results have been confirmed by analyzing a subgroup of hospitals providing data continuously from 2015 to 2018.

Conclusions: The surveillance data show a slight decrease of total antimicrobial consumption in German hospitals primarily driven by a decline of the use of second generation cephalosporins, which is partly compensated by an increase of penicillins. The data may indicate an effect of antibiotic stewardship activities and encourage for further enforcement and continuation of efforts.

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Abstract 7078

**Synergistic activity of a three-drug combination against clinical isolates of Mycobacterium abscessus complex**

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**Background:** Infections by nontuberculous mycobacteria (NTM) are increasing, affecting mainly patients with chronic pulmonary disease, being bronchiectasis the most frequent. *M. abscessus* complex (MAB) and *M. avium* complex are the most common NTM in these patients. To start treatment is a difficult decision, since to differentiate between contamination and infection is complicated and the response to antibiotic treatment is not optimal. The guidelines recommend the use of combinations including 3-4 drugs. The objective of this study was to test the activity of two combinations (including two and three drugs) against clinical isolates of MAB using an *in vitro* microdilution model.

**Materials/methods:** Ten clinical isolates of MAB were recovered from patients with bronchiectasis. A previous drug sensitivity testing (DST) showed that 6 were susceptible to clarithromycin and 4 had inducible resistance. The isolates were tested against amikacin, tigecycline and clarithromycin, using Mueller-Hinton (+cat) broth. The range of concentrations were 16 to 0.125 µg/mL for amikacin and clarithromycin and 1 to 0.0005 µg/mL for tigecycline. The combinations tested were amikacin-tigecycline (AT) and amikacin-tigecycline-clarithromycin (ATC). The range of concentrations were the same than for drugs alone. Plates were incubated at 30°C and the MIC results were obtained at 3 days. MBC was determined by subculturing the 4 higher concentrations to MIC and incubating them 3 additional days.

**Results:** Table 1 shows the results. The combination AT shows a MIC90 lower than the MIC90 for individual drugs, although not significant (decreasing one dilution). The combination ATC obtained a MIC90 decreasing two dilution, then individual drug. This combination showed synergism for 7/10 isolates tested. MBC90 for AT and ATC increased one dilution with respect to the MIC90.

**Conclusions:** Both combinations showed better activity than drugs alone. The combination amikacin-tigecycline-clarithromycin showed *in vitro* synergism against *M. abscessus*, compared to the individual activity of the drugs.

Table 1. Activity of individual drugs and combinations against *M. abscessus*.

<table>
<thead>
<tr>
<th>DRUG</th>
<th>MIC50</th>
<th>MIC90</th>
<th>MBC50</th>
<th>MBC90</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin [A]</td>
<td>4</td>
<td>16</td>
<td>Nd</td>
<td>Nd</td>
</tr>
<tr>
<td>Tigecycline [T]</td>
<td>0.5</td>
<td>1</td>
<td>Nd</td>
<td>Nd</td>
</tr>
<tr>
<td>Clarithromycin [C]</td>
<td>0.5</td>
<td>1</td>
<td>Nd</td>
<td>Nd</td>
</tr>
<tr>
<td>AT</td>
<td>4/0.25</td>
<td>8/0.5</td>
<td>16/1</td>
<td>16/1</td>
</tr>
<tr>
<td>ATC</td>
<td>0.5/0.003/0.5</td>
<td>4/0.25/4</td>
<td>4/0.25/4</td>
<td>8/0.5/8</td>
</tr>
</tbody>
</table>

Nd: not determined

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Detection of the novel variant of NDM-type metallo-β-lactamase: significance of D130N amino acid substitution

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Abstract third-party references: The Russian Science Foundation (grant number 18-75-10117) supported this work

Background: To date 28 variants of NDM-type carbapenemase have been identified. NDM-type metallo-β-lactamase (MBL) positive Klebsiella pneumoniae isolate 1970_kpn was recovered from the urine of male patient in oncology center. Molecular analysis presented in the current study revealed the new variant of NDM-type metallo-beta-lactamase.

Materials/methods: The isolate 1970_kpn was sequenced on Illumina MiSeq platform (NexteraXT libraries, 300-bp paired-end reads), followed by de novo assembly using the SPAdes v.3.10.0 algorithm. The 1139 bp DNA fragment carrying NDM-type MBL and its own promoter was amplified, and cloned in pJET1.2 cloning vector. The chemical transformation was performed with XL10-Gold Escherichia coli strain. The same manipulations were performed with blaNDM-1 gene from validated clinical strain as a control. Sanger sequencing was used to confirm the cloned inserts. Antimicrobial susceptibility testing of transformants was performed by broth microdilution method according to the EUCAST recommendations to imipenem, meropenem, aztreonam, ceftazidime and piperacillin/tazobactam.

Results: NGS sequencing revealed that isolate 1970_kpn belongs to ST147 and carries new variant of NDM-type MBL. The contig with new blaNDM was deposited in GenBank - accession number MN624980. New blaNDM variant differed from blaNDM-1 by single amino acid substitution [AAS] – D130N [G→A]. Similar AAS is presented in NDM-7 and NDM-19. However, additional AAS are presented in above-mentioned enzymes: M154L – in NDM-7 and M154L + A233V – in NDM-19. Phenotypes of NDM-1 and new variant transformants are presented in Table and it is obvious that MIC’s of carbapenems against both transformants are similar. We can speculate that though D130N AAS did not provide significant evolutionary advantages it may be an important point in the emergence of new types of NDM. Alternative scenario of D130N acquisition as secondary mutation in NDM-type enzymes cannot be excluded.

Conclusions: D130N amino acid substitution plays significant role in the evolution of NDM-type MBL’s.

<table>
<thead>
<tr>
<th>Strain</th>
<th>Imipenem</th>
<th>Meropenem</th>
<th>Aztreonam</th>
<th>Ceftazidime</th>
<th>Piperacillin/Tazobactam</th>
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</thead>
<tbody>
<tr>
<td>1970_kpn</td>
<td>64</td>
<td>64</td>
<td>nd</td>
<td>256</td>
<td>nd</td>
</tr>
<tr>
<td>Transformant NDM-1</td>
<td>4</td>
<td>4</td>
<td>0.12</td>
<td>&gt;512</td>
<td>128</td>
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<tr>
<td>Transformant NDM-29</td>
<td>8</td>
<td>4</td>
<td>0.25</td>
<td>&gt;512</td>
<td>256</td>
</tr>
</tbody>
</table>

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Abstract 7081

Characterisation of ZIKV NS1 protein and development of ZIKV-specific monoclonal antibodies for rapid diagnosis

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Background: Zika virus (ZIKV), a member of the flavivirus, was declared a global public health emergency and causes microcephaly and other neurological diseases. Zika virus has a single-stranded positive-sense RNA genome and viral proteins consist of three structural proteins (capsid, membrane and envelope) and 7 non-structural proteins (NS1, NS2A, NS2B, NS3, NS4A, NS4B and NS5). Non-structural protein 1 (NS1) plays a crucial role in the early stage ZIKV infection and NS1 protein is a potential diagnostic marker.

Materials/methods: The gene coding for the NS1 protein of ZIKV was synthesized and cloned into bacterial expression vector. Recombinant NS1 proteins were purified, characterized and used for the development of monoclonal antibodies for rapid diagnosis of ZIKV. The purified recombinant ZIKV NS1 proteins were characterized by size-exclusion chromatography (SEC), circular dichroism (CD) spectroscopy and multi-angle light scattering (MALS). ZIKV-specific monoclonal antibodies were selected using dot blot assay with ZIKV NS1 protein expressed in mammalian cells.

Results: To validate the folding of ZIKV NS1 recombinant protein after purification, its secondary structure was determined by CD spectroscopy and its oligomeric state was confirmed by SEC and MALS. This indicates that the purified recombinant ZIKV NS1 protein is well-folded and forms a dimer in solution. A large number of monoclonal antibodies were produced and the binding of ZIKV NS1 and antibody was verified by dot blot experiments. We selected two monoclonal antibodies for lateral flow assay (LFA) and development of rapid diagnostic test (RDT) kit for point-of-care is in progress.

Conclusions: In this study, we purified recombinant ZIKV NS1 proteins and developed ZIKV-specific antibodies. Characterization of recombinant viral antigen protein and production of virus-specific monoclonal antibodies are useful for both the early diagnosis of viral infection and biophysical studies of viral antigens and virus-specific antibodies.

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Abstract 7082

Use of short- and long-read sequencing for the identification of antimicrobial resistance genes from pig oral fluid samples

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Background: Antibiotic resistance driven by antibiotic overuse and bacterial evolution is a global problem not only in healthcare, but also in agriculture and the meat industry. Detection of the genes causing resistance is key to prevent further spread and to treat patients and animals suffering from an infection in the most optimal way. Shotgun metagenomic sequencing (SMg) has the potential to detect all antimicrobial resistance genes (ARG) and the possible transmission of ARG through horizontal gene transfer between different individuals. Here we report the presence and expression of ARG in pig oral fluid (OF) samples.

Materials/methods: Nucleic acids were extracted using MagMAX nucleic acid purification Kits from OF samples obtained from ropes. For long read sequencing (LRS), libraries were generated using the Rapid Barcoding Kit and sequenced on a FLO-MIN106 R9.4 flow cell. For short read sequencing (SRS), libraries were generated using the KAPA HyperPlus kit and sequenced on a NextSeq. SRS reads were trimmed and assembled using CLC workbench. MinION data was basecalled with Albacore, demultiplexed with Porechop, assembled with Flye and polished twice with Medaka. Finally, the LRS assembly was polished with MaxBin2 and annotation using PATRIC.

Results: Overall, we detected 32 different ARG conferring resistance to 9 different antibiotic classes (Table 1). Five ARG were actively being expressed. A novel IncQ plasmid of 18156 bp containing the MCR 1.1 gene, insertion sequence 26 and the gene encoding for the HicAB toxin-antitoxin was detected. MCR was detected both on a DNA and RNA level, with metagenomic binning and BLAST identifying E. coli as the most probable host. Other ARG were detected on plasmids, phages and in the chromosome and were frequently flanked by mobile genetic elements.

Conclusions: We show the potential of combining long and short read sequencing to not only detect, but also characterize ARG directly from samples. In addition, OF sampling has the potential for broad microbial screening in pig farms on the herd level.

Table 1: AMRFinder results of sample S.3. Cutoffs: Coverage >80%, identity >95%. ARG present on multiple alleles are presented in bold and expressed ARG are represented in blue.

<table>
<thead>
<tr>
<th>Gene symbol</th>
<th>Class</th>
<th>Coverage of reference sequence (%)</th>
<th>Identity to reference sequence (%)</th>
<th>Multiple alleles</th>
<th>Expression (RNA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>aadA1, aadA27, aadA31, aadS, aph(3’)-Ia, aph(3’)-Ib, aph(6’)-Id</td>
<td>Aminoglycoside</td>
<td>100</td>
<td>99.62 - 100</td>
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<tr>
<td>blaACI, blaEC, blaROB, blaRTG, blaTEM-1, cfxA</td>
<td>Beta-Lactam</td>
<td>93.31 - 100</td>
<td>97.82 - 100</td>
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<td>mcr-1</td>
<td>Colistin</td>
<td>100</td>
<td>100</td>
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<tr>
<td>erm(B), erm(C), mph(E), mrs(E)</td>
<td>Macrolide</td>
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<td>catA3, floR</td>
<td>Phenicol</td>
<td>94.06 - 100</td>
<td>99.47 - 100</td>
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<td>sat4</td>
<td>Streptomycin</td>
<td>100</td>
<td>100</td>
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<td>Sulphonamide</td>
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<td>99.12</td>
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<td>Tetracycline</td>
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<td>Trimethoprim</td>
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</tr>
</tbody>
</table>

Presenter email address: l.schuele@web.de
Abstract 7083

**Changing the hospital microbiome: a cluster-randomised controlled trial to analyse the influence of environmental cleaning on hospital-acquired infections using disinfectant, soap or probiotic agents**

Rasmus Leistner*1, Britta Kohlmorgen1, Jennifer Golembus1, Desiree Gruh1, Elke Lemke1, Bastian Raguse2, Gregor Zakonsky2, Petra Gastmeier1

1Charité Universitätsmedizin Berlin, Institute of Hygiene and Environmental Medicine, Berlin, Germany, 2Charité Universitätsmedizin Berlin, Charité Facility Management, Berlin, Germany

**Background:** Environmental cleaning is an important pillar of hospital infection prevention and control. However, in international and even national comparisons different substances are used for identical indications. Besides disinfecting agents and soap-based cleaning substances, a new type of agent was introduced recently: probiotic agents. In order to assess the effect of those different cleaning agents we designed an experimental study.

**Materials/methods:** From June 2017 to August 2018 we performed a 3-armed cluster-randomized-controlled trial. In each arm a different cleaning agent was employed in the routine maintenance cleaning (disinfection, soap, probiotic). The setting was the main building of Charité Universitätsmedizin Campus Mitte including 18 wards of different non-ICU disciplines. A hospital-acquired infection (HAI) was diagnosed if a patient had a clinically relevant pathogen in a microbiology specimen and fulfilled the criteria of CDCs HAI definition. The latter was based on the review of the patients’ files.

**Results:** Altogether, we analyzed about 17,702 patients (between 5,905 and 6,127 in each arm) with similar underlying diseases, age and gender in each arm. The hand hygiene compliance on all wards was between 50% and 66%. We found an overall HAI incidence of 1.7% [1.9% for probiotic cleaning, 1.5% for disinfection cleaning and 1.6% for soap-based cleaning]. The 95% confidence intervals of the three arms overlapped largely showing no relevant difference. The most common HAIIs were UTI [31.8%], BSI [22.6%], SSI [19.2%], LRTI [8.3%]. The most commonly detected pathogens were *E. coli* [32.8%], *S. aureus* [14.2%], *Enterococcus spp.* [32.8%], coagulase-negative staphylococci [8.8%], *Klebsiella spp.* [8.1%], *C. difficile* [6.4%], *P. aeruginosa* [4.1%]. There was no clinical detection of one of the used probiotic species (*Bacillus subtilis, Bacillus pumilus, Bacillus megaterium*).

**Conclusions:** In this RCT the measured rate of hospital-acquired infections did not depend on the agent that was used for environmental cleaning. However, each cleaning agent offers different advantages that could trigger their deployment.

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**Abstract 7084**

**Enterococcal bacteraemia: epidemiology, clinical characteristics and causes of inappropriate treatment**

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**Background:** The frequency of enterococcal blood stream infections is rising due to the increasing aging and comorbidities prevalence among general population.

The aim of this study was to assess the epidemiological and clinical characteristics and outcomes of enterococcal blood stream infections (E-BSI) and to evaluate the causes of inappropriate empirical antibiotic treatment (EAT).

**Materials/methods:** Design: Observational retrospective study. Setting: Acute care hospital. Period: January 2017-December 2018. Patients: All consecutive EB-foci were included. The EAT appropriateness was evaluated (appropriate EAT was defined as the use of an antibiotic with in vitro activity). Variables: demographic and clinical characteristics, appropriateness of EAT and outcomes.

**Results:** Eighty-two E-BSI were identified, representing 7.2% of global BSI episodes, 40 (48.8%) caused by *E. faecalis* and 42 (51.2%) by *E. faecium*. Median age was 68y, 60 (73.2%) cases were men. Median Charlson index was 2. Ten (12.2%) E-BSI were community-acquired, 39 (47.6%) hospital-acquired and 33 (40.2%) health-care related. The most prevalent sources of infection were urinary (20 [24.4%]) and abdominal-biliar (34 [41.5%]). In-hospital mortality was 28%.

We compared E-BSI that received appropriate-EAT (35 [42.7%]) with those with inappropriate-EAT (47 [57.3%]). Urinary focus (13 [34.3%] vs 8 [17%], p=0.07), Pitt Index >3 (5 [14.3%] vs 1 [2.1%], p=0.06) and control of the infectious focus (39 [82.9%] vs 28 [59.6%, p=0.03) were more common among patients with appropriate-EAT, whereas the identification of *E. faecium* (12 [34.3%] vs 30 [63.8%], p=0.008), vascular focus (5 [10.3%] vs 0, p=0.07), oncologic patients (8 [17%] vs 1 [2.9%, p=0.07) and continuous bacteremia (6 [13%] vs 1 [2.9%, p=0.01) were more frequent among patients with inappropriate-EAT. There were no differences in duration of antibiotic treatment, days of hospitalization or in-hospital mortality.

**Conclusions:** Almost one third of patients with E-BSI dies during admission. E-BSI are mostly health-care related. More than a half cases are produced by *E. faecium*. The risk of inappropriate-EAT was higher among patients with E-BSI due to *E. faecium*, in oncologic patients and in those with vascular focus. It is important to identify patients at risk of receiving inappropriate-EAT.

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Colistin hetero-resistance in Acinetobacter baumannii blood isolates
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Background: Colistin is used as drug of last resort for the treatment of infections caused by multidrug-resistant Gram negative bacteria. Together with the increased usage, colistin resistance and heteroresistance (HR) have been described in Acinetobacter baumannii. The inability to detect HR by routine diagnostic testing results in strains being misclassified as susceptible.

The aim of this study was to evaluate the presence of resistance and heteroresistance to colistin in A. baumannii blood isolates.

Materials/methods: A total of 169 A. baumannii blood isolates recovered from hospitalized patients between January 2014 and April 2018 were included in the study. Minimum inhibitor concentrations (MICs) were determined by broth microdilution method (BMD). For detection of HR, population analysis profiling (PAP) was applied. For investigation of colistin HR, we selected either the isolates which colonies were observed within the inhibition zone of colistin gradient test (n=7) [Etest, BioMérieux, France] or the ones with colistin MICs ranging from 1 to 2 μg/ml (n=68) Heteroresistance was considered if the antibiotic concentration exhibiting the highest inhibitory effects was at least 8-fold higher than the highest noninhibitory concentration.

Results: Among 169 A. baumannii blood isolates, 48 isolates (28.4%) were found as resistant to colistin by BMD method. The overall incidence of colistin heteroresistance was 27.2% (n=46). HR detected in %55.8 (n=29) of 52 isolates which had colistin MICs of 1 μg/ml and %76.2 (n=16) of 21 isolates which had colistin MICs of 2 μg/ml.

Conclusions: In this study, we found high HR incidence among colistin susceptible A. baumannii blood isolates. The frequency of HR was MIC dependent. The number of solates demonstrating heteroresistance increases with increasing colistin MICs.

The rates of colistin HR can vary according to the center, isolation source and treatment of colistin. Therefore investigation of HR is very important for understanding of clinical implications of this phenomenon.

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Cross-reactivity of antigenic enterococcal proteins against *Staphylococcus aureus* for the development of a vaccine to fight Gram-positive ESKAPE pathogens

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Abstract third-party references: Supported by European Union’s Horizon 2020 research and innovation programme for funding work on this topic under the Marie Skłodowska-Curie grant agreement BactiVax No. 860325

**Background:** The ESKAPE bacteria are pathogens of great clinical concern. These bacteria are major causes of nosocomial infections worldwide being able to escape the bactericidal action of many antimicrobial agents. Despite efforts targeted at these organisms, few novel antimicrobials are available, and therapeutic options remain limited. Therefore, non-antibiotic alternative treatments such as vaccines are valuable approaches to fight these diseases. Gram-positive ESKAPE pathogens (*i.e.* *Enterococcus faecium* and *Staphylococcus aureus*) possess similar components in their cell wall envelope that could be targeted by these immunotherapies. We have previously described cell-wall associated *E. faecium* proteins able to raise opsononic and protective antibodies against enterococci1–3 especially *Enterococcus faecium*, are well-known pathogens of hospitalized patients and are frequently linked with resistance against multiple antibiotics, which compromises effective therapy. Rabbit immune serum raised against heat-killed *E. faecium* E155, a HiRECC clone, was used in an opsonophagocytic assay, an inhibition assay and a mouse bacteraemia model to identify targets of opsonic and protective antibodies. Serum against whole heat-killed bacteria was opsonic and recognized a protein of about 72 kDa that was abundantly secreted. This protein, identified as SagA by LC-ES-MS/MS, was expressed in *Escherichia coli* and purified. Rabbit serum raised against the purified protein showed opsonic killing activity that was inhibited by almost 100% using 100 µg purified protein ml⁻¹. In this study, we evaluated antibodies targeting these immunogenic *E. faecium* proteins for their ability to cross-react with *S. aureus*.

**Materials/methods:** We performed *in silico* analysis to determine whether the previously immunogenically characterized *E. faecium* proteins have homologies in *S. aureus*. In addition, *in vitro* assays mimicking the protective immune responses were performed to determine if antibodies directed against the selected proteins mediate opsonophagocytosis of *S. aureus*. To this end, sera before and after immunizations with the proteins were compared in opsonophagocytic assays (OPA).

**Results:** Bioinformatic analysis showed that, previously characterized *E. faecium* proteins have homologies between 36 and 74% in *S. aureus*. The zinc ABC transporter substrate-binding lipoprotein (AdcAₕ), low-affinity penicillin-binding 5 (PBP5), manganese ABC transporter substrate-binding lipoprotein (PsaAₕ), peptidyl-prolyl cis-trans isomerase (PpiC) and secreted antigen A (SagA) proteins were selected to be tested in OPA. Sera raised against three out of the five selected proteins (*i.e.* AdcA, PpiC, and SagA) showed more than 40% killing activity against different *S. aureus* strains.

**Conclusions:** AdcAₕ, PpiC, and SagA are promising protein antigens that could be used alone or conjugated to bacterial polysaccharides to develop a vaccine against the Gram-positive ESKAPE pathogens. Currently, the protective efficacy of the antibodies against *S. aureus* is being tested. Moreover, identification of the specific cross-reactive epitopes could lead to a more potent formulation.


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Abstract 7093

Evaluation the presence of leukocytes and bacterial communities of sputum from cystic fibrosis patients

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Abstract third-party references: Supported by: INPRA (Instituto Nacional de Pesquisa em Resistência Antimicrobiana), FIPE/HCPA

Background: Cystic Fibrosis (CF) is a recessive genetic disease, which affects mainly the respiratory tract of patients causing chronic and persistent bacterial infection of the airways. The lungs of CF patients can be colonized by a complex of microbial communities. It is consider that the composition of these communities may be relate to the CF lung disease progression. The aim of this study was to correlate the diversity of the bacterial communities with the presence or absence of leukocytes in sputum samples from CF patients.

Materials/methods: In order to evaluate the microbiome of the sputum of the CF patients we performed 16S rRNA sequencing using the Illumina MiSeq platform. Eleven CF sputum were submitted to DNA extraction with QIAamp DNA Mini Kit (QIAgen, Valencia CA), with proteinase K pre-treatment (60 minutes at 56°C), followed by bead-beating with zirconia/silica beads in a FastPrep 24 5G system (Qbiogene, CA), for 10 seconds at 6.0 m/sec (repeated 3 times). The 16S rRNA gene library was prepared according to 16S Metagenomic Sequencing Library Preparation Illumina protocol, using V5V6 region. A set of sputum was evaluate in triplicate in order to evaluate the reproducibility of the technique. The presence or absence of leukocytes was evaluate using a differential slide counting of sputum smears stained with May-Grunwald-Giemsa. Alpha diversity measures were calculate based on OTU counts rarefied to the minimum sample size.

Results: The triplicate analysis presented homogeneous results indicating reproducibility of our methods for DNA extraction, amplification and sequencing. The metagenomics analysis indicated that the microbiome profile is particular of each patient. It was also possible to observe that the absence of leukocytes was associated to the heterogeneity of the sputum microbial community. In fact, the less diverse bacterial communities were related to an increase number of leukocytes \( p= 0.004329 \).

Conclusions: This study results indicated that the presence of leukocytes in a sputum sample are directly correlate to a homogeneous bacterial community. Further studies are necessary to evaluate other inflammatory markers, which will give a better understanding of the relationship between bacterial infection and host responses in CF patient.

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Abstract 7094

Rapid distinction of capsulated Acinetobacter baumannii using a density gradient method

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1National Laboratory for Antibiotic Resistance and Investigation of Outbreaks in Medical Institutions, Ministry of Health, Israel; National Institute for Antibiotic Resistance and Infection Control, Ministry of Health, Israel, Tel-Aviv, Israel, 2Sackler Faculty of Medicine, Tel Aviv University, Ramat-Aviv, Israel, Tel-Aviv, Israel

Background: Gram-negative bacterial capsules are associated with hypervirulence and overproduction of extracellular polysaccharide matrix, resulting in a mucoidic phenotype. Capsule production confers antiphagocytic and antibacteriolytic activity and immune evasion. Recently, fatal clinical cases involving capsulated carbapenem-resistant A. baumannii (CRAB) were reported in Israel. A rapid screening tool to identify capsulated isolates is needed. We present a simple method to distinguish A. baumannii based on capsule size.

Materials/methods: The sample consisted of 46 CRAB clinical isolates: 21 mucoid and 25 non-mucoid. Mucosity was determined by visual inspection after overnight incubation at 35±2°C on blood agar. Our method is based on migration of bacterial cells through a gradient matrix composed of colloidal silica particles of 15–30nm suspended in phosphate buffer saline. To determine the optimal number of layers and the silica concentrations (density of each layer) needed to obtain separation of capsulated from non-capsulated isolates, several combinations with a range of concentrations (20-80% V/V) were evaluated. Each test was performed by centrifugation of an aliquot (600µl) of the bacterial culture for 30 minutes at 3,000xg. Results were read by visual inspection. To eliminate subjectivity, we normalized a quantitative value (Rt-OD600) based on the ratio of optical density values (at 600nm) of the top and bottom layers. Capsule thickness was confirmed for five isolates by transmission electron microscopy and lipopolysaccharides (LPS) quantification. A highly mucoid (string test positive) Klebsiella pneumoniae was used as a positive control and a non-mucoid A. baumannii (ATCC19606) as a negative control.

Results: A set of two layers with silica concentrations of 30% (upper layer) and 50% (bottom layer) V/V was optimal. Twenty-three of the 46 isolates migrated to the lower layer (Rt-OD600 range: 0.0-1.5), while the other 50% remained in the upper layer (Rt-OD600 range: 4.2-75.9). Two isolates with a non-mucoid phenotype by visual inspection were detected as capsulated. Mean capsule thickness was 58±2nm for non-mucoid isolates and 103±20nm for mucoid capsulated isolates. ATCC19606 had no visible capsule. LPS concentration was 2.20ng/10⁸CFU for non-mucoid isolates, 2.22ng/10⁸CFU for mucoid isolates, and 1.92ng/10⁸CFU for ATCC19606.

Conclusions: We validated a rapid tool to screen for the presence of capsulated CRAB.

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Is there any association between microbiological variables and toxigenic *Clostridioides difficile* infection (CDI) in a tertiary hospital?

Ledicia Alvarez Paredes¹, Cristina Labayru Echeverría¹, María Andrés Franch², María Ángeles Mantecón*¹, Cristina Losa Pérez¹, María Ortega Lafont¹, Eleda Coletta¹, Gregoria Megías Lobon¹

¹Hospital Universitario de Burgos, Burgos, Spain

**Background:** According to several studies, specific microbiological factors can be related to poor outcome in CDI patients. The objective of the study was to analyze the documented microbiological factors and to assess its relationship with CDI.

**Materials/methods:** Between September 2013 and December 2018, patients >2 years old with unexplained and new-onset ≥3 loose stools in 24 h were included. Microbiological diagnosis of toxigenic strains was confirmed by real time PCR (Xpert® *C. difficile*) in stool samples. Microbiological risk factors associated to a severe episode or recurrence were analysed. Recurrence is defined as a relapse of CDI symptoms within 2 - 8 weeks of successful treatment of the initial episode. Clinical definition was categorised according to current guidelines. To assess possible differences between variables, Chi-square and U-Mann Withney were performed.

**Results:** 250 patients were included. The presence of binary toxin was detected in 58 (23%) of them. In 5 patients 027 ribotype was detected. Association between toxin B Ct (cycle threshold) and recurrence was found to be statistically significant. Additionally, when Ct were categorised according with a multicenter study (*Reigadas et al, Anaerobe. 2019 Jul 26:102079*), the association remained. (Table 1).

**Table 1**

<table>
<thead>
<tr>
<th>Binary toxin (n/total (%))</th>
<th>Initial episode, non-severe¹</th>
<th>Initial episode, severe¹</th>
<th>p-value</th>
<th>Recurrence</th>
<th>Non-recurrence</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>40/179 (22%)</td>
<td>20/71 (28%)</td>
<td>7/23 (30%)</td>
<td>0.331</td>
<td>41/195 (21%)</td>
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<table>
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<tr>
<th>Ribotype 027 (n/total (%))</th>
<th>Initial episode, non-severe¹</th>
<th>Initial episode, severe¹</th>
<th>p-value</th>
<th>Recurrence</th>
<th>Non-recurrence</th>
<th>p-value</th>
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<tbody>
<tr>
<td>1/179 (1%)</td>
<td>4/71 (6%)</td>
<td>1/29 (3%)</td>
<td>0.024</td>
<td>2/244 (1%)</td>
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<td>0.287</td>
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<table>
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<th>Toxin B Ct (median/interquartile range)</th>
<th>Initial episode, non-severe¹</th>
<th>Initial episode, severe¹</th>
<th>p-value</th>
<th>Recurrence</th>
<th>Non-recurrence</th>
<th>p-value</th>
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<tbody>
<tr>
<td>179 (24.7/22.40,28.20)</td>
<td>71 (26.6/22.70,28.40)</td>
<td>23 (22.9/22,20,25.70)</td>
<td>0.483</td>
<td>104(24.95)</td>
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<table>
<thead>
<tr>
<th>Binary Toxin Ct (n/median/interquartile range)</th>
<th>Initial episode, non-severe¹</th>
<th>Initial episode, severe¹</th>
<th>p-value</th>
<th>Recurrence</th>
<th>Non-recurrence</th>
<th>p-value</th>
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<tbody>
<tr>
<td>38 (25.5/22.5,28.15)</td>
<td>20 (22.7/21.48,26.08)</td>
<td>7 (22.9/20,8,23.2)</td>
<td>0.229</td>
<td>39 (23.7/22,2,28.1)</td>
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<td>0.178</td>
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<table>
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<th>Toxin B Ct*</th>
<th>Initial episode, non-severe¹</th>
<th>Initial episode, severe¹</th>
<th>p-value</th>
<th>Recurrence</th>
<th>Non-recurrence</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>&lt;23.5 (n/%)</td>
<td>66 (37%)</td>
<td>25 (35%)</td>
<td>0.806</td>
<td>14 (61%)</td>
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<tr>
<td>≥23.5 (n/%)</td>
<td>113 (63%)</td>
<td>48 (65%)</td>
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<td>63 (32%)</td>
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<table>
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<tr>
<th>Binary toxin Ct*</th>
<th>Initial episode, non-severe¹</th>
<th>Initial episode, severe¹</th>
<th>p-value</th>
<th>Recurrence</th>
<th>Non-recurrence</th>
<th>p-value</th>
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<tbody>
<tr>
<td>&lt;23.5 (n/%)</td>
<td>15 (39%)</td>
<td>11 (65%)</td>
<td>0.258</td>
<td>6 (86%)</td>
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<tr>
<td>≥23.5 (n/%)</td>
<td>23 (61%)</td>
<td>9 (45%)</td>
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<td>17 (44%)</td>
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</table>

**Conclusions:** According to other authors, Ct, as a surrogate for the amount of toxin in the sample, could be a predictor of poor outcome in CDI patients. In our number of cases, toxin B Ct, might be a strong marker associated with recurrence. Microbiological factors will be included in robust scores that allow predicting recurrence.

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Abstract 7098

Antibiotic resistance pattern and prevalence in occupied Palestinian territories (oPt): evidence for guiding empiric antibiotic therapy

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Background: The emergence of carbapenem and colistin resistant Klebsiella pneumonia in the oPt has complicated patients’ treatment and increased the risk of health care associated infections. The study aimed to investigate the burden of ARO colonization and differences in prevalence among oPt districts.

Materials/methods: A retrospective analysis of the ARO surveillance program at Augusta Victoria Hospital (AVH) targeting nasal and anal cultures of newly admitted patients has been carried out. The target group comprised 968 adult and pediatric oncology patients admitted between January and August 2018. All patients referred from other hospital or with a history of ARO on prior admission were included. Samples were microbiologically processed according to the American Society for Microbiology standard guidelines to isolate bacterial pathogens. Antimicrobial resistance was identified following the Clinical and Laboratory Standard Institute standards. Statistical analysis (Odds ratios) compared the prevalence of colonization in samples from specific districts, focusing on the Gaza Strip (GS) and the West Bank (WB). Comparison between groups was performed using the Chi-Squared test and the corresponding P-value.

Results: Overall 2,708 screening swabs were collected (1265 nasal and 1443 anal samples), 36% of samples came from GS patients. Anal swabs’ analysis revealed that 71% of the GS samples and 55% of the WB samples were AROs. There was a significantly higher prevalence (P<0.001) of 3rd generation cephalosporin-resistant (3GCR) bacteria in GS 56% (95%CI 52-60) compared to 43% (95%CI 40-66) from WB, and a significantly higher prevalence (P<0.001) of carbapenem-resistant Enterobacteraceae (CRE) from the GS (5.3%, 95%CI 3.7-7.5) compared to 1.9% (95%CI 1.2-2.5) in WB. The odds of having 3GCRs (OR 1.7, 95%CI 1.4-2.1) and CRE (OR 2.9, 95%CI 1.6-5.4) in GS is significantly higher than WB (P<0.001). Nasal swabs indicated there was a significantly higher prevalence of methicillin-resistant Staphylococcus aureus (MRSA) in GS compared to WB samples (GS: 11.9%, 95%CI 9.1-15 versus WB: 7.3%, 95%CI 5.7-9.4; P=0.009).

Conclusions: These results suggest an overall elevated anal colonization of AROs (3GCS, CREs and MRSA) among GS patients seem to be at higher risk of having. Introducing antimicrobial stewardship programs will help in reducing the spread of resistant bacteria in the oPt.

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Spectrum overly broad and duration too long: an assessment of appropriateness of antimicrobial prescriptions in older patients admitted to an Australian tertiary teaching hospital

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Background: Elderly patients are at higher risk of infections and are prescribed more antimicrobials compared to younger patients. As the prevalence of infections, polypharmacy, and comorbidities increases, inappropriate antimicrobial prescribing also increases. We evaluated antimicrobial prescribing in elderly patients admitted to a South Australian tertiary hospital to identify targets for improvements in antimicrobial prescribing.

Materials/methods: Antimicrobial prescriptions in 280 patients admitted to the Geriatric Evaluation and Management Unit (GEMU) of The Queen Elizabeth Hospital between December 2017 and June 2018 were evaluated using a national antimicrobial prescribing survey tool. Appropriateness of antimicrobial prescriptions was assessed using Australian therapeutic guidelines recommendations.

Results: Of the 280 GEMU patients, 142 (50.7 %) were prescribed at least one antimicrobial. The mean age of antimicrobial-prescribed patients was 84.2 ± 7.0 years. 342 antimicrobial prescriptions were assessed for appropriateness. The most common documented indications for antimicrobials were cystitis (n = 118, 34.5 %), and empiric therapy for community-acquired pneumonia (n = 34, 10.8 %). Twenty-eight (23.7 %) cystitis, and 10 (27.0 %) community-acquired pneumonia prescriptions were assessed as inappropriate. Indications of 341 (99.7 %), and review or stop date of 337 (98.5 %) prescriptions were documented. The most commonly prescribed antimicrobials were amoxicillin-clavulanic acid (n = 67, 19.6 %), and cephalexin (n = 45, 13.2 %). The most common inappropriately prescribed antimicrobials were amoxicillin-clavulanic acid (n = 34, 50.7 %), and ciprofloxacin (n = 4, 36.4 %). Overall, 178 (52.0 %) prescriptions were compliant with guidelines, while 96 (28.1 %) were non-compliant. 261 (76.3 %) prescriptions were deemed appropriate, and 80 (23.4 %) inappropriate; with the main reasons for inappropriateness being incorrect duration (n = 129, 37.7 %), and prescription of overly broad-spectrum antimicrobials (n = 54, 15.8 %).

Conclusions: Usage of broad spectrum antibiotics for an excessive duration was common in this elderly patient cohort, with suboptimal adherence to national prescribing guidelines. A low threshold to empirically treat for infection without clear infective symptoms and diagnostic uncertainty were likely important drivers of inappropriate prescribing in this group; needs for antibiotics should be weighed against the risk of adverse effects and the development of antibiotic resistance.

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Impact of the inpatient infectious disease consultations at a tertiary care university hospital

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Background: The purpose of this study is to report the value of infectious disease consultation in the inpatient setting.

Materials/methods: This is a prospective cohort study that took place in a tertiary care university hospital. During the period from April to June 2016, 224 cases of patients receiving antibiotics in the hospital with the request of an infectious diseases' consultation, were evaluated. The following variables were assessed: the referring department, purpose of the consultation, the antibiotic used before the infectious diseases consultation was requested, the antibiotic modifications (changing the type, dose or range of the antibiotic when applicable), the duration of antibiotic use (decreased or increased), whenever the antibiotic usage was switched to a mono or bi-therapy.

Results: The most frequent requesting departments were oncology (23.2%) and urology (21.4%). The purpose of the consultations was diagnostic (29%), therapeutic (41%), both diagnostic and therapeutic (21%) and prophylactic (9%). An infectious diseases consultation was given at a rate of 4.9 consultations per 100 hospitalized patients. Consequently, there was no indication for the antibiotic treatment in 11.6% of cases, antibiotherapy was discontinued in 14.7% of cases and modified in 25.4% of cases. Adjusting the antibiotic dosage was done in only one case. Carbapenem antibiotics were discontinued in 31.6% of cases and Quinolones discontinuation accounted for 22.7% of cases. Prolonging or shortening the duration of antibiotherapy was carried in 7 and 13 cases respectively. Changing the treatment to a monotherapy was performed in 54.1% (13 out of 24 cases). Antibiotic was already started in 132 cases (59%) before an ID consultation was requested.

Conclusions: Infectious disease consults contributed to the optimization of the diagnostic and therapeutic approaches for suspected or established infections in hospitalized patients. Furthermore, the de-escalation and interruption of the antibiotherapy are essential to reduce bacterial resistance.

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Clinical management of serious infections attributable to carbapenem-resistant Gram-negative pathogens in Spanish hospitals

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1Vall d’Hebron University Hospital, Barcelona, Spain, 2Marqués de Valdecilla University Hospital, Santander, Spain, 3University Hospital La Paz, Madrid, Spain, 4Hospital Universitaria y Politécnica de La Fe, Valencia, Spain, 5Hospital Universitario La Coruña, La Coruña, Spain, 6Merck Sharp & Dohme, Madrid, Spain, 7IQVIA Real World Solutions, Barcelona, Spain, 8Merck & Co., Inc., Kenilworth, NJ, United States

Background: The treatment of Gram-negative (GN) infections is a major and growing challenge as bacteria become increasingly resistant to commonly used antibiotics. The objective of this study was to characterize the clinical management of patients diagnosed with complicated urinary tract infections (cUTI), complicated intra-abdominal infections (cIAI), or hospital-acquired/ventilator-associated bacterial pneumonia (HABP/VABP) due to carbapenem-resistant (CR) GN bacteria in Spain.

Materials/methods: Hospitalized adults with a diagnosis of cUTI, cIAI, or HABP/VABP caused by CR GN pathogens from February 2015–July 2017 were consecutively enrolled from five hospitals in Spain (all >600 beds). Patient characteristics, medical history in the year prior to index hospitalization, and treatment patterns were abstracted from patient records in a retrospective chart review.

Results: 100 patients were included: mean age 65.9 years, 70% male. In the year before index admission, over half (52%) received antibiotics, most frequently penicillins (n=35, 67.3%), 58% were previously admitted to hospital, and 57% underwent invasive procedures. Most index infections were hospital-acquired (71%) and the most common index infections were HABP/VABP (47%), cUTI (42%), and cIAI (6%). K. pneumoniae was most frequently implicated (51% of patients) followed by P. aeruginosa (44%). 63 isolates were tested for carbapenemase type (isolates could be tested multiple times); 45 (71.4%) were OXA-producers, 3 (4.8%) VIM, and 15 (23.8%) ‘other’. The most common therapies given immediately after culture collection were carbapenems (21%), penicillins (15%), and macrolides (8%). Immediately prior to susceptibility results the most common were carbapenems (41%), colistin (20%), aminoglycosides (19%), and penicillins (19%). After test results were available, patients received carbapenems (41%), colistin (28%), and aminoglycosides (27%). Treatment patterns for patients receiving carbapenems at any timepoint (n=57) are shown in Figure 1.

Conclusions: Carbapenems are frequently used to treat cUTI, cIAI, HABP/VABP caused by CR GN bacteria in Spanish hospitals. Carbapenem use, particularly in combination with other agents, persists after confirmation of carbapenem resistance. New agents which restore bacterial susceptibility to carbapenems will support this prescribing behavior and provide an alternative to colistin use, which was seen to increase over the course of the treatment period.

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Abstract 7108

**Microdiversity of Enterococcus faecalis isolates from infective endocarditis**

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**Background:** Infective endocarditis (IE) due to *Enterococcus faecalis* are severe infections which relapse in almost 10% of cases, despite effective antimicrobial therapy. We recently hypothesized that treatment failure could be linked with the selection of isolates lacking the virulence factor Ebp. Ebp is a protein belonging to microbial surface component recognizing adhesive matrix molecules, and is an important target of the host’s immune system. For that reason, deletion of Ebp may be involved in immune evasion. In order to evaluate the frequency Ebp deletions in IE, we analyzed the microdiversity within 5 heart valves from patients with IE due to *E. faecalis*.

**Materials/methods:** Five heart valves from patient with *E. faecalis* IE were inoculated onto Polyvitex agar plates for 48h under aerobic, anaerobic and microaerophilic atmospheres. A total of 9 isolates (3 for each condition) per patient were selected according to the macroscopic aspect. The resulting 45 isolates were sequenced by Illumina. We analyzed the sequence type, the resistance and virulence genes (Resfinder and VFDB) of the isolates. Moreover, we searched for SNPs and large deletions between all pairs of isolates among each patient using Breseq.

**Results:** All isolates from each patient belonged to the same ST. However, the precise comparison of the isolates identified differences ranging from a few SNPs to large deletions of thousands of bases particularly for two patients. As expected, we found a 15 000 bp deletion involving the virulence factor ebpA/B/C and srtC into 2 of 9 isolates from a first patient. We also detected a deletion of more than 40 000 bp which probably results from a phage excision into 1 of 9 isolates in a second patient. Interestingly, the genetic analysis of this phage showed the presence of the *pblA* and *plbB*-like genes implicated in adhesion to human platelets.

**Conclusions:** Although poorly described, the bacterial microdiversity seems to be frequent during IE due to *E. faecalis*. The deletion of important genetic determinants such as ebp that we previously observed or other determinants such as gene *pblA* and *plbB*-like genes involved in adhesion to human platelets could allow immune evasion and facilitate IE relapses.

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Abstract 7109

Genomic characterisation of CTX-M-15/DHA-1/OXA-48-producing Klebsiella pneumoniae of ST15/ST11/ST307 lineages from companion animals in France

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Background: Dissemination of multi-drug resistance (MDR) is a worldwide problem in both human and veterinary medicine. Among MDR bacteria, WHO considered extended spectrum β-lactamase (ESBL)-producing Klebsiella pneumoniae as a major global concern. Recently, ESBL- and carbapenemase-producing Enterobacterales have been increasingly isolated from companion animals, stressing their potential role as a reservoir for humans. In this study, molecular features of ESBL- and carbapenemase-producing K. pneumoniae isolates recovered from companion animals in France were investigated.

Materials/methods: Between 2010 and 2018, 116 K. pneumoniae isolates collected in France from diseased companion animals (mostly dogs (n=65) and cats (n=35)) were included in the study based on phenotypic ESBL isolation/testing. Antimicrobial susceptibility was tested using disk diffusion. Clonal relatedness was assessed by PFGE and Multi-Locus Sequence Typing (MLST). ESBLs and carbapenemases genes were detected by PCR and sequencing. S1-PFGE, Southern blotting and PCR-based replicon typing (PBRT) were performed for plasmid characterization. For phylogenetic purposes, all isolates were whole-genome sequenced using the NovaSeq technology and genomic analyses were performed through appropriate bioinformatics tools.

Results: Among the 116 K. pneumoniae isolates analysed, 62 isolates (53.4%) carried the ESBL gene blaCTX-M-15. Most isolates harbouring blaCTX-M-15 belonged to the Sequence Type ST15 (n=17) or ST307 (n=11), while the remaining blaCTX-M-15-positive isolates showed a great diversity of STs. Three K. pneumoniae isolates belonging to ST15, ST48 and ST37 co-harboured the blaCTX-M-15 and blaOXA-48 genes. The AmpC β-lactamase gene blaDHA-1 was identified in 54 (46.5%) isolates, for which thirty-five belonged to ST11. Besides, nine ST11 isolates co-harboured the blaOXA-48 gene. Results from S1-PFGE showed that blaCTX-M-15 was mostly carried by IncFIIk plasmids, whereas blaOXA-48 was mainly harboured by IncR plasmids. The blaOXA-48 gene was systematically carried by IncL plasmids. Phylogenetic analysis using Illumina data is ongoing.

Conclusions: This study showed the predominance of two ESBL-producing K. pneumoniae lineages spreading in cats and dogs in France, i.e. ST15 blaCTX-M-15 and ST11 blaOXA-48. Notably, we also identified the emergence of the human-related ST307 blaCTX-M-15 K. pneumoniae lineage and the circulation of OXA-48-positive K. pneumoniae isolates.

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Abstract 7110

Extending the NeuMoDx CTNG test to liquid-based cytology specimens: a performance evaluation

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Background: Detection of infection using a variety of specimen types in symptomatic and asymptomatic subjects is critical to effectively combat the spread of Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) infection. The NeuMoDx CTNG Test is currently CE/IVD certified for use with neat urine and endocervical/vaginal swab specimens. The goal of this study was to demonstrate performance of the NeuMoDx CTNG Test in liquid-based cytology specimens. Effective implementation of the NeuMoDx CTNG Test in such specimens would enable rapid & effective screening of women during their routine Pap exam. Results of performance verification of the NeuMoDx CTNG Test in ThinPrep® liquid-based cytology specimens are presented here.

Materials/methods: A risk-analysis was performed considering the differential characteristics of cytology specimens, and specific analytical & clinical studies deemed essential to demonstrating the performance of the NeuMoDx CTNG Test in Thin Prep specimens were executed including Limit of Detection (LoD), interference testing, specimen stability on-board the system, and pilot method comparison. Testing was performed using 550 µL specimen volume.

Results: The NeuMoDx CTNG Test demonstrated an LoD of 20 EB/mL for CT and 5 cells/mL for NG in Thin Prep medium with excellent inclusivity across the 15 CT serovars and 20 NG isolates. The sensitivity of each target (CT or NG) was maintained in the presence of high target concentration (~1E6 cells/mL or EB/mL) of the other target (NG or CT) demonstrating the robustness of the assay. Turnaround time was only 60 minutes and specimens were stable for at least 8 hours on board the System. No adverse effect on the detection of low target levels was observed in the presence of common interfering agents. The included Sample Process Control was an excellent monitor of sample processing efficacy and demonstrated its ability to also monitor for inhibition in these specimens. Finally, the pilot method comparison study performed using a combination of clinical and contrived specimens demonstrated excellent correlation to the results obtained using the reference FDA-cleared assays (with ThinPrep specimen indication) for CT/NG.

Conclusions: The NeuMoDx CTNG Test was demonstrated to be effective for detection of CT and NG directly from Thin Prep specimens.

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Bezlotoxumab in real-life treatment of Clostridioides difficile infections in a tertiary centre in Spain

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Background: Recently the Spanish public health system has approved the use of Bezlotoxumab for CDI patients, who meet the following criteria: 1) Immunosuppressed patients (oncological, or transplanted), 2) patients with hypervirulent strains and 3) patients older than 65 years of age with one of the following: a) severe CDI episode (WBC count ≥15,000 cells/mm$^3$ or Cr ≥1.5 x baseline); b) previous episode in the last 6 months, or c) persistent diarrhea after 5 days despite adequate treatment. Our aim was to assess the use and effectiveness of the drug in real-life.

Materials/methods: Ongoing prospective study in a tertiary care center with a very active C. difficile program including a registry of cases and a bedside intervention in which all the cases are evaluated daily by an infectious disease specialist. Patients treated with Bezlotoxumab were compared to a cohort of 84 patients who survived a CDI, had risk of recurrence and were treated by our group before the drug was commercially available in our country. These control patients frequently received vancomycin tapering and sometimes with Fecal Microbiota Transplantation. Recurrence was defined as a second episode between 15-60 days after the initial episode.

Results: From January to October 2019, a total of 297 patients with CDI were evaluated and 20 (6.7%) met the Bezlotoxumab financing criteria of the public health system. Patients had a median age of 68.5 years and 18 (90%) were immunosuppressed {4 (20%) solid organ transplant recipients; 6 (30%) solid tumor and 3 (15%) cirrhosis}. As for CDI severity 2 (15%) were severe, 7 (35%) were severe-complicated and 10 (50%) were considered mild. Only one case (5%) was due to ribotype 027.

During the episode treated with Bezlotoxumab, 17 out of the 20 patients received vancomycin as concomitant treatment and 3 received fidaxomicin. Two patients treated with Bezlotoxumab died of non-related causes. When compared with the control cohort the recurrence rate was 3/18 (16.6%) vs 27/84 (32.1%), p=0.25

Conclusions: Preliminary experience with Bezlotoxumab in our institution was associated with a very good tolerance and a reduction in the incidence of recurrent episode of CDI.

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A new approach for the quantification of clinical samples viral load based on virtual qPCR standard curves

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Background: Quantification of clinical samples viral load in qPCR traditionally requires the presence of a calibrated standard curve in every run. The innovative V-Quant System (AB ANALITICA) allows the viral load quantification using a specific virtual standard curve (VSC), included in the AB V-Quant Software. The VSC is calculated based on dataset of standard curves and it is pre-loaded on software database. In this way, the user do not need to run standard curve. This approach permits to reduce costs associated with including standard curves on every qPCR run, increasing the number of available tests, and to save time during the plate set up and results analysis.

Materials/methods: V-Quant CMV device consists of a qPCR kit and the correlated software for the interpretation and quantification of Cytomegalovirus (CMV). 319 Samples (218 CMV positive and 101 CMV negative), previously identified with a reference IVD method or belonging to QCMD panels, were tested. The samples have been quantified in parallel using a real quantification standard included in the qPCR runs and by using the AB V-Quant Software. Furthermore, diagnostic sensitivity and specificity, Limit of Detection (LoD) and precision of the device have been evaluated.

Results: The quantifications of CMV loads obtained with the real standards have been compared with the quantification obtained with the virtual one. The mean difference stands around 0.1 Log10 copies/mL, which is far from the commonly recognized limit value of 0.5 Log10 copies/mL. As for the performances, the device shows a diagnostic sensitivity and specificity around 99 %, a LoD of 5 viral genome copies/reaction and a precision percent coefficient of variation below 5%.

Conclusions: The V-Quant System demonstrate to be a reliable tool for the quantification of clinical samples viral load without including the traditional quantification standards in qPCR runs by saving the diagnostic costs. Similar assays for other clinically relevant pathogens are under development.

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Global assessment of neonatal sepsis incidence and case fatality

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Abstract third-party references: World Health Organization

Background: Neonates are at major risk for sepsis, which is the common final pathway of death from infection. Data on sepsis incidence in this age group is scarce. We assessed the global burden of neonatal sepsis by updating and expanding a systematic review and meta-analysis (Fleischmann-Struzek Lancet Respir Med 2016).

Materials/methods: We searched 13 electronic databases for studies on the population-level incidence of neonatal sepsis. We included studies that used a clinical sepsis definition, e.g. the 2005 consensus definition (Goldstein Pediatr Crit Care Med 2005), or relevant ICD-codes. The search of the original systematic review was updated for studies published between 05/2016-05/2019 and complemented by a search targeting studies from low- and middle-income-countries (LMIC) published between 01/1979 and 05/2019. We performed a random-effects meta-analysis on sepsis incidence and case fatality and estimated between-study heterogeneity based on the I² statistic.

Results: 4,729 abstracts were identified, of which 18 met the inclusion criteria. Adding these studies to the 8 studies of the original review, we meta-analyzed 26 studies. The majority of these studies originated from middle-income-countries, predominantly from the South-East-Asian Region. We estimated a pooled incidence of 2876.9 [95% CI, 1924.3; 4280.5] neonatal sepsis, 1903.2 [979.5; 3665.4] early-onset sepsis (EOS) and 1026.7 [271.5; 3802.7] late-onset sepsis (LOS) cases per 100,000 live births. We observed large between-study heterogeneity. The pooled estimate for community-based studies was more than twice as high as for hospital-based studies. Stratified by WHO regions, we found that the highest pooled incidence of neonatal sepsis in the African Region was two-fold higher than in the Pan-American Region, where the lowest incidence was observed [5243.6 [2504.6; 10,650.6] vs. 2461.2 [857.1; 6859.6]/100,000 live births]. An estimated 16.4% [9.8%; 26.1%], 9.1% [2.1%; 32.5%] and 17.7% [10.3%; 28.7%] of neonatal sepsis, EOS and LOS patients died, respectively.

Conclusions: Although neonatal sepsis is common and often fatal, its incidence in most countries remains unknown. Further epidemiological research is needed to address this gap, particularly using community-based designs, as estimates from hospital-based studies seem to miss sepsis cases occurring outside the hospital and therefore, are likely to underestimate the burden of neonatal sepsis.

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Clinical outcomes in oncological patients with *Clostridioides difficile* infection in Catalonia: a cohort study

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**Background:** Oncological patients suffer high rates of *C. difficile* infection (CDI) due to the frequent presence of risk factors such as recurrent hospitalizations, immunosuppression, antibiotic use, chemotherapy and the use of enteral and parenteral nutrition. Data on specific risk factors and clinical outcomes of CDI in this group of patients are scarce. The aim of this study was to evaluate clinical outcomes (clinical cure, recurrence and mortality) in a cohort of oncologic patients with CDI in Catalonia.

**Materials/methods:** Prospective observational study in 28 hospitals participating in the VINCat program (Infection Control and Antimicrobial Stewardship Catalan Program), which represent 46% of all adult acute hospital beds. Cases were defined as oncological adult patients visited during 2018 in the participating hospitals who meet the case definition of CDI. Colonized and asymptomatic patients (even if they carried a toxin-producing strain), patients with previous CDI episodes or those admitted to specific convalescent and palliative care units were excluded. Comorbidities, CDI specific treatment and evolution at discharge and after 90 days were recorded for each case.

**Results:** During the study period 122 cases were included, 58.2% were male and the mean age was 71.6 years. After 90 days follow-up the evolution of cases was: 81 cases (66.4%) were cured; 17 cases (13.9%) had a recurrent CDI (rCDI), and 24 cases (19.7%) died. From the 122 cases, 2 (2.5%) developed megacolon and 3 (3.7%) required intensive care unit admission. The proportion of cure was higher when cases were treated with vancomycin vs metronidazole (78.1% vs 64.7%). From cases treated with metronidazole, those with active chemotherapy showed a statistical significant lower proportion of cure (47.6% vs 76.7%, p=0.033). No comorbidities present in cases were associated with a higher frequency of mortality or rCDI.

**Conclusions:** A fifth of the oncological patients presented an rCDI at 90 days. Metronidazole was clearly inferior to vancomycin in this population, especially in patients with active chemotherapy. Despite the lack of severity at the onset of the CDI, the mortality at the end of the follow-up was high, suggesting that the CDI has a great impact on the health status of oncological patients.

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Detection of unexpected emerging extensively drug-resistant bacteria: experience of a French university hospital, 2012-2018

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**Background:** One control measure to manage the spread of emerging extensively drug-resistant (eXDR) is based on early identification of carriers and spread evaluation from carriers by screening contact patients (CP). The incidence of colonization by eXDR has increased, and it is not unusual to detect in CP an eXDR different from those isolated in index patients. The objective of this study is to describe the frequency of detection of unexpected eXDR in a French university hospital.

**Materials/methods:** An eight-year prospective study was conducted in a French university hospital. Until November 2017, CP were those shared the same ward with the index patient for at least 24 h. Since December 2017, the definition was modified and patient was considered as contact if the index patient was not under additional precautions. Secondary case was defined by the discovery of the same bacterial species and resistance mechanism as the index case. Unexpected eXDR was considered if species or resistance mechanism were different from those in index case.

**Results:** Between 2012 and 2018, the number of eXDR carriers has increased 11-fold (table 1). The first case of unexpected discovery of eXDR occurred in 2015, followed by 4 cases in 2016, 4 in 2017 and 11 in 2018 (P<10<sup>-3</sup>).

**Conclusions:** The unexpected discovery of eXDR other than those being researched is a growing phenomenon. These data suggest a higher than expected dissemination of eXDR carrying and probably an underestimated prevalence in France. Further investigations are needed to confirm this epidemiological trend and to evaluate the efficacy of actual strategy to manage eXDR.

<table>
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<th>CP, n</th>
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<th>Probable secondary cases, n [%]</th>
<th>Unexpected eXDR in screened patients, n [%]</th>
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**In vitro activity of novel propionohydrazide derivatives BG-354 and KTU-341 against multidrug-resistant Candida auris**

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**Background:** Candida auris (C. auris) is an emerging multidrug-resistant fungal pathogen responsible for increasing morbidity and mortality worldwide. Increasing numbers of outbreaks caused by C. auris, limited treatment options, and emergence of resistance require urgent development of new therapeutics. We therefore aimed to investigate in vitro antifungal activity of novel propanohydrazide derivatives BG-354 and KTU-341 against clinical isolates of C. auris.

**Materials/methods:** Antifungal activity of BG-354 and KTU-341 was evaluated against a panel of C. auris (n=15) and C. albicans (n=5) isolates using broth microdilution methods as described by CLSI. Activity against C. auris biofilm integrity and viability was also evaluated using a crystal violet assay and measured by spectrophotometry.

**Results:** BG-354 and KTU-341 demonstrated antifungal activity against multi-drug resistant C. auris (n = 15) and pan-susceptible C. albicans (n = 5) isolates with EC_{50} of 5.38 µM and 5.89 µM, respectively. BG-354 and KTU-341 demonstrated selective antifungal activity against C. auris as measured by MIC (10.7 µM and 11.7 µM respectively) but showed no significant effect against C. albicans. Both BG-354 and KTU-341 demonstrated fungicidal activity with MFC of 10.7-21.4 µM for BG-354 and 23.4 µM for KTU-341. After 24 hour of incubation, BG-354 significantly reduced C. auris biofilm integrity in comparison to growth controls (OD_{570nm. 1.032 vs. 0.448, p<0.05}). More studies are needed better understand antimicrobial activity, safety, synergistic relationship, and therapeutic potency of propionohydrazide derivatives.

**Conclusions:** Novel propionohydrazide derivatives BG-354 and KTU-341 demonstrated favorable activity against multidrug-resistant C. auris making this class as selective and pathogen-directed antifungals.

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An epidemiological overview of intestinal parasitoses in a non-endemic setting: a comparison between Italians and immigrants from developing countries during the years 2011-2018

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Background: Intestinal parasites are now being diagnosed with increasing frequency in industrialized countries probably as a consequence of the globalization of the food supply, of the immigration/adoption from endemic regions, and of travels through the same areas.

This study reports the investigation of imported intestinal parasitoses in Parma, Italy, a non-endemic setting, during 2011-2018 with a comparison between those revealed in Italians and in immigrants from developing countries.

Materials/methods: In our laboratory, from 2011 to 2018, conventional diagnosis of intestinal parasitosis (microscopic examination of fresh/concentrated faeces and cultivation in Robinson’s medium) was performed on 20,978 faecal samples belonging to 13,596 patients, all presenting with the clinical suspicion of intestinal parasitosis; the foreigner patients included in the study were from developing countries, mainly from Sub-Saharan Africa. Real-time PCR assays for the differentiation of Entamoeba histolytica and E. dispar and for the detection of Dientamoeba fragilis were also used when clinical manifestation and/or risk factors for parasitic infections were reported, and/or when diagnostic stages of intestinal parasites were detected by microscopy.

Results: Intestinal parasitosis was diagnosed in 2671 patients (19.6%), about half of whom were immigrants from developing countries. For 15% of Italians and 36.2% of Foreigners at least one intestinal parasite was detected. The most common intestinal protozoa detected were Blastocystis hominis, D. fragilis and Giardia intestinalis, while the most prevalent helminths were Strongyloides stercoralis, Enterobius vermicularis, and Taenia saginata. A total of 204 (71%) helminthic infection was revealed in Foreigners. For 2.6% of Italians and 13% of Foreigners a mixed infection was found. The total of 663 mixed infections (co-infection by protozoa, helminths and/or by protozoa and helminths) detected, 380 were revealed in Foreigners.

Conclusions: The data presented confirm the importance of suspecting parasitic infections together with the use of appropriate diagnostic tools even in non-endemic areas, where, besides autochthonous intestinal parasites, imported ones are frequently diagnosed. The probability to reveal the presence of such agents increase also as a result of the high number of “forced migrants” coming during recent years from their origin countries afflicted by inadequate sanitation and poor hygiene conditions.

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Modulating the microbiota of the hospital environment by microbial cleaning: impact on infections and antimicrobial resistance

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Background: Healthcare–associated infections (HAIs) are a global concern, whose major causes include the persistent microbial contamination of the hospital environment, and the growing antimicrobial-resistance (AMR) of HAI-associated microbes. The control of contamination has been so far addressed by the use of chemical-based sanitation, which however does not prevent recontamination, have a high environmental impact and can select resistant microbes. Inspired by the studies on the human microbiome and by the recent acquisitions on the built-environment microbiomes, we set-up a microbial-based sanitation (MBS), testing the possibility to modulate the hospital microbiome by a biological approach based on competitive exclusion. Specific elimination of peculiar pathogens by bacteriophage application was also tested.

Materials/methods: MBS was tested in 10 healthcare settings, for 1-6 months, by substituting conventional chemical-based cleaning procedures with the microbial system. In the study including 6 Italian public hospitals and 5 Italian Universities the hospital bioburden and healthcare-associated infection (HAI) incidence were simultaneously analyzed for 18 months. Environmental contamination was examined by microbiological and molecular methods, including characterization of the resistome of the contaminating population. In parallel, rate of HAI onset and therapy costs were evaluated. The impact of bacteriophage addition on specific contaminants was also evaluated.

Results: Over 40,000 environmental samples were analyzed and about 12,000 patients surveyed. The MBS system was shown to induce a stable remodulation of hospital microbiota, obtaining a stable control of both bioburden (-80% pathogen load on treated surfaces compared to conventional disinfectants) and AMR (up to -99% of resistance genes in the residual contaminants). Microbiome modulation was associated with a significant reduction of HAIs (-52%) and of associated therapy costs (-75%). Bacteriophage treatment in addition to probiotic sanitation determined a further reduction (>90%) of targeted bacteria in less than 24 hours.

Conclusions: Collected data highlight the possibility to modulate hospital microbiota and suggest that microbiota remodulation can be associated with a consistent reduction of associated HAIs. The results thus suggest that such systems, based on the microbiome balance principles, might be considered as one of the tools for AMR and infection prevention and control.

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Abstract 7133

**Diagnostic performance of two novel semi-quantitative cryptococcal antigen assays**

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**Introduction:** Early cryptococcal disease can be detected via circulating antigen in blood before fulminant meningitis signs develop—where early antifungal therapy improves survival. Serum cryptococcal antigen (CrAg) titer predicts meningitis probability and outcome with fluconazole preemptive therapy. Two new semi-quantitative CrAg lateral flow assays have been developed but with undefined diagnostic performance.

**Materials/Methods:** Cryopreserved serum samples from 100 HIV+ Ugandans obtained as part of a prospective CrAg-screening cohort were tested in duplicate for cryptococcal antigen by the CrAg-SQ (IMMY) and CryptoPS (Biosynex) lateral flow assays. The tests were retrospectively run and read by two independent, trained readers. Inter-reader discrepancy was adjudicated by a third reader, as a tiebreaker. Diagnostic performance was measured using the FDA-approved CrAg LFA (IMMY) as a reference standard via McNemar’s test.

**Results:** Of 100 samples, 57 were CrAg+ by the CrAg LFA reference standard. By CrAg-SQ, 57 were positive, with 98% sensitivity (56/57) with 98% specificity (42/43) (P=.99). The CrAg-SQ false negative had a titer <1:5; while the false positive yielded a 1+ result. By CryptoPS, 53 were positive, with 88% sensitivity (50/57) and 93% (40/43) specificity (P=.34). The CryptoPS false negatives included samples with titers <1:5 (n=6) and 1:30 (n=1). The median CrAg titer values for the CrAg-SQ LFA at 2+ was 1:40 and at 3+ was 1:320. The median CrAg titer values for the CryptoPS at positive was 1:40 and at strong positive was 1:320. In assessing inter-reader variability, 14 incidents of reader discrepancy occurred for the CrAg-SQ (for grade of positivity) versus 10 incidents for CryptoPS. Qualitative reads were 97% concordant for CrAg-SQ and 96% concordant for CryptoPS.

**Conclusions:** The new semi-quantitative CrAg LFAs allow for a rapid estimation of titer level in easy-to-perform platforms, providing the potential to stratify clinical risk, and therefore determine clinical management. The CrAg-SQ demonstrated better qualitative sensitivity and specificity over CryptoPS in comparison to the reference standard. Both tests could delineate a low titer versus a higher titer [considering a 1:160 breakpoint]. The exact grade of CrAg-SQ does have some subjectivity with inter-reader variability; however, qualitative reads were generally concordant for both assays.

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**Abstract 7134**

**Risk factors for prosthetic joint infections caused by Gram-negative bacteria: experience at an infectious disease referral centre**

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**Background:** In recent years, a significant increase of prosthetic joint infections caused by Gram-negative bacteria (GNB-P JIs) has been described. Currently, in the absence of a pre-operative aetiological diagnosis, a broad-spectrum antimicrobial therapy is used for patients undergoing surgical treatment of P JIs, pending the results of intra-operative cultures. This strategy may lead to a widespread use of GNB-coverage, increasing resistance selections and costs.

The aim of our study is to identify the risk factors for GNB-P JIs, in order to select patients who would really benefit from an empirical GNB-coverage.

**Materials/methods:** Observational, single-centre, retrospective study (June 2010-December 2018) on patients at their first episode of hip or knee PJI, managed at a referral centre for P JIs in Italy.

**Results:** We enrolled 322 consecutive patients, 33 (10.2%) having a GNB-PJI. We found a trend toward increased incidence of GNB-PJI over time, that did not reach statistical significance (8.7% in 2011, 11% in 2012, 9% in 2013; 5% in 2014; 15% in 2015; 17% in 2016; 18% in 2017, 15% in 2018, p=0.48). A pre-operative synovial fluid culture was obtained in 110 patients (34%), and it was positive in 71 (64.5%); after surgery, 224 patients (69.5%) received a broad-spectrum antibiotic therapy with GNB-coverage.

At multivariate logistic regression analysis, an early infection [aOR 2.73, 95%CI 1.10-6.82, p=0.03] and the presence of a sinus tract both in early and delayed infections [aOR 2.46, 95%CI 1.14-5.33, p=0.03] were independently associated with GNB-P JIs.

**Conclusions:** To identify risk factors for GNB-PJI may reduce the use of empirical GNB-coverage when treating P JIs without a pre-operative aetiological diagnosis. GNB-PJIs are still uncommon, so large multicentre studies are urgently needed to address this issue.

<table>
<thead>
<tr>
<th></th>
<th>All patients (n=322)</th>
<th>GNB-PJI (n=33)</th>
<th>Others (n=289)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age [years] – median[IQR]</strong></td>
<td>66[55-73]</td>
<td>64[53-71]</td>
<td>66[55-73]</td>
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<tr>
<td><strong>Males</strong></td>
<td>165(51%)</td>
<td>19(58%)</td>
<td>146(50.5%)</td>
<td>0.71</td>
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<tr>
<td><strong>Charlson index – median[IQR]</strong></td>
<td>3[2-5]</td>
<td>3[1-5]</td>
<td>3[2-5]</td>
<td>0.40</td>
</tr>
<tr>
<td><strong>Hip prosthesis</strong></td>
<td>148(46%)</td>
<td>20(61%)</td>
<td>128(44%)</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>Timing of PJI</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early</td>
<td>41(12.5%)</td>
<td>8(24%)</td>
<td>33(11%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Delayed</td>
<td>250(78%)</td>
<td>22(67%)</td>
<td>228(79%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Acute late</td>
<td>31(9.6%)</td>
<td>3(9%)</td>
<td>28(10%)</td>
<td>0.91</td>
</tr>
<tr>
<td><strong>Clinical presentation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sinus tract</td>
<td>78(24%)</td>
<td>13(39%)</td>
<td>65(22%)</td>
<td>0.03</td>
</tr>
<tr>
<td><em>Rubor, tumor, dolor, calor</em></td>
<td>147(46%)</td>
<td>18(54%)</td>
<td>129(45%)</td>
<td>0.28</td>
</tr>
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<td>C-reactive protein [mg/dL]</td>
<td>1.81[0.56-5.02]</td>
<td>3[1.37-7.16]</td>
<td>1.69[0.55-4.49]</td>
<td>0.02</td>
</tr>
</tbody>
</table>

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Development of a ery-C recombinant protein-based ELISA approach for differentiating brucellosis infected cattle from vaccinated ones

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Introduction: Serological tests used for diagnosis of bovine brucellosis are usually depending on smooth lipopolysaccharides (S-LPS) as a diagnostic antigen for most of serological tests (mainly ELISA) which usually gives false positive reactions with sera of S19 vaccinated cattle. The eryC gene is absent in Brucella abortus S19 only but it is present and functional in all other Brucella strains. Aim: according to previous facts, this study aimed to develop and evaluate a diagnostic kit for accurate diagnosis of bovine brucellosis able to differentiate between vaccinated and infected cattle and exclusion of false positive cases. The present study evaluated antibody responses of brucellosis infected and S19 vaccinated cattle to purified recombinant EryC protein in an indirect enzyme-linked immunosorbent assay (I-ELISA) as an alternative diagnostic antigen.

Materials/methods: In this study, 114 samples of naturally infected, 78 sera from S19 vaccinated cattle and 25 sera samples from Brucella free cattle were used after screening with Rose Bengal test. Sera samples were tested with I-ELISA using S-LPS and periplasmic proteins as a coating antigen [a gold standard test] also with I-ELISA using ery-C protein as a coating antigen.

Results: The results revealed that in case of sera of naturally infected cattle, sero-positivity was 94.7%, 100%, 100% and 100% with EryC-ELISA, LPS-ELISA, periplasmic-ELISA and Rose Bengal test, respectively. Where in case of sera of S19 vaccinated cattle, all samples were negative when tested with EryC-ELISA while in case of LPS-ELISA, periplasmic-ELISA and rose Bengal test, the sero-positivity was 92.3%, 84.6% and 100%, respectively. Sera samples from Brucella free cattle react negatively with all types of coating antigens.

Conclusions: It could concluded that the EryC protein could be used in serological tests for diagnosis of bovine brucellosis and differentiation between infected and Brucella abortus S19-vaccinated cattle but further studies are demanded to be performed on large scale accompanied with bacteriological isolation to detect the sensitivity and specificity of this protein as a diagnostic antigen and also for validation.

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Comparative evaluation of the Phoenix and Vitek2 systems for ceftaroline-susceptibility testing in clinical isolates of methicillin-resistant Staphylococcus aureus (MRSA)

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Abstract 7138

Background: Ceftaroline (CPT) is a cephalosporin active against MRSA. Previous data suggest that the E-test® underestimates MIC values and that disk diffusion (both CLSI 30µg and EUCAST 5µg) performs poorly compared to broth microdilution (BMD), with categorical concordances (CC) of 51%, 55%, and 36%, respectively. This data make the evaluation of other methods necessary. The aim of the study was to compare CPT susceptibility testing determined by two automated systems, Phoenix-100™ (Becton Dickinson) and Vitek®2 XL (bioMérieux), with results from BMD in clinical isolates of MRSA.

Materials/methods: In vitro activity of CPT was evaluated in 320 clinical MRSA isolates collected between 1999-2018, in nine hospitals in Santiago, Chile. Identification was confirmed by MALDI-TOF MS. BMD was performed following CLSI-2019 guidance. Susceptibility for Phoenix-100™ and Vitek®2 was performed according to the manufacturer’s instructions, using the PMIC/ID 89 panel and AST-GP78 cards, respectively. CC, categorical agreement (CA), essential agreement (EA), minor errors (ME), and major errors (VME) were evaluated. Susceptibilities were analyzed using CLSI-2019 breakpoints.

Results: The MIC50/MIC90 by BMD was 2 μg/mL. No CPT-resistant (i.e. MIC >8µg/mL) strains were found, but 206/320 (64%) strains were categorized as susceptible dose-dependent (SDD) with an MIC between 2-4µg/mL (previously reported). For Phoenix-100™, the MIC50/MIC90 was 2µg/mL; 69/320 (22%) strains were classified as CPT-susceptible (MIC <2µg/mL), 218/320 (68%) as SDD (MIC = 2µg/mL) and 33/320 (10%) could not be cataloged, since the highest concentration of CPT included in PMIC/ID 89 panel is ≥4µg/mL. For Vitek®2, the MIC50/MIC90 were 0.5/2 µg/mL respectively, 192/320 (60%) strains were classified as CPT-susceptible and 128/320 (40%) as SDD. The CA, EA and mE between Phoenix-100™ and BMD were 81-98-19%, respectively. The CA, EA and mE between Vitek®2 and BMD were 64-98-30%, respectively. No ME and VME could be detected.

Conclusions: The Phoenix-100™ system showed good performance; however, the percentage of mE was unacceptable. Modifications of CLSI 2019 cut-off values did not allow the classification of 10% of the strains. Vitek®2 severely underestimated CPT MICs and its routine use in clinical MRSA isolates needs further evaluation.

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Abstract 7139

A comparative phenotypic study of aggregate versus non-aggregate Candida auris isolates

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Background: Candida auris, first reported in Japan in 2009, has recently emerged on five continents and it is considered a serious global health threat. Due to a particular persistence on a large range of surface types, this Candida species has been associated with outbreaks in healthcare settings.

Materials/methods: Candida auris isolates collected during an outbreak in Colombia were identified by MALDI-TOF analysis and ribosomal DNA (rDNA) gene sequencing targeting ITS1 regions. Aggregative and non-aggregative C. auris isolates were selected for a comparative phenotypic study including sterol composition, cell wall characterization, stress resistance, biofilm-forming capacity on catheter pieces and pathogenicity in a Galleria mellonella insect model.

Results: C. auris isolates with aggregating phenotype have a greater biofilm-forming capacity. This capacity is even higher if the medium contained glucose as in EUCAST method. In the latter medium, the biofilm formed by this phenotype is superior to that formed by C. albicans. Aggregating strains are more sensitive to heat stress while they are more resistant to osmotic shock. In contrast, there is no difference in sterol composition. Finally, in the in vivo Galleria mellonella model, aggregating phenotype isolates have a lower virulence than those of non-aggregating phenotype (Figure 1).

Figure 1: The virulence of Candida auris strains in Galleria mellonella larvae at 37°C. Non-aggregate (red) and aggregate (green) strains.

Conclusions: Our data suggest that using the Galleria mellonella infection model, non-aggregating C. auris strains exhibit higher pathogenicity which could be related to resistance to heat stress.

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Abstract 7141

Real-world treatment patterns observed in patients with carbapenem-resistant Gram-negative infections in Italian hospitals

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Background: Antibiotic resistance is highly prevalent in Italy. The increase in resistance has made the treatment of bacterial infections very challenging. The study aimed to describe the current clinical management of complicated urinary tract infections (cUTI), complicated intra-abdominal infections (cIAI), and hospital-acquired/ventilator-associated bacterial pneumonia (HABP/VABP), specifically infections attributable to carbapenem-resistant (CR) Gram-negative (GN) bacteria

Materials/methods: Four Italian hospitals participated in a retrospective chart review in which hospitalized adults with cUTI, cIAI, or HABP/VABP caused by CR GN pathogens between February 2015 and July 2017 were consecutively enrolled; their records were evaluated for baseline characteristic, medical history, and details of antibiotic treatment.

Results: 100 patients were included (the majority were male [64%], mean age: 64.1 years). In the 12 months prior to index admission, 57% had prior hospital admissions, 45% had prior invasive procedures, and 32% were treated with antibiotics, most commonly penicillins [n=24, 63.2%]. HABP/VABP was the most common infection type [56%], followed by cUTI [34%] and cIAI [10%]; the majority of index infections were hospital-acquired [78%]. Klebsiella pneumoniae was the most commonly isolated pathogen [66%]. Acinetobacter baumannii and Pseudomonas aeruginosa were detected in 23% and 12% of patients, respectively. 34 isolates [all K. pneumoniae] were tested for carbapenemases and all were found to be Klebsiella pneumoniae carbapenemase (KPC)-producers. Prescribing choices were evaluated immediately after culture collection [most common: carbapenems [19%], colistin [14%], and penicillins [14%]), immediately prior to susceptibility test results [carbapenems [44%], colistin [25%], and penicillins [17%]), and after test results were available [carbapenems [68%], colistin [61%], macrolides (16%), and aminoglycosides [16%]]. Carbapenems were typically given as part of combination therapy. Antibiotic treatment patterns for 67 patients who received carbapenems are presented in Figure 1.

Figure 1. Sankey diagram of treatment patterns for patients treated with carbapenems.

Conclusions: Carbapenem use was detected at every stage of the treatment period (pre- and post-susceptibility test results confirming carbapenem resistance), indicating the importance of this antibiotic class for the management of serious GN infections. The detection of KPC production in every tested isolate demonstrates that activity against this resistance mechanism should be considered when making treatment selections in Italy.

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Usefulness of serum as a non-invasive sample for the detection of Histoplasma capsulatum: comparative analysis of different diagnostic techniques

Leticia Bernal Martinez¹, Paula De La Cruz¹, Sara Gago¹, Laura Alcazar-Fuoli¹, María José Buitrago*¹

¹Carlos III Health Institute, Majadahonda, Spain

Background: A rapid, sensitive and specific method is essential for the diagnosis of histoplasmosis in laboratories with limited resources and also in regions that lack experience in the management of these patients. The diagnostic accuracy of different techniques using serum as a non-invasive sample has been evaluated. Techniques based on the detection of antibodies, antigens and DNA have been tested.

Materials/methods: Sera samples from patients with proven and probable histoplasmosis were analyzed (40). Four techniques were used. Histoplasma GM EIA test kit (IMMY, Palex), not used to date in serum, Platelia™ Aspergillus Ag (Bio-Rad), “ID Fungal Antibody System” kit (IMMY, Palex) and a Real time PCR method (RT-PCR) previously described (Gago et al., 2014). For Histoplasma GM EIA test kit, sera samples were pretreated and a cutoff of ≥0.2 ng/ml was used to determine positivity, according to the manufacturer´s recommendations.

Results: Analysis of the results was performed taking into account the clinical picture and the immune status of patients. Sensitivity of GM EIA test kit in patients with Aids and a disseminated disease was 94% and in immunocompetent patients was 66%. Detection of antibodies by ID antibody System was positive in 84% of immunocompetent patients and 68% HIV+ patients. Platelia™ Aspergillus Ag had a low performance in both groups (38% S in HIV+ and 21% S in HIV-) and finally RT-PCR obtained moderate results being more useful for immunosuppressed patients (47% S in HIV+ vs 26% S in HIV-).

Conclusions: i) Sera samples could be used to a rapid diagnosis of histoplasmosis but their performance depends on the clinical picture of the patient and the technique used. ii) GM EAI test kit seems to be a suitable option in disseminated disease. More validation studies are required. iii) The ID technique is useful to detect H. capsulatum antibodies in immunocompetent patients. iv) RT-PCR showed a moderate performance, being better option for the detection of histoplasmosis disseminated in HIV+ than in immunocompetent travelers. v) Further studies are warranted including control patients and patients with other invasive fungal infections to evaluate the specificity of these techniques and their usefulness.

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Abstract 7143

Molecular detection of mutations involved in *Helicobacter pylori* antimicrobial resistance in Ecuador

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Background: *Helicobacter pylori* (HP) infection is one of the most common chronic bacterial infections. Eradication of HP infection has been proven to reduce the incidence of gastric cancer. The efficacy of the HP eradication treatment has decreased dramatically because of antibiotic resistance. The most recent international consensus reports recommend the selection of treatment based on local resistance patterns, however, HP testing is rarely performed. In this study, we analyzed the prevalence of HP and main mutations involved in resistance.

Materials/methods: A total of 330 gastric biopsies of older than 18 years’ Ecuadorian patients were analyzed. PCR and sequencing were performed to amplify the regions *rdxA* (metronidazole [MTZ] resistance), *23S* ribosomal RNA (rRNA) [clarithromycin (CLA) resistance], *gyrA* (levofloxacin [LVX] resistance), *pbp1A* (amoxicillin [AMX] resistance) and *16S* rRNA regions (detection of infection) of HP. The mutations were determined using the MEGA 7. HP 26695 [access number CP003904.1] was reference strain. The biopsies were collected between March and September 2019.

Results: The prevalence of HP was 67.87% (224/330). The antimicrobial resistance rates associated with mutations are shown in Figure 1. The main mutations for CLA were A2142G and A2143G in the *23S* rRNA gene. For LVX were N87I, N87K, D91N, D91G, D91Y in the *gyrA* gene. For MTZ were D50E, S88P, H97T, M56V, M56I, R16H, A118T, R90K, G98S, L62V in the *rdxA* gene and for AMX were N562Y, T593A, G595S, V374L, N504D in *pbp1A* gene.

Conclusions: HP is present in a high percentage (67.82%). The high resistance of HP to metronidazole, clarithromycin and levofloxacin found in this study requires systematic monitoring to optimize the selection of treatment regimens. Clarithromycin-containing regimens are no longer suitable for unconditional empiric use because of resistance rates (43%). A limitation of this study was that sensitivity tests were not performed in parallel, only searching for mutations in genes and as in the case of AMX, MTZ, there are still no specific mutations that correlate the genotype with the phenotype, as in the case of LVZ, CLA.

Figure 1. Antimicrobial resistance rates in HP associated with mutations for metronidazole (MTZ), clarithromycin (CLA), levofloxacin (LVX) and amoxicillin (AMX).

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Abstract 7144

Blue-Carba complete

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Background: The Blue-Carba test is a rapid, low cost test for carbapenemase detection but does not allow the differentiation between metallo-β-lactamases (MBL) and serine carbapenemases. With the introduction of ceftazidime-avibactam (CAZ-AVI) in clinical use it is critical to rapidly detect and differentiate these two carbapenemase groups.

Materials/methods: Blue-Carba complete (BCC) consisted of four microplate wells: 1 - 0.4 mg/ml bromothymol blue in water pH 6.8; 2 - 6mg of imipenem/cilastatin in bromothymol blue solution [BTB]; 3 - 6mg/ml of imipenem/cilastatin plus 0.55mg/ml of DPA in BTB; 4 – 6mg of imipenem/cilastatin plus 5mg/ml of CAZ-AVI, both commercial products for injection in BTB. A total of 163 strains, mostly Enterobacterales, previously characterized by PCR and spectrophotometric imipenem hydrolysis [54 NDM-1; 7 SMP-1; 41 KPC-2; 10 KPC-2+NDM-1; GES-20, IMP-1, VIM-1, BKC-1, one of each; 8 OXA-carbapenemases; 39 non-carbapenemase producers] were cultured on CPS-Elite, Mueller-Hinton and Sheep blood agar. BCC tests were incubated in ambient air at 36°C. Readings were performed after 15, 30, 60 and 120 min. Positive and negative concordance values were calculated using spectrophotometry and PCR as the gold standards.

Results: Concerning NDM-1 producers, 44/54, 52/54 and 54/54 were identified as metallo-β-lactamase producers [no color change in the wells containing imipenem plus DPA] after 30, 60 and 120 min, respectively. There was 100% positive concordance with PCR. For KPC-2 producers, 41/41 strains were identified as serine-carbapenemase producers [no color change in the wells containing imipenem plus CAZ-AVI] after 30 min of incubation. There was 100% positive concordance with PCR for blaKPC. None of OXA-type carbapenemases producers were positive in the well containing imipenem only. Most (6/10) of the strains co-producing KPC-2 and NDM-1 were identified [color change to yellow in the wells containing imipenem plus CAZ-AVI and in the wells containing imipenem plus DPA] after 30 min and all were identified after 60 min; consequently there was 100% positive concordance for KPC-2 plus NDM-1 co-producers. All strains negatives for carbapenemases showed a negative result in BCC test, resulting in 100% negative concordance.

Conclusions: The Blue-Carba complete can differentiate serine-carbapenemase producers from metallo-β-lactamase producers and identify co-production of these carbapenemases.

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Abstract 7145

**Invasive pneumococcal disease in children: the risk of a moving target**

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**Background:** Invasive pneumococcal disease (IPD) causes life-threatening illnesses including meningitis and bloodstream infections. The highest disease incidence is associated with young children and older adults. Seven and 13-valent pneumococcal conjugate vaccines (PCV7/PCV13) were introduced into the Irish paediatric schedule in 2008 and 2010 to target the predominant serotypes. The aims of this work were to evaluate the effectiveness of PCVs in reducing paediatric IPD, examine potential vaccine-failures and identify emerging replacement-serotypes in the post-PCV era.

**Materials/methods:** Cultures submitted from children <16 years of age from July 2007 to June 2018 were assessed by serotyping and antimicrobial susceptibility testing. Whole genome sequencing was performed on strains of interest.

**Results:** The number of paediatric IPD cases decreased by over 50% since the introduction of PCVs. The most substantial reductions were in the numbers of PCV7/PCV13 serotypes in children aged <2 years, a 97% decline (incidence rate ratio [IRR]:0.03, 95% confidence interval [CI]:0.00-0.21, p=0.0005), and a 78% decline (IRR:0.22, 95%CI:0.05-1.04, p=0.0558), respectively. There was an increase in non-PCV13 serotypes during the same period (IRR:2.82, 95%CI:1.02-7.84, p=0.0463), with similar trends observed for older children. The predominant serotypes included 23B,15B/C,22F,33F,12F,24F,38,10A,15A,9N,11A and 35B, with variability within each age group and year. There were no clear vaccine replacement serotypes; instead a number of different serotypes emerged and were non-susceptible to antimicrobials.

Of sixteen vaccine failures/breakthrough identified, ten cases received all three doses of PCV, while six were mixed schedule or incomplete due to age. Most failures/breakthroughs (n=10, 63%) were serotype 19A and resistant to antimicrobials. Serotype 19A isolates were associated with a virulent clonal complex, CC320, but displayed considerable genetic divergence in comparison to strains reported elsewhere.

**Conclusions:** Reducing the incidence of IPD is more challenging as the number of non-PCV13 serotypes has expanded and are now less susceptible to antimicrobials. Consequently, higher valency or broader target vaccines are required to further prevent IPD.

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Abstract 7146

The burden of nosocomial pneumonia caused by Pseudomonas aeruginosa and Staphylococcus aureus for ventilated patients in European intensive care units: a weighted multi-state analysis

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Abstract third-party references: On behalf of COMBACTE-MAGNET Consortium

Background: Nosocomial pneumonia (NP) remains a major complication for ventilated patients in European intensive care units (ICUs). Among the most common causative agents are Pseudomonas aeruginosa (PA) and Staphylococcus aureus (SA).

Materials/methods: The prospective, observational, multi-center cohort study ASPIRE-ICU provides detailed information on the consequences of NP for eleven European countries. Patients in the sample (n=1929) are matched according to SA colonization status at ICU admission (50% SA-colonized). This study sample is embedded within a large surveillance population (n=9841) of which baseline characteristics are available. Additional detailed clinical and pathogen-specific variables as well as follow-up information beyond hospital discharge up to 90 days is collected for the matched sample.

Using up-to-date statistical methods, we investigate the burden of PA NP and SA NP. Multistate methodology is used to account for the time-dynamics of subsequently occurring events. Moreover, weights based on the information available from the surveillance population are calculated in order to make the matched sample representative of the surveillance population. The weighted sample is used to analyze 90-day mortality as well as extra length of ICU and hospital stay. The weighted multistate model analysis allows us to draw conclusions from the matched sample for the complete surveillance population.

Results: PA NP (n=46) was associated with increased length of stay in the ICU (8 extra days, 95%-CI: [3;24]) and 90-day mortality (adjusted weighted hazard ratio=1.88, 95%-CI: [1.05;3.36]). Subsequent hospital stay after ICU discharge was not found to be affected by PA NP (4 extra days, 95%-CI: [-1;9]). In contrast, no association between SA NP (n=131) and ICU-length-of-stay was detected (0 extra days, 95%-CI: [-4;4]). However, subsequent hospital stay was significantly increased (9 extra days, 95%-CI: [1;17]). Effects on 90-day mortality were not significant (adjusted weighted hazard ratio=1.36, 95%-CI: [0.90;2.06]).

Conclusions: PA NP remains a major complication for ventilated patients in the ICU with severe consequences. While SA NP was neither found to be associated with increased length of ICU stay nor with 90-day mortality, subsequent hospital stay was significantly increased. For cost calculations follow-up beyond ICU discharge provides important additional information on the economic burden of NP SA.

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Abstract 7148

Real-world treatment of patients diagnosed with serious infections due to carbapenem-resistant Gram-negative pathogens in Greek hospitals

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Background: Gram-negative (GN) infections which are resistant to key antibiotic classes pose a major threat to patients and clinicians. This issue is especially acute in southern European countries, including Greece. Our study objective was to characterize the real-world treatment of carbapenem-resistant (CR) GN complicated urinary tract infections (cUTI), complicated intra-abdominal infections (cIAI), and hospital-acquired/ventilator-associated bacterial pneumonia (HABP/VABP).

Materials/methods: Hospitalized adults with cUTI, cIAI, or HABP/VABP caused by CR GN pathogens between February 2015-July 2017 were consecutively enrolled from five participating hospitals across Greece. Baseline characteristics, medical history in the 12 months preceding index hospitalization, and treatment patterns were retrospectively reviewed through chart abstraction.

Results: 100 patients were identified from the five hospitals, with a mean age of 66.2 years; most (72%) were male. Index infections were largely hospital-acquired (90%) and the most common index infection types were HABP/VABP (81%), cIAI (10%), and cUTI (7%). A. baumannii was the most common pathogen identified (64%) - K. pneumoniae and P. aeruginosa were isolated in 37% and 9% of patients, respectively. After culture collection the most common antibiotics were carbapenems (43%), colistin (29%), glycopeptides (16%); prior to susceptibility test results: colistin (65%), carbapenems (57%), aminoglycosides (23%); post-susceptibility test results: colistin (79%), carbapenems (46%), tigecycline (39%). The majority of carbapenem use was as part of combination therapy. Antibiotic treatment patterns for patients who received carbapenems (n=71) are shown in Figure 1. Enrolled patients demonstrated considerable comorbidity in the pre-index period; in the year prior to index admission, 43% of patients received antibiotics, most commonly fluoroquinolones (n=20, 46.5%), 51% were admitted to hospital, and 37% had undergone prior invasive procedures.

Figure 1. Sankey diagram of treatment patterns for patients treated with carbapenems.

Conclusions: Carbapenems were the most commonly used empiric treatment, with continuing use observed just prior to, and after, susceptibility test results. High levels of colistin usage was observed in this cohort which may be linked to the high antibiotic resistance levels in Greece. The comorbid nature of these patients and the toxicity concerns associated with colistin suggest a need for alternative therapies which are efficacious against resistant pathogens and with improved tolerability profiles.

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Early, potent and sustained virus-specific antibody-dependent complement-mediated inactivation activity in HIV-2 infection

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Background: Despite significant improvements in therapy, the HIV/AIDS pandemic remains globally an important threat to public health. While there is hope that elimination of proviral HIV-1 DNA can be achieved, several approaches to reach a functional cure [control of HIV-1 replication in the absence of antiretroviral therapy] are also under investigation. HIV-2 is known to be less pathogenic than HIV-1, translating into slower disease progression. HIV-2 infection, therefore, represents a natural model for studies on HIV functional cure. In the present study, we examined longitudinally antibody-dependent complement-mediated inactivation (ADCMI) during the course of HIV-2 infection.

Materials/methods: Swedish teams, in collaboration with Guinea-Bissau, initiated in 1990 a police cohort, from which longitudinal plasma samples have been collected. In this study longitudinal plasma samples obtained between 1992 and 2010 (median four time points per subject) from seven HIV-2 seroincident individuals (median follow-up 14 years) were studied. Neutralizing and ADCMI activities of plasma were determined using a plaque reduction assay with GHOST(3)-CCR5 cell line. Pooled human AB serum was the source of complement. The cut-off for neutralization was 30% reduction in the number of plaques. For determination of the magnitude of neutralizing activity and ADCMI plasma samples were tested against three HIV-2 isolates.

Results: ADCMI developed at 6-13 months after estimated time of infection and plasma titers raised to 1:10 000-1:100 000 000 after five years and were thereafter sustained against tested HIV-2 isolates throughout the follow-up period. Moreover, complement enhanced plasma neutralizing activity 10-1000 times, depending on which HIV-2 isolate tested against.

Conclusions: This study represents the first longitudinal HIV-2 infection study of ADCMI, from early infection to years of follow-up, and shows that ADCMI develops earlier and to higher titers than that previously described for HIV-1. This suggests that complement may contribute to the relative benign outcome of an HIV-2 infection.

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Abstract 7152

**Sepsis-3: a prospective clinical study of the clinical diagnosis and blood culture performance**

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**Introduction:** Microbiological diagnosis of sepsis is crucial for appropriate treatment of patients with sepsis. Blood cultures (BC) are the gold standard method in sepsis. The performance of BC in detection of microorganisms in patients with the recently defined sepsis-3 definition has scarcely been studied.

**Aims:** The primary aim of the study was to analyze the association of clinical sepsis-3 diagnosis with BC results in patients who were identified through a sepsis alert system. Secondary aims were to describe the clinical characteristics in BC positive vs. BC negative sepsis.

**Materials/methods:** Patients that were treated according to a sepsis triage model were included prospectively in the emergency department. In total six blood culture bottles were collected from each patient that fulfilled the criteria for triage. BC were defined as having clinically relevant growth, contaminant growth or no growth by standard methods. The clinical and laboratory data were collected from patient journals and the laboratory information system. Foci of infection included in the study were: upper respiratory tract, lower respiratory tract, urinary tract, abdominal, skin/soft tissue/joint/skeletal, central nervous system and others. Correlation between the clinical diagnosis of sepsis and BC results were analyzed using Pearson's χ²-test.

**Results:** 652 suspected sepsis episodes were studied, the final analysis included 549 episodes. 387/549 (70.5%) episodes fulfilled sepsis-3 criteria. BC were positive in 140/387 (36.1%) episodes with sepsis. In patients without sepsis, BC were positive in 30/162 (18.5%) episodes (p < 0.001). In patients with sepsis, the BC positivity rates were correlated to infection focus. Patients with urinary tract infections (49.8%) had higher BC positivity rates compared to lower respiratory tract infections (31.4%) (p < 0.001).

**Conclusions:** BCs had low performance in detection of relevant clinical growth in patients with sepsis and could detect microorganisms in only 36% of the episodes. A higher proportion of positivity was detected in patients with sepsis compared to patients without sepsis. Urinary tract focus had the highest association with BC positivity.

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**Abstract 7153**

**Comparative effectiveness of ceftolozane/tazobactam versus aminoglycosides or polymyxins in multidrug-resistant *Pseudomonas aeruginosa* infections**

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**Background:** *Pseudomonas aeruginosa* infections are challenging to treat, due to multi-drug resistance (MDR) and the complexity of the patients affected by these serious infections. As new antibiotic therapies come to market, limited data exists about the effectiveness of such treatments in clinical practice among varied clinical populations. The objective of our study was to assess the comparative effectiveness of ceftolozane/tazobactam (C/T) compared with aminoglycosides or polymyxins in MDR *Pseudomonas aeruginosa* infections in Veterans Affairs (VA) hospitals.

**Materials/methods:** This retrospective cohort study included VA hospitalized patients with positive MDR *P. aeruginosa* cultures between January 2015 and April 2018. Inclusion criteria were 1) treated with C/T versus aminoglycosides or polymyxins for ≥48 hours, without overlapping therapy between C/T and aminoglycosides or polymyxins for >48 hours and 2) isolates were susceptible to the treatment of interest (C/T and aminoglycosides/polymyxins). Adjusted odds ratios (aOR) and 95% confidence intervals (CI) were calculated using automatic stepwise logistic regression for inpatient mortality, 30-day mortality, 30-day readmission, persistent positive culture, and microbiological eradication.

**Results:** We included 57 patients treated with C/T compared with 155 patients treated with aminoglycosides/polymyxins for MDR *P. aeruginosa* infections. Patients treated with C/T were younger (mean age 67.5 vs 71.1, p=0.03), and had a higher comorbidity burden prior to hospitalization [median Charlson 5 vs 3, p=0.01], as well as higher rates of spinal cord injury (38.6% vs 21.9%, p=0.02), *P. aeruginosa* positive bone/joint cultures (12.3% vs 0.7%, p<0.0001), and positive *P. aeruginosa* cultures in the 30 days prior to admission (54.4% vs 38.7%, p=0.04). Median time to initiation of the treatment of interest from culture was 3 days for both groups. Inpatient mortality was significantly lower in the C/T group compared with aminoglycosides/polymyxins (15.8% vs 27.7%, aOR 0.39, 95% CI 0.16-0.93) adjusting for prior positive *P. aeruginosa* culture, treating specialty, and previous antibiotics exposures prior to the initiation of the treatment of interest. There were no significant differences observed for the other outcomes assessed.

**Conclusions:** In hospitalized patients with MDR *P. aeruginosa*, the risk of inpatient mortality was 61% lower among patients treated with C/T compared with those treated with aminoglycosides or polymyxins.

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Outcomes and predictors of outcomes of serious infections attributable to carbapenem-resistant Gram-negative pathogens in southern European hospitals

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Background: Carbapenem resistance is increasing, particularly in southern Europe. This study characterized how patients with serious infections [complicated urinary tract infections [cUTI], complicated intra-abdominal infections [cIAI], and hospital-acquired/ventilator-associated bacterial pneumonia [HABP/VABP]] attributable to carbapenem-resistant [CR] Gram-negative [GN] bacteria are treated and the outcomes of treatment.

Materials/methods: Retrospective chart review in 300 patients from 14 Spanish, Italian, and Greek hospitals. Adult patients were enrolled consecutively if hospitalized with cUTI, cIAI, or HABP/VABP caused by CR GN pathogens from February 2015 to July 2017. Baseline patient characteristics, treatment patterns, and clinical outcomes [clinical cure, death/discharge] were abstracted. Univariate/multivariate cox regression models were performed to determine significant predictors of observed outcomes.

Results: In the included cohort, most infections were hospital-acquired (79.7%) and the most common infection types were HABP/VABP (61.3%), cUTI (27.7%), cIAI (8.7%); the remainder were mixed infections. Klebsiella pneumoniae was the most common pathogen (51.3%), followed by Acinetobacter baumannii (30.0%) and Pseudomonas aeruginosa (21.7%). Overall, 46.7% of patients reported clinical cure; rates ranged from 34.6% [cIAI] to 73.5% [cUTI]. Median time from culture collection to clinical cure was 16 days (11-24 days). On the date of discharge, 50.7% of patients were deceased; median time from culture collection to death was 27 days (12-84 days). Having cUTI was a predictor of clinical cure [hazard ratio [HR]: 1.728, 95% confidence interval [CI]: 1.172, 2.548, p=0.0057]; colistin use was inversely associated with clinical cure [HR: 0.625, 95% CI: 0.429, 0.912, p=0.0148]. cIAI [HR: 1.068, 95% CI: 1.011, 1.127, p=0.0177], receiving more drugs post-antibiogram availability [HR: 1.096, 95% CI: 1.052, 1.142, p=0.0001], and receiving carbapenems [HR: 1.583, 95% CI: 1.096, 2.287, p=0.0143] were all significantly associated with death.

Conclusions: cUTI, cIAI, and HABP/VABP attributable to CR GN infections were fatal in just over half of included patients. Infection type and antibiotic choices were predictive of outcomes, specifically, colistin and carbapenem use were associated with poor clinical outcomes. The trend between treatment decisions and outcomes warrants further exploration; patients identified as candidates for carbapenem or colistin therapy may benefit from newer treatments with enhanced activity against carbapenem-resistant pathogens and improved toxicity profiles.

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Real-world drug resistance profile of hepatitis C patients who failed direct-acting antivirals: SHARED

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Background: Hepatitis C patients who failed Direct-Acting Antivirals (DAA) often selected viruses with drug resistance-associated substitutions (RAS), which limits treatment options. High response rates from DAA therapy make it challenging to study HCV drug resistance. SHARED, the Surveillance of Hepatitis C Antiviral Resistance, Epidemiology and Methodology, is an international consortium with the goal of better understanding and avoiding HCV drug resistance and transmission through the development, application, and sharing of HCV genomic data, methods, software and technologies. Our aim was to characterize HCV resistance after unsuccessful DAA in real-world settings.

Materials/methods: HCV sequences and clinical data from >1900 DAA-failures were collected from 17 countries. Variants within NS3, NS5A, and NS5B were examined for resistance-associated substitutions (RAS) at positions according to the 2018 EASL guideline.

Results: Of the 1543 patients who failed NSSA inhibitor (NS5AI)-containing regimens, 83% selected RAS following therapy. Notably, 63% of patients with RAS had intricate patterns with ≥2 NSSA RAS suggesting a high level of resistance. In the 244 patients treated with a combination of NS5AI and protease inhibitor (PI), 63% had RAS in both drug-targets, and only 6% failed with no RAS. There was no difference in the frequencies of RAS selected between the first-generation NS5AI+PI regimens versus glecaprevir/pibrentasvir after treatment failure. The prevalence of NS5A-RAS was lower in genotype (GT) 1a (77%) but higher in GT2 (100%) and GT4 (99%). Each genotype/subtype had distinct RAS patterns, usually at positions 28, 30, 31, and 93. In general, GT2a virologic failures selected L31M while non-GT2 selected T24S+F28C; none of them harbored Y93H. In GT3, Y93H was most prevalent (61%) followed by mutations at position 62 (45%) and A30K/S (17%). Intriguingly, all GT3b/g harbored A30K+L31M mutations without Y93H. Overall, the prevalence of an unfit sofosbuvir mutation, S282T, was low in GT1a (2%), GT1b (1%), GT2 (3%) and GT3 (1%), but high in GT4 (18%).

Conclusions: SHARED is currently gathering a critical mass of data from virological failures worldwide, including uncommon GT and subtypes, to characterize the modality of DAA failure comprehensively. This information provides valuable insight to optimize rescue treatment options and to track resistant virus transmission.

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Abstract 7159

Rapid reduction in rotavirus gastroenteritis in children aged 0-59 months following the introduction of universal rotavirus vaccination in Palestine

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Background: Universal vaccination with a monovalent rotavirus vaccine (Rotarix GSK) was introduced in Palestine in May-2016 in collaboration between Palestine Ministry of Health and the Rostropovich & Vishneskaya Foundation (RVF). In November-2018 it was switched to the newly approved monovalent vaccine, Rotavac (Bharat Biotech) to foster program sustainability with the support of RVF. The study aims to examine the changes in rotavirus gastroenteritis hospitalizations following the introduction of universal rotavirus immunization among children aged 0-59 months.

Materials/methods: An ongoing laboratory-based surveillance of RVGE was launched in January-2016 till October 2019 among children aged 0-59 months living in Bethlehem and Hebron regions. Stool samples were collected from children hospitalized for gastroenteritis and analyzed for rotavirus antigen by immunochromatography. The year 2016 was considered as the reference period.

Results: Overall, 3341 hospitalizations for gastroenteritis occurred during 2016-March 2019. The median age of the patients was 7 months. Rotavirus tested positive in 709 (21.2%) samples. Rotavirus positivity was 389/1317 (29.5%), 149/889 (16.8%), 129/917 (14.1%) and 42/218 (19.2%) in 2016, 2017, 2018 and 2019 respectively. The number of hospitalizations for all-cause gastroenteritis decreased by 32.5% and 30.4% in 2017 and 2018, respectively compared to 2016. The corresponding reduction (p<0.001) in the percentage of rotavirus positive tests was 43.3% (95% CI 31.3, 54.8), and 52.4% (95% CI 40.9, 63.5). This reduction (p<0.001) was of stronger magnitude in infants aged 0-11 months: 62.0% (95% CI 46.4, 76.9) in 2017 and 59.2% (95% CI 43.9, 74.0) in 2018. In toddlers aged 12-23 months the respective reduction (p<0.05) was 22.9% (94% CI 1.9, 43.1) and 53.2% (95% CI 32.3, 72.1). In children aged 24-59 months, a small and non-significant reduction was documented: 28.5% (95% CI 1-3, 56.6) and 18.0% (95% CI 12.8, 47.4), in 2017 and 2018, respectively.

Conclusions: The introduction of universal immunization with a monovalent vaccine was followed by a rapid and significant reduction in rotavirus hospitalizations in children aged 0-59 months in Palestine. Preliminary data suggest that there is no difference between the clinical impact of Rotavac vaccine and the previously used Rotarix.

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Abstract 7161

**Light scatter AST for positive blood cultures, how impactful on antimicrobial therapy management of septic patient?**

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**Background:** Improving blood culture turnaround time (TAT) is pivotal in the management of septic patients. Faster reporting of results can significantly impact on patients’ outcomes and costs associated to inappropriate antimicrobial therapy.

**Materials/methods:** Positive blood cultures have been consecutively screened, and 50 septic patients have been enrolled so far. Each sample was processed according to the standard protocol (SP) consisting of preliminary ID by MALDI-TOF MS and preliminary AST both performed on short-term colony incubation, and definitive AST on isolated colony. A rapid protocol (RP) consisting of light scatter technology (ALFRED 60AST) direct AST from positive monomicrobial blood cultures coupled to ID by MALDI-TOF MS was tested, by choosing the appropriate antibiotic panel after Gram stain results. Clinicians were presented with the RP and SP results and interviewed to assess the potential impact of the RP results on the antimicrobial therapy management.

**Results:** The RP instrument TAT was significantly lower than that of the preliminary SP (6h 31’ vs 19h 12’ – p<0.001), and even more so was the real-life TAT (7h 31’ vs 26h 27’ – p<0.001). Overall concordance between RP and definitive SP was 93.4% (Cohen K 0.82 – excellent concordance) and no very major errors were found. The concordance between antimicrobial therapy decisions based on RP and PSP results was 91.7% (Cohen K 0.79 – good concordance). Based on RP results, there would have been 22.9% antibiotic therapy changes one day earlier. In 8.3% of cases, therapy management decisions were not concordant, half of which were motivated by antibiotics not tested in the RP.

**Conclusions:** The results represent a halfway analysis of an ongoing study that is designed to reach a sample size of 100 patients. The RP TAT is considerably lower than the SP TAT, and its diagnostic accuracy is excellent. The preliminary data suggest that rapid reporting of AST results could benefit more than 1 out of 5 patients thanks to changes of the empirical antibiotic therapy to a targeted one with one day in advance.

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Resource utilisation associated with infections attributable to carbapenem-resistant Gram-negative pathogens in southern European hospitals

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Background: Gram-negative (GN) bacterial infections are known to be clinically burdensome, particularly when the causative pathogens are resistant to antibiotics. This study characterizes the economic burden by describing the healthcare resource use (HCRU) associated with serious carbapenem-resistant (CR) GN infections in three southern European countries.

Materials/methods: HCRU, including length of stay (LOS), procedures, and readmissions, was assessed in 300 hospitalized adult patients with complicated urinary tract infections (cUTI), complicated intra-abdominal infections (cIAI), and hospital-acquired/ventilator-associated bacterial pneumonia (HABP/VABP) caused by CR GN pathogens from February 2015-July 2017, identified through a retrospective chart review conducted in 14 hospitals in Spain, Italy, and Greece.

Results: Patients had HABP/VABP (61.3%), cUTI (27.7%), cIAI (8.7%), or mixed infections (2.3%). Patients were most often admitted to medical wards (53.7%). Median LOS from admission to discharge was 39.5 days (interquartile range: 23-67 days), varying from 33.5 days (cIAI) to 41.0 days (HABP/VABP); from culture collection to discharge median LOS was 21.0 days [12-42 days]. 64.3% of patients spent time in the intensive care unit (ICU) during their hospitalization. Median ICU LOS was 27.0 days [13-47 days] from admission, and 7 days [0-18 days] from culture collection date. During index hospitalization, the most frequently performed tests were blood cell counts (in 92.7% patients, mean: 13 per patient), biochemistry tests (88.0%), and blood cultures (87.0%). The most common invasive procedures were vascular catheterization (33.7%), mechanical ventilation (18.3%), and urinary catheterization (16.3%). 143 patients had readmission data for six months post-discharge: 57 (39.9%) were readmitted. The cause of readmission was recurrence of infection for 10 (16.7%) of the 69 reported readmissions. Median time from discharge to readmission was 32.0 days [5-70 days]; mean LOS once readmitted was 4.9 days. 16.3% of discharged patients reported outpatient or emergency visits in the six months post-discharge, most commonly under the care of a specialist.

Conclusions: cUTI, cIAI, and HABP/VABP caused by CR GN infections were associated with substantial HCRU, including LOS and ICU LOS, procedures, and readmissions. These data highlight the considerable financial burden associated with these infections and highlight the urgent need for enhanced clinical management of these difficult-to-treat infections.

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Genomic features involved in intra-hospital transmission of *Pseudomonas aeruginosa*

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**Background:** *Pseudomonas aeruginosa* causes life-threatening nosocomial infections. Moreover, it is known to easily spread within hospitals, particularly during long-term outbreaks. However, little is known about the genomic and phenotypic features of successful outbreak strains since outbreaks are usually only detected when multidrug resistant strains are involved.

**Materials/methods:** We performed whole genome sequencing of 650 *P. aeruginosa* strains from 384 patients collected during active screening at our hematology department at the University Hospital Tübingen, Germany. We included the first isolate of all patients regardless of their antimicrobial susceptibility pattern. Further strains from the same patient were included when they differed in their antimicrobial susceptibility profile or were isolated from different specimen collection sites. Room occupation and transfer data from each patient was extracted from the clinical database system.

**Results:** Maximum likelihood phylogeny revealed 187 clusters of various sizes including strains from one or more patients. We determined likely transmissions for each cluster based on genetic and epidemiological links. In linear regression models, the number of transmissions was associated with direct contact days (standard coefficient 15.53, p = 0.06) and indirect contact days (standard coefficient 14.79, p = 0.03). Based on this data, we determined a weighted transmission efficacy for each cluster and found 9 clusters having a high transmission efficacy and 44 clusters having a low transmission efficacy, together comprising of 423 strains (65% of all strains). A group of four genes was found to be significantly enriched in the high transmission clusters (OR 119.94, FDR = 3.15 x 10^-49, sensitivity = 78.19%, specificity = 97.07%).

**Conclusions:** Our study shows a strong relationship between number of patient contacts and transmission counts, suggesting that transmission events are clearly driven by the hospital setting and logistics. Furthermore, our data suggest that genomic features of *P. aeruginosa* strains contribute significantly to intra-hospital transmission and could be used as biomarkers indicating strains with high transmission risk.

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Within host genetic comparison of *Escherichia coli* strains isolated from patients with urosepsis

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**Background:** *E. coli* is the most common cause of urinary tract infections (UTIs) and urosepsis worldwide. Whether these infections are caused by single clonal strains ascending the urinary tract, or whether more diverse *E. coli* populations are involved in these severe infections is not yet fully understood. In this project we assess the genetic diversity between *E. coli* strains isolated from paired blood or urine samples.

**Materials/methods:** We isolated and whole genome sequenced *E. coli* strains (*n*=129) from 63 patients with urosepsis. We compared the genomic sequences of strains isolated from the bloodstream (*n*=63) to strains isolated from the urinary tract (*n*=66) of the same patient. The samples were compared in terms of Average Nucleotide Identity (ANI), whole genome single nucleotide polymorphisms (SNPs) and for differences in gene content. In a subset of patients, we picked ten random colonies from blood and urine culture plates to assess the genomic diversity within the patient samples.

**Results:** We found that in 86% of patients with urosepsis (*n*=54/63), the *E. coli* isolates from blood and urine were closely related with >99.5% ANI (median number of SNPs=4; interquartile range=1-13) whereas in 14% of patients with urosepsis (*n*=9/63), the bloodstream isolated *E. coli* strains shared <99.5% ANI (median number of SNPs=79,631; interquartile range=31,189-82,557) to those isolated from the urine of the same patient. As a next step we assess the diversity of *E. coli* strains in urine and bloodstream samples of ten urosepsis cases, by comparing ten randomly picked colonies per sample material.

**Conclusions:** These findings suggest for patients with urosepsis with distantly related *E. coli* strains isolated from urine and blood, multiple *E. coli* strains may ascend the urinary tract to cause UTI. Assessing the diversity of *E. coli* strains in urine and bloodstream samples could increase our understanding and anticipation of disease progression.

![Core genome phylogeny of *E. coli* strains isolated from bloodstream (*n*=63) and urinary samples (*n*=66). Distantly related strains of the same clinical case are labeled with the case ID.](image-url)
Co-production of two types of carbapenemases in Enterobacterales from Poland
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Background: Since the first identification of carbapenemase-producing Enterobacterales (CPE), VIM-2 positive isolate, in Poland over decade, various types of carbapenemases including VIM, IMP, KPC, NDM, OXA-48-like and GES-5 have been recognized by the National Reference Centre for Susceptibility Testing (NRCST). Recently, the major CPE problem is NDM-producing Klebsiella pneumoniae, which continues its dissemination in the country since 2013. Here we present the first Polish strains coproducing of two different types of carbapenemases.

Materials/methods: A total of 26 Enterobacterales isolates: K. pneumoniae [n=20], Klebsiella oxytoca [n=3], Enterobacter cloacae cpx. [n=2], Escherichia coli [n=1] collected by NRCST were examined. The strains were isolated in 13 microbiological centers, 6 cities: Warsaw, Łódź, Lublin, Cracow, Rybnik and Grodzisk Mazowiecki. Species were identified by Vitek2 (bioMérieux). Carbapenemase detection was carried out by Carba NP and CIM tests, and phenotypic methods. blaNDM, blaVIM, blaKPC, blaOXA-48-like genes were identified by PCR. Susceptibility of isolates was tested by MIC Test Strips (Liofilchem) and the results were interpreted according to the EUCAST guidelines. Whole genome sequencing (WGS) was performed for the 23 isolates using the Illumina MiSeq.

Results: The first strain coproducing of two carbapenemases - K. pneumoniae NDM/KPC emerged in Warsaw in 2016. Since then, the following pairs of carbapenemases have been confirmed in 25 other isolates: NDM/KPC (Warsaw, n=2; Rybnik, n=7), KPC/VIM (Warsaw, n=5; Cracow, Lublin, n=1), KPC/OXA-48 (Cracow, n=4; Łódź n=1), NDM/VIM (Warsaw n=2; Łódź, Lublin, n=1), NDM/OXA-48 (Grodzisk Mazowiecki, n=1). NDM/KPC-producing K. pneumoniae isolates discovered in Rybnik represented the hyperepidemic clone ST23, while strains isolated in Warsaw - ST11. KPC/OXA-48-producing K. pneumoniae belonged to two STs: ST512 and ST395 which was previously observed in Cracow in strains with OXA-48. KPC/VIM E. cloacae and K. oxytoca isolates were classified as ST96 and ST145 respectively, both STs were observed previously in Poland in VIM-producing Enterobacterales. The studied strains showed multidrug-resistance patterns. A more detailed analysis of the genetic context of the carbapenemase encoding genes is currently underway.

Conclusions: Our research has revealed the occurrence of Enterobacterales coproducing of two carbapenemases in different type combinations. This new phenomenon is observed in Poland since 2016.

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Genomic analysis of Group B streptococci colonising pregnant women in Portugal reveals the emergence of novel genetic lineages resulting from capsular switching

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Background: Diversification of group B streptococci (GBS) clones causing invasive disease has been reported, together with emerging resistance within previously stable genetic backgrounds. Our aim was to use high throughput sequencing (HTS) to characterize the genetic lineages circulating among GBS colonizing pregnant women and to compare them with those causing neonatal infections in Portugal.

Materials/methods: GBS isolates (n=252) recovered from vaginorectal swabs of pregnant women (35-37 weeks gestation) in three hospitals in the Lisbon metropolitan area were sequenced (Illumina, San Diego, CA, USA) and analyzed by both mapping and de novo assembly approaches. Capsular serotypes, multilocus sequence typing (MLST) and antimicrobial resistance determining genes were extracted from the genomes.

Results: Serotype Ia was the most frequent (24%), mainly representing ST23 and ST24 and respective single-locus variants (SLVs). In ST24 a novel serotype combination - V/ST24 – was found (39%), possibly resulting from capsule switching. Serotype III accounted for 21% of the isolates, mostly representing the hypervirulent CC17 clone, including one isolate carrying multiple resistant determinants. Serotypes V (19%) and Ib (14%) represented mostly CC1, a lineage previously almost exclusively expressing serotype V. All Ib/CC1 isolates carried the ermB gene, accounting for the majority of isolates carrying macrolide resistance determinants within CC1 (66%). In total sixty isolates (24%) contained a macrolide resistance gene and a tet gene (mostly tetM, 95%) was found in 87% of the isolates.

Conclusions: In the past years, the emergence and expansion of the Ib/CC1 lineage, which we showed to have emerged from recombination of a large genomic region including the capsular locus, has been mostly restricted to non-pregnant adult disease. This lineage has been the major driver of the increase in macrolide resistance in Portugal, despite decreases in consumption. While only a small number of cases were found among neonatal infections, the expansion of Ib/CC1 lineage among GBS colonizing pregnant women, together with novel serotype/genotype combinations identified by genomic analyses, may be a harbinger of a shift in the serotypes and clones causing neonatal disease, which may impact the vaccine formulations currently under development.

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Abstract 7169

Detection of antibodies to hepatitis C virus using the Ortho VITROS: evaluation of the signal-to-cutoff ratio

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Background: Diagnosis of HCV infection is based on the detection of HCV specific antibodies (HCV-Ab) and serum HCV genome (HCV RNA). HCV-Ab chemiluminescence immunoassays are characterized by higher specificity compared to enzyme immunoassay methods, but a false positive results are possible specially in low-prevalence population. Several studies have shown that the use of signal / cut off ratio (S/Co) may reduce false positive results and they have correlated higher S/Co values to persistent HCV infection. The aim of this study is to correlate patients HCV-Ab absorbance values to HCV viremic status, in order to understand the clinical significance of S/Co ratio and reduce the use of second level tests.

Materials/methods: HCV antibodies results from 12901 serum samples, collected from January 2018 to July 2019, tested by Vitros ECi Anti-HCV assay (Ortho-Clinical Diagnostics), were extrapolated from the management system of a tertiary hospital. A part of HCV-Ab Vitros S/Co ≥1 positive samples (65/501) were re-tested using the LIAISON® XL murex HCV Ab assay (DiaSorin). Furthermore, the correlation between HCV-Ab S/Co ratio results and HCV RNA detection by CobasAmpli/Prep CobasTaqman (Roche) have been analyzed for 356 HCV-Ab positive samples

Results: Among 12901 samples, 501 (3.8%) samples have been resulted positive (Vitros S/Co ≥1) for anti-HCV, S/Co ratio resulted high (≥ 20) in 257/501 (51.3%) positive samples, intermediate (10 ≥ - <20) in 76 (15.1%), low (5 ≥ - < 10) in 35 (6.9%) and very low (≥ 1 - <5) in 133 (26.5%). Fifty/133 samples with very low S/Co have been re-tested with LIAISON and 32/50 of them resulted HCV-Ab negative (LIAISON, S/Co < 1). These samples have been confirmed as HCV-Ab Vitros false positive because they also resulted HCV-RNA negative. We demonstrated the correlation between high S/Co ratio and patients viremic status, 252/257 (98%) samples with S/Co ≥ 20 resulted HCV-RNA positive (> 100.000 UI/ml). Instead, only 30% and 18% of samples with intermediate to low S/Co ratio are also result HCV-RNA positive

Conclusions: Anti-HCV S/Co value definition, specific assay, allows to define false positive samples and therefore reduce the use of supplementary testing

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Clinical characteristics and outcome of patients with plasmid-borne AmpC β-lactamase-producing Klebsiella pneumoniae bacteraemia at a tertiary medical centre

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Background: Third-generation-cephalosporin-resistant (3GCR) Klebsiella pneumoniae infections are associated with significant morbidities and mortalities worldwide. Extended-spectrum β-lactamases (ESBL) and plasmid-borne AmpC β-lactamases are major resistance mechanisms in 3GCR K. pneumoniae. Carbapenem are considered the most effective therapeutic option for patients with ESBL-producing K. pneumoniae infections, but carbapenem-sparing regimens were proposed recently. However, the treatment regimens for 3GCR K. pneumoniae bacteraemia with plasmid-borne AmpC β-lactamases were rarely reported in the literature. We aimed to study whether non-carbapenems are suitable agents for bacteraemia caused by 3GCR K. pneumoniae with plasmid-borne AmpC β-lactamases.

Materials/methods: This single-centre, retrospective study enrolled 124 adult inpatients with 3GCR K. pneumoniae bacteraemia from January 2016 to September 2018. 3GCR K. pneumoniae strains were determined for genes coding for ESBL (including SHV, TEM, CTX-M) and plasmid-borne AmpC β-lactamases (including DHA and CMY) by PCR. Clinical characteristics of these patients infected with 3GCR K. pneumoniae strains were demonstrated and we further compared carbapenem and non-carbapenem regimens in patients infected with plasmid-borne AmpC β-lactamases-producing K. pneumoniae bacteraemia.

Results: Among 124 patients with 3GCR K. pneumoniae bacteraemia, 42 (33.9%) isolates harboured only plasmid-borne AmpC β-lactamases, 45 (36.3%) harboured only ESBL, 33 (26.6%) harboured both ESBL and plasmid-borne AmpC β-lactamases, and the remaining 4 isolates had unknown resistant mechanism. All strains with plasmid-borne AmpC β-lactamases were DHA-1-producing strains. The 14-day mortality of DHA-1-producing K. pneumoniae bacteraemia was similar to that of ESBL-producing strains (9.5% vs 15.6%, p=0.398). Thirty-seven patients with exclusive DHA-1-producing K. pneumoniae bacteraemia received appropriate antibiotics, including 19 patients with carbapenem and 18 with non-carbapenem group (5 with cefepime, 2 with piperacillin/tazobactam, 5 with fluoroquinolone, 3 with cefoperazone/sulbactam and 3 with ceftiraxone). There’s no difference in 14-day mortality and 28-day mortality between carbapenem and non-carbapenem treatment (5.3% vs 0%, p=0.324, 15.8% vs 0%, p=0.079). The time to clinical success was also similar between the group with carbapenem and those with non-carbapenem treatment [3 (2-6) vs 4 (2-5) days, p=0.613].

Conclusions: The 14-day mortality of patients infected with plasmid-borne AmpC β-lactamases K. pneumoniae strains was similar to those with ESBL-producing strains. Non-carbapenem regimes was as effective as carbapenems in the treatment of DHA-1-harbouring 3GCR K. pneumoniae bacteraemia.

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Abstract 7172

Hetero-resistance to colistin in *Stenotrophomonas maltophilia* isolates: challenges in colistin susceptibility testing

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**Background:** Colistin is one of the last –line antibiotic used for multidrug-resistant Gram negative bacilli. The increasing use of colistin has led to emergenge of resistant and heteroresistant isolates. The heteroresistance (HR) raised a diagnostic and therapeutic dilemma for clinicians because HR isolates could be misclassified as susceptible by routine diagnostic testing.

The aim of this study was to determine colistin heteroresistance in *Stenotrophomonas maltophilia* clinical isolates.

**Materials/methods:** A total of 212 *S. maltophilia* clinical isolates recovered from hospitalized patient between December 2015-April 2018 were included in the study. The colistin MICs were determined by both broth microdilution method (BMD) and gradient test (bioMérieux Etest). All tests were repeated twice. Heteroresistance was suspected if incompatible results were detected between BMD and gradient test or when colonies were observed within the inhibition zone of colistin gradient test. Heteroresistance was confirmed by applying population analysis profile (PAP) method. Heteroresistance was considered if the antibiotic concentration exhibiting the highest inhibitory effects was at least 8-fold higher than the highest noninhibitory concentration.

**Results:** Of the 212 *S. maltophilia* isolates, 54 (25.5%) were found as heteroresistant to colistin by PAP. In all of the HR isolates, category differences was detected with BMD test between two runs.

**Conclusions:** The results of this study shows that colistin susceptibility testing remains a challenging issue for routine microbiology laboratories. Although the recommended method is BMD, it cannot detect heteroresistance. The rate of colistin HR in *S. maltophilia* was found high in this study. In *vitro* and in *vivo* studies involving more isolates are needed to determine the true clinical outcome of HR to colistin.

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**Abstract 7173**

**Therapeutic equivalence between brand name antibiotics versus generics: a systematic review and meta-analysis**  
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**Background:** The use of generic drugs (GD) as an alternative to reference brand-name drugs (BD) is justified by the reduction in costs. Regulatory authorities authorize the clinical use of GD based on bioequivalence studies, which is the evaluation of single-dose pharmacokinetics in vitro or in healthy patients. There is little data on a therapeutic equivalence between BD and GD antimicrobials.

The objective was to synthesize and analyze the available evidence regarding the efficacy and safety of generic antibiotics compared with their original formulations.

**Materials/methods:** A systematic review of the literature was conducted in Medline (Pubmed) and Embase and validated through Epistemonikos and Scholar Google. The last search was in March 27th, 2019.

**Results:** The literature search retrieved 1179 unique studies. At the end of the selection process, 8 studies were included in this review. 1 was an RCT and 7 were non-randomized studies of intervention, totaling 11787 participants: 8522 received generic antibiotics and 3625 received the original formulation. Microbiological cure was reported in 6 studies that included a total of 2372 individuals. Overall, no significant differences were observed between the generic and original formulation groups (OR=0.89, 95% CI: [0.61-1.28]). However, in this analysis, there was significant heterogeneity (I²=70%, p=0.005).

Drugs contain pharmaceutical solids that may exist in different conformations in the crystal structure, which may interfere with the processability of the drug, and slight differences in production processes can cause distortions in therapeutic equivalence. The efficacy and safety of GD products are ensured by relying on the scientific principles of bioequivalence studies.

Nevertheless, there may be distinct differences in terms of outcome and adverse events when used in a clinical setting. The validity of current bioequivalence criteria depends on the existence of a clear relationship between active metabolite concentration, therapeutic efficacy, and tolerability.

In this review, most studies had an observational design that resulted in considerable heterogeneity. The length of follow up, participant characteristics, and sites of infection were different between studies.

**Conclusions:** It is not possible to contraindicate the use of GD, but we must maintain a surveillance posture in their use. Evidence of therapeutic equivalence is weak.

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Abstract 7174

**Sub-inhibitory concentrations of beta-lactam, aminoglycoside and polymyxin antibiotics induce differential proteomic responses in Pseudomonas aeruginosa**

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**Background:** *P. aeruginosa* is one of the main causes of hospital-acquired pneumonia associated with high mortality and morbidity. Growing evidence suggest that select antibiotics such as imipenem/carbapenems induce biofilm formation and have clear influence on colony composition. Moreover, organisms recovered from respiratory samples from hospital-acquired pneumonia patients are polymicrobial, however, the microbial diversity is reduced in presence of *P. aeruginosa*. We questioned whether sub-MIC challenge of common empirically prescribed antibiotics induce upregulation of specific responses including those capable of killing non-pseudomonal bacteria.

**Materials/methods:** Four strains of *P. aeruginosa* (PAO1, ATCC27853, and 2 clinical isolates) were challenged for 5 hours with 1/4 MIC of imipenem or tobramycin and both cytosolic and secreted proteins were studied using TMT-tagged mass spectrometric analyses. We further validated these findings by qPCR.

**Results:** Proteomic analyses showed that imipenem pressure significantly increased expression of AlgR and AlgC (1.6–1.8 fold, P < 0.05), while B-type flagellin protein was reduced (1.5 folds, P = 0.08) indicating a switch to biofilm formation. Imipenem also significantly induced expression of main T6SS structural components, Hcp1 (2.3 fold, P < 0.05) and ClpV1 (1.6 fold, P = 0.07). Hcp1 was also significantly upregulated in secreted fraction (5.8 fold, P < 0.01), indicating an activated T6SS. Tobramycin induced a significant increase of several components of branched chain amino acid (BCAA) metabolism such as lipoamide acyltransferase component (BkdB) (2.2 fold, P < 0.01), LpdV, a dihydrolipoyl dehydrogenase, (1.9 fold, P < 0.01), MmsA and MmsB (2.4 fold, P < 0.001 and 2.5 fold, P < 0.01 respectively). Displaying a shift in metabolism towards BCAA catabolic processes.

**Conclusions:** This study identified unique pathways upregulated as a consequence of subinhibitory concentrations of antibiotics thus gaining further insight in the potential resistance mechanisms and cellular physiology. The significance of our research is in identifying the proteomic changes occurring in different *P. aeruginosa* isolates when stressed with sub-inhibitory concentrations of different antibiotic classes, conditions that are also known to occur in patients. The specific pathways identified here could be co-targeted along with already existing antibiotics for treatment purposes.

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Implementing an antibiotic stewardship programme without increasing the surgical site infection rate in a highly antibiotic-resistant setting

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Background: The Bar Elias Hospital, along the road from Damascus to Beirut, in the Bekaa Valley, Lebanon, was started in October 2018 in response to the minor general surgical and chronic wound care needs of populations in the surrounding areas. Excessive prescription of broad-spectrum antibiotics is typical practice in Lebanon. For this reason, priority was set on establishing an Antibiotic Stewardship Program (ASP) and a surgical site infection (SSI) surveillance system to guarantee rational antibiotic use whilst ensuring the SSI rate did not increase. This report shares the lessons learnt in implementing an ASP and SSI surveillance system in this context.

Materials/methods: Preparation for implementing the ASP began before the hospital was opened. Staff were trained on ASP on initiation of employment. Tools for monitoring the pre- and post-operative prophylaxis, antibiotic prescriptions and SSI monitoring are used and data is collected in an Excel database. The ASP Committee was established in October 2018 and includes the Deputy Medical Director, Pharmacist, Health Promoter, Laboratory Manager, Nurse Responsible, Medical Manager and Data Manager. Modified AWaRe classifications were used to limit access to antibiotics. For the SSI surveillance system, monitoring during follow-up visits was performed, along with outpatient department nurses contacting patients by phone 30 days after surgery.

Results: During the first 12 months of operation, 420 surgeries were performed; 326 clean surgeries (Class I Altmeier) and 94 clean-contaminated (Class II Altmeier) were performed. There was 99.7% compliance with guidelines for pre-prophylactic antibiotics during anaesthesia; however one case received a restricted antibiotic without appropriate approval. Four percent (13) of clean surgeries received post-surgical prophylaxis in conflict to guidelines, whilst 69% (65) of clean-contaminated surgeries received post-surgical prophylaxis in concordance with guidelines. Of the 326 clean surgeries performed, there was one SSI case reported, whilst there were no cases of SSI reported for the 94 clean-contaminated surgeries.

Conclusions: The results from the initial 12 months of this program are promising, and indicate that an ASP and SSI surveillance system can be employed in a culture of high antibiotic prescribing activity. There was no indication that the application of an ASP affected the SSI rate.

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Genomic surveillance of *Bordetella* pertussis in Austria

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**Background:** Pertussis is a respiratory disease affecting mostly children and reemerging since the introduction of the acellular vaccines (ACVs) in the 90s. Strains that differ from the vaccine strain are a possible explanation for its increase worldwide. In Austria, the pertussis incidence in 2018 almost doubled in comparison to 2017. To explain this, we aimed at setting up an isolate-based surveillance system that complemented the case-based surveillance system, in order to characterize the collected isolates through whole genome sequence-based typing and to compare them with the vaccine strain.

**Materials/methods:** The surveillance system consisted of several microbiology laboratories servicing GPs and pediatricians in different Austrian provinces. Nasopharyngeal swabs for PCR and culture were collected from each pertussis case from May 2018 onwards. In the recovered isolates we identified 1) variants and mutations in the genes used as vaccine antigens (*ptxP, ptxS1, prn, fim2, fim3 and fhaB*) 2) genetic profiles, defined as the combination of the vaccine antigens genes 3) a new core genome Multi Locus Sequence Typing (cgMLST) scheme, comprising 2,938 genes, to detect clusters and assess the genetic relatedness among the isolates.

**Results:** Since May 2018, 60 isolates from 60 pertussis were recovered, being half of those vaccinated. Five genetic profiles were detected being the most frequent *ptxP3/ptxS1A/prn2/fim2/fim3-1/fhaB1*. None of them had the vaccine strain antigen profile. In addition, 42% of the isolates presented mutations in the *prn* gene causing pertactin deficiency, mostly originating from cases living in the same district, and more than the half of those were vaccinated. cgMLST revealed low variability among the clinical isolates (0-22 alleles), which was even lower (0-3) when intra-household transmission was confirmed, and high variability between the vaccine strain and the clinical isolates (>120 alleles). With a preliminary cluster threshold of ≤6 alleles, we identified 7 clusters. One of those grouped almost all pertactin-deficient isolates.

**Conclusions:** In conclusion, the circulating strains in Austria are different from the vaccine strain, being pertactin-deficient strains frequent, especially among vaccinated. cgMLST facilitated linking clusters with epidemiological data and therefore, we recommend its use together with vaccine genes typing to alert on *B. pertussis* outbreaks.

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Abstracts 2020

Abstract 7180

One Health investigation of Chlamydia psittaci in Denmark in 2019
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Background: Ornithosis or psittacosis caused by Chlamydia (C.) psittaci is a zoonosis primarily transmitted from birds. Ornithosis is often regarded as sporadic events, and cases are rarely investigated by molecular or epidemiological analysis. Since the beginning of 2019 both the human and veterinary diagnostics of C. psittaci has been performed at Statens Serum Institut (SSI)/Dansk Veterinær Konsortium (DK-VET), allowing investigation of infections in a one-health perspective. This has provided excellent insight into an outbreak-situation of C. psittaci in Northern Zealand in the summer 2019

Materials/methods: The owner of a large private homing pigeon flock in Northern Zealand was hospitalised with pneumonia. Atypical pneumoniae was suspected and C. psittaci was detected by PCR on a sputum sample. Samples were collected from the trachea of the pigeon flock (30 birds) owned by the patient, and as these were found positive, 31 contact flocks were sampled and analysed. A total of 961 swab samples from the pigeons were collected and pooled 3 by 3 into 329 sample

At SSI a new C. psittaci specific qPCR was designed. A database was constructed based on all available Chlamydia assemblies from the NCBI RefSeq genomic database (ftp://ftp.ncbi.nlm.nih.gov/genomes/refseq/bacteria), in order to identify genes unique to C. psittaci. The target was chosen to include a psittaci-specific region. This region is absent in C. abortus as well as other closely related Chlamydia species.

Results: Ornithosis was laboratory confirmed in the hospitalised index patient. Six out of 10 pooled samples from his pigeon flock were confirmed C. psittaci positive, and a total of 40 samples were C. psittaci positive (12%) from 12 flocks (36%) of the 31 investigated contact flocks.

Conclusions: As 36% of the contact flocks were found positive, the question is raised whether there is a large silent pool of C. psittaci infected birds in Denmark that can cause a continuous spread of the infection, and cause cases of ornithosis in humans. The co-localization of the C. psittaci diagnostics for both humans and animals, supplemented with molecular identification and epidemiological analysis gives us the opportunity to investigate a potential C. psittaci reservoir in Denmark

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Abstract 7182

The impact of H-NS-like protein on IncX3 plasmid dissemination and stability

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Background: IncX3-type plasmids largely mediate the dissemination of NDM genes in China. IncX3 plasmid could stabilize in host strains for 1000 generations and bring host advantage to the strain. It remains unclear which protein can regulate bla_{NDM}-bearing IncX3 plasmids adapting to new hosts and further spreading in this bacterial family. We focus on a DNA stabilized protein H-NS-like protein harbored by the IncX3 plasmid backbone and explore its role in plasmid stability.

Materials/methods: After knocking down IncX3 plasmid-encoded hns gene, we used conjugation experiments to evaluate the difference of conjugation frequency of parent strain and hns-knocking-down strain at different temperatures. Then we estimated the expression levels of different pilX genes. Plasmid stability in host was tested by serially passaging for 10 days. Mice infection models were employed to check strains virulence.

Results: Under different temperatures, IncX3 from parent strain J330 could transfer to Ec600 at 37°C with highest conjugation frequency. (6.22X10^{-5} for 25°C, 3.34X10^{-5} for 30°C, 1.19X10^{-4} for 37°C, 4.57X10^{-5} for 42°C). Plasmid-encoded HNS-like protein could decrease conjugation frequency at different temperature. Transcription of several pilX genes (pilX4, 5, 9 10, conjugation-related genes) from IncX3 are upregulated in cells depleted of H-NS-like proteins. Plasmid stability test showed that HNS-like protein could decrease the percent of strains maintaining IncX3 plasmid(at day 10, 0.71% for J330 vs 3.93% for strains losing plasmid-encoded hns). J330 could not infect balb/c mice successfully, so the impact of HNS-like protein on strain virulence is unclear.

Conclusions: Plasmid-encoded HNS-like protein could repress plasmid tranfer between the same species at different temperature, as well as the plasmid stability. The actual role of HNS-like protein in strain virulence could not be detected and IncX3 plasmid is a resistance plasmid more than a virulence plasmid.

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Abstract 7189

**Neuraminidase antibody response in a population vaccinated with split and adjuvant influenza vaccines**

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**Background:** Current licensed seasonal influenza vaccines (SIV) are only standardised for the hemagglutinin protein. Even so, clinical studies demonstrate that those vaccines contain immunogenic amounts of neuraminidase (NA), but the contribution of its immunogenicity to vaccine efficacy is currently not well studied. This study analyzes the increase in antibodies titers against the NA of different A(H1N1) viruses after SIV administration in two different age groups.

**Materials/methods:** The study included 160 pre and post-vaccination sera from adults [G1 = 80; 15-64yrs] and ≥65 years [G2 = 80], vaccinated with split and adjuvant influenza vaccine (AIV) against subtype A(H1N1)pdm09, respectively. Anti-neuraminidase antibodies (NAI) analysis was performed by using enzyme-linked-lectin-assay (ELLA) against five seasonal influenza strains of subtype A(H1N1) and the A/California/07/2009 strain of subtype A(H1N1)pdm09. Geometric means of NAI titers (GMTs) were analyzed. The increase of GMTs after vaccination (RIC) was compared according to the type of vaccine administered (α=0.05).

**Results:** Both split and AIV increased the titers of homologous and heterologous NAI against all influenza strains analyzed. The pre- and post-vaccination GMTs as well as the statistical comparison in the RIC according to the type of vaccine administered are described in Table 1.

Table 1. GMTs pre and post-vaccination and RIC of the NAI titers according to the seasonal influenza vaccine (SIV).

<table>
<thead>
<tr>
<th>A[H1N1] influenza viruses</th>
<th>Split-vaccine (G1=80)</th>
<th>Adjuvant-vaccine (G2=80)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GMTs pre</td>
<td>GMTs post</td>
<td>RIC</td>
</tr>
<tr>
<td>A/PR/8/1934</td>
<td>106.5</td>
<td>166.6</td>
<td>1.3</td>
</tr>
<tr>
<td>A/Weiss/1943</td>
<td>369.6</td>
<td>716.0</td>
<td>2.3</td>
</tr>
<tr>
<td>A/FM/1/1947</td>
<td>169.5</td>
<td>351.9</td>
<td>1.9</td>
</tr>
<tr>
<td>A/Brazil/11/1978</td>
<td>448.5</td>
<td>269.0</td>
<td>1.5</td>
</tr>
<tr>
<td>A/Brisbane/59/2007</td>
<td>222.3</td>
<td>251.0</td>
<td>1.8</td>
</tr>
<tr>
<td>A/California/07/2009</td>
<td>100.2</td>
<td>136.9</td>
<td>3.4</td>
</tr>
</tbody>
</table>

**Conclusions:** Our results showed the homologous and heterologous humoral response against neuraminidase influenza viruses after vaccination. Split vaccine induced a greater increase in the NAI titers with respect to the AIV against A/Weiss/43 and A/FM/1/47 strains. This difference seems to be linked to the fact that the population ≥65 years that received the adjuvant type vaccine had already very high NAI titers prior to vaccination against these two strains. Not only the type of vaccine administered seems relevant in the response to neuraminidase, but also the immunity previously acquired against the first infections during the life of an individual.

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Abstract 7191

**Epidemiology and outcomes of respiratory syncytial virus Infection in haematopoietic cell transplant recipients: findings from a multinational respiratory viral infection consortium (RVIC)**

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**Background:** Respiratory syncytial virus (RSV) is a common infection with serious consequences in immunocompromised cancer patients especially in recipients of hematopoietic cell transplant (HCT). Due to the seasonal nature, limited resources, and non-standard reporting practices, the studies examining these infections have been limited to single, large, cancer centers. We aimed to establish a multinational respiratory viral infection consortium (RVIC) of 11 cancer centers from US, Canada, and Brazil to study RVI in HCT recipients.

**Materials/methods:** We employed consensus-based data collection instruments and trained data entry personnel to collect demographics, risk factors, diagnosis, treatment, and outcomes of all HCT recipients with laboratory confirmed RSV infections diagnosed between January 2010 and December 2016 in a comprehensive data repository and performed descriptive statistical analyses on completed records.

**Results:** Of the 325 HCT recipients, majority were non-Hispanic white (66%), males (56%) with a median age of 57 years (range: 18 – 79 years) presenting with a community acquired (90%) RSV infection of the upper respiratory tract (80%). Patients had undergone autologous HCT (33%) or allogeneic HCT matched related [21%], matched unrelated [23%], mismatched donor [4%], cord [15%], and haploidentical [4%] and most were in complete or partial remission (78%) of acute myeloid leukemia [27%] or multiple myeloma [24%] at the time of RSV diagnosis. Acute (13%) or chronic (19%) graft versus host disease was common and treated with more than >2mg/kg/week of systemic corticosteroids in 36% of patients. RSV was mainly detected by nasal wash (43%) or swab (51%) and progressed from URI to LRI in 12%. Both oral (53%) and aerosolized (47%) ribavirin-based antiviral therapy using a continuous (21%) or intermittent schedule (79%) over a median duration of 10 days (range: 1 to 28 days) was administered in 64% of the study cohort for URI or LRI. Burden of RSV included need of hospitalization (32%), ICU admission (15%), mechanical ventilation (8%), and RSV-associated death (15%).

**Conclusions:** RSV remains a common and significant infection in HCT recipients with substantial burden on patient and cancer centers. RVIC has been a successful endeavor in bringing together a multinational, multidisciplinary team to study RSV in this vulnerable population.

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Abstract 7192

Plazomicin activity against carbapenemase-producing Enterobacterales carrying aminoglycoside-modifying enzymes from European and United States hospitals

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Abstract third-party references: This study was performed by JMI Laboratories and supported by Cipla Ltd., which included funding for services related to preparing this abstract.

Background: Plazomicin is a next-generation aminoglycoside recently approved by the United States (US) Food and Drug Administration (FDA) for complicated urinary tract infections, including acute pyelonephritis caused by certain Enterobacterales species. We evaluated the activity of plazomicin and clinically available aminoglycosides against CPE isolates collected in European and US hospitals that also carried AMEs.

Materials/methods: Among 7,913 Enterobacterales isolates collected in European and US hospitals during 2017-2018 and susceptibility tested by CLSI reference broth microdilution methods, 280 were carbapenem-resistant Enterobacterales (CRE; CLSI criteria). These isolates were submitted to whole genome sequencing and data analysis to detect β-lactamases, AMEs and 16S rRNA methyltransferases (RNAmet).

Results: A total of 232 (82.9% of CRE and 2.9% overall) CPEs were identified among the 280 CRE isolates. These isolates carried genes encoding KPC-2, KPC-3, NDM-1 and OXA-48-like enzymes (48, 64, 29 [6 producing OXA-48] and 19 isolates, respectively). RNAmet that encode resistance to all aminoglycosides, including plazomicin (US FDA breakpoint) were detected in 66 (28.4%) CPE isolates. All but 1 of these isolates was from Europe and armA was the most common RNAmet (56 isolates). Among the 166 isolates that did not carry RNAmet, 110 harbored AMEs (91 from Europe and 19 from US). Among the most common AME genes that modify clinically important aminoglycosides were aac(6’)-Ib [57 isolates], aac(6’)-Ib-cr [41] and aac(3)-Ila [39]. Amikacin and gentamicin were only active against 40.9% and 43.6% of these isolates (EUCAST breakpoints), respectively. Plazomicin inhibited 97.3% of the CPE isolates carrying AME genes at the US FDA approved breakpoints. Gentamicin displayed greater activity against Enterobacterales isolates when compared to US isolates (47.3% and 26.3%, respectively), but the activity of amikacin (40.7%/42.1% susceptible [Europe/US]) and plazomicin (100.0%/96.7%) was similar for both regions. Tobramycin had limited activity against these isolates (<2.0% susceptible). Only 1 NDM-1-producing Providencia stuartii from Romania carried the gene aac(2’)-Ia, which encodes the AME that modifies plazomicin.

Conclusions: Plazomicin displayed greater in vitro activity when compared to amikacin and gentamicin against CPE isolates that do not carry RNAmet and its activity is not affected by commonly detected AMEs in US and European hospitals.

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Validation of three MicroScan antibiotic susceptibility testing microplates designed for low-resource settings

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Abstract third-party references: Médecins Sans Frontières

Background: The Mini-lab is a Médecins Sans Frontières (MSF) project for the development of an all-in-one clinical bacteriology laboratory (CBL) deployable in low-resource settings (LRS). AST is essential in CBL, to improve patient treatment and limit the emergence of antimicrobial resistance. Three microplates were designed by choosing a list of antibiotics based on bloodstream infection (BSI) pathogens, MSF field needs, surveillance and public health importance. MicroScan lyophilized broth microdilution plates (Beckman Coulter Inc., Sacramento, USA) were chosen, co-developed and tested as they provide standardized, long shelf life, robust and easy-to-use by none-expert microbiology technicians.

Materials/methods: The MSF MicroScan Gram Pos microplate (C32698) for Staphylococcus and Enterococcus species, MSF MicroScan Gram Neg microplate (C32699) for Gram-negative bacilli and MSF MicroScan Fastidious microplate (C32700) for Streptococcus and Haemophilus species were validated with frozen isolates from routine clinical laboratories and challenging isolates coming from low resource settings, following ISO20776-2:2007 guidance. In total, 123 Gram-positive isolates (representing 7 different Gram-positive species), 157 Gram-negative isolates (representing 15 different gram-negative species), and 107 fastidious isolates (representing 8 different fastidious species), were tested. The three microplates were tested against EUCAST V9 recommended Disc diffusion, gradient diffusion method (E-test) or standard micro-broth dilutions.

Results: From the 16 antibiotics present on the three panels for treatment orientation all of them had a percentage of Category Agreement (CA) above 90% and major (MAJ) and very major error (VMJ) below 3%. On the MSF MicroScan Gram Pos panels for Staphylococcus spp, penicillinase-stable beta-lactams indicators had a CA of 99%, inducible clindamycin had a CA of 100%, while for Enterococcus spp, high-level aminoglycoside resistance indicators had a CA of 96% with only 2% MAJ and VMJ. On the MSF MicroScan Gram Neg panels, Extended Beta Lactamase, colistin and carbapenem indicators had presented a CA of 99%, 98% and 100% respectively for all species.

Conclusions: The 3 MSF MicroScan AST microplates was to that excellent performances with the clinical isolates from LRS and also other including pathogens such as Non-typhi Salmonella, Streptococcus pneumoniae and Haemophilus influenza. These often cause BSI in LRS but have been rarely tested on these microplates.

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Abstract 7196

Characterisation of Group B streptococci (GBS) colonising pregnant women in Belgium, 2018: antimicrobial susceptibility profile and distributions of capsular-types, pili-types and sequence-types

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Background: To update the knowledge of key epidemiological features of group B streptococcus (GBS) colonizing pregnant women’s vagina and/or rectum is important in the process of development of a vaccine to prevent GBS neonatal disease. As in 2013, the Belgian National Reference Center Streptococcus agalactiae (NRC) renewed in 2018 an epidemiological surveillance study.

Materials/methods: GBS strains isolated from pregnant women’s vagino-rectal swabs were sent to the NRC between October 2017 and March 2018 by laboratories of the Belgian sentinel network and of Luxembourg. Five isolates were expected per laboratory. For each strain, the capsular-poly saccharide (CPS) type and the pili-type were determined by multiplex-PCR. The antimicrobial susceptibility testing was performed according to EUCAST criteria by disk-diffusion and broth-microdilution. Multiple-Locus Sequence-Typing (MLST) was performed on serotype III strains and the gene hvgA was detected by PCR.

Results: A total of 228 strains of GBS have been sent from 46 laboratories. Serotype III, Ia and V were the 3 predominant serotypes, representing 25%, 23.7% and 23.7% of the cases, respectively, followed by serotype II in 14.47% of the cases. All GBS strains expressed at least one of the three pili proteins, with the couple Pi1, Pi2a being predominant (51.75%). All strains remained susceptible to penicillin. The resistance rates to erythromycin and clindamycin were 27.63% and 24.56%, respectively. Among these macrolides/lincosamides resistant GBS, the constitutive resistance phenotype was predominant [56.06%] and ErmB and ErmTr were the most frequent detected genes, in 37.88% and 27.27% of cases, respectively. The most prevalent sequence-type among serotype III GBS was ST17 in 40.35% of cases.

Conclusions: Among GBS isolated from colonized pregnant women in Belgium in 2018, we observed, compared to our previous 2013 data, an increase of serotypes Ia and V, being now practically equal to serotype III. On the other hand, pili distribution and MLST profiles among type III strains were quite similar. All the strains remained totally susceptible to penicillin and the resistance rate to macrolides and lincosamides was stable compared to 2013.

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Abstract 7200

Dynamic interactions between methicillin-resistant *Staphylococcus aureus* and methicillin-sensible *Staphylococcus aureus* contamination of the near patient and extended environment and patient colonisation revealed by whole genome sequencing in a tertiary referral hospital

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**Background:** The transmission dynamics of methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) between patients, their near environment and extended-environmental sites on nine wards of a tertiary referral hospital was investigated using whole-genome sequencing (WGS) during a non-outbreak period.

**Materials/methods:** Nasal-swab and oral rinse samples were obtained from consenting patients over three collection phases, 2017-2019. Samples were also taken from patient lockers, bedframes and mattress using sterile-neutralisation swabs. Air samples (500 L) were taken in each ward using an air sampler (Oxoid/Thermo Scientific). All samples were cultured on MRSAselect and SAselect chromogenic agars (Colorex) with methicillin-resistance confirmed using 30-μg cefoxitin disks (Oxoid). Additional MRSAselect and SAselect contact plate samples were taken from frequent hand-touch sites. Representative patient and environmental isolates selected on their antibiogram susceptibility profiles underwent Illumina whole-genome sequencing (WGS) and whole-genome multilocus-sequence typing (wgMLST; BioNumerics). Isolates exhibiting <24 wgMLST allelic differences were deemed related.

**Results:** MRSA and MSSA were recovered from 27/388 (6.9%) and 129/388 (33.2%) patients, respectively. A total of 1164 samples from near-patient environment sites yielded 13 MRSA and 58 MSSA corresponding to 57/388 (14.7%) near-patient environments. Air samples from 445 locations yielded 23 MRSA and 65 MSSA, whereas 21 MRSA and 73 MSSA were recovered from 1110 samples from frequent hand-touch sites. WGS was undertaken for environmental isolates associated with 29/57 near-patient environments including 12 colonised and 17 uncolonised patients whose near environments yielded MRSA or MSSA. Relatedness determined by wgMLST analysis was detected in 4/12 instances between pairs of isolates recovered from a colonised patient and their near environment. Isolates from the remaining eight colonised patients were unrelated to isolates from their near environment. Isolates recovered from air or additional environmental sampling were unrelated to patient isolates recovered from the 29 patients or near environments.

**Conclusions:** Considerable contamination of patients’ near and extended ward environment sites with MRSA and MSSA was detected. WGS identified patients as the likely source of near-environmental site contamination in 4/29 (13.8%) instances, implying another source of contamination in the majority of cases. This underpins the importance of regular decontamination and cleaning of ward surfaces in the acute setting.

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Plasticity in a bacterial global regulator drives the switch to antibiotic resistance and virulence

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Background: The ability to adapt rapidly to a changing environment is key for bacteria to be able to survive the ever-changing conditions they are exposed to. The inducible MexEF-OprN efflux pump, involved in antibiotic resistance, substrate import, toxin export and quorum sensing, is regulated by the global transcriptional regulator MexT, which is suppressed by MexS. Mutations in mexT and mexS in P. aeruginosa are associated with changes in antibiotic sensitivity and virulence. We investigated why such mutations arise so frequently and assessed their phenotypic impact.

Materials/methods: 151 clinical and environmental P. aeruginosa isolates were collected and sequenced. Strain PAO1 was used to construct a strain with an 8bp deletion in mexT (PAΔ) and select for a ciprofloxacin resistant strain with a mutation in mexT (PAn). All strains had MICs of ciprofloxacin, chloramphenicol and imipenem determined. Antibiotic-resistant mutants and subsequently antibiotic-sensitive revertants were selected from 33 strains in vitro, and sequenced. The strains PAO1, PAΔ and PAn underwent transcriptomics, virulence assays in Galleria mellonella, and metabolic phenotyping of 626 compounds.

Results: Analysis of strains PAO1, PAΔ, PAn, and in vitro selected strains, showed that P. aeruginosa switches from an antibiotic-sensitive to an antibiotic-resistant phenotype through MexT-induced increased efflux due to inactivating mutations in mexS. Transcriptomics showed altered expression of 1/6th of the genome (~900 genes) in the MexT-active/MexS-inactive strains PAΔ and PAn relative to PAO1, including reduced expression of virulence-related genes. Strains PAΔ and PAn were less virulent than PAO1 in the G. mellonella infection model, and were less metabolically active. In the absence of selective pressure, antibiotic-resistant strains reverted to sensitivity through mutations in mexT rather than a reversion to the ancestral genotype (i.e. reactivation of mexS).

Conclusions: Exposure to antibiotics selects for a loss of homeostatic control of efflux, which is not regained upon removal of antibiotic selection. This suggests that an evolutionary ratchet drives bacteria towards switching between an antibiotic-resistant but less virulent phenotype and an antibiotic-sensitive virulent phenotype, but does not enable a return to the ancestral state. This then enables subsequent unrelated antibiotic resistance mutations to produce strains that are simultaneously highly resistant and virulent.

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Abstract 7205

**Evaluation of Myco-TB TM kit for decontamination of urine and stool specimens to detect mycobacteria**

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**Background:** During the last decade, remarkable progress has been made in the diagnostics of pulmonary tuberculosis; however, diagnostic challenges in extra-pulmonary tuberculosis (EPTB) remain to be addressed. Diagnosis of EPTB is difficult due to the pauci-bacillary nature of disease. Most of the extra-pulmonary specimens (such as body fluids, aspirates, pus, urine and stool) need decontamination but certain decontaminating agents eliminate a substantial number of mycobacteria together with the contaminants, while others are too weak to destroy them. The resulting consequence is a costly delay in detecting the tubercle bacilli thereby slowing down the process of initiation of therapy. The aim of this study was to evaluate Myco-TB TM (Copan Italia, Brescia) in sample pretreatment, compared to the N-acetyl-L-cysteine–sodium hydroxide (NALC-NaOH) decontamination and fluidization method, for the detection of the *Mycobacterium tuberculosis* complex (MTBC) and Non Tuberculous Mycobacteria (NTM) in urine and stool specimens.

**Materials/methods:** A total of 120 urine and 90 stool specimens has been collected from clinically suspected cases of EPTB. Each sample has been divided into two equal parts and decontaminated by using the ready-to-use kit Myco-TB TM kit and classical NALC-NaOH decontamination protocol then investigated using Ziehl-Neelsen method, the Lowenstein-Jensen culture and the Real-Time PCR Anyplex MTB/NTM test.

**Results:** Stool and urine treated with Myco-TB system shown a significant reduction in bacteria load compared to NALC-NaOH decontamination (reduction of 11% for urine and 20% for stool). The Anyplex MTB/NTM test underlined an improvement in for samples treated with Myco-TB system. Furthermore, no contamination was detected following the treatment with this innovative system.

**Conclusions:** Our findings suggest that Myco-TB is an effective and faster decontamination tool for extrapulmonary clinical specimens as urine and stool. Particularly, this approach allows to reduce microbial contaminants and to efficiently remove inhibitors for molecular assays increasing the specificity and significantly reducing the invalid tests.

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Abstract 7208

Long-lasting outbreak of *Serratia marcescens* in a veterinary hospital due to contaminated chlorhexidine

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**Background:** Companion animals can be infected or colonized by bacteria, some of them representing both an animal and public health issue. These bacteria can spread within veterinary settings and cause Healthcare-Associated Infections (HAI) with various epidemiological facets. Our aim was to characterize the long-term occurrence of HAI due to *S. marcescens* in a French veterinary hospital.

**Materials/methods:** The study was conducted from September 2009 to September 2018 on 66 animals (45 dogs, 19 cats, 2 rabbits) from which one *S. marcescens* isolate was collected. Identification was performed using MALDI-TOF and antimicrobial susceptibility was tested by disc diffusion. All isolates were typed by XbaI-PFGE and five representative isolates were whole-genome sequenced using the NovaSeq technology.

**Results:** Epidemiological data unambiguously indicated that 32 isolates were HAI cases, mostly associated with surgical site infections. *S. marcescens* isolates were also found as surgical site colonizers without infection (n=22). The monthly incidence of *S. marcescens* isolation showed two clusters (September to December 2009, and March 2014 to September 2018) belonging to two distinct PFGE profiles. All isolates showed the intrinsic antibiotic resistance profile of this bacterial species. In January 2019, a large environmental sampling of the clinic demonstrated that *S. marcescens* was only present in 1% chlorhexidine impregnated gauze tubes, and that these environmental isolates shared exactly the same PFGE profile as animal isolates, which was further confirmed by the NGS data. All animal *S. marcescens* isolates also showed high MIC values for chlorhexidine (128 mg/L). Chlorhexidine tubs were banned from the hospital and disinfection gauzes are now prepared instantly.

**Conclusions:** This study reports the first long-term occurrence of HAI due to *S. marcescens* in a veterinary hospital due to contaminated chlorhexidine. The mode of transmission was undoubtedly direct inoculation of the bacteria onto the surgical site during skin disinfection procedures. The absence of any detection of *S. marcescens* between 2009 and 2014 is most likely due to the relocation of the clinic in new premises at the end of 2009, but without changes in hygiene procedures. Measures have now been taken and no *S. marcescens* was found at the time of writing (6 months).

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Abstract 7210

Brucellosis in different types of transplantation
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Background: Brucellosis, a bacterial disease caused by Brucella species, is one of the most important zoonotic diseases worldwide. Brucella can affect all organs of the human body and has different and numerous manifestations. It is an intracellular microorganism with particular immunologic response, which is different from other intracellular bacteria. In addition, it is less likely to theoretically transmit through various organs in body. The behavior and manifestations of Brucella in transplant recipients has not yet been comprehensively studied. The purpose of this study was to evaluate brucellosis in all types of transplant patients.

Materials/methods: Total cases of brucellosis in transplant patients with no time and language limitations were searched and retrieved using the following keywords: Brucella, Brucellosis, Transplant, and Transplantation through medical databases, including Google Scholar, Scopus, PubMed, and SID. All clinical features, including the time of transmission (before, during, and after transplantation), considered treatments and patients’ outcomes were investigated.

Results: Fifteen cases reported in 15 studies (out of 777 studies) were retrieved. Kidney (46.6%), liver (26.6%), and hematopoietic stem cell transplantation (HSCT) (13.3%) were the most reported types of transplantation. The majority of cases were related to the Middle East countries, including Turkey (five studies), followed by Saudi Arabia (4 studies) and Iran (2 studies). The presentation of brucellosis in 40% of the patients has been occurred in the early post-transplantation period, whereas in 60% of the cases it was late-onset. Transmission by donor had been reported in rare cases of HSCT. The most clinical features of the disease were fever (80%), headache (33.3%), musculoskeletal pain (33.3%), and sweating (26.6%).

Conclusions: Brucellosis in transplant recipients seems to be uncommon even in the endemic regions. However, rare cases could be transmitted through bone marrow transplantation and transfusion. Precise screening and meticulous supervision during and after transplantation can lead to a reduction in the frequency of brucellosis.

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**Background:** The plasma exposures of posaconazole improve with the newer formulations of intravenous (IV) injection and delayed-release tablet. The targeted plasma concentrations (Cp) of posaconazole are >700 ng/mL for prophylaxis and >1250 ng/mL for treatment. Lack of consensus on the upper limit of therapeutic range but 1830, 2000, or 3750 ng/mL was proposed to prevent hepatotoxicity. This study aimed to compare posaconazole Cp between IV and tablet and to explore the association between Cp and hepatotoxicity.

**Materials/methods:** This retrospective study enrolled adult patients who received IV posaconazole in a 2600-bed medical center in Taiwan between December, 2018 and September, 2019. The use of posaconazole IV and tablet formulations and trough Cp were evaluated. Liver function tests such as ALT, AST, ALP, GGT and bilirubin were documented. Nonparametric tests were applied due to small sample size. Statistical analyses were conducted with SPSS with a two-tailed $\alpha$ value of 0.05 as statistical significance.

**Results:** Twenty-eight patients receiving IV posaconazole were included and all of them had haematological malignancies. Their median age was 53.3 years old (range: 22-74) and more females (18/28, 64.3%) in the study. There were 23 patients (82.1%) on posaconazole for prophylaxis. The overall median posaconazole Cp was 1100 ng/mL (range 160-3480). No significant difference of Cp was observed between IV (1310 ± 747 ng/mL) and tablet (1240 ± 742 ng/mL). Approximately 25% of Cp failed to achieve targets: 13/77 Cp (16.9%) on prophylaxis with 1 breakthrough invasive fungal infection and 16/39 on treatment (41.0%). Elevations of ALT and bilirubin were the most frequent laboratory abnormalities. Although ALT elevation was generally mild, there was a significant association between increased ALT and individual posaconazole Cp >1830 ng/mL (P=0.02). Increase of direct bilirubin was associated with average Cp >2000 ng/mL in therapy courses (P=0.005).

**Conclusions:** Similar distribution of posaconazole Cp in IV and tablet formulations was demonstrated in this study. One fourth of patients had sub-therapeutic Cp. Elevation of liver enzymes most likely occurred when Cp >1830 ng/mL. Clinicians should consider monitoring of Cp during IV and tablet posaconazole therapy to improve effectiveness and safety.

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Abstracts 2020

Abstract 7212

Detection of Zika and Chikungunya viruses circulation in Pointe Noire district (Republic of Congo) during the 2019 Chikungunya outbreak

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Background: On 9 January 2019, the health authorities notified to the WHO and outbreak of chikungunya in the Republic of Congo. A risk assessment was carried out by the Italian Istituto Superiore di Sanità in collaboration with ENI and the Department of Health of Pointe-Noire to evaluate the potential exposure to chikungunya virus (CHIKV) and other vector-borne virus infections.

Materials/methods: Mosquitoes were collected in different sites of the urban and sub-urban area of Pointe-Noire, which was considered the epicenter of the outbreak, to detect the possible presence of CHIKV and other arboviruses. Field collected mosquitoes were identified, pooled and analyzed by real-time RT-PCR for the presence of genome of Zika, dengue, chikungunya, West Nile, Usutu, Yellow fever, Rift Valley, and Japanese encephalitis viruses. Culex was the most commonly detected genus.

Results: The identification of some mosquito species and full genome analysis of virus isolates are in progress. However, preliminary analyses showed the positivity of 3 Culex quinquefasciatus mosquito pools to Zika virus (ZIKV). Furthermore, molecular tests performed on the blood of a symptomatic child showed a double infection by CHIKV and ZIKV. The girl lived in the same district of Pointe-Noire where the ZIKV positive Culex mosquitoes were collected.

Conclusions: Our results show the circulation in the region, beside CHIKV, also of ZIKV, and highlight the possible role of the genus Culex in the transmission of ZIKV. The low level detection of Aedes spp. mosquitoes was probably due the limited number of typical Aedes larval breeding sites compared to other more suitable for Culex species in the dry season.

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Abstract 7214

First case of osteomyelitis caused by hypervirulent Klebsiella pneumoniae spread within a family in Korea

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Background: A new “hypervirulent” K. pneumoniae (hvKP) with hypermucoviscosity has emerged as a clinically significant pathogen causing highly invasive infections, such as liver abscesses, in both healthy and immunocompromised individuals. We present a case of osteomyelitis due to hypervirulent K. pneumoniae spread within a family reported in Korea.

Materials/methods: We characterized two isolates from blood sample of patient and stool sample of husband for their antimicrobial susceptibility, VITEK-2 system and genetic relatedness using capsular typing, multilocus sequence typing (MLST). Whole genome sequencing and comparative genomics analysis of strains of K. pneumoniae were determined by MiSeq (300bp paired end) by (Chunlab, Seoul, Korea).

Results: Both isolates were susceptible to all antibiotics except for ampicillin and showed hypermucoviscosity by a positive string test. K. pneumoniae isolates found to be a K1 serotype, sequence type 23 (ST23). Comparative genomics analysis presented with a phylogenetic tree analysis (Fig. 1.) and Venn diagram. A phylogenetic tree shows that two isolates of this case are closely related to liver abscess isolate in Taiwan and femoral bone isolate in United States. Carbapenem-resistant K. pneumoniae strain and carbapenem-resistant hypervirulent K pneumoniae strains in China are closely related. Venn diagram depicts the comparative Venn diagram of 6 hypervirulent K pneumoniae sharing a lot of genes (4475) and two isolates of this case are closely related than other isolates.

Conclusions: we report a first case of osteomyelitis caused by hypervirulent Klebsiella pneumoniae spread within a family in Korea. Microbiologists and clinicians need to become more aware of the possible severity of infections caused by this strain of K. pneumoniae.

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Evaluation of the Revogene Carba C assay for detection and differentiation of carbapenemase-producing bacteria
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Background: Rapid confirmation of carbapenemase production (CP) is essential not only for an effective therapy, but also for the prompt implementation of infection control measures in order to prevent CP-Enterobacterales (CP-E) dissemination. We have evaluated the performance of the novel, real-time PCR-based Revogene® Carba C Assay for the detection of blaKPC, blaNDM, blaVIM, blaOXA-48-like, and blaIMP genes.

Materials/methods: Revogene® Carba C Assay is a multiplex nucleic acid-based in-vitro diagnostic test that runs on the microfluidic Revogene platform (Meridian Bioscience, Cincinnati, OH, USA) and intended for CP-E detection from cultured colonies. It was evaluated on colonies of 120 well-characterized Enterobacterales with reduced susceptibility to carbapenems, on 50 MDR Pseudomonas aeruginosa (Pa) and 40 MDR Acinetobacter baumannii (Ab).

Results: The GenePOC™ Carba Assay’s performances were high as it was able to detect the five major carbapenemases in Enterobacterales with nearly 100% sensitivity, except for OXA-48 with 97.4%, as one distantly related variant OXA-535, was not detected. All double and triple carbapenemase producers were detected. When extrapolating the results to the French CP-E epidemiology between 2012-2018, the Revogene® Carba C Assay would have detected 99.3% of the 9624 CPEs sent to the F-NRC, missing 69 CPEs [2 GES-5; 10 OXA-23; 2 TMB-1; 1 SME-4; 54 IMI, 1 FRI].

Similarly, when extrapolating the results to the French epidemiology of CP-Pa it would have been able to detect 94% of them, missing only one DIM, 11 GES-variants and two rare IMP variants [IMP-31 and IMP-46]. However, only 15.9% of CP-Ab could be detected, as the most prevalent carbapenemase in that species is OXA-23.

Conclusions: The Revogene® Carba C Assay showed excellent sensitivity and specificity for the five most common carbapenemases, including IMP variants that are not detected by all molecular assays. It is well adapted to the CP-E and CP-Pa epidemiology of many countries worldwide. Its simplicity and short turnaround time make it suitable for use in the routine microbiology laboratory. It can provide results from colonies that grew on MH but also from selective screening media. This assay needs now to be evaluated directly on clinical samples.

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In vitro activity of delafloxacin against highly-levofloxacin-resistant invasive isolates of Streptococcus pneumoniae

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Background: The emergence of multidrug-resistant non-PCV-13 Streptococcus pneumoniae isolates causing invasive disease is a cause of concern. Delafloxacin is a new anionic fluoroquinolone equally potent against topoisomerase IV and DNA gyrase, with high intracellular penetration and enhanced bactericidal activity under acidic conditions. We studied the activity of delafloxacin against highly-levofloxacin-resistant invasive strains of Streptococcus pneumoniae.

Materials/methods: A total of 114 highly-levofloxacin-resistant (MIC >32 mg/L) S.pneumoniae invasive isolates received at a Reference Laboratory from March 2008 to June 2019 were studied. The origins were blood (n=109), pleural fluid (n=3), cerebrospinal fluid (n=1) ascitic fluid (n=1). Capsular serotypes were analysed by the Pneumotest-Latex and by the Quellung reaction using commercial antisera (Statens Serum Institut, Copenhagen, Denmark). Delafloxacin, levofloxacin, penicillin, cefotaxime, erythromycin, and vancomycin MICs were determined by the gradient diffusion method (Etest®; bioMerieux, France).

Results: The distribution of serotypes/serogroups were 8 (n=60), 19V (n=22), 4 (n=12), 15A (n=9), 19A (n=2), 33 (n=2), 31 (n=1), 11A (n=1), 12F (n=1), 15C (n=1), 18C (n=1), 35B (n=1) and 35F (n=1), being 87.7% non-PCV-13 serotypes. A total of 47 (41.2%) isolates were penicillin non-susceptible (MIC>0.06 mg/L), 27 (23.7%) were cefotaxime non-susceptible (MIC>0.5 mg/L), and 80 (70.2%) were erythromycin resistant (MIC>0.5 mg/L). Delafloxacin MIC50 and MIC90 (mg/L) values against the 114 levofloxacin-resistant isolates were 0.06 and 0.19, respectively, (range 0.01 - 1.0 mg/L). All isolates were susceptible to vancomycin. MIC distributions for delafloxacin against the pneumococcal strains is shown in the table.

Conclusions: This study shows that delafloxacin is a very active agent against multi-drug resistant invasive isolates of S.pneumoniae including highly-levofloxacin-resistant isolates, being at least >32-fold more potent than levofloxacin. The potency of delafloxacin makes it a good addition to the therapeutic arsenal for the treatment of multidrug resistant pneumococci.

Table. Antimicrobial activity of delafloxacin tested against highly-levofloxacin-resistant (MIC>32 mg/L) S. pneumoniae.

| Number and cumulative % of isolates inhibited at delafloxacin MIC (mg/L) of: | 0.01 | 0.02 | 0.03 | 0.04 | 0.05 | 0.06 | 0.09 | 0.12 | 0.19 | 0.25 | 0.38 | 0.50 | 0.75 | 1 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2 | 3 | 6 | 7 | 37 | 64 | 90 | 99 | 104 | 108 | 111 | 112 | 113 | 114 |
| 1.8 | 2.6 | 5.3 | 6.1 | 32.5 | 56.1 | 78.9 | 86.8 | 91.2 | 94.7 | 97.4 | 98.2 | 99.1 | 100.0 |

MIC<sub>50</sub> | MIC<sub>90</sub>
---|---

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Obesity affects interstitial space fluid of subcutaneous adipose tissue concentrations of meropenem after single application: a controlled clinical trial

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Abstract third-party references: Supported by Department of Anesthesiology and Intensive Care, University of Leipzig Medical Center, Leipzig, Germany, On behalf of Dr. Philipp Simon

Background: Antibiotics are often administered at a fixed dose, often without taking into account essential individual pharmacokinetic influencing factors. Obesity influences the pharmacokinetics of antibiotics due to changes in distribution volumes, blood flow and elimination rate. Underdosing of antibiotics promotes the development of multi-resistant bacteria in addition to severe consequences for individual patients. In this clinical study, perioperative antibiotic prophylaxis prior to abdominal surgery was used as a clinical-pharmacological model for the single administration of antibiotics. We investigated the hypothesis that meropenem plasma and subcutaneous interstitial space fluid (ISF) exposure in obese patients are lower compared to non-obese patients.

Materials/methods: The study was approved by the local Ethics Commission and the Federal Institute for Drugs and Medical Devices of Germany (EudraCT No. 2012-004383-22). We included patients prior to elective abdominal surgery with BMI ≥ 35 kg/m² or 18.5 ≤ BMI ≤ 30 kg/m² matched for age and sex. An intravenous bolus of 1000 mg meropenem was infused for 30 min starting 60 min prior to skin incision. The determination of meropenem concentration in ISF was performed by microdialysis via catheters placed subcutaneously in both upper arms, preoperatively. Catheters were calibrated by retrodialysis. Serial blood and tissue samples were collected in fractions from 0.5 to 8 h after infusion and meropenem was determined in the samples by HPLC and UV detection. Noncompartmental analysis was performed in R 3.6.0 and the PKNCA package (v0.9.1). P-value < 0.05 was considered statistically significant.

Results: 30 patients were included (15 obese BMI = 49 ± 11 kg/m²; 15 non-obese BMI = 24 ± 2 kg/m²). In contrast to plasma, meropenem concentrations in ISF in the obese group (Figure 1) were lower than in the non-obese group with significantly lower maximum concentrations (median Cmax 11.9 vs. 18.0 mg/L, p = 0.011). The distribution volume in the obese group was higher (25.9 vs. 22.9 L, p = 0.013), the half-life longer (1.6 vs. 1.3 h, p = 0.014) and clearance comparable (12.5 vs. 10.9 L/h, p = 0.41).

Conclusions: During the first hours after single administration of meropenem obese patients had significantly lower ISF concentrations. Depending on different MICs this may have an effect on target attainment. Therefore further analyses are necessary.


Figure 1: Concentration-time-curves (mean ± standard deviation) of meropenem in plasma and interstitial space fluid (ISF) of subcutaneous adipose tissue; dashed lines show relevant MIC for meropenem (EUCAST breakpoints 2019)

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Abstract 7219

Positive respiratory viral panel results moderately shorten antibiotic duration in patients with presumed respiratory tract infections

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Background: Respiratory viral panels (RVPs) can detect multiple viral pathogens and give clinicians diagnostic confidence to discontinue antibiotics. However, relatively little is known about how these tests influence antibiotic prescribing in hospital settings.

Materials/methods: This was a retrospective chart review of patients who had RVPs performed while receiving antibiotics. Hospitalized adults receiving antibiotics at the time of the RVP were included. Exclusion criteria included ICU care, solid organ transplantation (SOT), positive RVP for influenza, positive bacterial cultures, and antibiotic administration for other bacterial infection or prophylaxis. A multivariate linear regression model was created to investigate associations with longer antibiotic use after the RVP result.

Results: 2587 patients were screened and 451 met inclusion criteria; 249 in the positive RVP group and 252 in the negative RVP group. Primary reasons for exclusion were SOT, ICU, and influenza diagnosis. No significant differences existed between groups. Of the patients with a positive RVP, rhinovirus was isolated in 156 (64.5%), followed by metapneumovirus (35, 14.9%) and RSV (32, 13.3%).

Table. Characteristics of patients by test

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RVP+ (n=249)</th>
<th>RVP- (n=202)</th>
<th>Total (n=451)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>60.2 (14.3)</td>
<td>59.3 (15.5)</td>
<td>59.8 (14.9)</td>
</tr>
<tr>
<td>Male gender, n [%]</td>
<td>89 (35.7)</td>
<td>76 (37.6)</td>
<td>165 (36.6)</td>
</tr>
<tr>
<td>Length of stay, mean (SD)</td>
<td>5.4 (3.8)</td>
<td>5.8 (4.8)</td>
<td>5.6 (4.3)</td>
</tr>
<tr>
<td>Immunocompromised, n [%]</td>
<td>53 (21.3)</td>
<td>32 (15.8)</td>
<td>85 (18.8)</td>
</tr>
<tr>
<td>PMH Asthma, n [%]</td>
<td>87 (34.9)</td>
<td>66 (32.7)</td>
<td>153 (33.9)</td>
</tr>
<tr>
<td>PMH COPD, n [%]</td>
<td>120 (48.2)</td>
<td>85 (42.1)</td>
<td>205 (45.4)</td>
</tr>
<tr>
<td>PMH Heart failure, n [%]</td>
<td>60 (24.1)</td>
<td>34 (16.8)</td>
<td>94 (20.8)</td>
</tr>
<tr>
<td>Antibiotic duration, mean days (SD)</td>
<td>3.8 (2.4)</td>
<td>3.6 (2.4)</td>
<td>3.7 (2.4)</td>
</tr>
<tr>
<td>Antibiotics discontinued within 24 hours of RVP, n [%]</td>
<td>109 (43.8)</td>
<td>93 (46)</td>
<td>202 (44.8)</td>
</tr>
</tbody>
</table>

On multivariate analysis, factors that were significantly associated with longer antibiotic duration after RVP were length of stay (0.22 days, p=<0.0001), immunocompromised state (0.32 days, p=0.001), and a PMH of asthma (0.2 days, p=0.0355). A positive RVP was associated with a shorter duration of antibiotics after the test result (0.22 days, p=0.0133).

Conclusions: Positive RVP results were associated with a moderately shorter duration of antibiotics. More rapid assays may hasten time to discontinuation of unneeded antibiotics.

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Abstract 7220

**Graphene oxide-linezolid combination as potential new anti-TB treatment**

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**Background:** Tuberculosis (TB) remains one of the most alarming worldwide infectious disease and there is an urgent need for improved drugs and treatments, particularly for the emergence and spread of drug-resistant Mycobacterium tuberculosis (Mtb) strains. New nanotechnologies based on carbon nanomaterials are now being considered to improve anti-TB treatments and graphene oxide (GO) showed interesting properties as anti TB drug. GO preferentially accumulates in the lungs and it is quickly degraded by macrophagic peroxidases. Additionally, it has a high drug loading capacity and intrinsic antibacterial properties. GO can trap Mycobacterium smegmatis and Mtb in a dose-dependent manner, reducing entry of bacilli into macrophages, but not much is known about interaction with anti-TB drugs.

**Materials/methods:** Combination of anti-TB drugs and GO anti-mycobacterial properties have been evaluated on Mtb H37Rv by using a modified synergy checkerboard assay. Isoniazid (INH), Amikacin (AMK) and Linezolid (LZD) have been selected and minimal inhibitory concentration (MIC) assessed in presence of GO. Murine macrophages (J774) were used as in vitro infection model, and colonies forming units (CFUs) were evaluated at 4 hours and 24 hours post infection.

**Results:** Synergy checkerboard assay highlighted different activity of the GO when incubated with INH, AMK or LZD. Interestingly, INH and AMK activity inversely correlated with GO concentrations. Conversely, LZD MIC was reduced when GO was co-administered. We studied the interaction between GO and the selected anti-TB drugs observing a strong interaction with INH and LZD. GO-INH/AMK interaction, and not GO-LZD, promoted a significant aggregation in solution. Combinations of GO and LZD were tested in an in vitro infection model highlighted a higher anti-TB activity than the single compounds at four hours post infection. Surprisingly, a capacity to reduce CFUs were still observed when GO-LZD was administrated 4 hours post infection and CFUs evaluated at 24 hours.

**Conclusions:** GO-LZD co-administration is potentially a new promising anti-TB treatment at the forefront in fighting emerging antibiotic resistant Mtb strains. Importantly, LZD is suggested to treat MDR-TB together with fluoroquinolones and bedaquiline. Even though other studies are needed, this innovative pharmacological approach leads to reduce treatment periods and decrease or mitigate antibiotic adverse effects.

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Abstract 7221

Regional outbreaks of Enterobacter cloacae complex NDM-1 in Poland, 2015-19

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Background: Since 2011 Poland has recorded NDM-producing Enterobacteriaceae, including large Klebsiella pneumoniae ST11 NDM-1 multi-regional outbreak, approaching rapidly to endemic situation, and much smaller regional outbreak of K. pneumoniae ST147 NDM-1 imported in 2015 from Tunisia. Here we extend our previous observations, by presenting two regional dissem-
inations of Enterobacter cloacae complex NDM-1 based on the WGS data.

Materials/methods: The study comprised 82 unique NDM-positive E. cloacae complex isolates, since the first identification in October 2015 till the end of August 2019. NDMs were detected by CarbaNP and PCR, followed by sequencing. All isolates were
typed by MLST. Polymorphism of blaNDM-carrying Tn125-like elements was assessed by PCR-mapping. Twenty-seven isolates
representing the temporal and geographical scale of the outbreak, as well single K. pneumoniae and Escherichia coli NDM-posi-
tive isolates co-identified with E. cloacae complex in the same materials were subjected to WGS by Illumina MiSeq. The polymor-
phism of blaNDM-carrying Tn125-like elements was re-analysed using the DNASTAR software. Resistomes of the isolates were
determined using ResFinder.

Results: The MLST analysis revealed 7 profiles: ST89 (n=59), ST146 (n=16), ST114 (n=2), ST1303 (n=2), ST56 (n=1), ST198 (n=1) and ST231 (n=1). Five Tn125 derivatives were found, with the most numerous comprising 2994bp fragment from the up-
stream ISAba125 3' end (253bp) to the 5' part of the tat gene (806bp) characteristic for K. pneumoniae/ST11/NDM-1 outbreak
(n=71) and 5353bp element from 253bp 3'end of tnpA ISAba125 to 1250 5'end of groEL typical for “Tunisian” K. pneumoniae/
ST147/NDM-1. “Endemic” variant of Tn125 was detected among ST89 (n=8), all ST146, ST1303 (n=2), ST114 (n=1) and ST198
(n=1), whereas “Tunisian” only in ST89 (n=8). K. pneumoniae and E. coli NDM-positive isolates represented identical Tn125
polymorphs as co-morbid E. cloacae complex isolates, revealing horizontal transfer between species. Analysis of resistomes
of two main clones, ST89 and ST146, showed very similar profiles within groups, with ST146 possessing much less acquired
resistance genes.

Conclusions: The results documented horizontal transfer of Tn125 polymorphs from K. pneumoniae ST11 and ST147, followed
by clonal dissemination of two E. cloacae complex clones in Poland: ST89, recently described as E. hormaechei ssp. steiger-
waltii, and ST146.

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Development of two new techniques based on real-time PCR for the detection of Candida auris in clinical settings
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Background: Candida auris is an emerging fungal pathogen associated with nosocomial outbreaks and high mortality rates. This species is often misidentified as it is phylogenetically close to other Candida spp. In order to improve their detection in clinical settings, specific primers and probes for C. auris were designed and included in a multiplex real-time PCR (MRT-PCR) technique previously described (Fortun et al., 2014). The assay was standardized and validated with strains and sera samples spiked with DNA. A technique based in High Resolution Melting (HRM) was also developed to fast identify clinical strains.

Materials/methods: For MRT-PCR assay, Beacon Designer 9.1 software (Premier Biosoft,) was used to design specific primers and a molecular Beacon probe targeting rDNA region. The technique was optimized and included in a previous assay that detected C. glabrata, C. krusei and C. guilliermondii. Sensitivity, specificity and reproducibility were determined: i) Standard lines were constructed by using 5 repetitions of dilutions of genomic DNA from 1 ng to 1 fg / µl of each pathogen, ii) specificity was tested including other fungal species and human DNA. Validation was performed by using clinical strains and sera samples spiked with different DNA amounts (10ng to 200 fg). For HRM assay the ITS2 region of the rDNA was amplified using the universal primers ITS3 and ITS4. Six species of Candida spp. close-related to C. auris were included in the HRM assay.

Results: The MRT-PCR assay presented a high reproducibility detecting up to 100 fg of DNA/µl of sample. No cross-reaction was detected when other fungal species were included in the assay. Coefficient of variation was 3 %. The technique detected all strains included (7/7) and all sera samples (7/7). The analysis of HRM allowed to discriminate the six species included in the assay.

Conclusions: 1) The new MRT-PCR assay that detects four species of the genus Candida including C. auris presented a high sensitivity, reproducibility and specificity, although further validation will be required. 2) The method developed to identify C. auris based on HRM, was able to discriminate the species included and it could be a simple tool to identify this emerging species.

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Abstract 7229

**Antibiotic resistance and efflux pump inhibitor effect in Acinetobacter baumannii strains isolated from Cajamarca, Peru**

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**Abstract third-party references:** Universidad Peruana de Ciencias Aplicadas, Instituto de Investigación Nutricional

**Background:** Acinetobacter baumannii is a nosocomial pathogen that thrives alarmingly in intensive care units due to its ability to adapt and develop mechanisms of antibiotic resistance. Recent studies in Peru show that most infections are caused by multi-resistant (MDR) and extremely resistant (XDR) strains of this pathogen. Efflux pumps represent an important mechanism for resistance development on this bacteria.

**Materials/methods:** In this study, the antibiotic susceptibility of 47 A. baumannii strains isolated from Cajamarca, Peru were evaluated. Antibiotic susceptibility was assessed by disk diffusion on Mueller-Hinton agar plates, following the Clinical and Laboratory Standards Institute (CLSI) guidelines for the following antibiotics: ampicillin-sulbactam, piperacillin-tazobactam, cefotaxime, cefazidime, cefepime, gentamicin, amikacin, levofloxacin, doxycycline, tetracycline, meropenem, imipenem, trimethoprim-sulfamethoxazole and colistin. The effect of phenylalanine-arginine B-naphthylamide on the Minimum Inhibitory Concentration [MIC] of levofloxacin, tetracycline and amikacin was determined based on a 4-fold or greater reduction as the criterion for significance.

**Results:** All the isolates were resistant to at least one antibiotic agent in three or more categories. One isolate (2.13%) proved to be resistant to all the antibiotics tested and was classified as pan-drug-resistant (PDR) and 25 isolates (53.19%) presented an XDR phenotype, the majority being susceptible to colistin. The remaining 21 isolates (44.68%) were considered MDR. After phenylalanine-arginine B-naphthylamide addition: 8.51% of the isolates (4/47) showed a significant reduction with levofloxacin, 59.57% (28/47) with tetracycline and 31.91% (15/47) with amikacin.

**Conclusions:** Acinetobacter baumannii strains demonstrated MDR and XDR profiles of antibiotic resistance, which is an important nosocomial and public health concern. The addition of the efflux pump inhibitor PABN resulted in a reduction of the non-susceptibility for levofloxacin, tetracycline and amikacin. Efflux pump inhibitors may be useful as adjunct therapy for this pathogen if they significantly improve antimicrobial susceptibility in further larger studies and prove to be safe.

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Abstract 7231

**Evaluation of T2MR for the diagnosis of bloodstream infections in paediatric patients**

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**Background:** Bloodstream infection (BSI) is one of the major sources of mortality among hospitalized patients. A prompt and appropriate antibiotic therapy is critical to reduce morbidity and address a favorable clinical outcome. Cultural methods are the "gold standard" although they require too long times.

The molecular technology T2 magnetic resonance (T2MR) uses two diagnostic panels (T2Candida and T2Bacteria) to detect yeasts and bacteria directly from whole-blood samples within 3-5 hours, in a fully automated process.

Objective of the study is to evaluate the T2MR for rapid detection of pathogens in blood samples of paediatric patients with suspected BSI. Results were compared with those of blood culture (BC) and with the LightCycler Septifast test, a PCR Real-Time for the identification of bacterial and fungal DNA.

**Materials/methods:** A total of 226 paediatric patients, admitted to the Bambino Gesù Children's Hospital from May 2018 to November 2019, were included in the study and blood samples were contextually analyzed for T2Bacteria and/or T2 Candida, BC and Septifast. The recommended minimal blood volume samples for T2 testing is 3 ml. When less volume was occurring, samples were diluted or loading was performed through direct pipetting of whole blood directly onto the T2 cartridge.

**Results:** For T2Bacteria a 76% overall PPA was detected and a NPA of 95%. For T2Candida panel PPA was 100% and NPA 98%. Statistical analysis was elaborated for T2 bacteria including only not diluted samples and an increase of sensitivity and specificity was obtained (PPA 83%; NPA 96%). A total of 70/282 (25%) samples provided discordant results due to these possible reasons: BC and Septifast not performed or with discordant result. A T2 positive result, not confirmed by BC and Septifast, was evaluated in conjunction with clinical presentation and/or other laboratory markers.

**Conclusions:** T2MR assay can be used to efficiently diagnose BSI caused by bacteria and yeasts from paediatric specimens. This technology shows a significantly faster time to identify microorganisms than a culture-dependent system and this could result in improved time to appropriate pharmacological therapy.

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Characteristics of the initial phase of tick-borne encephalitis
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Background: TBE usually has a biphasic course. Reliable information on the initial phase is limited. Recognition that febrile illness was the initial phase of TBE typically occurs only after the onset of the second, meningoencephalitic phase of the disease and development of antibodies to TBE virus (TBEV). In the initial phase the infection can be confirmed by the presence of TBEV in serum but this is not a routine diagnostic approach.

Materials/methods: 98 patients, seen at the initial and second phase of TBE at our centre during 2003–2019, in whom infection with TBEV was identified with PCR in the initial phase serum specimens, qualified for the present report. The samples were obtained either during a prospective study on the etiology of febrile illness after a tick bite (78 patients, 80%) or represented remnants of the samples collected as a part of routine diagnostic testing of a patient with a febrile illness in whom TBE later developed (20 patients).

Results: Of 98 patients (median age 51, IQR 39–61 years), 47 (48%) were males. The most common signs/symptoms were malaise/fatigue [98% of patients], fever [89%; the highest temperature 38.5 (38.0–39.0) ºC], headache [86%], myalgias [54%], arthralgias [43%], gastrointestinal symptoms [46%; nausea/vomiting 38%, mild diarrhea 16%], and respiratory symptoms [18%; sore throat 10%, cough 10%]. 88% of patients had leukopenia, 51% thrombocytopenia, and 60% at least one abnormal liver function test result. IgM antibodies to TBEV in serum were present in 2 patients, none was IgG positive. Duration of the initial phase of TBE was 7 (6–8) days. 37 (38%) patients were hospitalized for median 3 (1–5) days.

Of 78 patients who were included in the prospective study and systematically followed for ≥2 months, 5 (6%) did not develop any further symptoms, 5 had mild and unimpressive symptoms potentially suggesting nervous system involvement but did not undergo CSF examination, while 68 (87%) patients developed clear-cut neurologic involvement associated with CSF pleocytosis. All the patients seroconverted.

Conclusions: The initial phase of TBE may be quite severe. A large majority of patients with initial phase of TBE later develops meningoencephalitis.

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Nasal colonisation with *Staphylococcus aureus* is a risk factor for ventricular assist device infection in the first year after implantation: a single-centre cohort study

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**Background:** *S. aureus* nasal colonization is a risk factor for the acquisition of post-operative wound infections. *S. aureus* infections in patients with implanted ventricular assist device (VAD) have detrimental effect on the overall morbidity and mortality. In this study we prospectively investigated *S. aureus* nasal colonization as the source of endogenous infections in this vulnerable patient group with a special focus on the onset of *S. aureus* infection. Better knowledge on the temporal component of *S. aureus* infection dynamics in VAD patients may provide the necessary evidence for optimized preventive interventions.

**Materials/methods:** Single-center, prospective cohort study (n=49) to (i) evaluate the risk of *S. aureus* nasal colonization for VAD-related *S. aureus* infection in patients with implanted VAD and (ii) determine the time to infection onset after implantation. Patients admitted for VAD implantation were screened for *S. aureus* colonization prior to surgical intervention with follow-up until heart transplant, death or end of study period. Endogenous infections were confirmed by WGS.

**Results:** Among 49 patients (17 colonized, 32 non-colonized), *S. aureus* VAD-infections by *S. aureus* occurred after 60 days post-implantation. Those colonized with *S. aureus* were at a significantly higher risk of acquiring VAD-related *S. aureus* infections compared to non-carriers (9/17, 52.9% vs. 4/32, 12.5%, P=0.005; IRs 2.81 vs. 0.61/1000 pdys; IRR 4.65, 95% CI 1.30-20.65, P=0.009). 75% (6/8) of paired *S. aureus* samples from colonized patients with VAD-infection showed concordant core genomes.

**Conclusions:** In patients with durable VAD, *S. aureus* nasal colonization is a source of endogenous infection throughout the first year after device-implantation, affecting mostly the driveline, and accounting for about half of VAD-infections. Due to the late infection onset, VAD-patients may still benefit from post-operative decolonization if pre-operative decolonization could not be performed. Our findings suggest that decolonization strategies may need to be adapted and optimized for this patient group to accommodate for late onset of infection.

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Abstract 7237

One-year evaluation of Genelead VIII combined to Deeplex-MycTB to detect rapidly the genotype and the resistance profile of Mycobacterium tuberculosis complex directly from clinical samples

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Background: For quickly starting suitable treatment to increase the chance of cure and reduce transmissibility of the disease, early and accurate identification of complete tuberculosis (TB) drug resistance profile is needed. The Genelead VIII is a new all-in-one system that extracts and detects Mycobacterium tuberculosis complex (MTBC) DNA from clinical samples. Deeplex-MycTB is based on the next-generation sequencing of PCR fragments amplified from extracted DNA and can predict the genotype and the resistance profile of 13 anti-tuberculous drugs. This study reports a one-year routine evaluation of the coupling of these two technologies applied directly to clinical samples.

Materials/methods: 52 clinical samples, with a positive (N=35) or a negative (N=17) microscopic examination, were tested from May 2018 to June 2019 in the French National Reference Center for Mycobacteria (CNR MyRMA). The results were compared (i) with the culture for Genelead VIII, and (ii) with the standard genotypic and phenotypic drug susceptibility testing for Deeplex-MycTB. When a spoligotype was shared by at least two strains, the MIRU-VNTR typing was performed for these strains.

Results: Overall, the combination of Genelead VIII to Deeplex-MycTB identified MTBC and drug resistance in 27 of the 35 (77%) smear positive- and 3 of the 17 (18%) smear negative samples. The Genelead VIII results were fully concordant with those of the culture for smear-positive samples and were 65% concordant for the tests carried out on smear-negative samples. The Deeplex-MycTB assay following Genelead VIII extraction gave interpretable results in 52% of the tests done in the study. Most of the failed tests corresponded to samples with a negative microscopic examination or less than 1 AFB per field. Deeplex-based drug susceptibility predictions were 83% concordant with the phenotypic method, and 91% with the genotypic ones. The median time to obtention of full results from clinical samples was 8 days.

Conclusions: The combined approach Genelead VIII-Deeplex-MycTB represents real progress for quickly identifying (8 days) MTBC and for determining the drug resistance profiles of M. tuberculosis directly from clinical samples. This tool could be very helpful, especially for choosing the most suitable therapeutic regimen to treat multidrug- and extensively drug-resistant TB.

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Comparative analysis of kitome identification methods in viral metagenomic data
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Background: Viral metagenomics next-generation sequencing (mNGS) enables the comprehensive characterization of viral communities in clinical samples. Despite a wide range of potential applications, several hurdles need to be overcome before its implementation in clinical lab. In particular, reagent contaminations (kitome) may critically impair the interpretation of the results. A growing number of studies have developed methods to address this issue, but mainly evaluated for the identification of bacterial contaminants. In this study, we aimed to compare various approaches for the detection of viral contaminants in mNGS data.

Materials/methods: We used a data set corresponding to 236 plasma samples, prospectively collected from multiple myeloma patients. These samples were sequenced in 19 batches using a validated mNGS protocol. One no-template control (NTC) per batch was also processed through the complete workflow. The detection of viral contaminants was performed through (1) the batch effect analysis [2] the comparison of viral abundances between NTC and clinical samples with DESeq2 and [3] Decontam package which includes two methods; one is based on the relationship between read counts and biomass and the second is based on the comparison of the prevalence between NTC and patient samples.

Results: We found that the batch effect approach and methods of the Decontam package identified at random the contaminant status of viral families or genera. Conversely, the differential approach comparing viral abundances between clinical samples versus NTC provided much better classification performances. This classification was based on three criteria, including fold change, significance and background noise. Using these criteria, we generated a list of potential contaminants that mainly derived from bacteriophages or plant viruses. Interestingly, some of these contaminants were found differentially abundant between patients and could have been misinterpreted as clinically relevant.

Conclusions: To our knowledge, this is the first study assessing different computational methods for the kitome identification in viral metagenomic data. Our data highlight that specific approaches are needed to detect viral contaminants and should be systematically applied to avoid clinical misinterpretation.

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Candida auris compared to other Candida spp. candidaemia: a two-year experience in a Spanish tertiary hospital

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Background: Candida auris is a novel Candida species, first reported in Japan in 2009, which is associated with nosocomial outbreaks, especially in intensive care units. In our setting, a 500-bed tertiary hospital, there is an ongoing C. auris outbreak since September, 2017; and, despite the implementation of different control measures (e.g. periodic screening for C. auris colonization), we still report cases. The aim of this study is to describe the characteristics of patients with C. auris compared to other Candida spp. candidaemia episodes.

Materials/methods: Candida species were isolated by our routine laboratory procedure. Briefly, blood samples are incubated in BD Bactec® FX for 14 days. When the sample flags positive, and the gram stain reveals the presence of yeasts, subculture is performed in Sabouraud-Chloramphenicol. Candida isolates are further identified by MALDI-TOF (Bruker®) and susceptibility testing is carried out. Demographic and clinical relevant data were retrospectively collected in a 2-year period of all candidaemia episodes from the beginning of the C. auris outbreak (September 2017 to September 2019).

Results: The main results of the study are shown in the table below. Among all clinical underlying conditions, digestive disease/abdominal surgery was selected for being the most frequent. Some patients were infected by two or more different species simultaneously or in the same hospitalization period.

<table>
<thead>
<tr>
<th></th>
<th>Total (%)</th>
<th>Candida auris (%)</th>
<th>Candida spp. (no C. auris)* (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>91</td>
<td>30 (33.0)</td>
<td>68 (74.7)</td>
</tr>
<tr>
<td>Male</td>
<td>68 (74.7)</td>
<td>26 (86.7)</td>
<td>49 (72.1)</td>
</tr>
<tr>
<td>Average age (years)</td>
<td>63.1</td>
<td>56.5</td>
<td>65.4</td>
</tr>
<tr>
<td>&gt;75 years</td>
<td>20 (22.0)</td>
<td>5 (16.7)</td>
<td>17 (25.0)</td>
</tr>
<tr>
<td>Digestive disease/abdominal surgery</td>
<td>48 (52.7)</td>
<td>21 (70.0)</td>
<td>34 (50)</td>
</tr>
<tr>
<td>Mortality at day 30</td>
<td>40 (44.0)</td>
<td>9 (30.0)</td>
<td>34 (50.0)</td>
</tr>
</tbody>
</table>

*C.albicans [36/91, 39.6%], C.glabrata [18/91, 19.8%], C.parapsilosis [8/91, 8.8%], other species [13/91, 14.3%].

Conclusions: C. auris is the second cause of candidaemia following C. albicans two years after the outbreak started [33.0%]. Most patients had an underlying condition of digestive disease. This is especially important in C. auris, reaching 70.0%. C. auris seemed to cause less mortality at day 30 than other Candida spp. This could be related to the younger age of patients affected by C. auris.

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Dengue virus infects HBMEC cell model and regulates proteins related to the blood-brain barrier function

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Background: The clinical characteristics of dengue are changing, and neurological manifestations in dengue cases with fatal outcomes are being reported more frequently, although dengue was long regarded as a non-neurotropic virus. Although dengue antigen has been detected with different laboratory techniques in the brain, it is still not completely understood how dengue virus (DENV) gains entry into the CNS.

Materials/methods: Human brain microvascular endothelial cells (HBMEC) cell model was used to study the mechanism of DENV crossing the blood-brain barrier. We identified the susceptibility of four serotypes of dengue virus to HBMEC cells, and applied transcriptome sequencing to find genes that were differentially expressed when HBMEC cells were infected with DENV3. Finally, the dynamic changes of proteins with different gene expression were detected to verify key regulatory proteins related to the blood-brain barrier function.

Results: All four serotypes of DENV are susceptible to HBMEC cells, of which DENV3 is the strongest. DENV persistent virus replication was observed after infection, accompanied by CPE. Infection of the CNS by DENV3 may correlate with the expression of specific chemokines, tight junction proteins (TJPs), and cell adhesion molecules (CAMs). The expression of GM-CSF, GRO-α, MCP-2, MIG, and RANTES shown significant increase, especially RANTES increased by 1.5 fold at day 1 after MOI-5 infection, and remained significantly high at days 2 and 3 compared to uninfected cells. As the TJP, the expression of ZO-1 and claudin-1 sharply increased at day 1, and declined to near baseline levels at day 2. It is worth noting that, we did observe an obviously increase in VCAM-1 transcripts at post infection, while no significant increase in CAM expression was observed in control cells. However, the increase in VCAM-1 protein levels was not observed.

Conclusions: DENV manifests strong infectivity in blood-brain barrier-associated HBMEC cell model. Dynamic changes in protein, such as RANTES for specific chemokines, ZO-1 and claudin-1 for TJPs, and VCAM-1 for CAMs, imply that DENV infection of HBMECs could destroy the integrity of the BBB, which facilitate the entry of cell-free virus into the CNS.

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Abstract 7246

Epidemiology, risk factors and treatment of anaerobic bloodstream infections: a 7-year study

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Background: Anaerobic bacteria can cause life threatening bloodstream infections. Anaerobic bloodstream are rare, but have high mortality. The objective of this study is to describe the epidemiology of bloodstream anaerobic infections from blood culture, clinical risk factors and the use of empirical treatment over 5 years, between January 2014 and January 2019, at a tertiary care hospital with 680 beds.

Materials/methods: Retrospective and descriptive study of patients with bloodstream infections. Between January 2014 and December 2018, blood cultures bottles were submitted 42,607 for analysis from 25,565 patients. The medical records of patients with positive blood cultures, microbiological data of the isolates and the epidemiological, clinical and therapeutic variables of the patients have been reviewed.

Results: 79 clinical cases of true anaerobic bacteremia were identified. The mean age was 68.53 years (range 30-90), 40 were male and 39 were female. The majority 46 (58.22%) had at least one comorbidity, and 10 (12.65%) had two or more comorbidities, in 33 (71.73%) of the cases it was a neoplasm. The main focus of bacteremia was abdominal (70.87%), followed by skin and soft tissues (21.51%). The most frequently isolated anaerobes were the following: Bacteroides fragilis (35.44%), Bacteroides thetaiotaomicron (20.25%), Bacteroides spp. (7.59%), Clostridium perfringens (6.32%), Clostridium septicum (3.79%), Parabacteroides distasonis (1.26%), Prevotella spp. (1.26%), Fusobacterium nucleatum (2.53%) Finegoldia magna spp. (1.26%), Peptostreptococcus (1.26%). The most commonly used empirical antibiotic treatment was Piperacillin / Tazobactam in 46.83% of the cases, followed by amoxicillin / ac. clavulanic 13.92% and ertapenem 7.59%. Mortality was 20 (25.31%) directly related to bloodstream infections.

Conclusions: Cancer patients have a greater predisposition for anaerobic bloodstream infections (71.73%). The prevalence of Bacteroides spp. (63%) and Clostridium spp. (10%) may reflect the dominance of intra-abdominal sepsis in anaerobic bloodstream infections. In most cases the empirical antibiotic treatment was adequate.

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Abstract 7247

**Delivering antibiotics locally to biofilms by targeted drug delivery and prodrug therapy**

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**Background:** Antibiotic treatment of biofilm infections often fail because the dose that can be administered safely is insufficient to eradicate the biofilm, which contains antibiotic-tolerant persister cells. We hypothesize that treatment will be more effective if drugs are delivered or synthesized at the site of infection, leading to a high local concentration with minimal side effects. We aimed at delivering a high local dose of antibiotics through two different approaches: i) targeted delivery of encapsulated antibiotics, and ii) local drug synthesis through prodrug therapy.

**Materials/methods:** Targeted drug delivery uses drug encapsulation, accumulation in the biofilm, and a triggered burst release. We encapsulated vancomycin and rifampicin in temperature-sensitive liposomes decorated with aptamers that bind specifically to *Staphylococcus aureus*. Accumulation, drug release, and kill efficiency was quantified on *S. aureus* biofilms in vitro.

Prodrug therapy uses immobilized enzymes (glucuronidase) to convert non-toxic glucuronide prodrugs to the active drug. We developed a novel method for synthesizing glucuronide prodrugs, opening the door for antimicrobial prodrug therapy for the first time. We immobilized the catalyst (β-glucuronidase) in a layer-by-layer coating on titanium implants. Glucuronide prodrugs of moxifloxacin was administered in solution, and the effect on *S. aureus* viability and biofilm formation was quantified.

**Results:** Aptamer-targeted liposomes accumulated in *S. aureus* biofilms, resulting in eradication of biofilms in vitro, while non-targeted liposomes were less effective. Although this result is promising, the burst release offers little control over dosage and exposure time. We therefore proceeded with prodrug therapy. The embedded enzyme continuously converted the inactive moxifloxacin prodrug to active moxifloxacin at the implant surface, which prevented biofilm formation, even under continuous flow where the synthesized drug could not accumulate locally.

**Conclusions:** Targeted drug delivery and pro-drug therapy enable local antibiotic therapy. The exposure time and concentration is better controlled in prodrug therapy, and we believe that our encouraging results will pave the way for implementing more potent drugs that target persister cells in treatment of biofilm infections.

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Etiological structure of exanthema subitum in children of younger age

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Background: Exanthema subitum is a common disease of early childhood caused by a primary infection with Human betaherpesvirus 6B and less frequently by Human betaherpesvirus 7 (HHV-7). 90% of cases occurring in children younger than two years old. In some cases inaccurate diagnosis and subsequent inadequate treatment at the beginning of the disease often lead to the development of undesirable complications requiring longer-term hospital treatment.

Materials/methods: The study involved 47 patients with primary infection, which were hospitalized at the infectious department of the children’s city hospital in Moscow: 24 male and 23 female with median age 12 months (ranged 6 – 36 months). DNA of Human betaherpesvirus 6A/B (HHV6-A/B), HHV-7, Human gammaherpesvirus 4 (EBV), Human betaherpesvirus 5 (HCMV), Human alphaherpesvirus 3 (VZV), Human alphaherpesvirus 1/2 (HSV-1/2), Primate erythroparvovirus 1 and RNA of Rubella virus, Enterovirus spp. in samples of whole blood were detected using qualitative or quantitative real-time PCR assays.

Results: 97.9% (46/47) children had a fever of 37.6 – 40.1 ºC. Most of them (76.6% (36/47) cases) had a small, rose-pink or red papules. Febrile seizures were observed in 4.3% (2/47) cases. HHV-6A/B DNA was detected in whole blood in 68.1% (32/47); HHV-7 – 17.0% (8/47); HHV6-A/B and HHV-7 co-infection – 8.5% (4/47); HHV-6A/B and EBV – 6.4% (3/47) cases. The concentration of HHV-6A/B DNA was 1.68–2.97 (median 2.20); HHV-7 – 1.95–3.28 (median 2.53) log10 copies/10^6 cells. Another viruses was not detected.

Conclusions: We have obtained data on etiological interpretation of exanthema subitum in children of younger age. HHV6-A/B was found in whole blood in 83.0% [39/47, 95% CI 69.86 – 91.11] cases, HHV-7 – in 25.5% [12/47, 95% CI 15.25 – 39.51]. 14.9% [7/47, 95% CI 7.41 – 27.69] patients had multiple concurrent viremia events.

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The effects of introduction of a syndromic PCR sputum testing in intensive care unit pneumonia patients in a tertiary trauma centre

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**Background:** Pneumonia is one of the most common diagnoses in ICU and carries up to 50% mortality rates. It is also associated with high healthcare costs. Microbiological diagnosis allows targeting of antimicrobial therapy and has been shown to improve patient outcomes. Standard culture of sputum samples has limitations due to time required to obtain results. BioFire offers a syndromic panel of multiplex PCR to identify pathogens rapidly. It is currently unknown if this molecular diagnostic test improves patient outcomes or what effect it has on pneumonia management.

**Materials/methods:** The study analysed notes of pneumonia patients admitted to ICUs in Hull hospitals between 1st August and 31st December 2018 and 2019, before and after the introduction of BioFire testing. The primary outcome of this observational study was the length of ICU stay and the secondary outcomes included the following: 1) ventilation duration, 2) mortality, 3) number of antibiotics before and after microbiological testing, 4) time from sample collection to a) management change, b) extubation and c) discharge from ICU.

**Results:** The review of all sputum samples received in the laboratory during the set time period in 2018 identified 120 patients with radiologically confirmed pneumonia. So far, 78 patients have been identified in the 2019 period. Although there was no reduction of median ICU stay duration, a reduction of prolonged ICU stay frequency was observed in 2019 in comparison to 2018 (61.5% and 65% respectively). We observed a reduction in number of antibiotics prescribed per patient following microbiology results in both groups. This reduction occurred sooner in 2019 group, within 1.2 days, compared to 3.3 days in 2018 group from the time of sample collection (p<0.001). There was a reduction in time from sample collection to extubation of 3.4 days and to ICU discharge of 5.4 days in 2019 compared to 2018 group. We also observed a reduction in mortality rates within 30 days of ICU discharge (28.3% vs 24.4% in 2018 and 2019 groups respectively, p<0.05).

**Conclusions:** Rapid molecular diagnostics allows adjustment of antimicrobial therapy and has potential for improving patient outcomes.

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Ultra high-resolution mass spectrometry database improves identification of clinical yeasts from blood cultures by the Acrion system

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Background: Bloodstream infections caused by yeasts can lead to devastating complications and markedly increase the costs of hospital care and is a big challenge as a life-threatening condition with increasing prevalence. Mortality remains high, especially when effective antifungal drug therapy is not promptly administered. Consequently, rapid and accurate identification of the causative organism is critical for successful treatment. Bloodstream yeast species are frequently identified by MALDI-ToF in the clinical laboratory. Due to their cell wall structure and low cell count they give higher quality identifications when the samples are prepared with manual purification, sub-culturing on a plate and lysis steps either offline or on the MALDI-ToF plate. This poster demonstrates the performance of bloodstream yeast identifications using a novel integrated high resolution mass spectrometry system and a spectral database containing a diverse range of bloodstream clinical yeasts.

Materials/methods: A novel workflow applying high resolution accurate mass spectrometry (HRAM MS) was applied to identify bloodstream yeast infections. The protein extracts from each species were introduced to the mass spectrometer in Acrion™ system. Mass spectra were evaluated for the individual protein masses detected. Different identification approaches were compared.

Results: A comprehensive HRAM MS database covering 22+ clinical yeast species causing bloodstream infections has been developed. In the highly automated workflow in Acrion™ system, hands on time for the sample preparation is limited to pouring directly from the positive blood culture bottle such that user handling variability is thereby reduced, and a second culturing step is not needed. The high resolution mass spectrometry analysis yields good performance and identification of challenging yeast taxa.

Conclusions: Applying the proposed rapid and user-friendly workflow in Acrion™ system and benefiting from high resolution Orbitrap™ mass spectral data in the database significantly improved identification of yeast species from blood culture including challenging taxa.

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Epidemiology, characteristics and outcomes of bacteraemia and endocarditis caused by Staphylococcus aureus in cancer patients

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Background: Cancer patients with Staphylococcus aureus bacteraemia (SAB) could have different clinical characteristics, risk of endocarditis and outcomes than the general population.

Materials/methods: Retrospective multicentre cohort study of consecutive patients with SAB admitted in two tertiary hospitals in Spain, from January 2011 to December 2017. Patients with active cancer (PAC) were defined as patients with recently diagnosed solid cancer or haematologic malignancy, who underwent chemotherapy/radiotherapy within the prior 3 months or who had metastatic cancer. SAB and S. aureus endocarditis in PAC were compared with patients without cancer (PWC).

Results: Among 789 episodes of SAB, 217 (27.5%) occurred in PAC. Compared to PWC, PAC were younger (mean age 59.5y vs 66.6y, p<.001), had less comorbidities such as cardiopathy (11.5% vs 39.9%, p<.001), diabetes mellitus (13.8% vs 36.7%, p<.001) and chronic renal failure (8.3% vs 29.6%, p<.001). They had less often osteoarticular prostheses than PWC (3.2% vs 10.3%, p<.001). PAC had less commonly community-acquired SAB (6.9% vs 26.6%, p<.001). Catheter-related SAB (39.6% vs 26.4%, p<.001) and skin and soft tissues infection (18.4% vs 12.9%, p<.001) were more common in PAC, whereas they presented less frequently osteoarticular infection (3.2% vs 14.0%, p<.001) and endocarditis (2.3% vs 8.7%, p<.001). Thrombocytopenia was more commonly observed in PAC (30.9% vs 0.3%, p<.001) but it was not significantly associated with a lower risk of endocarditis. Septic shock at presentation (12.0% vs 17.3%, p=.040) and septic embolisms (8.3% vs 29.2%, p<.001) were less frequent in PAC. Overall, methicillin-resistant SAB was observed in 177 patients (22.5%), without differences between groups. Thirty-day mortality was also similar between groups (24% vs 20.8%, p=.245). Independent risk factors for 30-day mortality in PAC were unknown source of infection (OR 2.89, 95%CI 1.10-7.55, p=.030), septic shock (OR 5.29, 95%CI 1.87-15.0), and persistent bacteraemia (OR 4.34, 95%CI 1.70-11.08, p=.002).

Conclusions: Endocarditis in PAC with SAB was less frequently observed than in PWC. Relevant differences in the sources of SAB, baseline comorbidities and site of acquisition could explain the different risk observed between both populations. Thirty-day mortality was high in both groups of patients.

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Abstract 7253

Performance evaluation of the new automated chemiluminescent immunoanalyser-based interferon-gamma releasing assay in comparison with the QuantiFERON-TB Gold Plus to detect latent tuberculosis infection

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Background: laboratory diagnosis of latent tuberculosis infection (LTBI) is performed with interferon-gamma release assays (IGRAs). We compared the performance of a new automated chemiluminescent immunoanalyzer-based IGRA test (CLIA-IGRA; LIAISON, DiaSorin, Italy) with the commonly used QuantiFERON-TB Gold (Qiagen, Germany) Plus performed on two ELISA instruments, the Dynex DS2 (Qiagen) and ETIMAX-3000 (DiaSorin, Italy).

Materials/methods: 50 healthcare workers (HCWs), 50 TB contact subjects and 200 patients were consecutively enrolled in two University hospitals from June to October 2019. They were tested by the two assays per the manufacturers’ protocols and results were compared qualitatively as positive, negative and indeterminate results.

Results: ELISA-QFT-Plus and CLIA-IGRA detected 18% (54/300) and 19.3% (58/300) positive samples, respectively. CLIA-IGRA demonstrated 98.4% positive and 97.7% negative percentage agreement with ELISA-QFT-Plus, with a Cohen’s kappa value of 0.95 (strong agreement).

In addition, 13 samples were indeterminate with both tests. With regard to the threshold of 0.35 UI/mL, discordant results were detected in 6 subjects (2%). 5 samples were ELISA-QFT-Plus(-)/CLIA-IGRA(+) and one provided ELISA-QFT-Plus(+)/CLIA-IGRA indeterminate results. However, taking into account the range of uncertainty of measure published as 0.2-0.7 UI/mL, only 1 sample was really discordant: an ELISA-QFT-Plus(+)/CLIA-IGRA indeterminate with a high IFN-γ level (7.25) in the Nil tube. IFN-γ values between ELISA-QFT-Plus and CLIA-IGRA showed a strong correlation between TB1 and TB2 tubes (Pearson’s correlation coefficients 0.93 and 0.96 respectively). Of note, the rate of positive test for HCWs was 8% whereas it was 34% for people presenting for TB contact investigation or screening for recent immigration (all foreign-born from high endemic countries). For patients hospitalized for immunosuppression patients, or waiting for immunosuppressive therapy or with TB suspicion, the positivity rate was 18.4%

Conclusions: CLIA-IGRA showed similar performances as QFT-Plus whatever the indication of the test. CLIA-IGRA represents a useful reliable alternative tool of ELISA-based IGRA, especially in large-scale LTBI screening because of ease-of-use and automation.

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Genomic and phenotypic diversity of carbapenemase-producing Enterobacteriaceae isolates from bloodstream infections: a multi-centre epidemiological, microbiological and genetic study in China

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Background: Globally, carbapenemase-producing Enterobacteriaceae (CPE) isolates are recognized as one of the most severe threats to public health due to their association with hospital outbreaks and high mortality. However, the population structure and genomic characteristics of CPE among bloodstream infections (BSIs) are largely unknown. We report the first comprehensive survey on the prevalence of CPE in patients with BSIs in China and present a detailed genomic framework for CPE isolates based on whole genome sequencing (WGS).

Materials/methods: In this study, we included patients with clinically significant BSIs due to Enterobacteriaceae isolates recruited from 26 sentinel hospitals in China (2014-2015). CPE isolates were microbiologically and genomically characterized, including susceptibility profiles, molecular typing, phylogenetic features and genetic context analysis of carbapenemase-encoding genes.

Results: Of the 2,569 BSI Enterobacteriaceae isolates enrolled, 42 (1.6%) were carbapenemase-positive. Moreover, 1,111 (49.6%) extended-spectrum β-lactamase (ESBL)-producing isolates were identified in Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, and Klebsiella oxytoca (n = 2,242). WGS analysis uncovered the clonal spread of ST11 KPC-2-producing Klebsiella pneumoniae and ST167 NDM-5-producing Escherichia coli in our collection. Plasmid analysis revealed that carbapenemase-encoding genes were located on multiple plasmids. A high prevalence of biofilm-encoding type 3 fimbriae clusters and yesiniabactin-associated genes was observed in K. pneumoniae isolates.

Conclusions: Our study demonstrates the high prevalence of ESBLs and wide dissemination of CPE among BSI isolates in China, which represent real clinical threats. The clonal spread of KPC-2-producing K. pneumoniae ST11 and NDM-5-producing E. coli ST167 needs to be closely monitored.

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Abstract 7257

**Persuasive antimicrobial stewardship intervention in the context of a KPC outbreak: a controlled interrupted time-series analysis**

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**Background:** Antimicrobial resistance is a major public health threat. Antimicrobial stewardship (AMS) is one of the key strategies to overcome resistance, but robust evidence on the effect of specific interventions is lacking. We report an interrupted time series (ITS) analysis of a persuasive AMS intervention implemented during a KPC producing *Klebsiella pneumoniae* outbreak.

**Materials/methods:** A controlled ITS for carbapenem consumption, total antibiotic consumption and antibiotic-free days, between January 2012 and May 2018 was performed, using segmented regression analysis. The AMS intervention was implemented in the Vascular Surgery ward starting on April 2016 in the context of a KPC outbreak and included two strategies, diabetic foot infection treatment institutional guideline and prospective audit and feedback. The General Surgery ward was taken as a control group. Data were aggregated by month for both wards, including 51 pre-intervention and 26 intervention points.

**Results:** The AMS intervention produced a level change in carbapenem consumption of -9.92 DDDs/100 patient-days accompanied (Figure 1) by a reduction of total antibiotic consumption and an increase of 4% in antibiotic-free days in Vascular Surgery ward. These differences were not apparent in the control group. No differences in mortality or readmission rates between pre-intervention and intervention periods were noticed in any of the groups.

**Conclusions:** Persuasive AMS interventions on top of previously implemented restrictive interventions can reduce carbapenem consumption and increase antibiotic-free days. Starting persuasive AMS interventions in an outbreak setting does not compromise the sustainability of the intervention.

![Carbapenem Consumption Jan2012 - May2018](image)

Figure 1 - Interrupted time series for carbapenem consumption. Continuous line: predicted trend based on the level change model. Dashed line: counterfactual scenario.

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Suitability of ceftolozane/tazobactam (ZERBAXA) via continuous infusion in outpatient parenteral antimicrobial chemotherapy (OPAT)

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Abstract third-party references: On behalf of Members of the BSAC Working Group for Drug Stability Testing

Background: Ceftolozane/tazobactam is a broad-spectrum cephalosporin/beta-lactamase inhibitor combination with activity against a range of pathogens including expanded spectrum beta-lactamase (ESBL) producing strains of Enterobacteriaceae and multi-drug resistant strains of Pseudomonas aeruginosa. It is given three times daily, making it unsuitable for OPAT services at this dose frequency. This study assessed the stability of ceftolozane/tazobactam via continuous 24-hour infusion in two different commercially available elastomeric devices 1) FolFusor LV10 (Baxter Healthcare) and 2) Easypump® II (B.Braun), in accordance with the UK National Health Services Yellow Cover Document (YCD) standards.

Materials/methods: Ceftolozane/tazobactam was diluted in 0.9% w/v saline, pH 7.0 at two therapeutic concentrations of the drug combination (5 mg/mL and 20 mg/mL). Devices were refrigerated at 2-8°C for 8 days, followed by a 3-hour warm up period at room temperature and a simulated infusion period up to 24 hours at 32°C. Concentrations of ceftolozane/tazobactam were determined using a stability indicating HPLC-DAD method developed for use in this study. Testing was carried out in triplicate at five timepoints.

Results: Results indicate ceftolozane is less chemically stable than tazobactam. At 12 hours the concentration of ceftolozane remaining was within the 95% YCD limit; at the end of the 18-hour testing period the concentration remaining for ceftolozane had marginally dropped below the 95% limit; the concentration was a minimum of 93.78±0.19% remaining after 24 hours.

Conclusions: HPLC-DAD assay results from this study show that ceftolozane, while relatively stable at fridge temperature, undergoes degradation during the administration “in-use” period at 32°C. Tazobactam, in contrast to ceftolozane, remains relatively stable even at 32°C. Depending on the acceptance criteria applied, the data supports a shelf life assignment of between 12-24 hours “in use period” at 32°C after storage for up to 8 days in fridge (2-8°C), following a three hour warm up period for ceftolozane/tazobactam solutions in both elastomeric devices tested, within the concentration range of 5-20 mg/mL.

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Abstract 7261

Prospective evaluation of BinaxNOW for rapid identification of Streptococcus pneumoniae from positive blood culture bottles

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Background: BinaxNOW Streptococcus pneumoniae is a rapid immunochromatographic test (BNT-SP) for detection of pneumococcal antigen in urine and cerebrospinal fluid to aid rapid diagnosis of pneumococcal pneumonia and meningitis in conjunction with cultivation. The main drawback of BNT-SP is potential cross-reactivity with viridans streptococci (particularly S. mitis group) as well as some Enterococcus species. While rapid identification of S. pneumoniae from positive blood culture (BC) has important clinical impact, the usefulness of rapid identification methods such as MALDI-TOF is lacking. The aim of our prospective study was to determine the usefulness of BNT-SP performed on positive BC and the frequency of false positive results due to cross-reactivity.

Materials/methods: Positive BCs from 1.1.2018 until 31.7.2019 were included in the study. BNT-SP was performed when Gram positive cocci in chains were observed in the Gram stain and direct MALDI-TOF test did not reliably identify bacterial species. BNT-SP was performed by collecting 10 drops of blood from the positive BC bottle into a tube. A swab was dipped into the tube, then inserted into the test card and reagent added. After 15 minutes the test result was interpreted visually. The results of BinaxNOW were compared to the results of overnight culture, S. pneumoniae was identified using optochin or bile solubility test, other bacterial species were identified using MALDI-TOF.

Results: In total 119 BCs were included in the study. BinaxNOW was positive in 95 cases, in 94 (98.9%) of them S. pneumoniae was isolated from overnight culture, in one case S. mitis was isolated. In the remaining 24 cases BinaxNOW was negative and bacterial species other than S. pneumoniae were isolated from overnight culture, in 19/24 cases other streptococci and 5/24 enterococci. Sensitivity was 100%, with good specificity 96.0%, positive 98.95% and negative predictive value 100%.

Conclusions: The results of our prospective study show very low rate of false positive results due to cross-reactivity with S. mitis, however, only two S. mitis were isolated among 119 isolates and no cross-reactivity with other species was detected. Our study has demonstrated that BinaxNOW is a valuable addition to rapid identification of S. pneumoniae bacteremia.

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Evaluation of the whole blood spot on plasma separation card as a sample type for serological screening for hepatitis B and hepatitis D infection

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Background: Viral hepatitis elimination is one of the WHO objectives; this includes increasing diagnosis rate of hepatitis B. Access to a laboratory is not always possible, especially in remote areas, and certain regions with special populations, in these scenarios a method to stock and transport blood samples for long periods and distances can be useful to bring near the laboratory based assays. Dried blood spots have been found useful to evaluate viral load of HCV an HIV, however there isn’t a wide experience using this sample to perform serological assays which is the first step in the diagnosis of viral hepatitis. The aim of this study was to evaluate the performance of the Cobas Plasma Separation Card (PSC) as alternative sample for serological testing compared to serum.

Materials/methods: We recovered whole EDTA venous blood from clinical samples with positive (n=101) and negative HBs (n=81). All samples HBs positive with anti-HDV results (n=24) were also tested for this assay. PSC samples were prepared by spotting 140µL of whole EDTA venous blood and drying it at room temperature over a minimum of 4 days. One spot of each PSC was eluted in 600µL of Elecsys universal diluent, incubated at 37ºC over one night and centrifuged at 3000rpm over 10min. Serum and PSC eluted samples were analyzed by elecsys HBs II and elecsys anti-HBc in cobas 8000 system (Roche, Switzerland) and XL MUREX anti-HDV in Liaison (DiaSorin, Italy). The results were compared by paired.

Results: Sensitivity of PSC compared to serum for HBsAg was 97.0% (n=101; 95% CI: 91.6 - 99.4%), for anti-HBc was 98.9% (n=94, 95% CI: 94.2 to 100%) and 43.75% (n=23, 95% CI: 38.5 to 80.3%) in HBsAg positive and HBsAg negative (solved hepatitis B) cases, respectively. For anti-HDV sensitivity was 100% (n=7, 95% CI: 59.0 to 100%). Specificity for all tests was 100%.

Conclusions: PSC demonstrated a good concordance with standard serum samples as an alternative sample type for serological testing used for screening of HBV and HDV infection. These results support the feasibility of PSC as an alternative sample for serological screening of patients in resource limited settings.

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Abstract 7264

A broad-spectrum bacterial gyrase inhibitor with a novel scaffold

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Background: There is an alarming scarcity of novel chemical matter with bioactivity against multidrug-resistant Gram-negative bacterial pathogens. Studying natural products arguably remains the most fruitful strategy to discover novel antibiotic lead structures, since more than 80 % of marketed antibiotics are secondary metabolites found in nature or derivatives thereof. In 2014, we identified cystobactamids as novel myxobacterial natural products that exhibit potent broad-spectrum antibacterial properties through the inhibition of bacterial topoisomerases. We accomplished the full chemical synthesis of these natural products and embarked into a medicinal chemistry and biological profiling program to advance cystobactamid leads to pre-candidates.

Results: Cystobactamids exhibit an unusual chemical structure, composed of oligomeric para-aminobenzoic acid moieties. Medicinal chemistry optimization has enabled some improvements in the spectrum coverage, which comprises some clinically important Gram-negative and Gram-positive pathogens (MIC90 on Escherichia coli of 0.06 µg/mL, n=12; MIC90 on Acinetobacter baumannii of 1 µg/mL, n=13; MIC90 on Staphylococcus aureus of 0.25 µg/mL, n=14), with some existing gaps currently being addressed (most notably Klebsiella pneumoniae and Proteus mirabilis). Although fluoroquinolones (FQ), albicidin and cystobactamids share the same molecular targets (GyrA/ParC subunits of topoisomerases), no cross-resistance is observed with the current frontrunners. In some species we observed rapid emergence of resistance in vitro through off target mutation. However, in vitro and in vivo efficacy data indicate that this liability may be overcome by adequate dosing of the compound. Indeed, in a mouse model of thigh infection by Escherichia coli the frontrunner led to three log kill of bacterial loads when administered intravenously at 40 mg/kg/day. The physico-chemical and ADMET profiles of the frontrunners are also acceptable at this stage.

Conclusions: Taken together, these data suggest that cystobactamids are promising lead structures, and more broadly that there is still a chemical space to identify novel broad-spectrum gyrase/topo-isomerase antibiotics against infections caused by Gram-positive and Gram-negative bacterial pathogens.

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Rapid diagnostics of bloodstream infections using sybodies and nanobodies as capturing agents

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Background: Sepsis caused by bloodstream infections (BSIs) affects 18 million people world-wide every year and has unacceptably high mortality rates of 10-20% in Western countries. BSI diagnostics typically takes several days which forces clinicians to treat sepsis patients with empiric broad-spectrum antibiotics. However, cephalosporin- and carbapenem-resistant Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa are often treated with inadequate antibiotics. We aim to drastically shorten the routine BSI diagnostics by extracting pathogenic bacteria from blood using single domain antibody fragments, called nanobodies to omit long-lasting blood cultures necessary for BSI diagnostics.

Materials/methods: Nanobodies from immunized alpacas and synthetic nanobodies (sybodies) were raised against non-essential but highly conserved outer membrane proteins (OMPs) of E. coli, K. pneumoniae and P. aeruginosa, namely OmpX, OmpA and OmpF [E. coli], OmpA [K. pneumoniae] and OprF [P. aeruginosa]. Enriched pools were then deep-mined using our recently developed NestLink technology to identify nanobodies and sybodies binding to OMPs in the native outer membrane context of the respective pathogens. Target binding was verified by cellular binding assays using fluorescently labelled nanobodies and sybodies, complex runs using size exclusion chromatography, and FACS.

Results: Nanobodies and sybodies were first selected against purified OmpX [E. coli], OmpA [K. pneumoniae] and OprF [P. aeruginosa]. In case of OmpX, enrichment of both nanobodies and sybodies turned out to be difficult. Therefore, nanobodies against OmpA and OmpF [E. coli] were raised, which are less conserved than OmpX, but both are necessary to achieve coverage of all E. coli strains. Binding various E. coli strains in a cellular context was shown by the above mentioned methods. Finally, nanobodies and sybodies binding to OmpA [K. pneumoniae] and OprF [P. aeruginosa] were successfully enriched and will be further analysed.

Conclusions: We have established an elaborate platform to generate binders that recognize highly conserved OMPs in their native context of the outer membrane of gram-negative pathogens. These binders will be further developed to capture these bacteria directly from blood samples of patients suffering from life-threatening BSIs. Thereby, time-consuming blood culturing is omitted, allowing for rapid antibiotic susceptibility testing.

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Abstract 7268

**Novel taxonomic and functional cervical microbiome biomarkers of persistency and histological progression to CIN2+ in women infected with high risk human papilloma virus**

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**Background:** Predictors of viral persistence and development of prestage cancer in high risk human papillomavirus (HR HPV) infected women would allow better risk stratification in cervical cancer screening.

**Materials/methods:** Previously a prospective German cohort of 10,040 women was established and 411 test-positive (HPV and/or cytology) women were followed for up to six years with yearly intervals. Shotgun metagenomics from the first cervical smear taken at the baseline was performed in 100 HR HPV infected women. Of these, 43 women showed a persistent HR HPV infection with the same HR HPV type (> 24 months) including 10 women who developed histological progression to CIN2+. The remaining 57 women had cleared their infections spontaneously within 24 months.

**Results:** Potential biomarkers for persistent HR HPV infection and histological progression to CIN2+ were identified using a univariate Wilcoxon rank sum test followed by multivariate logistic regression. Different machine learning classifiers built from six taxonomic and functional biomarkers allow to stratify women with a high risk of persistent HR HPV infection (OR=2.77; p=0.03) from those that cleared spontaneously (ROC-AUC 0.96 - 1.0). The six biomarkers are the relative abundance of three bacterial taxa (2 genera: Catenulispora, Oleiphilus; 1 phylum: Chlamydiae), the relative abundance of two metabolic microbial pathways (UDPNAGSYN-PWY, PWY-621), and the relative abundance of the fungal genus Aureobasidium. Furthermore, we trained machine learning classifiers on prediction of a high risk for incident CIN2+ (OR=15.5, p = 0.001) based on the relative abundance of two bacterial taxa (2 genera: Leisingera, Devosia), the relative abundance of a metabolic microbial pathway (PWY-2941), and the relative abundance of the two fungal genera Thermothelomyces und Marssonina (ROC-AUC 0.77 - 1.0). All biomarkers were further investigated using a Ward-cluster analysis that demonstrated excellent discrimination of the respective groups.

**Conclusions:** Applying machine learning algorithms to shotgun metagenomics data from cervical smears in women infected with HR HPV seems to enable prediction of the establishment of persistent HPV infections and more important an increased risk of incident CIN2+.

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Abstract 7269

**Large diffusion of Optra- and Poxta-producing linezolid-resistant Enterococcus spp. among healthy children from rural communities of the Bolivian Chaco**

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**Background:** The spread of antimicrobial resistance is increasing worldwide in both healthcare and veterinary field. Since now, little is known about the prevalence of oxazolidinone resistant enterococci bacteria among healthy children in rural communities. In this study, a surveillance was set up for the colonization by oxazolidinone and phenicol resistant Enterococcus spp. in two communities of the bolivian Chaco.

**Materials/methods:** 100 faecal samples obtained from healthy children from two rural communities of the bolivian Chaco (Ivamirapinta and Palmarito) in 2018 were studied. The samples were grown on selective plates for enterococci [Columbia CNA Agar with 5% Sheep blood] supplemented with 16 mg/L of florfenicol. Each colony characterized by a different morphology was isolated and identified by MALDI-TOF mass spectrometry. Each isolate was subjected to Real-Time PCR in order to detect the most common acquired oxazolidinone resistance genes (optra, poxta, cfr, cfr (B)), and RAPD (Random Amplification of Poly-morphic DNA) PCR was executed to detect the clonal relatedness of isolates from the same patient. Antimicrobial susceptibility testing for ampicillin, florfenicol, linezolid and vancomycin was performed by reference broth-microdilution method according to ISO 20776:1-2006, and interpreted according to EUCAST clinical breakpoints (when available).

**Results:** 59 samples yielded some growth on the selective medium and 83 different morphologies were detected. 75 isolates resulted positive for optra gene (including 64 Enterococcus faecalis, 8 Enterococcus faecium, one Enterococcus hirae, one Enterococcus casseliflavus and one Vagococcus spp.) and 8 for poxta gene (6 Enterococcus faecium, one Enterococcus gallinarum, and one Enterococcus hirae). The results confirmed a high MIC to florfenicol (>8 mg/L) for the 95% of the isolates. Additionally, 89% of the samples were also linezolid resistant, whereas only few of them showed ampicillin resistance (5%) or vancomycin resistance (2%, only E. gallinarum and E. casseliflavus isolates).

**Conclusions:** An unexpected high prevalence of antibiotic resistant enterococci carrying the optra and poxta resistance genes were detected among healthy children in two rural communities. The possible causes of this diffusion of oxazolidinone and phenicol resistance genes among enterococci are still unknown and this study highlights the importance of future surveillance studies at veterinary, environmental and clinical level in Bolivia

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Abstract 7271

Genetic mutations in drug-resistant paediatric tuberculosis: experience from a paediatric tertiary care centre in north India

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Background: The emergence of multidrug-resistant MDR-TB and extensively drug-resistant XDR-TB are serious threats to global TB control. Molecular tests like GenoType MTBDRplus has revolutionized MDR-TB diagnosis by rapid detection of resistance, leading to early and appropriate management of DR-TB. Information about common mutations imparting resistance to Rifampicin and isoniazid helps in understanding the disease epidemiology in various regions.

The study was conducted to determine the genetic mutation in drug resistant tuberculosis in children less than 12 years with pulmonary or extrapulmonary tuberculosis.

Materials/methods: Retrospective analysis was done over a period of 54 months from January 2015 to June 2019 to study the resistance pattern and mutations present in DR-TB in children less than 12 years with suspected pulmonary or extrapulmonary tuberculosis using Hain’s GenoType MTBDRplus VER 2.0.

Results: Over a period of 54 months, samples from 3461 patients with suspected TB were received for MGIT culture, out of which, 347 were positive for Mycobacterium tuberculosis. 250 of these 347 isolated were tested for drug resistance by Hain’s GenoType MTBDRplus VER 2.0. 61.1% were sensitive to isoniazid and rifampicin while 38.9% were DR-TB (38 out of 250). Out of these 38, 22 were MDR TB, 13 were isoniazid monoresistant (34.2%) and 3 were rifampicin monoresistant. The most common genotypic resistance for rifampicin was absence of rpoB WT8 band and presence of rpoB MUT 3 band (88%). 84.6% of the INH monoresistant isolates showed high level isoniazid resistant. All these isolates showed presence of katG MUT 1 band. On comparing Hain’s GenoType MTBDRplus VER 2.0 with Xpert MTB/Rif Assay, most common mutation for rifampicin resistance at SS31L which can be detected by Xpert MTB/Rif Assay [probe E]. However, two cases with rifampicin resistance had mutation in codon region 509-513 and 513-519 which could be missed by Xpert MTB/Rif Assay.

Conclusions: We cannot solely rely on Xpert MTB/Rif Assay for detection of drug resistance due to the risk of missing the isoniazid monoresistance. The higher frequency of mutation in codons of rpoB (SS31L) and katG (S315T) gene may help to design simple, new and less expensive molecular techniques to use in peripheral laboratories.

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Abstract 7273

Comparison of Candida PCR and blood culture results in high-risk patients with candidaemia in the intensive care unit

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Background: Candida isolates are responsible for 70 to 90% of invasive fungal infections in intensive care units. Early diagnosis and treatment is important in candidemia. Improper diagnosis and treatment can significantly increase mortality and morbidity. The aim of this study was to investigate the feasibility of Candida PCR as a rapid diagnostic method in patients with suspected candidiasis in intensive care units.

Materials/methods: Ninety patients with a high risk of candidiasis were evaluated prospectively in our study. Urine, perineum, axilla, tracheal aspirate culture and 2 sets of blood cultures were obtained from the patients. In Candida multiplex PCR ITS1, ITS2, ITS2D, CA3, CA4 primers were used. In Candida real-time PCR species-specific primers were used to distinguish species.

Results: 41 (45.5%) of the patients were female and 49 (55.5%) were male. The mean age of the patients was 58.1 (± 18.4) years. The blood culture was positive only for 3 (3.3%) patients. Candida multiplex PCR and Candida real-time PCR were positive in 17 (18.9%) patients. Candida species found in the blood culture and PCR test were compatible with each other (Table). PCR was significantly more positive than the blood cultures (p=0.006). The difference in candida score between patients with PCR positive and PCR negative was statistically significant (p=0.015).

Conclusions: In our study, we found that the probability of detecting candidemia with PCR was higher. Therefore, it can be seen that molecular methods should be used in the diagnosis especially in patients with high risk of candidiasis.

<table>
<thead>
<tr>
<th>Species</th>
<th>Blood culture, n [%]</th>
<th>Candida PCR, n [%]</th>
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<tbody>
<tr>
<td>C. albicans</td>
<td>-</td>
<td>1 [% 5,9]</td>
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<tr>
<td>C. krusei</td>
<td>-</td>
<td>6 [% 35,3]</td>
</tr>
<tr>
<td>C. parapsilosis</td>
<td>2 [% 66,7]</td>
<td>4 [% 23,5]</td>
</tr>
<tr>
<td>C. tropicalis</td>
<td>1 [% 33,3]</td>
<td>2 [% 11,7]</td>
</tr>
<tr>
<td>C. dubliniensis</td>
<td>-</td>
<td>3 [% 17,6]</td>
</tr>
<tr>
<td>C. glabrata</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>C. krusei+C. parapsilosis</td>
<td>-</td>
<td>1 [% 5,9]</td>
</tr>
<tr>
<td>Toplam</td>
<td>3 [% 3,3]</td>
<td>17 [% 18,9]</td>
</tr>
</tbody>
</table>

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**Abstract 7274**

**In vitro activity of cefiderocol, a siderophore cephalosporin, against multidrug-resistant isolates of Gram-negative bacilli from France**

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**Background:** Antimicrobial resistance has reached in many countries an extremely worrying situation, threatening the achievements of modern medicine and requiring urgently novel antibiotics to cope with this problem. Here, we have evaluated the in vitro activity of cefiderocol (S-649266), a novel siderophore cephalosporin against Multidrug resistant Gram-Negative Bacilli from France.

**Materials/methods:** The in vitro activity of cefiderocol was determined against a collection of carbapenem-resistant clinical isolates of Enterobacteriaceae \(n = 220\), multidrug-resistant (MDR) Acinetobacter baumannii \(n = 52\), MDR Pseudomonas aeruginosa \(n = 51\), Stenotrophomonas maltophilia \(n = 15\), and Burkholderia cepacia \(n = 10\) using the Clinical and Laboratory Standards Institute (CLSI) standard broth microdilution method. Iron-Depleted cation-adjusted Mueller-Hinton broth (ID-CAMHB), used to test cefiderocol while for all the other antimicrobial agents (ceftolozane-tazobactam, cefepime, ceftazidime, ceftazidime-avibactam, aztreonam, meropenem, amikacin ciprofloxacin, colistin, and tigecycline) were tested using CAMHB. MIC breakpoints were those of EUCAST or CLSI in case they were not available at EUCAST.

**Results:** The concentration of cefiderocol inhibiting 90% \(\text{MIC}_{90}\) of isolates of carbapenem-nonsusceptible Enterobacterales was 4 \(\mu\)g/ml; cefiderocol MICs ranged from 0.03-64 \(\mu\)g/ml, and 93.0% \(\text{MIC}_{90}\) of isolates demonstrated cefiderocol MICs of \(\leq 4 \mu\)g/ml. The MIC90s for cefiderocol for MDR A. baumannii, MDR P. aeruginosa, and S. maltophilia were 64, 2, and 0.06 \(\mu\)g/ml, respectively, with 81% \(\text{MIC}_{90}\), 100% \(\text{MIC}_{90}\), and 100% \(\text{MIC}_{90}\) of isolates demonstrating cefiderocol MICs of \(\leq 4 \mu\)g/ml. Cefiderocol MIC90 for B. cepacia were 1 with MICs ranging from 0.003 to 8 \(\mu\)g/ml. Cefiderocol was the most active antibiotic against these MDR Gram negative bacilli.

**Table 1: Antibiotic susceptibility of the 348 tested XDR isolates**

<table>
<thead>
<tr>
<th></th>
<th>S. 649266</th>
<th>C/T</th>
<th>MEM</th>
<th>CAZ</th>
<th>CZA</th>
<th>CST</th>
<th>ATM</th>
<th>AMK</th>
<th>CIP</th>
<th>FEP</th>
<th>TGC</th>
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<tr>
<td><strong>P. aeruginosa</strong></td>
<td>% R</td>
<td>100</td>
<td>100</td>
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<td>91</td>
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<td>83</td>
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<tr>
<td><strong>A. baumannii</strong></td>
<td>% R</td>
<td>81</td>
<td>81</td>
<td>81</td>
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<tr>
<td><strong>B. cepacia</strong></td>
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</table>

**Conclusions:** Cefiderocol demonstrated potent in vitro activity against a collection of highly drug resistant Gram-negative bacteria (Enterobacteriales, MDR A. baumannii, MDR P. aeruginosa, S. maltophilia, and B. cepacia isolates) as >93% of all \(320/348\) isolates tested had cefiderocol MICs of \(\leq 4 \mu\)g/ml. Interestingly 100% of the tested \(P. aeruginosa\) isolates being mostly susceptible only to colistin had cefiderocol MICs of \(\leq 4 \mu\)g/ml.

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Management of MDR-TB cases: roadmap towards TB elimination in Italy

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Background: Drug-resistance poses a major threat to global progress to end tuberculosis. In 2017 558,000 new cases of multidrug-resistant tuberculosis (MDR/RR-TB) emerged globally. In 2018 a total of 170 cases of MDR/RR-TB were notified in Italy, an incidence of 0.28 cases per 100,000 population. The WHO End TB Strategy aims at strengthening the capacity to manage the MDR-TB cases, providing new models for the implementation of out-patient management and shorter regimens.

Materials/methods: Findings of a two year (April 2017 - April 2019) observational study on the pilot implementation of four interventions for MDR TB management at the Infectious Disease Department of ASST Spedali Civili of Brescia. The project was funded by the Italian Ministry of Health. The intervention consisted on shorten definition of sensitivity pattern in MDR-TB strains through whole genome sequencing (WGS); adoption of shorter regimen (following the WHO criteria); MDR-TB out-patient treatment as initial care in the intensive phase whenever possible; treatment of MDR-TB contacts using fluoroquinolone containing regimens.

Results: Eleven MDR-TB cases were observed (1 XDR-TB, 1 PRE XDR-TB, 1 RR-TB). Four cases had extra-pulmonary TB (kidney; pleura; lymph node; miliary), two cases had HIV co-infection and one patient was under chronic immunosuppression due to Chron’s disease. The average time between Xpert positivity to MTB-RIF and start second line TB treatment based on WGS result was 10 days. MDR-TB patients treated ab-initio in out-patient setting were 2 out of 7 eligible (28%): (contraindications in XD; PRE XDR; cerebral location; social reasons). Of the 11 patients 7 had a resistance pattern not compatible with shorter regimen and one had TB meningitis. Of the 3 eligible cases, shorter regimens were started in 2 (66%). Among 20 identified MDR-TB contacts 3 received fluoroquinolone based preventive therapy (15%). Reasons for no treatment was mostly clinician preference. Treatment was completed by 1/3 contacts (treatment interruption due to side effects).

Conclusions: Selection of second line regimens based on WGS results in TB cases with rifampicin resistance measured through rapid test is feasible in this setting. The proportion of MDR-TB cases who are eligible and adopt shorter regimens according to current WHO guidelines is very limited.

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Abstract 7282

Genetic variability of Trypanosoma cruzi, in clinical samples from Latin American immigrant patients, living in Barcelona, Spain

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Abstract third-party references: Vall d’Hebron Research Institute (VHIR), São Paulo Research Foundation - FAPESP

Background: Chagas disease (ChD) has as its etiological agent the hemoflagellate protozoan denominated Trypanosoma cruzi. The species has a genetic structure that allows subdivision into six distinct DTUs (TcI to TcVI) and TcBat, which has shown differences in geographical distribution, biological properties and drug susceptibility. The predominance of TcII, TcV and TcVI DTUs is known in several regions of Latin America, associated with both the domestic and wild, Chagas Disease cycle. However, little is known about the circulation of different T. cruzi genotypes in Latin American chagasic immigrants living in the European continent. Thus, it was intended with this work, to verify the genotypes of parasites present in patients with ChD attended in Universitary Hospital Vall d’Hebron, Barcelona - Spain.

Materials/methods: 116 chronic chagasic patients with positive serology (residents in Barcelona, Spain), with different nationalities were included in this study. It was collected 5ml of blood in Guanidine/EDTA eluate, for subsequent DNA extraction, to evaluate the parasite load and molecular characterization of the parasites in their appropriate DTUs. Genotyping was performed using conventional multilocus PCR and Nested PCR, using amplification of different genes (SLIRac, SLIR, 24Sα rDNA and A10). Parasite loading was performed according to standard protocol in our laboratory, using a standard curve containing epimastigote forms of T. cruzi, SO3cl5 strain (DTU/TcV).

Results: An extremely low bloodstream parasitic load was observed in all 116 chronic patients included in the study, with an average of approximately 10fg of T. cruzi DNA in each patient sample. Regarding genotyping, we found the presence of TcV DTU in Bolivian patients, as reported in the specific literature, in addition to the presence of TcII/TcVI, TcII/TcV/TcVI genotypes in patients of different nationalities.

Conclusions: We can conclude from these data that the parasitic loads in all evaluated patients are really low, and that the genotypes found are very variable due to the different geographical origins of each patient. Thus, by better understanding the genetics of the circulating parasite, it is possible to perform control measures, treatment and clinical intervention with greater efficiency, bringing improvements to patients.

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Abstract 7283

Two-year experience of meningitis/encephalitis multiplex PCR assay on cerebrospinal fluids in comparison with conventional methods: advantages and disadvantages

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Background: Central nervous system (CNS) infections, including meningitis and encephalitis, are associated with significant morbidity and mortality; rapid and accurate detection of pathogens in the cerebrospinal fluid (CSF) can improve clinical care. The aim of this two-year study was to prospectively evaluate the multiplex PCR FilmArray Meningitis and Encephalitis Panel (FA-MEP, BioFire Diagnostics/bioMérieux) for the rapid (1 h) and simultaneous detection in CSF of 14 life-threatening agents (6 bacteria, 7 viruses and 1 yeast) in comparison with the reference methods currently used in case of CNS infection suspicion.

Materials/methods: A total of 173 CSFs (November 2017-November 2019) belonging to as many patients were analyzed by FA-MEP in comparison with the reference methods for bacteria, including the mandatory direct microscopic examination (DME) and the identification by MALDI-TOF MS from either agar or liquid conventional cultures. For virus confirmation, when a FA-MEP positive result for virus was obtained, the samples were submitted to agent specific PCRs (except for paraechovirus not routinely detected).

Results: The FA-MEP gave a positive result in 24 cases (13.9%), in 23 cases (95.8%) for a single agent (5 Streptococcus pneumoniae, 3 Haemophilus influenzae, 2 Neisseria meningitidis, 1 Streptococcus agalactiae, 7 enterovirus, 2 human herpesvirus 6, 2 varicella zoster virus and 1 paraechovirus) and in 1 case (4.2%) for H. influenzae in combination with cytomegalovirus. The FA-MEP positive results were concordant, with regard to the agents recognized by the molecular assay, with those obtained by the reference methods in all cases (83.3%) except in 4 culture-negative cases: 2 samples containing S. pneumoniae (DME-positive for Gram positive cocci, patients under antibiotic therapy) and 2 DME-negative samples containing S. pneumoniae and H. influenzae, respectively. In addition, the reference bacterial methods gave positive results in 12 CSFs, all agents not targeted by FA-MEP.

Conclusions: This study suggests that FA-MEP, despite high costs, can have comparable diagnostic yield and more rapid time-to-diagnosis than conventional methods in patients with suspected CNS infection and proves the potential for significant clinical impact including optimization of antimicrobial therapy and reduction of unnecessary use. However, for the definitive diagnosis reference methods remain mandatory for both bacteria and viruses.

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Abstract 7284

An evaluation to assess the performance of the Fungiplex Aspergillus real-time PCR and the Fungiplex Aspergillus Azole-R IVD real-time PCR Kits following the implementation of an extraction control

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Background: This Performance Evaluation was designed to test contrived samples spiked into serum, plasma and BAL material to assess the impact of a new extraction control on the limit of detection of the Fungiplex Aspergillus and Fungiplex Aspergillus Azole-R IVD Real-Time PCR Kits and to ensure sensitivity was unaffected by this change.

Materials/methods: Simulated samples were prepared and analysed by the clinical evaluators. Samples prepared in serum, plasma and BAL were spiked with specific concentrations of Aspergillus fumigatus or Aspergillus terreus genomic DNA prior to extraction. Aspergillus fumigatus wild type strains were used as well as resistant strains containing DNA mutations TR34 and TR46 in the Cyp51A gene. Samples were prepared in replicates of five and negative controls were included for each sample type.

Results: When tested with the Fungiplex Aspergillus IVD Real-Time PCR Kit, the limit of reproducibility for Aspergillus fumigatus and Aspergillus terreus samples was 5 ge (genome equivalents). No difference in sensitivity was observed when the results from two different extraction platforms were compared, however, on average the resultant Ct (cycle threshold) values were 1.2 cycles higher when the EZ1™ platform was used.

When tested with the Fungiplex Aspergillus Azole-R IVD Real-Time PCR Kit, the limit of reproducibility for Aspergillus fumigatus samples containing mutations TR34 and TR46 was 50 ge. This higher limit of reproducibility was expected as the Cyp51A gene is single copy. The limit of reproducibility was consistent between all sample types, where in a previous study, without an extraction control, the limit of reproducibility had been reported between 50 and 75 ge depending on which sample type was used.

Conclusions: 100% sensitivity was reported for the Fungiplex Aspergillus Kit when analysing Aspergillus samples at 5 ge and for the Fungiplex Aspergillus Azole-R Kit when analysing resistant strains at 50 ge. The sensitivity is not dependent on sample type and the new extraction control implemented in these products did not affect the performance of either Kit. Data has shown that results from this study are equivalent, and in some cases, superior to previous studies performed.

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Abstract 7285

Multimodal analysis of *Escherichia coli* isolates from patients and carriers with EPISEQ CS, a next-generation sequencing service for epidemiological surveillance

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Abstract third-party references: bioMérieux

**Background:** In hospital environments, the presence of antibiotic resistant and/or virulent strains are of particular concern. In this work, we present a new, fast and high-resolution multimodal epidemiological analysis of WGS data with bioMérieux EPISEQ® CS that easily provides information on the relatedness, resistance and virulence of strains.

**Materials/methods:** We analyzed WGS data of 22 *E. coli* publically available isolates from either patients with symptoms typical of an *E. coli* infection and asymptomatic carriers. This online application starts from raw reads with de novo assembly, and allows a multimodal approach for epidemiological surveillance including phylogenetic analysis based on whole genome multi-locus sequence typing (MLST), 7-gene MLST, resistome and virulome analysis.

**Results:** After upload of the metadata and fastq.gz files, EPISEQ® CS allowed the analysis of the 22 *K. pneumoniae* isolates with a turnaround time of just over one hour. The analysis outcome provides insight in the quality of the different steps in the pipeline, and clustered all isolates together in the final phylogenetic tree. Five different STs were detected in the set, and four clusters of related strains, two clusters from asymptomatic carriers, one cluster of symptomatic patients and one mixed cluster. The virulome shows the unique presence of stx2 in the cluster of patients, confirming current knowledge on this virulence factor. The strains in the mixed cluster have an identical resistome and virulome suggesting a recent transmission even between carrier and patient.

**Conclusions:** As WGS is also becoming feasible to smaller clinical laboratories, there is a need for automated and standardized analysis of these data. EPISEQ® CS is a fast, high-resolution, easy-to-use and automated WGS application, providing phylogenetic analysis, typing and resistome analysis. The phylogenetic analysis next to the quality information and uploaded metadata provides a useful overview to detect and allow the analysis of possible transmission events and will enhance rapid and accurate epidemiological surveillance in clinical environments.

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Comparison of humoral response against both haemagglutinin and neuraminidase after seasonal influenza vaccination

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Background: Vaccine serological efficacy is performed by analysing the production of antibodies against haemagglutinin (HA). However, seasonal influenza vaccines (SIV) have a non-standardized amount of neuraminidase (NA) and also its immunogenicity to the serological efficacy of the vaccine is not evaluated. The objective of the study is to analyze and compare anti-Neuraminidase (NAI) and anti-Hemagglutinin (HAI) antibodies response after seasonal influenza vaccination.

Materials/methods: Retrospective observational analysis of pre and post-vaccination sera from 160 vaccinated individuals, distributed in two age groups: adults (G1=80;15-64yrs) and elderly (G2=80≥65 years). Both groups received SIV that included the A/California/07/2009 strain of subtype A(H1N1)pdm09. HAI and NAI serological response was analyzed against five influenza strains of seasonal subtype A(H1N1) (A/PR/8/1934; A/Weiss/1943; A/FM/1/1947; A/Brazil/11/1978; A/Brisbane/59/2007) and the A/California/07/2009 strain of subtype A(H1N1)pdm09. Seroconversion rate (SCR) and Increment Ratio (RIC) of HAI and NAI titers against different analyzed influenza strains were compared according to age group. SCR was defined as an increase of at least four times the titres between pre and post-vaccination serum.

Results: Mean age of young-adults was 51.0 years (CI95%:48.2-53.4) and 78.6 years (CI95%:76.6-80.6) in elderly. Seasonal vaccination increased HAI and NAI titers against all influenza strains analyzed in both age groups. The highest SCR of HAI and NAI was observed in elderly against A/California/07/2009 strain. RIC against seasonal subtype A(H1N1) strains ranged from 1.3 to 36.3%. Statistical comparison between SCR and RIC of HAI and NAI titers is described in Table 1.

Table 1. SCR and RIC of HAI and NAI titers against different influenza strains in adults and elderly.

<table>
<thead>
<tr>
<th>A[H1N1] Influenza viruses</th>
<th>Age group</th>
<th>SCR(%)</th>
<th>RIC</th>
<th>p-value</th>
</tr>
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<tr>
<td></td>
<td>HAI</td>
<td>NAI</td>
<td></td>
<td>HAI</td>
</tr>
<tr>
<td>A/PR/8/1934</td>
<td>15-64</td>
<td>8.8</td>
<td>8.8</td>
<td>1.000</td>
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<td></td>
<td>≥65</td>
<td>11.3</td>
<td>11.3</td>
<td>1.000</td>
</tr>
<tr>
<td>A/Weiss/1943</td>
<td>15-64</td>
<td>1.3</td>
<td>31.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>≥65</td>
<td>7.5</td>
<td>13.8</td>
<td>0.227</td>
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<tr>
<td>A/FM/1/1947</td>
<td>15-64</td>
<td>8.8</td>
<td>21.3</td>
<td>0.052</td>
</tr>
<tr>
<td></td>
<td>≥65</td>
<td>13.8</td>
<td>12.5</td>
<td>1.000</td>
</tr>
<tr>
<td>A/Brazil/11/1978</td>
<td>15-64</td>
<td>8.8</td>
<td>15.0</td>
<td>0.267</td>
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<tr>
<td></td>
<td>≥65</td>
<td>3.8</td>
<td>18.8</td>
<td>0.008</td>
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<tr>
<td>A/Brisbane/59/2007</td>
<td>15-64</td>
<td>7.5</td>
<td>17.5</td>
<td>0.057</td>
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<td></td>
<td>≥65</td>
<td>22.5</td>
<td>36.3</td>
<td>0.080</td>
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<td>≥65</td>
<td>45.0</td>
<td>55.0</td>
<td>0.185</td>
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</table>

Conclusions: Results of our study show that SIV against subtype A[H1N1]pdm09 induced a similar serological response of HAI and NAI antibodies in adults and elderly. However, compared to some older A[H1N1] strains, seasonal vaccination induced a significantly greater heterotypic response in terms of NAI antibodies. This increased NAI response occurred despite the fact that the seasonal vaccine does not contain a standardized amount of neuraminidase.

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Dissemination of OXA-244-producing *Escherichia coli* in Germany

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**Background:** Because of their enzyme-mediated antibiotic resistance, carbapenemase-producing Enterobacterales (CPE) are of major public health concern. For diagnostic laboratories in Germany, the National Centre for Multidrug-resistant Gram-negative Bacteria (NRC) provides the cost-free phenotypic and genotypic identification and characterization of carbapenemases. From 2017 to 2019, an annually increasing number of OXA-244-producing *Escherichia coli* prompted the Robert Koch Institute (RKI) to initiate detailed investigations.

**Materials/methods:** Between January 2017 and mid-August 2019, a total of 255 OXA-244-producing *E. coli* isolates from 86 diagnostic laboratories were identified at the NRC, of which 150 isolates were successively subjected to whole genome sequencing (Illumina). We performed *in silico* multi-locus sequence typing (MLST), core genome (cg)MLST and high-resolution SNP analyses.

**Results:** Sequencing of 150 OXA-244-producing *E. coli* isolates identified a total of 16 different sequence types (ST). The majority of isolates (n=102) belonged to ST38, for which results of cgMLST and SNP-based mapping analyses revealed close genetic relatedness, particularly among 63 isolates segregating into a distinct cluster. Distribution of these ST38 *E. coli* isolates was not geographically restricted. Detailed *in silico* analyses showed cluster-specific resistance gene patterns and chromosomal integration of \( \text{bla}_{\text{OXA-244}} \) in all 150 isolates. However, \( \text{bla}_{\text{OXA-244}} \) was found to be integrated at different sites of the chromosome dependent on the clonal background.

**Conclusions:** Here we present a country-wide spread of OXA-244-producing *E. coli* in Germany that is predominantly driven by ST38 variants. Continuous characterization of newly identified isolates and complementary sequencing approaches are needed to identify routes of transmissions as well as the underlying mechanisms leading to the chromosomal plasticity of the \( \text{bla}_{\text{OXA-244}} \) gene.

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Abstract 7291

Comparative evaluation of the effectiveness of prophylactic agents based on bacteriophages, liquid soap and skin antiseptics for hand disinfection

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Background: Comparative evaluation of the effectiveness of prophylactic agents based on bacteriophages, liquid soap and skin antiseptics for hand disinfection.

Materials/methods: The study included 22 students. According to the method of how the students’ hands were disinfected, they were divided into 3 groups. Group I treated hands with soap (n=7), Group II - with skin antiseptic (n=7), and Group III - with gel containing a bacteriophage (n=8). Students’ hands were evaluated on the subject of microbial colonization of the palmar surface before and after treatment with smear imprints on the surface of Petri dishes (d=140) containing blood agar (Oxoid, Great Britain). Grown colonies on blood agar before and after the treatment were counted. Identification of the isolated microorganisms was carried out using Autoflex III mass spectrometer (Bruker Daltonics, Germany).

Results: Before washing and the treatment, all students’ hands were colonized by a large number of microorganisms. After treatment of hands in Group I (liquid soap) and Group II (gel with antiseptic) an increase in colonization by microorganisms post-treatment was observed in 57.1%. 42.9% however demonstrated a reduction in the number of microbes on the surface of the hands. In Group III (bacteriophage gel) 50% of cases showed a significant decline in the number of bacteria grown on Petri dishes. Bacteria belonging to 15 genera were isolated from the surface of the hands as follows: Staphylococcus aureus, Staphylococcus spp., Bacillus spp., Moraxella spp., Micrococcus luteus, Acinetobacter spp., Brevundimonas diminuta, Pseudomonas spp., Kocuria spp., Bergeyella spp., Lactobacillus spp., Enterococcus spp., Corynebacter spp., Brevibacillus spp., Paenibacillus spp., Bacteroides spp.

Conclusions: The main microorganisms colonizing the hands of the students were Staphylococcus spp., Bacillus spp., Micrococcus luteus, Acinetobacter spp., Kocuria spp., Lactobacillus spp. 13 participants (59.1%) carried S.aureus on their hands surface. It has been demonstrated that the treatment with bacteriophage gel is more effective compared to the treatment of hands with liquid soap and gel with antiseptic. Since 12 children had in fact an increase in the number of microbes after the treatment compared with the original colonization on their dirty hands, pupils were given recommendations on effective hand washing.

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Emergence of Klebsiella quasipneumoniae carrying New Delhi metallo-β-lactamase (blaNDM-1) gene in a Brazilian hospital

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Background: Klebsiella pneumoniae carbapenemase-resistant carrying the blaKPC gene is highly prevalent in some Brazilian hospitals. Recently, isolates of K. pneumoniae carrying blaKPC gene have been described in Brazil. K. pneumoniae were phylogenetically described in four groups (KpI, KpII-A, KpII-B and KpIII), but recently the KpII and KpIII groups were reidentified as K.quasipneumoniae and K.variicola. K.quasipneumoniae can be as virulent as K.pneumoniae carrying and spreading antimicrobial resistance genes. The aim of this study is to characterize through the whole genome sequence (WGS) isolates carrying the blaNDM-1 gene.

Materials/methods: We studied eight isolates of K.pneumoniae carrying blaNDM-1 causing infection in a Brazilian tertiary hospital located in the city of São Paulo in the period of 18/01/2018 – 05/07/2019. They were isolated from bone fragment, blood, catheter, rectal swab and urine. The WGS was performed in an Illumina® MiSeq 2x250 bp platform with paired-end mode. Sequences were assembled using Newbler 3.0 and Ray 2.3.1 software. Automatic annotation was performed using Prokka software, and manual validation was performed using NCBI Blast and the website bigsdb.web.pasteur.fr/klebsiella and genomicepidemiology.org/.

Results: The ribosomal multilocus sequence typing (rMLST) analyzes showed four K.quasipneumoniae isolates; these findings were confirmed by identifying the bla_oxa gene considered chromosomal in this species. In addition, the presence of blaKOP-A and blaKOP-B was used to characterize the subspecies K.quasipneumoniae subsp. quasipneumoniae in two isolates and K.quasipneumoniae subsp. similipneumoniae in another two. All isolates had a multidrug resistance profile including bla TEM-1A, blaCTX-M-15, blaNDM-1, and oxacillinase blaOXA-9, were detected in three isolates. All isolates were susceptible to amikacin and polymyxin B. Through Multilocus Sequence Typing (MLST), we found ST-735 [2] and ST-334 [1]. Single nucleotide Polymorphisms (SNPs) analysis showed that the two K.quasipneumoniae subsp. quasipneumoniae were identical and the two K.quasipneumoniae subsp. similipneumoniae were related.

Conclusions: Extensively drug-resistant K.quasipneumoniae carrying several antimicrobial resistance genes, including metallo-β-lactamase blaNDM-1 is present at this hospital warranting a surveillance in other Brazilians hospitals.

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Bacteriocin production in *Staphylococcus aureus* CC398 and CC130 lineages, potential strategies to antimicrobial resistance

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**Background:** *Staphylococcus aureus* (*S. aureus*) frequently colonize the skin and mucous membranes of humans and animals, also being an opportunistic pathogen. Recently, the *S. aureus* genetic lineages CC398 (mostly the livestock-associated methicillin-resistant MRSA) and CC130 (mostly the MRSA containing the mecC gene, frequent in wild animals) have gained public health relevance. Moreover, bacteriocins are antimicrobial peptides secreted by bacteria, with ecological and biotechnological implications. The objective was to determine the bacteriocin production (BP) in CC398 and CC130 strains of different origins with antimicrobial activity against indicator bacteria of public health significance and characterize at genomic level BP-strains.

**Materials/methods:** 43 *S. aureus* isolates CC398 (*n*=25) and CC130 (*n*=18) from (red-deer, magpie, vulture, rabbit, stork, small-mammals, chicken, goat, sheep, water and human) were included in the study. Isolates were methicillin-susceptible *S. aureus* (MSSA, 80% in CC398 and 28% in CC130) and MRSA (20% in CC398 and 72% in CC130, both mecC/meca). All 43 strains were tested for BP by the spot-in-the-lawn method against 19 indicator bacteria (different genera/species), including multi-drug-resistant (MDR) bacteria and relevant pathogens, including zoonotic ones. The presence of bacteriocin related genes was studied in the whole-genome-sequence of the 43 strains (previous studies), using the programs Bagel4 and Geneious.

**Results:** Only one of the 43 *S. aureus* tested showed BP. This BP-strain (C5802, of water origin) was MSSA-CC130-t843 and showed an intense antimicrobial activity against 74% of bacterial indicators tested including MRSA, *Streptococcus suis* and *Listeria monocytogenes*, among others. Bagel4 analysis revealed the presence of possible bacteriocins, mainly sactipeptides and the putative bacteriocin (lactococcin 972, accession nº PF09683). Sequence alignment between the reference sequence (accession nº WP_000726502), the BP-strain and other isolate genetically similar (CC130, t843, MRSA), revealed that all of them have the same nucleotidic/aminoacidic sequence and identical genetic environment. *S. aureus* strain C5802 contained only the resistance gene *blaZ*, and the virulence genes *lukME*, *lukED*, *etD2*, *hlgAB*, *hlgCB*, *edinB*, *splA/B*, *aur*.

**Conclusions:** BP is an unusual character in *S. aureus*; nevertheless, the detection of a BP-strain MSSA-CC130, with low resistance gene content but intense inhibitory action against zoonotic and MDR bacteria, open new therapeutic and biotechnological futures strategies.

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Abstract 7302

Streptococcus suis infection: a series of 37 cases from a community-based hospital, Thailand
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Background: Streptococcus suis (S. suis) is a gram-positive bacterial pathogen which can cause severe infections in human, including meningitis, and septicemia resulting in serious complications. This study is aimed to describe the clinical features and determine the risk factors for mortality of this life-threatening.

Materials/methods: We conducted a retrospective cohort study among patients diagnosed with culture-confirmed S. suis infection in a community-based hospital in eastern of Thailand from 1 January 2017 to 31 October 2018. All patients’ demographic data, diagnosis, and treatment were retrieved. Median with interquartile range (IQR) and frequency (%) were used to describes patients’ characteristics. Risk factors for mortality were determined by logistic regression analysis.

Results: Thirty-seven patients (22 men and 15 women, mean age 57 years) with S. suis infection were identified. The most common risk of S. suis infection was eating undercooked pork (72.4%). Blood cultures were confirmed S. suis in 36 (97.3%) patients. Clinical presentations included acute meningitis (48.6%), sepsis (21.6%), endocarditis (10.8%). 29.7% were presented with septic shock at the emergency department. Hearing loss was observed in 8.1% and was associated with meningitis. The overall mortality rate was 16.2%. On univariate analysis, acute respiratory failure and septic shock at the emergency department was significantly correlated with a high mortality rate.

Conclusions: S. suis infection is common in Eastern of Thailand, commonly presents with acute meningitis or sepsis. The mortality rate is high. The risk factors for mortality are septic shock and acute respiratory failure at emergency department. High suspicion and early detection are essential and could lead to a successful clinical outcome. The public health educations are crucially needed.

<table>
<thead>
<tr>
<th></th>
<th>Total (37)</th>
<th>Alive (31)</th>
<th>Death (6)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (IQR) onset, hours</td>
<td>48 [24-144]</td>
<td>48 [20-26]</td>
<td>120 [48-168]</td>
<td>0.34</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>7 (18.9)</td>
<td>5 (16.1)</td>
<td>2 (33.3)</td>
<td>0.33</td>
</tr>
<tr>
<td>Alcohol drinking</td>
<td>13 (35.1)</td>
<td>10 (32.3)</td>
<td>3 (50.0)</td>
<td>0.41</td>
</tr>
<tr>
<td>Positive hemoculture</td>
<td>36 (97.3)</td>
<td>30 (96.8)</td>
<td>6 (100)</td>
<td>0.66</td>
</tr>
<tr>
<td>Meningitis</td>
<td>18 (48.7)</td>
<td>16 (51.6)</td>
<td>2 (33.3)</td>
<td>0.41</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>4 (10.8)</td>
<td>2 (6.5)</td>
<td>2 (33.3)</td>
<td>0.05</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>1 (2.7)</td>
<td>0</td>
<td>1 (16.7)</td>
<td>0.66</td>
</tr>
<tr>
<td>Toxic shock</td>
<td>4 (10.8)</td>
<td>2 (6.5)</td>
<td>2 (33.3)</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Presenter email address: subencha@gmail.com
Post-artesunate delayed haemolysis presenting with positive direct antiglobulin test: are steroids a therapeutic option?
Tommaso Ascoli Bartoli*, Luciana Lepore1, Alessandra D’abramo1, Angela Corpolongo1, Andrea Mariano1, Nazario Bevilacqua2, Maria Letizia Giancola1, Claudia Palazzolo1, Laura Scorzonelli1, Pierre Buffet2, Emanuele Nicastri1
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Background: After the widespread introduction of artesunate as first-line severe malaria treatment, several cases of "post-artesunate delayed hemolysis" (PADH) have been reported. PADH is defined as a drop >10% of the hemoglobin level, combined with hemolysis blood markers, occurring more than 7 days after the start of intravenous artesunate. PADH pathophysiology is thought to be related to the "pitting" phenomenon and the synchronous delayed removal of once-infected erythrocytes, spared during the parasite killing. However, few PADH cases presenting with positive direct antiglobulin test (DAT) have been reported, suggesting a possible autoimmune pathogenesis. We reviewed published PADH episodes that explicitly included the results of DAT.

Materials/methods: PubMed database was investigated using a string of MeSH terms ("hemolysis" OR "anemia, hemolytic") AND ("artemisinins" OR "artemisinine" OR "artesunate" OR "artemether" OR "artemether, lumefantrine drug combination" OR "dihydroartemisinin") and all the articles published before October 31, 2019 were reviewed. Titles and abstracts were independently screened by two Infectious Diseases specialists and data regarding patients diagnosed with PADH, for whom DAT had been performed, were extracted. Uni- and multivariate analysis of features potentially related to DAT results were performed using SPSS. Mann-Whitney U-test and Fisher’s exact test were respectively used to analyze continuous and categorical variables, while multivariate logistic regression was used to detect features independently associated with outcomes.

Results: Twenty-two studies reporting 39 PADH cases were included: 13 patients (33.3%) were women, median age was 44 years (IQR: 24.5-51.5), median baseline parasitemia was 20.8% (IQR: 11.2-30.0) and DAT was positive in 17 cases (45.5%). Upon univariate analysis, DAT positive patients were older (49.5 vs 31; p=0.01), had higher baseline parasitemia (27% vs 17%; p=0.03) and were more commonly treated with systemic steroids (11 vs 3 patients, p=0.003). Upon multivariate analysis, steroids use was independently associated to positive DAT result (p<0.01).

Conclusions: In this case series focused on immunohematological results, almost half of severe malaria cases with PADH had a positive DAT. Whether the positivity of DAT contributes to anemia and whether the use of steroids is justified requires prospective studies.

Presenter email address: tommaso.ascolibartoli@gmail.com
Amikacin or colistin monotherapy for complicated urinary tract infections by extensively drug-resistant 
Pseudomonas aeruginosa

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Abstract third-party references: On behalf of PROA-PSMAR group

Background: To compare the performance of amikacin/colistin monotherapy with other antibiotic regimes in treating complicated urinary infections (cUTI) caused by extensively-drug-resistant (XDR) Pseudomonas aeruginosa (PA).

Materials/methods: Study performed at a 450-bed teaching hospital from 2012 to 2018. All consecutive adult patients with XDR-PA monomicrobial urinary-culture and diagnosed of cUTI were retrospectively reviewed. XDR phenotype was defined according to Magiorakos et al. Clinical failure was considered if: persistence/worsening of infection signs/symptoms, modification of antibiotic therapy or death.

Results: 281 cases with XDR-PA were identified; 133 asymptomatic bacteriuria/non-cUTI and 91 polymicrobial cultures. Overall, 57 cUTI episodes were included. Most XDR-PA were susceptible to amikacin 35 (61.4%) and colistin 57 (100%). History of urinary catheter 34 (59.6%), recurrent UTI 30 (52.6%), benign prostatic hyperplasia 19 (33.3%) and urologic malignancy 13 (22.8%) were frequent. The most frequent antibiotic regimens were: amikacin/colistin 26 (45.6%), amikacin/colistin+carbapenem 13 (22.8%), antipseudomonal-cephalosporins 6 (10.5%) and amikacin/colistin+aztreonam 4 (7%). Median days of treatment: 10 (IQR 7-13.5). Table below summarizes main differences between patients treated with amikacin/colistin alone vs other treatments (including combinations with either of these).

<table>
<thead>
<tr>
<th></th>
<th>Amikacin/colistin alone (n=26), n(%)</th>
<th>Other (n=31), n(%)</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, m[10R];years</td>
<td>74 [66.7-80.2]</td>
<td>77 [69-84]</td>
<td>0.23</td>
</tr>
<tr>
<td>Charlson, m[10R];points</td>
<td>8 [5.75-9.25]</td>
<td>7 [5-9]</td>
<td>0.65</td>
</tr>
<tr>
<td>Renal disease</td>
<td>7 [26.9]</td>
<td>8 [25.8]</td>
<td>0.92</td>
</tr>
<tr>
<td>SAPS-II</td>
<td>33 [27.7-37.2]</td>
<td>36 [29-45]</td>
<td>0.18</td>
</tr>
<tr>
<td>SOFA</td>
<td>1.5 [0.3-3.2]</td>
<td>1 [0-4]</td>
<td>0.76</td>
</tr>
<tr>
<td>Sepsis/shock</td>
<td>5 [19.2]</td>
<td>10 [32.3]</td>
<td>0.27</td>
</tr>
<tr>
<td>Bacteraemia</td>
<td>2 [77]</td>
<td>6 [19.4]</td>
<td>0.27</td>
</tr>
<tr>
<td>Adequate source control</td>
<td>26 [100]</td>
<td>29 [93.5]</td>
<td>1</td>
</tr>
<tr>
<td>72h-delay to adequate treatment</td>
<td>14 [53.8]</td>
<td>16 [51.6]</td>
<td>0.87</td>
</tr>
<tr>
<td>Failure (day-7)</td>
<td>8 [30.8]</td>
<td>10 [32.3]</td>
<td>0.9</td>
</tr>
<tr>
<td>Failure (end-of-treatment)</td>
<td>6 [23.1]</td>
<td>3 [9.7]</td>
<td>0.27</td>
</tr>
<tr>
<td>Microbiological eradication</td>
<td>9/21 [42.9]</td>
<td>20/22 [90.9]</td>
<td>0.001</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>11 [42.3]</td>
<td>10 [32.3]</td>
<td>0.43</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>0 [0]</td>
<td>5 [16.1]</td>
<td>0.05</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>4 [15.4]</td>
<td>5 [16.1]</td>
<td>1</td>
</tr>
</tbody>
</table>

In a logistic-regression model, amikacin/colistin monotherapy was associated with neither clinical failure nor in-hospital mortality. Urologic malignancy (OR 6.44, 95%CI, 1.03-40.3) and prior renal disease (OR 5.39, 95%CI, 1.02-25.6) were independent predictors of clinical failure whereas a high SAPS-II (OR 1.09, 95%CI, 1.01-1.19) was independently associated with in-hospital mortality.

Conclusions: Amikacin/colistin monotherapy showed good efficacy and safety profiles in treating cUTI by XDR-PA.

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Impact of porin deletions on the in vitro antimicrobial activity of cefepime-taniborbactam (formerly cefepime/VNRX-5133) in Klebsiella pneumoniae

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1VenatoRx Pharmaceuticals, Inc., Malvern, United States

Background: Taniborbactam (formerly VNRX-5133) is an injectable, cyclic boronate β-lactamase inhibitor that inhibits all classes of β-lactamases and restores antibacterial activity of cefepime against Enterobacterales and P. aeruginosa producing both serine-β-lactamases and metallo-β-lactamases. A Phase 3 trial of the cefepime-taniborbactam combination is currently ongoing in patients. Herein, we report the mechanisms of resistance to cefepime-taniborbactam in Klebsiella pneumoniae, and evaluate the impact of deletion of porin genes (ompK35, ompK36 and ompK35/ompK36) and/or the master regulator gene ramA on the activity of cefepime-taniborbactam in K. pneumoniae isogenic strains.

Materials/methods: Minimum inhibitory concentrations (MICs) were determined by broth micro-dilution following CLSI methods. Isolation of mutants less susceptible to cefepime-taniborbactam was performed by selection of K. pneumoniae strains producing NDM-1. Whole genome sequencing was used to identify the mutation sites. Klebsiella pneumoniae isogenic strains lacking OmpK35, OmpK36 and/or RamA, and/or expressing KPC-3 β-lactamase were obtained from Kemyth Biotech.

Results: Selection of K. pneumoniae with cefepime-taniborbactam yielded less susceptible mutants. Genome sequencing revealed a deletion of 2 base pairs in the ompK36 gene that caused frameshift at the codon 159 in one of the mutants, and also lack of OmpK35 in the parent and mutant strains. Because deletion of the OmpK35 and OmpK36 porins reduces permeability to antibiotics, we examined whether porin deletions affected the activity of the β-lactamase inhibitors. The MIC results showed that deletions of the porins reduced the activities of cefepime synergistically with KPC-3. However, restoration of the cefepime activity by the addition of taniborbactam, were not affected significantly by deletion of the porins. Furthermore, the deletion of the two major porins reduced the susceptibility to ceftazidime-avibactam and meropenem-vaborbactam.

Conclusions: In K. pneumoniae, OmpK35 and OmpK36 were the major porins for penetration of cefepime through the outer membrane into the periplasm. By contrast, taniborbactam does not show a strong dependence on OmpK35 or OmpK36 for periplasmic accumulation.

<table>
<thead>
<tr>
<th>K. pneumoniae strain description</th>
<th>Cefepime MIC (µg/mL)</th>
<th>Ceftazidime MIC (µg/mL)</th>
<th>Meropenem MIC (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>K. pneumoniae parent strain</td>
<td>Alone</td>
<td>+Taniborbactam (4 µg/mL)</td>
<td>+Avibactam (4 µg/mL)</td>
</tr>
<tr>
<td>N/T1001 (parental strain)</td>
<td>16</td>
<td>0.08</td>
<td>2</td>
</tr>
<tr>
<td>ΔompK35ompK36KPC-3</td>
<td>&gt;1024</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>ΔramRKPC-3</td>
<td>32</td>
<td>0.25</td>
<td>8</td>
</tr>
<tr>
<td>ΔompK35ompK36ΔramRKPC-3</td>
<td>&gt;1024</td>
<td>4</td>
<td>16</td>
</tr>
</tbody>
</table>

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Abstract 7311

Measuring the impact on turnaround time by implementation of a new fully-automated random, continuous-access molecular platform in a large microbiology department

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Abstract third-party references: Abbott Molecular

**Background:** Availability of automated platforms for accurate molecular diagnosis and rapid turnaround time is key to provide an adequate and timely treatment and consequently to reduce transmission rates. The Abbott Alinity m system (Alinity m) is utilizing proprietary ReadiFlex technology, when processing time across different assays is synchronized. This study aimed to evaluate the impact on the reduction of turnaround time after Alinity m implementation, comparing the Alinity m workflow to the current molecular methods used in a tertiary hospital with >30,000 molecular tests per year for HIV/HBV/HCV/HPV and STIs.

**Materials/methods:** Every day, all samples for HIV, HBV, HCV quantification, HPV detection, and STI diagnosis arriving in the laboratory were registered, stored and tested by the routine methods (kPCR for HIV, c6800 for HBV/HCV, c4800 for HPV, and Seegene for STI) and by Alinity m. Two times were evaluated in the comparative study: total turnaround time (from sample arrival to result reporting) and onboard time (from onboard sample registration for Alinity m or start processing for routine methods to result reporting). Two times were measured specifically for Alinity m: time from sample aspiration until result reporting, and processing time for urgent samples.

**Results:** Total turnaround time was analyzed for 860 samples. Fifty percent of samples results were reported within 3 (HBV, HCV, and HPV), 4 (STI) and 7 days (HIV) using the routine methods, while Alinity m reported 100% of the results within 10h. Moreover, 1,229 samples were included into the comparative evaluation of the onboard time. The time until completion of 95% of results was 7:30h for routine methods compared to only 4:15h for Alinity m (including time between sample aspiration and result reporting which was <2h in 100% of the samples). The onboard time for prioritized urgent samples on Alinity m was ≤2:45h.

**Conclusions:** The Alinity m system allows rapid result reporting. It reduces the turnaround time on board by faster sample processing, ReadiFlex technology, and truly random access, compared to the routine methods. The implementation of the Alinity m system in molecular diagnostics could optimize the workload/day and the workflow by avoiding sorting, freezing and thawing steps.

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Impact of antibiotic stewardship strategies for Clostridioides difficile infection

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Abstract third-party references: Diftec network

Background: Clostridioides difficile infection (CDI) remains a frequent and severe complication for inpatients. In 2017, metronidazole prescription counted for more than 70% of CDI treatment in our institution. Local guidelines diffused in May 2018 put oral vancomycin or fidaxomicin (OVF) as first-line treatment for CDI instead of metronidazole. Impact of different antimicrobial stewardship (ASM) strategies towards antibiotic prescription for CDI and its clinical outcomes is undescribed. Our objective is to compare 3 different stewardship periods for CDI management in a tertiary universitary hospital in France.

Materials/methods: All patients with a CDI bacteriologically diagnosed on stool samples were included prospectively from Jan. 1st 2018 to July 31st 2019. Patients whose first documented-on-place episode was a second or more relapse were excluded. Three phases were defined according to stewardship strategies: free prescription (P1, from Jan. 1st to April 30th 2018), local guidelines by printed and numeric flyer (P2, from May 1st to Oct. 30rd 2018) and systematic intervention of the ASM team (from Nov 1st 2018 to July 31st 2019). Primary endpoint was OVF prescription as first-line treatment. Secondary endpoints were mortality and recurrence rates after 90 days and OVF prescription for first relapse.

Results: 213 CDI episodes – 171 first episodes (E1), 31 first relapses (R1), 11 further relapses - were recorded in 232 patients (median age: 67.3 years old (IQR= [56.8-76.5]), 105 female) 16 patients during P1, P2=69 and P3=101. Sixty-four episodes (30.0%) were severe or complicated according to ESCMID definition (P1=46.7%, P2=28.6%, P3=30.2%). We did not show significant difference between different ASM periods for OVF prescription as first-line treatment (P1=85.7%, P2=81.8%, P3=80.2%, p=0.87). In the 171 E1 patients, 17.0% relapsed and 20.4% died before 90 days. We did not show significant difference for relapses or global mortality (p=0.52 and 0.42 respectively).

Conclusions: With more than 80% of adapted prescription during the study periods antibiotics management for CDI is almost adapted to local and international guidelines. We could not show significant impact of our strategies evaluated by improvement of accordance between practice and guidelines for CDI infection by active stewardship compared to free or guided prescription.

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Abstract 7314

Molecular characterisation of 15 strains of OXA-181-producing Klebsiella pneumoniae in Spain
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Background: OXA-181 was suggested to be originated in India, from where it has spread worldwide causing sporadic cases. However, there are no cases of clonal dissemination of OXA-181-producing Enterobacteriales reported in Spain. Our objective is to characterize these isolates by using molecular methods and to determine their epidemiological relatedness.

Materials/methods: Retrospective revision and characterization of all OXA-181-producing Enterobacteriales isolated in our hospital between June-2018 and August-2019. OXA-181-producing isolates were identified by in-house PCRs or LAMP-based assay (EazyplexCRE®). Whole genome sequencing (WGS) was used in certain isolates to perform MLST and cgMLST by Ridom software and SNP analysis by SNIPPY pipeline. Antimicrobial resistance markers were identified by Resistance Gene Identifier (version 4.2.2), virulence determinants by VFanalyzer and plasmid incompatibility groups by the PlasmidFinder 2.0 web-based tool. A subset of 23 ST147 Klebsiella pneumoniae (Kp) isolates were additionally used for an in silico comparison of antimicrobial resistance genes, plasmid carriage and typing.

Results: We identified fifteen OXA-181 Kp isolates from urine (11), rectal swab (2), blood (1) and wound (1). Five episodes were considered hospital-acquired infections without epidemiological relationship, 1 healthcare-associated infection and 9 community-acquired infections, with no apparent epidemiological relationship. WGS of 10 isolates revealed that all belonged to ST147. Typing analysis revealed that they only showed 0-1/2513 alleles of difference by cgMLST and 5 variable positions (range 0-5) by SNP analysis. All carried bla_{OXA-181}, bla_{CTX-M-15}, dfrA14, aph[6]-Id, aph[3’]-Ib and amino acid substitutions in GyrA (S83I), ParC (S80I) and MarR (S3N). All presented enterobactin and yersiniabactin siderophores and carried IncFII, IncFIB, IncR, ColKP3, Col440I and Col440III plasmid incompatibility group. Maximum likelihood comparison with isolates belonging to ST147 lineage revealed that they were genetically closer to previously described bla_{OXA-181} isolates identified in Oman, Canada and United Arab Emirates (range 34-50 polymorphic sites) than previously isolates detected in Spain non-OXA-181-producers (range 117-176 polymorphic sites).

Conclusions: Genomic characterization of the OXA-181-producing Kp isolated in our hospital suggests that clonal dissemination of a ST147 strain has been produced, although no epidemiological relationship has been evidenced among the patients. As far as we know this represent the first clonal dissemination of OXA-181-producing Kp isolates in Spain.

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Assay for screening of Enterococcus faecium susceptibility to the disinfectant Sodium Dichloroisocyanurate plus detergent

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Background: Nosocomial infections caused by hospital-associated clones of Enterococcus faecium have increased globally over the last decades. Enterococci are intrinsically resistant to a number of first-line antibiotics, which makes treatment challenging. Vancomycin is an important drug for the treatment of severe E. faecium-infections, but in Denmark, there has been an alarming increase in the proportion of invasive cases with vancomycin-resistant E. faecium (VREfm) and vancomycin-variable E. faecium (VVEfm) from 0.5% in 2008 to 12% in 2018.

This study investigated whether different hospital clones of E. faecium could survive exposure to relatively high concentrations of Sodium Dichloroisocyanurate plus detergent (NaDCC Plus), possibly contributing to difficulties controlling VREfm/VVEfm outbreaks. Furthermore, we compared to survival of non-hospital isolates.

Materials/methods: 59 Danish clinical isolates divided into six representative groups (hospital-associated “outbreak” clones [VREfm and VVEfm], hospital-associated VREfm of less common ST/CT types, hospital-associated, human community-associated or animal community-associated vancomycin-sensitive E. faecium [VSEfm]) were included. Screening was performed in 96-well plates containing disinfectant in increasing concentrations [50 to 1000 ppm]. Isolates, grown in brain hearth infusion broth [BHI broth] overnight at 37 °C, were diluted to a final concentration of 10⁵ bacteria per well. Exposed to NaDCC Plus. After 10 minutes, the disinfectant was inactivated by adding a neutralizing agent. Plates were spun down, washed with 0.9% NaCl-water and spun down again. The supernatants were discarded and BHI broth was added. Plates were incubated overnight at 37 °C and each well was checked for growth or no growth.

Results: Growth indicated survival of theoretically at least one bacterium. No growth indicated eradication of the inoculum. The average concentration of disinfectant resulting in growth for the 59 isolates was 398 ppm [SD ± 74 ppm]. When the data was grouped into the six groups, according to the classification described above, no statistically significant differences between groups were found.

Conclusions: The results indicate that E. faecium could survive exposure to relatively high concentrations of NaDCC Plus, which could be of concern regarding disinfection in hospital settings. “Outbreak” clones were not less susceptible to NaDCC Plus compared with other E. faecium clones.

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Abstract 7317

The role of microbiological surveillance in ensuring the safety of endoscopes reprocessing

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Background: Failure in reprocessing of thermolabile flexible endoscopes has been reported as one of the top ten most important threats to patient health. Microbiological surveillance may be used to identify systematic errors in reprocessing or damaged endoscopes and equipment. Implementation of a microbiological surveillance of endoscope reprocessing is appropriate to detect early colonization and biofilm formation in the endoscope and to prevent contamination and infection in patients after endoscopic procedures.

Materials/methods: The study was conducted in two digestive endoscopy centers of a teaching hospital (29,000 endoscopies/year, of which 550 ERCP). Microbiological surveillance was performed according to the "Duodenoscope Surveillance Sampling and Culturing Protocols" protocol, CDC, 2018, with slight modification. Duodenoscopes were sampled monthly, automatic washer-disinfectors and endoscopes every three months and the medical cabinet twice a year

Results: In the 9 months of surveillance, 43 endoscopes were sampled (13 colonoscopes, 9 gastroscopes, 19 duodenoscopes and 2 echoendoscopes), 12 washer-disinfector machines and 8 medical cabinets. The analyzes were conducted both on the outer surfaces (valve ports, distal end, bridge elevator) and each endoscope channel. High microbial count were detected in 6% (9/154) of valves, with >100 CFU in 3 valves; E. coli was isolated on a bioptic valve of a gastroscope and of a colonoscope, while K. pneumoniae was isolated from the bridge elevator of a duodenoscope.

39% (17/43) of the internal channels of the endoscopes resulted contaminated; E. cloacae were isolated in 10% (2/19) of duodenoscopes, P. aeruginosa in 15% (2/13) of colonoscopes and in 11% (1/9) of gastroscopes. K. pneumoniae was identified in 10% (2/19) of duodenoscopes and NDM-producing K. pneumoniae was isolated in 22% (2/9) of gastroscopes, after the use on a colonized patient. The inlet and final rinsing water of washer-disinfectors resulted always conformed to the parameters required by National low D.Lgs. 31/2001 and by ISO 15883-4, as medical cabinets to the limits required by ISO 16442.

Conclusions: Implementation of a microbiological surveillance of endoscope reprocessing is appropriate to detect early colonization and biofilm formation in the endoscope and to prevent contamination and infection in patients after endoscopic procedures.

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Type I interferon in viral and bacterial infections in children
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Background: Type I interferons (IFNs) are involved in the antiviral response and in the pathophysiology of some autoimmune disease such as type I interferonopathies. Secreted at femtomolar concentrations during course disease, detection of type I IFN in these patients remains challenging. This issue has led several groups to develop an alternative strategy for the detection of this group of cytokines. Based on quantification of expression of IFN-stimulated genes, blood transcriptional IFN signatures have been developed and are currently used for the screening of patients with interferonopathies.

Distinguishing between bacterial and viral infections etiologies in febrile patients remains challenging, especially in children. Misdiagnosis of disease etiology are responsible of inappropriate antibiotic prescription. We hypothesized that specific host biomarkers for viral infections, like type I-IFN, could help clinicians decisions and limit antibiotic overuse.

Materials/methods: This is an ancillary study of the prospective multicentric protocol ANTOINE (NCT03163628). Paxgene® tubes and serum were collected from febrile children aged from 7 days to 36 months with proven viral (n=17) or bacterial (n=33) infection admitted in pediatric emergency departments in France. We have assessed the performance of IFN signature calculated using Nanostring® technology and plasma IFNα quantified by digital ELISA technology (Quanterix®).

Results: Serum level of IFNα were below the quantification threshold (30fg/mL) for 6% (1/17) and 67% (22/33) of children with proven viral and bacterial infection respectively. IFNα levels were significantly higher in viral compared to bacterial infection (median [IQR] 511.2 [559; 1014.1] and 132 [37; 3708] fg/mL respectively, p<0.001). We noticed a strong correlation between serum IFN-α concentrations and IFN score (r=0.83 [CI 0.75, 0.89]). Both serum level IFN-α and IFN score robustly discriminated (AUC 0.88 [CI 0.78, 0.99] and 0.85 [0.72, 0.97] respectively) between viral and bacterial infection in febrile children.

Conclusions: Our study suggests that measurement of IFNα femtomolar concentrations as well as IFN signature could offer new perspectives for improving diagnosis and limiting antibiotic overuse in febrile children. Our patient recruitment and investigations are still ongoing to ultimately confirm if these markers could become key biomarkers in the decision-making process of clinicians dealing with febrile children.

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Abstract 7320

**Antimicrobial activity, synergy and toxicity of a new gold(III) complex (AuC2) against multidrug-resistant pathogens with no detectable resistance**

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**Background:** The worldwide emergence and spread of infections caused by multidrug-resistant (MDR) bacteria endangers the efficacy of current antibiotics in the clinical setting. The lack of new antibiotics in the pipeline points the need of developing new strategies. Gold(III) complexes could be a promising alternative due to their antibacterial activity. We evaluate the effectiveness of a gold(III) complex alone and in combination with antibiotics against MDR clinical isolates as well as its in vitro and in vivo toxicity.

**Materials/methods:** Susceptibility of gold(III) complex (AuC2) was assessed in planktonic and biofilm growth, by both microdilution and crystal violet staining respectively, against MDR strains of Pseudomonas aeruginosa, Methicillin-resistant Staphylococcus aureus, Stenotrophomonas maltophilia, Acinetobacter baumannii, and Escherichia coli. Antimicrobial interactions in vitro were determined by the checkerboard method. Point-of-resistance studies were determined by 30-daily sequential passages in sub-MIC concentrations of AuC2. Cytotoxicity assays were performed in HepG2 and THLE-2 cell lines by MTT assay and hemolysis detection in human erythrocytes. For acute toxicity in vivo, CD1 female mice were treated by single intravenous 2.5 mg/Kg doses, toxicity signs were monitored for 14 days after treatment and Organ Weight/Body Weight (OW/BW) coefficients were calculated to assess organ toxicity.

**Results:** Susceptibility studies in planktonic and biofilm state showed high efficacy of AuC2, markedly against MRSA, presenting MIC=0.125-0.25 mg/L and MBIC=0.5-1 mg/L. Drug interaction checkerboard method showed a synergistic effect of AuC2 when combined with colistin or aminoglycosides in all MDR gram-negative strains tested. No resistant mutants were obtained after 30 days of sequential cultures. No hemolysis or cytotoxicity was detected at AuC2 therapeutic concentrations. Mice showed no significant weight loss or other toxicity signs within the 14 days post-treatment. No statistically different BW/BW values were obtained when compared to the untreated control.

**Conclusions:** Newly described gold(III) complex AuC2 has shown antimicrobial activity against MDR pathogens, specially MRSA strains in planktonic and biofilm state. Its potent synergistic effect combined with colistin or aminoglycosides in gram-negatives, its inability to produce resistant mutants, as well as its low in vitro and in vivo toxicity, makes it a promising candidate in the fight of antimicrobial resistance.

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Abstract 7321

The 2017 epidemic of pulmonary plague in Madagascar
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Abstract third-party references: pneumalgia

Background: Plague, Yersinia pestis (YP), is a zoonotic infection of rodents, transmitted to humans by flea. Plague is a reportable disease that is endemic to Madagascar with bubonic plague being the most common seasonal manifestation. In 2017 an unexpected epidemic of pulmonary plague (PP), a rare clinical form, occurred in Madagascar involving 2348 patients (791 cases of pulmonary plague (22% confirmed, 34% probable and 44% suspected), 341 cases of bubonic plague, a case of septicemic plague and 215 cases of unspecified type. There were 202 deaths during this epidemic. Confirmed, probable or suspected plague cases were reported to WHO by the Malagasy Ministry of Public Health. This epidemic of pneumonic plague raised many questions and issues related to diagnosis, treatment and prophylaxis, socio political and cultural aspects some of which remain unanswered. We report a summary of the challenges that local healthcare professionals faced during this unprecedented outbreak.

Materials/methods: Symptoms were frequently severe with brutal onset, high fever, profound deterioration of the general condition. Severe respiratory signs were observed: cough, hemoptoid sputum, chest pain, cyanosis. Without treatment death occurred in 1-3 days in 100% of the cases. Confirming the diagnosis was challenging and relied on culture for YP, rapid diagnostic test detecting F1 capsular antigen, detection of antibodies. Testing was performed at the Laboratoire Central de la Peste which led to delays in getting results to clinicians.

Results: Additionally, the RDT proved to have inadequate sensitivity for pneumonic plague. Treatment was with intramuscular streptomycin which was poorly tolerated by patients. Supplies (gloves, gowns and surgical masks) required for infection control measures were not readily available and waste disposal was a major challenge. Communication between hospitals proved to be challenging. Protection rules and special burial protocol were applied leading to a big source of conflict with the patient’s families.

Conclusions: YP remains a major public health problem in Madagascar and the pneumonic plague outbreak presented numerous challenges to clinicians and healthcare workers charged with identifying and controlling outbreaks. Improving the health infrastructure with basic supplies is critical for those at the front line.

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Recruiting donors for faecal microbiota transfer: a one year experience

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Background: Prior to performing fecal microbiota transfer (FMT), eligible donors undergo comprehensive screening to prevent potential infectious and non-infectious disease transmission. The difficulties to find eligible relatives from which to obtain stool samples can be solved by using universal screened donors, which can also increase the cost-effectiveness of the procedure. The aim of the study was to evaluate the success of finding eligible donors in our hospital.

Materials/methods: University students were informed and received a prescreening questionnaire about lifestyle habits, medical history and general health conditions to identify any exclusion criteria. Those who met the inclusion criteria were called for a personal interview in which they received detailed information, signed the informed consent and were subjected to medical examination, blood and fecal analyses. Any major alteration implied their exclusion and those qualified as donors were asked to avoid eating common allergens within 5 days prior to stool donation. They received a donation bag containing the necessary material for sample collection and a second questionnaire to report any change in their health status between screening and donation day. The samples were collected within 4-6 hours before being delivered to our laboratory. Donors provided samples during the following 2 weeks after screening.

After their participation, all volunteers received an economic compensation. Donors were asked to fill in a satisfaction questionnaire to obtain information about their experience during the recruitment process.

Results: Table 1. Results from stool donors screening and their characteristics.

<table>
<thead>
<tr>
<th>Invited to participate</th>
<th>Pre-screening survey</th>
<th>Blood and stool screening</th>
<th>Bring valid sample</th>
<th>Mean Age</th>
<th>Gender</th>
<th>Mean BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=100</td>
<td>n=53</td>
<td>n=28</td>
<td>n=22</td>
<td>23 (range 20-38)</td>
<td>64.29% female</td>
<td>21.21kg/m² (range 18.6-24.9 kg/m²)</td>
</tr>
</tbody>
</table>

The satisfaction questionnaire showed that 62.5% (n=10) of respondents knew about FMT prior to participating in our study although the same percentage didn’t know about stool donation. Only 31.25% (n=5) would repeat as donors without receiving any remuneration.

Conclusions: The eligibility success in this population was 22%, showing higher rates than other studies. Although general population is not aware of FMT, university students showed interest in being stool donors favored by economic motivation.

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Abstract 7328

Mupirocin exposure in the preceding year is associated with mupirocin resistance among methicillin-resistant *Staphylococcus aureus* in a tertiary care hospital in the United States of America

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Abstract third-party references: University of South Florida, Department of Infectious Diseases, Tampa General Hospital

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) infections are associated with increased morbidity and mortality in nosocomial settings. Active surveillance and decolonization with mupirocin are vital components of MRSA control strategy. Emergence of mupirocin resistance (MR) poses an increasing threat to MRSA control efforts. Hence, this study aims to identify risk factors for emergence of MR among MRSA isolates in a 1040 bed tertiary care academic center in the United States of America.

Materials/methods: We conducted a retrospective cohort study. All consecutive hospitalized patients who screened positive for MRSA from May to August 2019 were eligible for inclusion. We tested for MR among MRSA culture positive isolates and reviewed risk factors for development of MR. The association between MR and risk factors was assessed using binary logistic regression and summarized as odds ratios (OR) along with 95% confidence intervals (CI). Statistical analyses were carried out using IBM SPSS software.

Results: A total of 326 MRSA positive samples were obtained during the study period. Of these, 235 patients had MRSA that were culture proven, and were tested for mupirocin susceptibility. MR was seen in 38.7% of the patients. Patients with mupirocin sensitive and resistant strains were similar in gender, location of transfer (hospital to hospital transfer, transfer from rehab facilities), presence of diabetic ulcers and chronic skin disorders. Following risk factors for mupirocin resistance were associated with MR: pressure ulcers (OR: 2.53, 95% CI 1.25-5.14; p=0.01), nursing home placement prior to admission (OR 2.48, 95% CI 1.01-6.07; p=0.047), mupirocin exposure within one year of admission (OR 7.01, 95% CI 3.90-12.59; p<0.001), age >59 years (OR 2.77, 95% CI 1.6-4.8; p<0.001) and intranasal mupirocin administration within one year (OR 6.58, 95% CI 3.68-11.78; p<0.001).

Conclusions: Prior mupirocin exposure within one year of admission poses increased risk of MR. Further investigation is needed to understand the effect of pressure ulcers and prior nursing home placement on the emergence of MR. These findings warrant early testing strategies for detection of MR and use of alternative decolonization strategies in patients with high risk for MR.

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Comparing the financial burden of hospitalised patients within the same Diagnosis Related Groups (DRGs) with and without an infection: a multi-centre evaluation in the USA

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Abstract third-party references: This study is supported by Merck & Co., Inc., Kenilworth, NJ, USA

Background: Slow uptake of new antimicrobials may be due to perceived higher cost relative to generic comparators. We compared the mortality and financial outcomes of similar hospitalizations that did or did not have an infection to determine the attributable total cost of an infection.

Materials/methods: We analyzed 92 hospital’s microbiology, general laboratory, antimicrobial orders and administrative data from 10/2015-7/2018 [BD Insights, Franklin Lakes, NJ USA]. Infection positive was defined as adult [≥ 18 yrs] admissions prescribed ≥ 72 hours of antibacterial therapy meeting the following: 1) infection ICD10 code [pneumonia, sepsis, urinary tract infections, skin/wound infection, or intra-abdominal infection] regardless of culture, 2) no infection ICD10 code but culture collected. Admissions with a length of stay (LOS) ≥ 3 days not meeting infection criteria and no antimicrobials prescribed was classified as no infection. We evaluated hospital mortality, LOS, intensive care unit (ICU) LOS, hospital cost, payment, and gain/loss per case within each non-infection diagnosis related group (DRG) that included an infection in the same DRG but without infection. Pair-wise comparisons were analyzed using t tests followed by Cohens d for the effect size.

Results: Across 704,559 total admissions, 303,650 met the study criteria. Of these, there were 133,423 with an infection and 170,227 without an infection. The DRG adjusted outcomes were significantly higher with versus without infection as follows: avg. additional LOS (4.5 days, p < 0.0001); avg. additional ICU LOS (1.3 days, p < 0.0001); avg. hospital cost ($10,953, p < 0.0001); avg. additional loss (-$3,087, p < 0.0001). Outcome differences varied by DRG type. The top 10 DRGs with infection in frequency are in table below.

<table>
<thead>
<tr>
<th>Top 10 DRGs by Total Infection (per definition) Admits</th>
<th>Total Adm</th>
<th>Uniq. Admits w Infection</th>
<th>Uniq. Admits w/o Infection</th>
<th>% w/o Infection</th>
<th>Avg. Add'l LOS</th>
<th>Avg. Add'l Cost</th>
<th>Avg. Add'l Margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grand Total</td>
<td>309,650</td>
<td>133,423</td>
<td>170,227</td>
<td>56.06%</td>
<td>4.5</td>
<td>$10,953</td>
<td>($3,087)</td>
</tr>
<tr>
<td>Heart failure &amp; shock w MCC (DRG 391)</td>
<td>10,811</td>
<td>5,732</td>
<td>5,079</td>
<td>46.98%</td>
<td>3.2</td>
<td>$6,726</td>
<td>($5,327)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease w MCC (DRG 190)</td>
<td>6,140</td>
<td>5,693</td>
<td>447</td>
<td>7.28%</td>
<td>1.4</td>
<td>$2,096</td>
<td>($1,855)</td>
</tr>
<tr>
<td>Pulmonary edema &amp; respiratory failure (DRG 189)</td>
<td>5,092</td>
<td>4,026</td>
<td>1,066</td>
<td>20.93%</td>
<td>2.5</td>
<td>$5,277</td>
<td>($3,312)</td>
</tr>
<tr>
<td>Other kidney &amp; urinary tract diagnoses w MCC (DRG 698)</td>
<td>2,801</td>
<td>2,726</td>
<td>75</td>
<td>2.7%</td>
<td>1.9</td>
<td>$3,082</td>
<td>($1,579)</td>
</tr>
<tr>
<td>Renal failure w MCC (DRG 682)</td>
<td>4,057</td>
<td>2,664</td>
<td>1,393</td>
<td>34.3%</td>
<td>4.4</td>
<td>$8,880</td>
<td>($4,320)</td>
</tr>
<tr>
<td>Esophagitis, gastritis &amp; misc. digest disorders w MCC (DRG 392)</td>
<td>4,431</td>
<td>2,409</td>
<td>2,022</td>
<td>45.6%</td>
<td>1.4</td>
<td>$1,875</td>
<td>($1,288)</td>
</tr>
<tr>
<td>Respiratory system diagnosis w ventilator support &lt;96 hours (DRG 706)</td>
<td>2,701</td>
<td>2,406</td>
<td>295</td>
<td>10.9%</td>
<td>4</td>
<td>$10,227</td>
<td>($5,704)</td>
</tr>
<tr>
<td>Renal failure w CC (DRG 683)</td>
<td>4,355</td>
<td>2,071</td>
<td>2,284</td>
<td>52.3%</td>
<td>1.9</td>
<td>$3,458</td>
<td>($7,317)</td>
</tr>
<tr>
<td>Major small &amp; large bowel procedures w MCC (DRG 329)</td>
<td>2,149</td>
<td>2,004</td>
<td>145</td>
<td>6.7%</td>
<td>9.4</td>
<td>$23,304</td>
<td>($8,852)</td>
</tr>
<tr>
<td>LEMU or trach w MV &gt;1 hrs or P/F &lt;200 face, mouth &amp; neck w maj O.R. (DRG 3)</td>
<td>1,973</td>
<td>1,964</td>
<td>9</td>
<td>0.5%</td>
<td>23.7</td>
<td>$113,347</td>
<td>($12,950)</td>
</tr>
</tbody>
</table>

Conclusions: The financial burden of admissions with an infection are significantly greater than the same DRGs without an infection. It is important to identify these groups with high risk of infection and high resource utilization that may be in need of treatment optimization. The cost of appropriate use of newer antimicrobials could be offset if there are benefits derived from decreased resource utilization in these patient groups.

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**Abstract 7331**

**Limited value of fluorescence in situ hybridization for the detection of *Coxiella burnetii* in tissue samples of patients with chronic Q fever.**

Sheila Bianca Buijs*, Tim Jensen², Mirjam Hermans³, Mette Boye⁴, Peet Nooijen¹, Andy I.M. Hoepelman¹, Chantal Bleeker-Rovers³, Jan Jelrik Oosterheert¹, Peter Wever³

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**Background:** Chronic infection with *Coxiella burnetii* is notoriously difficult to diagnose and is based on a combination of clinical, microbiological and radiologic characteristics. When *C. burnetii* is detected in blood or tissue, the diagnosis is considered proven. However, culturing *C. burnetii* is time-consuming and only possible in a biosafety level 3 lab, and polymerase chain reaction (PCR) on formalin-fixed tissue samples lacks sensitivity. Fluorescence in situ hybridization (FISH) is a promising technique, but its diagnostic value alone or in comparison to PCR has not been determined. We evaluated the diagnostic value of FISH for the detection of *C. burnetii* in formalin-fixed tissue samples.

**Materials/methods:** *C. burnetii* FISH and *C. burnetii* PCR were performed on formalin-fixed tissue samples from Dutch chronic Q fever patients collected during surgery or autopsy. A positive percentage agreement was calculated. Patient and disease characteristics were collected from electronic medical records.

**Results:** From 19 chronic Q fever patients, 27 tissue samples were available: 19 (70%) vascular walls, three (11%) tissues surrounding prostheses, two (7%) placentas, two (7%) lung tissues, and one (4%) heart valve were examined by both FISH and PCR. Of 24 PCR positive samples, 9 (37.5%) were also FISH positive. Two PCR negative tissues, both placentas, were FISH positive. FISH positive and negative results had similar time before fixation (<1h, 63.6% vs. 66.7%, p=0.41), PCR CT values (mean, 21.68 vs. 24.94, p=0.39), similar treatment during retrieval of samples (27.3% vs. 20.0%, p=0.21), *C. burnetii* PCR serum positivity (45.5% vs. 60.0%, p=0.50), and phase II IgG titers during retrieval of samples (mean, 2,048 vs. 4,096, p=0.12). Sampling error might have occurred given discordant FISH results in tissue sections from one patient obtained at the same moment.

**Conclusions:** As compared to PCR, FISH had a positive agreement percentage of 37.5%. Given the FISH positive results in PCR negative placentas, FISH does seem to have an additional value in combination with PCR and remains an interesting technique to further examine in patients with chronic Q fever.

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Abstract 7336

An innovative model to analyze anti-biofilm immune response in vivo
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Background: Due to its ability to form biofilms, *Staphylococcus aureus* (*S. aureus*) is responsible for an increasing number of infections on implantable medical devices with a high mortality rate. In order to simulate this, a mouse model of infection consisting of microbeads coated with *S. aureus* biofilm has been developed to analyze the dynamics of anti-biofilm inflammatory responses by intravital imaging.

Materials/methods: *In vitro*, silica microbeads were coated by a biofilm of *S. aureus* (fluorescent strain SH1000 mCherry+). Then, biofilm was injected intradermally into the ear tissue of LysM-EGFP transgenic mice (fluorescent polymorphonuclear neutrophils and macrophages). Different kinds of inocula were compared: microbeads coated by biofilm, a mixture of microbeads and planktonic bacteria, microbeads alone. The inflammatory responses in ear tissue were studied in real time by confocal microscopy at early (4h) and late time point (24h) after injection. The displacement properties of immune cells (average velocity, trajectory linearity) were analyzed.

Results: *In vitro*, we confirmed coating of microbeads by biofilm by labeling matrix components and observing biofilm ultrastructure at the microbeads surface by scanning electron microscopy. In vivo, the global analysis of inflammatory responses showed a massive recruitment of EGFP+ cells between early and late time points. Observation of cell recruitment in real time at the injection site revealed a difficult access to biofilm bacteria for immune cells. At 4h, the average velocity of cells after infection was decreased for planktonic and biofilm forms compared to control mice (p < 0.01). In tissue areas with direct contact between immune cells and bacteria, the average cell velocity and linearity were decreased regardless of the form (p < 0.001 and p < 0.05 respectively). At 24h, we observed a decrease in the mean velocity for both bacterial forms in direct contact with bacteria (p < 0.05).

Conclusions: This original model provides an innovative way to analyze the specific immune responses against biofilm infections on medical devices. It paves the way for live evaluation of the effectiveness of immunomodulatory therapies combined with antibiotics.

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Abstract 7339

**Multidrug-resistant A. baumannii beyond colistin era: in vitro synergy of ceftazidime/avibactam in combination with antibiotics**

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**Background:** Multi-drug resistant (MDR) A. baumannii presents a global threat for hospital-acquired infections and colistin-resistance is rapidly evolving in the hospital setting. A number of patients, especially in ICU, are co-infected by other MDR organisms, mainly K pneumoniae. This study investigates the possible in vitro synergy effect of ceftazidime/avibactam, which is a potent compound for KPC+ K pneumoniae, with colistin, tigecycline and fosfomycin against MDR A. baumannii strains.

**Materials/methods:** Forty MDR A. baumannii strains, resistant to carbapenems and colistin were included in the study. Strain identification and antibiotic susceptibility was originally performed by Vitek2 system (bioMerieux) and susceptibility to colistin tested by broth dilution method (ComASP Colistin, Liofilchem srl) according to EUCAST guidelines. All strains were screened for MIC by E-test (Liofilchem srl), against colistin (COL), fosfomycin (FOS), tigecycline (TIG) and ceftazidime/avibactam (CAZAVI) and the in vitro synergistic effect of combinations COL+CAZAVI, FOS+CAZAVI, TIG+CAZAVI was determined by E-test cross onto Muller Hinton agar plates (Oxoid), according to published methods. All strains were clinical isolates from blood, bronchial secretion or pus cultures, collected from January to October 2019. Synergy effect of all antibiotic combinations was calculated using the Fractional Inhibition Concentration index formula (MIC\(AB\)/MIC\(A\) + MIC\(BA\)/MIC\(B\)) and result was interpreted as: Synergy < 0.5, Additive 0.5-1.0, Indifference >1.0 - <4.0 and Antagonism >4.0.

**Results:** All strains were resistant to colistin both by broth dilution method and E-test, with MICs ranging from 4 to 64 mg/l, as well to CAZAVI with MICs from 12 to 32 mg/l. MICs to FOS were ranging from 1 to 64 and TIG from 0.50 to 16.

<table>
<thead>
<tr>
<th>Synergy</th>
<th>COL+CAZAVI</th>
<th>FOS+CAZAVI</th>
<th>TIG+CAZAVI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>29/40 (72.5%)</td>
<td>26/40 (62.5%)</td>
<td>29/40 (72.5%)</td>
</tr>
<tr>
<td>Additive</td>
<td>2/40 (5.0%)</td>
<td>3/40 (7.5%)</td>
<td>0</td>
</tr>
<tr>
<td>Indifference</td>
<td>9/40 (22.5%)</td>
<td>3/40 (7.5%)</td>
<td>0/40 (20.0%)</td>
</tr>
<tr>
<td>Antagonism</td>
<td>0</td>
<td>9/40 (7.5%)</td>
<td>3/40 (7.5%)</td>
</tr>
</tbody>
</table>

**Conclusions:** The findings of this study suggest that a significant synergy effect is observed with all tested combinations of CAZAVI. The combination with no antagonism effect was COL+CAZAVI, whereas FOS+CAZAVI showed the most antagonism effects. There is an indication of testing for synergy all MDR A. baumannii strains, even colistin-resistant ones, as there are high possibilities of achieving a synergistic effect.

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Abstract 7340

Genomic insights into the dynamic of OXA-48-producing Enterobacterales in a veterinary hospital

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Background: Carbapenem-resistance is still rare in Europe in animals due to the prohibition of carbapenem use in the vet sector. There are nevertheless a few specific exceptions, including the VIM-1 spread in the food chain in Germany and the sporadic detection of OXA-48 throughout Europe in companion animals. In this study, we characterized the dynamics of resistance to carbapenems in Enterobacterales in dogs in a French veterinary hospital.

Materials/methods: Between February and May 2017, 124 healthy dogs admitted for non-infectious surgery at a veterinary hospital in Paris were sampled on their arrival (t0) and when they left (t4). Environmental samples within the hospital were also taken. Bacteria were isolated on selective media for the detection of carbapenem-resistant Enterobacterales. Identification was performed by Maldi-TOF. Non-duplicate isolates were characterized by antimicrobial susceptibility testing (disc diffusion) and whole-genome sequencing (NGS) using the NovaSeq technology. Analyses were performed using the CGE website.

Results: Fifteen OXA-48-producing Enterobacterales were identified: one Citrobacter freundii, 3 Klebsiella pneumoniae, 4 Escherichia coli and 7 Enterobacter cloacae. Six E. cloacae originated from the environment within the hospital. One OXA-48-positive dog arrived and left with the same OXA-48-producing K. pneumoniae, whereas a second one entered with an OXA-48-producing E. coli that was not detected when the dog left. Three additional dogs most probably acquired OXA-48 during their stay in the hospital, of which two animals presented respectively two and three OXA-48-producing Enterobacterales. A wide genetic diversity was observed except for K. pneumoniae, which all belonged to the sequence type [ST]11. All blaOXA-48 genes were carried by an IncL plasmid.

Conclusions: OXA-48-producing Enterobacterales were resident, transient and/or acquired in the veterinary hospital. NGS data suggest a complex dynamic of OXA-48 clonal and plasmid spread, and most likely highlight E. cloacae as a local reservoir of carbapenem-resistance. Since one dog left with the same OXA-48-positive E. cloacae recurrently identified in the environment, a direct transmission is also plausible. Two dogs presented several OXA-48-producing Enterobacterales, proving the high mobility of the OXA-48/IncL plasmid. In the absence of carbapenem prescription, such a significant OXA-48 epidemiology remains unclear but of major public health concern.

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Regional dissemination of Klebsiella pneumoniae ST147 NDM-1 in Poland

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Background: Since 2011 the large countrywide Klebsiella pneumoniae ST11 NDM-1 outbreak has been observed in Poland, with rate growing exponentially year by year, reaching over 2000 cases in 2018 and over 7000 affected patients in total. In March 2015 three Polish nationals were seriously injured in terrorist attack in the Bardo National Museum located in Tunis, Tunisia, and after surgical intervention on place they have been transported to hospital in Warsaw. From all three patients K. pneumoniae blaNDM-1 gene localized in Tn125 derivative and represented ST147 were detected at admission. Here we present contribution of ST147 in NDM-1 outbreak in Poland from first isolation till the end of 2017 providing molecular data, including the whole-genome sequencing (WGS) results.

Materials/methods: The study comprised 4504 unique NDM-positive K. pneumoniae isolates identified between April 2015 and December 2017. NDMs were detected by CarbaNP and PCR. Polymorphism of blaNDM-carrying Tn125-like elements, being a screening molecular marker, was assessed by PCR-mapping. Isolates representing variant Tn125F, characteristic for ST147 from Tunisia, were subjected to further analysis. All Tn125F-variant isolates were typed by PFGE and randomly by MLST. Seventeen K. pneumoniae ST147 NDM-1 outbreak isolates were subjected to WGS by Illumina MiSeq. Their sequences were analyzed by cgMLST and compared with 23 international ST147 isolates of the Institut Pasteur Klebsiella MLST database.

Results: One hundred and five K. pneumoniae isolates with Tn125F-variant, containing 5353bp fragment harbouring blaNDM-1 from 253bp 3’end of tnpA ISaba125 to 1250bp 5’end of groEL, were analysed. The material were collected in 24 medical centres in 13 cities in 2015 (n=9), 2016 (n=13) and 2017 (n=83), including one centre in Warsaw with 70 cases. All isolates represented single PFGE type and were classified to ST147. Based on WGS the outbreak ST147 isolates formed a separate cluster of closely-related genotypes, differing in 1-7 locus each at all 629 target loci.

Conclusions: The results documented the progressing spread of K. pneumoniae ST147 NDM-1 in Poland, with serious problem in one centre in Warsaw, being far behind of endemic K. pneumoniae ST11 NDM-1.

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Abstract 7342

10 years surveillance of West Nile virus neuroinvasive disease
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Abstract third-party references: The research was funded through CCCDI-UEFISCDI project PN-III-P1.2-PCCDI-2017-0005/2018.

Background: During the last 10 years have been observed major changes in West Nile virus human infections, with spread in new regions and increasing mortality.

Materials/methods: We analyzed patients hospitalized with West Nile virus neuro-invasive disease (WNND) in a tertiary infectious diseases hospital from May 2010 to November 2019, in order to characterize patients and to identify the prognostic factors associated with the severe outcome of patients.

Results: In this period, a total of 115 cases of WNND, median age 64 years, 51.3% males, were hospitalized with the overall mortality rate at discharge 2.1% (25 patients). Most cases have been in the years 2016 (15 cases), 2017 (23 cases), 2018 (41 cases) and 2019 (22 cases). All deaths were recorded during 2016-2019. In addition other 3 patients died in first month of follow-up after discharge [3.33% from survivors at discharge]. The median age of deceased patients was significantly higher than that of survivors [78 years (IQR 75.0-84.5) vs 64 years (IQR 50-77.25), p<0.001]. Average days of hospitalization was 16.3 days [from 1 to 64 days]. Long rank test (Mantel-Cox) indicates significant differences between the days of hospitalization depending on the clinical forms. Deceased patients had clinical forms of meningo-encephalitis (72%) or encephalitis (28%), and associated several cardio-vascular co-morbidities: ischemic heart disease (80% vs. 34.4%), arterial hypertension (80% vs. 57.8%) or congestive heart failure (28% vs. 8.9%). Clinical signs associated with severe prognosis were coma (92% vs. 23.3%), Glasgow coma score [9.16 (IQR 7.89-10.43) vs. 13.39 (IQR 12.89-13.89)], change in consciousness [100% vs. 51.1%], obtundation [96% vs. 37.8%], disorientation [96% vs. 66.7%] and speech disorders [76% vs. 35.6%], 70% of deceased patients died in the first 20 days after hospital admission [Figure]. Of all survivors at discharge 51 (44.3%) had sequelae and at one month follow-up still had sequelae 47 patients (40.8%). The most frequent sequelae were weakness, tremor of the extremities and ataxia.

Conclusions: Severe outcome of WNND is associated with age, cardio-vascular co-morbidities and several neurological signs. WNND remains an important cause of morbidity and mortality with long length of stay in hospital with re-emergence in our region.
Abstract 7351

**OXA-48 producing Klebsiella pneumoniae in non-hospitalised elderly patients in Zagreb, Croatia**

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**Background:** During 2016 epidemic spread of OXA-48 positive *Klebsiella pneumoniae* strains from northwest to other regions of Croatia was noticed. In the early stage of dissemination only hospitals were affected, but during the last three years spread to the long-term care facilities was observed. The aim of this research was to analyse 98 *K. pneumoniae* strains positive for OXA-48 carbapenemases isolated from urine of non-hospitalized elderly patients from 2016-2018 in Zagreb.

**Materials/methods:** Antimicrobial susceptibility profiles and production of carbapenemases were assessed phenotypically. PCR was used to detect genes encoding extended-spectrum β-lactamases (ESBLs), plasmid-mediated AmpC β-lactamases, carbapenemases of class A, B and D, and qnr encoding fluoroquinolone resistance. Transferability of cefotaxime resistance was tested by conjugation using *E. coli* J53 resistant to sodium azide. Ertapenem resistance was transferred to recipient strain by transformation.

**Results:** The isolates were uniformly resistant to amoxicillin alone and combined with clavulanic acid, piperacillin/tazobactam, cefazoline and cefuroxime. Colistin resistance was observed in only two strains. Fifty five isolates (56%) were phenotypically positive for ESBLs. ESBL-positive isolates exhibited resistance to expanded-spectrum cephalosporins, cefepime, gentamicin and ciprofloxacin. Fourteen out of 32 ESBL-positive organisms tested harboured CTX-M-15 β-lactamase, and 12 TEM-1. PCR revealed OXA-48 class D carbapenemase as the sole carbapenem-resistance mechanism. The transformants were positive for blaOXA48 genes and harbouring L plasmid. Out of 98 strains tested 54 (55%) were isolated from long long-term care facilities patients. Those isolates exhibited significantly lower rates of additional ESBL positivity than isolates collected from 44 elderly outpatients (p<0.01). Moreover, they showed very low MICs of both imipenem and meropenem with the majority of isolates being in the susceptible range (MIC< 2mg/L).

**Conclusions:** OXA-48 producing *K. pneumoniae* isolates from long-term care facilities patients were predominantly non ESBL-positive, like isolates from hospitalised patients in Zagreb, suggesting transmission from hospitals. CTX-M-15 was the dominant type of ESBL coproduced by OXA-48 positive strains from outpatients. OXA-48 was the sole carbapenemase detected in isolates from geriatric non-hospitalized population in Zagreb.

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Speeding up identification and antimicrobial susceptibility testing of bacteria from positive blood cultures by the use of Alifax HB&L system

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Background: Rapid identification and antimicrobial susceptibility testing (AST) of the causative agents of bloodstream infections can lead to prompt appropriate antimicrobial therapy and decrease the mortality rate of patients. In this study we evaluate the workflow of combination of Alifax HB&L system with MALDI-TOF MS and VITEK 2 Compact system on how it can speed up the identification (ID) and AST of bacteria from positive blood cultures (BC).

Materials/methods: Two hundred and eighteen positive BC from BACTEC FX system (BD) were tested. After subculture onto agar plate, isolates were identified by VITEK MS (bioMérieux) and AST was performed by VITEK 2 Compact (bioMérieux), which were used as reference methods.

15 μl of positive monomicrobial BC, which was confirmed by Gram stain, was inoculated in the HB&L culture kit vial and incubated tilled the 1.00±0.25 McFland. Two tubes of 1 ml positive broth were centrifuge at 13,000 rpm for 5 min. Discard the supernatant and wash with 300 μl of distillate water. Vortex and centrifugate at 13,000 rpm for 5min. Spot the pellet onto target slide and identified by VITEK MS. Prepare the pellet into 0.5 McFland suspension and perform AST by VITEK 2 Compact using N334, N335 or P639 cards.

Results: In the 218 positive BC, 216 (99.1%) were reported positive by Alifax HB&L. Compared to the reference method, 212 (97.3%) were identified correctly. Four samples were reported as no identification. By Alifax HB&L, 92.4% positive BC can be tested by direct identification and AST within 4h. For Enterobacteriaceae (n=87), Acinetobacter baumannii (n=11), Pseudomonas aeruginosa (n=65) and Enterococcus (n=39), the percentages of CA/E/A/VME/ME were 96.5%/97.3%/1.5%/0%/0.8%, 95.0%/94.2%/0%/0.8%, 95.2%/91.7%/3.1%/1.0% and 98.1%/96.8%/0%/0.3%, respectively. The concordance rate of ESBL, methicillin resistant Staphycoccus, inducible clindamycin resistance and gentamicin high Level were 98.6%, 94.1%,100% and 100%, respectively.

Conclusions: Alifax HB&L system can shorten the TAT for BC with accurate ID and AST results, which would help clinicians to promptly confirm or adjust the antimicrobial therapy for patients with BSI.

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Abstract 7358

Caco-2 permeability assessment and in vivo pharmacokinetics of VRT001-C (oral ceftriaxone)

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Background: Ceftriaxone, a BCS Class III drug, is a widely used broad-spectrum cephalosporin antibiotic that is only available in parenteral formulation due to its polar nature and poor permeability in the small intestine. Stealth Targeted Nanoparticles (STN) is a platform technology that uses polymeric nanocarriers, appended with a highly specific targeting ligand, for increased drug uptake in the small intestine. In this study, we report the Caco-2 permeability and in vivo pharmacokinetics of VRT001-C [a formulation of ceftriaxone developed using STN] after intraduodenal (ID) administration in mice. ID administration was preferred over oral to have a better assessment of intestinal permeability.

Materials/methods: Caco-2 study was conducted in accordance with ICH guidelines. Caco-2 cells were obtained from ATCC. 10μM concentration of either VRT001-C or ceftriaxone control was added to apical/basolateral chamber and samples from both chambers were collected at 0 and 120 mins to assess permeability and efflux. Collected samples were analysed using LCMS-MS. For the PK study, 72 healthy swiss albino mice (25-30g, both sex) were fasted overnight and divided into two groups. One group received ceftriaxone control [200 mg/kg given IV; n=18] and the second group received VRT001-C [200mg/kg given ID; n=54]. After a single dose of either drug, plasma samples were withdrawn at various time points up to 12hrs and drug concentration was analysed using a validated HPLC method. PK parameters were calculated using noncompartmental analysis.

Results: In Caco-2 assay, VRT001-C observed a 44-fold greater absorption than the ceftriaxone control, as evidenced by their apparent permeability coefficients [apical to basolateral] of 38.90*10^-6 cm/s and 0.88*10^-6 cm/s respectively. These results corroborated with the in vivo study, with VRT001-C group reporting a mean bioavailability of 55% [AUC0-inf of 229.49±38.3 mg/L·h vs. 419.25±5.36 mg/L·h]. Half-life of the drug was longer in the VRT001-C group [3.67 hrs vs. 0.82 hrs].

Conclusions: Both in vitro and in vivo results reflect high intestinal permeability of VRT001-C. Further, as ceftriaxone exhibits time-dependent killing, a longer half-life can improve the pharmacodynamic activity by prolonging the therapeutic window. Overall, these results encourage the further development of VRT001-C.

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Abstract 7362

Evaluation of the RESIST-4 O.K.N.V. K-SeT test for the detection of carbapenemase production in Enterobacterales

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Background: The emergence of antibiotic resistance in bacteria poses an increasing threat to healthcare worldwide. The production of carbapenemases is an especially dangerous mechanism that is spreading especially among Enterobacterales species. Due to the severity and mortality rates associated with infections caused by carbapenemase producing Enterobacterales (CPE), it is crucial to rapidly detect and identify the type of carbapenemase. The goal of this study was to evaluate the RESIST-4 O.K.N.V. K-SeT, which is a newly developed ready-to-use immunochromatographic test kit. The test is based on an reaction that can directly detect the four most prevalent carbapenemases (OXA-48-like, KPC, NDM and VIM) within 15 minutes. The aims of the study were to determine the sensitivity and specificity of the test and to compare the results with different methods capable of identifying carbapenemases.

Materials/methods: The RESIST-4 O.K.N.V. K-SeT [Coris BioConcept], Carbapenemase Nordmann-Poirel [CarbaNP] and Modified Carbapenemase Inactivation Method (mCIM) tests were conducted using 96 Enterobacterales isolates previously characterized by PCR originated from Hungarian hospitals, each of which were resistant to at least one carbapenem. Most of the isolates were CPE isolates, which included OXA-48-like [n=17], KPC [n=10], NDM [n=18], VIM [n=28] and NDM+OXA-48-like [n=2] producers, while the remaining non-CPE were ESBL and/or AmpC producers [n=21].

Results: The overall sensitivity/specificity values were 85.3%/100% for the RESIST-4 O.K.N.V. K-SeT, 93.3%/100% for the CarbaNP and 95.9%/98.6% for the mCIM, respectively. For the detection of OXA-48-like, sensitivity/specificity values were 89.5%/100%, 78.9%/100% and 89.5%/98.7%, respectively. In the case of KPC isolates, the values were 100%/100%, 100%/100% and 100%/98.8%. For the NDM enzyme, values were 95%/100%, 100%/100% and 100%/98.6%. And lastly, for the detection of VIM, sensitivity and specificity of the three tests were 71.4%/100%, 96.4%/100% and 96.3%/98.5%.

Conclusions: The RESIST-4 O.K.N.V. K-SeT showed good sensitivity and excellent specificity values overall and proved to be a highly efficient tool for the detection of the four carbapenemases. The lower sensitivity for detection of VIM-producers could be explained by the higher frequency of Klebsiella pneumoniae with mucoviscous phenotype and probably low level production of VIM-4-type carbapenemase. Thus modification of protein extraction method could be advised.

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Abstract 7368

**Faster and more sensitive diagnostics of Shigella by Shigella specific PCR and improved culture**

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**Background:** *Shigella* is known to cause gastroenteritis with symptoms varying from mild diarrhea to colitis and dysenteria. Traditionally diagnosis is based culture but in recent years PCR-methods are becoming more common. The PCR targets used to detect *Shigella* in faeces (eg ipaH) are shared with enteroinvasive *E. coli* (eiec), hence discrimination between *Shigella* and eiec by PCR in the fecal sample is not possible. Attempts to culture *Shigella* often fails, typically 70-80 % of PCR-positive samples remains culture negative. In Sweden and many other countries *Shigella* is a notifiable disease but eiec not. Treatment with antibiotics is often recommended for *Shigella* infection but not for eiec. The unsatisfactory diagnostic result therefore poses a clinical problem.

**Materials/methods:** A new strategy for detecting *Shigella* in fecal samples was established, based on a novel *Shigella* specific PCR and a modified protocol for *Shigella* culture. The primers described by Kim et al, proposed to be specific for detection of *Shigella*, were combined with newly designed TaqMan probes in a triplex real time PCR method for detection of *Shigella* species. In an attempt to increase the outcome of *Shigella* culture a new routine was introduced. The fecal sample was diluted to a suitable concentration and spread over the whole surface of the agar plate resulting in many more free lying bacterial colonies for inspection and further analysis. This new strategy was applied to faecal samples positive for *Shigella*/eiec (ipaH). The result of *Shigella* specific PCR and the improved culture method was compared and the overall result of the new strategy was compared with historical results from diagnostic outcome of traditional methods.

**Results:** The combined result of modified culture and *Shigella* specific PCR increased the detection of *Shigella* from 20-30 % (historical data) to 52 % of the ipaH positive samples. The average time for a positive result was shortened by at least 3 days due to faster result from *Shigella* specific PCR.

**Conclusions:** The here described protocol for detecting *Shigella* in fecal samples increased the diagnostic outcome and decreased the time to result substantially.


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Impact of a multimodal intervention on non-sterile glove use in the intensive care unit

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Background: Incorrect use of non-sterile gloves increases the risk of cross contamination. We sought to explore and improve compliance with the glove use protocol in the ICU of our University hospital.

Materials/methods: Direct observations of the use of non-sterile gloves were performed. Incorrect use was defined as missing glove switches and missed hand hygiene moments that can lead to contamination of the patient or the hospital environment. The multimodal intervention included feedback of the audit results, visual reminders in the workplace and an interactive lecture for all health care workers targeting hand hygiene moments and indications for glove use or switch. After two months observations were repeated.

Results: In total, 195 observations were performed. Non-sterile gloves were used during 160 patient care episodes and in 147 moments glove use was appropriate. Switching gloves when needed (n=57) occurred in 38.6% (95%CI, 27.1-51.6). Hand hygiene compliance was 38.6% (95%CI, 28.8-49.3) before glove use and 18.2% (95%CI, 7.3-38.5) during a switch. Two months after the intervention the compliance of switching gloves when needed was 50% (95%CI, 37.9-62.1). Hand hygiene compliance before glove use was 48.4% (95%CI, 36.3-60.4). Other hand hygiene moments did not change. The overall risk of contaminating the patient or the patient surroundings was 47% (95%CI, 36.6-57.6) before and 39.1% (95%CI, 28.1-51.3) after the intervention.

Conclusions: Non-sterile gloves are used in most patient care episodes by nurses caring for patients on the ICU. Failure to change gloves when necessary and not applying hand hygiene before and in between glove use appear to be the biggest risks for transmission of microorganisms to the patient and the hospital environment. Our multimodal approach did not significantly increase compliance of correct use of non-sterile gloves, although a positive trend was achieved in switching gloves appropriately. The risk of contaminating the patient or the environment did not improve significantly, although a positive trend was achieved in adherence to the glove use protocol. Although the low number of observations might impede these results, investigating the underlying causes of non-compliance and barriers is needed to adjust the program to achieve clinical relevant effects.

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Abstract 7370

Gut microbiota of full-term and late preterm newborns in Moscow

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¹National Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V.I. Kulakov of Ministry of Healthcare of Russian Federation, Moscow, Russian Federation

**Background:** It is obvious that gut microbiome has important meaning in establishment of life-critical systems of newborns. The aim of the study was to assess the formation of the gut microbiota of full-term and late premature newborns.

**Materials/methods:** Fecal samples of 50 healthy full-term newborns (25 were born by vaginal delivery and 25 – by Caesarean section) and 51 babies with gestational age 34-37 weeks (25 were born by vaginal delivery and 26 – C-section) were investigated by culturomics and mass-spectrometry at 1st, 7th and 30th day of life. Most of them were given by breast milk or mixed feeding. Preterm babies were given by probiotics (lactobacilli and bifidobacteria).

**Results:** Meconium was sterile in 58% of babies, more often in C-section groups. In other groups microbiota was isolated in a low titer and mainly represented by gram-positive cocci. Anaerobes and lactobacilli were found in rare cases in vaginal delivery groups. At 7th day levels of all microorganisms have riced up to $10^{10-12}$ CFU/g. Lactobacilli and bifidobacteria have found in vaginally delivered newborns more often (up to 70% and 50%, respectively). The relative high frequency of the occurrence in preterm babies may be define of more application of probiotics. Bacteroids at high titer were isolated in all children except preterm C-section babies. Large frequency and species diversity in vaginal delivery babies were shown as compared with C-section newborns (8%). Clostridia were isolated approximately with equal frequency (11-20%) in all newborns. At 30th day the frequency of lactobacilli did not change essential as compared with first week. Bacteroids frequency have riced substantial in vaginal delivery babies and did not changed in full-term C-section. Among preterm C-section babies bacteroids were isolated only in two newborns. Clostridia were more often isolated in C-section babies with 1.5 times more often in preterm newborns.

**Conclusions:** Thereby, there is delay in development of microbiome of preterm infants and full-term C-section babies as compared with full-term vaginally delivery children. This is especially noticeable by low frequency of gut colonization by bacteroids and higher – by clostridia, that do not include in probiotics and mixes formula in contrast to lactobacilli and bifidobacteria.

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Impact of calmodulin inhibition by fluphenazine on susceptibility, biofilm formation and pathogenicity of caspofungin-resistant Candida glabrata

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Abstract third-party references: ECOS Nord

Background: In recent decades, Candida glabrata has emerged as a frequent cause of life-threatening fungal infection. In C. glabrata, echinocandin resistance is associated with mutations in fks1/ fks2 [β-1,3-glucan synthase]. The calmodulin/calci-neurin pathway is implicated in response to antifungal stress and calcineurin gene disruption specifically reverses Fks2-mediated resistance of clinical isolates. We evaluated the impact of calmodulin inhibition by fluphenazine on two caspofungin-resistant Candida glabrata isolates.

Materials/methods: Candida glabrata isolates were identified by ITS1/ITS4 sequencing and the echinocandin target FKS1/ FKS2 genes were sequenced. Susceptibility testing of caspofungin in presence of fluphenazine was performed by a modified CLSI microbroth dilution method. Effect of fluphenazine/caspofungin combination on heat stress (37°C or 40°C), oxidative stress (0.2 and 0.4 mM menadione) and on biofilm formation (polyurethane catheter) was analyzed. A Galleria mellonella model using 1x10⁹ UFC/mL blastospores were developed to evaluate the impact of this combination on larva survival.

Results: The F659del was found in FKS2 gene of both resistant strains. In these clinical isolates fluphenazine increases susceptibility to caspofungin and reduces their thermotolerance. Furthermore, fluphenazine/caspofungin combination significantly impairs biofilm formation in an in vitro polyurethane catheter model. All these features could participate in the increasing survival of infected Galleria mellonella after combination treatment in comparison to caspofungin alone.

Conclusions: In a repurposing strategy, our findings confirm that calmodulin could provide a relevant target for life-threatening fungal infectious diseases.

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Evolution of teicoplanin susceptibility pattern of *Staphylococcus aureus* and coagulase-negative *Staphylococcus* spp. related to orthopaedic infections

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**Abstract third-party references:** University of Sao Paulo

**Background:** *Staphylococcus aureus* and coagulase negative *Staphylococci* (CoNS) infections are highly associated with biofilm formation, which is a major concern in orthopedic implants because of its implications in antibiotic resistance. Glycopeptides, including teicoplanin, have often been used in empirical and rational therapy in infections caused by these species. Long-term use of glycopeptide antibiotics can be related to emergence of resistant strains.

**Materials/methods:** Retrospective observational study that included all isolates of *S. aureus* and CoNS regarded as causative agents of surgical site infections (SSI) related to orthopedic procedures at a reference hospital in São Paulo, Brazil. Diagnosis of SSI followed criteria defined by the Centers for Disease Control and Prevention (CDC). Isolates were obtained from culture of bone and deep soft tissues specimens, collected following extensive removal of devitalized tissues during surgical debridement procedures as part of infection treatment. Positive samples were identified through automated VITEK2 and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry systems. Antibiotic susceptibility testing was done using the VITEK2 system. Breakpoints used in categorical interpretation for teicoplanin were those effective each year according to the Clinical and Laboratory Standards Institute (CLSI) M100 document. Cumulative antibiograms were performed in accordance with CLSI standards.

**Results:** From 2011 to 2018, 209 isolates of *S. aureus* and 179 isolates of CoNS were related to cases of SSI following orthopedic procedures. Among *S. aureus* isolates, teicoplanin susceptibility remained at 100% throughout the study period. For CoNS, however, there was a wide variation in susceptibility values observed, which reached a minimum of 43% in 2014. The trend line for the entire observed period shows the progressive decrease in susceptibility.

**Conclusions:** During the period of this study, an important variation of CoNS susceptibility to teicoplanin was observed, with a tendency to decrease in the global evaluation. The same phenomenon was not observed for *S. aureus*, showing a dissociation in the susceptibilities of different species of *Staphylococcus* spp. against this glycopeptide that needs to be taken into consideration in clinical practice.
Abstract 7380

**Improved NG-test Carba5 assay for the detection of previously undetected IMP-variants**

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**Background:** The NG-Test Carba5 immunochromatographic assay (ICA) (NG Biotech, Guipry, France) accurately identifies the five most widespread carbapenemase families in Enterobacterales (CPEs) (KPC, NDM, VIM, IMP and OXA-48-like enzymes). In a recent study Potron et al. has identified IMP variants (IMP-13 clade (IMP-13 and IMP-37), IMP-14, IMP-15, IMP-18 clade (IMP-18 and IMP-71) and IMP-63) mostly encountered in *P. aeruginosa*, were not detected by the NG-Test Carba5. Here we have evaluated the NG-Test Carba5v2, with additional antibodies for detection of all IMP-variants.

**Materials/methods:** Monoclonal antibodies (mAbs) derived from IMP immunized mice were further tested against IMP-13. The NG-Test Carba5v2 tests (strip + cassette) were manufactured by NG Biotech using the IMP-13-selected mAbs and evaluated on a collection of 147 GNB (134 carbapenemase-producers (CP) including 31 IMP variants corresponding to the different branches of the IMP phylogeny and 13 non-CPs). Results were compared to those obtained with the NG-Test Carba5v1.

**Results:** Both versions of the NG-Test Carba5 gave similar results except for IMP, suggesting that the novel IMP- mAbs did not interfere with the other target. The NG-Test Carba5v2 allowed the detection of 100% of the IMP-variants tested (n=31/31), unlike NG-Test Carba5 that detected only 67% (n=21/31). The NG-Test Carba5v2 identified all VIM- (n=12), and NDM- (n=14) producers with no false- result. All OXA-48 carbapenemase variants were correctly identified, even the distantly-related OXA-535 variant. However, as already shown OXA-163 and OXA-405, two OXA-48 variants lacking carbapenemase activity were also detected. Two/19 (10%) KPC-producers were not detected. They corresponded to KPC-31 and KPC-33, two rare D179Y variants of KPC-3, known to be responsible for ceftazidime/avibactam resistance and for not being detected using ICA. All 13 non-CPs and the 13 isolates producing a non-targeted carbapenemase (different from the 5 main) gave negative test results demonstrating excellent specificity.

**Conclusions:** All tested IMP-variants were accurately detected, without impairing detection of the other carbapenemases. Thus NG-Test Carba5v2 is now well adapted to countries with high IMP-prevalence and to the epidemiology of CP-*P. aeruginosa* where IMPs are mostly detected.

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Abstract 7381

**Performance evaluation of a new screening and viral load monitoring HIV-1 assay on the NeuMoDx molecular system**

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**Background:** As no cure exists for HIV-1 infection, current treatment regimen requires characterizing HIV-1 viral loads in infected patients to monitor disease progression and efficacy of anti-retroviral therapies. The NeuMoDx HIV-1 Quant Assay is a novel fully automated, “sample to result” in-vitro diagnostic test specifically designed for the accurate detection and quantitation of HIV-1 RNA with broad variant coverage including group O, P and the major CRFs directly from plasma. The NeuMoDx Molecular Systems allow the flexibility to use either primary blood tubes or secondary tubes, with options for qualitative reporting for screening purposes, or quantitative reporting for viral load monitoring.

**Materials/methods:** The objective of this study was to characterize performance metrics including analytical sensitivity and specificity, linearity, precision, inclusivity, turnaround time, as well as quantitative correlation to FDA-approved/CEIVD-certified reference tests. Analytical sensitivity was determined using a calibrated WHO Standard HIV-1 reference material and the quantitation limits (LLoQ/ULoQ) were determined using the Total Analytical Error (TAE) ≤1.0 criterion. Secondary standards traceable to the Calibrated WHO Standard were used for the rest of the analytical testing.

**Results:** The NeuMoDx HIV-1 Quant Assay demonstrated a limit of detection (LoD) and a lower limit of quantitation (LLoQ) of 35 IU/mL (equivalent to ~12 copies/mL) in plasma. Excellent linearity was demonstrated across a ~7-log dynamic range (R²>0.99) with ULoQ of 7.7 Log10 IU/mL. The assay showed equivalent detection across all HIV-1 groups M-P, subtypes (A, C-H) and CRFs, and provided extremely accurate results with a time to first result of ~85 minutes. Excellent within-lab precision was demonstrated in a multi-day study across 3 instruments including both NeuMoDx 96 and NeuMoDx 288 Molecular Systems. No cross-reactivity or interference was observed against a panel of phylogenetically similar or co-habiting pathogens. An in-house method correlation study confirmed excellent linear correlation (R²>0.95) and minimal bias [<0.5 Log] relative to reference test results. Finally, all reagents used in the study were stable at ambient conditions and demonstrated in-use shelf life of >14 days.

**Conclusions:** The NeuMoDx HIV-1 Quant Assay provides a rapid, easy-to-use, rapid, and automated method for sensitive HIV-1 screening and accurate viral load monitoring.

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Abstract 7382

**Carbapenem hetero-resistance in blood isolates of OXA-48-producing Klebsiella pneumoniae and Escherichia coli**
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**Background:** Carbapenem-resistant Enterobacteriaceae have become an important problem during the last decade. The major mechanism which lead to carbapenem resistance is the production of carbapenemase enzymes such as KPC, OXA-48, NDM, VIM and IMP. Heteroresistance concept is another important issue about carbapenem resistance. Although, the mechanism of heteroresistance is not fully understood, it is thought to be effective on treatment success. The aim of this study is to determine carbapenem resistance and heteroresistance in Klebsiella pneumoniae and Escherichia coli blood isolates.

**Materials/methods:** A total of 301 Enterobacteriaceae (105 E.coli and 196 K.pneumoniae) blood isolates which were recovered in University Hospital of Hacettepe in the period from January 2016 to August 2018, were included in the study. Carbapenem resistance was evaluated by using gradient test, disk diffusion test, sensititre microdilution test and Phoenix automated systems. Polymerase chain reaction (PCR) was used for the detection of the KPC, VIM, IMP, NDM-1 and OXA-48 gene regions. Carbapenem heteroresistance was investigated with the disk diffusion method and gradient test (Etest, bioMérieux, Fransa). Heteroresistance was suspected when colonies were detected in the Etest/disk diffusion inhibition zone. It was confirmed by applying population analysis profile (PAP).

**Results:** Resistance or decreased susceptibility to carbapenems was detected in 160 blood isolates by at least one method. The presence of at least one carbapenemase gene were detected in 147 (91.8%) of the isolates that were intermediate or resistant to carbapenem. OXA-48 (142/160; 88.7%) was the most common carbapenemase enzyme, following by NDM-1 (14/160; 8.7%), VIM (5/160; 3.1%) and KPC (1/160; 0.6%). IMP enzyme was not observed in any of the isolates. In this study carbapenem heteroresistance was confirmed by PAP in 21 (16 K.pneumoniae and 5 E.coli) (6.9%) isolates. In 18 (85.7%) of these isolates OXA-48 enzyme was obtained.

**Conclusions:** The clinical significance of heteroresistance is still unknown. Therefore, there is a great need for studies involving larger numbers of isolates to determine the clinical effect of heteroresistance to carbapenems and the likelihood that the resistant subpopulations of carbapenem susceptible isolates will become fully resistant under drug action.

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Abstract 7383

Association of IL-27 and STAT3 genetic polymorphism on the susceptibility of tuberculosis in western Chinese Han population

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Background: Host immune response has a pivotal role in latent tuberculosis infection and active tuberculosis. Interleukin-27 plays both pro-inflammatory and anti-inflammatory activities in infectious diseases via STAT1/STAT3 mechanism, as well as malignant tumor and autoimmune disease. To investigate the association of single nucleotide polymorphisms (SNPs) of IL-27 and STAT3 on the susceptibility of tuberculosis, we conducted a large size of case-control study in western Chinese Han population.

Materials/methods: A total of seven SNPs were genotyped by using multiplex ligation detection reaction method in 900 patients with tuberculosis and 1534 healthy controls.

Results: Variants of three SNPs (rs181206, rs17855750, rs26528) within IL-27 gene, the genotype and allele frequencies of rs17855750 were significantly different (p = 0.013, p = 0.004, respectively). Subjects carrying C allele for rs17855750 showed a decreased tuberculosis risk (OR=0.75, 95% CI=0.62-0.91, p = 0.004). Genetic modal analysis revealed that dominant modal was associated with decreased TB risk (OR=0.74, 95% CI=0.60-0.92, p=0.042). Haplotype of A-C-G (representing rs181206, rs17855750 and rs26528) showed a reduced risk to TB (OR=0.79, 95% CI=0.65-0.96, p=0.017). There were no significant differences between TB cases and healthy controls in the variants of four SNPs (rs1053005, rs2293152, rs744166, rs4796793) within STAT3 gene.

Conclusions: The polymorphisms of IL-27, rs17855750, but not rs181206 and rs26528, plays a protective role on the susceptibility to TB.

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Loop-primer endonuclease cleavage loop-mediated isothermal amplification technology for singleplex or multiplex target detection and single-nucleotide polymorphism identification

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Background: Loop-mediated isothermal amplification (LAMP) provides effective infectious disease pathogen detection and is compatible with inexpensive instrumentation for use in disease-prevalent developing regions. However, simultaneous multiple-target detection and single nucleotide polymorphism (SNP) identification, essential properties of nucleic acid diagnostics, is difficult to achieve using LAMP. This study introduces Loop-Primer Endonuclease Cleavage (LEC)-LAMP, a singleplex or multiplex LAMP technology with single-base specificity for variable SNP identification. We developed a singleplex LEC-LAMP assay demonstrating single-target detection and SNP identification, and further evaluated this assay in terms of analytical specificity, sensitivity and clinical application. Modified versions of this assay were subsequently used to demonstrate single-tube wild-type and mutant allele differentiation, and simultaneous multiple-pathogen detection.

Materials/methods: Target templates used to exemplify this technology were bacterial meningitis pathogens, Neisseria meningitidis, Streptococcus pneumoniae and Haemophilus influenzae, and synthetic DNA templates containing SNPs. Single-target detection and SNP identification was demonstrated using a singleplex LEC-LAMP N. meningitidis assay. The analytical specificity of this assay was established using a panel of bacterial reference strains and limit of detection (LOD) was determined using Probit analysis. Clinical application of this assay was evaluated using DNA from blood and cerebrospinal fluid samples of confirmed bacterial meningitis cases. Modified versions of this singleplex assay were developed to demonstrate differentiation of wild-type and mutant allele templates using an allele-specific (AS) LEC-LAMP N. meningitidis assay, as well as simultaneous multiple-target detection using a multiplex LEC-LAMP N. meningitidis, S. pneumoniae and H. influenzae assay.

Results: The singleplex LEC-LAMP N. meningitidis assay demonstrated complete analytical specificity, a LOD of 3.1 genome copies per reaction, and 100% diagnostic specificity and sensitivity for all clinical samples tested. The single-base specificity of this assay indicated effective variable SNP identification within a specific 6 base region. The AS LEC-LAMP assay successfully demonstrated single-tube wild-type or mutant allele differentiation, and the multiplex LEC-LAMP assay successfully demonstrated simultaneous detection of all bacterial targets in a single reaction.

Conclusions: LEC-LAMP is the first report of a single-tube, real-time, multiplex LAMP method with variable SNP identification capabilities, providing state-of-the-art transferable isothermal nucleic acid amplification technology for POC infectious disease diagnostics.

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Utility of Xpert Carba-R in identifying carbapenem resistance in blood culture isolates in critically ill patients
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**Background:** Xpert® Carba R (Cepheid, Sunnyvale, USA) is a real-time PCR test for the detection and differentiation of carbapenemase producing genes like KPC, NDM, VIM, OXA-48 and IMP in under 60 minutes. It is used for detection of colonization with carbapenem resistant gram negative organisms (CROs) in rectal swabs or feces to enable early isolation of such patients. However, there are fewer studies on the use of Xpert® Carba R to identify CROs in blood culture isolates to enable early identification to guide empiric treatment with Polymyxins. We aimed to study the utility of Xpert® Carba R to identify CROs in gram negative blood culture isolates.

**Materials/methods:** Retrospective study of cases in whom Xpert® Carba R had been done on gram negative blood culture isolates during the period between September 2018 till October 2019.

**Results:** Xpert® Carba R was done on 31 critically ill patients in the study period. Of the 32 blood culture isolates, 20 were Carbapenem Resistant Enterobacteriaceae (CRE) [E. coli 8, Kleb. species 12]. Sensitivity and specificity of Xpert® Carba R to detect carbapenem resistance was 67% and 78% in all isolates, and 85% and 75% respectively, in CRE. In concordant cases, average turnaround time for Xpert® Carba R was 2 days vs. culture at 3.75 days. Resistance genes in CRE were OXA 48 (8), NDM (3) and both (3).

**Conclusions:**
1. Xpert® Carba R detects carbapenem resistance in CRE earlier and faster in critically ill patients and can help guide empiric therapy.
2. OXA-48 was the commonest carbapenamase detected in this series.
3. It did not detect any resistance in non-enterobacteriaceae in this series.

**Table:** Organism Profile and Test Results

<table>
<thead>
<tr>
<th>Organism (n)</th>
<th>Carbapenem resistance on culture</th>
<th>Carbapenamase detection on Xpert Carba R</th>
<th>Concordance</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>NDM [3]</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDM and OXA-48 [1]</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nil [2]</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>NDM and OXA-48 [2]</td>
<td></td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td>0</td>
<td>Nil</td>
<td>100%</td>
</tr>
<tr>
<td>[1]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>1</td>
<td>Nil</td>
<td>0%</td>
</tr>
<tr>
<td>Acinetobacter sp. [8]</td>
<td>4</td>
<td>Nil</td>
<td>50%</td>
</tr>
<tr>
<td>Burkholderia cepacia</td>
<td>1</td>
<td>VIM [1]</td>
<td>0%</td>
</tr>
<tr>
<td>[1]</td>
<td></td>
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</tbody>
</table>

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**Abstract 7388**

**Echinocandin blood and peritoneal concentration in patients with Candida peritonitis**

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**Background:** Echinocandin pharmacokinetics-pharmacodynamics (PK/PD) during abdominal candidiasis has not been evaluated systematically. Recently it has been announced the development of resistance to echinocandins especially in patients with candida peritonitis related to sub-optimal levels at peritoneum. The aim of this study was to describe the PK of echinocandins in patients with candida peritonitis (CP).

**Materials/methods:** Methods. Peritoneal and serum concentrations of anidulafungin (AND) micafungin (MCF) and caspofungin (CAS) were analyzed in 23 surgical patients with suspected candida peritonitis. After four days of starting therapy, serum [S] and peritoneal fluid [PF, through peritoneal drainage] were collected at baseline, 1 h, 6 h, 12h and 24 h of echinocandins administration. The PK/PD analysis was performed by using a non-compartmental approach [PKsolver, excel plug-in].

**Results:** The three echinocandins showed large interindividual variability in this study. Table shows the main PK parameters obtained in serum and peritoneal fluid.

<table>
<thead>
<tr>
<th>Antifungal (number of patients)</th>
<th>S</th>
<th>PF</th>
<th>Ratio PF/serum [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AND [11]</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cmax (mg/L)</td>
<td>7.96±5.40</td>
<td>2.57±2.19</td>
<td>32,356</td>
</tr>
<tr>
<td>Cmin (mg/L)</td>
<td>3.99±2.73</td>
<td>0.64±0.35</td>
<td>16,130</td>
</tr>
<tr>
<td>AUC₀⁻２₄ (mg*h/L)</td>
<td>126.84±78.66</td>
<td>34.38±20.17</td>
<td>27,10</td>
</tr>
<tr>
<td><strong>MCF [4]</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cmax (mg/L)</td>
<td>8.45±3.24</td>
<td>0.88±0.69</td>
<td>10,44</td>
</tr>
<tr>
<td>Cmin (mg/L)</td>
<td>2.04±1.34</td>
<td>0.66±0.47</td>
<td>32,47</td>
</tr>
<tr>
<td>AUC₀⁻２₄ (mg*h/L)</td>
<td>98.52±34.55</td>
<td>18.83±14.05</td>
<td>19,11</td>
</tr>
<tr>
<td><strong>CAS [8]</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cmax (mg/L)</td>
<td>5.30±2.66</td>
<td>0.49±0.39</td>
<td>9,236</td>
</tr>
<tr>
<td>Cmin (mg/L)</td>
<td>1.43±0.73</td>
<td>0.24±0.27</td>
<td>16,86</td>
</tr>
<tr>
<td>AUC₀⁻２₄ (mg*h/L)</td>
<td>66.90±32.71</td>
<td>8.78±7.83</td>
<td>13,13</td>
</tr>
</tbody>
</table>

**Conclusions:** We found that peritoneal exposure of echinocandins were a small fraction of that in blood. Using therapeutic doses, the minimal peritoneal concentrations were 0.64, 0.66 and 0.24 mg/L for AND, MCF and CAS in this study. Peritoneal exposures were above the MIC₉₀ for most of the *Candida* species responsible of CP. However, it is likely that Candida FKS mutations can emerge within the abdominal cavity in the face of prolonged subinhibitory echinocandin concentrations. Further researches including sanctuary compartments are needed to provide evidence for the development of candida resistance.

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Abstract 7389

Clinical management of alveolar echinococcosis in Germany: a retrospective cohort study of 275 patients

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Background: Alveolar echinococcosis (AE) is a progressive parasitic disease caused by the larval stage of Echinococcus multilocularis. Surgical resection is the only curative treatment, however, most patients are not eligible due to the advanced stage. Limited treatment options, treatment failure and severe side effects remain a challenge in the management of AE.

Materials/methods: This retrospective cohort study included 275 patients presenting at the University Hospital Ulm from 2011 to 2018. Descriptive statistics included demographics, stage of disease, initial symptoms, treatment options, side effects and complications. Adverse outcomes (follow-up at least one year, n = 242), risk and protective factors were analysed using regression models adjusting for confounders.

Results: Incidence rates increased over the years (21 patients in 2011, 43 patients in 2018). Median age at diagnosis was 55 years, 55% were female. When diagnosis was established, more than 60% reported no specific symptoms, yet 62% presented in an advanced stage (P3 or P4 according to PNM classification). While 29% underwent curative surgery, AE was inoperable in the majority (57%) and hence treated with benzimidazoles (BMZ). Within this group, 9% received a structured treatment interruption (STI), i.e. the termination of BMZ therapy with sustained follow-up. A follow-up period of 803 cumulative patient-years was monitored. While 26% of patients were cured, 71% were stable (with or without BMZ) and 3% suffered from progressive disease. Risk factors for adverse outcomes included advanced stage, vascular and biliary complications, BMZ toxicity and relapse after STI. Surgical treatment was identified as protective.

Conclusions: We noticed an increasing incidence of AE cases due to either increased awareness, infection rates or alterations in immune response. Curative surgery was strongly associated with a favourable outcome. BMZ allowed for a long-term stable disease. However, cases with non-response to BMZ or BMZ toxicity resulted in adverse outcomes with complex clinical management. In carefully selected patients, a STI can present an valuable alternative to life-long BMZ treatment. Due to increasing incidence, high treatment costs and possible complications, a screening in high risk groups to identify AE in early stages seems reasonable and probably cost-effective.

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Clinical features and outcomes of patients with Elizabethkingia meningoseptica infection: an emerging pathogen

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Background: Elizabethkingia meningoseptica, formerly known as Chryseobacterium meningosepticum, is a non-motile, non-fastidious, catalase and oxidase-positive, aerobic, glucose-non-fermentative Gram-negative bacillus. It is an important emerging opportunistic bacterium that primarily occurs in nosocomial settings. Given its ubiquitous nature, arsenal of multi-drug resistant genes, and affinity to infect primarily the immunosuppressed; it is paramount that more resources be devoted to study this emerging pathogen. It is also unclear as to which treatment regimen is most effective and what are the factors associated with adverse outcomes. The aim of this study is to describe the clinical features and outcomes of Elizabethkingia meningoseptica infections in a tertiary care center at Karachi, Pakistan.

Materials/methods: We conducted a retrospective case series on all patients identified to have any clinical culture specimen positive for Elizabethkingia meningoseptica over a period of 6 years between 2014 and 2019 at the Aga Khan University Hospital Karachi. Data was collected on a structured proforma on patient demographics and clinical factors. Descriptive analysis was performed for demographic features with median and IQR reported for quantitative variables such as age and lengths of hospital stay and frequencies (percentage) for qualitative variables such as gender, co-morbid conditions and mortality. All p value ≤0.05 will be taken as significant.

Results: Sixteen patients with E. meningoseptica were identified. The median age was 35 years with 44% males and 56% females. The most common co-morbidities were diabetes (31%) and hypertension (37.5%). 56% (n=9) had bacteremia with E. meningoseptica. Among other sites of infection, three had urinary tract infection, n=3 had meningitis and one had pneumonia. 61% (n=8) had monomicrobial growth whereas 38% had polymicrobial growth in culture. 56% required intubation and mechanical ventilation. E. meningoseptica was sensitive to beta lactam and quinolones in 68%. Three of the E.meningosepticum isolates were extensively drug resistant with sensitivity only to minocycline. Four out of 16 patients died and median length of hospital stay was 13 days.

Conclusions: E. meningosepticum is an emerging nosocomial infection and associated with good survival especially if isolates are susceptible to quinolones and can be treated with them.

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Background: India is a recognized endemic region for melioidosis. However, there are no data on the environmental occurrence of *B. pseudomallei* from the country. Environmental surveillance is crucial to assess the risk of infection to humans and animals in different parts of the country. The study aimed to determine the environmental prevalence of *B. pseudomallei* in the vicinity of cases of melioidosis diagnosed in India and to further understand the effect of various physicochemical properties of soil on the presence of the pathogen in the environment.

Materials/methods: We performed environmental sampling close to the home of melioidosis patients from July 2016 – November 2018. A total of 1204 soil samples at 20 sites were screened for *B. pseudomallei* by using a recently developed quantitative real-time PCR including *B. pseudomallei* specific qPCR target. Further, the various physicochemical factors such as pH, conductivity, Salinity and levels of micronutrients such as Iron, Phosphorous, Manganese, Sodium, Potassium, Copper were determined in subset of samples (N= 120).

Results: So far, our molecular analysis revealed 30.2% (374/1228) of soil samples, including samples from all different sampling-sites to be *B. pseudomallei*-positive. However, the number of qPCR positive samples varied significantly between sites and time of the year, with the highest positivity rate detected in samples taken during the rainy season (47.5%). Presence of *B. pseudomallei* was negatively associated with presence of Iron ($p <0.001$) and Manganese ($p =0.02$). Further on multivariable logistic regression model, the presence of *B. pseudomallei* was negatively associated with Iron (OR: 0.98; CI: 0.97-0.99; $P=0.001$).

Conclusions: Our molecular approach proved to be a valuable tool to detect *B. pseudomallei* in the environment in southwest India. Our study suggests that *B. pseudomallei* survive in nutritionally deprived environment with lower levels of micronutrients. Such studies might help to develop a pragmatic framework of a wide network for monitoring and evaluating the environmental exploration of the bacteria in the nation. Targeting the overall population at an initial stage might be challenging, in such a scenario identifying the areas of risk would be a beneficial approach to increase the case detection.

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Abstract 7394

Performance evaluation of a novel *Trichomonas vaginalis* and *Mycoplasma genitalium* assay in urine and swab specimens

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**Background:** *Trichomonas vaginalis* (TV) is the most widespread, non-viral sexually transmitted infection accounting for nearly half of all curable STIs globally with infection rates as high as 26% among STD clinical patients. In addition, only 30% of TV infections are symptomatic, making consistent & easy detection a critical component of patient management and infection control. *Mycoplasma genitalium* (MG) is a well-known cause of male urethritis as well as a major cause of clinical cervicitis in women. As culture techniques for MG are egregiously slow (sometimes taking up to 6 months), nucleic acid amplification testing is highly preferable for prompt diagnosis. The NeuMoDx TVMG Assay is a rapid, duplex test enabling the simultaneous detection of both pathogens from a single urine or swab specimen in a "sample-to-result" mode on the NeuMoDx molecular systems.

**Materials/methods:** Studies were performed to characterize relevant analytical parameters of the NeuMoDx TVMG Assay including sensitivity, inclusivity, exclusivity, and impact of interfering substances. Additionally, an in-house method correlation study was performed to assess concordance with a reference test using a combination of prospectively collected and archived clinical specimens.

**Results:** The NeuMoDx TVMG test demonstrated a Limit of Detection of 0.025 cells/mL for TV and 8.4 copies/mL for MG for urine and 0.04 cells/mL for TV and 15 cp/mL for MG in vaginal swabs with excellent inclusivity across an additional five TV variants (including two metronidazole resistant strains) and four MG variants. Over 80 phylogenetically similar or co-habiting pathogens were assessed for cross-reactivity and interference, with no adverse results observed. A panel of potentially interfering endogenous and exogenous substances, commonly associated with swab and urine samples, were tested in the presence of low levels of TV and MG targets and were shown to have no adverse effect on the quality of results. An in-house method comparison study showed excellent concordance (>95%) with FDA-cleared reference tests for both targets.

**Conclusions:** The NeuMoDx TVMG Assay provides an easy to use, reliable, low-cost and rapid method of detection of TV and MG directly from urine or swab specimens with no need for special preservatives or cumbersome storage requirements

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Abstracts 2020

Abstract 7400

Pharmacokinetics of amikacin and gentamicin in the setting of burn patients with Gram-negative bacterial infections
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Abstract third-party references: University of Turin

Background: Aminoglycosides (AG) pharmacokinetic (PK) is variable in critically ill patients, including patients with severe burn injuries, requiring frequent dose changes to achieve therapeutic antibiotic concentrations. Our aim is to prospectively describe the PK and pharmacodynamic (PD) parameters of AG in a cohort of burn patients.

Materials/methods: This was a prospective study on the PK/PD of amikacin (AMK) and gentamicin (GEM) in severe burn patients admitted in a regional referral center in Turin, Italy. Antibiotics were prescribed at the standard doses usually for gram negative bacterial infections. Target PK/PD ratio was defined as a $C_{\text{max}}$ above 8 x highest MIC. Samples were performed immediately before the antibiotic administration (T0) and at the end of the infusion (T1).

Results: Four patients in the AMK and GEM group were enrolled in the study. The most common sites of infection were bloodstream (5; 62.5%) and lungs (4; 50%). The most frequently isolated bacteria were Pseudomonas aeruginosa, followed by Klebsiella pneumoniae and Acinetobacter baumannii. The administration of standard doses of AMK (15-20mg/kg) or GEM (3-5 mg/kg) never achieved the target peak concentration of 60mg/L and 30mg/L, respectively (Table 1). At the standard dosage, the PK/PD target of $C_{\text{max}} > 8 \times$ highest MIC was reached for 8 (53.3%) out of 15 isolated pathogens. No Acute Kidney Failure (AKI) was reported during aminoglycosides treatment. We observed that standard dose of AMK and GEM in burnt population never achieved the target peak concentration of 60 mg/L and 30 mg/L, with low mean $C_{\text{max}}$ (33.1 and 14.3 mg/L, respectively).

Conclusions: in a population of septic burn patients, standard dosing of AG most often leads to unsatisfactory plasma concentrations, below the pk/pd target of efficacy. The use of elevated dosages along with TDM may help to optimized the treatment.

Table 1. S.D.: standard deviation; GEM: gentamicin; AMK: amikacin; BMI: body mass index; M: male; F: female; TBSA: total burn surface area; RBS: revised BAUX score; CVVH: continuous veno-venous hemofiltration; MIC: minimum inhibitory concentration; C: concentration

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<th>TBSA (%)</th>
<th>RBS</th>
<th>Septic Shock</th>
<th>Creatinine clearance [ml/min]</th>
<th>CVVH</th>
<th>Cmin (mg/L)</th>
<th>Cmax (mg/L)</th>
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<td>26 (F)</td>
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</table>

Mean ± S.D. 53.8 ± 22 15.3 ± 3.2 35.6 ± 14.7 104.5 ± 29.5 132.9 ± 75.4

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Abstract 7401

Evaluation of the whole blood spot on plasma separation card as a sample type for hepatitis B virus viral load quantification on the COBAS 6800 system

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Background: Viral hepatitis elimination is one of the WHO objectives; increasing diagnosis of hepatitis B is one of the main tools to achieve it. Viral load is necessary to aid in the management of patients with hepatitis B virus (HBV) infection, facilitate sample transportation over long distances and in harsh environmental conditions is a useful method to achieve optimal laboratory results in samples from populations with suboptimal infrastructure or special characteristics that hinder a proper diagnosis. Dried blood spots from whole blood samples have been found useful to evaluate viral load of HCV an HIV, however there is no experience using this kind of sample to perform HBV viral load monitoring.

The aim of this study was to evaluate the performance of the PSC as alternative sample type for HBV viral load quantification compared to plasma.

Materials/methods: We recovered whole EDTA venous blood from clinical samples with positive HBs and HBV viral load determination. PSC samples were prepared by spotting 140µL of whole EDTA venous blood and drying it at room temperature over a minimum of 4 days. One spot of each PSC was eluted by incubating at 56ºC with Specimen Pre-Extraction Reagent for 10min at 1100rpm on a preheated thermo-shaker. Plasma EDTA direct samples and PSC eluted samples were analyzed by cobas HBV Test in cobas 6800 system (Roche, Switzerland) and results were compared by paired.

Results: Correlation between PSC and plasma samples was linear [slope=-1.14, intercept=0.81, R²=0.90]. For these samples, the mean viral load difference between plasma and PSC samples was -1.81 log10IU/mL (95%CI: -2.22 to -1.40). Detection for PSC >1000IU/mL occurred in all samples tested with PSC.

Conclusions: Using PSC as an alternative sample type demonstrated a linear correlation to plasma viral load when tested with cobas HBV test, indicating that a correction factor could be applied to better align the PSC and plasma viral load. All samples with a viral load >1000IU/mL were detected with PSC. These results support the feasibility of PSC as an alternative sample type for detection and viral load monitoring of HBV.

Figure 1. Comparison of results for PSC samples and Plasma-EDTA

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Increasing importance of reservoir hosts in viral infections: Hantavirus infection in rodents in East Anatolia of Turkey

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Background: Hantaviruses are emerging pathogens that have a significant impact on human health. Hantaviruses cause two important life-threatening diseases including hemorrhagic renal syndrome (HFRS) and fever pulmonary syndrome (HPS, also known as Hantavirus cardiopulmonary syndrome). Hantaviruses are not transmitted by arthropods, but mechanically can spread. Hantavirus can be transmitted by inhalation of feces and urine of rodents. Dobrava-Belgrade and Puumala hantaviruses have previously been reported from Anatolia, in rodents in case reports and occasional outbreaks. This study was performed for the purpose of molecularly screening of rodents as possible reservoirs for hantavirus in East Anatolia, Turkey.

Materials/methods: In this survey for rodent-borne hantaviruses, 498 small rodents representing different genera were trapped in Turkey (Erzurum city and all districts in and around) from May-2016 to Oct-2016 and screened for hantavirus RNA by reverse transcription–polymerase chain reaction (RT-PCR).

Results: Rodents were identified morphologically as Microtus spp., Apodemus spp., Mesocricetus spp. and Cricetinae spp. tissues (lung, liver, spleen, kidney) from all rodents were screened by RT-PCR. In 24/498 (4.8%) of the scanned tissues, PCR products of the expected size for Hantavirus were obtained. Geographically, the city of Erzurum, where the study is made, consists of 20 different districts. Positivity was detected in 10 different districts (Figure 1).

Conclusions: This is the first comprehensive study in our region. This report describes important information of the circulation of hantavirus and its potential reservoir in East Anatolia of Turkey. When the identified location are examined, it can be seen that the disease is a bridge between east and west in this disease (Figure 1). As a result, hantavirus is an important pathogen in terms of public health. The region we are conducting our study is quite suitable for rodents which are the reservoir of the hantavirus. These data indicate that hantavirus poses a risk in our region and the necessary precautions should be taken. In the future studies need to be investigating the alternative hosts of Hantavirus, zoonotic aspects of the disease, and rodent-human contact in this region.

Figure 1. Representation of Hantavirus detected regions on the map in Erzurum, Turkey.

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The use and impact of a rapid molecular assay in the diagnosis and management of bloodstream infections in Botswana: a prospective clinical trial

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Abstract third-party references: McMaster University, University of Botswana, Botswana-UPenn Partnership, FIND

Background: The mortality and morbidity attributable to bacterial sepsis can be mitigated by timely, appropriate antimicrobial therapy; determination of what is ‘appropriate’ is dependent on pathogen identification and susceptibility. In resource-limited settings, manual blood culture systems are often utilized, followed by traditional manual microbial identification methods, which often greatly delays definitive results. Novel molecular assays, such as the FilmArray (FA) BCID panel (bioMérieux, France), can identify pathogens present in culture almost immediately, potentially facilitating earlier initiation of optimal antibiotic treatment. The objective of this study was to explore the use of the FA BCID panel at Princess Marina Hospital (PMH), a tertiary care centre in Botswana, as an add-on to the standard processing of positive blood cultures.

Materials/methods: Positive blood cultures from PMH inpatients, incubated using the manual Oxoid Signal system (Thermo Fisher, UK), were randomized 1:1 to standard PMH microbiologic processing (control arm) or standard processing plus FA BCID testing (intervention arm). The results of both were compared to the MicroScan WalkAway (Siemens, USA) automated system at a separate, accredited, hospital. If the FA BCID identified a pathogen, specific antimicrobial(s) were also recommended to the clinical team.

Results: Between May 2018-Nov 2019, 279 participants were enrolled, the case-fatality rate in these inpatients with bacteraemia was 20%. FA BCID results were available on the day of enrolment, with a median time-to-result of 4.8 hours (IQR 3.9-6.8h); standard testing results were available at a median of 55 h (IQR 51-66h). 54% of cultures grew isolates judged to be contaminants. In the intervention arm, there were 15 specimens (5%) that were misidentified only by standard processing, 2 (0.7%) that were misidentified only by FA BCID, and 2 (0.7%) that were misidentified by both FA BCID and standard workup. 8 specimens (3%) tested by FA BCID grew isolates that were not targeted by the panel, but only 2 (0.7%) of these were pathogenic (Burkholderia cepacia, Aeromonas caviae); both of these were misidentified by standard PMH testing.

Conclusions: In a referral hospital in a resource-limited setting, FA BCID testing provided identifications much more rapidly and more accurately than standard microbiologic processing.

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Abstract 7406

External quality assessment panel on detection of carbapenem-resistant Gram-negative pathogens within the NeoOBS study
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Abstract third-party references: NeoOBS Study Team

Background: An external quality assessment (EQA) was carried out to reflect the performance of the laboratories involved in a neonatal observational study (NeoOBS) looking at mortality risk factors in hospitalised infants less than 60 days of age who are being treated for significant sepsis. NeoOBS is funded by the Global Antibiotic Research and Development Partnership (GARDP).

Materials/methods: Twenty well-characterized Gram-negative isolates were sent blinded to 16 global labs taking part in the NeoOBS study, located across Africa, Asia, Europe and South America between May and August 2019. The panel included both carbapenem-resistant and susceptible strains (Table 1). Labs were asked to perform identification and antimicrobial susceptibility testing (AST) using their local routine procedures. Results were collected via two online questionnaire forms which were built to capture data on the detection methods used, as well as on the identification and susceptibility data for each of the 20 strains. After submitting the results, labs were given feedback and were asked to repeat some of the strains, if necessary.

Results: Fifteen labs reported results by 11 November 2019. The most commonly used routine methods for identification were Vitek (60%) and conventional biochemical tests (30%). Gram-stain was also used by 40% of the labs. All labs used either disc diffusion or gradient MIC testing methods to perform antimicrobial susceptibility testing. The majority of the labs (93%) interpreted the AST results according to the CLSI guidelines. Five labs (33%) reported all strains correctly. Every strain was identified correctly by 2/3 of the labs and the remaining labs mis-identified only one isolate. The susceptibility results of 5 labs (33%) matched fully the baseline results. The success rate of the other 10 labs varied between 70% and 95%. After results re-submission, the number of labs that reported all results correctly increased to 7 (47%).

Conclusions: The EQA panel allowed us to assess the capabilities of participating labs for detection of carbapenem resistance. Based on the results we were able to highlight certain carbapenem-resistant phenotypes that could be challenging for some of the labs in the NeoOBS study.

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</tr>
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<td>20</td>
<td>KPC-3</td>
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</table>

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Abstract 7410

Evaluation of in vitro susceptibility and molecular resistance mechanisms to ceftazidime-avibactam in clinical isolates of Pseudomonas aeruginosa from five Latin American countries

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Background: Ceftazidime/avibactam (CZA) is the combination of a third-generation cephalosporin and a non-β-lactam β-lactamase inhibitor capable of inactivating class A, class C and several class D β-lactamases, without activity against metallo-β-lactamases (MBL). Resistance mechanisms to CZA in P. aeruginosa (Pae) are diverse, and resistance has been reported even before the introduction of CZA into the clinic. The aim of this study was to identify the susceptibility and molecular mechanisms responsible for the in vitro resistance to CZA in a group of clinical Pae strains from Latin America.

Materials/methods: Clinical isolates of Pae (n=504) were collected between 2016 and 2017 in Argentina, Brazil, Chile, Colombia, and Mexico. Minimum inhibitory concentrations to CZA were determined by standard broth microdilution and interpreted according to CLSI M100-S28 breakpoints. Production of carbapenemases in Pae isolates displaying resistance to CZA was assessed by carba-NP followed by PCR to detect blaKPC, blaNDM-1, blaVIM, blaIMP, and blaSPM-1. Illumina whole-genome sequencing (WGS) was performed for 30 isolates in which resistance to CZA was not mediated by MBL. The presence of mutations of several genes involved in regulation of MexAB-OprM (mexR, nalC, or nalD), mutations leading to AmpC hyperproduction and ftsI (PBP3) was compared with PAO1, was evaluated.

Results: Overall, 28.5% (144/504) of all clinical isolates of Pae were resistant to CZA. Table 1 summarizes the results obtained by PCR and WGS. In 27.1% of the CZA resistant isolates, at least one MBL was detected. In all of the 30 isolates, which underwent WGS, mutations in MexAB-OprM regulator genes were observed, most frequently a G71E substitution in NalC (66.7%), followed by V126E substitutions in MexR (26.7%). Furthermore, amino acid substitutions in PBP3 and the AmpC/AmpD system were observed in 36.7% and 20% of CZA resistant isolates, respectively.

Conclusions: Susceptibility of Pae isolates to CZA was high. Further studies are warranted to establish the role of the novel substitutions found in many isolates, which were CZA resistant and did not harbor MBL or previously reported mutations.

Table 1. Molecular analysis of CZA resistant strains

| Country | Number of CZA resistant isolates | blaKPC | blaNDM-1 | MexR/Amr | MexR/Amr-NalC/NalD | ftsI/Amr | PBP3
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<td>0</td>
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<td>21</td>
<td>23</td>
<td>CEX-2(2)</td>
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<td>1</td>
<td>0</td>
<td>34</td>
<td>CEX-2(2), G165A, N1725</td>
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</table>

Each amino acid substitution was identified only once, unless indicated otherwise following each substitution. Amino acid substitutions highlighted in red color have been described previously.

(*) either the presence of acquired β-lactamases or amino acid substitutions in β-lactamases naturally expressed in Pae.

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Abstract 7412

**Fourier-transform infrared spectroscopy for bacterial typing and real-time outbreak analysis**

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**Background:** Outbreaks of multidrug-resistant organisms or cases in which suspicious resistance patterns emerge over a short time demand quick information at the strain level. Typing of bacterial strains can aid in outbreak investigation when classical epidemiological methods are inconclusive. Typing can reveal clonality and possible routes of transmission, and can link clinical isolates to environmental reservoirs. Recently, a new automated system for characterization of bacterial strain typing was commercialized. This system is based on FT-IR spectroscopy and performs same-day strain typing. Here, we summarize the advantages and the limitations of using this system for real-time outbreaks investigations.

**Materials/methods:** This study included specimens collected during seven outbreaks in Israeli hospitals in 2018-2019. The investigations involved different microorganisms: A. baumannii, MRSA, VRE, P. aeruginosa, ESBL-producing K. pneumoniae, IMI-producing E. cloacae and S. marcescens. Typing was performed using an FT-IR spectroscopy-based system (Bruker, Germany) and hierarchical cluster analysis was generated using OPUS 7.5 software (Bruker, Germany). We compared FT-IR results to results of genomic fingerprinting methods using DNA amplification (REP/BOX/ERIC-PCR and blaOXA-51LIKE typing), spa typing, and genome-based sequencing (cgMLST and core genome alignment). Typeability, discriminatory power (Simpson Index of diversity), and the influence of the cut-off value were evaluated.

**Results:** In each outbreak, the analysis based on FT-IR spectroscopy confirmed the presence of a predominant clone and concurred with epidemiological findings. In three outbreaks (of P. aeruginosa, S. marcescens and MRSA), there was complete concordance between FT-IR and REP-PCR, BOX-PCR and spa typing, respectively. In 2 outbreaks (A. baumannii and VRE) there was partial concordance between FT-IR and blaOXA-51LIKE and BOX-PCR typing, respectively. FT-IR was overdiscriminatory in analyzing an ESBL-producing K. pneumoniae outbreak when compared to cgMLST and core genome alignment. FT-IR had a discriminatory power >0.7 in each outbreak. The discrepancies observed between FT-IR spectroscopy and other typing methods would not have affected outbreak interpretation or management.

**Conclusions:** Because of its technical simplicity, short turn-around time, and low cost, FT-IR biotyping has the potential to become an essential tool for outbreak investigation.

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Abstract 7413

**Education for diagnostic stewardship needs fresh approaches in the digital era: lessons from an attempt to reduce inappropriate urine cultures**

Alicia Xin Yu Ang*

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**Background:** Inappropriate urine cultures can result in inappropriate treatment of asymptomatic bacteriuria, promoting antimicrobial resistance, increasing length of hospital stay, adverse drug reaction and possible missed diagnoses. We embarked on a series of interventions in a tertiary hospital in Singapore to reduce inappropriate urine cultures in hospitalised patients.

**Materials/methods:** Gap analysis identified that root causes of inappropriate urine culture orders included convenience of urine cultures, and lack of knowledge regarding indications for urine cultures, and consequences of inappropriate urine cultures. All urine culture orders were audited via electronic medical records review by trained reviewers, and deemed inappropriate if sent in the absence of any symptoms of urinary tract infection, unless they were in pregnancy or before a urological procedure. The interventions and continuous audit spanned 1 February to 1 November 2019. Initial interventions planned for 1 February to 30 June 2019 included educational efforts during hospital-mandated training sessions for junior doctors, and nurses questioning doctors on the indication of urine culture at the point of urine collection.

**Results:** At baseline in February 2019, 40.5% of urine cultures were inappropriate. Interventions planned between 1 February to 30 June 2019 could not be effectively carried out. Hospital-mandated training sessions had poor attendance, with limited presence even for doctors who signed in. Nurses were overwhelmed with reminder fatigue and could not undertake the additional task of questioning doctors at the point of urine collection. The rate of inappropriate urine cultures was 33.3%, 39.0%, and 35.7% in March, April and May 2019 respectively. New educational interventions were designed, including daily text reminders to junior doctors, and e-posters on ward computers used for electronic ordering. The prevalence of inappropriate urine cultures dropped to 32.6%, 28.6% and 21.1% in September, October and November 2019 respectively.

**Conclusions:** Diagnostic stewardship can improve patient care. Our experience suggests that utilising digital platforms in place of traditional means of education via face-to-face contact may be more effective in reaching out effectively to doctors.

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Abstract 7416

**Preliminary evidence of absence of cystic echinococcosis in the Dibrugarh district of Assam state, North-East India**

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**Background:** Cystic Echinococcosis (CE) is a cosmopolitan zoonosis caused by the tapeworm *Echinococcus granulosus*. In India, the disease has been estimated to have a significant socioeconomic impact. However, exact data on the epidemiology of the disease are lacking. We present findings from a cross-sectional ultrasound-based survey conducted to evaluate the prevalence of CE between March and April 2019 in rural communities in the state of Assam, North-East India.

**Materials/methods:** In the absence of published data on the presence of CE cases in animals and humans in the studied area, seven villages from the Dibrugarh district where randomly selected from communities where pastoral activities with goats are commonly carried out. Residents aged 5 to 90 years were invited to undergo a free ultrasound examination of the abdomen to check for the presence of CE cysts and stage lesions according to the WHO-Informal Working Group on Echinococcosis (WHO-IWGE) classification of CE cysts. A commercial Rapid Diagnostic Test (VIRAPID HYDATIDOSIS, Vircell, Spain) was performed using sera of patients with possible CE lesions.

**Results:** A total of 1464 participants were enrolled, 629 were female (42.91%). The median age was 35 (range 5-90, IQR 20). Only two patients (0.13%) presented with possible CE cystic lesions in the liver and the spleen respectively. Both lesions were found in patients who were over 60 years old, were solid with well-defined margins and no liquid component (possible CE5) and were negative at serology testing.

**Conclusions:** Our preliminary data suggest CE to be absent or at least very scarcely present in humans in the studied area, as we found no patient carrying cysts with pathognomonic signs detectable by ultrasound. Our results suggest the lack of an ongoing active CE transmission. This is most likely due to the scarcity of sheep raising activities in the region, as while other potential hosts such as goats and cows are present, sheep are known to be the most fertile intermediate host for *Echinococcus granulosus*. Physicians dealing with patients from this area carrying suspect CE lesions should carefully consider other differential diagnoses.

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Abstract 7419

Therapeutic drug monitoring of isavuconazole in patients undergoing antifungal therapy in Denmark

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Background: Isavuconazole is the newest approved broad-spectrum triazole antifungal agent. It is found non-inferior to voriconazole in the treatment of invasive aspergillosis and to have an effect on mucormycosis similar to amphotericin B. The pharmacokinetic features of isavuconazole identified during clinical development did not provide a clear need for therapeutic drug monitoring (TDM). Nevertheless, a recent study recommended a relatively narrow therapeutic range between 2.5 and 5 mg/L. We have monitored the serum levels since 2017 and present the results of isavuconazole TDM at Statens Serum Institut, Denmark

Materials/methods: Blood samples referred for isavuconazole TDM March 2017 to August 2019 were included. The serum concentration levels were determined by fluorescent detection on a UHPLC using an azole TDM kit from ChromSystems adapted and validated for isavuconazole determination [Jørgensen et al., 2017]. The therapeutic index aimed for was initially 2-10 mg/L, but recently adjusted to 2.5-5 mg/L. For invasive Aspergillus flavus infections a trough level ≥4 mg/L is recommended (due to a two-fold higher MIC compared to that for A. fumigatus) and in mucormycosis a trough level well above the individual MIC was preferred until fungal control.

Results: A total of 244 isavuconazole serum concentrations from 30 patients were analysed. The group of patients included 15 females/15 males with a median age of 59.5 years ranging from [7-80 years]. The median value of isavuconazole concentration in all patients was 4.5 mg/L range [0.0 – 15.4 mg/L]. The patients were divided into four disease groups, haematology (non-Mucorales), haematology (Mucorales), pulmonary disorders and other with median values of 4.1, 5.3, 4.3 and 2.2 mg/L, respectively, but with noticeable inter and intra patient variability (Fig. 1).

Conclusions: Although observing a median value of 4.5 mg/L, well within the recently recommended therapeutic range, the range of measured serum levels is very broad for all patient groups. This may in part be explained by variations in administration, sampling and influenced by drug-drug interactions. We recommend a targeted antifungal treatment according to species identification. Consequently, the serum levels for mucormycosis patients are higher compared to other patient groups although significant interpatient variability is seen for all groups.

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Abstract 7420

Implementation of intravenous artesunate for severe malaria in France: analysis of outcome in 1391 patients

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Background: Intravenous artesunate has been deployed in Europe and in the USA through a diversity of distribution programs. Its efficacy and safety have been analyzed in observational studies relatively limited in size.

Materials/methods: We collected outcome features in patients treated with intravenous artesunate during the first seven years [from May 2011 through December 2017] of a national implementation program through the French National Drug Agency. Data were collected from the national pharmacovigilance system and by the Malaria National Reference Center.

Results: Artesunate distributed in local hospitals became the most frequent treatment for severe malaria in France in 3 years. In 2017, 71.4% of severe malaria patients were treated with IV artesunate. 1391 patients with severe (1370) or uncomplicated (21) malaria were treated during the study period. Death rate was estimated at 4.1% from patients with reported outcome (41/1011). Median (IQR) length of stay in the hospital and in ICU were 6 (4-8) and 2 (1-4) days respectively. Treatment failure was recorded in 27 patients but resistance-associated mutations in the parasite Kelch-13 gene were not observed. Main reported adverse events were anemia and/or hemolysis (136 cases), cardiac events (24), elevations of liver enzymes (23), and kidney failure (15). No increase in adverse events incidence was noted in children, over or under-weighted, HIV-positive patients or during pregnancy. Incidence of post-artesunate delayed hemolysis (PADH) was 42.8% when specifically assessed in a sub-cohort of 98 patients, and was twice higher in patient of European origin than in patients of African origin (57.9% vs 29.2%, p<0.0009). Compared to the general population, higher mortality rate and prolonged stay in the hospital [total and in ICU] were observed in patients with initial parasitemia > 10%, age >50 years and European origin; mortality was lower in children <15 years [1.0%] and in patients of African origin. Conversely, mortality rate was similar in the general population and in over- or under-weight, HIV-positive patients or pregnant women.

Conclusions: Artesunate was rapidly deployed on a nation-wide scale and confirmed its superior clinical benefit in the general population and main subgroups, justifying a wide implementation in imported severe malaria.

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Infections associated with kinase and antiapoptotic Bcl-2 inhibitors in a cohort of real-life haematological patients

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1Hospital Clínic, Barcelona, Spain, 2Hospital General Universitario de Castellón, Castellón, Spain, 3Hospital Universitario de Gijón, Gijón, Spain

Background: Ibrutinib, idelalisib and venetoclax are novel oral agents for the treatment of hematologic neoplasias that have changed the landscape of hematology, but the knowledge of potentially associated infectious complications is scarce. We aimed to describe the incidence and epidemiology of infections in a current cohort of real-life treated patients.

Materials/methods: Retrospective descriptive study of the patients treated with ibrutinib, idelalisib or venetoclax in a tertiary center from June 2014 to September 2019. According to our hospital protocols, patients with idelalisib received prophylaxis with cotrimoxazole after March 2016 and also patients treated with ibrutinib if they had received 3 or more prior lines of therapy or concomitant corticosteroid therapy, after September 2018.

Results: A total of 167 patients were analyzed: 123 received ibrutinib, 17 idelalisib and 27 venetoclax. Median age was 72 years (IQR 62-78) and 67.1% were male. Underlying disorders were chronic lymphocytic leukaemia (89, 53.3%), non-Hodgkin lymphoma (55, 32.9%) and acute leukemia (22, 13.2%). Overall, 53 (31.7%) patients had at least one episode of microbiologically documented infection, and 110 different isolates were reported: 72.7% bacterial, 20.9% viral and 6.4% fungal. Patients receiving ibrutinib had a lesser risk of infection, while this risk was higher in those receiving venetoclax (p=0.001 each). Acute leukemia patients had a higher risk of infection (p=0.048) and those having received at least two previous lines of therapy for their baseline disease and those receiving corticosteroids had a non-significant trend for increased risk of infection (p=0.262 and p=0.121, respectively). In multivariate analysis, acute leukemia (OR 2.933, CI 1.154-7.456) and use of corticosteroids (OR 2.514, CI 1.048-6.033) were independently associated with higher risk of infection.

Conclusions: Patients with hematologic neoplasias treated with kinase and antiapoptotic protein Bcl-2 inhibitors face a high incidence of infection, especially those with acute leukemia and corticosteroids use. These results are important in order to establish preventive approaches.
### Table 1. Microbiological characteristics.

<table>
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<th>Microorganism isolated</th>
<th>Ibrutinib</th>
<th>Idelalisib</th>
<th>Venetoclax</th>
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<tbody>
<tr>
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<td></td>
<td></td>
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Abstract 7422

Comparison of PCR assays for detection of Echinococcus multilocularis from human formalin-fixed paraffin-embedded tissue preparations

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Background: Molecular identification and pathology examination performed on lesions are the two pathways for confirmation of alveolar echinococcosis in patient. Molecular diagnosis can be performed on various samples containing parasite DNA, such as tissue, biopsy, liquid, or formalin-fixed paraffin-embedded preparation (FFPE). The present study aims to assess molecular diagnosis on FFPE samples.

Materials/methods: Molecular diagnosis was tested from 30 alveolar echinococcosis lesions isolated after surgery from 1997 to 2018 and included in paraffin, in order to test the best PCR conditions from different published DNA targets. DNA was extracted twice with commercial kit. Eleven PCR assays were tested, which targeted four mitochondrial genes (NADH1, COX1, 12S-rrnS-rRNA and 16S-rrnL-rRNA), and generated PCR products from 84 to 529 bp.

Results: Except for few samples (from 1997 and 2000), the PCR results were better for FFPE samples less than 10 years old. PCR was successful for half of the tested samples when the size of the PCR product was below 250 bp. The PCR targeting part of the 16S-rrnL-rRNA (84 bp) was the most successful PCR and allowed us to amplified 75% (22/30) of the FFPE preparations tested. When quantitative PCR technique was used, the target was amplified in 90% of the samples.

Conclusions: Retrospective molecular studies performed on FFPE preparations is a key point in epidemiology of rare or emerging diseases as alveolar echinococcosis. Methods of FFPE preparation have changed this last decade and have impact on DNA conservation. In FFPE, DNA can be partially degraded and the use of short PCR targets is essential. Quantitative PCR, instead of conventional PCR, could be performed to increase the sensitivity, especially in retrospective FFPE studies. Confirmation by sequencing requires appropriate DNA target size, with PCR products about 200 bp.

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Abstract 7423

Unexpected genomic variability among Enterobacterales causing bloodstream infections in European neonates and infants less than 90 days

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Background: Mortality in neonates with Gram-negative bloodstream infections (BSIs) has remained unacceptably high over the last decade (10-15%), despite improvements in neonatal care. This was a case-series study including European infants with culture-proven sepsis caused by Enterobacterales to investigate significant determinants of neonatal mortality.

Materials/methods: 92 strains were isolated from 90 infants <90 days with proven Enterobacterales BSIs from six European countries between 2010-2015. Patient-level clinical data, treatment and 28-day outcome were available. Bacterial isolates from blood were identified by MALDI-TOF mass spectrometry and antibiotic susceptibilities obtained with disk diffusion tests (EUCAST guidelines 2019). Strains were further characterised by Whole-Genome Sequencing (Illumina MiSeq platform).

Results: Among the 92 bacterial isolates (UK: 50; Estonia: 21; Greece: 11; Italy: 7; Lithuania: 2; Spain: 1) the majority were Escherichia coli (37/92), Enterobacter spp. (25/92), Klebsiella spp. (20/92), Serratia spp. (9/92), and Proteus mirabilis (1/92). 28% (26/92) isolates were multi-drug resistant and 21% and 19% were resistant to 3rd-generation cephalosporins and gentamicin, respectively, while 99% were susceptible to amikacin and meropenem and 93% to piperacillin/tazobactam and ciprofloxacin. Twenty-five isolates harboured blaTEM-type genes, two non-Klebsiella spp strains the blaSHV-type determinant, and two E. coli strains the blaCTX-M-type genes. One K. pneumoniae Sequence Type (ST) 17 carried blaVIM-12 gene, and two Enterobacter asburiae (ST484) the mcr-9 determinant. A total of fifty different STs were found, with ST131 and ST90 as the most frequent in E. coli and Enterobacter cloacae, respectively. E. coli strains showed the highest mean number of virulence genes [105 vs <65 in the other species overall], mainly those involved in fimbriae production. The fatality-rate among the cohort was 21% (19/90).

Conclusions: The fatality-rate was higher than that reported in literature, with potential confounders being the high proportion of pre-terms and/or comorbidities. Genomic analyses revealed an unexpected genetic variability among the isolates, in terms of the number of STs and resistome/virulome composition, compared to the published adult literature. This could be due to age-specific factors, such as pathogenetic and immunological mechanisms, which should be further investigated to develop a tailor-made therapeutic strategy. This genetic heterogeneity needs to be confirmed in global neonatal sepsis cohorts.

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Evaluation of ResistancePlus GC assay for the detection of Neisseria gonorrhoeae and markers associated with ciprofloxacin-susceptibility and resistance

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Background: Most European guidelines recommend ceftriaxone 500 mg intramuscular as a single dose together with azithromycin 2 g oral as a single dose for empirical treatment of uncomplicated gonorrhoea. Ciprofloxacin is an option if antimicrobial susceptibility test results are available before treatment.

The aim of this study was to evaluate the ResistancePlus GC assay (SpeeDx Pty Ltd) for the simultaneous detection of Neisseria gonorrhoeae (GC) and gyrA S91 markers of susceptibility (Wild Type) and resistance (S91F) to ciprofloxacin from clinical samples and GC isolates

Materials/methods: Performance was assessed on 150 GC strains and 97 GC-positive clinical samples (positive culture and Seegene Allplex STI Essential Assay). The gonococcal DNA extraction was performed using NucliSens easyMAG (bioMérieux, France) and Seegene Allplex STI Essential Assay (Seegene, Seoul, Korea) from isolates and clinical samples, respectively. Amplification and detection were performed using the LightCycler 480 II instrument (Roche, Spain).

Results were compared with phenotypic resistance profiles determined by gradient diffusion technique (E-test) using EUCAST breakpoints.

Results: Both GC strains and GC-positive clinical samples were correctly detected by the ResistancePlus GC (beta) assay. The test demonstrated a 100% sensitivity for GC detection. E-test results determined that 60.8% of clinical samples were resistant to ciprofloxacin and we observed a 100% concordance between the phenotypic-based susceptibility data and the detection of the S91F mutation or S91 Wild Type respectively. No isolates provided an indeterminate result for gyrA detection.

Conclusions: The ResistancePlus GC (beta) assay is an appropriate assay for simultaneous detection of N. gonorrhoeae and markers of susceptibility and resistance to ciprofloxacin in gyrA gene directly from clinical samples or GC isolates. Therefore, this assay could be implemented in a healthcare laboratory as a routine technique for the rapid detection of GCs as well as its ciprofloxacin susceptibility. Consequently, ciprofloxacin could be used for gonorrhea treatment in order to improve antibiotic stewardship and conserve extended-spectrum cephalosporins.

Conflict of interests: SpeeDx Pty Ltd supplied all the reagents for molecular testing.

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Molecular epidemiology and spatiotemporal analysis of carbapenem-resistant Enterobacteriaceae among network hospitals in southern Thailand

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**Background:** Carbapenem-resistant Enterobacteriaceae (CRE) become a worldwide concern in nosocomial infections. The data epidemiology, risk factors, and outcomes of CRE infections among hospitalized patients are still insufficient.

**Materials/methods:** We prospectively collected data of inpatients in network hospitals (1 university hospital, 3 referral centers and 5 provincial hospitals) who infected and colonized with CRE from October 2018 to September 2019. Thus we also investigated for the environmental contamination of these organisms in those studied hospitals. Carbapenemase genes were identified and sequencing was used to obtain a complete genetic context of the plasmid-harboring those genes. A spatiotemporal analysis was performed by admission ward, hospitals, time of infection and similar groups of genes and plasmids.

**Results:** There were 1096 isolates of CRE identified among 985 patients. *Klebsiella pneumonia* is the most common species accounting to 51% following with *Escherichia coli* (28%). Only 25 patients (with 25 isolates) accounting 2 % was identified with community-acquired infection. The only one significantly risk factor is previous use of carbapenems [OR 2.3 [1.9-5.8], P = 0.031]. Among K.pneumoniae and E.coli, the MIC50 and MIC90 of both imipenem and meropenem were 32 µg/ml and 64 µg/ml, respectively. Nine hundred and ninety-seven (91%) isolates were positive for *bla_

**Conclusions:** CRE transmitted both within hospitals and between hospitals in the network. The data served the better understanding to control the spreading of these organisms.

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Genital tuberculosis in a low prevalence setting: an unsuspected cause of infertility and severe gynaecological disease

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Background: Genital tuberculosis is an unusual site of extra-pulmonary tuberculosis, usually with a non-specific clinical presentation and thus underdiagnosed. However, a correct diagnosis is mandatory to avoid infertility. Our aim was to define clinical characteristics of female genital tuberculosis (FGTB), population at risk, sequelae and genotypic features of the strains involved, in a city with a low-rate of tuberculosis around 10/100,000 people.

Materials/methods: Retrospective study in a tertiary care Hospital from January-2003 to August-2019. All tuberculosis cases were evaluated and cases with FGTB were included. Clinical records were reviewed. The isolates were analyzed by MIRU-VNRT to assign their genotypes, analyze potential clusters, determine the lineage and evaluate possible polyclonal infections.

Results: During study period, a total of 1804 tuberculosis cases were identified. Five of them (0.3%) corresponded to FGTB. All cases were from migrant women: Dominican Republic [3], El Salvador [1] and Ecuador [1], median age was 31-years (range:20-60). Three patients had infertility upbringing. The most frequent symptom were abdominal pain and fever [3]. Diagnosis was performed by PCR MTB-GenXpert and culture on biopsy specimens (endometrial, fallopian tube and placenta). All isolates were susceptible to first-line anti-TB drugs. Three patients had a disseminate tuberculosis (pulmonary and genital). However, two cases required treatment adjustment due to adverse effects. Two pregnant patients required intensive unit care due to severe respiratory failure, and one of them died; 80% responded to treatment. Histopathology assessment contributed only in one case. Genotypic analysis determined that the strain involved in each case was different and all corresponded to lineage (Euro-American). In one case, a polyclonal infection involving two variants was detected in the respiratory specimen. For the cases with respiratory and extra-respiratory involvement, no clonal compartmentalization was observed.

Conclusions: Genital tuberculosis in Madrid is uncommon and under diagnosis disease because of its low suspicion. It should be considered as potential diagnosis especially in patients with pelvic inflammatory disease symptoms and migrants from endemic tuberculosis countries, and maybe associated to severe disease leading to infertility and even death. This presentation did not involve a specific strain; one polyclonal infection, likely due to diagnostic delay, was identified.

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Abstract 7433

Antimicrobial resistance among bacteria causing asymptomatic bacteriuria in pregnant women, rural Burkina Faso
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Background: To determine antimicrobial resistance (AMR) in a rural community in sub-Saharan Africa, we assessed healthy pregnant women for asymptomatic bacteriuria.

Materials/methods: From 2016 to 2018, we recruited consenting pregnant women attending antenatal clinics in Nanoro district, Burkina Faso. Urine routinely sampled for glucose and protein testing was inoculated on-site on the Uricult system (LifeSign). Bacteria growing in quantities ≥10^4 colony (CFU) forming units/ml were processed for identification and antibiotic susceptibility testing (AST, disk diffusion according to CLSI-M100-S29). Skin bacteria, non-fermentative Gram-negative rods and bacteria from mixed flora (≥3 species) were considered as contaminants. For comparison, AST results from clinical isolates obtained from a diagnostic accuracy study in Nanoro [2017 – 2018] were used (ClinicalTrials.gov, NCT02669823). Multidrug resistance was defined as resistance to ≥3 antibiotic classes.

Results: On 6018 participating women, 92 (1.5%) had urine cultures grown at quantities ≥10^4 CFU/ml, and 132 (2.2%) had quantities ≥10^5 CFU/ml, meeting the criteria of asymptomatic bacteriuria. Among a total of 238 isolates, the top-3 pathogens included Escherichia coli (71.0%), Klebsiella pneumoniae (13.5%) and Staphylococcus aureus (9.2%). Proportions of susceptibility and MDR for the urine and clinical isolates were as follows:

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>E. coli Urine n=149</th>
<th>E. coli Clinical isolates n=21</th>
<th>p-value</th>
<th>S. aureus Urine n=22</th>
<th>S. aureus Clinical isolates n=8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ampicillin</td>
<td>35.5%</td>
<td>14.3%</td>
<td>0.05</td>
<td>oxacillin</td>
<td>100%</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>37.9%</td>
<td>9.5%</td>
<td>0.01</td>
<td>cotrimoxazole</td>
<td>100%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>84.6%</td>
<td>38.1%</td>
<td>&lt; 0.001</td>
<td>clindamycin</td>
<td>100%</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>97.0%</td>
<td>66.7%</td>
<td>&lt; 0.001</td>
<td>gentamicin</td>
<td>100%</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>96.4%</td>
<td>71.4%</td>
<td>&lt; 0.001</td>
<td>MDR</td>
<td>0%</td>
</tr>
<tr>
<td>MDR</td>
<td>3.0%</td>
<td>57.1%</td>
<td>&lt; 0.001</td>
<td></td>
<td>0%</td>
</tr>
</tbody>
</table>

Klebsiella pneumoniae (n=36) isolates were susceptible to cotrimoxazole (66.7%), ciprofloxacin (94.4%), ceftriaxone (97.2%) and gentamicin (100%), with only 2.8% MDR. Results were similar for isolates grown in quantities ≥10^4 CFU/ml versus ≥10^5 CFU/ml.

Conclusions: AMR rates of Escherichia coli from the urinary tract in healthy pregnant women were considerably lower compared to AMR rates in clinical isolates. Integration of urine culture in the routine of antenatal care in a rural setting in sub-Saharan Africa proved to be feasible and effective and can be used as a proxy for monitoring community AMR in remote areas.

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Hospital outbreak of *Klebsiella pneumoniae* producing GES-1 or GES-5 β-lactamases in Poland

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**Background:** The first representative of the GES family (GES-1) was identified in France in 1998 in the clinical strain of *Klebsiella pneumoniae*. Among the variants of GES β-lactamases described so far are both ESBLs, e.g. GES-1, and carbapenemases, e.g. GES-5, which is the most commonly identified carbapenemase in the world from the GES family. Here we extend our previous ECCMID report, by incorporating all GES-producing isolates from Poland and providing new molecular data.

**Materials/methods:** This work covered 12 clinical *K. pneumoniae* strains: 11 from Cracow isolated in 2017 (n=1), 2018 (n=8), 2019 (n=2) and 1 from Bytom identified in 2019. The strains were from new-borns and infants up to 6 months hospitalized in intensive care and cardiology wards. All strains were obtained by the National Reference Centre for Susceptibility Testing to carbapenemase confirmation. Species identification was performed by Vitek2 (bioMérieux). Carbapenemase activity was studied by phenotypic methods, including CIM test. The presence of the *bla*GES genes were confirmed by PCR. MICs were determined using antibiotic strips (Liofilchem) and the results were interpreted according to the EUCAST guidelines. All isolates were subjected to whole genome sequencing (WGS) by Illumina-Miseq.

**Results:** The first *K. pneumoniae* strain producing GES-5 in Poland was isolated in Cracow in 2017. Molecular studies revealed the presence of *bla*GES-5 on the plasmid pKRA-GES-5 (25.004bp), belonging to the IncP6 family. *bla*GES-5 was identified within class 1 integron - In1525. Afterwards, *bla*GES genes were identified by PCR in the next 11 *K. pneumoniae*. WGS analysis confirmed *bla*GES-5 in two and *bla*GES-1 in eight isolates from Cracow. *bla*GES-1 was also present in strain from Bytom. In all cases *bla*GES were located on the plasmid pKRA-GES-5 within In1525. All strains represented ST45 and were indistinguishable in cgMLST. In the studied genomes a total of 24 SNPs was identified with 7-17 SNPs in comparison with isolate from 2017. All GES-5-producing strains were resistant to carbapenems and they were positive in CIM test.

**Conclusions:** This study showed the first hospital outbreak of *K. pneumoniae* ST45 producing GES-1 or GES-5 in Poland with *bla*GES localised on plasmid pKRA-GES-5.

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Long lasting outbreak of severe Mycobacterium chimaera infection among cardiac surgery patients operated with contaminated heater-cooler devices: Italy, 2010 to 2019

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Background: Mycobacterium chimaera is a non-tuberculous Mycobacterium (NTM) belonging to the Mycobacterium Avium Complex (MAC) species. It is spread in the environment ubiquitously and harmless for healthy subjects, while vulnerable patients may develop severe infections. We report a long lasting outbreak of M. chimaera infection related to contaminated heater-cooler devices (HCD) used during open chest surgery interventions in Italy, between January 2010 and October 2019.

Materials/methods: We collected data since 2010 retrospectively, from the mandatory surveillance of human infections due to NTM, regulated by Ministerial Decrees 15/12/1990 and 29/7/1998. We adopted the case definition indicated by the European Centre for Disease prevention and Control (ECDC) referring to clinical and exposure criteria.

Results: We identified 36 lab-confirmed cases (median age: 66y, range: 35-82y; 91.4% male), included 21 death. Cases were notified from North (91.7%) and South (8.3%) Italy. Two cases were diagnosed in 2015, 6 in 2016, 8 in 2017, 6 in 2018, 11 in 2019 [3 dates were missing]. The median time between surgery and diagnosis was 3y. Mostly, patients referred fever (10.8%), leukopenia/thrombocytopenia (9.5%), night sweats (8.2%), endocarditis (8.1%), hepatitis (8.1%), asthenia (6.8%), weight loss (6.8%), nephritis (6.8%), multiple granulomas (6.8%), pulmonary involvement/pneumonia (5.4%), splenomegaly (5.4%), nausea (4.1%). Mostly, contaminated HCD were located in the North (84.6%), while 13.8% in the Centre and 1.6% in the two islands. Phylogenetic analysis is ongoing.

Conclusions: The different geographical distribution of cases and contaminated HCD possibly relay to a greater use of these devices and/or compliance in the notification flow procedures in Northern healthcare settings compared to those in other regions. We gave information to aware clinicians and general practitioners to guarantee patient safety and follow-up, together with the device cleaning and decontamination procedures spread by the Manufacturer. We recommend increased collaboration among all the actors at local and regional level to improve both case and HCD notifications in order to operate adequate and prompt health interventions. The correct cleaning, disinfection and maintenance procedures are key routine actions to guarantee appropriate HCD functioning and patient safety, avoiding spreading of infectious agents through the aerosol generated from the heating water contained in HCD.

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Abstract 7441

**Evaluation of *Stenotrophomonas maltophilia* non-susceptibility and associated risk factors: a multi-centre analysis**

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**Background:** *Stenotrophomonas maltophilia* is a lactose, nonfermenting gram-negative organism with few treatment options due to intrinsic resistance to most antimicrobials. Trimethoprim-sulfamethoxazole (TMP-SMX) and levofloxacin have traditionally high rates of *in vitro* susceptibility and are considered first line agents for *S. maltophilia*, with tigecycline, ceftazidime, and polymyxins also showing activity. Little is known regarding the prevalence of *S. maltophilia* non-susceptibility among these commonly used agents as well as potential risk factors associated with resistant isolates.

**Materials/methods:** A retrospective, multicenter analysis was performed at 5 centers in the southeastern United States. Inpatients that had a positive culture with susceptibility results between October 2015 - September 2018 were evaluated. The first isolate per patient per year was included. The primary outcome was the prevalence of non-susceptible isolates among any agent tested with typical activity vs. *S. maltophilia*. Intermediate and resistant results were grouped together and considered non-susceptible for evaluation. The secondary outcome was factors associated with *S. maltophilia* non-susceptibility based on historical risk factors associated with Pseudomonas species resistance. Data collected included baseline demographics, culture and susceptibility results, and clinical outcomes. Statistical analysis was performed using SPSS software, version 26.0 (IBM). Categorical data were analyzed using the Chi-square or Fisher exact test, and continuous data were analyzed using the Student t-test or Mann-Whitney U test, as appropriate. An alpha of ≤0.05 was deemed statistically significant.

**Results:** A total of 325 isolates met inclusion and exclusion criteria and were included in the study. Most isolates (76.3%) were sputum/respiratory cultures. Non-susceptibility was present in 43/325 (13.2%), 53/324 (16.4%), and 105/172 (61%) to TMP-SMX, levofloxacin, and ceftazidime, respectively. In centers that tested tigecycline, non-susceptibility was present in 11/16 (68.8%) isolates. The only factor predictive of non-susceptibility was isolation from a urine culture (13.3% vs. 5.4%; p=0.014). Presence of mechanical ventilation (37.7% vs. 21.5%) and ICU admission (35.3% vs. 18.4%) were predictive of susceptibility to these agents (p<0.001).

**Conclusions:** *S. maltophilia* non-susceptibility had a prevalence of almost 50% to at least one first-line or commonly used agent. Further research should evaluate national/international prevalence of, as well as risk factors associated with non-susceptibility, as treatment options are limited.

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Abstract 7450

**Resistance to azithromycin in *Mycoplasma genitalium* from patients of a tertiary hospital from Madrid, Spain**

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**Background:** *Mycoplasma genitalium* (MG) is an etiological agent of sexually transmitted diseases, increasingly diagnosed thanks to the new commercial PCR assays. MG is associated mainly with nongonococcal urethritis, cervicitis, pelvic inflammatory disease and proctitis. Azithromycin is recommended for empirical treatment but some studies report significant rates of macrolide resistance suggesting that selection for resistance may be widespread. Our aim is to study the prevalence and characteristics of azithromycin resistance in *Mycoplasma genitalium* at La Paz-Cantoblanco-Carlos III University Hospital, a tertiary care hospital from Madrid, Spain.

**Materials/methods:** Between April 2018 and November 2019, we collected clinical samples from patients with symptoms of nongonococcal urethritis, infertility, pelvic inflammatory disease and proctitis that were positive for MG by Mycoplasma-Ureaplasma – QSR for BD MAX™ (BioGX), a real-time multiplex PCR-assay that detects *M. genitalium*, *M. hominis*, *Ureaplasma urealyticum* and *U. parvum*. The macrolide-resistance study was performed with Allplex™ MG & AzI R assay (Seegene), a real-time multiplex PCR-assay that detects MG and six azithromycin resistance mutations in the 23S rRNA gene: A2058G, A2058T, A2058C, A2059G, A2059T and A2059C.

**Results:** Seventy-one clinical samples were MG positive by BD MAX™: 27 urines, 42 rectal swabs and 2 semen. Fifty-three percent of the clinical samples had azithromycin resistance mutations detected with Allplex™ (38/71). The mutations detected were: 40% (15/38) A2058G, 34% (13/38) A2058T and 26% (10/38) A2059T.

**Conclusions:** The data obtained in our study indicate a high resistance rate compared to other studies in Spain. This situation makes it necessary to implement resistance detection assays for *M. genitalium* to facilitate the optimization of antibiotic treatment in these patients and potentially reduce the transmission of resistance.

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Abstract 7451

Prospective surveillance of multidrug-resistant Gram-negative bacteria in a UK intensive care unit using whole genome sequencing

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Background: The prevalence of multidrug-resistant Gram-negative bacilli (MDRGNB, defined as resistance to 3 or more antibiotic classes) is increasing globally. In 2017 ECDC estimated that 8.3% of patients staying in an intensive care unit (ICU) for more than two days acquired at least one healthcare associated infection (HCAI). Routine surveillance for MDRGNB differs between different units, hospitals and countries, reflecting uncertainty about best practice. The impact of asymptomatic carriage of MDRGNB on rates of HCAI is unclear.

Materials/methods: We conducted a six-month prospective surveillance study for ESBL-producing and/or carbapenem-resistant Gram-negative bacteria in an adult ICU in the United Kingdom. Samples were collected from multiple sites (respiratory, urine, stool / rectal swabs, wound swabs) from all participants on admission, weekly, and on discharge from the ICU. Samples were cultured on selective media (Brilliance ESBL and chRomeID Carba/Smart) and underwent identification (MALDI-TOF MS), antimicrobial susceptibility testing (Vitek2) and whole-genome sequencing (illumina HiSeq).

Results: Between June and December 2016 461 participants were recruited. 14.1% were positive for MDRGNB on admission to ICU; 11.2% carried MDRGNB in their stool. The most frequently identified organisms were Pseudomonas aeruginosa (41.4%), Escherichia coli (24.1%) and Klebsiella pneumoniae (15.5%). 8.8% of patients acquired MDRGNB during their ICU stay. Whole-genome sequencing identified epidemic lineages and genomic populations consistent with UK national data. An outbreak of carbapenem-resistant K. pneumoniae was identified by surveillance, which would have been missed on routine diagnostic testing. A distinct lineage of ESBL-producing E. coli was identified in hepatology patients.

Conclusions: Asymptomatic carriage and infections with MDRGNB in ICU patients were higher than previously reported. The majority of patients were colonised on admission to ICU. Transmission between patients was minimal, suggesting effective infection control practices on ICU. We rapidly identified and controlled an outbreak of carbapenem-resistant K. pneumoniae. WGS data provided rapid, high resolution information during the outbreak. Distinct lineages of MDRGNB in particular patient groups may indicate target populations for more frequent surveillance. These findings have potential implications for infection control strategies and interventions.

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Latent tuberculosis infection screening in persons with new diagnosis of HIV infection in Italy: a multi-centre study promoted by the Italian Society of Infectious and Tropical Diseases

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Background: Italian guidelines for the management of people living with HIV (PLWH) indicate screening for latent tuberculosis infection (LTBI) in those recently diagnosed with HIV. The Italian Society of Infectious and Tropical Diseases performed a survey on the current practice and yield of LTBI-screening [tuberculin skin test (TST) or QuantiFERON TB Gold-In tube (QFT-IT), QuantiFERON TB Plus (QFT-P)] in recently diagnosed PLWH in Italy. Primary endpoint was the LTBI prevalence. Secondary endpoints included rate and features of LTBI-screening (compared to other suggested screening test for HCV and HBV), the rate of offer and acceptance of TB-preventive therapy and its outcome.

Materials/methods: We retrospectively enrolled recently diagnosed PLWH from 9 centres, from January 2016 to December 2017. We used binary logistic regressions and multinomial logistic regressions to identify factors associated with LTBI-screening [by TST, QFT or both] and QFT-results respectively.

Results: Among the 801 participants, 774 patients were included [after excluding active TB]. LTBI tests was significantly more frequently executed in foreign vs Italian born [OR:2.52, p<0.001], AIDS diagnosis [OR: 1.81, p=0.013] and in case of CD4 count <100 cells/mm³ vs CD4≥500 cells/mm³ [OR: 2.30, p=0.059]. HBV and HCV tests were done in 98% of the patients and this was significantly different compared to LTBI-screening that was done in 65.5% [p<0.001]. LTBI was diagnosed in 32 subjects (6.5%) of the 495 patients evaluated by QFT. Positive QFT-results were significantly associated with being foreign [RRR 23.32, p<0.001], high CD4 T-cell count (100 cell/mm³ increments RRR 1.26, p<0.001) and low HIV-RNA load (log10 copies/ml increments RRR 0.59, p=0.003). Indeterminate results were significantly associated with old age [10 year increments RRR 2.08, p<0.001], low CD4 T-cell count (100 cells/mm3 increments RRR 0.09, p<0.001), high HIV-RNA load (log10 copies/ml increments RRR 2.23, p=0.006) and AIDS diagnosis [RRR1768 p<0.001]. Sixteen LTBI-subjects started LTBI treatment and 8 completed it.

Conclusions: In a low prevalence country LTBI was found in a minority of newly diagnosed PLWH. LTBI-screening is not consistently performed in PLWH in Italy and preventive-TB-therapy is not offered to all LTBI. Next updated national guidelines need to consider these observations.

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Abstract 7454

**Epidemic clonal lineages of Enterobacteriales producing VIM-type carbapenemases in Poland, 2013-18**

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**Background:** Carbapenemase-producing Enterobacteriales (CPE) with MBLs of the integron-encoded families VIM and IMP have been recorded in Europe from 2001 and in Poland from 2006. The analysis of all 121 VIM/IMP CPE isolates from 2006-12, revealed their striking specificity, with prevailing organisms *Enterobacter cloacae* cpx (~53%), mainly *E. hormaechei* clones ST90 and ST89, and *Klebsiella oxytoca* (20%), mainly ST145. Here we present a remarkable increase of VIM/IMP CPE cases in 2013-18 with detailed species distribution.

**Materials/methods:** 623 non-duplicates VIM/IMP CPE isolates confirmed by the National Reference Centre for Susceptibility Testing (NRCST) in Warsaw from 2013-18 were analyzed. The isolates were derived from various infections or colonization cases in 180 hospitals all over the country (16/16 administrative regions). Species identification were confirmed by the VITEK 2 system (bioMérieux, France). In all isolates the MBL production was detected biochemically by the Carba NP test, and phenotypically by the EDTA double-disk synergy test. The *bla*\_vim\_ and *bla*\_imp\_like genes were detected by PCRs.

**Results:** Following 2012, the NRCST has been observing continuous significant increase in numbers of VIM/IMP CPE in Poland, from 36 isolates in 2013, 78 in 2014, 63 in 2015, 89 in 2016, to 174 cases in 2018. Altogether, 623 VIM/IMP CPE cases were confirmed, representing 12 taxa with the most numerous being: *E. cloacae* cpx (n=231), *Klebsiella pneumoniae* (n=168), *Citrobacter freundii* cpx (n=69), *K. oxytoca* (n=64), *Escherichia coli* (n=58) and *Serratia marcescens* (n=16) followed by *Morganella morganii* (n=5), *Citrobacter braakii* (n=3), *Proteus mirabilis* (n=3), *Klebsiella aerogenes* (n=2), *Citrobacter farmeri* (n=1) and *Enterobacter asburiae* (n=1). PCR analysis revealed a total predominance of VIM types with over 98% (n=614) of the isolates, and marginal contribution of IMP-like MBLs (n=9).

**Conclusions:** Comparison with the first phase of VIM/IMP CPE dissemination (2006-12), apart from the increasing tendency, showed a remarkable change in the species distribution. In 2018 *K. pneumoniae* became the leading species, probably as a result of several dynamic regional outbreaks, like in Lubelskie (45 isolates in 2018). If to consider all species, some regions (and specific hospitals) have been arenas of extensive VIM CPE expansion, like Mazowieckie (n=129), Łódzkie (n=91) or Pomorskie (n=69).

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Abstract 7457

Prevalence and molecular characteristics of Staphylococcus aureus carrying Panton-Valentine leukocidin genes isolated from patients accessing at emergency department in 2016-2018 period

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Background: Panton-Valentine leukocidin (PVL) represents a key determinant of community-acquired methicillin-resistant S.aureus (CA-MRSA) virulence, although not all CA-MRSA produce PVL and its presence is recently found also in hospital–acquired MRSA (HA-MRSA). HA and CA infections due to PVL-positive methicillin-susceptible S.aureus (MSSA) have also been described with clinical characteristics similar to that produce by PVL-positive MRSA suggesting that PVL-positive MSSA may be reservoirs for PVL-positive MRSA via the integration of the Staphylococcal Cassette Chromosome mec (SCCmec) mobile elements. We aimed at determining the frequency of PVL genes in S.aureus isolates collected from clinical samples at the emergency department in Milan, during the 2016-2018 period.

Materials/methods: The identification of the bacterial species and the antibiotic susceptibility were performed by MALDI-TOFF and VITEK.2, respectively. Samples were tested for the presence of PVL gene using RT-PCR. Whole genome sequencing was performed on PVL-positive isolates.

Results: We analyzed 25 stains carrying PVL genes (15 MSSA and 10 MRSA). We identified 14 different STs: the most frequent was ST512 (16%) followed by ST18 and ST1472 (12% each). The SCCmec typeIVa was the most frequent. In the minimum spanning tree we identified 3 distinct groups without common alleles with others: group A involving exclusively ST152, group B encompassing ST10, ST30, ST121 and ST1472, and group C including other STs. A median of 2.8 resistance genes were detected for 6 different classes of antibiotics. Most frequent detected genes were blaz (88%) and mecA (40%). By integrating phenotypic and genotypic data only one isolate showed a full sensitive profile. A median of 49 virulence genes was detected; MRSA isolates had more virulence genes compared to MSSA (53.6 vs. 46.5, p=.013).

Conclusions: Our data showed a high frequency of PVL in the MSSA strains which, despite their sensitivity to antibiotics, may have a high pathogenetic potential. The MRSA strains characterized showed the typical genetic characteristics related to CA infections such as a high number of virulence genes and a marked heterogeneity, representing a potential source of exchange of genetic material for the strains associated with hospitalization.

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Alarming high occurrence of multidrug resistance of *Mycoplasma genitalium* in a cohort of men who have sex with men using pre-exposure prophylaxis in Belgium (Be-PrEP-ared study)

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**Background:** Increasing antimicrobial resistance in *Mycoplasma genitalium* (Mg) has been described in men who have sex with men (MSM). We report on the occurrence of macrolide and fluoroquinolone resistance associated mutations (RAMs) in a cohort of MSM using pre-exposure prophylaxis in Belgium (Be-PrEP-ared study).

**Materials/methods:** Mg detection in urine, anorectal and pharyngeal (U-A-P) samples was performed every three months for 1.5 years using real-time PCR in 179 participants. Remnant specimens were genotyped via Sanger sequencing. RAMs were detected in the 23S rRNA which corresponds to high level resistance to azithromycin. Furthermore, quinolone resistance determining regions (QRDR) of the *parC* gene and the *gyrA* gene were sequenced to detect mutations conferring resistance to fluoroquinolones.

**Results:** At baseline, the prevalence of Mg was 19.3% (n=31). At follow-up, 139 additional Mg infections were detected (33.5% U; 59.4% A; 7.1% P). Genetic resistance data is available for 116 samples and is presented in Table 1. Only nine samples (7.8%) did not present any mutation. Macrolide resistance mediating mutations were detected in 90.5% of the samples (n=105). Mutations conferring resistance to fluoroquinolones were found in almost 45% (n=51). A total of four gyrA alterations were found (all anorectal samples), two of them coincided with a ParC mutation. The most frequent mutation of the QRDR of the ParC gene was S83I (n=27/49; 55.1%), followed by P62S (n=8/49; 16.3%).

Multidrug resistant strains were found in more than 40% of the samples (n=49; 42.2%) and were almost equally detect in the anorectum (41.3%) and urethra (44.9%).

Of those multidrug resistant cases, only eight (16.3%) presented symptoms. We linked 15 mutations to possible treatment failures; 11 with azithromycin (7/11 A2058G and 4/11 A2059G) and four with moxifloxacin (three S83I and one V112V).

**Conclusions:** The high rate of macrolide and fluoroquinolone resistance in Mg among MSM using PrEP demands attention. Nearly half of all Mg infections were multidrug resistant to azithromycin and moxifloxacin which are the first and second line treatment of Mg. Most of the cases were asymptomatic. Detection and treatment of asymptomatic cases of Mg among MSM will do more harm than good and should be avoided.

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**Table 1.** Presence of Mycoplasma genitalium macrolide and fluoroquinolone resistance associated mutations (RAMs) in the Be-PrEP-ared study.

<table>
<thead>
<tr>
<th>RAM Type</th>
<th>All samples (n=116)</th>
<th>Anorectal (n=63)</th>
<th>Urine (n=49)</th>
<th>Pharyngeal (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Presence of fluoroquinolone and macrolide RAMs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of fluoroquinolone RAMs only</td>
<td>2</td>
<td>1 (0.21-6.1)</td>
<td>1 (0.4-6.5)</td>
<td>0.0 (0.0-10.9)</td>
</tr>
<tr>
<td>Presence of macrolide RAMs only</td>
<td>56</td>
<td>48.3 (38.9-57.7)</td>
<td>44.4 (31.9-57.6)</td>
<td>51.0 (36.3-65.6)</td>
</tr>
<tr>
<td><strong>Macrolide RAMs (23S rRNA)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A2059G</td>
<td>105</td>
<td>90.5 (83.7-95.2)</td>
<td>85.7 (74.6-93.3)</td>
<td>95.9 (86.0-99.5)</td>
</tr>
<tr>
<td>A20587</td>
<td>56</td>
<td>48.3 (38.9-57.7)</td>
<td>46.6 (37.1-58.0)</td>
<td>42.6 (31.7-56.4)</td>
</tr>
<tr>
<td><strong>Fluoroquinolone RAMs (gyrA gene)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M98W (G207A)</td>
<td>4</td>
<td>3.4 (0.9-8.6)</td>
<td>6.3 (1.8-15.5)</td>
<td>0.0 (0.0-7.3)</td>
</tr>
<tr>
<td>M95W (G205C)</td>
<td>2</td>
<td>50.0 (17.1-100.0)</td>
<td>50.0 (17.1-100.0)</td>
<td>0.0 (0.0-30.2)</td>
</tr>
<tr>
<td>A79V (C236T)</td>
<td>112</td>
<td>87.9 (58.7-99.7)</td>
<td>89.4 (65.8-99.9)</td>
<td>100.0 (69.8-100.0)</td>
</tr>
</tbody>
</table>

**Conclusions:** The high rate of macrolide and fluoroquinolone resistance in Mg among MSM using PrEP demands attention. Nearly half of all Mg infections were multidrug resistant to azithromycin and moxifloxacin which are the first and second line treatment of Mg. Most of the cases were asymptomatic. Detection and treatment of asymptomatic cases of Mg among MSM will do more harm than good and should be avoided.

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Ugandan increase in malaria cases is reflected in imported cases to Norway of which surprisingly many have mixed infections identified by PCR

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Background: In August 2019 the Ugandan ministry of health reported a 40% increase in malaria cases since June 2018. In the same time period, we have noticed an increase in malaria cases imported from Uganda.

At Oslo University Hospital malaria is initially diagnosed by rapid diagnostic tests (RDT) and microscopy. In addition, the Department of Microbiology offers a nationwide service for species-specific Plasmodium PCR to confirm suspected malaria cases and identify Plasmodium species, and mixed infections.

Materials/methods: EDTA blood samples were analyzed by in-house real-time PCR targeting the five human pathogen Plasmodium species. PCR-data from patients analyzed for Plasmodium infections in the period 2017 until November 2019 were collected.

Results: A total of 220 patients with suspected or confirmed malaria were analyzed at our department in the given time period. Of these, 75 patients had been residing in Uganda and 63 patients were PCR positive for malaria. A major part of patients infected in Uganda were Plasmodium falciparum positive of which 28.2% were mixed infections. None of these mixed infections were identified by microscopy.

<table>
<thead>
<tr>
<th>Year</th>
<th>Patients analyzed: positive /total</th>
<th>Patients infected in Uganda [% of total positives]</th>
<th>Plasmodium falciparum in Ugandan patients</th>
<th>Double infections from Uganda [total tests analyzed]</th>
<th>Triple infections from Uganda [total tests analyzed]</th>
</tr>
</thead>
<tbody>
<tr>
<td>2017</td>
<td>18/39</td>
<td>2 [11.1%]</td>
<td>1</td>
<td>1 [1]</td>
<td>0 [0]</td>
</tr>
<tr>
<td>2018</td>
<td>17/43</td>
<td>6 [35.3%]</td>
<td>4</td>
<td>1 [2]</td>
<td>0 [0]</td>
</tr>
</tbody>
</table>

Table 1

Conclusions: Malaria is a potentially fatal infection, and correct diagnosis is important to provide adequate treatment. In 2019 we have noticed an increased number of malaria infections from Uganda, and a significant proportion of these are double and even triple infections. We urge our colleagues to be aware of the current situation and recommend PCR testing as a supplement to primary diagnostic in order to detect mixed Plasmodium infections in this patient group.

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**Abstract 7461**

**The antimicrobial role of a commonly used mucolytic agent in Chlamydia pneumoniae infection**

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**Background:** Chlamydia pneumoniae (Cpn) is an obligate intracellular bacterium, with characteristic biphasic lifecycle, causing respiratory infections. It is thought to be responsible for approximately 10% of community-acquired pneumonia cases. Ambroxol (Ax) is a widely used drug in the treatment of respiratory infection due to its effect on mucus viscosity. Ax-treatment showed anti-chlamydial activity *in vitro* on A549 cells, however, this effect was not observed *in vivo* in Cpn-infected mice when human equivalent dose of Ax was applied. In this study, our aim was to examine whether an increased dose of Ax could influence the growth of Cpn *in vivo*.

**Materials/methods:** Balb/c mice were infected with Cpn intranasally and treated with higher dose of Ax than the commonly used human equivalent dose. The recoverable Chlamydia inclusions from the mouse lungs and the growth rate *in vitro* were detected by an indirect immunofluorescent assay. The seroconversion of mice, IFN-γ and IL-6 quantity in the lungs were tested with ELISA. Furthermore, the relative mRNA expression of IL-12, IL-23, IL-17-{A,F}, IFN-γ, IDO-{1,2}, surfactant-proteins [SP-A1,B,C,D] in the lungs were analysed with RT-qPCR. Moreover, *in vitro* apoptotic assay on A-549 cells was carried out with fluorescence-activated cell sorting.

**Results:** The Ax-treatment of mice resulted in a significantly lower [2.3-times] Cpn load in the lungs and a higher Cpn specific IgM seropositivity rate. The mRNA expression level of surfactant proteins [SP-A1, B, C,D], IL-12, IL-23, IL-17-[A,F] and IFN-γ was elevated in the Ax-treated mice compared to that in the non-treated group. The quantity of IFN-γ on protein level was significantly higher in the Ax-treated group of mice. Based on the *in vitro* results, the antimicrobial activity of Ax affects the early phase of the infection and it increases the apoptosis of the cells. Furthermore, the SP-A1 showed significant anti-chlamydial effect in *in vitro* conditions.

**Conclusions:** According to our results, the higher dose of Ax-treatment had beneficial effect during Cpn infection by increasing the bacterial clearance from the mice. The antimicrobial effect of Ax treatment is complex and might be due to the increased expression of inflammatory cytokines and surfactant proteins and the apoptosis of infected cells.

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Abstract 7466

**Very good results for the use of the RAST methodology and for identification of agents of sepsis directly from the blood cultures by MALDI-TOF to optimise antibiotic therapy**

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**Background:** Rapid blood cultures identification and antibiotic susceptibility profile are of the main microbiological informations for appropriate management of sepsis.

**Materials/methods:** We evaluated the performance of the Rapid Antimicrobial Susceptibility Testing (RAST) proposed by the European Committee on Antimicrobial Susceptibility Testing (EUCAST), for blood cultures with the direct identification of the agents by MALDI-TOF (Bruker®) with the Bruker’s methodology, in an University and Reference Hospital in Brazil. We followed all the procedures of version 1.1 RAST EUCAST May 2019. We compared the results with the PHOENIX BD® antimicrobial susceptibility test and we also included the comparison of the screening for carbapenemase with the Blue–Carba test and final confirmation by BDMAX® resistance panel.

**Results:** From July first to 25 November 2019, 176 blood samples were included and the antibiogram completed and compared. For *E.coli* (n=35), *K. pneumoniae* (n=50), *S. aureus* (n=38), *S. pneumoniae* (n=9), *P. aeruginosa* (n=13) and *A. baumannii* (n=15) the performance of ≥90% of correct results was achieved since the 6hs reading. Only for *E. faecalis* (n=12) and *E. faecium* (n=4) the results were around of 70% of correct results on 4, 6 and 8hs reading. The VME was acceptable for *E. coli* and *K. pneumoniae* for 6 and 8hs, *S. aureus* and *S. pneumoniae* for 4, 6 and 8hs, *P. aeruginosa* for 8hs. *E. faecalis* no VME, but ME 5% for 4hs and *E. faecium* no VME but 5% ME in all the readings. For *A. baumannii* we get no so good results: VME of 5.7% at 4, 6 and 8hs. The screening of carbapenemase when compared with Blue-Carba for 6 and 8hs was respectively: sensibility 90/100%, specificity 95/90%, VPP 86/77% and VPN 97/100%. The Blue carba results were confirmed by BDMax®. The polymicrobial blood cultures occurred in 5%, and the MALDI-TOF detected only the predominant bacteria, and the Gram stain did not helped to detect the mixture.

**Conclusions:** The RAST methodology is easy, fast, with good accuracy and very useful for the antibiotic therapy choice for bacteremia and septic patients. The inclusion of MALDI-TOF and a rapid carbapenemase test like Blue-Carba can improve these critical informations.

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Abstract 7470

**Malaria outbreak response in a nomadic pastoralist setting, Kenya 2019**

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**Background:** On 22nd August 2019, Baringo County health department, Kenya notified of a suspected malaria outbreak. As at 26th August 2019, a total of 301 cases had been line-listed with six deaths (CFR=2.0%), all under the age of five years. We carried out response activities to investigate the suspected outbreak with the specific objectives to confirm, determine the magnitude and describe the epidemiology of the suspected cases. We also proposed and initiated appropriate public health actions.

**Materials/methods:** The outbreak epicenter was in Tirioko ward, Baringo county. A suspect case was defined as a case presenting with fever (axillary temperature ≥ 37.5°C), chills, malaise, headache or vomiting at examination or 1–2 days prior. A laboratory confirmed case was a suspect case with detection of *Plasmodium* species by either rapid diagnostic antigen or detection of malaria parasites by microscopy. Collected data was cleaned and analyzed using Microsoft Excel software’s and Epi info 7.2 software (CDC Atlanta, GA). Descriptive statistics was performed using means and medians for continuous variables and frequency and proportions for categorical variables.

**Results:** A total of 1242 cases were line listed with 8 deaths (CFR=0.6%). Females were 697 (56.1%) with those <5 years old being 424 (34.1%). Of the sixty three (63) laboratory samples collected, RDT positives were 40 (63.4%) and Microscopy positive were 28 (44.4%). Additional arboviral screen testing yielded 2/13 (15.3%) positives for Dengue fever. All were negative for Chikungunya, Riftvalley fever, Yellow fever, West Nile fever and Crimean Congo hemorrhagic fever. We observed that the epicenter was poorly served by health facilities, social amenities and experienced security incidents occasion by cattle rustling. Short rains had been experienced a month prior and pools of water were evident in the environment. Additionally, the communities did not always use mosquito nets due to their temporary housing structures.

**Conclusions:** We recommended the establishment and operationalization of a health facilities in the region. Additionally, strengthen Integrated Disease Surveillance and response activities to proactively mitigate future outbreaks. There is also a need to customize malaria social behaviour change communication to fit the community’s nomadic lifestyle

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Abstract 7471

**Evaluation of fungi isolates from cystic fibrosis adult patients in a tertiary hospital of Madrid, Spain**

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**Background:** There is a great variability in the clinical manifestations of the respiratory fungal diseases in patients with cystic fibrosis (CF). The role of fungi isolations from these patients, is sometimes uncertain, specially, in the context of the emerging fungi and the new methods of identification. We aimed to assess the epidemiological data, of fungi isolations, in adult CF patients.

**Materials/methods:** Data of fungal isolates from sputum samples of adult patients with CF from the University Hospital of La Princesa, were collected retrospectively. Six year (November 2013 to November 2019) of fungal cultures, and epidemiological data were analyzed.

Sabourdau dextrose agar with chloramphenicol was used as growth medium. Fungal identification, was performed by at least one of the following techniques: lactophenol blue stain [optical microscopy], MALDI-TOF MS [Bruker], and chromogenic medium. Patient data, were collected from their medical records.

**Results:** 2773 sputum samples of 130 patients [medium age 28 years, 51.1% males] were analyzed. 1240 [44.7%] of these samples, from 92 [70.8%] patient [medium age 28 years, 50.3% males] were positive for fungi culture, of wich, 353 [28.5%] where positive for two or more fungi.

The global fungi identification data were:

- **Candida** sp. [44.1%], from wich, main species: *C. parapsilopsis* [44.2%], *C. albicans* [27.7%], *C. lusitaniae* [19.9%].
- **Aspergillus** sp. [29.9%]; main species: *A. fumigatus* complex [78.6%], *A. flavus* complex [13.1%], *A. terreus* complex [5.7%].
- **Scedosporium apiospermum complex** [14.6%], *Lomentospora prolificans* [6.4%], *Exophiala dermatitidis* [3.1%] and other species (*Fusarium* sp., *Paecilomyces* sp., *Penicillium* sp., *Aureobasidium pullulans*, and *Trichoderma* sp.) [1.9%].

Annual data evolution are summarized in the following graphic:

Regression line for **S. apiospermum** \( r=0.93 \)

**Conclusions:** *Candida* sp., *Aspergillus* sp., and *S. apiospermum complex*, were the most prevalent fungi, being consistent data with the literature. The data evolution by year, seems to indicate an ascendant trend for *S. apiospermum complex*. Further studies are needed to track epidemiological evolutions and to deepen the role played by these fungical isolates in the patient’s clinic.

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Clinical spectrum of infections by new members of the Staphylococcus aureus complex
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Background: Staphylococcus argenteus and Staphylococcus schweitzeri are new members of the Staphylococcus aureus complex that were first described in 2015. Differentiation of these species from Staphylococcus aureus in routine diagnostic microbiology reports is not recommended by the ESCMID Study Group for Staphylococci and Staphylococcal Diseases. One of the reasons is to minimise misinterpretation of these new species as non-pathogenic. Given limited clinical reports of this new species, this study was performed to review the clinical features of patients from whom clinical isolates of Staphylococcus argenteus or Staphylococcus schweitzeri were detected.

Materials/methods: Laboratory records between 1 April to 31 July 2019 were reviewed to identify potential Staphylococcus argenteus and Staphylococcus schweitzeri based on matrix-assisted laser desorption/ionization (MALDI-TOF) score >2.000 on Bruker Biotyper (BD, Bremen, Germany) following upgrade to the latest software version. Susceptibility testing was routinely performed using Vitek 2 (bioMérieux, Marcy l’Etoile, France) and interpreted according to EUCAST breakpoints. Only clinical samples were included. Screening samples for epidemiology were excluded. Electronic medical records of patients were retrospectively reviewed.

Results: 38 methicillin-susceptible isolates were identified from non-duplicate patients. Majority (27/38, 71.1%) of the samples were associated with skin and soft tissue infections, including post-operative wound infections. Two of these cases were associated with bacteraemia. Other sites include nasal swabs of patients with bacterial sinusitis (2/38, 5.3%), empyema (1/38, 2.6%), urinary tract (2/38, 5.3%), nasal swab (1/38, 2.6%), and female genital tract (1/38, 2.6%). High susceptibility rates were seen to most tested antimicrobials, including trimethoprim-sulphamethoxazole (38/38, 100%), erythromycin (34/38, 89.5%), clindamycin (34/38, 89.5%), quinupristin-dalfopristin (38/38, 100%), minocycline (37/38, 97.4%), gentamicin (35/38, 92.1%), ciprofloxacin (37/38, 97.4%).

Conclusions: The spectrum of clinical disease of other members of the Staphylococcus aureus complex is similar to Staphylococcus aureus. Although higher mortality for Staphylococcus argenteus bacteraemia has been reported, additional studies are required to confirm this. Further studies may aid our understanding of these new species and whether a different treatment approach is required. All clinical isolates were methicillin-susceptible and remained susceptible to the majority of tested antibiotics.

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Mediastinitis: an incidence study and case series in an elderly adult centre

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Background: Mediastinitis is a rare complication of cardiovascular surgery. Most studies report an incidence between 0.34 and 8% and a high mortality, ranging from 12 to 47%. Numerous risk factors has been described in the literature such as diabetes mellitus (DM), obesity, duration of the surgical procedure and extracorporeal circulation (ECC), prophylaxis used, packed red blood cell transfusions, hyperglycemia in the short term postoperative period.

Materials/methods: The medical records of all patients undergoing myocardial revascularization surgery (MRS) and/or valve replacement surgery (VRS) were retrospectively analyzed. Demographic information, comorbidities and information related to surgery were collected from December 2017 to September 2019 at César Milstein Hospital in Buenos Aires Argentina.

Results: We included 287 patients undergoing cardiovascular surgery. Fifty three percent of them were males with a mean age of 74.6 (SD 7.3). Thirteen cases of mediastinitis were diagnosed (4.53% CI 2.5 to 7.4). Within this group, six cases were in the context of MRS, two were due to VRS, and three were due to MRS + VRS. Sixty-days mortality was 23.77% (95% CI 6.23 to 50.8) in patients with mediastinitis. Surgical duration was between 90 and 300 minutes, 7 patients required ECC. Only 3 patients required packed red blood cell transfusions.

Ten of 13 patients developed hyperglycemia within 48 hours after surgery (range: 195-455 mg/dL). In patients receiving inadequate surgical antibiotic prophylaxis, mortality was 37% (n=8), while in the group receiving adequate prophylaxis it was 20% (n=5) p 0.98. None required reoperation for bleeding. Sternal dehiscence was found in 5 patients. The most common isolated agent was Staphylococcus coagulase negative (SCN) (39.13%), followed by gram negative bacilli (BGN). Initial antibiotic treatment was inadequate in two cases only, although both had a favorable outcome. The most common comorbidities were DM, obesity and smoking. Three patients developed other concomitant infections.

Conclusions: The incidence and mortality of post-surgical mediastinitis in our study was similar to other reported in other studies. One of the weaknesses of our study is that the incidence reported is inaccurate due to the small sample size.

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Abstract 7478

A machine learning-based model to predict bloodstream infections

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Background: Clinical identification of patients with bloodstream infection (BSI) is challenging. Efficient predictive scores to quickly identify patients at increased risk of BSI are highly desirable. The aim of this study was to use a machine learning algorithm-based approach for identifying the best predictors of BSI and, then, to validate a clinical algorithm based on these predictors in hospitalized patients suspected of having a BSI.

Materials/methods: The study included all the patients from infectious diseases consultancies at 1100-bed University Hospital in Rome (Italy) between 2016 and 2018, for whom blood cultures (BCs) were collected upon the suspect of a BSI. We used data from patients with positive BCs for significant pathogens (i.e. excluding clear contaminants) and from patients with negative BCs concerning the demographic and clinical features that have been described in the published literature as risk factors for BSI. Data were extracted automatically from multiple hospital database sources which are connected through GENERATOR (Gemelli big-data Network for Retrospective Analysis and Test in Oncology and medical Research) infrastructure. Then, the dataset was split into training and validation data (Figure 1). A logistic regression (LOG) algorithm was used to compute the model and the final performance was assessed on the validation data by measuring accuracy, specificity and negative predictive value (NPV).

Results: 6619 consultancies, of which 1231 (19%) were BSI cases and 5388 (81%) non-BSI controls, resulted in 4691 training data and 1928 validation data. Among 41 explored features, the model identified 14 predictors (dialysis, solid tumor, dyspnea, hypoxemia, central venous catheter, previous BSI, renal failure, urea, white blood cells, platelets, hypotension, tachycardia, fever, urinary catheter) with an accuracy, specificity and NPV of 81%, 97% and 82%, respectively.

Conclusions: Despite preliminary, our model performs extremely well in ruling out the BSI while the BSI prediction can be used as an at-risk warning.

Figure 1: Data analysis workflow for selecting the features and developing and validating the predictive model

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Abstract 7480

**Genomic analysis of multi-resistant *Mycobacterium tuberculosis* strains in France: evolution from 2006 to 2018**

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**Abstract third-party references:** On behalf of the National Reference Center for Mycobacteria (CNR-MyRMA)

**Background:** Multidrug-resistant *M. tuberculosis* (MDR) strains isolated in France are sent to the National Reference Center for Mycobacteria (CNR-MyRMA) for expertise and epidemiological surveillance. We report the evolution at the phylogenomic level of MDR isolates received at the CNR-MyRMA over a 13 years period. A transborder analysis allowed to detect some potential pathways of diffusion in the EU.

**Materials/methods:** Between 2006 and 2018, 921 MDR strains were genotyped by MIRU-VNTR 24 loci and Sanger sequencing. Illumina whole-genome sequencing (WGS) was performed for 273 strains [172 MDRs]. Data assembly and phylogenomic analysis were performed on GALAXY and BIONUMERICS-7.6.°

**Results:** MIRU typing showed that the main phylogenetic lineages among French MDR strains are Beijing-38%, T-20%, LAM-14%, and Haarlem/X-8%. Beijing fluctuated from 21% in 2006-07 to 48% in 2013-14 (wave of former USSR-patients), then 39% in 2017-18. The dominant lineages vary according to the region of birth, e.g. Beijing in Georgia-Armenia (82%); L4 (30%) in Eastern Europe; Haarlem/X (30%) in the Maghreb. The lineages of patients born in France were diverse: L4-23%, LAM-21%, Beijing-21%, Haarlem/X-18%. The MIRU/WGS analysis revealed 81 episodes of genetically linked cases (“clusters”), including 12 XDR. Almost all were family and/or friends close contact cases, excepted one 9-cases outbreak in a workplace and one XDR intra-hospital transmission. The WGS-resistance SNPs of the 132 MDRs and 18 XDR strains showed a perfect correlation with Sanger sequencing. The WGS allowed the differentiation of clusters amongst strains non-distinguishable by MIRU, especially for Beijing [53/273 strains in clusters]. A comparison of our Beijing genomes with a genome database established by the EuSeqMyTB consortium [24 countries] indicated that two Beijing strains isolated in France in 2017-2018 displayed less than 12 SNPs with a single Beijing strain isolated in another European country in 2008.

**Conclusions:** WGS offers ultra-high resolution in the determination of the resistance profiles and the phylogenomic comparison of MDR strains, and is efficient to trace the origin of clusters which are circulating in France but started to spread more than 10 years ago in countries of the EU. Dissemination of MDR strains out of family or close friend’s circles is exceptional in France.

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Monitoring and control of the heater-cooler unit colonisation by Mycobacterium chimaera and other NTMs used during open-heart surgery
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Background: Recent reports have suggested an association between heater-cooler devices and NTM infections among patients undergoing cardiac surgery potentially through the aerosolization of bacteria from contaminated water used in these devices. The Italian Ministry of Health, in the communication n.000067 4/2019 issued recommendations for the control of M. chimaera infections, requesting the microbiological surveillance of all the HCUs.

Materials/methods: In three cardiac surgery centers, water and aerosol samples were collected to determine the microbiological parameters required by the Directive 98/83/CE and to assess the presence of NTMs according to the protocol proposed by the ECDC (ECDC, 2015). Genotyping was performed by sequencing the hsp65 gene, ITS1-rDNA and 16S-rDNA regions. HCUs were decontaminated according to the manufacturer’s guidance, except for the 3T-Heater-Cooler System, LivaNova, where weekly cycles of treatment with 4,5% peracetic acid and maintenance with 22% hydrogen peroxide were performed; moreover the replacement of internal tubing was also carried out to eliminated the presences of biofilm

Results: We sampled 22 HCUs (n.9 3T-Heater-Cooler System, LivaNova, n.3 1T-Heater-Cooler System, LivaNova, n.1 HX2-Heater-Cooler, Terumo and n.9 Heater-Cooler Unit HCU 40, Maquet) for a total of 114 samples (45, 8, 2 and 59 respectively). All the microbiological parameters were compliant, excepted for total microbial load at 36°C that exceed 100 CFU/ml in 50% (57/114) of samples and for the presence of P. aeruginosa in 10.5% (12/114) of them. NTMs were detected in 15.8% (18/114) of HCUs. M. chimaera was identified in 11.4% (13/114) of samples and in 4% (5/114) M. gordonae. All aerosol samples were negative for NTMs, but in the Heater-Cooler Unit HCU 40, Maquet, B. cereus was detected in 7% (4/59), K. oxytoca in 2% (1/59), B. ursincola in 2% (1/59) and S. paucimobilis in 3% (2/59) of the samples. Only S. paucimobilis was isolated also in the same HCU water sample

Conclusions: The implementation of maintenance and disinfection procedures of HCUs devices was able to reduce the risk of contamination and aerosolization by M. chimaera but not of other microorganisms

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Abstract 7482

**French health students' knowledge about human papilloma virus infections and vaccine: it is time to fill the gaps**

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Abstract third-party references: Supported by Plan Cancer, on Behalf of PREV'HPV Study Group

**Background:** In France, vaccine coverage against HPV is around 20 % in girls. Prev'HPV is a research project to co-construct and evaluate interventions to increase HPV vaccine acceptability. Health students (HS) will be involved in educational interventions. Our aim was to evaluate the knowledge of HS about HPV infections and HPV vaccine.

**Materials/methods:** An anonymous online questionnaire was sent to HS involved in 3 French Universities. We describe the results with the percentages [with 95 % CI] of answers.

**Results:** Five hundred and ninety six HS (mean age 21.4 ± 4.1 years, 30.2 % Nurses, 51.1 % medical students, 15.9 % future pharmacists, 81 % were in 2nd or third year, 74.3 % were female) answered the questionnaire. The role of persisting HPV infection for cervical cancer was known by 81.2 % (78-84.3%) of the HS. For 70.2 % (66.8-74.1) of the HS, HPV infects both males and females. Only 33.7 % (29.9-37.5) agreed that HPV will infect the half of the population during the life. The association between HPV and anal cancer and HPV and genital warts were respectively known by 30.5 % (26.8-34.2) and 40.1 % (36.1-44.1). HPV was wrongly considered as responsible for urinary tract infections by 23.3 % of HS (19.9-26.7). HPV vaccine protects from cervical cancer, other HPV related cancer and genital warts for respectively 83.2 % (80.2-86.2), 41.2 % (37.2-45.1) and 16 % (15.4-21.7) of HS. Condoms were considered as prevention tools for HPV infection by 65.1 % (61.2-68.9). The proportion of HS considering HPV vaccine is safe was 46.1 % (42.1-50.1). The proportion of HS reporting to be vaccinated was 35.9 % (32-39.7). If the HPV vaccine was recommended for them, 70.5 % (66.8-74.1) of the HS would agree to get vaccinated.

**Conclusions:** The role of HPV infection is well known for cervical cancer. However, the role of HPV in other cancers and genital warts is under-recognized by HS. Our results highlight the need for training on HPV infection and their prevention for HS before their involvement in interventions, particularly, whereas the HPV vaccine for boys would be recommended.

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Abstract 7484

Evaluation of a new tool in diagnostic process of sepsis: reporting results to a smartphone

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Background: A pilot study [PS] was designed to change on of antibiotic treatment in patients with sepsis-code, results of Antimicrobial-Susceptibility-Testing [AST] performed using Accelerate Pheno [Accelerate-Diagnosis] was reporting to smartphone by means of institutional email and Electronic-Clinical-History [EHC].

Materials/methods: 7 clinical services collaborate in these study [intensive care unit, internal-infectious medicine, emergency, digestive, resuscitation, general surgery, microbiology]. SB septic patients with positive blood cultures [BC+] were included, from May-November 2019. In PS 24 patients were included whereas the other 34 were admitted to non-participating services, constituted as Control-Group [CG]. Data of treatment changes were collected in each phases of results reported of BC+: Gram stain, a Maldi-Tof [Bruker-Daltonics] identification, ID/AST by Accelerate-Pheno [ACC-AST] and AST by Microscan-Walkaway [Beckman-Coulter]. Treatment modifications at each stage were collected and evaluated according to next criteria: Escalation, De-escalation, Equivalent.
**Results:** There were 57 modifications on treatment of 39 (67.2%) patients: 16 Escalations, 36, de-escalation and 5 Equivalent, as shown on Table 1.

<table>
<thead>
<tr>
<th>Adequations on treatment</th>
<th>Gram stain (n=58)</th>
<th>MALDI-TOF-identification (n=58)</th>
<th>ACC-AST (n=58)</th>
<th>Global ACC-AST (n=58)</th>
<th>Micro-SCAN-AST (n=58)</th>
<th>Total actions 5?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escalation (%)</td>
<td>13(26.5)</td>
<td>1(25)</td>
<td>3(33.3)</td>
<td>3(32.5)</td>
<td>6(35.3)</td>
<td>6(31.6)</td>
</tr>
<tr>
<td>De-escalation (%)</td>
<td>3(17.6)</td>
<td>2(50)</td>
<td>6(66.7)</td>
<td>4(50)</td>
<td>10(58.8)</td>
<td>11(57.9)</td>
</tr>
<tr>
<td>Equivalent (%)</td>
<td>1(5.9)</td>
<td>1(25)</td>
<td>-</td>
<td>1(12.5)</td>
<td>1(5.9)</td>
<td>2(10.5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Total treatment adequation (%)</th>
<th>Gram stain (n=58)</th>
<th>MALDI-TOF-identification (n=58)</th>
<th>ACC-AST (n=58)</th>
<th>Global ACC-AST (n=58)</th>
<th>Micro-SCAN-AST (n=58)</th>
<th>Total actions 5?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>17(29.3)</td>
<td>4(6.9)</td>
<td></td>
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</tbody>
</table>

| Treatment First modification | 1?                | 3(1DE, 1ES, 1ED)                | 4(3DE, 1ES)    | 6(3DE, 2ES, 1ED)      | 10(6DE, 3ES, 1ED)    | 9(6DE, 3ES)      | 39              |
| Treatment Second modification | 1(1DE)            | 5(3DE, 2ES)                     | 2(1DE, 1ES)    | ?                     | 6(4DE, 3ES)          | 4(1DE, 2ES, 1EQ) | 14              |
| Treatment Third modification  |                   |                                  |                |                       |                       |                  | 4               |

Comparing changes in treatment between both, PS and CG groups, when ACC-AST were reported, no significant differences were found (p=0.25). It is possible due to small sample size.

**Conclusions:** Use of fast Identification/AST devices has an important impact in antibiotic management of patients with severe infections or sepsis and use of mobile device to receive and analyze AST results on real time and in point of care is a good strategy for a rational use of antimicrobials.

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Pharmacokinetics of radiolabeled anti-mouse PD-L1 in immune-challenged tumour-bearing mice

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Background: Clinical studies recently demonstrated that nuclear imaging using radiolabeled anti-programmed-death ligand-1 (PD-L1) antibodies can be used to detect and quantify PD-L1 expression on a whole-body scale in vivo. As cancer patients may suffer from secondary infections, it’s important to know whether this affects the biodistribution and tumour uptake of anti-PD-L1 antibodies. Therefore, we investigated the effects of lipopolysaccharide (LPS), Staphylococcus aureus and Candida albicans-mediated immune activation on the in vivo biodistribution of radiolabeled anti-mPD-L1 in a tumour-bearing mouse model.

Materials/methods: Anti-mouse-PD-L1 antibodies were labelled with the radionuclide Indium-111 (111In-anti-mPD-L1). The effect of different infectious stimuli on anti-PD-L1 in vivo biodistribution was evaluated in healthy and Renca tumour-bearing BALB/c mice in 4 conditions; LPS-challenged, heat-inactivated Candida Albicans-challenged, local Staphylococcus aureus infection-bearing and vehicle control mice. Mice were intravenously injected with 30 or 100 µg 111In-anti-mPD-L1. Pharmacokinetics were assessed by taking blood samples and biodistribution was quantified by microSPECT/CT and ex vivo biodistribution studies 24h post injection. PD-L1 expression in relevant organs was evaluated with immunohistochemistry.

Results: There were no statistically significant differences in in vivo biodistribution of 111In-anti-mPD-L1 between tumour-bearing and non-tumour-bearing mice, except for the tumour. In LPS-challenged mice, however, bone marrow, lung and splenic 111In-anti-mPD-L1 uptake significantly increased compared to vehicle control (spleen: 44.6±5.0 vs. 14.8±3.5 %ID/g; p<0.01), thereby accelerating blood clearance and reducing tumour targeting (blood: 2.1±0.7 vs. 8.9±2.6 %ID/g; p<0.05, tumour: 9.2±4.5 vs. 22.2±5.95 %ID/g; p<0.05). Local Staphylococcus aureus infection significantly increased tracer uptake in affected muscles (8.3±0.2 vs. 1.8±0.65 %ID/g; p<0.01) and decreased tumour uptake (13.6±0.03 vs. 22.2±5.95 %ID/g; p<0.15). Candida albicans-challenge only affected blood clearance. Although spleen, bone marrow and lymph node uptake remained higher in LPS-challenged mice, increasing the 111In-anti-mPD-L1 dose to 100 µg resulted in normalized biodistributions, blood clearance and tumour targeting in all conditions.

Conclusions: Our preliminary data show that systemic and local inflammatory responses can significantly alter anti-PD-L1 antibodies’ pharmacokinetics and tumour targeting. Increasing the anti-PD-L1 antibody dose saturates splenic uptake and restores efficient tumour targeting. This information is essential to better understand alterations in in vivo anti-PD-L1 antibody biodistribution and allows exploration of these host responses in infectious conditions.

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Evaluation of the MGIT 960/EpiCenter TB eXiST system for drug susceptibility testing for Mycobacterium abscessus group

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Abstract third-party references: FAPESP #2014/50094-4

Background: Species of the Mycobacterium abscessus group (MAG) are capable of infecting different types of organs and tissues, being the third most isolated non-tuberculous mycobacteria, and are responsible for 80% of pulmonary infections caused by fast-growing mycobacteria (MCR). Their infections are difficult to resolve due to their intrinsic and acquired resistance to most commonly used antibiotic classes, making this group a major public health concern. Drug susceptibility testing (DST) is the minimum inhibitory concentration indicated for therapeutic follow-up, and the only validated methodology is that recommended by the Clinical & Laboratory Standards Institute. This project aimed to evaluate DST by BACTEC MGIT 960/TB eXiST system for MAG isolates.

Materials/methods: M. abscessus ATCC 19977T was used to develop the protocol, and subsequently DST for four antibiotics was performed against 31 clinical isolates using both REMA method and MGIT system.

Results: Comparison between both methods showed that there were no critical errors. Thus, overall, the MGIT system correctly provided the clinically relevant information, with the sole exception being a minor discrepancy. All isolates tested were susceptible to amikacin with the exception of one resistant isolate. For imipenem, all isolates were resistant, while for cefoxitin only two isolates were susceptible. Regarding clarithromycin, 14 isolates were susceptible while the remaining were resistant.

Conclusions: This study describes a protocol for performing DST of rapidly growing mycobacteria using the MGIT 960/TB eXiST system and that applying the method to a set MAG of clinical isolates demonstrated that the MGIT 960 system was reliable and highly reproducible.

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Predictors of asymptomatic *Clostridioides difficile* colonisation on admission: prospective cohort study in a French university hospital

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**Background:** *Clostridium difficile* is the most common cause of hospital-acquired infectious diarrhea and can result in asymptomatic carriage. Rates of asymptomatic colonisation on hospital admission range from 1.4%-21%. The objective of this study was to evaluate factors associated with colonization on admission in a French university hospital.

**Materials/methods:** An ongoing prospective cohort study was conducted in the following wards the hospital: intensive care unit (ICU, 3 units), geriatrics (3 units) and nephrology (one unit). Stool or rectal swabs were obtained for microbiological analysis within 48h of admission in participating wards. Multivariate logistic regression was performed to identify factors associated with colonization by *Clostridium difficile* at inclusion in this study.

**Results:** A total 539 patients were included. The mean of age was 71.6 years (min-max: 18-99) and there were 52.9% male and 47.1% female. Most of included patients (92.8%) suffered from at least one underlying disease. The mean length of hospital stay was 23.7 days (min-max: 2-252). The mean incidence density of testing at admission was 61.3/100 admitted patients. *C. difficile* was isolated at inclusion in 20 asymptomatic (no diarrhea) patients (3.7%; 12 had toxigenic *C. difficile*) while 519 included patients had a negative screening. The factors independently associated with colonization by toxigenic strain at inclusion were described in the table below.

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR (95%CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>21.64 (1.42-329.74)</td>
<td>0.03</td>
</tr>
<tr>
<td>Past medical history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI</td>
<td>10.22 (0.77-135.52)</td>
<td>0.08</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>12.37 (1.16-131.52)</td>
<td>0.04</td>
</tr>
<tr>
<td>Hospitalization in the last 90 days</td>
<td>6.38 (1.42-28.61)</td>
<td>0.02</td>
</tr>
<tr>
<td>Exposure in the last 30 days before inclusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parenteral nutrition</td>
<td>8.88 (1.36-57.88)</td>
<td>0.02</td>
</tr>
<tr>
<td>Statins</td>
<td>2.88 (0.72-135.52)</td>
<td>0.13</td>
</tr>
<tr>
<td>Exposure in the last 60 days before inclusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>9.98 (1.72-57.90)</td>
<td>0.01</td>
</tr>
<tr>
<td>C4G</td>
<td>13.06 (1.07-158.78)</td>
<td>0.04</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>5.54 (1.39-22.08)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

C4G: Cephalosporin’s 4th generation, CDI: *C. difficile* infection; CI: confidence interval; OR: odds ratio.

**Conclusions:** There are identifiable risk factors among asymptomatic *C. difficile* carriers that could help for optimizing their detection and provide a basis for targeted screening at admission.

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Abstract 7501

Surveillance culture-guided empirical therapy for febrile neutropaenia: low prevalence of inappropriately treated Gram-negative bloodstream infections

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Background: Prompt initiation of empirical treatment with broad-spectrum antimicrobial therapy reduces the risk of death for patients with febrile neutropenia. Broad-spectrum antimicrobial therapy is however associated with increased antimicrobial resistance. Therefore tailored antimicrobial therapy is needed to reduce inappropriate antimicrobial therapy without endangering high risk febrile neutropenic patient. Two university hospital hematology centers in Amsterdam, historically employed different empirical regimens: carbapenem monotherapy in one center (center A) and ceftazidim monotherapy, with a pre-emptive escalation option for patients colonized with 3GCR-GNB (further referred to as surveillance-culture-guided empirical therapy) in the other center (center B). This provided a unique opportunity to retrospectively compare these different empirical therapy regimens in the same city.

Materials/methods: Retrospective cohort study conducted in both centers. Diagnostic blood cultures drawn from patients > 18 years at risk for protracted febrile neutropenia (ASCO guideline definitions: < 100 neutrophils/μL for > 7 days) in which surveillance cultures were routinely performed, from the first day of chemotherapy until the recovery of neutrophils (> 500 neutrophils/μL) over a time period of 3 years were included. Blood cultures positive for Gram-negative rods (GNB) and candida species were further assessed.

Results: In both centers, 20% of blood cultures were positive. Prevalence of GNB in all blood cultures was 4.2% in center A and 2.4% in center B. In center A 19/38 (50%) of all GNB BSI were resistant to third generation cephalosporin (3GCR), 74% of these were preceded by a culture with a 3GCR-GNB. In center B, 4/22 (18%) 3GCR-GNB BSI were detected of which 3 (75%) were preceded by a 3GCR-GNB in surveillance cultures. Candida prevalence differed between the two centers where 19 candidemias occurred in center A versus 1 candidemia in center B.

Conclusions: In both centers Gram-negative BSI were rare (2.4-4.2%) and therefore 3GCR-GNB which constitute 18-50% of GNB, were even less prevalent. 75% of all 3GCR-GNB BSI were preceded by surveillance cultures and therefore led to escalation of empirical therapy. A surveillance-culture guided empirical therapy approach could reduce the number needed to treat with carbapenems, without compromising appropriate empirical antibiotic treatment for high risk febrile neutropenic patients.

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Abstract 7502

Use ESwab in sexually-transmitted disease diagnosis by STD Direct Flow Chip Kit

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**Background:** The aim of this study was to evaluate the use of soaked swabs (Copan ESwabs (Biomerieux)) for Sexual Transmission Disease (STD) diagnosis using STD Direct Flow Chip-Kit (Master-Diagnóstica).

**Materials/methods:** For STD Direct Flow Chip-Kit, dry swabs (DS) and soaked swabs (SS) can be used. However, only for SS is recommended an additional washing step prior to sample processing.

This study compared 200 samples: 100 DS and 100 SS parallel collected from 39 cervix and 61 urethral exudates coming from 98 patients with STD symptoms, between May-August/2019 at Hospital U. la Princesa.

Diagnosis was made using STD Direct-Flow-Chip-Kit, a molecular diagnosis test based on Multiplex PCR and automatic reverse dot blot on a Microarray Chip under DNA FLOW Technology (hybryspot). DS samples, according to manufacturer guidelines, were suspended in 1mL saline solution, vortex homogenated and concentrated by centrifugation (3’, 12,000rpm). 5µL of suspended pellet was processed. Processing SS was performed as DS removing the above mentioned washing step.

**Results:** STD Positive results: 60/100 (60%) SS and 56/100 (56%) DS. Results were analyzed considering DS as gold standard. No positive result was detected for H.ducreyi, T.pallidum, T.vaginalis and LGV.

A discrepant result in SS for C.trachomatis was confirmed in urine sample with STD Direct Flow Chip-Kit.

None discordant result Ureaplasma/M.hominis had a count >10^4 CFU/mL (Mycoplasma-IST2, Biomerieux) and 8 samples presented count >10^4 CFU/mL, all detected by DS and SS.

**Conclusions:** Please copy and paste the corresponding text here Copan ESwab would be appropriate for STD Direct Flow Chip-Kit diagnosis use, improving laboratory process, optimizing sample processing and contamination possibility. Possible major detection of STD pathogens should be considered. More studies should be performed.

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Common and distinctive genomic features of clinical and environmental third-generation cephalosporin-resistant Klebsiella pneumoniae

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Background: Third generation cephalosporin-resistant Klebsiella pneumoniae are clinically relevant pathogens also widespread in the environment. The hypothesis of this study is that the genomes and phenotypes of clinical and environmental isolates evidence some specialization to both types of habitat. To test this hypothesis clinical and environmental cefotaxime-resistant K. pneumoniae isolates were compared based on their genetic and phenotypic traits and capacity to infect the model organism Galleria mellonella.

Materials/methods: A collection of 59 isolates (25 environmental and 34 clinical) of cefotaxime-resistant K. pneumoniae were characterized based on antibiotic resistance phenotype, plasmids content, and conjugative capacity. A subset of these isolates was also tested for infection capacity in Galleria mellonella (23 environmental and 24 clinical). The whole genome sequences of a subset of clinical (n=11) and environmental (n=7) K. pneumoniae isolates together with others available in public databases (66 environmental and 67 clinical) were compared.

Results: Most environmental (80%, 20/25) and clinical isolates (94%, 32/34) were multidrug resistant. Most clinical isolates (76%, 26/34) were able to horizontally transfer part of their antibiotic resistance genes, compared with the environmental isolates (40%, 10/25). The presence of ≥2 plasmids was observed in clinical isolates (59%, 20/34) and in environmental isolates (72%, 18/25). G. mellonella health index was lower after infection with clinical isolates (10/24 scored ≤3) than with environmental isolates (5/23 scored ≤3). A screening of the whole genome sequences searching genes involved in antibiotic and metal resistance, virulence, efflux systems, oxidative stress and quorum sensing, resulted in 1,383 gene variants, 438 of which were common to clinical and environmental isolates. Both types of isolates differed in a large set of genes, with 460 found exclusively in environmental isolates and 485 in clinical isolates. The comparison of the whole genome-deduced amino acid sequences revealed a common putative proteome in environmental and clinical isolates (n=2715). Exclusive amino acid sequences were more frequent in clinical (n=577) than in environmental (n=205) isolates.

Conclusions: These results may reflect the adaptation of K. pneumoniae to environmental or clinical niches, although suggest that putative clinically relevant traits may persist in K. pneumoniae when thriving in the environment.

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**Abstract 7506**

**Antimicrobial susceptibility of Neisseria gonorrhoeae in southern Spain and co-infection with other sexually-transmitted pathogens**

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**Background:** Chlamydia trachomatis (CT) and Neisseria gonorrhoeae (NG) are the common prevalent sexually transmitted bacteria. Mycoplasma genitalium (MG) is an emerging agent of sexually transmitted infection (STI). Increasing rates of NG antimicrobial resistance is becoming a public health problem. The aim of this study is to present the most recent data on antimicrobial susceptibility of NG in Southern Spain and to describe coinfection with other STI pathogens.

**Materials/methods:** From May 2018 to November 2019, 1589 cervical and 1193 urethral exudates samples received at the Clinical Microbiology Unit of San Cecilio University Hospital (Granada, Spain) for STI diagnosis were analyzed by the FDA approved Aptima Assays (Hologic, San Diego, USA) or the RT-PCR Allplex™ STI Essential Assay (Seegene, Seoul, Korea) to CT, NG, MG and Trichomonas vaginalis (TV). Culture for NG was made in Martin Lewis broth in CO2 conditions. Susceptibility to cefotaxime, azithromycin, ciprofloxacin, tetracycline and penicillin was determined by E-test using EUCAST 2018 and 2019 breakpoints.

**Results:** NG was isolated from 157 patients (5.6%), 89% men; average age 27 years [IQR, 22-34], 136 from urethral exudates and 21 from endo-cervix. 132 cases were NG PCR/positive culture and 25 cases were NG PCR positive/negative culture. In those with positive culture, susceptibility was 64.3% to ciprofloxacin, 96.5% to cefotaxime, and 27% to penicillin and tetracycline.

From may to december 2018, azithromycin susceptibility was 78%, determined using EUCAST breakpoints 2018 (MIC values S<=0.25 mg/L; R>0.5mg/L). From 1st January 2019 following EUCAST recomendations, as the ECOFF is 1 mg/L, no resistance was found to azithromycin.

Coinfection with CT was detected in 26.1% (41/157) of patients and with MG in 4.5% (7/157); no co-detection with TV was found. Three male were CT, NG and MG co-infected.

**Conclusions:** In southern Spain, NG is highly susceptible to cefotaxime. As in another countries, susceptibility to penicillin is low. Given the low susceptibility to tetracycline and ciprofloxacin, their use should be avoided, due to the high risk of therapeutic failure. Molecular methods and monitoring of NG antimicrobial susceptibility are needed.

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Abstract 7507

**Fungal prosthetic vascular graft infections: beware of aorto-enteric fistulas!**

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**Background:** Prosthetic vascular graft infections (PVGIs) are often polymicrobial, especially when complicated by aorto-enteric fistulas (AEFs). Fungal PVGIs are rarely described in literature but quite frequent in our practice.

**Materials/methods:** We reviewed retrospectively all cases of fungal PVGIs in our retrospective cohorts (Bordeaux and Lille-Tourcoing University Hospitals) of vascular infections between January 1st, 2006 and October 31, 2019.

**Results:** Of 384 patients, 41 had a fungal infection. One patient with an abdominal aortic aneurysm complicated by AEF was excluded. Of the 40 patients (10.4%) with a fungal PVGI, 92% were men, median age was 64 years, all had an aortic PVGI and the great majority were late infections (87.5%). Mortality rate was high (55%), especially before the 28th day (25%), as early and late relapse rates, 22.5% and 20%, respectively. Only two patients were intravenous drug users, one had parenteral nutrition, six were immunosuppressed, two were splenectomised, three suffered from malnutrition including one with cirrhosis, and the last one had lung cancer. Most patients had an AEF (80%), mainly duodenal (26 patients), but also jejunal (5), and caecal (1). Two grafts were close to digestive structures (jejunum, pancreatic abscess). Bacterial coinfection was diagnosed in 90% of the cases, including 28 polymicrobial infections. Only 24 graft samples were sent to both mycology and bacteriology laboratories, fungal direct examination was positive in 13 cases. In six cases, *Candida* were exclusively isolated on mycological media (Sabouraud or/and Candida Chromogenic agar). Six patients had two and one patient had four different species of *Candida*. *Candida albicans* was clearly predominant (28 isolated strains), followed by *Candida glabrata* (8), *Candida tropicalis* (6), *Candida kefyr* (4), *Candida krusei* (2), one *Candida inconspicua*, and one "non-Candida albicans yeast". Most of patients underwent surgery (95%), only 47.5% received an empiric antifungal therapy peroperatively, mainly caspofungin. Six patients had no antifungal therapy at all, one had an early and a late relapse, one had a late relapse and two others died very early after surgery.

**Conclusions:** In PVGIs, coinfections with *Candida* sp. are frequently associated with AEF, and an empiric antifungal treatment should be introduced peroperatively in these particular cases.

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Abstract 7509

Local and national diagnostic and typing capacity for *Clostridioides difficile* infection, Europe, 2018

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Background: Suboptimal diagnostic testing for *Clostridioides difficile* infection (CDI) affects patient management, surveillance and prevention. In 2011 and 2014, ECDC ECDIS-Net surveys in 33 European countries recorded optimal diagnostic practices in 19% and 46% of the participating laboratories, respectively. In 2014, 16/32 (50.0%) countries had capillary-based (CE) PCR ribotyping capacity.

In 2017, ECDIS-Net-2 organised a ‘train-the-trainer’ workshop for European national reference laboratories promoting use of 2016 ESCMID diagnostic guidance and algorithms. This survey sought to describe European CDI diagnostic and typing capacity in 2018.

Materials/methods: In December 2018, ECDIS-Net-2 sent a web-based questionnaire on national CDI diagnostic practices, to national-level experts, designated by ECDC’s National Focal Points for Healthcare-Associated Infections, in all 34 European countries. These experts forwarded another web-based questionnaire on local CDI diagnostic practices to local laboratories in their country. In countries with >20 responding laboratories, we randomly selected 20 responses.

Results: By March 2019, 31/34 (91.2%) countries and 364 local laboratories had responded.

15/31 (48.4%) countries reported changes in national CDI diagnostic guidelines since 2014. 22/31 (71.0%) countries had diagnostic algorithm(s) in national guidelines, adopting ESCMID algorithms fully (11/22) or partially (7/22).

22/31 (71.0%) countries with national guidelines and two countries with guidelines in progress had stool selection criteria. 15/20 (75.0%) countries tested on a physician’s request, including 11/15 (73.3%) only testing diarrhoeal samples and 4/15 (26.7%) testing all stool samples. In 5/20 (25.0%) countries, local laboratories defined test criteria.

197/364 (54.1%) local laboratories in 24/29 (82.8%) countries had adopted ESCMID algorithms. In the nine countries that fully adopted ESCMID algorithms and had local laboratory responses, 93/132 (70.5%) laboratories had adopted ESCMID algorithms, while 15/132 (11.4%) had adapted them.

13/31 (41.9%) countries indicated a need for additional training in routine laboratory CDI testing.

25/31 (80.6%) countries had routine *C. difficile* typing capacity, including 21 (84%) with CE PCR ribotyping and eight (32.0%) with next-generation sequencing.

Conclusions: Europe has further improved its capacity to diagnose CDI, measure prevalence and identify subtypes, thus permitting better targeting of local and national public health actions. Countries should consider promoting and providing training on ESCMID-aligned diagnostic and typing practices.

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Abstract 7511

Impact of the anti-coagulant therapy before hospitalisation on cerebrovascular complications and mortality in infectious endocarditis

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Background: Infective endocarditis (IE) is still a highly mortal disease. The high rate of cerebrovascular complications (CVC) is one of the main reasons for this. The evidence does not support the initiation of anticoagulant therapy in IE, but many patients have an indication for it before. Intracranial hemorrhage and, therefore, mortality rate, may be increased in these patients. The aim of this study is to compare the risk of death and CVCs in patients with IE under anticoagulant therapy.

Materials/methods: Retrospective study conducted in one referral center, selecting all adult patients that had a definite IE according to modified Duke criteria from January 2013 to December 2018.

Results: One hundred thirty-two patients were recruited, 58 of them were under anticoagulant therapy before the hospitalization. Most of them (81%) were in treatment with acenocoumarol.

CVCs occurred in 55 patients (41.7%) during the active phase of IE, with the same rate in those with and without anticoagulant therapy (p=0.86). There was a non-statistical association between the previous anticoagulant therapy and the increase in the major bleeding events (p=0.23), with a bigger rate of intracerebral hemorrhage (8 vs 12%) and subarachnoid hemorrhage (7 vs 16%).

The mortality rate was 31%. There was a statistical association between the presence of previous anticoagulant therapy and the increase in the mortality rate: 20 vs 45% (p=0.004). We did not find association between the presence of CVCs and death. The group of patients that met surgery criteria but could not be operated had the highest mortality (49%, p<0.001), sixty-five percent of those had previous anticoagulant therapy. When using propensity score matching adjustment we cannot demonstrate the independent association between previous anticoagulant therapy and mortality rate: Odds ratio (OR) 1.95 (CI95%: 0.77, 4.91).

Conclusions: In our study, the presence of previous anticoagulation therapy selects a group of patients with a much higher mortality rate (45% vs 20%). This group presents a non-statistical higher rate of major bleeding events. Most of them could not be operated despite meeting surgery criteria, which is the variable that is most related to a higher mortality rate.

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Chikungunya virus: neuromotor evaluation of infants born to infected mothers
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Background: Chikungunya virus (CHIKV) is an arbovirus transmitted by the Aedes mosquitoes. The disease in humans is characterized by a disabling skeletal muscle inflammatory syndrome with fever, polyarthralgia, myalgia, rash and/or headache. Due to the recent awareness of the Zika Virus epidemic, studies have also found CHIKV poses a risk to newborns if the mother has acute viremia close to or during labor due to vertical transmission.

The Epidemiological Bulletin of Health reports that in the first half of 2019 60,987 probable cases of CHIKV were reported in Rio de Janeiro, corresponding to an incidence of 355.40 cases per 100,000 inhabitants.

In July 2019, the Health Department issued a technical note reporting the risk of CHIKV vertical transmission and included information regarding the clinical management of the newborn. Symptomatic or asymptomatic newborns to mothers with positive CHIKV test near delivery date were scheduled for an interdisciplinary evaluation at our institution.

The purpose of our report is to describe the neuromotor development of children born to mothers infected with the CHIKV during the end of their gestation.

Materials/methods: This is a prospective cohort study evaluating the neuromotor development of CHIKV-exposed children during pregnancy from July to November 2019.

Results: Fifteen infants were evaluated. Eleven were female (73%), the average age at the evaluation was 3 months. Fourteen infants (93%) were born at full-term and one was considered small for gestational age.

One child (7%) was hospitalized due to seizure following birth.

All mothers reported symptoms of CHIKV in the 3rd trimester of pregnancy. The average age of mothers was 26 years, only 4 (27%) had vaginal delivery. More than half of the mothers (60%) still complained of CHIKV symptoms at the time of the evaluation.

None of the infants presented neuromotor developmental delays or changes in reflexes or postural reactions. Muscle tone was normal in 14 infants (93%) and one was hypotonic requiring physical therapy follow-up.

Conclusions: The evaluations did not show alterations in the neuromotor development of these infants. Longitudinal follow-up is necessary to continue observing the development and delays which may become more evident at a later age.

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Abstract 7514

Comparative effectiveness of combined favipiravir and oseltamivir therapy versus oseltamivir monotherapy in critically-ill patients with influenza virus infection

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Abstract third-party references: National Key Research and Development Program of China [2018YFC1200102]

Background: A synergistic effect of combination therapy with favipiravir and oseltamivir has been reported in pre-clinical models of influenza. However, no data are available on the clinical effectiveness of combination therapy in severe influenza.

Materials/methods: Data from two separate prospective studies of influenza adults were used to compare outcomes between combination and oseltamivir monotherapy. Outcomes includes rate of clinical improvement, defined as a decrease of 2 categories on a 7-category ordinal scale, and viral RNA detectability over time. Sub-hazard ratio (sHR) was estimated by Fine and Gray model for competing risks.

Results: In total, 40 patients were treated with combination therapy and 128 with oseltamivir alone. Clinical improvement on Day 14 occurred in the combination group was higher than in monotherapy group (62.5% vs 42.2%, p=0.0247). The adjusted sHR for combination therapy was 2.06 (95%CI: 1.3-3.26). The proportion of undetectable viral RNA at day 10 was higher in the combination group than oseltamivir group (67.5% vs 21.9%, p<0.01). No significant differences were observed in mortality or other outcomes.

Conclusions: Favipiravir and oseltamivir combination therapy may accelerate clinical recovery compared to oseltamivir monotherapy in severe influenza, and this strategy should be formally evaluated in a randomized controlled trial.

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Abstract 7521

**Prospective nested case-control study on colistin-resistant Enterobacterales in the Netherlands**

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Abstract third-party references: On behalf of the CCRE survey study group in the Netherlands.

**Background:** There is a rapid emergence of multidrug-resistant Gram-negative bacteria worldwide. Importantly, polymyxins, such as colistin, are last-resort treatment options. Aim of this study was to obtain insight into the prevalence and epidemiology of colistin-resistance in the Netherlands.

**Materials/methods:** As part of a pan-European ECDC multicenter study, a 6-month surveillance project was performed with a prospective nested case-control design on occurrence, geographic distribution, population dynamics and risk factors of colistin-resistant Enterobacterales. Twenty-two Dutch participating laboratories with 36 associated hospitals were requested to send colistin-resistant *Escherichia coli* or *Klebsiella pneumoniae* (ColRE) from a maximum of five patients with a colistin MIC>2 mg/L (confirmed via broth microdilution) and/or a mcr-gene (1-8); and no carbapenem-resistance. For each ColRE isolate, a colistin-susceptible isolate (ColSE) was sent, matched on species, location of collection (hospital/community) and material of origin. Microbiological and epidemiological data were added.

**Results:** In total, 74 ColRE and 67 ColSE isolates from 16 laboratories were collected. Of the ColRE, 72% were *E. coli* and 28% *K. pneumoniae*. The majority was derived from urine samples (70%). Of all ColRE isolates, 60% were collected in a hospital, 32% at a general practice and 8% in other healthcare facilities. Only four ColRE isolates contained a mcr-1 gene (5%). When comparing ColRE-ColSE pairs (*n*=67), the median age was 70 years old in both groups and the proportion of females was similar (ColRE: 75%; ColSE: 70%). Of the ColRE isolates, 68% was reported as infection, similar to 64% in the ColSE group. Of patients with ColRE isolates, 30% had used colistin and 82% other antibiotics in the previous 6 months, which was more than the 7% colistin and 50% other antibiotics observed in the ColSE group (*p*=0.026 and 0.013, respectively). Twenty-three percent of ColRE and 7% of ColSE isolates were from patients that resided in long-term care facilities (*p*=0.044).

**Conclusions:** Seventy-four ColRE isolates were sent by 16 of 22 participating laboratories. The majority of ColRE isolates were *E. coli* and did not contain known mcr-genes. Patients with ColRE had used more colistin and other AB and/or resided more frequently in long-term care facilities compared with patients with ColSE.

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**Abstract 7523**

**Evaluation of the efficacy of rezafungin in the treatment of Candida albicans endophthalmitis using a rabbit model**

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**Background:** Candida endophthalmitis is a devastating disease. Echinocandins are first-line therapy for candidemia and invasive candidiasis, however, due to poor penetration of currently approved echinocandins into the eye, once Candida eye involvement is demonstrated, current guidelines recommend a switch to azole therapy. The aim of this study was to evaluate the efficacy of rezafungin, a novel echinocandin with unique PK properties, in the treatment of endophthalmitis in a rabbit candidiasis model.

**Materials/methods:** New Zealand White rabbits with indwelling catheters were inoculated intravenously with $5 \times 10^6$ colony-forming units (CFU) of *Candida albicans* SC5314 and divided into groups: rezafungin 10mg/kg (n=6), micafungin 6.2mg/kg (n=5), voriconazole 10mg/kg (n=4) and vehicle control (n=5). Treatments were administered IV at 0 and 80h post-inoculation. Day 8, the rabbits were anesthetized and indirect ophthalmoscopy performed. Tissues were collected for assessment of fungal burden. Eye scores were given based on the number and size of lesions and total ocular damage caused by infection. The severity of each lesion was scored on a 1-4 scale: 1+, lesion barely visible; 2+, lesion small but easily visible; 3+, lesion large but less than one disk diameter in size; and 4+, lesion larger than one disk diameter.

**Results:** In the kidneys, the voriconazole and vehicle groups had the highest CFU counts, while the rezafungin group showed the lowest [Fig. 1A]. The rezafungin- and micafungin–treated groups showed significantly lower bioburden when compared to the voriconazole and vehicle groups ($P<0.001$). In the retina, humor body, and vitreous humor, the greatest bioburden was observed in vehicle control-treated animals as expected. Animals treated with rezafungin demonstrated no detectable CFU. The rezafungin–treated group compared with the micafungin, voriconazole and vehicle groups showed significantly fewer CFU in the retina ($P<0.05$), humor body ($P<0.001$), and vitreous humor ($P<0.05$). Eye Score—The rezafungin-treated group demonstrated no eye lesions [Fig.1B], while the micafungin, voriconazole and vehicle [Fig.1C] groups showed average eye scores of 1.9, 2.5, and 3.2, respectively.

**Conclusions:** Our findings show that rezafungin is effective in the treatment of endophthalmitis caused by *C. albicans*.

**Figure 1.** Average log CFU/g ± SD fungal burden in tissue (A). Evaluation of lesions in the rezafungin-treated group (B) and those treated with micafungin, voriconazole, or vehicle (C).

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Background: Globally, Choosing Wisely® campaigns warn against the overtreatment of asymptomatic bacteriuria. Regardless, clinicians often prescribe antibiotics to patients with evidence of bacteriuria or localized inflammation on urinalysis independent of localizing symptoms. This study examines leukocyte deformability, a measure of host immune activation, for predicting outcomes of patients presenting to the Emergency Department (ED) due to a genitourinary process.

Materials/methods: We enrolled 120 adult patients presenting to the ED with signs or suspicion of genitourinary infection. Demographic, clinical, and outcome data were abstracted from the medical record. EDTA-anticoagulated blood was analyzed using deformability cytometry [1]. Treating clinicians did not have access to assay results. Patients were stratified into three categories of immune activation: low, intermediate, and high. Chi-square and Mann Whitney U tests were used.

Results: Of the 120 patients, 40 (33.3%) were classified as low, 47 (39.2%) as intermediate, and 33 (27.5%) as high states of immune activation. Patients in the high immune activation group were older than patients in lower immune activation groups. There were no significant differences in positive urine cultures, hematuria, or pyuria across the three groups. Patients in the high immune activation group had significantly higher admission rates, lengths of stay, positive blood cultures, severity of illness scores (APACHE, SOFA and PIRO), as well as hospital mortality (Figure 1). Patients in the high immune activation group (87.9%) were more likely to receive antibiotics. However, 55% of patients in the low immune activation group and 66% of patients in the intermediate immune activation group also received antibiotics.

Conclusions: Leukocyte deformability can risk stratify patients with genitourinary processes by important clinical outcomes, independent of pathogen detection and urinalysis. Examining host immune activation could result in reduced antibiotic exposure and improved hospital resource utilization.


Figure 1. Outcome data for the Low, Intermediate, and High Immune Activation (IA) Groups. Note: *p<0.05, **p<0.01, ***p<0.001

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Abstract 7532

Rectal isolates display high-negative predictive value for bloodstream infections with (ESBL+) Gram-negative bacteria in neonates with suspected sepsis in a low-resource setting neonatal care unit

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Background: There is scarce evidence around the potential value of understanding bacterial colonization in neonates in guiding empiric treatment for neonatal sepsis. We aimed to analyze the concordance of rectal swab isolates and blood culture isolates with gram negative bacteria (GNB) in neonates with suspicion of neonatal sepsis in Port au Prince, Haiti.

Materials/methods: Due to repeated outbreaks of sepsis in a neonatal care unit in an obstetric emergency hospital between 2014 and 2018, we enhanced microbiological and epidemiological surveillance for all neonates with suspected sepsis after admission. We analyzed data from rectal and blood samples that were taken simultaneously, on the date of onset of suspected sepsis and before the administration of antibiotics. Samples were cultured and tested for antibiotic susceptibility. We calculated the concordance for GNB genus and species of rectal and blood pair isolates. We also calculated the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for GNB and Extended Spectrum Beta-Lactamase (ESBL) producing (ESBL+) GNB for all rectal and blood pair isolates.

Results: We included 238 rectal-blood pairs with 238 and 309 microbiological results from blood and rectal samples respectively; 171 pairs (72%) had a single isolate or no isolate identified in either sample. Klebsiella sp. isolates were the most commonly isolated bacteria from all samples (160/313 isolates). Concordance between blood and rectal isolates was 21% (95%CI:16-26) and 22% (95%CI: 17-28) for species and genus respectively. For GNB and ESBL+GNB isolates we estimated: sensitivity (84%, CI95%:70-93 and 71%, CI95%:59-85), specificity (16%, CI95%:11-22 and 61%, CI95%:54-68), PPV (19%, CI95%:13-25 and 23%, CI95%:16-33) and NPV (82%, CI95%:66-92 and 93%, CI95%:87-96).

Conclusions: Our analysis shows that rectal swab cultures can have added value in choosing and adjusting antibiotic therapy due to the high NPV for mainly ESBL+ GNB. Therefore, the use of rectal swab microbiological surveillance in neonates can improve prudent antibiotic use and stewardship neonatal care units in low resource settings. We recommend that these findings are validated in other contexts in neonatal care settings.

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Abstract 7538

Susceptibility profile of Pseudomonas species in a tertiary care hospital over a 9-year period and impact of antimicrobial stewardship

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Background: Novel therapeutic options can be helpful, but many older molecules are still effective depending on the susceptibility profile. Resistance pattern of Pseudomonas spp. (Ps) is very variable making aggregate data analysis complicated.

Materials/methods: We retrieved from the antimicrobial stewardship (ASP) database at Saint George Hospital (SGH), a 333-bed tertiary care center in Lebanon from January 2010 till December 2018:

- the susceptibility profiles of all recovered Ps isolates
- the antibiotic consumption expressed in daily defined dose [DDD]/1000 PD.

Isolation density is the number of isolates/1000 patient days [PD]. All identified isolates were then categorized according to the Centers for Disease Control and Prevention definitions: multidrug-resistant (MDR), extensively drug-resistant (XDR) and pandrug-resistant (PDR). We compared the rates of resistance on antimicrobial consumption for period 1 (2010-2014) vs. period 2 (2015-2018).

Results: The isolation density of Ps significantly decreased from an average of 5.57/1000PD for the years 2010-2014 of whom 0.19 were PDR to 3.34/1000PD for the years 2015-2018 of whom 0.07 were PDR (p-value= 0.006, CI 95% [0.872, 3.583]). The rest were roughly equally divided between MDR and XDR. The yearly detailed resistance profile is illustrated in figure 1. Carbapenems consumption significantly dropped in period 1 from 176 to 126 DDD/1000PD in period 2 (p-value=0.031, CI 95% [0.026, 0.035]). 51% of the isolates carbapenems were resistant in period 1 vs 47% in period 2. Piperacillin/tazobactam consumption was stable 30 vs 31.4 DDD/1000PD in period 1 and 2 with 32% of the isolates TZP resistant in period 1 vs 21% in period 2. Cefepime consumption dropped from 31.4 to 21.2 DDD/1000PD with 24% cefepime resistant in period 1 vs 16% in period 2.

Conclusions: There have been many reports describing an alarming rise in pseudomonas resistance. In our institution, there has been a significant drop in pseudomonal burden of disease with relatively very few isolates with limited therapeutic options and even more interesting a significant improvement in the overall resistance pattern over the last 4 years maybe due to an improvement in antimicrobial consumption.

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Abstract 7542

Posaconazole therapeutic drug monitoring in high-risk haematology patients receiving antifungal prophylaxis (SAPHIR-study)

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Background: The SAPHIR study described the diagnostic and therapeutic management of haematology patients at high risk of Invasive Fungal Disease (IFD) under antifungal prophylaxis (AFP) in France. We evaluated therapeutic drug monitoring (TDM) adopted in French haematology services during this study.

Materials/methods: SAPHIR was an observational, prospective, multicentre, non-comparative study. The included patients were ≥18 years, in a context of myelosuppressive chemotherapy for acute myeloid leukaemia and initiated an AFP treatment.

Results: 404 patients were included (mean age: 56.4±14.0 years). The intensive chemotherapy started 1.06±4.49 days before inclusion and was either induction 79.0%, consolidation 12.6% or treatment of relapse 8.4%. 91.6% patients had experienced a profound and durable neutropenia period with 1.08±0.51 periods during 23.3±16.6 days. For 373 patients (92.3%), the primary AFP prescribed was posaconazole using either tablets (366 patients, 98.1%), or suspension (7 patients, 1.9%). The mean AFP period was 24.2±32.1 days. Twelve of 23 participating services performed TDM during the patients’ AFP period. Therapeutic target was defined as plasma trough levels (PTL)>0.7 mg/L for prophylaxis. A total of 278 posaconazole PTLs were measured in 139 patients (1 to 10 PTLs per patient). Median posaconazole PTL achieved during AFP was 0.94 mg/L (IQR: 0.6-1.5). PTLs were not different in patients with concomitant mucositis or diarrhoea. 29% of the patients whose PTLs were measured after AFP initiation (median=6 days) had concentrations <0.7 mg/L. After AFP period, 267 patients (66.8%) stopped AF treatment because they were at the end of the high-risk period and 126 (31.2%) switched to a non-prophylactic AF treatment (2/3 empirical, 1/3 pre-emptive/curative), mainly because of fever (67.1%). Among these 126 patients, posaconazole PTLs were measured in 57 patients before AFP stopping (median=3 days), 16 patients (28%) presented a PTL<0.7 mg/L.

Conclusions: This real-life study of AFP in France shows that half of services use posaconazole TDM. Almost 30% of patients undergoing TDM have concentration below the target. The prevalence of patients with posaconazole concentration <0.7 mg/L reported in our study with posaconazole tablets is higher than early observational studies. Parameters associated with this lower probability have to be explored.

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Evaluating the extraction and molecular detection of *Candida auris* strains using commercial kits

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**Background:** *Candida auris* is a multidrug resistant, emerging agent of invasive fungal infection in the intensive care setting, and has been responsible for recent outbreaks in healthcare institutions. Real-time PCR methods for the detection of *C. auris* could provide quick results for both colonisation and infection, help to control spread in the clinical setting and, with accurate identification, could lead to more appropriate patient management.

**Materials/methods:** A diverse sampling of *Candida auris* strains collected worldwide were grown from glycerol stocks in 5 mL of Sabouraud broth and streaked on Sabouraud agar. Strains were grown for 24 hours at 37°C. Following incubation, serial dilutions of 1/10, 1/100 and 1/1000 of each *C. auris* strain were prepared and extracted using three different extraction methods; (i) Qiagen's manual DNeasy PowerLyzer Microbial Kit, (ii) Hain Lifescience's manual FluoroLyse Kit, and (iii) Qiagen's automated EZ1 extraction platform with a DSP Virus Kit. PCR was carried out using Bruker’s Fungiplex Candida Auris RUO Real-Time PCR Kit.

**Results:** No target was detected after extraction using the Qiagen DNeasy PowerLyzer Microbial extraction kit and in all of these samples the internal control failed, highlighting inhibition within the PCR reaction.

*Candida auris* was detected in all samples extracted using both the Hain Lifescience FluoroLyse Kit and the Qiagen DSP Virus Kit for the EZ1. As expected, Ct values increased with increasing dilution factor. When comparing the results from each of the successful extraction methods, Ct values were higher in gDNA samples extracted using the EZ1 system with differences ranging from 2 to 5 Cts higher than the manual extraction values, suggesting that the manual system is more efficient at extracting gDNA compared to the automated platform.

**Conclusions:** This study has shown that the extraction method used in the molecular detection of *Candida auris* is critical. It is clear from comparison of Ct values between a manual and an automated system that the Hain Lifescience manual extraction FluoroLyse kit is more efficient in extracting gDNA compared to the EZ1 system. When extraction was successful, a sensitivity of 100 % was achieved with the Fungiplex Candida Auris Kit.

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Abstract 7551

Emergence of “high risk clone” Klebsiella pneumoniae ST307 producing KPC-3 and NDM-1 in Argentina

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Background: KPC carbapenemase production constitutes the main resistance mechanism in K. pneumoniae. KPC-K. pneumoniae global expansion has been associated with the clonal dissemination of ST258, however the emergence of new lineages was observed in Argentina. Less frequently KPC has been reported in other Enterobacterales. Also, an increased detection of NDM metallo-enzymes is been observed in our region. Objective: to characterize carbapenem resistant Enterobacterales isolates recovered from inpatients at a hospital in Buenos Aires city, during Nov 2018 - March 2019.

Materials/methods: Antimicrobial susceptibility to clinically relevant antibiotics was assessed by automated system (Phoenix, BD). Coding genes for VIM, IMP, SPM, NDM, KPC, OXA-48 were screened according to Poirel et al, 2011. Further identification of carbapenemase coding genes was performed by complete gene amplification, using plasmid DNA as template, and sequencing. KPC-K. pneumoniae typing was conducted by XbaI-PFGE and MLST. Plasmids were characterized by conjugation assays using E. coli J53 as receptor strain and replicon typing according to Carattoli et al, 2005. Genetic contexts of carbapenemase coding genes were studied by PCR mapping and sequencing.

Results: Eight carbapenem resistant isolates were included (7 K. pneumoniae and 1 Providencia stuartii). They were resistant to ciprofloxacin, levofloxacin and gentamicin and 5/8 were resistant to amikacin. Minimal inhibitory concentration for colistin was >4µg/ml. Six out of 8 isolates harbored carbapenemase coding genes. Among carbapenemase producing K. pneumoniae isolates 2 pulsetypes were observed, belonging to ST258 (n:1) and ST307 (n:4). Three out of 4 K. pneumoniae-ST307 harbored blaKPC-3 and blaNDM-1 and the remaining harbored blaKPC-3. K. pneumoniae-ST258 was positive for both blaKPC-2 y blaNDM-1. In P. stuartii only blaNDM-1 was detected. All blaNDM-1 plasmids were transferred by conjugation and corresponded to IncA/C group. ISKpn14 was detected upstream blaNDM-1 and bleMBL and trpF were detected downstream. Genetic context for both blaKPC-2 and blaKPC-3 corresponded to Tn4401.

Conclusions: The presence of the "high risk clone" K. pneumoniae-ST307 producing both KPC-3 and NDM-1 constitutes a worrisome scenario, as this clone combines hypervirulent and resistance features making it difficult to eradicate. The presence of blaNDM-1 plasmid in different species and lineages indicates the epidemic feature of this mobile element.

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Abstract 7553

Preclinical evaluation of liposomes carrying bioactive lipids as an immune therapeutic tool against in vitro and in vivo infection with Mycobacterium abscessus

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Background: MA abscessus (MA) in an emerging pathogen that affect individuals with lung pathologies such as chronic obstructive pulmonary disease (COPD), bronchiectasis and, especially, cystic fibrosis (CF). Apoptotic-body like liposomes (ABLs) carrying bioactive lipids have been demonstrated to significantly enhance bactericidal response in macrophages from CF patients and in bronchoalveolar lavage (BAL) cells from non-CF patients with pneumonia caused by different bacterial pathogens, irrespective of bacterial species and multidrug resistance. Our murine model of MA respiratory chronic infection was useful to assess the therapeutic effect of different ABLs against this pathogen. Furthermore the MA infection in vitro allowed us to study the mechanism of action of ABLs on macrophages phagocytosis mechanism.

Materials/methods: We established a chronic pulmonary infection in immunocompetent C57Bl/6N mice up to 36 days with MA ATCC 19977 and at different time point mice were treated with 3 different ABLs [PA, PI3P and PI5P]. Mice lungs were processed for microbiological and inflammatory analysis to establish the therapeutic effect of ABLs. We set up in vitro MA infection on human macrophages to investigate the effect of ABLs on phagocytes mechanism. We set up infection.

Results: In vitro results showed that ABL/PA, PI3P and PI5P were able to statistically increase the phagocytic and the intracellular microbicidal activity of human macrophages infected with MA. The in vivo experiments revealed that after 30 days of treatment all the 3 ABLs induced a statistical reduction of bacterial count in the total lung when compared to the control mice. The results also revealed that these 3 immunomodulatory compounds induced a statistical reduction of the recruitment of total leukocytes, in particular of neutrophils and macrophages, into the bronchoalveolar lung spaces compared to the control mice. Despite the absence of effect in granuloma reduction at parenchymal level, analyzed by histological lung sections, ABLs were also able to statistically decrease the IFNy production during the course of treatment.

Conclusions: ABLs treatment statistically reduced both lung’s bacterial burden and inflammatory response during chronic MA infection. ABLs, combined with an antibiotic therapy, could represent a novel immunotherapeutic strategy to treat pulmonary infection induced by drug-resistant MA.

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Monitoring of interactions with clarithromycin: evaluation of routinely performed drug interaction checks
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Background: Clarithromycin is a potent inhibitor of cytochrome P450 (CYP) 3A4, which is involved in the metabolism of commonly used drugs. Therefore, clarithromycin may increase the steady state concentrations of drugs that depend primarily on CYP3A4 metabolism.

Materials/methods: Every order of clarithromycin tablets or infusion in the pharmacy department of the Munich university hospital triggers a check for interactions of clarithromycin with the co-prescribed medication. Information on the medication are obtained by contacting the ward over the phone or - if available – retrieved from the electronic medication record. Whenever a relevant drug interaction was identified, a pharmacist contacted the prescriber to discuss the interaction and its management (e.g. discontinuation of a drug, monitoring of serum levels or side effects). Each check was documented in the drug information database and a written information was provided to the prescriber if requested. The clinically relevant interactions were classified according to Lexicomp® Drug Interactions Database into three categories (X = contraindicated; D = avoid combination; C = monitor therapy).

Results: From August 2014 to July 2017, 1160 checks were performed, 829 (71.5%) contained at least one interaction with clarithromycin. Each patient took on average 9.2 drugs (1 – 31) and had 1.4 interactions with clarithromycin. 330 (28.4%) drug regimens contained at least one X-rated drug. Of the 1891 identified interactions 397 (21.0%) were rated as X, 960 (50.8%) as D and 395 (20.9%) as C. 139 interactions (7.3%) were not rated as the drug was not included in the database but were regarded as relevant. The most commonly prescribed X-rated interactants were simvastatin (150, 12.9%), apixaban (44), and (es-) citalopram (40). Other highly relevant interactants included azole antifungals (87), tacrolimus (47), phenprocoumon (28), and colchicine (4). A preliminary evaluation of the effect of the counselling showed an inconsistent implementation of the recommendations.

Conclusions: Though the risk for relevant drug interactions is established, it is not always accounted for when prescribing clarithromycin. There is a need for active interaction testing in clinical practice. Measures need to be taken to raise awareness of the importance of the problem and ensure appropriate implementation of recommendations made.

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Abstract 7555

**Improved prediction of mortality in sepsis using peripheral capillary oxygen saturation to estimate the respiratory dysfunction score: a cohort study**

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**Background:** The Sepsis-3 criteria are based on sequential organ failure assessment (SOFA) score, which was developed for intensive care units (ICU). Yet, more than half of sepsis patients are admitted to other hospital wards where possibilities to assess full SOFA-score is limited. The respiratory component of SOFA is based on PaO2/FiO2 ratio, which requires arterial blood gas analysis. Peripheral capillary oxygen saturation (SpO2) is a more accessible measure, but this has not been validated in the Sepsis-3 criteria. Current methods to translate SpO2 to PaO2 results in cut-offs at SpO2 96 or 95% without oxygen treatment to get 1 SOFA point. The aim was to assess the association between SpO2 and in-hospital mortality in a population with suspected infection outside ICU.

**Materials/methods:** Subjects were identified in electronic health records from Karolinska University Hospital between July 2012 and December 2013. All adult patients admitted for >24-hours with a suspected infection, defined as any culture taken and administration of at least 2 doses antimicrobials, were included. Time during ICU was censored. Patients were followed until discharge or death. Logistic regression was used to assess the association between worst SpO2 and in-hospital mortality, adjusted for age, gender, comorbidity and other SOFA-score components.

**Results:** In total, 19396 admissions in 14871 patients were included, and 17805 had at least one SpO2 measurement coinciding with the time of suspected infection. The in-hospital mortality was 5.4%. Compared to SpO2 100-97% (reference), SpO2 96 or 95% were not significantly associated with increased mortality. At SpO2 94%, the odds ratio for mortality was 1.62 [95% CI 1.13-2.31] and increased gradually below this level (Figure). The findings were robust to sensitivity analyses and preliminary results shows adding information on oxygen delivery (SpO2/FiO2-ratio) didn’t improve predictability.

**Conclusions:** Current cut-offs for respiratory dysfunction in Sepsis-3 using SpO2 does not seem to be associated with increased mortality in the non-ICU setting. Our results support a gradually increased mortality starting from SpO2 94% and less, which could have implications for SOFA-scoring to define sepsis in the non-ICU setting. These findings are planned to be validated in a prospective cohort with suspected sepsis in Sweden.

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Abstract 7556

**Bridging the gap between human and animal antimicrobial resistance and consumption surveillance data, antibiotic policy and stewardship: the EPI-Net and ARCH projects**

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**Background:** Guidance on how surveillance data on antimicrobial resistance (AMR) and consumption (AMU) should be provided to stewardship teams to drive empiric therapy, policy recommendations and whether a One-Health approach could be practically implemented is unclear.

**Materials/methods:** The COMBACTE-Magnet EPI-Net and JPIAMR projects joined their networks to connect multisector specialists in human and animal settings aiming to bridge the gap between human and animal surveillance data, antibiotic policy and stewardship (ARCH) by studying surveillance of AMU, AMR and frontline AS providers. We carried out a scoping review of the literature (January 2009-June 2019) to draw up a list of actions addressing 3 topics: AS team, AMU and AMR surveillance data throughout both animal and human settings (i.e. hospital, outpatients, long term care facilities-LTCF, and veterinary clinics). Evidence were provided to experts from 34 international networks from high and low medium income countries in a two round RAND-modified Delphi. The panel evaluated the sets of actions based on criteria of relevance, feasibility, and adaptability. Agreement was expressed on a 9-point Likert scale. Then, a 2-day face-to-face consensus meeting was held to discuss results, finalise the recommendations and expand the list of research priorities.

**Results:** A total of 189 papers were reviewed. 32 statements were developed for the hospital, 18 for the outpatient, 19 for the LTCF, and 65 for the animal settings. Recommendations were classified as essential [37] or desirable [32] according to clinical relevance, feasibility and applicability to settings and resources. Agreement was reached for 116 statements; 18 concerning modalities of AMR monitoring were qualified for discussion [median score ≥8 but <70% of all scores in the highest tertile]. 19 statements were deleted after first review and recommendations on topics for future research agenda were developed and agreed.

**Conclusions:** The EPI-Net/ARCH set of actions represents a new, practical and flexible tool to guide the development of calibrated AS intervention in human and animal settings based on surveillance systems collecting AMR and AMU data. The advantage of the tool relies in the One-Health approach used in a practical way to synergize and connect adequate decisions on AS in different compartments.

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Co-existence of blaNDM- and mcr-1-producing Escherichia coli isolated from human, poultry and environment water from Pakistan: a One Health problem

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Background: Emergence and spread of New Delhi metallo-β-lactamase (NDM) and mcr-1 producing Escherichia coli is a serious “ONE HEALTH” threat around the globe particularly in developing countries like Pakistan. NDM producing bacteria showed resistance against multiple antibiotics. mcr-1 is a novel plasmid-mediated gene conferring resistance to colistin which is considering a last resort to treat clinical infection caused by carbapenem resistant pathogens. The aim of the study was to determine the prevalence of both blaNDM and mcr-1 producing E. coli in different settings.

Materials/methods: A 100 each poultry cloacal swabs, environmental water and human samples (blood, urine, pus) were collected from Faisalabad metropolitan. Samples were screened for NDM and mcr-1 producing E. coli using colistin and meropenem (4μg/mL) containing MacConkey agar. Further, isolates were confirmed using UTI ChromoSelect agar and API 20E. Antibiogram and phenotypic confirmation of carbapenemase and metallo-β-lactamase was carried out as per CLSI 2018 guidelines. Molecular identification of mcr-1 and NDM gene was performed by PCR.

Results: Of 100 poultry samples; 22 E. coli were positive for mcr-1. Of 100 water samples, 17 E. coli were NDM producers and 4 were positive for mcr-1. Of human samples, 15 E. coli were NDM producer and none for positive for mcr-1. E. coli from poultry displayed 100% resistance to colistin, tetracycline and doxycycline and 31% to cefepime while 83% sensitive to meropenem. E. coli from water samples also displayed 100% resistance to β-lactam, β-lactam inhibitors followed by 88% to meropenem and 73% to ciprofloxacin while 90% to colistin. Moreover, NDM producing E. coli from human samples also displayed 100% resistance against β-lactam and inhibitors and 80% to levofloxacin moxifloxacin and all were sensitive to colistin.

Conclusions: Dissemination of blaNDM and mcr-1 producing E. coli from clinical, poultry and environmental water is a matter of great concern for both livestock and public health. A “One Health” approach is necessary to further explicate the variability of these high-risk genes.

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SAVE: Stewardship Antibiotica VErona: a new model of stewardship to reduce antimicrobial overuse in a setting with high levels of antimicrobial resistance rates

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**Abstract 7559**

**Background:** According to the ECDC estimates, Italy is the country with the highest burden of disease due to antimicrobial resistance (AMR) in Europe. Aim of this study is to measure efficacy and safety of a new model of antimicrobial stewardship (AS) intervention in reducing inappropriate use of antibiotics in a 1350-beds University hospital with high AMR rates.

**Materials/methods:** The SAVE program is a 12-months, multifaceted, educational AS intervention with a stepped-wedge implementation started in June 2018. The core elements of the intervention are: 1. provision of a full time ID specialist to the intervention ward for 6 weeks; 2. mandatory CME-accredited training for at least 2 physicians per intervention ward; and 3. development of customized guidance on empirical antibiotic therapy followed by periodic audits and feedbacks. Primary outcome of the study is the overall consumption of systemic antibacterials (ATC-J01) per 1000 patient-days (PDs) measured as Days of Therapy (DOTs) and Daily Defined Doses (DDDs) with an interrupted time series (ITS) analysis over a 24-months period. Secondary outcomes are rate of inappropriate therapy (compliance with local guidance documents); single classes’ DOTs and DDDs. As clinical indicators we measured *Clostridium difficile* infections and crude in-hospital mortality.

**Results:** Four medical wards with a total of 150-bed completed the intervention, 8 non-ID physicians were trained in antibiotic prescribing, 1113 prescriptions were revised, and inappropriateness decreased by 13.8%. A significant change in level of overall antibiotic consumption was measured both in terms of DOTs/1000 PDs (-160.5; p<0.05) and DDDs/1000 PDs (-181.4; p<0.05). Comparison between pre- and post-intervention slope showed a reduction in DDDs/1000 PDs per month (-16.2; p<0.05) and in DOTs/1000 PDs per month (-1.5; p 0.08). Level of fluoroquinolones consumption decreased significantly by 24.2 DOTs/1000 PDs (p<0.05) with a significant drop in slope (-4.4 DOTs/1000 PDs per month; p<0.05). Rates of mortality and *C. difficile* infections remained stable throughout the post-intervention period.

**Conclusions:** The SAVE intervention demonstrated to be effective and safe in reducing antimicrobial consumption and increasing appropriateness of prescription in internal medicine units. Although promising, generalizability of the model and cost effectiveness must be further explored in different clinical and cultural settings.

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**Abstract 7560**

**Gut colonisation with carbapenemase-producing Enterobacterales: predicting factors for prolonged colonisation among adults**

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**Background:** The spread of CPEs represents a major public health issue. As 10% of CPE carriers will develop a CPE infection it is important to understand the risk factors for colonisation and for prolonged colonisation. The aim of this work was to follow a cohort of colonised patients over one-year period to identify predicting factors for prolonged colonisation.

**Materials/methods:** This is a two years mono-centric prospective observational study. Patients newly colonised starting 2017 were included. Rectal swabs were taken during their hospitalisation, once a week, and at every novel hospitalisation or consultation. The following definitions were used: Non-Excretors (NE) are patients with 3 negative rectal swabs in three consecutive weeks and Excretors (E) are patients with positive CPEs culture from their rectal swabs. Comorbidities, reasons for hospitalisation, antibiotic treatment and length of hospitalisation were recorded.

**Results:** 109 patients colonised CPE (44F/65M) were included in the study. 124 bacteria were isolated: E. coli (60), K. pneumoniae (47), E. cloacae (7), C. freundii (10). The detected carbapenemases corresponded well to the French epidemiology of CPEs: OXA-48-like (95), NDM-like (20), and KPC-like (9). 35 patients were lost during follow up. The number of NE was 21/74 (28%), 27/74 (36%), 36/74 (49%) and 40/74 (54%) at 1, 3, 6 and 12 months, respectively. The NEs were initially colonised with NDM 4/20 (20%), OXA-48like 29/60 (48%), KPC 7/9 (77%). 34 patients remained Es after 12 months (46%). Characteristics of Es and NEs at 12 months are displayed below.

<table>
<thead>
<tr>
<th>Characteristics of patients at 12 months</th>
<th>Excretors</th>
<th>Non-excretors</th>
<th>P value (kh2)</th>
</tr>
</thead>
<tbody>
<tr>
<td># of patients</td>
<td>34</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Median age (years)</td>
<td>72</td>
<td>74</td>
<td></td>
</tr>
<tr>
<td>Charlson score</td>
<td>6</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Reasons of hospitalisation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection with non-CPE</td>
<td>8 (24%)</td>
<td>4 (10%)</td>
<td></td>
</tr>
<tr>
<td>Neurological disorder</td>
<td>10 (29%)</td>
<td>7 (17%)</td>
<td>0.22</td>
</tr>
<tr>
<td>General surgery</td>
<td>7 (21%)</td>
<td>5 (13%)</td>
<td>0.35</td>
</tr>
<tr>
<td>Orthopaedic surgery</td>
<td>8 (24%)</td>
<td>2 (5%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Heart and lung disorder</td>
<td>14 (41%)</td>
<td>9 (23%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Antibiotic treatment</td>
<td>14 (41%)</td>
<td>10 (25%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Median length of hosp (days)</td>
<td>30</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Infection with CPE</td>
<td>10 (29%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** In our cohort, 1/3 of the patients spontaneously became NEs after one month, and nearly ½ after 12 months. Statistically significant predicting factor for prolonged colonisation was orthopaedic surgery. Thus, our data suggest that prolonged carriage depends on factors inherent to the patients [length of hospitalisation and underlying pathology] but also on the bacteria. Indeed, it seems that OXA 48-like or NDM producers are linked to a prolonged carriage. Our results need to be confirmed in larger studies.

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Abstract 7561

**What are the reasons behind high handrub consumption? A national in-depth qualitative assessment**

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**Background:** Hand hygiene (HH) is the most important prevention measure of healthcare-associated infections (HAI) and transmission of multidrug-resistant (MDR) bacteria. Significant correlation between alcohol-based handrub consumption (AHRC) and observed HH compliance rates - and between AHRC and MDR bacteria reduction - has been established. In France, publicly-reported AHRC displayed a large heterogeneity across healthcare facilities (HCFs). The present study aimed to assess factors and mechanisms leading to a high AHRC score in a panel of French HCFs and to describe programs in the top and medium scorers.

**Materials/methods:** Qualitative comparative case study based on semi-structured, in-depth interviews of the Infection Prevention and Control Team (IPCT) members (n=67), quality managers/CEOs (n=20) and frontline workers (n=5) of the 16 highest scoring HCFs (4 university hospitals (UH), 4 large non-university hospitals, 3 cancer centers and 5 rehabilitation hospitals), and 7 medium scoring UH, using an iterative thematic approach.

**Results:** 84 interviews were performed. There was a large heterogeneity in IPCTs’ structures and objectives with specific patterns associated with high AHRC. Four meta-themes emerged: strong IPCT internal organization; external organization with integration into the hospital; active support from the institution; and leadership and role models. The following factors were associated with top scorers: a good intrinsic IPCT organization with joint activity of IPC physicians and nurses; a proactive attitude in defining priorities and anticipation; a continuous IPCT presence in clinical wards with adaptation to local context, time or staff constraints; involvement of link nurses; active participation in an IPC hospital network; institutional support and the role of “champions” (with the highest impact in small HCFs). Agreement with the national AHRC indicator was variable among IPCT members, with top scorers using the score as a tool for change and medium scorers frequently doubting its value.

**Conclusions:** This qualitative study highlights that IPCT structure and activity is heterogeneous, with mainly behavioral characteristics associated with high AHRC score. Our work enhances the importance of strong IPCT structure and behavioral approaches in implementing key IPC programs. It offers material to rethink IPCT’s functioning with several strategies for improvement.

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Abstract 7562

Study on the diagnostic value of serum amyloid A (SAA) in pathogen classification and clinical stage identification of hand, foot and mouth disease

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Background: To explore the titer distribution characteristics of SAA in the main enteroviral types of hand, foot and mouth disease and its relationship with severe cases, so as to provide a new reference for the diagnostic value of SAA in hand, foot and mouth disease.

Materials/methods: A total of 815 laboratory confirmed cases of HFMD in our hospital during the epidemic period of 2017-2018 were randomly selected as the study objects. SAA level was detected by turbidimetry, and EV71, CA16, CA6, CA10 and other enteroviruses of HFMD were detected by fluorescence quantitative RT-PCR. SAA was statistically analyzed with enterovirus typing, clinical staging and other relevant indicators.

Results: The SAA values of EV71 (n=108), CA16 (n=39), CA6 (n=472), CA10 (n=63) and the unclassified enteroviruses (n=133) were 13.85 (8.2, 37.05) mg/L, 73.10 (25.7, 158.3) mg/L, 156 (122.1, 176.6) mg/L, 148 (131.172.9) mg/L and 146.9 (121.9, 171.5) mg/L respectively. The titer difference of SAA among common enterovirus types was statistically significant (kruskal-wallis value: 204.94, p=0.000). The AUC of SAA for the diagnosis of EV71 HFMD was established as 0.907 (95%CI:0.884-0.926). SAA= 92.1 ml/L was taken as the threshold, with a sensitivity of 93.52% and specificity of 81.05%. The SAA values were 17.00 (5.80, 24.30) mg/L in critical cases (n=11), 18.00 (9.30, 49.90) mg/L in severe cases (n=82), 148.90 (112.20, 174.60) mg/L in mild cases (n=722) respectively, and the difference among them was statistically significant (kruskal-wallis value: 119.882, p=0.000). With the clinical stage of severe and above as the dependent variables and SAA, enterovirus typing, gender and age as the independent variables, the binary Logistic regression analysis showed that EV71 was highly correlated with severe HFMD (p < 0.05), while SAA value was not correlated with severe HFMD (Wald value 0.3275, p=0.5671).

Conclusions: The distribution of SAA value among common enteroviral types of HFMD was statistically different, and the SAA value ≤ 92.1 ml/L was highly sensitive and specific for the differential diagnosis of EV71 HFMD. Multivariate regression analysis showed no relationship between SAA and severe hand, foot and mouth disease.

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Host- and pathogen-related factors for acute cardiac events in pneumococcal pneumonia

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Background: Acute cardiac events are increasingly recognized as a major complication in pneumococcal community-acquired pneumonia (CAP). Host- and pathogen-related factors for these serious complications, including sero- and genotypes of pneumococcal strains, have not been identified.

Materials/methods: Observational study of a prospective cohort of hospitalized patients for CAP in a university hospital from January 1996 to December 2016. Pneumococcal strains were serotyped and molecular typed (PFGE and/or MLST). A logistic regression and funnel plot analysis to determine host- and pathogen-related factors for the development of acute cardiac events was performed.

Results: A total of 1553 patients with pneumococcal CAP were included. One or more acute cardiac events occurred in 265 (17.1%) subjects being the most frequent arrhythmia (n=182), heart failure (n=116) and acute coronary syndrome (n=23). The majority of cardiac events (74.4%) occurred within 48 hours of hospitalisation. Older age, pre-existing heart conditions, pneumococcal bacteraemia, septic shock at admission and high-risk pneumonia (PSI>90) were independently associated with the development of acute cardiac events; whereas pre-hospitalization antibiotic treatment for the acute episode of pneumonia tended to have a protective effect. A propensity score matching of the treatment with antiplatelet drugs, oral anticoagulation, statins, ß-blockers, ACE inhibitors or angiotensin II receptor blockers and diuretics showed no protective effect. Out of 916 pneumococcal isolates, 797 (87%) were serotyped and 694 (75.8%) molecular typed. The funnel plot analysis did not show any significant association between any particular serotype or clonal complex and acute cardiac events; although there was a trend towards a higher risk of developing these complications in cases caused by strains harbouring clonal complex CC230. Patients with acute cardiac events had a higher 30-day case fatality rate than those without (14.3% vs. 5%, p<0.01).

Conclusions: Host factors appear to be more important than pathogen-related factors for developing acute cardiac events in pneumococcal pneumonia. The host factors delineated in this study may help identify those patients who should undergo a strict follow-up and monitoring, particularly during the first 48 hours of hospitalization, for early detection and treatment of acute cardiac events. These high-risk patients should be a target for future preventive intervention strategies.

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Abstract 7566

Microbiome ecology drives the epidemiology of antibiotic resistance and the efficacy of antibiotic stewardship interventions: a mathematical modelling study

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Background: Commensal bacteria of the host microbiome (‘flora’) can both support and suppress colonization by bacterial pathogens, through cross-feeding, niche competition, horizontal gene transfer (HGT) and other inter-species interactions. At the within-host level, antibiotics disrupt flora and select for the proliferation of antibiotic resistance-encoding genes, while at the between-host level, recent antibiotic therapy is a colonization risk factor for many pathogens. Here we explore how narrow- and broad-spectrum antibiotics affect flora ecology and its mediating influence on pathogen transmission dynamics, including consequences for antibiotic stewardship.

Materials/methods: We developed a mathematical Susceptible-Colonized transmission model including ecological interactions between flora and pathogens. Numerical simulations were conducted to explore transmission dynamics in the hospital setting. The model was parameterized to several high-risk nosocomial multidrug-resistant pathogens, including MRSA, Clostridiodes difficile and ESBL-Enterobacteria. Across these pathogens, relative reductions in bacterial colonization were compared for two antibiotic stewardship interventions: (i) reduced overall prescribing and (ii) restriction of broad-spectrum antibiotics.

Results: Within-host flora-pathogen interactions shape acquisition dynamics of multidrug-resistant nosocomial bacteria (Figure). For a generic pathogen, in the absence of interactions and across all possible combinations of antibiotics, cross-transmission explains much more pathogen acquisition (55.3–65.4%) than either HGT (21.7–30.6%) or endogenous acquisition (12.7–15.5%). Conversely, when within-host interactions with flora are strong, cross-transmission explains less acquisition (29.5–43.6%) than the endogenous route (37.0%–43.1%), with a similar quantity due to HGT (19.1%–27.3%). These findings are consistent with simulations showing dominance of endogenous acquisition over cross-transmission in species with complex within-host interactions, for instance in ESBL-E. coli.

Differences in pathogen acquisition routes are consistent with simulations showing species-specific differences in how colonization responds to antibiotic stewardship interventions. Interestingly, given identical baselines, a 30% reduction in broad-spectrum prescribing resulted in a 20.2% reduction in hospital prevalence in C. difficile, 10.8% in K. pneumoniae and 6.9% in E. coli, but an increase of 7.6% in MRSA.

Conclusions: This work illustrates the importance of within-host ecology in driving the colonization behavior of pathogens and responses to different antibiotic regimens, and how modelling can help to design and inform effective control strategies in the absence of data.

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Evaluation of a multiplex real-time PCR for the diagnosis of intestinal protozoa

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Background: The diagnosis of intestinal parasitosis is a very important challenge for many laboratories, in fact it requires a high degree of specific competences from the microbiologist. A lot of studies report that molecular biology, compared to microscopy, has numerous advantages such as greater sensitivity and specificity. The aim of this study is to evaluate an RT-PCR for the detection of intestinal protozoa from faecal samples.

Materials/methods: 164 samples were collected in seven Italian hospitals (Bergamo, Napoli, Pavia, Legnano, Modena, Bologna and Treviso) stored at -20 or -80 °C. The samples were examined using traditional techniques: macro- and microscopic examination after concentration, Giemsa or TrichRome stain, Giardia lamblia, Entamoeba histolytica/dispar or Cryptosporidium parvum antigens and amoebae culture. DNA was extracted with Microlab [NIMBUS]. All samples were examined with RT-PCR multiplex (Biorad, CFX96, Real Time system) using the Allplex GI-Parassite Assay, Seegene kit.

Results: On the 164 samples the traditional investigations allowed to identify the following protozoa: 41 non-pathogenic, 107 pathogens (34 G. lamblia, 65 D. fragilis, 4 C. parvum, 4 E. histolytica), 5 antigen positive only (2 G. lamblia, 2 E. histolytica, 1 C. parvum), 2 RT-PCR positive only, 1 negative from a patient with positivity for antibodies anti-E. histolytica. RT PCR confirmed 126/164 concordant positive and 31/164 concordant negative. RT-PCR detected D. fragilis in 9 samples positive for another parasite with the traditional technique: 6 confirmed with slide revision. RT-PCR detected E. histolytica in a patient with positive serology, but antigen and microscopy negative. C. parvum was also detected, in a reported positive sample only for B. hominis.

Conclusions: RT-PCR detected 6 D. fragilis, 1 C. parvum and 2 E. histolytica undiagnosed by traditional techniques [one of which was positive with the E. dispar/histolytica binary antigen]. Furthermore, RT-PCR confirmed 13 false positives for D. fragilis due to incorrect microscopic interpretation, justifying B. hominis in the Allplex panel. The impossibility of rereading 3 slides did not allow a better evaluation of sensitivity. The detection of E. histolytica in patients with positive serology alone, is important. The RT-PCR technology could therefore improve the limits of diagnosis of intestinal protozoan infections with time resolution.

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Dose-dependent *in vitro* interactions of colistin with meropenem against carbapenem-resistant Gram-negative bacteria

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**Background:** Due to limited therapeutic options, the colistin and polymyxin B are often considered antibiotics of last resort. However, the optimal dosage regimen is not universally agreed upon. We aimed to assess the *in vitro* effect of different combinations of colistin and meropenem against CRGN clinical isolates collected from patients enrolled in the AIDA trial in 2013-2017.

**Materials/methods:** The sample consisted of 354 CRGN isolates (A. baumannii n=276, Enterobacterales n=68, P. aeruginosa n=10). Broth microdilution was used to determine MICs of colistin and meropenem alone. The checkerboard method was used to evaluate colistin-meropenem interactions. A total of 32 combinations of drug concentrations were tested on each isolate (0.12 to 1µg/ml for colistin; 0.5 to 64µg/ml for meropenem). The fractional inhibitory concentration (FIC) index for each combination and the cumulative FIC (ΣFIC) index were calculated for each isolate. Synergy was defined as ΣFIC ≤0.5, additivity as ΣFIC >0.5 to ≤4, and antagonism as ΣFIC >4. In the subsample of meropenem-resistant, colistin-susceptible isolates (n=280), we determined the optimal colistin concentration (1/2, 1/4, or 1/8 MIC) needed to reach bactericidal activity when meropenem concentration is ≤8µg/ml.

**Results:** Synergy was observed in 56.7% of A. baumannii (156/276), 10.0% of P. aeruginosa (1/10), and 7.4% of Enterobacterales (5/68) strains synergism (ΣFIC: 0.1-0.5). Antagonism was detected for 1.5% of the A. baumannii (4/276), 42.6% (29/68) Enterobacterales and 40.0% P. aeruginosa (4/10) isolates [ΣFIC: 4.1-4.5]. One P. aeruginosa isolate exhibited both synergism [FIC₅₀: 0.5] and antagonism [FIC₅₀: 4.1]. Additivity was found in 42.0% of the A. baumannii (116/276), 50.0% of the Enterobacterales [34/68] and P. aeruginosa (5/10) isolates. In the subsample colistin-susceptible isolates, the highest percentage of isolates (48.9%) reached bactericidal activity [at meropenem concentration ≤8µg/ml] when combined with 1/4 MIC colistin concentration. At both 1/2 and 1/8 MIC colistin concentration, only 7.4% of isolates reached bactericidal activity.

**Conclusions:** Although meropenem-colistin combination therapy for CRGN infections has been advocated based on the assumption of synergy, we found in vitro synergy in less than half of isolates. In order to achieve the optimal bactericidal effect of meropenem, the initial MIC of the isolate to colistin must be considered.

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**Abstract 7573**

**In vitro evaluation of barrier function against foodborne bacteria and oral streptococci on polytetrafluoroethylene membranes**

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**Background:** In the guided bone regeneration (GBR) process, it is important to choose the optimal biomaterial, which will not degrade rapidly, and which, upon completion of GBR, will maximally contribute to osteogenesis in order to completely close the bone defect. It is equally important to ensure that the processes of bone healing take place without microbial contamination from the oral cavity. New generation of nonresorbable, membranes include dense polytetrafluoroethylene (D-PTFE) tetra fluoroethylene membranes. As they are not degradable, d-PTFE membranes are removed 4 weeks after tooth extraction, creating pre-conditions for possible infection. Commonly used d-PTFE membranes are Permamem (Botiss biomaterials, Zossen, Germany) and Cytoplast (Osteogenics Biomedical, Texas, USA) membranes. The aim of this study was to evaluate adhesion properties, biofilm formation and consequently barrier function of foodborne bacteria *Staphylococcus aureus*, *Enterococcus faecalis*, *Escherichia coli*, and oral streptococci (*Streptococcus mutans*, *S. mitis* and *S. salivarius*) on Permamem and Cytoplast membranes.

**Materials/methods:** Bacterial adhesion and colonization on a two d-PTFE membranes of varying openness [Cytoplast and Permamem] and polystyrene were evaluated. The surfaces of tested membrane and polystyrene were challenged with tested bacteria and incubated statically for 2-48 h. At the end of the incubation, plate were three times washed with PBS and sonificated in a water bath at 40 kHz for 1 min. Bacteria were enumerated by culturing on MH agar or Salivarius Mitis agar up to 2 days until colonies were observed. At the same time, the characteristics of bacteria in the biofilm using fluorescence microscopy and SEM were examined.

**Results:** Numbers of all tested bacteria increased over time on all surfaces. Oral Streptococci showed better adhesive properties than foodborne bacteria. Comparing different materials, all bacteria showed significantly lower biofilm formation [reduced by app. 4 log] on d-PTFE membranes compared to polystyrene. Oral streptococci and foodborne bacteria adhered better on Cytoplast than Permamem membrane [app. to 2 log].

**Conclusions:** Tested PTFE membranes showed to be effective barriers against bacterial colonisation in vitro. Permamem membrane showed the lowest bacterial adhesion and biofilm formation, compared to Cytoplast and polystyrene, suggesting their better resistance towards foodborne bacteria and streptococci.

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Abstract 7574

**Clinical effectiveness of temocillin in a French university hospital**
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**Background:** Temocillin is a narrow spectrum antibiotic that is indicated to treat infections due to *Enterobacteriaceae* producing extended spectrum beta-lactamase (ESBL). The purpose of this study is to evaluate the clinical effectiveness of temocillin in a French University Hospital.

**Materials/methods:** From July 2018 and September 2019 all patients who received more than 1 day of treatment by temocillin were prospectively included in the study. Characteristics of patients, microbiology and treatment data and outcome were retrospectively analysed for each prescription. The effectiveness of temocillin was defined by the clinical improvement and the absence of recurrent infection.

**Results:** Twenty-two patients received temocillin: 19 adults [mean age: 70.3 [36; 95]], 3 children [12 men, 10 women]. Nine patients were immunocompromised, including 5 renal transplant and 1 hepatic transplant patients. One patient was treated twice with temocillin during the study period.

The indications were urinary tract infections (82.6%; 19/23), bacteriemia from unknown source (13.0%; 3/23) and respiratory tract infection (4.4%; 1/23). Temocillin was used after a documented, monomicrobial infection. Bacteria identified were *Escherichia Coli* (54.2%; 13/24), *Enterobacter cloacae* (25.0%; 6/24), *Klebsiella pneumoniae* (12.5%; 3/24), *Serratia marcescens* (4.2%; 1/24), *Morganella morganii* (4.2%; 1/24). In one case, two bacteria were identified. In all cases, MIC was ≤ 8 mg/mL.

The mean duration of antibiotherapy was 12 days ([5; 21]). Temocillin was either administered as a continuous infusion (52.2%; 12/23) or over 30 minutes (47.8%; 11/23). Dosages were adapted to renal impairment. Before temocillin, all patients were initially treated by a broad-spectrum antibiotic: a third-generation cephalosporin (52.2%; 12/23), piperacillin/tazobactam (26.1%; 6/23) or a carbapenem (21.7%; 5/23).

The clinical evolution was favorable in 87.0% (20/23) of cases. A recurrence was observed in 34.8% (8/23) of cases, including all transplant patients. Patients infected with *Escherichia Coli* or *Enterobacter cloacae* recurred in 61.5% (8/13) and in 16.7% (1/6) of cases respectively.

**Conclusions:** Temocillin seems be an effective alternative to broad-spectrum antibiotics to treat documented urinary tract infections in immunocompetent patients. However, this study highlights an important recurrence rate especially in immunocompromised patients despite a favorable initial evolution.

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Abstract 7575

Comparison of rifampin synergy in high versus low biofilm-forming Staphylococcus epidermidis

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Background: The role of rifampin in the treatment of biofilm-associated Staphylococcal infections remains controversial. Staphylococcus epidermidis is frequently implicated in medical device infections due to its propensity to form biofilm on foreign materials. We sought to describe synergistic combinations of antibiotics with rifampin and determine if its activity differed when used in high biofilm-forming vs low biofilm-forming S. epidermidis.

Materials/methods: A methicillin-resistant high biofilm-forming S. epidermidis strain RP62a (Hi-BF) and its accumulation-negative mutant M7 (Lo-BF) were utilized in a 24-hour high-inoculum time kill assay to detect synergy with rifampin. An inoculum of 10^7 CFU/mL was used for this assay to simulate high-inoculum biofilm infections. The antibiotics that were tested were levofloxacin, vancomycin, daptomycin, ceftaroline, and minocycline at 0.25x, 0.5x, 1x, and 2x the minimum inhibitory concentration with and without the addition of rifampin. As previously described, synergy was defined at 24 hours as a ≥2-log10 decrease in colony-forming units CFU/mL from the most single active agent, antagonism was defined as an increase of a ≥2-log10 CFU/mL, and indifference was defined as any CFU/mL that was in between this range.

Results: In the Hi-BF isolate, rifampin synergy was observed with daptomycin, vancomycin, and levofloxacin (Table 1). However, rifampin was not synergistic with daptomycin, vancomycin, ceftaroline, levofloxacin, or minocycline in the Lo-BF isolate. Of interest, antagonism was noted with minocycline and rifampin in the Lo-BF isolate.

Conclusions: This study demonstrated that rifampin improved the bactericidal activity of some antibiotics against a Hi-BF S. epidermidis isolate, but not with a Lo-BF isolate. The difference in kill is likely dependent on biofilm formation capability of the isolate. This may explain why the literature is inconsistent in regards to the role of rifampin in therapy. The antagonistic activity of minocycline in combination with rifampin in low biofilm-forming S. epidermidis is of concern and warrants further investigation. Identification of the mechanism behind increased kill with rifampin in biofilm is critical to determining its role in combination therapy for infections.

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Table 1. Results from the high-inoculum biofilm time-kill assays.
Performance of the rapid molecular assay BioFire FilmArray Meningitis/Encephalitis for the diagnosis of CNS infections: a one-year evaluation in a tertiary care hospital

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Background: The BioFire FilmArray Meningitis/Encephalitis System, BF-ME (bioMérieux) is a rapid (1 h) molecular assay for the diagnosis of meningitis and encephalitis. The test provides a qualitative result for 14 pathogens. We aimed to evaluate the reliability and the added-value of this assay one year after its introduction in our hospital.

Materials/methods: In November 2018, the BF-ME was made available for physicians 7/7 days/8am-10pm. Pathogens for which in-house PCRs were available, were retested within 24h; this included Haemophilus influenzae, Listeria monocytogenes, Neisseria meningitidis, Streptococcus agalactiae, Streptococcus pneumoniae, Cytomegalovirus, Enterovirus, Herpes simplex virus 1 and 2, Human herpes virus 6 and broad range 16S rRNA gene PCR. Clinico-laboratory assessment was achieved to investigate discrepant results.

Results: We analysed results (n=144), obtained during a one year period after the introduction of the ME panel (Nov. 2018 to Nov. 2019) with the following results: sensitivity 90.9% (30/33), specificity 98.6% (139/141), positive predictive value 93.7% (30/32) and negative predictive value 97.9% (139/142). Two adult patients that tested positive for E. coli K1 with the BF-ME panel were negative with in-house PCR, among whom only one of them could eventually correspond to a true positive by clinico-laboratory assessment. Two patients with a clinico-laboratory assessment compatible with a viral encephalitis tested negative for HSV-1 with the BF-ME panel but positive with in-house real-time PCR with very low DNA copy number. One patient with a Listeria monocytogenes rhombencephalitis and bacteraemia tested negative with the BF-ME panel but positive with in-house real-time PCR.

Conclusions: The overall performance of the test appeared intermediate. However, important unexpected discrepant results - false positive and false negative - occurred. This may be problematic for a first line assay expected to support decision making in the setting of a life-threatening disease. In conclusion, the BF-ME provided rapid results with a better sensitivity than Gram staining. However, our study similarly to previous studies re-inforces that: i) a carefully clinico-laboratory assessment is mandatory for the interpretation of any BF-ME results (both negative and positive results) and ii) confirmation with in-house molecular test, ideally quantitative tests, appears to be necessary.

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Sulbactam and colistin susceptibility pattern among multidrug-resistant Acinetobacter isolates from respiratory samples

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Background: Healthcare-associated lower respiratory tract infection (LRTI) is one of the major causes of morbidity, prolonged average length of stay, exorbitant healthcare expenses and mortality related to antimicrobial resistance. The most common bacterial agents of LRTI in the Intensive Care Unit (ICU) are Pseudomonas spp., Acinetobacter spp., Klebsiella pneumoniae, Citrobacter spp., and Escherichia coli. Acinetobacter baumannii has emerged as a major cause of nosocomial outbreaks. A unique feature of A. baumannii in particular, is their intrinsic resistance to multiple antibiotics.

Sulbactam being a beta-lactamase inhibitor has been traditionally combined with beta-lactams to treat ESBL producing Acinetobacter. Studies have also described a unique intrinsic bactericidal effect of Sulbactam against Acinetobacter baumannii.

Materials/methods: A prospective study was conducted for six months in the medical ICU of a 500 bedded tertiary care hospital and medical teaching institution in India. Identification of organisms causing LRTI obtained from sputum or invasively collected samples were done by conventional phenotypic and/or VITEK 2 Compact System™. Antimicrobial susceptibility was tested by Kirby-Bauer disc diffusion method according to standard guidelines. Minimum inhibitory concentrations were measured for Acinetobacter spp. to colistin and sulbactam by E-strips and micro broth dilution technique.

Results: A total of 542 respiratory samples were received, 109 of which showed growth of significant colony count of one or two organisms, yielding a sum of 115 isolates. Among these isolates, 51 were (44.35%) Klebsiella pneumoniae, 32 (27.83%) Pseudomonas spp., 30 (26.09%) Acinetobacter spp. and 2 (1.74%) Stenotrophomonas maltophilia. All the Acinetobacter isolates were resistant to ceftazidime, cefepime, piperacillin-tazobactam, cefoperazone-sulbactam, ciprofloxacin, amikacin, gentamicin, tobramycin, meropenem and imipenem. No significant independent intrinsic bactericidal effect of sulbactam was observed against the Acinetobacter isolates.

Conclusions: The common Gram-negative pathogens causing healthcare-associated LRTI were highly resistant to most drugs except polymyxins. Acinetobacter baumannii isolates were not susceptible to either free sulbactam or in combination with cefoperazone. The alarming situation of antimicrobial resistance in these isolates remarkably demonstrates the need for immediate investment in newer and alternative therapeutics.

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Abstract 7580

Epidemiology of non-tuberculous mycobacteria in bronchiectasis and non-bronchiectasis patients in a university teaching hospital in Madrid

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Background: Non-Tuberculous Mycobacteria (NTM) includes species other than M. tuberculosis and M. leprae. These microorganisms are opportunistic pathogens recognized as a cause of pulmonary infection. Patients with pre-existing lung disease, such as bronchiectasis, are predisposed to developing a NTM infection. The aim is to describe the NTM prevalence and etiology of patients suffering bronchiectasis (excluding cystic fibrosis) in relation to non-bronchiectasis patients.

Materials/methods: Retrospective study from 2009 to 2019 in a university hospital in the community of Madrid, Spain. All respiratory samples for mycobacteria diagnosis were included. Microbiological diagnosis was carried out by an automated culture (MGIT™ 960 system, Becton Dickinson). Bacterial identification was obtained by mass spectrometry (MALDI-TOF) or DNA studies.

Results: 2 124 samples from 762 bronchiectasis-patients were processed. NTM were isolated from 811 (38.18%) samples from 228 (29.92%) of these patients. Comparing to general population (1 7163 patients; 606, 3.53% NTM isolates), the presence of NTM was more common in patients suffering bronchiectasis (11.67 OR, 95% CI 9.79-13.90). The most prevalent NTM was M. avium (490 isolates, 54.08%) following by M. abscessus and M. lentiflavum (80 isolates, 9.85% each one) and M. fortuitum (65 isolates, 8.00%). There were not important differences among species found from bronchiectasis and non-bronchiectasis cultures (Table 1). An increase number of NTM isolates is observed: from 15 in 2009 to 84 in 2019.

Conclusions: the NTM isolation from bronchiectasis-patients are common and becoming more frequent. The risk of NTM infection in this patients comparing to general population are much higher although the species found are similar. Therefore, it is necessary to take into account NTM to get a correct diagnosis of infection and optimal management of patients suffering from this disease.

<table>
<thead>
<tr>
<th>Mycobacterium avium complex</th>
<th>Non-bronchiectasis</th>
<th>Bronchiectasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>754</td>
<td>52.43%</td>
<td>420</td>
</tr>
<tr>
<td>Mycobacterium abscessus</td>
<td>157</td>
<td>10.92%</td>
</tr>
<tr>
<td>Mycobacterium lentiflavum</td>
<td>132</td>
<td>9.18%</td>
</tr>
<tr>
<td>Mycobacterium fortuitum complex</td>
<td>131</td>
<td>9.11%</td>
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<td>Mycobacterium gordonae</td>
<td>120</td>
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<tr>
<td>Mycobacterium xenopi</td>
<td>52</td>
<td>3.62%</td>
</tr>
<tr>
<td>Mycobacterium chelonae complex</td>
<td>26</td>
<td>1.81%</td>
</tr>
<tr>
<td>Mycobacterium kansasii</td>
<td>20</td>
<td>1.39%</td>
</tr>
<tr>
<td>Other NTM</td>
<td>46</td>
<td>3.20%</td>
</tr>
<tr>
<td>1438</td>
<td>100.00%</td>
<td>812</td>
</tr>
</tbody>
</table>

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Faecal microbiota in Romanian ankylosing spondylitis patients
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Background: Ankylosing spondylitis (AS) is a chronic inflammatory autoimmune disease characterized by new bone formation causing syndesmophytes and enthesitis, and represents the prototype of spondyloarthritis inflammatory disorders (SpA). A strong correlation between SpA and gut dysbiosis has been made since up to 50-70% of SpA patients display subclinical gut inflammation and 5-10% of them evolve toward inflammatory bowel disease (IBD).

Materials/methods: Diversity of the gut bacterial microbiome was studied in 25 Romanian patients diagnosed with AS (sex ratio 4:1, 22-68 years) and 16 clinically healthy control individuals with no history of rheumatic disease and IBD. Fecal DNA was used for PCR amplification of hypervariable regions of 16S rRNA gene using Ion 16S™ Metagenomics Kit. High-throughput sequencing was performed on an Ion PGM™. Taxa identification was performed with QIIME within Ion Reporter™ (Thermo Fisher Scientific). Alpha diversity was assessed by richness (Chao1) and diversity (Shannon, Simpson). Beta diversity was evaluated by principal-coordinate analysis plot (PCoA) with Bray-Curtis dissimilarity. LefSe analysis was employed to reveal the significant differences in abundance between the patients and controls.

Results: The rarefaction curves showed a clear tendency toward a saturation plateau, suggesting that most of the diversity was captured. Bacteroidetes, Firmicutes, Proteobacteria, and Actinobacteria were found as dominant taxa in both groups. The number of detected families was significant lower in patients than in control group (p< 0.01). At the genus level, Eubacterium and Roseburia were significantly greater in AS than in controls whereas Herbaspirillum, Lactococcus, Oxalobacter and Paraprevotella were significantly lower in AS than in controls. Examination at species level showed that Blautia producta and Blautia luti are significantly represented in AS patients, and some species such as Alistipes shahii, Alistipes putredinis, Lactococcus lactis, Ruminococcus flavefaciens and Sutterella sp., are underrepresented comparing with controls.

Conclusions: The gut microbiome of AS patients was clearly different from that of controls. There was a loss of richness of the gut microbiome in AS patients. As other previous reports, we conclude that some biomarkers might be involved in the pathogenesis or development process of AS.

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Development of in vitro and ex vivo wound biofilm models for the assessment of wound dressings
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Abstract 7585

Background: Increasing evidence suggests that the chronicity of wounds is linked to infection and presence of biofilm, thus, novel biofilm targeting wound care products are being developed. It is crucial to have appropriate analytical methods to quantitatively assess these anti-biofilm properties. The aim of present study was to develop in vitro and ex vivo wound biofilm models for assessing the antibiofilm properties of wound dressings.

Materials/methods: For the in vitro model thermally crosslinked electrospun gelatine (GEL) matrix as an artificial skin was used. Ex vivo model was developed using pig ear skin. For wound biofilm model development different pathogenic bacteria (S. aureus, E. coli, S. epidermidis) and media as wound exudate were tested. Biofilm formation was studied according to the schematics. Filter papers immersed into the artificial wound exudate were placed at the bottom of the 24-wellplates, then either GEL matrix or pig skin was positioned on top. Bacterial dispersion was added after which chloramphenicol (CAM)-loaded electrospun wound dressings were applied. These systems were incubated for 24, 48 and 72h, subsequently planktonic bacteria were removed, biofilm disrupted and quantified. Confocal microscopy and scanning electron microscopy were used for the characterisation of the biofilms and wound dressings.

Results: GEL matrix is suitable for being used as an artificial skin in in vitro biofilm model as bacteria adhered to its surface and formed a biofilm (up to 10^8 CFU/cm^2). Compared to GEL matrix, the ex vivo model on pig skin appeared to be a better surface for biofilm formation resulting in 2-10 times higher CFU/cm^2. Application of CAM-loaded dressings effectively reduced the biofilm formation in both models compared to the blank dressings without CAM.

Conclusions: Designed in vitro and ex vivo models allow comparing and evaluating the antibiofilm properties of wound dressings. Both models exhibit their specific advantages, GEL matrix has a defined chemical composition and structure and pig skin has its durability allowing longer experiments over several days. Next studies investigate the efficacy of the dressings for the treatment of already formed biofilm.

Acknowledgements: PUT1088P, PRG335, L’ORÉAL Baltic “For Women In Science” scholarship.
Abstract 7586

Efficient inactivation of clinically relevant antimicrobial drug concentrations by two resin-containing media in simulated paediatric blood cultures

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Background: Diagnosis of bloodstream infection in paediatric patients is a major challenge for clinical microbiologists. Improvements in blood culture (BC) media and the availability of automated growth detectors enhance the recovery of bloodstream pathogens and decrease the time to detection (TTD) of microbial growth. However, antimicrobial treatment administered before drawing BCs can reduce or delay pathogen recovery, especially in paediatric patient settings where low-level bacteraemias and small blood sample volumes often complicate the situation. The aim of this study was to evaluate the BacT/Alert PF Plus (bioMérieux) or BACTEC Peds Plus (Becton Dickinson) resin-containing media for their capability of inactivating clinically relevant antimicrobial drug concentrations in simulated paediatric BCs.

Materials/methods: We tested eight antimicrobial-organism combinations in BacT/Alert PF Plus or BACTEC Peds Plus bottles, which were inoculated with 2 or 10 mL of banked whole blood, 0.5 mL of antimicrobial drugs at peak or trough serum concentrations, and 0.5 mL of bacterial suspensions containing 5 or 30 CFU of per bottle. This resulted in eight conditions (each was tested in triplicate) for each combination. Positive and negative controls were included. All bottles were incubated in both BacT/Alert Virtuo and BACTEC FX systems. Results were reported as organism’s recovery rates and mean TTDs, and differences were assessed using the McNemar’s test or the paired t test, as appropriate.

Results: The overall recovery rate of organisms with the BacT/Alert PF Plus medium was 39.1% (75/192 bottles), whereas the rate with the BACTEC Peds Plus medium was 25.0% (48/192 bottles) for all the antimicrobial-organism combinations tested. We found that this difference was statistically significant (P < 0.001). The mean TTDs were 14.26 h and 16.37 h for the BacT/Alert PF Plus medium or the BACTEC Peds Plus medium, respectively (P < 0.05). There was no recovery at any condition with ceftriaxone tested against Streptococcus pneumoniae for both the media and with vancomycin tested against S. pneumoniae only for the BACTEC Peds Plus medium.

Conclusions: Despite preliminary, our findings show that the BacT/Alert PF Plus medium is more efficient than the BACTEC Peds Plus medium in a simulated paediatric BC setting.

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Abstract 7587

Five different Borrelia species identified in synovial fluids from patients in Sweden
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Background: Sweden is an endemic area for Lyme borreliosis. Serology is the routine diagnostic method while detection of Borrelia specific DNA is considered a complementary diagnostic tool. At the clinical microbiological laboratory in Lund, Sweden, a 16S real-time PCR has been in use since 2007. A cohort of patient samples originating from joints is presented with demographic data together with species and subspecies characterization.

Materials/methods: Patient samples originating from joints referred over the years 2007 to 2018 to the laboratory for Borrelia DNA detection was studied. Two 16S rDNA PCR tests are run in parallel, one targeting the Borrelia genus and the other one targeting Lyme Borrelia species (Borrelia burgdorferi sensu lato). For species and subspecies characterization a nested ospA based PCR followed by sequencing is performed.

Results: During 12 years 1414 of 2495 (56.6 %) samples referred to the laboratory for a Borrelia PCR test were material from joints. Joint samples originated from synovial fluids and occasional synovial membranes from patients living in Sweden and a few cases from Denmark, Norway and Finland. Borrelia DNA was detected in the 16S rDNA PCR in 155 of 1414 (11.0 %) joint samples. Species identification was successful in 116 unique patients by the ospA PCR and sequence analysis. Borrelia afzelii was the most common species identified in 58 samples (50.0 %), followed by Borrelia burgdorferi, Borrelia garinii, Borrelia bavarensis, Borrelia spielmanii identified in 35 (30.2 %), 11 (9.5 %), 9 (7.8 %), 3 (2.6 %) samples, respectively. Female to male ratio was 28.2 % to 71.8 %. Mean age was 31.8 (range 4 to 78 years).

Conclusions: Synovial fluids was the most common material sent for a Borrelia PCR test and there was a year around request. Borrelia DNA is predominantly detected in males. Of the five species found Borrelia burgdorferi sensu stricto was the second most prevalent species in synovial fluids a species much more seldom found in ticks. Molecular based tests in routine diagnostics can provide new important epidemiological data into Lyme borreliosis.

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Abstracts 2020

Abstract 7590

qPCR to detect mecA in faecal samples: a tool for assessing resistance burden amongst pets and their owners in the microbiological ‘fast age’?

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Abstract third-party references: This work was supported by a JPI-EC-AMR grant funded by the Medical Research Council [Grant MR/R000042/1], This work is a part of the PETRisk Consortium.

Background: Current sampling and detection methods for carriers of pathogenic methicillin-resistant staphylococci (MRS) such as MR-Staphylococcus pseudintermedius and MR-S. aureus can be challenging in animals and time-consuming. Developing a faster method to identify mecA in a convenient-to-collect sample, such as faeces, would benefit surveillance efforts and may aid in management of MRS-carrier animals which could be a zoonotic risk to owners. This study aimed to identify whether a quantitative polymerase chain reaction (qPCR) method could be optimised to detect mecA in faecal samples and distinguish MRS-carriers from non-carriers.

Materials/methods: Faecal samples (0.5g) were collected from ten MRS-carriers (n=6 dogs, n=4 humans) and 51 non-carriers (n=21 dogs, n=30 humans); carriage was determined using nasal swabs processed with enrichment salt broth. Bacterial DNA was extracted from faeces using a commercial kit and verified by 16S PCR. A qPCR method previously used for pure bacterial culture was optimised to ensure accuracy and detection of low copy numbers of mecA. A robust method with a single melt curve peak was achieved, and the product confirmed as mecA by Sanger sequencing. Faecal mecA abundance was compared between MRS-carriers and non-carriers (Kruskal-Wallis test).

Results: The limit of detection (LOD) of mecA was approximately 70 copy numbers in 6µL DNA, with a melt curve temperature of 75°C and extraction efficiency of 97.1±3.2% across all plates used for analysis. In 8 individuals (n=2 human carriers, n=4 canine non-carriers, n=2 human non-carriers) mecA was detected [74-36756 copy numbers]; in all others mecA was below LOD. Faecal mecA abundance did not correlate with nasal MRS-carriage (P=0.83).

Conclusions: Using the optimised qPCR method, we could identify mecA directly from faeces of MRS-carrier humans, and in individuals who were not MRS-carriers based on nasal swabbing. Further development and validation of this method may be warranted to enable future large, easy-sampling population screening for resistance gene abundance. We could not discriminate between MRS-carriers and non-carriers in this population. This is possibly due to the small sample size but more likely due to the presence of mecA-positive coagulase-negative staphylococci, or possibly other bacterial species carrying mecA homologues, in the gut microbiota of both groups.

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Abstract 7593

Typing of Clostridioides difficile isolates by MALDI-TOF MS

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Background: Clostridium difficile infection (CDI) associated with emerging ribotypes is increased both in Europe and worldwide; more than 800 different ribotypes and 34 different toxinotypes of C. difficile are known and the ribotype 027 strain is currently considered the most virulent. In Europe, nosocomial CDI are typically associated with ribotype 027 and 078 strains, while in Italy, the predominant ribotypes are associated to 356/607 (27%) and 018 (12%) strains. Unlike other European countries, the hypervirulent ribotypes 027 and 078 emerged in Italy only recently and accounted for 8% and 4% respectively. In this study MALDI-TOF mass spectrometry was used as a potential innovative method for C. difficile strains typing, compared with the widely known PCR-Ribotyping method.

Materials/methods: Fifty strains of C. difficile isolated in our hospital were typed both by PCR-Ribotyping, according to Bidet et al., and by MALDI-TOF MS. The spectra obtained in the range 2-20 kDa, with the instrument Autoflex speed (Bruker Daltonics, Germany), were analyzed and subsequently imported into the ClinProTools software version 2.2 (Bruker Daltonics) to carry out a statistical analysis in order to verify the presence of specific peaks for each ribotype.

Results: The two typing methods used showed a concordance of 76%. Using PCR-Ribotyping, 5 different ribotypes (named PR1-PR5) were observed, 2 of these, PR1 and PR3, associated to ribotypes 018 and 0126, respectively. MALDI-TOF MS, based on the presence/absence of 13 different peaks, differentiates the 5 ribotypes identified by PCR-Ribotyping. For eight strains (16%) the spectra obtained were classified by the MALDI-TOF MS statistical software as one of such 5 ribotypes but differently to the classification of PCR-Ribotyping. For 4 strains (8%) a protein profile different from each other and from those characterizing the 5 ribotypes observed was obtained, making them unique and belonging to different classes (PR6-PR9).

Conclusions: MALDI-TOF MS typing compared to other molecular typing methods was faster and cheaper. However, the typing of strains, although possible as demonstrated in this study and presenting significant advantages, is currently applicable to the most frequently circulating ribotypes, as a first-level epidemiological investigation in the nosocomial setting.

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The role of local high microbial load in predicting the outcome of diabetic foot ulcers

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Background: Diabetic foot ulcers (DFUs) are common and lead to infections with high morbidity-mortality. Diagnosis of DFU infection by clinical signs and conventional-qualitative cultures is sometimes difficult. We aimed to evaluate the role of quantitative cultures from DFUs in predicting the outcome of ulcers.

Materials/methods: Prospective multicenter study (3 Spanish referral centers) including patients with DFUs. At baseline visit, we performed a biopsy from ulcers clinically infected (signs of inflammation, purulent secretion) or not, and quantitative bacterial counts were obtained. Patients were followed-up at 1, 3 and 6 months to evaluate DFU cure; we compared characteristics and outcome of cases with high (≥10E6 UFC/ml) or low microbial load (<10E6 UFC/ml).

Results: 65 DFU cases (28% toes, 72% midfoot-backfoot) were studied; 80% were men (median age 65 years, IQR 59-71) with a chronic diabetes (17 years, IQR 8.5-25). At baseline, 24 (37%) DFU cases were considered clinically infected but only 33% (8/24) presented a high microbial load, whereas 27% of not-infected DFUs (11/41) had high bacterial counts. DFUs had mainly polymicrobial population (74%), S. aureus and Gram-negative bacilli (GNB) being present in 48% and 46%, respectively.

The group with high load in comparison with that with lower bacterial load had more frequently a young ulcer (<4 weeks, 37% vs 13%, p=0.03), a higher percentage of GNB (68% vs 37%, p=0.02) and S. aureus (63% vs 41%, p=0.1). No differences between groups were observed in the value of glycosylated hemoglobin, degree of vasculopathy and the consumption of antibiotics one month before obtaining the biopsy (58% vs 48%, p=0.3). Cases with high bacterial counts required more antibiotic therapy during the first month after biopsy (76% vs 45%, p=0.03), and at 6-month visit they presented more amputations (38% vs 22%, p=0.2) and lower cure rate (44% vs 73%, p=0.04).

Conclusions: Relationship between clinical diagnosis of infection and high bacterial load from DFUs was poor. However, cases with higher bacterial counts presented more frequently GNB strains and a worse prognosis. Our results suggest a potential role of quantitative cultures in predicting the outcome of DFUs that should be further evaluated.

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Continuous infusion of cefoxitin is associated with higher probability of target attainment in patients infected with ESBL-producing Enterobacteriaceae

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Background: Cefoxitin (FOX) is a cephamycin still active against most extended spectrum beta-lactamase (ESBL) producing Enterobacteriaceae. The currently recommended dosages are 3 to 6 gr. Per day. However, few data of therapeutic drug monitoring are available on the use of cefoxitine for ESBL producing Enterobacteriaceae related infections.

Materials/methods: The objective was to compare the use of prolonged or continuous infusion versus intermittent administration of FOX for the treatment of infections caused by ESBL-producing Enterobacteriaceae. We performed a multicentric retrospective cohort study to evaluate continuous, prolonged or intermittent infusion of FOX. Firstly, we analyzed patients’ plasmatic concentrations according to the infusion duration and secondly, we performed a simulation of the percentage of patients who would reach the PK / PD targets set at 100% \( T > \text{MIC} \) or 100% \( T > 4 \times \text{MIC} \).

Results: Seventy-eight patients were enrolled with a median [IQR] age was 68 [56 – 77] years. Seventy-four patients were treated for Escherichia coli related infections and four for Klebsiella pneumoniae related infections. The major source of infections was urinary tract (91%). All patients were treated with 6 gr./day or renally adjusted equivalent.

In all patients infected with strains with MICs ≤ 6 mg/L, PK/PD objectives (100% \( T > \text{MIC} \)) was achieved with prolonged or continuous infusion. In contrast, when MICs was 8 mg/L only continuous infusion was sufficient to achieve the PK/PD objectives (100% \( T > \text{MIC} \)). In contrast, PK/PD objectives (100% \( T > 4 \times \text{MIC} \)) were achieved by prolonged or continuous infusion only when FOX MICs ≤ 2 mg/L.

Conclusions: Only prolonged or continuous infusion of FOX provided sufficient coverage to achieve sufficient probability of target attainment for ESBL PE with MICs ≤ 6mg/L. For more severe patients or in case of MICs to FOX at 8mg/L, only continuous infection of FOX seems sufficient to achieve probability of target attainment.

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Abstract 7600

**Screening for carbapenemase-producing Enterobacteriaceae**

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**Abstract third-party references:** Imperial College London, Chelsea and Westminster Hospital Foundation Trust

**Background:** Screening for Carbapenemase-producing Enterobacteriacea (CPE) enables early isolation and prevention of transmission in inpatient healthcare settings. The UK Department of Health detailed a national approach to screening in 2013. Implementation of this policy has been variable and challenging given the increasing prevalence of patients who meet these criteria and the limited number of isolation facilities.

**Materials/methods:** We undertook a point prevalence study in a central London teaching hospital in 2019, to ascertain patient risk factors for CPE and the frequency of per-policy screening. We then modelled variations in screening approaches to optimise risk assessments in the context of isolation room availability.

**Results:** We assessed screening compliance on the tertiary Burns Unit, Paediatric High Dependency Unit (PHDU), Acute Admissions Unit (AAU) and general surgery. 141 patient notes were assessed against the three screening criteria: 47/141 met the screening requirements due to previous admission to high risk UK healthcare institutes, 3/141 because of healthcare admission abroad, and 0/141 previously identified CPE carriers. Screening as per national guidelines was performed in only 30% (15/50) of patients that met the eligibility criteria. The highest rate of screening was noted in Burns unit (5/5). The factor most likely to result in screening, was previous admission to a hospital abroad (3/3).

The national toolkit advises that patients who meet eligibility criteria should be isolated immediately. Our data shows that the number of patients that should have been isolated surpasses the capacity of available side rooms in the hospital by 135%.

**Conclusions:** Screening for CPEs is complex and 6 years after role out of a national toolkit there is still variation in adherence to screening policy. In light of a revised national toolkit, due to be published in 2019, reworking of the risk stratification is needed. We suggest that education on risks of carrying CPEs as well as electronic healthcare records may enable better screening adherence.

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Abstract 7604

Incidence and utility of follow-up blood cultures in haematology/oncology patients with Gram-negative bacteraemia

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Background: Follow-up blood cultures (FUBC) in gram-negative bacteremia are commonly performed; however, recent data demonstrated no benefit in non-cancer patients. This study sought to determine the incidence of FUBC within hematology/oncology patients with gram-negative bacteremia and evaluate potential impact of FUBC on clinical outcomes.

Materials/methods: A multicenter retrospective chart review across 3 centers was performed in adult cancer patients (age ≥ 18 years) admitted to an oncology unit who had microbiologically defined gram-negative bacteremia between January 2018-December 2018. Data collected included: demographics, cancer diagnosis, type of treatment if applicable, microbiologic and clinical data. Primary outcome was incidence of FUBC in the hematology/oncology population with gram-negative bacteremia. Secondary outcomes included central venous catheter removal, presence of infectious diseases (ID) consultation, hospital length of stay, and in-hospital mortality in patients with FUBC versus those without FUBC. Descriptive statistics were calculated to characterize all study variables. Chi-square analyses (or Fisher’s Exact tests), t-tests (or Wilcoxon rank-sum tests), and bivariate regression (logistic and Poisson) analyses were conducted to examine the associations between FUBC and outcomes.

Results: Gram-negative bacteremia was identified in 55 patients. The vast majority of patients received FUBC (50/55; 90.9%). Patient characteristics, such as cancer diagnosis or receipt of cytotoxic chemotherapy, did not differ between those with versus without FUBC. Of 50 patients with FUBC, the average patient received 3.6 FUBC (SD 4.2; range 1-29) with a total of 179 FUBC performed. No growth was demonstrated in 163/179 (91.1%) of FUBC with only 11/179 (6.1%) growing the same initial pathogen and 5/179 (2.8%) growing different pathogen. Patients with FUBC were no more likely to have catheters removed or receive ID consultation than those without FUBC (p=0.6 and p=0.67, respectively). Patients receiving FUBC had greater lengths of stay (coefficient=0.47, CI 0.21-0.73) with median of 13 vs 9 days, respectively, while in hospital mortality was not different between groups (p=0.39).

Conclusions: FUBC are frequent in hematology/oncology patients with gram-negative bacteremia despite lack of supporting evidence. Our data demonstrated increased length of stay for patients receiving FUBC. Future studies should prospectively evaluate effect of FUBC on clinical outcomes to further clarify these findings.

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Abstract 7605

**Group B Streptococcus vaginal colonisation from antenatal screening to 2 months after delivery: results from a prospective cohort study in France**

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**Background:** Maternal vaginal colonization with Group B Streptococcus (GBS) is the major risk factor for neonatal early onset disease. GBS vaginal colonization fluctuates during pregnancy but host factors and bacterial characteristics that may impact GBS colonization and persistence remain poorly investigated. The objective of the study was to identify maternal demographic factors and features of GBS isolates associated with persistent GBS colonization.

**Materials/methods:** GBS vaginal colonization was prospectively recorded during a screening program of pregnant women in France from 2012 to 2016. Clinical data including place of birth were recorded. Vaginal swabs were collected at antenatal screening, at delivery, 21 +/- 7 days (D21) and 60 +/- 7 days (D60) after delivery. Colonization was defined as persistent when all samples from antenatal screening to D60 were positive for GBS. Capsular serotype genotyping and detection of the hyper-virulent CC-17 GBS were performed.

**Results:** A total of 906 women were included. In women screened GBS positive antenatally, GBS colonization was persistent in 63% of the cases, and GBS eradication either at D21 or at D60 was observed in 8% of the cases. Women screened negative remained uncolonized until D60 in 85% of the cases. Loss of colonization at D21 and D60 was more frequent in women born in France whereas persistent colonization was more frequent in those born in Sub-Saharan Africa. The dynamics of GBS vaginal colonization was not associated with any capsular serotype. The hypervirulent CC-17 GBS was over-represented in women born in Sub-Saharan Africa compared to women born in Europe and North Africa.

**Conclusions:** The place of birth which likely reflects the ethnicity impacts the dynamics of GBS colonization. Besides, women born in Sub-Saharan Africa are more frequently colonized with the hypervirulent CC-17 clone. These observations might be related to variations of the vaginal microbiota depending on the geographical origin and the vaginal community state types.

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Impact of selective decolonisation of critically ill extreme elderly patients using invasive devices with chlorhexidine 2% daily bath on healthcare-associated infection rates

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Background: Healthcare-associated infections (HAIs) in critically ill elderly patients are frequent and have a major impact on mortality and healthcare costs. These populations are more vulnerable to infections acquired in intensive care units (ICUs) due to frailty related to aging. Additionally most HAIs in Brazil are caused by multidrug-resistant gram-negative bacteria (MDR-GNB). Previous work developed on these populations by our group showed a significant reduction (26%) in colonization by carbapenem-resistant MDR-GNB using universal decolonization with chlorhexidine 2% daily bath.

Materials/methods: A prospective cohort study was conducted at an ICU of a private hospital in Rio de Janeiro with the care of extreme elderly (+80 years-old) populations from January 2016 (beginning the decolonization strategy with daily bath with chlorhexidine 2% in January 2017) through October 2019. A comparative analysis before-after of the adjusted rates of the HAIs (ventilator-associated pneumonia [VAP], catheter-associated urinary tract infection [CAUTI] and central line-associated bloodstream infection [CLABSI]) were done in three periods: Baseline period (January to December 2016); period 1 with universal decolonization in all patients admitted at the ICU (January 2017 to October 2018) and period 2 with selective decolonization only for patients with invasive devices (April 2019 to October 2019).

Results: In total, HAI rates were analyzed following 1,955 extreme elderly critically ill patients (summarizing 24,646 patient-days; baseline period-2016: 6,157 patient-days; period 1:14,608 patient-days; and period 2:23,891 patient-days) [Graph 1]. Following the introduction of the universal decolonization strategy with chlorhexidine 2% daily bath, we observed a significant reduction in all HAIs rates (VAP: 27 to 7.3 episodes/1000 patient-days; CAUTI: 56.8 to 1.9 episodes/1000 patient-days; and CLABSI:63.8 to zero episodes/1000 patient-days). After targeting the strategy to patients with invasive devices only, we observed similar HAI rates in the ICU (VAP: 7.3 to 4.6 episodes/1000 patient-days; CAUTI: 1.9 to 1.8 episodes/1000 patient-days; and CLABSI: zero to 1.1 episodes/1000 patient-days).

Conclusions: The selective decolonization strategy with chlorhexidine 2% daily bath, in addition to decreasing the colonization rate by MDR-GNB, protects the populations of extreme elderly critically ill from healthcare-associated infections. This strategy to reduce use chlorhexidine 2% daily bath is necessary.
Graph 1. Impact of stopping universal decolonization with chlorhexidine 2% daily bath on healthcare-associated infections rates of critically ill extreme elderly patients

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Abstract 7612

Screening for latent tuberculosis infection among asylum seekers in Brescia, Italy: results from the E-DETECT Project

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Background: Screening and treatment for latent tuberculosis infection (LTBI) among asylum seekers (AS) is a key element of tuberculosis (TB) elimination in low incidence countries. Screening strategies are heterogenous among countries and completion rates are known to be low. The E-DETECT project aimed at identifying enablers of the cascade of TB prevention in this population.

Materials/methods: The intervention consisted in a modified centralized, system for LTBI screening in AS in the Province of Brescia, Northern Italy. During the intervention phase, all the steps of the LTBI screening cascade were performed at a single site. The cascade consisted of an initial tuberculin skin test (TST) followed, if reactive ≥10 mm, by a confirmatory IGRA. Subjects with double positive tests performed a chest X-ray and those without any abnormality started an LTBI regimen of rifampicin/isoniazid for three months. Results were compared with historical data in the same setting, with similar procedures, but with a fragmented site (consultations at at least three health sites with independent management).

Results: In 2017-2018, 1,356 AS arrived in Brescia. They were mainly male (1178, 86.8%) from sub-Saharan Africa (1034, 76.2%) with mean age of 23.1 (SD 10) years. The standard LTBI screening organization was offered to 1,206 (88.9%) AS at arrival, while 145 (10.7%) received the intervention approach. LTBI diagnosis was more frequent in delayed screening (28.9% vs 17.7%, OR 1.89 p<0.01) without difference in the number of AS coming from high incidence TB countries (cut-off 150/100,000). Screening completion rate was significantly higher during the intervention (98.6% 143/145 vs. 55.1% 665/1206 OR 63.64, p<0.01). Treatment initiation rate also increased in the intervention phase (100%, 42/42 vs 83.6%, 87/104), as well as treatment completion (88.1%, 37/42 vs 71.3%, 62/87, p<0.05).

Conclusions: The LTBI cascade among AS can be significantly improved by a centralized approach to treatment and screening practices. Higher prevalence of LTBI in delayed screening could reflect recent (either during travel or in Italy) acquisition of the infection.

### Multivariate analysis of variables associated with LTBI screening completion

<table>
<thead>
<tr>
<th>Screening completion</th>
<th>AOR</th>
<th>IC95%</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delayed centralized</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No 685 (55.1)</td>
<td>63.84</td>
<td>15.64-258.85</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Yes 143 (98.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No 206 (54.2)</td>
<td>0.66</td>
<td>0.51-0.86</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Yes 602 (58.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F 98 (55.1)</td>
<td>1.19</td>
<td>0.84-1.67</td>
<td>0.3118</td>
</tr>
<tr>
<td>M 710 (60.6)</td>
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<td></td>
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</tr>
<tr>
<td>High influx period</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>No 67 (61.5)</td>
<td>1.20</td>
<td>0.76-1.89</td>
<td>0.4294</td>
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<tr>
<td>Yes 373 (59.6)</td>
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<tr>
<td>Age</td>
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<td>1.00</td>
<td>0.99-1.01</td>
<td>0.2871</td>
<td></td>
</tr>
</tbody>
</table>

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Abstract 7613

**Delafloxacin activity against moxifloxacin-resistant *Clostridiodes difficile* clinical isolates**

Salud Rodríguez-Pallarés¹, Fatima Galan-Sanchez¹, Jorge Arca Suárez¹, Fátima Cano¹, Manuel Rodriguez-Iglesias¹

¹Hospital Universitario Puerta del Mar, Cádiz, Spain

**Background:** *Clostridioides difficile* infection (CDI) is the leading cause of antibiotic associated diarrhea in hospitalized patients worldwide. Fluoroquinolone resistance in *C. difficile* has been blamed to play a key role not only in the occurrence or recurrence of the disease, but also to contribute to the selection of epidemic strains in the hospital environment. Recently the anionic fluoroquinolone delafloxacin has been approved by the FDA. Its combined structural features directly impact on the activity of delafloxacin, with very low minimal inhibitory concentrations against a large array of grampositive and gramnegative organisms and may explain its enhanced potency at acid pH. The aim of this study is to evaluate the activity of delafloxacin against a collection of *C. difficile* with moxifloxacin-resistant phenotype.

**Materials/methods:** Fifteen isolates of *C.difficile*, recovered from non-formed stool specimens from patients with suspected CDI at the Hospital Universitario Puerta del Mar, Cádiz, Spain, with moxifloxacin MICs≥32 ug/ml were included in the study. Susceptibility to moxifloxacin and delafloxacin were determined by the E-test method. Total bacterial DNA extraction was carried out using the EZ1 Advanced XL (Qiagen). The clonal relatedness of the 15 clinical isolates was assesed by PCR-ribotyping. The *C. difficile* PCR ribotypes001, 014, 078, and the epidemic NAP1/027 were used as references. The presence of mutations in the QRDR was assessed by partial sequencing of the *gyrA* and *gyrB* genes.

**Results:** Delafloxacin was more active than moxifloxacin (range 0.01-2 μg/ml; MIC₅₀ and MIC₉₀, 0.38 and 0.75 μg/ml, respectively). Four isolates belonged to ribotype 078, which was the most prevalent (26.6%), followed by ribotype 014 (13.3%). None of the isolates belonged to ribotype 027. The aminoacid substitution Thr82Ile in the *Gyr* A was found in the majority of the isolates (14/15). Six different mutations outside the QRDR of *Gyr*A were also found. Evaluation of the *Gyr*B sequences revealed the presence of mutations in eight isolates, located outside the QRDR.

**Conclusions:** Delafloxacin was active against non-027 moxifloxacin-resistant *C. difficile*, with 100% of isolates being inhibited by delafloxacin at ≤1 μg/ml. Classical Thr82 to Ile substitution, the main genetic event leading to high-level resistance to quinolones, seems not to affect delafloxacin.

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Abstract 7615

**Artificial intelligence to support antibiotic decision-making processes in haematological patients with febrile neutropaenia**

Carolina Garcia Vidal*, Gemma Sanjuan-Gomez, Pedro Puerta, Estela Moreno, Mariana Chumbita, Nicole Garcia-Pouton, Marta López-Garrido, Cristina Pitart, Celia Cardozo, Marta Bodro Marimont, Laura Morata, José Antonio Martínez Martínez,Montserrat Rovira, Jordi Esteve, José Mensa, Alex Soriano

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**Background:** We aimed to predict which microorganisms would be isolated in our hematological patients' cultures at febrile neutropaenia (FN) onset in order to personalize empirical antibiotic treatments.

**Materials/methods:** A total of 1.11 billion pieces of high-quality data retrieved from electronic health records concerning consecutive episodes of FN at a tertiary hospital in Barcelona were used to feed-forward 4 neuronal networks (NNs). Patients were classified per their predicted risks of infections caused by: 1) *Pseudomonas aeruginosa* (PA) 2) PA multidrug-resistant (MDR) 3) ESBL-Enterobacteriaceae or 4) none of the prior. In the first retrospective phase, algorithms were trained with 70% of the data and tested with the other 30% (2008-2017). In the second phase (2018), the algorithms worked within a prospective setting.

**Results:** A total of 2263 FN episodes were documented [2067 retrospective/196 prospective]. Bacterial infections were documented in 497 patients, with the majority (355, 71.4%) being positive blood cultures. Overall, 104 patients had PA infection, 54 PA-MDR, 49 ESBL-Enterobacteriaceae, and 2111 none of the prior infections. Table 1 summarizes the sensitivity, specificity, positive prediction value, and negative predictive value of NN predictions provided in both the retrospective and prospective phases of the study.

**Conclusions:** NNs analyzing a large amount of high-quality data obtained from EHRs are helpful in predicting which microorganisms will be reported in our patients' cultures. This tool serves as a revolutionary approach, maximizing the power of an artificial intelligence decision support system to personalize empirical antibiotic treatments.

<table>
<thead>
<tr>
<th>MDR Enterobacteriaceae</th>
<th>PA</th>
<th>MDR-PA</th>
<th>None of the prior infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restroactive</td>
<td>Prospective</td>
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<td></td>
</tr>
<tr>
<td>44</td>
<td>5</td>
<td>99</td>
<td>49</td>
</tr>
<tr>
<td>Total cases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prediction</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>given to this category</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>True positive</td>
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<td></td>
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<tr>
<td>False positive value</td>
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<td></td>
</tr>
<tr>
<td>False negative value</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specificity</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Predictive positive value</td>
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<td></td>
</tr>
<tr>
<td>Predictive negative value</td>
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</tr>
</tbody>
</table>

**Table 1. NN predictions**

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Prevalence of ST131 in community-acquired Escherichia coli urinary tract infections in Gauteng, South Africa

Keegan John Hoog1, Johann Pitout2, Ebrahim Hoosien3, Marthie M. Ehlers1, Marleen Kock*1

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Background: The spread of the pandemic clone, ST131 extra-intestinal pathogenic Escherichia coli (ExPEC) harboring resistance to cephalosporins and fluoroquinolones poses a great risk to patient health. The dissemination of the ST131 E. coli clone and the diversity of its drug resistant associated clades has not been widely documented in South Africa. A study was designed to characterize community acquired E. coli urinary tract infections (UTIs) acquired from a private diagnostic laboratory in South Africa during a three-day period in October 2019.

Materials/methods: A multiplex PCR screened isolates for the E. coli specific gene uidA and ST131-specific single-nucleotide polymorphisms in genes mdh and gyrB. Isolates that screened positive for ST131 were subjected to a published ST131 clade PCR assay for the identification of ST131 clades A, B and C (including subclades C1, C2 and C1-M27).

Results: From the 232 isolates recovered from the diagnostic laboratory, the overall prevalence of pure ST131 E. coli isolates was 17% (n=37). The clade diversity of the ST131 isolates included subclades C1 (n=23), C2 (n=8), clade A (n=3) and subclade C1-M27 (n=3). No isolates screened positive for clades B or C0.

Conclusions: The rapid method for detection of ST131 and its subclades allows for easy surveillance of the dissemination of highly-epidemic pathogen strains as well as their associated antibiotic genes. Clade C of ST131 is of high concern due to the presence of fluoroquinolone resistance in the clade as well as the beta-lactamase cefotaximase-Munich-15 in subclade C2 and presence of the IncF1: A2: B20 plasmids in subclade C1. The presence of the global C1 subclade C1-M27, which is associated with blaCTX-M-27, further poses risk of increased antibiotic resistance. Our results highlight, for the first time, the diversity of the high-risk ST131 ExPEC clone, with associated antibiotic resistance, circulating amongst communities in South Africa. Proper infection control strategies and future vaccination against certain strains would limit the spread of these high-risk clones.

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Abstract 7618

18 years of surveillance of nasopharyngeal pneumococcal carriage before, during, and after PCV7 then PCV13 implementation in children with acute otitis media

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**Background:** To determine whether the use of 7-valent pneumococcal conjugate vaccine (PCV7) then 13 valent (PCV13) caused a shift in *Streptococcus pneumoniae* serotypes distribution and influenced the antibiotic susceptibility.

**Materials/methods:** Between 2001 and 2019, 121 pediatricians obtained nasopharyngeal swabs from children with acute otitis media aged 6 to 24 months. The swabs were analyzed by the French National Reference Centre for Pneumococci. Demographics, medical history and physical examination findings were recorded.

**Results:** From the 10,740 nasopharyngeal swabs, we observed a slight reduction in the overall pneumococcal carriage, a marked decrease of vaccine serotypes (VT), and an increase in non-vaccine serotypes (NVT). Among the VT, the only serotype still carried at a low level (<3%) were 19F, 19A, and 3. The most frequently (5 to 10%) carried NVT were 15B/C, 23B,11A,15A,10A, and 35B. A significant reduction (40%) in the rate of penicillin-non susceptible (PNSP) strains has been observed. PNSP were mostly represented by NVT 35B, 11A and 15A. No penicillin resistant strain has been found since 2016.

**Conclusions:** Since the PCV13 implementation, in carriage, replacement appears almost complete, the serotype distribution tending to a new equilibrium without emergence of highly resistant pneumococci to date.

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**Abstract 7619**

**High-resolution mass spectrometry database (Acrion) improves identification of clinical yeasts**

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**Background:** Yeast species are frequently identified by MALDI-ToF in the clinical laboratory. Due to their cell wall structure, they give higher quality identifications when they are prepared with manual lysis steps either offline or on the MALDI-ToF plate. While highly effective, it adds both sample preparation time and variability between laboratories, such that protein databases are sometimes less effective elsewhere. A second variability comes from the accuracy of the protein masses, dependent on the mass spectrometer used. By decreasing the mass resolution, the universality of the database improves, but the likelihood of false matches rises, yielding reduced species identification accuracy. We explore the performance a novel integrated high resolution mass spectrometer (HRMS) with automation and a spectral database to investigate whether the Acrion™ system can overcome these two sources of variability and improve yeast identification accuracy.

**Materials/methods:** 37+ clinical yeast species, multiple strains each, were cultured on saboraud dextrose agar and measured with a HRMS to create a comprehensive database of protein masses against which unknown strains could be identified. These measurements were collected with a resolution of <10 ppm, and protein masses in the range of 5-30 kDa were detected for each strain. A classifier was created to identify species. A test set of strains [not used in classifier development] were measured on the Acrion™ system and classified to species level.

**Results:** A comprehensive HRMS database covering clinical yeast species causing >95% of yeast infections was developed. In the highly-automated workflow for this system, hands on time for the sample preparation is limited to sample picking (<30 seconds per sample) and user handling variability is thereby reduced. The HRMS analysis yielded good performance and discrimination even between challenging taxa; for example, we challenged the database with strains from each of the C. auris global lineages and all strains identified correctly.

**Conclusions:** By reducing the user and system variability through automated sample processing we were able to realise the improvement that high resolution mass spectrometry can yield in yeast species identification. Key to this was a comprehensive database enabling discrimination between challenging taxa that are frequently mis-identified in the clinical laboratory.

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Limited multidrug-resistant efflux pump overexpression among multidrug-resistant Escherichia coli of ST131
Johannes Camp*1, Sabine Schuster1, Martina Vavra1, Tobias Schweigger1, John Rossen2, Winfried Kern1

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Background: The development of multidrug resistance (MDR) phenotypes among bacteria presents a threat for patients and an ever-growing challenge for physicians. Gram-negative bacteria rely partly on efflux pumps to facilitate growth under stressful conditions and to increase resistance to a wide variety of commonly used drugs. Over the past years E. coli ST131 has emerged as a major cause of extraintestinal infection frequently exhibiting an MDR phenotype. The contribution of efflux to MDR in emerging E. coli MDR clones however, is not well studied.

Materials/methods: We investigated 34 strains from an international collection of clinical MDR-E. coli isolates within the framework of the Innovative Medicines Initiative (IMI) project “translocation”. Phenotypic analyses included MIC testing with and without addition of the AcrAB-TolC efflux inhibitor 1-(1-naphthylmethyl)-piperazine (NMP). MIC data for in total 17 agents and their reversion by NMP were analysed by Principal Component Analysis (PCA) in order to identify an efflux phenotype. Whole genome sequencing (WGS), multilocus sequence typing (MLST) and qRT-PCR of multiple efflux-related genes were performed.

Results: PCA revealed a group of 18/34 MDR-E. coli exhibiting increased susceptibility to treatment with NMP suggesting enhanced contribution of efflux pumps to antimicrobial resistance in these strains. This phenotype was termed “efflux phenotype”. Conversely, MICs in 16/34 strains remained relatively unchanged after treatment with NMP. In the latter group 11/16 strains belonged to the ST131, whereas in the former only 2/18 did. WGS revealed marked differences in efflux-related genes, with the majority of notable amino-acid substitutions occurring in AcrR, MarR and SoxR. Analysis of qRT-PCR data showed that strains exhibiting the “efflux phenotype” showed a significant overexpression of the AcrAB-TolC system, whereas in the remaining strains we found a trend towards enhanced expression of alternative efflux proteins (Figure 1).

Conclusions: We conclude that a proportion of MDR-E. coli exhibit an “efflux phenotype” which is linked to an overexpression of the AcrAB-ToIC-efflux-pump. Associated with this phenotype we find distinct genomic variations that could together be viewed as constituting an “efflux genotype”. Members of the ST131 are less likely to exhibit the “efflux-phenotype” which bears potential implications for the management of the ST131 pandemic.

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A combined strategy of antimicrobial stewardship and hospital-acquired infection control reduced the incidence of bacterial infection in a kidney transplantation programme (Hippomenes-PACTA-PROA study)

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**Abstract**

Infection is a major complication in kidney transplant recipients (KTR), compromising graft and patient survival. Both antimicrobial stewardship programs (ASP) and hospital-acquired infection control (HAIC) initiatives have demonstrated their utility in reducing the incidence of infection in the overall hospital population. We performed a quasi-experimental study to evaluate this combined approach in the setting of KTR.

**Background:** Infection is a major complication in kidney transplant recipients (KTR), compromising graft and patient survival. Both antimicrobial stewardship programs (ASP) and hospital-acquired infection control (HAIC) initiatives have demonstrated their utility in reducing the incidence of infection in the overall hospital population. We performed a quasi-experimental study to evaluate this combined approach in the setting of KTR.

**Materials/methods:** During the intervention period (June 2015-March 2016) an ASP was developed by a dedicated Infectious Diseases specialist who reviewed all antimicrobial treatments among consecutive KTR admitted to the hospital and made recommendations to optimize therapy. An intensive HAIC program was concurrently implemented to reinforce actions among healthcare workers oriented to decrease in-hospital spread of multidrug resistant microorganisms (MDR). The main study outcomes were days of treatment (DOT) for some relevant antimicrobials and incidence rates of overall and MDR infection per 1,000 transplant-days. Results in the intervention cohort were compared with a historical pre-intervention cohort of KTR during the immediately preceding period (June 2014-March 2015). Both cohorts were followed-up for 6 months after transplantation.

**Results:** We included 100 KTR (mean age: 53 years; 70% males) in the intervention cohort and 100 KTR in the pre-intervention cohort. During the intervention period there was a reduction in the consumption of meropenem (incidence rate ratio [IRR]: 0.61; 95% confidence interval [CI]: 0.51-0.72; \(p<0.001\)), vancomycin (IRR: 0.62; 95% CI: 0.5-0.77; \(p<0.001\)) and ciprofloxacin (IRR: 0.64; 95% CI: 0.52-0.78; \(p<0.001\)), and an increase of ceftriaxone (IRR 2.44; 95% CI: 2.0-3.0; \(p<0.001\)) and fosfomycin (IRR: 2.0; 95% CI: 1.3-3.2; \(p=0.001\)). There was a reduction in the incidence of global bacterial infection (IRR: 0.53; 95% CI: 0.35-0.82; \(p=0.002\)) and, specifically, upper urinary tract infection (IRR: 0.51; 95% CI: 0.28-0.90; \(p=0.01\)) and cystitis (IRR: 0.37; 95% CI: 0.15-0.83; \(p=0.01\)). A non-significant trend for a lower incidence of infection due to extended-spectrum beta-lactamase-producing Enterobacteriaceae was observed (IRR: 0.53; CI 95% 0.20-1.34; \(p=0.15\)). No differences were found for incidence rates of bloodstream or *Clostridioides difficile* infection.

**Conclusions:** A multifaceted approach based on ASP and HAIC was effective to optimize the use of antimicrobials and to reduce the incidence of bacterial infection among KTR.

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Abstract 7623

**The role of mobile genetic elements and virulence factors in the typing of vancomycin-resistant Enterococcus faecium outbreak isolates of a successful MLST ST117 cluster type 24**

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**Background:** The vancomycin-resistant E. faecium (VREfm) is a successful nosocomial pathogen able to survive in hostile environments, ultimately causing hospital outbreaks. The rapid emergence of certain VREfm lineages makes it difficult to distinguish isolates based on the core genome. Here we explored if characterization of mobile genetic elements and virulence factors of VREfm isolates from two different outbreaks belonging to the same cgMLST CT24 could be useful for typing.

**Materials/methods:** Twenty-eight E. faecium isolates from patient and environmental samples from two different outbreaks in 2014 and 2017 were sequenced with Miseq of which two isolates were also sequenced using MinION. De novo assemblies were performed in CLC Genomics Workbench and the hybrid assemblies were obtained through Unicycler. The genomes were analyzed by molecular typing (using SeqSphere) and investigated for known E. faecium virulence factors (VirulenceFinder), antimicrobial resistance genes (ResFinder), bacteriocins (BAGEL4), and prophages (PHASTER).

**Results:** All isolates belonged to the MLST ST117, CT24. They were resistant to vancomycin, trimethoprim, macrolides (except for one isolate in which the ermB gene was absent) and aminoglycosides. cgMLST analysis showed that the isolates belonged to two distinct genetic clusters with a minimal allelic difference of 10 between the closest related isolates of each cluster. The vanB carrying transposon Tn1549 was present in all isolates, however its genomic position was different between isolates 2014 and 2017. The gene conferring resistance to Chloramphenicol (cat) was exclusively present in isolates from the 2014 outbreak. All isolates contained the adhesion factors acm, efaAfAm and Esp. In all genomes, Enterocin A and Enterolysin A were identified, but isolates from 2017 additionally contained bacteriocins: Enterocin P, Bac43, Bacteriocin78 and HiracinJM3. In the majority of investigated isolates, three main plasmid families (Inc18, RepA_N and Rep3) were identified. Finally, all isolates carried three prophages: Entero_phiFL1A, Entero_EFAP-1 and Lister_238. In the majority of investigated isolates, three main plasmid families (Inc18, RepA_N and Rep3) were identified. Finally, all isolates carried three prophages: Entero_phiFL1A, Entero_EFAP-1 and Lister_238. Interestingly, isolates of 2014 additionally carried two phages: Entero_vbIME-197 and EnteroIMEEFm-5 while isolates of 2017 contained Lactoc_TP901-1.

**Conclusions:** Closely related isolates from separate VRE outbreaks could be distinguished by phage typing and different genomic location of the Tn1549 carrying vancomycin resistance. Also, the arsenal of bacteriocins was unique for the isolates of each outbreak cluster.

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Incidence of hospital-acquired bloodstream infections caused by *Klebsiella pneumoniae* and impact of different preventive strategies: need to going back to basics?

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**Background:** *Klebsiella pneumoniae* (Kp) is a frequent cause of hospital acquired bloodstream infections (HA-BSI), as well as a challenging pathogen due to its intrinsic or acquired antimicrobial resistance. Surveillance of Kp epidemiology still provides valuable information for its prevention and control.

**Materials/methods:** We conducted a retrospective observational study at the 1200 acute-care beds “San Martino” Policlinic Hospital, located in Genoa, Liguria, North-West Italy. We analyzed all patients with an HA-BSI caused by Kp from January 2008 to December 2018. Incidence was reported as number of events per 10,000 patient-days.

**Results:** We observed 994 Kp-related HA-BSIs during the study period, 610 caused by carbapenem resistant Kp (CRKp) and 384 by non-carbapenem resistant Kp (nCRKp).

Patients’ median age was 69 years (IQR 58-77), without differences between the two groups. Median onset time and median length of hospital stay were, respectively, 23 and 50 days for CRKp and 18 and 39 days for nCRKp group. Survival was significantly lower in CRKp group ($\chi^2$ p < 0.05 for 7th days all-cause mortality and p < 0.001 for 30th days all-cause mortality). Trends of CRKp and nCRKp incidence rates were different: while CRKp HA-BSIs increased from zero in 2008 to 2.12 in 2015 and then decreased to 0.81 in 2018, nCRKp HA-BSIs trend show a slow grow from 0.62 in 2008 to 1.21 in 2018. Stratifying this data for ward specialty we observed that intensive care units showed the highest incidence for CRKp HA-BSI, with a nadir observed in 2010 (25.47) followed with a marked decrease in the last years (6.94 in 2018).

In Figure 1 we reported the annual incidence of CRKp and nCRKp HA-BSIs observed at “San Martino” Policlinic Hospital and the chronological sequence of the main preventive intervention implemented in the period.

**Conclusions:** Although incidence of CRKp HA-BSI considerably decreased during the last years, the slow and steady increase of nCRKp in our hospital highlights the need to reconsider all the intensified strategies implemented to prevent and control Kp HA-BSI, focusing our attention on a stricter adherence to standard precautions and going back to the basics of prevention.

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Seasonal patterns in the burden of common bacterial pathogens in south-east Michigan post-acute care facilities

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Background: Knowledge of specific pathogens’ seasonal incidence patterns can improve epidemic surveillance and guide timing and efficacy of infection prevention initiatives. Influence of seasonal patterns on colonization with key pathogens among high-risk older adults in institutional settings is unknown. Through longitudinal screening of older post-acute care (PAC) patients and their immediate environment for two consecutive years, we investigated seasonal variation in patient and environmental burden of common bacterial pathogens in 6 SE Michigan PAC facilities.

Materials/methods: 1370 patients were screened between December 2013 and December 2015. Consenting patients’ hands, nares, groin, oral cavity, perianal area, and room objects (side table, bed control, call button, curtain, TV remote control, railing, toilet seat, wheelchair, door knob) were sampled for vancomycin-resistant enterococci (VRE), methicillin-resistant Staphylococcus aureus (MRSA), Klebsiella pneumoniae, ciprofloxacin sensitive and resistant E. coli. Three-month averaged incidence rates were plotted alongside average maximum temperature for the region.

Results: 418 unique MRSA, 679 VRE, 294 K. pneumoniae, and 443 E. coli were isolated from 640 patients and their rooms. A significant seasonal variation, correlated with regional monthly temperatures with a 1-month lag was observed for K. pneumoniae in patient and room isolates (0.17 and 0.19 unique isolates, respectively, per newly admitted patient and room in March, doubling to 0.34 and 0.38 in July).

Interestingly, there were marked seasonal differences between ciprofloxacin-susceptible and ciprofloxacin—resistant E. coli isolates, and only for the latter the trend was correlated to average regional temperatures (0.08 for patients and 0.02 for rooms in January, more than doubling to 0.19 and 0.09 respectively in June-July). The ratio between incidence of resistant and susceptible E. coli reached a trough of 0.26 in January, and doubled in May-July [up to 0.54]. No clear seasonal variation was observed for MRSA and VRE.

Conclusions: We report seasonal variability in two common gram-negative pathogens in high-risk post-acute care patients, and observe that antimicrobial-resistance may affect such patterns. Unlike some previous reports in hospitals, we did not observe seasonality patterns in MRSA and VRE among our post-acute care patients. Further investigation is warranted on the causes and geographical extension of such patterns in PAC.

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Abstract 7631

**Participatient: Patient Engagement Counter Catheter-associated urinary tract infections with an App (PECCA)**

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Abstract third-party references: The Netherlands Organisation for Health Research and Development; project 522004007

**Background:** Catheter-associated urinary tract infections (CAUTI) are the main cause of healthcare associated infections (HAI), leading to additional morbidity, increased antibiotic use and prolonged hospital stay. Inappropriate indication of a urinary catheter and avoidable prolongation of use causes for an increased and preventable risk of infection. This project aims to reduce unnecessary use of urinary catheters.

**Materials/methods:** In a multicentre, interrupted time series study, the smartphone application for patients called ‘Participatient’ (ECCMID2018:P0243) is introduced on thirteen wards in four hospitals in the Netherlands. The fraction of inappropriate use of urinary catheters is the primary endpoint. Secondary endpoints are catheter use and (CA)UTI reduction; increase in patient satisfaction-, involvement-, and trust in health care; measure and improve patient satisfaction with the Participatient app; and obtain analytical data on app use to optimize usefulness and ease of use. Data was collected every other week. This resulted in 12 data points during both the baseline and the post-intervention phase, of both 6 months. Preliminary analyses compared incidence rates before and after the intervention.

**Results:** Data were obtained from 6556 observed patients. App use was 9% of admitted patients, with a range of 6-12% between hospitals. The rate of inappropriate indication for use of urinary catheters dropped from 21.9% (n=175; 95%CI: 19.2-24.9%) to 7.0% (55; 5.4-9.0%) (P<0.0001; OR 0.27; 95%CI: 0.19-0.37). The overall urinary catheter prevalence was stable around 24% (798/3285 to 786/3271). The UTI rate decreased from 8.1% (267) to 4.9% (161), with CAUTI cases nearly halved from 141 to 78. Subsequent analyses will take into account the trends in the time series design, subgroup analyses, and eHealth outcomes.

**Conclusions:** The Participatient bundled eHealth intervention reduces unnecessary use of urinary catheters, with a substantial reduction in catheter-associated UTI. Patient involvement in infection prevention via eHealth is an effective way to improve the quality of care.

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<th>Appropriate % (n)</th>
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<td>Post-intervention</td>
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Does selective mandatory vaccination affect vaccine coverage of recommended vaccinations?
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Abstract 7632

Background: Maintaining high vaccination coverage is important in order to protect the individual and the community. Mandatory vaccination is an option in case of declining coverage. Widely used in the USA, it is considered a rather controversial issue in Europe. In Italy, after a decrease of vaccination coverage for the hexavalent [tetanus, diphtheria, pertussis, polio, hemophilus influenzae, and HBV] and the MPR vaccine under the optimal threshold, a new law which extended the number of mandatory vaccines from 4 to 10 and reinforced coercive measures, was introduced on July 2017.

Materials/methods: Vaccine specific data were collected at the Regional level and reported to the Ministry of Health. The information is analyzed in collaboration with the Istituto Superiore di Sanità in Rome. To the purpose of this analysis, data collected before and after the introduction of the law were compared (2016 and 2018, respectively).

Results: After two years, vaccination coverage increased for all mandatory vaccines. Interestingly, vaccination coverage increased also for other two recommended vaccines [from 89% to 92% for anti-pneumococcal and from 81% to 85% for anti-meningococcal C vaccination in 2016 and 2018, respectively]. Vaccination coverage for HPV, which is included among the recommended vaccines for the adolescents in the National Plan but is not listed among recommended vaccines in the law, remained at relatively low vaccination coverage levels.

Conclusions: Although it is not possible to disentangle the role of other factors contributing to the positive outcome, consistently with the results of studies conducted in the USA, vaccine mandates appeared to be successful in increasing vaccination coverage in Italy for both mandatory and recommended vaccinations. The long-term sustainability of the effect of mandatory vaccination and the potential negative drawbacks of the coercive measures need to be evaluated to generate scientific evidence in public health.

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Abstract 7637

**Ranking antibiotic classes by their potential impact on in-hospital selection of resistance: an ecological approach**

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**Background:** Antibiotic stewardship is a cornerstone strategy to combat antimicrobial resistance (AMR). However, evidence is scarce concerning which antibiotics have the strongest global impact on AMR and should be restricted first. Here, we leverage ecological modeling of hospital-based data to estimate the potential effect of 9 classes of antibiotics on the cumulative incidence of bacterial infections with resistance to either third-generation cephalosporins (3GCs) or carbapenems.

**Materials/methods:** Data were collected in 2016-17 from 357 wards in 4 hospital groups in Lyon, France. Using the ward as the statistical unit, we calculated the cumulative incidences of infection with ESKAPE pathogens and *Escherichia coli* with intrinsic or acquired resistance to 3GCs and carbapenems (3GCR and CR infections, respectively; total = 4,089). Ward-specific antibiotic pressure was estimated from consumption data for 9 antibiotic classes including cephalosporins, carbapenems or fluoroquinolones. We used Poisson regression in a metapopulation ecology framework to model the relationship between antibiotic consumption and the incidence of 3GCR and CR infection. Models were adjusted for sampling bias and the estimated frequency of introduction of 3GCR and CR pathogens from other wards.

**Results:** Consumption volumes of 3 out of 9 antibiotic classes had a positive and significant association with the incidence of 3GCR or CR infections: non-antipseudomonal 3GCs (CTX/CRO), carbapenems and piperacillin-tazobactam (TZP). 3GCR incidence was predicted by CTX/CRO and TZP use, but not carbapenems. CR incidence was predicted by carbapenems and TZP use, but not CTX/CRO. Strikingly, TZP coefficients outweighed other coefficients by a large margin in terms of amplitude and significance in both models.

**Conclusions:** Our approach illustrates how ecological modeling can be used to analyze hospital-wide data on infection incidence and antibiotic consumption while controlling for major sources of bias, including pathogen introduction from other wards. The controlled models identified a strong association between TZP use and the incidence of both 3GCR and CR infections in our setting. This is intriguing because TZP has been repeatedly considered as an alternative drug of choice in carbapenem-sparing strategies. If confirmed in other settings, our findings might call for a reevaluation of the rationale of recommending TZP over other drugs for ecological reasons.

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Estimation of cystic echinococcosis prevalence in an endemic region in Uzbekistan

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Background: Cystic echinococcosis (CE) is a cosmopolitan zoonosis caused by the tapeworm Echinococcus granulosus. While Uzbekistan and other countries in Central Asia are considered endemic, estimates of disease burden are lacking. We present findings from a cross-sectional, ultrasound-based survey evaluating the prevalence of CE in the Samarkand region of Uzbekistan.

Materials/methods: Study villages were selected based on the presence of human cases recorded by the national CE surveillance system. The survey was conducted in September 2019 in the Payaroq district of Samarkand in six rural communities. Residents aged 5 to 90 years underwent a free ultrasound examination of the abdomen. The World Health Organization-Informal Working Group on Echinococcosis (WHO-IWGE) classification was used to stage cysts. During the survey, information was also collected on individuals who had been previously diagnosed with CE and surgically treated.

Results: Over a total population of 34,968 inhabitants, 2,057 individuals (5.88%) agreed to undergo an abdominal ultrasound. Of these, 498 were males (24.2% males). Thirteen patients had abdominal CE (0.63%). Four of the 13 had previously been surgically treated for CE, while one was currently undergoing treatment with albendazole while awaiting surgery for an inactive cyst. In total, there were 5 active and transitional cysts (1 CE1, 1 CE2, 3 CE3b) and 10 inactive cysts (8 CE4, 2 CE5). Four patients had CL lesions and are currently receiving a one month course of albendazole as part of their diagnostic algorithm. Twenty-seven additional individuals reported previously undergoing surgery for CE. Surgeries had been conducted to remove CE cysts from the liver (67.7%), lungs (14.8%), spleen (3.7%), and liver and lungs (14.8%).

Conclusions: Our findings confirm the presence of CE in the Samarkand region of Uzbekistan. Surgical overtreatment of CE patients appears to be common and no conservatively managed patients were found even though most cysts were inactive. Further studies on the epidemiology of CE in Uzbekistan are needed. The local medical community must also be informed about current standards for the clinical management of this neglected disease.

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Abstract 7639

**Antimicrobial stewardship in oral and maxillofacial surgery: melting the iceberg**

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**Background:** Irrational antibiotic consumption leads to increasing antimicrobial resistance, significant side effects for patients and rising costs. The key aim of modern antimicrobial stewardship (AMS) is the rational antibiotic use by implementing restrictive as well as supporting measures. In oral and maxillofacial surgery, national or international guidelines regarding antibiotic prophylaxis and therapy are lacking for many clinical entities and antibiotic consumption is traditionally high.

**Materials/methods:** We determined the antibiotic consumption in the Oral and Maxillofacial Surgery clinic of a large German university hospital by using defined daily dose (DDD) per 100 patient days. We then implemented weekly ward rounds by a member of the AMS team, recording data from all patients [name, date of admission, diagnosis, indication, substance, route of application, duration of antibiotic therapy]. Recommendations regarding antibiotic therapy and/or further diagnostics were given. A mandatory consensus guideline covering antibiotic prophylaxis and therapy was developed and implemented. We determined the point prevalence of antibiotics prescribed for therapy and prophylaxis.

**Results:** Before the intervention, prevalence was high with up to 90% of patients receiving antibiotics, mainly amoxicillin/clavulanic acid or clindamycin. Median duration of antibiotic therapy and prophylaxis was 12 and 9 days, respectively. Antibiotic consumption was 97.9 DDD/100 patient days. This value was significantly higher than the national estimates [median 78.55 DDD/100 patient days]. During one year of intervention, antibiotic prevalence dropped to below 50% and the duration of antibiotic therapy and prophylaxis was reduced to 7 and 4 days, respectively. Accordingly, antibiotic consumption decreased and is now below the national estimates [Figure 1]. Interestingly, the ratio of patients receiving antibiotic prophylaxis or therapy did not change considerably.

**Conclusions:** Antibiotic consumption is high in oral and maxillofacial surgery. We show that regular ward rounds by the AMS team as well as the development of consensus guidelines can reduce antibiotic consumption substantially. Consensus guidelines furthermore help define quality indicators that can be used to evaluate long term effects of the AMS measures. However, such interventions are time-consuming and require appropriate personal and financial support of the antimicrobial stewardship team.

Figure: Antibiotic consumption in the Department of Oral and Maxillofacial Surgery 2018/2019

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Implementation of a homegrown electronic antimicrobial prescribing authorisation process at King Abdulaziz Medical City (KAMC) in Saudi Arabia

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Abstract third-party references: King Abdulaziz Medical City

Background: The misuse of antimicrobials is multifactorial and is related to knowledge deficits, resource limitations, and socio-behavioral prescribing trends. The Antimicrobial Stewardship Program at KAMC - Jeddah has been working on several interventions to improve antimicrobial prescribing including education, prospective audit and feedback, surgical prophylaxis improvement, and an electronic antimicrobial prescribing authorization (EAPA) process. This study describes the experience of implementing EAPA and its effect on days of therapy (DOT).

Materials/methods: The EAPA process implementation took 4 years in total from theory to implementation. This process involved proposing a workflow, creating electronic authorization request and reply forms embedded into the available prescribing process, an intensive face-to-face education on the workflow to all pharmacists, nurses, and prescribers, and establishing a dedicated team to handle all requests with an initial 24 hour oncall service for the first two weeks of implementation. The detailed reply form ensured complete recommendation documentation and facilitates electronic extraction of appropriateness evaluation and recommendations. The approving team also communicated recommended changes and inquiries to the prescriber. EAPA was piloted on 4 medications during phase 1 and 4 antimicrobials were later added.

Results: From March 2019 till October 2019, an average of 16 consults were automatically generated per working day [Total = 2701 consults]. Days of Therapy (DOT) of all antimicrobials was 927.6/1000 patient days in October 2018 and 779.2/1000 patient days in October 2019. DOT for the restricted antimicrobials was 239/1000 patient days for October 2018, and 123.3/1000 patient days for October 2019. There was a sharp drop in carbapenem utilization, 85.8/1000 patient days to 32.8/1000 patient days. There were no serious safety drug reports relating to the new process.

Conclusions: The EAPA workflow by the ASP at KAMC - Jeddah is effective at reducing inappropriate antimicrobial use. Further evaluation is required to evaluate the reasons for inappropriate prescribing and the long term effect on resistance patterns.

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Abstract 7642

**Amikacin nomogram for treatment of adult cystic fibrosis exacerbations based on an external evaluation of a population pharmacokinetics model**

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**Background:** Acute pulmonary exacerbations (APE) expose cystic fibrosis (CF) patients to life-threatening complications and contribute to the progression of the disease. The current guidelines recommend treating an APE with a combination of two antipseudomonal agents (beta-lactams and aminoglycosides). Amikacin is gradually used as a therapeutic alternative to tobramycin in patients harboring tobramycin-resistant pathogens. However, no optimal dosing has been described for amikacin despite important pharmacokinetic (PK) changes in adult CF patients. Current amikacin dosing is quite variable across CF accredited care centers. The main objectives of this study were to perform the external evaluation of the single population PK model available and revise amikacin dosing recommendations in adult CF patients if needed.

**Materials/methods:** Demographic, biological and clinical data of adult CF patients treated with amikacin at the McGill University Health Center (Montreal, Canada) were collected retrospectively. The predictive performance of the previously published two-compartment model was evaluated by determining both bias and inaccuracy. The model included creatinine clearance and weight as covariates on clearance and central volume of distribution, respectively. Monte Carlo simulations (n=1000) were performed with different doses [15-45 mg/kg] to determine the optimal regimen in order to reach the target ratio of the maximum serum concentration (Cmax) to the minimum inhibitory concentration (MIC) ≥8 mg/L.

**Results:** The model predicted the central tendency of amikacin concentrations measured in our patient population, that included 19 patients (age: 18-68 y.o.; weight: 28.1 -92.5 kg) treated for 30 APE episodes in total. The values for bias and inaccuracy were sound for clinical application with values of 7.2% (CI 95%: -0.65 - 15.0%) and 18.2% (CI 95%: 12.0 - 24.4%), respectively. The simulations showed that amikacin doses ranging from 20 to 45mg/kg/day should be adjusted according to the patient’s weight and creatinine clearance (Figure1).

**Conclusions:** This model can be generalized to adult CF patients and is suitable for predictive dosing. Initial doses should be adapted according to the patient’s weight and creatinine clearance. We developed a nomogram to optimize amikacin dosing regimens, which should be validated in a prospective study.

![Amikacin nomogram](image)

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Clones diversity of ESBL-producing Escherichia coli from vultures in Canary Islands

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Abstract third-party references: The authors gratefully acknowledge the financial support of “Fundação para a Ciência e Tecnologia” [FCT – Portugal], through the reference SFRH/B0/133266/2017 [Medicina Clínica e Ciências da Saúde]. This work was financed by “Dirección General de Protección de Lucha Contra el Cambio Climático y Medio Ambiente del Gobierno de Canarias” and also from “Fondo Europeo de Desarrollo Regional [FEDER]”.

Background: Although wild animals are not directly exposed to clinically relevant antibiotics, the antimicrobial resistance in these animals has been increasingly reported worldwide, in parallel to the situation in human and veterinary medicine. The high prevalence of infections with organisms producing extended spectrum β-lactamases (ESBL, particularly those of the CTX-M type) is threatening the future of the β-lactam drugs. This study was carried out to investigate the molecular epidemiology and genetic characteristics of ESBL-producing *E. coli* isolates originating from wild vultures (*Neophron percnopterus var. majorensis*) from Fuerteventura and Lanzarote (Canary Islands), in Spain.

Materials/methods: Fecal samples of 23 apparently healthy vultures were collected during July 2019. Samples were seeded in MacConkey agar supplemented with cefotaxime (2µg/ml), and *E. coli* identification was performed by Maldi-TOF-MS. Antimicrobial susceptibility was done by disk-diffusion (CLSI, 2018), and phenotypic detection of ESBL or carbapenemases were done by double-disk tests. The presence of *blaCTX-M* [different groups], *blaSHV*, *blaTEM*, and *blaOXA-48* genes, as well as *mcr-1* [colistin resistance], *tetA/tetB* [tetracycline resistance] and *int1* gene [integrase of class 1 integrons], was tested by PCR/sequencing. Furthermore, phylogenetic groups and MLST were tested by PCR/sequencing.

Results: ESBL producing-*E. coli* were detected in 6 of the 23 vultures samples (26%). All of them carried *blaCTX-M* genes, specifically: *blaCTX-M-15* (4 isolates) and *blaCTX-M-55* (2 isolates). ESBL-positive isolates were ascribed to phylogenetic group D (2 isolates), B1 (2 isolates) and A (2 isolates), and 4 sequence types were detected [ST/phylogenetic-group/ESBL]: ST1290/A/CTX-M-15, ST38/D/CTX-M-15, ST457/D/CTX-M-55 and ST6448/B1/CTX-M-55; this suggest a genetic diversity among these isolates. Three CTX-M-15 producing isolates contained the *blaTEM* gene and two carried the *tetA* gene. Four strains contained the *int1* gene.

Conclusions: Vultures frequently are fecal carriers of *E. coli* producer of ESBLs of epidemic CTX-M-15 and CTX-M-55 subtypes. ESBL-positive *E. coli* belonged to different clones [some of them very unusual], what suggest the implication of mobile genetic elements in the dissemination of this relevant mechanism of resistance. This underlies the complexity of bacterial resistance in wild animals and the possible interspecies transmission between humans, domestic animals, wildlife, interspecies and in the environment.

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An extreme chain reaction-based multiplex assay for detection of group A/C/G streptococci directly from throat swab specimens

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Background: Group A beta-hemolytic streptococci (GAS) are the most frequently isolated pathogens in acute bacterial pharyngitis. In addition, group C and G streptococci (GCS or GGS) have been increasingly recognized as causes of non-group A streptococcal pharyngitis in children. Diagnosis has traditionally been performed through rapid antigen detection test or culture. Both approaches suffer from significant drawbacks. The NeuMoDx Strep A/C/G Vantage Assay is a multiplex, “sample to result” nucleic acid test implemented using XCR technology to provide ultra-fast results on the NeuMoDx molecular systems. The assay detects and differentiates DNA of GAS and GCS/GGS simultaneously. All reagents and consumables used are stable at ambient conditions and come in ready-to-use configurations requiring no user mediated steps.

Materials/methods: Assay performance was characterized using throat swabs in liquid Amies transport medium. Multiple studies were performed to characterize the assay’s ability to detect GAS (both the M1 and M3 strains), GCS, and GGS. Studies included determination of the analytical sensitivity for all types, analytical specificity across non-target organisms, clinical sensitivity and specificity, and robustness in the presence of interfering substances.

Results: The Limit of Detection of the NeuMoDx Strep A/C/G Vantage Assay for the GAS M1 and M3 strains was established to be 70 and 170 CFU/mL respectively, 2.0E3 CFU/mL for GCS, and 1.0E4 CFU/mL for GGS. No interference was demonstrated in the presence of 20 endogenous and exogenous substances and 44 pathogens. No cross-reactivity was observed against the 44 relevant pathogens tested (meaning the assay displayed 100% analytical specificity). Turnaround time for the complete test was <50 minutes. Finally, excellent sensitivity (GAS: 100%; GCS/GGS: 95.9%) and specificity (100% for GAS and GCS/GGS) against FDA-cleared reference tests was demonstrated in a pilot method comparison study analyzing 230 clinical residual specimens.

Conclusions: The NeuMoDx Strep Vantage Assay is the only test developed for detection of Group A and Group C/G Streptococcus directly from throat swab specimens providing ultra-fast turnaround time and high throughput while requiring minimal (<5 min) user mediated steps to perform the testing.

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Abstract 7645

**Performance of the Allplex Assay in comparison to microscopy and in-house real-time PCR for the detection of helminths in Tanzanian stool samples**

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Abstract 7645

Although detection of helminths in stool samples is still mainly done by microscopy, real-time PCR and latest commercial multiplex PCR panels become more and more available. The primary objective of this study was to assess the performance of the Seegene Allplex™ GI-Helminthiasis Assay (Seegene) in comparison to Kato Katz (KK) and standard in-house real-time PCR (PCR).

A total of 310 stool samples, collected at the baseline in the framework of a randomized clinical trial for *Trichuris trichiura* in 2017 in Tanzania were analysed. All participants were *Trichuris* positive in at least one of two stool samples evaluated by Kato Katz for inclusion to the study. The three diagnostic methods studied detected the following helminths: (i) KK detecting *Trichuris*, *Ascaris* and hookworm (species differentiation not possible), not suitable for *Strongyloides*; (ii) PCR detecting *Ascaris*, *Trichuris*, *Ancylostoma*, *Necator* and *Strongyloides*; and (iii) Seegene detecting *Ascaris*, *Trichuris*, *Ancylostoma*, *Necator*, *Strongyloides*, Enterobius, *Taenia*, *Hymenolepis*, *Microsporidia*.

Three helminths (*Trichuris*, *Necator* and *Ascaris*) were detected in all three assays. *Strongyloides* was detected by PCR and Seegene only. Positivity for KK, PCR and Seegene for *Trichuris* was 100% (inclusion criteria), 92% and 85%, for *Ascaris*: 60%, 59% and 54%, for *Necator*: 44%, 49% and 48%, respectively. In comparison to KK, sensitivity of PCR and Seegene was for *Trichuris*: 92% and 85%; for *Ascaris*: 87% and 81%; for *Necator*: 81% and 91%, respectively. Overall rates of agreement of PCR and Seegene compared to KK were for *Trichuris*: 92% and 85%; for *Ascaris*: 86% and 84%; for *Necator*: 76% and 75%, respectively. Only four samples were positive for *Strongyloides* by PCR and three by Seegene. Seegene compared to PCR showed overall rates of agreement >90% for all detected species.

Overall, Seegene Assay and in-house PCR showed comparable results, however both molecular methods missed positive participants detected by microscopy due to uneven and irregular shedding of eggs. The Seegene Assay can be recommended as screening tool for its ease to use in molecular settings; however microscopy remains the most cost-effective method in developing countries and allows the detection of helminth eggs not covered by the used molecular assays.

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A new menace emerges in South America: yellow fever outbreak looms in Venezuela

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Abstract third-party references: The working group on emerging and re-emerging diseases in Venezuela

Background: In South America, yellow fever virus (YFV), an arbovirus, maintains enzootic transmission in sylvatic areas. YFV emerges in cyclic epizootic outbreaks among nonhuman primates associated or not with human cases, every 7-10 years. Venezuela is endemic for YF with urban transmission eradicated ~100 years ago. The last outbreak of sylvatic YF (epizootic wave) was recorded in 2005 comprising several regions of the country and a mortality in humans close to 50%. At the time of writing, a potential new YF epizootic outbreak is evolving and affecting vulnerable indigenous populations and rural areas of southeastern Venezuela. Around 3.5 million people live in high-risk areas for YFV transmission.

Materials/methods: Information published by the Venezuelan Public Health Society and Let’s Defend The National Epidemiology Network, by WHO Disease outbreak news, and unofficial information obtained locally was used. Further information will be gathered and presented at the time of the Congress.

Results: In September 2019, PCR-confirmed YFV infection was reported in a 46-year old male Pemón Amerindian resident of Bolivar State (southeast Venezuela). This is the first confirmed autochthonous case diagnosed since 2005. The patient became severely ill developing renal failure and was hospitalized. There are unconfirmed reports of more (severe) cases from Bolivar and from individuals living in rural areas from another region of the country. The worry that a large epizootic epidemic and eventual expansion to urban transmission occur is due to the low vaccine coverage and to the ubiquitousness and high prevalence of the urban vector Aedes aegypti that currently infests >20% of houses, well over the WHO transmission threshold. Moreover, illegal gold mining activities in Bolivar are fueling transmission, as people live in precarious conditions, there is no surveillance, low vaccination and high human mobility between these areas and the rest of the country increasing the risk of spillover into urban areas.

Conclusions: The potential for a similar or bigger epidemic as the one that took place in Brazil during 2016/18 is a threat that is augmented by the economic and humanitarian crisis affecting Venezuela with the collapse of the vector surveillance and control system and low vaccine coverage.

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Abstract 7647

Whole genome sequencing (WGS) and antifungal susceptibility testing of Candida glabrata (C. glabrata) reveals new associations of antifungal resistance (AFR) with gene variants

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Background: The incidence and severity of C. glabrata infections have increased at an alarming rate over the last few years. Studies have attempted to evaluate the epidemiology and investigate the genetic contribution towards AFR. WGS is a powerful tool for establishing the relationship between genetics and AFR.

Materials/methods: Thirty C. glabrata isolates were cultured from the blood of hospitalized patients. The susceptibility to fluconazole, voriconazole, caspofungin, and flucytosine were carried out using the broth dilution according to the EUCAST’s guidelines. WGS was deployed to obtain MLST profiles, and WGS sequence data was also compared with genes associated with AFR: (FKS1, FKS2, FKS3 with echinocandins; FCY1, FCY2, FUR1, FPS1, FPS2 with flucytosine and ERG9, ERG11, CDR1, PDR1, FLR1, SNQ2 with azoles).

Results: Sixteen MLST sequencing types (STs) were identified with ST3 and ST7 were predominantly present in 8 and 3 isolates, respectively. There were also 6 potential new ST profiles. The majority of isolates were resistant to fluconazole (29/30, 97%), while 19, 13 and 1 isolates were resistant to flucytosine, voriconazole and caspofungin, respectively (63%, 43% and 3%). Interestingly, the response to the two tested azoles was not consistent, with 12 isolates being resistant to fluconazole and susceptible to voriconazole or vice-versa. None of the isolates were either susceptible or resistant to every antifungal. The non-synonymous variants found in genes involved in AFR did not characterise resistant isolates, however, significant associations were found between almost every genetic variant and the degree of susceptibility. Eleven genes (FKS1, FKS2, FKS3, FCY2, FUR1, FPS1, ERG9, ERG11, CDR1, PDR1, FLR1, SNQ2) had at least 1 SNP associated with the resistance to a class of antifungals that has not been reported previously. Similarly, associations were also observed between the responses to the antifungals and the copy numbers of AFR genes (FCY2, FKS1, FKS2, FLR1 with fluconazole and FCY2, FKS1, FKS2, FLR1 with caspofungin).

Conclusions: Our study demonstrates increased AFR in bloodstream infections and suggests that C. glabrata clinical isolates may be acquiring AFR through new mechanisms.

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Abstracts 2020

Abstract 7648

**Melioidosis in patients suspected with recurrent tuberculosis: a disease in disguise**

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**Background:** Melioidosis is a known endemic infectious disease in many Asian countries with India predicted to have the highest burden for the disease. However, it remained too long neglected in the country and now is gaining the status of an emerging infectious disease. The disease is well known as a great mimicker and the presentation can be very similar to that of tuberculosis thus making difficult for physicians to come up with a clinical diagnosis.

**Materials/methods:** A prospective observational study was conducted from January 2016 to December 2018, to determine the proportion of melioidosis diagnosed among patients suspected with recurrent Tuberculosis infection in the endemic coastal region of the country. All cases suspected of recurrent TB were simultaneously tested for the presence of *B. pseudomallei* in the sample based on enrichment culture and TTSS1 PCR. Basic demographics and clinical details were analyzed to identify predictors of melioidosis infection.

**Results:** A total of 11,138 patients were admitted to the hospital with suspected tuberculosis infection in the last 2 years. 586 (5.2%) patients were diagnosed with primary tuberculosis. Among the confirmed cases, recurrent infection with microbiologically confirmed tuberculosis was documented in 1.8% cases whereas 1.2% of patients showed growth of *B. pseudomallei* in culture. Bone and joint infection, hepatomegaly with deranged liver function, and uncontrolled diabetes were predictors of melioidosis infection. Among the seven patients diagnosed with melioidosis, two died (29%). Five patients had a history of soil exposure.

**Conclusions:** This is the first study estimating the occurrence of melioidosis among patients presenting with recurrent tuberculosis from India. The study foreshadows the need for prompt microbiological diagnosis along with a high index of suspicion from the clinicians in endemic countries thus leading to prevent the abuse of Anti-TB treatment or prophylaxis.

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Evaluation of the BACT/ALERT VIRTUO in terms of time to detection, performance, workflow efficiency and impact on patient management, compared to the BACTEC FX automated blood culture system

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**Background:** Bloodstream infections are associated with high rates of morbidity and mortality, therefore prompt identification and antimicrobial susceptibility testing of the causative organism(s) are critical. We compared the microbiological/clinical performance of BacT/ALERT®-VIRTUO™-(BioMerieux) to that of the BACTEC™-FX-(BD) instrument, with time-to-detection (TTD, from loading into system until positivity) as the primary outcome. Secondary microbiological outcomes were positivity and contamination rates, hands-on-time, turn-around-time (TAT) and time-to-identification.

**Materials/methods:** We performed a prospective cross-over study using blood cultures from patients (>18 years) suspected of bacteremia/fungemia, localized in different wards into two strata (Stratum-1: Emergency Department-ED-; Stratum-2: in-hospital patients). Testing was performed in BACTEC™-PlusAerobic/F and BACTEC-Lytic/10-Anaerobic/F bottles and incubated in BACTEC™-FX, or BacT/ALERT®FA-Plus and FN-Plus bottles and incubated in VIRTUO™. Initially, each strata was randomly assigned to one of the incubators and then alternated every 2-weeks for 6 months (October-16th-2018 to April-16th-2019). All samples were processed in parallel with the same work-flow from the moment they were flagged positive. Maximum incubation time was 5 days.

**Results:** We included a total of 3898 extractions (776 1 bottles) in VIRTUO and 4179 (8306 bottles) in BACTEC. The median age was 69 years for both groups and the samples were equally distributed for each ward (ED: VIRTUO 80.9%, BD 75.1%). The number of blood cultures with at least one positive extraction was 278(7.1%) for VIRTUO and 193(4.6%) for BACTEC (p<0.0001). TTD and proportion of aerobic/anaerobic bottles is shown in Table. Hands-on-time was reduced by 15 minutes/day when using VIRTUO.

<table>
<thead>
<tr>
<th></th>
<th>VIRTUO</th>
<th>BACTEC</th>
<th>P value</th>
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<tbody>
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<tr>
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</table>

**Conclusions:** We have compared in a large scale and in a "real world" setting the performance of two automatic blood culture incubators. TTD differed in both systems depending on the type of bottle {aerobic vs. anaerobic}. The number of positive extractions was significantly higher for the VIRTUO incubated samples, which might impact antimicrobial prescription and clinical outcomes.

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Enteroaggregative Escherichia coli in mid-Norway

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Background: Enteroaggregative E. coli (EAEC) has been associated with acute diarrhoea in children, travellers’ diarrhoea and persistent diarrhoea in people residing in low-income regions. Other studies have not found any association between EAEC and diarrhoeal illness. The aim of this study was to examine the EAEC prevalence among people in mid-Norway and investigate the association between EAEC and diarrhoea.

Materials/methods: This study included faecal samples from 9511 diarrhoeal episodes and 381 randomly invited healthy controls from March 1st 2017 to February 28th 2019 with multiplex PCR for 19 pathogens. Request forms (diarrhoeal episodes) and questionnaires (healthy controls) provided clinical information. We investigated the relationship between EAEC and diarrhoea with unadjusted analyses on gender, age and concomitant pathogens, and performed multivariate logistic regression analysis on the significant variables.

Results: We detected EAEC in 440 (4.6%) of the diarrhoeal episodes, and eight (2.1%) of the healthy controls. Among diarrhoeal episodes, the prevalence was 4.8% in females, 4.7% in males, 18.8% in those with travel history, and 2.2% in those without. The age group 20-29 had the highest prevalence (9.2%). We detected other pathogens in 65.5% of all diarrhoeal episodes with EAEC, most commonly enteropathogenic E. coli (29.1%), enterotoxigenic E. coli (25.1%), norovirus (10.9%) and Campylobacter spp (9.8%). 80.5% of EAEC positive samples from persons with travel history had concomitant pathogens. Among healthy controls, we detected EAEC in 2.3% of females, 1.9% of males, and 0% of travellers. The prevalence was highest in the age group 60-69 (4.9%). No EAEC positive healthy controls had concomitant pathogens. EAEC was significantly associated with diarrhoea (OR=2.26, 95%CI=1.12-4.59), also when adjusting for age and gender (OR=2.11, 95%CI=1.04-4.29). No significant association was found when adjusting for concomitant pathogens (OR=1.54, 95%CI=0.73-3.17).

Conclusions: EAEC was a common finding in faecal samples in mid-Norway, and it was significantly associated with diarrhoea. The prevalence of concomitant pathogens was high, and the analysis was no longer significant when corrected for these. Further studies on bacterial virulence-related genes to distinguish pathogenic from non-pathogenic strains, as well as on the relevance of pathogens’ coexistence in the gut, are warranted.

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Abstract 7655

Aging influences effector functions of neutrophil granulocytes in *Pseudomonas aeruginosa* lung infection

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**Background:** With the increasingly aging population, the incidence and mortality of *P. aeruginosa* induced lung infections simultaneously rise. This might in part be due to the age-dependent dysregulation of the immune system, including the function of neutrophilic granulocytes. Therefore, the aim of this study was to investigate the impact of the host’s age on the immune response towards *P. aeruginosa* induced pneumonias using precision-cut lung slices (PCLS) and isolated neutrophils.

**Materials/methods:** PCLS prepared from young adult (11-15 weeks) as well as old (18-22 months) C57BL/6NCrl-mice were infected with the *P. aeruginosa* standard lab strain PAO1 or a late clinical *P. aeruginosa* isolate [D61], derived from a chronically infected cystic fibrosis patient. The resulting infection and induced host response were analysed by assessing bacterial load and cytokine production by means of counting colony-forming units and performing ELISA. Furthermore, neutrophils and bacteria were co-cultivated and neutrophil extracellular trap (NET)-formation was quantified and imaged using SYTOX green and antibody staining. Additionally, colony-forming units were quantified to evaluate bacterial clearance by neutrophils.

**Results:** Bacterial load in lung tissue was comparable in PCLS of young and old mice, but was lower when using the clinical isolate D61 as compared to PAO1. Interestingly, an age-dependent increase of pro-inflammatory cytokines such as TNF-α, IL-1β, MIP-3α, KC and IL-17A was observed in PCLS of old mice compared to young animals, with significant differences particularly for D61. Regarding neutrophil effector functions, NET-formation and bacterial clearance were lower when using D61 compared to PAO1. Additionally, NET-release was increased in an age-dependent manner when using neutrophils of old mice in response to PAO1.

**Conclusions:** In line with the increased pro-inflammatory status reported in the elderly population, ex vivo lung tissue of old mice displayed an increased cytokine response towards *P. aeruginosa* infection predominantly for the clinical isolate D61, despite the lower bacterial load compared to PAO1. Furthermore, neutrophil effector functions were impaired for D61 compared to PAO1 in an age-dependent manner. Conclusively, aging seems to be a relevant factor in terms of host immune response and resolution of infection, suggesting that elderly individuals could benefit from therapies restoring effective immune responses.

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Multiple mutational possibilities allow ceftazidime-avibactam resistance in KPC-type carbapenemase

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Background: KPC carbapenemases have a broad substrate profile, including penicillins, cephalosporins, carbapenems and most beta-lactamase inhibitors. The association ceftazidime-avibactam can inactivate KPC-type carbapenemases offering a significant advance over some antimicrobials agents, and it keeps an in vitro activity against carbapenem-resistant Enterobacteriaceae (CRE). Mutations in genes such as blaKPC or in genes encoding porins can lead to resistance to ceftazidime-avibactam, limiting the benefit of this last resort strategy. We recently described the impact of anticancer drugs on the bacterial mutation rate, but also on the widening of the beta-lactamase spectrum of the KPC-type carbapenemase towards ceftazidime-avibactam. The aim of this study was to evaluate the KPC mutational possibilities conferring ceftazidime-avibactam resistance.

Materials/methods: We studied a hundred mutants from an in vitro selection of clinical isolates of Enterobacteriaceae. The strains carried either blaKPC-2 or blaKPC-3, and they became resistant to ceftazidime-avibactam after a culture with anticancer drug chemotherapy. To confirm their phenotype, we cloned the KPC genes of a subset of resistant mutants in the plasmid pBR322 and we determined their susceptibility to various beta-lactams +/- inhibitors.

Results: We identified several point mutations in the KPC gene and particularly in the omega loop. The positions 164 and 179 were the most mutated sites. Although several mutations have been previously described in clinical isolates, other mutants, not yet described, showed insertions or deletions within the beta-lactamase, either in the omega loop or close to the position 274. The increase in the MIC to ceftazidime-avibactam is associated with a decrease of MIC to several other beta-lactams +/- inhibitors.

Conclusions: KPCs evolve rapidly and mutations are increasingly described in clinical isolates. We show that many ways lead these enzymes to become resistant to ceftazidime-avibactam, an antibiotic of the latest therapeutic line. These possibilities include insertions or deletions at certain key positions suggesting a common pattern across different class A beta-lactamases responsible for the extension of the substrate spectrum. The MIC results indicate that the acquired mutations in KPC expand its substrate profile by increasing catalytic efficiency for ceftazidime hydrolysis at the cost of carbapenemase activity.

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The flow cytometry-assisted susceptibility test (FAST) accurately predicts colistin MICs for Gram-negative bacilli directly from positive blood culture in less than four hours

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Background: Bloodstream infections require rapid, effective treatment to safeguard patient lives: every hour without appropriate antimicrobial therapy increases cumulative risk of death. Current best practice recommends the use of an automated blood culture incubation system, with subsequent antimicrobial susceptibility testing. Against a background of rising resistance to carbapenems, rapid colistin susceptibility results for Gram negative organisms from positive blood culture are becoming increasingly important. We present the use of the Flow Cytometry-Assisted Susceptibility Test (FAST) to rapidly assess colistin susceptibility of Gram negative bacilli direct from blood culture.

Materials/methods: Using expended and simulated clinical specimens, we tested n=106 positive blood cultures confirmed by Gram stain to contain Gram negative bacilli. Simulated specimens were created by inoculating 3 colonies from an overnight blood agar plate into BD BACTEC™ Plus Aerobic bottles already containing donor blood drawn after informed consent by a phlebotomy service. Bottles were incubated in a BD BACTEC™ blood culture analyser until positive. An aliquot of blood culture mixture was briefly centrifuged, and the supernatant inoculated directly into a Sensititre™ GNX3F plate using a Sensititre™ auto-inoculator module. Plates were incubated at 35°C for 2 or 3 hours, diluted 1:4 with a staining buffer containing 5 µM SYTO® 9, and read using an Attune™ NxT flow cytometer with an autosampler. Data were analysed using bespoke software to predict colistin MIC and susceptibility in ≤ 4 hours. Identification of unknown organisms in specimens was performed by Bruker MALDI-Biotyper® analysis and available within the assay window.

Results: We determined colistin MICs for organisms from the following categories: Enterobacterales (n=71, 3 resistant), pseudomonads (n=23, 4 resistant), A. baumannii (n=12, 1 resistant). The distribution of flow cytometry data proved to be complex when compared with other classes of antimicrobial agents. Essential agreement and categoric agreement compared to BMD were 100% across all 106 isolates tested.

Conclusions: The rapid mutation and dissemination of MCR variants underscores the need for phenotypic tests to capture all colistin resistance phenotypes. We present FAST as a new rapid method to correctly assay colistin susceptibility from positive blood culture, with results in ≤ 4 hours from blood culture positivity.

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Abstract 7660

**Pilot study of reimbursement model to ensure access to new critical antibiotics in Sweden**

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**Background:** Sweden has low levels of resistance, a restrictive antibiotic use and is a small market. Consequently, some antibiotic products face such low demand that there is a risk that pharmaceutical companies do not choose to have them available on the Swedish market. The Public Health Agency of Sweden (PHAS) was in 2018 commissioned by the Government to pilot a new reimbursement model for new antibiotics of special medical value. The aim of this pilot study is to ensure availability of new antibiotics for critical pathogens. The pilot study will run until 2022.

**Materials/methods:** PHAS has developed an algorithm to identify products for the reimbursement model. To define the need and specific medical value, the algorithm include evaluation of sales, number of Market Authorization Holders, evaluation of products activity, ecological profile and role in the Swedish treatment guidelines.

The reimbursement model implies that a minimum annual revenue to the pharmaceutical companies is guaranteed at national level. In return, the companies warrant high availability for all Swedish hospitals and a security stock. The health-care providers will continue to pay for their use. Annual reconciliation will be done. If the revenue of companies is lower than the guaranteed level, the difference will be paid from national level. If the revenue of companies is higher than the guaranteed level, the companies will be paid 10 percent of the value of the security stock (Figure). The guaranteed annual revenue is based on clinical need.

**Results:** The contracting process is set as a public procurement process. The call will be opened for antibiotic products identified by the algorithm and with effect against multi-resistant Enterobacteriaceae, carbapeneme-resistant *Pseudomonas aeruginosa* and/or carbapeneme-resistant *Acinetobacter baumannii*.

**Conclusions:** Existing financing models fail to secure a steady supply of new drugs in small markets like Sweden. This novel reimbursement model is predictable for pharmaceutical companies and the total revenue over the contract years will be higher. The model may possibly be adapted and scaled up to similar countries.

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Abstract 7661

**Prospective evaluation of bacteraemia rates and infectious complications among patients undergoing endoscopic retrograde cholangiopancreatography**

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**Background:** Endoscopic retrograde cholangiopancreatography (ERCP) is becoming a common procedure for diagnosis or treatment of biliary and pancreatic illness worldwide. Although improvements in the technical and hygienic standards led to reduce the complications, infections still remain one of the most serious complications of ERCP. In this study, infectious complications of ERCP and patient characteristics were evaluated prospectively in a tertiary-care hospital.

**Materials/methods:** Patients undergoing ERCP were evaluated prospectively in a 15 months period. Patients' demographic features, underlying diseases, reasons for ERCP, antimicrobial prophylaxis, type of infections, causative agents, antimicrobial susceptibility of microorganisms, duration of hospital stay, and prognosis of all were recorded.

**Results:** Totally 788 patients underwent to ERCP in study period. Infectious complications were developed in 13 (1.66%) patients (eleven males and two females). Mean age of the patients were 38 years (range 34-87 yrs.). All the patients were admitted to the tertiary referral centre were retrospectively included. Therapeutic intervention was the primarily indications in 11 (84.4%) patients due to choledocholithiasis and stenosis in biliary tract system. Diabetes mellitus (in 2 patients) and malignancy (in 2 patients) were the underlying diseases. All the patients were received ciprofloxacin + metronidazole (8 patients; 61.5%) either ceftriaxone + metronidazole (5 patients; 38.5%) prophylaxis. Bacteraemia occurred in 11 (84.4%) patients, liver abscess detected in 2 patients (one was with bacteraemia). The most prevalent isolates detected during bacteraemia were *Klebsiella pneumoniae* (6/13), *Escherichia coli* (4/13). Five of *Klebsiella pneumoniae* and 3 of *Escherichia coli* isolates were ESBL+. One of the patients had to be admitted to the intensive care unit. Carbapenems were the most frequently used agents (8/13). Mean duration of antibiotic use was 16 day (5-30 days) and mean hospital stay was 21 day (5-90 day).

**Conclusions:** ERCP-related infectious complications are decreasing but infections with resistant microorganisms are becoming a serious problem. All centres need to evaluate their own cases and to develop strategies to prevent the infectious complications.

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Analysis of chloramphenicol susceptibility in metallo-beta lactamase producing Enterobacterales

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Background: Systemic use of chloramphenicol has been limited by rare adverse effects including aplastic anemia. However with increasing antimicrobial resistance it is sometimes necessary to consider all therapeutic options for multidrug-resistant Enterobacterales including Carbapenemase Producing Enterobacterales (CPE) and for Acinetobacter species.

Materials/methods: Ninety-two class B Metallo-Beta Lactamase (MBLs) isolates of CPE and Acinetobacter spp. from throughout Ireland submitted to the national reference laboratory service during the period February to August 2019 were included. Duplicate isolates were excluded. Isolates from CPE screening samples and general diagnostic samples were included. Isolates were identified by Maldi-TOF. CPE production was confirmed by immunochromatographic detection enzyme and by whole genome sequencing performed using Nextera XT (Illumina) library preperation and MiSeq (Illumina). Species included were Escherichia coli, Enterobacter cloacae complex, Citrobacter species, Klebsiella pneumoniae, Klebsiella species, Klebsiella oxytoca, Proteus mirabilis, Serratia species and Acinetobacter baumannii complex. Chloramphenicol susceptibility testing was performed by broth microdilution.

Results: MIC values were as follows ≤8 (n=58), 16 (n=8), 32 (n=3), 64 (n=22), 128 (n=6) and >128 (n=15) mg/L. Among the 58 isolates with MIC values of ≤8 mg/L 36 had no genes encoding resistance to chloramphenicol, 18 encoded catB3 and 4 contained a combination of catB3 and catA2. All but one isolate with chloramphenicol MICs of >64 mg/L contained catA1 or floR while no isolates containing these genes had MICs ≤32 mg/L. There was poor correlation between chloramphenicol MICs and the presence of catB3, catA2 and cml. EUCAST (≤8 mg/L = susceptible, >8 mg/L = resistant) and CLSI (≤8 mg/L = susceptible, 16 mg/L = intermediate and ≥32 mg/L resistant) have different interpretative criteria. Among the 34 isolates classified as resistant by EUCAST CLSI would categorise 8 as intermediate and 26 as resistant.

Conclusions: Chloramphenicol may be an option for treatment of metallo-β-lactamase producing CPE and Acinetobacter species when other options are very limited. Detection of catA1 and floR genes predict high level resistance to chloramphenicol (MIC≥64 mg/L) but this is not the case for catB3, catA2 and cml. Many isolates that were called resistant by EUCAST criteria had no chloramphenicol resistant genes detected. This was less of an issue when using CLSI criteria as many of these would be classified as intermediate.

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**Abstract 7665**

**Real-world multi-centre experience with eravacycline at academic hospital systems**

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**Background:** Eravacycline (ERV) received Food and Drug Administration (FDA) approval for the treatment of adults with complicated intra-abdominal infections (cIAIs) in 2018. ERV is a novel fluorocycline with broad-spectrum activity against Gram-positive, Gram-negative and anaerobic bacteria including those with tetracycline-acquired resistance mechanisms. Real-world data regarding ERV use in FDA and non-FDA approved indications is limited. We evaluated the clinical and safety outcomes of patients treated with ERV for various infections.

**Materials/methods:** Multi-center, retrospective, observational study from September 2018 to November 2019. Adult patients treated with ERV for ≥72 hours were included. Primary outcome was 30-day survival. Secondary outcomes were 30-day lack of infection-recurrence and resolution of signs/symptoms of infection.

**Results:** Overall, 31 patients were included from 5 geographically distinct medical centers across the United States. Median age was 56 years (45-67); 58.1% were male and 54.8% were Caucasian. Median APACHE II and Charlson Comorbidity scores were 16 (11-20) and 3 (2-7), respectively. Common sources of infection were intra-abdominal (35.5%), respiratory (29.0%), and bone/joint (12.9%). The most common pathogens were *Klebsiella pneumoniae* (22.6%), and *Enterococcus faecium* (22.6%), followed by *Escherichia coli* (19.4%). Infectious diseases consultation was obtained in 96.8%, and surgical interventions in 64.5%.

Most patients received active therapy prior to ERV initiation (61.3%). Median ERV therapy duration was 9.1 (4.5-19.4) days. Among cases with documented cultures, ERV was initiated within a median of 6.9 (4.1-14.8) days. Combination therapy ≥48 hours was given in 48.4%. Among clinically evaluable population (n=26), 73.1% (19/26) achieved the primary endpoint. Of patients who died, majority had positive blood cultures (4/7), intra-abdominal as a source (4/7), were critically ill (4/7), and on monotherapy (4/7). For secondary outcomes; 88.5% (23/26) lacked 30-day infection-recurrence and 53.8% (14/26) resolved signs/symptoms of infection. Overall, only 7/31 switched to an alternative agent. Four patients experienced a probable ERV-related adverse event [n=4, 3: gastrointestinal, 1: rash], but only one led to drug discontinuation.

**Conclusions:** 30-day survival was achieved in majority of patients treated with ERV for various infections. Studies with longer follow-up and more patients are required to assess the effectiveness and safety of ERV, particularly compared to standard of care.

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Does the new recommendations of treatment for non-severe Clostridiodes difficile-associated diarrhoea ensure a better outcome?

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Background: In February 2018 IDSA and SHEA published updated guidelines for Clostridium difficile associated diarrhea (CDAD). We followed this recommendation for patients admitted with the first episod of CDAD during this year. The purpose of our study was to evaluate the outcome of CDAD by monitoring patients for recurrences or death for 2 month after the first episod.

Materials/methods: A comparative study, including all adult patients who were admitted for or who developed the first episod of CDAD in our hospital (GDH and toxin A/B positive) regarding outcome: cure, recurrences and death. Patients were monitored for 2 months after CDAD. Cases were considered: non-severe, medium and severe according with ATLAS score published by Mark A Miller and colleagues in 2013. The outcome of non-severe CDAD [ATLAS score < 4] was compared for patients admitted during 2012-2016 treated according with the previous CDAD IDSA guidelines and patients admitted during summer 2019 (June-Sept) treated with vancomycin. We compared the outcome for all non-severe cases and also for non-severe cases without co-administered antibiotics during CDAD, considering that as a risk for recurrences.

Results: 61 patients were admitted between 1st of June-30th of Sept 2019, 37 women (61%), average age 64 years (min22, max92, median 66 years). 42 (69%) patients had an ATLAS score less than 4, were treated with oral vancomycin and 7 patients (17%) died or had recurrences. From 39 patients with non-severe CDAD without concomitant antimicrobials during CDAD treatment, 7 (18%) had unfavorable outcome. During 2012-2016, 768 patients were admitted with the first episod of CDAD, 412 female (54%), average age 65.6 years (min 18, max 97, median 69). 539 (70%) were non-severe and were treated with: metronidazole 258, vancomycin 63 and vancomycin plus metronidazole 199 patients. 128 (31%) patients died or had recurrences. From 202 patients with non-severe CDAD without concomitant antibiotics, 63 patients died (31%).

Conclusions: New IDSA/SHEA guidelines recommendation for CDAD decreased the risk of death/recurrence for patients with non-severe disease, possible due to a real resistance of C. difficile to metronidazole in our country and to a better effect of vancomycin.

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First insight into the genome sequence of *Clostridioides difficile* strains isolated from Romanian patients

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**Background:** Recurrent *Clostridioides difficile* infections (rCDI) are difficult to treat, due to various factors, including antibiotic resistance profiles. Here we investigated the background of antibiotic resistance and virulence in *C. difficile* strains isolated from Romanian patients.

**Materials/methods:** The analyzed *C. difficile* strains were isolated from stool samples of male patients with recurrent *C. difficile* infection, aged 67 - A, 78 - B and 84 - C. The stool samples were screened using CoproStrip *C. difficile* GDH+ToxA+ToxB (Savyon Diagnostics). The strains were cultured on Columbia Agar with 5% sheep blood and identified by MALDI-TOF MS. The strains were subjected to whole genome sequencing using Illumina HiSeq System. The ribotype was determined *in silico* based on genomic sequences. The antibiotic resistance genes (ARGs), virulence factors and multilocus sequence typing profiles were analyzed.

**Results:** The phenotypic analyses revealed the presence of ToxA and ToxB in A and B strains, while for strain C both toxins were absent. *In silico* ribotyping revealed that all three strains belong to 027 ribotype (RT), previously described in our country and to the ST1 sequence type. The bioinformatic analysis of sequencing data revealed similar patterns of ARGs in strains A and B (respectively vanG-like operon, nimB <nitroimidazole resistance>, cdeA <multi antimicrobial extrusion protein>, dfr-like genes), present also in strain C which also harboured aminoglycoside modifying enzymes (namely ant(6)-Ib and aph(2")-Ia). Genome sequences revealed also the presence of toxA and toxB genes in all strains, despite the absence of toxA and toxB production by strain C.

**Conclusions:** The WGS analysis of clinical *C. difficile* isolates demonstrated that the strains belong to the epidemic ribotype 027, but harbor a considerable genetic diversity, suggesting diverse reservoirs for CDI. The presence of multiple resistance determinants to glycopeptides, imidazoles, trimethoprim sulfamethoxazole and aminoglycosides could explain the recurrency of underlying infections.

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Abstract 7673

**Dalbavancin as a sequential treatment for Gram-positive infective endocarditis: 2-year experience at the University Hospital 12 de Octubre (Madrid)**

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**Background:** Dalbavancin is a second-generation lipoglycopeptide antibiotic with a broad spectrum of activity against virtually all important gram-positive pathogens, being a potent bactericidal drug against methicillin-resistant Staphylococcus aureus (MRSA). It demonstrated an excellent safety profile in different studies. Its main advantage is its long half-life, having an attractive role in outpatient (OPAT) intravenous therapy. It is only approved for skin and skin structures infections. This study aims to expand the evidence of the effectiveness and safety of prolonged treatment with dalbavancin in Gram-positive infective endocarditis (IE) after the clearance of the bacteremia.

**Materials/methods:** Prospective observational study conducted in one referral center, including all consecutive possible or definite IE according to modified Duke criteria treated with dalbavancin from January 2018 to November 2019.

**Results:** During the study 22 patients were enrolled, with a median age of 84.4 years. Sixteen were males (73%), with a mean of 7.5 points in the Charlson Comorbidity Index (CCI). Sixty-eight percent presented some type of valvulopathy. Fifty-five percent had prosthetic intracardiac material. The most common microorganism was methicillin-sensitive Staphylococcus aureus (MSSA) (32%), followed by Enterococcus faecalis (21%), coagulase-negative staphylococcaceae (16%) and viridans streptococci (11%). Only one MRSA was isolated. All the enterococci were ampicillin-susceptible. There was a high rate of complications (68%), being valve regurgitation (45%) and central nervous system emboli (32%) the most frequent. Fifty-five percent of the patients met surgery criteria, but only half of them could be operated. All the patients had been previously treated with another active antibiotic, for a mean of 27.4 days (SD: 11.8). Dalbavancin was used as OPAT extended therapy for a median of 14 days (IQR: 14-31.5). This led to a reduction of approximately 283 days of hospitalization (14.2 per patient). Two patients presented adverse events not attributable to dalbavancin: mild diarrhea and neutropenia. Two patients died of unrelated causes during follow-up.

**Conclusions:** This study shows the effectiveness and safety of prolonged treatment with dalbavancin in IE, even in the elderly population with a high comorbidity score. Furthermore, its potential cost-saving associated with hospitalization-shortening and avoidance of long-dwell intravenous lines should be taken into consideration.

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Abstract 7675

**Recurrent bacteraemia with Enterococcus faecalis is predominantly caused by the same clone**

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**Background:** Enterococcus faecalis is a member of the normal gut microbiome and causes several clinical infections such as the urinary tract infection (UTI) and bloodstream infection. *E. faecalis* is a common cause of infective endocarditis (IE) associated with high mortality and morbidity. Isolation of the causative pathogen from blood culture is a major criterion for establishing the diagnosis. We report the clinical and microbial characteristics from a Swedish cohort of patients diagnosed with recurrent monomicrobial *E. faecalis* bacteremia (MEFsB).

**Materials/methods:** From 2012 to 2016, medical record data from patients with more than one episode of MEFsB were retrospectively analyzed, together with the bacterial blood culture isolates from the corresponding episode. *E. faecalis* isolates obtained from both the first and subsequent episodes of bacteremia were subjected to whole genome sequencing (WGS). From the WGS data, multilocus sequence typing (ST) was performed using the microSAL T pipeline [https://github.com/Clinical-Genomics/microSALT].

**Results:** Clinical data and bacterial isolates from 27 patients were available for inclusion in the study. 24/27 (88%) of the patients had two episodes and 3 patients had three episodes of MEFsB. The median time to a recurrence was 57 days (IQR: 30-97 days). During the first episode, the source of infection was identified in 9/27 (33%) of the cases but in only 3/27 (11%) in the last episode (p=0.10); with UTI (8 and 3 cases, respectively) dominating. IE was diagnosed in 1/27 (4%) and 11/27 (41%) of the cases during the first and second episodes (p<0.001), respectively. Isolates from both episodes in a patient were of the same sequence type (ST) in 26/27 (96%) of the patients. The ST distribution among the study isolates was diverse. Half of the patients diagnosed with IE were infected with ST6 and ST179 (3 cases each).

**Conclusions:** Multiple episodes with blood culture positive for *E. faecalis* was significantly correlated to IE. In recurrent infections, the vast majority of the coupled episodes in a patient are due to strains with the same ST, suggesting it is likely the same strain.

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Epidemiology and genetic diversity of *Plasmodium falciparum* in Kobeni, south-eastern Mauritania

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**Background:** *Plasmodium falciparum* malaria is endemic in the Sahelian zone of Mauritania where intense internal and trans-border human movement occurs. The risk of spread of drug-resistant parasites needs to be regularly assessed in this region. Our objective was to assess the malaria epidemiological situation in Kobeni, a potential ‘hotspot,’ using parasitological and molecular tools.

**Materials/methods:** Patients with fever or history of fever, presenting at the health centre of Kobeni, were screened for malaria using a rapid diagnostic test (RDT) and microscopic examination of blood smears in 2015–2017. The diagnosis was confirmed by PCR. *P. falciparum* microsatellites and *Pfcr*t, *Pfmdr1*, and *Pfk13* markers were genotyped to assess genetic diversity and resistance to artemisinin-based combination therapies (ACT), respectively.

**Results:** A total of 2,326 febrile patients (mean age, 20.2 yrs) were screened. The presence of malaria parasites was detected by RDT and microscopy in 53.0% and 49.3% of patients, respectively, and was confirmed by PCR in 59.7%. Of 1,361 PCR-positive samples, 1,205 (88.5%) were *P. falciparum*, 47 (3.5%) *Plasmodium vivax*, and 100 (7.3%) *P. falciparum-P. vivax* mixed infection. Malaria transmission occurred mostly during and shortly after the rainy season. *Plasmodium falciparum* populations in Kobeni exhibit high genetic diversity (He >0.7) consistent with a high level of malaria transmission. Molecular analysis suggested an absence of resistance to ACT.

**Conclusions:** *P. falciparum* is the predominant species in the Sahelian zone, and malaria transmission is seasonal. *P. falciparum* parasites in Kobeni were heterogeneous and characterized by a high genetic diversity.

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Abstract 7682

Screening, diagnosis and treatment of latent tuberculous infection in rheumatic patients candidate to biological therapy: experience of a tertiary tuberculous control unit

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Background: Patients who receive biological treatment have a significant risk of infections, including tuberculosis. Previously these patients have LTI that is reactivated under the influence of biological treatments. The programs of detection and treatment of LTI have been carried out in these patients for many years, especially in rheumatologic patients and here we present our data.

Materials/methods: During 2014-2019 all patients with rheumatic diseases who were candidates for biological treatment were tested with both the Mantoux test and the IGRA test, Quantiferon tb plus (QF TB plus). Any of the tests that were positive (except in patients vaccinated with BCG who had to have the PPD and the QF TB plus positive) were considered positive. In all positive cases, a chest Rx was performed to rule out active disease and in all of them the treatment of LTI was considered. Here we exposed our data in screening of LTI and treatment in those patients.

Results: During these years a total of 440 rheumatologic patients were analyzed and a total of 84/410 (21%) patients were registered with a positive test according to the before mentioned criteria. In no case was an active disease detected. The agreement between the different techniques analyzed was high, 86%, while QF TB plus was more sensitive than the Mantoux. All patients received treatment: 85% with isoniazid, 10% with rifampicin and 5% with the combination of rifampicin + isoniazid. Hepatic toxicity was recorded in 10/84 (12%) patients, although only two patients had to stop treatment. No cases of active tuberculosis were detected during follow-up. The average follow-up is 3.4±1.2 years. The average time from the beginning of LTI diagnosis to the start of the biological treatment was 48±12 days.

Conclusions: The combination of Mantoux test and IGRA test proved to be a good tool to detect cases of LTI. The agreement between them was good, although QF TB plus were more sensitive. The patients were very adherent to the treatment. There were no cases of active disease in the follow up. The toxicity was low and all the patients finished therapy.

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Fever of unknown origin: a prospective observational study from a tertiary university hospital

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Abstract 7686

Background: According to the latest definition, classic fever of unknown origin (FUO) is characterized as a condition of temperature exceeding 38.3 °C on at least three measurements over a period of at least three weeks, with no diagnosis made despite 1 week of in-patient investigation or 3 outpatient visits or 1 week of “intelligent and invasive” ambulatory investigation. The aim of the study was to update the data relating FUO, as the last available published series, in Greece, was 9 years ago.

Materials/methods: Clinical data were prospectively collected from patients meeting the criteria of classic FUO hospitalized in the 3 departments of internal medicine of “Laiko” General Hospital in Athens, Greece, a tertiary university hospital, from November 2017 to November 2019.

Results: During the study period, 87 cases fulfilled the criteria of classic FUO, yielding an incidence of 4,98 cases per 1000 patient-days. The patient sample consisted of 44 men (50.6%) and 43 women (49.4%), 76 natives (87.4%) and 11 foreigners (12.6%). The median patient age was 59 years (IQR: 43.5 – 77.5). The median time interval from onset of fever until study enrollment was 30 days (IQR: 21 – 54). 31 patients (35.6%) were included in the study on the 21st day of fever. The median hospital stay was 11 days (IQR: 7 – 22). The etiology of FUO was determined in 57 cases (65.5%), whereas 30 cases (34.5%) remained undiagnosed. The most common group of diagnosed cases was that of non-infectious inflammatory diseases (23 cases – 26.4%), followed by infections (17 cases – 19.5%), neoplasms (15 cases – 17.2%) and miscellaneous conditions (2 cases - 2.3%).

Conclusions: There is a rise in the frequency of non-infectious inflammatory diseases at the expense of infections as classic FUO diagnoses, compared to older data. There also seems to be a rise in the proportion of the undiagnosed cases of FUO. This can be explained by the advances in diagnostics which allow a quicker diagnostic approach to cases presenting with prolonged fever, which are no more considered as classic FUO cases.

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The burden of enteric fever from three urban centres: a multi-centre, multi-component prospective epidemiological study with 626,219 person years of observation

Abstract 7689

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Background: Enteric fever is a serious public health concern in many low- and middle-income countries. Numerous data gaps exist concerning the epidemiology of Salmonella Typhi and Paratyphi, the causative agents of enteric fever, in different global contexts. A comprehensive epidemiological study was conducted to quantify the burden of disease and to generate the evidence for typhoid Vi-conjugate vaccine implementation.

Materials/methods: In this multicentre, multicomponent prospective study, a demographic census was used to enumerate an open cohort of approximately 100,000 individuals in each of three urban sites in Africa (Malawi) and Asia (Nepal and Bangladesh). Facility-based passive surveillance was conducted for two years with blood-culture collection for febrile illness. Healthcare utilisation surveys performed in a sample of households enabled adjustment of incidence estimates for healthcare-seeking behaviour. Community-based serological surveillance was performed on an age-stratified cohort of over 24,000 randomly selected individuals, with blood samples collected at baseline and three months to provide an estimate of seroincidence.

Results: Between November 2016 and December 2018, 626,165 participants were enrolled in the demographic census across the three sites. From this population, 625 S. Typhi and 107 S. Paratyphi A isolates were cultured from the blood of 11,529 febrile patients. Multi-drug resistance was observed in 44% and fluoroquinolone resistance in 61% of S. Typhi isolates. The overall crude incidence rates of blood-culture confirmed S. Typhi per 100,000 person-years of observation were 58 (95% confidence interval [CI]: 48-70) in Malawi, 74 (95% CI: 62-87) in Nepal and 161 (95% CI: 145-179) in Bangladesh. Adjusted incidence rates were highest in the 5-9-year age group in all three sites, with overall adjusted rates per 100,000 person-years of 477 (95% CI: 372-770) in Malawi, 1,256 (95% CI: 827-2,074) in Nepal and 1,312 (95% CI: 1,037-1,701) in Bangladesh. Through serological surveillance, seroconversion rates suggest higher rates of exposure and infection than captured through passive surveillance.

Conclusions: S. Typhi is a major cause of febrile illness in young children in the populations studied. Combined with high rates of anti-microbial resistance, the introduction of typhoid conjugate vaccines and improvements in water and sanitation infrastructure are a necessity to control this pathogen.

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Abstract 7691

Ceftriaxone and cefotaxime have similar impact in emergence of resistance in gut microbiota from hospitalised patients

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Background: Resistance to third generation cephalosporins (3GC) in Enterobacteriaceae is a major concern. Most risk factors associated with colonization and infection with 3GC-resistant Enterobacteriaceae included healthcare exposure, travel in high endemic region and recent antibiotic therapy [especially 3GC]. ceftriaxone and cefotaxime, two intravenous administered 3GC, have different pharmacokinetics characteristics, mostly regarding elimination half-life and route. In previous studies, ceftriaxone could be responsible for the selection of 3GC-resistant Enterobacteriaceae. However, these datas are still controversial today.

Thus, the objective of this study was to compare the impact of ceftriaxone versus cefotaxime on emergence of resistance in gut microbiota from hospitalized patients.

Materials/methods: We conducted a prospective study in patients hospitalized in internal medicine and treated with ceftriaxone or cefotaxime. Patients were included during two periods according to the 3GC received: ceftriaxone during the first period (ceftriaxone group) and cefotaxime during the second period (cefotaxime group).

A dynamic collection with 3 fecal samples was collected from each patient [at days 0, 3, 7 or at the cessation of antibiotic therapy] in order to determine intestinal colonization with 3GC resistant Enterobacteriaceae (ESBL-PE and AmpC-hyperproducing Enterobacteriaceae) and their relative faecal abundance, and emergence of toxigenic Clostridium difficile, yeasts and vancomycin resistant Enterococci. Total cultivable aerobic bacteria and total Gram-negative Enterobacteriaceae were also counted.

Results: During the study period, 28 patients were included in the ceftriaxone group and 17 in the cefotaxime group. No differences in the counts of 3GC resistant Enterobacteriaceae was observed in both groups over time. Carriage of toxigenic Clostridium difficile was observed in 3 patients [2 in the ceftriaxone-group and one in the cefotaxime group] but was associated with clinical infection in only one case in cefotaxime group.

Conclusions: In our prospective study, Ceftriaxone and cefotaxime seems to have the same impact on the emergence of 3GC resistant Enterobacteriaceae or toxigenic C. difficile in gut microbiota of hospitalized patients. These results need to be confirmed on a larger cohort in order to use safely ceftriaxone.

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Abstract 7692

Development of an extraction control in Fungiplex Candida IVD real-time PCR Kit

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Background: This study is designed to test contrived samples spiked into serum, plasma and whole blood material to assess the impact of a new extraction control on the limit of detection of the Fungiplex Candida IVD Real-Time PCR Kits and to ensure sensitivity was unaffected by this change.

Materials/methods: Simulated samples have been prepared and analysed for this study as well as synthetic DNA. Samples prepared in serum, plasma and whole blood were spiked with specific concentrations of Candida DNA prior to extraction. Samples were prepared and tested using the control material both as an extraction control and as a PCR inhibition control. This study has included limit of detection analysis, dynamic range determination, interference testing, extraction efficiency calculation. Extraction was performed using the BioRobot® EZ1™ by Qiagen. The PCR was prepared using the Fungiplex Candida IVD Real-Time PCR Kit and tested across 5 common laboratory thermal cycler platforms.

Results: When tested with the Fungiplex Candida IVD Real-Time PCR Kit, the limit of reproducibility for various Candida species samples was 1 – 5 CFU. No difference in sensitivity was observed between the different sample types. With plasmid DNA samples the LOD remained at 20 input copies as defined by previous studies and Candida DNA was detected between 20 and $2 \times 10^6$ input copies. Detection was not affected by the presence of inhibitors or interfering substances. The extraction control was detected in every sample analysed with no significant differences observed in Ct value reported. Depending on the extraction method/protocol used, the amount of DNA in the resultant extract varied and in some instances a 50% loss was observed. The extraction control has been developed to endure differences in extraction efficiency.

Conclusions: 100% sensitivity was reported for the Fungiplex Candida Kit when analysing Candida samples at the predefined limits of detection of 20 input copies or 1 – 5 CFU. The sensitivity is not dependent on sample type and the new extraction control implemented in this product did not affect the performance of the Kit.

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Evaluation of MediScout for the planning, operationalisation and monitoring of community-based tuberculosis active-case finding interventions: a prospective study in the Democratic Republic of Congo

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Background: To find the 3 million missing tuberculosis (TB) cases worldwide — 50% of TB cases in Africa—, the WHO recommends to perform community-based screening in populations where the incidence of the disease is above 1% per year. In practice, no country presents such a high incidence at national level, and TB programs limit active case finding to the households of TB cases, people living with HIV and people living in prisons or mines. Additional tools are required to identify pockets of high TB incidence at the sub-national level.

Materials/methods: The MediScout© (Savics, Belgium) approach is a two-step triage process aiming to identify communities and individuals at high risk for TB. The first step consists in using artificial intelligence and open data (population, satellite images, TB reports) to build a map which gives a risk score for TB to each area of a country or a province. The second step consists in performing door-to-door verbal screening using a scoring system based on questions related to symptoms and exposure to TB. We performed a prospective community-based study in the South-Kivu province of the Democratic Republic of Congo to evaluate the performance of this approach.

Results: Between March and October 2019, 7,714 interviews were performed by community health workers using the MediScout mobile application in 8 different locations (Figure 1A), among which 3,849 (50%) in 3 zones predicted to show an incidence rate above 1%. Individuals categorized at high risk for TB were referred for Ziehl-Neelsen microscopy test. Overall, positivity rate was 3.5 times higher in the 3 zones predicted to be at high risk (42 people tested positive) compared to the 4 zones predicted to be at lower risk (12 people tested positive).

Conclusions: Community-based screening should be performed in communities where the incidence of TB is expected to be above 1% per year. MediScout© is the first commercial solution which allows to efficiently target these communities at sub-national level and to operationalize the required targeted community-based interventions. In this study, combining artificial intelligence technologies with smart application resulted in high yield of detection of previously unrecognized active TB infections.

(A) Predicted TB intensity based on artificial intelligence analysis for Africa, with a zoom on the South-Kivu province of the Democratic Republic of Congo.
(B) Correlation between the predicted incidence rate for TB and the actual yield of community-based TB screenings. The WHO recommends to perform active case finding when the expected incidence is higher than 1%.

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Clinical and laboratory study on invasive infections due to Fusarium species in critically ill adult and paediatric patients in Serbia: ten years' experience of National Laboratory for Medical Mycology

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Abstract third-party references: Ministry of Education, Science and Technology Development Grant OI 174034

Background: Invasive mold infections (IMIs) are being increasingly recognized as a major threat in critically ill adult and paediatric patients. Data from Serbia reported Fusarium as the second most common IMIs pathogen, especially in paediatric critically ill patients [Tortorano AM et al, 2014, Arsic Arsenijevic V and Denning D, 2018]. This study aims to investigate the epidemiology of fusariosis in Serbia, during ten years. The clinical and laboratory data were launched.

Materials/methods: Fusarium cases analyses performed from January 2009 to January 2018. Onychomycosis due to Fusarium were excluded. A total of 16 proven cases collected, and Fusarium identified by sequencing the translation elongation factor 1α gene. Antifungal susceptibility was done by broth microdilution method.

Results: In adult patients sporadic ocular infections were seen (n=7), while in paediatric patients (n=9) deep site infections occur. Ocular Fusarium infections were proven by microscopy and culturing, and deep site infection by blood culture (n=8) or tissue sample culture. Risks for adults were the increased use of corticosteroids and trauma, and for pediatrics nosocomial route of infection. As the result of fungal dissemination the skin involvement was common in children. Gibberella fujikuroi species complex (SC), including Fusarium verticillioides and F. proliferatum, and F. solani SC were identified. Amphotericin B was the most potent, and itraconazole the least effective. The azoles exhibited lower minimum inhibitory concentrations against F. verticillioides strains, with posaconazole having a slightly better performance. F. solani SC isolates were resistant to all azoles.

Conclusions: Beside relatively low number of proven IMIs due to Fusarium two different spectrum of infections seem to be age dependent in critically ill patients in Serbia, ocular form found in adults and disseminated form in pediatric patients. Fusariosis is a rare but difficult to treat IMIs, and this is important because Serbia is agriculture reach country and further surveillance of these predominant plant pathogens causing severe human infections is urgent need. New proven cases and epidemiology data are important for development of effective prevention strategy for fusariosis among high-risk patients.

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Optimisation of bacterial whole genome sequencing workflow for implementation in routine clinical and epidemiological applications

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Background: Whole genome sequencing (WGS) of bacterial pathogens has several advantages over current diagnostic methods. WGS can provide clinically and epidemiologically useful information related to pathogen identification, antimicrobial resistance and typing. Further, the exhaustiveness and the digitalization of the results are major advantages compared to conventional analysis which have to be repeated when new parameters need to be assessed. Large scale adoption WGS in the clinical environment is lagging however due to cost and complexity of data analysis which are mainly driven by the cost of reagents, multiple manual steps and finally the time required by bio-informaticians to process the data. Here we present a novel integrated, high-throughput and highly automated workflow that significantly decreases, cost, turn-around-time and data analysis complexity of bacterial WGS.

Materials/methods: We optimized several aspects of the workflow. First, we validated the Nextera XT (Illumina) library preparation on the Echo (Labcyte) acoustic liquid handling system. This system allows to work with minimal amounts of reagents, as small as nanoliters, and to work on large series of samples with minimal hands-on time. Second, we allowed automated transfer of sequencing data to a cloud-based repository. Third, we developed and automated two pathogen-specific cloud-based pipelines. To improve functionality and compatibility, we integrated these modules as Docker images to make the entire system modular and easy to share. Such system could easily be transferred to partner laboratories willing to perform bacterial WGS without investing in laborious bioinformatical development, validation and maintenance.

Results: In this proof-of-principle study, we successfully performed 454 WGS analysis. The optimized workflow compared to the conventional workflow resulted in significant decrease in reagents cost (40%) and hands-on time in the lab (90%). Automated data processing after demultiplexing was typically finalized after 49 minutes (Streptococcus pneumoniae) and 55 minutes (Mycobacterium tuberculosis).

Conclusions: Considering the higher automation and the better traceability of this new approach together the decreased cost and time-to-result, this optimized bacterial WGS workflow meets our quality standards and cost constraints. This evaluation allows to reconsider the place of bacterial WGS for clinical diagnostic and surveillance purposes in our University Hospital.

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Abstract 7700

Evaluation of a multiplex real-time PCR assay for detection of the aetiologic agents of vaginitis
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Background: Vaginitis is one of the most common reasons women seek professional assistance. Vulvovaginal candidiasis, trichomoniasis and bacterial vaginosis (BV) are the main infectious syndromes that cause abnormal vaginal discharge. Diagnosis of these disorders presents several barriers such as low tests sensitivity and the need of experienced microscopists. The aim of this study is to evaluate the Allplex™ Vaginitis Screening Assay for the detection of etiologic agents of vaginal pathology from clinical samples

Materials/methods: Between July and September 2019, a total of 100 vaginal swabs (11 Candida albicans positive, 5 Candida spp. positive, 4 Trichomonas vaginalis (TV) positive, 39 BV, 5 C. albicans and BV coinfection and 36 samples with healthy vaginal microbiota) were collected from women with symptoms of vaginitis. Test was performed using the multiplex RT-PCR Allplex™ Vaginitis Screening Assay (Seegene, Korea), DNA extraction was performed in the Starlet platform (Seegene, Korea) and Real-time PCR was performed in a CFX-96-real-time thermocycler (Bio-Rad, USA), according to the manufacturer’s instructions. Results were compared with reference methods: yeast culture (BBL™ CHROMagar Medium) and Gram staining for C. albicans and Candida spp. and Gram staining (Nugent score) for BV. We compared TV-PCR results with culture (Roiron Medio, DIFCO).

Results: Results are displayed in table 1. Sensitivity of Allplex™ assay was 93.8% [n=16; 95% CI: 69.7–99.8%] for C. albicans, 100% [n=5; 95% CI: 48.0–100%] for Candida spp., 100% [n=4; 95% CI: 39.7–100%] for TV and 84.1% [n=44; 95% CI: 69.9–93.4%] for BV. Specificity was 88.1% [n=84; 95% CI: 79.2–94.1%] and 89.3% [n=56; 95% CI: 78.1–96.0%] for C. albicans and BV, respectively. This lack of specificity is due to the fact that 10 C. albicans and 6 BV were detected by Allplex™ assay but not by the reference method. Moreover, two TV-culture negative were detected by Allplex™ assay.

Conclusions: Allplex™ Vaginitis Assay demonstrated good concordance with conventional methods what supports the feasibility of this assay as an alternative test for screening of women with abnormal vaginal discharge. However, due to the high sensitivity of RT-PCR, Allplex™ assay detected several cases that had not been detected by reference method, probably due to low microorganism load, and this fact could be a disadvantage since it could lead to over-diagnose.

Table1:

<table>
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Abstract 7701

**Digital antimicrobial dashboard facilitates antimicrobial stewardship in a large London teaching hospital**

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**Background:** Our antimicrobial stewardship (AMS) programme routine consumption reporting revealed a 20% increase in carbapenem usage between 2016/17 and 2017/18 (154-186 DDDs/1000 admissions), placing our usage 40% above the London mean and 1.3% above the Shelford hospital group mean. This rise was compounded by fragile drug supply lines and local resistance patterns.

A patient-level audit of 62 patients showed 7% of 688 meropenem days of therapy were potentially inappropriate; primarily due to delays between treatment initiation and infection specialist advice. This identified the need for a robust real-time method to identify patients on antimicrobials within our newly adopted electronic prescribing system (Cerner powerchart) and facilitate stewardship interventions.

**Materials/methods:** An AMS dashboard (figure 1) was developed within Cerner which identifies all in-patients currently prescribed antimicrobials. It shows patient details, antimicrobial information (drug, route, dose, duration, missed doses), and recent laboratory results (cultures and susceptibilities and inflammatory markers). This links directly to patient records and can be filtered (by location/drug/treatment duration), annotated to flag patients requiring review, and record stewardship interventions. The dashboard was piloted between August and October 2019 with refinements on-going and improvements to stewardship practices measured.

**Results:** The pilot confirmed the dashboard accurately identifies patients on antimicrobials, albeit with some missing data (allergies and route of anti-infective administration). It was used to facilitate the Trust antimicrobial point prevalence survey (August 2019), reducing the time burden of data collection, and to facilitate AMS rounds in high carbapenem consumption areas. Reductions in average time taken to identify patients requiring intervention were seen (from 24 to 10mins per ward round). It also facilitated intervention (in 53% of patients), particularly stopping unnecessary antimicrobials (30% of patients reviewed). Carbapenem consumption fell by 12% to 163 DDDs/1000 admissions in 2018-19.

**Conclusions:** Implementation of a digital AMS dashboard facilitated both audit and timely patient level review of antimicrobials. Work is ongoing to optimise both data display and utilisation of this novel stewardship strategy within the larger AMS and infection prevention and control programme. Expansion to the out-patient setting and linking to clinical decision support systems are also longer term ambitions.

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Abstract 7703

The case for pharmacokinetic/pharmacodynamic studies during epidemics of high consequence pathogens: Tekmira for Ebola virus disease in Sierra Leone

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Background: Pharmacokinetic/Pharmacodynamic (PK/PD) studies during epidemics pose substantial logistical and safety challenges. However, data generated can be used in dose optimisation, and delineating toxicology thresholds [TT]. It is possible to draw conclusions from relatively small numbers of subjects. PK can alter in the disease state, making measurements from patients invaluable, particularly in the haemodynamic destruction caused by Ebola virus. For example: isolated PK measurements were used to evaluate Favipiravir concentrations in EVD patients [1] and a PKPD study of Tekmira (TKM-130803) in EVD patients yielded sufficient information to develop an in silico model presented below.

Materials/methods: TKM-130803 is a specific anti-EBOV therapeutic comprised of two small interfering RNAs (siRNA) siLpol-2 and siVP35-2. During the clinical trial [Sierra Leone, 2015], patients were infused with 0.3 mg/kg of TKM-130803 over 2 hours daily for up to 7 days [2]. The trial was discontinued having reached a predefined statistical endpoint which indicated a low probability of demonstrating overall therapeutic benefit compared to historic controls [2]. Plasma concentration of siRNA was compared to survival at 14 days. PK data were fitted to two-compartment models then Monte Carlo simulated PK profiles were compared to Efficacy Thresholds (Cmax 0.04-0.57 ng/mL and mean concentration 1.43 ng/mL), and TT (3000 ng/mL).

Results: SiRNA was in quantitative excess of virus genomes throughout treatment, a level considered needed for efficacy, but the 95% percentile exceeded TT. The maximum AUC for which the 95% percentile remained under TT was a continuous infusion of 0.15mg/kg/day. Plasma concentration of both siRNAs were higher in subjects who died compared to subjects who survived (p<0.025 both siRNAs).

Conclusions: Subjects who died exhibited impaired drug clearance, justifying caution in dosing strategies for such patients. This analysis is the first PK model derived from EVD subject and indicates that such studies are possible, if challenging. It has given a useful insight into the pharmacokinetics of the siRNA in the disease state and illustrates the value of designing PKPD studies into future clinical trials in epidemic situations.


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Multi-centre validation of a EUCAST method for the antifungal susceptibility testing of microconidia-forming dermatophytes

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Abstract

Background: Terbinafine resistance is increasingly reported in Trichophyton rubrum and Trichophyton interdigitale rendering susceptibility testing important particularly in non-responding cases. We performed a multicentre evaluation of a recently proposed EUCAST method implementing medium supplemented with chloramphenicol and cycloheximide (CC) to avoid contamination.

Materials/methods: A blinded panel of wild-type and squalene epoxidase [SOLE] target gene mutant T. rubrum and T. interdigitale strains were distributed to 10 laboratories. Susceptibility to terbinafine, itraconazole, voriconazole and amorolfine were performed according to the EDef 9.3.1 method with and without addition of chloramphenicol and cycloheximide [final concentrations 50 mg/L and 300 mg/L]. Plates were incubated at 25°C [one laboratory used 28°C] for 5-7 days until sufficient growth. MICs were determined visually [ignoring trailing growth for itraconazole] and spectrophotometrically with 90% and 50% endpoints [total 7,829 MICs]. A. flavus ATCC204304 and A. flavus CMM-C1813 were included as controls. Very major errors VME [mutant MICs\(\geq 6\)-WT-UL] and major errors ME [wild-type MICs WT-UL] were determined.

Results: 100%/96% [itraconazole] and 84%/84% [itraconazole] MIC determinations fell within the QC ranges for the two QC methods, respectively, and 99%/96% terbinafine MICs fell in a 0.25-1 \(\mu\)g/mL range suggesting a high interlaboratory reproducibility. Across the six methods, the number of terbinafine MEs varied from 2-5 [2.6%-6.6%] for T. rubrum and between 0-2 [0%-2.0%] for T. interdigitale [lowest for the CC-method [2.6%-4.4%/0-1% for T. rubrum/T. interdigitale]]. The difference between the modes for the wild-type and mutant population were \(\geq 7\) two-fold-dilutions in all cases [Table]. If excluding a F397L/V237I T. rubrum mutant, and two mixed T. interdigitale strains, the number of VMEs were CC visual: T. rubrum: 1/77 [1.3%], CC spec-90%: 3/68 [4.4%] and CC spec-50%: 1/76 [1.3%], and none for T. interdigitale. The activity of voriconazole, itraconazole and amorolfine were quite uniform against T. rubrum and T. interdigitale, but unacceptably wide MIC ranges were found for the visual and spec-90% inhibition methods for itraconazole.

Conclusions: Although none of the laboratories perform dermatophyte testing at a regular basis an acceptable interlaboratory agreement and good separation between SOLE wt and mutants were found with very low error rates, suggesting a robust performance of the proposed method.

Table. Comparison of terbinafine MICs determined using the EUCAST CC-method for 20 wild-type and 18 SOLE mutant T. rubrum and T. interdigitale isolates. MICs were read visually (with a no growth endpoint) and by spectrophotometer using a 90% and 50% inhibition endpoints.

<table>
<thead>
<tr>
<th>Laboratory specific distance between modes (range) 2-fold dilutions among strains</th>
<th>N (%)/MIC determination of mutant strains</th>
<th>MIC strates overlapping with wt range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wild type</td>
<td>Mutant strains</td>
<td>N (%)</td>
</tr>
<tr>
<td>N</td>
<td>Mode ((\mu)g/mL)</td>
<td>Mode ((\mu)g/mL)</td>
</tr>
<tr>
<td>T. rubrum</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| CC Visual | 77 0.008-0.5 | 0.01 0.03 | 0.06 0.06 | 4 4 | 7 (1/7) 6 (0.8)% | 0 (0%)
| CC spec-90% | 68 ±0.008-1 | 0.03 0.03 | 0.03 0.03 | 4 4 | 7 (3/9) 6 (10.2%)
| CC spec-50% | 76 ±0.008-0.5 | 0.008 0.008 | 0.06 0.06 | 2 1 | ≤75-88 5 (7.5%)
| T. interdigitale | | | | | |
| CC Visual | 76 0.008-0.5 | 0.06 0.06 | 0.16 0.16 | 8 8 | 7 (5-16) 11 (11.0%)
| CC spec-90% | 69 ±0.008-0.25 | 0.06 0.06 | 0.08 0.08 | 4 4 | 7 (5-16) 11 (12.2%)
| CC spec-50% | 99 ±0.008-0.125 | 0.06 0.06 | 0.08 0.08 | 2 2 | 7 (5-10) 13 (13.0%)
| T. interdigitale Excluding strain \#26 & 31* | | | | | |
| CC Visual | 99 0.008-0.5 | 0.06 0.06 | 0.18 0.18 | 4 4 | 16 (5-88) 0 (0%)
| CC spec-90% | 89 ±0.008-0.25 | 0.06 0.06 | 0.2 0.2 | 4 4 | 7 (5-86) 0 (0%)
| CC spec-50% | 99 ±0.008-0.125 | 0.06 0.06 | 0.18 0.18 | 4 4 | 7 (5-10) 0 (0%)

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**Abstract 7707**

**Distribution during 10 years of the genotypes A and B of *Giardia intestinalis* among the infected subjects attending to an Italian tertiary care hospital**

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**Background:** *Giardia intestinalis* is considered one of the principal causative agents of diarrhea and an important waterborne disease pathogen that infects animals and humans worldwide. Investigations such as host specificity and transmission patterns require the direct genetic characterization of parasites from fecal samples. *G. intestinalis* is distributed into eight distinct genetic assemblages (A-H), however only assemblages A and B are known to infect humans. The present study aims to investigate the distribution, among the infected subjects, of the genotypes A and B of *G. intestinalis* in the last 10 years (2009-2018) in a tertiary care hospital.

**Materials/methods:** A total of 162 DNAs extracted from human stools positive for *G. intestinalis* was analyzed for the Assemblages identification. The DNA extracted was used to amplify, by a real-time PCR assay based on melting curve analysis, the translation initiation factor, and the cathepsin L precursor genes for assemblage A and B, respectively. Chi-square test was used for the comparison of the frequency of Assemblage A and B between Italians and foreigners, between adults and children and between male and female. Statistical significance was set at p< 0.01.

**Results:** Out of 162 samples analyzed, 72 samples were assigned to Assemblage A, 37 to Assemblage B, 7 were mixed and 15 were not amplified. The frequency of Assemblage A in association with origin was 70.8% in Italians and 47.7% in foreigners, while the frequency of Assemblage B was 25% in Italians and 43.2% in Foreigners: this different Assemblages distribution resulted significant (p=0.0229). On the contrary, no significant difference was observed in the frequency of Assemblage A and B in association with age (p=0.119) and sex (p=0.3948). The 15 not amplified samples are at present under investigation to assess if they could be included in a non-A non-B Assemblage.

**Conclusions:** The performed real-Time PCR was able to amplify *G. intestinalis* DNA in 90.7% of the tested samples. The result show that Assemblage A, related to a major risk of zoonotic transmission, is prevalent, as already described in Italy. Assembly B is less common in our area, with a frequency attributable mainly to immigrants from developing countries.

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Clinical characteristics and mortality-related factors of bloodstream infections in patients with acute leukaemia: a single-centre experience with 152 patients

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Background: Bloodstream infection (BSI) is an important cause of morbidity and mortality in patients with acute leukemia (AL) undergoing chemotherapy or stem cell transplantation. BSI was documented in 11-30% of the febrile neutropenia (FN) episodes. The epidemiology of BSI in FN constitutes the basis for selection of empiric antibiotic therapy for febrile neutropenia.

Objectives: To establish the incidence, microbial etiology, risk factors and prognosis of BSI in patients with AL.

Materials/methods: Retrospective observational study. All patients with AL and FN (absolute neutrophil count of <500/mm³) consecutively hospitalized between June 2011 and December 2018 were included. The package Infostat 2014 program was used for statistical analysis.

Results: 365 episodes of FN (in 152 patients) were evaluated, 126 BSI were documented (34.5%), including 13 (10.3%) episodes polymicrobial bacteremia. The mean age of the patients was 34.11 ± 7.2 years and 58% were male. Low-risk group (according MASCC Risk Index) 294 episodes (80.5%). Twenty-five (6.8%) patients died. Gram-negative bacteria (GNB) were found in 62.5%, Gram-positive bacteria (GPB) 36.6% and one patient had fungemia (C. parapsilosis) of the isolates. Clinically documented infections could be observed in 162 of 365 febrile episodes (44.3%). The majority of them localized in the abdomen 44 cases (12%), catheter-associated infections 39 cases (10.6%) and lung infections 36 cases (9.8%). Risk factors associated with BSI were relapse of hematological disease (p = 0.009), hospitalization in the last 30 days (p = 0.003), antibiotics in the last 30 days (p = 0.03). In the group of BSI patients mortality was higher than in non-bacteremic patients (p = 0.0003).

Conclusions: Bacterial epidemiology and antimicrobial resistance in these patients should be regularly monitored, which will provide guidance for local policies for the use of antimicrobial agents for empirical antibiotic therapy in FN. Mortality in BSI and FN is worse than in non-bacteremic patients. Reducing the fatality rate of bacteremia remains a major challenge.

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Abstract 7712

**Microbial predictive virulence factors for pyelonephritis caused by extended-spectrum beta-lactamase-producing Escherichia coli in children harbouring such strains in their gut microbiota**

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**Background:** Emergence of extended spectrum beta-lactamase (ESBL) Escherichia coli strains causing pyelonephritis in children is increasing worldwide and questions empirical antimicrobial therapy. However, implementing carbapenems as first line antibiotics would probably lead to an increase of carbapenem-resistant strains. Fecal carriage monitoring of resistant strains can be used to adapt the choice in patients hospitalized during long periods of time. However these patients are more frequently carriers of multidrug resistant bacteria and thus more frequently treated with carbapenems.

In this study we have analyzed the virulence factors of ESBL-producing E. coli strains causing pyelonephritis in children in comparison with those encountered in fecal carriage by asymptomatic children in order to identify a pyelonephritis-associated virulence profile

**Materials/methods:** From March 2014 to March 2017, 218 ESBL-producing E. coli isolates were recovered from French pediatric pyelonephritis cases. From October 2010 to July 2017, 154 ESBL-producing E. coli were isolated from fecal carriage among French children aged 6 to 24 months in the community.

Strains were sequenced with the Nextera kit (Illumina, San Diego, CA, USA). We used the Centre for Genomic Epidemiology (CGE) website to characterize the strains and 180 virulence factor genes were searched using the NCBI BLAST tool.

**Results:** The most frequent phylogroup was B2 both in pyelonephritis (64%) and carriage isolates (60%). The most frequent ST was ST-131 (44%) in both collections. We found no significant difference between pyelonephritis and carriage isolates in terms of phylogroup, ST or serotype. Among the 180 virulence genes searched 27 were present in > 20% of pyelonephritis isolates. After Bonferroni correction, five (papC, papGII, hlyC, hek and traJ) remained significantly associated with pyelonephritis. The strongest association with pyelonephritis was found for individual genes with adhesin papGII (54% vs 16%) and for gene combinations with papGII and/or traJ (63% vs 24%).

**Conclusions:** ESBL-producing E. coli strains found in fecal carriage genetically resemble those causing pyelonephritis in children with the exception of few genes. Combining the detection of two genes (papGII and/or traJ) would permit to attribute a risk-associated genetic profile to 63% of pyelonephritis isolates versus only 24% of healthy carriage isolates

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Central nervous system infections caused by herpes simplex virus and varicella zoster virus in France, 2014-2018: a nationwide retrospective study

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Background: Herpes simplex virus 1 and 2 (HSV-1 and HSV-2) and varicella-zoster virus (VZV) remain major causes of sporadic meningoencephalitis worldwide. The French National Reference Centre for Herpesviruses-Associated Laboratory Pitié-Salpêtrière [Paris] performed a nationwide retrospective observational study to examine epidemiological and clinical characteristics of alphaherpesvirus central nervous system (CNS) infections during the period 2014-2018.

Materials/methods: Forty-eight public or private microbiology laboratories throughout France participated in this study. Participants indicated the total number of cerebrospinal fluids (CSFs) tested for HSV-1, HSV-2 and VZV and the diagnosis procedures used. For each positive result, data related to patient demography, clinical presentation, biological features, and antiviral treatment were collected.

Results: A total of 189,010 CSFs from 181,559 distinct patients were analysed by the 48 laboratories, and 3,860 patients had a positive result: 1,247 (32.3%) for HSV-1, 822 (21.3%) for HSV-2, 1,791 (46.4%) for VZV. The overall prevalence of alphaherpesvirus CNS infections was 2.13%: 0.69% for HSV-1, 0.45% for HSV-2, 1.12% for VZV. Molecular diagnosis on CSF was performed by real-time PCR in all laboratories. The most common platforms used were easyMAG/EMAG (BIOMERIEUX) for nucleic acid extraction (50%) and LightCycler (Roche Diagnostics) for gene amplification (35%). R-GENE® kits (ARGENE, BIOMERIEUX) were used by 59% of participants. Only 13 (28%) laboratories used a sample-to-answer instrument (LIAISON MDX, DiaSorin or FilmArray, BIOMERIEUX). Data for patients with a positive CSF result have been analysed so far for 36 (75%) laboratories. CSF positivity for any alphaherpesvirus did not differ according to gender (men, 49.5%; female, 50.5%) and was not associated with immunosuppression. The median age of patients with a positive CSF result was 61 years for HSV-1, 39 years for HSV-2, 58 years for VZV. HSV-1 prevalence was similar among men and female, whereas HSV-2 prevalence was almost twice higher among female than men. Among patients with a positive CSF, 19.3% had a normal white blood cell count <5/mm3, and 25.2% had a normal protein level ≤5g/L. Analyses are still in progress for remaining laboratories and items.

Conclusions: This national study will permit to improve our knowledge regarding HSV and VZV CNS infections in France.

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Abstract 7715

**Pan-bacterial cumulative antibiograms**

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**Background:** Cumulative antibiograms are increasingly used to inform antimicrobial stewardship and to monitor antimicrobial resistance (AMR). Cumulative antibiograms are typically defined on a species-specific basis and, thus, focus on acquired resistance. However, the overall AMR burden also depends on the distribution and selection of bacteria with intrinsic resistance to key antibiotics. We propose that pan-bacterial cumulative antibiograms, that aggregate all species to consider both acquired and intrinsic resistance, can complement species-specific antibiograms by providing a less detailed but more complete picture of AMR. Here, we examine and overcome the challenges of computing such antibiograms and we illustrate their relevance to linking ward-level antibiotic use and resistance.

**Materials/methods:** Routine susceptibility testing involves different antibiotics depending on the isolate's species and other factors. To obtain comparable resistance profiles across multiple species, we implemented a 3-step data enrichment pipeline comprised of: (1) inclusion of EUCAST intrinsic resistances; (2) application of EUCAST deduction rules; and (3) random-forest-based imputation of remaining missing data. The pipeline was used to calculate cumulative antibiograms for 14 drugs from 73,962 non-duplicate, non-screening clinical isolates collected in 2015-2017 from 381 wards in 4 hospitals in Lyon, France. We examined the correlation of ward-level consumption (in DDD/bed/y) of cefotaxime and ciprofloxacin with their respective resistance rates using either *E. coli*-specific or pan-bacterial cumulative antibiograms.

**Results:** The input dataset contained 615,430 tested drug-isolate pairs out of 10.3x10^6 possible pairs (59.4% completeness). Data enrichment increased completeness to 82.5% (+23.1%) with a major contribution from intrinsic resistance inclusion (+18.3%). Using linear regression, cefotaxime consumption explained only 2.6% of the variance of *E. coli*-specific resistance across wards (P=0.01) but 10.3% of pan-bacterial resistance variance (P<1x10^{-6}). Likewise, ciprofloxacin consumption explained a higher proportion of the variance of resistance rates in pan-bacterial antibiograms (12.9%) than in *E. coli*-specific antibiograms (8.5%).

**Conclusions:** Automated data enrichment enables the computation of pan-bacterial cumulative antibiograms reflecting both intrinsic and acquired AMR. Compared to *E. coli*-specific resistance to cefotaxime and ciprofloxacin, pan-bacterial resistance was more strongly associated with cefotaxime and ciprofloxacin consumption, possibly reflecting the local antibiotic pressure. Pan-bacterial cumulative antibiograms could facilitate the comparison of global AMR rates across hospital wards.

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Abstract 7719

A real-time PCR for the detection of Mucormycetes: Fungiplex Mucorales

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**Background:** Mucorales have been increasingly reported as causes of invasive fungal infections in immunocompromised subjects, particularly in patients with haematological malignancies, uncontrolled diabetes mellitus or those undergoing dialysis. Mucorales are now also being reported in Aspergillus-positive patients who are not responding to first line treatments.

Histology and culture are still the most important diagnostic approaches for mucormycosis because of the lack of molecular diagnostic methods available, and β-d-Glucan detection is not useful due to the extremely low content of the biomarker in the Mucorales order. Timely diagnosis of invasive mucormycosis is essential due to the rapid progression of the disease, and because signs and symptoms of the infection are consistent with other invasive fungal infections. PCR would improve detection of Mucorales and complement the current Bruker offering within the area of invasive fungal disease.

**Materials/methods:** The Bruker real-time PCR assays are designed in an easy to use format with minimum hands on time and results generated 1 hour after extraction. Universal primer and probe sequences have been designed to target the internal transcribed spacer (ITS) region of the rRNA gene for the genera detailed in Table 1. The probes associated with each pathogen have been labelled with different fluorescent dyes enabling some differentiation within the multiplex reaction. A specific control material has been developed to give the users an option of running it as an extraction control or a PCR inhibition control.

**Table 1: Genera detected by the Fungiplex Mucorales Real-Time PCR Kit**

|------------------|---------------|------------|

**Results:** The coverage specified in Table 1 has been confirmed using a range of simulated samples prepared from plasmid and genomic DNA. The limit of detection for species representing the highest prevalence of IFD for each genus has been assessed over six thermocycler platforms to ensure accuracy across a variety of systems.

**Conclusions:** Bruker have developed a Mucorales assay which identifies a wide range of clinically relevant genera. The assay has been developed into a kit to provide rapid detection of the main causative agents in invasive mucormycosis.

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Non-B subtypes are a major driver of clustered HIV-1 transmission in north Italy in recent years

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Background: To evaluate the dynamics and phylogenetic relationships of HIV-1 strains circulating in North Italy in the last years.

Materials/methods: HIV-1 pol sequences were obtained from 272 drug-naïve individuals diagnosed for HIV-1 infection at ASST GOM Niguarda Hospital (Milan, Italy) between 2012 and 2018. Phylogenetic trees were built using GTR model and 1000 bootstrap with maximum-likelihood method using PhyML. Transmission clusters (TCs) included large TCs (≥3 sequences, LTCS) and pairs [2 sequences]. Factors associated with TCs were evaluated by uni-multivariable logistic regression analysis.

Results: Most patients were men (82.4%) and caucasian (65.4%), with a median age of 39 (IQR:30-48) years. Heterosexual intercourse were the main route of transmission (46.7%), followed by men who have sex with men contact (MSM; 36.0%). Patients were infected mostly by B (64.3%), BF recombinant forms (11.0%) or CRF02_AG (8.1%) clades. Non-B subtypes, and particularly recombinant forms, were increasingly represented across years (from 26.9 to 44.1% and from 13.9 to 30.1%, respectively, p=0.01 2 and 0.006).

Overall, 67 (24.6%) individuals took part in TCs, including 39 (58.2%) in small TCs and 28 (41.8%) patients in LTCS. Non-B subtypes were increasingly represented across LTCS (60.7% of non-B subtypes vs. 39.3% of B subtypes were involved in LTCS, p=0.004). Respect to other patients, LTCS-individuals were more frequently MSM (p=0.003), and infected by CFR02_AG and CRF42 BF (p=0.016 and 0.010, respectively). None of the identified LTCS carried transmitted drug resistance. By multivariate logistic regression, the HIV-1 infection by non-B subtypes was the only factor significantly associated with higher probability to be in LTCS (odds ratio: 3.29 [1.37-7.93]). No other factors, including risk factors, were significantly associated with LTCS.

Conclusions: Remarkable changes in HIV-1 infection occurred in Italy over the last years, with active spreading among large TCs, and contributing to the epidemiological shift from B to non-B subtypes in North Italy. Our results highlight the role of molecular epidemiology in HIV-1 non-B diagnoses, suggesting the need to promptly identify local outbreaks, particularly those characterized by large clusters of transmission. This can help in decreasing the rate of transmission, and in improving the efficacy of HIV-1 therapy.

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Pharmacokinetic/pharmacodynamic informed assessment of pyrazinamide phenotypic resistance testing and pncA sequencing in multidrug-resistant tuberculosis

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Background: Pyrazinamide (PZA) is a key drug in therapy of multidrug-resistant tuberculosis (MDR TB). Despite one-third to two-thirds of MDR-TB isolates being phenotypically resistant, PZA is often administered to all patients with MDR-TB because of difficulties in phenotypic testing. Most PZA-resistant isolates demonstrate mutations in the pncA gene and sequencing technologies may offer an alternative. However, neither phenotypic nor genotypic PZA resistance testing has been fully informed by a pharmacokinetic / pharmacodynamic (PK/PD) analysis.

Materials/methods: Patients with at least rifampicin resistant TB were recruited in KwaZulu-Natal, South Africa. Baseline positive sputum samples were evaluated with phenotypic drug susceptibility testing, PZA minimum inhibitory concentrations (MICs) in the BACTEC MGIT 960 system and whole-genome sequencing. Pharmacokinetic sampling was performed at 0,1,2,4,6 and 8 hours post-dose at steady-state, PZA concentrations quantified using high performance liquid chromatography-mass spectrometry and population pharmacokinetic analysis performed using NONMEM® (from which area under the PZA time-concentration curve (AUC_{0-24}) values were derived). Attainment of a PZA PK/PD efficacy target (AUC_{0-24}:MIC >11.3 mg/L/h) was assessed after stratifying by phenotypic or genotypic PZA resistance testing results using Monte-Carlo simulations.

Results: Ninety-two PZA MICs and fifty PZA AUC_{0-24} values were available for simulation. Using the MIC distribution for all isolates from this population, 39.1% achieved the efficacy target. Target attainment was 0% and 63.9% when using the MIC distribution from isolates with and without a pncA mutation respectively. Whereas target attainment was 0 and 82.7% when using an MIC distribution from isolates with an MIC ≤100µg/ml (the current critical concentration) or >100µg/ml respectively. Only by using an MIC distribution from isolates with an MIC of ≤40µg/ml did ≥95% achieve the target.

Conclusions: Amongst patients with MDR TB, the presence of pncA mutations identify those where PZA is unlikely to be of use. In contrast, the absence of pncA mutations does not reliably distinguish those in whom PZA is likely to be of benefit versus those in whom it is unlikely to be beneficial. These results question the rationale for MDR TB regimen design based on pncA sequencing. Phenotypic testing provides better discrimination, but the current critical concentration may be too high.

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A multi-centre study of dalbavancin use in Italy (DALBITA Study): which could be the appropriate place for this easy-to-manage antibiotic to treat Gram-positive infections?

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Background: Dalbavancin is approved for the treatment of Acute Bacterial Skin and Skin-Structure Infections (ABSSSI); the efficacy in the treatment of osteomyelitis and endocarditis is still under investigation. Few data are available about Dalbavancin use in real-life settings. We aimed to evaluate the efficacy and safety of Dalbavancin in Italy.

Materials/methods: Retrospective multicenter study involving 11 Italian hospitals. Patients that received \( \geq 1 \) dose of Dalbavancin (May 2016–June 2019) were enrolled. The primary outcome was clinical cure at the end of treatment (improvement of lesions and resolution of infection as defined by clinicians); secondary outcomes were safety and tolerability. ABSSI and other infections will be compared. Chi-square and Mann-Whitney test were used for statistics.

Results: 206 patients were enrolled (males 50%, median age 62 years, Charlson index 3). 60.2% were ABSSI; non-ABSSI (39.8%) included: osteomyelitis, prosthetic joint infections, septic arthritis, catheter-related bloodstream infections, and sepsis. 151/194 (77.8%) of patients received previous and concomitant antibiotic treatments for the same infection, respectively. A microbiological isolation was available in 38% of patients (12% MRSA). Clinical cure was obtained in 82.5% of patients. 62.1% had no relapse at the follow-up visit (1-6 months). 11/167 (5.4%) patients had adverse events, mostly non-severe. No difference in efficacy and safety was found according to ABSSI and non-ABSSI diseases (Table 1).

Conclusions: Dalbavancin demonstrated an overall success rate of more than 80% in a multicenter Italian cohort. The efficacy and safety were similar in both ABSSI and infections with off-label indication. In this real-life setting Dalbavancin is often used as maintenance therapy and in a combination regimen. Further data are needed about the use of this long-acting lipoglycopeptide in non-ABSSI in order to optimize therapeutic strategies.
### Abstracts 2020

#### Table 1

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Population (N=206)</th>
<th>ABSSSI (N=124)</th>
<th>Other than ABSSSI (N=82)</th>
<th>p-values</th>
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</thead>
<tbody>
<tr>
<td>Age, median (IQR)</td>
<td>62 (50-76)</td>
<td>62 (47-73)</td>
<td>61 (54-78)</td>
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<td>Gender (males), n(%)</td>
<td>103 (50%)</td>
<td>62 (51%)</td>
<td>40 (48%)</td>
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<tr>
<td>Charlson comorbidity index, median (IQR)</td>
<td>3 (1-5)</td>
<td>3 (1-5)</td>
<td>4 (1-6)</td>
<td>0.022</td>
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<tr>
<td>Previous antibiotic therapies, n(%)</td>
<td>151/194 (77.8%)</td>
<td>83/119 (69.7%)</td>
<td>68/75 (90.7%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Concomitant antibiotic therapy, n(%)</td>
<td>82/173 (47%)</td>
<td>50/108 (46.3%)</td>
<td>31/64 (32.2%)</td>
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<td>Setting, n(%)</td>
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<tr>
<td>Hospital-admission</td>
<td>83 (40.3%)</td>
<td>46 (37%)</td>
<td>37 (45%)</td>
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<tr>
<td>Day-Hospital</td>
<td>57 (27.7%)</td>
<td>34 (27%)</td>
<td>23 (28%)</td>
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<td>Outpatient-services</td>
<td>62 (30.1%)</td>
<td>42 (34%)</td>
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<td>Unknown</td>
<td>4 (1.9%)</td>
<td>2 (2%)</td>
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<tr>
<td>LOS, median (IQR)</td>
<td>7 (0-18)</td>
<td>3 (0-11.7)</td>
<td>13.5 (5.5-22)</td>
<td>&lt;0.0001</td>
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<td>Outcome:</td>
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<td>0.459</td>
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<tr>
<td>Recovery</td>
<td>170 (82.5%)</td>
<td>106 (85.5%)</td>
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<tr>
<td>Interruption for AE</td>
<td>3 (1.5%)</td>
<td>1 (0.8%)</td>
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<tr>
<td>Failure</td>
<td>22 (10.7%)</td>
<td>12 (9.7%)</td>
<td>10 (11.9%)</td>
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<tr>
<td>Unknown</td>
<td>11 (5.3%)</td>
<td>5 (4%)</td>
<td>9 (10.8%)</td>
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<td>No</td>
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<td>Serious</td>
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<td>Unknown</td>
<td>39 (18.9%)</td>
<td>18 (14.5%)</td>
<td>24 (28.6%)</td>
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</tr>
</tbody>
</table>

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Abstract 7730

In-hospital and midterm out-hospital complications of hospitalised respiratory syncytial virus-positive adults in France

Alexandre Descamps*1, Paul Loubet1,2, Nezha Lenzi2, Florence Galtier2,3, Laine Fabrice2,4, Zineb Lesieur2, Philippe Vanhems2,5, Xavier Duval2,6, Fabrice Carrat7, Odile Launay1,2

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Background: Although respiratory syncytial virus (RSV) is recognized as an important cause of respiratory infections among older adults with comorbidities, associated hospital burden and long term complications are still underestimated. We aimed to compare baseline characteristics, comorbidities, in and out-hospital outcomes of RSV versus influenza infected adult patients.

Materials/methods: Adults hospitalized with acute respiratory infection (ARI) were included in a prospective, multicenter study conducted in five French university hospitals during two consecutive winter seasons (2017/2018 and 2018/2019). RSV and influenza virus were detected by multiplex RT-PCR in nasopharyngeal swabs. Poisson regression models with a robust error variance approach were used to estimate the prevalence ratio (PR) associated with in/out-hospital outcomes between RSV positive patients and influenza positive patients after adjustment for potential confounders.

Results: Overall, 1,428 hospitalized adults with ARI were included, median age was 72 years (IQR 60-82), 55% were male (790/1,428) and 87% had underlying chronic conditions (1,250/1,428). RSV was detected in 8% (114/1,428) and influenza virus in 31% (437/1,428). After excluding RSV-influenza co-infections (n=6), there was a higher proportion of patients aged ≥60 years or more in adults hospitalized with RSV compared to those with influenza (86% vs 76%; p=.02). Patients with RSV were more likely to have chronic respiratory diseases (52% [56/108] vs 39% [166/431], p=.012) and chronic cardiac diseases (52% [56/108] vs 41% [176/431], p=.039) than those with influenza. Median hospital length of stay was higher for RSV than influenza positive [8 (IQR, 5-13) vs 6 days (IQR, 4-11), p<.001]. In-hospital complications prevalence ratios were significantly higher among RSV patients: respiratory failure (aPR=1.7; 95%CI 1.2-2.4), acute respiratory distress syndrome (aPR=1.9; 95%CI 1.2-3.0), ICU admission (aPR=2.1; 95%CI 1.5-3.1) and invasive mechanical ventilation (aPR=1.8; 95%CI 1.2-2.7). No differences were observed in out-hospital outcomes defined as new hospital admission and mortality within 1 or 3 months after hospital discharge.

Conclusions: In our setting, RSV positive patients had more severe in-hospital outcomes than influenza positive patients. Improvement in the early diagnosis and management of RSV infections in hospitalized adults are needed with specific new therapeutics to protect older adults and those with high risk conditions.

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Abstract 7734

Development of a dried blood spot assay to quantify levofloxacin drug concentrations for personalised dose adjustment in multidrug-resistant tuberculosis in endemic settings

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Abstract third-party references: Acknowledgement: This project was financially support by the Bill & Melinda Gates Foundation, Grant Challenges program (grant number OPP1191221). Sagal Mohamed’s work was supported by the NIH T-32 AI007046 grant.

Background: Levofloxacin is one of the two fluoroquinolones recommended as a group A drug to treat multidrug-resistant tuberculosis (MDR-TB), but is subject to considerable individual pharmacokinetic variability where low circulating levofloxacin exposures drive poor treatment outcomes. Measurement of serum drug concentrations for personalized dose adjustment has been limited in TB endemic settings due to inability to preserve the cold chain for serum analyses and lack of access to specialized equipment for quantification.

Materials/methods: A dried blood spot (DBS) based assay was developed to bypass the need for serum which could be transported at room temperature by conventional mail services. Our previous method to detect levofloxacin concentrations from serum for analysis by high performance liquid chromatography (HPLC) was adapted for the DBS platform on Whatman™ FTA™ DMPK-C paper filter cards. Spiked filter paper punches were extracted and precipitated by perchloric acid in acetonitrile. A levofloxacin standard curve, concentrations (μg/mL): 50, 40, 30, 25, 20, 12, 8, 4, 2, 0.5, was tested as well as the controls of serum only and 20 μg/mL of levofloxacin only without blood, and using difloxacin as an internal control. Linearity, intra-day and inter-day variability were compared over different environmental conditions and durations from time of blood spotting.

Results: No degradation of levofloxacin or the internal control was observed. The assay was linear over the testing concentration range with R2 of >99%, with a lower limit of quantification of 0.5 μg/mL, which extended above and below the commonly observed peak concentration range (8-12 μg/mL). Intra-day and inter-day variability demonstrated acceptable precision up to 42 days from spotting with relative standard deviation (RSD) < 15%. The assay was replicated onsite with transport condition and local laboratory equipment at Kibongo to Infectious Diseases Hospital and Kilimanjaro Clinical Research Institute.

Conclusions: A DBS based assay for levofloxacin quantification was successfully developed and adapted for a TB endemic setting in Tanzania. Ongoing studies include comparison of the DBS assay to a novel saliva-based methodology for implementation strategies in Tanzania.

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Abstracts 2020

Abstract 7740

Arakki: a workflow-based system for virus identification in the clinic
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Background: The recent advances in next generation sequencing (NGS) provided a fast and cost effective means to characterize viral infections in clinical samples. Many NGS data analysis tools have been developed to identify the virus genomes in samples. However, the clinical use of NGS technology requires extra analysis options not existing in these tools, such as identification of multiple types/sub-types in the population, the discovery of mutations in the viral genomes, and annotating the mutations with relevant information. Moreover, the tool should be fast, flexible to configure, and easy to use.

Materials/methods: We introduce the Arakki system, which provides functionalities to support analysis of viral samples in the clinic. The Arakki workflow is composed of four phases: First, viral identification, including taxonomy classification. This is achieved by mapping the NGS reads to all available viral genomes in the public databases. Second, viral de novo assembly, to check for novel sequences. Third, variant identification and annotation. The annotation is based on a user defined database of clinically relevant positions [for example, substitutions in the core positions 70 and 91 of HCV virus]. Fourth, report generation and visualization. Each of these steps provides a list of candidate hits, to detect multiple types/sub-types in the population. Arakki is developed using the Tavaxy workflow engine and it is so flexible that the users can re-configure the workflow using graphical user interface [Figure below]. Users can add/remove steps, select NGS platform, or even select among programs for mapping and assembly.

Results: Arakki is available for free (www.arakki.org), for local installation or in the cloud. Arakki achieved using many clinical samples infected with HCV, HBV. Some samples were sequenced using Illumina and the others using Ion Torrent. The analysis time takes few minutes per sample.

Conclusions: Arakki is an efficient system for analysis of viral samples in the clinic. It is efficient in terms of time and resources. A recent study using Arakki could prove that the sample has HPgV co-infection and not only HCV infection, as primarily thought according to PCR analysis.

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Short versus extended antibiotic treatment with a carbapenem for high-risk febrile neutropenia in haematology patients (SHORT trial): results from a randomised multi-centre non-inferiority trial

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Abstract third-party references: ZonMW [The Netherlands Organisation for Health Research and Development], Fonds NutsOhra

Background: In haematology patients with high risk neutropenia due to intensive chemotherapy the optimal antibiotic treatment duration for fever of unknown origin [FUO] is unknown. Early antibiotic discontinuation has been advocated to reduce unnecessary exposure to broad-spectrum antibiotics, but there is limited evidence for the safety of this strategy. We aimed to assess if short treatment with carbapenems is non-inferior to extended treatment for neutropenic patients with FUO.

Materials/methods: Multicentre, open-label, randomised clinical trial in 6 centres in the Netherlands. Haematology patients with FUO during high risk neutropenia [≥7 days] were eligible for participation. Eligible patients were randomly assigned (1:1) to either the short treatment arm, where the carbapenem was discontinued after 72 hours, irrespective of presence of fever, or the extended treatment arm, where the carbapenem was continued for ≥9 days until afebrile for 5 days or end of neutropenia [EON], whichever came first. The primary endpoint was treatment failure defined as a composite of recurrent fever or a carbapenem-sensitive infection between day 4 and day 8 and septic shock or death from day 4 until EON. Secondary endpoints included all-cause and infection-related mortality until 30 days post-EON. We used 10 percentage points as non-inferiority margin.

Results: Between December 2014 and August 2019 268 patients were included. Risk of treatment failure in the modified intention-to-treat analysis [mITT] was 23.7% (32/135) in the short treatment versus 18% (24/133) in the extended treatment arm [adjusted risk difference (ARD) 4.0% [90% CI: -2.3% to 10.3%]] and in the per-protocol analysis 28.2% (29/103) versus 18% (22/122) [ARD 9.3% [90% CI 0.8% to 17.7%]]. In both analyses the confidence intervals included the non-inferiority margin of 10%. All-cause mortality until 30 days post-EON was significantly higher in the short treatment group: 3.7% (5/135) versus 0.8% (1/133) [ARD 2.9%, 95% CI 1.3 to 4.4%], but infection-related mortality until 30 days post-EON was not statistically different between the treatment arms: 2.2% (3/135) in the short and 0.8% (1/133) in the extended treatment arm [ARD 1.6%, 95% CI 0.6 to 3.7%].

Conclusions: Early discontinuation of carbapenem treatment in neutropenic patients with fever was not non-inferior to extended treatment.

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Prevalence of non-tuberculous mycobacteria in patients with cystic fibrosis in a tertiary hospital

Diego Ortega Larrea*1, Eric López1, Miguel Moreno Hijazo1, Saray Mormeneo Bayo1, Sandra Nabal Díaz1, Emilio David Valverde1, María Antonina Arias1, Blanca Fortuño1, Margarita Elu1, Jesús Viñuelas1

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Background: Nontuberculous mycobacteria (NTM) are increasingly insulated and with higher frequency in adults and children with Cystic Fibrosis (CF). Data from the US CF Patient Care Registry reveal that 19% of patients who were cultivated over a 4-year period (2011-2015) had one or more species of isolated MNT.

Materials/methods: Review of the last 8 years of the MNT isolations from respiratory samples of patients with CF diagnosis from the Pneumology Clinic of the Miguel Servet University Hospital in Zaragoza.

Results: The identification of MNT was performed from culture by mass spectrometry (MALDI Biotyper System, Bruker) and molecular methods (GenoType Mycobacterium CM and AS, Hain). During the last 8 years 1147 samples were received from 297 patients with CF, 73 MNT isolates were found in 16 patients, 15 adults with an average age of 32 years and 1 pediatric patient. There was no difference respect the sex, 8 women and 8 men. In most of these patients the same MNT isolation was repeated (3, 5 and up to 10 times). Single isolates were considered contaminations. Two different species of MNT were isolated in two patients. The most isolated MNT was *M. lentiflavum* (29), followed by *M. intracellulare* (19), *M. abscessus* (12), *M. chimaera* (6), *M. gordonae* (4), *M. mucogenicum* (1), *M. xenopi* (1) and *Mycobacterium sp.* (1), which could not be identified and was considered a contaminant.

Conclusions: The increase in MNT isolates in recent years is related to the search and the value of these mycobacteria as pathogens and the new liquid culture media and the new species identification techniques, which help to detect them. The prevalence of MNT in CF patients has increased in recent years. Its role is difficult to determine and should always be individualized according to the clinical and radiological characteristics of the patient and once other more frequent pathogens in these patients have been ruled out.

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Abstract 7746

**Human papilloma virus 16 viral load quantification using droplet digital PCR and correlation with cervical lesion**

Marianna Martinelli*, Chiara Giubbi, Rosario Musumeci, Federica Perdoni, Federica Paola Sina, Robert Fruscio, Fabio Landoni, Clementina Cocuzza

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**Background:** Human Papillomavirus (HPV) infection is known to be associated to cervical cancer development. Presently, many countries are changing their screening policy switching to HPV testing as primary screening as suggested by European guidelines. Even if cytology is the preferred triage method, HPV viral load measurement has been suggested to be a predictor of cervical lesion progression. The aim of this study was to evaluate the correlation between HPV16 viral load and cervical lesion grade using droplet digital PCR (ddPCR) among women referred to colposcopy.

**Materials/methods:** Cervical samples were collected from women attending the Colposcopy Clinic, San Gerardo Hospital (Monza, Italy) for abnormal cervical cytology. All samples were extracted using NucliSENS easyMAG and HPV detection was carried out using AnyplexII HPV28. All HPV16 positive samples were tested using ddPCR and read in a QX Droplet reader (Bio-Rad). PCR was set up in duplex, combining HPV16 with the CCR5 gene to obtain cell quantification. Viral copy number/cells were calculated as: HPV16 copies/(CCR5 copies/2).

**Results:** Currently, 47 HPV16 positive samples collected from women with different grade of lesion have been tested. A higher mean viral load/cells value was observed among women with a high-grade lesion (HSIL) compared to women with lower grade lesion (36.3 vs 21.9 copies/cells). The same result was obtained comparing viral load quantification with biopsy (22.1 vs 6.0 copies/cells, CIN2+ vs <CIN2). Moreover, 4 women showing HPV16 persistent cervical infection were followed-up at different time points to evaluate viral load changes with cervical cytology. Preliminary results show a possible correlation between HPV16 viral load and progression/regression of the cervical lesion [Figure1].

**Conclusions:** Preliminary data suggest that ddPCR method represents a promising tool for HPV viral load estimation. Viral load measurement could represent a useful biomarker in the follow up of HPV-positive women although larger longitudinal clinical studies are required to assess its clinical value.

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Fayssoil Fouad1, Magali Lemaitre1, Antoine Bessou1, Fabrice Carrat2, Pascal Crépey3, Jacques Gaillat4, Gaetan Gavazzi5, Odile Launay6, Anne Mosnier7, Marie-Cécile Levant8, Mathieu Uhart9

1iqvia, Courbevoie, France, 2Sorbonne Université, Paris, France, 3ehesp, Rennes, France, 4Centre Hospitalier Annecy Genevois, Épagny Metz-Tessy, France, 5chu Grenoble, Grenoble, France, 6cochin, Paris, France, 7open Rome, Paris, France, 8sanofi, Lyon, France, 9sanofi, Lyon, France

Background: Seasonal epidemics caused by influenza viruses lead to 2 to 6 million influenza cases each season in France. Severe influenza disease can result in hospitalisations due to the virus itself or due to a secondary infection, making it difficult to estimate the overall burden. The objective of the study was to estimate the burden attributable to influenza in terms of hospitalisations between 2010 and 2018 in France.

Materials/methods: The number and the characteristics of patients hospitalised due to influenza for the period 2010 to 2018 were obtained from the French national hospital administrative database (PMSI). This analysis was supplemented by an ecological approach for estimating excess hospitalisations, costs and mortality (CepiDc) attributable to influenza. Cyclic regression models were developed integrating different parameters [trend, season, and incidence of influenza syndromes (sentinel network)].

Results: The mean number of influenza hospitalisations was 19,280 [min: 8,627; max: 44,024] per season with an average stay of 8 days. Patients aged 65 years old and over experienced the longest stays [11 days] and accounted for the largest share of hospitalisations, with a mean of 57% of hospital-days [ranging from 17% of the 2009/10 pandemic season to 80% for the 2016/17 season]. Among patients aged 65 and over, 29% were re-hospitalized within 90 days post-discharge. A mean average of 32,424 respiratory hospitalizations were attributable to influenza [min: 13,075, max: 48,672] per season, with 68% of excess respiratory hospitalisations accounted for by patients aged 65 years and over. The number of deaths attributable to influenza was estimated at 9,656 on average per season between 2010/11 and 2014/15, 90% of which were among patients aged 65 years old and over.

Conclusions: The combination of two complementary approaches allowed the estimation of the hospital burden attributable to influenza in France. These results highlight the major public health burden represented by influenza and its complications among hospitalised cases, which is particularly evident in individuals aged 65 years and over.

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Prospective evaluation of three rapid multiplex PCR assays for the detection of gastrointestinal pathogens from stool samples

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Background: The detection of gastrointestinal (GI) pathogens (bacteria, parasites and/or viruses) by conventional methods is time-consuming, requires strong technical experience, and lacks sensitivity. Several rapid multiplex PCRs (mPCR) have recently been developed to improve the identification of such pathogens and their relative performance should be evaluated. The aim of the present study is to assess the performance of 3 rapid mPCR GI assays (FilmArray® gastrointestinal panel [bioMérieux], QIAstat-Dx® gastrointestinal [Qiagen] and Novodiag® gastrointestinal panel [Mobidiag] - bacteria search only).

Materials/methods: Enteric pathogens were detected in stool samples using the 3 mPCR kits as well as conventional methods (standard stool culture, GenXpert PCR [Cepheid] for Clostridioides difficile, parasitological stool examination and/or in-house PCR). The patients enrolled were adults consulting for digestive disorders in the emergency department or the infectious diseases department of Bichat Hospital (Paris). We used a composite gold standard considering the conventional method, the positivity of 2 out of 3 mPCRs or the results of the national reference center (NRC).

Results: 85 stool samples were studied, including 77 collected prospectively from April to September 2019 and 8 stored at -80 °C. Prevalence of bacterial pathogens was 45.9% (n=39) including Clostridioides difficile at 9.4% (n=8). Prevalence of parasites and viruses was 12.9% (n=11) and 2.4% (n=2), respectively. For bacteria detection, 95.7% (732/765) of the overall results and 70.6% (36/51) of positive results were concordant between the 3 mPCRs. We observe a concordance between FilmArray® and QIAstat-Dx® for parasites and viruses, at 99.4% (338/340) and 99.8% (424/425) of overall results and 90.9% (10/11) and 100.0% (2/2) of positive results, respectively. Performances of the 3 kits are detailed in the table below. The discrepancies in Yersinia sp. detection were explained because Novodiag® only detects toxigenic Yersinia sp. whose absence was confirmed by the NRC. Discrepancies in the detection of Campylobacter sp. were also investigated by the corresponding NRC.

<table>
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<tr>
<th>Pathogen</th>
<th>Gold standard (n = 85)</th>
<th>Conventional method (n = 85)</th>
<th>FilmArray® GI Panel (bioMérieux) (n = 85)</th>
<th>QIAstat-Dx® GI Panel (Qiagen) (n = 85)</th>
<th>Novodiag® GI Panel (Mobidiag) (n = 85)</th>
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<td>Bacteria</td>
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<td>8 9.4 2</td>
<td>11 100.0 96.1</td>
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<td>5 100.0 97.6</td>
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<td>8 80.0 100.0</td>
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</table>

(Se = Sensitivity, Sp = Specificity, NA = Not applicable, NR = Not realized)
* Prevalence of Campylobacter sp. includes results given by the NRC
** No toxigenic Yersinia sp. was detected by the NRC which is consistent with the results found with Novodiag® (n=0; Sp=100 %)

Conclusions: All tested rapid molecular methods have identified more enteric pathogens than conventional methods. Although some discrepancies were identified, the 3 mPCR assays showed good agreements.

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What clinicians and researchers should know about machine learning for infection management: review of methods, targeted outcomes and reporting of future technologies

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Background: Machine learning (ML) is already used in many healthcare areas. Recent reviews have identified an increasing albeit still experimental use of ML for diagnosis and management of infections. These reviews focused on introducing ML to practitioners in the field and investigated the underlying data source. We aimed at extending this introduction by assessing methods, targeted outcome, and reporting quality of ML research in infection management.

Materials/methods: A Medline search was performed to identify ML research for infections between 2014-01-01 to 2019-08-20. Studies were included if routinely available electronic hospital record data from an inpatient setting with a focus on bacterial and fungal infections were used. Articles were assessed on their research focus and definitions of the targeted/labelled outcome (e.g. sepsis onset). ML techniques and performance metrics were extracted. A special focus lied on reporting of (missing) data handling, availability of software code, and information on external model validation.

Results: Most studies the 52 included studies focused on the detection/prediction of sepsis (n = 19). Target outcome definitions in this group were heterogeneous and comprised bacteraemia, sepsis by ICD code, clinical sepsis definitions, and sepsis-associated mortality. Similar heterogeneity was found for studies on hospital-acquired infections (HAI; n = 11), surgical site and other postoperative infections (n = 11), microbiological test results (n = 4), infections in general (n = 2), musculoskeletal infections (n = 2), and other topics (n = 3). Of 35 ML techniques, neural networks showed best performance by AUROC for sepsis and HAI outcomes. Overall, detailed information on data handling and software code was often lacking. Validation on new datasets and/or in other institutions was rarely done. Despite existing reporting guidelines, documentation of ML approaches was often poor.

Conclusions: Not all clinicians and researchers need to be experts in ML, but it is crucial to get acquainted with ML concepts and their application. Promising approaches of ML use in infection management were identified (e.g. early identification of septic patients). However, building trust in these new technologies will require improved reporting. Explainability and interpretability of the used models was rarely addressed and should be further explored.

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Abstract 7760

**MALDI-TOF MS as new tool for the identification of serological biomarkers for diagnosis of hepatitis B and C viruses infections**

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**Background:** Hepatitis B virus (HBV) and Hepatitis C virus (HCV) represents two of the major health problem worldwide. Only few studies investigate by MALDI-TOF MS the presence of specific peptides/proteins that can be considered predictive indicators for HBV infection. In this study, we used MALDI-TOF MS to examine serum samples aiming at searching peptides/proteins that can be used as serological biomarkers to detect HBV and HCV.

**Materials/methods:** Fifty-six serum samples, received for diagnostic purposes with suspected HBV and/or HCV infection, previously analyzed with the diagnostic assays currently used in our laboratory and resulted positive or negative for HBsAg or HCVcoreAg, were examined by MALDI-TOF MS.

**Results:** In the first step, 3 different protein extraction approaches were evaluated to obtain valid, reliable and reproducible results. The protocol adopted involved ultracentrifugation of serum samples with water. The analysis performed at low molecular weight showed the presence of unique peaks for each class of sera (HBV-positive, HCV-positive or both negative), while the analysis carried out at high molecular weight showed the absence of significantly discriminating peaks. In particular, the detection of HBV-positive sera is associated with 8 discriminating peaks; similarly, detection of HCV-positive sera is associated with 8 discriminating peaks. Noteworthy the trend of the intensity of 3 peaks (3224, 6632, 7478 Da) showed a significant increase or decrease depending on the virus responsible for the infection. However, it was not possible to identify the protein/peptide matching to the markers found. The second step involved the creation of statistical models able to differentiate the three different categories of serum analyzed on the basis of these peaks. In particular, using this model it was correctly classified all 56 sera.

**Conclusions:** Our results demonstrated, on a limited number of sera with high concentration of specific antigen, the presence of peaks differentiating classes of positive sera, for both HCV, for the first time to our knowledge, and HBV, as already reported by other Authors. This could be a starting point to add MALDI-TOF MS as a tool for the diagnosis of such infections, being independent of antigen mutations that could affect the conventional assays.

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Abstract 7764

**Metanet: synchronisation and quality assessment of methods for rapid metagenomics-based pathogen detection**

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**Background:** Adoption of rapid metagenomics-based pathogen detection by clinical microbiology laboratories is accelerating. However, integration into routine diagnostic practice requires standardization, quality control, and objective result interpretation. The “Metanet” network includes 6 laboratories across Europe and North America and was established to optimize standardization of wet-lab and bioinformatic methods for this disruptive technology.

**Materials/methods:** In phase 1, DNA and RNA extracted from 8 spiked samples were distributed to Metanet sites. DNA and cDNA libraries were prepared by each laboratory and sequenced (NextSeq, Illumina) using a common standard operation procedure (SOP). In phase 2, DNA and RNA extracted from 18 pooled bronchoalveolar lavage samples were distributed to participating sites and processed with the same SOP. In phase 3, residual DNA and RNA from phase 2 was tested by 2 sites with optimized methods, additional training, and after standardization of processing steps that were found to affect reproducibility. Sequence data were analyzed using the Explify Platform (IDbyDNA).

**Results:** In phase 1, all sites reported identical results, except for one sample spiked with *Klebsiella pneumoniae* at a low concentration [detected by 3 of 5 laboratories]. Phase 2 demonstrated QC below expected ranges for 50% of runs and 27.8% of samples, as well as higher inter-laboratory and inter-run variation. Comparing sequence data from across the 6 sites highlighted variable quality of sequencing libraries as a source of error. Laboratory protocols were optimized and residual DNA and RNA retested. In phase 3, sequencing data was consistent, high quality with all runs and 31 of 32 samples (96.9%) passing sequencing QC. In addition, reproducibility of pathogen detection was also significantly improved. Respiratory viruses were detected in 42 of the expected 45 times (93.3%, compared to 79.7% in phase 2). Two of the 3 missed detections were in samples that did not meet internal control requirements, which would have flagged results as invalid.

**Conclusions:** As clinical microbiology laboratories adopt rapid metagenomics, standardized methods and comprehensive QC are critical. Easy-to-use software supporting QC and objective result interpretation are essential for clinical laboratories. Multi-center networks like Metanet help refine QC, optimize workflows, standardize methods, and inform future guidance documents.

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Plasmodium ovale curtisi and wallikeri infections in imported malaria: a 2013-2018 retrospective study from the French National Malaria Reference Centre

Valentin Joste*, Justine Bailly1, Veronique Hubert1, Eric Kendjo2, Nicolas Argy1,3, Sandrine Houze1,3

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Background: Plasmodium ovale curtisi (Poc) and Plasmodium ovale wallikeri (Pow) are two sympatric human malaria species despite their identical morphology[1] and the resulting burden of disease is not known. Dimorphism in defined genes has led to P. ovale parasites being divided into classic and variant types. We hypothesized that these dimorphs represent distinct parasite species.

METHODS: Multilocus sequence analysis of 6 genetic characters was carried out among 55 isolates from 12 African and 3 Asia-Pacific countries.

RESULTS: Each genetic character displayed complete dimorphism and segregated perfectly between the 2 types. Both types were identified in samples from Ghana, Nigeria, São Tomé, Sierra Leone, and Uganda and have been described previously in Myanmar. Splitting of the 2 lineages is estimated to have occurred between 1.0 and 3.5 million years ago in hominin hosts.

CONCLUSIONS: We propose that P. ovale comprises 2 nonrecombining species that are sympatric in Africa and Asia. We speculate on possible scenarios that could have led to this speciation. Furthermore, the relatively high frequency of imported cases of symptomatic P. ovale infection in the United Kingdom suggests that the morbidity caused by ovale malaria has been underestimated.

In France, Plasmodium ovale (Po) was responsible of 6% of imported malaria cases in 2018[2].

Materials/methods: We used data from the French National Malaria Reference Center (FNMRC) over 6 years (2013-2018) to analyze epidemiological, clinical and biological data, and malaria diagnosis corresponding to Poc or Pow mono-infection, confirmed using HRM-qPCR[3].

Results: We included 311 Poc and 372 Pow cases, imported from 27 countries, mainly in Africa with no difference between Poc and Pow (p=0.49). There was no difference in parasitic density median with 1882 p/µL for Poc and 1658 p/µL for Pow (p=0.088), in white blood cells count [5.6 G/L for Poc versus 5.2 G/L for Pow; p=0.054] and hemoglobin [127 g/L for Poc versus 126 g/L for Pow; p=0.94] but Pow infected patients presented deeper thrombopenia than Poc infected patients [94.5 G/L versus 111 G/L; p=0.0001]. Rapid Diagnostic Test (RDT) using aldolase detected respectively 45 and 55% of Poc and Pow infections whereas pan-LDH RDT detected respectively 4 and 16% of Poc and Pow infections.

Poc and Pow infected patients were comparable in age, sex ratio and ethnic origin. No difference in symptoms, clinical presentation (97% of uncomplicated malaria for both species), and taking-care of patients (hospitalization in respectively 56 and 61% of Poc and Pow cases; p=0.45) was observed. But, delay between last exposure to Po and symptoms was longer for Poc than Pow infections [34 days for Pow, 72 days for Poc; p=0.0001]. Relapses were observed in 16 Pow and 8 Poc infected patients, with no difference in delay [89 days for Poc, 78 days for Pow, p=0.92]

Conclusions: Pow caused more severe thrombopenia and had shorter appearance of symptom after leaving endemic area than Poc. There is no clear evidence of difference in clinical presentation. Thus, Po spp diagnosis without Poc/Pow differentiation is sufficient in patient’s management.

Aldolase RDTs were more efficient in Poc and Pow diagnosis than p-LDH RDTs. Furthermore, p-LDH RDTs were more efficient to detect Pow, as previously described[4].

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Abstract 7767

Letermovir reduces rehospitalisations among cytomegalovirus-seropositive allogeneic haematogenous stem-cell transplant recipients

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Background: CMV infection post A-HSCT is associated with substantial morbidity, mortality, and resource utilization. Letermovir was shown to prevent clinically significant CMV infection (CS-CMVi) in CMV-seropositive A-HSCT recipients and lower mortality at week 24. We evaluated letermovir’s impact on rehospitalization post-transplant.

Materials/methods: We used data from a phase-3 multicenter RCT to assess CMV-associated and all-cause rehospitalizations at weeks 14, 24, and 48 post-transplant among recipients of letermovir versus placebo (study drug started between day 0 and 28 post-transplant and given up to 14 weeks). We reported unstandardized rehospitalization rates, estimate standardized rates accounting for censoring due to death or early study discontinuation, and average rehospitalization days. We calculated 95%CI using Clopper–Pearson’s exact method.

Results: Of 495 patients in the primary efficacy study population, 325 received letermovir and 170 received placebo. Unstandardized rates of CMV-associated rehospitalization in letermovir vs. placebo recipients at weeks 14, 24, and 48 were 0.6% vs. 7.1% (95%CI 0.1%-2.2% vs. 3.7%-12.0%), 2.8% vs. 7.6% (95%CI 1.3%-5.2% vs. 4.1%-12.7%), and 3.1% vs. 8.8% (95%CI 1.5%-5.6% vs. 5.0%-14.1%), respectively. Unstandardized rates of all-cause rehospitalization in letermovir vs. placebo recipients at weeks 14, 24, and 48 were 36.6% vs. 47.6% (95%CI 31.4%-42.1% vs. 39.9%-55.4%), 49.2% vs. 55.9% (95%CI 43.7%-54.8% vs. 48.1%-63.5%), and 55.7% vs. 60.6% (95%CI 50.1%-61.2% vs. 52.8%-68.0%), respectively. Standardized rehospitalization rates per 100 patient-months in letermovir vs. placebo recipients at weeks 14, 24, and 48 were 12.8 vs 19.6, 9.5 vs. 11.1, and 6.3 vs. 7.2, respectively. In addition, the mean duration (days) of rehospitalization was shorter among letermovir vs. placebo recipients at weeks 14, 24, and 48: 14.4 vs. 17.9, 15.9 vs. 17.9, and 16.5 vs. 19.2, respectively. Standardized total length of rehospitalization per 100 patient-months in letermovir vs. placebo recipients at weeks 14, 24, and 48 were 264.4 vs 462.6, 267.3 vs. 308.0, and 202.5 vs. 245.2.

Conclusions: Letermovir, apart from preventing CS-CMVi in A-HSCT recipients and reducing all-cause mortality, is consistently associated with lower rates of CMV-associated and all-cause rehospitalizations with a shorter length of stay (especially within first 14 weeks post-transplant). Letermovir prophylaxis can significantly reduce healthcare utilization among CMV-seropositive A-HSCT recipients.

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Abstract 7768

**Epidemiology of carbapenemases isolated from Enterobacteriaceae other than Klebsiella pneumoniae and Escherichia coli in Belgium (2015-2018)**

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**Background:** The epidemiology of carbapenemase-producing Enterobacteriaceae (CPE) among species other than Klebsiella pneumonia (KP) and Escherichia coli (EC) is less explored. We retrospectively analyzed a large collection of isolates to determine the distribution and the epidemiology of non-KP non-EC CPE isolates (NKPECCPE) in Belgium.

**Materials/methods:** 119 Belgian hospital-based (n=95) and community-serving (n=24) laboratories referred 1237 non-duplicate EOTKpEc collected from various clinical specimens between 2015 and 2018 to the National Reference Center (NRC) for suspicion of CPE. The species identification was confirmed by MALDI-TOF and the antimicrobial susceptibility profile was determined by disk diffusion. Carbapenemase production was tested by Beta-Carba test (BioRad). Carbapenemases were identified by immunochromatographic lateral flow assay (LFA) RESIST-4 OKVN (Coris) or by multiplex PCR.

**Results:** Of the 1237 referred isolates, 531 (43%) EOTKpEc isolates including Enterobacter cloacae (n=249), Citrobacter freundii (n=119), Klebsiella oxytoca (n=67) and 13 other Enterobacteriaceae species (n=96) collected from 87 laboratories were confirmed as CPE. Carbapenemase types were mostly OXA-48-like (n=282; 53%), VIM (n=167, 31%), NDM (n=59; 11%), and six other types (n=25; 5%). Eight isolates coproduced two different types mostly OXA-48-like combined to another one (n=7). OXA-48 and VIM producing EOTKpEc were widely reported by 69 (79%) and 39 (45%) laboratories, respectively whereas 18 (21%) found NDM producing EOTKpEc. NDM and OXA-48 isolates were widely distributed in the three regions of the country, whereas VIM producers were reported more frequently in Wallonia including 8 hospitals with clusters (>1 cases with the same carbapenemase).

**Conclusions:** Our data shows a high diversity of carbapenemase producing EOTKpEc with E. cloaceae, C. freundii and K. oxytoca representing the three main species. Despite the predominance of OXA-48 type carbapenemase, VIM carbapenemase was found much more frequently in NKPECCPE than in E. coli and K. pneumoniae (less than 5% of VIM producers according to the NRC data during the same period). These data highlight the importance to conduct active survey that includes or targets other species of CPE to have a comprehensive epidemiology with representative distribution of different major carbapenemase types.

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Bacterial and fungal infections associated with influenza virus in hospitalised patients

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Background: The aim of this study was to describe the clinical characteristics, antiviral treatment and outcome of patients with influenza virus infection and bacterial and fungal co-infection.

Materials/methods: Prospective observational study conducted in a third level hospital between December 2016 and March 2019. Patients > 18 years of age, admitted to the hospital who met the criteria for severe influenza disease (pneumonia, respiratory distress, multiorgan failure, septic shock, admission to ICU) were included.

Results: We included 351 patients with influenza virus infection: 60% (209/351) had influenza B infection. Fifty one percent were women; mean age was 72.4 ± 17.74 years. One hundred and twenty-six patients were vaccinated, of these 86 (68%) developed influenza B and 40 (31%) influenza A (p < 0.001). Sixty-four patients were admitted to the ICU: 46 (71%) with influenza A and 18 (28%) with influenza B (p = 0.02). Seventy-nine patients had coinfections: 27 (34%) were admitted to the ICU and 52 (66%) in conventional ward (p < 0.001). Bacterial or fungal coinfection occurred in 22.5% (79/351) of patients. The most common bacteria were S. pneumoniae (35 patients-10%), S. aureus (6 patients-2%) and H. influenzae and P. aeruginosa in 5 patients (1.4%) each. Four patients had fungal infection: 1 P. jirovecii and 3 A. fumigatus (IFI). All 3 patients with IFI (2 influenza A and 1 B infection) were immunosuppressed (1 Lymphoma, 1 lung adenocarcinoma and 1 infliximab treatment); no immunocompetent patients (0/278) had IFI (p = 0.008). Oseltamivir treatment was prescribed in 87% (69/79) of patients with coinfections and in 77% (209/271) without coinfections (p = 0.04). Death within 30 days after the diagnosis of influenza was similar in patients with (7/77) or without (25/274) coinfections (p > 0.05); and no statistically significant differences were observed in mortality between patients with influenza type A or B (p > 0.05) or those vaccinated or not vaccinated (p > 0.05).

Conclusions: Patients with influenza A virus infection required admission to the ICU more frequently. S. pneumoniae was the most frequent bacteria isolated. Only immunosuppressed patients had fungal coinfection. Patients with coinfections received more Oseltamivir treatment. Thirty-days mortality was similar in patients with or without bacterial coinfections and in those vaccinated or not vaccinated.

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Public health impact of similar ESBLs/pAmpC-producing Escherichia coli causing urinary tract infections in non-related companion animals and humans

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Background: This study aimed to characterize ESBL/AmpC β-lactamases producing E. coli strains causing urinary tract infections (UTI) in companion animals (CAs) and non-related humans from the community (H).

Materials/methods: 3GC-resistant E. coli (companion animals n=35; humans n=85) isolated from patients with UTI were tested against 14 antimicrobials. PCR was used to detect E. coli phylogenetic groups, Pathogenicity associated-islands (PAIs), urovirulence genes, ESBLs/pAmpC resistance genes. ESBL/pAmpC-producing E. coli isolates were typed by MLST. Subclades C2 (H30-Rx) and C1 (H30-R1) by PCR. Genetic relationships among E. coli isolates were visualized by the goeBURST algorithm based on the PHYLViZ software (v.2). Molecular epidemiology was investigated using rep-PCR typing method.

Results: The frequency of resistance against fluoroquinolones (CAs=74.3%, H=88.2%), trimethoprim/sulphamethoxazole (CAs=71.4%, H=74.1%) and gentamicin (CA=40%, H=37.6%) was higher in 3CG-resistant E. coli from both groups. All isolates were susceptible to carbapenems. Considering phylogenetic group 3GC-resistant E. coli strains from CAs and humans mainly belonged to group-D and B2 (48.6%, 67.1%, respectively). The most frequent PAIs and virulence genes among isolates from CAs and H were: PAI IV536 (CAs=72%, H=91.8%, p=0.017) and PAI ICFT073 (CAs=54.3%, H=78.8%, p=0.013); ecpA (CAs=100%, H=100%) and iucD (CAs=48.6%, H=83.5%, p=0.0002). MLST typing of the ESBL/pAmpC producing E. coli strains revealed a heterogeneous population of E. coli clonal groups in CAs and in non-related humans with UTI. CAs and humans E. coli strains shared two MDR high-risk clonal lineages: ST131, and ST648, an emergent virulent lineage. The blaCMY-2 and blaCTX-M-15 were the most frequently ESBL/pAmpC detected genes in CAs and human strains. ST131 strains from CAs and humans mostly belonged to subclade C2 (H30-Rx). Rep-PCR confirmed that similar high-risk clonal lineages occur between non-related CAs and humans.

Conclusions: Considering that CAs with UTI are generally treated at home by the owners, measures should be implemented to avoid the spread of multidrug-resistant high-risk clones to the environment.

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Broiler farms and carcasses are an important source for dissemination of ESBL/mcr-1-producing Escherichia coli in Ecuador

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Background: Critical antibiotics in human medicine are being used in industrial poultry production in Ecuador (e.g. colistin). This practice has led the emergence and dissemination of resistance mechanisms of last resort antibiotic compounds. The aim of this study was to identify and characterize CTX-M-type extended spectrum β-lactamases (ESBL) and evaluate the prevalence of mcr (1 to 5) genes; in cefotaxime resistant Escherichia coli which were isolated from broiler carcasses, farms and extraintestinal human infections in Ecuador.

Materials/methods: Sampling was carried out in Quito (2018-2019), 126 samples from poultry batches, 319 carcasses from markets and 624 third generation cephalosporins resistant E. coli (3GC E. coli) isolates from human extraintestinal infections were considered. Samples were screened for the presence of 3GC E. coli inoculating a representative amount of sample in TBX + cefotaxime (3 mg/l). Antibiotic susceptibility profiles were established by Vitek® 2 system with AST-N27 cards. MIC for colistin were tested by microdilution. The mcr and bla\textsubscript{CTX-M} genes were identified by PCR and further characterized by sequencing.

Results: 92.9% (117/126) of caecum samples and 78.4% (250/319) of carcasses were positive for 3GC E. coli. None of the isolates were resistant to carbapenems and amikacin. Low resistance was registered for gentamycin. A half of the isolates were resistant to quinolones and fosfomycin and high percentage of the isolates were resistant to trimethoprim/sulfamethoxazole. Colistin resistant isolates showed MICs from 2 to 16 µg/ml. The most prevalent bla\textsubscript{CTX-M} allele was bla\textsubscript{CTX-M-55} (53%), followed by 28.4%. Other genes were found in less than 10% of the samples (bla\textsubscript{CTX-M-1},  bla\textsubscript{CTX-M-2},  bla\textsubscript{CTX-M-3},  bla\textsubscript{CTX-M-17},  and  bla\textsubscript{CTX-M-23}). The mcr-1 was found in 18.8% and 10.6% of farms and carcasses respectively. One isolate positive to mcr-1 and one isolate positive to mcr-4 were identified from human samples.

Conclusions: Poultry production in Ecuador is an important reservoir of ESBL and mcr positive E. coli. The prevalence of mcr-1 and mcr-4 in ESBL-E. coli from extraintestinal infections remains low. Further research is needed to find the most possible sources of these bacterium.

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Model-informed exposure response analyses for ceftazidime and levofloxacin against *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* in murine thigh infection models

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**Background:** Exposure response (E-R) analyses based on robust pharmacokinetic (PK) and pharmacodynamic (PD) data play a critical role in antimicrobial development. However, model-informed approaches are less common in preclinical settings. This study aimed to characterize E-R relationships for ceftazidime and levofloxacin in murine thigh infection models with *K. pneumoniae* and *P. aeruginosa* using an integrated experimental and optimal design strategy informed by population modeling.

**Materials/methods:** Strains *K. pneumoniae* ATCC 43816 (MIC <sub>CAZ</sub>: 0.25 mg/L, MIC <sub>LVX</sub>: 0.0625 mg/L) and *P. aeruginosa* ATCC 27853 (MIC <sub>CAZ</sub>: 2 mg/L, MIC <sub>LVX</sub>: 0.50 mg/L) were employed in neutropenic murine thigh infection models. Ceftazidime and levofloxacin were subcutaneously administered as single or multiple doses in dose range and dose fractionation studies. Doses for PK/PD studies and PK sampling times were based on D-optimal designs. Drug concentrations and protein binding in plasma were analysed by LC-MS/MS and modelled via population methods. E-R relationships were determined using viable count data at 24 h and PK/PD targets calculated.

**Results:** Apparent clearances differed slightly with the infecting pathogen for ceftazidime, but not levofloxacin [Table]. The fAUC/MIC was most predictive for levofloxacin and fT>MIC for ceftazidime. However, the PK/PD targets for stasis and 2-log<sub>10</sub> killing differed between strains [Table, n=1,397].

<table>
<thead>
<tr>
<th></th>
<th>Ceftazidime</th>
<th>Levofloxacin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><em>K. pneumonia</em></td>
<td><em>P. aeruginosa</em></td>
</tr>
<tr>
<td>Apparent total clearance (mL/h)</td>
<td>38 (4%)</td>
<td>30 (5%)</td>
</tr>
<tr>
<td>Coefficient of determination (r²) for free Cmax-over-MIC (fCmax/MIC)</td>
<td>0.26</td>
<td>0.26</td>
</tr>
<tr>
<td>Coefficient of determination (r²) for free AUC-over-MIC (fAUC/MIC)</td>
<td>0.25</td>
<td>0.38</td>
</tr>
<tr>
<td>Coefficient of determination (r²) for free time-above-MIC (fT&gt;MIC)</td>
<td>0.94</td>
<td>0.87</td>
</tr>
<tr>
<td>PK/PD indices at 24 h, bacteriostasis</td>
<td>fT&gt;MIC 34%</td>
<td>fT&gt;MIC 60%</td>
</tr>
<tr>
<td>PK/PD indices at 24 h, 2 log&lt;sub&gt;10&lt;/sub&gt; killing</td>
<td>fT&gt;MIC 47%</td>
<td>fT&gt;MIC 84%</td>
</tr>
</tbody>
</table>

**Conclusions:** This study presents an integrated experimental, optimal design and modeling strategy that efficiently identified the most predictive PK/PD indices and targets for ceftazidime (fT>MIC) and levofloxacin (fAUC/MIC) against two common pathogens. This serves as a case study for how to implement this translational approach in future pre-clinical drug development programs. This model-informed approach was valuable to efficiently generate robust and informative E-R relationships.

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Emergence of penicillin non-susceptible Group B streptococci within the hypervirulent CC17 clone colonising pregnant women in Portugal: a genomic analysis

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Background: Group B streptococci (GBS) have been considered uniformly susceptible to penicillin. However, increasing reports from Asia and North America are finding penicillin-non-susceptible GBS (PRGBS) with mutations in the pbp genes. We used a high throughput sequencing approach to characterize three PRGBS isolates colonizing pregnant women in Portugal.

Materials/methods: Three out of 252 GBS isolates (G0305, G0503 and G0516) recovered from vaginorectal swabs of pregnant women showed decreased penicillin susceptibility [MIC>0.12µg/ml]. The isolates were sequenced (Illumina, San Diego, USA) and analyzed by both mapping and de novo assembly approaches. Capsular serotype, multilocus sequence type (MLST), surface-associated structures and pbp genes were extracted from the genomes.

Results: Genomic analysis revealed that all isolates contained the type III capsular polysaccharide locus, carried the rib surface protein gene, pilus islands 1 and 2b, and were represented by sequence type (ST)109, a single-locus variant of ST17, founder of the hypervirulent CC17 clone. Comparison of the PBPs with those of the susceptible strain 2603V/R revealed, in all isolates, the presence of 4, 3, 1 and 2 amino acid substitutions in PBP1A, PBP2A, PBP2B and PBP2X, respectively. All these changes are commonly found among other susceptible isolates. Additionally, the isolates carried a G398A substitution in PBP2A, previously found among PRGBS isolates in Japan. The core-genome MLST comparison of the 3 isolates with a reference genome (COH1, ST17) and a penicillin susceptible representative of ST17 in the collection (G0235) revealed that the ST109 isolates are more similar to each other (between 46 and 86 allelic differences) than to the ST17 isolate, which is closer (94 allelic differences) to the COH1 reference (Figure).

Conclusions: Recent reports of PRGBS in America and Europe suggest a widespread distribution of PRGBS outside Asia where they were first described. Our results show the emergence of PRGBS within the hypervirulent CC17 clone. Although PRGBS are reported at an increasing rate, the clinical significance of in vitro penicillin non-susceptibility is still not fully understood. The possible emergence of penicillin resistance in GBS, particularly among the most prevalent and invasive clones, may have significant implications for the prevention and management of GBS disease.

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Abstract 7778

**Bacteroides as a next-generation of probiotics in neonatology**

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**Background:** Most healthy adult microbiota are dominated by *Bacteroides* which used to be the "pioneers" in colonization of newborns gastrointestinal tract after vaginal delivery. It plays the key role anti-inflammatory effects inducing the maturation of enterocytes in newborns. We are trying to define the differences in the process of colonization involving *Bacteroides* in two groups of infants after vaginal (group I) and caesarean section (group II) delivery.

**Materials/methods:** We examined the feces of 66 term healthy infants both from group I (n=33) and group II (n=33) on the 1st, 7th and 30th day of life using cultural methods. As a tool for identification of bacterial species, MALDI-TOF mass-spectrometry was used. In case if the ID score was less than 2.0 the 16S rRNA gene-sequencing has been chosen as an alternative to complete the identification.

**Results:** Among all the participants on the 1st day after birth, only 13 infants had any bacteria in meconium samples. We found the abundance of *Propionibacterium* in the samples whereas *Bacteroides* has been cultivated just once and only in the group I. Further, we also determined *Bacteroides* only in the group I. In comparison with the 1st day the 7th day of life was characterized with the higher rate of colonization of *Bacteroides* in the group I (3% and 36% of infants respectively), while *Bifidobacterium* and *Propionibacterium* dominated. Out of all *Bacteroides* species present in feces, we identified *Bacteroides uniformis, Bacteroides fragilis, Bacteroides ovatus, Bacteroides vulgatus*. On the contrary, the group II lacked *Bacteroides* whereas *Bifidobacterium, Lactobacillus, Clostridium* and *Veillonella* were most commonly identified. The 30th day results in both groups demonstrated the comparable microbial taxa (*Bifidobacterium, Lactobacillus* and *Veillonella*) with the 7th day results of the group II. It is important that the 30th day also demonstrated the abundance of *Bacteroides* and the lack of *Clostridium* in group I (37.5 %) with the absence of the first one in the group II, except one patient. While the group II results exhibited reciprocal prevalence of *Clostridium*.

**Conclusions:** We think *Bacteroides* helps to prevent colonization of GI-tract by *Clostridium* and might be used as a probiotic candidate.

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Abstract third-party references: Collaboration des 17 CPias

**Background:** In France, the HAI notification was written in the law, since 1998 and implemented in 2001 by decree. The system aimed to early detection of unusual events at local, regional and national level for their prompt investigation and control. An HAI has to be notify to health care authorities if: (i) it is unusual, unexpected according to identification, pathogenicity or antimicrobial resistance of the causative micro-organism or according to its localisation or mechanism; (ii) it occurs in a cluster of cases; (iii) death of the patient is related to HAI, (iv) it is included in the list of mandatory notifiable disease. The first step of notification is the regional level (Health authorities (ARS) and Regional centre for HAI prevention (CPIAS). Secondarily, the national level Sante publique France is informed. In 2012, a secure web system was implemented called “e-Sin”.

**Materials/methods:** In 2017, according to the evolution of antimicrobial resistance epidemiology and the spread of Carbapenem-resistant Enterobacteriaceae (CRE) and Glycopeptide Resistant Enterococci (GRE), a new specific module was added. It can be used to report infections and colonisations. Further information as implemented control measures are included, to assess their compliance with national recommendations.

**Results:** Since 2012, near 20 000 notifications including around 5000 CRE and GRE have been reported. In 2018, Sante publique France received more than 3000 notifications, 62 % of them were CRE or GRE, mostly colonisations and 3% of bacteremia. Despite the spread of these MultiDrug Resistant Bacteria, the French level of CRE (E. coli and K. pneumoniae) and GRE in European Antimicrobial Resistance Surveillance Network remains very low (<1%). Moreover, this notification system allows us to identify and control other emerging micro-organisms as *Candida auris* in immunocompromised patients, non-tuberculosis Mycobacteria in cardiac surgery, *Bacillus cereus* spreads in neonates.

**Conclusions:** The system has some limits rely on professional adhesion and data quality. However, it has an added value to HAI and AMR surveillance for immediate implementation of investigations and control measures, information and potential support of Regional and national level to Health care facilities.

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Fluoroquinolone and Macrolide resistance-associated mutations in *Mycoplasma genitalium*

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**Background:** We analyzed the macrolide and fluoroquinolone resistance in *M. genitalium* positive samples collected from symptomatic patients, attending an STI center in Milan (Italy) between March 2017 and October 2019.

**Materials/methods:** A total of 99 *M. genitalium* positive samples (73% males and 26% females), including 71 urethral swabs, 25 vaginal swabs and 3 anal swabs, were analyzed at the Virology Laboratory of the Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy. The samples were tested using two commercially-available multiplex qPCR assay [ResistancePlus™ MG, Speedx and Allplex™ MG & AziR assay, Seegene] for simultaneous detection of *M. genitalium* and mutations responsible for resistance to macrolides in region V of the 23S rRNA. Moreover, 99 samples were analyzed with Allplex™ MG & MoxiR assay, Seegene to evaluate clinical performance of new assay. The resistant specimens were subsequently sequenced with the Sanger method.

**Results:** From 99 *M. genitalium* positive specimens 52 (52.5%) and 51 (51.5%) resulted resistant to macrolide with the ResistancePlus™ MG kit and MG & AziR assay, Seegene respectively. The presence of a single point mutation was confirmed in 51 of 52 samples with the Sanger Sequencing, while 1 sample resulted wild type (WT). The most common mutations were A2059G (35/51, 68.6%) and A2058G (10/51, 19.6%), while the least frequent were A2058T (7/51, 13.7%).

Moreover, 14/99 (14.1%) *M. genitalium* positive specimens resulted positive for moxifloxacin resistance with a frequency of mutations of G259A (4/14, 28.6%), G248T (4/14, 28.6%), G259T (3/14, 21.4%), G248A (2/14, 14.3%), A247C (1/14, 7.1%).

Interestingly, 11/99 (11.1%) positive specimen presented both macrolide and fluoroquinolones resistance.

**Conclusions:** *M. genitalium* was found to represent an important microbial pathogen in patients presenting with genital symptoms in Milan, Italy. In Italy azithromycin is still widely used for the treatment of *Chlamydia trachomatis* infections, therefore a rise of the percentage presented in this analysis is expected in the next few years. Our findings support the need for ongoing antibiotic resistance surveillance and the importance of using molecular assays to tailor treatment.

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**Abstract 7787**

**Invasive *Acinetobacter baumannii* infections in paediatric infectious disease intensive care unit**

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**Background:** *Acinetobacter baumannii* has become an important cause of nosocomial infections and has displayed increasing antimicrobial resistance over the last decade. The goal of this study was to examine the occurrence, clinical presentation, risk factors, antimicrobial susceptibility and mortality of invasive *A. baumannii* infections in pediatric infectious diseases intensive care unit (PICU).

**Materials/methods:** We conducted a retrospective cohort study that included patients treated for invasive *A. baumannii* infection in PICU at the University Hospital for Infectious Diseases in Zagreb, Croatia, in a 9-year period (2010 – 2019).

**Results:** Seven children [eight infection episodes]; 4 girls and 3 boys with median age 14 months [range 4 months – 13 years] were treated during the studied period. They all had hospital-acquired *A. baumanii* infection (6 in other hospitals and 2 in our PICU). All patients had some predisposing factors for invasive infection [ventriculo-peritoneal drainage in 4/7 (57.1%), combined heart defect in 1/7 (14.3%), tracheostomy in 1/7 (14.3%) and systemic erythematous lupus in 1/7 (14.3%)]. *Acinetobacter* was isolated mainly from cerebrospinal fluid (5/8, 62.5%) and blood cultures (3/8, 37.5%), while 3 patients (37.5%) had concomitant isolate from tracheal aspirates.

5 infection episodes (62.5%) were postoperative shunt-meningitis with bacteria isolated from cerebrospinal fluid. The average CSF cell count was 7168 [range 240-17920] cells in 3mm3. One patient had concomitant pneumonia. Patients were treated with meropenem (4 patients) and colistin (1 patient); two patients received intrathecal amikacin. 3 patients had sepsis (37.5% infection episodes), treated with ampicillin-sulbactam (2 patients) and meropenem (1 patient). Two of them had external source [central venous catheter] and one had origin in pneumonia/tracheal colonization [due to chronic tracheostoma]. Four isolates (50%) had good antimicrobial susceptibility, 3 (37.5%) were susceptible only to ampicillin-sulbactam and colistin while one (14.3%) was susceptible solely to colistin. Mortality rate was 50% (2 patients with sepsis and 2 with shunt-meningitis died).

**Conclusions:** *Acinetobacter baumannii* predominantly causes severe invasive infections in conditioned pediatric patients with exposure to hospital enviroment. Although *Acinetobacter* infections are not common in our PICU, the isolation of this nosocomial pathogen should be of particular concern due to high antimicrobial resistance rate and significant mortality.

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Background: In Tunisia, coastal regions are ecosystems of economic importance; however, they are highly subjected to potential anthropogenic impacts. Over the past decade, Enterobacterales producing extended-spectrum β-lactamases (ESBLs) and carbapenemases have emerged among animals and animal products. Those multidrug resistant bacteria have been recognized from non-human sources and were found in rivers and hospital wastewater, suggesting that aquatic organisms are a reservoir of such enzymes. Here, we investigated the presence of ESBLs and carbapenemases in Enterobacterales isolated from Mediterranean clams (Ruditapes decussatus).

Materials/methods: Between March and April 2016, 1075 clams originating from the Bizerte region and bought at retail were distributed in 215 pools of 5 clams each. Resistant Enterobacterales were selected on MacConkey agar plates either supplemented with imipenem or cefotaxime (final concentration of 2µg/ml). Antimicrobial susceptibility was performed by disk diffusion and ESBL and carbapenemase genes were detected by PCR and sequencing. Plasmids were characterized by rep-typing (Diatheva) and southern blot on S1-PFGE gels. Clonality was assessed by PFGE and MLST.

Results: Among the 215 analyzed pools, 21 gave a positive result on the cefotaxime-enriched medium, including 16 ESBL-producing Escherichia coli and 5 ESBL-producing Klebsiella pneumoniae isolates. In E. coli isolates, CTX-M-1, CTX-M-14, CTX-M-15 and CTX-M-27 were produced by 8, 5, 2 and one isolate(s), respectively. PFGE demonstrated 13 different profiles and genetic backgrounds [10 different STs]. Two E. coli ST131 were identified, suggesting a human contamination. ST147, already identified in Tunisian mussels, was also found in two samples. Plasmid characterization is ongoing. For K. pneumoniae, all isolates (n=5) produced CTX-M-15. Three of them, all belonging to ST147, co-produced the OXA-48 carbapenemase.

Conclusions: This is the first report of OXA-48 producing Enterobacterales isolate from mollusks in Tunisia. Next to the recent finding of KPC-3 in Mytilus galloprovincialis at retail, we confirm that other filter feeder mollusk species are at risk to concentrate carbapenem-resistant Enterobacterales from the human reservoir.

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**Evaluation of Novodiag C. difficile and GenePOC CDiff test for quick and accurate detection of Clostridioides difficile infection**

Ann-Cathrine Petersson*, Lealdina Rebihic†, Sara Karlsson Sobirk‡

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**Background:** *Clostridioides difficile* is the most important cause of hospital-acquired diarrhoea and antibiotic-associated pseudomembranous colitis. Rapid identification of strains producing toxin B is necessary for appropriate treatment of the patients and for infection control. Over the last decade diagnostic tests have switched from culture and cytotoxicity assays or enzyme immunoassays (EIAs) to more rapid techniques such as PCR. The aim of the present study was to compare the performance and workflow of molecular methods suitable for decentralized rapid detection of toxigenic *C. difficile* in stool samples, to the routine method used at the central laboratory in Region Skåne.

**Materials/methods:** Two new fully automatic PCR systems, Novodiag® *C. difficile* (MobiDiag, Espoo, Finland) and GenePOC™ CDiff test (GenePOC Diagnostics, Quebec, Canada), were evaluated for the detection of the *C. difficile* toxin B gene (*tcdB*) direct from stool samples. Included were fresh samples with stool type 5-7 according to Bristol Stool Scale, from patients >2 years of age, which could be analyzed consecutively within 48 h from time of sampling. Culture on CHROM-agar *C.difficile* (CHROMagar, Paris, France) followed by test for toxin A and B of cultured strains, using Vidas (bioMérieux, Marcy l’Etoile, France), was used as reference method. In total 212 samples were analyzed in parallel with all three methods. PCR’s were performed according to instructions by the manufacturers.

**Results:** Both systems showed high concordance (both 99.1 %) with the results obtained with the reference method where 77 samples were positive for toxin producing *C. difficile*, 4 had indeterminate, and 131 had negative results. Diagnostic sensitivity and specificity, compared to the reference method, were identical for both systems: 100 % and 98.5 %, respectively.

Evaluation of the workflow showed few differences between Novodiag and GenePOC. Differences were random access versus batches of 1-8 samples, possibility to analyse samples in eSwab versus only fresh stool samples, and calibration of instrument versus evaluation of amplification curves.

**Conclusions:** Both Novodiag *C. difficile* and GenePOC CDiff provide quick and accurate results, are easy to handle, and are suitable for decentralized diagnostics of *C. difficile* infection.

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Abstract 7794

Evaluation of association between immune modulation and incidence of cytomegalovirus reactivation in sepsis-induced immunosuppression

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Abstract third-party references: National Health and Education Society, P. D. Hinduja Hospital and Medical Research Center

Background: Sepsis is a global health priority, often accompanied by transient immune paralysis due to progressive immunosuppression and increased susceptibility to secondary infections. Reactivation of Cytomegalovirus (CMV) has been associated with adverse outcomes and mortality in immunocompetent patients, including sepsis. We aimed to evaluate the relationship between incidence of CMV reactivation and immune alteration in sepsis-induced immunosuppression in patients with prolonged sepsis.

Materials/methods: Prospective observational study, including consecutive patients admitted to hospital ICU, with severe sepsis and length of stay >48 hrs. Patients with immune-suppression due to other disorders/steroids/anti-CMV treatment were excluded. Blood sampling was done on enrolment and further weekly until 21 days or death/discharge. Quantification of CMV viremia was done using RT-PCR (qPCR). Determination of immune cell subsets (CD3+, CD19+, CD16+CD56-, CD4+, CD8+ and CD25+CD127- regulatory T cells) and surface receptor expression of HLA-DR on monocytes, PD-1 on T lymphocytes were analyzed by flow cytometry. Measurement of Th1/Th2/Th17 cytokines was done using CBA assay by flow cytometry.

Results: Among 25 CMV seropositive analyzed patients, CMV reactivation occurred in 80% (n=20) of the population. CMV viremia >1000cp/ml were detected in 60% (n=12) patients while, <1000cp/ml were detected in 40% (n=8) patients at any time point. Median time for reactivation was 7 days. Patients with CMV reactivation had T lymphopenia. Elevation in inhibitory expression of PD-1 on both CD4+, CD8+ T cells was observed in CMV reactivated group, which found decreased in non-reactive group over time (515.9±526.8 vs 580.12±246 vs 174.2±47.8, p <0.01). Levels of IL-10 were significantly higher in CMV reactivated group which continued to elevate, compared to non-reactive group (18.7±30.8 vs 5.0±2.95, p <0.01). HLA-DR expression on monocytes was significantly low in all patients however, did not show major difference in CMV reactive vs non-reactive patients.

Conclusions: Our study suggests impairment in immune defense is a major cause of sepsis-induced immune tolerance and risk factor for viral reactivation. Incidence of CMV reactivation was associated with PD-1-related T lymphocyte dysfunction and IL-10 suppressive activity. Targeted and individualized immune therapy with PD-1 blockade and immune stimulation can effectively help prevent CMV reactivation and improve clinical management of patients with severe sepsis.

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Abstract 7795

**Identification of DNA virus in conventional culture by MALDI-TOF MS**

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**Background:** Traditionally, gold standard method for viral diagnosis has been cell lines culture. Nowadays qPCR and other genomic techniques are extended. Proteomic techniques implanted for bacterial and fungal identification, like MALDI-TOF/MS, are quick and cheaper, but are not available for viral identification. Thus the aim of this study was MALDI-TOF/MS apply for viral identification.

**Materials/methods:** An in house library was created following manufacturer instructions (Bruker Daltonics, Germany). It contains 104 spectrums of viruses (54 HSV, 4 VZV, 13 CMV and 16 ADV) and cell lines (8 MRC5, 7 VERO and 2 MDCK), used to define background spectrums. Strains used to do this library were also checked by immunofluorescence and qPCR.

Pellet and supernatant of cell cultures from: 50 positive samples for HSV1 [27] and HSV2 [23], 50 positive for ADV grown in conventional cultures [MRC5 and VERO], and 50 non infected cell cultures [25 MRC5 and 25 VERO] were assayed. Each strain was identified by IF and qPCR.

**Results:** In pellet, 45 (90%) of HSV strains were identified, while 27 (54%) were detected in supernatant. For HSV1, 25 (92.59%) strains were detected in pellet and 17 (62.96%) were detected in supernatant. For HSV2 strains, 20 (86.95%) were detected in pellet while 10 (43.47%) were detected in supernatant. About ADV strains, 32 (64%) were detected in pellet, while 46 (92%) were identified in supernatant. All strains were positive by IF and/or qPCR. In any not-infected cell line assayed any virus was detected. This table shows the identified virus and the score of MALDI-TOF/MS.

<table>
<thead>
<tr>
<th>Virus Identified</th>
<th>Pellet</th>
<th>Score over 2.00</th>
<th>Score 1.7&lt;x&lt;1.99</th>
<th>Supernatant</th>
<th>Score over 2.00</th>
<th>Score 1.7&lt;x&lt;1.99</th>
</tr>
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<tbody>
<tr>
<td>HSV (n=50)</td>
<td>45 (90%)</td>
<td>6 (13.33%)</td>
<td>13 (28.88%)</td>
<td>27 (54%)</td>
<td>16 (59.25%)</td>
<td>7 (25.93%)</td>
</tr>
<tr>
<td>HSV1 (n=27)</td>
<td>25 (92.59%)</td>
<td>0 (0%)</td>
<td>10 (40%)</td>
<td>17 (62.96%)</td>
<td>10 (58.82%)</td>
<td>3 (17.64%)</td>
</tr>
<tr>
<td>HSV2 (n=23)</td>
<td>20 (86.95%)</td>
<td>5 (25%)</td>
<td>4 (20%)</td>
<td>10 (43.47%)</td>
<td>6 (60%)</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>ADV (n=50)</td>
<td>32 (64%)</td>
<td>3 (9.38%)</td>
<td>15 (46.88%)</td>
<td>46 (92%)</td>
<td>28 (60.86%)</td>
<td>10 (21.74%)</td>
</tr>
</tbody>
</table>

**Conclusions:** MALDI-TOF/MS is able to recognize and genotype HSV and ADV viruses grown in conventional cell cultures. Supernatant could be used to do a quick screening of the samples doing less processing.

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Infectious complications in patients with multiple sclerosis treated with monoclonal antibodies (anti-CD20 and anti-CD52) and autologous stem cell transplantation

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Background: Novel therapies for multiple sclerosis (MS) include autologous stem cell transplantation (ASCT) and monoclonal antibodies targeting CD20/CD52 antigens. Although similar treatments have been used for non-neurological conditions, risk of infections may vary in MS population. The aim of our work was to compare the incidence and severity of infections in patients receiving anti-CD20 (ocrelizumab [OCR] and rituximab [RTX]), anti-CD52 (alemtuzumab [ALM]) antibodies and ASCT for MS treatment.

Materials/methods: Three-year follow-up records of MS patients treated with monoclonal antibodies or ASCT at the Neurology Unit of San Martino Hospital (Genoa, Italy) were retrospectively reviewed. Demographic, clinical and laboratory data were collected. Severe infections were defined as grade ≥3 [Common Terminology Criteria for Adverse Events v5.0-2017]. Rate of infections requiring systemic antibiotic use per 1000/patients-year was compared between treatment groups using RTX as reference. Univariate and multivariate Cox regression analyses were performed to evaluate risk factors using rate of infections requiring systemic antibiotic use as dependent variable.

Results: We collected data of 254 patients (64.6% female, median age 44 years, 48% with relapsing-remitting form), 33 treated with ALM, 84 with OCR, 84 with RTX and 54 with ASCT. Overall infection rate during the three-years follow-up was 63.6%, 52.4%, 69% and 89% for, respectively, ALM, OCR, RTX and ASCT, and severe infections were observed in 3%, 3.6%, 1.2% and 83.3% respectively. Rate of infections requiring systemic antibiotic use per 1000/patients-year was significantly higher in the groups treated with ASCT (IRR 4.75 [2.27 -9.94], p<0.001), ALM (IRR 3.35 [1.54-7.30], p=0.002) and OCR (IRR 2.15 [1.09-4.24], p=0.028) compared to RTX. In multivariate analysis, higher number of previous therapeutic lines (IRR 1.76 [1.09-2.85]; p=0.02) was associated with increased risk of moderate to-severe infections in ALM group, while more recent treatment start with an increased risk in ASCT group (IRR 1.15 [1.09-1.20], p<0.001), and RTX group (IRR 1.76 [1.20-2.59], p=0.004). Rate of infections decreased substantially after the engraftment in the ASCT group, conversely remained stable during treatment with monoclonal antibodies [Fig.1].

Conclusions: Risk of severe infections was low during monoclonal antibodies treatment, and the rate of infections requiring systemic antibiotics was the lowest in RTX group.

Figure 1. Overall incidence of infections

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**Prevalence, antimicrobial susceptibility and molecular typing of **Legionella pneumophila** **in hot water systems in Morocco**

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**Background:** The aims of this study were to determine the prevalence of **Legionella pneumophila** in hot water systems in Morocco, assess the antimicrobial susceptibility and investigate the molecular distribution of **Legionella pneumophila** serogroup 1.

**Materials/methods:** A total of 149 water samples from 111 different hotels were analyzed. The minimum inhibitory concentrations (MICs) of sixty environmental **Legionella spp.** strains were tested for twelve antimicrobial agents, including Macrolides, fluoroquinolones, ketolide and rifampicin. Moreover, a selection of 20 **L. pneumophila** sg1 strains were typed by monoclonal antibodies, pulsed field gel electrophoresis and new generation sequencing.

**Results:** Out of the 149 samples, 77 (51.7%) were positive for **L. pneumophila**. Serological typing of the isolates revealed that 54 (70.1%) are **L. pneumophila** serogroup2-15 and 23 (29.9%) are **L. pneumophila** serogroup1. Counts were over 1000 cfu/l in 44% of all building. Contamination was strongly correlated with temperature in the circulation, the age of the premise plumbing and the size of the building. All tested strains of **L. pneumophila** were inhibited by low concentrations of fluoroquinolones and macrolides. Rifampicin was the most effective antibiotic against the isolates in vitro. All isolates were inhibited by the following antibiotics (MICs): doxycycline < cefotaxime < tigecycline. MAb typing results showed a prevalence of MAb 3/1 negative isolates (n = 100%) with 6 subgroups of Camperdown (30%), 7 Oxford (35%) and 7 OLDA (35%). The pfge analysis showed five different profiles, some of which are present at several buildings in different cities of Morocco. After sequencing, SBT analysis revealed 3 sequence type (STs) with a high prevalence of ST1 found in 13 strains (65%), followed by ST560 in 4 (20%) and a new ST was found in 3 (15%). 46% of ST1 are Oxford, 23% of Camperdown and 31% of OLDA.

**Conclusions:** The results show a relevant exposure to **L. pneumophila** in the community and the identified risk factors can serve as indicators for risk assessment and relevant actions. This study revealed the genetic diversity of environmental **L. pneumophila** sg1 isolates in Morocco, providing also a useful data for future epidemiological investigations, especially of travel associated Legionnaires’ diseases.

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**Abstract 7801**

**Impact of unique blood culture sampling in the emergency departments of Strasbourg University Hospital, France**

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**Background:** Bacteremia are responsible for a high morbi-mortality worldwide. Detection of bacteremia is directly related to the quality of blood culture (BC) sampling.

The purpose of this study is to evaluate the impact of a resensibilisation action to good practices of BC sampling. During this action, unique sampling (US) of 3 pairs of HC was also promoted.

**Materials/methods:** A retrospective before/after observational study was conducted. Two groups were compared: one ‘before’ (October-December 2017) and the other ‘after’ intervention (October-December 2018). Patient inclusion criteria was the sampling of at least one BC in the emergency department during these periods.

The following indicators were used to compare the 2 groups:
- The rate of patients who had a US
- The positivity rate (excluding contamination)
- The isolation rate of commensal skin microorganisms, which could be linked to contamination
- BC sampled by venipuncture
- The average volume of blood per blood culture bottle

**Results:** In 2017 1450 patients and 1462 patients in 2018 were included, which represented 1804 pairs of BC in 2017 and 3579 pairs of BC in 2018.

Table 1 summarizes the values of the indicators and the statistical significance of the difference before/after.

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<tr>
<td>US</td>
<td>%</td>
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<tr>
<td>Positivity rate</td>
<td>?</td>
<td>11</td>
<td>0,001</td>
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<tr>
<td>Contamination rate</td>
<td>38</td>
<td>28</td>
<td>0,07</td>
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<tr>
<td>Rate of BC sampled by</td>
<td>69,2</td>
<td>90,6</td>
<td>&lt; 0,001</td>
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<td>venipuncture*</td>
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*Percentage calculated on sites with prescription information.

The average filling volume of the vials did not increase and remains low at 3 mL per vial.

**Conclusions:** The adhesion of US of three pairs of BC was good. This led to a significant increase of the BC positivity rate. However, this increase is not as high as it can be found in the literature, the low filling volume per bottle is undoubtedly the cause of it.

Raising awareness of good sampling practices has reduced the rate of contamination and direct punctures were preferred.

The adoption of US increases the number of BC sampled, this increase may also lead to the need to clarify the indications of this laboratory testing.

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Abstract 7803

**HEV infection as an emergent public health issue: is it a concern for Italian blood donors?**

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**Background:** In high-income countries, HEV infection is usually associated with an asymptomatic, self-limiting, acute or mild hepatitis. However, the risk of HEV transmission through blood or blood products raises concerns, especially in the setting of immunosuppressed patients. The aim of the present study was to determine the presence of HEV infection in blood donors at ASST GOM Niguarda Hospital using a combined approach (HEV-RNA/seroprevalence).

**Materials/methods:** From January to July 2019, 9,081 sera and plasma samples from blood donors were retrospectively analysed. Pools of 6 plasma donations were assessed to detect HEV-RNA using the commercial Cobas® HEV Test (Roche Molecular Diagnostics, LLOD 18.6 IU/mL). Among them, 7,771 serum samples were tested for anti-HEV total IgM/IgG with ELISA test (DIA.PRO Diagnostic Bioprobes srl).

**Results:** Overall, the blood donors were predominantly men (73.6%; 5,720/7,771) with a median age of 42 (IQR: 31-50). HEV-IgM/IgG positivity was found in 4.3% (334/7,771) of blood donations, however none of them carried detectable HEV-RNA.

The rate of HEV-infection in this healthy population was compared with that of symptomatic patients [with altered transaminases]. HEV-IgM/IgG positivity was found in 4.3% (14/324) and 10.6% (50/472) of patients, respectively. Among them, 1.6% (3/184) of patients had detectable HEV-RNA: two of them were mother and son from Egypt with acute HEV-infection and the third was an Italian man with chronic HEV-infection.

**Conclusions:** The circulation of HEV-RNA in blood donations at Niguarda Hospital results to be absent, with an HEV-IgM/IgG prevalence of 4.3%, one of the lowest reported among blood donors in Italy [8.7%; Spada et al., Blood Transfusion 2018]. At the same time, HEV active infection has been detected in few patients whose HEV-RNA was assessed for hepatic symptoms [elevated ALT]. From these data, the screening for HEV-RNA appears not to be crucial in our population of blood donors, while further studies are warranted to define its relevance in case of liver pathologies.

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ABSTRACT BOOK – 30th ECCMID 2020

Abstracts 2020

Abstract 7811

**LUISA: Low Cost Unit for Sequencing Applications**

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**Background:** Over the last years, next generation sequencing had a revolutionary advance for molecular biology, made microbial genome sequencing cheap and accessible with high accuracy and throughput. However, short-reads length limits its ability to resolve repetitive and/or high %GC content regions, hindering the mobile genetic elements spread tracking creating implications for Global Health since these elements have the ability to transport antibiotic resistance genes and virulence factors. In this regard, this is one of the reasons that led to the development of long-read sequencing, such as generated by Oxford Nanopore Technologies (ONT) platforms, that has a portable real time sequencer (MinION), with potential to render other sequencing technologies obsolete. Although, high error rates pose a challenge for generating accurate genome assemblies, emerging a demand of paramount importance focused on developing new tools able to deal efficiently with the high error rate. Generating a subsequent avalanche of development of new tools and computational algorithms, as well as the application of machine learning (ML) in order to reduce error rate. But most of tools require a high computational cost causing a performance bottleneck which involves high financials costs. In this regard, we develop LUISA.

**Materials/methods:** In this regard, we develop LUISA (Low Cost Unit for Sequencing Applications) embedded with custom carrier board, Ubuntu OS, Bioinformatics tools and two options versions that can be powered by solar energy: GPU-based, option 1: Jetson TX2 NVIDIA board, 8GB RAM, SSD M.2 1Tb, wifi 802.11 b/g/n 5GHz) and option2: Mini ITX board, Intel i7-4300Y, 16GB RAM, SSD M.2 1Tb, wifi 802.11 b/g/n 2.4GHz.

**Results:** Benchmarking of LUISA provided results that consensus calling, de novo assembly and machine learning training model in GPU-based version can be five times faster than LUISA CPU-based version. Additionally, it offers a cost-effective solution compared to other available options.

**Conclusions:** LUISA will lead benefits to genomic surveillance and epidemiological studies of the endemic diseases for low income countries. In this context, LUISA is currently the most cost-effective option available for nanopore data analysis. Providing the analysis of sequencing feasible, open solution, low cost and also an alternative powered by renewable energy.

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Evaluation of different methods for the detection and differentiation of mechanisms of resistance in carbapenemase-producing Enterobacterales at a large district hospital, UK

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Background: Carbapenemase-producing Enterobacterales [CPE] have been increasing rapidly globally and are considered to be significant health threat. The accurate, simple, cost effective and rapid detection of carbapenemases in laboratories is an important step to control the spread of CPE. However, no consensus has yet been reached with regards to the single most optimal method and hence the detection of CPE represents a substantial challenge for many laboratories. The aim of this study is to evaluate the performance of four different carbapenemase detection tests to develop guidance in Microbiology laboratory.

Materials/methods: A total of 69 samples were included in this study. MASTDISCS combi Carba plus disc D73C, Coris RESIST-4, BD MAX™ and Gene Xpert Carba-R were challenged, according to the manufacture’s instruction, with Enterobacterales isolates molecularly characterised by the reference laboratory (PHE, Colindale) including NDM, OXA-48, VIM and NDM and negative CPE. Additional 14 of the isolates were not characterised by the reference laboratory were excluded but tested by the other detection methods. We considered equivocal results by D73C as negative. IMI, OXA-23 and OXA-51 were only included when tested by D73C.

Results: The overall sensitivity for the carbapenemase detection tests were 100% for each of BD MAX™, Gene Xpert Carba-R and D73C. While, the sensitivity of RESIST-4 was 97%. The specificity was 100% with Gene Xpert Carba-R and Coris RESIST-4 while dropped to 68.8% and 36.8% with BD MAX™ and D73C respectively. Interestingly, additional detection of NDM gene was reported on five isolates by BD MAX™ where only OXA-48 was detected by the reference laboratory. The other methods were in concordance with the reference laboratory report for these five isolates. BD MAX™ was unable to differentiate between VIM and IMP. The turnaround time was fastest with Coris RESIST-4 (15mins), followed by Gene Xpert Carba-R (53mins), BD MAX™ (2.5hrs). D73C takes longest time as overnight incubation is required.

Conclusions: In this study, except for MASTDISCS combi Carba plus disc D73C, all other methods showed high sensitivity. Lower specificity was detected by BD MAX™. The very low specificity of D73C made it necessary to have additional confirmatory test.

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Abstracts 2020

Abstract 7819

ESBL- and/or carbapenemase-producing *Klebsiella pneumoniae* with multidrug-resistant phenotypes as a main cause of non-*Escherichia coli* Enterobacterales healthcare-associated bacteraemia of urinary origin episodes in Spain

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Abstract third-party references: Merck Sharp & Dohme (MSD)

**Background:** *Escherichia coli* (*Ec*) is the main pathogen causing healthcare-associated bacteraemia of urinary origin (HCA-BUO), but other Enterobacterales are also involved. We assessed the prevalence and microbiological characteristics of ESBL and/or carbapenemase producing non-*Ec* Enterobacterales causing HCA-BUO in Spain (ITUBRAS-2 project) and compared with those previously obtained in 2011 (ITUBRAS project).

**Materials/methods:** Patients with HCA-BUO [Sep-2017 to Apr-2019] from 12 tertiary hospitals were prospectively included and blood isolates were stored. Bacterial identification (MALDI-TOF) and antimicrobial susceptibility (microdilution, EUCAST-2019) were performed. Isolates were classified as multi-drug (MDR), extensively-drug (XDR) and pan-drug-resistant (PDR) (Maggiorakos, 2012). ESBL and carbapenemase production were screened by double-disk synergy and colorimetric (CarbaNP, BioMerieux) tests, respectively. Genes encoding ESBLs (*bla*<sub>SHV</sub>, *bla*<sub>TEM</sub>, *bla*<sub>CTX-M</sub>) and carbapenemases (*bla*<sub>OXA-48</sub>, *bla*<sub>VIM</sub>, *bla*<sub>KPC</sub>) were characterized (PCR, sequencing).

**Results:** 372 episodes with 389 Enterobacterales isolates were collected; 42.9% (167/389) corresponding to non-*Ec* species. Among them, *Klebsiella pneumoniae* (*Kpn*) (57.5%) was the most prevalent, followed by *Proteus mirabilis* (*Prm*) (11.4%) and *Enterobacter cloacae* (*Eclo*) (8.4%). Overall, 45.5% [76/167] of non-*Ec*-Enterobacterales were MDR, 3.6% [6/167] XDR and 0.6% [1/167] PDR. Resistance to ceftolozane/tazobactam (CMI>2 mg/L) was detected in 10.7% of isolates [18/167; 5 *Eclo*, 4 *Klebsiella aerogenes* and 9 *Kpn*; all of them producing carbapenemases, AmpC or ESBL enzymes]. Prevalence of ESBL-producers increased from 9% (15/167) in 2011 to 26.3% [44/167] in 2019 (p<0.01). The majority of ESBL-producers were *Kpn* [39/44] with MDR phenotype [36/39]. CTX-M-15 [70.4%] was the dominant enzyme. ESBL-producers showed higher resistance rates than non-producers to tobramycin [95.5% vs 9.7%], trimethoprim/sulfamethoxazole [93.2% vs 19.5%], ciprofloxacin [93.2% vs 22%], gentamicin [72.7% vs 8.1%], and amikacin [13.6 vs 2.4%] (p<0.01 for all comparisons). Carbenpenemase production was detected in 10 isolates [6%] [6 *Kpn*, 2 *Eclo*, 1 *Klebsiella oxytoca* and 1 *Morganella morganii*], while carbapenemase-producers were not identified in 2011. OXA-48 was the most frequent enzyme [n=7]. Other types were VIM-1, OXA-244 and KPC-19. ESBL co-production was presented in six isolates which were classified as MDR [1 *Kpn*], XDR [3 *Kpn* and 1 *Eclo*] and PDR [1 *Kpn*].

**Conclusions:** We describe a significant increase of ESBL/carbapenemase-producing *Kpn* with MDR/XDR/PDR phenotypes causing HCA-BUO in Spain among non-*Ec*-Enterobacterales episodes.

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Risk factors for daptomycin-induced eosinophilic pneumonia: a matched case-control study in a population with osteoarticular infections

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Background: The use of daptomycin in osteoarticular infections is widespread and usually prolonged for long periods because of its remarkable anti-biofilm activity. Daptomycin-induced eosinophilic pneumonia (DEP) is an unusual but severe adverse effect. As issues for developing DEP are still not well known, we aimed to determine the risk factors through a case-control study.

Materials/methods: Retrospective, matched case-control study performed in our Bone-Joint Infection Unit (BJIU, January 2014-December 2018). Patients with osteoarticular infections treated with daptomycin were included as cases if they developed DEP [fever, dyspnea with increased oxygen requirement, pulmonary infiltrates and improvement following daptomycin withdrawal]. Controls (2:1) were matched by the total cumulative dose of daptomycin (TCDD, daily dose-mg · X days of treatment), sex and the closest date of drug administration. Data of daptomycin consumption for all patients attended in BJIU during the same period of study was collected.

Results: We identified 11 cases of DEP; 1 patient died (respiratory insufficiency), and 10 cured with daptomycin withdrawal and corticosteroids (6/10, 60%). Percentage of DEP cases increased progressively with days of daptomycin therapy [1% (<7 days), 3.3% (7-14d), 13.3% (≥15d); P<0.001], and with TCDD [1.9% (TCDD<10g), 9.8% (10-15g), and 16.7% (>15g); P<0.001].

In case-control study we found DEP cases were older than controls [median age, 77years –IQR 71-82 vs 62.5 –IQR 50-71; p=0.006, respectively], but they did not differ in the presence of previous pulmonary or cardiac disease nor in renal function. While median values of daily dose of daptomycin and days of treatment were similar between case and controls [700mg/d IQR 700-750 and 19days IQR 12-25 vs 700mg/d IQR 700-850 and 19days IQR 12-23, respectively], the number of eosinophils was higher in DEP cases either with half treatment administered [490x10⁶/mL –IQR 250-850 vs 160x10⁶/mL –IQR 100-310 after median 9.5days; P=0.006] or at the end of treatment [1010x10⁶/mL –IQR 570-1420 vs 210x10⁶/mL –IQR 110-340; p=0.0008].

Conclusions: Older patients with high TCDD (>15g) and prolonged daptomycin therapy (>15 days) are at high risk for developing DEP. Monitoring the increase in the eosinophil counts after 1 week of treatment may be helpful to identify patients at risk for DEP.

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Does tigecycline have a place in therapy for rickettsial infections of the central nervous system?

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Background: Rickettsial infection may present as meningitis. The treatment of these infections can be challenging, as the antimicrobial options are restricted.

Materials/methods: The aim of this retrospective study was to describe the efficacy and safety of tigecycline in a case series of patients with rickettsial infections of the CNS. The conditions of all patients responded well to tigecycline therapy. Although tigecycline is not approved for CNS infections, it was the best available option for the treatment of these five cases.

Results: Herein, we report a case series of five patients with rickettsial infections of the CNS. The diagnosis was based on clinical and CSF findings. Focal neurologic signs were rare, and cerebrospinal fluid profiles were similar to those of viral and tuberculous meningitis. Other major organ involvement (renal, liver, or lungs) occurred in all five patients. Three patients were immediately intubated and placed on mechanical ventilation; initial laboratory investigations showed severe acidosis with elevated lactic acid in these patients. Chest radiography, head CT, and MRI were normal. The finding of abnormalities on electroencephalogram (EEG) during the course of aseptic meningitis was considered to be indicative of parenchymal brain involvement. Cerebral spinal fluid and blood cultures were negative. Investigation for herpesvirus, enterovirus, arbovirus, Borrelia, and Mycobacterium tuberculosis was negative. Serological blood studies were all negative. The diagnosis was confirmed by serology (immunofluorescence assay) that showed a seroconversion, with an eightfold increase of IgG antibodies for Rickettsia rickettsii in 2 weeks (with titres of 128 and 1024). Intravenous tigecycline was administered for 7-10 days with progressive improvement. All patients evolved favourably with remission of symptoms and had no sequelae. Treatment was changed to oral doxycycline as patients were able to take the tablets correctly. Our patients completed 5-10 days of doxycycline.

Conclusions: To the best of our knowledge, this is the first report of tigecycline therapy for CNS infections caused by Rickettsia rickettsii. Tigecycline will be most useful as therapy for rickettsial meningitis and encephalitis, especially in cases in which parenteral therapy is needed. Further research is necessary to determine the role of tigecycline in the treatment of rickettsial infections of CNS.

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Fighting a rare cystic fibrosis pathogen: characterisation of Burkholderia cenocepacia cell division machinery

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Background: Burkholderia cenocepacia is multidrug-resistance dangerous cystic fibrosis (CF) pathogen associated with heightened mortality.

The benzodiotiazol derivative C109 showed efficacy against B. cenocepacia and other CF pathogens inhibiting the GTPase and polymerization activity of FtsZ.

In order to expand our knowledge on the cell division machinery of this rare pathogen, we identified and characterized the components involved in this essential mechanism.

Materials/methods: Using molecular biology techniques, the structure and regulation of the dcw operon has been studied.

Then, taking advantage of a bacterial two hybrid system, we clarified the interaction among FtsZ and the other divisome components like FtsA, ZipA, SulA and other later proteins in vivo and in vitro through co-sedimentation, co-polymerization, biochemical assays and electron microscopy studies. Finally, using microfluidics and time-lapse microscopy, we characterized the behaviour of B. cenocepacia cells treated with C109.

Results: First, we identified the binding site of MraZ regulator upstream the dcw operon, the transcription start site and its minimal promoter of this operon in B. cenocepacia. We confirmed the interaction among FtsZ and the other components of the cell division machinery of B. cenocepacia, in vivo and in vitro.

Moreover, our results on time-lapse microscopy of B. cenocepacia cells with C109, showed how the treatment induces an elongated phenotype in a sub-population of B. cenocepacia cells that could be considered “persisters”.

On the other hand, we screened C109 derivatives against B. cenocepacia cells and FtsZ to identify more powerful molecules.

Conclusions: Our final goal is to explore the B. cenocepacia divisome machinery to identify new druggable targets suitable for antibacterial therapies effective against B. cenocepacia.

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Evaluation of FT-IR spectroscopy in vancomycin-resistant enterococcal nosocomial outbreak investigation

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Abstract 7825

Background: Early detection of nosocomial outbreaks due to multidrug-resistant pathogens is very important to reduce their spread. Limitations of existing typing methods necessitate more rapid, economical and easy-to-apply techniques, such as Fourier Transform Infrared (FT-IR) spectroscopy. We retrospectively compared the IR-Biotype® (Bruker Daltonik GmbH) to MLST and WGS for detection of vancomycin-resistant E. faecium (VREfm) nosocomial outbreaks.

Materials/methods: VREfm strains (n=106) were provided by the National Reference Centre for Enterococci, collected from 12 Belgian hospitals during 7 different outbreaks over a three-year period (2016-2019). All strains were analysed by FT-IR and MLST. For FT-IR, isolates were clustered using the average linkage algorithm and displayed as dendrograms using the IR-Biotype® software. Seventy-seven strains were sequenced using Nextera XT (2×250bp), Miseq (Illumina), followed by core genome SNP based phylogeny using ParSNP. We applied the adjusted Wallace coefficient (AW) to compare partitions and Simpson’s diversity index (SDI) to compare the discriminatory power of the different techniques.

Results: FT-IR accurately clustered 77% (82/106) and 74% (57/77) of strains within outbreaks according to MLST and WGS respectively. For each outbreak FT-IR suggested the presence of a predominant clone in agreement with epidemiological findings. Overall, 16 partitions obtained by FT-IR were compared with the corresponding 8 MLST- and 16 ParSNP-types. AW showed that FT-IR is predictive of MLST-types, but less predictive of clonality (see table). This finding might be due to genetic variation in closely related strains. The discriminatory power of FT-IR was slightly higher than that of MLST.

Conclusions: FT-IR seems a sensitive rather than a specific typing method in detecting nosocomial outbreaks, making it suitable for screening. Yet, confirmation of clonality is warranted by alternative techniques. Further research is needed to explore the role of FT-IR in optimising outbreak investigation and ensuing impact on infection control.

Table: Congruence between typing methods determined by SDI and AW [95% CI]

<table>
<thead>
<tr>
<th></th>
<th>SDI (95% CI)</th>
<th>AW (95% CI) when compared with</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>MLST</td>
</tr>
<tr>
<td>Biotyper</td>
<td>0.854 [0.086-0.902]</td>
<td>0.541 [0.340-0.743]</td>
</tr>
<tr>
<td>MLST</td>
<td>0.785 [0.739-0.831]</td>
<td></td>
</tr>
<tr>
<td>ParSNP WGS</td>
<td>0.916 [0.897-0.936]</td>
<td></td>
</tr>
</tbody>
</table>

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Abstract 7832

Complex sharing of *Klebsiella pneumoniae* carbapenemase (KPC) plasmids in patients harbouring multiple KPC-positive organisms

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**Background:** Our understanding of inter-species dissemination of carbapenemase-encoding gene *bla*KPC, which is typically plasmid-associated, has been limited due to genomic sequencing efforts using short-read technology alone. Herein, we describe sharing of similar incompatibility-group KPC-carrying plasmids between multiple bacterial species in patients using long read sequencing.

**Materials/methods:** We evaluated all patients colonized with multiple KPC-producing organisms (KPCOs) from a single University Hospital between August 2007 and March 2017. Short-read and long-read sequencing was performed on all available isolates from patients with distinct species having *bla*KPC. Species identification and genomic relatedness were determined from short-read data alone. Bacterial genomes were assembled using Unicycler’s hybrid assembly-approach, followed by incompatibility-group assignment of circularized plasmid structures using in-silico replicon typing schema. Inter-species plasmid similarity and sharing was assessed by pairwise comparisons of their incompatibility-groups and MASH k-mer distribution distances.

**Results:** 158 longitudinal isolates from 37/507 (7%) patients colonized with two or more distinct KPCOs were sequenced and analyzed as described above. Species identification and chromosomal relatedness from genomic data showed the isolates belonged to 67 distinct bacterial clades, spread across 22 species. Of the 37 patients, two patients were colonized five distinct species, one with four, and three or two. A total of 578 circularized plasmid structures were obtained from the assemblies. As shown in the figure, five incompatibility-group plasmids – IncN, IncL/M, IncA/C2, IncX5 and a novel non-typable repA plasmid (pKPC_UVA01), were the most prevalent KPC-plasmid types across multiple species harboring the *bla*KPC gene with all other incompatibility-groups aggregated into Other group. Pairwise comparisons of longitudinal isolates showed sharing of at least one KPC-carrying plasmids between 39 distinct species pairs in 24/37 patients.

**Conclusions:** Longitudinal sampling paired with long read sequencing of from patients colonized with more than one species of KPCOs demonstrate a complex pattern of plasmid transmission and horizontal gene transfer of *bla*KPC within patients. There was little narrow host range plasmid sharing and a single non-typeable novel plasmid (pKPC_UVA01) demonstrated frequent movement and an apparent broad host range.

**Figure:** Prevalence of KPC-carrying plasmids in patients. Heatmap showing presence [red] and absence [white] of *bla*KPC harboring plasmids in patients isolates.

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Abstract 7833

**Heterogeneity of antimicrobial prescribing in large paediatric tertiary centres: implications for future interventions and benchmarking of antimicrobial stewardship activities**

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**Background:** Dedicated paediatric antimicrobial stewardship programmes (pAMS) within the UK are emerging and there is currently debate ongoing about which metrics should be included in pAMS. Three centres decided to compare simple AMS metrics to allow for benchmarking. Centre 1 (C1) and 2 (C2) are acute admitting tertiary centres whilst centre 3 (C3) is a non-acute quaternary specialist centre. All three centres are geographically close and have had increasing support for pAMS programmes over the last four years.

**Materials/methods:** 2019 Antimicrobial Point Prevalence Survey (PPS) results were reviewed. Prescribing quality indicators (number of patients on antibiotics including intravenous, percentage of documented indications and those prescriptions with a 48-72 hour review) together with examining the top indications and antimicrobials used in a variety of patient groups

**Results:** C1 and C2 had approximately 30% of patients on antimicrobials (C1:39/1 34, C2:67/198) compared to 56% (153/272) in C3. In C1, 89 antimicrobials were prescribed of which 66% were intravenous compared to 76% in C2 (n=99) and 65% in C3 (n=396). 100% of antimicrobials in C1 had a documented indication and 48-72 hour review. Indication documentation was lower in C2 (96%) and in C3 (85%) as was 48-72 hour review with C2 84% and C3 70%. C1 and C2 amongst neonates, sepsis was the most common indication with benzylpenicillin & gentamicin predominating. In C3 the antimicrobial spectrum was broader including amikacin, piperacillin-tazobactam and meropenem covering indications such as NEC, sepsis and central nervous system infections. Within paediatric intensive care, C1 respiratory infections predominated with piperacillin-tazobactam driving prescribing compared to co-amoxiclav in C2. C3 prescribing saw slightly more WHO reserve category antimicrobials due to the complexity of infections. Both C1 and C2 aminoglycoside of choice was gentamicin compared with amikacin in C3. Medical prophylaxis and febrile neutropenia treatment predominated within immunocompromised patients at both C1 and C3.

**Conclusions:** These relatively simple PPS results between three geographically close centres highlights the heterogenous nature of prescribing in paediatric populations of differing acuity and complexity. Local and national interventions to optimise and benchmark AMS activities need to be carefully implemented to ensure stewardship efforts are both effective and sustainable.

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Abstract 7836

Evaluation of the MDR/MTB ELITe MGB assay for the detection of Mycobacterium tuberculosis complex and resistance to rifampicin and isoniazid

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Abstract third-party references: On behalf of the National Reference Center for Mycobacteria [CNR-MyRMA]

Background: Antibiotic resistance being the main threat to tuberculosis control, early and accurate detection of Mycobacterium tuberculosis complex (MTB) and resistance to first-line antibiotics rifampicin and isoniazid are needed for efficient patients care. MDR/MTB ELITe MGB® Kit is a novel fully automated real-time PCR assay designed for the simultaneous detection of the DNA of MTB and of resistance to rifampicin and isoniazid. Here, we report the first evaluation of the MDR/MTB ELITe MGB® in comparison with the phenotypic and molecular tests routinely performed in our laboratory.

Materials/methods: Forty-seven clinical samples including sputa, tracheal aspirate, bronchoalveolar lavage, gastric aspiration, vertebra, lymph node, and 6 strains of MTB formerly isolated were analyzed. Detection of MTB in clinical samples was compared to microscopic observation and identification by MTB-specific PCR. Resistance typing results, which were obtained from DNA extracted from both smear positive samples and strains, were analyzed using the Genotype MTBDRplus (Hain) assay as gold standard.

Results: MTB detection from smear-positive clinical samples was observed in 34/36 tests (94%), the 2 discordant results awaiting for culture results to be interpreted. The smear negative samples (n=11) were all tested negative. Overall, MDR/MTB ELITe displayed a positive predictive value of 100% and a negative predictive value of 85%. Among the 6 strains tested, 5 grew on solid and liquid medium and 1 in liquid medium only. The 6 (100%) were detected by the new assay. Regarding resistance typing, 25/26 (96%) of the rpoB mutations, 7/7 (100%) of the inhA mutations and 22/22 (100%) of the katG mutations were detected. The only discordant result observed for rpoB was caused by a L533P mutation not detected by the MDR/MTB ELITe assay and conferring a low-level of resistance to rifampicin. There was no false-positive result.

Conclusions: With a sensitivity of 94% and a specificity of 100 % for MTB detection, and a single discordant result for resistance typing, this first assessment from clinical samples of the fully automated MDR/MTB ELITe MGB® assay looks very promising, even if further investigation with a larger set of samples is required.

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Abstract 7838

**Multi locus sequence typing of Treponema pallidum subspecies pallidum in Barcelona**

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1 Vall d’Hebron University Hospital, Barcelona, Spain, 2 Universitat Autònoma de Barcelona, Bellaterra, Spain, 3 Parc Taulí University Hospital, Sabadell, Spain

**Background:** Enhanced CDC Typing (ECDCT) has been widely used as the reference methodology for molecular characterisation of Treponema pallidum subspecies pallidum. The new Multi Locus Sequence Typing (MLST) system consists in the sequence analyses of the TP0136, TP0548 and TP0705 loci. The objective was to determine the MLST profiles of clinical samples and to compare them with the ECDCT types.

**Materials/methods:** A total of 213 samples were collected from subjects diagnosed with syphilis at the STI Unit Vall d’Hebron-Drassanes during 2015. MLST was performed by Sanger-sequencing on samples with positive PCR result. The ECDCT types (arp, tpr and TP0548 genes) and the genetic azithromycin and doxycycline resistance (mutations within 23S rRNA and 16S rRNA genes respectively) were previously determined.

**Results:** Until now, a total of 29 samples could be characterised following the MLST typing system (analyses in process). Six different sequence-types were identified, two of them have not been described (table 1). The most frequent MLST profile was 1.3.1 (72%) and all of them were genetically resistant to azithromycin but sensitive to doxycycline. A higher number of types were identified following the ECDCT typing system: 1.3.1 samples were previously classified into 6 different ECDCT types and 1.1.1 were previously classified into 2 different ECDCT types.

**Table 1. MLST profiles and ECDCT types**

<table>
<thead>
<tr>
<th>Sequence-type</th>
<th>MLST profiles</th>
<th>23SrRNA+ (N)</th>
<th>Genetic group</th>
<th>N (%)</th>
<th>ECDCT types (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.3.1</td>
<td>R8(21)</td>
<td>SS14-like</td>
<td>21</td>
<td>13d/g (1) 14a/g (1) 14d/g (9) 14b/g (2) 14g (6) 14p/g (2)</td>
</tr>
<tr>
<td>2</td>
<td>1.1.1</td>
<td>R8(2)S(1)</td>
<td>SS14-like</td>
<td>3</td>
<td>14d/f (2) 14d/f (1)</td>
</tr>
<tr>
<td>28</td>
<td>1.17.9</td>
<td>R8(2)</td>
<td>SS14-like</td>
<td>2</td>
<td>14ff (2)</td>
</tr>
<tr>
<td>6</td>
<td>3.2.3</td>
<td>R8(1)</td>
<td>Nichols-like</td>
<td>1</td>
<td>14d/c (1)</td>
</tr>
<tr>
<td>Non-described</td>
<td>1.17.1</td>
<td>R8(1)</td>
<td>SS14-like</td>
<td>1</td>
<td>14a/t (1)</td>
</tr>
<tr>
<td>Non-described</td>
<td>9.7.8</td>
<td>S(1)</td>
<td>Nichols-like</td>
<td>1</td>
<td>14/d (1)</td>
</tr>
</tbody>
</table>

*Macrolide resistance: S=sensitive, R8=A2058G mutation*

**Conclusions:** Preliminary results showed that 1.3.1 and 1.1.1 profiles are the most frequent MLST types according to literature. Moreover, the discrimination power of the ECDCT seems to be higher than of the MLST. However, the techniques used for arp and tpr determination (molecular weight and restriction fragment length polymorphism) are more subjective than Sanger-sequencing, used for TP0136, TP0548 and TP0705 characterisation.

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Abstract 7840

**The association of antibiotics and *Clostridioides difficile* infections in allogeneic stem cell recipients**

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**Background:** Oncological patients receiving allogeneic stem cell transplantation (aSCT) are at risk of contracting hospital-acquired *Clostridium difficile* infection (CDI) followed by severe diarrhea.

**Materials/methods:** We conducted a cohort analysis based on aSCT recipients treated at the Department I of Internal Medicine at the University Hospital of Cologne between 01/2016 and 12/2018. We extracted demographic, clinical, and microbiological data, as well as the antibiotic therapeutic and prophylactic medication from the Cologne Cohort of Neutropenic Patients. The 100-day CDI incidence rates from onset of conditioning chemotherapy were computed. Antibiotic usage and further covariates from onset of conditioning chemotherapy were assessed in an adjusted multivariable backward-stepwise logistic regression. Patients with signs of CDI infection before aSCT were excluded.

**Results:** We included 253 patients, of whom 23 were positive for CDI. Among these patients, the incidence rates for the 100-day CDI was 9.1 with a rate of 19.2 per 10,000 patient days. The median time from conditioning chemotherapy to CDI was 34 days (interquartile range: 15-41 days). In 15 patients, an acute graft-versus-host disease was present at onset of CDI. In 12 patients, CDI occurred during neutropenia (neutrophils <500/μL [×10^9/L]). The two most frequently administered therapeutic antibiotics were piperacillin and tazobactam (group without CDI: 147/230 [63.9%], group with CDI: 13/23 [56.5%]) and meropenem (group without CDI: 128/230 [55.7%], group with CDI: 10/23 [43.5%]). Antibiotic prophylaxis was administered in 44/230 (19.1%) and 2/23 (8.7%) of patients for the group without and with CDI, respectively. The adjusted logistic regression analysis revealed no significant association of antibiotics and CDI.

**Conclusions:** In contrast to other studies, in our analysis, we could not find an association of antibiotics and CDI. For further conclusions, a time-dependent and time-varying consideration of further covariates and risk factors in a larger and multi-centric cohort is needed.

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Abstract 7844

**ComParison of patients' brain microdialysate and cerebrospinal fluid concentrations versus time profiles of cefotaxime and metronidazole as representative antibiotic substrates or not of efflux transport systems**

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**Background:** Cefotaxime (CTX) is used as an empirical therapy for bacterial meningitis, ventriculitis, and cerebral abscesses associated with metronidazole (MTZ) [1-2]. The aim of this study was to develop a population pharmacokinetic (PK) model to characterize and compare their PK in central nervous system (CNS), from extracellular fluid (ECF) or cerebrospinal fluid (CSF) concentrations in ICU patients.

**Materials/methods:** The trial received ethical approval. Patients received 500 mg of MTZ (n=8) or 2 g of CTX (n=10), every 8 h through a 30-min IV-infusion. Half of the patients (n=4 in the MTZ group and n=5 in the CTX group) were equipped with an external ventricular drainage system into their lateral brain ventricles, and half with microdialysis probes placed in brain tissue. Unbound antibiotic concentrations were measured in CSF or dialysates samples, as well as in concomitant plasma ultrafiltrates, by LC-MS/MS. Measured dialysate concentrations were corrected for probes recoveries. A population PK model was developed, with bidirectional transfer across the blood brain barrier (BBB) and blood cerebrospinal fluid barrier (BCSFB) characterized by clearance in (CLin) and out (CLout). Parameters values were estimated using NONMEM 7.4.

**Results:** CSF concentration-time profiles were flat compared with brain ECF concentration-time profiles, for both MTZ and CTX. The model successfully described the unbound PK profiles of both drugs in plasma, ECF and CSF. MTZ distribution was faster in ECF (CLin=303 mL/h) than in CSF (CLin=70 mL/h) but CLin equals CLout in both fluids, consistent with passive bidirectional diffusion across the BBB and the BCSFB. By comparison, CTX distribution was slower both in ECF (CLin=21 mL/h) and in CSF (CLin=1.4 mL/h). Furthermore CLout values (88 and 11 mL/h) were several fold higher (4 and 8) than corresponding CLin, consistent with efflux transport systems, and leading to limited CNS exposure (AUC_{ECF}/AUC_{Plasma} = 24% and AUC_{CSF}/AUC_{Plasma} = 13%).

**Conclusions:** Brain microdialysis and CSF sampling can be used for the assessment of antibiotics CNS distribution, but may not exhibit similar results, especially for efflux transport system substrates.

**References:**


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Abstract 7848

An unusual cluster of community-acquired skin infections by a multidrug-resistant MRSA harbouring genes that encode for exfoliative toxins

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Background: The Netherlands has a low prevalence of MRSA and an active surveillance. Cultured strains from all colonised and infected patients are collected nationally and typed using multiple locus variable number of tandem repeat analysis (MLVA). Next-generation sequencing (NGS) based whole genome MLST (wgMLST) is applied on a selection of isolates.

Materials/methods: Between June and October 2019, an outbreak of skin infections with MRSA occurred. The first case discovered was a child admitted to hospital with impetigo bullosa. Contact tracing led to identification of several positive family members, some living in elsewhere in The Netherlands. In that area, an increase was observed of patients with impetigo not responding to treatment with fusidic acid. Therefore, general practitioners in the area were encouraged to submit samples for culture and to use mupirocin in case of MRSA.

Results: In total, 54 cases were identified, including 45 children. The cases focussed around two villages in the east of the country. All but one were community acquired. Resistance was found for beta-lactams, fusidic acid, erythromycin, clindamycin and co-trimoxazole, and sensitivity for mupirocin, vancomycin, rifampicin, linezolid, doxycycline and ciprofloxacin. Typing showed the isolates had MLVA-type MT4627 and were negative for PVL. This MLVA-type was found only three times before in our country. NGS of 23 isolates revealed the isolates had classical MLST-type ST121 and clustered closely together in wgMLST, including one isolate from 2018 from the same region. Two isolates from children living in another part of the country differed slightly more. These children had recently visited family in Morocco.

The strains harboured exfoliative toxin genes eta, etb and edinC. This combination was not present in any other of the 3,800 sequenced isolates in our collection. ComParison to 460 publicly available genomes showed a clear distinction of the Dutch isolates with 482 genes difference to the nearest isolate in wgMLST. After putting in place active case finding and appropriate treatment, as of October 11, 2019, no new cases occurred.

Conclusions: An outbreak with community acquired fusidic acid resistant MRSA occurred with a rare strain, harbouring exfoliative toxin genes. Most cases were children with impetigo-like skin lesions.

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**Abstract 7849**

**Genomic epidemiology and antimicrobial resistance surveillance of gonococci in Spain**

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**Background:** Gonorrhea is the second most common sexually-transmitted bacterial infection at global scale. Its increasing incidence along with the growing number of antimicrobial resistant (AMR) strains, has made Neisseria gonorrhoeae (NG) a major threat to Public Health. Our aim was to analyse the population structure of NG circulating in Spain and to identify the AMR determinants present in this population.

**Materials/methods:** DNAs from 342 NG isolates from three main urban areas of Spain were collected, and their whole-genome sequences were obtained with Illumina NextSeq platform. Sequence Types (STs) were inferred using SRST2. AMR determinants were detected using ARIBA. Reads were mapped against FA1090 strain and a maximum-likelihood phylogenetic tree was constructed using IQTREE. Additionally, reads were assembled de novo to verify SRST2 and ARIBA results by using the contigs and BLAST, and to find other elements such as plasmids and gonococcal genomic islands.

**Results:** 45 different STs were found, with ST 7363 and 1901 being the majority. For cephalosporins, 53.6% of isolates were phenotypically susceptible. Mutations in penA were found in resistant isolates, most of them being mosaic forms XXXIV and X. 63.1% of isolates were resistant or had reduced susceptibility to penicillin, carrying mutations in porB1b and/or ponA, or having bla TEM plasmid. Regarding azithromycin, 20.1% had some resistance, all of them with C2597T mutation in 23S rDNA. 24.9% were resistant to doxycycline, mostly by tetM plasmid than by mutations in rpsJ. 21.1% had resistance to fluoroquinolones, with mutations in both parC and gyrA.

**Conclusions:** The use of whole-genome sequences (WGS) has led to more a accurate depiction of NG population structure in Spain than MLST schemes, e.g. ST 7363 is polyphyletic in this population, this could be detected by using WGS and can be explained by recombination. NG shows a great diversity in the regions studied. The detection of AMR determinants is comparable to phenotypic analyses, improving the AMR surveillance. Spanish NG show high number of resistant isolates for penicillin, doxycycline, and fluoroquinolones. Most cases in which an AMR determinant was not detected but phenotype was resistant might be explained by inactivation of the MtrCDE efflux pump repressor.

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Impact of total laboratory automation systems on efficiency, cost and clinical outcomes: a systematic review

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Background: Total laboratory automation (TLA) is usually defined as the automation of the diagnostic workflow including all steps from inoculation to final result. A systematic review of the literature was conducted to evaluate the impact of TLA on clinical microbiology laboratory efficiency/productivity, quality, and to ask the question whether faster, more accurate lab results are linked to improved clinical and economic outcomes.

Materials/methods: A search string was conducted in Embase and PubMed from 1999 to present. Various study designs including randomized controlled trials, cohort studies/longitudinal studies, case-control studies, cross-sectional studies, reviews, and prospective-retrospective (pre-post) were included. Human and English publications were included, and no exclusions were made based on age, gender, race or other demographics. After data extraction, a meta-analysis was ruled out due to high data heterogeneity.

Results: After double-blind review, 31 publications were selected for inclusion into this clinical microbiology TLA-system systematic review. The relevant publications addressed at least one of the following commercial TLA platforms: BD Kiestra™, Copan WASP®. The included publications addressed multiple laboratory endpoints that included accuracy and quality, efficiency and workflow, cost savings and cost-effectiveness, or clinical outcomes. Eight publications demonstrated improvements in lab accuracy and quality. Seventeen publications discussed efficiency and workflow, fourteen of which, demonstrated improvement due to TLA. Two publications demonstrated significant cost savings due to reduced labor costs, with additional gains in quality, efficacy, reduced ergonomic injuries, and improved laboratory safety due to TLA implementation. Only one study demonstrated a statistically significant reduction in the duration of empirical therapy and 30-day crude mortality rate for patients with mono-microbial bloodstream infections; this was attributed to shorter time-to-result following processing of samples by BD Kiestra™ TLA.

Conclusions: TLA consistently created positive impact for a variety of laboratory endpoints and measurements; demonstrating the potential of TLA for improving clinical laboratory efficiency in the future. This review identifies the need for further research on TLA and effects on clinical outcomes and overall hospital costs.

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Abstract 7855

The role of complement and diabetes in invasive candidiasis
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Background: Complement is an important link between the innate and the adaptive immunity and has several crucial functions in first line defense against non-self structures. To avoid detrimental effects, complement activity is tightly controlled by several regulators, one of which is factor H (fH). *Candida albicans* (CA) has developed mechanisms to escape complement. One of these is to bind fH on its surface via the “high affinity glucose transporter 1” (Hgt1p), whose expression is glucose-dependent. Hence, we aimed to study the effect of glucose and complement on CA pathogenesis.

Materials/methods: Immunocompetent (wt), diabetic and C3-deficient (DC3) mice were intravenously infected with CA wild-type (wt) or a mutant lacking Hgt1p (Dhgt1). Survival and clinical status were monitored over 14 days. Immunological and inflammation parameters and fungal load were analyzed at defined time points.

Results: The murine model revealed that the CA wt strain is less virulent in immunocompetent mice than the Dhgt1 strain, with a lower risk of lethal outcome and a slower pathogenesis. No significant difference in virulence was detected between diabetic and wt mice infected with Dhgt1 or between diabetic mice infected with the different *Candida* strains. In contrast, CA wt showed a significant higher virulence in diabetic and, in particular, DC3 mice, compared to wt mice. This proves that diabetes is a relevant risk factor for a worsened outcome of candidiasis and the causal association to complement. The higher fungal load in the urine as a parameter of a pronounced kidney infection and consecutive inflammation confirmed the survival data. Furthermore, the higher granulocyte numbers correlated with the virulence of the different *Candida* strains.

Conclusions: The complement system is linked to the virulence of CA in diabetic animals. This might be due to lower C3b deposition on the surface of CA. Despite this, the depletion of Hgt1p cannot be attributed to be beneficial for the survival in the murine model. An explanation might be that this depletion could lead to either an up-regulation of other fH-binding molecules or other virulence factors.

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Changes in the laboratory diagnosis of CDI in Wales after the introduction of *C. difficile* toxin gene detection

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**Background:** UK and European guidelines recommend a 2-step algorithm for the laboratory diagnosis of *C. difficile* infection (CDI). Detection of glutamate-dehydrogenase (GDH) or toxin gene[s] are acceptable as the first screening method. During 2018 toxin gene (*toxB*) detection was introduced to all Public Health Wales laboratories whilst others continued to use GDH assays. Changes in laboratory detection rates and PCR ribotyping results between October 2014 and September 2019 are presented.

**Materials/methods:** More than 290,000 results for GDH, *toxB* PCR, toxin EIA, *C. difficile* culture and PCR ribotyping were extracted for comparison. GDH and toxin EIA testing was performed using a variety of commercial methods. Toxin B gene detection was accomplished using the Serosep EntericBio *C. difficile* PCR assay.

From December 2017, all first screen positive samples referred to the UK Anaerobe Reference Unit (UKARU) were cultured for *C. difficile* with ribotyping performed for all toxin positive samples. From January 2019, all culture positive-GDH/PCR positive samples referred to the UKARU, regardless of toxin result, were ribotyped.

**Results:** Between October 2014 and September 2019 first screen positivity declined annually using both test modalities (10%-7.9% for GDH; 5.7-5.3% for PCR) with test numbers increasing in every year except 2016-17 (43770 in 2014-15 to 50091 in 2018-19). Toxin EIA positivity showed an overall decline (30% in 2014-15 & 25%-GDH/27%-PCR in 2018-19).

Between December 2017 and September 2019 *C. difficile* culture positivity for toxin positive samples was >99% for samples tested by both GDH and PCR. For toxin EIA negative samples, it was 78% and 89% respectively. In 2019 culture positivity for toxin EIA positive samples remained >99% but decreased to 76% for GDH, and increased to 91% for PCR, from toxin EIA negative samples.

RT027 is no longer common within our CDI patients. Toxin negative/variable strains were isolated more commonly from GDH positive compared with PCR positive samples.

**Conclusions:** *C. difficile* toxin gene detection, within a 2-step algorithm, has not lead to an increase in laboratory CDI diagnosis in Wales. In fact, the added specificity of PCR as a frontline screen may be beneficial in excluding patients that harbor toxin negative/variable strains.

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Phenotypic and genotypic examination of Dientamoeba fragilis and Blastocystis isolates in patients with ulcerative colitis and irritable bowel syndrome

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Background: The aim of this study is to compare the efficacies of different diagnostic methods in the recovery of D. fragilis and Blastocystis in stool samples of patients with active and remittent ulcerative colitis (UC), and irritable bowel syndrome (IBS) and identification of their subtypes.

Materials/methods: A total of 100 patients (35 IBS, 35 active UC and 30 remittent UC) were enrolled in the study between April 2018 and March 2019. Initial diagnoses of all UC patients and IBS patients were based on Mayo Score and Rome IV Criteria, respectively. Stool samples were investigated by iodine, trichrome staining, Kinyoun acid-fast staining, bacteriological cultures and by conventional-PCR, nested-PCR with amplification of cysteine peptidase, serine peptidase and metallopeptidase genes and q-PCR. All amplicons were sequenced and interpreted according to data on GenBank.

Results: Four patients were diagnosed with D. fragilis by iodine and trichrome staining; 4 by conventional PCR; 6 with the amplification of cysteine peptidase by nested-PCR; 6 with serine peptidase; 6 with metallopeptidase; and 8 by q-PCR. Five patients were diagnosed with Blastocystis spp by iodine; 6 by trichrome staining; 9 by conventional PCR. 5 active UC, 1 remittent UC, 3 IBS patients were diagnosed with Blastocystis, 2 active UC, 2 remittent UC, 4 IBS patients were with D. fragilis. D. fragilis was most common in IBS patient group whereas Blastocystis in active UC. Most D. fragilis isolates were identified by q-PCR. All D. fragilis isolates were evaluated as Genotype 1 by sequencing; whereas all Blastocystis as Subtype 3. Examination of Kinyoun stained smears revealed no Coccidians (Cryptosporidium, Cyclospora and Cystoisospora), while the bacterial cultures were negative.

Conclusions: Our findings demonstrated that nested PCR is relatively more sensitive than conventional-PCR, compared to q-PCR which is the golden standard for D. fragilis. All D. fragilis isolates were found as Genotype 1, which is the predominant genotype worldwide. To our knowledge, this is the first study investigating D. fragilis genotypes in Turkey. Further assessments involving the assessment of gut microbiota together with these results may help unveil the interactions between the microorganisms in gut and their outcomes on human health.

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Performances evaluation of the first sample-to-result system for detection and quantification of *Pneumocystis jirovecii* in respiratory tract samples

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Abstract third-party references: ELITechGroup SPA

**Background:** The most common pathogenic fungi are *Candida, Aspergillus, Cryptococcus,* and *Pneumocystis spp.* — causing more than 90% of reported deaths due to fungal disease. The top ten fungal infections are responsible for at least as many deaths as tuberculosis or malaria. Traditionally considered a protozoan, *Pneumocystis* has been shown to belong to the family of fungi. It is estimated that approximately 400,000 individuals are affected by *Pneumocystis jirovecii* pneumonia (PCP) every year. In the Western world, PCP used to be the most common opportunistic infection in HIV-positive individuals. Today, the principal risk group comprises patients who are iatrogenically immunocompromised because of either malignancy, transplantation or rheumatological disease. This study describes the performance of the first quantitative Real-Time PCR assay “Pneumocystis ELITe MGB® Kit” (ELITechGroup Spa, Turin, Italy) in association with ELITe InGenius® instrument (ELITechGroup Spa, Turin, Italy), for highly sensitive *Pneumocystis jirovecii* detection and quantification, in Bronchoalveolar lavage (BAL) and Sputum.

**Materials/methods:** The clinical performance evaluation study of Pneumocystis ELITe MGB Kit on ELITe InGenius instrument was carried out by “Azienda per l’Assistenza Sanitaria n. 5 Friuli Occidentale” (Pordenone, Italy) on 102 BAL and 73 sputum retrospectively collected samples.

**Results:** Pneumocystis ELITe MGB Kit LoD, calculated on BAL samples and confirmed in BAL and Sputum samples, is equal to 97 copies/mL. Inclusivity was verified on different clinical samples and by analysis of a QCMD proficiency panel. Cross-reactivity was tested against 18 respiratory tract pathogens. The diagnostic specificity for BAL was equal to 96.6% and for sputum to 97.1%. The diagnostic sensitivity for BAL was equal to 100% and for Sputum to 84.2%. The turnaround-time was about 100 minutes.

**Conclusions:** Pneumocystis ELITe MGB Kit in association with ELITe InGenius instrument constitutes a highly sensitive and timely system for detection and quantification of *Pneumocystis jirovecii* in BAL and sputum samples. This innovative and fast solution simplifies the laboratory workflow, dramatically cut the report time and provide a valuable add on tool to clinician for correct patient management.

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Abstracts 2020

Abstract 7860

Fighting antimicrobial resistance with breath analysis
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Background: Identification of bacterial respiratory tract infection (RTI) is key to alleviating antimicrobial resistance via improved antibiotic stewardship. The aim of this observational study is to discriminate adult participants with suspected upper or lower RTI with bacterial infection from those without, using breath analysis. Breath samples were tested using a gas chromatography – ion mobility spectrometry (GC-IMS) to measure volatile organic compounds (VOCs) components. Confounding factors, such as age, smoking habits and gender will be investigated to demonstrate the efficacy of results.

Materials/methods: 1229 subjects were recruited, all suspected of a RTI from 8 NHS sites across the UK. Patients were recruited from both primary (397 subjects) and secondary care (832 subjects) settings. Breath samples were analysed using a commercial GC-IMS (G.A.S. BreathSpec®, Dortmund, Germany).

Results: Initial data analysis indicates that the G.A.S. BreathSpec® GC-IMS was able to separate between diagnostic groups well. Ongoing VOC analysis indicates that certain compounds play a crucial role in distinguishing between diagnostic groups. Analysis of possible confounding factors indicate that gender, age and smoking habits have insignificant influence on breath content.

Conclusions: This observational study confirms the utility of exhaled breath analysis to distinguish between bacterial RTI and those without. This potential diagnostic power would reduce antibiotic prescribing by over 30% in a primary care setting alone. Therefore, the G.A.S. BreathSpec® GC-IMS instrument offers great potential as a non-invasive, high-throughput, diagnostic tool for RTI in a clinical setting while reducing antimicrobial resistance through improved antibiotic stewardship.

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Abstract 7863

The management of Enterococcus bloodstream infections in cancer patients: impact of central venous catheters

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Background: There has been a rise in Enterococcus species Central Line-Associated Bloodstream Infections (CLABSIs) ranking as the third overall causative organism according to the Centers for Disease Control and Prevention (CDC) report issued in 2014. Central Venous Catheter (CVC) management including the need and timing of removal is not well defined for enterococcus bacteremia (EB) in the 2009 Infectious Diseases Society of America (IDSA) management guidelines given the paucity of studies addressing CVC management.

Materials/methods: We conducted a retrospective chart review on 542 patients diagnosed with EB between 2010 and 2018. We excluded patients without an indwelling CVC. We further subgrouped the remaining 397 patients into the following three groups based on the IDSA definition for catheter-related bloodstream infection (CRBSI) and the CDC definitions for CLABSI (with and without MBI) and non-CLABSI: CRBSI and CLABSI without MBI, CLABSI with MBI, and non-CLABSI. Impact of catheter removal was evaluated at different intervals; less than 3 days (early) and at 3–7 days (late). The composite primary outcome included: absence of microbiologic recurrence, 90-day infection related mortality, and 90-day infection related complications. Failure to meet any of those parameters was designated as failure.

Results: Early catheter removal within 3 days was associated with higher success rate compared to removal in 3-7 days (88 and 63 percent respectively, P = 0.08). We also noted that bacteremia with a vancomycin resistant isolate was associated with higher all-cause mortality (53 percent, P = 0.018), however multivariate analysis identified isolation of Enterococcus faecium to be associated with higher all-cause mortality (OR 2.38, 95% CI 1.54, 3.68). The use of combined antimicrobials that are potentially effective and previously studied was not associated with differences in outcome.

Conclusions: Early CVC removal within 3 days is recommended as it is associated with a better outcome compared to later CVC removal in 3-7 days. Further prospective data is needed to decide optimum CVC management. Enterococcus faecium (vancomycin resistant) is associated with a worse outcome in cancer patients.

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Abstract 7865

Understanding the Corynebacterium diphtheriae population through whole genome sequencing
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Background: The UK has high diphtheria immunisation coverage, the majority of cases being sporadic and imported. However, a small number of cryptogenic cases and clusters are raising concerns about transmission within communities with low immunisation coverage. Increasing numbers of isolates with detectable diphtheria toxin genes but which do not express the toxin have also been seen, and are of uncertain significance. We used whole genome sequencing (WGS) to investigate the Corynebacterium diphtheriae population in the UK to improve the evidence base for public health measures.

Materials/methods: Public Health England receives all UK C. diphtheriae isolates for toxigenicity testing. All toxigenic and non-toxigenic tox-gene bearing (NTTB) C. diphtheriae strains referred since 2003, and where possible a geographically and temporally similar non-toxigenic strain, were sequenced using HiSeq-2500 (150 isolates). MASH distances were calculated to construct a dendrogram of isolate assemblies (Unicycler) and complete Corynebacterium genomes (RefSeq). The tox gene and promoter were extracted and aligned to identify genetic changes likely to lead to a loss of toxin production.

Results: The dendrogram showed several clusters of highly related isolates. For two clusters, WGS demonstrated relatedness where epidemiological links had been suspected, but not previously identified. High genomic similarity suggests cases were closely linked to known transmission events, rather than reflecting more widespread undetected disease in the community. Two NTTB clones were identified and showed different loss-of-function mutations; one, the loss of the promoter region, and the other, both a single base deletion and a large deletion of the second half of the tox gene. Penicillin non-susceptibility was distributed throughout the dendrogram and, with the exception of isolates with known links, did not suggest a single resistant clone within the population.

Conclusions: WGS of C. diphtheriae can define isolate characteristics and contribute to outbreak detection and management. However, without developing a more robust phylogeny of the current global population, it is difficult to contextualise these relationships and set specific thresholds for similarity. Substantial gene disruption in NTTB clones suggests reversion to toxigenicity is highly unlikely in the UK and public health measures should be reviewed; however, genomic surveillance of NTTBs would be beneficial.

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Abstract 7866

**Piperacillin-tazobactam resistance developed during febrile neutropenia**

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**Background:** Emerging resistance solely to piperacillin/tazobactam (pip-taz) due to its use has surfaced with few cases documented worldwide. The main mechanism of resistance are beta-lactamases, out-membrane protein mutation and efflux pumps.

**Materials/methods:** Three patients [P1, P2 and P3] from the BMT unit developed [pip-taz] resistant *K. pneumoniae* bloodstream infections, one of them after stem cell infusion. All of the samples were submitted to routinely VITEK® antibiogram, susceptibility testing by disk diffusion (DD), broth microdilution (BMIC) with and without Carbonyl Cyanide 3-Chlorophenylhydrazone (CCCP) assay, clonality was assessed by pulsed field gel electrophoresis (PFGE). Whole genome sequence (WGS) was also performed.

**Results:** The VITEK® antibiogram showed that P1 and P3 isolates were only resistant to pip-taz and ampicillin, while P2 showed resistance to quinolones, cephalosporins, aminoglycosides and ampicillin. All isolates were resistance to pip-taz by DD whereas P2 isolate was intermediate by BMIC. None of the microdilution tiles were affected by CCCP.

PFGE analysis showed that P1 an P3 were closely related and shared 94% of similarity while P2 isolate seemed to belong to a different clone with 69% of similarity. These patients were not hospitalized at the same time, but P1 and P3 did use the same hospital room with a twenty day gap period.

WGS analysis demonstrated different resistance genes to b-lactams [Table1], only P2 showed blaTEM-1b a gene already portrayed as pip-taz resistant. Unknow mutations were found in porin genes (*ompk36* and *ompk37*) and in the efflux pump regulators genes (*acrR* and *ramR*) except for P2 that lacked *ramR* mutations. The 3D protein structure prediction showed that mutated *ramR* gene presented differences in morphology that may lead to functional alterations. No modification in penicillin binding proteins was identified.

**Conclusions:** These data indicate pip-taz resistance as an emerging problem that should be carefully investigated and surveilled. More data is needed to better understand this important new mechanism of resistance.

**Table 1. Description of the bone marrow transplant patients (P1,P2,P3) and the K. pneumoniae Phenotypic and Genotypic profile when Piperacillin-Tazobactam Resistance was evaluated.**

<table>
<thead>
<tr>
<th></th>
<th>Patient</th>
<th>Neutropenia</th>
<th>Previous Antibiotic</th>
<th>Central Line</th>
<th>Previous Pip-taz use duration</th>
<th>Antibiotic (VMAX)</th>
<th>PhenoxMBL</th>
<th>DD</th>
<th>BMIC</th>
<th>CCCP</th>
<th>MIC</th>
<th>Resistance genes</th>
<th>MDR</th>
<th>piv-taz</th>
<th>Efflux pump mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>Autograft</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>3 days</td>
<td>R pip-taz</td>
<td>R ampicillin</td>
<td>R</td>
<td>R</td>
<td>Negative</td>
<td>Yes</td>
<td>blaTEM-1b</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>P2</td>
<td>Autograft</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>3 days</td>
<td>R piv-taz</td>
<td>R ampicillin</td>
<td>R</td>
<td>R</td>
<td>Negative</td>
<td>No</td>
<td>blaTEM-1b</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>P3</td>
<td>Autograft</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>3 days</td>
<td>R pip-taz</td>
<td>R ampicillin</td>
<td>R</td>
<td>R</td>
<td>Negative</td>
<td>Yes</td>
<td>blaTEM-1b</td>
<td>Yes</td>
<td>No</td>
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Abstracts 2020

Abstract 7868

**Adjuvants that contain saponin may be an important component of influenza peptide vaccines to induce broadly reactive functional antibodies**

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**Background:** Broadly reactive peptide vaccines that contain conserved epitopes to Hemagglutinin (HA), Neuraminidase (NA) and Matrix Ectodomain (M2e) antigens that promote functional activity against contemporary Group 1 and 2 influenza strains may provide new and useful strategies for influenza epidemic and pandemic control. The ability of different adjuvants to promote robust immune responses against influenza antigens should be assessed to improve vaccine efficacy. Here, we evaluate the interaction of three adjuvants: Saponin-derived, Squalene-based sorbitan-trioleate, and Squalene-based block copolymer, with HA, NA and M2e peptides, and report a comparative analysis of their binding profiles to influenza antigen epitopes and functional activities across Group 1 and 2 influenza viruses.

**Materials/methods:** A composite peptide (HA, NA and M2e, in combination) vaccine conjugated to CRM was administered subcutaneously to mice using Saponin-derived Quil-A®, Squalene-based AddaVax™ or Squalene-based TiterMax® Gold adjuvant. Serum antibody titers were analyzed using an anti-influenza ELISA on peptides and live influenza contemporary viruses (H3N2 and H1N1) with isotype-specific detection. Functional activity was evaluated in vitro using a micro-neutralization assay.

**Results:** The composite peptide vaccine given to mice in the Saponin-derived adjuvant group produced higher serum anti-influenza titers across HA, NA and M2e, and induced broad isotypes (IgG1, IgG2a, IgG2b) to all the peptides. However, the Squalene-based block copolymer adjuvant preferentially promoted antibody responses mainly to M2e. Binding activity of serum antibodies to live contemporary viruses (H3N2 and H1N1) was superior for the Saponin-derived group compared to the Squalene-based groups. Neutralization activity against influenza A (H3N2 and H1N1) contemporary strains was demonstrated in all groups; however, it was markedly enhanced in the Saponin-derived group.

**Conclusions:** The Saponin-derived adjuvant with composite peptide CRM-conjugate vaccine induced broadly reactive serum antibodies across surface peptides, matrix and live influenza viruses, and demonstrated a more robust humoral response across isotypes. Functional activity against contemporary influenza strains was greater for the Saponin-derived group, compared to Squalene-based groups. Antibody-Dependent Cellular Cytotoxicity (ADCC) assays are currently in progress and in vivo protection studies are being designed. Saponin-derived adjuvants may play an important role in the induction of key immune responses that are critical for immunity to influenza.

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**Abstract 7872**

**Genetic context of the poxtA gene that confers resistance to linezolid in enterococci**  
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**Background:** Acquired resistance to linezolid (LZD) is rising worldwide among enterococci, especially due to the spread of resistance genes carried by mobile genetic elements (cfr, optrA and poxtA). Whereas the genetic context of cfr and optrA genes has been well studied, little is known about the most-recently reported gene poxtA. The aim of this study was then to characterize the genetic support and environment of poxtA in enterococcal clinical isolates from France.

**Materials/methods:** All enterococcal isolates suspected to be LZD-resistant enterococci (LRE) received at the National Reference Center for Enterococci from 2016 to 2018 were included. These strains were screened for the presence of cfr-like, optrA and poxtA genes by PCR and phenotypically characterized. The genome of poxtA-positive strains was sequenced using the Illumina technology (MiSeq) while a long-read sequencing approach (MinION, Oxford Nanopore Technologies) was also used for one strain (18-276). Bioinformatic analysis was performed with the CLC Genomic Workbench software (Qiagen) and a homemade pipeline.

**Results:** A total of 12 non-clonally related strains were positive for poxtA [11 Enterococcus faecium, 1 Enterococcus faecalis], including 2 strains that co-carried optrA. Note that only 3 strains were resistant to vancomycin [2 vanA and 1 vanB]. In all strains, poxtA was identified in 3-kb contig and flanked by IS1216 elements. The hybrid assembly for the genome of 18-276 (ST80) showed that poxtA was part of a 35-kb plasmid (named p18-276) that co-carried 3 other resistance genes [tet(M), tet(L), fexB]. Note that the vanA operon in 18-276 was not co-located on p18-276. The association of poxtA-tet(M)-tet(L)-fexB was also detected in 4 other strains [16-021 (ST323), 16-164 (ST650), 17-318 (ST324) and 18-204 (ST18)], suggesting the potential presence of p18-276.

**Conclusions:** The poxtA gene is emerging among LRE clinical isolates collected in France. Concerning its genetic environment, poxtA is linked to IS1216 elements that could drive its mobilization. For one strain, it is part of a plasmid that co-carries genes responsible for resistance to tetracyclines and phenicols, which is likely involved in horizontal genetic transfer of resistance gene[s]. Additional hybrid genome analyses are in progress to confirm the plasmidic support of poxtA.

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Abstract 7875

Community faecal carriage of extended-spectrum beta-lactamase-producing Escherichia coli in Niger

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Background: Little is known about the epidemiology of extended-spectrum beta-lactamase-producing E. coli (ESBL-E. coli) in Sub-Saharan Africa. Here, we studied the molecular epidemiology of ESBL-E. coli in the faecal carriage of a community population in Niger.

Materials/methods: Between April 22, 2017, and May 18, 2017, 383 stools of healthy people were collected from 20 villages in the district of Madarounfa, in rural southern Niger. Stools were plated on MacConkey agar media containing 1 mg/l cefotaxime. Of 383 people, 354 (92.4%) were carriers of cefotaxime-resistant Enterobacteriales (CTX-R-E). 90 stools with CTX-R-E were randomly selected for further analysis. Colonies of different morphologies obtained on cefotaxime containing agar plates were identified by mass spectrometry (MALDI-TOF-MS). Antimicrobial susceptibility was tested by the disk diffusion method according to the EUCAST, and ESBL detection was performed using the synergy test. Genomes of ESBL-E. coli isolates were sequenced on HiSeq (2×100 bp) (Illumina, San Diego, CA) and assembled with SPAdes (v3.12.0). Resistance and virulence genes were searched using abricate (v0.7), resfinder and VFDB. Phyllogroup were determined by ClermonTyping method. PlaScope was used to discriminate the plasmidome from the genome. Genome distances were estimated using Mash.

Results: A total of 109 ESBL-E. coli were recovered from 90 stools: 72, 17 and 1 people carried a single, two or three different ESBL-E. coli, respectively. Most ESBL-E. coli isolates (91/109, 83%) belonged to phylogroup A. 41 different sequence types (ST) were identified; ST10 was most frequent (10/109, 9%). ESBL-phenotype was mostly associated with blaCTX-M-15 (107/109, 98%). blaCTX-M-15 gene was integrated into the chromosome for about one-third of isolates (32/109), in various integration sites. Phylogenetic analysis displays a high diversity of circulating clones within and between different villages.

Conclusions: CTX-M-15 producing E. coli are highly prevalent in the community in Niger and are mainly phylogroup A isolates, associated with commensalism, and have different genetic backgrounds, suggesting co-circulation of many distinct clones. Given these surprising results, enhanced monitoring in this region will be essential.

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Abstract 7876

**Performance assessment of MDR/MTB ELiTé MGB Kit for tuberculosis diagnosis**

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**Background:** Tuberculosis (TB) is a worldwide public health concern. Mycobacterium tuberculosis complex (MTB) culture still is the reference method for TB diagnosis, but it is time-consuming. To accelerate the TB diagnostic, guidelines from the Centers for Disease Control and Prevention recommend performing a TB NAAT (nucleic acid amplification tests) directly on specimens from patients. Here, we evaluated the performance of MDR/MTB ELiTé MGB® kit.

**Materials/methods:** Forty-nine specimens were selected retrospectively, among the left-overs of the Mycobacteria Laboratory of the University Hospital, Lyon, France. All samples were collected before anti-mycobacterial treatment and included forty-two specimens with MTB positive culture (6 pulmonary smear-positive with isoniazid (INH) and/or rifampicin (RIF) resistant MTB, 27 pulmonary smear-negative, 7 extra-pulmonary smear-negative) and 7 pulmonary samples with a non-tuberculous mycobacteria culture. Specimens were stored at -20°C before testing by MDR/MTB ELiTé MGB® kit in association with ELiTé Ingenius system and SP200 or SP1000 extraction kit.

**Results:** Interpretable results were obtained for forty-seven samples, excluding 1 MTB pulmonary smear-negative sample and 1 MTB extra-pulmonary smear-negative sample. Overall performance of MDR/MTB ELiTé MGB® kit for TB detection and for each samples category was collected in table below:

<table>
<thead>
<tr>
<th>Category</th>
<th>Samples number (MTB/no-MTB)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All samples</td>
<td>47 (40/7)</td>
<td>77.5% [61.5-89.2]</td>
<td>100.0% [59.0-100.0]</td>
<td>100.0% [88.8-100.0]</td>
<td>23.0% [19.8-70.1]</td>
</tr>
<tr>
<td>Smear-negative samples</td>
<td>41 (34/7)</td>
<td>73.5% [55.6-82.1]</td>
<td>100% [59.0-100.0]</td>
<td>100% [86.3-100.0]</td>
<td>23.0% [19.8-70.1]</td>
</tr>
<tr>
<td>MTB pulmonary smear-positive samples</td>
<td>6</td>
<td>100.0% [54.1-100.0]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTB pulmonary smear-negative samples</td>
<td>26</td>
<td>80.7% [60.6-93.4]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTB extra-pulmonary smear-negative samples</td>
<td>8</td>
<td>50.0% [15.7-84.3]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTB pulmonary smear-negative samples using SP200 kit</td>
<td>13</td>
<td>76.9% [46.2-94.9]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTB pulmonary smear-negative samples using SP1000 kit</td>
<td>13</td>
<td>84.6% [54.6-98.1]</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

95% confident interval [-]

For TB-resistance detection performance, MDR/MTB ELiTé MGB® kit was performed on the 6 MTB pulmonary smear-positive samples including 1 strain multi-resistant-TB, 1 strain RIF-R and 4 strains INH-R. Overall sensitivity for resistance detection was 100.0%.

**Conclusions:** MDR/MTB ELiTé MGB kit display good performance for detection of TB infection and TB resistance, notably for pulmonary specimens with a very good sensitivity on pauci-bacillary smear-negative respiratory samples (80.7%), equivalent to the sensitivity of GeneXpert MTB/RIF Ultra on the kind of specimens.

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Evaluation of carbapenem resistance in Enterobacteriaceae isolated from intensive care unit using phenotypic and genotypic methods

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Abstract third-party references: National Health and Education Society, PD Hinduja Hospital & Medical Research Centre

Background: Carbapenemase-producing Enterobacteriaceae (CPE) are a global emerging threat with high transmissibility, multidrug-resistance and limited treatment options. Reliable detection is important for prevention, containment of these pathogens as well as for antimicrobial stewardship.

The aim of this study was to investigate the phenotypic and genotypic features of carbapenem-resistant Enterobacteriaceae (CRE) strains isolated from Intensive Care Unit (ICU).

Materials/methods: A total of 107 rectal swabs were collected and cultured in MacConkey broth with meropenem (1µg/ml). Identification and susceptibility testing by disk diffusion method. Carbapenem resistant was confirmed by meropenem and imipenem E-Test. Carbapenemase enzyme production was confirmed by Modified Hodge Test (MHT), Carba-NP, modified carbapenem inactivation method (mCIM) according to the Clinical and Standard Institute (CLSI) guidelines (M100-S27). In-house Real-time PCR was performed to confirm carbapenemase genes (KPC, NDM, VIM, IMP, OXA-48).

Results: Based on phenotypic results, our study depicted that out of the 107 patients screened, 71 patients were found positive for harbouring CRE mainly E.coli (n=30), K.pneumoniae (n=24), Enterobacter spps (n=13), and K.oxytoca (n=4) strains. All isolates were resistant by E-test. Carba-NP test was positive in 62 isolates whereas it was negative in 9 isolates.

Of the 71 isolates analyzed by real-time PCR, 36 isolates expressed blaNDM and 3 isolates expressed blaOXA. Twenty-nine isolates showed co-expression of blaNDM and blaOXA. One showed co-expression of blaNDM and blaVIM. One K.pneumoniae and one K.oxytoca showed co-expression of blaNDM and blaVIM.

The sensitivity of mCIM, CARBA NP and MHT were 100%, 84.5% and 74.6% respectively. mCIM showed higher sensitivity than CARBA NP & MHT. The mCIM assay perfectly correlated with the genotypic findings of the 71 isolates with 100% sensitivity and specificity for CPE detection.

Conclusions: The results of our study show high prevalence of colonization of CPE isolates. The predominant genes harboured by CPE strains were blaNDM and blaOXA. Therefore, CRE should be rapidly determined in high risk patients and strict infection control precautions should be immediately taken to prevent spread of these pathogens.

Also our results showed mCIM is a suitable and reliable method for detecting CPE than CARBA NP and MHT and is an economical alternative to molecular method.

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Diagnostic challenges in Whipple’s disease: an update
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Background: Whipple’s disease (WD) is a rare infection with Tropheryma whipplei that is fatal if untreated. Diagnosis is challenging, and it is based mainly on invasive sampling. We previously reported on a kidney biopsy, where we observed morphologically intact bacteria within the glomerular capsular space and tubular lumen. This lead to evaluation of polymerase chain reaction (PCR) testing of urine as a diagnostic test for WD. Here we give insights into WD using fluorescence in situ hybridization (FISH) and update on the performance of urine testing for the diagnosis of WD.

Materials/methods: In selected cases, we used FISH to localize T. whipplei directly within the patients’ tissue (duodenal biopsies, lymph node, skin, and heart valves). We prospectively investigated urine samples of 25 newly diagnosed and treated WD patients by PCR. As controls, we investigated samples from 110 healthy volunteers and patients with excluded WD or acute gastroenteritis.

Results: Out of 25 urine samples from independent, therapy-naive WD patients, 19 were positive for T. whipplei PCR. In three patients, FISH visualized T. whipplei in urine. All control samples were negative, including those of 11 healthy carriers with T. whipplei-positive stool samples. In our study, the detection of T. whipplei in the urine of untreated patients correlated in all cases with WD. In other specimens, FISH visualized T. whipplei in the intercellular spaces and showed impressive biofilms on heart valves. One case of relapse in T. whipplei endocarditis yielded a mixed infection of the heart valve prosthesis with T. whipplei and Cardiobacterium hominis pointing to insufficient therapy.

Conclusions: We showed that T. whipplei is detectable by PCR in the urine of the majority of therapy-naive WD patients. With a low prevalence but far-reaching consequences upon diagnosis, invasive sampling for WD remains mandatory, but must rely on a strong suspicion. Recent results from the Consilary Laboratory strengthen the approach of urine testing as a novel, easy-to-obtain specimen for guiding the initial diagnosis of WD, in particular in patients with extra-intestinal WD. FISH sheds light on the invasiveness and biofilm potency of T. whipplei.

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Impact of early infectious diseases intervention and microbiologically led antimicrobial therapy in patients with idiopathic granulomatous mastitis

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Background: Idiopathic Granulomatous Mastitis (IGM) is a poorly understood entity defined by the presence of granulomata on histology in the context of mastitis with a reported association with the presence of lipophilic Corynebacterium spp. IGM has a variable response to classical mastitis treatment and optimal management is controversial. We conducted a retrospective review of early specialist infection intervention in a group of IGM patients at our centre.

Materials/methods: We reviewed referrals to our infection service who had a presumptive diagnosis of IGM over a 3 year period. We defined IGM as the presence of at least one of: Gram positive rods on histology, granulomata identified on histology or bacteriological evidence of Corynebacterium spp. Data regarding clinical features, interventions and outcome were collected through case note review.

Results: 13 of the patients referred to our service met our inclusion criteria. The median age of patients at referral to our service was 42.02 years, all patients were female and 1 was HIV positive. The median time between review in breast clinic and review in our Infectious Diseases Service was 47.5 days.

9 patients (69.2%) underwent biopsy of which 7 (77.8%) were granulomatous on histology. 1 patient showed evidence of Gram positive bacilli on histology. Corynebacterium spp. was isolated on culture in 7 cases (53.8%), with 2 further cases identified on 16S rRNA PCR.

Operative drainage of abscess was performed in 7 patients (53.8%), with over half of these (4/7 57.1%) receiving more than one procedure [range 1-7 procedures].

Interventions by the infectious diseases team included extended and sensitivity targeted antimicrobial therapy [12/13 patients, 92.3%], and corticosteroid therapy [7/13 patients, 53.8%]. We will present details of culture results, antimicrobial strategies and steroid management.

At 6 months 11/13 (76.9%) had symptomatically resolved. We will present extended follow up data and treatment response chronologies.

Conclusions: IGM remains a challenging clinical entity to treat and we will present data which inform the management of this condition and demonstrate the impact of early specialist assessment. This will lay the foundation for the development of a multidisciplinary integrated care pathway for this condition.

Antibiotic Initiated on Infectious Disease Review

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Clinical metagenomics next-generation sequencing for diagnosis of suspected clinical infections, a prospective multi-centre cohort study

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Background: Timely and precise pathogen identification is crucial for clinical approaches to infectious diseases. Metagenomics next-generation sequencing (mNGS) is a powerful culture-independent tool for direct microbes detection, and we conducted a multi-center prospective study to set up a standard filter mNGS pipeline and evaluated its clinical diagnostic value in suspected infections.

Materials/methods: 205 clinical samples including bone marrow, plasma, BALF, sputum, CSF, and hydrothorax were used to build the standard pipeline to identify positive mNGS threshold for different pathogens. Then, we prospectively collected 2247 samples and medical data from patients with suspected respiratory, CNS, focal and bloodstream infections between August 2017 to August 2018, from 6 hospitals. Each sample was sent for culture and mNGS synchronously. After nucleic acid extraction and library construction, single-end sequencing was performed on BGISEQ platform and bioinformatics and statistical analysis were conducted.

Results: We generalized standardized mNGS-positive identification cutoff, which achieved 83.4%, 80.0%, 86.8%, 0.945 in accuracy, sensitivity, specificity, and AUC. During clinical evaluation, mNGS detected an overall 1501 pathogenic organisms [54% bacteria, 23% virus, 13% fungi, 7% mycobacteria and 3% parasites]. Top 3 identified bacterias were Klebsiella, Streptococcus, and Acinetobacter, while top 3 identified viruses were Epstein-Barr virus, Cytomegalovirus and Herpes simplex virus 1. Compared to culture, mNGS reported 79.21% in sensitivity and 94.53% of specificity. Compared to clinical diagnosis, extra detection rate of mNGS in culture-negative specimens was 94.25%, 37.60%, 28.10%, and 26.97% in respiratory, focal, CNS and bloodstream infections respectively. mNGS had a higher sensitivity in bacteria than fungi and mycobacteria (80.28% vs 61.54% and 75.00%, P<0.0001). The sensitivity of mNGS in CNS infection was statistically higher than focal and respiratory infection (89.66% vs 81.03% and 68.46%, p<0.05). The average time for mNGS to identify culturable pathogens was within 48 hours, significantly lower than 5.28 days of traditional culture, P<0.0001. Bacteria (excluding Mtb.) and fungi culture took an average of 3.56 and 4.32 days, while culture of Mtb. took 23.24 days, significantly longer than mNGS.

Conclusions: This study demonstrated that mNGS, combined with traditional laboratory methods, may provide a potentially powerful tool in the rapid diagnosis of suspected clinical infections.
Figure 1 A-C. Standardized mNGS-positive identification cutoff set up. A. The rank of mNGS pathogen sample percentage of positive validation for different types of pathogen (Bacteria, Virus, Fungi, Mycobacterium). B. The receiver operating characteristic (ROC) curve (blue line) of mNGS pathogen identified for all validated positive and negative samples. C. Pathogen identification efficiency evaluation for different type of samples. AUC: Area Under Curve. D. The diagnostic ability of mNGS and culture for different pathogens. E. The diagnostic sensitivity of mNGS in different types of pathogens among different types of samples and infections. F. Time to diagnosis by traditional culture and mNGS infections.

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Why don’t hospital prescribers stop antibiotics when it would be safe to do so? Results of a discrete choice experiment

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Abstract third-party references: The study is funded by the National Institute for Health Research (NIHR) Programme Grants for Applied Research (Grant Reference Number RP-PG-0514-20015).

Background: Early antibiotic prescription review is a cornerstone of hospital antimicrobial-stewardship practice worldwide. The ability to decide whether to continue or rationalize antibiotics at the time of review is a key competency for hospital prescribers. In England this approach is set out in government guidance (“Start Smart then Focus”) but in reality <10% of hospital empiric antibiotic prescriptions are discontinued at review, despite evidence that 20-30% could be discontinued safely. We have quantified the factors that influence prescriber decision-making in this situation.

Materials/methods: We conducted an online choice experiment, a survey method for eliciting preferences for alternative healthcare options. Prescribers working in acute/general hospital medicine in England were asked whether they would continue or discontinue antibiotic-treatment in 15 hypothetical scenarios. Scenarios were described in terms of six attributes, including patient presenting symptoms and whether antibiotic discontinuation would conflict with local guidelines. Respondents’ choices were analysed using conditional fixed-effects logistic regression.

Results: 100 respondents completed the survey. Respondents were more likely to continue antibiotics when discontinuation would ‘strongly-conflict’ with local guidelines [average marginal effect (AME) on probability of continuing 0.194 (p<0.001) relative to ‘no-conflict’]; when presenting symptoms more clearly indicated antibiotics [AME of typical symptoms of urinary tract infection 0.173 (p<0.001) relative to unclear symptoms]; and when patients had severe frailty and comorbidities [AME=0.101 (p<0.001) relative to patients previously fit and well]. Respondents were less likely to continue antibiotics when there was no external pressure to continue [AME=-0.101 (p<0.001) relative to heavy pressure]. Decisions were also influenced by the competing risks of continuing treatment (e.g. antibiotic resistance) [AME of 1% higher risk -0.013 (p<0.001)] versus discontinuing (e.g. treatment failure) [AME of 1% higher risk 0.026 (p<0.001)]. Respondent feedback also highlighted that perception of treatment response influences decision making at antibiotic review.

Conclusions: Antibiotic guidelines that conflict with empiric antibiotics being discontinued at review (e.g. by pre-specifying durations) may be a major barrier to prescribers stopping antibiotics at review. Making guidelines less prescriptive about duration, but conditional on patient factors and treatment response, could help prescribers discontinue antibiotics in hospitalised patients as diagnostic information suggesting they are no longer indicated becomes available.

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**Abstract 7889**

**Outbreak of cryptosporidiosis among responders to a rollover of a truck carrying calves: Normandy, France, October 2019**

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**Background:** In October 2019, the Fire and Rescue Center medical Officer of Neufchatel (Normandy, France) notified the French CNR-Laboratoire Expert Cryptosporidioses of one case of cryptosporidiosis among emergency responders to a tractor-trailer rollover. On 1st of October, the truck was carrying approximately 140 two week old calves that were not reportedly suffered from diarrheal disease.

**Materials/methods:** An outbreak investigation was led. A case was defined as a person with diarrhea, or at least two of the following symptoms: vomiting, nausea, abdominal pain, fever, or identification of Cryptosporidium in a stool sample; and onset of symptoms up to two weeks after the intervention. DNA was extracted from stools and PCR was performed to identify Cryptosporidium sp., C. hominis and C. parvum.

**Results:** Nine cases of cryptosporidiosis were identified among the 11 individuals who entered the trailer to evacuate calves. The median incubation period was 7 days [3-15]. Nine (100%) individuals reported diarrhea and abdominal pain, 3 (33%) reported vomiting. Four had to stop or significantly reduce work for at least one day. The median duration of illness was 2 weeks [1-3]. PCR analysis revealed presence of Cryptosporidium DNA in 8 out of 9 stools tested and sequencing of the hypervariable gp60 gene of isolates revealed the parasite responsible as C. parvum, strain Ilia15G2R1. One proved and two probable secondary cases were identified.

**Conclusions:** Disease was associated with carrying calves and contact with fecal matter. Because of the age of the calves and the conditions at the rollover scene, a high potential existed transmission of Cryptosporidium. The same C. parvum Ilia15G2R1 subtype, the most commonly genotype detected in calves in Normandy, was found in stool samples which supports a transmission of Cryptosporidium attributed solely to direct contact with animals and their feces. This is the first report in France of emergency responders contracting cryptosporidiosis. Cryptosporidiosis resulting from contact with animals during an emergency response might be minimized if 1) people are aware of potential zoonotic transmission, 2) education is provided on proper animal handling with appropriate protective equipment, and 3) thorough hand hygiene and clothing decontamination following contact with feces are practiced.

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Abstract 7891

**Early cytomegalovirus reactivation and bacterial infections affect the mortality of patients after kidney transplant**

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**Background:** Kidney transplant (KT) recipients are prone to develop bacterial infections (BIs) and Cytomegalovirus reactivation (CMVr). Here we report a single-centre real-life experience of a cohort of KT recipients followed up after renal transplant.

**Materials/methods:** A single-centre retrospective study including patients undergoing KT between 2012 and 2016 was performed. Infectious complications [BIs and CMVr], were recorded during an observation period of 6 months after kidney replacement. Statistical analysis was performed using GraphPad Prism ver. 6.0.

**Results:** 191 (124 males, 66%) CMV seropositive KT recipients were enrolled, with a median age of 54 years (range 19-75). CMVr and BIs occurred in 92 (48.2%) and 41 (21.5%) patients, respectively, during the six-month observation period after KT. BI episodes were associated to CMVr, considering that 31/92 patients in the CMVr group compared to 10/99 in the non-CMVr group had BI (Chi-Squared test p <0.001). Considering all the BI episodes, Gram negative isolates were more frequent than Gram positive, without any statistically significant difference between CMVr and non-CMVr groups (25 vs 6, and 9 vs 1, respectively).

Overall mortality was assessed and associated to CMVr and BIs. Globally, patients with BIs showed an increased mortality compared to patients who did not experience BIs (7/41 vs 6/150, respectively; Chi-Squared test p= 0.003). After stratifying patients in CMVr and non-CMVr, BIs were associated to increased mortality in the CMVr group only (6/31 vs 3/61, respectively; Chi2 test p= 0.028), while no differences in mortality were found in the non-CMVr group after comparing patients with and without BIs.

**Conclusions:** In our cohort of KT recipients CMVr was associated to bacterial infections. The occurrence of both infectious complications in the six months after kidney replacement seems to increase the overall mortality. Larger studies addressing the interactions between bacterial infections and CMVr should be performed in KT recipients, in order to understand the causal and temporal relationship of these two infectious complications.

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Abstract 7893

**Studying the association of the human vaginal microbiome with HPV infection using enriched metagenomic sequencing**

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**Background:** We investigated the association of the vaginal microbiome with human papillomavirus (HPV) infection in young women participating in a HPV vaccine monitoring study using metagenomic sequencing enriched for HPV.

**Materials/methods:** Cervical samples were analysed from seven hundred twenty-nine women (mean age 22.4 y) participating in a HPV vaccine monitoring program who also filled in a questionnaire. DNA extracts from ThinPrep underwent rolling circle amplification (RCA) to amplify circular DNA aiming for HPV and sequenced on Illumina MiniSeq. Quality checked reads were filtered by mapping to the human reference genome. Samples were considered positive for an HPV genotype if concordantly mapping paired reads covered at least 100bp of a HPV reference genome. Taxonomic assignment was performed by mapping remaining reads via Bowtie2 against an in-house compilation of bacterial NCBI reference of complete genome sequences. For each sample, bacterial genera were reported if at least 10 reads were assigned to the respective reference genomes. Samples with >1000 bacterial reads were considered for further analysis (N=591). Alpha diversity was calculated using the Shannon diversity index. Beta diversity was calculated by computing pairwise Bray-Curtis distances between samples. Inter-sample distances in beta diversity were linked to metadata-derived groups using PERMANOVA.

**Results:** Overall, 72.1% reads mapped to human, 3.8% to bacteria, 1.1% to HPV and 0.005% to fungi. A substantial proportion 332/729 (45.5%) were HPV positive. Cluster analysis identified two main bacterial community clusters, Lactobacillus and Gardnerella genera dominant in 67% and 30% of the samples, respectively (Fig 1). Difference in beta diversity is associated with nationality (Luxembourgish, Portuguese and other migrants), but not by HPV status, abnormal cytology, condom use, smoking status, age and sexual behaviour. The alpha diversity was significantly higher for participants of non-Luxembourgish nationality and smokers.

**Conclusions:** Our results suggest that RCA enriched metagenomic sequencing has the potential to characterize both the bacterial cervical microbiome and HPV, but not fungi. As the RCA enrichment may introduce some bias, further investigation is required to compare this approach with both targeted 16S sequencing and direct shotgun sequencing.

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Nasal microbiota: is it the war between staphylococci and corynebacteria?

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Abstract third-party references: This research was promoted and has been funded by the University Hospital of St-Etienne.

Background: *Staphylococcus aureus* (SA) nasal carriage is a well-recognized risk factor of infection with this bacterium. Nasal decolonization procedures help in reducing this risk, with the risk of emergence of antibiotic resistant strains. We aimed to characterize the microbial communities associated with SA carriage at 3 nasal sites, in order to uncover antagonistic interactions between SA and other bacteria of the nasal flora that might be used to prevent or eliminate SA colonization.

Materials/methods: 15 SA carriers and 15 matched non-carriers, were sampled at 3 nasal sites (vestibule, spheno-ethmoidal recess, nasopharynx) by an otolaryngologist specialist. 16S rDNA V3 PCR and Ion Torrent PGM sequencing were performed. Reads were filtered with BBduk and VSEARCH, then BLASTn aligned to the NCBI 16S database with 16S-copy number normalization. Species-level resolution of taxonomies was refined using an in-house algorithm. Alpha- and beta-diversities were compared across sites and depending on the presence of SA. Indicator species were characterized using Linear discriminant analysis Effect Size (LEfSe).

Results:

Comparison between sites: Alpha- and beta-diversity indices were similar across the 3 nasal sampled sites, with the exception of a higher Shannon index-based diversity in vestibule samples\((p<0.05,\) Mann-Whitney test). LEfSe analysis showed an increase of *Propionibacteriaceae* in the vestibule and the recess, while *Streptococcaceae* and *Prevotellaceae* were mostly found in the nasopharynx.

Comparison depending on SA carriage: Shannon and Simpson alpha-diversity measurements showed a significant increase in diversity in SA carriers compared to non-carriers after exclusion of SA reads, but not by keeping SA reads. These results suggest that SA is a major factor in the stability of the community. Beta-diversity PCoA profiling suggests that both carrier groups differ significantly with and without SA. Based on LEFSE analyses, several *Corynebacterium* species were discriminant in non-carriers while non-*aureus* staphylococci were associated to SA carriage.

Conclusions: This study brings new insights into the microbial communities colonizing various nasal sites. Results point towards a war between staphylococci and corynebacteria when SA is involved, suggesting antagonistic relationships. The role of corynebacteria as SA competitors should be further examined to determine if corynebacteria nasal inoculation can prevent or displace SA colonization.

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Abstract 7897

The growth dynamics of *Pseudomonas aeruginosa* isolated from peritoneal fluid, blood and homogenates of the organs of septic mice

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Background: To detail the patterns of development of sepsis, taking into account the increased etiopathogenetic role of *P. aeruginosa*, it is important to study the dynamics of the spread of the pathogen in the body.

Materials/methods: For sepsis modeling, we used strain *P. aeruginosa* 1623 isolated from bronchial flushing of a patient under cystic fibrosis and cultivated on Columbia agar. 42 male C57Bl/6 mice were administered intraperitoneally at a dose of $7 \times 10^6$; 3 control animals were injected with saline. Infected animals were opened 15, 30, 60, 120, 180, 240, and 480 min after infection. Samples weighted, homogenates in porcelain mortars, cultured on Columbia agar, calculated of CFU and logarithmized. Throughout the experiments, the animals were processed according to the ethical guidelines for the care of laboratory animals.

Results: 15 minutes after infection, seeding of *P. aeruginosa* 1623 from peritoneal fluid was $1.34 \times 10^5$ CFU / ml (lg5.13); while CFU from the blood increased from 0 to $2.01 \times 10^4$ CFU (lg4.3). By 15-30 min, the level of seeding of the pathogen from the peritoneal fluid was maintained and a slight increase in seeding from the blood was recorded. Seeding from liver homogenates sharply increased - $2.85 \times 10^6$ CFU (lg6.45); from kidneys - $2.04 \times 10^6$ CFU (lg6.31); from lungs - $4.24 \times 10^5$ CFU (lg5.63); from spleen - $8.3 \times 10^5$ CFU (lg5.92). From 60 to 120 minutes, pathogen seeding rates from organs decreased slightly, although it remained at a sufficient level. By 240 min, the number of CFU from liver, spleen and kidney decreased, and remained almost unchanged in the lungs. A new rise in the CFU of the pathogen from the blood and a small increase in CFU from the peritoneal fluid were recorded.

Conclusions: Analysis of the growth of *P. aeruginosa* 1623 during the first 480 minutes of the development of sepsis was revealed a chronological vector of the spread of the pathogen in the body and of its potential reproduction in the studied organs.

**Diagram:**

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Activity of imipenem-relebactam against Enterobacterales and Pseudomonas aeruginosa isolates collected in Latin America and Brazil from 2017-2018: results from the Study for Monitoring Antimicrobial Resistance Trends [SMART]

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Background: In Latin America, especially Brazil, Gram-negative bacterial (GNB) infections are increasingly difficult to treat due to antimicrobial resistance. imipenem-relebactam (IMI/REL) is a β-lactam/β-lactamase inhibitor combination with activity against carbapenem-resistant Enterobacterales. The Study for Monitoring Antimicrobial Resistance Trends [SMART] evaluates the in vitro activity of various Gram-negative antimicrobial agents since 2002 and includes IMI/REL since 2015. We compared the activity of IMI/REL against clinical isolates, focusing on Enterobacterales and Pseudomonas aeruginosa, collected in LATAM from 2017-2018.

Materials/methods: 13,843 Gram-negative bacterial isolates including Acinetobacter baumannii, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa and other Enterobacterales from 36 sites in LATAM (08 Brazilian) were collected in the period. Samples were consecutive and non-duplicated; each site collected up to the indicated number of isolates in 2017/2018 from lower respiratory tract infections (RTI), complicated urinary infections (cUTI), complicated intra-abdominal infections (cIAI) and blood. Minimum inhibitory concentrations were determined by broth microdilution for several antibiotics including ceftolozane-tazobactam, colistin, imipenem-relebactam and meropenem. Antimicrobial susceptibility results were interpreted by CLSI criteria and molecular resistance mechanisms were also evaluated.

Results: 46% of isolates came from RTI and blood. Among Brazilian centers, E. coli (N=537), K. pneumoniae (N=423), P. aeruginosa (N=353), P. mirabilis (N=110), S. marscenses (N=107) and A. baumannii (N=101) were the 6 most prevalent pathogens isolated. Susceptibility to imipenem-relebactam ranged from 41.8% to 100%. Susceptibility of K. pneumoniae to imipenem-relebactam was 96.9% (MIC50/90 0.25/1 µg/mL). For E. coli, imipenem-relebactam inhibited 100% (MIC50/90 0.12/0.25 µg/mL) of the microorganisms. The susceptibility to IMI-REL of P. aeruginosa, P. mirabilis, S. marscenses and A. baumannii was 87.3% (MIC50/90 0.5/4 µg/mL); 41.8% (MIC50/90 2/4 µg/mL); 72.8% (MIC50/90 1/2 µg/mL); and 14.9% (MIC50/90 >32/>32 µg/mL), respectively. An analysis was performed to describe the profile of resistant mechanisms in 432 isolates. From which KPC-producing K. pneumoniae were 67% from 209 analyzed isolates. The majority of IMI/REL-non susceptible isolates were ENT class B (metallo beta-lactamase) and class D (OXA-48 like) producers.

Conclusions: Imipenem-relebactam has shown relevant activity against a variety of the analyzed microorganisms, especially KPC-producing K. pneumoniae, collected from multiple LATAM centers, showing it is an option for addressing infections caused by MDR strains.

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Genetic relatedness, antimicrobial resistance, virulence and biofilm-forming abilities of Klebsiella pneumoniae from healthy broilers and turkeys

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Background: Klebsiella pneumoniae (Kp) belongs to the ESKAPE pathogens, which are important causes of nosocomial infections. Kp is a well-studied human pathogen and antimicrobial resistant high-risk clones and hypervirulent clones have emerged globally. Kp is also present in a variety of environmental niches, but currently there is a lack of knowledge on the occurrence and characteristics of Kp from non-human sources. Certain environments may be associated with high Kp abundance and Kp in these niches may constitute a reservoir for further transmission of strains and genetic elements. The aim of this study was to explore and characterize Kp from healthy broilers and turkeys.

Materials/methods: A total of 565 faecal samples [broiler n=404, turkey n= 161], included in the Norwegian monitoring program on antimicrobial resistance in the veterinary sector [NORM-VET] in 2018, were screened for Kp by culturing on SCAI agar. Susceptibility testing was performed using disc diffusion (EUCAST) and the isolates ability to produce biofilm was investigated in a crystal violet microtiter plate assay. All Kp isolates (n=203) were whole genome sequenced and genomes were analysed using bioinformatic tools.

Results: A total of 203 (36%) samples were Kp positive; 70% of the samples from turkey and 24% of the samples from broiler. The overall antimicrobial resistance occurrence was low, with 23 (11%) isolates [17 turkey, 6 broiler] showing resistance, mainly against tetracycline and sulfamethoxazole. The 203 isolates grouped into 64 different sequence types (STs), with ST35 identified in 14% and ST290-LV in 7% [figure]. Forty-three different capsule types were identified. Plasmid (IncFII) mediated virulence genes iuc5 and iro5 encoding siderophores were identified in 15 clonal ST290-LV from turkey. Chromosomally encoded yersiniabactin (ybt) was found in 13 of the ST290-LV isolates. Isolates from both poultry species displayed good biofilm forming abilities with an average of OD595 0.69 and 0.64.

Conclusions: Detection of Kp was significantly higher in samples from turkey, than broilers. The overall antimicrobial resistance occurrence among Kp from Norwegian poultry was low. Plasmid-located and chromosomal virulence genes encoding siderophores were detected in some isolates. High genetic diversity was found with some STs overlapping with STs commonly described from humans.

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Abstract 7900

**blaCTX-M-55/mcr-1/IncHI2 plasmids in Escherichia coli from foodstuffs in Tunisia**

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**Background:** Antimicrobial resistance (AMR) in bacteria represents one of the most important challenges for public health worldwide. As such, plasmid spread of resistances to broad-spectrum cephalosporins and colistin in foodborne zoonotic Gram-negative bacteria of animal origin is of concern. The objective of this study was to characterize mcr-1/ESBL plasmids in Enterobacterales recovered from foodstuffs in Tunisia.

**Materials/methods:** From March to June 2017, 148 cefotaxime-resistant Gram-negative bacteria were isolated on selective medium from 100 food samples (raw milk, chicken meat, beef minced meat and merguez). Antimicrobial susceptibility was performed by disc diffusion and the mcr-1 gene was specifically searched by PCR and sequencing within this collection. Plasmids were characterized by rep-typing (Diatheva) and Southern blot on S1-PFGE gels. Clonality was assessed by XbaI-PFGE and phylogrouping.

**Results:** The collection comprised 80 Escherichia coli, 20 Klebsiella pneumoniae and 16 Enterobacter cloacae cefotaxime-resistant isolates. The mcr-1 gene were detected in 9 E. coli isolates (11.3%) from chicken meat, merguez or minced meat, together with blaCTX-M-1 (5 isolates) and blaCTX-M-55 (4 isolates) and among diverse E. coli genetic backgrounds. Notably, mcr-1 was co-harbored with blaCTX-M-55 on IncHI2 plasmids. All mcr-1-positive E. coli isolates were multdrug resistant, exhibiting resistances to common antimicrobials such as tetracyclines, florfenicol, sulfonamides or fluoroquinolones.

**Conclusions:** It is the first report of mcr-1-positive E. coli in meat at retail in Tunisia. More importantly, the co-occurrence of mcr-1 and blaCTX-M-55 on IncHI2 plasmids in meat is reminiscent of previous data obtained in our country where mcr-1/bluCTX-M genes were also identified on IncHI2 plasmids in livestock. Work is in progress to further characterize those plasmids using advanced NGS technologies. Those data highlight the wide spread of mcr-1 in the food chain in Tunisia, most likely through dominant ESBL plasmids, which is of major importance for public health.

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Abstract 7902

**Exploring posaconazole pharmacodynamics against Candida krusei isolates: determination of EUCAST PK/PD susceptibility breakpoints**

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**Background:** Posaconazole has some activity against the intrinsically fluconazole resistant species C. krusei, however, paucity of clinical data prohibit establishment of clinical breakpoints. We assessed the pharmacodynamics of posaconazole in an in vitro pharmacokinetic/pharmacodynamic (PK/PD) dilution model and determined EUCAST PK/PD susceptibility breakpoints for the available posaconazole formulations.

**Materials/methods:** Three clinical C. krusei isolates (EUCAST posaconazole MICs 0.03, 0.06 and 0.25 mg/L) were tested in a one compartment in vitro PK/PD dilution model using a 10⁴ CFU/mL initial inoculum. Steady state posaconazole serum concentration-time profile of 400 mg b.i.d. was simulated for 48h with fCmax 0.15, 0.85, 2.25 and 5 mg/L and with t1/2=36 h. The 48h log₁₀ CFU/mL - fAUC₀-2⁴/MIC relationship was analyzed with the Emax model and the exposure associated with 50% of maximal activity (EI₅₀) was determined. The probability of attaining the EI₅₀ was calculated with Monte Carlo analysis for isolates with EUCAST MICs 0.015-4 mg/L in patients treated with 400 mg oral posaconazole b.i.d. (Ullmann et al, AAC 2006) or 300 mg tablet/i.v. posaconazole o.d. (Duarte et al, AAC 2014, Maertens et al, AAC 2014) attaining tAUC₀-2⁴ of 17.15±14.71 and 34.17±14.68 mg.h/mL, respectively, adjusted for fAUC based on the 99% protein binding

**Results:** Posaconazole reduced >1 log₁₀ the fungal burden of isolates with MIC 0.03 and 0.06 mg/L at fCmaxs ≥0.85 mg/L whereas the same effect was observed for the isolate with MIC 0.25 mg/L only at fCmax 5 mg/L. The in vitro PK/PD relationship followed a sigmoid curve (R²=0.96) with a mean (95% CI) EI₅₀ of 31 (18-52) fAUC/MIC. Monte Carlo showed that the PTA for C. krusei isolates with MICs ≤0.125, 0.25, 0.5, 1 and ≥2 mg/L were 96%, 76%, 46%, 13% and <2% for the oral formulation and 100%, 100%, 96%, 51%, and <4% for the tablet/i.v formulation, respectively.

**Conclusions:** The PK/PD susceptibility breakpoints 0.125 and 0.5 mg/L was determined for the oral and tablet/i.v. formulations of posaconazole, respectively. Given the corresponding EUCAST epidemiological cutoff value [ECOFF 0.5 mg/L], posaconazole tablet/i.v. may be used for the treatment of C. krusei infections provided that adequate exposure is attained.

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Abstract 7904

**Mycoplasma genitalium: evaluation of macrolide resistance in a very large setting of sexually-transmitted infections**

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**Background:** *Mycoplasma genitalium* (MG) is a slowly growing microorganism causing inflammation of the urogenital tract. Azithromycin is the most used antibiotic, nevertheless a recently increased number of treatment failure was observed. Macrolide resistance is associated to single nucleotide mutation on gene 23S rRNA. The aim of this project was a retrospective evaluation of macrolide resistance on positive samples for *M. genitalium* on our population.

**Materials/methods:** From 15th March 2018 to 15th November 2019, samples positive for MG were assessed with Anyplex II STI™ (Seegene). Results were confirmed with STI PLUS ELItE MGB® kit and with Macrolide-R/MG ELItE MGB® kit (detection of A2058C, A2058G, A2058T, A2059G, A2059C mutations) on ELItE InGenius platform (ELITechGroup S.p.A.).

**Results:** 4100 samples were analysed for sexual transmitted infections: 2940 were negative, whereas 1160 were positive for at least one pathogen. The most commonly isolated microorganisms was *U. parvum* in 17.1% (701) samples, followed by *U. urealyticum* 7.98% (327), *M. hominis* 4.9% (201), *C. trachomatis* 1.9% (78), *N. gonorrhoeae* 1.05% (43), *M. genitalium* 0.95% (39), and *T. vaginalis* 0.93% (38). The 39 positive samples for MG were urine 56.4% (22), anal swab 20.5% (8), uretral swab 7.7% (3), cervical swab 10.3% (4), vaginal swab 2.6% (1) and one fetal placenta 2.6%, belonging to 34 patients: 70.6% (24) were males, 23.5% (8) were females and 5.9% (2) were transgender. Among them, 55.9% (19) declared at risk sexual intercourses; 35.3% (12) were symptomatic, 5.9% (2) were controlled for sterility problems and 2.9% (1) had a corioamnionitis. Regarding the sensitivity to macrolide, 52.9% of strains (18) were sensitive, while 47.1% (16) were resistant. Among the latter, 43.7% (7) belonged to symptomatic patients; 56.3% (9) had at risk sexual intercourses.

**Conclusions:** *M. genitalium* shows a low prevalence (0.95%), among patients tested for sexually transmitted infections, but remarkably high level of macrolide resistance (47.1%). Since azithromycin is the first choice of empirical treatment in Italy also for *C. trachomatis*, the spreading of MG strains resistant to macrolides may further increase in the following years. Hence, multicenter studies aimed at the national evaluation of resistance of MG to macrolides is warranted.

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Changes in epidemiology, treatment and outcomes of candidaemia at a tertiary care children’s hospital

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Background: Candidemia, a serious infection in hospitalized children, is associated with significant morbidity and mortality. Highest incidence is reported in premature neonates (premie). *C. albicans*, consistently sensitive to fluconazole, has been the most common species. Infection prevention measures to reduce central line infections (CLABSI) were implemented widely. Resulting epidemiologic changes may impact prevention and treatment.


Results: 195 (133 and 62) subjects had 233 (154 and 79) candidaemia episodes (periods 1 and 2 respectively); overall rate per 1000 discharges decreased between periods (-52.5%; 1.98 to 0.94); rate decrease was larger in premie (-61.5%) than oncology (-37.5%). Comparing period 1 with period 2 respectively; intestinal failure (IF) occurred in 28.6% and 69.4% of subjects; *C. albicans* (37.7% to 28.1%) and *C. parapsilosis* (33.1% to 28.1%) decreased while *C. glabrata* (11.7% to 12.2%) and *C. krusei* (3.3% to 6.1%) increased; fluconazole MIC (mcg/ml) 50 and 90 (1 and 16 in each period) remained constant while % sensitive (MIC < 4) decreased (84% to 76.8%) and mortality increased (19.5% to 25.8%). End organ involvement was identified in 32 (19.2%) of 167 events with metastatic evaluation. Micafungin (98), fluconazole (62) or the combination (41) were most common antifungal agents used for initial treatment. Temporary renal and liver toxicity was common. (table)

<table>
<thead>
<tr>
<th>Initial</th>
<th>Maximum</th>
<th>Final</th>
<th>Initial vs Maximum</th>
<th>Initial vs Final</th>
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<tbody>
<tr>
<td>Creatinine</td>
<td>0.33(0.27 – 0.6)</td>
<td>0.5(0.38 – 0.8)</td>
<td>*</td>
<td>- 5/33 (p&lt;0.05)</td>
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<tr>
<td>AST</td>
<td>45(30 – 87)</td>
<td>87(57 – 166)</td>
<td>45(31 – 77)</td>
<td>- 7.48 (p&lt;0.001)</td>
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<tr>
<td>ALT</td>
<td>42(24 – 83)</td>
<td>91(46 – 149)</td>
<td>45(29 – 80)</td>
<td>- 6.79 (p&lt;0.001)</td>
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<tr>
<td>Bilirubin</td>
<td>0.9(0.5 – 2.1)</td>
<td>1.4(0.8 – 3.9)</td>
<td>0.7(0.4 – 1.8)</td>
<td>- 4.79 (p&lt;0.05)</td>
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Median [1 – 3 quartile]. Comparison sum rank by Mann-Whitney
* Not enough had final creatinine measured.

Conclusions: CLABSI reducing measures substantially decreased candidemia incidence, particularly in premie, yet candidemia associated mortality increased. IF emerged as a common comorbidity in these patients. Non-albicans Candida species increased, particularly fluconazole resistant ones; > 25% have elevated MIC or are fully fluconazole resistant impacting future treatment options. Fluconazole and micafungin are well tolerated. Evaluation for end organ involvement is important.

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Development of bovine herpesvirus 4-based vaccines as an antibiotic-free strategy to control bacterial infection in livestock

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Abstract third-party references: Dr Michael Jarvis, The Vaccine Group, Plymouth

Background: Bovine herpesvirus 4 (BoHV-4) is a benign gamma-herpesvirus common across multiple ruminant species that is being developed as a vaccine vector platform. BoHV-4 has been shown to induce high levels of durable antibody and T cell immunity against encoded heterologous pathogen target antigens, in many cases, following only a single dose. Unlike many other vaccine platforms, DNA encoding multiple target antigens can also be inserted into a single BoHV-4 vector and prior immunity does not prevent reuse. Deletion of ORF73, a gene required for persistence of BoHV-4 in the host, provides an additional level of safety without impacting immunogenicity. Herpesvirus-based vaccines are also inexpensive to produce, with a related commercial vaccine (Bovilis IBR) being marketed at £3/dose wholesale. For many bacterial diseases in livestock there are either no vaccines available or they induce suboptimal protection and require multiple rounds of vaccination.

Materials/methods: Our strategy is to use the BoHV-4 vaccine vector platform to reduce the occurrence of antimicrobial resistance (AMR) by stimulating the host immune system against these difficult to control bacterial infections, thereby decreasing the need for antibiotics. Target pathogens include Streptococcus suis, bovine tuberculosis (bTB) and mastitis caused by E. coli, all of which are high priority vaccine targets. It will also be possible to develop vectors targeting currently unknown bacterial diseases through this pipeline as they emerge.

Results: BoHV-4 prototype vectors expressing target antigens from these three bacterial pathogens were constructed. Following complete in vitro characterization, these vectors were tested in a rabbit model, and shown to induce antibody responses against the targeted pathogen. In future work, we will determine the impact of this immunity on replication and viability of the bacteria in vivo.

Conclusions: We propose that BoHV-4 based vaccines targeting these key livestock bacterial pathogens will provide an additional means by which antibiotic usage can be reduced in these agricultural animals to decrease the incidence of antimicrobial resistance and prevent spread of antibiotic resistant strains into the human population.

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Abstract 7911

Procalcitonin serum concentration is higher in patients with meningococcal meningitis and/or invasive diseases: the MeningItaly study, preliminary results

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Background: Meningitis and related invasive bacterial diseases (IBD) are life-threatening infections with severe morbidity and mortality. Recently, several outbreaks of meningococcal meningitis were reported from different countries and Italy too. Procalcitonin (PCT) is a marker of systemic bacterial infection. Thomas-Ruddel et al (Critical Care, 20018) described the possibility that PCT levels could be associated to specific pathogens and foci of infection. The aim of the present study is to evaluate this possible association in patients with meningitis and IBD.

Materials/methods: All patients with meningitis or IBD due to S. pneumoniae (SP), N. meningitidis (NM) and L. monocytogens (LM) previously enrolled in the MeningItaly study were considered. The MeningItaly study is a prospective observational multicentric study on epidemiology, clinical, laboratory and microbiologic characteristics and therapeutical approaches in patients with meningitis and/or IBD; it involved 11 centres in Italy.

Results: We enrolled 151 patients; 128 patients had an infection due to SP, NM or LM. Table 1 report on the main characteristic of the study population. In particular, NM is associated with higher PCT levels (mean 35 for NM, vs 9.25 for SP and 4.25 for LM), less comorbidity – described as Charlson comorbidity index – and younger patients.

Conclusions: PCT serum concentration is significantly higher in patients with NM meningitis invasive infections than in patients with SP or LM infections. This finding could be useful to quickly hypothesize NM etiology and, as a consequence, to start appropriate therapies and public hygiene measures.

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<tr>
<th>Study population</th>
<th>LM</th>
<th>NM</th>
<th>SP</th>
<th>P</th>
<th>P_LM,NM</th>
<th>P_LM,SP</th>
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<td>Charlson Comorbiditù Index</td>
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<td>Procalcitonin</td>
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<td>C-RP (mg/dl)</td>
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<td>SOFA score</td>
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<tr>
<td>mortality</td>
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Usefulness of flow cytometry as a screening technique in the detection of bacterial vaginosis and vaginitis

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Background: Vaginal symptoms are typical and common in the general population and about 30% of women with complaint of vaginal discharge or irritation remain undiagnosed despite extensive testing. The most common causes of vaginitis/vaginosis are bacterial vaginosis (BV), vulvovaginal candidiasis (VVC), and trichomoniasis. BV is the most common cause of vaginal discharge in reproductive-aged women. VVC is the second most common cause of vaginitis in reproductive-aged women. Gram stain and culture are conventional methods for diagnosis BV/VVC but they are time-consuming methods. Automated molecular methods have been introduced to increase sensitivity and facilitate workflow. Flow cytometry is frequently used in the screening of urine samples and other biological samples. Our objective has been to implement flow cytometry in BV/VVC screening.

Materials/methods: Five-hundred-fifty-four vaginal samples from patients with symptoms of BV/VVC were collected in liquid transport medium (ESwab, Copan). The samples were processed by microscopy, culture, and realtime PCR (BDMax Vaginal Panel, Becton Dickinson). Previously, all the samples were analysed by cytometry (UF4000, Sysmex) for the detection of bacteria, yeast, epithelial and inflammatory cells per microliter.

Results: Realtime PCR were positive in 158 samples for BV (28.5%), 183 for VVC (33.0%), and 14 (2.5%) for trichomoniasis. Sixteen samples were positive for bacterial vaginosis and vaginal candidiasis. The samples positive for BVs were a median of 39029.9 bacteria/μl with an AUC of 0.727. The cutoff value was 8965.5 bacteria/μl for 85% and 42.7% of sensitivity and specificity respectively. In samples positive for VVC we found a median of 435.3 yeast/μl with an AUC of 0.717. The cutoff value was 117.4 yeasts/μl for 85% and 37.9% of sensitivity and specificity respectively.

Conclusions: The results show that the BV samples have a higher bacterial count than the samples in which VVC is detected and the negative samples. On the other hand, in VVC samples, cytometry detects, in addition to a greater number of yeasts, as the inflammatory status is reflected by the presence of a greater number of leukocytes and squamous cells. These preliminary data show that flow cytometry could be a quick and inexpensive screening technique to detect situations of vaginosis and vulvovaginitis.

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Evaluation of the FluoroType mycobacteria assay for the detection and differentiation of clinically relevant mycobacteria
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Background: The genus Mycobacterium includes many species that can be divided into three large groups: i) Mycobacterium tuberculosis complex (MTBC) causing tuberculosis which is one of the major health problems worldwide, ii) Mycobacterium leprae; iii) non tubercular mycobacteria (NTM), environmental opportunistic pathogens frequently associated with human diseases.

In the last few years, infections caused by NTM have been steadily increasing in western countries, while tuberculosis is more prevalent in low-income countries.

In order to limit the diffusion of mycobacterial infections, specific and rapid diagnostic methods for detection of MTBC and NTM are urgently needed.

The aim of this study was to evaluate the novel FluoroType Mycobacteria assay (FTMA) (Hain, Germany), a rapid molecular method based on the innovative LiquidArray technology, which allows detection of MTBC and differentiation of most relevant clinical NTM in only one tube.

Materials/methods: FluoroLyse DNA extracts of 43 positive liquid cultures, inactivated at 95°C for 30 min, were tested with the FTMA on the FluoroCycler XT. The results, obtained within 2.5 hours (handling and analysis time included), were compared with routine diagnostic methods - GenoType Mycobacteria CM/AS, GenoType NTM-DR, and/or genetic sequencing.

Results: The FTMA identification of 39 NTM (4 Mycobacterium abscessus abscessus, 4 Mycobacterium abscessus bolletii, 4 Mycobacterium abscessus massilense, 5 Mycobacterium avium, 2 Mycobacterium chelanae, 2 Mycobacterium chimaera, 2 Mycobacterium fortuitum, 5 Mycobacterium xenopi, 4 Mycobacterium intracellulare, 3 Mycobacterium gordonae, 1 Mycobacterium kansasii, 2 Mycobacterium malmoense) resulted identical with reference diagnostic methods, while Mycobacterium flavescens and Mycobacterium arupense were not identified at the species level (but only as Mycobacterium spp.), due to database limitations. Moreover, the new method detected the presence of two MTBC in accordance with reference methods.

Conclusions: The FTMA showed to be a powerful tool for automated detection of mycobacteria, correctly identifying 39 clinically relevant NTM and 2 MTBC from liquid culture in 2.5 hours. Testing of additional samples is in progress, with simplified extraction protocol in order to confirm the performance of this novel technology.

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Abstract 7919

**Extended-spectrum β-lactamase in Escherichia coli and Klebsiella pneumoniae of chicken meat in butchers in Algeria, with detection of ESBL-CTX-M-55 and E. coli-B2/ST131**

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**Background:** ESBL constitute a mechanism of resistance of great clinical relevance that is spreading not only in the human niche but also among food-producing animals and derived-food. This study was designed to determine the prevalence and the genetic content of ESBL-producing *Enterobacteriaceae* recovered from food sold in butchers of Djelfa area (Algeria).

**Materials/methods:** 136 broiler livers randomly purchased in chicken butchers were collected. Analysis was performed by enrichment in BHI broth and isolation on Hektoen agar. Bacterial identification was performed using API 20E system and Mal-di-TOF MS. Susceptibility against 13 antimicrobials was evaluated by disc diffusion method. PCR/sequencing were adopted for the detection of ESBL and other resistance genes, phylogenetic grouping and molecular typing. Ultimately, transferability of associated ESBL-genes was checked-up through conjugation experiments.

**Results:** 78 *Enterobacteriaceae* isolates were recovered (one/sample: 73 *Escherichia coli* and 5 *Klebsiella pneumoniae*). In *E. coli* strains, the highest resistance levels were expressed to tetracycline (98.6%), nalidixic acid (86.3%) and trimethoprim/sulfamethoxazole (72.6%). ESBL activity was detected in 8 *E. coli* and the 5 *K. pneumoniae* isolates (rates of 5.9% and 3.7% in analyzed samples, respectively). The following ESBLs were detected (number of isolates): *blaCTX-M-15*(8), *blaCTX-M-1*(3), *blaCTX-M-55*(1) and *blaSHV-12*(1); all ESBL-*K. pneumoniae* isolates carried the *blaCTX-M-15* gene. ESBL producing *E. coli* isolates were assigned to lineages: A/ST48, B1/6448, B1/ST5087, B1/ST23, and B2/ST131 [two *blaCTX-M-15* *E. coli* isolates]. *K. pneumoniae* isolates were ascribed to sequence types ST2010 and ST3483. The four ESBL subtypes were successfully transferred by conjugation. Transconjugants carrying the *blaCTX-M* genes acquired either the IncK or the IncI1 plasmids, while the transfer of the *blaSHV-12* was associated with the acquisition of IncFIB or IncI1 plasmids. In non-ESBL *E. coli* isolates, the most commonly observed resistance genes were: *aac-(3)-ii* (100%), *tetA* (75%), *cmlA* (70%), *blaTEM* (57.1%) and *sul2* (43.5%) genes.

**Conclusions:** Relevant ESBL genes (*blaCTX-M-15* and *blaCTX-M-55* in *E. coli* or *K. pneumoniae*), as well as epidemic clones (B2/ST131) are detected among ESBL-producing *E. coli* from Algerian chicken markets. These findings reveal a serious public health concern, given that, such isolates could be transmitted to human consumers via the food chain.

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Background: Even with newer molecular diagnostic instruments offering an "open channel" for LDT automation, these implementations can be constrained by slow operation, forced batching, and significant hands-on time. The NeuMoDx 96 and NeuMoDx 288 Molecular Systems allow for complete standardization of LDTs with solutions to overcome the above-mentioned drawbacks of LDT automation, while offering significant advantages of room temperature stable reagents with long in-use life as well as extremely fast turnaround times and integration with laboratory information systems. Ability to implement these LDTs from CSF, transport medium, and whole blood specimen types is presented here.

Materials/methods: Whole blood, swabs in transport media, and CSF specimens spiked with following model DNA/RNA targets: Chlamydia trachomatis (CT) in 400µL vaginal swabs in UVT, Cytomegalovirus (CMV) in 200µL CSF and 250µL whole blood, and Enterovirus (EV) in 200µL CSF and 400µL nasal swabs in UVT was used to demonstrate efficacy of LDT implementation. Once extraction and PCR parameters were optimized, LDTs were processed automatically using the NeuMoDx Master Mix Test Strips (for PCR or RT-PCR) coupled with analyte specific reagents (ASRs). Studies to determine limit of detection, linearity, effectiveness of the sample process control, and the effect interfering substances testing were performed for each matrix and target set to determine effectiveness.

Results: Excellent sensitivities were obtained for all five specimen and target combinations tested: 10 EB/mL for CT in vaginal swabs in UVT, 0.0032 TCID₅₀/mL for EV in nasal swabs in UVT, 20 IU/mL for CMV in CSF, 0.0032 TCID₅₀/mL for EV in CSF, and 200 IU/mL for CMV in whole blood. All LDTs demonstrated excellent linearity (slopes of -3.1 to -3.4, efficiencies of 96-108%) across the range tested. The incorporated sample process control was determined to be an effective indicator of the extraction process for all tested targets and specimen types. No interference was observed at clinically relevant levels of endogenous/exogenous substances tested in any of the matrices.

Conclusions: This study demonstrated the extreme ease and excellent performance of LDT implementation using CSF, Transport Medium and Whole Blood specimens on the NeuMoDx Molecular System.

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Cationic antimicrobial polymers as new anti-biofilm agents
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Background: The rational design of new antibiotic agents is of imminent global necessity; more than 10 million deaths and an immense cost in health systems are predicted by 2050 due to multidrug bacterial infections. Inspired by natural antimicrobial peptides, cationic polymers can be developed as a new category of antibiotics to treat bacterial and biofilm infections.

Materials/methods: Cationic polymers mimicking antimicrobial peptides were synthesized by reversible addition-fragmentation chain transfer (RAFT) polymerization with various organizations of cationic regions. The positively charged moieties (guanidinium and ammonium) mimicking arginine and lysine amino-acids respectively. Standard antimicrobial susceptibility tests were performed using Staphylococcus aureus, following the Clinical Laboratory Standards Institute (CLSI) guidelines. Mammalian cell proliferation was tested following the XTT assay. Potential haemolytic activity of the compounds was tested in sheep red blood cells (RBC). The antibiofilm activity was evaluated using a synthetic collagen wound biofilm model.

Results: The synthesized cationic polymers showed good antimicrobial activity against S. aureus strains in Muller-Hilton broth (MHB) and in synthetic wound media (SWM) which is more representative for a clinical wound infection environment. The compounds were non-hemolytic, which is promising for future application as intravenous treatment for systemic infections. However, the polymers (especially guanidinium compounds), showed some toxicity against fibroblast cells (3T3).

The activity against S. aureus biofilms was tested in a collagen wound model. The artificial collagen wound was loaded with a polymeric solution and then a bacterial inoculum was added. Total biofilm inhibition was observed. In order to test biofilm disruption, a mature biofilm was formed in the collagen-wound model and afterwards treated with a polymeric solution. A significant decrease in colony forming units (CFU) in the treated wound can be observed.

Conclusions: Antimicrobial cationic polymers possess promising antibacterial and anti-biofilm activities as a new class of antibiotics. However, the toxicities against mammal’s cells need to be further studies in more complex models for further application in vivo.

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Nosocomial respiratory syncytial virus infections: a two-season European multi-centre cohort study

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Background: Respiratory syncytial virus (RSV) is a well-known cause of respiratory infection in infants, but the data about adult infection is scarce, especially regarding nosocomial infections. Despite the usual mild disease that it causes in healthy adults, those with cardiopulmonary diseases can be severely affected.

Materials/methods: We collected data from all patients with a positive PCR result for Influenza or RSV virus on oropharyngeal swabs who were admitted to the three centers represented in the study – Lisbon, Turin and Nicosia, during the 2017-2018 and 2018-2019 season. Patients included were older ≥ 18 years old, admitted for admission to a hospital ward and/or intensive care unit and had both positive PCR and clinical manifestations only take place at least 48h after admission. Univariate analysis was conducted using chi-square tests. Multivariate analysis used logistic regression including variables which showed associations with p values <0.25 on univariate analysis.

Results: Of the 1151 patients with positive PCR swabs, 246 met the inclusion criteria. Median age was 73 years and 59% (101) were female. Regarding comorbidities, 36% (88) had COPD/asthma, 26% (65) DM, 19% (47) CKD, 15% (37) interstitial disease, 13% (33) were smokers and 8% (19) had a solid neoplasm. 5% were co-infected with Influenza A (mostly H3N2) and only 1.6% co-infected with Influenza B. There were 32 deaths (13%) registered during the course of admission, 53% (17) during the four first weeks of the year (2018 or 2019). Median length of stay was 15 days. 16% (40) needed ventilatory support with non-invasive ventilation (NIV) and 6% (15) were submitted to invasive mechanical ventilation (IMV). Patients with solid neoplasms were more prone to die (p= 0.02, OR 3.5, CI95% [0,1 -0,8]). There was a trend relating co-infection of RSV and Influenza B with NIV but with no statistical significance (p= 0.3) was reached.

Conclusions: January was the deadliest month, in every year, for patients with nosocomial infections with RSV. Co-infection with Influenza B seems to be related with higher need for NIV. Oncologic patients are more prone to die due to nosocomial VSR infections.

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Severe viral respiratory infections in paediatric intensive care unit: a 4-year experience in an Italian paediatric hospital

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Background: Viral respiratory infections (VRIs) are one of the main causes of hospitalization in children; 2-3% of cases need Intensive Care Unit (ICU) admission. Herein we describe a series of pediatric patients affected by severe VRIs requiring ICU admission in an Italian tertiary care pediatric hospital to explore the determinants for mechanical ventilation requirement and prolonged ICU hospitalization.

Materials/methods: We described demographical and clinical characteristics of all children aged between 0 and 18 months admitted to the Bambino Gesù Children’s Hospital in Rome over a four-year period (2015-2018) because of a VRI requiring ICU admission. Categorical data were compared through Chi square test; continuous data were expressed as median and interquartile range (IQR) and compared through the Wilkoxon test.

Results: 132 patients were included in the study; the median age was 3 months (IQR 2-9) and the median weight was 5 kg (IQR 4-8). Comorbidities affected 37% of patients. The main viruses isolated in the respiratory tract were VRS-A (31.1%) and Rhinovirus (22.7%). 41% and 57% of children required mechanical ventilation and prolonged ICU admission, respectively. The median stay in ICU was 8 days (IQR 6-16). Patients younger than 7 months and with a weight below 6 kg had more frequently an ICU hospitalization longer than 8 days (p<0.001). Comorbidities, previous admissions for a respiratory infection, the type of virus and viral co-infections did not result to be risk factors for mechanical ventilation and prolonged ICU hospitalization. Otherwise, bacterial co-infections, mainly caused by Haemophilus influenzae, led commonly patients to endotracheal intubation and longer ICU stays (p<0.001).

Conclusions: VRIs can be an important cause of morbidity, especially in young children and children with comorbidities. Many patients with VRIs require endotracheal intubation and need a prolonged ICU hospitalization that can expose them to further complications, such as hospital-acquired infections and tracheostomy. Studies are necessary to identify tools such as specific antiviral therapies to reduce the severity of these infections and to improve the outcomes.

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Abstract 7933

Next generation sequencing of influenza A virus from environmental samples at the human-animal interface
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Background: The 2009 pandemic influenza A virus [H1N1] highlighted gaps in surveillance of influenza viruses of swine origin, specifically at the human-animal interface. Current influenza surveillance systems are costly and labour-intensive, often under-prioritizing zoonotic sources of emergent strains with pandemic potential. The genetic diversity and reassortment of influenza A virus in swine underscores the need for a non-invasive, population based surveillance technique to improve pandemic preparedness. Aggregate, environmental samples from agricultural settings can be analyzed using a next-generation sequencing (NGS) techniques, providing an alternative approach to classic surveillance methods for influenza viruses of public health importance.

Materials/methods: Environmental samples consisting of 88 pooled oral fluids from swine, 183 room-level and personal breathing zone bioaerosols and 45 surface swabs were collected from a swine barn in Southern Ontario, Canada. Room-level air samples were obtained using two low and two high volume bioaerosol samplers. All samples were analyzed by RT-PCR for detection of the matrix gene. Suspect positive and positive samples were subject to target enrichment using captured probes against influenza genomic segments, designed by Fusion Genomics Corporation. Enriched libraries were sequenced using an Illumina NextSeq sequencing instrument at a read depth of 2-5 million reads per sample.

Results: Among 76 rooms deemed positive by oral fluids, 23.8%, 33.3%, 11.5%, and 45.2% were positive by PTFE, NIOSH, Coriolis, and swabs, respectively. Suspect positive samples were detected in 23.8%, 50%, 38.4%, and 23.8% by PTFE, NIOSH, Coriolis, and swabs, respectively. NGS recovered 35%, 18%, 6% of the viral genome by oral fluids, swabs, and bioaerosol samples, respectively. Hemagglutinin and neuraminidase segments showed the highest percent coverage in all sample types. Non-structural and polymerase segments (excluding polymerase basic protein 2) were unable to be sequenced.

Conclusions: Environmental sampling of swine barns could provide a non-invasive option for the detection of influenza A virus, however complete characterization of influenza A virus requires whole genome sequencing of all segments. Further optimization of environmental sampling is needed to enhance sequencing yield, prior to consideration as a stand-alone method for surveillance.

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Impact of a multiplex PCR in the management of viral meningitis

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Background: Infectious meningitis and meningo-encephalitis are life-threatening conditions associated with high morbidity and mortality. In emergency departments, their diagnoses are still a challenge for the clinician since pleiocytosis is not specific of infectious meningitis. Recently, multiplex PCRs have been developed to improve this diagnosis and optimize patient management and treatment. The objective of this study was to measure the impact of multiplex PCR in the management of viral meningitis.

Materials/methods: We conducted a retrospective monocentric study in the Emergency department of our University hospital including all patients who underwent lumbar puncture with pleocytosis (> 5 leukocytes / mm3). The study was divided into two periods: Period 1 from April 2014 to March 2017 before the implementation of the FilmArray® ME test (bioMérieux) and Period 2 from April 2017 to March 2019 after implementation. Microbiological and clinical data were collected from hospital informative systems.

Results: Out of 7,674 CSF (7,341 patients) analyzed, 1,121 (1104 patients) showed pleocytosis (587 in Period 1 and 534 in Period 2). Meningitis or meningo-encephalitis were diagnosed in more cases in Period 2 than in Period 1 [325 [60.9%] vs. 312 [53.2%], respectively (p=0.009)]. The proportion of pathogens identified among those covered by the FilmArray® ME test was not different between period 1 and period 2 (127/312, 40.7% vs. 153/325, 47.1%, p=0.1). For the subgroup of Enteroviral (EV) meningitis, patients were less often hospitalized in Period 2 than in Period 1 (38/58, 65.5% vs 32/88, 36.4%, p<0.001). The duration of hospitalization for patients with EV or HSV-2 meningitis was significantly shorter (mean duration of 1.63 days vs 2.54 for EV and 3.6 days vs 6.6 for HSV-2, p<0.001 and p=0.01 respectively). Empirical prescription of acyclovir was reduced during Period 2 for patients with EV (10/58 vs 6/88, p=0.05) or VZV meningitis (20/25 vs 7/18, p=0.01). The prescription of antibiotics was also reduced in Period 2 for patients with HSV-2 meningitis (4/9 vs 0/25, p=0.002).

Conclusions: The implementation of a rapid multiplex PCR in the diagnosis of community meningitis in emergencies appears to have an impact on the management of viral meningitis and may reduce inadequate antimicrobial treatments.

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Abstract 7940

Evaluation of the performances of BD MAX enteric bacterial panel and extended enteric bacterial panel for detection of gastrointestinal pathogens in clinical stool specimens using FecalSwab

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Background: The goal of this study was to evaluate the analytical performance of BD MAX enteric bacterial panel (EBP) and extended EBP (xEBP) for identification of bacterial pathogens.

Materials/methods: 982 prospective stool specimens collected on FecalSwab® (Cary-Blair) were screened by molecular biology using BD Max EBP and xEBP assays (MB). Results were compared to i) standard culture routinely used in the laboratory (Hektoen before and after selenite enrichment, Karmali and CIN agar), ii) new specific cultures (chromogenic or selective agar) inoculated on the MB results.

Results: Utilization of MB elevated the overall detection rate from 5.6% (55/982) to 7.9% (78/982) for the detection of Campylobacter spp, Salmonella spp, Shigella spp, Yersinia spp and Plesiomonas spp. It also allowed the detection of 3.6% (35/982) positive specimens for pathogens not usually identified by standard culture such as ETEC, EHEC (shigatoxins+) and Vibrio spp. Five samples were positive by MB for 2 or more pathogens (2 pathogens, n=4; 5 pathogens, n=1). All discrepancies corresponded to MB+/culture-, except one case for which culture was positive for Salmonella and MB- but MB+ when retested. The rough overall agreement between MB and culture (including both standard culture and specific culture) were as follows: 17/18 Salmonella spp, 37/47 Campylobacter spp, 1/2 Y. enterocolitica, 0/2 Vibrio spp and 1/1 P. shigelloides. For the detection of shigatoxins, 14/21 specimens were confirmed with home-made PCR. 11 samples were positive for Shigella spp/EIEC by MB among which 6 Shigella were detected in culture. Complementary investigations (Biofire assays and specific tests in French National Reference Centers) are underway to investigate further some specimens with MB+/culture- and for the detection of EIEC for Shigella spp/EIEC positive samples by MB. The selected use of specific media for specimen with MB+ allowed the additional culture of 6 Campylobacter and 2 Salmonella compared to standard culture.

Conclusions: BD Max EBP and xEBP showed higher number of positive samples compared to culture and very good performances for the detection of enteric bacterial pathogens. The use of specific media based on MB results allowed the increase of isolation of pathogens implicated in diarrhea, in particular Campylobacter and Salmonella.

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**Abstract 7942**

**Drug repurposing as an effective strategy to treat multidrug-resistant infections: teaching old drugs new tricks**

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**Background:** Antibiotic resistance has become one of the main health crises of the 21st century. Due to the lack of new molecules, the repurpose of "old" drugs used to treat different conditions is becoming attractive. The antipsychotic Thioridazine (TZ) has been reported as an efflux pump inhibitor with demonstrated activity against *Mycobacterium tuberculosis*, *Acinetobacter baumannii*, etc. but its mechanism of action has never been fully described. The main aims of this study were to uncover the mechanism of action of TZ in *Salmonella Typhimurium* (model bacterium) and assess its use as an adjuvant to treat infected macrophages.

**Materials/methods:** The in vitro antibacterial activity of TZ was determined based on its minimum inhibitory concentration (MIC). Membrane permeability assays were performed with sub-MIC concentrations of TZ and fluorescence measured using the Ethidium-Bromide accumulation assay. *Salmonella* was exposed to sub-MIC of TZ and its effects on membrane potential and cell wall assessed by flow cytometry and Transmission Electron Microscopy, respectively. Effects on the bacterial proteome were assessed through 2D gel electrophoresis. Cytotoxicity was determined in THP-1 cells. Infection assays were performed in THP-1 and RAW 264.7 cells treated and non-treated with TZ.

**Results:** The MIC of TZ against *Salmonella* was 200mg/L. Our in vitro data demonstrates that TZ mechanism[s] of action involves primarily *Salmonella*’s membrane by affecting its permeability and potential after 15 minutes of exposure to TZ. At half of the MIC, and only after 15 minutes, TZ disrupts the bacterial membrane leading to leakage of the cellular contents and lysis of *Salmonella*. Proteomic profiling revealed 75 upregulated and 62 downregulated proteins, among which were TolC and AtpD, involved in cell energetics. TZ demonstrated no cytotoxicity on human cells at clinically relevant concentrations. Infected macrophages treated with sub-MIC of TZ, showed a reduction on intracellular CFU/mL compared with the control. This may be indicative of TZ’s ability to enhance the killing activity of infected macrophages.

**Conclusions:** TZ seems to act in vitro by targeting the bacterial cell-envelope. Due to its effect on infected macrophages, TZ can be considered a adjuvant to current therapeutic regimens to treat multidrug resistant infections.

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Identification and quantification of microdialysis variability using an integrated in vitro, ex vivo and in silico approach

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Background: For the antibiotic linezolid (LIN), a catheter-based microdialysis (µD) study [1] investigated its pharmacokinetics in obese and non-obese patients at target site [1]. However, the observed µD technique variability prompted investigations to identify and quantify its sources to optimise study designs of future clinical trials. Hence, LIN inter- and intracatheter variability assessed by relative recovery (RR) was compared in an in vitro dynamic µD system (dIVMS) in different matrices and an ex vivo approach in human subcutaneous interstitial space fluid (ISF) with different locations of µD catheter to quantify their influence on the observed in vivo variability of the µD technique.

Materials/methods: The typical in vivo LIN concentration-time profile in ISF [2] was mimicked in the dIVMS using Ringer’s solution (RS) and mimicked artificial ISF (pooled plasma + saline 0.9%, 1+1) as in vitro matrices, respectively. Retrodialysis was performed as a calibration method in vitro and ex vivo with sampling from three µD catheters (CMA 60, cut-off 20kDa) simultaneously.

Statistical analysis of catheter variability was performed in R (3.6.0) using one-way ANOVA and linear mixed-effects modelling with the R-package lmer (v1.1-21).

Results: RR between catheters was significantly different in the ex vivo setting (p<0.001), but not in the in vitro approaches in the dIVMS in RS and artificial ISF (p=0.741 and p=0.890).

RR variability was split in intercatheter and residual variability (including intracatheter variability) being slightly smaller ex vivo (RSO=21.4%CV and 10.4%CV) compared to in vivo (RSO=16.0%CV and 18.1%CV).

Conclusions: The integrated in vitro, ex vivo and model-based analysis approach provided quantitative and qualitative insights into the µD technique variability of the clinical µD study. Changing of matrices from RS to artificial ISF seem to have no significant influence on the µD technique variability, whereas different localisations of the inserted µD catheters in the ex vivo setting can partially explain the observed in vivo variability. Further investigations are warranted to unveil sources of the remaining unexplained variability such as handling of µD equipment or the staff experiences.

References:

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Abstract 7945

Development and preliminary evaluation of Multidrug Resistance Direct Flow Chip kit, a molecular method for a rapid detection of multiple antibiotic resistance markers

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Background: The preliminary evaluation of the new commercial assay Multidrug Resistance (MDR) Direct Flow Chip (Master Diagnóstica, Spain) for the simultaneous detection of multiple resistance markers in multidrug resistant bacterial causing several infections is described.

Materials/methods: MDR is a multiplex PCR followed by automatic flow-through hybridization, colorimetric detection and image analysis, which detects 5 pathogens and 47 resistance markers in 4 hours. Both steps were simultaneously performed in the fully automated HS12 PCR auto platform. DNA from multidrug resistant (MDR) clinical isolates was purified with the automatic extraction by the system NucliSens EasyMag using a generic protocol. Direct PCR was also tested starting from blood cultures, rectal or nasal swabs.

Results: A total of 70 clinical isolates and 24 clinical samples were tested with MDR assay. Figure 1 shows the antibiotics resistance genes detected and correlation with the antimicrobial susceptibility tests (AST).

Conclusions: The resistance markers detected by MDR Direct Flow Chip could explain the antibiotic resistance profile in approximately 90% of the isolates. Furthermore, preliminary results showed a correct performing of the test in direct PCR from clinical samples such as blood cultures, rectal and/or nasal swabs, thus this test could be a useful tool for a rapid detection of multiple resistances in a single assay avoiding the spreading of resistances and overuse of broad-spectrum antibiotics. An ongoing study is being carried out with a larger number of samples in order to provide unbiased sensitivity and specificity values of MDR kit.

Antibiotic resistance genes detected with MDR

<table>
<thead>
<tr>
<th>Antibiotic resistance genes detected with MDR</th>
<th>Isolates/resistance genes</th>
<th>Phenotypic resistance</th>
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<tbody>
<tr>
<td>3 mecA</td>
<td>1 S. epidermidis, 2 S. aureus</td>
<td>Penicillin/cephalosporin</td>
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<td>2 mecC</td>
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<tr>
<td>5 CMY</td>
<td>3 K. pneumoniae, 2 E. coli</td>
<td></td>
</tr>
<tr>
<td>9 CTX</td>
<td>3 K. pneumoniae, 4 E. coli, 1 P. aeruginosa, 1 Enterobacter</td>
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<td>2 SIV (one SK mut.)</td>
<td>1 Enterobacter, 1 Providencia</td>
<td></td>
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<tr>
<td>2 GES</td>
<td>2 P. aeruginosa</td>
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<tr>
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</tr>
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<td>1 K. oxytoca</td>
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<td>3 S. aureus</td>
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<td>17 ace (F) 6b</td>
<td>4 P. aeruginosa, 6 K. pneumoniae, 4 E. coli, 2 Enterobacter, 1 K. oxytoca</td>
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<td>4 mox-1</td>
<td>4 E. coli</td>
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Abstract 7946

Histoplasmosis epidemiology in Costa Rica
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Background: Histoplasmosis has a worldwide distribution, with major areas of high endemicity in USA and in some Latin America countries. To our knowledge, no epidemiological studies have been published from Central America. This paper describes the epidemiological behavior of histoplasmosis in Costa Rica from 2001 to 2015.

Materials/methods: This is a retrospective, descriptive study based on the national discharge registry of Costa Rica’s public health care system. The cumulative incidence of histoplasmosis per 100,000 persons per year, gender, distribution by age, co-morbidities, clinical form and in-hospital mortality rate were determined. In this analysis the period was divided into 5-year intervals.

Results: During this period, 424 Histoplasma capsulatum infections were recorded for a cumulative incidence of 0.64 cases per 100,000 persons-years. A significant increase in the incidence between the first (0.51 cases/100,000 per persons) and second quinquennium (0.71 cases/100,000 per persons) was observed (RR = 1.28; 95% CI 1.01-1.64), to subsequently a mild decrease. Men were affected more than women (RR = 2.68; 95% CI 2.14-3.29). Median age was 31 years (interquartile range of 18 to 43 years), 26% of cases occurred in children under 19 years and 59% between 20 and 49 years. More frequent associated co-morbidities were: HIV-infection (49%), cancer (5%), chronic liver disease (2%) and kidney transplant (3%), just 5% of the individuals did not possess any underlying illness. The proportion of histoplasmosis in non-HIV infected patient gradually increases among the periods, from 44% to 54% but it was not statistically significant. The clinical form of histoplasmosis was classified as pulmonary (48%) and disseminated disease (52%). The in-hospital mortality by quinquennium was 12, 15% and 17% respectively due to a significant rise in HIV-infected group mortality.

Conclusions: The incidence of histoplasmosis in Costa Rica had a significant growth. A clear predominance of the disease was observed in young men HIV-infected. In-hospital mortality rate in HIV patients experienced a significant increase during this period.

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Abstract 7947

**Acquisition of antimicrobial resistance organisms by US international travellers**

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**Background:** Antibiotic-resistant bacteria are an increasing health threat in the U.S., with an estimated 2.8 million cases and 35,000 deaths annually. Carbapenem and polymyxin antibiotics, including colistin, are the “last resort” treatment for highly antibiotic-resistant Gram-negative organisms. Increasing evidence shows that international travelers asymptotically acquire antibiotic-resistant bacteria in the gut while abroad and may contribute to the global spread of these medically important organisms.

**Materials/methods:** We recruited subjects seen for pre-travel health evaluation in select Global TravEpiNet network (GTEN) sites. GTEN is a consortium of 25 travel clinics across the U.S. that provide pre-travel health consultations to U.S. international travelers. Data were collected from December 2017 to August 2019. Participants self-collected stool samples before and after international travel and sent them for processing through the U.S. postal service. Using selective media, we screened the stool for extended spectrum beta-lactamase producing *Enterobacteriaceae* (ESBL). All identified isolates subsequently underwent whole-genome sequencing using Illumina technology.

**Results:** We collected a total of 570 stool samples. 44 U.S. study subjects had ESBL prior to departure. We identified 219 U.S. international travelers who had positive post-travel samples for ESBL. The most common destinations associated with travel-associated acquisition of ESBL were India, Ghana, and Peru. Most ESBL were *E. coli* (90% pre-travel and 97% post-travel). Eighty-five of the ESBL colonized travelers (39%) experienced diarrhea on their trip, and 29 (34%) took antibiotics. Whole-genome sequencing of the bacterial isolates revealed the vast majority of ESBLs were of the CTX-M type. CTX-M group 55 predominated in South East Asia and South America.

**Conclusions:** This study highlights the acquisition risk of antimicrobial resistance organisms, including ESBL, in association with international travel. These acquisition rates are similar to smaller European studies. Prevention measures and screening policies, including genomic surveillance, for U.S. international travelers may be needed to help contain the global spread of drug resistance elements.

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Cytomegalovirus reactivation as a diagnostic and prognostic indicator of increased risk of cardiovascular diseases

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Background: The pro-inflammatory status related to chronic infection by human cytomegalovirus (HCMV) has been associated with an increased cardiovascular risk and formation of atherosclerotic plaques, that could lead to acute clinical manifestations. We aimed to investigate the potential correlation among the occurrence of an acute coronary syndrome with a cardiac and/or systemic HCMV-reactivation.

Materials/methods: Between January and November 2019, 200 patients were enrolled in the study; 11 have been excluded (lack of adequate sampling, informed consent missing, etc). Therefore 189 subjects were evaluable, and divided as follows: 123 with acute coronary disease, 49 with chronic coronary disease (classified as acute or chronic “cases”, respectively) and 17 healthy patients (classified as “controls”). All cases underwent to a coronary angiography and to HCMV-DNA quantification from culprit coronary withdrawal. HCMV-DNA in peripheral blood and HCMV total IgM/IgG were quantified in all patients through real-time PCR assay (ELITech group) and ELISA test (Diasorin Molecular), respectively. HCMV-DNA was tested in triplicate in 22 patients, according to samples’ availability.

Results: Most patients were men (74.1%; 140/189), caucasians (67.2%; 127/189), with a median age of 66 (IQR: 55-73) years. HCMV seroprevalence was higher in acute/chronic cases (91.5/100%, respectively) than in controls (9/17, 52.9%), the latter in line with the seroprevalence in general population (50-70%, Lachmann et al., Plos One 2018) (p<0.001). IgG-positive acute/chronic cases also had detectable (but not quantifiable) HCMV-DNA in peripheral blood more frequently than IgG-positive controls (22/132, 20.0% vs. 1/9, 11.1%, p=n.s.). At coronary level there was a trend of higher prevalence of HCMV-DNA positivity in patients with acute disease, compared to chronic controls (15.3% vs 8.2%). Of note, 43.5% of acute patients showed a HCMV-DNA positivity only in coronary plasma sample, while in chronic patients the HCMV-DNA was detected only in peripheral plasma samples or in both specimens (p=0.018).

Conclusions: Our results show a higher CMV seroprevalence (90-100%) relative to the Italian population. Furthermore, the increased presence of CMV-DNA in coronary samples is somewhat associated with acute cardiovascular disease. This finding should be confirmed by a uni-multivariable logistic regression analysis for the epidemiological confounding factors, currently ongoing.

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Penicillin-binding protein 2 (PBP2), PBP2a and PBP4 clone-specific polymorphisms are not associated to ceftaroline (CPT) susceptibility in Chilean clinical isolates of methicillin-resistant Staphylococcus aureus (MRSA)

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Background: CPT is a last-generation cephalosporin active against MRSA due to its affinity for PBP2a. CPT-resistance (CPT-R) is well-described, with mutations in the active transpeptidase domain of PBP2a associated to high-level resistance. The accumulation of changes in the non-penicillin-binding domain of PBP2a has been linked to elevations of the minimal inhibitory concentration (MIC) to CPT to levels around 2-4ug/mL (susceptible dose-dependent [SDD]). PBP4 and PBP2 have also been implicated as potentially relevant mecA-independent mechanisms of CPT-R. We recently reported high rates of CPT-non-susceptibility in clinical MRSA strains from Chile. However, the mutational landscape of PBPs in clinical MRSA isolates from Chile and its relation to CPT susceptibility has not been assessed.

Aim: To assess the mutational profile of PBP2, PBP2a and PBP4 in clinical MRSA isolates from Chile and compare it to CPT-susceptibility obtained by broth microdilution (BMD).

Materials/methods: We analyzed 180 MRSA isolates collected from 2000-2018 in Santiago, Chile. Identification was confirmed by MALDI-TOF and methicillin resistance with cefoxitin disk-diffusion. CPT susceptibility was performed by BMD following CLSI-2019 guidance. Whole-genome sequencing was performed for all isolates, the mutational profile of PBPs was determined using reference sequences for PBP2 (AGY89563.1), PBP2a (NG_047938.1) and PBP4 (X91786.1).

Results: All isolates were phenotypically-confirmed MRSA and harbored mecA. The MIC50/MIC90 by BMD was 2/2μg/dL; only 71 (39%) isolates were CPT-susceptible (MIC <1µg/mL). Most isolates belonged to ST5/SCCmecI (70%,126/180), ST105/SCCmecII (10%,18/180) and ST8/SCCmecIV (5%, 9/180). All ST5/SCCmecI isolates carried the mutations in PBP2 (Y156D), PBP2a (M122I and E150K), and PBP4 (T189S, L234H, and T409A); CPT-susceptibility among ST5/SCCmecI was only 22%. On the other hand, all ST105/SCCmecII isolates had mutations in PBP2 (S707L) and PBP4 (T189S, L234H, and T409A) and exhibited a higher CPT-susceptibility rate (67%). All 9 isolates belonging to the ST8/SCCmecIV lineage harbored a non-coding mutation in PBP2a (g-6t) and the previously observed L234H change in PBP4. Importantly, no association between specific polymorphisms and MIC to CPT was found.

Conclusions: Changes in the studied PBPs were frequent among MRSA circulating in Chile and were conserved among different genetic backgrounds. However, these changes were not associated with the level of CPT MIC among these isolates.

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Abstract 7955

**Varicella zoster: a complicated primoinfection in an elderly patient**

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**Background:** Chickenpox is a primary infection caused by Varicella-Zoster virus (VZV), highly contagious and characterized by a pruriginous vesicular exanthema, preceded by systemic symptoms. It is common in children and generally has a benign course, however in adults and immunocompromised patients might have a more severe presentation and serious complications. Viral pneumonia is one of the most common complications with an incidence 25 times higher in adults compared with children. Treatment with acyclovir is recommended in adults, immunocompromised and patients with severe presentations, because it reduces the viral replication and frequency of complications.

**Materials/methods:** case report: Man, 91 year-old, totally dependent and institutionalized, examined at the emergency room with fever, pruriginous vesicular exanthema with two day onset associated with cough, respiratory distress and low peripheral oxygen saturation.

He presented with exuberant, disseminated cutaneous lesions, in different development stages, some of them infected, sparing the palmar, plantar and anterior region of the lower limbs. Pulmonary auscultation with wheezing in both lungs. Analytically without leucocytosis, PCR 6 mg/dl (<0.50 mg/dl), hepatic alterations with cytolysis pattern and hypoxemia. It was performed a swab of the lesions that revealed VZV positivity (PCR). IgM and IgG VZV antibodies were negative. Chest radiography showed interstitial infiltration and the abdominal ultrasound was unremarkable. The patient was admitted with chickenpox, superinfected lesions and viral pneumonia and started treatment with acyclovir and amoxicillin/clavulanate. VZV serology was repeated and IgM and IgG antibodies turned positive which was compatible with recent infection.

**Conclusions:** The authors intend to show a clinical case of chickenpox primoinfection due to its rarity in elderly patients and exuberant presentation. This infection is associated with severe complications in adults, therefore it is necessary to promptly recognise and initiate antiviral therapy.

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Abstract 7958

**Tuberculosis in elderly patients**

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**Background:** The geriatric population among all ethnic groups represents the largest reservoir of tuberculosis (TB) infection, particularly in developed nations. The rate of progression from infection to disease is substantially modified by age and multiple other immunosuppression factors. Clinical features of tuberculosis in older adults may be atypical, non specific and confused with concomitant age related disease. Mortality even with treatment is increased with age. The aim of this study was to describe the characteristics of elderly patients with TB.

**Materials/methods:** We conducted a retrospective study analyzing the characteristics of patients over 65 years of age who were treated for a TB disease in a French hospital between 2009 and 2019.

**Results:** We included 40 patients aged 65 years or older with TB disease. Mean age was 78 [65-92] and sex ratio was 0,9. Pulmonary TB was found in 29 patients (72,5%). Other types of extra pulmonary TB were lymph node (5), gastrointestinal (4), bone (3), neurological (2), cardiac (2), and ophthalmologic TB (1). Among the patients 35% were born in France and 35 % had African origin, 10% Asian, 5% other European countries, 7,5% Caribbean and 7,5% with unknown origins. The Charlson comorbidity index scores was high (>4) for 29 (72,5%) patients. TB was bacteriologically proven in 72,5% (1 resistance to isoniazid was found), histologically in 12,5% and clinical/radiologically in 15% of cases. Thirty seven patients received an antituberculosis quadritherapy including isoniazid, rifampin, pyrazinamide (PZA) and ethambutol at diagnosis. 3 patients received triple therapy; 2 without PZA, 1 without ethambutol (renal failure). Adverse effects of treatment were recorded in 17 cases (42,5%), particularly hepatic dysfunction (41,1%), occurred more commonly. In 8 cases, the anti-tuberculosis treatment initiated had to be suspended and reintroduced after normalization of the liver function, in 3 cases without pyrazinamide. Nine patients were lost to follow-up before the end of treatment.

**Conclusions:** More drug-induced adverse reactions are experienced by this population during TB therapy according to the literature. Optimal treatment of associated chronic diseases, minimization of invasive procedures, limitation of polymedication and adequate nutritional support are essential for this vulnerable population.

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The microbial aetiology of the acute appendicitis: the possible role of microbiota in the disease

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Background: Acute appendicitis (AA) is the most common cause of abdominal pain in emergency. It appears that complicated (perforated) and uncomplicated (non-perforated) AAs are two distinct disease forms most likely having different pathophysiology. However, the cause and etiology of these two forms remains poorly understood. The differentiation between disease forms is essential prior the determination of the optimal treatment since over two thirds of cases are of uncomplicated nature. Thus, appendectomy is not necessity in every case. Further, promising results have been reported in treating uncomplicated AA by antibiotics. Our MAPPAC (Microbiology Appendicitis Acuta) trial aims to determine the microbiological etiology and possible microbiological and immunological differences between the two AA forms. Further, the possible mediating role of both appendiceal and gut microbiota in the disease is investigated.

Materials/methods: Disease form has been confirmed by computed tomography (CT). Two appendiceal lumen swabs, one for culture and one for microbial DNA extraction (Puritan DNA/RNA Shield Tube), were collected right after the removal of appendix. In addition, two rectal swabs have been collected from the same patient during the stay in an emergency. Appendiceal content were cultured on six different plates both aerobically and anaerobically. Morphologically distinct colonies were selected from primary cultures and identified with MALDI-TOF Mass SpectRometry. DNA was extracted as previously described. Microbiological profiles were assessed by 16S rRNA sequencing (V3+V4 area, Illumina MiSeq).

Results: Majority of the appendix samples exhibited polymicrobial growth. In both disease forms common aerobic species were Esherichia coli, Pseudomonas aeruginosa, Streptococcus anginosus and S. constellatus. In complicated AA, P. aeruginosa was frequent. Commonly found anaerobes were Bacteroides fragilis, B. ovatus, B. thetaiotaomicron, B. vulgatus and Clostridium innocuum in both disease.

Conclusions:

Based on culture complicated and uncomplicated AA may differ microbiologically. Ongoing NGS analysis will provide crucial addition to the abovementioned results.


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Delayed diagnosis of neuroschistosomiasis in a non-endemic country: a tertiary referral centre experience

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Background: Neuroschistosomiasis is a severe complication of schistosomiasis, triggered by the local immune reaction to egg deposition, with spinal cord involvement the most well recognised form. Early treatment with praziquantel and high dose steroids leads to a reduction of neurological sequelae. The rarity of this condition in returning travellers to high income countries can result in delayed diagnosis and treatment. We aimed to evaluate the diagnosis and management of neuroschistosomiasis in a UK national referral centre.

Materials/methods: A retrospective review of confirmed clinical cases of neuroschistosomiasis referred to the Hospital for Tropical Diseases, UK, between 2016 and 2019 was undertaken. Electronic referral records were interrogated and patient demographic, clinical, laboratory, and radiological data collected.

Results: Four cases of neuroschistosomiasis were identified. The median age at diagnosis was 28 (range 21 to 50) with three male patients. All patients had epidemiological risk factors for schistosomiasis based on travel history and freshwater exposure; two in Uganda (River Nile), one in Malawi and one in Nigeria. All patients presented with features of transverse myelitis including back pain, leg weakness, paraesthesia and urinary dysfunction. Mean time from presentation to health services to definitive treatment was 40.5 days (range 16-74 days). Diagnosis was confirmed with CSF serology for schistosomiasis in all cases. Radiological features on MRI spine included enhancement focused predominantly in the lower thoracic spinal cord in three cases and the conus in one patient. All patients received a minimum of three days of oral praziquantel and high dose steroids. At three month follow-up, two patients had complete resolution of symptoms and two had residual deficit; one patient was left with urinary and faecal incontinence whilst another had ongoing leg weakness.

Conclusions: We observed a marked delay in diagnosis of neuroschistosomiasis in a non-endemic country. We advocate undertaking a thorough travel history, and early use of imaging and CSF schistosomal serology to ensure early diagnosis of neuroschistosomiasis in patients presenting with consistent symptoms. If Schistosomal diagnostics are not immediately available, presumptive treatment under the guidance of a tropical medicine specialist should be considered, to minimize the risk of residual disability.

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Abstract 7965

Identification of central nervous system infection in children without cerebrospinal fluid pleocytosis using a syndromic meningitis/encephalitis panel

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Background: The syndromic approach for the diagnosis of Central Nervous System (CNS) infections enables the rapid detection of multiple pathogens in cerebrospinal fluid (CSF) specimens. The aim of the study was to evaluate the use of CSF pleocytosis as an indicator for the optimal utilization of BIOFIRE® FILMARRAY® Meningitis/Encephalitis (FA) panel.

Materials/methods: In the first period of the study (06.2018-05.2019), FA was performed only in children with suspected CNS infection and CSF pleocytosis >15 cells/mm³. In the second period (06.2019-11.2019) there was no cut-off and all CSF samples were tested with FA. Pathogen detection rate (%) was compared between children with CSF ≤15 or >15 cells/mm³, within two age groups (>3 or ≤ 3 months of age).

Results: A total of 170 children were included in the study with median age 2.5 months (IQR: 0.7-27). Pathogen detection rate (%) with FA in the first and second study period was 46.3% (37/80) and 21.1% (19/90), respectively (P-value: 0.001). In CSF samples without pleocytosis which were tested with FA, the pathogen detection rate was 15.3% (9/59). Enterovirus was detected in 5 CSF samples (6.7%), HHV-6 in 3 (5.1%) and parechovirus in 1 (1.7%). The median age of children without pleocytosis, but with a pathogen detected was 0.66 months (IQR:0.41-4.75). In children >3 months (n=68) with CSF ≤15 or >15 cells/mm³, a pathogen was detected in 2/15 (13.3%) and 26/53 (49.1%), respectively (P-value: 0.013). In children ≤3 months (n=102) with ≤15 or >15 cells/mm³, a pathogen was detected in 7/44 (15.9%) and 21/58 (36.2%) samples, respectively (P-value: 0.023). No difference in detection rate was found in newborns ≤1 month (n= 65) between CSF ≤15 or >15 cells/mm³, 6/29 (20.7%) and 9/36 (25%), respectively, (P-value: 0.682).

Conclusions: Absence of CSF pleocytosis does not exclude CNS infection, especially in infants less than 3 months of age and newborns.

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Intravenous amoxicillin in patients with various degrees of renal function: are we dosing adequately?

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Background: Amoxicillin dosing is often adjusted in patients with renal impairment (RI). The dosing recommendations for these patients differ remarkably in the literature. Our objectives were to determine if the pharmacodynamic target of 40% fT>MIC (time that the free concentration exceeds the MIC) was achieved with the local dosing guidelines in patients with and without RI and to compare amoxicillin concentrations and half-lives in both groups.

Materials/methods: Seven internal medicine ward patients treated empirically with intravenous amoxicillin/clavulanic acid were included. Median estimated Glomerular Filtration Rate (eGFR, measured by CKD-EPI) was 27 ml/min/m² (range, 21-33) in RI patients (n=4) and 99 ml/min/m² (range, 78-121) in non-RI patients (n=3). Amoxicillin dose was 1000mg four times daily for all patients. Five blood levels per patient were drawn after two or three days of therapy. Total amoxicillin concentrations were determined by liquid chromatography with mass spectrometry. Unbound concentrations were calculated using a protein binding of 20%. Non-compartmental pharmacokinetic analysis was performed using PKsolver. The %fT>MIC was calculated for a MIC of 8 mg/L (EUCAST breakpoint for Enterobacterales).

Results: One patient without micturition had an unreliable eGFR of 99, indicated by high amoxicillin levels and a prolonged half-life, and was transferred to the RI group (now n=5). Amoxicillin half-life was higher in the RI group: median 3.6h (range, 2.2-4.4) compared to 0.8h and 1.3h in the 2 non-RI patients. In all patients fT>MIC was at least 40%, although the fT>MIC was higher for the RI patients (median 100%, range 94-100%) than the non-RI patients (48 and 51%). The concentrations 3h after start of infusion were higher in the RI group (median 22.9 mg/L, range 15.3-48.9) than in the non-RI patients (7.8 and 11.5 mg/L).

Conclusions: All subjects attained the 40% fT>MIC target, concluding that the current amoxicillin dose of 1000mg four times daily is sufficient for patients with and without RI. Concentrations in RI subjects are much higher than in non-RI patients, which raises the question if their dosing is not unnecessary high. However, as the supratherapeutic concentration limit is unknown, more research is necessary to suggest a new dosing regimen in RI.

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Efficacy of an engineered protegrin-1 analogue in a murine model of Pseudomonas aeruginosa sepsis

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Abstract: Sepsis is a leading cause of death among hospitalized patients where the increasing prevalence of multidrug-resistant organisms complicates treatment. Protegrin-1 (PG-1) is a cationic peptide that exhibits broad-spectrum antimicrobial activity; however, proteolysis limits its use. Our group has developed a novel approach of engraving PG-1 into a cyclotide that increases its protease stability. The purpose of this study is to evaluate in vitro antipseudomonal activity, in vivo safety and efficacy of our engineered cyclotide MCo-PG1.

Materials/methods: PG-1, MCoTI-1 (cyclotide scaffold), and MCo-PG1 were prepared using Fmoc synthesis. In vitro stability was assessed using mass spectrometry on active human serum. In vitro antimicrobial activity was determined using microbroth dilution susceptibility testing and time-kill kinetics with laboratory and clinical isolates of P. aeruginosa. The maximum tolerated dose (MTD) of MCo-PG1, PG-1, and colistin was determined following single ascending intraperitoneal doses in 8-10-week-old Balb/c mice. Sepsis was established by an intraperitoneal injection of 1.5×10⁷ CFU/mouse of P. aeruginosa (ATCC 27853). Treatment was administered immediately by intraperitoneal injection with saline, 15 mg/kg colistin, 5 mg/kg PG-1, 10 mg/kg MCo-PG1 or 25 mg/kg MCo-PG1. Animals were monitored for seven days and/or euthanized if moribund appearances were observed.

Results: MCo-PG1 in vitro stability improved in comparison to PG-1 (81 and 53 hours, respectively). MCo-PG1 retained antimicrobial activity with MICs against laboratory and clinical isolates of P. aeruginosa (MCo-PG1: MIC₅₀ and MIC₉₀ of 1.5 and 3 μM, respectively, PG1: MIC₅₀ and MIC₉₀ of 0.2 and 0.78 μM, respectively). Time-kill experiments demonstrate rapid, concentration-dependent antimicrobial activity with ≥10³ CFU/mL reduction at concentrations ≥4× MIC. Considering molarity, MCo-PG1 had an increased tolerability in mice in comparison to PG-1 (25 mg/kg and 5 mg/kg, respectively) while the MTD for colistin was 5 mg/kg. Single-dose administrations of 10 mg/kg and 25 mg/kg MCo-PG1 were associated with a high survival rate of septic mice (Hazard ratio (HR): 11.4 and 20.8 respectively, p <0.001) comparable to 5 mg/kg PG-1 considering molarity and 15 mg/kg colistin administration (HR: 24.8, p <0.001).

Conclusions: MCo-PG1 exhibited potent antipseudomonal activity in vitro, improved tolerance and demonstrated reduced mortality in a murine model of P. aeruginosa sepsis.

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Abstract 7969

**Impact of different components of a national intervention on CLABSI rates**

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**Background:** Central line-associated bloodstream infection (CLABSI) is one of the most common preventable infectious complications among intensive care unit (ICU) patients. In 2012, the Israeli National Center for Infection Control (NCIC) initiated a country-wide intervention to reduce the incidence of CLABSI. The objective of this study is to evaluate the impact of different components of the intervention on CLABSI rates.

**Materials/methods:** All medical-surgical ICUs in Israel were included in the national intervention. CLABSI prevention guidelines were distributed in 2011. National surveillance of hospital-acquired BSI and CLABSI rates was initiated in January 2012 with bi-annual feedback to hospital management and local infection control teams. A national workshop on effective prevention measures was conducted in June 2013. Public reporting of CLABSI rates was announced in 2015. In 2017, additional steps were implemented: setting national targets, providing quarterly feedback to hospitals, assessing local infection control measures using an online survey and conducting site visits by a physician and infection control nurse from the NCIC. We calculated incidence rate difference between each year and the year prior. The number of cases prevented was calculated by comparing the expected number of CLABSI based on the 2012 rate to the observed number.

**Results:** A total of 121 ICUs in 30 hospitals were included in the national intervention. The pooled average rate in 2012 was 7.2/1000 line-days [Figure]. Following the introduction of surveillance and feedback in 2012, a significant decrease in CLABSI rates was observed during 2013. (IRD: -2.8, 95% CI: -3.7 - -1.8, P<0.001). Between 2013 and 2017, no significant change was observed (IRD range -0.7 - 0.1). In 2018, a significant decrease was observed: (IRD -1.4 95% CI: -2.0 - -0.8, P<0.001). The decrease in CLABSI incidence since 2012 translates into approximately 1500 CLABSI cases prevented between 2013-2019.

**Conclusions:** National surveillance and data feedback resulted in an initial reduction in CLABSI rates but the effect was limited. In the wake of additional interventions, including more frequent and detailed feedback, goal setting and site visits, a further sustained reduction was observed.

**Figure:** CLABSI rates in Israeli medical-surgical ICUs, by year

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Virulence profile and comparative genomics analysis of the emerging Klebsiella pneumoniae genotypes ST45, ST101 and ST629

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**Background:** Klebsiella pneumoniae isolates associated with hospital-acquired infections have primarily been assigned to CC258 and to the additional emerging genotypes ST45, ST101, ST629 in Europe and worldwide. The aim of this study was to analyze the virulence profile and to perform comparative genomic analysis of a collection of K. pneumoniae isolates, from different sources and human or non-human hosts, assigned to the ST45, ST101 and ST629 genotypes.

**Materials/methods:** The virulence profiles of K. pneumoniae strains was assessed using the Galleria mellonella infection assay. Genome sequencing of K. pneumoniae isolates was performed using Illumina MiSeq. Genes associated with virulence, heavy metal resistance, and drug resistance were identified using the Large-Scale Blast Score Ratio pipeline.

**Results:** ST45, ST101 and ST629 K. pneumoniae strains were isolated from either human or non-human hosts and from different body sites. Among them, human clinical K. pneumoniae isolates showed multidrug-resistant profiles. High variability in the infectivity of G. mellonella larvae was observed among K. pneumoniae isolates assigned to different genotypes, with lethal dose 90% (LD$_{90}$) values ranging from dozens of cells [isolates M1A and SB5970 assigned to ST45] to more than ten million of cells [isolate Kp-Mo-5 assigned to ST629]. Kaplan-Meier survival curves confirmed the different pathogenicity of the strains in this infection model. Overall, K. pneumoniae isolates assigned to ST45 showed higher virulence than those assigned to ST101 or ST629, with LD$_{90}$ values $10^2$ to $10^3$-fold lower than those of ST101 or ST629 isolates. Notably, a hyper-virulent phenotype was found in some ST45 K. pneumoniae isolates irrespective of their source of isolation. The distribution of virulence and/or resistance genes among ST45, ST101 and ST629 K. pneumoniae isolates is currently under investigation.

**Conclusions:** Our data highlight a trend toward increased virulence in K. pneumoniae strains assigned to the ST45 genotype. Comparative genomics is ongoing to verify whether an association exists between this phenotype and the acquisition of specific virulence determinants.

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**Abstract 7971**

**Patients related barriers for delay in seeking confirmatory test and treatment of hepatitis C in treatment naïve patients visiting a tertiary care hospital in Karachi, Pakistan**

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**Background:** Hepatitis C virus (HCV) is a leading cause of chronic liver disease worldwide, resulting in significant morbidity and mortality. Though it is a preventable disease but has turned into an epidemic in South-Asia, with the disease burden in Pakistan being one of the highest in the world. Researches from various countries have identified factors for the poor uptake for the diagnosis and treatment at three different levels: patient level, physician level and organizational level. This study aims to determine the reasons for patient level delay in seeking confirmatory diagnosis and treatment of hepatitis C as it is important to ascertain these factors to reduce unnecessary complications and mortality from a curable disease.

**Materials/methods:** A cross-sectional survey conducted between 2014 to 2016 in HCV treatment naïve patients visiting out-patient family medicine clinics at a free tertiary care hospital. Patients were interviewed using a pre-coded questionnaire. Delay was defined as taking greater than 3 months at any stage as follows: Delay 1: not going to a doctor for advice after initial diagnosis; Delay 2: not getting a confirmatory PCR test after being advised; Delay 3: delay in initiating treatment.

**Results:** A total of 368 participants with positive HCV antibody status constituted the study population. The mean age of the participants was 33.2 years (SD ± 8.3), with the majority two-thirds being women (n=242; 66%). Types of delay with their frequencies can be consulted in Figure 1. Most common reasons for type 1 delay was financial constraints (47.9%), followed by assuming it was curable through alternative treatment (33.6%), and lack of time due to household responsibilities (24.3%). Delay 2 and Delay 3 also showed inability to afford the test (80.2%) and treatment (66.2%) as being the leading cause.

**Conclusions:** Barriers to Hepatitis C testing and treatment vary at different care stages and are not entirely patient-related. However, understanding the patient related barriers for the delay will not only help in the successful delivery of Hepatitis C care in a resource poor country, but also decrease the morbidity and mortality associated with this chronic disease.

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Impact of interferon gamma on Staphylococcus aureus internalisation within human osteoblasts

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Background: Staphylococcus aureus is responsible for difficult-to-treat bone and joint infection, partly due to its ability to constitute an intraosteoblastic bacterial reservoir associated with chronic and relapsing infections. We evaluate here the impact of the interferon gamma (IFNg)-mediated host cellular response against this intracellular infection.

Materials/methods: The ability of the S. aureus wild-type strain SA113 (ATCC35556) to adhere and to invade bone cells were evaluated in an ex vivo model of MG63 human osteoblast infection (gentamicin protection assay) pre-treated or not by recombinant human IFNg at 1, 10 or 100 ng/mL. Our results led us to further investigate: i) the impact of the supernatant of MG63 cells pre-treated or not by IFNg on bacterial adhesion and internalization (gentamicin protection assay); and ii) the effect of IFNg on the cellular expression of the β1 intergrin (RT-q-PCR) which represent the osteoblastic receptor of S. aureus during the internalization process.

Results: Pre-exposition of MG63 cells to IFNg resulted in a significant and dose-dependent reduction of SA113 internalization rate, from 4.0% (95% confidence interval [CI], 3.1 -4.8) for untreated cells to 1.2% (95%CI, 0.8- 1.6) for osteoblasts treated by 100 ng/mL of IFNg (p<0.001) (figure, panel A), due to a significant reduction of SA113 adhesion to bone cells (figure, panel B). This observation was not due to a cell-released soluble factor, as preincubation of SA113 with the supernatant of osteoblasts pre-treated by IFNg did not influence bacterial survival or adhesion to MG63 cells. Surprisingly, the observed reduction of adhesion and internalization was not related to a decrease in cellular expression of the β1 intergrin.

Conclusions: During the acute inflammatory phase of bone and joint infection, IFNg secretion might prevent the constitution of an intraosteoelastic reservoir of S. aureus, limiting bacterial adhesion to bone cells. The involved mechanism is not related to a decreased expression of the cellular β1 intergrin, and remains to be clarified.

Figure. Internalization [A] and adhesion [B] rates of S. aureus SA113 in a ex vivo model of infection of MG63 osteoblastic cells pre-treated or not by increasing concentrations of interferon gamma [IFNg].

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Abstract 7975

**Early (within 7h) phenotypic detection of fluconazole-resistant Candida glabrata isolates**

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**Background:** The wild-type *Candida glabrata* population is susceptible to increased exposure of fluconazole (800 mg/12 mg/kg daily). However, acquired resistance is common. Rapid detection of fluconazole resistance is important for early effective antifungal therapy. We therefore developed a phenotypic test based on EUCAST E.Def 7.3 protocol for the detection of fluconazole resistant isolates utilizing the colorimetric dye XTT.

**Materials/methods:** Twenty-five clinical *C. glabrata* isolates were included: 14 fluconazole resistant (MICs >16 mg/L) and 11 Susceptible Increased exposure (MICs ≤2-16 mg/L). For the XTT assay, 0.5-2.5×10^5 CFU/mL of each isolate was added to RPMI1640+2% glucose medium containing different concentrations of XTT/MEN in 96-flat bottom microtitration plates (200 μL/well). In order to find the optimal concentration 100-400 mg/L of XTT with 0.39-25 μM of menadione were tested. Fluconazole at a concentration of 32 mg/L corresponding 1 two-fold to EUCAST R breakpoint (16 mg/L) was added and together with drug-free wells, plates were incubated at 37°C. The metabolic activity in each well was kinetically assessed by measuring absorbance at 450nm every 15min for 18h in a microplate reader (Tecan Infinite F200). The differences in XTT absorbance between the drug-free and the drug-treated wells for resistant and susceptible to increased exposure isolates were assessed with student t test at different time points.

**Results:** The optimal conditions discriminating between resistant and susceptible to increased exposure isolates were: 100mg/LXTT/0.39μM MEN after 7h incubation. The mean±SD XTT-absorbance in drug-free and wells containing 32 mg/L were 0.32±0.11 and 0.25±0.10 for the resistant isolates and 0.32±0.06 and 0.15±0.03 for susceptible to increased exposure isolates, respectively. The XTT-absorbance differences of the 32 mg/L containing well from the drug-free well were 0.07±0.06 for the resistant isolates significantly lower than the 0.17±0.05 (p=0.0005) for the susceptible to increased exposure isolates.

**Conclusions:** A simple, cheap and fast phenotypic test was developed using the XTT dye with high specificity in detecting fluconazole-resistant *C. glabrata* isolates within 7h.

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Risk factors [derived from host, pathogen and disease] did not affect the efficacy of delafloxacin monotherapy in acute bacterial skin and skin structure infections trials

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Background: DLX is a new anionic fluoroquinolone available as IV and oral formulations that has been recently approved in Europe for the treatment of ABSSSI. It is characterised by a broad-spectrum of activity, including MRSA strains and a favourable safety profile in terms of cardiac effects and phototoxicity.

Specific factors such as age, diabetic status or type of infection represent risk factors that are recognised to impact the response to treatment. This analysis assesses the impact of these factors on the efficacy using data from pooled phase 3 ABSSSI trials.

Materials/methods: Risk factors relative to the host, the pathogen or the disease were examined in the pooled population of two pivotal trials performed in ABSSSI patients \(n=1510\) comparing DLX single agent IV/OS \(n=754\) vs the combination of Vancomycin/Aztreonam IV \(\text{VAN/ATZ}; n=756\) given for 5 to max 14 days in order to explore their potential impact on the success [cure + improvement] rate at end of treatment [EOT] and at follow-up [FU, i.e. 14 days after EOT].

The following risk factors at baseline were considered: age \(>65\) years; BMI \(\geq 30\) kg/m\(^2\); diabetes; prior antibiotic treatment; MRSA; bacteraemia; polymicrobial infection; >3 signs of systemic infection; type of infection: wound infection; and erythema area: \(\geq 4\)th quartile.

Results: The ABSSSI population was split into 2 categories based on the median number of baseline risk factors: lower risk \(<3\) risk factors \(n=881\), and higher risk \(\geq 3\) risk factors \(n=629\).

In patients treated with DLX, comparable success rate has been achieved in higher vs lower risk patients at the EOT [90.3% vs 90.8%] as well as at the FU [82.9% vs 86.0%]; no significant difference was observed when the two categories of patients are compared between treatment groups.

Conclusions: The number of risk factors did not affect the efficacy of DLX for the treatment of ABSSSI, with a high success rate being confirmed also in difficult to treat patients.

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Examining the urinary tract infection patient journey to identify opportunities to enhance the role of community pharmacists

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Background: Community pharmacists are involved in antimicrobial stewardship by providing patients with self-care advice and recommending over-the-counter treatments for common infections. The aim of this study is to identify opportunities to enhance the role of community pharmacists specifically in the management of urinary tract infections (UTI) by exploring the journey of service users with urinary symptoms.

Materials/methods: We collected data about the management of suspected or confirmed UTI through different sources: interviews and electronic questionnaires with community pharmacists and electronic and paper surveys with service users. Interviews were recorded, transcribed and coded using NVivo 12. Data were analysed using the classic grounded theory approach.

Results: We conducted 31 interviews and collected 38 questionnaires from 22 pharmacists working in 20 pharmacies. Eight pharmacists (36%) were women with a median of 15 years (IQR, 5-30) since qualification. Fifty service users completed the survey, 92% women, median age 50 years (IRQ, 27 -60), 41% suffering from recurrent UTIs. Triangulating responses from pharmacists and service users, 70% of the service users with urinary symptoms come to the pharmacy following a GP visit after an antibiotic prescription and 30% seek help first from a pharmacy. Pharmacists identified a number of barriers and facilitators of giving advice in the pharmacy [Table]. Sixty-four percent of the service users were comfortable discussing their urinary symptoms with pharmacists and even reported an enhanced role when compared with GPs; but stressed the importance of privacy. We collected the most important self-care advice given by pharmacists and their reasons for referral to the GP. Pharmacists declared that they could be the first contact for patients with urinary symptoms but pointed out the lack of a specific pathway to refer patients, the need for additional funding and staff to do so and the importance of increasing the possibilities to prescribe antibiotics for pharmacists.

Conclusions: We collected qualitative data among community pharmacists and service users about the journey of patients with suspected or confirmed UTI. This work could be useful to inform future strategies in England and other settings to enhance the role of community pharmacists in the management of patients with urinary symptoms.

Table: Barriers and facilitators of giving advice in the pharmacy

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Pharmacists n=22 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of time or staff</td>
<td>17 (77)</td>
</tr>
<tr>
<td>Language barrier</td>
<td>13 (59)</td>
</tr>
<tr>
<td>No access to the medical record</td>
<td>9 (41)</td>
</tr>
<tr>
<td>Not recognised or funded by health authorities</td>
<td>5 (23)</td>
</tr>
<tr>
<td>No possibilities to prescribe medication</td>
<td>5 (23)</td>
</tr>
<tr>
<td>Outside the scope of expertise of pharmacists</td>
<td>3 (14)</td>
</tr>
<tr>
<td>Waiting time is unpredictable for service users</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Some service users prefer information from doctors</td>
<td>2 (9)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Facilitators</th>
<th>Pharmacists n=22 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacists are confident and trained in giving advice</td>
<td>22 (100)</td>
</tr>
<tr>
<td>No appointment needed</td>
<td>17 (77)</td>
</tr>
<tr>
<td>Long opening hours</td>
<td>14 (64)</td>
</tr>
<tr>
<td>Ease of access</td>
<td>13 (59)</td>
</tr>
<tr>
<td>Multiples languages spoken by the staff</td>
<td>12 (55)</td>
</tr>
<tr>
<td>Financial incentive to give additional advice</td>
<td>10 (45)</td>
</tr>
<tr>
<td>Availability and use of a consultation room</td>
<td>9 (41)</td>
</tr>
<tr>
<td>Close contact with the service users</td>
<td>8 (36)</td>
</tr>
<tr>
<td>Flexible time for consultation (no time limit)</td>
<td>6 (27)</td>
</tr>
<tr>
<td>Counter assistants and sufficient staff</td>
<td>5 (23)</td>
</tr>
<tr>
<td>Local presence / community-based</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Possibility to give advice on the phone</td>
<td>2 (9)</td>
</tr>
</tbody>
</table>

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Abstract 7983

**Outcome and characteristics of invasive fungal infections in critically ill burn patients: a multi-centre retrospective study**

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**Background:** Characteristics and outcome of Invasive fungal infection (IFI) in critically ill burn patients have been poorly explored. We report the epidemiology and factors associated with 90-day mortality in a multicenter retrospective European study.

**Materials/methods:** All burn patients with confirmed IFI admitted between January 2010 to December 2015 in 10 centers in France and Belgium were included. Data were collected from mycology laboratories and from medical records of burn centers patients and reviewed by an expert committee including an infectious disease specialist and two burn care specialists.

**Results:** During the study period, 8503 burn patients were admitted to burn centers of whom 94 (1%) presented an IFI with a total of 110 IFI collected. Patients with IFI were mostly male (62%), with a median age of 50 [42-68] years, with high severity scores (median SAPS II score of 40 [28-49]), and with a median Total Burn Surface Area (TBSA) of 43 % [25-60]. Among the 110 IFIs collected, 77 were proven and 33 probable, 79 [72%] were yeast infections (Candida albicans (57% of yeasts), C. parapsilosis [20%] and C. glabrata [10%]), and 31 [28%] were filamentous infections (Mucorales infections [52 % of filamentous infections], Aspergillus sp. [26%] and Fusarium sp. [19%]). The 90-day mortality was 37% for all IFIs combined, 52% for filamentous infection and 32% for yeast infection (p: 0.08). Patients with more than one IFI had a higher 90-day mortality than patients with only one episode (62% vs 34 % (P = .006)). In multivariate analysis, higher SAPS II (OR= 1.05 (95%CI: 1.02-1.09) P = .002), bacterial co-infection (OR= 5.6 (95% CI: 1.6-19.6), P = .007) and use of allograft at the time of IFI diagnosis (OR= 5.3 (95% CI: 1.6-17.1), P = .005) were associated with 90-day mortality.

**Conclusions:** Although rare, invasive fungal infections remain associated with poor outcome in burn patients. The mortality appears however lower compared to control historical cohorts, suggesting improved survival over time. Bacterial co-infection and presence of allograft at time of IFI were factors independent associated with mortality and potential modifiable factors.

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Pharmacodynamic properties of amoxicillin-clavulanic acid in a neutropenic mouse thigh infection model

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Background: Amoxicillin (AMOX)-clavulanic acid (CLAV) has been used for decades. Various formulations with different AMOX:CLAV-ratios are available, but the rationale between these differences is unknown. The minimum CLAV concentration (Ct) required for efficacy has not been determined. We evaluated the pharmacodynamic properties of AMOX:CLAV combination against 3 bacterial species in a murine thigh infection model.

Materials/methods: 10^6-10^7 CFU of 1 Escherichia coli (No 39), 1 Klebsiella pneumoniae (No 17) and 2 Staphylococcus aureus isolates (ATCC 29213 and MUP2273) with AMOX/AMOX+CLAV MICs of >2048/16, >2048/32, 1/0.5 and 0.5-1/0.25-0.5 mg/L were used in a thigh infection model in neutropenic mice. Two hours after infection mice were treated with 256, 128 and 64 mg/kg q2h of AMOX alone. For combination studies, AMOX 64mg/kg q2h (S. aureus) and 128mg/kg q2h (E. coli, K. pneumoniae) was combined with 0.5-16 mg/kg q2h and 2-128mg/kg q8h CLAV, respectively. After 24h the mice were euthanized and the number of CFU in thigh homogenates were counted with serial quantitative cultures. For AMOX %fT>MIC and for CLAV %fT>Ct were calculated using the pharmacokinetic analysis (NONMEM) using different target Ct’s for each species.

Results: AMOX monotherapy up to total daily doses (TDD) of 2048 mg/kg had no effect against E. coli and K. pneumoniae. High TDD of 1072-3297mg/kg for stasis and 2423-3201 mg/kg for 1log kill were needed for S.aureus, resulting in %fT>MIC of 95.1-100%. When AMOX was combined with CLAV, q2h regimens were more efficacious than the q8h regimens for all 3 species. TDDs to obtain stasis/1logkill were 100/486, 64.1/328, and 1.0-1.1/1.2-1.6 mg/kg for E. coli, K. pneumoniae and S. aureus, respectively. For AMOX:CLAV combination with AMOX TDD of 1536 mg/kg (E. coli, K. pneumoniae) and 768 mg/kg (S. aureus), target Ct’s of CLAV for E. coli, K. pneumoniae, and S. aureus were 0.5, 1, and 0.031 mg/L, respectively, resulting in %fT>Ct of 29.1%, 10.4%, and 3.7% (SD 1.2) for stasis, respectively.

Conclusions: The addition of CLAV to AMOX increased the efficacy. Target concentrations for CLAV needed for efficacy are lower for S.aureus as compared to E.coli and K. pneumoniae. The effect of CLAV is time-dependent. These results can be used to optimise human dosing regimens.

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Epidemiology of Neisseria meningitidis infections over a 17-year period in a tertiary hospital in Madrid, Spain

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Background: Non-B non-C meningococcal infections are rising in European countries. The knowledge of the epidemiology of these infections is crucial to establish preventive actions in risk population. The aim of this work was to study the epidemiology of Neisseria meningitidis (Nm) infection diagnosed in a 17-years period in a tertiary hospital in Madrid, Spain.

Materials/methods: All patients with Nm isolation in blood cultures and/or cerebral spinal fluid (CSF) from 2003 to 2019 were included. Microorganism identification was performed by biochemical tests (API-NH biochemical gallery, Biomérieux) and/or mass spectrometry (MALDI-TOF MS, Bruker Daltonics). Serogroup identification was assigned by agglutination (BD). Antibiotic susceptibility testing was performed by disk diffusion and/or Etest (Biomérieux) and results interpreted according to CLSI/EUCAST criteria. Epidemiological and clinical data were collected from patients’ clinical records.

Results: Forty-two patients (50% men, median age 33 years; IQR: 9.25-72.25) with meningococcemia (n=24, 57.1%), meningitis (n=7, 16.7%) or both (n=11, 26.2%) were included. Patients were mainly hospitalized at Infectious Diseases (20, 47.6%), Pediatric (13; 30.9%) or Internal Medicine (5; 11.9%) Departments. Almost half of them (19; 45.2%) needed intensive care admission and mortality rate was 7.1% (3 patients died). Most of the cases occurred in 2004, 2005, 2006 (5 each year; 35.7%) and 2019 (6; 14.2%). Serotyping was only feasible in half of the isolates (n=21) that belonged to serogroups: C (10; 47.62%), B (5; 23.81%), W135 (3; 14.29%), A (2; 9.52%); and Y (1; 4.76%). Nm serogroup W135 was only isolated during 2019 and these cases presented with meningococcemia and respiratory symptoms but did not associated meningitis. All isolates were susceptible to third generation cephalosporins, rifampicin, quinolones and only two isolates were resistant or had intermediate susceptibility to penicillin.

Conclusions: Nm infection has remained low in our setting over a 17 years period. An increase in the number of cases has been observed in the last years along with a switch in serotypes circulation. Monitoring this epidemiological change should be a priority in surveillance programs.

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Abstract 7991

**Performances of BD MAX Cdiff assay for detection of toxigenic *Clostridioides difficile* in 1321 clinical stool specimens using FecalSwab**

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**Background:** The goal of this study was to evaluate the analytical performance of BD MAX Cdiff assay for detection of toxigenic *C. difficile*.

**Materials/methods:** 1321 prospective stool specimens collected on FecalSwab (Cary-Blair) were screened with BD Max Cdiff assay (BD) from October to November 2019. Results were compared to routine algorithm including immunochromatographic testing for glutamate dehydrogenase (GDH) and toxinA/B by *C. diff* QuickChek Complete (Abbott) (QC) completed by Xpert *C. difficile* assay (Cepheid) (GX) when GDH+/Tox-. In case of discrepant results (BD-/GDH+/Tox+ or BD+/GDH-Tox-), GX was performed.

**Results:** The overall agreement between BD and routine algorithm was 97.4%. The prevalence of toxigenic *C. difficile* was 7.6% (n=99) using BD versus 5.4% (n=71) using the routine QC/GX algorithm (see table 1). Among the 99 BD+ specimens:

- 29% (n=29) were confirmed GDH+/Tox+ using QC.
- 42% (n=42) were GDH+/Tox- using QC and were therefore tested using GX. Among these 42 samples, 41 were GX+ confirming BD results.
- 28% (n=28) were GDH-/Tox- using QC. 16 were confirmed GX+ while 12 remained negative. Interestingly, three out of these 12 specimens showed a late positive Ct (>37 cycles) interpreted as negative by GenXpert platform.

Of note, one specimen was found QC+ but both BD- and GX-. Complementary analyses are underway for the fourteen specimens in bold characters in table 1.

**Conclusions:** BD Max Cdiff assay shows good performances for the detection of toxigenic *C. difficile* and has a good agreement with the routine algorithm used in the laboratory. However, it shows an increased sensitivity for ICD. Nevertheless, the potential lost of specificity due to asymptomatic carriage of toxigenic strains must be taken into account to avoid overestimation of ICD. Complementary analyses, that are underway, will allow to compare accurate sensitivity and specificity of BD and routine algorithm.

<table>
<thead>
<tr>
<th>GDH + / Tox +</th>
<th>BD +</th>
<th>BD -</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>29</td>
<td>1</td>
</tr>
<tr>
<td>(GX also confirmed -)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GDH - / Tox -</td>
<td>GX +</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>GX -</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>GX Not tested</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>1180</td>
<td></td>
</tr>
<tr>
<td>GDH + / Tox -</td>
<td>GX +</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>GX -</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>41</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Results of BD versus QC/GX results.

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Abstract 7992

**Bacteriophage therapy in the treatment of burn wounds**

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**Background:** Purulent-septic infections are a major problem in combustiology. The search for alternative methods of treatment of wound infections is relevant at the time of the rise of antibiotic resistance. Phage therapy is one of the most promising directions in this field of medicine. The unique features of bacteriophages attract physicians since the 20-ies of XX century. Researchers around the world are exploring alternative ways of combating infections, in particular, the treatment of bacteriophages.

To define the algorithm of complex therapy with antibiotics and bacteriophages of burn wounds caused *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

**Materials/methods:** The results of research of 187 separated wounds samples of 100 patients with burns less than 30% of body surface have been analyzed. All the patients were treated at the burn center F.I. Inozemtsev City Clinical Hospital. Identification of the bacteria and determination of the sensitivity was performed on the analyzer AutoScan 4 (Siemens, USA). Strains of *S. aureus* and *P. aeruginosa* were tested for sensitivity to the drug of domestic production "Bacteriophage staphylococcal liquid" and "Bacteriophage pseudomonas aeruginosa" [FSUE NPO "Microgen", Russia].

**Results:** In the study 272 strains of microorganisms have been isolated. *S. aureus* – 44.2%, *Acinetobacter baumannii* – 37.7%, *P. aeruginosa* – 27.3%, *Klebsiella pneumoniae* – 11.7%, other -26.0%. In the study of antibiotic susceptibility strains *S. aureus* (n=120) received 20.8% (n=25) methicillin-resistant (MRSA) and 79.2% (n=95) – methicillin-sensitive strains of *S. aureus* (MSSA) were obtained. Among MSSA sensitivity to bacteriophage made 90.5% and among MRSA strains it was 92.0%. Among the *P. aeruginosa* strains (n = 74) were sensitive to Meropenem – 54.0%, Imipenem – 59.5%, Ceftazidime – 67.6%, Cefepime – 68.9%, Amikacin – 64.9% and Ciprofloxacin – 60.8%, panresistance – 21.6% strains *P. aeruginosa*. Among the *P. aeruginosa* strains (n = 74) were sensitive to bacteriophage – 85.7%.

**Conclusions:** The results of the study show the high sensitivity of strains of *Staphylococcus aureus* and *Pseudomonas aeruginosa* in relation to drugs with bacteriophages domestic production [FSUE NPO "Microgen", Russia] and the feasibility of their use in the treatment of burn wounds. The special relevance gains bacteriophages in the treatment of burn infections caused by antibiotic-resistant bacteria.

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Amphotericin B as rescue therapy for alveolar echinococcosis in patients with benzimidazole treatment failure or toxicity

Johannes Bloehdorn¹, Sanne Burkert*, Lynn Peters¹, Julian Schmidberger¹, Andreas Hillenbrand¹, Tilmann Gräter¹, Martina Furitsch¹, Thomas Barth¹, Doris Henne-Bruns¹, Wolfgang Kratzer¹, Nina Eberhardt¹, Ambros Beer¹, Beate Grüner¹

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Background: Curative resection is the treatment of choice for alveolar echinococcosis (AE) with circumscribed manifestation. However, in most cases complete resection is impracticable due to extended involvement of critical anatomic structures. Benzimidazole treatment (BMZT) is the only available medical treatment approved in such cases, but may be limited due to inefficacy or intolerance. Thus, new drugs are urgently needed. Amphotericin B treatment (AMBT) has been used with success in desperate situations.

Materials/methods: We report long-term follow-up data from 5 patients with AMBT at our centre who were diagnosed with unresectable AE and BMZT intolerance or treatment failure. Initial AMBT loading phase of 2 weeks was followed by 1-3 applications per week, depending on response. Close monitoring was conducted for the first month and afterwards every 3 months. Responses were confirmed by PET-CT scan, showing stable or regressive metabolic activity or lesion size. Furthermore, clinical evidence of response was documented with healing AE associated cutaneous fistulae and regression of abdominal discomfort.

Results: All patients had complex disease manifestation requiring repeated surgical interventions due to complications. Three patients exhibited disseminated disease with pulmonary, cardial, vertebral and cerebral manifestations. Patients showed intolerance (n=2) and progression (n=3) under BMZT. Age at diagnosis ranged from 29-58 years and AMBT was initiated 10-25 years after diagnosis and a median of 3 previous lines of systemic therapy. With AMBT, 4 patients achieved stable disease (SD), of which 2 are still on therapy after 2 months and 13 years, respectively. The other two patients died after having achieved SD for 4 months and 3 years, respectively, but AMBT had to be discontinued due to an ileus or renal toxicity. One patient had shown only a partial remission for 17 months and achieved SD with alternative treatment. Side effects under AMBT were mostly manageable, however deteriorating renal function after 3 years prompted the halt of AMBT in one patient.

Conclusions: Salvage AMBT might be a valuable treatment option in cases of BMZT failure and can induce persistent disease control, although with potentially significant side effects, high treatment costs and the need for repeated intravenous therapy.

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Abstract 7994

**Potential role of procalcitonin in antimicrobial stewardship programme in febrile neutropenic cancer patients**

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**Background:** The assessment of cancer patients with chemotherapy-induced neutropenic fever in the emergency center could be challenging. Clinical decision should be made regarding initiation of antimicrobial agents and need for hospitalization. Cancer patients are often subjected to overuse of antimicrobial therapy which contributes to the emergence of multidrug-resistant pathogens. Procalcitonin (PCT)-based algorithm has been proposed as part of antimicrobial stewardship programs to guide and reduce antibiotic use in patients with sepsis and respiratory tract infections. Initiation of intravenous antibiotics in patients with baseline PCT levels <0.25 μg/L has been strongly discouraged whereas levels ≥0.25 dictate hospitalization and antibiotic use. We evaluated the role of PCT in febrile neutropenic cancer patients.

**Materials/methods:** We conducted a retrospective study of all febrile neutropenic cancer patients who presented to our emergency center and had a serum PCT level collected from April 1, 2018 to April 30, 2019. Fever was defined either as a documented temperature of ≥100.4 °F or a chief complaint of fever reported at home. Neutropenia was defined as an absolute neutrophil count ≤500 cells/mL.

**Results:** We identified 550 neutropenic febrile cancer patients of whom 440 (80%) were hospitalized for a median duration of 5 days. Among all patients, 70% had hematological malignancies. Bloodstream infections (BSI) were diagnosed in 24% of patients with gram negative organism in 56%, gram positive in 41%, and both in 3%. A PCT level ≥0.25 was significantly associated with BSI and overall mortality (P<0.0001). Among the 110 patients who were treated as outpatient, 37% had a PCT ≥0.25 and 15% had a BSI of whom 71% had a PCT ≥0.25. Among the 440 patients who were admitted to the hospital, 48% had a PCT level <0.25.

**Conclusions:** A PCT level ≥0.25 in febrile neutropenic cancer patients is significantly associated with BSI and mortality and may prompt initiation of intravenous antibiotics and hospital admission. PCT < 0.25 is associated with a low mortality and may suggest treatment of the patient in the ambulatory setting. PCT may reduce inappropriate use of antibiotics in an oncologic emergency center and may contribute to an antibiotic stewardship program.

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Evaluation of the CAMPYLOBACTER QUIK CHECK to detect Campylobacter in stool samples

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Background: Campylobacters are the main cause of bacterial diarrhea in the world. Antibiotic therapy in Campylobacter diarrhea is of interest in the first 3 days in order to shorten carriage and duration of the disease. For a long time, stool culture was the reference test to detect Campylobacters but the result was obtained in a minimum of 48 hours. Now, several different rapid tests are available. One of them is a rapid membrane enzyme-linked immunosorbent assay, the CAMPYLOBACTER QUIK CHEK™, commercialized by Abbott and providing a result in less than 30 minutes. The aim of this study was to evaluate its performance.

Materials/methods: This retrospective study was conducted in the Bacteriological Laboratory of Bordeaux University Hospital, France. One hundred and eight samples were analyzed: 88 were issued from patients hospitalized at the Bordeaux University Hospital and 22 were kindly provided by a private laboratory (Exalab, Le Haillan, France), and transported at +4°C in an e-swab medium. Culture was systematically performed, then specimens were frozen at -80°C until use. After thawing, specimens were tested by the rapid CAMPYLOBACTER QUIK CHEK™ following the manufacturers’ instructions, and by a molecular method (in house RT-PCR and/or BOMAX (Beckton Dickinson) and/or Rigadene (r-Biopharm)). The reference test was a composite reference standard: a positive case corresponded to a positive culture and, in case of a negative culture result, by the association of a positive molecular test and the ELISA (Ridascreen, r-Biopharm).

Results: Following the composite reference test, 53 stools were positive and 55 were negative. The Abbott test detected 1 additional positive sample and missed 2 cases, corresponding to e-swab stools, whereas culture did not detect 5 positive samples. Sensitivity of the CAMPYLOBACTER QUIK CHEK™ was 97% and specificity was 98%. In contrast, culture sensitivity was 90% and its specificity was 100%.

Conclusions: The CAMPYLOBACTER QUIK CHEK™ showed an excellent performance. It is a very easy test to use and does not require any specific automation. Its main advantage is the rapidity in obtaining a result, enabling an adapted medical care if needed. The place of this test in daily clinical practice needs to be evaluated.

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Abstract 7997

Serum galactomannan antigenaemia of HIV-positive patients in an endemic area for Talaromyces marneffei

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Background: Cross-reactivity of serum galactomannan (GM) test (Platelia, Bio-rad) has been demonstrated in patients with cryptococcosis, talaromycosis marneffei, and paecilomycosis. In our previous study, we have demonstrated significant elevation of serum GM in HIV-positive patients with symptomatic talaromycosis. We prospectively evaluated prevalence of serum GM antigenemia in HIV/AIDS patients in an endemic area of talaromycosis.

Materials/methods: From January-2009 to August-2019, we prospectively tested serum GM of all patients within one week after their confirmation of HIV-infection. A GM optic density index (O.D.) more than 0.5 was considered to be positive. CD4 T cell count, HIV viral load and serology testing for syphilis, cryptococcosis and toxoplasmosis were also determined during the initial assessment of these patients. Diagnosis of talaromycosis was defined as having positive culture of T. marneffei from blood, sputum, sterile site fluid or any biopsied tissue. Medical records regarding further management were obtained.

Results: A total of 1143 adult HIV/AIDS patients were enrolled and followed at our institute during study period (man: woman= 1100:33). Thirty-six patients (3.1%, all male) were positive for serum GM test at their initial evaluation (O.D. index; range: 0.508-4.763, mean±S.D.: 1.2 15± 1.019) with a median CD4 count of 299 cell/μl (range, mean±S.D.: 7 - 1 305, 404.2±317.6). None of these patients was considered to have aspergillosis or talaromycosis judged by their physician according to clinical presentations therefore no anti-mold agents were ever prescribed. Other co-infections included 8 syphilis, one cryptococcosis, one toxoplasmosis and one amebiasis.

Conclusions: GM antigenemia of HIV/AIDS patients were not rare in endemic area for T. marneffei. A close follow up of their symptoms rather than initiate antifungal treatment may be more suitable for these patients.

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**Abstract 7998**

*In vitro comparative activity of cefepime/taniborbactam against metallo-beta-lactamase-producing Pseudomonas aeruginosa and Klebsiella pneumoniae isolates*

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**Background:** Multidrug resistant bacteria are a major problem for public health. Treatment with last-line antibiotics becomes less and less effective. Taniborbactam (VNRX-5133) is a newly developed β-lactamase inhibitor (BLI) which directly inhibits all four classes of β–lactamases (Class A, C, D Serine- and VIM/NDM class B metallo-β-lactamases). To evaluate the efficacy of BLI taniborbactam combination with cefepime we used MIC determinations and compare them with a panel of antimicrobial agents that are used in clinical practice, against metallo beta-lactamase (MBL) producing Pseudomonas aeruginosa and Klebsiella pneumoniae isolates.

**Materials/methods:** Fifty phenotypically characterized MBL producing (VIM and NDM) P. aeruginosa (N=25) and K. pneumoniae (N=25) clinical strains isolated in the last two years in two major hospitals in Athens were tested against amikacin (0.06-128 mg/l), aztreonam (0.03-64 mg/l), cefepime (0.03-64 mg/l), cefepime/tazobactam (0.03-64/8 mg/l), cefepime/taniborbactam (0.03-64/4 mg/l), levofloxacin (0.016-32 mg/l), gentamicin (0.016-32 mg/l), ciprofloxacin (0.008-16 mg/l), levofloxacin (0.016-32 mg/l), imipenem (0.016-32 mg/l), meropenem (0.016-32 mg/l), meropenem/vaborbactam (0.03-64/8 mg/l), piperacillin/tazobactam (0.06-128/4 mg/l), tigecycline (0.016-32 mg/l) and MICs were determined using the broth microdilution ISO standard. Classification of isolates to susceptible (S), intermediate (I) and resistant (R) was performed according to EUCAST breakpoints (for cefepime/tazobactam the breakpoints of cefepime were used whereas for cefepime/taniborbactam the S/R ≤8/>16 breakpoints were used). The quality control (QC) strains Escherichia coli ATCC25922, Pseudomonas aeruginosa ATCC27853 and Klebsiella pneumoniae ATCC700603 were used.

**Results:** High levels of resistance (>84%) were found for K. pneumoniae MBL isolates to most antimicrobial agents tested except cefepime/taniborbactam for which only 16% were resistant (Table). High levels of resistance (>82%) were also found for P aeruginosa MBL isolates to all drugs except amikacin, aztreonam and cefepime/taniborbactam for which 67%, 29%, and 54% were resistant, respectively (Table). Taniborbactam reverse resistance to cefepime in 84% of K. pneumoniae isolates and in 46% P aeruginosa MBL isolates.

<table>
<thead>
<tr>
<th>Antibacterial Drug</th>
<th>Kisebsiella pneumoniae (N=25)</th>
<th>Pseudomonas aeruginosa (N=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%S</td>
<td>%I</td>
</tr>
<tr>
<td>Amikacin</td>
<td>NTa</td>
<td>NT</td>
</tr>
<tr>
<td>Aztreonam</td>
<td>8%</td>
<td>0%</td>
</tr>
<tr>
<td>Cefepime</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Cefepime/Tazobactam</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Cefepime/Taniborbactam</td>
<td>64%</td>
<td>0%</td>
</tr>
<tr>
<td>Ceftriafoline/Tazobactam</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>12%</td>
<td>4%</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
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<td>NT</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>4%</td>
<td>0%</td>
</tr>
<tr>
<td>Imipenem</td>
<td>NT</td>
<td>NT</td>
</tr>
<tr>
<td>Meropenem</td>
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</tr>
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<td>Meropenem/Vaborbactam</td>
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</tr>
<tr>
<td>Piperacillin/Tazobactam</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Tigecycline</td>
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<td>0%</td>
</tr>
</tbody>
</table>

*aNot tested

**Conclusions:** The BLI+b-lactam combination cefepime/taniborbactam was very effective against MBL producing K. pneumoniae and P. aeruginosa isolates reversing b-lactam resistance in 88% and 61% of the isolates, respectively.

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Efficacy and safety of intravenous fosfomycin in patients with periprosthetic joint infection: preliminary results from the PROOF study: a prospective multi-centre study

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Background: Fosfomycin exhibits bactericidal activity against a broad-spectrum of bacteria and has good tissue and bone penetration. We evaluated the efficacy and safety of treatment regimens based on combinations with 15g/d intravenous fosfomycin followed by oral antibiotics for totally 12 weeks for the treatment of periprosthetic joint infection (PJI).

Materials/methods: Consecutive patients with PJI caused by at least one of the following isolates were prospectively included: staphylococci (MIC ≤32 mg/l), streptococci (MIC ≤128 mg/l), enterococci (MIC ≤128 mg/l), Enterobacteriaceae (MIC ≤32 mg/l) and Pseudomonas spp. (MIC ≤128 mg/l). Follow up with clinical (joint function and quality of life scores), laboratory and radiological evaluation at 3, 12 and 24 months after last surgery is performed. The probability of infection-free survival was estimated using the Kaplan-Meier survival method.

Results: 50 patients were screened for eligibility, of which 2 were excluded due to intolerance or allergy to fosfomycin, 1 due to isolation of fosfomycin resistant pathogen and 2 patients died due to unrelated cause to infection. The remaining 45 patients were included. The infection occurred postoperatively in 31 patients (69%) and hematogenously in 14 (31%). Two-stage exchange was performed in 27 (60%), debridement with retention in 13 (29%) and one-stage exchange in 5 patients (11%). Due to persistence of infection, 3 patients underwent prosthesis explantation after initial debridement and retention, 1 patient underwent debridement of Girdlestone-situation; all 4 infections were caused by S. aureus. 41 patients were infection-free (91%) after a median follow-up of 6 month (range, 1 - 14 months). Nausea (n=14) and hypokalemia (n=13) were the most frequent adverse events and resolved after fosfomycin discontinuation. Isolated pathogens were staphylococci (n=30), streptococci (n=3), enterococci (n=5) and gram-negative rods (n=2). Cultures were negative in 9 patients and polymicrobial in 2 patients.

Conclusions: The applied PJI treatment algorithm including intravenous fosfomycin in the initial postoperative period was associated with infection-free outcome of 91% after a median follow-up of 6 month. The Kaplan-Meier survival method showed the probability of infection-free survival of 88.5% after 1 year. Adverse events occurred in 21 patients (46%) mostly nausea and hypokalemia. Adverse events were mild and resolved completely.

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Haematology/oncology patients might have different risks for MDR according to different types of chemotherapy

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Background: Few studies analyzed chemotherapy schemes regarding the risk of infections by multidrug resistant bacterial (MDR) infections. The goal of this study was to analyze risk factors for laboratory confirmed bloodstream infection (LCBI) by MDR among hematological cancer patients submitted to chemotherapy.

Materials/methods: We performed retrospective cohort study that included all patients with hematologic malignances submitted to chemotherapy between January-2017 and June-2018 with LCBI within 30 days of the end of chemotherapy. The outcomes evaluated were LCBI by MDR bacteria and LCBI by carbapenem resistant Gram-negative bacteria (CRGNB). The independent variables analyzed were gender, age, hematological diagnosis, type of chemotherapy, chemotherapy drug, outpatient or inpatient chemotherapy, number of chemotherapy cycles, neutropenia on LCBI diagnosis, lymphopenia on LCBI diagnosis, invasive devices use, ICU stay at LCBI diagnosis, site of infection, ECOG, Karnofsky performance score. The analysis was performed by LCBI episode. Statistical analysis was performed by chi-square, Fisher and Mann-Whitney test when appropriated and logistic regression for multivariate analysis.

Results: During study period 1467 patients were submitted to chemotherapy. It was identified 167 LCBI in 135 (9.2%) patients. The most common hematological diagnosis was acute myeloid leukemia, 41 (24.6%). 118 (70.7%) episodes occurred during neutropenia period. The most common site of infection was intrabdominal infection, 59 (35.3%). MDR bacteria were identified in 60 (35.9%) episodes, and LCBI by CRGNB occurred in 35 (21.0%) cases. 12 (7.2%) LCBI by MDR were identified in patients under ambulatory chemotherapy. Variables identified in final model of risk factors for LCBI by MDR were: chemotherapy during hospital stay (p<0.02, OR 2.60 CI95% 1.20-5.67), mechanical ventilation in previous 7 days of LCBI (p<0.001, OR 3.45, CI95% 1.46-7.17), and chemotherapy with cytarabine (p<0.06, OR 1.91 CI95% 0.95-3.85). Risk factors for LCBI by CRGNB in final model were chemotherapy during hospital stay (p<0.02, OR 3.66, CI95% 1.27-10.56), mechanical ventilation in previous 7 days of LCBI (p<0.001, OR 4.08, CI95% 1.79-9.32), chemotherapy with vincristine (p<0.10, OR 1.98 CI95% 0.86-4.55).

Conclusions: Hospital assistance is the most important determinant of MDR infections among hematological patients. Different types of chemotherapy drugs maybe associated to different risks for MDR infections.

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Distribution of minimum inhibitory concentration of ceftriaxone to gonococcal strains in a reference sexually-transmitted disease clinic in Madrid, Spain

Clara Lejarraga*1, Blanca Menendez1, Estela Tello1, Flor Geriz1, Oskar Ayerdi1, Teresa Puerta1, Mar Vera Garcia1, Juan Ballesteros1, Petunia Clavo1, Giovanna Delia1, Carmen Rodriguez1, Jorge Del Romero1

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Background: Sexually transmitted infections (STI) are increasing all around the world. Considering that N.gonorhoeae is a common STIs worldwide, with an estimated 87 million new cases in 2016, lack of effective treatment would result in a major public health problem. Some isolated ceftriaxone-resistant strains of N. gonorhoeae have recently been reported. Overall, stronger surveillance is needed to better characterize the extent of antimicrobial resistance among gonococcal strains. The aim of this study was to know the minimum inhibitory concentration (MIC) for ceftriaxone to gonococcal strains in a reference STI/HIV clinic in Madrid.

Materials/methods: A total of 240 N. gonorrhoeae isolates were collected, from June until October 2019 in Centro Sanitario Sandoval. Urethral, pharyngeal, rectal and endocervical swabs were cultured on Chocolate agar PolyViteX VCAT3 [BioMérieux]. Neisseria gonorrhoeae was identified using API®NH [Biomerieux]. Moreover, all samples were identified using RT-PCR [Abbott RealTime CT/NG]. Consequently, we determined the MIC for ceftriaxone by using the E-test strip [Liofilchen srl], after 24 hours of culture. MIC (mg/l) values were interpreted according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

Results: 240 gonococcal isolates were tested for ceftriaxone susceptibility. Seventy-nine strains were urethral infection, 126 were rectal infection, 31 were pharyngeal infections and 4 were endocervical infections. Distribution by ages and gender shows that 91.7% of the samples were collected from men with ages between 16 and 58 years old, and 73.3% of them were men who have sex with men (MSM). Ceftriaxone MICs ranged from less than 0.002 to 0.016 mg/L. The MICs distribution for ceftriaxone are shown in Table 1.

Conclusions: Not only none of the strains have a decrease in the sensitivity but also the 50% of the isolates have a MIC below 0.003, therefore, we should consider ceftriaxone as monotherapy.

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Abstract 8006

Pulmonary mucormycosis: a large French survey
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Background: Mucormycosis is a rare and life-threatening invasive fungal infection occurring mostly in immunocompromised patients. The most common presentations of mucormycosis are pulmonary, rhinocerebral and cutaneous. New therapeutic and diagnostic tools have become available. We aimed to describe current pulmonary mucormycosis presentation, diagnosis, therapeutic management and outcome.

Materials/methods: A multicenter retrospective survey was conducted in six French tertiary hospitals. Patients diagnosed with pulmonary mucormycosis, localized or disseminated, according to modified EORTC/MSG criteria were enrolled. Patients with positive results of quantitative PCR (qPCR) in serum without other mycological criteria were classified as putative mucormycosis.

Results: From January 2008 to January 2019, 112 patients were recruited including 49 proven, 43 probable and 20 putative cases. Mucormycosis was disseminated in 40% patients. Eighteen percent of patients were diagnosed post-mortem. Main risk factors for mucormycosis were hematological malignancy (48%), allogeneic hematologic stem cell transplantation (21%), and solid organ transplantation (17%). Fourteen percent of patients developed mucormycosis while on posaconazole prophylaxis. Median time to diagnosis was 13 [7-23] days after first symptom, which was isolated fever in 67% cases.

CT-scan showed vascular involvement in 19% cases. Ground-glass opacity was more frequent in neutropenic patients than in non-neutropenic patients (64% vs 32%, p<0.01). A bronchoalveolar lavage contributed to diagnosis in 54/94 cases (57%). A qPCR was positive in serum in 32/40 patients (80%). The most frequent Mucorales genus were Rhizopus (31%), Rhizomucor (30%) and Lichtheimia (26%). Histological analysis revealed more frequently angio-invasion in patients with disseminated mucormycosis than with localized mucormycosis (58% vs 10%, p<0.01). Antifungal therapy was initiated in 86% patients and based on liposomal amphotericin B in 91/96 cases. Surgical excision was performed in 14% patients. Post-operative complications occurred in 5/16 patients, contributing to death in 3 patients. Fifty-three percent patients were admitted in ICU. Mortality rate was 33% at day 14 and 59% at day 90.

Conclusions: There are several different clinical pictures of pulmonary mucormycosis. A high mortality rate is observed despite the use of early liposomal amphotericin B treatment. Non-invasive diagnostic techniques such as qPCR assays should be used as a screening tool in febrile patients at risk for mucormycosis.

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**Abstract 8010**

**A retrospective study of rhinoviruses molecular diversity in three Paris hospitals: differential behaviours of HRV groups?**

Oshra Haddad¹, Mélanie Bertine¹, Nadhira Fidouh¹, Donia Bouzid¹, Xavier Duval¹, Vincent Bunel², Raphael Borie³, Jean-Christophe Lucet⁴, Diane Descamps¹, Benoit Visseaux*¹⁶


**Background:** Rhinoviruses are commonly thought as only the “common cold” agent. Recent diagnosis improvements revealed their high frequency among lower respiratory tract infection. The role, molecular epidemiology and patients’ characteristics associated to these viruses are still unclear today.

**Materials/methods:** We retrospectively included all nasopharyngeal or bronchoalveolar-lavages positive for rhinovirus using multiplex PCR assay in three Paris hospitals, France, from January to September 2018. The VP2/VP4 region was sequenced for subtyping. Associated clinical data were retrieved.

**Results:** Rhinoviruses were identified among 178 patients during the study period, mostly male (56%), with a median age of 62.2 [IQR:46.8-71.4] and frequently presenting chronic respiratory diseases (56%) and/or immunosuppression (46%). 63% of patients presented respiratory distress. Pneumonia diagnostic was retained for 25% of all patients. 95 (53%), 27 (15%) and 56 (32%) were HRV group A, B and C positive, respectively. HRV-B, compared to HRV-A and -C, appeared associated with immunosuppressor (56 vs 31 and 34% of patients, respectively, p=0.058), higher ICU admission rates (30 vs 17 and 9%, p=0.055) higher coinfections rates (52 vs 35 and 23%, p=0.04), and longer hospitalisation duration. Inversely, HRV-A was more frequently associated to a final diagnostic of pneumonia (54 vs 31 and 11% for HRV-B and -C, p=0.01). 137 HRV positive samples were identified <48h of hospitalisation and 41 >96h of hospitalisation. The latter were associated to higher ICU admission rates (29 vs 12%, p=0.01) and longer hospitalisation duration (22 vs 4 days, p<0.0001).

**Conclusions:** In this retrospective study, we highlight the high proportion of rhinovirus positive patients with chronic respiratory diseases or immunosuppression (69%) and observed some differences between rhinoviruses group regarding patients’ population or retained pneumonia diagnosis.

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>HRV-A</th>
<th>HRV-B</th>
<th>HRV-C</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>N</td>
<td>178</td>
<td>95</td>
<td>27</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>Immunosuppressive treatments</td>
<td>63 [35.4%]</td>
<td>29 [30.5%]</td>
<td>15 [55.5%]</td>
<td>19 [33.9%]</td>
<td>0.058</td>
</tr>
<tr>
<td>Chronic respiratory diseases</td>
<td>100 [56%]</td>
<td>53 [56%]</td>
<td>16 [61%]</td>
<td>31 [55%]</td>
<td>1</td>
</tr>
<tr>
<td>Coinfection</td>
<td>60 [33.7%]</td>
<td>33 [34.7%]</td>
<td>14 [51.8%]</td>
<td>13 [23.2%]</td>
<td>0.04</td>
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<td><strong>Bacterial</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Viral</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>16 [9.0%]</td>
<td>10 [10.6%]</td>
<td>5 [18.5%]</td>
<td>1 [1.8%]</td>
<td></td>
</tr>
<tr>
<td>Hospitalisation duration-median [IQR]</td>
<td>6 [1-13.75]</td>
<td>6 [1-14.5]</td>
<td>10 [5-18.5]</td>
<td>5 [0.75-12]</td>
<td>0.051</td>
</tr>
<tr>
<td>Death</td>
<td>11 [6.2%]</td>
<td>7 [7.4%]</td>
<td>1 [3.7%]</td>
<td>3 [5.3%]</td>
<td>0.8</td>
</tr>
</tbody>
</table>

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In vitro antibacterial activities of cefiderocol (S-649266) against multidrug-resistant Acinetobacter baumannii

Jacinda Abdul-Mutakabbir*1, Logan Nguyen1, Philip Maassen2, Kyle Stamper2, Katherine Lev2, Razieh Kebriaei3, Keith S. Kaye4, Michael J. Rybak5

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Background: The propensity for Acinetobacter baumannii to develop mechanisms of resistance against antimicrobials has rendered most therapeutic options ineffective. Nevertheless Cefiderocol (FDC), a siderophore-antibiotic conjugate, has shown success in overcoming the dependence on the outer membrane porins for bacterial entry. In A. baumannii, FDC has demonstrated potent activity against MDR isolates. However, the activity of FDC in combination with additional antimicrobials has yet to be evaluated. The objective of this study was to determine the activity of FDC alone and in combination with other antimicrobials through minimum inhibitory concentration (MIC) testing and time-kill experiments (TKE).

Materials/methods: One hundred and fifty carbapenem-resistant isolates, including 32 COL-resistant (COL-R) strains, were evaluated using MIC testing and TKE. MIC testing via broth micro-dilution was performed for FDC, colistin (COL), meropenem (MEM), amikacin (AMK), tigecycline (TGC), minocycline (MIN), ampicillin (AMP), sulbactam (SUL), and ceftazidime (CAZ). Four representative strains, displaying the highest MICs to FDC (16-32 mg/l), were selected for synergy testing via 24-h TKE. A bacterial reduction of $\geq 3 \log_{10}$ CFU/ml from the starting inoculum was considered bactericidal activity, while a $>2 \log_{10}$ CFU/ml reduction from the most active single agent was considered synergistic activity.

Results: The MIC testing revealed a lower range of MIC values for FDC in comparison to the other agents evaluated, with both the FDC MIC50 and MIC90 demonstrating 1 mg/l for the COL-S strains. While in the 32 COL-R strains, the MIC50 and MIC90 was 1 mg/l and 4 mg/l, respectively. In the TKEs, we observed synergistic activity with FDC and all other Gram-negative agents tested. Most notably, each of the TKEs demonstrated both synergistic and bactericidal activity, indicated by an average 4 $\log_{10}$ CFU/ml reduction in bacterial counts, with the FDC +AMK and FDC+MEM combinations. The enhanced activity occurred despite the increased MICs of 256 mg/l and 64 mg/l for AMK and MEM, respectively.

Conclusions: Susceptibility testing demonstrated that FDC is highly active against carbapenem-resistant A. baumannii including COL-R isolates. The combination of FDC with other agents showed promise in eradicating MDR A. baumannii. Further research is warranted to solidify the role of FDC-based combination treatment in current therapy.

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Abstract 8012

Prevalence of *Mycoplasma pneumoniae* infections during six years (2014-2019) in two hospitals of Saint Petersburg

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**Background:** Epidemics of *Mycoplasma pneumoniae* (Mp) infections typically occur in 3–7 year intervals, with seasonal peaks in autumn and winter. The diagnostics of mycoplasmosis is carried out by detection of DNA or antigens of pathogen in sample and specific antibodies in serum because of the lack of pathognomonic signs. The purpose is to assess an incidence of MP among children and adults from Saint Petersburg, that have a community-acquired pneumonia or other respiratory infections.

**Materials/methods:** During six years between 2014 and 2017, 1471 patients of Kolpino district of Saint-Petersburg [945 children and 526 adults] were screened for Mp. Specimens were mostly nasopharyngeal (NPS) or oropharyngeal (OPS) swab (n=1302), sputum (n=167), pleural fluid (n=2). Specimens were extracted using AmpliSens®RIBO-prep [InterLabService Ltd.] and detection was performed on CFX96 [Bio-Rad] with AmpliSens® Mp/Cp [InterLabService Ltd.]. Specific antibodies were detected with Mp-IgG-EIA-BEST and Mp-IgM-EIA-BEST [Vector-Best].

**Results:** Mp was detected among 222 of 1471 specimens, moreover the percentage of patients with DNA of pathogen was higher among children than adults [16.3 children:11.8% adults]. A frequency of detection of Mp during 2014-2016 years was 3.1-3.6%, during 2017-2019 years the frequency had increased to annual average 11.1-23.0% (children) and 9.4-16.9% (adults). The maximum level of Mp detection was registered from September of 2018 till January of 2019: 18.2-38.8% (children) and 11.1-31.6% (adults).

IgG, IgM antibodies to Mp were detected in 28 children with positive and in 6 children with negative results of PCR of specimens from the upper respiratory tract. 23 (82.1%) patients with Mp had antibodies [IgG, IgM], 1 patient with Mp had IgG, that verified the diagnosis of mycoplasma pneumonia; 4 patients with Mp hadn’t IgG, IgM. Among 6 children with PCR negative results, only 1 patient had IgM, the antibodies in serum of other 5 patients weren’t detected.

**Conclusions:** At 2017-2019 years there was an increase Mp detection till 38.8% [children] and till 31.6% [adults] at the hospitals of Saint-Petersburg, mainly in autumn and winter. For accurate diagnosis of a community-acquired pneumonia the molecular biology test should be supply the serological diagnostic methods.

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**Evaluation of the efficacy of combination of antifungals against invasive aspergillosis in an invertebrate animal model**

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**Background:** Evaluation of new therapeutic strategies for the treatment of aspergillosis is needed due to emergence of azole-resistance in Aspergillus fumigatus (Af). Galleria mellonella is a promising invertebrate model to estimate antifungal efficacy in vivo. The aim of the study was to evaluate the efficacy of antifungal combination against azole-resistant Af in G. mellonella model.

**Materials/methods:** Two Af clinical strains have been used: HEGP064, a susceptible strain without any Cyp 51A mutation, and HEGP2666, an azole-resistant strain with TR34/L98H mutation. Groups of 10 G. mellonella larvae were infected with the LD90 (inoculum concentration that gave 90% mortality at 7 days post-infection) and treated by voriconazole (VRZ, [Vfend®]) at 0.5, 1, 2, 4, and 8 µg/larva. Subsequently, HEGP064 or HEGP2666-infected larvae were treated by VRZ at 4 µg/mL alone and in combination with caspofungine (CSP) at 4, 2 or 1 µg/larvae. The mortality was estimated daily for 7 days. The pharmacokinetics of VRZ in the hemolymph was established in uninfected larvae and in HEGP064-infected larvae by recovering the hemolymph after injection of VRZ at 1, 4, 8 and 16 µg/larva. Dosage was performed by mass spectrometry coupled with high performance liquid chromatography.

**Results:** The LD90 values for the HEGP064 and HEGP2666 strains were 4.38x10^7 and 1x10^8 CFU/mL, respectively. In untreated groups, mortality was at least 90% on day 7 post-infection. VRZ at 4 µg/larva increased significantly the mortality of HEGP064-infected larvae (p=0.0007) but not HEGP2666-infected ones (p=0.25). Bitherapy (VRZ 4 µg/larva and CSP 4 µg/larva) lead to a more significant decrease in mortality compared to monotherapy (VRZ 4 µg/larva) and control group infected by HEGP064 (p=0.002) or HEGP2666 (p=0.0018) strain. Combination of CSP (1 and 2 µg/larva) decreased significantly mortality of HEGP2666-infected larvae compared to untreated larvae (p=0.037 and 0.024, respectively). Residual doses of VRZ in hemolymph were higher in infected versus non-infected larvae.

**Conclusions:** The combination VRZ-CSP showed its effectiveness in G. mellonella model especially when larvae were infected with an azole-resistant strain. This model could be used for screening and evaluation of different therapeutic strategies for the treatment of aspergillosis.

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**Abstract 8016**

**Predict to prevent: system dynamic modeling for healthcare-associated influenza**

Martina Sansone*, Lars-Magnus Andersson, Johan Westin, Rickard Norden

*Sahlgrenska University Hospital, Institute of Biomedicine, Gothenburg, Sweden*

**Background:** System dynamic modelling is a way to illustrate complex problems including non-linear relationships and multiple interactions. Our aim was to develop a model to estimate healthcare-associated influenza (HCAI).

**Materials/methods:** By using ithink® computer simulation software1, we constructed a model for predicting the accumulated number of healthcare associated influenza cases per season. The model was constructed based on hospital data obtained from previous seasons regarding patient flow and management as well as national surveillance data and relevant published data. Multiple step-wise simulations were performed to identify potential strategies in order to reduce nosocomial influenza transmission.

**Results:** Seasonal scenarios regarding the number of patients exposed for influenza by shared ward room, diagnostic accuracy at the emergency ward, the extent of antiviral treatment as well as post-exposure prophylaxis were investigated. In total, 240 simulations were performed. The single most effective preventive measure was post-exposure prophylaxis followed by reduced number of exposed patients per ward room (Table 1). Antiviral treatment of symptomatic cases may have individual benefits but seem to have limited impact on in-hospital transmission in the current model.

**Conclusions:** System dynamics is a valuable tool which may help hospitals to improve infection control policies. Preventive measures rely on early identification of influenza cases, and antiviral prophylaxis seem to be the most effective way to reduce in-hospital transmission.

Table 1. Accumulated seasonal estimates of HCAI-cases according to share of exposed patients treated with antiviral prophylaxis and mean number of exposed patients per room.

<table>
<thead>
<tr>
<th>Exposed patients/room (n)</th>
<th>100%</th>
<th>75%</th>
<th>50%</th>
<th>25%</th>
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<tr>
<td>3</td>
<td>54</td>
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<td>304</td>
<td>432</td>
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</tbody>
</table>

1 See Systems Inc., New Hampshire, U.S.A; iseesystems.com

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Abstract 8017

Urine alkaline pH effect on ciprofloxacin and fosfomycin efficacy in a murine urinary tract infection model by Escherichia coli

Marta Claudia Carretero Ledesma*1, Tania Cebrero Cangueiro1, Gema Labrador Herrera1, Younes Smani1, Jose Miguel Cisneros Herreros1, Jeronimo Pachon-Diaz1, Jesus Blazquez2, Elisa Cordero Matias1, Maria Eugenia Pachon-Ibáñez2

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Abstract third-party references: University Hospital Virgen del Rocío/CSIC, Institute of Biomedicine of Seville (IBiS), University of Seville

Background: The high incidence of urinary tract infections (UTI) by Escherichia coli in renal transplant recipients, in the era of antimicrobial resistance, prompts to optimize treatments. This work evaluates the effect of urinary alkaline pH on the efficacy of ciprofloxacin (CIP) and fosfomycin (FOS) in a UTI model and the development of resistance.

Materials/methods: An UTI murine model by E. coli using a wild-type [NU14], 2 low-level quinolone resistant [LLQR, NU14-D87G and NU14-S83A] and 3 low-level fosfomycin resistant [LLFR, NU14-glpT, NU14-uhPT and NU14-cyaA] strains. Seventy-two hours before infection, 5% glucose or 5% glucose plus 0.5% sodium bicarbonate was added to the drinking water. C57BL/6J female mice were transurethral inoculated with 50 x 10^5 cfu/ml. Forty-eight hours post-infection, therapy was initiated. Groups: i) control, infected not treated, ii) CIP [20mg/kg/ip/12h/24h], and iii) FOS [500mg/kg/ip/8h/24h]. After 24h, bacterial concentrations in aseptically collected urine and bladder were analysed (U Mann-Whitney test) and MIC of CIP and FOS were determined.

Results: CIP and FOS were similarly effective, independently of the urine pH (table). The treatment with CIP increased its MIC against the LLQR strains from 0.125/0.25 to 64/1.28 mg/l. Treatment with FOS did not increase its MIC for LLFR.

Conclusions: CIP and FOS are effective in UTI model, at both urinary pH. CIP resistance appeared after 24 hours of treatment.

<table>
<thead>
<tr>
<th>Strains</th>
<th>Groups</th>
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<th>Alkaline pH</th>
<th>Neutral pH</th>
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<tr>
<td></td>
<td></td>
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<td>log cfu/g</td>
<td>log cfu/ml</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>bladder</td>
<td>urine</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>bladder</td>
<td>urine</td>
</tr>
<tr>
<td>NU14wt</td>
<td>Control</td>
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<td>7.02±0.43</td>
<td>6.24±1.19</td>
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<td>6.63±0.54</td>
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<tr>
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<td>CIP</td>
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<td>2.51±0.32</td>
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<td>2.67±0.43</td>
<td>2.18±1.67</td>
</tr>
<tr>
<td>NU14-glpT</td>
<td>Control</td>
<td>7</td>
<td>5.64±1.68</td>
<td>5.11±0.96</td>
</tr>
<tr>
<td></td>
<td>FOS</td>
<td>10</td>
<td>2.72±0.35</td>
<td>1.54±1.68</td>
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<tr>
<td>NU14-cyaA</td>
<td>Control</td>
<td>7</td>
<td>6.12±0.84</td>
<td>6.22±1.22</td>
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<tr>
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<td>10</td>
<td>1.81±1.56</td>
<td>2.65±2.04</td>
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<tr>
<td>NU14-uhPT</td>
<td>Control</td>
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<td>2.10±1.47</td>
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*p<0.05 and **p<0.01 vs. controls

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Abstract 8018

**Catheter-associated urinary tract infections in patients hospitalised in intensive care unit**

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**Background:** The occurrence of urinary tract infections in patients referred for intensive care is almost inevitable; it is proportionally related to the duration of bladder catheterization.

We aimed to determine the causative agents of Catheter-associated urinary tract infections in patients hospitalised in intensive care unit and antimicrobial susceptibilities of the pathogens.

**Materials/methods:** This is a retrospective study from January 2012 to July 2019, where the positive results of urines performed in patients surveyed with at least one clinical sign (fever, hypothermia, sepsis) hospitalised in intensive care are selected for study. A threshold of $10^5$ CFU/ml is used for the diagnosis of urinary tract infection. The antimicrobial sensitivity test of isolated strains is performed according to CLSI recommendations. The Whonet 5.6 software is used to analyze the antibiotic sensitivity of the main bacterial species found.

**Results:** CA-UTI rate was 17.24% (95% CI: 15.01-19.72%). A total of 214 patients (mean age 40.2 years, sex ratio m/f: 1.27) had positive urinary tract infections with 245 strains distributed as follows:

- 58% of gram-negative bacilli, with *Escherichia coli* (48, 34%), *Klebsiella pneumoniae* (31, 22%), *Acinetobacter baumannii* (30, 21%)
- Gram-positive cocci account for 23% (57 strains) dominated by *Enterococcus* sp and *Staphylococcus* non-aureus with 51% and 23% respectively and 19% (46) yeasts, mainly *Candida albicans*.

The resistance of *Escherichia coli* to ampicillin, cotrimoxazole, ciprofloxacin and gentamicin is of the order of 80%, 45%, 25% and 20% respectively.

More than half (53%) of *Klebsiella pneumoniae* produce extended spectrum beta-lactamase (ESBL), 80% of *Acinetobacter baumannii* are resistant to imipenem. The same germ was isolated at least twice in 116 patients after the catheter was changed.

Bacteremia were recorded in 42 patients with mainly *Klebsiella pneumoniae* and *Acinetobacter baumannii*, 4 cases of candidemia due to *Candida albicans* were reported.

**Conclusions:** Gram-negative rods (58%) represent the main isolated germs of urinary tract infections with high rates of antimicrobial resistance which forms an important reservoir of multidrug-resistant bacteria.

The proportion of *Candida* spp is not negligible (19%) probably due to the use of broad-spectrum antibiotics in intensive care unit.

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Abstract 8019

Genome sequencing of Leishmania infantum causing cutaneous leishmaniosis from a Turkish isolate: meta-analitic study for evaluation of proteins with polymorphism

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Background: It has been nearly 13-14 years since the completion of the first whole-genome sequence (WGS) of a Leishmania parasite. However, much information about these parasites remains to be elucidated, such as the causes of differences in tissue tropism. The aim of this study is to evaluate of proteins with polymorphism on the WGS of L.infantum causing cutaneous leishmaniosis from a Turkish isolate.

Materials/methods: Genomic sequencing was performed on the Illumina HiSeq 2500 platform. The TruSeq Nano DNA Low Throughput Library Prep Kit, compatible with the Illumina HiSeq 2500 platform, was used to generate the library. Synthesis sequencing (SBS) was performed with a HiSeq Rapid SBS Kit v2 to generate single-fragment reads (2 x 150 bp; PE) with two fragment end-to-end assemblies. Bioinformatics analyses were performed on the Geneious 11.0.5. (www.genius.com) platform. L.infantum JPCM5 strain was used as the reference genome for genome mapping. Polymorphic regions were determined by using the Find Variations/SNPs program on the Geneious platform. The literature review was searched by using PubMed database for this proteins with polymorphism.

Results: In our study, a high-quality WGS of L.infantum was successfully generated, and a total of 32,009,138 bp of genomic DNA from 36 chromosomes were obtained. The genomic DNA sequence was submitted to the NCBI GenBank (www.ncbi.nlm.nih.gov) database and registered under the name Leishmania infantum_TR01. The accession numbers of the 36 chromosome of the L.infantum genome available from the NCBI [BioProject PRJNA433593]. As a result of the annotation of the genome, 3153 polymorphisms, 8324 genes, 8199 CDSs, 8109 mRNAs, 6 T tRNAs, 11 rRNAs and 58 ncRNA were identified.

Conclusions: The protein-coding-polymorphisms were found 166 among the 3153 polymorphisms, affecting 63 different proteins. In literature, it was determined that 14 studies of these 63 proteins have been done before. Of the 14 proteins mentioned herein, 5 are related to virulence, 2 to vaccine candidate, 4 to diagnosis / typing, 2 to drug resistance, 3 to drug target and 1 to vital function. The data obtained in our study contributes to sciences, provides a basis for Leishmania genome studies in Turkey and will contribute to studies a global level.

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Abstract 8020

A review of the resistance to integrase inhibitors in HIV-1 patients in a third level hospital: a four-year experience
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Background: The Integrase inhibitors [INIs] have been the last drug family to join the antiretroviral therapy for human immunodeficiency virus type 1 (HIV-1) infection. Currently the resistance prevalence to these drugs remains unknown, perhaps due to the lack of commercialized and standardized detection methods, for that reason our laboratory has implemented a “home-made” INIs resistance detection technique. The objectives of our study are to determine the prevalence of INIs resistance in our Hospital and to share the diagnostic approach used in our laboratory.

Materials/methods: A retrospective and descriptive study was carried out. All the requested samples to determine Raltegravir (RAL), Elvitegravir (EVG), Dolutegravir (DTG) and Bictegravir (BIC) resistance, between September 2015 and October 2019, were analysed, excluding those with viral load < 700 copies/mL or non-interpretable sequences. The genetic material extraction was made using the EZ1 system (QIAGEN) and the sequencing reactions were performed according to the Sanger method using primers RT-INTF , RT-INTR, INT-SF and INT-SR. Raw data was edited with Bioedit software and analysed with Geno2Pheno (Max Planck Institute) and HIV Drug Resistance Database (Stanford University).

Results: Out of the 188 samples submitted, 131 could be included and 17 (13%) showed resistance mutations. Major resistance mutations were observed in 10 (58.8%) of the samples, being the N155H the most frequent mutation with resistance to RAL and ELV. In the remaining 7 (42%) samples, accessory mutations were observed, all of them related to the presence of potential low-level resistance to any of the four drugs.

Conclusions: Prevalence of INIs resistance in our centre was observed at considerable proportion. Samples carrying the N155H mutation were mainly associated to RAL and ELV resistance, supporting the known high genetic barrier of DTG and BIC. The relevance of the strains with accessory resistance mutation is still unknown, therefore, more studies, greater number of cases and a standardized PCR technique may be useful to assess what could be a future concern.

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Abstract 8027

Rapid identification of methicillin-resistant Staphylococcus aureus (MRSA) in clinical microbiology labs by infrared spectral fingerprinting following growth on agar supplemented with cefoxitin

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Background: Staphylococcus aureus is a leading cause of bacterial infections in humans, ranging from skin, wound, and surgical-site infections to potentially life-threatening invasive endocarditis and bloodstream infections. It is critical to rapidly identify the causative agent as methicillin-susceptible (MSSA) or methicillin-resistant S. aureus (MRSA) for appropriate treatment of invasive infections. In previous work, we employed Fourier transform infrared (FTIR) spectroscopy as a rapid and cost-effective technique for discrimination between S. aureus and coagulase-negative staphylococci (CoNS) by developing a spectral database. In this study, we use this database in conjunction with a modified growth protocol, employing cefoxitin to inhibit growth of MSSA, for FTIR-based MRSA identification with high sensitivity and selectivity.

Materials/methods: Blood agar plates (BAP) were made using Columbia agar (5% sheep blood) supplemented with colistin (10 mg/L) and nalidixic acid (15 mg/L) (CNA) to inhibit Gram-negative bacteria and with cefoxitin at levels of 4 mg/L (4FOX) and 8 mg/L (8FOX). 234 staphylococcal isolates (previously identified by MALDI-TOF MS) were cultured on BAP, 4FOX-CNA-BAP, 8FOX-CNA-BAP and MRSA selective chromogenic agar. Isolated colonies were deposited onto IR-reflective slides for FTIR spectral acquisition and identified as S. aureus or CoNS by matching their spectra against the FTIR spectral database. Isolates were identified as MRSA if colonies growing on cefoxitin-containing agar were spectrally identified as S. aureus.

Results: All S. aureus (n = 86) and CoNS (n = 144) isolates were correctly identified by matching their FTIR spectra against the spectral database, irrespective of whether they had been cultured with or without antibiotics. Based on comparison with VITEK 2 AST results, MRSA was identified with 100% sensitivity and 100% specificity at 24 hours incubation when isolates were grown on 8FOX-CNA-BAP, whereas growth on 4FOX-CNA-BAP yielded 100% sensitivity and 97% specificity. These results were comparable to those obtained with MRSA selective chromogenic agar (97.8% sensitivity and 100% specificity).

Conclusions: This new FTIR-based methodology achieved high sensitivity and specificity for MRSA identification through accurate identification of S. aureus isolated on cefoxitin-containing agar. As an MRSA screening tool, this methodology may provide an alternative to the use of costly chromogenic media at substantially lower cost.

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The role of procalcitonin as a predictor of severity, prognosis and appropriate empirical antibiotic therapy in community-acquired pneumonia of bacterial aetiology

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Background: The role of procalcitonin (PCT) in patients hospitalized for community acquired pneumonia (CAP) outside the ICU is still undefined, as well its role as predictor of appropriateness of antibiotic therapy. In this study we aimed to define the prognostic role of PCT and its association with appropriateness of antimicrobial treatment in patients with bacterial CAP (BCAP) admitted to Internal Medicine wards.

Materials/methods: We retrospectively analyzed consecutive patients with BCAP (defined by bacterial isolation from sputum, bronchoalveolar lavage, blood cultures or recovery of urinary antigens). We evaluated the association of PCT at admission (APCT), subsequent 1 (∆-24h-PCT), 4-5 days (∆4-5d-PCT) variations with in-hospital mortality and need of intensive respiratory and vasopressor support (IVRS). We also explored the relationship between appropriateness of initial empirical antimicrobial therapy (IET) and APCT, ∆-24h-PCT, ∆4-5d-PCT and clinical evolution identified by MEWS score variations 0-72 hours.

Results: 356 patients with CAP were screened; 56 (15.7%) had BCAP. The median values of APCT were higher in BCAP with positive cultural analysis of sputum or bronchoalveolar lavage versus patients with no isolation at the same diagnostic exams (2.87 vs 0.33; p=0.006). We found neither association between APCT, nor its variations, and in-hospital mortality. In patients with BCAP, APCT was an independent predictor of IVRS at multivariate analysis, and the most accurate cut-off was 3.4 ng/ml (OR 16.67; 95%CI 2.9-95; p<0.001. PPV 81% NPV 68%). ∆-24h-PCT and ∆4-5d-PCT values were not associated with an increased risk of IVRS. PCT values and variations were not predictive of inappropriate IET, which was an independent predictor itself of in-hospital mortality (OR 68.2; 95%CI 1.7-271.87; p= 0.025). Only worsening of MEWS was related to inappropriate IET (OR 4; 95%CI 1.18-13.49; p=0.022).

Conclusions: APCT revealed to be a useful predictor of bacterial etiology of CAP. Moreover, APCT was an independent predictor of IVRS but not of in-hospital mortality. PCT values and variations were not predictive of appropriateness of IET. PCT it doesn’t appear useful for identifying the appropriateness of antimicrobial therapy, suggesting that upgrading empirical antibiotic therapy based on PCT variation is not an appropriate strategy subsequently leading to antibiotics overuse.

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Abstract 8037

Potential use of data from a national HIV testing surveillance system to improve community-based testing strategies, Ireland

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Background: An estimated 10% of people living with HIV in Ireland do not know their HIV status. Data from surveillance of national voluntary community-based HIV testing (VCBT) can be used to improve targeting of hard-to-reach groups and reduce the proportion of undiagnosed individuals.

Materials/methods: National monitoring of VCBT commenced in Ireland in 2018; data are provided by statutory and non-statutory organisations to the Health Protection Surveillance Centre. This study includes available case based data on individuals who underwent VCBT (using rapid point-of-care-test methods) during the period 01st January 2018 to 31st December 2018. Analysis was conducted of reactivity rates by country of birth, and whether clients were first-time or repeat testers.

Results: In all, data on 2,643 results were reviewed.

Twenty-one (0.8%) people had a reactive HIV test result, 20 of whom were male and one was female. Age was available for 76% of cases, median age was 29 years (range: 19 - 60 years).

Of 21 individuals with a reactive test result, 19 were men who have sex with men. By country of birth, the highest proportion of people who had a reactive test were born in Latin America (n=10; 48%), six were born in Ireland, two in sub-Saharan Africa, and three in other countries.

Information on whether or not the client had previously tested for HIV was available for 2,443 tests. Of those, 776 (32%) were first time testers and 1667 (68%) were repeat testers.

HIV test reactivity rate was similar among first-time testers (0.8%) and repeat testers (0.9%) overall. We found a higher reactivity rate in first time testers born in Latin America (6.3%) and in sub-Saharan Africa (3.7%).

Conclusions: Data from surveillance of VCBT can be used to improve targeting and increase uptake of community HIV testing among people at risk of HIV. Design of future VCBT strategies, including information and promotion campaigns, should take into account differences in HIV test reactivity among demographic subgroups, and by history of having tested previously. Separate messaging campaigns designed to reach first-time testers and repeat testers may help to increase/retain uptake in both groups.

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Abstract 8038

In vivo virulence of different growth states of Pseudomonas aeruginosa

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Background: Pseudomonas aeruginosa biofilms are often involved in chronic or recurrent infections and associated with high mortality. Inducing dispersal of cells in the biofilm is a strategy that is being explored to regain effectiveness of antibiotics in biofilm related infections. However, prior in vitro data suggest that these induced dispersed cells express more virulence factors. Here, we employ a pneumonia model to study in vivo virulence and immune responses against different P. aeruginosa biofilm and dispersed phenotypes.

Materials/methods: 1E6 CFU of biofilm, planktonic form (bacteria collected from broth cultures), and uninduced (naturally dispersed from biofilm) and induced dispersed cells by either nitric oxide treatment or depletion of c-di-GMP were intratracheally inoculated in mice. As control, sham animals were utilized where mice were inoculated with saline. Animals were monitored for 24 hours before euthanization after which bacterial counts were estimated in bronchoalveolar lavage fluid, lungs, liver and spleen. Cytokines were studied from serum by a meso-scale discovery panel containing IFN-γ, IL-10, IL12p70, IL-1β, IL-2, IL-4, IL-5, IL-6, KC/GRO and TNF-α.

Results: Animals treated with induced dispersal methods (nitric oxide treated or c-di-GMP depleted) showed a significant drop in survival within 24 hours compared to animals treated with other P. aeruginosa cell phenotypes. Dissemination in hematopoietic organs was significantly higher in induced dispersed cells and planktonic cells compared to biofilm and untreated biofilm cells. In serum, the similarities observed in CFU counts were also reflected in the cytokine measurements with planktonic cells showing significant upregulation for KC/GRO and IL-6 compared to other groups.

Conclusions: Here we show that induced dispersed cells lead to higher mortality and dissemination in hematopoietic organs when compared to biofilm cells or uninduced dispersed cells. These data suggest that although induced dispersal might decrease biofilm mass, an increased in vivo virulence observed in this study warrants a more careful re-evaluation of the clinical use of the dispersal agents.

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Letermovir pre-existent mutations in human cytomegalovirus UL56 terminase in solid organ and haematopoietic stem cell transplant recipients

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Abstract third-party references: Group for the Study of Infection in Transplantation (GESITRA) & Spanish Network for Research in Infectious Diseases (REIPI)

Background: Letermovir (LMV) is a HCMV terminase inhibitor recently approved for hematopoietic stem cell transplant (HSCT) prophylaxis. LMV presented better safety and tolerance profiles, however, LMV-resistance mutations selected in vitro emerged much earlier than for current anti-CMV DNA polymerase inhibitors, suggesting a lower LMV-resistance genetic barrier. Many LMV resistance mutations have been described from clinical samples in the pUL56 terminase subunit, but studies of UL56 polymorphisms before treatment are scarce. We aimed to study preexistent mutations in UL56 prior LMV treatment in solid organ transplant (SOT) and HSCT recipients.

Materials/methods: UL56 sequences from HCMV clinical strains of 50 SOT and HSCT patients comprised into the Spanish Network for Research in Infectious Diseases (REIPI) and the Group for the Study of Infection in Transplantation (GESITRA) were analyzed by Sanger sequencing. Phenotypic assay by recombinant bacmid technology, LMV antiviral susceptibility test and growth assays were performed for previously undescribed mutations found by genotypic assay in collaboration with the French Reference Center. All patients accomplished the suspected resistance criteria for current anti-CMV drugs. None of them received LMV previous the study.

Results: Missense mutation R246C was detected in the UL56 gene of 2 patients (4%) located within the LMV resistance mediating region [codons 230-370] and adjacent to the leucine zipper [249-271]. Recombinant bacmid assay showed no LMV-resistance association. However, its replicative capacity was much higher than the HCMV backbone strain AD169 (figure 1). No other gene variations were found in the remaining patients.

Conclusions: New LMV sensitive polymorphism R246C was found in two transplant patients. This mutant was positively selected in both cases due to its increased replicative capacity, which confirms it does not alter the HCMV fitness although it is located next to the catalytic site of the pUL56. Its position also confirms the phenomenon of vicinity of resistance and natural polymorphism in UL56, previously described for UL97 phosphotransferase, corroborating that mutations phenotypes cannot be predicted by their gene position.

Figure1. Growth assay performed on MRC5 cell line of the mutant recombinant strain R246C compared to the reference strain AD169 after 7 days post-infection.

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Abstract 8043

Host transcriptome analysis accurately diagnoses and prognoses acute infections and sepsis in emergency department patients

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Background: Rapid diagnostic tests for the detection of acute bacterial and/or viral infection and sepsis are needed in the emergency department (ED). Current diagnostic and prognostic tests are impeded, e.g. by slow turnaround time for blood cultures. Differentiating between bacterial and viral infections as well as managing the appropriate level of care are critical deliverables. Thus, over-treatment leading to antimicrobial resistance, as well as Clostridium difficile infection or late diagnosis and treatment of sepsis may result.

Materials/methods: In a prospective single-site study at the ED of the Charité University Hospital (Campus Benjamin Franklin) we investigated the efficacy of a novel host response test from blood which uses 29 host response mRNA targets and a machine learning algorithm (HostDx Sepsis) to quickly and accurately differentiate between viral and bacterial infections including co-infections and non-infected patients and predict the probable clinical course. Patients who presented with signs of acute infection were enrolled. All patients were adjudicated using chart review by two expert physicians using clinical data, radiological and laboratory tests (incl. C-reactive protein [CRP] and procalcitonin [PCT]) but blinded to the HostDx Sepsis results.

Results: We here present an interim analysis of 125 patients enrolled and adjudicated since January 2019. The accuracy of HostDx Sepsis predictions was compared to standards of rapid bacterial infection detection, such as CRP and PCT. The Area Under the Receiver Operating Characteristics (AUROC) for HostDx Sepsis at predicting bacterial and co-infections vs. non-infected and virally infected patients was 0.89 compared to 0.87 for PCT and 0.83 for CRP. HostDx Sepsis also predicted viral and co-infections vs. non-infection and bacterial infection with an AUROC of 0.85. When combined with quick Sequential Organ Failure Assessment (qSOFA)-scores the test predicted multiorgan failure with an AUROC of 0.85, compared to 0.80 for qSOFA-scores alone.

Conclusions: Our results suggest that the use of a host-response test to determine the infection status and severity allows for more informed rapid decisions on antibiotic treatment and further level of care in the ED.

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**Influenza immunoglobulin in hospitalised patients with serious influenza A**

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**Background:** Seasonal influenza remains a significant burden in the US and worldwide, and there are no approved treatment for hospitalized patients with severe influenza. FLU-IGIV is a human immunoglobulin produced from healthy donor plasma; final product contains high titers of antibodies against seasonal influenza A strains.

**Materials/methods:** Adults with NEW score ≥3 hospitalized in the US and Europe over two flu seasons (2017-2019) with laboratory-confirmed influenza A infection were randomized 1:1:1 in a double-blind Phase 2 study. Subjects received either a fixed volume low dose (approx.16 g) or high dose (approx. 32 g) of FLU-IGIV or placebo, in addition to standard of care (oseltamivir; 75 mg BID/5 days). The primary study objective was to evaluate safety of FLU-IGIV and determine an optimal dose. Analysis of PK parameters and clinical benefit (6-category ordinal scale) is ongoing.

**Results:** The study randomized 65 subjects, with 60 dosed (safety population, 50% female and 50% male). Five subjects (8%) discontinued prior to dosing. Subjects 18 to 87 years old (median 54.5), within the weight range of 46 to 184 kg (median 87.9 kg), were randomized to receive FLU-IGIV high dose (19, 32%), low dose (19, 32%), or placebo (22, 37%). Oseltamivir ≥80% compliance was 93% in the safety population. There were 6 adverse events (AEs) considered related to FLU-IGIV; nausea, peripheral edema, infusion site warmth, and headache (2). There were 19 serious AEs (15 treated vs 4 placebo) reported in 8 subjects (7 FLU-IGIV-treated vs 1 placebo) and none were considered related to study medication. No deaths were reported. Constipation was the most common AE (1 [5.3%] high dose vs 3 [13.6%]) placebo group. Duration of hospitalization was 2 to 40 days (median 4) vs. 2 to 16 days (median 5) in the treatment vs placebo group. Subjects that completed Day 8 (36 treated vs 21 placebo) will have their ordinal outcome assessed.

**Conclusions:** Administration of FLU-IGIV was well tolerated at both dose levels compared to placebo in hospitalized patients with serious influenza A infection.

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Abstract 8046

**SOS response to a novel inhibitor of DNA replication**

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**Background:** SOS response is a protective mechanism against antibacterial molecules that affect DNA replication. In this study, we used analysis of DNA content by flow cytometry to measure the impact of SOS response after antibiotic treatment and differentiate the mechanism of action of several antibiotics, including a novel scaffold ATB-93.

**Materials/methods:** Bacterial DNA content was labeled by picogreen after cell fixation.

**Results:** This study compares ATB-93, with Ciprofloxacin and Mitomycin C. Strains with deletion of several SOS response effectors were treated with those compounds and their DNA content was compared to determine which components of SOS response are involved in the bacterial response to treatment. This study demonstrates that RecB is necessary to observe replication following ATB-93 treatment. It also shows that SulA deletion does not prevent filamentation after ATB-93 treatment contrary to Mitomycin treatment.

**Conclusions:** Analysis of DNA content by flow cytometry is a potent tool to compare inhibitors of DNA replication.

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**Abstract 8048**

**Candidaemia: a decade-long experience from India**

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**Background:** Candidemia is one of the leading causes of mortality in healthcare associated infections. There is an increase in the incidence because of various invasive procedures and complexities of patients. This study was conducted to analyze the prevalence, risk factors, antifungal susceptibility and outcome of candidemia in a tertiary care unit.

**Materials/methods:** This study was performed in a 600 bedded tertiary care centre in South India. A retrospective analysis of all patients between January 2010 and October 2019 was done from the laboratory and hospital information system.

**Results:** In this ten-year study, a total of 11269 blood cultures were positive. Out of which 508 patients (4.5%) grew Candida species. Only the first isolate of the patient was considered for further analysis. The median age of the patients was 52 years (range, 7 days to 90 years), and 315 of the patients (62%) were male. Among the top five isolates, Candida tropicalis was the most common fungal species (141/508, 27.8%), followed by Candida haemulonii (95/508, 18.7%), Candida albicans (76/508, 15%) and Candida parapsilosis (62/508, 12.2%). Candidemia was diagnosed while admitted in the wards in 55.9% of patients, 35.2% in intensive care units and 8.9% in outpatients. Analysis of the risk factors has shown that 17.5% of these patients had uncontrolled diabetes, 16.1% had malignancies, 11.3% had lung infections, 9.9% developed candidemia in post-surgical turn of events and others. The most frequently isolated Candida species, i.e., C. tropicalis was sensitive to fluconazole in 95.7%, voriconazole 98.6%, flucytocine 96.7% and 100% susceptible to amphotericin B, caspofungin and micafungin. 54% of these patients recovered, 40% expired and 6% were discharged against medical advice.

**Conclusions:** C. tropicalis was the most frequently isolated species. This report shows that invasive candidiasis is a significant source of morbidity in Indian healthcare settings, causing substantial burden of disease in immunosuppressed and uncontrolled diabetic patients. An important and high alert issue is that mortality remains unacceptably high. This type of data analysis is needed to track trends of serious infection and to develop guidelines for infection control strategies and antimicrobial stewardship program.

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Abstracts 2020

Abstract 8050

Diversity of capsular switch among carbapenemase-producing Klebsiella pneumoniae
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Background: Klebsiella pneumoniae (Kp) is a leading cause of intractable multidrug-resistant (MDR) infections in hospitals. Most of the Kp clinical isolates produce capsule (CPS) as a major virulence factor. Extensive recombination events at the cps locus are frequent and responsible for capsule diversity in Klebsiella spp. Capsular diversity may also occur within the same bacterial population, generating differences in colony aspect, i.e. mucoid and non-mucoid. Our objectives were to characterize colony variants appearing among eight clinical carbapenemase-producing Kp isolates: capsulated, mucoid (M) and non-capsulated, non-mucoid (NM) phenotype.

Materials/methods: The M and NM colony variants were distinguished by appearance on solid medium. Whole genome sequencing of 74 NM variants was used to infer mutations causing phenotypic differences. CPS was quantified by uronic acid assay and visualized by India Ink staining. The frequency of CPS switching on Tryptic-Soy agar (TSA) was determined. Antimicrobial susceptibility testing (AST), biofilm and autoaggregation assays were performed to unveil putative differences in resistance.

Results: Spontaneous loss or reduction of CPS results from point mutations and IS elements hopping into essential genes for capsule synthesis. Frequency of mutations was strain-dependent but overall higher at later growth stages on solid medium. Little or no capsule was produced by the NM variant. Strikingly, differences in carbapenem susceptibility, in vitro biofilm formation and autoaggregative properties were observed between the two variants.

Conclusions: Reduced or loss of capsular production led to various phenotypic changes that might lead to different in vivo adaptation according to the Kp strain. However, as the colony opacity differences in stored isolates may go undetected, researchers might unconsciously work with mixed populations. This could be problematic for many studies, especially those involving virulence and resistance.

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Abstract 8052

**Active surveillance mitigates the risk of donor-derived infections in solid organ transplant recipients: the role of infection control**

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**Background:** Unexpected donor-derived infections (DDIs) are a major concern in SOT. Our SOT center is located in Sicily, an endemic area for Multidrug-resistant (MDR) gram-negative bacilli (GNB), especially Carbapenem-Resistant Enterobacteriaceae (CRE) infections. To prevent and manage MDR DDIs, an active surveillance system was implemented.

**Aim of this study is to evaluate the effectiveness of an active surveillance system for DDI prevention in SOT recipients.**

**Materials/methods:** Since December 2015, together with the organ, our surgical team collects donor blood culture and transport liquid for all organs, urine for kidney and broncho-aspirate for lung donors. These specimens are cultured at our microbiology lab. The Infection Control Nurses (ICN) check results of donor cultures every day and maintain a prospective database. In case of significant positive result, ID physician starts immediately targeted treatment following internal guidelines. ICN inform Regional Transplant Center in case of significant positivity to protect other recipients. ICN perform surveillance of potential DDI in the 30 days after transplant for every HR recipients. In case of suspected DDI, NGS will be performed on donor and recipient strains.

Recipients were considered at High Risk (HR) of DDI when the donor had positive blood culture or infection at transplanted organ.

**Results:** During study period (Dec 2015-Jun 2019) 489 SOT were performed, 124 (25%) were at HR of DDIs. In particular 26 (5.3%) of recipients were at HR for MDR-GNB DDI (11 carbapenem-resistant *Acinetobacter baumannii*, 13 Carbapenem-Resistant Enterobacteriaceae, 2 ESBL).

Active surveillance system allowed prevention of 93% of DDI infections in HR recipients (115), 7% of recipients (9) developed a DDI but they were promptly diagnosed and effectively treated, see Table 1.

**Conclusions:** Active surveillance system managed by ICN is effective for prevention or prompt management of unexpected DDI. Given the shortage of organs for transplantation, this innovative approach, together with reinforcement of infection control practices in the donor intensive care units, should be consistently applied to improve the quantity, quality, and allocation of organs for transplantation, and survival of patients and grafts after transplantation.

<table>
<thead>
<tr>
<th>Case</th>
<th>Organ</th>
<th>Pathogen Transmitted</th>
<th>Type of DDI</th>
<th>Post Tx Days</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Liver</td>
<td><em>Candida albicans</em> BSI</td>
<td>BSI</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Liver</td>
<td>CRKP</td>
<td>BSI</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>Liver</td>
<td>CRKP</td>
<td>BSI</td>
<td>3</td>
</tr>
<tr>
<td>4</td>
<td>Liver</td>
<td>CRKP</td>
<td>IAI</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>Kidney</td>
<td>CRKP UTI</td>
<td>UTI+BSI</td>
<td>17</td>
</tr>
<tr>
<td>6</td>
<td>Lung</td>
<td>Aspergillus niger+ CRAB UTI</td>
<td>PNL</td>
<td>4</td>
</tr>
<tr>
<td>7</td>
<td>Liver</td>
<td>MSSA</td>
<td>PNL</td>
<td>21</td>
</tr>
<tr>
<td>8</td>
<td>Kidney</td>
<td>E. coli-S</td>
<td>UTI</td>
<td>21</td>
</tr>
<tr>
<td>9</td>
<td>Lung</td>
<td>P. aeruginosa LRTI</td>
<td>PNL</td>
<td>14</td>
</tr>
</tbody>
</table>

Table 1: Donor Derive Infection

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Abstract 8053

**Comparison between Bedside Blind Bone Biopsy (B4) and Basic Bone Biopsy (B3) in the management of diabetic foot osteomyelitis**

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**Background:** Bedside Blind Bone Biopsy (B4) performed by a diabetologist has been recently shown as a reliable tool to manage antimicrobial therapy in case of Diabetic Foot Ulcer (DFU) with suspected osteomyelitis. Here, we evaluated the performance of B4 compared to the conventional procedure (Basic Bone Biopsy, B3) performed either by surgery or interventional radiology.

**Materials/methods:** A bi-centric, observational, retrospective study was conducted in two different diabetes departments. B4 was performed by a diabetologist from December 2015 to September 2018 (33 months) in Center A. B3 was performed by a surgeon or an interventional radiologist from September 2013 to September 2018 (62 months) in Center B. The primary endpoint was complete healing with Exclusive Medical Treatment (EMT) and no recurrence (EMT=offloading, wound care ± antimicrobial therapy) at 6 months. The secondary endpoints were the rates of contaminations and sterile Bone Biopsies (BB).

**Results:** Among 1112 patients with Diabetes Mellitus (DM) admitted with foot ulcer, 127 consecutive patients (11.4%) had clinically and/or radiological suspicion of osteomyelitis, eligible for EMT and consequently with an indication of BB. 81/415 (19.5%) patient in center A underwent a B4 and 46/697 in center B underwent a B3 (6.6%, surgery n=31/46 [67.4%], radiology n=15/46 [32.6%]). Patients characteristics were similar between the 2 groups: males (76.4%), mean age (69 ± 12 years), mean duration of DM (19 ± 10 years), mean glycated hemoglobin (8 ± 2%). Bacterial strains were comparable between the two groups with a similar proportion of *Staphylococcus aureus* (B4 18.2% vs B3 23.3%, p=0.58). The rate of patients with complete healing with EMT and no recurrence at 6 months was similar between the two groups (B4=59% B3=58.7%, p=1.00). The mean duration of follow up was 604+/−446 days. No statistical difference was observed for the rate of contaminations (B4=13.7% [31/236 bone samples], B3=11.1% [7/63 bone samples], p=0.55). The rate of patient with sterile bone biopsies was significantly higher in B4 group (43/83, 51.8%) than in B3 group (11/46, 23.9%), p=0.002.

**Conclusions:** B4 is a simple and valid diagnostic procedure to manage DFU with suspected osteomyelitis. It results in similar healing rate to more sophisticated and expensive procedures.

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Next-generation sequencing for kinetics of the respiratory microbiota of intensive care unit intubated patients

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Abstract: Ventilator associated pneumonia (VAP) remains a public health concern in the intensive care units (ICU) due to its related increase in hospital stay, mortality and over costs. Nowadays, the pathophysiology from colonization to infection is still not fully understood. A better understanding of the respiratory microbiota changes during mechanical ventilation (MV) could help to better target patients with increased risks of VAP. The objective of the study was to describe, thanks to next-generation sequencing (NGS), the kinetics of the respiratory tract microbiota during MV in ICU patients.

Methods: This is a pilot monocentric prospective observational study enrolling 10 adult ICU patients under MV for at least 48h for neurological issue with no past medical history of respiratory diseases and without antibiotic use since one month. Endotracheal aspirates (ETA) were collected daily from intubation until extubation (7 patients, 51 ETA samples) or until prescription of antibiotics for suspected VAP (3 patients, 13 ETA samples). After human cells depletion and DNA extraction of all ETA samples, 16S rRNA-encoding gene amplification was performed with the Ion 16S Metagenomics Kit. After libraries preparation, the Ion GeneStudio S5 platform was used. Twenty ETA samples were sequenced per chip to assure a high sequencing depth. Bioinformatic analysis was performed with the IonReporter® and the Shaman software. Semi-quantitative conventional culture was performed in parallel following ESCMID recommendations. Results were compared to culture.

Results: NGS results were in agreement with culture, all pathogens being detected. Respiratory microbiota and kinetics were very different from one patient to another. For each patient, changes in the respiratory microbiota were highly variable from one day to the other. Anaerobes were systematically detected, sometimes at very high proportions even when pathogens were present at high concentrations. Interestingly, Bacteroidetes phylum was more represented in patients finally receiving antibiotics whereas uneventfully extubated patients had a higher proportion of the Actinobacteria phylum.

Conclusions: Following the kinetics of the respiratory microbiota of MV ICU patients shows interesting results with distinct profiles. NGS monitoring promises accurate results that could help on giving new perspectives to the understanding of pathophysiology of VAP in the ICU setting.

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Abstracts 2020

Abstract 8056

Low incidence of Gram-negative infections in people who inject drugs in Tennessee

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Background: People who inject drugs (PWID) are thought to be at risk of Gram-negative (GN) infections given non-sterile injection techniques or contaminated injection material. Despite limited knowledge about the incidence of GN infections in PWID, broad-spectrum antibiotics with are routinely prescribed. The objective of this study was to describe the infection microbiology in PWID, and to describe patient characteristics associated with GN infections in this population.

Materials/methods: Cross-sectional study with nested cohort performed at an academic medical center included patients with injection-drug related infections seen in an emergency department or admitted from 6/2017-6/2018. Urinary and respiratory tract infections were excluded. Injection drug use was defined as patient admittance or self-identification as a PWID within the past 30-days, admittance to a history of substance use with a positive urine drug screen for illicit substances on admission, and/or an infection determined to be related to injection drug use by an infectious diseases physician. Patient characteristics were described and compared.

Results: 250 patients were included: 25 (10%) had a GN infection. 140 (56%) were women, and the median [IQR] age was 36 [29-44] years. 96 (38%) patients had no insurance at time of care. 236 (94%) patients were admitted to the hospital; the median [IQR] length of stay was 6 [3-14] days. The predominant illicit drugs used were opioids (95%) and amphetamines (42%). Common infection types were: 40% skin/skin structure, 25% infective endocarditis, 14% unknown source, 12% osteomyelitis, 9% multiple infections. 195 organisms were identified from 166 (66%) patients; the most commonly identified organisms were: 41% methicillin-resistant Staphylococcus aureus, 18% methicillin-sensitive S. aureus, 17% streptococci, 5% enterococci, 2% P. aeruginosa, 1% Candida spp., 9% other Gram-positive organisms, 7% other GN organisms. 233 (93%) patients received empiric GN therapy; 215/233 (92%) had anti-pseudomonal coverage. In multivariable logistic regression, variables independently associated with GN infection was a history of mental health disorder [Table 1].

Conclusions: The incidence of GN infections, particularly P. aeruginosa, in PWID are low, but empiric anti-GN antibiotics are prescribed in the majority of patients. Antimicrobial stewardship actions targeted towards improved antibiotic use in this population are warranted.

Table 1: Variables associated with GN-infection in People who Inject Drugs

<table>
<thead>
<tr>
<th>Variable</th>
<th>UnadjOR (95% CI)</th>
<th>AdjOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of mental health disorder</td>
<td>2.7 (1.1-6.9)</td>
<td>2.7 (1.1-7.0)</td>
</tr>
<tr>
<td>Cocaine use</td>
<td>2.3 (0.8-6.7)</td>
<td>2.2 (0.7-6.8)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>1.8 (0.7-4.9)</td>
<td>Not Tested</td>
</tr>
<tr>
<td>Skin/skin structure infection</td>
<td>1.2 (0.5-2.8)</td>
<td>Not Tested</td>
</tr>
<tr>
<td>Previous hospitalization, 30-days</td>
<td>0.3 (0.04-2.5)</td>
<td>Not Tested</td>
</tr>
<tr>
<td>Intensive Care Unit on admission</td>
<td>0.14 (0.02-1.1)</td>
<td>Not Tested</td>
</tr>
</tbody>
</table>

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Mutations in *Aspergillus fumigatus* hmg1 confer increased expression of ergosterol biosynthesis and efflux pump encoding genes

Jeffrey M. Rybak*1, Wenbo Ge1, Nathan Wiederhold2, Vincent M. Bruno3, P. David Rogers1, Jarrod R. Fortwendel1

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**Background:** Triazole antifungals are relied upon as primary therapy for the treatment of infections caused by *Aspergillus fumigatus*. Recently, we have demonstrated that mutations in the *A. fumigatus* HMG-CoA reductase encoding gene, hmg1, represent a novel genetic determinant of clinical triazole resistance, conferring reduced susceptibility to all clinically available triazoles used for the treatment of invasive aspergillosis. In this work, we employ RNAseq-derived transcriptional profiling to determine the effects of hmg1 mutations on gene expression with or without voriconazole exposure.

**Materials/methods:** Three previously characterized hmg1 mutant strains with reduced voriconazole susceptibility (MIC 1 to 2mg/L), constructed in the *akuBΔKU80* background, as well as a hmg1WT control strain (MIC 0.25mg/L), were included in this study. All strains were subjected to RNAseq-derived transcriptional profiling in biological triplicate following growth in RPMI media without voriconazole, with 7 hours of voriconazole exposure, or with 48 hours of voriconazole exposure. Voriconazole was supplemented at half the minimum inhibitory concentration of each strain.

**Results:** Following growth in RPMI without voriconazole, transcriptional profiling revealed that expression of multiple ergosterol biosynthesis related genes including erg1, erg3B, erg24, erg24B, erg25, and srb8, as well as the efflux pump-encoding genes abcA and mdrA were increased 2 to 5-fold in all hmg1 mutant strains relative to the hmg1WT control strain. After growth in RPMI with 7 hours of voriconazole exposure, similar increases in the expression of ergosterol biosynthesis genes was observed among all hmg1 mutant strains, while the expression of the efflux pump-encoding genes abcA and mdrA further increased to 4 to 9-fold that of the hmg1WT control strain. Following growth in RPMI with 48 hours of voriconazole exposure, the expression of the efflux pump-encoding genes abcA, abcC, abcD, atrI, mdr1, and mdrA was observed to be increased 2 to 4-fold relative to the hmg1WT control strain.

**Conclusions:** These data demonstrate that mutations in *hmg1* are associated with increased constitutive and voriconazole inducible expression of multi-drug efflux pump encoding genes and ergosterol biosynthesis genes. Further research is needed to delineate the direct contributions of these changes in gene expression to clinical triazole resistance conferred by *hmg1* mutations.

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Identification of the extended-spectrum β-lactamase L2 in an extensively drug-resistant Pseudomonas aeruginosa isolate, United States

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Background: Pseudomonas aeruginosa, an opportunistic pathogen that causes >32,000 healthcare-associated infections each year in the United States, is known to harbor a variety of acquired β-lactamase genes. Here we report the first identification of the Stenotrophomonas maltophilia L2 extended-spectrum β-lactamase (ESBL) in a P. aeruginosa isolate.

Materials/methods: The isolate was submitted to CDC as part of the Emerging Infections Program, which conducted laboratory- and population-based surveillance for carbapenem-resistant P. aeruginosa from 2016-2018. We screened the isolate for carbapenemase activity using the modified carbapenem inactivation method (mCIM). Antimicrobial susceptibility testing (AST) was performed using reference broth microdilution according to Clinical and Laboratory Standards Institute guidelines. The isolate underwent whole genome sequencing (WGS) using both Illumina and PacBio platforms. We analyzed the WGS data with our custom QuAISAR-H pipeline and identified antimicrobial resistance (AMR) genes using publicly available databases (ResFinder, ARG-ANNOT, and NCBI AMRFinder).

Results: The isolate was mCIM-positive and extensively drug-resistant (XDR; non-susceptible to at least one agent in all but two or fewer antimicrobial categories), though it was susceptible to colistin and amikacin. Using WGS data, the isolate was identified as multilocus sequence type 3054 and the bla_{L2} gene was the only acquired β-lactamase detected. This gene was located on a 20.6kb plasmid along with tetracycline and aminoglycoside resistance genes, Figure 1).

Conclusions: S. maltophilia and P. aeruginosa are associated with water sources in healthcare environments, thus gene transfer events between the two gram-negative species may occur. While nominally an ESBL, the AST and WGS results suggested that the strain may produce a carbapenemase-like phenotype in a P. aeruginosa background. This work demonstrates the utility of WGS to rapidly identify potentially novel or unexpected pathogen-carbapenemase combinations, a crucial component for early containment of emerging antimicrobial resistance among healthcare-associated pathogens.

Figure 1. Annotation of the 20.6kb plasmid with bla_{L2} found in the XDR P. aeruginosa.

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Abstracts 2020

Abstract 8065

Evolutionary dynamics of carbapenem resistance genes among different international clones of Acinetobacter baumannii: resistance and dissemination implications

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Background: Carbapenem resistant Acinetobacter baumannii has been emerged as a global threat. A. baumannii genome has remarkable plasticity and undergo large scale homologous recombination events resulting in diverse lineages. In this study, we investigated the evolutionary dynamics of class D OXAs, NDM and its association with mobile genetic elements (MGEs) among different International clones (ICs) of A. baumannii.

Materials/methods: A total of 112 genomes of A. baumannii were analyzed which includes 31 Indian genomes from this study and 81 global genomes from Genbank. The phylodynamics of Indian genomes against global genomes with regards to carbapenem resistance and genomic diversification was studied using BEAST analysis. For a subset of 12 genomes from this study, complete genome was obtained using hybrid assembly of IonTorrent and MinION reads. Resistance profile and sequence types were identified using ResFinder and MLSTFinder respectively. Genetic arrangement of MGEs associated with bla\textit{OXA-23}, bla\textit{OXA-58}, bla\textit{NDM-1} and bla\textit{OXA-51} was determined. The diversity of A. baumannii Resistance (AbaR) islands was examined by manual cura-
tion.

Results: Phylodynamic analysis classified A. baumannii genomes into four globally disseminated ICs, IC1, IC2, IC7/CC25 and IC3 along with a few unknown clades. Transmission events predicted the evolution of A. baumannii in the late 18th century and the acquisition of carbapenem resistance genes by different clones at respective intervals thereafter. bla\textit{OXA-23} was the most widespread carbapenemase while bla\textit{OXA-24}, bla\textit{OXA-51} and bla\textit{NDM-1} was less prevalent. The 31 Indian isolates were distributed in all identified ICs with predominant group belongs to IC2. Variant of bla\textit{OXA-51} specific to ICs were observed. Analysis of the genetic environment of 12 complete genomes revealed novel findings like insertion of IS\textit{Aba1} upstream OXA-51 variant, bla\textit{NDM-1} and Tn125-like harboring bla\textit{NDM-1} with insertion sequence, IS\textit{Aba14}. Four diverse AbaR Island was identified, of which two were novel with Tn6166 like backbone.

Conclusions: The current study unveils the evolutionary dynamics of carbapenem resistance genes among different lineages. Emergence of less dominant clone, CC25/IC7 and predominance of AbaR4 like Resistance Island with its diverse variants were observed in this study. Transposons carrying bla\textit{OXA-23} and bla\textit{NDM-1} unleash the transposition events resulting in wide spread of carbapenem resistance among A. baumannii.

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Abstracts 2020

Abstract 8069

Travel health advice: do travellers follow the recommendations?

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Background: In the last decade, there has been a rapid growth in the number of international travels. Tropical destinations suppose increased risk of travel-related diseases. Many of them are preventable through vaccination, chemoprophylaxis or anti-vectorial personal protective measures (PPM). However, although PPM are easy to comply with, many travellers do not seek or adhere to these recommendations. We describe compliance with preventive measures in a cohort of Spanish travellers.

Materials/methods: Travellers attended at Travel Medicine Unit from the National Reference Centre Hospital La Paz- Carlos III, Madrid (Spain) between June 2017 and June 2019 were asked to complete an online questionnaire close after the travel. Demographics, travel characteristics (length of stay, reasons for travel, destination) and questions related to PPM were recorded.

Results: The survey was completed by 2338 travellers, of a total of 6354 requests (36.8%). Median age of respondents was 38 years (range 18-81); 59.5% (n=1391) were women. Most frequent destinations were Sub-Saharan Africa (31.2%) and South-east of Asia (24.4%). The median duration of the trip was 15 days (range 4-456), and the most frequent reason for travel was tourism (81.6%).

PPM were followed by most travellers (89.1%), although more than half [65.1%] applied them less than 2 times a day. Visiting Friends and Relatives [VFR] travellers were more likely to underuse skin repellents [P>0.001]. Up to half of travellers [50.9%] drunk uncontrolled beverages, and 57.6% ate fresh/undercooked food. No differences were found through different reasons for travel. Those travelling for business were more likely to avoid walking on barefoot [p>0.001], but nearly 55% of all travellers admitted to having done so. Finally, up to 34.6% of travellers bathed in fresh water. Table 1 summarize compliance with preventive measures according to reason for travel.

Conclusions: Most travellers followed PPM but they didn’t applied the recommended protective dose of repellent as well as most of them didn’t follow recommendations regarding safe food or drinks or avoid walking on barefoot. New approaches to motivate travellers’ compliance are required to increase the awareness of risk in travellers and to improve knowledge about the risks they are exposed to during international travels.

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Abstracts 2020

Abstract 8070

The rapid clinical diagnosis of lower respiratory infection by an unbiased real-time metagenomics methods in validated intensive care unit patients

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Background: Efficient and rapid detection of pathogens is an urgent need in lower respiratory infections (LRIs), especially for those validated ICU patients with life-threatening infections. Nanopore (ONT) has been reported as a promising diagnostic tool in infectious diseases.

Materials/methods: The single-center prospective study was conducted in Huashan Hospital affiliated to Fudan University, Shanghai, China from May 2019 to October 2019. Validated patients in ICU, aged over 16, were consecutively enrolled. All of the collected sputum samples were sent for Nanopore, culture and smear. Complete clinical microbiological data was available for all samples. Pneumonia severity index (PSI) was used to evaluate the clinical condition of the validated patients.

Results: A total of 23 patients with tracheal incubation were enrolled, and serial sputum of one patient with severe pneumonia was collected. Culture detected one or more pathogens in 20 specimens, while ONT detected all the culture-detected pathogens in 95.0% (19/20) specimens. ONT detected pathogens in 3 culture-negative specimens, which were confirmed by PCR later, representing an increase in sensitivity from 87.0% (20/23) to 95.7% (22/23) compared with culture. Average time of sample preparing and ONT process took 13-17 h per sample and showed an advantage over smear (critical value) and traditional culture in identification of the particular microorganisms (P < 0.05). Klebsiella pneumoniae can be detected precisely one hour after sequencing in a specific sample. For the above-mentioned sample there was 49.26% coverage within 2 h with 28257 specific reads. The condition and PSI of patients with severe pneumonia continuously deteriorated after treatment, a marked increase in Klebsiella pneumoniae sequencing reads was observed. Genome coverage increased to 99.64% after 48 h. Among the 10 resistance genes, 7 matched the phenotype seen.

Conclusions: Nanopore showed promising potential in pathogenic diagnosis and surveillance during validated patients in ICU with lower respiratory infection and might enable clinicians to make more timely and targeted therapeutic decisions. However, new bioinformatics analysis method for resistance gene detection deserves to be explored.

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**Abstract 8072**

**Daptomycin or vancomycin for methicillin-resistant Staphylococcus aureus infective endocarditis complicated by septic pulmonary emboli**

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**Background:** Methicillin-resistant Staphylococcus aureus (MRSA) causes serious infections including infective endocarditis (IE) and bacteremia. Septic pulmonary emboli (SPE) are complications more commonly observed in intravenous drug users (IDU). Daptomycin is an approved alternative to vancomycin for MRSA bacteremia and right-sided endocarditis treatment but it is inactivated by pulmonary surfactants. However, in vivo studies suggest that mechanisms necessary to inactivate daptomycin are not present during SPE. Its use in the presence of SPE has remained controversial with small studies describing mixed results of clinical success and failure. It is crucial to explore daptomycin effectiveness for MRSA bacteremia complicated by SPE as an alternative to vancomycin especially given concerns for reported vancomycin failures in MRSA bacteremia.

**Materials/methods:** This is a single-center retrospective cohort study of adult patients ≥18 years old with MRSA-positive blood cultures complicated by SPE between 2014 and 2019. Inclusion criteria were daptomycin or vancomycin for ≥72 hours initiated ≤48 hours of SPE suspicion or diagnosis. Exclusion criteria were concurrent pneumonia, polymicrobial bacteremia, and treatment with other anti-MRSA antibiotics during the initial 48 hours. The primary outcome was composite failure defined as 30-day mortality or worsening respiratory signs and symptoms. Descriptive statistics were used for baseline demographics. Bivariate analyses were used to compare differences between treatment groups.

**Results:** A total of 23 adults were included. Six (26%) received daptomycin and 17 (74%) received vancomycin. The median (IQR) age was 52 (36 – 59) years, 57% were male, and 57% were IDU. Almost half (43%, n = 10) had definitive infective endocarditis and source control (valvular repair) was pursued in one person. Two people experienced 30-day mortality, one in each treatment group. No one experienced worsening respiratory signs and symptoms.

**Conclusions:** This study represents real-world evidence describing daptomycin use in a vulnerable IDU population. No obvious signal of daptomycin failure was observed. However, the small number of people precludes statistical inferences and additional multicenter studies are needed to elucidate the role of daptomycin in MRSA bacteremia complicated by SPE. This research is important in the context of the opioid and IDU epidemic in the United States.

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Abstract 8074

**Dose optimization of carbapenems in critically ill patients for highly resistant *Klebsiella pneumoniae* environment: population pharmacokinetics and simulations**

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**Background:** Critically ill patients showed alteration in pharmacokinetics (PK) of carbapenems, backbone antibiotics for multiple drugs resistance (MDR) *K. pneumoniae*. This study aimed to optimize the doses of meropenem (MEM) and imipenem (IMI) for critically ill patients admitted to an intensive care unit (ICU) with highly resistant *K. pneumoniae*.

**Materials/methods:** Plasma samples were collected from 70 ICU patients at 0.5 and 3 h after prolonged infusion of MEM (27 patients) and IMI (43 patients). Population PK modelling was performed using nonparametric method with the help of Pmetrics on R v.3.5.3. Susceptibility data of *K. pneumoniae* were obtained from microbiology department. Monte Carlo simulations was performed for dose optimization with threshold to achieve 90 % probability of target attainment (PTA) for 100% $T>MIC$ and cumulative fraction of response (CFR) against *K. pneumoniae*.

**Results:** A one-compartment model best fit the PK data ($V$ and total clearance (CL): 16.5 L and 8.4 L/h for MEM and 22.4 L and 12.7 L/h for IMI, respectively). Eight-hour urine creatinine clearance was significant covariate of CL of both antibiotics while body weight and the indwelling drainage were predictors for $V_e$ of IMI and MEM, respectively. Prolonged infusion of MEM and IMI could cover sensitive pathogens only. Higher PTA and CFR were attained with continuous infusion, which can cover pathogens with MIC up to 8 mg/L. Target on pathogens of MIC $\geq$ 32 mg/L could not be achieved with regular dose (see Table)

<table>
<thead>
<tr>
<th>Susceptibility</th>
<th>All</th>
<th>Susceptible</th>
<th>Intermediate</th>
<th>Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Meropenem</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6000 mg CI</td>
<td>69.9</td>
<td>100.0</td>
<td>99.4</td>
<td>51.3</td>
</tr>
<tr>
<td>3000 mg q6h PI</td>
<td>62.0</td>
<td>95.2</td>
<td>84.7</td>
<td>41.7</td>
</tr>
<tr>
<td>2000 mg q8h PI</td>
<td>40.0</td>
<td>90.5</td>
<td>58.6</td>
<td>9.7</td>
</tr>
<tr>
<td><strong>Imipenem</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3000 mg CI</td>
<td>58.0</td>
<td>100.0</td>
<td>95.7</td>
<td>23.6</td>
</tr>
<tr>
<td>1000 mg q6h PI</td>
<td>45.3</td>
<td>91.6</td>
<td>75.2</td>
<td>11.2</td>
</tr>
<tr>
<td>1000 mg q8h PI</td>
<td>34.9</td>
<td>82.4</td>
<td>41.9</td>
<td>4.1</td>
</tr>
</tbody>
</table>

CI: continuous infusion, PI: prolonged infusion in 3 hours.

All: All isolated *K. pneumoniae*, Susceptible: MIC $\leq$ 2mg/L, Intermediate: 2mg/L < MIC $\leq$ 8mg/L, Resistant: > 8mg/L

**Conclusions:** Critically ill patients underwent suboptimal doses of carbapenems for isolated *K. pneumoniae* in ICU and therefore high dose by CI should be considered.

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**SNP-based phylogeny revealing establishment of ciprofloxacin-resistant Shigella sonnei lineage in India**

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1Christian Medical College, Vellore, India

**Background:** S. sonnei is replacing S. flexneri as the most common cause of shigellosis worldwide, particularly in countries undergoing economic development. Previous studies reported that South Asia as a hub for recent international spread of fluoroquinolone resistant S. sonnei. S. sonnei lineage III is widespread globally among the five reported lineages. This study investigated the local establishment of ciprofloxacin resistant S. sonnei in India through whole genome sequence analysis.

**Materials/methods:** A total of 444 S. sonnei genomes were studied. This includes 106 Indian isolates and 338 global isolates. Sequences were mapped to the S. sonnei Ss046 reference sequence (Accession number: NC_007384) using SMALT and SNPs were called against the reference and filtered using SAMtools. RAxML tree resulted was displayed and labelled using iTOL. Further establishment of ciprofloxacin resistance in India was investigated by temporal phylogenetic reconstruction of 76 Indian S. sonnei from 1990 to 2017 using BEAST analysis.

**Results:** Phylogenetic analysis in global context showed, all Indian isolates clusters within lineage III (Central Asia clade). Notably, 68% of the isolates within Central Asia III had triple (gyrA – S83L, D87G/N, parC – S80I) mutations for fluoroquinolone resistance. No PMQR genes were identified except in one isolate. Central Asia III lineage isolates had more number of AMR genes and different plasmid profile compared to isolates in other lineages. A time-scaled phylogenetic tree demonstrated the sequential accumulation of mutations and showed that all ciprofloxacin resistant S. sonnei comprised a distinct clade. The most recent common ancestor (MRCA) of the ciprofloxacin resistant clade in India was estimated to be at late 2005.

**Conclusions:** This is the first study to investigate the temporal structure of S. sonnei Central Asia III lineage in India. The successful global expansion of this lineage could be due to acquisition of double or triple mutations and mobile elements. This study indicates the continued surveillance of this lineage and recommends for an urgent re-evaluation of the empirical use of ciprofloxacin for a range of gastrointestinal infections.

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Abstract 8077

**Hospitalised patients with a label of penicillin allergy: which antibiotic therapy do they receive?**
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**Background:** About 10% of patients report being allergic to penicillin, while only 10% of them are skin-test positive. Reporting a notion of penicillin allergy (PA) (NPA) can lead to negative consequences for patients. The alternative antibiotic therapy can be: less efficient, more expensive or with a higher impact on the intestinal microbiota. Our study aimed to describe the consequences of a NPA on the antibiotic strategy in two tertiary care referent centers in France.

**Materials/methods:** We performed a multicenter, prospective study in hospitalized patients in 2 tertiary care hospitals between 01/02/19 and 31/08/19. Inclusion criteria were: requiring curative antibiotic therapy and a NPA reported by the patient (whatever the results of prior or subsequent skin-tests). Information were collected through a questionnaire developed for the purpose of assessing their allergy and the adopted antibiotic strategy. Information was checked in their medical records and through interviews of their general practitioner, and local pharmacist.

**Results:** 53 patients were included. 57% did not notified the type of allergy with an increased risk of serious side effects. Nine patients (17%) received a penicillin despite the NPA, of whom one presented a maculopapular exanthema during hospitalization. The most prescribed antibiotics in case of PA were cephalosporin’s (23% of prescriptions), fluoroquinolones (18%), glycopeptides (15%), and macrolides (11%). On the basis of the interview of the pharmacist and the general practitioner 8 (15%) patients had no penicillin allergy. A correct evaluation would have avoided the prescription of critical and expensive antibiotics in 5 (9.5%) cases. Regarding cephalosporin’s prescription, 26% of patients should not have received it according to the French guidelines in case of penicillin allergy but no side effects were reported.

**Conclusions:** Antimicrobial stewardship programs should include PA evaluation and proposition of alternative therapy algorithms to help practitioners on the management of possible PA.

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Next-generation sequencing for the research and development of novel antibiotics

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Background: Understanding the mechanism of action (MoA) and predicting resistance issues are key points in the development of novel antibacterials.

To document these properties and decipher structure activity relationship studies (SAR) during chemical optimization, we use transposon sequencing (TnSeq). TnSeq uncovers the genes that upon inactivation influence the efficacy of a drug candidate. The generation of a database with compounds of known classes allows comparisons and clustering analyses.

Here we present examples of the application of TnSeq to help the research and development of novel antibiotics.

Materials/methods: A saturated Tn5 transposon library was generated in Escherichia coli ATCC35218. Challenges were performed with reference or novel compounds. Next generation sequencing determined the fitness of each mutant.

First analysis probed efflux and influx properties, and predicted mechanisms of resistance. Differential analysis and clustering methods were applied to compare the profiles and predict potential target pathways of the novel compounds. The same approach was also used to guide chemical SAR optimization.

Results: Characterization of the Tn5 library confirmed a highly saturated collection with a 15bp-frequency of insertion.

Profiling existing compounds using TnSeq confirmed previously published data associated to influx and efflux liabilities. TnSeq also documents resistance and target pathways. Comparing profiles allowed to determine signatures. For instance, mutants implicated in DNA repair ([recN, dinG, xseA and hupAB] have a decreased fitness in presence of quinolones. Some have clear efflux liabilities like levofloxacin, minocyclin or tetracyclin, when others are clearly more active with short-LPS in waaP or waaG mutants.

The same approach applied to new compounds enables to rapidly predict their target pathways and resistance issues. For instance, we showed that a new compound targets DNA replication and has a dedicated influx pathway. In addition, we used TnSeq to compare three compounds of a novel series and document possible target deviation.

Conclusions: We have validated TnSeq as a powerful tool for the MoA identification, and guiding SAR making use of a robust collection of known molecules profiles.

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Abstract 8079

**Evaluation of clinical safety and efficacy of letermovir for cytomegalovirus infection prevention in allogenic haematopoietic cell transplant recipients**

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**Background:** Cytomegalovirus (CMV) infection remains a common opportunistic infection after allogenic haematopoietic stem cell transplantation (HSCT). Letermovir is a new antiviral drug indicated in CMV infection prophylaxis post allogenic HSCT. By interfering with CMV terminase complex, letermovir has a different mechanism of action from ganciclovir with the benefit of non-inducing nephrotoxicity or myelotoxicity. The aim of this study is to assess clinical safety and efficacy of letermovir in a French reference centre of HSCT.

**Materials/methods:** This is a monocentric observational prospective study conducted during 23 months (01/2018-11/2019). All patients treated by letermovir during this period were included. Patients with high risk of CMV reactivation are defined by criteria: haplo-identic or non-related donor, SCT collected from umbilical cord, Graft-versus-Host Disease (GvHD) grade 2 or more, requiring systemic use of corticosteroids.

**Results:** During the study, 23 patients received letermovir. The average age of patients was 52 +/- 14 years old [19;69] and the sex ratio was 1:1. The allogenic HSCT was indicated for aplastic anemia [n=2]; acute myeloid leukemia [n=7]; chronic myeloid leukemia [n=2]; Griscelli disease [n=1]; lymphoma [n=2] and myelodysplastic syndRome [n=9]. CMV serological statuses were: R+/D- [n=7], R+/D+ [n=14], R-/D+ [n=1], R-/D- [n=1]. Twelve patients received 240 mg per day of letermovir in association with ciclosporin whereas 11 patients were treated by 480 mg of letermovir per day without ciclosporin. In median, letermovir was started 88 days [2;299] after transplantation and lasted 140 days [20;326]. Nine patients (39%) had a GvHD when they began letermovir. Reasons to stop letermovir were: the planned end of treatment without CMV infection (n=17; 74%); hematological disease relapse (n=3); CMV infection because of unfulfilled treatment (n=1) or explained by a resistance mutation (n=1), and patient death (n=1).

**Conclusions:** Our experience demonstrates the efficacy of letermovir in a real-world setting for CMV prevention with an effective prevention for 74% of patients. The long duration of treatment by letermovir (> 100 days) in this study is explained by the profile of patients with high risk of CMV reactivation. A long term evaluation would be necessary to evaluate the proportion of CMV infection after the end of letermovir treatment.

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Evaluation of the PROMPT inoculation system with the MicroScan antibiotic susceptibility testing microplate designed for low-resource settings

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Abstract third-party references: Médecins Sans Frontières

Background: The Mini-lab is a Médecins Sans Frontières (MSF) project for the development of an all-in-one clinical bacteriology laboratory deployable in low-resource settings (LRS). Three microplates were designed for AST, covering most clinically-relevant bacteria found in bloodstream infections using MicroScan lyophilized broth micro dilution plates (Beckman Coulter, Sacramento, USA). PROMPT™ inoculation system (Beckman Coulter, Sacramento, USA) was chosen as an easy method to obtain a standardized inoculum by none-expert microbiology technicians.

Materials/methods: The PROMPT inoculation system was evaluated against standard turbidity method using frozen isolates from routine clinical laboratory and challenging isolates from LRS following ISO20776-2:2007 guidance's with the MSF MicroScan Gram Pos panels [C32698] for Staphylococcus spp and Enterococcus spp species and MSF MicroScan Gram Neg panels [C32699] for Gram-negative bacterial isolates. EUCAST V9 recommended Disc diffusion, gradient diffusion method (E-test) or standard Micro broth dilutions using turbidity method, were used as comparators. In total, 123 Gram-positive and 157 Gram-negative isolates were tested. All panels were read visually using manufacturer instructions.

Results: With the MSF MicroScan Gram Neg panels no difference in performances was evidenced, the percentage of category agreement (CA) were all above 90% and major (MAJ) and very major error (VMJ) were below the 3% ISO threshold when using the PROMPT or standard inoculum. With the MSF MicroScan Gram Pos panels, for Staphylococcus spp, category agreement was much lower using the PROMPT versus standard inoculum for amikacin (78% - 93%), erythromycin (88% - 96%) and trimethoprim-sulfamethoxazole (81% - 93%) with no difference in VMJ. However, MAJ error rate was higher with the PROMPT for ciprofloxacin (8% - 2%), amikacin (7% - 1%), gentamicin (9% - 3%), vancomycin (4% - 0%), erythromycin (9% - 1%), trimethoprim-sulfadiazine (14% - 1%) and linezolid (5% - 1%).

Conclusions: PROMPT inoculation system results in increased MICs, which results in increase of Major Errors for ciprofloxacin and erythromycin for Staphylococcus spp. In addition, we found that the use of the PROMPT increased as well MICs and MAJ rates for gentamicin, amikacin, vancomycin, trimethoprim-sulfamethoxazole, and linezolid. Our results confirm the manufacturer recommendation not to use the PROMPT for Staphylococcus spp, standard inoculum should be used instead.

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Abstract 8084

**Impact of saponin-based host DNA depletion on respiratory resistome measures**

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¹University of Pennsylvania, Philadelphia, United States

Abstract third-party references: National Institute for Allergy and Infectious Diseases, Centers for Disease Control and Prevention (CDC)

**Background:** The low ratio of microbial to host cell biomass poses a challenge to metagenomic studies of the respiratory tract microbiome. Saponin-based host DNA depletion improves the efficiency of metagenomic respiratory microbiome analysis using long-read sequencing. We sought to (1) define the impact of saponin-based host DNA depletion on short-read metagenomic analysis of the respiratory tract microbiome and (2) evaluate the potential for saponin-based host DNA depletion to improve detection of respiratory tract antimicrobial resistance (AMR) determinants.

**Materials/methods:** We enrolled a cohort of subjects on admission to an academic long-term acute care hospital (LTACH) for ventilator weaning and performed longitudinal sampling of endotracheal aspirates. From 37 subjects, we selected 100 respiratory specimens which were split for DNA extraction with and without saponin-based host DNA depletion prior to metagenomic sequencing (Illumina HiSeq). Taxonomic assignment was performed with Kraken; resistome analysis with CARD-RGI. Statistical analysis was performed with R and Stan; mixed effects models were fit to define microbiome and resistome differences.

**Results:** Saponin-based host DNA depletion produced more metagenomic reads per respiratory specimen after human read filtering (Kruskal-Wallis p < 0.002). At the family level, saponin-treated specimens demonstrated higher read counts of Enterobacteriaceae and Halomonadaceae. However, saponin-based host DNA depletion did not significantly increase the detection of AMR determinants, at either the drug-class or gene category level.

**Conclusions:** Saponin-based host DNA depletion improves yield of microbial reads from respiratory tract specimens to which short-read shotgun metagenomic sequencing is applied, but this does not significantly improve detection of AMR determinants in the respiratory microbiome.

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Epidemiology of candidaemia in Swiss tertiary care hospitals: a 15-Year Study 2004 to 2018
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Background: Candidemia is the most frequent fungal bloodstream infection. Its epidemiology has evolved over the last two decades. New antifungal agents and new management strategies such as antifungal prophylaxis and preemptive therapy have been recommended over the last decade. These changes may have resulted in a change of *Candida* species causing invasive infections. However, recent comprehensive longitudinal data from Europe are limited.

Materials/methods: We conducted a 15-year nationwide survey of candidemia in all five university and two university-affiliated tertiary care hospitals from 2004-2018. Incidences of candidemia per 1000 admissions and antifungal consumption in defined daily doses (DDD) per 100 patient days were calculated. Preliminary descriptive data are presented.

Results: The annual number of hospital admissions and solid organ/hematopoietic cell transplantations increased from 152,036 to 378,865/year and 830 to 1,410/year over 15 years, respectively. A total of 2,233 episodes of candidemia were observed. *Candida* species ranked 9-10 among etiologic agents (2-3% of all bloodstream isolates). The incidence of candidemia decreased from 0.86 to 0.44/1000 admissions over the 15-year period [Figure 1]. *Candida albicans* episodes decreased significantly over 2004-2018 [0.55 to 0.22/1000 admissions] by remaining the predominant cause of candidemia [63% to 50%]. *C. glabrata* ranked second, and while the number of episodes decreased [0.20 to 0.12/1000 admissions], the proportion increased from 19% to 27%. *C. krusei* remained a rare isolate [3%), other non-albicans *Candida* episodes remained stable (around 0.10/1000 admissions). No *C. auris* blood isolate was recovered until 2018. Notably, species distribution varied significantly by age. *Candida albicans* was more common in children and in adults >40 years, than in adults 18-40 years. Fluconazole and voriconazole consumption remained stable since 2007, whereas posaconazole, liposomal amphotericin B and echinocandin consumption increased significantly.

Conclusions: Despite increasing high-risk activities, the incidence of candidemia decreased over 15 years, with a predominant decrease of *Candida albicans* episodes and a relative shift to resistant species. These epidemiological trends are possibly due to the increased use of prophylactic and preemptive antifungal management strategies. Additional analyses will be performed to investigate the causes of the noted epidemiological trends.

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Ceftazidime-avibactam monotherapy for 7 days as treatment of KPC carbapenemase-producing Enterobacteriaceae bacteraemia in severely immunosuppressed patients

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**Background:** Bacteraemias caused by KPC carbapenemase-producing Enterobacteriaceae (KPC-CPE) in immunosuppressed patients have more than 50% mortality rate. Treatment usually includes a combination of 2 or more active antibiotics for ≥10 days. Ceftazidime-avibactam (CA) has an important microbiological activity against these microorganisms, being able to be used as monotherapy, even in severe infections. However, to our knowledge, there are not enough data regarding short treatment for bacteraemia in severely immunosuppressed patients.

**Materials/methods:** Immunosuppressed patients with KPC-CPE bacteraemia who received treatment with ceftazidime-avibactam for 7 days were prospectively included, between August 2018 to June 2019. Clinical success was assessed at the end of treatment and 30-day follow-up was performed to evaluate mortality and recurrence of bacteraemia.

**Results:** Seven patients were included. Median age (IQR 25-75): 47 (38-59), APACHE II score (IQR 25-75): 23 (19-25). Other baseline, clinical and microbiological features as well as outcome are described in table 1.

**Conclusions:** Immunosuppressed patients with KPC-CPE bacteraemia who have clinical resolution during treatment with ceftazidime-avibactam, could be treated with this drug as monotherapy for a short period of time.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Underlying disease</th>
<th>Immunosuppresion</th>
<th>Source of infection</th>
<th>Pathogen</th>
<th>Empirical treatment</th>
<th>Definitive treatment</th>
<th>Clinical outcome</th>
<th>Recurrence of bacteraemia</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kidney Transplant</td>
<td>Tacrolimus Prednisone 60 mg/ day ATG</td>
<td>Pyelonephritis</td>
<td>Serratia marcescens</td>
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<td>Dexamethasone 40 mg/day</td>
<td>Pyelonephritis</td>
<td>Klebsiella pneumoniae</td>
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<td>CA</td>
<td>-</td>
<td>No</td>
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<td>3</td>
<td>Allogeneic HSCT</td>
<td>Prednisone 60 mg/day</td>
<td>Enteritis CVC</td>
<td>Klebsiella pneumoniae</td>
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<td>CA</td>
<td>Succ</td>
<td>No</td>
<td>Alive</td>
</tr>
<tr>
<td>4</td>
<td>Multiple Myeloma</td>
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<td>Succ</td>
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<td>Succ</td>
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<td>7</td>
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<td>Enterobacter cloacae</td>
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</table>

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Intra- and inter-facilities spread of multidrug-resistant Enterobacteriaceae across a large nursing homes network

Clément Legeay1, Basile Fuchs2, Thomas Haudebourg3, Céline Poulain1, Françoise Raymond3, Stéphane Corvec2, Gabriel Birgand*3

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Background: Nursing homes (NH) may play a major role in the spread of multi-drug resistant Enterobacteriaceae (MRE) over the healthcare network. We assessed the prevalence of, and factors associated with, ESBL or carbapenemase producing Enterobacteriaceae (ESBLPE or CPE) carriage across a large network of NHs in western France.

Materials/methods: Fifty NH from the Pays de la Loire region were randomly selected according to the geographical situation and density of NHs. One resident every three rooms was included in the prevalence survey. Stool samples were collected with swab and cultured on selective chromogenic media (ESBL-chromID® and chromID CARBA-SMART ID®). Mass spectrometry (Vitek MS) was used to identify Enterobacteriaceae species. ESBL, AmpC or carbapenemase production was respectively confirmed with MAST® and CORIS® test. Antibiotic susceptibilities were assessed using Vitek 2. Demographic and clinical data were collected prospectively on the day of the survey. Clonal relatedness was investigated by pulsed-field gel electrophoresis (PFGE).

Results: 734 residents from 30 different NHs were included. 83 (11.3%) were found colonized with ESBLPE (59 [71%] Escherichia coli – E. coli, 12 [14%] Klebsiella pneumoniae - Kp). The prevalence varied from 0% to 45% according to NHs. 44 (6%) carried an AmpCPE (18 [41%] Citrobacter spp, 14 [31%] Enterobacter spp.). None CPE was identified. Demographic and clinical data were available for 698 residents. 75% were female with a mean age of 88 years old. 37% were dement, 4% travelled abroad in the prior 12 months, 4% had a urinary tract catheter, 0.7% had a peripheral venous catheter and respectively 58% and 67% had fecal or urinary incontinence. History of travel abroad was associated with the ESBLPE carriage (n=9 [31%] ESBLPE+ vs 67 [10%]; OR = 3.9; IC95 = 1.7 – 8.9; p < 0.01).

A total of 10 clusters of ESBL E.coli and 1 of Kp were identified within 9 NH. 7 similar E.coli strains were identified across 8 different NH and 1 Kp across 2 NHs.

Conclusions: This study suggests that NH play a role in the intra and inter spread of MRE. The ongoing whole genome sequencing of strains and analysis of residents’ movements will help understanding these findings.

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Abstract 8095

Effectiveness and safety of isavuconazole treatment for invasive fungal infections in solid organ transplant recipients

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Abstract third-party references: Supported by a grant from Pfizer

Background: IFI is a significant complication following solid organ transplantation. Voriconazole is the treatment of choice for invasive aspergillosis. However, it is associated with many serious adverse events and has an important interaction with anticalcineurin and mTOR inhibitors. Isavuconazole is an alternative for voriconazole in hematological patients affected with IFI. Evidence regarding its use in SOTR is lacking. Our aim was to study the safety and tolerability of isavuconazole in SOTR.

Materials/methods: We prospectively included all SOTR from January 2018 to November 2019 who received isavuconazole for treatment of an IFI. The study was performed in Vall d’Hebron University Hospital, Barcelona, Spain. The duration of treatment depended on the type of infection and the treating physician. All patients were followed at least for 3 months after treatment. IFI was defined by ISHLT criteria for lung transplant recipients (LTR) or revised EORTC/MSG criteria in non-LTR.

Results: We included 28 SOTR treated with isavuconazole. Most of them (26/28, 92.9%) were LTR. The most frequent IFI treated was tracheobronchitis (12/28, 42.9%). SOTR were infected with Aspergillus spp. (87.5%): A. terreus (7/28, 25%) and A. fumigatus (7/28, 25%); all of them with ISA MIC≤0.5 μg/mL. Other treated infections included Scedosporium prolificans, Alternaria alternata and Trichosporon ashii, one case each. ISA was the initial treatment in 15/28 (53.6%) SOTR and following voriconazole due to adverse events in 4/28 (14.3%). The median duration of treatment was 98 days (IQR 19-193). Hepatotoxicity (mild elevation of cholestatic enzymes) was the commonest adverse event (39.3%). Myopathy was reported in 5/28 (17.9%) SOTR related to combination with corticosteroids. None of the patients developed breakthrough IFI. ISA was prematurely discontinued in only one patient (3.7%) due to significant elevation of transaminases. Dose of anticalcineurin inhibitors was initially adjusted in 33% SOTR, and up to 66.7% on the first days of treatment with a median of 33% decrease (1.2 mg). Four patients received concomitantly mTOR inhibitors with overall good tolerance. Eight (28.5%) SOTR died while on isavuconazole treatment. Another patient died during follow-up.

Conclusions: We consider that ISA was well tolerated and proved to be an effective treatment for IFI in SOTR.

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**Abstract 8096**

*Staphylococcus aureus* dampen autophagy flux to survive inside a model of keratinocytes mimicking *S. aureus* nasal colonisation

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**Abstract third-party references:** This research was funded by a grant from the University of St-Etienne

**Background:** *SA* uses the eukaryotic cell as a Trojan horse to escape both the immune system and antibiotics unable to diffuse into the cell. *SA* can invade non-professional phagocytic cells and induce autophagy by damaging endosomes. A recent study has shown that *SA* is able to induce selective autophagy and to dampen the autophagy flux through MAPK14/p38α phosphorylation. Our study aimed to characterize a model of HaCaT cells mimicking *SA* nasal colonization in order to identify *SA* virulence factors involved in the slowdown of autophagosome maturation.

**Materials/methods:** HaCaT cells were inoculated with *SA* HG001 strain. *SA* intracellular survival was quantified by lysostaphin protection assay. Autophagy response was followed by western blot and immunofluorescence microscopy using either chemical inducers or inhibitors of autophagy.

**Results:** *SA* HG001 was found to invade and to multiply inside HaCaT cells without inducing cell death up to 5-hour post-infection (hpi).

*SA* was able to induce both p38α phosphorylation at 1 hpi (p-p38/p38 = 0.5) and a significant accumulation of LC3-II and SQSTM1 at 5 hpi. Interestingly, neither p-p38 nor LC3-II and SQSTM1 accumulation was observed when HaCaT cells internalize heat-killed *SA* cells.

*SA* intracellular survival at 2 and 3 hpi was significantly increased in cells treated with rapamycin compared to untreated cells. Rapamycin treated cells inoculated with *SA* showed a 3.5 fold-change increase of p-p38 at 2 hpi and a 4 and 6 fold-change increase of SQSTM1 and LC3-II respectively at 5 hpi compared to untreated cells inoculated with *SA*.

Using bafilomycin A1 (BafA1), the intracellular *SA* load doubled at 5 hpi compared to untreated cells. As expected, BafA1 was found to increase LC3-II while SQSTM1/actin and p-p38/p38 ratios were similar to those observed in untreated cells suggesting that *SA* has no need to further slowdown the autophagy flux in BafA1 treated cells.

**Conclusions:** Here, we showed that HaCaT cells are a useful in vitro model to decipher how *SA* is able to take advantage of autophagy by dampening autophagosome maturation and fostering its survival inside keratinocytes. Using targeted CRISPR/Cas9 technology, further experiments are underway to identify *SA* virulence factors involved in autophagy subversion in keratinocytes.

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The N-terminus of APOBEC3C regulates the antiviral activity against HIV-1
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Background: The APOBEC3 (A3) family of single stranded DNA deaminases defends hosts from retroviruses, including human immunodeficiency virus (HIV)-1 lacking viral infectivity factor (vif) [HIV-1 Δvif]. Within primates, A3s have evolved diversely via gene duplications and fusions. A3 enzymes catalyze the dC to dU deamination in the viral genome, causing hypermutation that abrogates the virus. Human APOBEC3C (hA3C) is a strong restriction factor of Vif-deficient simian immunodeficiency virus (SIV Δvif), but exhibit a weak inhibition against HIV-1 Δvif for reasons unknown. Here, we set out to address the mechanistic understanding of A3C’s antiviral function and identify the determinant(s) of functionality of A3C.

Materials/methods: HIV-1 reporter viruses containing A3s were generated by transfection in HEK293T cells. Luciferase-based infectivity assay was used for checking HIV-1 infectivity. Differential-DNA-denaturation (3D) PCR and in vitro DNA cytidine deamination assays were used to study G-to-A mutations on the plus-strand of viral DNA. Molecular docking and simulation were performed between the A3C and ssDNA structure. EMSA was performed to check the protein-DNA interaction. Relative L1 retrotransposition activity was determined by applying a rapid dual-luciferase reporter based assay.

Results: Here we demonstrate that modifying the WE residues in hA3C loop 1 to RK leads to stronger interactions with ssDNA substrate, facilitating catalytic function, which resulted in a drastic increase in both deamination activity and the ability to restrict HIV-1 and LINE-1 replication. Conversely, the modification hA3F WE resulted only in a marginal decrease in HIV-1 Δvif inhibition. The two series of ancestral gene duplications that generated A3C, A3D-CTD and A3F-CTD allowed neo/subfunctionalization: A3F-CTD maintained the ancestral RK residues in loop 1, while strong evolutionary pressure selected for the RK: WE modification in catarrhines A3C, possibly allowing for novel substrate specificity and function.

Conclusions: In conclusion, we have identified the loop 1 region of A3C might have a conserved role in anchoring ssDNA substrate for efficient catalysis and that hA3C’s weak deamination and anti-HIV-1 activity might have been the result of losing DNA interactions in loop 1 during its evolution.

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Abstract 8102

**Analysis of patients with severe complicated influenza in a hospital, 2015-2019**

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**Background:** Influenza, a viral respiratory infection, can cause mild to severe illness. Influenza A and B viruses are responsible for seasonal influenza epidemics every year. Elderly, young children and people with chronic diseases are high-risk groups for severe influenza with complications. In Taiwan, 7 % of patients having influenza with serious complications need intensive care, and about 20 % of whom died.

**Materials/methods:** The data was from the records of medical charts and microbiology laboratory at Jen-Ai Hospital - Dali, a 602-bed regional teaching hospital in central Taiwan. This study enrolled patients with severe complicated influenza from 1 January 2015 to 31 October 2019. Severe complicated influenza was defined as influenza followed by a complication (such as pneumonia, encephalopathy, invasive bacterial infection, or myocarditis) requiring hospital admission in the intensive care unit or leading to death within two weeks. The following information was collected: age, gender, chronic diseases, body mass index, vaccination, type of influenza viruses, concomitant bacterial infection, antimicrobial treatment, length of hospital stay, use of central venous catheter (CVC) or extracorporeal membrane oxygenation (ECMO), and outcomes.

**Results:** Totally 30 patients (15 men and 15 women) were enrolled. The average age was 65 years old (60 % were under 65 years old). The virus types included A/swH1 (60 %), AH3 (23 %), and B (17 %). Nearly half of patients had diabetes mellitus (47 %). Twenty percent of patients had hemodialysis. Forty percent of patients were overweighted (one fourth were obese) and ten percent of patients were underweighted. Only 4 patients received flu vaccine. *Klebsiella pneumoniae* was the most common bacteria isolated from sputum (23 %). Thirty percent of patients had CVC placement. Four patients received ECMO. The average length of hospital stay was 12 days. The mortality rate was 23 %.

**Conclusions:** In this study, patients with severe complicated influenza were mostly middle-aged, A/swH1 type, diabetes mellitus, overweighted, and had less flu vaccination. The patients with A/swH1 type had higher mortality rate and longer hospital stay.

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Assessment of the performances of the novel BioNumerics-7.6 MTBC plugin for phylogenomic analysis and drug resistance prediction from Mycobacterium tuberculosis whole genomes

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Background: There are 3 major challenges regarding tuberculosis which still kills 1.4 million people/year: 1) the delay of diagnosis, 2) the identification of multidrug resistance, and 3) the development of new diagnostic tools. BioNumerics-7.6 is a programs suite that offers modules allowing the analysis of whole genomes sequences. Recently, a new MTBC genotyping plugin has been implemented with 3 functionalities: species and lineage typing, spoligotyping and resistance prediction. Here, we report the first evaluation of this plugin from a large set of clinical isolates.

Materials/methods: 406 whole genomes were obtained by Illumina sequencing from clinical isolates collected between 2006-2019, then assembled by using a Galaxy pipeline and BioNumerics-7.6. The lineages were determined by 24-loci MIRU-VNTR typing. The most common resistance mutations were detected by the MTBDR(+) assay (Hain) and by Sanger sequencing of PCR amplicons. The phenotyping of the clinical isolates was done on solid medium.

Results: We analyzed 344 isolates for which the MIRU-VNTR results were available. Amongst the 17 different lineages identified by MIRU-VNTR, the BioNumerics typing was concordant with MIRU-VNTR for 100% of EAI [N=12], 97% of Beijing [N=109/112], 95% of Delhi/CAS [N=19/20], 84% of Haarlem [N=67/80], 94% of LAM [N=34/36], 62% of Cameroon [N=8/13], 85% of H37Rv [N=11/13], and 57% of S [N=4/7]. Concordance was 100% for TUR [N=6], URAL [N=12], Ghana [N=19], Ugandan [N=5], Ugandan II [N=2], M.bovis BCG [N=2], and West African 1 [N=1]. The single M.canetti was not identified. The curated database of BioNumerics contains mutations related to resistance to 12 antituberculosis drugs. The MTBC plugin correctly predicted the sensibility/resistance profiles in 99% [379/384] of the strains for rifampicin, 98% [378/384] for isoniazid, 90% [283/314] for pyrazinamide, 94% [306/327] for ethambutol, 99% [381/384] for fluoroquinolones, 97% [216/222] for injectable aminoglycosides, 100% [207/207] for linezolid, and 100% [158/158] for bedaquiline.

Conclusions: We report the first evaluation of the use of the BioNumerics MTBC module for genotyping and prediction of drug resistance of Mtb. The MTBC plugin of BioNumerics is very promising for routine analysis of whole genomes of M.tuberculosis, specially to characterize and better control the spreading of multidrug- and extensively-drug resistant tuberculosis.

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Abstract 8109

**Study of microbial adhesion to nanostructured and nanocoated orthoprosthetic material through dynamic models**

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**Background:** Bacteria can form submerged biofilms and are one of the most important causes in most states of chronic infectious diseases. Biofilms can also develop on abiotic surfaces, including medical devices such as orthopedic prostheses, artificial heart valves, coronary stents, intravascular and urinary catheters, breast implants, prosthetics eye devices.

**Materials/methods:** Two different types of nanostructured and nanocoated orthoprosthetic materials, crafted experimentally, were used to create coupons to be used inside the Drip Flow Reactor (DFR) bioreactor, TiAl6V4 titanium with and without coating in silver nanoparticles (TiAl6V4-AgNPs) and cobalt - chromium with and without coating (CoCr-AgNPs). The composition of coupons was verified by two different methods: X-ray fluorescence spectroscopy (XRF) and Laser-induced breakdown spectroscopy (LIBS). Biofilm formation on materials was evaluated according to the American Standards or Testing and Materials ASTM-E2647-13 on the Pseudomonas aeruginosa ATCC 700888 strain. Silver release during continuous flow was evaluated by ICP-MS spectrophotometric analysis. The expression level of the genes of the Las and Rhl system of Quorum Sensing was evaluated using the ΔΔCt method.

**Results:** The results showed an improved ability of cobalt-chromium to reduce microbial adhesion and biofilm formation, independently of the presence of silver nanoparticles [TiAl6V4-AgNPs] and cobalt - chromium with and without coating [CoCr-AgNPs]. The composition of coupons was verified by two different methods: X-ray fluorescence spectroscopy (XRF) and Laser-induced breakdown spectroscopy (LIBS). Biofilm formation on materials was evaluated according to the American Standards or Testing and Materials ASTM-E2647-13 on the Pseudomonas aeruginosa ATCC 700888 strain. Silver release during continuous flow was evaluated by ICP-MS spectrophotometric analysis. The expression level of the genes of the Las and Rhl system of Quorum Sensing was evaluated using the ΔΔCt method.

**Conclusions:** Nano-structuring and nano-coating of orthoprosthetic materials can be a valid strategy in the prevention of device-related infections, however their effectiveness should be evaluated with dynamic models that simulate the real dynamics of biofilm formation. The release of silver from the analyzed material resulted below the minimum inhibitory concentration, but this quantity found to promote the up-regulation of Rhl system. Furthermore investigation should be conducted to optimize the effectiveness of the coating.

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Abstract 8110

**Characterisation of multidrug resistant *Shigella sonnei* isolated from men who have sex with men in Zagreb, Croatia**

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**Background:** During 2018 epidemic spread of ciprofloxacin-resistant *Shigella sonnei* strains among men who have sex with men (MSM) in Zagreb was noticed. In MSM population *S. sonnei* infection is in most cases sexually transmitted and clusters are regularly reported. We investigated an outbreak of ciprofloxacin-resistant *S. sonnei* among MSM and studied its resistance profile.

**Materials/methods:** Eight isolates of *S. sonnei* from outbreak among MSM in 2018 in Zagreb were compared by antibiotic susceptibility testing and molecular typing by use of pulsed-field gel electrophoresis (PFGE). Isolates were tested for susceptibility to ampicillin, co-amoxiclav, cefazolin, cefuroxime, ceftriaxone, ceftazidime, amikacin, gentamicin, tetracycline, co-trimethoprim, pefloxacin, ciprofloxacin, and azithromycin. Disk diffusion and e-test were used for phenotypic characterisation of antibiotic resistance and PCR was used to detect genes encoding β-lactamases.

**Results:** The isolates were uniformly resistant to ampicillin, tetracycline, co-trimethoprim, pefloxacin, ciprofloxacin, and azithromycin (MIC>256). Ampicillin resistance was attributed to the production of TEM1 β-lactamase. PCR for SHV and OXA1 was negative. All isolates were resistant to co-amoxiclav according to disk-diffusion test with inhibition zone of 17-18mm, but susceptible according to e-test (MIC 2-6). Isolates collected during the outbreak from eight men with diarrhoea showed identical PFGE and resistance patterns and can therefore be regarded as clonally identical.

**Conclusions:** Asymptomatic and prolonged shedding in the reconvalescent phase may contribute to the transmission risk of shigella infection during oral-anal sexual practices. The risk of transmission of multidrug resistant *S. sonnei* in MSM population in Zagreb is further complicated by the resistance of shigella to usually used therapeutic options. Enhanced surveillance and risk-reduction interventions against the spread of shigellosis among MSM is needed.

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Biomarker profiles in streptococcal skin and soft-tissue infections with or without necrosis or shock: a prospective multi-centre study

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Background: β-haemolytic streptococcal (BHS) skin and soft tissue infections (SSTIs) range from mild superficial impetigo to necrotising soft tissue infections (NSTIs). Streptococcal NSTIs are associated with high rates of septic shock, organ failure and death. In the initial phase, symptoms can be vague and development can be rapid. Discriminating streptococcal NSTIs from less severe SSTIs can be difficult. The diagnosis of NSTIs is still, mainly based on clinical suspicion leading to surgical exploration, confirming the diagnosis. We aim to explore plasma biomarker profiles in severe and non-severe cases of streptococcal SSTIs, in an effort to detect biomarkers that could serve as novel diagnostic and prognostic tools.

Materials/methods: Cases were derived from the INFECT study, a prospective Scandinavian multicentre cohort study. Patients with monomicrobial NSTI or cellulitis caused by Streptococcus pyogenes or Streptococcus dysgalactiae were selected and plasma were analysed using a customised multiplex assay of 37 biomarkers (cytokines, chemokines, adhesion molecules and tissue remodeling factors). To identify immunological profiles associated with specific clinical endotypes, biomarker levels were evaluated in relation to type of infection, streptococcal species, presence of septic shock, and amputation or death using the Mann-Whitney U test, random forest plots and hierarchical cluster analysis.

Results: Altogether 125 monomicrobial streptococcal SSTIs (NSTI=102, cellulitis=23) were included. Significant differences in biomarker levels between streptococcal NSTI and streptococcal cellulitis were observed and several biomarkers showed area under receiver operating characteristic curve (AUROC) above 0.90. Within the NSTI cohort we identified several distinctions in biomarkers in those with or without septic shock, and some differences between deceased or amputated cases compared to those whom did not have these outcomes. Random forest plots predicted similar results. Hierarchical cluster analysis demonstrated distinct grouping of biomarker levels corresponding well to the different infections, clinical findings and outcome (Figure 1), substantiating the conventional analysis.

Conclusions: In a homogenous patient cohort of solely monomicrobial BHS SSTIs the measurement of a wide range of plasma inflammatory biomarkers allowed the characterisation of profiles from which candidate biomarkers for diagnostic or prognostic use can be further explored.
Application of direct MALDI-TOF MS analysis in routine study of gut microbiota of newborns

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Background: One of the main goals in studying microbiota of different biotopes is correct and relatively fast species identification of a large number of isolates of microorganisms, which became possible with the implementation of high-tech methods, including MALDI-TOF MS and sequencing of species-specific DNA loci. The aim of the study was to evaluate the possibility of using the direct MALDI-TOF MS analysis for reliable identification during the study of gut microbiota of newborns.

Materials/methods: Fecal samples of 50 healthy full-term newborns and 51 babies with gestational age 34-37 weeks were investigated by culturomics and mass-spectrometry. To isolate aerobic, facultative and obligate anaerobic microorganisms, method by "culturomics" with an extended set of nutrient media consisting of 17 selective and non-selective nutrient media was used. Microorganisms were identified by direct (non-extraction) MALDI-TOF MS analysis on the Autoflex LT mass spectrometer (Bruker Daltonics, Germany). Upon receipt of the SCORE value ≥2.1 a culture was considered identified to species with high probability. At values SCORE <2.0 isolates considered "hardly identified": species identification was considered controversial at SCORE from 1.6 to 2.0, not correct at SCORE<1.6. For all "hardly identified" isolates, verification control of identification was checked by sequencing the 16S rRNA gene on the 3130 Genetic Analyzer with BigDye™ Terminator v3.1 Cycle Sequencing Kit.

Results: At cultural study 1832 isolates of microorganisms were isolated: 1226 isolates of facultative anaerobes and 606 isolates of strict anaerobes. When evaluating the obtained SCORE values, it was found that in 1.5% of isolates SCORE value was <1.6; in 71.8% - was in the range of 1.6-2.0 and in 26.7% it exceeded 2.1. Eighty four "hardly identified" isolates were selected for sequencing. The correspondence of species identification obtained by both methods was 71%, with a SCORE above 1.8 all isolates were identified correctly.

Conclusions: The use of MALDI-TOF MS by direct application of the colony without extraction with a SCORE above 1.8 can be considered appropriate in routine microbiota research.

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Abstract 8114

Antimicrobial susceptibility of Neisseria gonorrhoeae in Málaga, Spain

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Background: Gonococcal infection is a public health problem as it is the second most common bacterial sexually transmitted infection. The analysis of antibiotic susceptibility data over a period of time allows knowing variations on it and helps in the selection of empirical treatment. Our objective was to analyze the evolution of Neisseria gonorrhoeae (NG) susceptibility to different antimicrobials over the last years in our hospital.

Materials/methods: We studied a total of 393 NG strains, isolated from genital samples processed in our laboratory from January-2012 to October-2019. We considered one strain per patient and year. Each antibiogram was performed by E-test or disk diffusion test, following EUCAST criteria. The tested antibiotics were penicillin, cefotaxime, cefixime, azithromycin, spectinomycin, ciprofloxacin and tetracycline.

Results: 83.7% of the strains were isolated from urethral exudate samples. The average age of our patients was 30 years and 88% were male. Antibiotic susceptibility is shown in the following table:

<table>
<thead>
<tr>
<th>Year</th>
<th>N=393</th>
<th>Penicillin</th>
<th>Cefotaxime</th>
<th>Cefixime</th>
<th>Azithromycin</th>
<th>Spectinomycin</th>
<th>Ciprofloxacin</th>
<th>Tetracycline</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>23</td>
<td>92,6%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>82,6%</td>
<td>82,6%</td>
</tr>
<tr>
<td>2013</td>
<td>59</td>
<td>66,1%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>42,3%</td>
<td>71,1%</td>
</tr>
<tr>
<td>2014</td>
<td>44</td>
<td>20,4%</td>
<td>100%</td>
<td>100%</td>
<td>95%</td>
<td>100%</td>
<td>34%</td>
<td>31,8%</td>
</tr>
<tr>
<td>2015</td>
<td>69</td>
<td>21,7%</td>
<td>100%</td>
<td>100%</td>
<td>94,2%</td>
<td>100%</td>
<td>33,3%</td>
<td>69,5%</td>
</tr>
<tr>
<td>2016</td>
<td>38</td>
<td>68,4%</td>
<td>94,7%</td>
<td>97,3%</td>
<td>94,7%</td>
<td>100%</td>
<td>57,8%</td>
<td>73,6%</td>
</tr>
<tr>
<td>2017</td>
<td>80</td>
<td>11,2%</td>
<td>93,7%</td>
<td>97,5%</td>
<td>78,7%</td>
<td>100%</td>
<td>40%</td>
<td>41,2%</td>
</tr>
<tr>
<td>2018</td>
<td>50</td>
<td>48%</td>
<td>96%</td>
<td>100%</td>
<td>86%</td>
<td>100%</td>
<td>50%</td>
<td>60%</td>
</tr>
<tr>
<td>2019</td>
<td>30</td>
<td>30%</td>
<td>93,3%</td>
<td>96,6%</td>
<td>53,3%</td>
<td>100%</td>
<td>56,6%</td>
<td>50%</td>
</tr>
</tbody>
</table>

Penicillin: we found a decrease in susceptibility in the studied period, which remains relatively low.

The susceptibility of cefotaxime and cefixime showed a minimal decrease, remaining above 90%.

Azithromycin: a decrease in susceptibility is observed in recent years, worrying in 2019, which should be carefully monitored.

Ciprofloxacin: presents a discreet increase in susceptibility since 2015, which should continue to be evaluated.

Tetracycline: an increase in susceptibility is observed in 2015-2016, but it decreases again in subsequent years.

Conclusions: We can recommend cephalosporins as an empirical treatment and use azithromycin cautiously, evaluating the trend over the next few years.

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Abstract 8115

**Supervised machine learning algorithms to predict the patient outcome during febrile neutropenia**  
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1University of Cologne, Faculty of Medicine and University Hospital Cologne, Department I for Internal Medicine, Cologne, Germany, 2German Center for Infection Research (DZIF), partner site Bonn Cologne, Cologne, Germany, 3University of Cologne, Faculty of Medicine and University Hospital Cologne, Institute for Medical Microbiology, Immunology and Hygiene, Cologne, Germany, 4Cologne Excellence Cluster on Cellular Stress Responses in Aging Associated Diseases (CECAD), University Hospital of Cologne, Cologne, Germany, 5Department of Internal Medicine, Hematology and Oncology, Goethe University Frankfurt, Cologne, Germany

**Background:** Prolonged febrile neutropenia despite broad-spectrum empirical antibacterial treatment remains a clinical challenge, as standard empirical treatment has failed and a broad spectrum of differential diagnoses has to be considered. A reliable prediction of patient outcome could indicate that experts need to be consulted and could provide information on the effectiveness of treatment.

**Materials/methods:** We analyzed retrospective data of the Cologne Cohort of Neutropenic Patients (CoCoNut) including highly granular clinical data of cancer patients treated at the university hospital of Cologne between 2008 and 2014. We predicted the patient outcome (28-day survival or death/admission to intensive care unit) after four successive days of febrile neutropenia (neutrophils < 0.5 × 10^9/L and body temperature ≥ 38°C). We implemented four supervised machine learning approaches in order to (i) identify the best prediction algorithm and (ii) better explain the interaction and importance of features.

**Results:** We included 927 episodes of prolonged febrile neutropenia in the analysis of which 61% (562/927) were male with median age of 52 years (interquartile range 42-62). 42% (390/927) had acute myeloid leukemia (AML) and 32% (297/927) lymphoma. 23% (211/927) adverse outcomes were identified. We computed 240 features describing changes and interactions of clinical parameters. After feature selection and model tuning using repeated cross-validation we obtained in the validation dataset (neutropenic episodes in 2014) following area under the operating characteristic curve (AUC), sensitivity/specificity, and number of selected features: random forest; 0.70; 0.41/0.99; 135, Adaptive Boosting; 0.63; 0.27/0.99; 239, neural networks; 0.65; 0.32/0.99; 241, naive Bayes; 0.67; 0.36/0.99; 180. The performance of random forest for specific underlying diseases and age groups was: AML; 0.78; 0.55/1.00, lymphoma; 0.68; 0.36/1.00, age <52; 0.67; 0.33/1.00, age ≥52; 0.72; 0.46/0.98.

**Conclusions:** Our findings in a retrospective setting indicate that supervised machine learning algorithms can be used to fuse medical events for a prediction of the patient outcome. The high specificity shows the potential to use the algorithm in the clinic. Classification performance could vary for specific patient groups.

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Abstract 8122

**Phylogenetic and taxogenomic approaches to elucidate the *Citrobacter* genus**

Teresa Gonçalves Ribeiro¹, Carla Rodrigues², Luisa Maria Vieira Peixe³

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**Background:** *Citrobacter* genus comprises members inhabiting different habitats, including human and animal gut, with some species being involved in human infections and presenting multidrug resistance. Recent phylogenetic analysis based on recN or multilocus sequence analysis (MLSA), and comparative genomics (ANI; Genome-to-Genome Distance Calculator-GGDC) unveiled novel species within this genus (*Citrobacter pasteurii*, *Citrobacter europaeus*, and *Citrobacter portucalensis*). Nevertheless, the polyphyletic structure of *Citrobacter* sp. observed in 16S rRNA gene-based phylogeny motivated a reassessment of *Citrobacter* spp. taxonomic position among other genera of *Enterobacteriaceae* family.

**Materials/methods:** MLSA, recN-based phylogenetic analysis, ANI and GGDC were conducted with type strains of *Citrobacter* spp. and closely related genera (*Salmonella*, *Escherichia*, *Kluyvera* and *Klebsiella*). Furthermore, a core-genome phylogeny from all publicly available genomes of *Citrobacter* spp. and type strains from closely related genera (n=243) was produced using Roary (BLASTP identity cut-off of 50% and presence in more than 90% of the isolates) and a maximum-likelihood tree inferred using FastTree.

**Results:** MLSA- and recN-phylogenetic tree clearly demonstrated that *Citrobacter* genus is not monophyletic, with *Citrobacter* species being grouped into two distinct clusters and one branch. The 2,211 core-genes-based phylogeny was highly consistent with MLSA- and recN-based phylogeny, and revealed that the type strain of *Citrobacter* genus (*Citrobacter freundii*) grouped with eight other species in cluster I, while *Citrobacter amalonaticus*, *Citrobacter farmeri*, *Citrobacter rodentium* and *Citrobacter sedlakii* were within cluster II, and *Citrobacter koseri* formed a distinct branch (Figure 1). Moreover, it is noteworthy that cluster II was more closely related to *Salmonella* spp. than to *Citrobacter* cluster I. ANI values between *Citrobacter* clusters (80.36-81.96%) and between each cluster and *Salmonella enterica* LT2 (80.38-81.30% and 80.67-81.12%, respectively) were similar. GGDC values between *Citrobacter* clusters (23.90-25.50%) and between each cluster and *C. koseri* (26.00-26.90%) were clearly below the criterion for bacterial species (70%) delineation.

**Conclusions:** These data strongly support that species included in cluster I should be assigned to *Citrobacter sensu stricto*, while species from cluster II and *C. koseri* should be reclassified into novel genera.

**Figure 1.** Maximum likelihood phylogenetic tree inferred based on the concatenated nucleotide sequence alignments of 2,211 core genes.

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Prevalence and clonal distribution of azole-resistant Candida parapsilosis isolates causing human bloodstream infections in a tertiary Italian hospital

Cecilia Martini*1, Margherita Cacaci1, Riccardo Torelli1, Elena De Carolis1, Theun De Groot3, Francesca Bugli1, Maurizio Sanguinetti1, Brunella Posteraro1, Jacques F. Meis3

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Background: Candida parapsilosis species complex is a common human opportunistic pathogen that causes invasive fungal infections, particularly bloodstream infections (BSIs) in hospitalized patients. Among three closely related species, C. parapsilosis sensu stricto is responsible for most of infections associated with this species complex. The spread of the fungus from the healthcare environment to susceptible patients and the increasing emergence of fluconazole-resistant isolates in hospital settings complicate the situation. Here we report on the molecular characterization of azole-resistant C. parapsilosis sensu stricto (hereafter designated as C. parapsilosis) isolates recovered from BSIs in order to define their clonal prevalence and distribution over a 5-year period in a large Italian university hospital.

Materials/methods: C. parapsilosis isolates were identified at the species level using MALDI-TOF MS analysis, and were tested for antifungal susceptibility against fluconazole and voriconazole using the broth-microdilution based CLSI reference method. The azole target ERG11 gene from each isolate was sequenced by PCR, whereas multilocus microsatellite typing was performed using a previously described panel of six short tandem repeat (STR) markers.

Results: During the study period (May 2014–September 2019), we isolated C. parapsilosis from 249 cases of BSIs, including 80 central venous catheter-associated BSIs. Forty-nine (19.6%) of 249 C. parapsilosis isolates were resistant to fluconazole (MIC, ≥4 mg/L; range, 16–128 mg/L) and non-susceptible to voriconazole (MIC, ≥0.25 mg/L; range, 0.25–2 mg/L) according to CLSI clinical breakpoints. Of these isolates, 40 harboured the Y132F substitution and nine of them the Y132F substitution in combination with the R398I substitution. STR typing of 49 azole non-susceptible and 10 susceptible isolates showed the presence of two major genotypes, which only included the 49 fluconazole-resistant isolates. This was consistent with the idea that Y132F mutation may relate to the persistence of isolates in the hospital, whereas R398I mutation may arise to compensate for azole resistance-associated mutations.

Conclusions: Fluconazole-resistant clonal isolates harbouring the Y132F mutation were circulating in our hospital. The presence of two clusters of isolates with identical genotypes that infected different patients seems indicate a patient-to-patient transmission or a direct infection of patients possibly via a common source.

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Abstract 8135

**Proinflammatory biomarkers are not useful as sepsis outcome predictors in patients older than 75**

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**Background:** Individual therapeutic approach to sepsis patients has been proposed recently based on the results of most studies. In the past, different biomarkers and their prognostic values for the outcome of sepsis have been studied, mostly on the population as a whole. A very few researches focus on immune response to sepsis taking into the consideration the patients age. Since the immune response is highly dependent on age, we have hypothesized that predictive value of different biomarkers could differ between age groups, and decided to examine predictive value of baseline measured C reactive protein, fibrinogen, procalcitonin serum levels as well as SOFA score on the outcome of septic patients, depending on their age.

**Materials/methods:** 514 consecutive septic patients were included. Patients were divided into two groups: younger and older than 75. Inflammatory biomarkers [C reactive protein, fibrinogen, procalcitonin] and SOFA score were compared within each group with the outcome through multivariate binary regression analysis.

**Results:** In the first group [18-75 years old], multivariate binary regression analysis revealed higher values of CRP serum levels, SOFA score, and lower PCT and fibrinogen serum levels as an independent predictor of lethal outcome (Table 1). In the second group [older than 75] binary logistic regression revealed only SOFA score as independent predictor of sepsis outcome \(p=0.025, \text{OR} 1.233 \ (95\%CI 1.027-1.481)\), while none of the proinflammatory biomarkers were noted as predictors of outcome.

**Conclusions:** The difference in the reactivity of immune system among different age groups enables the use of inflammatory biomarkers as predictors with regard to sepsis outcome in patients younger than 75 years of age.

<table>
<thead>
<tr>
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<th>MED (IQR)/(SD)</th>
<th>p</th>
<th>OR</th>
<th>95%CI</th>
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<tr>
<td><strong>CRP [mg/l]</strong></td>
<td></td>
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<tr>
<td>Survived</td>
<td>199.02 (±101.71)</td>
<td>0.010</td>
<td>1.004</td>
<td>1.001-1.008</td>
</tr>
<tr>
<td>Deceased</td>
<td>232.50 (±132.82)</td>
<td></td>
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<td></td>
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<tr>
<td><strong>PCT [ng/l]</strong></td>
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<td></td>
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<tr>
<td>Survived</td>
<td>14.45 [4.14-55.16]</td>
<td>0.005</td>
<td>0.989</td>
<td>0.981-0.987</td>
</tr>
<tr>
<td>Deceased</td>
<td>9.02 [2.03-30.89]</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Fibrinogen [g/l]</strong></td>
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<tr>
<td>Survived</td>
<td>6.00 [4.84-7.28]</td>
<td>&lt;0.001</td>
<td>0.692</td>
<td>0.577-0.829</td>
</tr>
<tr>
<td>Deceased</td>
<td>4.54 [2.99-5.91]</td>
<td></td>
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<td></td>
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<tr>
<td><strong>SOFA score</strong></td>
<td></td>
<td></td>
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<tr>
<td>Survived</td>
<td>3 [2-5]</td>
<td>&lt;0.001</td>
<td>1.286</td>
<td>1.132-1.462</td>
</tr>
<tr>
<td>Deceased</td>
<td>5 [3-8]</td>
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</table>

Table 1. Proinflammatory biomarkers and SOFA score in the group of patients 18 to 75 years of age

**Presenter email address:** miticsoso@gmail.com
Colistin heteroresistance in carbapenemase-producing *Acinetobacter baumannii*

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**Background:** Colistin is often the last therapeutic option against carbapenemase-producing *Acinetobacter baumannii*. We investigated the mechanisms of resistance in eight-colistin heteroresistant carbapenemase-producing *A. baumannii* strains isolated in 2010 from fatal bloodstream infections in elderly patients acquired during therapy.

**Materials/methods:** Heteroresistance to colistin was studied using E-test, broth microdilution and Levine-agar assay; ER-IC-PCR and MLST for genotyping; and whole genome sequencing. Biofilm formation and viability was determined by CFU’s determination and FilmTracer Live/Dead Biofilm Viability assay, respectively. Efflux activity was studied by MIC determination and time-kill assays for colistin in the presence of efflux inhibitors, real-time ethidium bromide efflux activity evaluation and analysis of mRNA transcriptional levels of selected efflux pump genes in response to colistin.

**Results:** All strains displayed heteroresistance to colistin demonstrated by E-test. Growth on Levine-agar supplemented with colistin revealed strain-variants exhibiting different colony morphologies, growth rates and susceptibilities to colistin. The colistin sub-population showed increased capacity to form biofilms. ERIC patterns showed the presence of three clusters comprising strains belonging to ST218 and ST350. All strains harbored mutations in the genes associated with colistin resistance: *lpxA*, *lpxC*, *lpxD*, *pmrA* or *pmrB*. Checkerboard assays showed MIC reductions ranging from 256- to 8-fold of colistin in the presence of the efflux inhibitor, thioridazine [TZ]. Real-time efflux assays demonstrated increased efflux activity in these strains, which could be inhibited by TZ. The efflux pump genes *adeB*, *adeJ*, *adeG*, *craA*, *amvA*, *abeS* and *abeM* were found overexpressed in these strains in response to colistin exposure.

**Conclusions:** This study provides a clear evidence of the impact of colistin-heteroresistant strains on patient outcome demonstrating the high versatility by which this bacterium manages to survive treatment. Under selective pressure, persistent colistin-resistant variants rapidly overtake the susceptible population and give rise to variants with high-level resistance. The use of efflux inhibitors as adjuvants of therapy may prevent the emergence of colistin resistant subpopulations during therapy. Understanding the mechanisms behind the development of colistin resistance will enable us to develop more effective therapies and give additional information on how to implement appropriate approaches for its detection.

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Abstract 8138

Real-world experience with prolonged courses of tedizolid at a large academic medical centre
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Background: Linezolid and tedizolid are important antibiotics in the management of infections due to resistant gram-positive organisms, including vancomycin-resistant Enterococcus (VRE). Tedizolid use has been purported to have a lower incidence of drug-induced thrombocytopenia compared to linezolid, although clinical experience, especially with administration for >6 days, is lacking. The primary objective of this study was to describe the real-world use of tedizolid, including tolerability and associated outcomes.

Materials/methods: We conducted a retrospective, observational study of patients receiving tedizolid for ≥ 10 days between September 2014 and October 2019. In patients without baseline thrombocytopenia, changes in platelets were evaluated. In patients with an intolerance to linezolid, subsequent tedizolid tolerability was evaluated. Clinical failure, microbiological failure, and 30-day all-cause mortality was also assessed.

Results: A total of 43 patients were included. The median duration of therapy was 20 days (IQR 15-37). 53% [23/43] had received linezolid; 13/23 had therapy discontinued due to an adverse drug event (ADE). The most common reason for linezolid discontinuation was thrombocytopenia [9/13]. Of these 9 patients, all but one went on to tolerate tedizolid for a median duration of 20 days [IQR 18-46]. In the overall cohort, only 3 [70%] patients had therapy interrupted for an ADE attributed to tedizolid. In the 17 patients without pre-existing thrombocytopenia, the average change in platelets was -4%, -11%, -4%, and -4% at days 10, 14, 21, and 30, respectively. Clinical failure was reported in 26% of patients [11/43] and 30-day all-cause mortality was 30% [13/43]. In patients with clinical failure,10/11 had documented VRE bacteremia with 6/10 experiencing microbiological failure (defined as a positive blood culture at ≥ 5 days from the index culture while receiving tedizolid).

Conclusions: Tedizolid administration for ≥ 10 days was well tolerated in this cohort of patients, including those with linezolid-induced thrombocytopenia. The high rate of clinical and microbiological failure in patients with documented VRE bacteremia warrants further investigation.

Baseline Demographics

<table>
<thead>
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<th>Tedizolid (n=43)</th>
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<tbody>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Male, n (%)</td>
</tr>
<tr>
<td>ICU admission, n (%)</td>
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<tr>
<td>Immunosuppressed, n (%)</td>
</tr>
<tr>
<td>Baseline platelet count, n</td>
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<tr>
<td>Platelet value &lt; 50 x 10⁹/L at baseline, n (%)</td>
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<table>
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<tr>
<th>Infectious Source</th>
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<td>Intraabdominal</td>
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<tr>
<td>Pulmonary</td>
<td>10</td>
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<tr>
<td>Cardiac Device</td>
<td>5</td>
</tr>
<tr>
<td>Skin and Soft Tissue</td>
<td>5</td>
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<tr>
<td>Primary Bacteremia</td>
<td>5</td>
</tr>
<tr>
<td>Bone/Joint</td>
<td>3</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
</tr>
<tr>
<td>Secondary Bacteremia</td>
<td>9</td>
</tr>
</tbody>
</table>

Maximum likelihood phylogeny showing the clustering of the nine outbreak cases and three matching food isolates against a background of 60 representative CC8 isolates encompassing the strain diversity collected through routine surveillance [2013-2019].

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**Construction and investigation of lncRNA-associated ceRNA network in chronic hepatitis B infection**

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2West China Hospital of Sichuan University, Chengdu, China

**Background:** Researches on the functional role and underlying mechanism of long non coding RNA(lncRNA)-associated competing endogenous RNA (ceRNA) network in hepatitis B virus (HBV) persistence are facing challenges and it is worthwhile devoting much effort to them. This study aims to explore novel RNA biomarkers or therapeutic targets, and the molecular mechanism in HBV persistence as well as searching via analyzing ceRNA network in chronic hepatitis B (CHB).

**Materials/methods:** This study recruited three patients with CHB and three patients with spontaneous clearance of HBV (group 1), and twenty spontaneous clearance of HBV and nineteen CHB (group 2) in West China Hospital. Gene expression profiles of patients in group 1 were analyzed using microarray analysis to identify differently expressed (DE) lncRNAs, mRNAs and miRNAs. miRNA-target interactions and lncRNA–mRNA co-expression pairs were predicted via bioinformatics analysis. A lncRNA-associated ceRNA network of HBV persistence was constructed based on systematical investigation through miRNA-target predictions and co-expression relationships. Finally, Reverse Transcription-Polymerase Chain Reaction (rt-PCR) was performed to validate the expression levels of key RNAs (n332762, AIFM2, EPSTI, and LY6E) in group 2.

**Results:** A total of 368 lncRNAs, 256 mRNAs and 48 miRNAs were detected to be differentially expressed in patients with CHB compared with patients with spontaneous clearance of HBV (fold change > 1.2 and P < 0.05). After bioinformatics analyses and systematical investigation, a ceRNA network in CHB constructed based on co-expressed relationships above, which included 12 lncRNAs, 7 miRNAs, and 7 mRNAs (Figure 1). Expression levels of n332762 and AIFM2 were significantly downregulated in CHB compared with spontaneous clearance of HBV group while LY6E showed the higher expression level in CHB than the latter. The expression level of EPSTI have no significant difference between them.

**Conclusions:** These results suggested that the ceRNA network in CHB included 12 lncRNAs, 7 miRNAs, and 7 mRNAs might involve in HBV persistence. The downregulation of AIFM2 is associated with malignant prognosis of HBV infection while upregulation of LY6E enhance the HBV infectivity. These findings might provide new insights into the pathogenesis of CHB and lay a foundation for further functional research.

**Figure 1:** a ceRNA network in CHB

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Abstract 8142

Comparative in vitro activity of ceftolozane/tazobactam, ceftazidime/avibactam, meropenem/vaborbactam, and imipenem/relebactam against susceptible and resistant Pseudomonas aeruginosa

Jason Pogue*, Keith S. Kaye1, Vincent Marshall1, Aaron Smith1, Carol Young1, Paul Lephart1, John P. Mills1, Owen Albin1, Twisha S. Patel1

1University Of Michigan Health System, Ann Arbor, United States

Background: β-lactam resistance in P. aeruginosa (PSA) is common and previous analyses have demonstrated high rates of cross-resistance between traditional anti-pseudomonal β-lactams, stressing the need for novel therapies. Four β-lactam/β-lactamase inhibitor combinations have recently been approved, but comparative in vitro susceptibility data against resistant PSA are lacking. The purpose of this analysis was to compare the in vitro activity of ceftolozane/tazobactam, ceftazidime/avibactam, meropenem/vaborbactam, and imipenem/relebactam against PSA at an institution that routinely tests all isolates to each agent.

Materials/methods: All non-duplicate PSA identified from patient samples at Michigan Medicine from 6/1/19 through 10/30/19 were included. Minimum inhibitory concentrations for antimicrobials were determined using TREK broth microdilution panels. CLSI breakpoints were used to determine susceptibility rates for all agents, except meropenem/vaborbactam where USCAST breakpoints were applied (≤8/8 mg/L).

Results: The table shows comparative susceptibility rates. All four novel therapies were more active than traditional β-lactams and retained high degrees of activity against resistant isolates. Importantly, even in the setting of resistance to one of the novel agents, the other agents often retained in vitro activity.

Conclusions: All four novel agents have improved in vitro activity compared to traditional β-lactams against resistant PSA at Michigan Medicine. Ceftolozane/tazobactam performed worse and meropenem/vaborbactam performed better in our isolates compared to published data. These results highlight the importance of understanding local susceptibility data and routinely testing all agents to inform both empiric and definitive therapy decisions.

<table>
<thead>
<tr>
<th></th>
<th>FEP</th>
<th>CAZ</th>
<th>IMI</th>
<th>MEM</th>
<th>TZP</th>
<th>CAZ- AVI</th>
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FEP-cefepime; CAZ-ceftazidime; IMI-imipenem; MEM-meropenem; TZP-piperacillin/tazobactam; CAZAVI-ceftazidime-avibactam; TOLTZAZ-ceftolozane/tazobactam; IMIREL-imipenem/relebactam; MEMVAB-meropenem/vaborbactam

β-lactam-R-resistance to all traditional β-lactams

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Abstract 8143

Role of glucose transporters in the intracellular proliferation of Toxoplasma gondii
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Background: The protozoan Toxoplasma gondii is an obligate intracellular parasite which produces the human disease toxoplasmosis, which can progress to death, mainly in immunocompromised patients. This parasite has the ability to infect animals and humans, through the invasion of all nucleated cells of the organism by tachyzoites, the rapid stage of infection. The presence and uptake of glucose could be essential for its optimal growth, survival and dissemination. The uptake is done by activation of GLUT 4 glucose transporters, which migrate from the nucleus to the host cell membrane.

Materials/methods: HFF cell culture were infected with T. gondii tachyzoites extracted from peritoneal lavage of a mousse BALB/c model. Some conditions included the preincubation with WZB 117, a GLUT4 blocker, which was added in different concentrations, 5mM and 10mM. T. gondii tachyzoites and GLUT4 were stained by indirect immunofluorescence. Subsequently, the staining was observed under phase contrast microscope, quantifying the number of parasites per parasitic vacuole. The amount of glucose, in and out of the cell was determined using an enzymatic kit.

Results: The proliferation of Toxoplasma gondii tachyzoites decreases by inhibiting GLUT4 glucose transporters by WZB 117. Apparently, the decrease in intracellular glucose is associated with the inhibition of parasitic division.

Conclusions: The presence of glucose at the intracellular level regulates the cell division of Toxoplasma gondii, which is mediated by GLUT 4 transporters.

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Abstract 8144

**Invasive aspergillosis caused by Aspergillus non-fumigatus in children and adults after haematopoietic stem cell transplantation (HSCT) & chemotherapy**

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**Background:** Invasive aspergillosis (IA) is a major cause of morbidity in hematological patients. Aspergillus caused by non-fumigatus species is poorly studied.

**Materials/methods:** We design the retrospective study in order to investigate the epidemiology of IA caused by *Aspergillus* non-fumigatus as a single agent in large cohort of patients after HSCT and chemotherapy from 2013 to 2018 in CIC725. According to EORTC/MSG 2008 criteria 1 proven and 29 probable cases were diagnosed in patients with hematological malignances and non-malignant hematological diseases. The median age was 26 (3-60) y.o., males – 53%. The median follow up time was 10 months; for survivors – 17,5 months.

**Results:** The most common underlying diseases in patients with *A. non-fumigatus* IA were acute lymphoblastic leukemia (37%) and acute myeloid leukemia (30%). *A. non-fumigatus* IA was more often diagnosed in allo-HSCT recipients (90%) then after chemotherapy (10%). Most of the patients at the moment of IA diagnosed received antifungal prophylaxis with fluconazole (83%) or echinocandins (6,7%). Breakthrough IA (prophylaxis with voriconazole – 2, posaconazole – 1) was diagnosed in 10% of patients. Etiology agents were *A. niger* – 60%, *A. flavus* – 34%, *A. glaucus* – 3%, and *A. terreus* – 3%. The main sites of infection were lungs (80%), paranasal sinuses (10%), or combination lungs and paranasal sinuses (10%). *A. non-fumigatus* IA developed in combination with other infections in 20% (n=6): *Klebsiella pneumonia* – 33,3%, *Pseudomonas aeruginosa* – 33,3%, *Kocuria kristinae* – 16,7%, *Trichoderma viride* – 16,7%. The median time of onset of *A. non-fumigatus* IA after allo-HSCT was 155 (19-922) days. Antifungal therapy was used in all patients: voriconazole – 73,3%, lipid amphotericin B – 6,7%, posaconazole – 6,7%, combination therapy – 13,3%. *A. non-fumigatus* IA developed on the background of acute graft-versus-host diseases (GVHD) grade 2-3 + glucocorticoids therapy (25%) and CMV reactivation (19%). Overall survival (OS) at 12 weeks from the IA diagnosis was 83,3%. Death could be attributed to IA was registered in one case.

**Conclusions:** *Aspergillus* non-fumigatus invasive aspergillosis affected patients predominantly with acute leukemia (67%) and allo-HSCT recipients (90%). *Aspergillus niger* was the main etiology agent. *Aspergillus* non-fumigatus IA developed on the background of CMV reactivation and acute GVHD. OS at 12 weeks from the IA diagnosis was 83,3%.

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Evaluation of efflux pump inhibitor combination with fluoroquinolones and aminoglycosides in resistant clinical isolates of Mycobacterium tuberculosis

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Abstract third-party references: This study was supported by the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) 2018/00163-0, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ grant 162676/2013-1)

Background: Since antibiotic resistance is a factor that negatively influences the effective treatment of tuberculosis, treatment alternatives have been sought to overcome the mechanisms of bacterial resistance. Efflux pumps (EP) are membrane proteins capable of expelling substrates and antibiotics (ATB) from the bacterial interior. Increased activity or expression of these EP may result in resistance, which may be the main mechanism or a parallel mechanism to the presence of genetic mutations. For this study were selected from a library of Brazilian clinical isolates, those resistant to fluoroquinolones or aminoglycosides and that did not show mutations in rrs and gyrA genes to evaluate how much EP may be responsible for such resistance, combining ATB with efflux pump inhibitors (EPI) potentials: verapamil, reserpine and carbonyl cyanide m-chlorophenyl hydrazine (CCCP).

Materials/methods: Two phenotypic methods were used, the first one combining EPI in non-toxic concentrations with ATB ofloxacin, streptomycin and amikacin in an adaptation of Resazurin drugs combination microtiter assay (REDCA) or Checkerboard method and the second method was the evaluation of Bromide accumulation. Ethidium (EtBr) and the clinical isolate was previously exposed to subinhibitory ATB concentrations for 24 or 48h and also removing this exposure for the same period.

Results: As a result, it was observed that the presence of EPI in some cases reversed ATB susceptibility in the REDCA assay. Regarding the EtBr accumulation assay, it was observed that in the presence of EPI, the accumulation of EtBr within M. tuberculosis was differently changed in the presence of pretreatment and for each EPI present, showing that there is no unique profile of EPI. Verapamil stands out as a potential inhibitor in the ABC family responsible for mainly aminoglycoside efflux and CCCP for the MSF family most related to fluoroquinolone efflux.

Conclusions: So, it can be concluded that the combination of EPI with ATB is a therapeutic possibility and perhaps does not exert as much selective pressure as the use of other antibiotic combinations.

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Contrast-enhanced ultrasound for the detection of abdominal complications in infective endocarditis

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Background: Embolic events are associated with increased morbidity and mortality in patients with infective endocarditis (IE). Contrast enhanced ultrasound (CEUS) is a highly sensitive imaging modality, which is safe, fast, cheap and omits the need for ionizing radiation or nephrotoxic contrast agents. The goal of this study was to assess the diagnostic potential of CEUS to detect abdominal complications of IE.

Materials/methods: This is a single-center cohort study. Abdominal CEUS was performed in 40 patients out of 235 prospectively registered patients with definite or possible IE between July 2013 and December 2016. Conventional B-mode ultrasound preceded CEUS in every patient. The definition of IE related lesions on CEUS included embolic infarction, metastatic abscesses and vascular aneurysms.

Results: CEUS was able to detect abdominal embolic events or metastatic infection in 12 patients (30%). Most commonly seen were splenic infarction (n=10), followed by renal infarction (n=2), liver abscess (n=1) and mycotic aneurysm (n=1). Six out of 14 lesions were only detected by CEUS and not by conventional ultrasound. Abdominal complications revealed by CEUS were associated with a detectable valve vegetation (P=0.04) and larger vegetation size (P=0.01). In three patients a non-IE related abdominal lesion (2 hepatocellular carcinomas, 1 psoas hematoma) was detected.

Conclusions: CEUS is a feasible diagnostic method in detection of abdominal complications of IE and enhances the detection rate of conventional ultrasound. Further prospective studies are needed to evaluate its diagnostic value in patients with IE, especially in comparison to other imaging modalities.

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Prevalence of non-B HIV-1 subtypes in north Italy and analysis of transmission clusters based on sequence data analysis

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Background: HIV-1 diversity is increasing in European countries due to immigration flows as well as travels and human mobility leading to the circulation of both new viral subtypes and new recombinant forms with important implications for public health.

Materials/methods: We analyzed 710 HIV-1 sequences comprising protease and reverse transcriptase (PR/RT) coding regions, sampled from 2011 to 2017 from naïve patients in Spedali Civili’s Hospital, Brescia, Italy. Subtyping was performed using a combination of different tools; the phylogenetic analysis with a structured coalescence model and Makarov Chain Monte Carlo was used on the datasets to determine clusters and evolution.

Results: We detected 304 (43%) patients infected with HIV-1 non-B variants, of which only 293 sequences were available, with 4 pure subtypes and 5 recombinant forms; subtype F1 (17%) and CRF02_AG (51.1%) were most common. Twenty-five transmission clusters were identified, three of which included >10 patients; belonging to subtype CRF02_AG and subtype F. Most cases of alleged transmission were between heterosexual couples. Probably due to strong migratory flows, we have identified individual subtypes with particular patterns of recombination or, as in the case of the subtype G (18/293, 6.1%), to a complete lack of relationship between the sequenced strains revealing that they are all singletons.

Conclusions: The methods of phylogenetic analysis are advancing rapidly and the timing of the nodes as well as directionality of transmission being ever more accurate, provide consistent data in phylogenetic inference. This knowledge is important to monitor the efficacy of public health interventions aimed at controlling the HIV epidemic.

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Abstract 8154

**Retrospective analysis of spinal infections over a 10-year period (2008-2018) in tertiary care hospital**

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**Background:** Pyogenic spinal infections (PSI) are an all-encompassing spectrum of conditions with debilitating morbidity and mortality risk. Prognosis depends on early multidisciplinary approach to diagnosis and initiation of appropriate anti-microbial therapy.

**Materials/methods:** This a retrospective descriptive study aiming to review management of patients admitted in our hospital with PSI over the last 10-year period. Demographic characteristics, clinical, microbiological, and radiological data and outcomes were collected from patients’ hospital electronic records between 01/07/2008 to 30/06/2018.

**Results:** 183 patients were included in our study, median age 64 [59.6% males]. Most frequent site of PSI was lumbar spine (40%), followed by thoracic (20%), whilst 34% presented with disease in multiple spinal levels. 44% had discitis, 4% osteomyelitis, 17% epidural abscesses, and 34% combination of all three. PSI due to Gram-positive bacteria was found in 53% of cases and *Staphylococcus aureus* (SA) was the most frequent pathogen isolated in all age groups (44%). Gram-negative pathogens were isolated in 9% of PSI, with *E. Coli* accounting for 5%. SA was isolated in 21% of blood cultures and a significant correlation between SA presence in blood culture and spinal tissue was identified (OR16.06, CI: 3.2 to 78.92, p<0.05).

70% of our patients had antibiotic treatment alone (ATG) and 30% received concomitant surgical treatment (STG). SA was associated with severe disease and need for STG (p<0.05). STG was more associated with neurological deficits than ATG [OR 4.04, CI 1.936 to 8.091, p<0.05]. There was no significant difference in median antibiotic treatment duration between ATG (56 days) vs STG (70 days). In-patient mortality was 6% and there was no difference in mortality between ATG vs STG group. 90-day readmission rate was 12% and was higher in ATG (15.5%) vs STG (4%) [OR 4.77, CI 1.151-21.19, p<0.05].

**Conclusions:** There was no significance in admission length, duration of antibiotic therapy and mortality rates between surgically- and medically-managed patients with PSI. SA was the most prevalent pathogen isolated (44%) and SA isolation from blood cultures was predictive for SA-related spinal infection. SA was associated with more severe disease, abscess formation and need for surgical management.

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The impact of candidaemia management on mortality: a 4-year retrospective study from a tertiary care hospital

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Background: EQUAL Candida Score is a tool that aggregates factors regarding diagnosis, treatment and follow-up of candidaemia that measures adherence to the strongest recommendations of ESCMID and IDSA guidelines. Association between this score and outcome is still unclear. We aimed to review its impact on patients’ mortality.

Materials/methods: Retrospective study of candidaemia during a 4-year period in a tertiary hospital. Candidaemia was defined by at least one blood culture (BC) positive for Candida species. Data were collected from individual medical records. Two groups (fatality and non-fatality) were compared regarding patients’ characteristics and infection-related variables present within 60 days of first positive BC. The parameters daily follow-up BC collection until negative, echocardiography, ophthalmoscopy, antifungal treatment, initial treatment with echinocandin, step-down to fluconazole and 14 days treatment after first negative follow-up BC were individually included in a multiple logistic regression analysis adjusted for the variables differently distributed between groups.

Results: Two hundred and four episodes of candidaemia were reported (mean age 65 ± 23 years, mortality rate 46.6%). Variables associated with increased mortality were older age (p-value 0.004), hospitalization in intermediate or intensive care unit at the time of BC collection (p-value < 0.001), previous total parenteral nutrition (p-value 0.028), mechanical (invasive and non-invasive) ventilation (p-value < 0.001), sepsis due to Candida spp. (p-value < 0.001) and gastrointestinal perforation (p-value 0.036). Mean EQUAL Candida Score was 9 ± 3 points in both fatality and non-fatality groups (p-value 0.484). After adjusting for the possible confounding effect of the aforementioned 6 factors, using multiple logistic regression analysis, only treatment for 1-4 days after first negative follow-up BC had predictive value for mortality decrease (OR 0.331, CI 0.127-0.862).

Conclusions: The only confounder-adjusted parameter with positive impact on mortality was antifungal treatment for 14 days after negative follow-up BC. However, EQUAL Candida Score was low in both groups. Optimization of adherence to international guidelines is mandatory in order to re-assess the impact of quality candidaemia management practices on patients’ survival.

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Use of whole genome sequencing for rapid detection of a national nosocomial outbreak of Listeria monocytogenes associated with contaminated prepacked sandwiches in England, 2019

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Abstract third-party references: Public Health England

Background: Prepacked sandwiches are commonly catered in hospitals in England. However, sandwiches are complex food items with multiple ingredients and serve as a potential vehicle for L. monocytogenes, a pathogen that can multiply and persist, particularly under suboptimal storage conditions. In April 2019, a national outbreak of listeriosis associated with the consumption of prepacked sandwiches served in hospitals was identified in England.

Materials/methods: The Public Health England (PHE) undertakes national surveillance of listeria, clinical data are collected from patients using a standard questionnaire, and food exposure data (30 days prior to onset of symptoms) are collected by direct interview. Isolates from cases and foods are voluntarily referred to the PHE Reference Laboratory for molecular typing. The isolates undergo whole genome sequencing (WGS) using Illumina, FASTQ files generated, the identification is confirmed using Kmer, MLST and clonal complex (CC) is derived (Pasteur) and SNP clustering tool is used to define the phylogeny and relatedness of strains.

Results: Between April- June 2019, nine confirmed cases of listeriosis associated with the outbreak were identified in England using WGS. The median age of cases was 75 years, six were female and all had received care at hospitals supplied by sandwich Supplier X prior to onset. All cases had underlying risk factors for listeriosis, seven have since died. The outbreak strain was L. monocytogenes serotype 1/2a, CC8, isolates from all cases and cooked meat sampled from Supplier X and Producer Y were phylogenetically linked and fell within a 5 SNP cluster (Figure 1). It was a unique strain and there are no isolates matching at a threshold of less than 25 SNPs in the PHE database.

Conclusions: This was one of the largest nosocomial outbreaks of listeriosis in the UK. WGS provided the highest level of strain discrimination, supported early detection and linked food isolates. This is especially important for listeria, which has a long incubation period and withdrawal of implicated food is an important control measure. The outbreak highlighted the risk of prepacked sandwich supply to vulnerable patients in healthcare settings.

Figure 1: Phylogenetic tree including confirmed cases and non-clinical isolates of L. monocytogenes outbreak strain
Impact of porin deficiency and expression levels of environmental CRH-1 and CRP-1 class A β-lactamases on carbapenem and ceftazidime resistance

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Background: CRP-1 and CRH-1 are class A β-lactamases (BLA) isolated from two environmental species, Chromobacterium piscinae and Chromobacterium haemolyticum, respectively. These enzymes have a high amino acid identity with KPC-2 (76% for CRP-1 and 69% for CRH-1) and were found to confer low-level resistance to carbapenems and oxyimino-cephalosporins in recombinant Escherichia coli clones. Here we assessed the impact of BLA expression on carbapenem and ceftazidime resistance levels in porin-deficient strains.

Materials/methods: CRH-1- and CRP-1-encoding genes were cloned in pMBLe vector, and transformed in E. coli TOP10, E. coli K12, and isogenic Omp-deficient strains. Since the pMBLe vector allows regulating the levels of protein expression by IPTG, MICs of carbapenems and ceftazidime were determined in recombinant E. coli TOP10 clones with increasing concentrations of this inductor. BLA expression was qualitatively measured by MALDI-TOF. For analyzing the porin-deficient clones, MICs were obtained with 50 µM IPTG, according to CLSI’s guidelines.

Results: MIC values of all β-lactams tested were higher in recombinant clones expressing CRP-1 that in those expressing CRH-1. E. coli TOP10 clones harboring CRP-1 and CRH-1 showed resistance towards imipenem and meropenem at all IPTG concentrations tested (50, 100 and 250 µM). MALDI-TOF assays showed that BLA expression in E. coli TOP10 clones was higher for CRP-1, compared to CRH-1. It also exhibited differences in CRP-1 and CRH-1 expression according to IPTG concentration, but such differences did not correlate with the MICs values. Absence of OmpF expression in CRP-1-producing clones yielded an increase in the MICs of meropenem (4 to 32 µg/ml) and ceftazidime (2 to 16 µg/ml). No changes were observed in the resistance phenotype of porin-deficient strains harboring CRH-1, probably due to lower protein expression.

Conclusions: Porin deficiency results in high-level carbapenem resistance in E. coli strains expressing CRP-1, indicating that some class A β-lactamases isolated from environmental bacteria can be expressed in E. coli and confer carbapenem resistance in combination with other resistance mechanisms like porin deficiency. This result supports the hypothesis that KPC-2 and other carbapenemases occurring in clinical pathogens could have evolved from environmental bacteria.

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Abstracts 2020

Abstract 8160

The rise and fall of a resistome: travel returners shed light on the dynamics of ESBL-producing Escherichia coli
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Abstract third-party references: Personalised Health Basel (PHB) Infectious Diseases Cluster

Background: Although ESBL E. coli are among the most studied microorganisms, a thorough understanding of their colonization and transmission dynamics in colonized people remains elusive. Travel returners from high-endemic countries pose a potential source for multi-drug resistance, but may help to understand ESBL-gene and -plasmid dynamics within colonized persons. We aimed to explore the AMR gene population (resistome) and plasmid population (plasmidome) of healthy travel returners being colonized with ESBL-E. coli strains over 5 years.

Materials/methods: We performed rectal swabs of 45 travel returners from South-East Asia and India prior to (H), directly after the travel (R0), and 3, 6, 12, 24 months after return, and for few participants, a follow-up 5 years (R5) later. A total of 82 ESBL E. coli strains were isolated on ChromID ESBL plates (Biomerieux). Whole genome sequencing (WGS) was performed via short-read sequencing (NextSeq500, Illumina), and R0 genomes additionally with long-read sequencing (Nanopore). Genome assemblies were screened for antimicrobial resistance (AMR) genes and plasmidic sequences with abricate, annotation was assigned using respectively the NCBI and PlasmidFinder database.

Results: Preliminary results indicate an immediate increase of AMR gene diversity after travel, and its progressive decrease over following months, correlating with loss of plasmid marker diversity. The resistome shows prominent patient specificity, which explained more than 50% of the resistome variance according to PERMANOVA (p-value=0.045, 1000 permutations). Large part of this patient specificity is linked to blaTEM genes fluctuations according to likelihood ratio test on fitted generalized linear models (p-value<0.05, 500 permutations). Interestingly, pairwise Wilcoxon-Mann-Whitney test showed a significant decreased detection of blaTEM.40 genes after 12 months, mirrored by the increased detection of blaCTX-M, seemingly in gene variant 27 and 55 (p-value<0.05).

Conclusions: Our results reveal a particular aspect of ESBL E. coli resistome dynamics in ESBL colonized otherwise healthy travel returners. Though the shift in resistome diversity may be somewhat expected, our results underpin the hypothesis of a pivotal role of blaTEM genes, which dynamically switches to blaCTX-M genes over time. This suggests a displacement of genetic elements or a succession of strains over time. Additional studies are needed to assess further the possible dynamics of the displacement itself.

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Abstract 8162

Persistence of antimicrobial resistance genes in treated sewage water intended for reuse

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Abstract third-party references: Supported by Fundação de Amparo à Pesquisa do Estado de São Paulo, Process n. 2016/06469-9.

Background: Water scarcity is a worldwide concern, and several countries use treated wastewater for varied purposes. Considering current Brazilian regulations do not define limits for antimicrobial resistance (AMR) determinants in reuse water, this study evaluated the persistence of AMR genes in raw and treated wastewater from sewage treatment plants in São Paulo, Brazil, during a one-year period using culture-independent methods.

Materials/methods: Samples of raw sewage (500mL), secondary effluent (activated sludge stage) (500mL) and reuse water (disinfection stage) (1L) were filtered through 0.45µm membranes and DNA was extracted directly from the membranes. Samples were also cultured to check bacteria viability. PCR was performed for the search of integrons and genes encoding resistance for β-lactams, Fluoroquinolones, Polymyxins, Aminoglycosides and Fosfomycins. Real time absolute quantification was carried out to enumerate total bacterial load (16S rRNA gene), Escherichia coli load (uid gene), and the genes encoding CTX-M and qnrB resistance proteins.

Results: Bacterial growth was observed in raw sewage and secondary effluent, but not on reuse water. PCR revealed that 88% (n=22) of the resistance genes were present in raw sewage, 72% (n=18) in secondary effluent and 40% (n=10) in reuse water. Mean total bacterial count was 9.7 log_{10}/L in raw sewage, 8.8 log_{10}/L in secondary effluent and 6.6 log_{10}/L in reuse water. Relative abundance (RA) of E. coli was 0.32% in raw sewage, 0.04% in treated wastewater and 0.05% in reuse water. For CTX-M, RA was 0.03% in raw sewage, 0.003% in treated wastewater and 0.004% in reuse water. Finally, qnrB concentration was 0.59% in raw sewage, 0.05% in secondary effluent and 0.06% in reuse water.

Conclusions: Results indicate that disinfection methods, although effective in attenuating culturable bacteria, do not remove all bacterial DNA. Resistance genes, which are easily spread due to their frequent location within bacterial mobile genetic elements, persisted throughout the treatment processes and got more concentrated from activated sludge to the disinfection stage. This is a concern due to the potential human exposure to AMR, even because treated wastewater is generally discharged into natural aquatic sources that can eventually contaminate water supplies, contributing to the resistance spread dynamics.

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Abstract 8170

Neglected tropical diseases contribute to the number of years with civil war
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Background: Both neglected tropical diseases (NTDs) and civil wars are strongly influenced by poverty conditions. However, while civil wars regularly lead to rising infectious diseases rates, the impact of NTDs on civil wars is less clear. On a micro level, high NTD prevalence is theorized in this study to influence civil wars via reinforced poverty conditions. On a macro level, high NTD prevalence is assumed to lead to a reduced tax income for the state and thus reduced state capacity.

Materials/methods: The prevalence rates of seven selected NTDs (leishmaniasis, schistosomiasis, trypanosomiasis, malaria, typhoid fever, filariasis and dengue fever) in 109 countries were analysed based on available epidemiological data. To circumvent causal inference problems, historic prevalence rates from the years 1944 and/or 1952-61 were used. The number of years with civil war was calculated for the period 1990-2011 to exclude Cold War dynamics. Proxies for poverty (bottom decile income/capita) and state capacity (road/telephone density and urban population) were included as mediator variables, while population size, percentage of mountainous terrain, previous civil war and a measure of regime authority were included as control variables. Zero-inflated negative binomial regressions were calculated to estimate effects.

Results: In our model, a one unit increase in a country’s NTD prevalence rate increased the number of years with civil war by a factor of 1.75 while holding all other variables in the model constant (0.56, CI 0.23-0.89, P = 0.001). Other significant variables included the percentage of mountainous terrain (0.21, CI 0.05-0.38, P = 0.01) and population size (0.26, CI 0.09-0.42, P = 0.002), which is consistent with civil war literature. Previous civil war events (-1.92, CI -3.23- -0.62, P = 0.004) and limited state capacity (6.53, CI 1.12-11.93, P = 0.018) were significantly associated with increased odds for a country to experience civil war.

Conclusions: We found an association between a high NTD prevalence rate and a country’s increased likelihood to experience civil war in the analyzed time period. Policies directed at affected populations in terms of prevention, diagnostics and treatment of NTDs may contribute to reduce the civil war risk profile of these countries.

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Abstract 8174

Slovenian national outbreak of *Salmonella* Paratyphi B variant Java between 2014 and 2016

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Abstract third-party references: Slovenian Society for Clinical Microbiology and Hospital Infections of the Slovenian Medical Association

**Background:** *Salmonella* Paratyphi B d-tartrate positive (*S. Paratyphi B var. Java, S. Java*) is a less virulent variant of serotype 1,4,12:b:1,2 which has been increasingly reported serovar in recent years with a number of recognized national or multinational outbreaks. In Slovenia the incidence of S. Java rose from 0.53/100,000 inhabitants in 2011 to 1.12/100,000 in 2014, peaking in 2015 with 2.28/100,000; in 2017 the incidence was 0.73/100,000. S. Java became the second most frequently reported serovar in 2015 and the third in 2016. Between 2011 and 2017 147 S. Java isolates were reported in Slovenia, 59.9% (88/147) from Central Slovenian region (CSR), majority of those were detected since 2014, transient increase was present in one additional region. At the time the cases appeared sporadic and no detailed epidemiological investigation was launched. The aim of the study was to analyse whether the S. Java isolates were related and to establish whether an epidemiologically unrecognized outbreak occurred.

**Materials/methods:** One S. Java isolate per month per region isolated between 2013 and 2017 was selected for genotyping. In total 64 S. Java isolates were included in the study (27 isolates from CSR, 37 isolates from 5 other regions including one environmental isolate). Pulsed-field gel electrophoresis (PFGE) was used to determine relatedness among selected isolates according to the Pulse-Net protocol. Whole-cell DNA was digested using XbaI restriction endonuclease. PFGE profiles were analysed using BioNumerics software, dendrogram was constructed using the Dice coefficient with 1.5 optimization and tolerance and unweighted-pair group method using average linkages (UPGMA) clustering.

**Results:** PFGE analysis demonstrated that 90.6% [58/64, 57 patients, 1 environmental isolate] of S. Java belonged to the same pulsotype which was present in 6 Slovenian regions spanning all investigated years. Remaining 6 isolates belonged to 5 different pulsotypes.

**Conclusions:** Our study has demonstrated that the majority of the S. Java isolates belonged to the same pulsotype and even though the cases between 2014 and 2016 clinically appeared to be sporadic, our findings indicate that there may have been a common source. Further investigation into epidemiological connections is needed as well as more detailed genotyping using whole genome sequencing.

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Abstract 8178

**Application of WISCA (Weighted Incidence Syndromic Combination Antibiogram) to guide empiric therapy in oncological paediatric patients with febrile neutropenia**

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**Background:** Febrile neutropenia (FN) is an acute potentially life-threatening oncological complication which should be treated promptly with antibiotics. With the spread of antibiotic resistance, the choice of an empiric therapy is driven by local epidemiology usually described by cumulative pathogens susceptibilities antibiograms. The WISCA attempts to address the unmet need for syndrome-specific local susceptibility data to guide empirical prescribing, providing estimates for different treatment regimens as a weighted average of pathogens susceptibilities. Our aim was to create a WISCA model to inform empirical antibiotic regimens selection for FN in children.

**Materials/methods:** We included all non-duplicate blood cultures from patients aged 0-17 years with FN admitted to the paediatric oncology/hematology wards in Padua from January 2016 to August 2019. WISCA was developed by estimating the sensitivity of 29 antibiotic regimens with a Bayesian probabilities distribution. Moreover, we created a second model with 57 blood cultures excluding potentially contaminant bacteria.

**Results:** We collected 69 blood cultures, 41 Gram- and 28 Gram+ bacteria. Considering most used combinations such as piperacillin-tazobactam + amikacin the median sensibility was 58% (BUI 33-84%) that increased to 70% (BUI 42-85%) in the second model. When adding a glycopeptide to this combination the median sensibility increased dramatically (Figure 1). The highest median sensibility for a beta-lactam + aminoglycoside combination was 66% (BUI 37-86%; meropenem + amikacin) in the first model and 75% (BUI 46-85%) in the second model; the lowest was 42% (BUI 26-75%; ceftriaxone + amikacin) and 50% (BUI 32-76%) respectively. Overall mono-treatments had median sensibility lower than 50%, except meropenem (65%; BUI 35-85) and gentamycin (60%; BUI 33-84%), but in the second model most median sensibilities increased above 50%. WISCA model with median sensibilities and uncertainty intervals is shown in Figure 1.

**Conclusions:** WISCAs represent a valid tool to maximize the clinical utility of microbiological surveillance data supporting appropriate empirical antibiotic treatment selection, while contributing to conservation of broad-spectrum antibiotics.
Figure 1

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Abstract 8179

Diagnostic approach for Aspergillus infection: performance evaluation of a new molecular assay for detection and quantification of Aspergillus spp. in clinical samples

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Background: The conventional diagnosis of Aspergillus infection is based on the presence of risk factors, radiological features, and microbiological results, i.e., histopathology and/or culture of Aspergillus spp. Important advances to the diagnostic field were brought by the introduction of non cultural tests in respiratory samples and blood, including PCR assay. Our study describes the performance of the new quantitative Real-Time PCR assay Aspergillus spp. ELItel MGB® Kit in association with ELItel InGenius instrument for Aspergillus spp detection in bronchoalveolar lavage (BAL) and plasma samples.

Materials/methods: Totally, 88 BAL and 82 plasma, collected in the period may-november 2019, were evaluated. The BAL were collected from patients undergoing bronchoscopy for monitoring or diagnosis of pulmonary infiltrates and blood samples were collected from immunocompromised and/or oncological patients in clinical follow-up. Clinical information was picked up during the routine diagnostic process; patients were classified as having IPA (proven/probable/possible) or no-IPA according to the EORTC/MSG diagnostic criteria. The Aspergillus spp. ELItel MGB® Kit in association with the ELItel InGenius® instrument (Elitech, Torino) is a quantitative real-time PCR with a target within the 28S rDNA. The volume of clinical sample required was 1ml. BAL fungal culture were also performed.

Results: The diagnostic specificity was 100% for BAL and 98% for plasma. The diagnostic sensitivity was 88.6% for BAL and 100% for plasma. The turnaround-time was about 150 minutes. PCR was positive in BAL from 24 patients: 6/24 (8.1%) had pulmonary chronic aspergillosis, 7/24 (9.4%) had invasive pulmonary aspergillosis and 11/24 (14.8%) had colonization.

Conclusions: Aspergillus spp. ELItel MGB® Kit in association with ELItel InGenius instrument is a highly sensitive method for detection and quantification of Aspergillus spp in BAL and plasma samples. This molecular system represents an innovative and fast solution with a simply laboratory workflow and a short report time. It is conceivable that the introduction of this assay in routine diagnosis and its incorporation into the patient care pathways could be a promising tool, in combination with other clinical information and biomarkers, for an improvement in detection and management of Aspergillus infection, and subsequently in the patient outcome.

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Abstract 8181

Molecular testing of the bone marrow in post-mortem samples for the detection of fatal disseminated infections

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Background: Although bone marrow (BM) samples are recommended for the diagnosis of certain infections in the living patient, little is known about the performance of BM in diagnostic autopsies. We aimed to investigate the performance of molecular testing in BM samples for the diagnosis of fatal disseminated infections.

Materials/methods: This study is part of the CaDMIA project; an observational study that included complete diagnostic autopsies (CDAs) for cause of death (CoD) ascertainment. Body fluids and tissue samples were collected for microbiological and histopathological analyses. For the present study, 61 cases from the Fundação de Medicina Tropical Doutor Heitor Vieira Dourado in Manaus, Brazil were included. The median age of the patients was 39 years-old [range 18-81] and 67% were male. Nucleic acid extractions of BM samples were performed using a semi-automated system and were tested for pathogens causing fatal disseminated infections using specific real time PCR assays.

Results: Twenty-seven disseminated infections were detected in the CDA, from which 21 (78%) were HIV infected. The aetiology of the fatal disseminated infections and the results obtained with the analysis of BM samples are shown in Table 1. Molecular testing of BM samples detected 23/27 (85.2%) disseminated infections causing death. Mycobacterium tuberculosis was the pathogen most frequently causing death and was detected in 6 out 7 deaths in BM samples. The pathogens could be also detected in cases dying of fatal localized infections and in cases dying of other etiologies.

Conclusions: Molecular investigation of BM samples detected most pathogens causing fatal disseminated infections. Some microorganisms such as cytomegalovirus can be frequently detected in postmortem BM samples.

Table 1. Aetiological agents identified in the CDA and bone marrow samples

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>CDA</th>
<th>Bone Marrow</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycobacterium tuberculosis</td>
<td>7/6</td>
<td>8</td>
</tr>
<tr>
<td>Histoplasma capsulatum</td>
<td>6/5</td>
<td>NT</td>
</tr>
<tr>
<td>Cryptococcus spp.</td>
<td>3/2</td>
<td>5</td>
</tr>
<tr>
<td>Toxoplasma gondii</td>
<td>3/2</td>
<td>5</td>
</tr>
<tr>
<td>Neisseria meningitidis</td>
<td>3/3</td>
<td>1</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>2/2</td>
<td>26</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>2/2</td>
<td>1</td>
</tr>
<tr>
<td>Leishmania spp.</td>
<td>1/1</td>
<td>NT</td>
</tr>
<tr>
<td>Total</td>
<td>27/23</td>
<td>85.2%</td>
</tr>
</tbody>
</table>

*include localized infections causing death and detections in cases dying of other etiologies. NT: not tested.

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Abstract 8183

Pragmatic ranking of antibiotics based on spectrum and ecologic impact for educational purposes: results from a Delphi survey for Dawaa

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Background: “Dawaa” is an educational board game aiming at raising awareness on antimicrobial resistance and teaching antibiotic use to medical students. It ranks antibiotic, based on spectrum and potential for selection of resistant strains. This ranking is difficult to achieve, because there is no clear hierarchy nor strong evidences, especially other than beta-lactam antibiotics. The aim of this work was to reach a consensus.

Materials/methods: We formed a scientific board which included six infectious disease specialists, one internal medicine physician and one microbiologist, among which six were academics. Twenty-three antibiotics were selected for ranking. Each expert was asked to attribute penalty points from 1 to 5 to each antibiotic. A Delphi process with successive rounds was conducted to reach an agreement. More than 70% of similar answers were necessary to reach a consensus.

Results: The study was carried out between February and July 2019. A consensus for all antibiotics except carbapenems was reached after three rounds. No experts attributed a penalty of 1. A penalty of 2 was attributed to penicillin M, penicillin A, piperacillin, 1st- and 2nd-generation cephalosporins, pristinamycin, rifampicin, vancomycin, aminoglycosides, macrolides, metronidazole, fosfomycin, cyclins, and aztreonam. A penalty of 3 was attributed to amoxicillin-clavulanate, 3rd- and 4th-generation cephalosporins, and clindamycin. A penalty of 4 was attributed to piperacillin-tazobactam, ticarcillin-clavulanate, and fluoroquinolones. A panel discussion was conducted at the beginning, and in the end of the survey. It appeared that antibiotics were first ranked by the broadness of their spectrum, and a penalty of 4 was attributed to antibiotics known for selecting resistant strains. Experts finally attributed a penalty of 5 to carbapenems to teach students to consider these molecules, with extremely broad spectrum, as last resort treatment.

Conclusions: Through a Delphi process with experts, we were able to attribute antibiotic penalties to most clinically-used antibiotics, including other than beta-lactam antibiotics, for “Dawaa”. These penalties first accounted for the broadness of the antibiotics’ spectrum, and then supposed ecologic impact, and carbapenems to be kept as last resort treatment.

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Abstract 8185

**Procalcitonin diagnostic performance for differentiating bacterial from viral infection in adults and children with lower respiratory tract infection**

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Abstract third-party references: MeMed diagnostics LTD.

**Background:** Distinguishing bacterial from viral etiology in febrile patients with lower respiratory tract infection (LRTI) is a frequent challenge faced by physicians at the emergency department (ED). Based on meta-analyses of published data, procalcitonin (PCT), a bacterial induced biomarker, was recently cleared to guide antibiotic treatment in adult patients with LRTI. However, prospective data on PCT accuracy in differentiating bacterial from viral infection is lacking. Here we evaluated its diagnostic performance for differentiating bacterial from viral infection in adult and pediatric patients presenting to the ED with LRTI.

**Materials/methods:** This is a sub-analysis of two European commission funded, prospective studies, conducted at European and Israeli EDs that recruited patients with suspicion of LRTI (OBSERVER; NCT03011515; grant #684599; adults>18 years old) or respiratory tract infection and fever without source (AutoPilot-Dx; NCT03052088, grant # 701088; 3 months<children<18 years). For every participant, we collected medical history, physical examination, routine lab, imaging and respiratory multiplex PCR data. The cohorts included patients with LRTI discharge diagnosis and PCT test results, who were assigned reference standard bacterial or viral by majority adjudication of an expert panel; children (n=293) and adults (n=139).

**Results:** 63 pediatric patients were assigned reference standard bacterial and 230 reference standard viral. LRTI included pneumonia (46%), bronchiolitis (6%), acute bronchitis (18%), influenza (21%) and unspecified LRTI (9%). 67 adult patients were assigned reference standard bacterial and 72 reference standard viral. LRTI included pneumonia (53%), acute bronchitis (36%), asthma or COPD exacerbation (8%) and unspecified LRTI (3%). PCT at cutoff of 0.25 μg/l displayed significantly decreased sensitivity and increased specificity in adults as compared to children (p<0.05; Table 1). Adherence to PCT guided antibiotic prescription for adults would have resulted in ~36% underuse rate (24 patients with PCT≤0.25 μg/l out of 67 reference standard bacterial) and ~10% overuse rate (7 patients with PCT>0.25 μg/l out of 72 reference standard viral).

**Conclusions:** PCT did not meet in adults or children the target product performance for differentiating bacterial from viral infection as defined by Foundation for Innovative New Diagnostics (FIND), indicating an unmet need for host-response biomarkers with higher performance to support improved antimicrobial treatment decisions.
Table 1: Diagnostic performance of procalcitonin in children and adults

<table>
<thead>
<tr>
<th>Cutoffs</th>
<th>Sensitivity % (95% CI)</th>
<th>Specificity % (95% CI)</th>
<th>PPV % (95% CI)</th>
<th>NPV % (95% CI)</th>
<th>Total accuracy % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Children (3 months to 18 years)</strong></td>
<td></td>
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<tr>
<td>0.25 ng/ml</td>
<td>80.9 (69.1-89.7)</td>
<td>60.8 (54.2-67.2)</td>
<td>36.1 (31.6-40.9)</td>
<td>92.1 (87.4-95.1)</td>
<td>65.1 (59.4-70.6)</td>
</tr>
<tr>
<td>0.5 ng/ml</td>
<td>73.0 (60.3-83.4)</td>
<td>79.5 (73.7-84.5)</td>
<td>49.4 (42.1-56.8)</td>
<td>91.5 (87.7-94.2)</td>
<td>78.1 (72.9-82.7)</td>
</tr>
<tr>
<td>1 ng/ml</td>
<td>65.1 (52.0-76.6)</td>
<td>91.7 (87.4-94.9)</td>
<td>68.3 (57.5-77.5)</td>
<td>90.5 (87.2-93.1)</td>
<td>86.0 (81.5-89.7)</td>
</tr>
<tr>
<td>2 ng/ml</td>
<td>53.9 (41.0-66.6)</td>
<td>96.5 (93.3-98.5)</td>
<td>80.9 (76.4-89.7)</td>
<td>88.4 (85.4-90.9)</td>
<td>87.3 (83.0-90.9)</td>
</tr>
<tr>
<td><strong>Adults (age &gt; 18 years)</strong></td>
<td></td>
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<tr>
<td>0.25 ng/ml</td>
<td>64.2 (51.5-75.5)</td>
<td>90.3 (80.9-96.0)</td>
<td>86.0 (74.8-92.7)</td>
<td>73.0 (66.0-79.0)</td>
<td>77.7 (69.8-84.3)</td>
</tr>
<tr>
<td>0.5 ng/ml</td>
<td>53.7 (41.1-66.0)</td>
<td>98.6 (92.5-99.9)</td>
<td>97.3 (83.5-99.6)</td>
<td>69.6 (63.8-74.8)</td>
<td>76.9 (69.1-83.7)</td>
</tr>
<tr>
<td>1 ng/ml</td>
<td>47.7 (35.4-60.3)</td>
<td>98.6 (92.5-99.9)</td>
<td>96.9 (81.8-99.5)</td>
<td>66.9 (61.7-71.8)</td>
<td>74.1 (65.9-81.1)</td>
</tr>
<tr>
<td>2 ng/ml</td>
<td>26.8 (16.7-39.1)</td>
<td>100 (95.0-100)</td>
<td>100 (95.0-100)</td>
<td>59.5 (55.9-62.9)</td>
<td>64.7 (56.2-72.6)</td>
</tr>
</tbody>
</table>

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Impact of a French regional centre infectiology hotline on antibiotic prescriptions in general medical practice

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Background: Since 2016 a regional hotline dedicated to antibiotic (AB) stewardship is available for physicians and especially used by general practitioners (GP). We aimed to measure the impact on GP’s AB prescriptions and to study the population of GP using this device.

Materials/methods: We conducted a prospective observational regional study from April to July 2019. All the AB queries from GP were identified. The AB suggested by the GP was compared to the AB prescribed by the infectious diseases (ID) specialist. D7 a survey was sent to all the GP in order to collect characteristics of the GP population and evaluated the reduction of AB consumption.

Results: Overall 783 calls were received, 176 came from a GP of which 122 were reviewed. Mean age of patients was 51.4 yr (+/-23.3), sex ratio 1.2. Urinary tract infections represented 40.2% (49/122) of inquiries, cutaneous infections 23.0% (28/122) and genital infections 9.0% (11/122). Before ID advice, GP would have prescribed an AB for 71.6% of patients (73/122). After ID advice, AB was stopped/delayed/not started in 18 cases (17.6%) and an AB with a narrower spectrum was chosen in 16 cases (15.7%). Altogether, the reduction in AB pressure was estimated of -30.4% (IC 95% -40.4 ; -20.3, p<10⁻³). ID advice led to an improvement in the AB use in 64.8% of cases (IC 95% : 55.6% ; 73.2%) concerning: indication (48.1%), molecule (41.8%), dose and duration (both 5.1%). The D7 survey was completed by 56.6% (69/122). Advices given by ID specialists were judged relevant by 94% of GP and were followed in 100% of the cases. The GP investigated, comparatively to the regional population of GP, seemed to be younger (55% under 35), more feminine (sex ratio 0.54) and 70% were regular users of the hotline.

Conclusions: Our study revealed a significant reduction of AB pressure thanks to an AB stewardship hotline. An improvement in the good use of AB and a reduction of AB consumption were major results, warranting the quality of the advice given by the ID specialists as well as the existence of the structure itself.

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Abstract 8194

Sulbactam-durlobactam (ETX2514) activity against carbapenemase-producing Acinetobacter baumannii in the presence or absence of imipenem or meropenem using an in vitro hollow-fibre infection model

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Background: Increased incidence of infections attributed to multidrug-resistant (MDR) Acinetobacter baumannii (Ab) has elevated the threat level to urgent as highlighted by the CDC Antibiotic Resistance Threats Report 2019. Infections caused by carbapenem-resistant Ab (CRAB) pose a particular threat due to a paucity of effective therapeutic options. Sulbactam-Durlobactam (SUL-DUR), a novel β-lactam/β-lactamase inhibitor combination, is currently evaluated in a Phase 3 clinical trial with carbapenem background therapy. This study sought to evaluate clinically relevant SUL-DUR dosage regimens with or without imipenem (IPM) or meropenem (MEM) using the dynamic in vitro hollow fiber infection model (HFIM) and translational, mechanism-based modeling (MBM).

Materials/methods: Concentration time profiles of SUL (1g Q6h), DUR, IPM (0.5g Q6h), and MEM (0.5g Q6h) at clinically relevant dosage regimens were simulated in the HFIM over 24-h and quantified via LC-MS/MS using three DUR exposures (i.e. average concentrations at steady state [Css,avg] of 0.44, 2.6 and 6.1 mg/L). We tested CRAB strain ARC5082 that produces the ADC, OXA-66, and OXA-23 β-lactamases [MIC: 128 mg/L for MEM and IPM; 4 mg/L for SUL-DUR]. All drug concentration and viable count profiles were simultaneously analyzed via population pharmacokinetic/pharmacodynamic modeling.

Results: SUL-DUR achieved 1.9 log10 bacterial killing at 8 h at a DURCss,avg of 2.6 mg/L. Three-drug combination regimens (with DURCss,avg of 2.6 and 6.1 mg/L) yielded at least 2.8 log10 killing at 8 h followed by regrowth. SUL-DUR plus imipenem yielded >5 log10 killing without regrowth by 24 h. In the MBM, one bacterial population was susceptible and the second less susceptible to SUL-DUR. The susceptible population was rapidly killed when DUR concentrations exceeded approximately 1 mg/L in presence of SUL (at Css,avg of 6 mg/L). β-Lactamase-related inactivation of carbapenems was inhibited at DUR exposures of 2.6 and 6.1 mg/L (Css,avg). Population fits were unbiased and reasonably precise.

Conclusions: SUL-DUR with or without a carbapenem achieved robust bacterial killing of CRAB at clinically relevant doses. Killing by SUL-DUR was enhanced by IPM (and MEM). As shown by MBM, these 2- and 3-drug combinations hold great promise to combat CRAB infections.

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Abstract 8198

Cost-effectiveness analysis for human papilloma virus mitigation strategies implemented since 2019 in the Republic of Moldova based on infectious disease modelling

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Background: Human papillomavirus (HPV), is a sexually transmittable virus infection, which is necessary risk factor for developing cervical cancer, first killer in working age women in Moldova (one of the poorest countries in Europe). Since 2018 Moldova has modified screening program and vaccination program [mainly externally funded]. The optimal preventive guidelines for cervical cancer are known: cervical screening practice, widespread vaccination and sexual education. However, interventions with the highest impact and lowest price should be prioritized in low resource setup.

Materials/methods: To assess the performance of the mitigation policy we propose cost-effectiveness analysis with mathematical model according to 2 already implemented strategies. (1) Vaccination of a single age-cohort, although vaccinating a single cohort may not have a substantial effect in other countries with distinct socio-economic situation. (2) Transition to more technologically advance screening ecosystem (changing from Romanowski to Pap smear), which might not necessary be cost-efficient in low resource settings [if GDP per capita will not growth substantially at the same time].

Results: (1) We verified that single cohort vaccination is both cost-beneficial [total costs reduction will balance intervention costs around the year 2040] and cost-efficient [with incremental impact in 20 years perspective on the level of 2300 EUR/QAL Y]. (2) Transition between Romanowski -> Pap smear cytology in screening benefits unquestionably in epidemiology e.g. due to higher specificity. However, further maintenance and higher procedure costs could exceed treatment costs, hence intervention costs would gather unacceptable share in whole national limited resources dedicated to public health.

Conclusions: (1) We recommend continuation of vaccination which is both financial [with GAVI substitute] and economic cost-effective. (2) In terms of screening technology transition: there is no way to go back, however screening costs have to be periodically monitored and national guidelines could be revisited [if necessary] according to economic situation in Moldova.

Fig. Simplified Moldovan history of pathogenic HPV strains costs. Intervention (int) costs [sexual education, vaccination, screening] and Total (tot) costs [intervention costs with mainly cervical cancer treatment as well as other treatment costs of pre-cancer abnormalities, anus cancer, genital warts] with tunable variables [vaccination coverage type and smear cost]

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Abstracts 2020

Abstract 8199

Comparison of the preclinical renal effects of piperacillin/tazobactam and imipenem-cilastatin/relebactam in combination with vancomycin

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Background: Vancomycin (V) is a commonly used antimicrobial against gram-positive bacteria that is associated with acute kidney injury (AKI) in a dose-dependent manner. Combination of V with select beta-lactams such as piperacillin/tazobactam (PT) has been associated with an increased risk for AKI. Imipenem-cilastatin/relebactam (ICR) is a recently approved agent that contains a novel beta-lactamase inhibitor R to restore I activity against I non-susceptible gram-negative bacteria, and C to inhibit I metabolism. Preclinical models have shown that C decreases the risk of drug-induced AKI. The objectives of this study were to compare the AKI potential of V in combination with PT and ICR, respectively.

Materials/methods: Ten to twelve week old male C57BL/6J mice (Charles River Laboratory) were used in these studies. Three mice per group were dosed with saline (control), 300 mg/kg of VAN by intraperitoneal injection once daily over 4-days period. V was also combined with PT at 2500 mg/kg/day and ICR at 320 mg/kg/day. These V combinations included fractionated doses of ICR and PT every 6 [V+ICR6 or V+PT6], 12 [V+ICR12 or V+PT12], and 24 [V+ICR24 or V+PT24] hours, respectively. Mice were sacrificed 24 hours after the 4th dose, blood collected for serum creatinine (SCr) and blood urea nitrogen (BUN) assays. The right kidney from each animal was graded for acute tubular damage (ATD) by histopathology (blinded to treatment group). Experimental procedures were repeated for V combinations with IMP-C/REL and P/T every 6 hours based on the results.

Results: Mice treated with V alone had a near doubling of their baseline SCr and BUN compared to control, and ICR or PT alone (Figure 1). Combinations of V and ICR and PT had numerically lower SCr and BUN values though this was statistically significant (p<0.05) for the V+ICR24 or V+PT24 groups for BUN and V+ICR24 for SCr compared to V alone. Renal tubular degeneration grade was higher in the V+PT6 group than V alone.

Conclusions: ICR and PT attenuate V induced AKI at single daily doses. ICR maintains a nephroprotective effect while PT does not with fractionated doses.

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Figure 1. Box and whisker plot of renal biomarkers against PT and ICR alone, control, and V alone along with fractionated combinations. The * symbol denotes statistical significance (p<0.05) relative to V alone.
Rapid detection and characterisation of the Ambler class of carbapenem-resistant Enterobacteriaceae with the mCIMplus assay

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Background: The spread of carbapenemase-producing Enterobacteriaceae (CPE) is a major public health problem. Recently, the mCIM (Modified Carbapenem Inactivation Method) assay was developed for carbapenemase detection, which reported a sensitivity and specificity of 99% and 100%, respectively. This test has been approved by the Clinical and Laboratory Standards Institute (CLSI). In this study, we evaluated the performance of a faster version, the mCIMplus, which allows the detection of carbapenemase in 8 hours (vs 20h for mCIM) and its characterization according to the Ambler classification in 20 hours.

Materials/methods: The performance of the mCIMplus assay was evaluated on a panel of 159 isolates, including 137 CPE isolates (17 KPC, 1 GES, 33 NDM, 7 VIM, 1 IMP; 59 OXA-48, 13 OXA-48-like and 6 NDM plus OXA-48) and 22 carbapenem-resistant isolates that do not produce carbapenemases. Briefly, 3 bacterial suspensions of the tested isolate each containing a meropenem disc were prepared, with respectively tryppticase soy broth (TSB) (Bio-rad), EDTA solution (0.05M) and phenylboronic acid solution (20 mg/mL) in TSB, respectively. At the same time, an Escherichia coli strain (ATCC 25922) was inoculated onto MH agar from a 0.5 McF suspension. After 4 hours of incubation at 37 °C, the meropenem discs were removed from the bacterial suspensions and placed on the seeded agar and incubated again at 37 °C. The inhibition diameters were read at 4h (detection only) and 16h (detection and characterization).

Results: For the detection of carbapenemase, the mCIMplus assay showed a sensitivity of 99.3% and 98.5% at 8 hours and 20 hours respectively, with a specificity of 100% regardless of the reading time. For enzyme characterization, the mCIMplus assay successfully identified the Ambler class in 98.5% of the CPE isolates tested. The characterization was correct for 100%, 95%, and 100% of Ambler class A, B, and D isolates.

Conclusions: The mCIMplus test shows excellent performance for detection and characterization of CPE. This test is easy to perform, inexpensive, effective and can be performed without specific equipment.

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Abstract 8201

Cell immunity in maxillofacial actinomycosis diseases
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Background: Actinomycosis is present in all parts of the world and makes up to 3-20% of chronic pus processes. Some types of actinomycosis (i.e. Actinomycesisraeli, Actinomycesodontolyticus) create actinomycosis in different parts of human organism and structures. They cause diseases when the relevant conditions occur. In addition, they have some obligate pathogen members as well. Medically and socially it is very important to research the spreading of such forms in various substrates. For better understanding of pathogenesis and prognosis of actinomycosis it is necessary to evaluate host’s immune status. Therefore, main aim of our research was to study host immune status in patients with maxillofacial actinomycosis.

Materials/methods: 14 patients in the age range of 25 to 60 with maxillofacial actinomycosis were involved in the study. The control group consisted of 40 healthy persons. In both groups subpopulation of T-lymphocytes (CD3, CD4, CD8) and also CD22 were detected by commercial test "Kolonospekt", which based on immune peroxidase staining of the cells. Conventional microbiology methods were used for identification of etiology agent and to detect association of actinomycetes with different bacteria.

Results: Actinomycetes were isolated in experimental group. Most prevalent microorganisms associated with actinomycetes were beta-hemolytic streptococcus, Helicobacter pylori, Staphylococcus aureus, Porphyromonas spp., Pseudomonas spp. and Candida spp. The rate of CD3 was 37%, CD4 -27%, CD8-12,7, CD22-3% in experimental group. The following rates were detected in control group: CD3 - 65,5%, CD4-38,5%, CD8-29,5%, CD22-12,8%.

Conclusions: Quantitative detection of T-lymphocytes (CD3, CD4, CD8) showed attenuation of cell mediated immunity in patients with maxillofacial actinomycosis. In addition, immunodeficiency was also detected in humoral immunity with decreased levels of CD22.

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Abstract 8203

The role of co-morbidities in the prescription of carbapenemes
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Background: Extended carbapenem use has been associated with the emergence of Carbapenem-resistant, difficult to treat Gram-negative nosocomial pathogens. Adequate empirical treatment is crucial for patient’s outcome and is based on estimation of risk factors for multi-drug-resistant (MDR) infection. We sought to investigate the presence of comorbidities in a cohort of severely ill patients being considered as high risk for MDR infections, for whom treating physicians prescribed a carbapenem.

Materials/methods: A retrospective analysis of data collected prospectively during an observational study, conducted at a 450-bed tertiary hospital of Athens from September 2013 to December 2015. In the context of an antimicrobial stewardship program (ASP) targeting carbapenem restriction, the Antimicrobial Stewardship Program team (ASPT) provided unsolicited face-to-face consultation for every patient with prescription of meropenem or imipenem. Treating physicians were advised to switch to carbapenem-sparing options for empiric or definite treatment based on risk estimation or microbiological data respectively. Comorbidities as predisposing factors for MDR infections were studied.

Results: The study included 304 patients classified into two groups based on the strategy of treatment; group A consisted of patients who were treated with alternative to carbapenem regimens following ASPT consultation, (N= 168) whereas group B (N= 136) consisted of those who were maintained on carbapenem following treating physician’s decision. The most common comorbidities observed in the study population were in decreasing frequency diabetes mellitus type 2 (T2DM) 74(26.3%), malignancy6 (2.1%), chronic obstructive pulmonary disease (COPD) 53 (18.8%) and immunosuppression51 (18%). Between two groups of study statistical results showed p-value =0.001 in COPD and 0.015 in T2DM. All cause of mortality of the cohort was 30 % (26,2% vs 35,3% in group A and B respectively). The survival analysis with Cox regression model for comorbidities showed p=0,96(OR=0,96, 95%CI for OR=0,06-7,21).

Conclusions: T2DM and in COPD were significantly more frequent in the group of patients who were maintained on a carbapenem regimen, despite ASPT consultation. Local antibiotic policies should further explore epidemiology of infections in these subgroups of patients and tailor relevant recommendations

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Abstract 8204

**Screening of colonisation for carbapenemase-producing Enterobacterales: impact in the empiric antibiotic choice of carbapenemase-producing Klebsiella pneumoniae infection in a Portuguese hospital**

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**Background:** Carbapenemase-producing *Klebsiella pneumoniae* (CPKP) infection is a major concern. Carbapenemase-producing Enterobacterales (CPE) colonization is associated with an increased risk of infection. Knowledge of CPE colonization can be relevant not only to infection control but also to antimicrobial stewardship. The purpose of this study was to evaluate infection caused by CPKP and understand the role of screening of CPE in empirical therapy management.

**Materials/methods:** Since January 2016 was implemented an active screening in selected patients admitted in our hospital with an increased risk of colonization for CPE. Rectal swab samples were screened by real time PCR (Xpert Carba-R® test and later BD MAX™ Check-Points-CPO). From 2016 to August of 2019 we evaluated retrospectively all clinical isolates with CPKP concerning the age, genre, source of infection, antibiotherapy and screening results.

**Results:** During the analysed period, 7233 patients were screened at admission, of which 327 (4.5%) were positive. We identified 110 CPKP in clinical isolates that corresponding to 91 infections, and 19 colonization. Only 42 (46%) were screened at admission, of which 28 (67%) had positive CPE screening. The mean age was 77.9 years (min 18; max 95) and 46 (53.5%) were females. The main source of infection was urinary (n=43; 47%), followed by respiratory infection and surgical site infection. Only nine had bacteremia. Piperacillin/Tazobactam was the most widely used empirical therapy (30%; n=27). The mortality of infected patients was 26.4% (24).

**Conclusions:** Our study demonstrates low adherence to assessment of risk factors to CPE colonization and active screening. Our results showed no difference in empirical therapeutic strategy in patients with positive CPE screening in Infections caused by CPKP.

<table>
<thead>
<tr>
<th></th>
<th>Positive EPC Screening (28)</th>
<th>Negative EPC Screening (14)</th>
<th>EPC Screening not realized (68)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection to Klebsiella spp (91)</td>
<td>26</td>
<td>11</td>
<td>54</td>
</tr>
<tr>
<td>Empirical ABT with coverage of EPC (4)</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Change of antibiotic after the microbiological identification (8)</td>
<td>1</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Change of antibiotic after antibiogram (52)</td>
<td>14</td>
<td>11</td>
<td>27</td>
</tr>
</tbody>
</table>

Table 1: Therapeutic strategy in patients with positive EPC screening in clinical isolates

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Molecular investigation of a 4-year outbreak of human adenovirus A31 (HAdV-A31) infection on a paediatric haematopoietic stem cell transplantation ward

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Background: Weekly adenovirus PCR blood screening revealed an increased incidence of adenovirus infections on the SickKids HSCT ward in early 2015. Institution of routine typing of all new cases identified a total of 20 cases of HAd-A31 infection occurring between October, 2014 and September, 2018. Sanger sequencing of the E3 and hexon genes was inconclusive regarding strain relatedness, so whole genome sequencing (WGS) was performed.

Materials/methods: Routine weekly HAdV blood monitoring was performed (day 0 to 100 post-HSCT), using the RealStar quantitative Adenovirus PCR assay (Altona Diagnostics, Hamburg, Germany). Urine, stool and nasopharyngeal samples were also tested after a first positive blood. Where possible, samples were genotyped using an in-house assay, followed by viral culture. Culture isolates were subjected to WGS. Additional isolates, specimens, DNA or sequences from pediatric HAd-A31 HSCT infections were obtained from 4 international pediatric HSCT centers for WGS. Disseminated infection was defined as ≥ 2 sites positive, e.g. plasma, stool, urine, respiratory, other.

Results: 20 HSCT patients were found to have disseminated infection with HAd-A31. During the same time period, there were 43 other cases of adenovirus infection (6 genotypes, 10 untypeable). 25/33 (76%) non-HAd-A31 patients (excluding non-typed) had disseminated infection. Urine and stool adenoviral loads were often very high (10⁷–10¹⁰ copies/ml) even in the absence of GI symptoms. WGS was successful in 19/20 HAd-A31 patients. 16/19 HAd-A31 sequences formed a distinct clade, with ≤ 8 SNP difference among them. 3/19 HAd-A31 sequences were unique, differing by at least 20 SNPs from any of the outbreak strains. Two of these strains had significant sequence similarity to strains from 3 of the 4 collaborating international centers. Intensive environmental cleaning, educational efforts directed at staff and family, and restriction of access to contaminated areas resulted in a one-year period since the last outbreak strain-associated infection.

Conclusions: Our findings strongly implicate nosocomial spread of HAd-A31 on an HSCT unit and demonstrate the value of molecular techniques in defining and mapping the anatomy of an outbreak. An as yet unexplained close sequence similarity to HAd-A31 strains from other international pediatric HSCT centers was observed.

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Abstract 8220

**Hunt for Leishmania RNA Virus (LRV) in transcriptome database of Leishmania species: which is best for bioinformatic analysis?**

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**Background:** Leishmaniasis is a vector-borne protozoal disease caused by *Leishmania* species and transmitted to humans by sandflies (Phlebotomus sp., Lutzomyia sp.). *Leishmania* RNA Virus (LRV; LRV-1 in the New World, LRV-2 in the Old World), present in some *Leishmania* isolates may worsen clinical manifestations through interactions with host’s immune system. Therefore, investigation of LRV is suggested in resistant cases. Described correlation between *Leishmania* species and LRV subtypes label them as epidemiological markers and may help researchers track infection's origin to reveal its causes and contributing factors. Since unveiling of LRV's interactions with disease pathology is relatively new, assessment of the older transcriptome data is essential to identify LRV (+) isolates. NCBI has recently introduced a next generation sequence data archive (SRA: Sequence Read Archive), which supplies faster sequencing with lower costs. The aim of this study is to test the efficacy of SRA in seeking LRV in Leishmania transcriptome database.

**Materials/methods:** The consensus sequence of LRV was sought in NCBI’s Sequence Read Archive (SRA) Blast for all recorded *Leishmania* transcriptomes before 20th of November 2019. All *Leishmania* transcriptome reads bearing positive signals were downloaded and their validity was tested by guided assemblies, using SPAdes® (Center for Algorithmic Biotechnology, St. Petersburg State University) and BBTools® (Joint Genome Institute). Geneious Prime® (Biomatters) was used to visualise the outcomes (Figure 1).

**Results:** LRV-1 and LRV-2 were present in 53 (11.1%) and 6 (1.3%) of 477 transcriptional data. Five of these LRV-positive transcriptomes were assembled (4 LRV1 and 1 LRV2) and 1 was found positive for LRV1.

**Conclusions:** Consequent guided assembly applied to five SRA-positive *Leishmania* transcriptomes confirmed that only one of them actually had LRV. Despite being fast and inexpensive for bioinformatic analysis, we suggest combined use of SRA followed by guided assembly to avoid false positives in searching LRV in Leishmania transcriptomes. This preliminary study also indicated that LRV can be an epidemiological marker of leishmaniasis.

Figure 1: LRV consensus sequences created from Leishmania Transcriptome.

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Abstract 8221

Controlled human infection with Neisseria lactamica induces B cell responses that are cross-reactive with Neisseria meningitidis

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Background: Neisseria lactamica (Nlac) is a commensal of the human oropharynx. Colonisation with Nlac significantly reduces colonisation by N. meningitidis (Nmen). We hypothesised that cross-reactive adaptive cellular immune responses were responsible for this effect.

Materials/methods: 31 volunteers were inoculated intra-nasally with 105 colony-forming units of viable Nlac or vehicle control. Nlac/Nmen colonisation status was assessed at baseline and at 7-, 14- and 28-days post-inoculation. ELISpot assays were utilised to detect Nlac- and Nmen-specific plasma cells (PCs) and memory B-cells in peripheral blood mononuclear cells (PBMCs) across study time points having coated ELISpot well membranes with Nlac/Nmen-derived outer-membrane vesicles.

Results: Nlac-specific PC frequencies increased significantly amongst Nlac-colonised volunteers (n=17). Median baseline vs. post-colonisation peak Nlac-specific PC frequencies/2x105 PBMCs were 0 (range 0-0.5) vs. 2 (0-31) for IgM (p<0.0001), 0 (0-1) vs. 5 (0-20.5) for IgA (p<0.0001), and 0 (0-1) vs. 3 (0-27) for IgG (p<0.0001). Nlac-specific IgG memory B-cell frequencies (as a proportion of total IgG memory B-cells) increased significantly amongst Nlac-colonised volunteers from 0.000% (range 0.000-0.0027%) at baseline to 0.04% (0.000-0.119%) at day 28 (p<0.0001). As expected, there was no induction of Nlac-specific PCs or memory B-cells in volunteers who received the vehicle control (n=10). Interestingly, there was also a significant increase in IgM, IgA and IgG Nmen-specific PCs amongst Nlac-colonised volunteers. Median baseline vs. post-colonisation peak Nmen-specific PC frequencies/2x105 PBMCs were 0 (range 0-0) vs. 0 (0-30) for IgM (p=0.008), 0 (0-1) vs. 0.5 (0-8.5) for IgA (p=0.01), and 0 (0-0.5) vs. 0.5 (0-10) for IgG (p=0.006).

Conclusions: The increase in Nmen-specific PCs in volunteers colonised with Nlac demonstrates the presence of cross-reactive B-cell epitopes between Nlac and Nmen. Cross-reactivity towards Nmen suggests that the previously observed protective effect of Nlac on Nmen colonisation may have an immunological basis. A plethora of animal models have demonstrated that Th1-polarised effector mechanisms are essential in mediating clearance of bacteria from mucosal epithelia, including Streptococcus pneumoniae and Staphylococcus aureus. Therefore, we plan to assess the frequency and effector phenotype of Nlac-specific CD4+ memory T-cells in response to Nlac colonisation. We hypothesise that cross-reactive CD4+ memory T-cells directed towards Nmen will be Th1.

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Colistin MIC determination by a rapid flow cytometry assay


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Abstract third-party references: This work received funding from the H2020 F7Pilot 2016 project nº 730713 'FAST-bact—A novel fast and automated test for antibiotic susceptibility testing for Gram positive and negative bacteria'.

Background: The increasing prevalence of multidrug-resistant Gram-negative bacteria worldwide leads to a re-evaluation of previously discarded antibiotics, such as colistin (CS), belonging to the class of polymyxins. Its use is being increasingly as a ‘last-line’ resort therapy. The emergence of clinical isolates with reduced susceptibility to this antibiotic has been reported. As susceptibility results obtained with automated systems are not valid due to technical issues, different minimum inhibitory concentration (MIC) assays appear in the market. Nevertheless, they are laborious and time-consuming (minimum of 24h). In present study we evaluate a rapid flow cytometry method that can easily and quickly determine CS MIC values in 2 hours versus 24h from pure colonies with standard broth microdilution.

Materials/methods: A total of 84 Enterobacterales isolates, including 12 QC control strains, with well characterized mechanisms were tested for MIC determination by flow cytometry and compared with broth microdilution (EN ISO 20776-1, 2016) interpreted according to CLSI and EUCAST criteria protocols. For flow cytometry assay (FC), bacteria were inoculated in a microplate containing colistin in variable concentrations (from 0-25 to 32 µg/L) together with a fluorescent dye that detect cell membrane lesion; after incubation (1h), the susceptibility of colistin was analyzed by CytoFLEX Flow Cytometer. FASTinov results were provided by a dedicated software. Categorical agreement (CA) and Essential agreement (EA) were calculated.

Results: The distribution of the strains by CS MIC are represented in Table 1. The CA was 100% and the EA 90.5% with 6 strains showing by FC MIC values 2 dilutions below the reference method and 2 strains 2 dilutions above.

Table 1. Distribution of strains by colistin MIC

<table>
<thead>
<tr>
<th>MIC values (µg/ml)</th>
<th>&lt;0.125</th>
<th>0.25</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>4</th>
<th>8</th>
<th>&gt;32</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of strains</td>
<td>11</td>
<td>10</td>
<td>20</td>
<td>9</td>
<td>2</td>
<td>9</td>
<td>5</td>
<td>3</td>
<td>15</td>
</tr>
</tbody>
</table>

Conclusions: Colistin induced cellular alterations when challenged with bacteria, regarding membrane lesion up to 1h of exposure, which allowed the determination of MIC value with high accuracy.

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Population pharmacokinetics and pharmacodynamics of colistin A and B in the murine thigh infection model with *Pseudomonas aeruginosa*: an integrated experimental and modelling approach

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**Background:** The pharmacokinetics (PK) and pharmacodynamics (PD) of colistin in murine infection models has been studied for colistin (i.e. the sum of colistin A and colistin B) via non-compartmental methods. No PK data exists on each component. This study aimed to characterize the PK of colistin A and colistin B individually and their PK/PD targets in the neutropenic murine thigh infection model with *P. aeruginosa*. An integrated experimental, optimal design, and population PK modeling strategy was leveraged. Secondly, we sought to determine the strain-to-strain variability in PD endpoints for twelve multidrug-resistant *P. aeruginosa* (MDR-PA) strains.

**Materials/methods:** Optimal designs were employed in the exposure response studies with *P. aeruginosa* strain ATCC 27853 (MIC<sub>90</sub>: 1.0 mg/L). The PK of colistin A and B was determined in murine thigh infection models at single subcutaneous doses of 3.5, 7, 10, 20 and 40 mg/kg and analysed by population PK. Robust and informative dose fractionation studies were designed at daily doses from 10 to 160 mg/kg given as Q3h, Q6h, Q12h or Q24h. The strain-to-strain variability in the dose required for PD targets was assessed in twelve MDR-PA strains (MIC<sub>90</sub>: 1-2 mg/L).

**Results:** Clearance and volume of distribution were comparable between colistin A and B (Table). The fAUC/MIC best predicted bacterial killing at 24 h. Strain-to-strain variability in the daily doses required for stasis and 1-log<sub>10</sub> bacterial killing was moderate (Table, n=1,157).

<table>
<thead>
<tr>
<th>PK parameters</th>
<th>Colistin A</th>
<th>Colistin B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apparent clearance (CL/F, mean±SD, mL/h)</td>
<td>6.4 (7.3%)</td>
<td>7.6 (10%)</td>
</tr>
<tr>
<td>Apparent volume of distribution at steady state (Vss/F, mean±SD, mL)</td>
<td>20 (6.7%)</td>
<td>20 (6.7%)</td>
</tr>
</tbody>
</table>

**Coefficient of determination (r²) for**

- Free Cmax-over-MIC (fCmax/MIC): 0.57
- Free AUC-over-MIC (fAUC/MIC): 0.83
- Free time-above-MIC (fT>MIC): 0.22

<table>
<thead>
<tr>
<th>Dose targets of colistin A&amp;B required in the twelve MDR-PA strains for</th>
<th>Colistin A</th>
<th>Colistin B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stasis (mg/kg/day, mean±SD)</td>
<td>27 ± 10</td>
<td>33 ± 16</td>
</tr>
<tr>
<td>1-log killing for the twelve MDR-PA strains (mg/kg/day, mean±SD)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** While the PK of both components was comparable, apparent total clearance of colistin B was slightly larger than that of colistin A. The fAUC/MIC best predicted bacterial killing. Moderate strain-to-strain variability was observed in the daily colistin dose required for PD endpoints.

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**Abstract 8225**

**Risk factors for mortality, intensive care unit admission, and bacteraemia of patients admitted with suspected infection in the emergency department**

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1Hasselt University, Faculty of Medicine and Life Sciences, Hasselt, Belgium; 2Jessa Hospital, Department of Infectious Diseases and Immunity, Hasselt, Belgium; 3Radboud University Medical Center, Department of Internal Medicine, Nijmegen, Netherlands; 4Jessa Hospital, Emergency Department, Hasselt, Belgium; 5Jessa Hospital, Department of Clinical Biology, Hasselt, Belgium

**Background:** In the latest sepsis guidelines, SOFA score was introduced as a risk-assessment tool for patient outcomes, including mortality, and has been evaluated in ICUs, clinical wards, and emergency departments (EDs). The objective was to identify other potential risk factors associated with all-cause mortality, ICU admission, and bacteraemia in the ED.

**Materials/methods:** A prospective observational cohort study was conducted in a 981-bed teaching hospital between February and August 2019. All adult patients admitted to the ED and suspected of infection for whom blood cultures were ordered were eligible. Clinical and laboratory data were collected from electronic medical files. For each outcome 2 multiple logistic regression models were calculated using SPSS Statistics (version 25; IBM). Model 1 included total SOFA score ≥2, model 2 included individual SOFA score variables.

**Results:** In total, 929 admissions of 868 unique patients were included. There were 131 (14%) admissions with true bacteraemia and 394 (4%) with contaminated blood cultures. Diagnoses were 162 (17.4%) pneumonia, 48 (5.2%) lower RTI, 48 (5.2%) urosepsis, 40 (4.3%) upper UTI, 76 (8.2%) intraabdominal infections, 72 (7.8%) ABSSSI, 38 (4.1%) primary bacteraemia, 45 (4.8%) influenza, and 131 (14.1%) other, mostly minor infections. In 269 (28.9%) admissions there was no diagnosis of infection. Of admissions with bacteraemia (n=131), 11 (8.4%) had pneumonia, 1 (0.8%) lower RTI, 48 (36.6%) urosepsis, 20 (15.3%) intraabdominal infection, 8 (6.1%) ABSSSI, and 5 (3.8%) other infections. Model 1 showed only age, serum lactate ≥2mmol/L, and abnormal WBC count, as independent risk factors for mortality (Table). For ICU admission, SOFA score ≥2 and serum lactate ≥2mmol/L were significant. For bacteraemia, serum lactate ≥2mmol/L, abnormal WBC count, and elevated bilirubin levels were significant. Last, for bacteraemia, serum lactate ≥2mmol/L, abnormal WBC count, and elevated bilirubin levels were significant.

**Conclusions:** Besides SOFA score ≥2, other independent risk factors for mortality, ICU admission, and bacteraemia were identified in this population. These factors can help to identify patients most at risk for severe infections, and guide management and empirical antibiotic therapy in the ED.

**Table.** Multiple logistic regression: factors measured on admission influencing 30-day mortality, ICU admission, and bacteraemia

<table>
<thead>
<tr>
<th>Variable</th>
<th>MODEL 1</th>
<th>p-value</th>
<th>MODEL 2</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>30-day mortality</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOFA score ≥2</td>
<td>1.911 (1.658-5.548)</td>
<td>.234</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>Age</td>
<td>1.088 (1.033-1.145)</td>
<td>.001</td>
<td>1.079 (1.019-1.144)</td>
<td>.01</td>
</tr>
<tr>
<td>Serum lactate ≥2mmol/L</td>
<td>2.856 (1.109-7.357)</td>
<td>.003</td>
<td>2.652 (.880-7.989)</td>
<td>.083</td>
</tr>
<tr>
<td>WBC*</td>
<td>3.153 (1.998-9.960)</td>
<td>.05</td>
<td>3.893 (1.031-14.706)</td>
<td>.045</td>
</tr>
<tr>
<td><strong>ICU admission</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOFA score ≥2</td>
<td>3.851 (2.072-7.158)</td>
<td>.000</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>Serum lactate ≥2mmol/L</td>
<td>1.794 (1.043-3.085)</td>
<td>.035</td>
<td>1.745 (.957-3.182)</td>
<td>.069</td>
</tr>
<tr>
<td>MAP* &lt;70mmHg</td>
<td>n.a.</td>
<td>n.a.</td>
<td>2.587 (1.260-5.314)</td>
<td>.01</td>
</tr>
<tr>
<td>Creatinine</td>
<td>n.a.</td>
<td>n.a.</td>
<td>1.324 (.687-.554)</td>
<td>.401</td>
</tr>
<tr>
<td>1.2 – 1.9 mg/dL</td>
<td>1.253 (1.02-6.393)</td>
<td>.045</td>
<td>12.649 (2.905-53.517)</td>
<td>.001</td>
</tr>
<tr>
<td>3.5 – 4.9 mg/dL</td>
<td>3.187 (.804-12.64)</td>
<td>.059</td>
<td>&gt;5 mg/dL</td>
<td></td>
</tr>
<tr>
<td><strong>Bacteraemia</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOFA score ≥2</td>
<td>1.742 (1.154-2.631)</td>
<td>.008</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>Serum lactate ≥2mmol/L</td>
<td>2.342 (1.858-3.520)</td>
<td>.000</td>
<td>2.477 (1.548-3.873)</td>
<td>.000</td>
</tr>
<tr>
<td>WBC*</td>
<td>1.571 (1.035-2.383)</td>
<td>.034</td>
<td>1.312 (1.844-2.041)</td>
<td>.228</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>n.a.</td>
<td>n.a.</td>
<td>1.944 (1.075-3.513)</td>
<td>.028</td>
</tr>
<tr>
<td>1.2 – 1.9 mg/dL</td>
<td>1.625 (.229-11.753)</td>
<td>.630</td>
<td>&gt;12.0 mg/dL</td>
<td>1.000</td>
</tr>
<tr>
<td>2.0 – 5.9 mg/dL</td>
<td>7.997 (3.706-17.257)</td>
<td>.000</td>
<td>12.0 mg/dL</td>
<td>1.000</td>
</tr>
</tbody>
</table>

*WBC: abnormal white blood cell count, (<4.5*10^9/L and >11*10^9/L); MAP mean arterial blood pressure; n.a.: not applicable because variable was not entered separately in the multivariate model; p<0.05 was considered significant.

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Abstract 8230

Development and validation of a questionnaire to explore tuberculosis knowledge, attitudes and practices in foreign-born subjects from high tuberculosis-incidence countries

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Background: Italy is a low tuberculosis (TB) incidence country, and TB cases cluster especially among foreign-born subjects from high TB incidence countries. Several determinants of health contribute to active TB development in this population and TB control strategies should address all. TB knowledge represents only one of these determinants, and all alone does not increase person’s empowerment. However, TB knowledge could represent a contribution to TB control, when integrated into a framework of actions. To our knowledge, there are no validated questionnaires to explore TB knowledge, attitudes and practices in foreign-born subjects from high TB incidence countries who are living in a low TB incidence country.

Materials/methods: The questionnaire’s item pool was compiled from literature reviews. The questionnaire collected demographic data, social determinants’ data, TB knowledge, attitudes and practices information. Questionnaire had to be performed face-to-face and answers were open-ended or multiple choice. Content validity was assessed by content validity index (CVI) and Delphi technique. Linguistic and cultural barriers were assessed performing a focus group and two pilot tests. Reliability was assessed calculating Cronbach’s alpha coefficient. We enrolled and interviewed 86 adult foreign-born subjects from high TB incidence countries in November 2019 in four different facilities (a school, a refugee centre, an infectious diseases unit and an immigrant-health ambulatory) in Ferrara, Italy.

Results: Seven TB experts evaluated the questionnaire with two Delphi technique rounds. Nineteen (50%) out of 38 items presented CVI <80% and were deleted. The focus group was conducted with four foreign-born subjects and two items were deleted. 11 subjects underwent the first pilot test and 40 subjects the second one: no items were deleted. Cronbach’s alpha coefficient was 0.65 for knowledge items (four items).

Conclusions: We developed and validated a questionnaire as a reliable and valid tool for measuring TB knowledge among foreign-born subjects from high incidence TB countries, who are living in a low TB incidence country. We hope this questionnaire could contribute to TB control.

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Abstract 8235

Characterisation of a Portuguese population with candidaemia in a tertiary care hospital

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1Saint John Hospital, Porto, Portugal

Background: Candidemia is an infection with increasing relevance due to its rising incidence and resistance to antifungal treatment. It is associated with substantial morbidity and mortality. The aim of our study was to describe the general characteristics of a population of patients with fungemia by Candida spp.

Materials/methods: We performed a retrospective cohort study of all patients admitted in our hospital during a 4-year period with isolation of Candida spp. in at least one blood culture. Candida species were identified using MALDI-TOF technology, VITEK1 MS, bioMérieux. Information regarding patients’ demographics, comorbidities, relevant clinical and microbiological parameters were collected from individual medical records.

Results: There were 204 episodes of candidemia, 47.1% of cases were male patients and the median age was 65 years. About a quarter of cases (23.8%) were previously colonized with Candida spp., most of them in urine. Patients had high comorbidity burden, with a significant number of them with previous surgery (56.9%), corticosteroid therapy (31.8%) and solid cancer (26.6%). Eighty-four percent of patients had more than one comorbidity. Eighty-two (43.4%) patients were in an Intermediate or Intensive Care Unit (ICU) at the time of diagnosis and 13.7% were admitted in ICU after the diagnosis. The most frequent isolated species was C. albicans (52.5%), followed by C. glabrata (20.6%), C. parapsilosis (17.2%) and C. tropicalis (3.9%). Nearly 1/3 of the patients did not receive any antifungal treatment and around 1/3 received empirical treatment with azoles. Daily follow-up blood cultures were performed in 5.6% of patients. Less than half of the cases had an evaluation by Ophthalmology (31.2%), echocardiography (40%) or by an Infectious Diseases physician (20.7%). The mortality rate was 47.3%.

Conclusions: Our series demonstrates a high prevalence of candidemia, most of the cases due to C. albicans. Most of the patients have important comorbidities and prolonged and frequently complicated admissions. Regarding management and follow-up, a low adherence to international candidemia guidelines was observed. It is thus important to raise awareness to this frequently ignored infection, to recognize potential cases, anticipate diagnosis and improve care measures, in order to ameliorate such reserved prognosis.

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Hospital admission for sepsis and mortality in Brazil from 2009 to 2018: analyzing 10 years of government database (Datasus) information

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Background: Sepsis is a common cause of death among patients in intensive care units (ICU) in Brazil and worldwide. We analyzed hospitalizations for septicemia and deaths in Brazil from 2009 to 2018, through data from Datasus.

Materials/methods: Data from Datasus (www.datasus.gov.br), government database for health information, about hospitalizations for septicemia and mortality from 2009 to 2018 in patients over 15 years old in Brazil. We analyzed length of hospital stay and mortality by gender and age group.

Results: From 2009 to 2018, 788,333 patients with diagnosis of septicemia were hospitalized, 408,865 males (51.9%) and 379,468 females (48.1%). Annual mortality rate was average 51.6%, with rates less than 50% in those below 60 years old and greater than 50% in those over 60 years old, reaching 67.2% in those over 80 years old. Mortality had little risen over the period, with 50.7% in 2009, 51.7% in 2013, a peak of 52.2% in 2016 returning to 50.8% in 2018. Analyzing age group, 298,138 patients (73.4%) were over 60 years old. The age group with highest number of deaths was over 80 years old with 118,454 cases (29.1%). Mean length of stay was 11.8 days, with minimum of 11.4 in 2018 and maximum of 12.2 days in 2013.

Conclusions: Mortality of septicemia at admission is high all over the world. In Brazil we observed rates averaging 50%. Advanced age is at highest risk. Length of hospital stay is average 12 days. Cases of septicemia not diagnosed during hospitalization, alternative diagnoses, or progression to septicemia only during hospitalization may disrupt the correct measurement.

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Abstract 8241

**Antibacterial and anti-biofilm activity of colistin-loaded nanoparticles against Acinetobacter baumannii**

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**Background:** Colistin (COL) is an antibiotic used in last resort against multidrug-resistant gram-negative bacteria such as Acinetobacter baumannii (AB). AB forms adherent biofilms on endotracheal tubes of ventilated patients. These biofilms limit access of COL to AB and require higher doses of COL than for the treatment of infections caused by planktonic bacteria. The aim of the study was to develop COL-loaded lipid-nanoparticles [NANO-COL] to improve COL antimicrobial and anti-biofilm activities in order to avoid the appearance of resistance to this antibiotic.

**Materials/methods:** NANO-COL were formulated using the method initially described by Heurtault et al. (Pharmaceutical research 2002). Various adjuvants (fatty acid, farnesol) were added to improve COL encapsulation efficiency and increase its efficacy against biofilm compared to free COL. Size and zeta potential of the NANO-COL were evaluated. The efficacy of NANO-COLs against an AB COL-resistant AbS2 (C1–D7-12, MIC = 32 mg/L) planktonically grown was tested by MIC measurements. Anti-biofilm activity was evaluated on 48-hours biofilms grown into 96-well microplates by evaluating their total biomass by crystal violet (CV) staining.

**Results:** Stable monodisperse NANO-COL with an average diameter around 120 nm were formulated. In the presence of fatty acid, the negative zeta potential was maintained around -9 mV, suggesting that the positively charged amphipathic COL was encapsulated in the NANO-COLs and not on their surface. Compared to free COL, NANO-COL reduced by 32 times the MIC of COL against planktonic AbS2. When present as NANO-COL, no CV staining was observed from a COL concentration greater than 4 mg/ml, whereas a staining was still observed at 256 mg/L of free COL.

**Conclusions:** The COL was successfully encapsulated in lipid nanoparticles, which allowed restoring the sensitivity to COL of a resistant Acinetobacter baumannii and improved the effectiveness of COL against an abiotic adherent biofilm of Acinetobacter baumannii.

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**Abstract 8242**

**Within-host genetic diversity of *Staphylococcus epidermidis* in prosthetic joint infections: consequences for microbiological diagnosis**

Micael Widerstrom¹,²; Marc Stegger³; Anders Johansson¹; Anders Rhod Larsen²; Tor Monsen¹

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**Background:** Prosthetic joint infection (PJI) is a devastating complication after arthroplasty with high hospital costs, increased in-hospital mortality, and both diagnosis and treatment are challenging. *Staphylococcus epidermidis* is a major pathogen in PJIs. The current guidelines of a definite PJI diagnosis is partly based on the finding of two or more periprosthetic cultures that yield the same organism (indistinguishable based on common laboratory tests including genus and species identification or common antibiogram). Since phenotypic morphological variation, including small colony variants and different antibiograms (clonal variability), as well as polyclonal infections has been reported in *S. epidermidis* infection, the definition of "phenotypically identical organisms" is ambiguous. The aim of the present study was therefore to evaluate the phenotypic and genotypic diversity among multiple *S. epidermidis* isolates identified in individual PJI patients.

**Materials/methods:** A retrospective cohort study of 62 consecutive patients with PJI due to coagulase-negative staphylococci in two hospitals in Northern Sweden from 2008 to 2011. Multiple *S. epidermidis* isolates (n=71) from multiple tissue samples (range 2-9 isolates/patient) were available from 16 PJI patients. WGS was performed using Illumina MiSeq. The sequence data was assembled using SPAdes v.3.9.0. Raw reads were aligned against the *S. epidermidis* ATCC 12228 reference chromosome for SNP detection using NASP.

**Results:** In 10 of 16 PJI, only a single ST (or a single locus variant) was identified (max. intrahost pairwise SNP difference = 64). In six (38%) of the cases, 2 - 5 different ST types were detected within each case showing a intrahost SNP difference of 3156 to 39 618. Colony polymorphism was detected in all cases. Importantly, we identified variations in phenotypic and genotypic antibiograms in 13/16 (81%) of cases and in 11 (68%) also variations between isolates of the same ST (Figure 1).

**Conclusions:** Morphologic, phenotypic and genotypic polymorphism is common in PJIs due to *S. epidermidis*. The present study underscore the complexity in assessing whether phenotypically different *S. epidermidis* isolates from multiple cultures meets the current criteria for microbiological diagnosis of PJI.

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Abstract 8243

Implementation of an antimalarial stewardship programme in a tertiary care hospital in South India

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Background: Increasing incidence of non-malarial acute febrile illness and the declining cost of anti-malarial drugs has resulted in inappropriate use of antimalarial drugs in the developing world. Implementation of antibiotic stewardship programs (ASP) reduced unnecessary antibiotics use in the hospitals. However, very limited data is available regarding the impact of Anti-malarial stewardship program (AMSP) in reducing anti-malarial drug usage in the hospitals. Here we assessed the impact on AMSP on anti-malarial drug usage pattern in a tertiary care hospital.

Materials/methods: This before and after intervention study was conducted in a 200 bed tertiary care referral hospital in South India. In before intervention phase (January 2017 to December 2018) malarial prescription audits was conducted in the post discharge period in the medical records room by physician assistant (PA) and results were discussed latter in the clinical meetings. During intervention phase (January 2019- October 2019) AMSP team consisting an infectious disease (ID) physician, clinical Pharmacist (CP) & PA was established, prescription audits and feedback regarding anti-malarial use indication, choice, dose and duration were immediately provided to the prescriber on the receipt of malarial by AMSP team. The number of malarial prescriptions were compared before and after intervention and analyzed.

Results: 27,020 patients were admitted during the study time. The important difference between pre & post intervention period were shown in the table 1 below

Table-1 Differences between before and after implementation of anti-malarial stewardship program

<table>
<thead>
<tr>
<th>Character</th>
<th>Before intervention</th>
<th>After intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study time</td>
<td>January 2017- December 2018</td>
<td>January 2019- October 2019</td>
</tr>
<tr>
<td>No of admissions</td>
<td>18827</td>
<td>8193</td>
</tr>
<tr>
<td>No of anti-malarial drugs started</td>
<td>34 (0.18%)</td>
<td>6 (0.03%)</td>
</tr>
<tr>
<td>Clinical malaria based on signs &amp; Symptoms</td>
<td>30 (30/34=88.24%)</td>
<td>3 (3/3= 50%)</td>
</tr>
<tr>
<td>Laboratory confirmed malaria</td>
<td>4 (4/34=11.76%)</td>
<td>3 (3/6=50%)</td>
</tr>
<tr>
<td>Anti-malarial drugs stopped by AMSP team when laboratory test for clinical malaria came negative</td>
<td>0/30 (0%)</td>
<td>3/3 (100%)</td>
</tr>
</tbody>
</table>

Conclusions:

1. Implementation of AMSP is feasible in a tertiary care hospital in South India
2. The implementation of AMSP nearly eliminated clinical malaria & stopped empirical anti-malarial drug on 100% occasion on the receipt of laboratory tests for malaria.

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Performance of a computerised decision support system for the semi-automated detection of healthcare associated infections: an explorative pilot study

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Abstract third-party references: Supported by Fonds National Suisse

Background: Current methods for surveillance of health care associated infections (HAI), such as Point Prevalence Surveys (PPS), may be time and resource intensive. With the development of healthcare information technologies, semi-automated real-time surveillance of HAI becomes a real option. Geneva University Hospitals (HUG) are currently involved in the COMPASS trial (NCT03120975), during which a computerised decision support system (CDSS) for antimicrobial prescription has been implemented. The CDSS is integrated into the electronic health record and each antimicrobial prescribed is linked to an indication. We aimed to assess the performance of the COMPASS tool to detect HAI by comparison with data collected in the yearly PPS.

Materials/methods: The annual PPS at HUG conducted in May 2019 was based on the ECDC protocol (version 5.3 for the ECDC-PPS II). In order to assess HAIs detected by the CDSS, we selected all the patients hospitalized in the 8 COMPASS intervention wards who received antimicrobials on the day of the PPS. We then selected patients with (1) indications containing a term referring to a HAI with no restriction for antimicrobial starting date (e.g. hospital acquired pneumonia (HAP)), (2) indications containing a term referring to a possible HAI (e.g. “pneumonia”) linked to antimicrobials prescribed at least 48 hours after hospital admission. HAIs considered were HAP, urinary tract infection (UTI), bloodstream infections (BSI), central-line associated BSI, and C. difficile infections. We compared HAIs detected by the CDSS and by the PPS. A manual chart review was performed for discordant cases and reasons underlying discrepancies were analyzed.

Results: Eight HAIs were correctly identified by both systems (4 HAP, 3 UTI). Five HAIs were only detected by the PPS (1 HAP, 4 UTI). Among them, 3 UTI were excluded by manual revision. Four HAIs were only detected by COMPASS but further excluded by manual review (3 HAP, 1 UTI). The main reasons for discordance were the use of a wrong indication in COMPASS and erroneous reporting during the PPS.

Conclusions: COMPASS is a promising semi-automated surveillance tool. We plan to assess its performance further in a prospective study, exploring different algorithms including other electronic data (e.g. microbiology data).

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Abstract 8257

**Invasive aspergillosis in solid organ transplantation: changes in epidemiology, therapy and prognosis: a national cohort (DIASPERTOS Study)**

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**Background:** Patients with SOT have an elevated risk of IA. In recent years several epidemiological and prognostic changes have been observed.

**Patients/methods:** Retrospective study, carried out in 8 centers in Spain, during the years 2010-2019.

**Results:** During the study period 91 IA were detected: EORTC criteria, (de Paw et al; CID 2008) and Blot et al. criteria [Am J Respir Crit Care Med. 2012]

<table>
<thead>
<tr>
<th></th>
<th>Lung tx</th>
<th>Kidney tx</th>
<th>Liver tx</th>
<th>Heart tx</th>
<th>Combined tx*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute rejection</td>
<td>5 (18%)</td>
<td>7 (30%)</td>
<td>4 (21%)</td>
<td>7 (44%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>Graft dysfunction</td>
<td>4 (14%)</td>
<td>3 (13%)</td>
<td>4 (21%)</td>
<td>3 (19%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Dialysis</td>
<td>5 (18%)</td>
<td>11 (48%)</td>
<td>8 (42%)</td>
<td>5 (31%)</td>
<td>3 (75%)</td>
</tr>
<tr>
<td>COPD$</td>
<td>14 (50%)</td>
<td>8 (35%)</td>
<td>4 (21%)</td>
<td>2 (12%)</td>
<td>0</td>
</tr>
<tr>
<td>CMV infection</td>
<td>5 (18%)</td>
<td>5 (22%)</td>
<td>5 (26%)</td>
<td>4 (25%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Previous AF#</td>
<td>19 (68%)</td>
<td>2 (9%)</td>
<td>11 (58%)</td>
<td>4 (25%)</td>
<td>3 (75%)</td>
</tr>
<tr>
<td>ICU requirement</td>
<td>8 (29%)</td>
<td>12 (52%)</td>
<td>12 (63%)</td>
<td>11 (69%)</td>
<td>3 (75%)</td>
</tr>
<tr>
<td>3-month mortality</td>
<td>2 (7%)</td>
<td>10 (43%)</td>
<td>11 (58%)</td>
<td>5 (31%)</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>12-month mortality</td>
<td>4 (14%)</td>
<td>12 (52%)</td>
<td>11 (58%)</td>
<td>6 (37%)</td>
<td>2 (50%)</td>
</tr>
</tbody>
</table>

*: liver-kidney [3], kidney-pancreas [1], liver-bowel [1]  # AF: antifungal (most in prophylaxis)

$ COPD: chronic obstructive pulmonary disease

Antifungal therapy administered was voriconazole [61%], lipid amphotericin [34%], candins [26%], nebulized amphotericin [19%], isavuconazole [6%] and posaconazole [7%]. Combination treatment was administered in 47% of patients. Length of therapy in those who survived >3 months was 24 weeks [lung. tx 30w, kidney: 13w, liver tx: 14w, heart tx: 28w].

**Conclusions:** IA in SOT presents a high mortality, slightly lower in lung transplant (specially in tracheobronchial forms). It is frequently associated with dialysis, rejection and COPD. Voriconazole is the most commonly used treatment but AmphotericinB is used in a third of cases. Near half of them receive a combination regimen. The length of therapy is prolonged, especially in lung transplant recipients.

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Abstracts 2020

Abstract 8261

**Comparison of the molecular-based test system hyborg Dx and culture for the diagnosis of prosthetic joint infections**

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**Background:** Prosthetic joint infection (PJI) remains one of the most serious complications of joint replacement. Due to the formation of biofilms the diagnosis of PJI may be difficult particularly in infections caused by low virulent microorganisms. The treatment decisions and the ultimate necessity of explantation of implants depend on a timely and precise diagnosis.

**Materials/methods:** 111 orthopedic samples (e.g. prosthesis, implants) suspicious for bone and joint infections were sonicated using the Bactosonic® (Bandelin, Germany) for biofilm removal, followed by culture within the scope of microbiological analysis. 100% (111/111) of the samples were used for the evaluation of the hyborg Dx using Real-Time PCR followed by compact sequencing technology (Cube Dx, Austria). After Real-Time PCR-based amplification of the bacterial 16S-rDNA followed by high resolution melting curve analysis, positive samples (Ct value <26) were analyzed by compact sequencing.

**Results:** 68.5% (76/111) showed microbial or mycotic growth of different pathogens. 42.1% (32/76) show more than 100 colony forming units (CFU) per milliliter (ml), 9.2% (7/76) between 10-99 CFU/ml and 50% (38/76) <10 CFU/ml (positive only after enrichment). For the molecular approach nucleic acid extraction was performed with the GINA 500 extraction kit (Cube DX, Austria). 41.4% (46/111) were tested positive with the hyborg Dx. 14.3% (5/35) were negative in culture but positive with the hyborg 93.75% (30/32) of the positive samples >100 CFU/ml were correctly identified with the hyborg DX resulting in a concordance of 94%. 71.4% (5/7) of the samples between 10-99 CFU/ml were correctly identified with the hyborg resulting in a concordance of 91.4% and 16% (6/38) of the samples below 10 CFU/ml, respectively.

**Conclusions:** The use of molecular biology based broad-range RT-PCR followed by comparative sequencing provides an assay complementary to culture to identify microorganisms from PJI and has a theoretical advantage of a rapid turnaround time and higher sensitivity than conventional microbiological methods, particularly for patients who received antimicrobials. It is also critical to evaluate the results of molecular testing as a stand-alone test, because of risk of contamination at any point of during procedure. However, the hyborg seem to be a useful tool to support microbiological analysis.

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**Abstract 8268**

**Novel mutations found in UL56 terminase subunit and UL54 DNA polymerase after human cytomegalovirus infection treatment with letermovir**

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Abstract third-party references: Group for the Study of Infection in Transplantation (GESITRA), Spanish Network for Research in Infectious Diseases (REIPI)

**Background:** Letermovir (LMV) is a HCMV terminase inhibitor recently approved for hematopoietic stem cell transplant (HSCT) prophylaxis. LMV presents better safety and tolerance profiles than current anti-CMV DNA polymerase inhibitors. However, its efficacy against HCMV infection during replication is currently being studied.

**Materials/methods:** A transplant recipient with persistent HCMV infection was treated with LMV as compassionate treatment after therapeutic failure with valganciclovir, ganciclovir, leflunomida or immunoglobulins. Immunosuppressive and antiviral treatments were adjusted to clinical response during the five HCMV reinfections until LMV was dispensed. Kidney function advised against the use of foscarnet.

Plasma CMV DNAemia was monitored with real-time polymerase chain reaction. Anti-CMV drugs target genes [UL56, UL54, UL97] of clinical samples before and after LMV treatment were analyzed by Sanger sequencing. Phenotypic assay by bacmid recombinant technology was performed for undescribed mutations found by sequencing at the French Reference Center. Anti-viral susceptibility test and growth assay are in progress at the moment and will be finished before February 2020.

**Results:** Two previously undescribed mutations were found after 20 days of LMV treatment which were not present prior LMV dispensation. F345L missense mutation was found within the LMV-resistance region (codon 230-370) of HCMV UL56. This mutation is located adjacent to previously described LMV-high-resistance-associated mutations (Y321C, C325Y, M329T, R369M/G/S).

Second S462P unknown mutation was detected in the HCMV UL54, located between the conserved functional domains IV and delta-C. S462P mutant emerged after 20 days valganciclovir withdrawal and LMV treatment. No resistance-associated mutation was detected until this point.

**Conclusions:** F345L and S462P are novel mutations found in HCMV UL56 and UL54 genes, respectively, at very early stage after LMV treatment. Based on evidence supporting a low LMV-resistance genetic barrier, emergence of the F345L mutant only under LMV selective pressure suggest its association to LMV resistance. The role of DNA polymerase S462P mutant is questioning. The potential replicative advantage conferred by this mutation has to be evaluated alone and in association with UL56 F345L.

Characterization of target genes variations from clinical specimens under different antiviral therapies is crucial for an early diagnosis of resistance and treatment adaption.

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Prevented ciprofloxacin resistance development in *Pseudomonas aeruginosa* by immunomodulatory S100A8/A9 in a murine biofilm wound model

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**Background:** *Pseudomonas aeruginosa* is known to contribute to pathogenesis of chronic wounds by establishing biofilm. Increased tolerance to host response and antibiotics, with development of antibiotic resistance *per se*, are consequences of biofilm formation in chronic wounds. The neutrophil factor S100A8/A9 has a promising adjuvant effect when combined with ciprofloxacin, measured by bacteriology, and increased anti- and lowered pro-inflammatory proteins. This raised the question "Can S100A8/A9 prevent ciprofloxacin resistance development in chronic wounds with *P. aeruginosa* biofilm?".

**Materials/methods:** Full-thickness necrosis (2.9 cm²) was inflicted on 33 mice. On day 4, 100µL of 10⁷ CFU/mL *P. aeruginosa* embedded in seaweed alginate was injected sub-eschar to mimic a biofilm infection.

Mice were randomized into groups: I) ciprofloxacin (500µL s.c. (2mg/mL)) and S100A8/A9 (200µL sub-eschar (5µg/mL)). Group II) Ciprofloxacin monotherapy and saline. Group III) Saline controls.

Half of the mice were terminated day 10 and the remaining on day 14. All mice were treated until sacrifice. The study was evaluated by means of quantitative bacteriology, appearance of ciprofloxacin resistant *P. aeruginosa* detected with E-tests, genetic characterization of resistance mechanism and cytokine production.

**Results:** Bacterial wound densities were significantly different between all groups (p=0.018). The osteopontin level, a chemokine that recruits inflammatory cells, was higher in the ciprofloxacin monotherapy group compared to the double treated group on both termination-days (p=0.0012, p=0.018). In contrast, IL-2 was highest in the double treated group and different from the ciprofloxacin group on both days (p=0.007, p=0.037).

Three mice receiving ciprofloxacin monotherapy had developed resistance after 10 days of ciprofloxacin therapy. These mice also had the highest osteopontin levels. None of the mice receiving combination therapy changed resistance pattern. Whole genome sequencing of these mice identified two high-resistant strains mutated in the DNA gyrase *gyrA* C248T. No mutation was found in the sample with low ciprofloxacin resistance (MIC 1.5 mg/L).

**Conclusions:** The present study indicates a protective effect of adjuvant S100A8/A9 in terms of hindered ciprofloxacin resistance development in biofilm infected chronic wounds. In addition, the adjuvant S100A8/A9 therapy resulted in reduced wound inflammation.

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Abstract 8271

**Epidemiology, management, and costs of syphilis in Germany: a public health analysis**

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**Background:** Syphilis is becoming a re-emerging public health concern in Europe. Because relatively little is known about the epidemiology and economic impact of syphilis in Germany, we analyze currently available statutory health insurance data to get deeper insights into the epidemiology and costs of syphilis in Germany from a public health perspective.

**Materials/methods:** The standardized incidence rate of syphilis is calculated, using the 2010 to 2012 claim data provided by one of the biggest German statutory health insurances “DAK-Gesundheit” and compared with the incidence of notified cases provided by the Robert Koch Institute (RKI) as well as the standardized seroprevalence for blood donors. In addition, we investigated the total number of treatments delivered and the number of diagnostic syphilis tests using claim data and proficiency testing reports as provided by INSTAND e.V, Düsseldorf to approximate costs and quality of diagnostics for syphilis in Germany.

**Results:** During the studied period, the average annual standardized incidence is 8/100,000, while the annual incidence for notified cases is 5/100,000 and the average annual standardized seroprevalence is 80/100,000. In average, 375 incident cases treated for syphilis are diagnosed annually in the cohort of 5.8 million insured DAK members. Extrapolation on the country level leads to 6,414 expected cases annually for Germany as a whole. Correspondingly, 72,234 screening tests (TPPA/TPHA) with a calculated sensitivity of 96.5% and specificity of 98.1% are performed annually in the outpatient sector alone, leading to approx. 1,006,727 annual syphilis tests for Germany as a whole with an annual cost of 4,491,607 €. For the blood donor cohort, 2,472,587 tests are estimated annually for donor screening in Germany with calculated positive predictive values of 2% and negative predictive values of 100%. For donor screening, the annual test cost amounts to 12,257,422 €. In addition, the total extrapolated average annual expenses calculated from claim cases leads to 13,904,813 € of syphilis in Germany.

**Conclusions:** Syphilis has an unexpectedly high economic impact on the German public health care system, therefore raising awareness of the disease and strengthening prevention is recommended for a reduction of the incidence and consequently economic burden of syphilis in Germany.

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Investigation of hypervirulent Group B Streptococcus ST17 clone by MALDI-TOF MS

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Background: Group B streptococci (GBS) is one of the leading causes of invasive infections in newborns and pregnant women and GBS Sequence-Type 17 (ST17) is defined as a hypervirulent clone by multilocus sequence typing (MLST). There have been reports that GBS ST17 clone can be detected during the identification of bacteria by evaluating the peaks in the spectra obtained using MALDI-TOF MS. In a previous study by our team, as a first report of circulation of the hypervirulent clone in our region, six out of 101 isolates were found as ST17 clone by MALDI-TOF MS and confirmed by MLST. The aim of this study is to determine the ratio of ST17 clone in a larger population of various clinical GBS isolates by MALDI-TOF MS.

Materials/methods: A total of 318 GBS isolates obtained from various clinical specimens between January 2015-July 2019 at the Clinical Microbiology Laboratory of a research hospital were included in the study. Identification was done by MALDI-TOF MS (Bruker, Daltonics). Detection of GBS ST17 was done by MALDI-TOF MS as described by Lartigue et al. A peak shift from 7650 Da to 7625 Da was used to distinguish ST17 clone

Results: Of the 318 GBS isolates from 212 urine, 75 cervicovaginal, 12 blood 10 abscess and 9 other samples, 19 (%6) were identified as ST17 clone. Samples yielding ST17 isolates were from obstetrics&gynecology [7 from nonpregnant patients], urology [4], nephrology [4] and pediatrics [4]. Of the 19 ST17 isolates, 15 were from urine and 4 were from cervico-vaginal samples.

Conclusions: Here we demonstrate hypervirulent GBS ST17 clone circulating in our population with a rate of 6% of all GBS isolates. Rapid detection of this hypervirulent clone by MALDI-TOF MS without the need for additional cost during bacterial identification may help develop strategies for the early treatment. Further investigation of this high-risk clone is essential for developing strategies for the control and prevention of invasive infections.

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Abstract 8278

Xpert MTB/RIF assay useful for paediatric patient tuberculosis disease diagnosis

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Background: Diagnosis tuberculosis in children is difficult because the incidence for extra-pulmonary sites such as lymphatic and meningeal tuberculosis, are more common in young children. Samples such as sputum (gastric lavage fluid), cerebrospinal fluid and lymphatic ganglion, may have very few tuberculosis bacteria in it (paucibacillary smear-negative disease). The Xpert MTB/RIF assay is a nucleic acid amplification (NAA) test that uses a disposable cartridge with the GeneXpert Instrument System. The test simultaneously detects *Mycobacterium tuberculosis* complex (MTBC) and resistance to rifampin (RIF).

Materials/methods: The investigational assay was used to test gastric lavage fluid, sputum, bronchial lavage, cerebrospinal fluid and lymphatic ganglion samples from 231 pediatric patients with tuberculosis disease presumptive diagnosis. All the collected samples were available for smear with microscopy for acid-fast bacilli, culture for mycobacteria, and for the Xpert MTB/RIF assay.

Results: This clinical study included 231 pediatric patients; female 53.2%, male 46.8%. Age groups affected 0-5 years: 56.75%, 6-15 years: 40.75% and > 15 years: 2.6%. 17 patients had tuberculosis disease (7.35%), 8 patients had pulmonary tuberculosis, 4 lymphatic tuberculosis, 3 disseminated tuberculosis and 2 meningeal tuberculosis. The Xpert MTB/RIF assay detected 16 of 17 cases for MTBC and one of these for resistance to rifampin, failure MTBC detected once for a ganglion sample. Culture for mycobacteria was positive in 16 of 17 cases, failure once for a gastric lavage fluid sample. Smear with microscopy for acid-fast bacilli was effective in 10 of 17 cases for tuberculosis. All the collected samples were paucibacillary.

Conclusions: The standard cultures can take 2 to 6 weeks for MTBC to grow and conventional drug resistance test can add 3 more weeks, but the Xpert MTB/RIF assay results are available less than 3 hours, and this information provided by the Xpert MTB/RIF assay aids in selecting treatment regimens very quickly. However, the Xpert MTB/RIF assay does not replace the need for smear with microscopy for acid-fast bacilli and the culture for mycobacteria.

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Decline of the Brazilian endemic clone and dominance of internationally disseminated lineages among MRSA from bacteraemic patients in Porto Alegre, Brazil

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Background: Methicillin-resistant Staphylococcus aureus (MRSA) is one of the most frequent causes of healthcare-associated (HA) and community-associated (CA) infections, with bacteraemic patients representing a particularly serious challenge. We aimed to investigate the clinical and molecular epidemiology of MRSA invasive infections.

Materials/methods: This cohort study was performed in four tertiary care public hospitals located in Porto Alegre, Brazil. Only MRSA bloodstream isolates were included and were prospectively collected - isolates from the same episode of bacteraemia were counted only once. The study period was from April 2014 until June 2018. The isolates were subjected to high throughput sequencing using Illumina technology. Clinical data was obtained from electronic records.

Results: A total of 91 MRSA isolates were included; 64 (70%) were from HA and 27 (30%) from CA infections. The patients were predominantly male (55%), median age was 58y. (IQR 39-68y.) and Charlson score median was 3 (IQR 1-6). The sequence types (ST) and clonal complexes (CC) identified were: ST5, ST105, ST1176 and ST552 (CC5, 36%); ST30 and ST5522 (CC30, 31%); ST8 and ST239 (CC8, 29%); ST669 (2%) and ST398 (2%). The Brazilian endemic clone (BEC–ST239–III–PVL), a previously prevalent lineage, was now represented by 3 isolates (3%). Both ST30 and its CC were associated with CA infections (p=0.005 and p=0.006 respectively; Fisher exact test). In contrast, CC5 was associated with HA infections (p=0.008). ST669 was present only in paediatric patients (p=0.006). Forty-nine isolates (54%) had the PVL encoding locus and were associated with CA infections (p=0.005). The ST8 and ST30/CC30 were associated with PVL presence (p=0.0001 for both) and the CC5 with PVL absence (p=0.0001) with all CC5 isolates being PVL negative. The major SCCmec type found was IV (67%), with subtypes IVa (31%), IVc (27%) and IVg (9%).

Conclusions: The major clones in our collection represent widely disseminated lineages, which, in our cohort, were associated with specific presentations and age groups. The low incidence of BEC in our study supports the replacement of this lineage by international clones in recent years in Latin America, as reported also in other centers in Brazil. A more detailed genomic analysis will reveal if there are specific sub-lineages of these international clones circulating in our region.

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Abstract 8282

**Intra-osteoblastic activity of dalbavancin during treatment of Staphylococcus aureus bone and joint infection**

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**Background:** Long-acting lipoglycopeptides such as dalbavancin are promising therapeutic options in the treatment of *Staphylococcus aureus* bone and joint infection (BJI). However, the ability of dalbavacin to eradicate the intraosteoblastic reservoir of *Staphylococcus aureus*, associated with BJI chronicity and relapse, has never been evaluated.

**Materials/methods:** In an *ex vivo* model of bone cell infection, osteoblastic MG63 cells were infected with a standardized inoculum of the *S. aureus* reference strain HG001 (multiplicity of infection, 100:1), and incubated for 24h with dalbavancin, vancomycin or rifampin using the minimal inhibitory concentration (MIC), 10MIC, 100MIC, and the intraosseous concentrations reached using standard therapeutic doses in humans [i.e., vancomycin, 10mg/L; rifampin, 2mg/L; and dalbavancin, 6mg/L]. The remaining intracellular bacteria were quantified by plating cell lysates. Four independent experiments in technical triplicates were performed. Results are expressed as means and 95% confidence intervals (95%CI).

**Results:** HG001 was fully susceptible to the three tested molecules, with MICs of 0.125, 1 and 0.004 mg/L for dalbavancin, vancomycin and rifampin, respectively. Dalbavacin was able to significantly reduce the intracellular inoculum of *S. aureus* starting at a concentration equal to the MIC, with a significant dose effect ranging from a reduction of 31.4% (95%CI, 19.3-43.5) at MIC to 51.6% (95%CI, 41.3-61.9) at 100MIC compared to untreated cells. At intraosseous concentrations [figure], dalbavancin reduced the intracellular inoculum by 49.6% (95%CI, 46.4-54.6) compared to untreated cells (p<0.001), with no difference compared to vancomycin [38.1%; 95%CI, 21.5-54.7; p=0.646], and was less efficient than rifampin [69.0%; 95%CI, 63.9-74.1; p<0.001].

**Conclusions:** Dalbavancin was able to decrease by 50% the intraosteoblastic *S. aureus* inoculum at intraosseous concentrations reached during standard human therapeutic dosing, with no difference compared to vancomycin, but remained less efficient than rifampin. Future studies should investigate its activity against internalized methicillin-resistant staphylococci, including vancomycin-intermediate isolates.

Figure: Ability of dalbavancin to eradicate the intraosteoblastic inoculum of *S. aureus* at intraosseous concentrations reached with standard human therapeutic dosing, in comparison with vancomycin and rifampin

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Abstract 8284

Effect of nikkomycin Z and caspofungin upon in vitro induction of echinocandin resistance by Candida tropicalis

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Abstract third-party references: This work was supported by Astellas and Grupo de Infeção e Sepsis (GIS) from Centro Hospitalar São João [Clinical Mycology Research grant].

Background: Echinocandins represent the first-line therapy for the treatment of invasive candidosis. They inhibit the \( \beta(1,3) \)-glucan synthase which is responsible for producing a key component of the fungal cell wall and is encoded by \( \text{FKS} \) genes. The increase in chitin content plays a role in maintaining fungal cell integrity following exposure to echinocandins. Nikkomycin Z (NZ), a peptidyl nucleoside that functions as a substrate analogue and inhibits chitin synthase at its catalytic site, may be a promising therapeutic drug. The aim of this study was to evaluate the effect of the chitin synthesis inhibitor, nikkomycin z, in the evolution of caspofungin resistance by \( \text{Candida tropicalis} \).

Materials/methods: One \( \text{C. tropicalis} \) clinical isolate susceptible to echinocandins (CTs strain) was incubated overnight at 35°C with sub-Minimal Inhibitory Concentration (sub-MIC) concentration (0.03 \( \mu \)g/mL) of caspofungin (CSF). The drug concentration was increased to double whenever yeast growth was prominent, reaching the final concentration of 8 \( \mu \)g/mL. In parallel, CTs strain was incubated overnight with 0.03 \( \mu \)g/mL of CSF plus 25 \( \mu \)g/ml (sub-MIC concentration) of nikkomycin Z (NZ) (CT_CS-F+NZ). \text{In vitro} induction experiment took 30 days. Every 5 days, MIC values of echinocandins were determined according to the broth dilution antifungal susceptibility testing from CLSI.

Following DNA extraction, random amplification of polymorphic DNA was performed using the primers OPE-18 and OPA-18. The HS1 and HS2 of the \( \text{FKS1} \) and \( \text{FKS2} \) genes were amplified and sequenced in an ABI PRISM 3130 Genetic Analyzer.

Results: After 30 days of exposure to CSF, a cross resistant echinocandin strain was obtained (CT_CSFr); with the exposure of CTs to CSF + NZ the phenotype remained susceptible to all echinocandins. CT_CSFr was sub-cultured for an additional 30 days in the absence of CSF and MIC values re-determined and the resistant pattern remained stable. All isolates were confirmed to be isogenic. A point mutation was found in CT_CSF, corresponding to an amino acid replacement of aspartate to valine at position 702 of Fks1p HS1.

Conclusions: Our results demonstrate that the presence of nikkomycin Z prevented the evolution of echinocandin resistance, suggesting therapeutic potential of nikkomycin Z-echinocandin combinations in managing echinocandin resistance.

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Abstract 8285

Extended-spectrum ß-lactamase-producing/carbapenemase-producing Enterobacterales prosthetic joint infection in patients with positive rectal screening

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Background: Gram-negative Bacilli represent approximately 10% of PJI (TANDE, CMR 2014). Since 2002, the incidence of ESBL Enterobacterales is growing (RAISIN network, 2016). In France, CPE infections remain rare but increasing (Santé Publique France, 2018). The rectal carriage of resistant Enterobacterales could play a role in the PJI due to these strains.

The aim of this study is to clarify if the results of rectal screening swabs should be taken in account for the adaptation of probabilistic antibiotic therapy for PJI.

Materials/methods: We performed a monocentric retrospective observational study, between January 2015 and June 2019, at the Reference Center for Osteo Articular Infections in Versailles.

All the patients with ESBL and CPE PJIs during the study period were included.

Phenotypes of Enterobacterales CPE and ESBL strains isolated from rectal swabs and strains isolated from PJIs were compared.

Results: 26 1 P JIs were treated in 227 patients during the study period. 85/227 (37%) patients had a ESBL/CPE positive rectal screening. Among them 15/227 (7%) had a ESBL or EPC PJI (16/26 1).

Sex ratio was 1.1 4 and average age was 7 4 years.

7/15 (47%) patients were immunocompromised. Patients underwent a median number of 3 surgeries.

9/15 (60%) patients [i.e. 10/16 PJI because 1 patient was infected twice] had positive rectal screening; 8 ESBL PJIs and 2 CPE.

5/8 (63%) ESBL infected patients [4 hip / 1 knee prosthesis] and 2/2 (100%) CPE infected patients [2 knee prosthesis] were infected with their carrying strain.

3 patients were infected with a different strain.

6/14 (43%) of ESBL-infected patients had negative rectal screening.

Conclusions: In our study, 5/14 (35,7%) and 2/2 (100%) of patients infected with ESBL or CPE were infected with the same profile of rectal carrying strain. Risk factors of infections to multiresistant Gram negative strains seem to be age, number of surgeries but have to be clearly identified. Today, it is not recommended to adapt the probabilistic antibiotic therapy of PJIs to the germs found in rectal screening. In patients with high risk of ESBL/CPE PJIs, enlargement of probabilistic therapy might be considered. Multicentric studies could be useful since more data are needed.

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**Abstract 8288**

**Mycobacterium tuberculosis** serostatus in patients with multiple sclerosis treated with anti-CD20/52: effects of treatment and lymphocytic asset on Quantiferon assay results

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**Background:** Tuberculosis screening is routinely carried out in patients with multiple sclerosis (MS) receiving anti-CD20/52 agents in order to minimize the risk of reactivation. Our study was aimed to investigate the prevalence of the different serostatus and the effect of such regimens and lymphocytic counts on Quantiferon TB-Gold In-Tube (QTF) results.

**Materials/methods:** QFT assay were performed before and after treatment with anti-CD20 (ocrelizumab/rituximab) and anti-CD52 (alemtuzumab) agents and results were compared according to time of testing. The effects of lymphopenia and treatment history on indeterminate QTF results were evaluated by logistic regression. Pre/post-treatment QTF results were compared in a subset of patients.

**Results:** Two-hundred forty-three patients were enrolled, 47% on ocrelizumab, 26% rituximab, and 27% alemtuzumab. Considering the time of testing, QTF assay was negative in 143/168 (85%) vs 95/108 (88%), indeterminate in 4/168 (2%) vs 6/108 (6%) and positive in 21/168 (13%) vs 7/108 (7%) of patients screened before and after treatment, respectively. Pre-treatment QTF results did not differ according to prior/ongoing treatments or immune status at sampling (Fig. 1). Post-treatment QTF results were significantly different based on prior fingolimod (p=0.047), lymphocytopenia (p=0.034), CD4+ counts<200 cells/μl (p=0.011), and median CD8+ counts (p=0.027) (Fig. 1). Indeterminate QTF results were recorded in 9 patients and main risk factors were evaluated. At multivariate analysis, no prior MS treatment was significantly associated with indeterminate results (OR: 2.4, p=0.039). Twenty-six patients were tested before and after treatment: changes in QTF assay results were recorded in 6 (23%) patients (median time-to-re-test: 320 days). In particular, in two patients QTF switched from negative to indeterminate (both on alemtuzumab, severe lymphopenia <100 cells/μl at re-testing); in two from positive to negative (both on rituximab and isoniazid prophylaxis, after 3 months); in one from indeterminate to negative (on alemtuzumab, with prior fingolimod and baseline lymphopenia); in one from negative to positive (after 15 months and 3 cycles of rituximab with no known risk factor, clinically negative).

**Conclusions:** Post-treatment QTF results in patients receiving anti-CD20/52 agents can significantly be affected by prior fingolimod exposure and lymphocytopenia. QTF changes and conversions were observed in a remarkable proportion of patients screened before and after monoclonal antibody treatment. No significant effect of lymphocytic levels and ongoing treatment was observed in patients with indeterminate QTF.

**Table 1:** Comparison of QTF assay results in patients receiving anti-CD20/52 agents screened before or after treatment.

<table>
<thead>
<tr>
<th>Treatment history</th>
<th>Pre-treatment QTF assay (n=168)</th>
<th>Post-treatment QTF assay (n=108)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive (n%)</td>
<td>Negative (n%)</td>
</tr>
<tr>
<td>Prior monoclonal agent</td>
<td>9 (21)</td>
<td>33 (75)</td>
</tr>
<tr>
<td>Prior fingolimod</td>
<td>4 (13)</td>
<td>28 (87)</td>
</tr>
<tr>
<td>Median number of treatment cycles</td>
<td>2 (1-3)</td>
<td>1 (1-2)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ongoing treatment</th>
<th>Pre-treatment QTF assay (n=168)</th>
<th>Post-treatment QTF assay (n=108)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive (n%)</td>
<td>Negative (n%)</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>7 (26)</td>
<td>20 (71)</td>
</tr>
<tr>
<td>Rituximab</td>
<td>9 (25)</td>
<td>32 (80)</td>
</tr>
</tbody>
</table>

**Immune-status at sampling**

<table>
<thead>
<tr>
<th>Median lymphocytic count</th>
<th>Pre-treatment QTF assay (n=168)</th>
<th>Post-treatment QTF assay (n=108)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1400 (975-1800)</td>
<td>1360 (950-1800)</td>
<td>2489 (815-3285)</td>
</tr>
<tr>
<td>Lymphocytopenia</td>
<td>3 (7)</td>
<td>38 (91)</td>
</tr>
<tr>
<td>Median CD4+ T cells count</td>
<td>Pre-treatment QTF assay (n=168)</td>
<td>Post-treatment QTF assay (n=108)</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>771 (565-1210)</td>
<td>631 (365-884)</td>
<td>1112 [32-537]</td>
</tr>
<tr>
<td>Median CD8+ T cells count</td>
<td>Pre-treatment QTF assay (n=168)</td>
<td>Post-treatment QTF assay (n=108)</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>284 (190-436)</td>
<td>284 (185-426)</td>
<td>466 (97-445)</td>
</tr>
<tr>
<td>CD4/CD8 ratio</td>
<td>Pre-treatment QTF assay (n=168)</td>
<td>Post-treatment QTF assay (n=108)</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>2.59 (1.55-3.81)</td>
<td>2.14 (1.48-3.00)</td>
<td>2.32 [0.33-2.32]</td>
</tr>
</tbody>
</table>

**Presenter email address:** e.zappulo@gmail.com
Identification of gene expression profiles of *Leishmania major* by integrated bioinformatics analyses

Ozlem Ulusan¹, Aygul Sadıqova², Ufuk Mert³, Sercan Öztürk³, Ayse Caner*¹,⁴,⁵

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**Background:** *Leishmania major* infection causes a localized cutaneous lesion in patients and has been widely used to study the development of vaccines against leishmanial infections in mice. *L. major* infected C57BL/6 mice are susceptible to infection and fail to control parasite replication due to the development of Th2 responses. In this study, our aim is to identify the changes in gene expression between mice with infected *L. major* and healthy mice and show molecular pathways and biological functions relate to the pathogenesis of *L. major*.

**Materials/methods:** We used GSE56029 data set from the GEO database for our study. In the whole-genome transcriptional analysis, the skin samples were obtained from healthy mice and mice infected intradermally with *L. major* for 4 weeks. Normalization of the raw data was performed with the Robust Multi-array Analysis. We performed paired t-test and fold change analysis to see for statistically significant changes in expression profiles between mice infected with *L. major* and control group. To define the molecular pathways of all the genes mapped within amplicons in *L. major*, Ingenuity pathway analysis was carried out with each set of significantly differentially expressed genes using IPA8.0 software. Then, we conducted macrophage cell culture infected with *L. major* strain to validate the expression level of some genes, which showed significantly increased/decreased gene expression.

**Results:** We showed the top 20 genes that have significantly increased and decreased expression in *L. major* infection. The top 5 significant genes, Arg1, FCGR4, CXCL9 and CXCL2, had more significant fold change and FDR values than the others and important positions in leishmaniasis. The expression levels of these genes in cell culture were compatible with bioinformatics analysis. The pathway analysis existed that the TREM 1 signaling was the most activated pathway in *L. major*. We showed the upregulated and downregulated genes in TREM signaling pathways in detailed and validated the gene expression levels in cell culture.

**Conclusions:** The results revealed that the activated TREM-1 signaling pathway is associated with *L. major* infection and has a pathogenic impact during parasitic infection in mice. Besides, *L. major* may modulate some genes relate to TREM-1 in macrophages.

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**Abstract 8291**

**Omics approaches for detection of unique features of *Mycobacterium tuberculosis* Beijing B0/W148 cluster**

Julia Bespyatykh*, Egor Shitikov, Dmitry Bespiatykh, Ksenia Klimina, Marine Dogonadze, Viatcheslav Zhuravlev, Elena Ilina

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**Background:** *Mycobacterium tuberculosis* Beijing B0/W148 is one of the most widely distributed clusters in the Russian Federation and in some countries of the former Soviet Union. Recent studies have improved our understanding of the reasons for the "success" of the cluster but this area remains incompletely studied. The aim of the present study was to investigate the features of these endemic strains on different -omics levels.

**Materials/methods:** We used 20 Beijing B0/W148 strains and H37Rv strain from our collection. WGS and transcriptome analysis were conducted on Illumina HiSeq 2500. Additionally, WGS data for 10000 *M. tuberculosis* isolates were obtained from NCBI. Proteome analysis was performed on a Q Exactive HF mass spectrometer.

**Results:** Overall, we identified 397 Beijing B0/W148 strains, which showed a restricted genetic diversity (a pairwise distance of 28 SNPs, ±SD 19 SNPs). Additionally, we described 59 cluster-specific SNPs, which can partly explain the "success" of the cluster. During the study whole (circular) genome of RUS B0 strain was obtained (CP030093.1). In turn, proteome and transcriptome studies allowed to confirm the genomic data and to identify a several features that have not previously been described. Our results demonstrated that expression of the *whiB6* which contains cluster-specific polymorphism (a151c) increased almost 40 times in RUS B0. Additionally, the level of *ethA* transcripts in Beijing B0/W148 was increased by more than 7 times compared to the H37Rv. A comparative quantitative proteomic analysis showed a statistically significant difference between cluster strains and H37Rv in the representation of 192 proteins. Functional analysis revealed differences in the representation of lipid metabolism proteins and proteins involved in the response to hypoxia, which was confirmed by the results of transcriptome analysis. Start sites for 10 genes were corrected based on the combination of proteomic and transcriptomic data. Additionally, based on the omics approach, we identified 5 new genes.

**Conclusions:** We presented the most complete description of the cluster Beijing B0/W148 cluster members. In summary, our results suggest that the specific features of Beijing B0/W148 strains are likely to contribute to their increased virulence and successful geographical distribution.

Supported by the RSF (№ 19-75-10109) and RFBR (№ 18-34-00168).

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Abstract 8293

**Introduction of automated blood culture in a resource-limited setting in West Africa**

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**Background:** Blood cultures (BC) have a high clinical relevance and are a priority specimen for surveillance of antimicrobial resistance. Manual BC (M-BC) is still most frequently used in resource-limited settings. Data on automated BC (A-BC) performance in Africa is scarce. We implemented A-BC within the African Network for improved Diagnostics, Epidemiology and Management of Common Infectious Agents (ANDEMIA) in the Ivory Coast. We compared the performance of A-BC and M-BC.

**Materials/methods:** Between June 2017 and January 2018, bottle pairs of BacT/ALERT® FA Plus (A-BC) and M-BC with self-made brain-heart infusion were compared at a university hospital in the Ivory Coast. BC bottles were inoculated each with a target blood volume of 10ml from the same venipuncture. A-BC’s were incubated for up to 5 days in the BacT/Alert 3D system, M-BC’s for up to 10 days at 37°C. Terminal subcultures were performed for M-BC’s only. Contamination was defined by the clinical microbiologist. The two systems were compared regarding yield, contamination and processing time. During the study period, clinicians were trained in best practice of BC sampling.

**Results:** A total of 337 matched pairs of BC specimens were included. Overall, 37% (95%CI: 31.3-41.9) of A-BC and 24% (95%CI: 19.6-29.0) of M-BC had a positive result with a contamination proportion of 48% (95%CI: 38.8-57.2) and 44% (32.7-55.3), respectively. Processing times were shorter with A-BC than with M-BC (see table). Most contaminants were members of the skin flora. Most common detected pathogens were *Klebsiella* spp. (32%) and *Staphylococcus aureus* (19%).

**Conclusions:** Implementing A-BC in a resource-limited setting is possible. A-BC increased yield and shortened turnaround times, but increased contamination. Training of clinicians has to be intensified to increase the number and the quality of BC sampling. Pre-analytical training to improve diagnostic stewardship is essential when implementing a new microbiological method.

<table>
<thead>
<tr>
<th>Time</th>
<th>A-BC</th>
<th>M-BC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turnaround-Time in days [95%CI]</td>
<td>5.5 [5.3-5.7]</td>
<td>11.1 [10.8-11.4]</td>
</tr>
<tr>
<td>(Blood culture collection until final result)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time-To-Detection in hours [95%CI]</td>
<td>24.0 [19.9-28.2]</td>
<td>101.7 [84.2-119.1]</td>
</tr>
<tr>
<td>(Loading on blood culture machine/incubator until blood culture flags positive)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time-To-Analysis in hours [95%CI]</td>
<td>37.9 [33.0-42.9]</td>
<td>108.9 [91.5-126.5]</td>
</tr>
<tr>
<td>(Loading on blood culture machine/incubator until removal and initial work)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Abstracts 2020

Abstract 8294

**Ceftaroline+rifampin versus vancomycin+rifampin in the treatment of methicillin-resistant Staphylococcus aureus meningitis in an experimental rabbit model**

Damla Akdağ1, Tuncer Turhan1, Elif Bolat1, Gamze Şanlıdağ1, Furkan İşbilen1, Şöhret Aydemir1, Tansu Yamazhan1, Husnu Pullukcu1, Bilgin Arda*1, Meltem Isiköz Tasbakan1, Berke Gökkilic1, Ekin Kartal1, Hilal Tipirdamaz Sipahi1, Sercan Ulusoy1, Oguz Resat Sipahi1

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**Background:** In this study it was aimed to compare the antibacterial activity of ceftaroline+rifampin with vancomycin+rifampin in the treatment of methicillin-resistant Staphylococcus aureus (MRSA) meningitis in experimental rabbit meningitis model.

**Materials/methods:** Meningitis was induced by direct inoculation of ATCC 43300 MRSA strain into cisterna magna of New Zealand rabbits. After 28 hours of incubation, rabbits were divided into three groups as ceftaroline+rifampin (S+R), vancomycin+rifampin (V+R), and control (C) groups. The S+R group received 58 mg/kg ceftaroline (Pfizer, Istanbul, Turkey) twice a day, the V+R group received 20 mg/kg vancomycin (Koçak Farma, Istanbul, Turkey) two dosages (at T0 and 5 h later). Rifampin (Koçak Farma, Istanbul, Turkey) was given 15 mg/kg at T0 and 5 h later. The C group did not receive any treatment but 0.9 NaCl. Quantitative bacterial cultures were performed in cerebrospinal fluid (CSF) samples, which were obtained at the beginning and 24th hours of the treatment.

**Results:** After 28 hours of incubation, 25 of 46 rabbits (8 C, 9 S+R, 8 V+R) met the criteria of meningitis. There was no difference in the number of bacteria [calculated as log10] between the three groups at the beginning of the treatment [C: 4.498±0.566 cfu/mL, S+R: 4.646±0.890 cfu/mL, V+R: 4.269±0.524 cfu/mL, p:0.506]. There was no statistically significant difference between the groups in terms of surviving rabbits at the end of treatment [C: 5/6, S+R: 8/9, V+R: 7/8, p:0.096]. At the end 24th hour of treatment, bacterial count decreased significantly in both treatment groups compared to the control group [C: +3.054±3.817 cfu/mL, S+R: -4.411±0.832 cfu/mL, V+R: -3.185±3.126 cfu/mL, p: 0.034]. However, there was no statistically significant difference between the S and the V groups (p:0.541).

**Conclusions:** Our results suggest that the antibacterial activity of both ceftaroline+rifampin and vancomycin+rifampin are similar in the treatment of MRSA meningitis in experimental rabbit model.

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A majority of adult hospitalised patients with community-acquired lower respiratory tract infections had viral infections

Nicklas Sundell1, Lars Gustavsson1, Magnus Lindh1, Lars-Magnus Andersson1, Johan Westin*

1Dept of Infectious Diseases, University of Gothenburg, Gothenburg, Sweden

Background: Community-acquired lower respiratory tract infections (LRTI) is a frequent reason for in-patient hospital care. Bacterial etiology is commonly suspected and antibiotic therapy initiated in these cases. We aimed to investigate the relative proportion of viral infections in this patient group and describe the clinical characteristics and outcome of such infections.

Materials/methods: We collected nasopharyngeal (NP) samples prospectively from adult hospitalized patients at the infectious disease unit of a 2000 bed teaching hospital in Western Sweden, during three consecutive winter seasons 2016-2019. Syndromic testing was performed using a multiplex PCR panel including 16 viruses and 4 bacteria. Medical records were reviewed for information regarding symptoms at presentation, antimicrobial therapy, microbiological and radiological findings, length of hospital stay, ICU admission, need for oxygen therapy, readmission rate as well as 30-day mortality.

Results: In total, 220 patients were included in the study of which 71 (33%) had viral infections, 51 (23%) had viral/bacterial coinfections, 66 (30%) had bacterial infections while the etiology remained unknown in 31 (14%) cases. The predominant viral agent was influenza (A or B) virus. Sporadic cases of respiratory syncytial virus, metapneumovirus and parainfluenza virus was detected. Rhinovirus was uncommon among viral infections but frequently detected as a potential bystander in viral/bacterial coinfections. Streptococcus pneumoniae was the predominant bacterial pathogen in bacterial and viral/bacterial coinfections. Absence of chest x-ray findings and low CRP level but not low CRB-65 or NEWS scores were associated with viral infections. Patients with viral infections had a shorter length of hospital stay (median 4 vs. 5 days) and received less antibiotics (median 4 vs. 10 days) than patients with bacterial or unknown etiology.

Conclusions: Syndromic testing by a multiplex PCR panel identified either viral infection or viral/bacterial coinfections in a majority of hospitalized adult patients with community-acquired LRTI. Identification of viral etiology based on clinical presentation and routine laboratory tests is challenging and clinical scoring systems like CRB-65 and NEWS add limited value, while chest x-ray and CRP remain relevant. Systematic use of syndromic testing for virus and bacteria may reduce overuse of antibiotics in adult hospitalized patients with LRTI.

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Abstract 8298

Relevance of EBV load monitoring in renal transplant recipients: a retrospective cohort study

Lilli Gard*1, Claudy Oliveira Dos Santos2, Willem Van Doesum2, Hubert G.M. Niesters2, Willem Van Son1, Arjan Diepstra1, Coen Stegeman1, Henk Groen1, Jan-Stephan Sanders1, Annelies Riezebos-Brilman3

1University Medical Center Groningen, Groningen, Netherlands, 2Certe, Groningen, Netherlands, 3UMC Utrecht, Utrecht, Netherlands

Background: EBV load monitoring after solid organ transplantation is used to predict post-transplant lymphoproliferative disorder (PTLD) development in high risk populations. We studied in a retrospective single center cohort, the additive value of EBV monitoring in renal transplant recipients (RTR).

Materials/methods: 373 RTR were included who received a kidney transplant between 2010 and 2012. The incidence of EBV-viremia in whole blood, graft and patient survival, PTLD and biopsy proven acute rejection (BPAR) was studied.

Results: 121 recipients were EBV-DNA negative in whole blood (32.4%), whereas EBV-DNA was detectable at least once in 252 recipients (67.5%). One patient developed histological proven PTLD (0.4%). Incidence of graft failure was not significantly different between the EBV-viremia group (n=25/247, 10.1%) and the EBV-viremia negative group (n=7/121, 5.8%) (RR=1.75, 95% CI 0.8-3.9, p=0.17). In recipients with EBV viral load > log 4 cp/ml graft loss occurred significantly more often (p=0.004). BPAR and mortality rate did not differ significantly between the groups with or without EBV-viremia.

Conclusions: EBV-viremia is common in RTR. With EBV viremia > log 4 cp/ml more graft loss was observed. However, no association with patient survival, PTLD and BPAR was found.

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Molecular epidemiology of Neisseria gonorrhoeae clinical isolates in Reunion and Mayotte: lessons from the study of island populations

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Background: Little is known about the epidemiology of Neisseria gonorrhoeae (NG) in the Indian Ocean. We characterized the main circulating genotypes of NG and their resistance profiles on two French islands in the Indian Ocean (Reunion and Mayotte).

Materials/methods: A retrospective study was performed between October 2016 and April 2017, within a network of laboratories on French overseas islands at which NG isolates are cultured. For 88 NG isolates, Minimum inhibitory concentrations (MICs) were determined for 6 antibiotics and genotyping was performed using the NG-MAST technique.

Results: NG isolates were recovered from symptomatic patients, 38 women (43.2%) and 50 men (56.8%), with a median age of 25 years. Genotypic diversity was low and the main genotypes belonged to ST5441 (19/88, 21.6%), followed by ST2318 (16/88, 18.2%) and ST2 (9/88, 10.2%). The ST5441 and ST2 isolates were fully susceptible to ceftriaxone and ciprofloxacin. All ST2318 isolates were resistant to ciprofloxacin, and 9/16 displayed a MIC of ceftriaxone above the ECOFF.

Conclusions: Our results show the circulation of three major clusters. ST5441 and ST2 belong to the most frequent genotypes in mainland France. All isolates with increased MICs for ceftriaxone belong to ST2318. This clonal complex is poorly represented in France but predominates in China, particularly in NG isolates with high MICs for ceftriaxone. Here, we highlight the link between the epidemiological features of NG and population flow in an island study model.

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Study of penicillin-susceptible Staphylococcus aureus in patients with bacteraemia. a multi-centre study in Spanish hospitals

Oluwafemi Mistourath Mama1, Carmen Aspiroz2, Laura Ruiz1, Emilia Cercenado1, José Manuel Azcona-Gutierrez3, Lorena Lopez-Cerero3, Francisco Javier Castillo2, Ana Isabel López-Calleja1, Carla Andrea Alonso4, Pilar Berdonces5, Jose Luis Torroba Alvarez5, Jorge Calvo6, Myriam Zarazaga1, Carmen Torres*1

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Abstract third-party references: *Study Group of LA-MRSA: Hospital de Vic, Barcelona (Maria Navarro and Anna Villamala), Hospital Arnau Villanova, Lleida (Mercé García); Hospital San Jorge, Huesca (Luis Torres, Ana Betrán), Hospital de Barbastro, Huesca (Pilar Robres, Javier Pereira), Hospital Univ. Miguel Servet, Zaragoza (Antonio Rezusta, Mª Cruz Villuendas, Pilar Palacian), Hospital Univ. Lozano Blesa (Cristina Seral), Clínica Universitaria de Navarra, Pamplona (José Leiva), Complejo Hospitalario de Navarra, Pamplona (Carmen Ezpeleta), Hospital Universitario de Burgos (Gregoria Megias), Hospital Universitario de Álava, Vitoria (Andrés Canut, Amaia Aguirre), Hospital Universitario de Donostia (María Gomáriz), Hospital Galdakao, Galdakao (Rafael Ayarza), Hospital Universitario Marqués de Valdecilla (María Siller). Partially supported by SEINORTE (Spain), Partially supported by project SAF2016-76571-R of AEI of Spain and FEDER of EU

Background: An increase of Staphylococcus aureus with penicillin susceptibility (SA-PENS) has been reported in several countries, which might be of therapeutic relevance. This work aimed to study the current situation in Spain, by determining the prevalence of SA-PENS isolates among patients with bacteraemia SA from Spanish Hospitals, and their molecular characteristics.

Materials/methods: A total of 852 SA isolates (MSSA, n=632) was recovered from blood cultures during 2018-2019 in 17 Spanish hospitals. Antimicrobial susceptibility profile was determined for all isolates [Vitek® (BioMérieux) and/or Microscan® (Beckman)] but only methicillin-susceptible SA (MSSA)-PENS isolates were included in this study. For all MSSA-PENS isolates, it was studied: 1) the presence of blaZ gene and of other non-beta-lactam antimicrobial resistance genes, according to the antimicrobial resistance profile, by PCR; 2) the spa-type by PCR/sequencing; 3) the presence of the genes coding for Panton-Valentine leucocidin (PVL, lukF/lukS-PV), exfoliative toxin A and B [eta, etb] and toxic shock syndrome toxin [tst], by PCR.

Results: Of 632 MSSA isolates, 132 were PENS [MIC: ≤0.12; 20.8%], all but five being blaZ-negative. MSSA-PENS-blaZ-negative represented 20.1% of MSSA and 14.9% of SA. Among MSSA-PENS-blaZ-negative isolates, 77 spa-types were detected with predominance of 1002/CC5 (11.02%) and 1571/CC398 (10.2%). 74.8% of MSSA-PENS-blaZ-negative isolates were pan-susceptible, while the remaining isolates were mostly resistant to macrolides (19%) and lincosamides (15%), harbouring one or a combination of these resistance genes: erm(A), erm(B), erm(C), erm(T), msr(A), lnu(A) and vga(A). Virulence genes were also detected among MSSA-PENS-blaZ-negative isolates (eta [n=8], etb [n=1] and tst [n=4]), however none of them carried the lukF/lukS-PV genes.

Conclusions: A high prevalence of MSSA/SA and MSSA-Pen-blaZ-negative/MSSA was detected among blood cultures SA isolates. Most of MSSA-PENS-blaZ-negative isolates were susceptible to non-beta-lactam antimicrobials. With 20% of invasive infections caused by MSSA-PENS, we can hypothesize that penicillin could be back as an antimicrobial option for MSSA. This situation raises therapeutic options which should be re-evaluated with wider studies and clinical assays.

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Abstract 8303

Genomic features of Argentinean KPC-2 producing *Klebsiella pneumoniae* ST25 and comparative genomics with carbapenem susceptible ST25 isolates

Daniela Cejas1,2, Vincenzo Di Pilato3, Lucia Henrici De Angelis4, Sabrina Di Gregorio1, Lucia Pallecchi4, Fabio Arena4, Gian Maria Rossolini3, Gabriel Gutkind*1,2, Marcela Radice1,2

1Universidad de Buenos Aires, Buenos Aires, Argentina, 2CONICET, Buenos Aires, Argentina, 3Università di Firenze, Firenze, Italy, 4Università di Siena, Siena, Italy

**Background:** The hypervirulent-*K. pneumoniae* (hvKp) strains display higher virulence potential, such as, an increased capsular production, giving a hypermucoviscous phenotype. Carbapenem resistance in hvKP has rarely been reported, and KPC-2 positive isolates are concentrated in four clonal lineages, ST11, 15, 101, 258/512. However, we have described the emergence KPC-2-hvKp strains, belonging to ST25, in Argentina. Objective: to explore the genomic features of these isolates and to establish the phylogenetic relationship with other worldwide ST25 strains, which did not displayed carbapenem resistance.

**Materials/methods:** KPC-2 producing isolates, hvKp2015 and hvKp2017, recovered in different hospitals in Buenos Aires, in 2015 and 2017, were included. These isolates displayed resistance to all beta-lactams, gentamycin and trimethoprim-sulphamethoxazole, susceptibility to amikacin and colistin, and intermediate to fluoroquinolones. WGS was performed on total DNA using Illumina MiSeq and reads were assembled using SPAdes. BLASTn, Plasmid Finder, Rest Finder, Kleborate, PROKKA, Roary, SnIPPy and GUBBINS, were used for sequence analysis. Phylogenetic studies were performed using IQ-Tree and RaxML.

Nineteen samples were analyzed, including hvKp2015 and hvKp2017, and all publicly available genomes of ST25 isolates from Australia(1), Belgium(1), Croatia(2), Denmark(1), Germany(2), Italy(2), Poland(1), Romania(2), Turkey(1), UK(3) and USA(1). All these genomes corresponded to clinical human samples.

**Results:** Genomes presented an approximate size of 5.0 Mb [6391 and 6088 CDS for Kp2015 and Kp2017]. *bla*KPC-2 plasmids belonged to IncL/M in both isolates. A capsular locus KL2-wzi72 resembling KN2 capsular type was detected, however the loci were not identical and genetic rearrangements were identified. Among resistance genes *bla*KPC-2, *bla*OXA-1, *aac(6')-Ib-cr, *aac(3)'-IIa, *aph(3'')-Ib, *aph(6)-Id, *dfrA14, *qnrB1, *oqxA* in both isolates and *bla*CTX-M-15 hvKp2015.

Whole and core genome phylogenetic analysis showed strong relationship and two main clusters could be recognized. Argentinean samples grouped together with Italy, Belgium and USA isolates. The same group setting was observed when a closely related ST (ST65) was used to route the phylogenetic tree.

**Conclusions:** Phylogenetic analysis of ST25 isolates including KPC-2-producing isolates is not available in indexed literature. Carbapenem-resistant *K. pneumoniae*-ST25 appear to have evolved from susceptible strains, indicating a confluence of virulence and carbapenem resistance, which might poses major problems in the management of *K. pneumoniae* infections.

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**Abstract 8304**

**Retrospective and prospective evaluation of the rapid carbapenem inactivation method test for AmpC-producers**

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**Background:** Simple, cost-effective and rapid differentiation methods between Enterobacterales that produce a carbapenemase and those that are carbapenem-resistant through non-enzymatic mechanisms are mandatory. Herein, we optimised the protocol of the rCIM for efficient use with AmpC hyper-producers.

**Materials/methods:** The classic rCIM was performed as previously reported. Experimentally, cloxacillin was added in the first step of the test. The test was initially validated on 48 well-characterized strains belonging of the various *Enterobacter* species. These consisted of 47 non-carbapenemase producing strains and one strain which harboured OXA-204. After validation, the test performance was evaluated on 6 clinically-relevant AmpC hyper-producing strains.

**Results:** Within the 48 validation strains, CarbaNP had a specificity of 95.74%, but did not detect an OXA-204 producing isolate. Using the standard rCIM protocol, the specificity was 91.49%, being falsely positive for 4 isolates. With the addition of cloxacillin, the rCIM’s specificity was 100% (95% CI: 92.45 - 100%). Both rCIM protocols correctly identified the OXA-204 producer. To evaluate test characteristics, 61 chromosomal and plasmid harbouring AmpC isolates have been evaluated. Using the standard rCIM protocol, the sensitivity and specificity of rCIM was 95.74% and 50%, respectively, being falsely positive for 7 isolates and negative for 2 isolates (one IMI-1, and one LMB-1-producers). Using the modified rCIM protocol, with the addition of cloxacillin, the sensitivity and specificity was 93.62% (95% CI: 82.46 - 98.66%) and 100% (95% CI: 76.84 - 100%), respectively. Three isolates were falsely negative: the LMB-1-, an NDM-1- and an IMI-3-producers. When colonies were tested off Uri4 and carbapenem-infused media all but the LMB-1-producing isolate gave a positive test, suggesting very low carbapenemase production in the absence of an inducer.

**Conclusions:** The addition of cloxacillin in the rCIM protocol can be used to improve the test’s performances for AmpC-producers as it can differentiate between a carbapenemase and AmpC-hyperproduction. The rCIM can therefore be successfully used as a rapid, cost-effective phenotypic test for carbapenemase detection in AmpC-producers in low resource laboratories.

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**Abstract 8305**

**Dengue awareness in patients with acute febrile illness in Sindh province of Pakistan**

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**Abstract third-party references:** Defense Threat Reduction Agency, Basic Research Award # HDTRA1-14-1-0022, to the University of Florida

**Background:** Dengue has been endemic in Pakistan since 2001 but large epidemics continue to occur every few years. It is important to know how the knowledge of dengue has affected arboviral disease occurrence over different socioeconomic backgrounds. We describe here the rate of awareness of dengue in febrile patients evaluated for arboviral infections in Sindh province of Pakistan, stratified over socioeconomic groups.

**Materials/methods:** Patients presenting with acute febrile illness at medical centers in five cities of Sindh, Pakistan, from April 2015 to July 2017 were enrolled in a study screening for arboviral infections: Dengue (DEN), West Nile (WN), Chikungunya (CHIK) and Japanese Encephalitis (JE). Dengue was confirmed with NS1 antigen, IgM ELISA positivity; CHIK diagnosed using IgM ELISA and PCR; WN and JE by IgM ELISA, further confirmed on Plaque Reduction Neutralisation Test (PRNT). Study participants were stratified by socioeconomic status into lower (LSE) quartile, middle half (MSE) and upper (USE) quartile. Dengue awareness was determined using a questionnaire pertaining to knowledge on dengue transmission, prevention, treatment, source of information, and preventive practices.

**Results:** A total of 989 patients between 6-86y were enrolled with five major febrile syndromes: arthralgia/myalgia (64.7%), headache (33.3%), neurologic (20.5%), petechial or macular rash (8.8%) and bleeding diathesis (6.2%). Of these, 40.6% tested positive for arboviruses: DEN (51.2%), CHIK (24.6%), WN (20.4%) and JE (3.7%). Only 54.9% LSE had knowledge of dengue compared with 72% MSE and 79.7% USE. Similar proportion of LSE, MSE and USE correctly identified how dengue was transmitted (54.6%, 70.5%, 79.7%), prevented (47.4%, 66.7%, 71.7%), and treated (50.5%, 69%, 78%), and had received public awareness messages (50.9%, 65.4%, 72%). All three groups similarly agreed on dengue and malaria being a major problem in Pakistan (84%, 82.7%, 86.7% respectively). 24.2% of LSE versus 49.4% MSE and 66.7% USE had covered drains in their homes, 62.8% LSE, 80.2% MSE and 84.7% USE covered their water storage containers, and 74% LSE, 84% MSE and 87.3% USE used indoor insecticide sprays.

**Conclusions:** Dengue awareness and preventive activities differ by socioeconomic status in febrile patients evaluated for arboviral infections.

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Diagnostic value of IgG avidity and/or Western blot test for the diagnosis of Rubella virus infection during pregnancy

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Background: Rubella infection during early pregnancy often results in congenital Rubella syndrome. Specific Immunoglobulin (Ig)M research is recommended for Rubella infection screening. However, the diagnosis of Rubella infection during pregnancy requires mostly the use of additional tests such as Rubella virus (RV) IgG avidity and/or IgG Western-blot test (WB). We aim to evaluate the interest of these two tests to distinguish old and recent Rubella infection in woman pregnancy.

Materials/methods: A retrospective study was conducted from January 2007 to November 2019 including 107 pregnant women with detectable anti-Rubella IgM, with or without clinical symptoms.

Anti-Rubella IgM and IgG were determined respectively using ELISA technique (PLATELIA RUBELLA IgM-Bio-Rad, France) and automated ELFA (VIDAS RUB IgG II, Biomerieux, France). RV IgG avidity and IgG WB were performed using commercial kits (Euroimmun, Lübeck, Germany). Old Rubella infection has been considered face to WB anti-E2 IgG detection.

Results: Among 107 women with suspected Rubella primary infection based on positive IgM, recent infection was concluded in only 21 cases (19.6%) by low IgG avidity and in 29 cases (27%) by negative WB anti-E2 IgG. Among 21 women having low IgG avidity, 14 have recent rubella western blot pattern. Only 38 from 50 women, with high IgG avidity, have a WB pattern concordant with an old infection. Therefore, concordance rate between the two techniques is around 73.2%.

The WB test allows us to exclude recent Rubella infection in patients with low (n=21) or intermediate IgG avidity (n=36) in 42% (n=24). However, high IgG avidity excludes recent Rubella infection in patients with non conclusive WB (n=16) or with negative WB anti-E2 IgG (n=29) in 26.66% (n=12).

Conclusions: Although a medium concordance rate between RV IgG Avidity and WB test, combination between the two techniques is highly required for a better Rubella infection diagnosis.

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Abstract 8310

**Evaluation of FAST-Prep Liquid Colony for early antimicrobial sensitivity testing of positive blood culture by disk diffusion method**

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**Background:** Conventional antimicrobial susceptibility testing (AST) of microorganisms from positive blood cultures (PBC) can take ≥ 2 days. In order to improve the turnaround time for AST on a PBC, CLSI and EUCAST have made efforts to standardize procedures for disk diffusion (DD) direct from a PBC. Qvella (Richmond Hill, ON, CA) has recently developed FAST-Prep, an automated centrifugal sample preparation system that rapidly delivers a Liquid Colony consisting of a purified, concentrated, viable cell suspension directly from a PBC. This study was performed to investigate the feasibility of DD AST off of a PBC using a FAST-Prep Liquid Colony.

**Materials/methods:** Contrived PBC samples were prepared by spiking 6 species of Gram-positive and 4 species of Gram-negative bacteria (3-5 strains per species) into FA® Plus bottles and incubating in the BACT/ALERT® VIRTUO® System (bioMerieux, Durham, NC). After positivity, 3 mL of PBC was added to the FAST-Prep cartridge. After 20 minutes of processing in the FAST-Prep instrument, the Liquid Colony was removed from the cartridge and a 0.5 McFarland sample was prepared for DD AST. In parallel, the DD AST from a PBC was performed using 4 drops of PBC (CLSI direct method). Both methods were compared to conventional colony-based DD AST. After 16-18 hours of incubation zone diameters and S/I/R interpretations were determined. Categorical agreement (CA) and errors for both DD AST methods were calculated. In addition, colony plate counting was performed on 0.5 McFarland suspensions of Liquid Colony and the plate colony to determine biomass recovery and sample purity.

**Results:** CA for a FAST-Prep DD AST for Gram-positive and Gram-negative bacteria was 95.6% and 98.6%, respectively, compared to CA for CLSI DD AST of 77.2% and 81.9%, respectively. Biomass in the Liquid Colony was 7.2x10^8 and 1.2x10^9 CFU for Gram-positive and Gram-negative bacteria, respectively. Cell concentration in the 0.5 McFarland suspension of the Liquid Colony was 3.7x10^7 and 5.9x10^7 CFU/mL for Gram-positive and Gram-negative bacteria, respectively, which was similar to the concentration for the reference colony suspension.

**Conclusions:** The results support the potential role of FAST-Prep in providing a Liquid Colony for use in rapid AST.

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Abstract 8317

Detection of \textit{blaKPC-2} in a conjugative IncP-6 plasmid in \textit{Escherichia coli} isolated from wastewater in Romania

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\textbf{Background:} \textit{Escherichia coli} is one of the leading causes of nosocomial and community-acquired infections worldwide which makes the emergence and dissemination of carbapenem-resistant strains a main risk for global public health. This is the first study reporting the molecular characterization of a carbapenem-resistant \textit{E. coli} strain isolated from a wastewater treatment plant in Romania.

\textbf{Materials/methods:} \textit{E. coli CE1} strain was isolated from a wastewater treatment facility in 2018, on CHROMID\textsuperscript{\textregistered} CARBA selective medium. The presence of carbapenemases was confirmed by the Blue-Carba phenotypic test and by PCR and sequencing. Transferability of carbapenem resistance was investigated by conjugation (liquid matting) followed by PCR confirmation, using the \textit{E. coli} J53 strain as a recipient. The \textit{E. coli} CE1 strain was subjected to paired-end whole genome sequencing using a MiSeq System Sequencer (Illumina). De novo assembling of the reads into contigs was performed with Spades software and annotation with CARD, BLAST, ResFinder, PlasmidFinder, VirulenceFinder. ISSs were annotated using ISFinder and INTEGRALL.

\textbf{Results:} The \textit{E. coli} CE1 strain (the nearest MLST result: ST3486) exhibited high resistance to \textit{β}-lactams correlated with the presence of \textit{blaNDM-1}, \textit{blaKPC-2}, \textit{blaTEM-1B}, \textit{blaOXA-1} genes, out of which only \textit{blaKPC-2} proved to be transferred by conjugation. Sequencing revealed plasmids harboring resistance genes belonging to 5 other classes of antibiotics apart from \textit{β}-lactams, namely aminoglycosides: (aac(3)-la, aac(6')-lb-cr, aph(3')-Ia, aadA1, aac(3)-Ila, rmtC); fluoroquinolones: qnrB19, aac(6')-lb-cr; phenicols: catA1, catB4; sulphonamides: sul1, sul2 tetracyclines: tet(D), and macrolide: md diluted (A). Some of these genes grouped on the same genetic platforms, such as [catB2, bla\textsubscript{GIM4}, aac(6')-lb-cr] or [bla\textsubscript{NDM1}, rmtC]. The genetic context of \textit{blaNDM1} gene exhibits same conserved region as other plasmids previously reported in Romania, comprising ISCR14-rmtC-ISAbac125-bla\textsubscript{NDM1}-ble\textsubscript{MBL}. The \textit{blaKPC-2} gene is integrated in a Tn3-like transposon [ISApu1 – ISApu2 – tnpA – tnpR – ISKpn27 – ΔblaTEM – blaKPC-2 – ΔISKpn6] within an IncP6 plasmid previously encountered in wastewaters in other countries.

\textbf{Conclusions:} The transferability of \textit{blaKPC-2} gene raises concern, as commensal bacterial strains may acquire and disseminate this gene. Therefore, the characterization of resistome from wastewater in our country is mandatory.

We acknowledge the financial support of UEFISCDI research projects PN-III-P3-1.1-PD-2016-2137, ERANET-JPI-EC-AMR-AWARE-WWTP, PN-III-P4-ID-PCCF-2016-0114, PN-III-P1.1-PD-2016-1798.

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Abstract 8318

Real-life experience with ceftazidime-avibactam in South Spain

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Background: Real-life studies in the treatment of carbapenem-producing Enterobacteriaceae and carbapenem-resistant P. aeruginosa are limited and new antibiotics have recently been launched. We aim to describe our clinical experience using Ceftazidime-avibactam for different severe infections.

Materials/methods: Retrospective study of episodes of infection treated with ceftazidimeavibactam. Efficacy and safety were evaluated as 14 and 30 day mortality and occurrence of adverse events.

Results: Twenty-one patients were included. The median age was 69 years (IQR: 22–72), 10 (47.6%) were male and the median Charlson index was 5 (IQR: 2-8). McCabe score was ultimately fatal in 6 (28.6%). The most frequent sources of infection were respiratory (23%) followed by intra-abdominal (24%) and urinary (29%). 14 (66.7%) were admitted in ICU. Median length of stay in hospital and ICU were 65 (IQR: 41-89) and 33 (2-65) respectively. Eighteen (86%) patients had a severe infection (defined as presence of sepsis or septic shock) and the median Increment score was 8 (IQR: 6-13). Median Giannella score 14 (IQR: 10-16). The 30-day and 90-day mortality rates were both 38.1%. Clinical cure was achieved in 14 (66.7%) of episodes. Only one (4.8%) patient presented adverse event (seizures) in the context of impaired renal function. Among patients with Increment score ≥7 (15, 71.4%), eight died by 30-day and only 7/15 received combine therapy. The most frequent associations with ceftazidime-avibactam were amikacin (4/8) and metronidazole (3/8).

Beside colonization, isolated pathogens in clinical samples were: OXA-48-like carbapenem producing Klebsiella pneumoniae (N=12), IMP (N=1), VIM (N=1) and OXA48 (N=2) producing Enterobacter cloacae and 2 (9.5%) carbapenem-resistant Pseudomonas aeruginosa. In one Klebsiella pneumoniae isolate the carbapenemases were confirmed to be IMP and OXA-48 types.

Conclusions: From our limited experience, ceftazidime-avibactam seems to be an effective drug with a convenient safety profile for the treatment of patients with severe infections due to carbapenem resistant pathogens and limited therapeutic options.

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Abstract 8319

**Beta-D-glucan to aid the diagnosis of Pneumocystis pneumonia in HIV-positive patients**

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**Background**: Confirmation of a PCP diagnosis often requires invasive procedures. Serum concentrations of beta-d-glucan (BDG) are elevated in HIV positive patients with *P. jirovecii* pneumonia (PCP) and more readily available to aid the diagnosis of PCP. We summarized the experience with BDG in HIV positive patients presenting to three hospitals in London, UK.

**Materials/methods**: We retrospectively identified HIV positive patients with a BDG result and bilateral infiltrates on chest x-ray from January 2018 to May 2019. A confirmed PCP diagnosis required demonstration of *P. jirovecii* on direct stain or by PCR in bronchoalveolar lavage, sputum or on lung biopsy specimens. A BDG concentration >80pg/mL measured using the Fungitell assay was considered a positive BDG result.

**Results**: Thirty-four patients (Median age 44; CD4 count 44; HIV Viral load 446684) including 21 (61.7%) with confirmed PCP, were studied. All patients with confirmed PCP, compared to 8 of 13 (61.5%) without confirmed PCP, had a positive BDG (p<0.01, NPV 100%, PPV 72.41%). Patients with confirmed PCP (both median and lower quartile >500pg/mL) compared to those deemed not to have PCP clinically (Median 47, IQR 10-95pg/mL) had significantly higher serum BDG levels (t 9.17, p<0.001). The distribution of BDG concentrations is shown in table 1.

**Conclusions**: We confirmed a high negative predictive value of serum BDG levels for confirmed PCP. This suggests that in HIV positive patients, BDG levels in combination with chest x-ray findings and clinical parameters may be useful to rule out PCP.

Table 1: The distribution of beta-d-glucan concentrations between patients with and without confirmed PCP

<table>
<thead>
<tr>
<th>Beta-D-glucan concentration (pg/mL)</th>
<th>Confirmed PCP</th>
<th>No Confirmed PCP</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;80</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>80-260</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>260-399</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>&gt;300</td>
<td>19</td>
<td>4</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>18</td>
</tr>
</tbody>
</table>

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Detection of Aspergillus spp. in bronchoalveolar lavage fluid of haematological and non-haematological patients with invasive aspergillosis by real-time PCR

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Background: To evaluate the sensitivity of real time PCR with High Resolution Melt analysis (mHRM-RT-PCR) test for detection of Aspergillus spp. in bronchoalveolar lavage fluid (BAL) of hematological and non-hematological patients with invasive aspergillosis (IA).

Materials/methods: The investigation included 60 BAL samples collected during 2014-2019 from 30 hematological and 30 non-hematological patients with diagnosis of IA confirmed by mycological methods according to ESCMID-ECMM-ERS, 2017. As controls, 50 BAL were collected from patients without mycoses. Clinical samples were examined by fluorescent microscopy and culture. Fungal DNA was extracted from BAL by a chloroform-isoamyl extraction method. DNA amplification was performed using aspergillus-specific primers and EvaGreen based mHRM-RT-PCR on Rotor-Gene 6000 cycler. Detection of galactomannan (GM) in BAL was performed using “Platelia Aspergillus Ag” (Bio-Rad). Sensitivity and specificity for the PCR assay and GM were calculated.

Results: Microscopy of 30 BAL from hematological patients with IA was positive in 50% cases. Aspergillus spp. were isolated in 83%: A. fumigatus [63%], A. niger [19%], A. flavus [6%], A. versicolor [2%]. From 3 patients (10%) two different species were isolated: A. fumigatus + A. niger [6%] and A. fumigatus + A. flavus [3%]. In 30 non-hematological patients with IA microscopy of BAL was positive in 60% of cases. Aspergillus spp. were isolated in 57%: A. fumigatus [31%], A. niger [31%], A. flavus [11%], A. ochraceus [1%]. From 8 patients (26%) two or more different species were isolated including A. ustus [6%] and A. versicolor [3%]. At similar specificity (83% vs. 86%) PCR assay performed in BAL yielded 89% sensitivity in hematological and 83% in non-hematological patients. GM test was positive in 77% BAL samples from hematological and 60% from non-hematological patients. The positive results of PCR assay correlated with positive results of microscopy and culture in 75% and 78% for hematological patients and in 72% and 80% for non-hematological patients with IA.

Conclusions: This study indicated that the mHRM-RT-PCR may be a very useful tool for detection of Aspergillus spp. in BAL of hematological and non-hematological patients with IA. Sensitivity of PCR assay in BAL was higher than sensitivity of GM test and basic mycological methods.

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Abstract 8324

Antimicrobial susceptibility of Enterobacterales and Pseudomonas aeruginosa to carbapenems and occurrence of carbapenemase producers: results from SMART study in South Serbia, 2012-2018

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Abstract third-party references: International Health Management Associates [IHMA]

Background: Bacterial resistance to carbapenems including occurrence of carbapenemase producers is an important growing threat to public health. We present the data of the antimicrobial susceptibility of Gram-negative bacilli to carbapenems as a part of the Study for Monitoring Antimicrobial Resistance Trends [SMART] in the Clinical Center Niš, South Serbia.

Materials/methods: The study included 1146 Gram-negative bacilli from the fam. Enterobacterales and 221 isolates of Pseudomonas aeruginosa collected from patients with intra-abdominal infections (IAI), urinary tract infections (UTI) and lower respiratory tract infections (LRTI), during 2012-2018. The isolates were processed at the IHMA laboratory. Minimal inhibitory concentrations [MICs] were determined by broth microdilution and susceptibility interpreted according to European Committee on Antimicrobial Susceptibility Testing guidelines. Multiplex PCR was used to detect carbapenemase genes.

Results: All enterobacterial isolates were tested for susceptibility to ertapenem and imipenem, and 535 of them tested to meropenem. Susceptibilities of all isolates to these carbapenems were 84.12%, 89.2% and 92.1%, respectively. Susceptibilities of isolates from different sources shown in the table. During the studied period, decrease in susceptibilities to ertapenem, imipenem and meropenem was noted for Klebsiella spp. resulting in 67.5%, 87.5% and 87.5%, respectively. For Escherichia coli, susceptibilities retained for all tested carbapenemes. Susceptibilities of 221 isolates of Pseudomonas aeruginosa to imipenem and meropenem were 56.1% and 51.8%, respectively. There was a trend of a decrease in susceptibility to imipenem, from 71.4% in 2012 to 34.4% in 2018. Susceptibility to imipenem and meropenem was the lowest for LRTI isolates [41.9% and 43.9%, respectively]; susceptibility for UTI that were 57.69% and 63.64%, respectively, and the highest susceptibility were for IAI (78.9 and 79.2%). Screening by multiplex PCR to detect β-lactamase genes among non-Proteae Enterobacteriaceae [NPE] showed that in Serbia 16.3% of all isolates were carbapenemase producers, with presence of NDM, OXA-48-like and KPC enzymes. In Pseudomonas aeruginosa isolates, this percent was 16.9%, with NDM and GES enzymes.

Conclusions: Increasing resistance to carbapenems and the onset of carbapenemase producers require continuous monitoring of resistance, and introduction of measures for its prevention.

<table>
<thead>
<tr>
<th>Specimen source of Enterobacterales</th>
<th>Percent (%) of susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ertapenem</td>
</tr>
<tr>
<td>IAI</td>
<td>91.48</td>
</tr>
<tr>
<td>LRTI</td>
<td>88.3</td>
</tr>
<tr>
<td>UTI</td>
<td>72.51</td>
</tr>
</tbody>
</table>

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Abstract 8325

**An automated data extraction from primary-care paediatricians' computers: a French paediatric ambulatory research in infectious diseases**

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**Background:** Infectious diseases account for 50-70% of ambulatory pediatric daily practice. In order to improve the diagnostic performance of primary-care pediatricians by providing real time data on epidemiology of several infectious diseases, we have set up a national surveillance network, PARI (Pediatric and Ambulatory Research in Infectious diseases) using an automated data extraction from the primary-care-pediatricians' computer. The participating pediatricians were specifically trained in diagnostic and treatment of infectious diseases and the use of rapid diagnostic tests.

**Materials/methods:** We daily prospectively collect anonymized data (age, sex, height, weight, daycare attendance, vaccines, diagnosis and prescriptions) of children with infectious diseases in 100 primary-care-pediatricians all over France using the same software (Axi5-Infansoft®, CompuGroup Medical).

**Results:** Between September 2017 and November 2019, data on 47,446 patients, 65,752 consultations, 92,204 diagnoses, 328,851 vaccines and 278,521 drug-prescriptions were collected. Mean age at diagnosis was 3.0 ± 2.7 years and boys accounted for 58.4%. Frequencies of the different infectious diseases were weekly and automatically provided on a dedicated website as graphs for all pediatricians, to allow them to monitor the epidemiology of the diseases, locally as well as at national level. If the epidemiology over the two years and half was identical for otitis, bronchiolitis, group A *Streptococcus* pharyngitis, gastro-enteritis and enterovirus infections, the peak for influenza had already been reached by the end of December in 2017, whereas it had just begun in December 2018.

**Conclusions:** For the first two years and half of this study, the seasonal distribution of the pediatric infectious diseases is perfectly stackable, except for influenza diseases. These robust results validate the PARI network as an efficient and reliable tool for monitoring infectious diseases and enforce the impact of this automated surveillance on the pediatricians’ practice and public health.

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Abstract 8334

Acquired resistance to colistin in Enterobacteriaceae isolated at university hospital of Algiers
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**Background:** The emergence of plasmid resistance to colistin currently fears evolution towards panresistance particularly in carbapenemase-producing Enterobacteria. Such strains begin to be described in our hospital. The aim of this work is to discriminate between colistin-resistant Enterobacteria, those involving the MCR-1 mechanism and those with a chromosomal mechanism.

**Materials/methods:** This is a five-year study (2015-2019) in which any Enterobacterial strain with reduced sensitivity to colistin [MIC ≥ 2 μg/ml] was studied. This MIC was determined by microdilution on Mueller-Hinton II broth (cation adjusted) as currently recommended by CLSI. For each of these strains, a PCR search of the mcr-1 and mcr-2 genes was performed. A rapid immunochromatographic detection test of MCR-1 (NG biotech® NG-Test MCR-1) was performed for strains with a PCR positive PCR result.

**Results:** Fifteen colistin-resistant Enterobacteriaceae strains were isolated in our hospital during this period. Nine strains isolated from infections [Four from blood culture, three from urine and two from pus] and six strains from rectal carriage. Among the isolated species we report:

- Six strains of *Escherichia coli*: four of them showed a colistin MIC of 4 μg/ml and were carbapenem sensitive. These strains showed mcr-1 positive PCR and a positive MCR-1 test. Two other strains of *Escherichia coli* having a colistin MIC of 16 μg/ml and 32 μg/ml gave a PCR mcr-1 and mcr-2 negative result and were carbapenem resistant strains.

- Nine strains of *Klebsiella pneumoniae*: all were carbapenem resistant strains and showed a colistin MIC greater than 32 μg/ml. The nine strains showed PCR mcr-1 and mcr-2 negative results.

**Conclusions:** This preliminary study demonstrates the existence of a plasmid support for colistin resistance in our hospital and emphasizes the risk of dissemination of this mechanism to other species that could become pan-resistant.

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Abstract 8335

**Inoculum effect of OXA-48-like-producing Enterobacteriaceae against ceftazidime-avibactam**

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**Background:** The spread of OXA-48 producing Enterobacteriaceae is a major issue in the diffusion of multidrug-resistance. Several studies have evaluated the clinical relevance of ceftazidime/avibactam (CAZAVI) in OXA-48-producing Enterobacteriaceae infections without exploring the impact of high inocula.

The aim of this study was to investigate in vitro the impact of high inocula of OXA-48-producing Enterobacteriaceae on minimum inhibitory concentrations [MIC] of CAZAVI and meropenem (MER).

**Materials/methods:** Enterobacteriaceae isolates were collected from January 2013 to June 2018. A total of 56 isolates were tested, including 37 *E. coli* (66%), 14 *K. pneumoniae* (25%), 4 *C. freundii* (7.2%), 1 *E. cloacae* (1.8%). For each isolate, 3 inocula: 0.5; 1 and 5 Mac Farland (MF) were prepared. Bacterial suspension was plated on Mueller-Hinton agar to determine by E-test (bioMérieux) for MER and CAZAVI according to EUCAST guidelines. After 24h, the MIC were compared to the averages MIC of MER and CAZAVI for each inoculum. Bacterial genomes of the isolates were sequenced with a NextSeq (2×151 bp; Nextera XT library, Illumina) and assembled with SPAdes (v3.1 2.0). Resistance genes were checked using abricate (v0.7) and resfinder. Averages MIC were compared according to the presence/absence of genes encoding for CTX-M enzymes.

**Results:** Among the 56 strains, 49 (87.5 %) were OXA-48 and 7 (13.5 %) were OXA-181 carbapenemase. Twenty isolates (36%) isolates carried genes encoding for CTX-M: CTX-M-15 (15; 27%) CTX-M-14, (4; 7%) and CTX-M-1 (1; 2%).

For all strains, we found that averages MIC for all tested inocula were not significantly different with the CAZAVI (p>0.5). In comparison we observed that averages MIC of MER for all inocula were significantly different (p<0.01). (Figure 1)

The presence of a CTX-M enzyme did not change the MIC results for both antibiotics.

**Conclusions:** In this study, we observed in vitro an inoculum effect of meropenem for Enterobacteriaceae-producing OXA-48 or OXA-181, which was not observed with the ceftazidime/avibactam combination. This result must be confirmed on a larger number of strains and suggests that ceftazidime/avibactam may be a better option than meropenem in high inoculum infections.

ComParison of different inocula of OXA-48-like producing Enterobacteriaceae on ceftazidime/avibactam and meropenem MIC

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ComParison of four ESBL detection tests directly from blood cultures and urine samples

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Background: The 3rd generation cephalosporins (3GC)-resistance in Enterobacteriales, mainly due to Extended-Spectrum Beta-Lactamase (ESBL) production, is increasing worldwide. Bacteremia, as urinary tract infections, due to ESBL-producing Enterobacteriales increase delays to initiate effective antibiotic therapies. In this context, we evaluated 4 ESBL detection tests directly from blood cultures (BC) and urine samples based on 4 different principles: colorimetry (β-Lacta Test (BLT), Bio-Rad), molecular biology (BCID-GN cartridge including the CTX-M target, ePlex apparatus [GenMark]), electrochemistry (BL-RED, Coris) and immunochromatography (NG-CTX, NG-Biotech).

Materials/methods: Between May and September 2018, 46 BC and 52 urine samples with Gram-negative bacilli (GNB) at the microscopy examination were tested. The ePlex and the BLT were prospectively tested and the BL-RED and NG-CTX were performed from samples conserved at -80°C. The results were compared to antimicrobial susceptibility testing interpreted according to EUCAST 2018 recommendations.

Results: Among the 46 GNB-positive BC, 32 Enterobacteriales including 9 ESBL-producers (CTX-M type), and 14 other GNB were identified. The 9 ESBL enzymes were detected by BLT, BL-RED and NG-CTX while ePlex detected 8/9. For the 37 remaining BC, no enzyme was detected by each test, except for the BL-RED which was positive for 1 S. maltophilia and 1 VIM-producing P. stutzeri-positive BC. Among the 52 GNB-positive urines, 52 were positives with Enterobacteriales, including 11 ESBL producers (10 CTX-M). BLT, ePlex, NG-CTX and BL-RED detected 9, 9, 10 and 11 of ESBL-producing Enterobacteriales respectively. No false positives were found except for the BL-RED which was positive for 5 urine samples with 3GC-susceptible Enterobacteriales.

The Sensibility/Specificity/Positive Predictive Value/Negative Predictive Value on BC and urine samples were 100%/100%/100%/100% and 91%/100%/100%/98% for the NG-CTX, 100%/100%/100%/100% and 82%/100%/100%/95% for the BLT, 89%/100%/100%/97% and 92%/100%/100%/95% for the ePlex, and 100%/95%/82%/100% and 100%/95%/65%/100% for the BL/RED, respectively.

Conclusions: Finally, ESBL detection tests may constitute valuable tools for ESBL-detection directly from blood cultures and urine samples, notably the BL-RED which has 100% of sensibility on both specimens. A combination of these tests could be a best way to improve probabilistic antibiotic therapy and save on broad spectrum antibiotics.

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Abstract 8337

Vancomycin plus piperacillin-tazobactam and the risk for acute kidney injury: what is the effect size?
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Background: Accumulating evidence suggests that vancomycin (V) combined with piperacillin-tazobactam (PT) is associated with increased risk of acute kidney injury (AKI) defined using serum creatinine. Meta-analyses suggest a greater risk of AKI with V+PT compared to PT, V, or other beta-lactams (BL) alone. However, the impact of heterogeneity between studies and potential publication bias on the minimum detectable effect-size has not been robustly evaluated.

Materials/methods: We performed a systematic literature to find systematic reviews comparing V+PT to comparators using PubMed. Meta-analyses were sought and study-level data were extracted to generate effect-size, heterogeneity, and random-effects estimates. Inverse-variance weighted random-effects meta-analyses were performed using the meta package in R. Trim-and-fill was used to adjust for publication bias. Effect-size estimates of increased risk of AKI with V+PT tested were: 10, 12, 14, 16, 18, or 20% vs. comparators. We used Monte Carlo simulation to generate 1000 trials for each of these mean effect-sizes in Microsoft Excel. The variance estimator tau was used as the standard deviation of the effect-sizes for all simulations. Simulated trial effect-sizes were compared against the lower bound of the 95% confidence interval (CI) the trim-and-fill random-effects model. If a given mean effect-size exceeded the lower bound of the 95% CI in 90% or more of simulated trials then it was considered as a detectable difference.

Results: The results of the MCS are shown in Table 1 below. Compared to V alone, V+PT was only considered a detectable difference if the risk increase was 18% or greater. Compared to BL or PT alone, V+PT was only considered a detectable difference if the risk increase was 16% or greater.

Table 1.

<table>
<thead>
<tr>
<th>Mean effect-size</th>
<th>10%</th>
<th>12%</th>
<th>14%</th>
<th>16%</th>
<th>18%</th>
<th>20%</th>
</tr>
</thead>
<tbody>
<tr>
<td>V+PT vs. V</td>
<td>60%</td>
<td>70%</td>
<td>80%</td>
<td>85%</td>
<td>93%</td>
<td>95%</td>
</tr>
<tr>
<td>V+PT vs. BL</td>
<td>82%</td>
<td>85%</td>
<td>88%</td>
<td>93%</td>
<td>95%</td>
<td>97%</td>
</tr>
<tr>
<td>V+PT vs. PT</td>
<td>58%</td>
<td>73%</td>
<td>83%</td>
<td>91%</td>
<td>96%</td>
<td>98%</td>
</tr>
</tbody>
</table>

Conclusions: Our simulation study suggests that small effect-sizes (i.e., less than 16% increased risk of AKI) cannot reliably be distinguished from a null effect, given the heterogeneity in the observed literature. Our findings have implications for sample size estimation for any future prospective comparative trials.

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Exploiting CRISPR-Cas9 to eradicate ESBL genes and tracing conjugative plasmids within complex microbial communities at single-cell resolution

Reetta Penttinen*1,2, Lara Ambrosio Leal Dutra2, Pilvi Ruotsalainen2, Ole Franz2, Cindy Given2, Kimi Nurminen2, Pauliina Salmi2, Marja Tiirola2, Matti Jalasvuori2

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Background: Bacteria acquire resistance towards antimicrobial compounds via resistance genes. These genes are often localized in mobile plasmids, which disperse between bacteria via conjugation and even across species boundaries. Besides the fact that the exposure to antibiotics selects for conjugative plasmids, they can also serve as life-buoys in cases where originally susceptible bacteria receive resistance from the resistant bacteria. This so-called evolutionary rescue can occur even after the exposure to lethal antibiotic concentration and efficiently rescue susceptible bacteria from extinction. Resistance genes could be eradicated from bacterial reservoirs by utilizing CRISPR-Cas9 system. It acts in a sequence-specific manner and is programmable to target any desired DNA sequence, such as antibiotic resistance genes. Yet, the challenge in recording the movements of conjugative plasmids has been the lack of efficient tools for analyzing complex bacterial populations at single-cell resolution.

Materials/methods: With genetic engineering, we generated a conjugative CRISPR plasmid system that targets ESBL-genes. Further, we developed a single-cell method on droplet digital PCR (ddPCR) platform in order to identify the bacteria that harbor the target plasmid. Briefly, individual bacterial cells are enclosed into droplets in a ddPCR reaction. During PCR, a fusion amplicon consisting of 16S rRNA and the desired target gene is produced. By amplicon sequencing, the subpopulation harboring the target gene can be identified.

Results: We show that the conjugative CRISPR-Cas9 system efficiently decreases the frequency of drug-resistant phenotypes within bacterial communities. Additionally, we demonstrate that the single-cell ddPCR technique allows the detection of plasmids together with their hosting bacteria within a heterogeneous bacterial population. We also discuss the potential challenges and limitations of using CRISPR-based molecular tools for eradicating antibiotic resistance as well as in bacterial sample preparation for single-cell analysis.

Conclusions: Our results suggest that CRISPR-based antimicrobials can be a promising weapon against antibiotic resistance. Furthermore, the single-cell ddPCR method is suitable for localizing the desired plasmid within bacterial populations and it may be applied to resolve various research questions where there is a need to identify which bacteria harbor the specific gene of interest.

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Prevalence of blaZ gene types and the inoculum effect with cefazolin among bloodstream isolates of methicillin-susceptible Staphylococcus aureus

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**Background:** Cefazolin, the first generation cephalosporin used as the second line of treatment in bacteriemia caused by methicillin susceptible Staphylococcus aureus (MSSA), offers certain advantages over drugs used in the first instance as cloxacillin. However there have been concerns about cefazolin treatment failure associated with b-lactamase production and inoculum effect. The aim of this study was to determine the prevalence of both blaZ gene and the inoculum effect.

**Materials/methods:** A total of 54 MSSA bloodstream isolates were included in the study. All isolates were identified using standard methods. The blaZ gene was detected using PCR. The MICs of cefazolin, were determined by the broth microdilution method using standard and high inoculum. A pronounced inoculum effect was defined as a ≥4-fold increase in the MIC between the standard and high inoculum.

**Results:** BlaZ gene was detected in 47/54 isolates (87%). Using standard inoculum, values for CMI50 and CMI90 were 0.5 and 4µg/ml, respectively. Using high inoculum, values for CMI50 and CMI90 were 0.5 and 16µg/ml, respectively. A pronounced cefazolin inoculum effect was observed in 4 isolates (7.4%) all of them harboured blaZ gene.

**Conclusions:** The phenotypic and genotypic detection coincided in the results in all the strains studied. The inoculum effect to cefazolin obtained has been low and this was detected in a low number of strains of all those that were positive for Gen BlaZ. The minimum inhibitory concentrations of both standard inoculum and high inoculum obtained were similar to the published studies. Further complementary studies of beta-lactamases subtyping are necessary to search for an association between beta-lactamases types and inoculum effect.

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Abstract 8344

The role of a monthly active surveillance programme for multidrug-resistant Gram-negative bacteria in a neonatal intensive care unit: impact evaluation of preventive measures

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Background: Antimicrobial resistance is a public health threat. Neonatal Intensive Care Unit (NICU) patients are particularly at risk, due to the large use of invasive devices and antimicrobial treatment.

Since 2014 an active surveillance program of multidrug-resistant organisms is in place in the five NICUs of Palermo, Italy. High prevalence of multidrug-resistant Gram-negative bacteria (MDR-GNB) carriage observed in one NICU suggested the need of a long-lasting approach to achieve effective control of MDR-GNB circulation.

Materials/methods: Rectal swabs were obtained every month from each hospitalized new-born. Samples were enriched in liquid cultures, plated in McConkey Agar with three antimicrobial discs (amoxicillin-clavulanate, meropenem, ceftazidime). Resistant colonies were isolated, identified and submitted for antimicrobial susceptibility testing and ESBL detection. Molecular characterization of MDR-GNB was performed using pulsed-field gel electrophoresis (PFGE).

From November 2017 multiple intervention measures were done:
- Strengthening of sample collection for two months;
- Stakeholders meetings;
- Standardized protocols for antimicrobial therapy and common procedures.

Prevalence of MDR-GNB carriage between the pre-intervention (November 2016-October 2017) and the post-intervention period (November 2017-October 2018) was compared by chi-square test. Clinical features were analysed in a subgroup of patients to identify possible risk factors. All associated variables with p-values <0.25 were included in a multivariate logistic regression model. P<0.05 was considered significant.

Results: 39 patients were included in the 2 months of strengthened microbiological surveillance. MDR-GNB and ESBL-Klebsiella pneumoniae (KP) were detected in rectal swabs (34.8%; 23.2%), nasal swabs (24.6%; 14.5%), oral swabs (14.5%; 5.4%), milk samples (32.1%; 17.9%) soother swabs (30.8%; 17.9%). ESBL-KP was also detected from a sub-intensive room surface. Thirteen ESBL-KP strains isolated from clinical and environmental samples showed identical or closely related PFGE patterns suggesting a common origin for all tested strains. Prevalence of MDR-GNB and ESBL-KP carriage after intervention significantly decreased compared to the year before (61.1% vs 20.6%; p<0.001 and 94.5% vs 53.8%; p<0.001). Admission in post-intervention period significantly reduced the risk of MDR-GNB carriage (OR=0.15, p=0.01).

Conclusions: MDR-GNB broadly circulate in NICU setting, can colonize different body sites and spread by various vehicles. Cooperation between epidemiologist and clinicians can effectively reduce diffusion of antimicrobial-resistant bacteria.

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Ceftazidime-avibactam/aztreonam synergism assay against carbapenem-resistant Enterobacteriales and Pseudomonas aeruginosa carrying metallo-beta-lactamases

Julia Barbosa¹, Kamilla Moraes²*, Evelyn Patricia Sanchez Espinoza¹, Lauro Perdigao Neto¹, Sânia Santos¹, Ana Paula Marchi², Roberta Cristina Ruedas Martins¹, Thais Guimaraes¹, Flávia Rossi¹, Silvia Figueiredo Costa¹

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Background: The emergency of carbapenem-resistant Enterobacteriales (CRE) has promoted the develop of new antimicrobials to target this bacteria, nevertheless none of the new antimicrobials covers one of the most difficult threats these days: metallo-beta-lactamases (MBL). The aim of this study is to analyze synergism between ceftazidime-avibactam and aztreonam in isolates with *blaNDM* and *blaSPM* obtained from three different hospitals in Sao Paulo-Brazil.

Materials/methods: Nine *Klebsiellas pneumoniae*, fourteen *Pseudomonas aeruginosa* and two *Serratia marcescens* carbapenem-resistant clinical isolates analyzed by Whole Genome Sequence (WGS) using MiSeq illumina and Ion Torrent as NDM and SPM respectively where included. All isolates were submitted to disk diffusion (DD) prior to the synergism assay and evaluated using the Clinical and Laboratory Standards Institute breakpoints. The synergism assay was performed using ceftazidime-avibactam and aztreonam disks, in duplicate by two different persons, the results were evaluated in duplicate as well.

Results: The DD assay showed all of the *K. pneumoniae* resistant to aztreonam and susceptible to ceftazidime-avibactam, the synergism assay was positive in all of these isolates (n=9) that were assigned 5 isolates to three ST (ST340, ST258, ST11). For the *S. marcescens* the DD showed one of them was resistant to both ceftazidime-avibactam and aztreonam while the other was susceptible to ceftazidime-avibactam, both isolates were positive in the synergism assay (n=2). Finally, among the fourteen *P. aeruginosa* analyzed half were portrayed as intermediate to aztreonam and the other half was susceptible, all of them were resistant to ceftazidime-avibactam in the DD assay. Only one isolate displayed synergism, moreover, the other thirteen isolates had undetermined results (Table 1). Eleven isolates were assigned to two ST (ST277, ST308).

Conclusions: The synergism between ceftazidime-avibactam and aztreonam seen in *Klebsiella pneumoniae* carrying NDM is promising and will probably need an animal model to corroborate the in-vitro results, for *Pseudomonas aeruginosa* other types of synergism for MBL should be tested.

Table 1: Evaluation of *Klebsiella pneumoniae*, *Serratia marcescens* and *Pseudomonas aeruginosa* by Disk Diffusion (DD), Whole Genome Sequence (WGS) and Ceftazidime-Avibactam-Aztreonam (Caz-Avi-Azt) Synergism

<table>
<thead>
<tr>
<th>Microorganisms</th>
<th>(n=25)</th>
<th>Caz-Avi-Azt Synergism</th>
<th>MBL gene</th>
<th>AZT DD</th>
<th>CAZ AVI DD</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>(n=9)</td>
<td>positive</td>
<td>NDM</td>
<td>R</td>
<td>S</td>
</tr>
<tr>
<td><em>Serratia marcescens</em></td>
<td>(n=1)</td>
<td>positive</td>
<td>NDM</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td><em>Serratia marcescens</em></td>
<td>(n=1)</td>
<td>positive</td>
<td>NDM</td>
<td>R</td>
<td>S</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>(n=1)</td>
<td>positive</td>
<td>SPM</td>
<td>S</td>
<td>R</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>(n=7)</td>
<td>undetermined</td>
<td>SPM</td>
<td>I</td>
<td>R</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>(n=6)</td>
<td>undetermined</td>
<td>SPM</td>
<td>S</td>
<td>R</td>
</tr>
</tbody>
</table>

R: resistant    S: susceptible    I: intermediate

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Non-tuberculous lymphadenitis in children: epidemiology and management strategy in France during the last decade

Cécile Le Brun*, Hélène Guet-Revillet, Olivia Peuchant, Alice Gaudart, Christelle Koebel, Caroline Piau, Julien Bador, Frédérique Canis, Anne Vachée, Camille Brehin, Lucas Ricco, Pascale Bemer, Philippe Lanotte, Claudia Carvalho Schneider, Zoha Maakaroun Vermesse, Aurélie Guillouzouic

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Abstract third-party references: On behalf of the MYCOMED group

Background: Nontuberculous mycobacterial (NTM) lymphadenitis is a rare disease. Its treatment is not standardized; even a "wait-and-see" approach is shown to be effective in the literature. The aims of this study were to describe characteristics, diagnostic approach, management and outcome of such infections in France.

Materials/methods: We performed a retrospective study of all children under 18 years-old with culture-confirmed NTM lymphadenitis documented in 10 French hospitals within the MYCOMED network from 2010 to 2018. The MYCOMED network was created on a voluntary basis and collects data on all culture-positive mycobacterial infections diagnosed in the participating hospitals. Demographic data, diagnostic tests, histological examination, treatment and follow up information were recovered.

Results: 211 cases were registered, with a mean age of presentation of 36 months (range 10 months – 14 years). The mean time between the symptoms onset and first consultation was 63 days (range 5 – 519 days). The most frequent location was cervical in 92/211 cases (43.6%), followed by sub-maxillar and parotid in 84 (39.8%) and 20 (9.5%) cases respectively. Fistulae were observed in 45 cases. Microbiological cultures were positive for Mycobacterium avium in 144 (68%), Mycobacterium intracellulare 30 (14%), and Mycobacterium lentiflavum 19 (11.1%) cases. There is no significant change in the number of cases or species distribution over the years. Histological examination was performed for 123 patients and granulomatous necrotizing lymphadenitis was retrieved in 94 (76%). Antibiotic susceptibility testing was performed for 98 strains. All were susceptible to clarithromycin. Surgical treatment alone was given in 57/192 cases (30%), medical treatment only in 55 (28%), and combined treatment of antibiotics and surgery in 49 (26%). 31 patients (16%) had no treatment. Surgical drainage was chosen for 45/114 patients (39%) and 57 (50%) underwent chirurgical excision. Antibiotic treatment was mostly clarithromycin (n = 100, 96%) alone or with rifampicin (n = 30, 29%). Median antibiotics duration was 92 days (range 3-671 days). Ten patients required a new surgery and 112/159 (70%) had a favorable evolution.

Conclusions: Epidemiology and numbers of NTM lymphadenitis appears stable in France since 2010. Surgical excision, antibiotic treatment or combination do not show difference in the evolution.

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Abstract 8350

*My*oc*ab*terium *tuberculosis* genotypes’ landscape in HIV-negative and HIV-positive tuberculosis patients in Russia

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**Background:** Genotyping of *M. tuberculosis* (MBT) isolates is widely used during the last decades for studies in genetic diversity of MBT molecular epidemiology, evolutionary and population genetics. Results of MBT genotypes’ assays are considered to be also useful for clinical management. We had analyzed MBT isolates from HIV- and HIV+ TB patients from different regions of the Russian Federation.

**Materials/methods:** TB patients’ MBT isolates from six regions of Russia (400 from HIV- and 117 HIV+ patients) were tested for 1st (rifampicin, isoniazid, streptomycin, ethambutol, pyrazinamide) and 2d line (amikacin, capreomycin, levofloxacin, moxifloxacin, prothionamide) drugs’ susceptibility (Bactec MGIT 960, BD), for mutations conferring drugs’ resistance by microbiochip technology (TB-TEST, Biochip IMB, Moscow, Russia). Spoligotyping analysis of 43 spacers’ nucleotide sequences was done by microbiochip technology (SPOLIGO-BIOCHIP, Biochip IMB, Moscow, Russia). Statistical evaluation was done with Statistica 11.

**Results:** MBT strains belonging to Beijing family constituted 64.5% and 72.6% in isolates both from HIV- and HIV+ TB patients (including 18.5 and 20.5% representatives of B0/W148 Beijing, correspondingly), p>0.05. Statistically significant difference were revealed in proportions LAM family of isolates (17.5% in HIV- and 6.8% in HIV+ patients, p<0.001), Ural family (7.5% in HIV- and 15.4% in HIV+ patients, p=0.018) and a group of minor genotypes’ families (10.5% in HIV- and 5.1% in HIV+ patients, p=0.035). Proportions of Beijing family strains were higher in MDR and XDR strains both in isolates from HIV- and HIV+ TB patients (86.4% and 81.1%, correspondingly) compared to isolates susceptible to anti-TB drugs and lacking mutations conferring drug resistance (41.8%), p<0.001 for all. Proportions of LAM and Ural families’ representatives was higher in susceptible strains (19.9% and 14.8% correspondingly) than in MDR strains (10.7%, p=0.013 and 2.8%, p<0.001, correspondingly).

**Conclusions:** Beijing family strains with high proportion of B0/W148 Beijing dominated in MBT isolates from HIV- and HIV+ TB patients. The proportion of Beijing strain was higher in drug resistant strains compared to susceptible ones. Diversity of minor genotype groups was higher in MTB isolates from HIV- TB patients compared with isolates from HIV+ TB patients.

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Abstract 8352

**Immunodominance Hierarchy after seasonal Influenza vaccination**

Laura Sanchez De Prada*, Iván Sanz1, Raúl Ortiz De Lejarazu2, Jose María Eiros3, Adolfo Garcia-Sastre4,5,6, Teresa Aydillo4,5

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**Background:** Hemagglutination inhibiting (HI) antibodies against the head of the haemagglutinin (HA) have been used as a correlate of protection for inactivated influenza vaccines (IIVs). Although, HA molecule comprises two major structural regions, head and stalk, the head remains the primary target for licensed IIVs. Five highly variable antigenic sites (Sb, Sa, Cb, Ca1, Ca2) have been described as immunodominant compared with other antigenic regions in the HA head. We aimed to characterize the antibody responses against these variable epitopes after influenza vaccination with an adjuvanted-trivalent-(ATIV) or quadrivalent-(QIV) IIV.

**Materials/methods:** Prospective human cohort study of 166 volunteers vaccinated with either ATIV (118, 71.1%, age ≥65 years) or QIV (48, 28.9%, age <65 years) during 2018/2019 influenza season. Sera was obtained pre- and 28 days post-vaccine. Antibody titers were measured by HI assay against recombinant PR8 (H1N1) virus expressing a pandemic-like A/Michigan/45/2015 (Wt) H1 HA protein and the counterpart modified viruses in which classically defined antigenic sites were partially substituted with heterologous antigenic sites from exotic H5 or H1 3 HAs: H1 - Sb, H1 - Sa, H1 - Cb, H1 - Ca1 and H1 - Ca2. Seroprotection was defined as an HI titer ≥40. Seroconversion was considered when a 4-fold induction occurred after influenza vaccination.

**Results:** Baseline seroprotection against the H1-Wt pandemic-like virus was 67.5% (112). Of these, only 14.3% (16) showed seroprotection against H1-ΔSbvirus, meanwhile 90.4% (90), 89.3% (100), 90.2% (101), 63.4% (71) were also seroprotected against H1-ΔSa, H1-ΔCb, H1-ΔCa1 and H1-ΔCa2, respectively. The seroconversion rate after influenza vaccination was 39.8% for both cohorts. No differences on baseline seroprotection or seroconversion were found between ATIV and QIV for the H1-Wt or any of the viruses containing the modified antigenic sites. A positive correlation was found (p<0.001) between de novo antibodies produced after ATIV and QIV vaccination between the H1-Wt and H1-ΔSa (r=0.74), H1-ΔCb (r=0.82), H1-ΔCa1 (r=0.82) and H1-ΔCa2 (0.67). No correlation was found with H1-ΔSb (0.13, p=0.09).

**Conclusions:** A significant reduction in baseline seroprotection was found for the viruses lacking single antigenic sites, especially for H1-ΔSb. No differences in seroconversion rates were found between ATIV or QIV for H1-Wt or the viruses containing the modified antigenic sites. Our results suggest that the HI responses mostly depend on the antigenic sites surrounding the sialic acid receptor binding domain such as Sb and Ca2.

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Abstract 8353

Identification of risk factors for extrapulmonary tuberculosis
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Background: Studies from developed countries have reported on host-related risk factors for extra-pulmonary tuberculosis (EPTB). However, similar studies from high-burden countries like Turkey are few. Therefore, we carried out this study to compare demographic, life-style and clinical characteristics between EPTB and PTB patients.

Materials/methods: A retrospective analysis was carried out on 589 tuberculosis (TB) patients diagnosed in a tertiary care hospital infectious diseases clinic between 2008-2018. We aimed to determine associations between the demographic, clinical, and life style characteristics of patients with tuberculosis (obtained from medical case records) and the risk factors for occurrence of extrapulmonary tuberculosis, by using logistic regression analysis.

Results: The study included 335 patients with EPTB (female:male ratio of 2.2) and 254 with PTB (male:female ratio of 1.17). The most commonly seen two types of EPTB were urogenital TB (26.2%) and lymph node TB (18.4%). Bone/joints, skin, peritoneal cavity/intestines, central nerve system (CNS), adrenal gland, eye and ear involvement occurred at a frequency ranging from 0.29% to 11.2%. Meningeal and bone/joint TB were more commonly observed among the male patients, while lymphatic, urogenital, peritoneal and skin TB cases were more frequently seen among females. Risk factors of PTB were smoking [Odds Ratio [OR] 3.98; 95% confidence interval [CI] 1.66–9.56], contact with patients with TB [OR: 2.51; 95% CI 1.06-5.95], diabetes mellitus [OR 1.69, 95% CI 1.12–2.56] and use of immunosuppressive drugs/steroids [OR: 2.82, 95% CI 1.59–5.00]. Treatment success rate for EPTB was 70.1% compared to 84.2% for PTB (p<0.001). In logistic regression, younger age [≤40 years] [OR 3.19; 95% CI 2.69–3.79], female gender [OR 1.59; 95% CI 1.35–1.88] were found to be significantly associated with EPTB compared with PTB. Being immunocompromised [OR 1.35; 95% CI 1.10–2.25] and having CNS TB [OR 3.88; 95% CI 1.14–13.23] were associated with mortality among EPTB patients.

Conclusions: Results suggest that younger age and female gender may be independent risk factors for EPTB. TB control programmes may target young and female populations for EPTB case-finding.

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Abstract 8354

**Development of an in-house cell-SELEX methodology for Acinetobacter baumannii aptamers selection**

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Abstract third-party references: Fundação de Amparo a Pesquisa do Estado de Sao Paulo

**Background:** Infections caused by multi-drug resistant agents are a worldwide health problem and are a leading cause of human disease with high mortality rates. Rapid identification of these infections is critical as they can be highly contagious, difficult to treat and have high hospitalization costs. In this context, the development of fast and economically viable detection methodologies, as well as development of new therapeutic alternatives are challenging. One of the promising solutions may be the development of nucleic acid aptamers capable of interacting with bacteria. These aptamers can be used for specific recognition of infectious agents as well as blocking their functions. Cell-SELEX technology currently allows the selection and identification of aptamers and is flexible enough to target any protein of interest or any target present in an entire bacterial cell without their prior knowledge. However, aptamer technologies still face many challenges including the difficulty of the screening process. The Main objective of this work was to standardize an inhouse methodology of aptamer selection and identification.

**Materials/methods:** A new inhouse methodology, based in whole cell-SELEX, for aptamer identification with rapid execution and low cost was described based on previously publications. The selected aptamer was identified by cloning in pGEM vector and sequenced by Sanger. The binding specificity was tested in *Acinetobacter baumannii, Klebsiella pneumoniae, Staphylococcus aureus* and *Candida albicans*. The ability to interfere in the bacterial growth was measured by time kill assays.

**Results:** This protocol is 10 times less expensive than other ones previously described and allowed the identification of the aptamer A01 with the whole *Acinetobacter baumannii* cell as target. Although its ability to bind to the bacteria cell, the aptamer did not affect the bacterial growth in the analyzed conditions. A01 also showed the ability to bind to other bacterial and fungal cells.

**Conclusions:** While studies in developing aptamers for clinical applications are still incipient, aptamers are promising molecules that may be widely used in bacterial detection and therapy with the improvement of selection methodologies. These data indicate that soon aptamer-based technology may become a tangible alternative to traditional approaches to infectious disease diagnosis and therapy.

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Abstract 8356

**Comparison of clinical characteristics and mortality between patients with pulmonary nocardiosis and patients with pneumonia**

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**Background:** Despite appropriate antibiotic therapy, mortality rate among pulmonary nocardiosis patients remains high. The current study compared clinical characteristics and mortality between patients with pulmonary nocardiosis and patients with pneumonia caused by other pathogens.

**Materials/methods:** A historical cohort study of adults hospitalized in a tertiary hospital during 2007-2018 was undertaken. Patients with nocardiosis (n=48) were matched by year of hospitalization to 96 patients with pneumonia caused by other pathogens. Data on both groups were retrieved from the medical charts and mortality was determined using the national death registry. Conditional logistic regression models were used to assess differences in clinical characteristics between the groups and the Cox proportional hazards model was implemented for survival analysis.

**Results:** In comparison to patients with pneumonia, pulmonary nocardiosis patients were younger by 15 years (P<0.001), were more likely to be solid-organ transplant recipients (OR 30.5 95% CI 4.0-230.7, P=0.001), and had a higher rate of corticosteroid therapy during the 90 days prior to diagnosis (OR 55.7 95% CI 7.6-408.0, P<0.001). One-month all-cause mortality rates were 8% and 20% among the pulmonary nocardiosis patients and in those with pneumonia, respectively (P=0.072); the respective one-year all-cause mortality rates were 38% and 37% (P=0.901). Patient’s age was the only variable significantly associated with mortality (HR 1.3 per decade, 95% CI 1.1-1.6, P=0.005). Exclusion of patients with central nervous system involvement did not change the results. Among pulmonary nocardiosis patients, the presence of malignancy significantly increased the risk for one-year all-cause mortality (OR 14.5, 95% CI 1.6-133.7, P=0.018), while corticosteroid therapy, a history of solid-organ transplantation and central nervous system involvement were not significantly associated with mortality.

**Conclusions:** A non-significant trend of higher one-month mortality was noted among patients with pneumonia than those with pulmonary nocardiosis. However, despite pulmonary nocardiosis patients had a substantially younger age, no significant differences were found in one-year mortality rates between the groups. This might be due to severe comorbidity among pulmonary nocardiosis patients, possibly malignant diseases.

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Abstract 8358

The case for infectious disease-centered antimicrobial stewardship: a 10-year experience at Saint George Hospital

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Background: In order to optimize antimicrobial prescription, Saint George hospital (SGH) implemented different educational modalities. Starting February 2012, an instant email forwarded to the infectious diseases (ID) consultant and the fellow on service upon prescribing a broad-spectrum antimicrobial, mandates a consult. The case is then reviewed for approval. Narrower spectrum antibiotics can be freely prescribed. Our antimicrobial stewardship program (ASP) also provides internal guidelines for best practices; for example, the carbapenems sparing strategy was implemented in July 2016.

Materials/methods: At SGH in Lebanon, a 333-bed hospital, the restricted antibiotics (RA) list consists of: carbapenems, amikacin, vancomycin, teicoplanin, ceftaroline, ceftolozane/tazobactam, piperacillin/tazobactam, cefepime, ceftazidime, tigecycline and colistin. Unrestricted antimicrobials are amoxicillin/clavulinate, first, second and third generations cephalosporins, ciprofloxacin and levofloxacin. We extracted from our ASP database consumption of each antibiotic reported as the daily defined dose (DDD) per 1000 patient days (PD) from January 2010 till June 2019. We also retrieved the number of ID consultations per 1000PD from 2012 till 2018.

Results: The unrestricted antimicrobial consumption was stable ranging from 295-345 DDD/1000 PD with a mean of 319. (Figure 1)

Shortly after adapting of our email notification system in February 2012, an absolute drop of 50 DDD/1000PD representing 15.6% of the total consumption of RA was noted. In 2013, this early success was difficult to maintain mainly due to an increase consumption of carbapenems that peaked in 2015.

However, after the implementation of strict carbapenems sparing strategy in 2016, consumption dropped from a peak of 208 DDD/1000PD to 33 DDD/1000PD in 2019. The total consumption of RA dropped from an average of 303 DDD/1000PD from 2010-2016 to 177 DDD/1000PD from 2017-2019.

The number of ID consultations was flat between 20-21 consults per 1000PD from 2012-2018.

Conclusions: Our 10 year experience in ASP favors that education, unlike restriction, did not result in any concrete change of consumption rates. Creating a system whereby an ID clinician enforces the best practices of the institution seems to yield interesting results without additive resources.

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Abstract 8369

**Serum Galectin-3 status in hospitalised patients with catheter-associated asymptomatic bacteriuria**
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**Background:** Urinary tract infections (UTI) are common in hospitalized patients with bladder catheters. Identifying new biochemical markers of urinary tract infection is an active line of research, since the management of UTI requires many resources. Galectin-3, which belongs to the lectin family able to bind to β-galactosides, plays an important role in the pathogenesis of numerous diseases such as cancer and inflammatory and metabolic disorders. It is known than its expression is increased by inflammatory stimuli such as microbial and non-microbial. Our study sought to evaluate alterations in inflammation-related Galectin-3 in patients with an indwelling catheter to assess their potential usefulness as biomarkers of infection.

**Materials/methods:** Patients (n=165) who had had the urinary catheter removed and healthy volunteers (n=72) were recruited and their medical records were also examined. Pertinent demographic data, comorbidities, bacteriologic and therapeutic data were recorded and were reviewed based on whether or not they have asymptomatic bacteriuria related to the catheter (CAAB). In all participants we measured plasma galectin-3, procalcitonin (PCT) and C-reactive protein (CRP).

**Results:** Patients with and without CAAB were significantly different in terms of percentages of sex, ischemic heart disease, chronic renal failure, history of malignancies and reception of antimicrobial treatment 24 hours before sample collection. Patients showed a higher inflammatory status than healthy individuals, with higher Galectin-3 concentration (17.15 ng/ml vs 6.15 ng/ml, p<0.01), CRP (24.60 mg/l vs 1.17 mg/l, p<0.001) and PCT levels (41.41 mcg/l vs <10 mcg/l, p<0.001). In patients, we observed that the galectin-3 concentration significantly correlated with age and with the number of days the urinary catheter was indwelling (Figure 1). The discriminatory capacity of the circulating concentration of these parameters was analyzed by means of the receiver operating characteristics (ROC) curves for patients with or without acute concomitant infection and CAAB, being galectin-3 the marker with the best area under the curve in both cases (Figure 1).

**Conclusions:** Our results suggest that the measurement of these biochemical variables may be useful in investigating complications of long-term use of these devices and can help to optimize antimicrobial treatment and shorten hospital stays.

**Figure 1**

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Detection and identification of intact carbapenemases using liquid chromatography and tandem mass spectrometry from microbial lysates in a rapid carba method using the Acrion system

William Mcgee*, Arvind Verma*, Marjaana Viirtola*, Scott Kronewitter†, Jason Neil†, Jaakko Haakana†, Jim Stephenson†

†Thermo Fisher Scientific, Cambridge, United States; †Thermo Fisher Scientific, Vantaa, Finland

**Background:** Carbapenemase-producing organisms (CPOs) pose a rapidly-growing global health threat, not only for the ability to metabolize the potent antibiotic family of carbapenems, but also for the frequent association of high morbidity and mortality rates from these infections. Effective treatment of these infections can be maximized by rapidly detecting the specific mechanisms of resistance. Mass spectrometry (MS) has been used to individually characterize the “big five” carbapenemases: KPC, VIM, IMP NDM and OXA-48-like. We have developed a single method that, following automated sample preparation from bacterial cultures, uses a combination of liquid chromatography and tandem mass spectrometry (LC-MS/MS) for direct detection of intact carbapenemases.

**Materials/methods:** Carbapenemase-producing and carbapenemase-non-producing isolates were used, including several species from Acinetobacter, Pseudomonas and Enterobacteriales. Bacterial colonies from either agar or blood culture were harvested and mechanically lysed, with the lysate being transferred directly to disposable columns for liquid chromatography (LC) for rapid separation and elution, followed by electrospray ionization (ESI) and MS analysis. Tandem mass spectrometry (MS/MS) is used to determine the presence of carbapenemases by dissociating the intact protein(s) in a data-independent manner. Diagnostic fragments produced directly from unique carbapenemase, each possessing specific characteristics as mass-to-charge (m/z) and charge state, are used to determine the presence of specific carbapenemases.

**Results:** To date, our methods have been used to determine the presence or absence of KPC, VIM, IMP NDM and OXA-48-like in Enterobacteriales; KPC, VIM and IMP in Pseudomonas, and VIM in Acinetobacter, based on isolate availability. Multiple variants from each of the big five are detected, with the exception of IMP, in which we focus specifically on IMP-1. Several isolates harboring multiple carbapenemases, most frequently of OXA-48-like and NDM, have been evaluated. Carbapenemase-non-producing isolates have shown negative carbapenemase results. Following carbapenemase detection, results of all claimed carbapenemases present are reported.

**Conclusions:** This research allows detection of the big five carbapenemases in an automated fashion, with the duration of the assay lasting under 5 minutes. The method presented takes advantage both of the ability of liquid chromatography to simplify complex protein mixtures and the high-resolution, targeted capabilities of mass spectrometry for confident detection of carbapenemases.

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**Goal achieved! Elimination of hepatitis C in three penitentiary centres**

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1Universitary Hospital Puerto Real, Puerto Real, Spain

**Background:** The WHO has purposed to eliminate the hepatitis C (HCV) in 2030. In order to achieve this objective it is essential to eliminate it in vulnerable and high prevalence population such as de Penitentiary Center (PC) which also present multiple difficulties for their approach. Therefore, an HCV elimination program was designed with the development of innovative strategies.

**Materials/methods:** In June 2016 a multidisciplinary team composed of doctors, nurses, pharmacist and officials was created in the PCs Puerto I, II and III. All the inmates, 2068, were included. A training program, diagnostic and follow-up protocols were developed and the prevalence of active infection was determined by viral load and core antigen positive serology inmates. Hepatic fibrosis was analyzed by Fibroscan and HCV was genotyped. The infectologist monthly attended consultations in the PC. The prescribed treatment was administered directly observed. Sustained virologic response (SVR) was used to measure effectiveness of HCV treatment.

**Results:** HCV active infection was positive in 214 of the 2068 inmates. The prevalence was 10.35%. In the table 1, co-infected with HIV, monoinfected and total patients results are shown.

<table>
<thead>
<tr>
<th>Fibrotic degree:</th>
<th>HCV: n(%)</th>
<th>HIV / HCV: n(%)</th>
<th>Globally: n(%)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>159 (74.3%)</td>
<td>55 (25.7%)</td>
<td>214 (100%)</td>
</tr>
<tr>
<td>F4</td>
<td>34 (21%)</td>
<td>20 (36%)</td>
<td>54 (26%)</td>
</tr>
<tr>
<td>F3</td>
<td>20 (13%)</td>
<td>8 (48%)</td>
<td>28 (13%)</td>
</tr>
<tr>
<td>F2</td>
<td>28 (18%)</td>
<td>10 (18%)</td>
<td>38 (18%)</td>
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<tr>
<td>F0-F1</td>
<td>68 (42%)</td>
<td>16 (26%)</td>
<td>84 (40%)</td>
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<th>Genotype:</th>
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<th>HIV / HCV: n(%)</th>
<th>Globally: n(%)</th>
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<td>G1a</td>
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<td>210 (97%)</td>
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</tr>
<tr>
<td>G1b</td>
<td>14 (84%)</td>
<td>40 (18%)</td>
<td></td>
</tr>
<tr>
<td>G2</td>
<td>12 (22%)</td>
<td>56 (26%)</td>
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</tr>
<tr>
<td>G4</td>
<td>8 (14.5%)</td>
<td>45 (21%)</td>
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</tbody>
</table>

<table>
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<tr>
<th>Most used therapies:</th>
<th>HCV: n(%)</th>
<th>HIV / HCV: n(%)</th>
<th>Globally: n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gilepaimv/obrentasv</td>
<td>51 (32%)</td>
<td>60 (28%)</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/velpatasv</td>
<td>32 (20%)</td>
<td>49 (23%)</td>
<td></td>
</tr>
<tr>
<td>Elbasvir/grazoprevir</td>
<td>36 (23%)</td>
<td>42 (20%)</td>
<td></td>
</tr>
<tr>
<td>Sofosbuvir/ledipasv</td>
<td>13 (6%)</td>
<td>25 (12%)</td>
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</tbody>
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<table>
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<tr>
<th>Completed treatment:</th>
<th>HCV: n(%)</th>
<th>HIV / HCV: n(%)</th>
<th>Globally: n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>157 (98.7%)</td>
<td>55 (100%)</td>
<td>212 (98.3%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Loss of follow-up:</th>
<th>HCV: n(%)</th>
<th>HIV / HCV: n(%)</th>
<th>Globally: n(%)</th>
</tr>
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<tr>
<td>Recurrence:</td>
<td>3 (1.9%)</td>
<td>2 (2%)</td>
<td>5 (2.4%)</td>
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<tr>
<td>Death</td>
<td>2 (1.3%)</td>
<td>0</td>
<td>2 (0.0%)</td>
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</table>

<table>
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<tr>
<th>SVR X 12:</th>
<th>HCV: n(%)</th>
<th>HIV / HCV: n(%)</th>
<th>Globally: n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>108/152 (90.0%)</td>
<td>61/54 (94.4%)</td>
<td>189/208 (91.7%)</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** The elimination of HCV in the CPs Puerto I, II and III has been achieved thanks to a multidisciplinary teamwork program. Directly observed therapy programs in prison improve treatment compliance. The efficacy of treatment in these group is lower to general population due to loss of follow-up.

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Risk factors for mortality in diabetic foot infections

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Background: Foot ulceration and infection represent an important source of morbidity and mortality in people with diabetes mellitus. We aimed to determine the risk factors for mortality in diabetic foot infection (DFI).

Materials/methods: Data of patients who were hospitalized for DFI between 2010 and 2019 were recorded retrospectively from the hospital records. The data of the patients who died and survived were evaluated statistically for predicting mortality.

Results: Data were collected for 401 patients including 280 (69.8%) men. The mean age was 59.6±11.1 (29-81) years. Thirteen (3.2%) of the patients were type 1 diabetes and mean duration of diabetes was 14.1±9.2 years. The causes of the DFI were as follows; ischemic ulcer (33.7%), trauma (13.5%), neuropathic ulcer (11.5%), venous ulcer (10.5%) burn injury (2.7%) and idiopathic (25.4%). Of these patients, 47.4% had right foot wound, 43.6% had left foot wound and 9% had bilateral foot wounds. Treatment modalities included medical treatment (146, 36.4%), debridement/drainage (88, 21.9%), minor amputation (71, 17.7%) and major amputation (96, 23.9%). Mean duration of follow-up was 23.7±22.9 months; 146 (46.8%) patients completely recovered, 63 (20.2) patients developed a chronic foot ulcer and 103 (33%) patients required re-operation. The overall mortality rate was found 3% (12/401).

Ischemic wound (p = 0.025), hindfoot wounds (p = 0.043), whole foot wound (p = 0.035), peripheral arterial disease (p = 0.005), high leukocyte levels (p < 0.001), high thrombocyte levels (p < 0.001) and high C-reactive protein levels (p = 0.018) were found to be significant factors in terms of mortality. Among these factors, peripheral arterial disease (OR:13.430, 95% CI: 1.129-59.692; p=0.040), high thrombocyte levels (>378000 K/ul) (OR:1.000, 95% CI:1.000-1.000; p=0.022) and isolation of multiple bacterial species from the tissue culture (OR:7.790, 95% CI: 1.592-38.118; p=0.011) were independent risk factors for mortality in DFI (Figure).

Conclusions: Early recognition of risk factors for mortality is crucial in terms of decreasing mortality rates. We conclude that these clinical parameters are simple, broadly available and cost-effective promising parameters for predicting mortality in DFI.
### Abstracts 2020

**Figure: Risk factors for mortality in patients with diabetic foot infection**

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Mortality (n=1,210)</th>
<th>Mortality (n=380, 33%)</th>
<th>P</th>
<th>Odds Ratio</th>
<th>95% Confidence Interval</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years, mean±SD)</td>
<td>64.36±5.9</td>
<td>59.56±11.1</td>
<td>0.030</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes (n=%)</td>
<td>7 (92.3%)</td>
<td>272 (92.1%)</td>
<td>0.060</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of diabetes</td>
<td>2 (16.7%)</td>
<td>32 (8.3%)</td>
<td>0.005</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI years</td>
<td>3 (25.6%)</td>
<td>72 (18.9%)</td>
<td>0.008</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment of diabetes</td>
<td>9 (69.7%)</td>
<td>247 (64.3%)</td>
<td>0.099</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral antidiabetic drug</td>
<td>3 (25.6%)</td>
<td>65 (16.9%)</td>
<td>0.009</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>0</td>
<td>91 (9.9%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of diabetic chronic overtreatment</td>
<td>9 (65.4%)</td>
<td>101 (40.1%)</td>
<td>0.003</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic overtreatment (≥1 year)</td>
<td>0</td>
<td>42 (10.6%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of invasive procedures</td>
<td>0</td>
<td>44 (11.2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of debridement/drainage</td>
<td></td>
<td>92 (15%)</td>
<td>0.100</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cause of foot injury</td>
<td>0</td>
<td>127 (32.9%)</td>
<td>0.002</td>
<td>3.10</td>
<td>0.074-12.12</td>
<td>0.942</td>
</tr>
<tr>
<td>Traumatism</td>
<td>1 (0.3%)</td>
<td>15 (3.9%)</td>
<td>0.000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurotrophic</td>
<td>1 (0.3%)</td>
<td>46 (11.9%)</td>
<td>0.000</td>
<td>3.53</td>
<td>1.043-11.73</td>
<td>0.150</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>1 (0.3%)</td>
<td>41 (10.5%)</td>
<td>0.000</td>
<td>3.10</td>
<td>1.043-11.73</td>
<td>0.386</td>
</tr>
<tr>
<td>Ename</td>
<td>0</td>
<td>11 (2.8%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Location of the infections</td>
<td>3 (25.6%)</td>
<td>107 (45.1%)</td>
<td>0.147</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right foot</td>
<td>3 (25.6%)</td>
<td>107 (45.1%)</td>
<td>0.147</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left foot</td>
<td>7 (58.3%)</td>
<td>105 (40.2%)</td>
<td>0.076</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral foot</td>
<td>2 (16.7%)</td>
<td>34 (13.7%)</td>
<td>0.294</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>3 (25.6%)</td>
<td>107 (45.1%)</td>
<td>0.147</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of diabetes</td>
<td>3 (25.6%)</td>
<td>107 (45.1%)</td>
<td>0.147</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of invasive procedures</td>
<td>3 (25.6%)</td>
<td>107 (45.1%)</td>
<td>0.147</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of debridement/drainage</td>
<td>3 (25.6%)</td>
<td>107 (45.1%)</td>
<td>0.147</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cause of foot injury</td>
<td>1 (8.3%)</td>
<td>106 (43.7%)</td>
<td>0.120</td>
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<td></td>
</tr>
<tr>
<td>Traumatism</td>
<td>3 (25.6%)</td>
<td>107 (45.1%)</td>
<td>0.147</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurotrophic</td>
<td>3 (25.6%)</td>
<td>107 (45.1%)</td>
<td>0.147</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Vascular disease</td>
<td>3 (25.6%)</td>
<td>107 (45.1%)</td>
<td>0.147</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ename</td>
<td>3 (25.6%)</td>
<td>107 (45.1%)</td>
<td>0.147</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laboratory parameters</td>
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<tr>
<td>Hemoglobin</td>
<td>10.9±2.3</td>
<td>11.1±1.5</td>
<td>0.700</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Leukocyte</td>
<td>22.69±7.9/5.4</td>
<td>14.92±6.3/0.005</td>
<td>0.004</td>
<td>1.000</td>
<td>1.000-1.000</td>
<td>0.004</td>
</tr>
<tr>
<td>Platelet</td>
<td>0.9±0.000</td>
<td>336±722/722/722</td>
<td>0.000</td>
<td>1.000</td>
<td>1.000-1.000</td>
<td>0.000</td>
</tr>
<tr>
<td>Glucose</td>
<td>29±10.9</td>
<td>29±10.9</td>
<td>0.000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat</td>
<td>13±5.1</td>
<td>13±5.1</td>
<td>0.000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>32±13±3.3</td>
<td>32±13±15.1</td>
<td>0.016</td>
<td>1.534</td>
<td>0.835-1.114</td>
<td>0.555</td>
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<tr>
<td>TRAP level</td>
<td>6.9±9.7</td>
<td>1±5.5</td>
<td>0.003</td>
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</tr>
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</table>

*Only the values found to be significant in univariate logistic regression analysis were evaluated in multivariate logistic regression analysis. The values are indicated by odds ratio in the table. CI: 99% confidence interval, SP: Significant p-value.***

**Presenter email address:** tunademirdal@hotmail.com
Genomic characterisation of MBL-producing non-aeruginosa Pseudomonas spp. in Saint-Louis University hospital in Paris, France

François Caméléna*, Manel Merimèche¹, Martine Rouveau¹, Sarah Delliere¹, Mourad Benyamina¹, Touratier Sophie¹, Matthieu Lafaurie¹, Beatrice Bercot¹

¹Saint-Louis, APHP, Paris, France

Background: Acquisition of antimicrobial resistance determinants, including metallo β-lactamase (MBL) carbapenemases have been reported in non-aeruginosa Pseudomonas spp. The aim of this study was to identify and characterize MBL-producing non-aeruginosa Pseudomonas spp. (MPP) isolated at Saint-Louis hospital in France.

Materials/methods: MPP isolates were collected retrospectively from patients hospitalized in several Units of the St Louis hospital from January 2011 to June 2019. Antimicrobial susceptibility was tested toward 19 antibiotics including last cephalosporin and β-lactamase inhibitor combinations [broth microdilution Sensititre™ (Thermofisher Scientific) and diffusion gradient E-test® (Biomérieux)]. Genomic characterization was performed by whole genome sequencing (NextSeq™ or MiSeq™, Illumina®). Sequences were analyzed for genes encoding acquired antibiotic resistance (ResFinder) and Core genome single nucleotide polymorphisms (SNP) from reference-based read alignment were used to infer phylogenetic relationships.

Results: Among the 19 carbapenems resistant non-aeruginosa Pseudomonas spp., 13 were MPP. Four were isolated from screening rectal swabs, 4 from blood cultures, 3 from stool samples, 1 from urine sample and 1 from skin sample. The bacterial species observed were P. putida (n=8), P. stutzeri (n=4) and P. mosselii (n=1). All isolates were resistant to all β-lactam antibiotics except 5 isolates which were susceptible to aztreonam. All were susceptible to colistin. MPP isolates produced VIM-type carbapenemase with VIM-2 (n=9), VIM-4 (n=3) and VIM-1 (n=1) enzymes.

The core-genome analysis identified several clusters with one cluster corresponding to 3 P. stutzeri. which suggest a potential transmission of MPP isolates in our hospital. Characterization of the genetic support and the environments surrounding carbapenemase genes are ongoing.

Conclusions: Non-aeruginosa Pseudomonas spp. with MBLs are emerging and may represent difficult-to-treat infections. Identification of MBLs in these species is essential for limiting the spread of carbapenemase-producing isolates in hospital which could occur via plasmid circulating in the Pseudomonas genus. Whole Genome Sequencing represents a powerful tool for investigation and traceability of strains circulating in the hospital.

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Abstract 8383

**Actinotignum schaalii bacteraemia: a ten-year retrospective analysis in a tertiary hospital in Madrid, Spain**

Adriana Rojas*, Luis A. Arroyo Pedrero, Carlos Sanchez Carrillo, Luis Alcala, Patricia Muñoz

1Hospital General Universitario Gregorio Marañón, Servicio de Microbiología y Enfermedades Infecciosas, Madrid, Spain, 2Hospital General Universitario Gregorio Marañón, Madrid, Spain

**Background:** *Actinotignum schaalii* is an emerging uropathogen which can be frequently overlooked in routine culture due to its special growth conditions. It has also been described as a rare cause of septicemia.

**Materials/methods:** *A. schaalii* isolates in blood cultures were identified retrospectively in the clinical laboratory database, comprising results from January 2009 to July 2019. Once cases were identified, the medical history of each patient was searched to extract variables such as age, sex, comorbidities, urogenital risk factors, the presence of septic shock (defined by use of vasopressors), clinical diagnosis of UTI (described by the treating physician) with or without positive urine cultures. All isolates were identified by MALDI-TOF, and antimicrobial susceptibility was determined via Sensititre®.

**Results:** A total of 10 isolates from blood cultures of 10 patients were identified, with 5 female and 5 male patients. The median age was 74.5 years. Only one case was associated with septic shock. 6 patients had predisposing urinary tract conditions upon admission, with an additional 3 requiring indwelling urinary catheters during hospitalization. All patients had significant comorbidities, including oncologic and neurologic diseases. 6 cases were clinically diagnosed as bacteremia secondary to UTI, despite there only being 2 urine cultures positive for *A. schaalii*. The susceptibility of only the 4 latest isolates could be obtained, with all 4 sensitive to penicillin, tetracycline, moxifloxacin and vancomycin, 2 out of 4 resistant to clindamycin, and all 4 resistant to metronidazole.

**Conclusions:** *A. schaalii* is a rarely reported cause of urinary sepsis, most commonly found in elderly patients with urinary tract disease and other comorbidities. In this study there is a clear disparity between positive blood cultures and urine cultures, indicating a need for protocols directed towards the isolation of emerging uropathogens in select populations.

<table>
<thead>
<tr>
<th>#</th>
<th>Date of culture</th>
<th>Sex</th>
<th>Age</th>
<th>Urinary tract disease</th>
<th>Comorbidities</th>
<th>Septic shock</th>
<th>Diagnosis of UTI</th>
<th>Positive urine culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>01/05/2010</td>
<td>F</td>
<td>41</td>
<td>Yes</td>
<td>Paraplegia, neurogenic bladder.</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<tr>
<td>2</td>
<td>04/09/2011</td>
<td>F</td>
<td>74</td>
<td>Yes</td>
<td>Renal carcinoma.</td>
<td>No</td>
<td>Unclear.</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>23/09/2013</td>
<td>F</td>
<td>88</td>
<td>Yes</td>
<td>Renal lithiasis, Parkinson’s disease</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>4</td>
<td>18/04/2014</td>
<td>M</td>
<td>71</td>
<td>No</td>
<td>Multiple myeloma</td>
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<tr>
<td>5</td>
<td>29/11/2015</td>
<td>M</td>
<td>75</td>
<td>Yes</td>
<td>Renal transplant, percutaneous nephrostomy</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
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<tr>
<td>6</td>
<td>25/05/2016</td>
<td>F</td>
<td>70</td>
<td>Yes</td>
<td>Ureteral dilation</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>7</td>
<td>10/09/2017</td>
<td>M</td>
<td>88</td>
<td>Yes</td>
<td>Urinary catheter</td>
<td>Colorrectal cancer.</td>
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<td>Unclear.</td>
</tr>
<tr>
<td>8</td>
<td>14/11/2017</td>
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<td>60</td>
<td>Yes</td>
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<td>Liver cirrhosis.</td>
<td>No</td>
<td>Yes</td>
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<tr>
<td>9</td>
<td>15/02/2019</td>
<td>M</td>
<td>88</td>
<td>Yes</td>
<td>Urinary catheter</td>
<td>Dementia.</td>
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<td>Unclear.</td>
</tr>
<tr>
<td>10</td>
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<td>M</td>
<td>90</td>
<td>Yes</td>
<td>Dementia.</td>
<td>No</td>
<td>Yes</td>
<td>Contaminated sample.</td>
</tr>
</tbody>
</table>

**Presenter email address:**acrojasd@gmail.com
In vitro model of Pseudomonas aeruginosa pulmonary biofilm to evaluate the efficacy of cationic antibiotics

Rana Awad1,2*, Frederic Tewes1,2, Sandrine Marchand1,2,3, William Couet1,2,3, Mohamad Nasser4

1INSERM U1070, Poitiers, France, 2Faculté de Médecine et de Pharmacie, Poitiers, France, 3Poitiers University Hospital, Poitiers, France, 4Lebanese University, Hadat Campus, Beirut, Lebanon

Background: Pseudomonas aeruginosa (PA) forms pulmonary biofilms in cystic fibrosis patients. These biofilms are aggregates of PA (50-100 μm) entrapped in a self-produced matrix of anionic polymers (alginate, eDNA), often surrounded by patient mucus. These conditions limit the efficacy of cationic antibiotics (ATB) used by inhalation, such as tobramycin (TOB) and colistin (COL). The aim of this study is to develop an in-vitro model composed of these anionic polymers (alginate, mucins, DNA) to mimic PA biofilms and evaluate the efficacy of these ATB.

Materials/methods: A constitutively bioluminescent PA01 strain was incorporated into calcium alginate beads dispersed in various growth media. The effects of the beads size (60 and 1200 μm) and the medium in which they were dispersed (Muller-Hinton (MH) or artificial pulmonary mucus (ASM)) were tested on TOB and COL efficacy by performing bioluminescence kinetics produced by PA for 40 h, followed by a measurement of bacterial concentrations (log10 CFU / ml). Then, the appearance of resistance to the ATB used in the surviving PAs was evaluated by measures of MIC.

Results: Below 10 MIC, TOB did not slow the growth of PAs under all conditions tested. Above 10 MIC, adding ASM or increasing the beads size further decreased TOB efficacy. TOB concentrations higher than 200 MIC allowed eradicating PA in beads dispersed in MH, but remained insufficient to eradicate those in beads dispersed in ASM. Compared to TOB, COL at this concentration allowed the total eradication of PA from large beads dispersed in ASM. For PAs loaded in large beads dispersed in MH, the apparition of small colony variants was observed from TOB concentrations ≥ 25 MIC. The percentage of this phenotype in the total bacterial population increased with the TOB concentration. This phenotype, which was not observed in the presence of COL, has been described in CF patients with chronic pulmonary infections.

Conclusions: PA incorporated into large alginate beads dispersed in ASM seems to be an in vitro model reproducing PA lung biofilms. In this model, COL was more effective than TOB, suggesting a better clinical efficacy of COL than TOB against pulmonary PA biofilms.

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Abstract 8393

Impact of the use of C-reactive protein in micro-methods on the prescription of antibiotics in case of suspected respiratory infection in children and adults in ambulatory care in France

Robert Touitou1, Corinne Levy1, Stéphane Béchet1, Emmanuel Pinto1, Alice Laplante1, Juliette Lion-Altmayer1, Blandine Trincard1, Camille Jung3, Robert Cohen2

1EFGH Croix Saint Simon, Paris, France, 2ACTIV, Créteil, France, 3CHI Créteil, Créteil, France

Background: Respiratory tract infections and particularly the “febrile cough” are the leading cause of unnecessary antibiotic prescriptions while a minority of them are linked to bacterial infections requiring antibiotics. These massive prescriptions contribute to increase bacterial resistance not only for respiratory pathogens but also for bacterial species of digestive microbiota. Point of care tests such as C-reactive protein micro-method (POCT-CRP) have been developed to help differentiate between viral and bacterial infections and thus contribute to the proper use of antibiotics. The decrease in antibiotics prescriptions due to POCT-CRP is likely to have a greater positive impact in countries such as France, where antibiotic consumption is high.

Materials/methods: 24 investigators were randomized in 4 clusters to conduct a stepped wedge randomized multicentric study. All clusters began the study at the same time, but they were randomized to start using POCT-CRP at different times: 3, 6, 9 and 12 months after the beginning of the study. Because of a too large number of subjects to enroll in a stepped wedge design, the study was early stopped after 8 months, and it was decided to conduct a second study. Nevertheless, the rate of antibiotic prescriptions during the first study were compared according to the use of the POCT-CRP. Results were also analyzed according to age group (3-17, 18-64, >64 years).

Results: Between June 2018 and February 2019, 404 patients were included in the first study. Mean age was 41.2 ± 24.5 years, with a minimum of 3 years and a maximum of 92 years and male accounted for 58.4% of patients. Seventy five (18.6%) POCT-CRP were used, for patients with mean age of 21.9 ± 32.8 years. Antibiotics were prescribed for 163 patients (40.5%): 147 (45.2%) when a POCT-CRP was not used and 14 (18.2%) when a POCT-CRP was used (p<0.001).

Conclusions: The use of POCT-CRP allowed to reduce the prescription of antibiotics in adults and children on an outpatient basis for suspected respiratory infection. We are confident that those results will be confirmed by the second study.

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Abstracts 2020

Abstract 8395

**Antimicrobial stewardship starts at home: in-house developed digital tool for real-time resistance surveillance**

Marta Gonzalez Sanz*, Natalie Marshall¹, Alleyna Claxton¹, Kate Woods¹

¹Homerton University Hospital NHS Foundation Trust, London, United Kingdom

**Background:** Accurate bacterial susceptibility surveillance data is a cornerstone of the fight against Antimicrobial Resistance (AMR). Hospital antibiotic guidelines are often based on regional and national data which might not be directly applicable to the local population served. Smaller hospitals may lack the necessary infrastructure for regular analysis of local susceptibility patterns. Our team designed a tool to semi-automate analysis of local susceptibility patterns in order to ensure our antibiotic guidelines are appropriate for current AMR patterns in the local population.

**Materials/methods:** We created a programme on SPSS® [software platform for statistical data analysis], to analyse data extracted directly from Winpath, our Laboratory Information Management System (LIMS). The syntax can be configured for any sample type, demographics or location; and output data can be compared with local antibiotic guidelines and national AMR data.

Urine samples which were culture positive between April 2016 and March 2019 were retrospectively extracted from Winpath, and analysed using the SPSS® tool. The target study group were Enterobacterales culture positive samples from patients older than 16 years.

**Results:** 26,192 Enterobacterales culture positive urine samples were identified. 19,767 (75.5%) from community/outpatient settings; 3,588 (13.7%) and 2,837 (10.8%) from acute/inpatient settings respectively. The most common organisms isolated were: *Escherichia coli* (75.7%), *Klebsiella pneumoniae* (9.1%), *Proteus mirabilis* (5.4%), *Citrobacter koseri* (2.6%), *Enterobacter cloacae* (1.3%). Among these organisms (N=24,657) the proportion of non-susceptible isolates to first-line antibiotics was: amoxicillin (78%), cefalexin (10.2%), nitrofurantoin (6.1%), trimethoprim (30.8%), fosfomycin (4.6%), pivmecillinam (4.1%) and ciprofloxacin (11.5%). Second-line susceptibilities were performed in 2,228/24,657 (9%) of samples: 1,183/2,228 (53.1%) were ESBL producers, 1,115/1,379 (8.2%) and 31/2,223 (1.4%) were gentamicin and amikacin resistant respectively; no carbapenemase producing organisms were identified. Resistance patterns have remained stable over time, however gentamicin resistance sharply increased to 26.9% from April 2018 to March 2019.

**Conclusions:** Homerton’s AMR tool is simple to use and enables rapid, detailed analysis of local antibiotic susceptibility data. It can be implemented with limited resources and by small Antimicrobial Stewardship teams. The data generated is essential to ensuring antibiotic policies are appropriate for local populations. The development of this tool and sharing the process with the international community could improve local AMR surveillance capabilities.

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Prevalence of Hepatitis E Virus in allogeneic-haematopoietic stem cell transplant recipients from Portugal

Sara Cruz*1, Nânci Santos-Ferreira2, Maria São José Nascimento1, Carlos Pinho Vaz1, Fernando Campilho1, Luís Leite1, Rosa Branca1, Antonio Campos Jr1, Rui Medeiros1, Hugo Sousa1,3

1IPO Porto, Porto, Portugal, 2Faculty of Pharmacy, University of Porto, Porto, Portugal, 3ICVS - Life and Health Sciences Research Institute, Braga, Portugal

Background: Hepatitis E virus (HEV) is an emerging cause of acute hepatitis in healthy individuals. In developed countries, locally acquired HEV infections can lead to chronic infection in immunosuppressed patients. Little is known of HEV infection in hematopoietic stem cell transplant (HSCT) recipients, and their prolonged immunosuppression state makes them an important risk group. We developed an epidemiology study to characterize HEV prevalence in a retrospective cohort of allogeneic-hematopoietic Stem Cell Transplant (allo-HSCT) recipients.

Materials/methods: A retrospective study was performed in a cohort of 196 patients submitted to allo-HSCT in a single center between 2016-2018. Allo-HSCT recipients were screened prior transplantation for HEV RNA by real-time RT-PCR and for anti-HEV IgM and IgG using an enzyme immunoassay.

Results: All 196 samples were tested for the presence of anti-HEV IgG, and 39 were positive, giving an anti-HEV IgG prevalence of 19.9%. Furthermore, we found a prevalence of recent/active HEV infection of 4.1% with 8 positive cases for HEV infection, of which 6 were positive for HEV RNA, and 2 were positive for both anti-HEV IgM and IgG.

Conclusions: Over the last years, some attention has been given to this group of immunocompromised patients, but there is still a small number of studies. This study shows that recipients of allo-HSCT are at risk for HEV infection. Therefore, allo-HSCT recipients should be screened prior transplantation, and during episodes of liver enzyme abnormalities post-transplantation, with HEV RNA testing as the preferred diagnostic method in these immunocompromised patients. Nevertheless, more studies are needed to increase our understanding of the epidemiology of HEV in HSCT recipients, as it may be an important factor in the outcome of patients.

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Dynamic study of microbial interactions in the skin microbiota of patients with epidermal necrolysis (DynaMiCut)

Justine Lavaud1,2, Christophe Rodriguez3, Saskia Oro1, Nicolas De Prost4, Guillaume Gricourt1, Floriane Kouby1,2, Vanessa Desmontant1, Camille Hua1, Françoise Battereli1, Bruno Costes1, Elise Melloul1, Lolita Roisin2, Pierre Wolkenstein1, Jean-Winoc Becquesp1, Olivier Chesidow1, Charlotte Bernigaud1,2,3, Olivier Chosidow1, Charlotte Bernigaud1,2,7,8, Paul-Louis Woerther2,6,8

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Background: Toxic epidermal necrolysis (TEN) is a potential life-threatening dermatologic disorder characterized by necrosis and bullous detachment of the epidermis and mucous membranes most often secondary to drug intake. Mortality is related to skin barrier disruption, colonization and infection with opportunistic bacteria [OP]: notably Staphylococcus aureus (SA) and Pseudomonas aeruginosa (PA). The study objective was to describe the evolution of the skin microbiota from the phase of skin detachment to the epidermization of patients with TEN.

Materials/methods: Patients hospitalized in the dermatology or ICU reference center department with a skin detachment > 10% were included. Swabs (Eswab*) were taken from healthy and detached skin three times a week until epidermization. At each time-point, seborrheic areas (thorax), moist areas (crook of the elbow, inguinal fold and umbilicus/abdomen) and dry areas (anterior forearm and anterior thigh) were sampled. For all samples, targeted sequencing of the 16S ribosomal RNA gene [V3-V4] on Miseq Illumina® was performed after automated extraction (QIAsymphony®).

Results: 153 samples from 5 patients included between 06/2018 and 03/2019 were analyzed. 11,023,208 sequences were used for the targeted metagenomic analysis. The OTUs (Operational Taxonomic Unit) allowed identification in 99.97% [99.82%-100%] of cases up to the genus. The alpha diversity (Shannon) between skin detachment and healthy or epidermised skin was significantly different (p = 0.0094) and between seborrheic and non-seborrheic areas (dry and wet) (p = 0.028). Beta-diversity was also significantly different in skin detachment in quantitative analysis (p = 0.007) and at the limit of significance in qualitative analysis (p = 0.082). The results of the targeted metagenomic analysis showed the predominance of four bacterial genera: Pseudomonas, Staphylococcus, Corynebacterium and Enterobacter.

Conclusions: We did not observe a specific microbiota associated with TEN [low number of patients included]. During the detachment phase, there was a homogeneous loss of the healthy microbiota in favor of OP. Diversity analyzes showed a significant difference between skin detachment and healthy skin. There was a predominance of Staphylococcus followed by Pseudomonas and finally the microbiota recovered during the epidermization phase with a reappearance of commensal bacteria [Corynebacterium] (fig1). Similar observations have been described in burn patients.

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Local prevalence of molecular resistance mechanisms in carbapenem-resistant Enterobacteriaceae at a tertiary healthcare centre in Lebanon

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Background: Clinical syndromes caused by carbapenem-resistant Enterobacteriaceae (CRE) vary in severity owing to the myriad of mechanisms of resistance harbored by these organisms. This often results in limited therapeutic options. These mechanisms have a well-documented geographic variation, with a predominance of OXA-48 and metallo-β-lactamases reported in the Mediterranean region. In practice, novel antimicrobial molecules marketed for treating CRE infections exhibit different levels of therapeutic success.

Materials/methods: We retrieved from the records of the antimicrobial stewardship program at Saint George Hospital, a 333-bed tertiary care center in Lebanon, the CRE isolation density defined as the number of isolates/1000 patient-days (PD) from January 2010-December 2018.

Results of real-time PCR identification of carbapenemase genes (Cepheid Xpert® Carba-R) performed from January 2015-November 2019 were retrieved from the laboratory electronic database. Descriptive analysis was done using SPSS© Version 25.

Results: Over eight years, the isolation density of CRE increased 25-fold from 0.05/1000PD in 2010 to 1.28/1000PD in 2018. A total of 113 CRE isolates from 106 patients were tested from January 2015-November 2019. Only two isolates were tested in 2015, 20 in 2016 and 2017, and 51 in 2018. Overall, 84 isolates were found to possess ≥ 1 gene. The most commonly detected molecular mechanism of carbapenem-resistance was OXA-48 (38/84 tested; 45%) followed by NDM (33/84; 39%). Fifteen isolates (18%) co-expressed NDM and OXA-48. One isolate expressing KPC was detected from the wound of a patient who had undergone CNS surgery in Latin America. The most frequent organisms tested were Klebsiella pneumoniae (42/84; 50%), followed by Escherichia coli (33/84; 39%) and Enterobacter sp. (9/84; 11%). The most tested isolates were wound and fluid samples (42/113; 37%).

Conclusions: Although our sample may not fully represent the CRE burden of disease, it is highly suggestive of the rise in CRE with an OXA-48 and NDM predominance in our area. This is very challenging as it points towards a lower than expected benefit from the novel antimicrobial agents currently on the market. Epidemiologic surveillance, diagnostics and antimicrobial stewardship are necessary to understand CRE dynamics.

<table>
<thead>
<tr>
<th>Total Number of CRE isolates tested</th>
<th>114</th>
</tr>
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<tbody>
<tr>
<td>Molecular Mechanism of Carbapenem-Resistance Detected (number of isolates; n=84)</td>
<td></td>
</tr>
<tr>
<td>OXA-48</td>
<td>38</td>
</tr>
<tr>
<td>NDM</td>
<td>30</td>
</tr>
<tr>
<td>NDM + OXA-48</td>
<td>15</td>
</tr>
<tr>
<td>KPC</td>
<td>1</td>
</tr>
<tr>
<td>Distribution of CRE Isolates by Organism (number of isolates)</td>
<td></td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>42</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>33</td>
</tr>
<tr>
<td>Enterobacter species</td>
<td>9</td>
</tr>
</tbody>
</table>

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Burden of tuberculosis in Nepal: where do we stand?
Prabin Shrestha*1

1Young Professional Development Society Nepal (YPDSN), Kathmandu, Nepal

Background: Tuberculosis is a communicable disease causing ill health and one of the top ten causes of death worldwide. In Nepal, tuberculosis is a major public health problem and seventh leading cause of death.

Materials/methods: Desk review was conducted. Various literatures, reports, policy documents and guidelines related to tuberculosis in Nepal were reviewed using policy review framework. Descriptive analysis was conducted to present the findings.

Results: The World Health Organization estimates 44,000 new tuberculosis cases every year in Nepal, however in 2017/18, only 32,474 cases were notified, depicting missing cases needed to be notified and brought into treatment. It is estimated around 13,000 incident tuberculosis cases are missed to be diagnosed or notified annually and everyday there are 123 new tuberculosis cases, 18 deaths because of tuberculosis and 34 cases are missed to be diagnosed. The case notification rate stands at 112/100,000 and this has remained almost constant. Among the notified cases, 97.7% were incident (New and Relapse) cases and 71% were pulmonary cases of which 80% were bacteriologically confirmed. Around 24% of the cases were reported from Province 3 of which Kathmandu district alone holds around 41% (3,183 cases) which accounts for 10% of national cases. In terms of eco-terrain, Terai region reported more than half of cases (18,590, 57%). Most cases were reported in the middle age group with the highest of 50% in 15-44 year of age. Men were nearly 1.73 times more than women and childhood tuberculosis was around 5.5%. Among the notified cases, 67% were tested for Human Immunodeficiency Virus and 0.90% (196) were found positive and 94% (185) were enrolled for antiretroviral therapy. In Nepal, tuberculosis prevalence survey is undergoing that will provide the latest estimates of the disease and the results are expected by the end of 2019.

Conclusions: Significant efforts are required to identify the missing cases. There is a need for more accountable, equitable and quality service delivery approach making services universally accessible and patient centered. Awareness, accessible services, private sectors involvement and screening programs for high risk groups definitely can help increase the case notification.

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Abstract 8404

The real-life impact of the Xpert MTB/RIF Ultra assay on the diagnosis of tuberculosis in a hospital in central Israel

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Background: The Xpert MTB/RIF Ultra assay (Cepheid, USA) has high sensitivity for Mycobacterium tuberculosis (TB) detection. Our aim was to assess the real-life impact of this assay.

Materials/methods: To assess the impact of the Ultra assay at the Wolfson Medical Center, a secondary hospital in Israel, we compared two periods: Period I (1.11.2015-31.10.2017) when diagnosis was based on the Xpert MTB/RIF assay to Period II (1.11.2017-31.10.2019) when diagnosis was based on the Ultra assay. The Xpert MTB/RIF reports semiquantitative results (very low, low, medium, and high). In addition to improved sensitivity the Ultra assay also identifies trace amounts of TB DNA. The significance of this is not clear and is left to clinical judgement.

Results: In period I 1,064 TB PCR tests were performed for 741 patients. In period II 1,451 tests were performed for 884 patients, (36.4% increase in PCR tests and 19.3% increase in patients tested). During Period I 21 (2.8%) patients had a positive PCR (1 high, 10 medium, 5 low, and 3 very low). 2 patients had a negative PCR with a positive culture. During period II 37 patients were positive (6 high, 9 medium, 8 low, and 14 very low), an increase of 76.2%. 14 additional patients had a trace result. In only one case the TB culture was positive. 5 (35.7%) of them were treated for TB in the past. In Period I and Period II 10 (47.6%) and 19 (37.3%) were African born, 6 (28.6%) and 17 (33.3%) were born in Eastern Europe, 5 (23.8%) and 14 (27.5) were born in Asia. Mean age was 47.0, and 53.2 years. 18 (85.7%) and 29 (78.4%) cases were susceptible to rifampicin Cultures susceptibility results were variable. All trace cases were not susceptible.

Conclusions: The Ultra assay enabled a higher diagnosis rate for TB. During the study there was no change in TB guidelines, nor in the epidemiology of patients served by the hospital. We suggest that this reflects a higher sensitivity of the Ultra test in patients with paucibacillary TB. Trace result pause a clinical challenge as it is not clear what is their clinical significance.

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Enterococcus species involvement in vascular graft infections

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Background: Vascular graft infections (VGI) are associated with significant mortality. Due to the lack of data and recommendations, treatment of VGI was historically regarded as similar to other material-related infections or endocarditis. Enterococcus species represent the second gram-positive cocci in VGI (10 to 15%) but are frequently involved in polymicrobial infections. This make them difficult to treat.

Materials/methods: We described vascular graft infections involving Enterococcus sp. from a cohort of 230 VGI followed in an infectious disease center between 2009 and 2019.

Results: We found 29 (13%) VGI associated with Enterococcus sp.. Patients were mostly men (86.2%) with a median age of 72 years. Most of the cases involved patients with few comorbidities (COPD = 17%; obesity = 20%; diabetes mellitus = 27%; moderate or severe kidney failure = 44%). Enterococcus sp. strains includes E. faecalis (75%), E. faecium (18%), E. avium (n=1) and E. casseliflavus (n=1). Only 3 VGI were monomicrobial (10%). The microbiological epidemiology of the polymicrobial cases is broken down as follows: Enterobacteriaceae (52%); Staphylococcus species (45%, including six strains of methicillin-sensitive Staphylococcus aureus and one strain of methicillin resistant Staphylococcus aureus); Streptococcus species (24%); Candida species (12%). VGIs concerned intra-cavitary prosthesis and extra-cavitary prosthesis in 16 (55%) and 13 (45%) cases, respectively. Infections were declared during the three months following surgery (76%) with few associated clinical symptoms and a mean rate of CRP at 94 mg/L. The mortality rate was 31%.

Conclusions: Enterococcus sp. vascular graft infections seem to occur in patients with few comorbidities and during the early period following surgery. Our study shows a high rate of intra-cavitary prosthesis infection. Taking all these factors into account could be of importance for choosing the right antibiotic regimen, for example Piperacilline-Tazobactam rather than Cefepim associated with Vancomycin or Daptomycin.

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Abstract 8406

**Artesunate-containing therapies and abnormal haemoglobin: do we need to adapt the treatment?**

Ronan Jambou 1, Eric G Adji 2, Andre Toure 0, Albert Gnondjui 2, Stephane Koussou Tossea 2, Landry Tiacoh 2, Serge Assi 3, Ibrahima Sanogo 4

1 Institut Pasteur, Global health Department, Paris, France, 2 Institut Pasteur de Côte d’Ivoire, Parasitology Department, Abidjan, Côte d’Ivoire, 3 Institut Pierre Richet/Programme National de Lutte contre le Paludisme, Abidjan, Côte d’Ivoire, 4 Yopougon University Hospital, Abidjan, Côte d’Ivoire

**Background:** Patients with sickle cell anemia have a lower risk of severe disease, but are not protected for malaria. Sickle cells are very different from normal ones and efficacy of artesunate containing therapy can varies. This project aims to explore in vivo and in vitro drug responses of Plasmodium infecting red cells with or without abnormal hemoglobin.

**Materials/methods:** In vivo response was investigated through retrospective data obtained during standard 42 days lumefantrine-artesunate response protocol with a 6 hours decay (WWARN) or a 24H decay (WHO) follow-up. A, S or C genotypes were determined using electrophoresis or FRET molecular typing. The threshold of in vivo decrease of drug resistance was set at 5 hours for the decay slope (WWARN) and 48h for WHO test.

**Results:** For the in vivo study, data from 1003 patients were analyzed (268 and 735 for WWARN and WHO protocols respectively). For 804 of them, hemoglobin status was defined successfully (196 and 608 for the two protocols respectively), and 127 patients (15.7%) had abnormal hemoglobin (20 and 107 for WWARN and WHO). Overall, during the 42 days of follow up, 6 out of 127 (4.6%) and 52 out of 677 (7.7%) patients experimented a clinical drug failure. Patients with abnormal hemoglobin experimented more parasite clearance retardation (both for WWARN and WHO protocols) than others, especially before 5 years.

**Conclusions:** In conclusion abnormal hemoglobin seems not associated with a treatment failure with ACT, but clearance retardation could sustain occlusive crisis. In vitro experiments could suggest a specific resistance to artesunate which needs to be explored deeper.

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Abstract 8408

Performance of XpertMTB/RIF Ultra assay on respiratory and extra-respiratory specimens in a high-resource setting with a low TB prevalence

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Background: Tuberculosis (TB) is a worldwide public health threat, including in countries with a low prevalence. Rapid diagnosis of TB and determination of rifampicin resistance are essential for disease management and effective public health interventions. The Xpert MTB/RIF assay is an automated molecular test that has improved the detection of TB and rifampicin resistance. However, its sensitivity for TB detection is limited in patients with paucibacillary disease (patients with sputum smear-negative or extrapulmonary TB) or HIV. Xpert MTB/RIF Ultra has been recently developed to overcome this limitation. We compared the diagnostic performance of Xpert Ultra with that of culture for the detection of TB and rifampicin resistance in a high-resource setting with a low TB prevalence.

Materials/methods: This study was conducted in 6 tertiary hospitals in Madrid, Spain. Respiratory and extra-respiratory specimens were obtained as part of standard patient care between April 2018 and October 2019 and processed using Xpert Ultra, auramine acid-fast staining (AFB), conventional culture, and drug phenotypic susceptibility testing.

Results: Of the 1,268 clinical samples, 419 (33%) were extra-respiratory and 849 (67%) were respiratory. In total, MTB was isolated in 187 specimens, 173 of which were positive with Xpert Ultra. Trace-positive results were obtained in 15 samples, 8 of which were confirmed by culture. The sensitivity, specificity, PPV, and NPV of Xpert Ultra were: 94.7%, 97.7%, 90.5% and 98.8% for respiratory samples and 83.3%, 96.7%, 71.4% and 98.3% for non-respiratory. The sensitivity, specificity, and predictive values of Xpert Ultra for smear-positive and smear negative respiratory samples are detailed in Table 1. Xpert Ultra detected 5 RIF-resistant samples, also confirmed by DST.

Conclusions: XpertMTB/RIF Ultra demonstrates excellent diagnostic accuracy for TB detection and simultaneous detection of rifampicin resistance in a low prevalence setting, including in individuals with paucibacillary forms. Further studies are needed to evaluate the interpretation of trace-positive results.

<table>
<thead>
<tr>
<th>Respiratory specimens</th>
<th>% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GeneXpert</td>
<td></td>
</tr>
<tr>
<td>Smear-positive</td>
<td>100.0 (96.3-100.0)</td>
</tr>
<tr>
<td>Smear-negative</td>
<td>84.0 (71.5-91.7)</td>
</tr>
</tbody>
</table>

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Abstract 8411

Performance of the PBP2a (Alere-Abbott) immunochromatographic test on early primary cultures from positive MRSA/MR-CoNS blood cultures

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Abstract third-party references: Resistance detection rapid assays

Background: Early detection of methicillin resistance in staphylococci is crucial for optimal early treatment of infected patients. Alere™ PBP2a SA Culture Colony Test is an immunochromatographic test allowing the detection of the expression of PB-P2a directly from a primary culture in 5 minutes. We evaluated the use of this test on early primary cultures for methicillin-resistant S. aureus and methicillin-resistant coagulase-negative staphylococci (MRSA and MR-CoNS) from blood-culture bottles.

Materials/methods: The performance of the test was evaluated on early cultures (4h) on COS agar (bioMérieux) of MRSA or MRCoNS strains obtained from BactALERT-FA bottles reported positive using the BactALERT VIRTUO platform (bioMérieux):

- Artificial spiking with human blood and an inoculum of 100 bacteria per bottle using MRSA harbouring mecA [n=100] and mecC [n=2] representative of the various clones circulating in France and Europe.

- Artificial spiking with human blood and an inoculum of 100 bacteria per bottle using 36 mecA+ MRCoNS (S. epidermidis [n=11], S. capitis [n=4], S. hominis [n=4], S. haemolyticus [n=4], S. lugdunensis [n=4], S. saprophyticus [n=4], S. warneri [n=5]).

In addition, we tested prospectively MRSA (mecA+) positive blood cultures [n=36] from patients.

At the same time, identification using Maldi-tof VITEK® MS (bioMérieux) was performed on the same early culture.

When species identification was inconclusive and/or PBP2a was negative at t=4h, the tests were repeated after 6, or even after 24h of reincubation of the primary culture.

Results: The results highlighted an excellent ability to detect methicillin resistance at an early stage for S. aureus, except for MRSA harbouring mecC gene, which have a very low prevalence in France. For MRCoNS, 6% of methicillin-resistant strains were classified as susceptible after 4h of incubation on COS.

<table>
<thead>
<tr>
<th>Early cultures 4h</th>
<th>Reincubation culture 6h or 24h</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Test PBP2A+ Identification</td>
</tr>
<tr>
<td>mecA+ MRSA</td>
<td>99/100</td>
</tr>
<tr>
<td>n=100</td>
<td></td>
</tr>
<tr>
<td>mecC+ MRSA</td>
<td>0/2</td>
</tr>
<tr>
<td>n=2</td>
<td></td>
</tr>
<tr>
<td>mecA+ MR-CoNS</td>
<td>34/36</td>
</tr>
<tr>
<td>n=36</td>
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</table>

Conclusions: These results show that the Alere™ PBP2a SA Culture Colony Test can be used on colonies after short incubation (4h) of primary cultures from positive blood-cultures to detect methicillin resistance in S. aureus, in combination with Maldi-tof for identification.

For MRCoNS, a negative result after only 4h of incubation should be interpreted with more caution. In addition, species identification using Maldi-tof is also less effective.

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Sero-prevalence and risk factors of brucellosis among suspected febrile patients attending a referral hospital in southern Saudi Arabia (2014-2018)

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Background: Human brucellosis is an infectious zoonotic disease caused by Brucella spp. It is one of the most public health problems that remains largely neglected in developing countries, including Saudi Arabia. Brucellosis is particularly prevalent among rural people who have constant contact with livestock. The Objectives To determine brucellosis prevalence and associated risk factors in suspected febrile human patients attending Aseer referral hospital between 2014 and 2018 in the Southern region of Saudi Arabia.

Materials/methods: A cross-sectional sero-epidemiological study conducted in Aseer Central Hospital, South Saudi Arabia, between 2014 and 2018 among 7567 patients. Serum samples were analyzed for Brucella antibodies using slide agglutination test. Serology results and patient’s demographic data were analyzed by GraphPad Prism. Results were presented as mean ± SEM and differences between two groups were assessed by t-test and p<0.05 was considered significant.

Results: The prevalence of brucellosis among the admitted suspected 7567 cases was 12.8% (10.4–15.7%; CI 95%). The highest prevalence rate was detected during 2015, the rate decreased to the lowest level during the last three years (p < 0.05). Higher rate of brucellosis was observed among males than females (p < 0.05) and most cases were reported during summer season (p < 0.05). The highest prevalence rate was observed in age group 21-40 year old (40.5%) followed by 41-60 years (27.7%). The lowest prevalence rate was noticed in old and young children (15 % and 3%, respectively). Cross-transmission of brucellosis was seen within family (1%) and high titers (>1280) was noticed in 22% of the hospitalized patients. The major symptoms were fatigue, hyperhidrosis, fever and joint pain.

Conclusions: Our findings showed a high prevalence of human brucellosis among suspected patients in Aseer region. This indicates that clinical suspicion is a valid criterion and the endemic nature of the disease. The disease status requires early laboratory detection and confirmation to start prompt

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Abstract 8415

The 2020 Dutch working party on antibiotic policy guideline for empirical antibacterial therapy of sepsis in adults

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Background: The Dutch Working Party on Antibiotic Policy (SWAB), in collaboration with scientific societies for Medical Microbiology, Internal Medicine, Intensive Care, Surgery, Hospital Pharmacy and Emergency Medicine, has updated the guidelines on antibacterial therapy of sepsis in adults in the Netherlands.

Materials/methods: The guideline committee generated key clinical questions (Table 1). For each question we performed a pragmatic literature search to summarize the quality of evidence for clinically relevant outcomes, assessed according to GRADE from high to very low. The committee formulated recommendations after structured discussions as strong or weak. When evidence could not be obtained, recommendations could be provided on the basis of opinions (good practice statements).

Results: Forty-eight recommendations were generated. Overall, the committee formulated 21 strong and 27 weak recommendations. Eleven recommendations were based on moderate to high quality evidence, 28 on low to very low quality evidence and nine on good practice statements.

Conclusions: Our multidisciplinary committee formulated evidence-based recommendations for antibacterial therapy of adults with sepsis in the Netherlands. We will ask relevant scientific medical disciplinary organizations to review and endorse these guidelines. We will subsequently implement them in routine daily practice after dissemination through the national SWAB website and its antimicrobial formulary.

Table 1. Key clinical questions

<table>
<thead>
<tr>
<th>Question</th>
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<tbody>
<tr>
<td>Which bacteria are most frequently isolated from patients with sepsis in the Netherlands?</td>
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<tr>
<td>What are the resistance patterns of the most frequently isolated bacteria in patients with sepsis in the Netherlands?</td>
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<tr>
<td>Which patients are at risk for sepsis due to 3rd generation cephalosporin-resistant Enterobacterales in the Netherlands?</td>
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<tr>
<td>What is the importance of appropriate empirical therapy in patients with sepsis?</td>
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<tr>
<td>What is the effect of double active empirical antibacterial therapy compared to monotherapy in patients with sepsis?</td>
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<tr>
<td>What is the optimal choice of empirical therapy in patients with sepsis in the Netherlands?</td>
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<tr>
<td>What is the optimal empirical antibacterial therapy of sepsis in patients with a penicillin allergy?</td>
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<tr>
<td>What is the optimal timing of empirical antibacterial therapy in patients with sepsis?</td>
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<tr>
<td>What is the optimal duration of antibacterial treatment for sepsis?</td>
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<tr>
<td>In patients with sepsis, should we recommend pharmacokinetic/pharmacodynamic dosing optimization for empirical antibacterial therapy?</td>
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</tbody>
</table>

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Abstract 8420

Performance of core genome multi-locus sequence typing compared to capillary electrophoresis PCR ribotyping of Clostridioides difficile

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Background: Clostridioides difficile is the most common cause of antibiotic-associated gastrointestinal infection. Capillary-electrophoresis (CE) PCR ribotyping is currently the gold standard for C. difficile typing, but lacks sufficient discriminatory power to fully resolve outbreaks. This study compares the performance of core genome (cg) and whole genome (wg) multi-locus sequence typing (MLST) with CE-PCR ribotyping.

Materials/methods: 528 sequenced C. difficile strains were obtained from the NCBI Sequence Read Archive (Illumina sequencing platform). Additionally, 74 known ribotypes from the Leeds-Leiden reference collection were included, resulting in 99 unique ribotypes [1-98 different strains/ribotype]. Two different cgMLST schemes [SeqSphere: 2270 genes; Enterobase: 2556 genes] and the Enterobase wgMLST scheme (pangenome; 13763 genes) were used. Backward compatibility and discordances between CE-PCR ribotyping and cgMLST were assessed. A neighbor-joining tree was produced (1 strain per ribotype) [Seqsphere]. Average inter- and intra-ribotype allele differences were calculated from produced distance matrices using the cg/wgMLST schemes. Discriminatory power of cgMLST was assessed in 3 outbreak settings with RT078, RT036/198 and RT181 in Europe [30 strains] using a threshold of ≤ 6 targets to define similarity.

Results: Of 99 ribotypes (n=602 strains), 78 ribotypes [78,8%] had a unique profile, whereas 21 ribotypes clustered [≤ 6 targets] with multiple ribotypes [ranging 1-4].These latter ribotypes belonged mainly to MLST Clades 2 and 5, followed by Clade 1. This clustering is shown in a neighbor-joining tree (Figure 1). Average intra-ribotype allele difference varied between different ribotypes, with RT001 (n=11) showing high average allele difference [56.7 with Seqsphere; 70.5 and 110.7 with Enterobase cg and wgMLST, respectively], contrary to RT027 [n=13] [8.5 with SeqSphere; 10.5 and 16.7 with Enterobase cg and wgMLST, respectively]. Application of cgMLST in outbreak settings of RT078, RT036/198 and RT181 showed clustering of the strains with unrelated control strains of the same ribotypes/Clades.

Conclusions: cgMLST has the potential to replace CE-PCR ribotyping of C. difficile as the standard typing method in centers where whole genome sequencing is accessible. The method is reproducible, easy to standardize and offers a higher discriminatory power, but its use is currently limited in an outbreak of strains belonging to MLST Clades 2 or 5.

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Enabling phyletic-based comParison and visualization of genomic islands for tens to hundreds of microbial genomes

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Background: Genomic islands (GIs), commonly defined as clusters of genes of probable horizontal origin, are of interest since they disproportionately encode environmental and medically important adaptations, including novel metabolic abilities, virulence factors (VFs) and certain antimicrobial resistance (AMR) genes. While microbial genome sequencing has become rapid and inexpensive, current computational methods for GI analysis are not amenable for rapid, user-friendly, and scalable analysis of the thousands of genomes being sequenced. To fill this gap, we have developed IslandCompare, an open-source computational pipeline and web-based visualization resource to compare GIs across several to hundreds of bacterial genomes.

Materials/methods: In IslandCompare, GI predictions are performed using two of the most accurate GI prediction tools based on nucleotide composition biases: SIGI-HMM\textsuperscript{\dagger}duplications or mutations. For a precise characterization, algorithms are needed that identify transfer events with high reliability. Frequently, the transferred pieces of DNA have a considerable length, comprise several genes and are called genomic islands (GIs and IslandPath-DIMOB v1.0.0). A bacterial core-genome phylogeny is computed using Parsnp\textsuperscript{\dagger}however existing whole-genome alignment methods are limited in their ability to perform sequence comparisons of multiple sequences simultaneously. Here we present the Harvest suite of core-genome, and visualization tools for the rapid and simultaneous analysis of thousands of intraspecific microbial strains. Harvest includes Parsnp, a fast core-genome multi-aligner, and Gingr, a dynamic visual platform. Together they provide interactive core-genome alignments, variant calls, recombination detection, and phylogenetic trees. Using simulated and real data we demonstrate that our approach exhibits unrivaled speed while maintaining the accuracy of existing methods. The Harvest suite is open-source and freely available from: http://github.com/marbl/harvest. The Harvest suite for rapid core-genome alignment and visualization of thousands of intraspecific microbial genomes and pairwise regions of similarity between isolates are calculated with Mauve\textsuperscript{\dagger}they undergo large-scale evolutionary processes that present a challenge to sequence comparison to other methods through extensive simulations of genome evolution. ComParison to other methods through extensive simulations of genome evolution.

Conclusions: IslandCompare will facilitate more robust, flexible analysis and comParison of GIs, complementing existing tools like IslandViewer\textsuperscript{\dagger}, and enabling more efficient larger-scale analysis of infectious disease outbreaks and microbial evolution. The genome visualization developed may be adapted to visualize any genome feature for hundreds of phyletically-organized linear genomes, with broad applications.
Abstracts 2020

References:

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In vitro antimicrobial activity of liposomal ceftriaxone and liposomal amoxicillin and clavulanic acid against clinical strains isolated from companion animals with urinary tract infections

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Background: In the face of rising antimicrobial resistance and subsequent absence of effective antibiotics, new approaches are required. A promising strategy to increase the bactericidal efficacy of an antibiotic is through their entrapment in drug carriers, namely liposomes. This promotes antibiotic accumulation at the infection site and enhances binding to bacteria, while avoiding systemic exposure.

Materials/methods: The evaluation of the antimicrobial activity, in vitro, of free and liposome-encapsulated ceftriaxone and amoxicillin and clavulanic acid combination, against 14 susceptible and resistant clinical strains (8 strains of Escherichia Coli, 3 of Klebsiella pneumoniae and 3 of Pseudomonas Aeruginosa), isolated from companion animals with a confirmed diagnosis of urinary tract infections was performed. Their antimicrobial activity was measured by means of MIC determination, through the broth microdilutions method, whereas the assessment of the bacterial growth was achieved by a colorimetric method.

Results: Ceftriaxone and amoxicillin and clavulanic acid were successfully encapsulated, in a liposomal formulation of phosphatidylcholine and negatively charged phosphatidylglycerol (PC:PG). The liposome-encapsulated ceftriaxone showed bactericidal activity however the MIC values of the encapsulated ceftriaxone were 4 to 16 times higher than those of the corresponding free antibiotic, against the E. coli and K. pneumoniae strains. This result was probably due to a low liposome-bacterium interaction. The liposome-encapsulated amoxicillin and clavulanic acid didn't show bactericidal activity against any strain. None of the studied liposomal forms exhibited bactericidal activity against the P. aeruginosa strains owing to its bacterial resistance related to low permeability and enzymatic hydrolysis.

Conclusions: The liposomal encapsulation of the antibiotics ceftriaxone and amoxicillin and clavulanic acid combination didn't enhance the in vitro antibacterial activity when compared to the existing drug. Nevertheless, the liposomal formulation showed bactericidal potential, suggesting that for further investigation the extent of the interaction with the bacteria should be improved through the variation of the physicochemical properties of the liposome, namely surface charge, bilayer fluidity and fusogenic properties.

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Abstract 8426

**Antimicrobial stewardship practices in Brazil: where are we?**

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**Background:** To know the essential elements for the creation and implementation of the Antimicrobial Stewardship Program (ASP) becomes a necessary strategy to improve hospital care outcomes, related to the use of antimicrobials with a safe and cost-effective approach, minimizing the development of antimicrobial resistance.

**Materials/methods:** This was a prospective, cross-sectional, multicenter study. A total of 453 hospitals with adult Intensive Care Unit (ICU) from all 27 Brazilian states were included. The evaluation criteria of the institutions with ASP were grouped into six essential elements for the implementation of these programs in a National Guideline for Creation of the Antimicrobial Use Management Program in Health Services, with validation by specialists with satisfactory internal consistency (five elements with Alpha Cronbach classification “Good / Excellent”). The elements are: (E1) Institutional support from the senior management; (E2) Definition of the responsibilities of each professional involved; (E3) Education of professionals and family members; (E4) Strategic actions to rationalize antimicrobial prescription; (E5) Monitoring of ASP indicators and (E6) Dissemination of the results in the institution. The data were collected through an online government platform called FormSUS. This is an unprecedented study carried out between July and August 2019.

**Results:** It was observed that 62% (SD ± 24.1) of the hospitals have an ASP. Of the 27 Brazilian states, a significant implementation of the ASP was observed in the states of: São Paulo 96 (21.2%), Rio de Janeiro 63 (13.9), Paraná 47 (10.4%) and Minas Gerais 39 (8.6%), with the southeast region standing out in this unprecedented investigation. Regarding the evaluated elements of the 453 (47.5%) Adult ICUs that had the ASP implemented, the medians were: E1 = 65.3%, E2 = 35.7%, E3 = 15.2%, E4 = 78.4%, E5 = 72.2% and E6 = 58.7%.

**Conclusions:** The results show that Brazil needs to improve all Elements, but special attention should be given to E2 and E3. This study outlined an important Brazilian characteristic of the level of implementation of adult ICU bed hospital programs in Brazil.

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Identification of new small-RNAs involved in growth and virulence of Enterococcus faecium

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Background: Thus far, only few sRNAs have been identified in the opportunistic pathogen Enterococcus faecium, and the study has been conducted only in laboratory conditions, to analyse the sRNA involved in antibiotic resistance. To gain insights on the sRNAs that may play a role during infection and/or in laboratory conditions, we conducted RNA-seq and Transposon sequencing (TN-seq) analysis on bacteria grown in laboratory condition and bacteria recovered after intraperitoneal infection.

Materials/methods: The study was conducted using the E. faecium strain AUS0004. RNA was extracted from bacteria grown in laboratory condition and from bacteria recovered after intraperitoneal infection. All reads from the in vitro and in vivo RNA samples were mapped on the AUS0004 genome. The transposon bank was constructed using the pZXL5 vector and the insertions were mapped on the genome.

Results: 35 intergenic small-RNAs and 40 antisense small-RNAs were identified by RNA-seq. The quantification of the expression of the sRNA candidates in the in vitro and in vivo conditions has been performed. E. faecium transposon bank grown over night, representing the input pool, and recovered after intra-peritoneal infection (output pool) was sequenced and transposon insertion sites were mapped onto the AUS0004 genome. The intergenic transcripts regions, identified above, were checked for the presence of transposon insertions. Six intergenic regions do not show reads neither in the input library nor in the output library, reflecting a putative essential or fitness function for bacterial growth in laboratory culture. Interestingly, two intergenic regions do not contain reads in the output pool, indicating a possible involvement in pathogenesis. Moreover, these two intergenic regions appear to be over-expressed in vivo in the RNA-seq analysis.

Conclusions: RNA-mediated regulation is an important aspect to understand bacterial response to different environments. This study allowed the identification of new sRNAs involved in E. faecium growth and infection process, using an innovative approach combining RNA-seq and TN-seq. The putative sRNAs identified will be confirmed by Northern-blot and RT-qPCR and their involvement in bacterial growth and virulence will be analyzed using deletion mutants. We expect this approach to stand as a powerful tool to predict bacterial essential sRNAs.

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**Abstract 8429**

**Dananase: discovery of a novel *Pseudomonas aeruginosa* active polyketide type-1 synthetase**

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**Background:** The urinary microbiome harbors a great repertoire of bacteria, which possess an immense potential for the biosynthesis of different biochemical products such as polyketide synthases. Traditionally such compounds have been utilized as pharmaceutical drugs, for example as antibiotics or cytostatic substances or agrochemical agents. While examining the urinary microbiome of patients during AKI and concomitant antibiotic treatment a remarkable decrease of *Candidatus solibacter usitatus* in one patient attracted our attention. Surprised about detecting a putative close relative of a bacterium, which originally has been found in Australian soil in our patient’s urine, we examined the genome and protein coding regions of *Candidatus solibacter usitatus*. Thereby we identified a biosynthetic pathway, which allowed us to clone and produce an up-to-now unknown polyketide type 1 synthase, which we named Dananase.

**Materials/methods:** The *dananase* gene was synthesized, cloned into the pEX-A258 for replication and inserted into the p-T0-PO-entry-D gateway vector following PCR amplification. The resultant insert was shifted into the pEXP1-DEST gateway vector. *E. coli* transformants were selected for *dananase* expression. BAP1- *E. coli* was transformed with the *dananase*-pEXP1-DEST expression plasmid and grown in liquid culture under induction with IPTG. The supernatant was filtered and utilized for antimicrobial activity testing against *Pseudomonas aeruginosa*. Metabolome analysis of BAP1- pEXP1-DEST-*dananase* following induction with IPTG was performed and compared to LB-media alone and supernatants of dummy plasmid transformed BAP1- *E. coli*. In addition, the molecular structure of *dananase* product was determined using trans-AT polyketide synthase predictor web application genome mining tool.

**Results:** The 1646 amino acid long polyketide synthase type 1 named *dananase* was cloned into pEXP1 expression vector and expressed in BAP1. The supernatant contained specific antimicrobial activity against clinical isolates of *Pseudomonas aeruginosa*. This highly active compound could be further purified by HPLC but not yet identified in its structure. In silico prediction analysis suggested a polyketide as follows CC[C(O)*]CC[CC][NC][K]CC[CC][CC][O]0=0=0. Mass spectrometric analysis revealed several Dananase-specific peaks representing most likely its product in the supernatant.

**Conclusions:** The *dananase* gene of *Candidatus solibacter usitatus* consists of 4941bp and encodes a polymodular polyketide synthase type-1, its product successfully inhibits growth of *Pseudomonas aeruginosa* in vitro.

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Abstract 8431

**Epidemiology and risk factors for mortality in patients with *Pseudomonas aeruginosa* bacteraemia**

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**Background:** Our study was conducted to identify the predictors of mortality in patients with *Pseudomonas aeruginosa* bacteraemia.

**Materials/methods:** A retrospective study was performed on data from patients (>16 years old) with confirmed clinical signs of *P. aeruginosa* bacteraemia between January 2010 and December 2017 at a tertiary teaching hospital in Spain. The data that were routinely collected included the patient’s age, sex, clinical service at the onset of bacteraemia, acquisition, source of infection, predisposing clinical conditions, as well as antimicrobial susceptibility of causative pathogens, antimicrobial therapy regimen and the outcome during hospitalization. To determine independent risk factors for mortality, a multiple logistic regression model was used to control for the effects of confounding variables.

**Results:** Overall, 349 episodes of *P. aeruginosa* bacteraemia were included, 67.9% of them were men with a median age of 61 years (range, 16–100 years). A predisposing condition was identified in 83.1% of episodes. The acquisition of bacteraemia was nosocomial in 153 (43.8%) cases and the most common primary site of infection was catheter-related [86 (24.6%)]. One hundred and thirty-one (37.5%) had a severe sepsis or septic shock. The isolates were multidrug-resistant in 20 (5.7%) cases and extremely-resistant in 13 (3.7%). Treatment was appropriate in 176 (50.4%) of episodes. The 30-day mortality rate was 26.6% (93 patients). By univariate analysis, variables significantly associated with mortality included having an underlying disease (COPD and heart failure) and a predisposing condition (chemotherapy or radiotherapy, steroids, neutropenia and parenteral nutrition), requiring invasive procedures (endotracheal intubation, nasogastric tube or urinary catheter), presentation with severe sepsis or septic shock, absence of fever, having pneumonia and an increasing SOFA score. Multivariate model is shown in table 1.

**Conclusions:** *P. aeruginosa* bacteraemia was a nosocomial acquired infection in nearly half of episodes and catheter-related was the most common primary site of infection. Presentation with septic shock, absence of fever, previous use of steroids and neutropenia were independently associated with mortality.

**Table 1: Multivariate model**

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<tr>
<th></th>
<th>OR (95% CI)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Septic shock</td>
<td>15.1 (7.69-30.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Absence of fever</td>
<td>3.19 (1.35-7.53)</td>
<td>0.008</td>
</tr>
<tr>
<td>Steroids</td>
<td>2.38 (1.19-4.76)</td>
<td>0.013</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>2.07 (0.92-4.40)</td>
<td>0.058</td>
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Typing of carbapenemase-producing Klebsiella pneumoniae: IR Biotyper meets NGS

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Background: KPC- and NDM-producing Klebsiella pneumoniae (KPC-Kp and NDM-Kp) represent a serious public health concern. The high-resolution molecular epidemiology techniques required to track its spread are often unaffordable and laborious to perform. In this study, we evaluated the resolution power of the Fourier Transform Infrared Spectroscopy (FTIRS) based IR Biotyper in comparison to whole genome sequencing (WGS).

Materials/methods: We used WGS of 46 clinical and surveillance K. pneumoniae isolates (n=33 KPC-, n=11 NDM- and 2 ESβL-producers) from the Bologna University Hospital on a NextSeq500 (Illumina) with core genome MLST clustering (Ridom Seqsphere+ v 6.0.2) as reference method, and compared results to clustering using IR Biotyper (IRBT - Bruker Daltonik). Infrared spectra were acquired in transmission mode from bacterial suspensions in water/ethanol, placed onto a silicon sample plate, and air dried. The IRBT software evaluated spectra in the range 1300-800 nm, applying hierarchical cluster analysis (HCA) with Euclidean metric and single linkage. We compared IRBT results with core genome multi-locus sequencing typing (cgMLST). We explored the resolution power of IRBT with subclusters and the presence of bla genes.

Results: 14 Multilocus Sequence Types (ST) were identified in the samples: ST-258, 512, 1519, 307, 101, 189, 39, 45, 628 (KPC-producers); ST-11, 16, 147 (NDM-producers); and ST-15 and 37 (ESβL-producers). Using cgMLST these represent 9 different clusters and 4 unique isolates (using a 15-allele cut-off). IRBT classified the isolates in similar clusters using a cut-off value of 0.30. The comparison of the two trees showed a good congruence, with only minor differences in the location within the Clonal Group (CG) 258, and two ST-258 isolates clustered outside the CG-258. Lowering the cut-off value for IR Biotyper, further subclusters could be defined for CG-258 and ST-307. Subclusters correlated with presence of bla genes variants.

Conclusions: IR Biotyper showed a resolution power comparable to cgMLST for carbapenemase-producing K. pneumoniae typing, and a promising potential to be explored for a differentiation at a deeper level. Although further detailed investigations are necessary, these results suggest that IRBT represents a promising typing method for carbapenemase-producing K. pneumoniae.

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Abstract 8434

One-year prospective analysis of carbapenem-resistant strains isolated from a tertiary urinary centre in Romania

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Background: Urinary tract infections (UTIs) caused by carbapenem-resistant microorganisms are a major public health issue as they are difficult to treat, leading to high morbidity rates and high costs for the healthcare system. The prevalence of carbapenem-resistant bacteria in UTIs in Romania is not known. Here, we studied carbapenem-resistance among Enterobacterales and non-fermenters isolated over one year at a Tertiary Urinary Center in Bucharest, Romania.

Materials/methods: Antibiotic susceptibility testing was performed using disc diffusion antibiograms. All bacteria with reduced susceptibility to carbapenems and compatible with EUCAST criteria for carbapenemase confirmatory testing (MIC for meropenem > 0.125µg/ml) were screened using CarbaNP test and rCIM tests. NG-test Carba5 (NG biotech) was used to determine the type of carbapenemase involved.

Results: During the study period 392 Gram negative bacilli were studied. Upon interpretation of the antibiograms, 152 isolates met EUCAST screening criteria for carbapenemase production. Of these, 85 isolates were confirmed as carbapenemase producers on the basis of CarbaNP or rCIM positivity. NG-test Carba5 revealed that 54 isolates produced NDM (27 K. pneumoniae, 20 E. cloacae, 3 P. stuartii and 1 E. hormachei, S. marcescens, P. mirabilis, Acinetobacter baumannii), 11 isolates produced OXA-48 (all K. pneumoniae), 5 isolates produced VIM (all in P. aeruginosa), and 2 co-produced KPC and NDM (in K. pneumoniae). 13 isolates presented a positive CarbaNP or rCIM test, yet it was not identified through the lateral flow assay. These isolates will be subjected to WGS in order to identify the underlying carbapenem-resistance mechanism. In enterobacteria, carbapenem resistance was associated with Ciprofloxacin resistance (95% of strains), Nitrofurantoin (95% of strains) and Cotrimoxazole (75% of strains) – according to EUCAST guidelines.

Conclusions: Carbapenemase production in isolates from urinary tract infections appears to be high in Bucharest (22%). NDM is the main carbapenemase identified in Enterobacterales while VIM was predominant in Pseudomonas aeruginosa. Resistance to other antibiotics useful in UTIs such as fluoroquinolones, fosfomycin or nitrofurantoin is high as well, leaving few therapeutic options for these patients.

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**Abstract 8436**

**Late presentation of HIV infection in a hospital in the community of Madrid**

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**Background:** Late presentation (LP) has become the leading cause related to mortality in HIV-infected people in Western countries. It increases the risk of opportunistic infections and medical costs in the short and long term in the affected population.

**Materials/methods:** Retrospective, observational study conducted in a 400-bed hospital in the Community of Madrid. Epidemiological, clinical, analytical variables were collected from all patients over 18 years of age with diagnosis of HIV infection from 2008 to 2017. The patients were compared by area of diagnosis, transmission mechanism and place of origin. The LP was defined as <350CD4+ and advanced disease as the presence of an AIDS event or <200 CD4+ at diagnosis. The regression analysis identified the factors associated with LP.

**Results:** 186 patients were included. The average age was 36 years (SD 11.5), 74% were men and 54% were immigrants. The route of transmission was heterosexual (HTS) in 54% and 46% of the diagnoses were made in Primary Care. At diagnosis, the median of CD4+ and CV were 418/µL and 44,117 copies/mL respectively.

LP was found in 41.8% of patients. The frequency of advanced disease and WHO category C diseases at diagnosis were 30.3% and 14.1% respectively.

Women had a higher LP (52%) compared to men (38.2%), (p:0.98). HTS patients had a higher risk of LP (55%) compared to MSM (27.4%), (p: 0.001). Diagnosis during hospitalization (69.7%) compared to other areas was associated with a higher LP (p:0.001). African immigrants presented 66% of LP, followed by patients from Latin America (46.8%) and Europe (30.9%), (p: 0.01).

In the multivariate analysis, being an African immigrant was associated with LP, increasing the risk of LP by 2.9 times, 95% CI(1.06–8.34) (p:0.038).

In our cohort 88.2% of patients started ART. After 12 months of follow up the median of CD4 was 607 (IQR399-824). Among treated patients 96.2% had undetectable CV (<20 copies/mL) at 35 (20-40) weeks.

**Conclusions:** Late presentation remains an area of improvement in the cascade of care of HIV patients. In our cohort, African patients have a higher risk of LP. Attention should be given to HIV screening in this population.

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**Abstract 8443**

**Laboratory evaluation of a cartridge-based multiplex PCR assay for the detection of gastrointestinal pathogens**

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**Background:** Acute infectious gastroenteritis can be caused by a wide range of pathogens, but symptoms are rarely pathognomonic. Whilst many causes are self-limiting, certain pathogens have significant morbidity or infection prevention implications, for which rapid diagnosis can inform appropriate management. Traditional methods can be time-consuming and slow, delaying these management decisions. Multiplex PCR panels offer a rapid, simple solution to screen samples for a broad-range of pathogens in a single process. The aim of this study was to evaluate the utility of the Qiagen QIAstat Gastrointestinal Panel (QSGP) in a diagnostic laboratory.

**Materials/methods:** Stool specimens that had been sent for diagnosis of gastrointestinal pathogens using routine culture, antigen detection or PCR methods (depending on the pathogen) were retrospectively tested with the QSGP. The QSGP detects 24 bacterial, viral and parasitic pathogens by real-time PCR in an enclosed cartridge format. Stool samples were inoculated into phosphate-buffered saline using a flocked swab and 200 µL was immediately transferred to the cartridge. This was loaded onto the QIAstat DX instrument which completed nucleic acid extraction, amplification and interpretation of results.

**Results:** Forty-nine stool samples were included in the study, providing 324 individual comparisons between QSGP target results and reference methods. QSGP overall sensitivity was 78.7% and specificity was 98.5%. QSGP detected an additional 15 pathogens from 10 specimens, predominantly pathotypes of *Escherichia coli* not covered by the routine methods. Sensitivity for *Salmonella* spp. was particularly low at 58.3%, with 5 specimens negative by QSGP, but culture-positive following selenite broth enrichment. Two specimens were positive for shiga toxin-producing *E. coli* by QSGP, but negative by reference laboratory PCR. One specimen (2.0%) gave an invalid result. Hands-on time was <5 minutes per specimen and results were available within 75 minutes.

**Conclusions:** The QSGP is a simple and rapid test for syndromic gastrointestinal infection testing. Performance was similar to other nucleic acid-based assays for detection of GI pathogens, displaying the ability to detect a wider range of pathogens than culture, but having reduced sensitivity in the detection of *Salmonella* spp. The ability to obtain rapid results using this system has the potential to improve patient management.

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Abstract 8447

Detection of Legionella spp. and Legionella pneumophila in environmental samples using culture and live/dead-qPCR

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Background: Legionella spp. are found in water bodies but the typical route of infection is inhalation of bioaerosols. The distribution of such aerosols is commonly linked to evaporative cooling systems, cooling towers and wet separators, but also sewage treatment plants, composting plants and surface waters. The identification of a possible source is typically done by culture on selective nutritive medium (ISO 11731, 2017). For correct interpretation of results, 10 days are required and commensal bacteria often prevent detection of legionella colonies.

In an effort to establish a catalogue of measures which contribute to contain the threat to civil security as quickly as possible, we have evaluated molecular and immunological approaches to detect, quantify and characterize Legionella in environmental samples.

Materials/methods: Water and air samples were screened for Legionella spp. and L. pneumophila. The samples were tested in parallel with standard culture methods and with live/dead qPCR using propidium monoazide (PMA). Through treatment with PMA we were able to differentiate between the cells with an intact membrane (living) and those with a damaged membrane (dead).

Results: In total, 107 water samples and 28 air samples were collected between November 2015 and January 2019. Using qPCR, Legionella spp. was found in 115 samples. L. pneumophila was found using qPCR in seven cooling towers, three wastewater treatment plants, two industrial water samples in concentrations between 100-25000 GU/100mL and between 3-550 GU/m³ in three air samples. Using the culture method, only seven samples were positive for L. pneumophila. The concentration of PMA was adjusted based on the bacterial and organic load of the samples.

Conclusions: qPCR detection of Legionella spp and Legionella pneumophila shows higher sensitivity than the culture based methods. The methods described have been mentioned as part of the VDI (Verein Deutscher Ingenieure) guideline: “Catalogue of measures in case of suspicion of emission-related Legionellosis outbreaks - Identification and investigation of aerosol-emitting environmental sources in the context of legionellosis outbreaks” (VDI-MT 4259-1).

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Abstract 8449

Contrasting molecular epidemiology of Klebsiella spp. and Escherichia coli bloodstream infections in Oxfordshire (UK) 2009-2017

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Background: The incidence of Gram-negative bloodstream infections (BSI) in England continues to increase with significant associated morbidity and mortality; the genetic mechanisms underpinning this remain unclear.

Materials/methods: We performed short-read whole genome sequencing of all (90-day deduplicated) E. coli (n=2964) and Klebsiella spp. (n=651) BSIs in Oxfordshire, UK, 2009-2017. AMR genes were identified using Abricate; in silico MLST using BLASTn. Stacked negative binomial regression models were used to compare change in presence/absence of AMR genes/STs over time. Healthcare-associated was defined as nosocomial-onset or ≤ 30 days since last discharge.

Results: 1415/2964 (48%) of E. coli isolates belonged to four dominant STs (131/95/73/69); the proportion of BSIs caused by these did not change over time (p=0.25). Most cases were community-onset (1802 community vs 1162 healthcare-associated); ST131 was more likely than other STs (except ST69/95) to be healthcare-associated (p=0.005). There was a significant increase in incidence of the relatively drug-susceptible ST127 [rate ratio/year (RR) = 1.20, p=0.01], which became the sixth largest ST. In contrast for Klebsiella spp., only 87/651 (13%) of cases belonged to the top four STs and the proportion caused by these significantly decreased over time (RR=0.97, p=0.004). Klebsiella BSIs were more likely to be healthcare-associated than E. coli (p < 0.001). In E. coli, the incidence of isolates with genes encoding amoxicillin (RR=1.17, p=0.01) and/or ceftriaxone (RR=1.26, p=0.003) resistance increased significantly over time. Ceftriaxone resistance genes were more commonly found in healthcare-associated cases (136/1162 vs 147/1802, p=0.002). For Klebsiella spp. there was a significant decrease in the incidence of genes associated with co-amoxiclav (RR=0.92, p=0.03), gentamicin (RR=0.92, p<0.001) and ceftriaxone (RR=0.98, p=0.03) resistance. Carbapenemase genes were not observed until 2014; there was an increasing trend over the remaining study period (RR=1.59, p=0.03).

Conclusions: As expected, E. coli BSIs were predominantly community-onset, and associated with a largely clonal population structure and increasing AMR carriage. Somewhat paradoxically for the more healthcare-associated Klebsiella BSIs the opposite was true. This contrasting epidemiology likely reflects different environmental reservoirs and modes of acquisition, and may require different control strategies. The emergence of E. coli ST127, a strain associated with virulence, warrants vigilance.
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Feedlot lambs, carcasses and nearby animals are implicated in the transmission of cephalosporin-resistant *Escherichia coli*

Caroline Silva¹, Marlon Barroso¹, Katia Suemi Gozi¹, Juliana Froes², Leticia Kalir Pradela³,⁴, Juliana Peiró⁴, Luiz Claudio Nogueira Mendes⁴, Mara Nogueira¹, Tiago Casella*¹,³

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Abstract third-party references: FAPESP [#2018/02691-4, #2018/16147-4, #2019/16003-5], CAPES, CNPq

**Background:** Transmission of cephalosporin-resistant *Escherichia coli* through the food-production chain has been reported by studies concerning beef, chicken and pork meat. This represents a public health concern since those bacteria can cause hard-to-treat infections or horizontally transmit resistance genes to the intestinal microbiota. Studies with sheep are scarce, thus we initiated investigation in this field in Brazil.

**Materials/methods:** Ninety-nine and 93 lambs were rectal sampled during feedlotting in 2017 and 2018, respectively, different herds in the same stockyard. Carcasses were also sampled after slaughtering. In 2017, 10 other mammals dwelling nearby were also sampled. Faeces were inoculated in MacConkey agar supplemented with 4 mg/L ceftiofur. Suggestive colonies of *E. coli* were identified and submitted to antimicrobial susceptibility test by disk-diffusion. Genes responsible for cephalosporin-resistance were sequenced, and *bla*-carrying plasmids were characterized. Isolates were typed by *Xba*I-PFGE.

**Results:** Fifty-seven *E. coli* were isolated from 43 lambs, four carcasses and two surrounding animals in 2017, 82.5% of them multidrug-resistant, and 51 were isolated from 44 lambs and two carcasses in 2018, 100% of them multidrug-resistant. The *blaCTX-M-55* gene prevailed (56.1% in 2017, 62.7% in 2018), but *blaCTX-M-2* (12.3%, and 17.7%), *blaCTX-M-8* (10.5% in 2017), *blaCTX-M-14* (7.8% in 2018) and *blaCMY-2* (21.0%, and 9.8%) were also detected. *Xba*I-PFGE revealed identical isolates carrying *blaCTX-M-2*, *blaCTX-M-55*, or *blaCMY-2*, each gene in the same plasmid, recovered from lamb faeces in either years, showing that such strains remained in that environment throughout a year. Very similar isolates carrying *blaCTX-M-14*- in a unique plasmid were recovered from feedlot lambs and external animals in 2017, which supports that surrounding fauna is also involved in the transmission of cephalosporin-resistant strains to/from food-producing animals. Finally, identical *blaCTX-M-14*-carrying *E. coli* and plasmids were isolated from faeces and carcass in 2018, corroborating the transferring of resistant bacteria from animals’ intestine to ensuing products.

**Conclusions:** Commensal cephalosporin-resistant *E. coli* of food-producing animals contaminate carcasses after animals’ slaughtering, and such bacteria are also in close contact with animals nearby a herd, as well as they can remain subsequent years in a single stockyard. Our results corroborate the movement of resistant bacteria through the food chain.

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Brain abscess in children: a retrospective single-centre experience
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Background: Brain abscess (BA) is an uncommon infection during childhood, occurring mostly in the 4-to-7-year age group. Most frequent causative pathogens are streptococci, usually from an otic focus or in patients with congenital heart disease (CHD). BA symptoms and signs vary. High index of suspicion, recognition of predisposing conditions and prompt radiologic evaluation are necessary for outcome improvement.

Materials/methods: Patients with BA aged <18 years, treated at University Hospital for Infectious Diseases “Dr. Fran Mihaljević” in the 10-year period (1 January 2009 – 31 October 2019) were included. Epidemiology, etiology and outcome were analysed.

Results: This study enrolled 21 patients with a male predominance of 71.4%, and the median age of 7.8 years (range 11 days - 17.2 years). The majority (52.3%) were older than 8 years, followed by 3-to-7-year (28.6%) and <3 years age group (19.0%). Predisposing conditions were identified in 16 (76.2%) patients. The most common were otitis/sinusitis (19.0%), followed by dental infection (14.3%), CHD (14.3%), previous neurosurgical procedure (14.3%), meningitis (14.3%), haematologic malignancy (9.5%), and brain trauma (4.8%). In majority of them initial symptom was fever (66.6%). The classic triad of headache, fever and focal neurological deficits was identified in 8 cases (38.1%). Median time from the onset of symptoms to the diagnosis was 7 days (range 0-30 days). 80.9% patients had a single BA. Among patients with multiple BA, 50% were newborns.

Causative pathogens were identified in 16 (76.2%) patients and included 12 bacterial and one fungal pathogen. Most frequently isolated bacteria were streptococci (43.8% of culture-positive cases), of which S.intermedius and S.gordonii were the most common. Mixed infections were detected in 6 cases (37.5% of culture-positive cases). In 76.2% of patients neurosurgical procedure was an integral part of treatment. Stereotactical puncture was performed in 10 and radical excision in 6 patients. The mortality rate was 14.3%.

Conclusions: BA remains a relatively rare disease in children. The spectrum of predisposing conditions is changing due to the increase in the number of postoperative cases and immunocompromised hosts. Early recognition of symptoms, radiologic evaluation and adequate microbiological culture techniques are necessary for positive outcome.

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Abstract 8455

Immunotherapy in patients with relapsed/refractory HIV-related lymphomas

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Background: Immune check point inhibitors (ICIs) is a new option for salvage therapy in relapsed/refractory (r/r) Hodgkin lymphoma (HL) and non-Hodgkin lymphoma. Patients with HIV-related lymphoma may benefit not only anticancer activity of ICIs, but also from its potential anti-HIV effect [1]. The publications on ICIs in HIV-related lymphomas is limited by a few case reports [2,3].

Materials/methods: Nine patients with r/r HIV-related lymphoma were treated with nivolumab [nivo] between 2017-2019. Median follow-up time was 397 days [45-889]. The end points were response to therapy, immune-related adverse effects (IRAЕ) and overall survival (OS) at 12 months. LYRIC criteria for assessing FDG-PET/CT were applied.

Results: The main characteristics of study population and outcomes are presented on picture 1. Median number of prior lines of therapy was 3 (range, 2-4). Four patients received low dose of nivo as monotherapy [NCT03343665] with median N of courses 12 [7-12], 5 patients in combi with bendamustine and gemcitabine [NCT03259529] with median N of courses 4 [3-11]. The median of CD4+ was 382 c/mcl (range, 45-560). The only one patient didn’t receive cART due acute renal failure who died early from undetermined cause. Overall response rate (ORR) was 89% with the median time 104 days [73-517]; complete remission (CR) was 67% with the median time 107 days [75-265]. IRAЕ was not registered. OS at 12 months was 88.9%

Conclusions: Overall response rate to nivo in patients with HIV-related lymphomas was 89%, one-year OS – 88.9%. Immune-related adverse effects were not registered. Preliminary data provide that nivo seems to be an effective and safety treatment option for r/r HIV-related lymphoma.

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Abstracts 2020

Abstract 8461

Clinical characteristics and treatment outcome of patients with sepsis treated in an infectious disease intensive care unit

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Background: In most countries of the European Union patients suffering from sepsis are commonly treated in general intensive care units (ICU). By contrast, in some European countries, as well as in Zagreb, Croatia, these patients are admitted to a specialized infectious disease intensive care unit (IDICU). The study aimed to evaluate the clinical and epidemiological features of patients with severe sepsis admitted to an IDICU and compare treatment outcome in IDICU with literature data on the outcome of patients admitted to a non-IDICU.

Materials/methods: This research is a retrospective data analysis on 408 patients with the diagnosis of sepsis admitted to the 18-bed IDICU of the University Hospital for Infectious Diseases in Zagreb, Croatia over a three year period (January 2016 to December 2018).

Results: The admitting diagnosis of sepsis represented 35% of all admitting diagnoses in the IDICU. Nearly 2/3 of admitted patients with sepsis were men and the age median was 65 (IQR 55-75), whereas the median of Charlson Comorbidity Index (CCI) was 3 (IQR 2-5). Septic shock was present in 40% of patients, while the median of Sequential Organ Failure Assessment Score (SOFA) was 7 (IQR 4-11). In the IDICU the median patient length of stay was 8 (IQR 3-19) days. The most commonly associated infections were neurological (16%), endocarditis (15%) and urinary tract infections (12%). The specific mortality rate among patients with sepsis was 14%. Around 10% of admitted patients with sepsis were discharged from the IDICU as independent and mobile, while 23% of patients were left with reduced functional disability and 27% of patients were completely dependent and immobile, with case fatality rate of 40%.

Conclusions: The proportion of admitted patients with sepsis in the IDICU was 35%, which is higher than in other ICU-s in Croatia (10-20%) according to literature. The specific mortality rate of IDICU patients of 14% was though in the lower portion of the compared specific mortality range for sepsis (10-50%). Taken into consideration that the admitted patients had higher CCI and SOFA scores, we observed that the type of ICU may have had an impact on the treatment outcome.

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Infectious complications in patients with relapsed/refractory Hodgkin's lymphoma during new agents' therapy

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Background: Despite of many reports on anti PD-1 antibody and brentuximab vedotin (BV) therapy the risk of infections is still unknown. We are the first to present the study on infectious complications in large cohort r/r HL patients treated with nivolumab (nivo) or BV.

Materials/methods: Since 2012 to 2018 in our clinic 287 patients with r/r HL received salvage treatment with nivo (n=112) and BV (n=175). In nivo and BV groups median age was 31 and 27 y, median lines of chemo before therapy was 6 (range, 1-9) vs 5 (range, 1-12). The median number of chemo courses was 20 (range, 1-30) vs 4 (range, 1-16), with the median follow-up time 3 years. Infection episodes and outcome analysis considered events at one year after first nivo or BV administration and were censored at the date of allo-HSCT or auto-HSCT.

Results: In 26 r/r HL patients during salvage therapy 31 infection episodes were registered: bacterial infections – 35.5% (n=11), viral infections – 35.5% (n=11), and IFD – 29% (n=9). The incidence of documented bacterial infection in nivolumab group was 6%, in BV – 3.4%, (p=0.19). The main etiology agent was Klebsiella pneumoniae (45%). The incidence of viral infection in nivolumab group was 5.3%, in BV – 2.8% (p=0.28). The main etiology agent was CMV (90%). The incidence of IFD in nivolumab group was 3.2%, in BV – 2.8% (p=0.30). The main etiology agents were Aspergillus spp. (100%). Median time to infection episode was 98 days (12-365) after first nivo administration and 144 days (33-363) after BV. Primary chemoresistant disease before nivo therapy was the only risk factor for the infectious complications during salvage therapy of r/r HL (p=0.029). Overall survival (OS) at 1 year after first nivo administration was 96.5%, in BV group – 72.1%. The only one death was attributed to infection in nivo group.

Conclusions: Infections after BV and nivo developed in 10.8% of patients with r/r HL. There was no difference in incidence of different type of infections during salvage treatment for relapsed/refractory Hodgkin’s lymphoma in BV and nivolumab group. Infections after BV and nivolumab can be managed successfully.

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Fecal lactoferrin is associated with severity at presentation but not relapse risk in *Clostridioides difficile* infection

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**Background:** Fecal lactoferrin (FL) has been shown to correlate with the severity of inflammation in the gastrointestinal tract. Data relative to *Clostridioides difficile* infection (CDI) is scarce.

**Materials/methods:** We investigated the accuracy of FL values to predict CDI severity or relapse in a prospective cohort of consecutive patients diagnosed with CDI over a 10-month period. A stool sample was collected at diagnosis and frozen at -80ºC. The ELISA kit DRG EIA-6038 was used to assess FL levels after sample extraction with the system EIA-5674 (both from DRG Diagnostics, Marburg, Germany). According to manufacturer’s recommendations, the cut-off for test positivity was 7.2 µg/ml. Second [Q2 (67.4 µg/ml)] and third quartiles [Q3 (213.8 µg/ml)] were also explored as alternative cut-off values.

**Results:** Overall, 170 samples (146 first CDI episodes, 26 recurrences) were included. The presence of FL values below Q2 was more frequent in patients with diabetes mellitus [64.3% [27/42] vs. 44.5% [57/128], P-value = 0.03], immunosuppression (62.0% [31/50] vs. 44.2% [53/120], P-value = 0.04), solid organ transplantation (71.9% [23/32] vs. 44.2% [61/138], P-value = 0.005) and chronic renal failure (70.2% [33/47] vs. 40.6% [50/123], P-value = 0.02). On the contrary, FL test positivity was associated with solid organ cancer (96.7% [29/30] vs. 77.1% [108/140], P-value = 0.016) and patient age (67.4 ± 18.9 vs. 58.4 ± 16.3 years, P-value = 0.014), as well as with acute renal failure (90% [45/50] vs. 79.3% [98/121], P-value = 0.09), fever (88.8% [79/89] vs. 67.9% [55/81], P-value = 0.007) and leucocytosis at presentation (92.5% [37/40] vs. 78.5% [95/121], P-value = 0.04). Patients with non-severe CDI exhibit more frequently negative FL test than those with severe or fulminant episodes (25% [28/112] vs. 8.6% [5/58], P-value = 0.01). FL values below Q2 were more common among patients with non-severe CDI (58.0% [65/112] vs. 34.5% [20/58], P-value = 0.004). No association was observed between a positive FL test and CDI relapse in the subset of 146 first episodes (86.7% [13/15] vs. 79.4% [104/131], P-value = 0.5).

**Conclusions:** Although immunosuppressed patients presented lower FL levels, a positive test was associated with severity at presentation of CDI (but not relapse).

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Phenotypic and genomic diversity of bacterial isolates from humans and healthy pigs in Thailand

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Background: Antibiotic drugs are frequently used in the rearing of farm animals in South East Asia either as direct treatments or as supplements in animal feed. However, there is limited information into the prevalence and dissemination antimicrobial resistance within these farms. Within this study we developed a bacterial isolate collection from small and medium sized pig farms in Thailand. Each farm had samples collected from the contact animal-handler (C), non-contact animal-rearing individual (NC), and from the health pigs (P) present on the farm.

Materials/methods: A total of 166 pig farms were included in this study, where 115 were from small-sized farms and 51 from medium sample farms. Farm size was categorized as, small-sized farms being <9 pigs and medium sized were categorized as ≥9 pigs. P samples were collected from rectal swabs, whilst all human (C and NC) samples were collected from fecal samples. Collected samples were cultivated on selective media plates, bacterial isolates were selected and species determined by MALDI-TOF. All bacterial isolates were tested for their antimicrobial susceptibility testing (AST) profile and whole-genome sequenced (WGS).

Results: Our bacterial collection consists of 492 E. coli and 43 K. pneumoniae isolates. From our AST testing we saw an abundance of multidrug resistance in both species (E. coli 358/492, 72.3% and K. pneumoniae 29/43, 67.4%). No significant differences between the three groups were found by using a three-way ANOVA statistical test of variance. From our WGS results, we observed a multitude of sequence types (ST) for both species (for E. coli 143 known and 51 novel STs whilst for K. pneumoniae 26 known and 10 novel STs) that will undergo further analysis for clonality and plasmid type testing.

Conclusions: MDR Gram-negative bacteria are prevalent in both small and medium sized Thai pig farms, amongst all sample groups. We demonstrate that NC individuals are at high MDR carriage risk due to close proximity but the societal risk needs to be explored further.

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Limitations of the diagnostic criteria for invasive aspergillosis in solid organ transplantation: a national cohort (DIASPERTOS study)

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Background: Diagnostic criteria for IA are well validated in hematological patients, but their application to other population, including SOT patients, has several limitations.

Patients/methods: Retrospective study, carried out in 8 centers in Spain from 2010 to 2019. EORTC criteria, Blot et al criteria and a new diagnostic algorithm based on the combination of the above criteria (DIASPERTOS criteria) were compared.

Results: During the study period, 91 IA were diagnosed. The distribution of patients according the different criteria were: "probed" in the same 29 patients for the three criteria; "probable or putative" in 32, 49 and 60 patients, respectively; “possible” in 3, 0 and 1 patients respectively; and “not classified” in 26, 12 and 1 patient, respectively. The contribution of diagnostic techniques according to the type of SOT was as follows:

<table>
<thead>
<tr>
<th></th>
<th>Lung tr.</th>
<th>Kidney tr.</th>
<th>Liver tr.</th>
<th>Heart tr.</th>
<th>Combined*</th>
<th>All</th>
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<tr>
<td></td>
<td>[n:28]</td>
<td>[n: 23]</td>
<td>[n: 19]</td>
<td>[n: 16]</td>
<td>[n: 5]</td>
<td>[91]</td>
</tr>
<tr>
<td>Respiratory sample culture</td>
<td>26 (93%)</td>
<td>19 (83%)</td>
<td>14 (82%)</td>
<td>15 (94%)</td>
<td>4 (80%)</td>
<td>78 (86%)</td>
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<td>GM blood &gt;0.7 (only in 44 p)</td>
<td>1 (33%)</td>
<td>8 (52%)</td>
<td>4 (33%)</td>
<td>8 (61%)</td>
<td>2 (100%)</td>
<td>23 (52%)</td>
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<tr>
<td>GM BAL &gt;1.0 (only in 34 p)</td>
<td>5 (71%)</td>
<td>7 (87%)</td>
<td>6 (54%)</td>
<td>5 (62%)</td>
<td>-</td>
<td>23 (68%)</td>
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<tr>
<td>CT &quot;halo-sign&quot;</td>
<td>2 (7%)</td>
<td>4 (17%)</td>
<td>1 (5%)</td>
<td>4 (25%)</td>
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<td>13 (14%)</td>
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<tr>
<td>CT &quot;air-crescent sign&quot;</td>
<td>1 (3%)</td>
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<td>0</td>
<td>1 (6%)</td>
<td>0</td>
<td>13 (14%)</td>
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<tr>
<td>CT &quot;nODULES&quot;</td>
<td>8 (28%)</td>
<td>14 (61%)</td>
<td>6 (31%)</td>
<td>9 (56%)</td>
<td>1 (20%)</td>
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<td>CT &quot;cavitation&quot;</td>
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<td>9 (39%)</td>
<td>4 (21%)</td>
<td>6 (37%)</td>
<td>1 (20%)</td>
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<td>CT &quot;tree-in-bud&quot;</td>
<td>7 (25%)</td>
<td>6 (26%)</td>
<td>4 (21%)</td>
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<td>CT &quot;ground glass opacities&quot;</td>
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<td>7 (30%)</td>
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<td>1 (20%)</td>
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</table>

Conclusions: The diagnostic of IA in SOT requires a different approach than of the hematological patient. EORTC and Blot et al. criteria have poor sensitivity in SOT patients with IA. GM in blood and GM in BAL have a sensitivity of 52% and 68%, respectively, in these patients. The most frequent radiological features in CT in SOT were nodules, ground glass opacities and tree-in-bud pattern.

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**Progressive multifocal leukoencephalopathy, still a challenge in the combined antiretroviral therapy era**

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**Background:** The aim of our study was to assess prevalence, clinical outcomes and survival in HIV-infected patients diagnosed with progressive multifocal leukoencephalopathy (PML) in a Romanian tertiary care facility.

**Materials/methods:** Retrospective study on HIV-infected patients hospitalized with PML at Victor Babes Hospital, Bucharest, between January 2006 and December 2018. PML diagnosis was based on clinical symptoms, neuroimaging, positive CSF PCR-DNA JC virus and neurohistopathology.

Statistical analysis was performed using SPSS vs. 20.0.

**Results:** During the study period 87 HIV-infected patients, 63.2% males, were diagnosed with PML, with a prevalence of 3.5/1000 PY [87/24,315]. Thirty patients were confirmed by positive CSF PCR-DNA-JCV. The median age at PML diagnosis was 27 years [IQR: 23, 33]. Modes of HIV acquisition were: parenteral, during early childhood (PI) 54.0%, sexual contact (SI) 40.2% and injecting drug use (IDU) 5.7%. The median CD4 cell count/µl and plasma HIV-RNA (log₁₀copies/mL) at PML diagnosis were 53 [IQR: 16,129] and 4.72 [IQR:2.92,5.40], respectively. The median HIV-RNA in CSF [log₁₀copies/mL] was 3.89 [IQR: 2.71,4.59]. Brain MRI showed lesions in brainstem and/or cerebellum in 25 (28.7%) patients and 4 were diagnosed with PML IRIS. Out of 62 patients previously diagnosed with HIV, 45 were on ART and 41 had severe immunosuppression due to poor adherence. PI patients were younger at PML and HIV diagnosis [p<0.0001] and had lower CD4 cell count [p=0.006] compared to SI and IDUs. The overall mortality and early mortality rates [within 3 months] were high, 49.4% and 29.8%, respectively. 44 patients (50.5%) were alive at the end of the study, with a median survival of 68.0 months [IQR: 41.4, 102.3]. The main risk factors for short survival were nadir CD4 cell count lower than 50/µl [p=0.014], severe immunosuppression [CD4 ≤ 80/µl] and HIV-RNA > 5.00 log₁₀copies/mL [p=0.006] at PML diagnosis [Figure].

**Conclusions:** PML prevalence was high due to late diagnosis and/or poor adherence to ART. SI and IDU patients were frequently diagnosed simultaneously with HIV and PML and had more severe immunosuppression, compared to PI. High HIV viral load at PML diagnosis was a predictor for short-term survival and increased mortality rate.

**Figure.**

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**Abstract 8477**

**Lower concentrations of immunoglobulins (IgM, IgG and IgA) in patients with septic shock compared with sepsis**

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**Background:** Septic shock is the subset of sepsis with the poorest prognosis. Early recognition of those patients is the keystone of successful treatment. Immune status is one of the key factors for sepsis outcome. We have hypothesized that concentrations of immunoglobulins at admission could reflect one part of the patients immune status, and might serve as biomarkers of sepsis severity. We aimed to compare immunoglobulin levels on the day of sepsis diagnosis in patients with sepsis and septic shock, and to compare immunoglobulin concentrations between the subgroups of survivors and non-survivors among the septic shock patients.

**Materials/methods:** 137 consecutive septic patients (Sepsis-3 definition) were included – 116 with sepsis and 21 with septic shock. All patients had available clinical and laboratory data: age, SOFA score, white blood cell count (WBC [$\times 10^9$]), C-reactive protein (CRP [mg/ml]), procalcitonin (PCT [ng/ml]), immunoglobulin levels (IgM, IgG and IgA [g/l]) on admission. Mann-Whitney test was used for comparison of evaluated parameters in two observed groups. For evaluation of sensitivity, specificity and cut-off values of immunoglobulin concentrations, we constructed ROC curves.

**Results:** IgM, IgG and IgA levels were significantly lower in patients with septic shock (Table 1). Despite the small number of patients in septic shock group, concentrations of immunoglobulins in survivors (n=12) and non-survivors (n=9) were compared. Significantly lower levels of both IgM (non-survivors: 0.36 [0.30-0.49] g/l; survivors: 0.64 [0.42-1.04] g/l; p=0.049) and IgG (non-survivors: 2.73 [2.12-3.94] g/l; survivors: 6.13 [3.01-10.89] g/l; p=0.023) were detected in non-survivors.

**Table 1. Evaluated parameters in sepsis and septic shock group**

<table>
<thead>
<tr>
<th></th>
<th>Sepsis Med(IQR)</th>
<th>Septic shock Med(IQR)</th>
<th>p</th>
<th>AUC ROC (95%CI)</th>
<th>Cut-off</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>64 (52-72)</td>
<td>63 (56-69)</td>
<td>0.971</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SOFA</td>
<td>5 (3-8)</td>
<td>8 (5-9)</td>
<td>0.007</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>15.3 (9.0-20.4)</td>
<td>8.4 (5.7-14.2)</td>
<td>0.008</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>224 (180-283)</td>
<td>213 (133-284)</td>
<td>0.496</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT</td>
<td>18.4 (5.3-70.9)</td>
<td>74.4 (9.0-106.5)</td>
<td>0.075</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IgM</td>
<td>0.90 (0.64-1.28)</td>
<td>0.48 (0.36-0.75)</td>
<td>&lt;0.001</td>
<td>0.774 (0.651-0.897)</td>
<td>0.67</td>
<td>71%; 73%</td>
<td></td>
</tr>
<tr>
<td>IgG</td>
<td>8.65 (6.22-11.43)</td>
<td>3.94 (2.57-9.09)</td>
<td>&lt;0.001</td>
<td>0.762 (0.631-0.892)</td>
<td>5.10</td>
<td>67%; 89%</td>
<td></td>
</tr>
<tr>
<td>IgA</td>
<td>1.82 (1.25-2.21)</td>
<td>0.98 (0.73-1.30)</td>
<td>&lt;0.001</td>
<td>0.787 (0.681-0.892)</td>
<td>1.36</td>
<td>81%; 72%</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** Patients with septic shock had lower concentrations of IgM, IgG and IgA than patients with sepsis. Early measurements of immunoglobulins concentrations could serve as potential biomarkers of septic shock development.

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**Abstract 8478**

**Diabetes and obesity reduce weight gain on tuberculosis treatment**

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**Abstract third-party references:** Department of Infectious Diseases London North West University NHS Trust

**Background:** Weight gain is used as a clinical indicator of satisfactory response to anti-tuberculosis treatment (ATT). Here we review weight change on ATT for our TB cohort, with a high prevalence of Type 2 diabetes mellitus (17%), to identify correlates of poor weight gain, and the effect of diabetes on weight change.

**Materials/methods:** Retrospective case-control study of patients treated in a North West London tuberculosis unit between 01.01.2015 and 01.01.2018. Diabetic patients (DM) were age-matched to non-diabetic (non-DM), and pre-diabetic patients were excluded. Weights at 0, 2 months and 6 months of treatment were extracted from the clinical record, and percentage weight change for induction (0-2months), continuation (2-6months) and overall (0-6months) were calculated.

**Results:**

- Older age negatively correlated with both induction and overall percentage weight changes ($r(147) = -.301 \ p=.0007$ and $-.357 \ p=.00003$ respectively).
- Higher start weight negatively correlated with continuation and overall percentage weight changes ($r(113) = -.185 \ p=.048$, $r(129) = -.195 \ p=.027$ respectively).
- Male sex was associated with significantly higher mean weight gains during induction, continuation and overall.
- Percentage weight change was not associated with smear-positivity, ethnicity, HbA1c or good treatment outcomes.

Diabetic patients had significantly less percentage weight gain at all treatment stages than age matched non-diabetic patients:

<table>
<thead>
<tr>
<th>Age-matched</th>
<th>Diabetic (n=67)</th>
<th>Non-diabetic (n=67)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>60</td>
<td>58</td>
<td>NS</td>
</tr>
<tr>
<td>Weight Start*</td>
<td>69.7kg ±14.5</td>
<td>66.5kg ±14.1</td>
<td>.11</td>
</tr>
<tr>
<td>Change Induction*</td>
<td>+0.4% ±4.0</td>
<td>+1.9% ±3.5</td>
<td>.024</td>
</tr>
<tr>
<td>Continuation*</td>
<td>+2.1% ±6.6</td>
<td>+4.1% ±5.5</td>
<td>.042</td>
</tr>
<tr>
<td>Overall*</td>
<td>+1.8% ±6.3</td>
<td>+4.9% ±6.4</td>
<td>.005</td>
</tr>
</tbody>
</table>

*Mean ±standard deviation

No significant differences in smear-positivity, ethnicity, sex or outcomes between diabetic and non-diabetic groups.

**Conclusions:** In our cohort lower percentage weight increase was associated with diabetes, higher start weight, older age and female sex.

Treatment outcome was good for a large proportion of patients despite the lack of significant weight gain for many.

Diabetic TB patients have less weight gain during treatment despite similar starting weights possibly due to the metabolic effects of diabetes or effects of glycaemic treatment. Consequently, weight gain as an indicator of TB recovery may therefore be less valid in heavier, older and diabetic populations.

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Abstracts 2020

Abstract 8484

Evaluating the healthcare utilisation of undocumented migrants in the Helsinki and Uusimaa hospital district, Finland: a protocol for a register-based cross-sectional study

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Background: It is estimated that 3000-4000 undocumented migrants reside in Finland. The majority live in the capital region of Helsinki. Evidence on the health status and utilisation of health care services by undocumented migrants in Finland is scarce. Their entitlement to municipal health care and social services is severely restricted, although considerable variation exists between municipalities. A description of these services is currently missing. We aim to describe the tertiary level health system for undocumented migrants in Finland and present the first characterization of the use of tertiary level health care and the prevalence of routinely screened resistant bacteria (e.g. MRSA, VRE) in undocumented migrants.

Materials/methods: By using legislative and administrative documents, we map the current health system for undocumented migrants in Finland. In addition, we perform a register-based cross-sectional study of the undocumented migrant population’s use of outpatient and inpatient services in the Helsinki and Uusimaa Hospital District between 2010-2020. The data are collected using two different methods to maximise capture rate. Firstly, in addition to a temporary personal identification code, the financial documentation on hospital billing include a specific code in the case of an undocumented migrant. Secondly, hospitals apply for state reimbursement from the Social Insurance Institution with a specific form. Combining records allows for the tracking of selected personal identification codes from the electronic patient record system. Information is collected on, e.g., the length of hospital stay, number of hospital visits, related diagnoses, and screening results on colonising resistant bacteria.

Results: The tertiary level health system available to undocumented migrants in Finland is shown in Figure 1. We have identified and mapped the registering basis for undocumented migrants in the HUS area and are currently collecting data.

Conclusions: We have created a model to be used to evaluate health care utilisation and needs of undocumented migrants. We will assess the prevalence of routinely screened resistant bacteria to test the applicability of our model in this particularly hard-to-reach population. The results can be used in developing health care services for undocumented migrants and improving their access to necessary preventative health interventions.

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Abstract 8487

Granulicatella sp. and Abiotrophia sp. as a rare cause of osteoarticular infections

Dorsaf Slama*, Philippe Morand*,1, Julien Loubinoux1,2, Anne-Laure Roux1, Luc-Jean Eyrolle1, Guillaume Aubeger1, Maya Enser3, Thomas Bauer4, Remy Gauzit1, Valérie Zeller5, Dominique Salmon-Ceron1

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Abstract:

Granulicatella and Abiotrophia are two bacterial genus close to streptococci, formerly known as “nutritional variants of streptococci”. The purpose of this work is to describe the characteristics of osteoarticular infections (OAI) due to Granulicatella and Abiotrophia and their antibiotic resistance pattern.

Background:

The background section describes the context and rationale for the study.

Materials/methods:

The methods section details the study design, patient selection, data collection, and analysis methods.

Results:

The results section presents the findings of the study, including patient demographics, clinical characteristics, and outcomes.

Conclusions:

The conclusions section summarizes the key findings and their implications for future research and clinical practice.

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Development of a new murine model for *Enterococcus faecium* intestinal colonisation

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**Background:** *Enterococcus faecium* is a ubiquitous organism usually present in normal human gut microbiota and natural environment, which is commonly responsible for healthcare-associated infections and hospital outbreaks. Understanding colonization mechanisms seems to be essential to manage those infections and to limit hospital spread. Several experimental models of intestinal colonization have been described using different antibiotic protocols. The aim of this study was to compare these different published models of intestinal colonization with a new one as close as possible to human conditions.

**Materials/methods:** Protocols were performed using 6-weeks specific-pathogen-free Swiss mice. Mice were treated with antibiotics to decolonize the intestinal tract, and then a calibrated suspension (ca. 10⁸ CFU/mL) of *E. faecium* was orally inoculated. The vancomycin-resistant vanB-positive Aus0004 reference strain (recovered from a bacteremic patient) was used. A fecal pellet was collected for each mouse before inoculation and at day (D) 3, D5, D7, D10 and D14 after colonization. Viable bacterial counts were determined in pellets by serially diluting homogenates and plating onto Trypticase-Soy agar and Bile-Esculin-Azide agar. Five antibiotic protocols were tested: clindamycin associated with gentamicin; ceftriaxone associated with cefoxitin; ceftriaxone alone; ceftriaxone associated with amoxicillin and cefoxitin; and ceftriaxone associated with amoxicillin. A group received no antibiotic as negative control.

**Results:** No *E. faecium* intestinal colonization was observed in the control group. At D3, fecal pellets contained on average 4.10⁹ CFU of *E. faecium* per gram of feces with all antibiotic protocols. With clindamycin-gentamicin association, we observed a decrease of about one log₁₀ CFU/g every two days from D3. With the other four antibiotic regimens, the bacterial load obtained at D3 was maintained and stable until D14. A concomitant colonization by *Enterococcus faecalis* was observed in groups treated with ceftriaxone alone and ceftriaxone-cefoxitin combination.

**Conclusions:** Both ceftriaxone-amoxicillin-cefoxitin and ceftriaxone-amoxicillin combinations provided significant and stable *E. faecium* colonization without co-colonization by *E. faecalis*. To be as close as possible to human situation, ceftriaxone-amoxicillin seemed to be the most appropriate for *E. faecium* intestinal colonization model. This model can be used to develop *in vivo* transcriptomic analysis by RNA-seq.

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Abstract 8491

A study to investigate the utility of confirmatory testing of oropharyngeal samples positive for Neisseria gonorrhoeae by Cobas 4800 CT/NG test

Sophie Jones*1, Rachel Drayton2, Carys Knapper1, Michael Perry1

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Abstract third-party references: Cardiff and Vale University Health Board, Aneurin Bevan University Health Board, Public Health Wales

Background: Neisseria gonorrhoeae (NG) is a sexually transmitted disease that infects the columnar epithelial cells of the urethra, cervix, rectum, conjunctiva and pharynx. We have previously shown that the positive predictive value for oropharyngeal swabs using the Roche cobas® 4800 CT/NG Test was 88.6% using an in-house assay for confirmation. In this study we set out to investigate the confirmation of cobas® 4800 CT/NG Test NG positive oropharyngeal samples using additional methods.

Materials/methods: Eighty-three patients with positive NG oropharyngeal cobas® 4800 samples from two Integrated Sexual Health clinics in Wales were consented for further NG investigations. Patients had two additional swabs taken for NG testing using the Hologic Aptima Combo 2® Assay and for culture using selective NG media. In-house confirmatory testing for opa and pap genes by real-time PCR was also performed on the remnant cobas 4800 specimens.

Results:

<table>
<thead>
<tr>
<th>Method</th>
<th>Agreement with cobas® 4800 CT/NG Test (n=83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-house real-time PCR</td>
<td>73.5% (n=61)</td>
</tr>
<tr>
<td>Aptima Combo 2® Assay (Aptima NG confirmatory assay negative)</td>
<td>66.3% (n=55)</td>
</tr>
<tr>
<td>Aptima Combo 2® Assay (Aptima NG confirmatory assay positive)</td>
<td>56.6% (n=47)</td>
</tr>
<tr>
<td>Any molecular method</td>
<td>73.5% (n=61)</td>
</tr>
<tr>
<td>Culture</td>
<td>19.3% (n=16)</td>
</tr>
</tbody>
</table>

The agreement for all three molecular methods was 66.3%, falling to 56.6% when the Aptima® NG confirmatory assay was performed.

All samples that were negative by in-house real-time PCR were also negative by the Aptima Combo 2® Assay and by culture; all samples positive by the Aptima Combo 2® Assay were also positive by the in-house assay.

Conclusions: The agreement between all four methods for NG detection was low at 19.3%, primarily due to the low sensitivity of culture, and no culture positive samples were negative by any molecular method. Twenty-two samples (26.5%) did not confirm NG by any method, it is unclear if these are true positives or are due to cross-reactivity with non-gonococcal Neisseria species. The further lack of agreement between the molecular confirmatory methods casts doubt onto the utility of confirmatory testing for this sample type when screening high risk patients where high sensitivity is required. Further work is required to determine the true nature of the unconfirmed NG positive samples.

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Abstract 8492

Microbiological performances and clinical impact of the FilmArray Pneumonia Panel Plus on critically ill with severe pneumonia
Alexia Verroken*1, Julien Favresse1, Hector Rodriguez-Villalobos1, Pierre-Francois Laterre1
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Background: Following international recommendations, patients suspected with severe pneumonia receive broad-spectrum empirical antibiotherapy subsequently reviewed upon availability of microbiological results. However laboratory analysis on respiratory samples requires up to 48 hours to obtain final results allowing instauration of optimal antibiotherapy (OAT). Molecular testing aims to reduce time to results. In this study we evaluated the microbiological performances and clinical impact of the BioFire® FilmArray® Pneumonia Panel (FA-PNEU) [bioMérieux] on critically ill suspected with severe pneumonia. This multiplex PCR allows the detection of 27 bacteria and viruses within 1h15 minutes directly from the respiratory sample.

Materials/methods: This prospective interventional study is conducted at the Cliniques universitaires Saint-Luc university hospital. Conditions for inclusion are: all adult patients admitted/remaining at the intensive care with suspicion of community acquired pneumonia class IV [CAP IV] or hospital acquired pneumonia (HAP) for which a lower respiratory tract sample was obtained. The study started in May 2019 and will last for 1 year. FA-PNEU testing is performed immediately following sample collection 24h/24 7days/7. Results were compared with routine testing including urinary antigen detection, immuno-enzymatic viral assays and bacterial cultures performed during working hours. FA-PNEU results were used to tailor patient’s antimicrobial treatment and time to OAT was measured.

Results: At present 34 patients have been included, comprising 20 men and 14 women with a mean age of 63 years. Final diagnosis was bacterial CAP IV and HAP for respectively 15 and 9 patients while pneumonia diagnosis was uncorroborated for 10 patients. Mean time to FA-PNEU result was 2h10 compared to 52h to complete routine laboratory results. A 100% concordance with routine testing was observed for all FA-PNEU strains detected with a minimum quantity of 10^6 copies/ml. 18/34 (52.9%) included patients benefitted from a speeded-up initiation of OAT following FA-PNEU result availability consisting of 11 cases of antibiotic streamlining and 7 cases of complete antibiotic stop.

Conclusions: FA-PNEU results show optimal concordance with routine testing and speed up instauration of the OAT in more than 50% of the included patients. Incoming study results confirm these observations and will be included in the presentation.

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Abstract 8495

Human metapneumovirus infections among patients with haematological malignancies including haematopoietic stem cell transplant: analysis of a 6-year period

Laura Labate1, Elisa Balletto1, Laura Magnasco*1, Anna Maria Raiola2, Fabio Guolo3, Emanuele Angelucci1, Lemoli Roberto Massimo1, Claudio Viscoli1,4, Matteo Bassetti1,4, Malgorzata Karolina Mikulska1,4

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Background: The pathogenic potential of human metapneumovirus (hMPV) infection among severely immunocompromised patients has yet to be fully elucidated. Previous studies reported a prevalence of hMPV infection in hematopoietic stem cell transplant (HSCT) recipients of 5-9% and a mortality up to 27% among patients with lower respiratory tract infections (LRTI). The aim of this study was to report the characteristics and outcome of hMPV infection among patients with hematological malignancies.

Materials/methods: We conducted a retrospective, single-centre study at a University Hospital in Genoa, Italy during the years 2012 to 2018. All adult patients with hematological malignancies and detection of hMPV in respiratory specimens by molecular search (Seeplex RV12 Viral) were included. Upper respiratory tract infection (URTI) and LRTI were defined according to ECIL criteria.

Results: Fifty-two patients met the inclusion criteria. Median age was 52 years; 30 patients (58%) were females. The infection was mostly detected during late winter/early spring (February to April). Clinical characteristics of included patients, data about specific antiviral treatment and outcome are outlined in table 1. Overall, incidence of hMPV LRTI among patients receiving HSCT was 10%. Attributable mortality to hMPV infection was 3.9%, with a crude mortality of 29%.

Conclusions: hMPV infections are frequent among immunocompromised patients with hematological malignancies and undergoing HSCT during the cold season, with a high rate of LRTI and attributable mortality of 4%. The optimal management strategy remains to be defined.

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>n=52 (100%)</th>
<th>Infection characteristics</th>
<th>n=52 (100%)</th>
<th>Antiviral treatment among patients with LRTI</th>
<th>n=28 (100%)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute myeloid leukemia</td>
<td>13 (25)</td>
<td>URTI</td>
<td>24 (46)</td>
<td>Any treatment</td>
<td>8 (29)</td>
<td>Overall mortality</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>12 (23)</td>
<td>LRTI</td>
<td>28 (54)</td>
<td>Treatment with RBV</td>
<td>2 (1)</td>
<td>Attributable mortality</td>
</tr>
<tr>
<td>Other hematological malignancies</td>
<td>27 (52)</td>
<td>Viral pneumonia</td>
<td>25/28 (90)</td>
<td>Treatment with IgA</td>
<td>4 (2)</td>
<td></td>
</tr>
<tr>
<td>HSCT</td>
<td>40 (77)</td>
<td>Viral coinfection</td>
<td>7 (13)</td>
<td>Treatment with RBV + IgA</td>
<td>2 (1)</td>
<td></td>
</tr>
<tr>
<td>Allageneic HSCT</td>
<td>36/40 (90)</td>
<td>Bacterial co-infection</td>
<td>16 (30)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Graft-versus-host reaction</td>
<td>18/36 (50)</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Steroid treatment at hMPV detection</td>
<td>28 (54)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocytopenia</td>
<td>36 (67)</td>
<td></td>
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</tr>
</tbody>
</table>

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Identifying drivers of acquisition of extended-spectrum beta-lactamase producing Enterobacterales in Malawi using whole genome sequencing and mathematical modelling

Joseph Lewis*1,2,3, Madalitso Mphasa1, Rachel Banda1, Emma Smith1,2, Christopher Jewell4, Brian Faragher1, Nicholas Thomson1, Nicholas Feasey1,2

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Background: In Blantyre, Malawi, extended-spectrum beta-lactamase producing Enterobacterales (ESBL-E) are a significant public health challenge: limited access to carbapenems often renders these infections locally untreatable. Sparse data suggest ESBL-E gut mucosal colonisation is common, making interventions to reduce colonisation potentially attractive to tackle invasive disease - but drivers of carriage are not understood. We performed a prospective cohort study to identify drivers of ESBL-E colonisation in this setting.

Materials/methods: Malawian adults with planned antimicrobial therapy were recruited on admission to Queen Elizabeth Central Hospital, Blantyre, Malawi, along with antimicrobial-unexposed hospital and community controls. ESBL-E carriage was defined at enrolment and 1, 4, 12 and 24 weeks with ESBL-selective stool culture. Isolates underwent short-read whole-genome sequencing as high-resolution typing. Multivariable logistic regression was used to identify associations with ESBL-E carriage at baseline and Markov models used to identify associations with ESBL-E acquisition/loss.

Results: 425 adults were recruited. 42% (95%CI 38-47%) of participants carried an ESBL-E at baseline, rising to 78% (95%CI 71-84%) in antimicrobial-exposed inpatients by day 7. Rainy season (aOR 2.2 [95%CI 1.4-3.4]), use of unprotected water source (aOR 3.0 [95%CI 1.1-8.8]), household crowding (aOR 1.2 [95%CI 1.0-1.4] per adult) and recent hospital admission (aOR 5.9 [95%CI 1.8-27.0]) were independently associated with colonisation. Longitudinal models showed that hospitalisation drives net acquisition of ESBL-E by increasing turnover (aHR for loss 10.0 [95%CI 1.2-52.3] and acquisition 27.8 [95%CI 3.6-143.1]) and antimicrobials act to prolong carriage by reducing loss (aHR 0.16 for loss [95%CI 0.05-0.58]), with a post-antibiotic effect (half-life 44 days [95%CI 15-98]) whereby antimicrobials act to prolong ESBL-E carriage long after they have been excreted. Whole-genome sequencing showed a dynamic process with rapid turnover of bacteria and mobile genetic elements.

Conclusions: In Malawian adults, ESBL-E colonisation is common, and environmental and person to person transmission routes may both play a role. Rapid turnover at the genomic scale suggests frequent exposure. Hospitalization and antimicrobial exposure act synergistically to produce rapid increase in and prolonged carriage of ESBL-E, driven in part by a prolonged post-antibiotic effect. The mechanism of this effect is unknown but warrants study as a potential therapeutic target.

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Abstract 8501

Development of a combination antibiogram for empiric treatment of Pseudomonas aeruginosa in the intensive care unit

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Background: The 2016 IDSA/ATS treatment guidelines for hospital-acquired or ventilator-associated pneumonia (HAP/VAP) endorse empiric double coverage for high-risk patients. An antipseudomonal β-lactam plus either a fluoroquinolone (FQ) or aminoglycoside (AG) are suggested, along with the recommendation that selection is guided by local resistance data. Therefore, the primary objective of this study was to develop a combination antibiogram to determine the most active empiric coverage for the intensive care unit (ICU) population.

Materials/methods: The first isolates of Pseudomonas aeruginosa from adult (>18 years) patients collected between 1/1/2017-12/31/2018 at two tertiary care medical centers were included. Isolates were analyzed if they were the first collected per patient per year and excluded if the patient was not in the ICU at the time of collection. Susceptibilities to amikacin (AMK), cefepime (FEP), ciprofloxacin (CIP), gentamicin (GEN), levofloxacin (LVX), meropenem (MEM), and piperacillin/tazobactam (TZP) were assessed by either disk diffusion or Vitek 2 per 2018 CLSI criteria. A combination antibiogram was then developed by including isolates that were non-susceptible to the β-lactam but susceptible to either the FQ or AG.

Results: In total there were 345 isolates included in the analysis; however, not all isolates were tested against each antibiotic. Culture sources included: 255 (73.9%) respiratory isolates, 46 (13.3%) urinary isolates, 8 (2.3%) bloodstream isolates, and 36 (10.4%) isolates from other sources. FEP was the most active β-lactam monotherapy agent (Table 1). Susceptibilities to non-β-lactams were: AMK, 96.7%; GEN, 87.8%; CIP, 74.8%; LVX, 71.8%. Isolates were 6% (95% CI; 2.7%-9.3%) more susceptible to the combination of FEP + AMK than FEP + LVX.

Table 1. β-lactam mono- and combination therapy susceptibilities

<table>
<thead>
<tr>
<th>All Isolates</th>
<th>Alone</th>
<th>+AMK</th>
<th>+GEN</th>
<th>+CIP</th>
<th>+LVX</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEP</td>
<td>86.9%</td>
<td>97.9%</td>
<td>95.8%</td>
<td>92.8%</td>
<td>91.9%</td>
</tr>
<tr>
<td>MEM</td>
<td>82.4%</td>
<td>97.5%</td>
<td>96.7%</td>
<td>87.1%</td>
<td>86.0%</td>
</tr>
<tr>
<td>TZP</td>
<td>85.6%</td>
<td>96.5%</td>
<td>96.7%</td>
<td>92.5%</td>
<td>91.6%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Respiratory Isolates</th>
<th>Alone</th>
<th>+AMK</th>
<th>+GEN</th>
<th>+CIP</th>
<th>+LVX</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEP</td>
<td>85.3%</td>
<td>97.2%</td>
<td>95.9%</td>
<td>92.2%</td>
<td>91.0%</td>
</tr>
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</tr>
<tr>
<td>TZP</td>
<td>84.0%</td>
<td>98.0%</td>
<td>95.5%</td>
<td>91.4%</td>
<td>90.6%</td>
</tr>
</tbody>
</table>

Conclusions: AGs provide greater additional activity than FQs. In ICU patients with suspected pseudomonal infection, TZP combined with AMK would offer the most active empiric coverage while MEM plus LVX offers the least.

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Abstract 8504

Non-steroidal anti-inflammatory drug administration impairs antibiotic treatment of orthopaedic device-related infection in a rat model

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Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are a mainstay of perioperative pain management in orthopaedic trauma surgery, although due to their anti-inflammatory properties, NSAIDs may also negatively impact on host immune responses. This could have negative consequences for their use in the context of orthopaedic device related infection (ODRI). The aim of this study was to determine the impact of NSAIDs on antibiotic therapy of ODRI in a rat model.

Materials/methods: A polyetheretherketone (PEEK) screw was inserted in the proximal tibia of 48 skeletally mature (24-week old) female Wistar rats: 12 control animals received a sterile screw, of which 6 also received NSAID therapy (carprofen, 5 mg/kg s.c. once daily); 36 animals received a S. epidermidis-inoculated screw, of which 18 also received NSAID therapy. Antibiotic therapy (cefazolin: 30 mg/kg; s.c., b.i.d. plus rifampin: 25 mg/kg; s.c., b.i.d.) was administered from day 7-21 in 9 animals from each group (i.e. +/- NSAID treatment) receiving S. epidermidis-inoculated screws. Bone changes were monitored using in vivo microCT scanning, performed postoperatively and at 3, 6, 9, 14, 20 and 28 days (euthanasia). Quantitative bacteriology of the implant, bone and overlying soft tissue was also performed to assess infection status.

Results: All animals receiving S. epidermidis-inoculated screws without antibiotics were confirmed as infected at euthanasia. Quantitative microbiology showed no difference in bacterial load control versus NSAID-treated animals (CTL = 53’686 CFU + 68’094; NSAID = 45’617 CFU + 36’057). However, NSAID administration dramatically impaired antibiotic efficacy, with 7/8 animals remaining infected versus 2/9 control animals.

Pronounced osteolysis was observed in infected control animals, which peaked at day 9. Reparative processes (periosteal proliferation and mineralization) in the vicinity of the screw was observed at day 14 and continued until day 28. NSAID treatment markedly prevented S. epidermidis-induced osteolysis but also markedly impaired reparative processes. Antibiotic treatment did not affect the bone changes in control or NSAID-treated animals.

Conclusions: NSAID administration dramatically affected the response of bone tissue to infection, reducing osteolysis but also dramatically reducing antibiotic efficacy. Given these observed negative effects, further investigations should be conducted to determine the underlying pathophysiological mechanism.

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Prevalence of resistance-associated mutations for ciprofloxacin in Neisseria gonorrhoeae and azithromycin and moxifloxacin in Mycoplasma genitalium

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Background: STI causing bacteria Neisseria gonorrhoeae (NG) and Mycoplasma genitalium (MG) are both listed on the CDC’s list of Antibiotic resistance threat in the US. For NG, ciprofloxacin has no longer been recommended for treatment as of 2007 because of increasing resistance. Resistance of MG to first-choice antibiotic azithromycin is high across the globe. Resistance to the alternative antibiotic moxifloxacin has already been reported. Because these bacteria are commonly diagnosed using PCR only, phenotypical detection of antibiotic resistance is hardly ever feasible for NG and impossible for MG. In this study, we determined the prevalence of resistance to abovementioned antibiotics for respectively NG and MG using molecular methods.

Materials/methods: All specimens received for routine STI diagnostics from December 2018 – May 2019 were tested for NG and MG and positive specimens were subsequently tested for the presence of resistance associated mutations (RAM). A prototype of the NG-FQres qPCR assay (NYtor B.V.) was used to detect ciprofloxacin RAM in NG. To detect RAM in MG, the RealAccurate® TVMgres PCR assay (Pathfinder) and a prototype of the MG-FQres qPCR assay (NYtor B.V.) was used for detection of azithromycin and moxifloxacin resistance respectively.

Results: From a total of 2644 specimens, 41 (1.6%) and 106 (4.0%) tested positive for NG and MG respectively. Thirty-three NG positives could be tested for ciprofloxacin RAM, of which 7 tested positive. In addition, 55 previously collected NG positive specimens were tested, of which 11 contained ciprofloxacin RAM. In total, 18 out of 88 (20.5%) contained ciprofloxacin RAM. For MG, 106 and 86 could be tested for azithromycin and moxifloxacin RAM respectively. Forty-three (40.6%) tested positive for azithromycin RAM, whereas 7 (8.1%) for moxifloxacin RAM.

Conclusions: Although treatment of NG with ciprofloxacin is not recommended, the use of ciprofloxacin might again be an option when testing individual patients for RAM since almost 80% is susceptible. This study shows that the prevalence of azithromycin RAM in MG is alarmingly high, indicating that azithromycin should not be used as first-choice treatment without prior susceptibility testing. Moxifloxacin is still an option, but the prevalence of the respective RAM should be monitored.

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Abstract 8506

Excessive antibiotic use and costs in hospitalised adults with chronic heart failure

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Background: Clinical presentation of chronic heart failure (CHF) can be easily confused with the signs and symptoms of lower respiratory tract infections such as pneumonia. Therefore patients with CHF worsening have a high probability of antibiotics (AB) overprescribing even if clinical suspicion for pneumonia is low. Our study aimed to evaluate the rate of inappropriate AB prescription and calculate direct costs due to excessive antibacterial therapy in hospitalized patients with CHF.

Materials/methods: Hospitalized adults with previously diagnosed decompensated CHF and suspected community-acquired or hospital-acquired pneumonia were included into a prospective two-centered observational study. Diagnosis of pneumonia was confirmed/excluded by multispiral computed tomography (MSCT) or chest radiography (evaluated independently by two radiologists) along with standard methods and procedures. Patients with any systemic infections were excluded. Unnecessary AB use and direct costs related to antibacterial therapy were calculated.

Results: Overall 140 patients, median age 77 (67; 82) years old, were enrolled, 56.5% were female. Diagnosis of pneumonia was excluded in 52 (37%) cases. Of them, 49 (94.2%) patients received systemic AB. The median duration of antibacterial therapy was 8 (7;11) days. Ceftriaxone, azithromycin and cefotaxime were the most commonly prescribed AB. The median direct cost associated with excessive antibacterial therapy was 101,34 (47,7; 141,1) Euro per patient.

Conclusions: Difficulties in verification of pneumonia among patients with CHF lead to high rate of unnecessary AB use and inappropriate expenditures. More reliable algorithm to differentiate pneumonia and CHF worsening is required to prevent potential adverse outcomes of AB overprescription.

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Abstract 8507

**Impact of intra-partum azithromycin on carriage of group A Streptococcus in Gambia: an ad hoc analysis of a double-blind randomised trial**

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**Background:** Group A Streptococcus (GAS) is an important cause of both maternal and neonatal sepsis. Asymptomatic bacterial colonization is considered a necessary step towards sepsis.

**Materials/methods:** We performed an adhoc analysis of a phase-III, double-blind, placebo-controlled randomized-trial (ratio 1:1) conducted in The Gambia to determine the impact of one oral dose (2g) of intra-partum azithromycin on maternal and neonatal GAS carriage. Biological samples (nasopharyngeal swabs, breast milk and vaginal swabs) were collected at different time points during the 4 weeks following the intervention. All samples were processed using conventional microbiology techniques. Statistical analysis was done using STATA 14. Whole Genome Sequencing (WGS) of GAS isolates was performed using the illumina Miseq platform. De novo assembly (SPAdes), gene annotation (prokka), core genome determination (roary), maximum likelihood phylogenetic tree construction (RAxML) and antimicrobial resistance gene analysis (abricate) were used to analyse sequence data.

**Results:** We randomized 829 mothers who delivered 843 babies. Among women who received azithromycin, there was lower GAS prevalence of post-intervention carriage in breast milk (2.40% vs 0.27%, Prevalence Ratio (PR)=0.11, 95% CI 0.01 -0.87, p=0.021) and in the nasopharynx (1.87% vs 0.27%, PR=0.14, 95% CI 0.02-1.16, p=0.069), but not in the vaginal tract (2.13% vs 1.87%, PR=0.88, 95% CI 0.32-2.39, p=1.000). Among neonates whose mothers had received azithromycin, there was also lower prevalence of GAS carriage in the nasopharynx (2.20% vs 0.56%, PR=0.26, 95% CI 0.06-1.21, p=0.107). Prevalence of carriage of GAS azithromycin resistant was low and similar in participants from both arms, except for a higher prevalence in the vaginal tract post-intervention among women from the azithromycin arm (1.88% vs 0.27%, PR=7.04, 95% CI 0.87-56.92, p=0.038). WGS revealed all azithromycin-resistant vaginal tract isolates from the azithromycin arm to be Group A carbohydrate-expressing Streptococcus dysgalactiae harbouring macrolide resistant genes msr(D) and mef(A). Other isolates were confirmed as GAS as expected, with low prevalence of genotypic macrolide resistance.

**Conclusions:** Oral intra-partum oral azithromycin reduced prevalence of GAS carriage among Gambian mothers and neonates. The prevalence of carriage in the maternal vaginal tract was not affected by the intervention due to azithromycin-resistant Streptococcus dysgalactiae isolates expressing Group A Lancefield antigens.

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Antimicrobial stewardship teams in candidaemia management: advise or take care of the patient?

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Background: It is known that the intervention of antimicrobial stewardship teams with infectious diseases specialist (AST-ID) improves compliance with the bundle of diagnostic and therapeutic measures in candidemia. The difficulty lies in establishing what type of intervention is the most efficient.

Materials/methods: Data regarding the management and evolution of candidaemia of a tertiary hospital without solid organ and hematopoietic transplantation, with 680 beds, from January 2015 to June 2019 have been collected. AST-ID interventions were making a non-impositive recommendation to the responsible physician or taking direct charge of the patient’s management. Adherence to standard recommendations and outcomes were evaluated. Categorical variables were compared with the chi-square test.

Results: A total of 110 episodes of candidaemia were evaluated in non-neutropenic patients. Of these 43 were women (39.1%) and 67 men (60.9%). 92 episodes were nosocomial (83.6%). They were managed without the help of AST-ID 47 (42.7%) episodes, in 24 (21.8%) AST-ID give non-impositive recommendations and in 39 (35.5%) episodes AST-ID took direct charge of patient management.

<table>
<thead>
<tr>
<th>Variable</th>
<th>AST-ID Management</th>
<th>AST-ID recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up blood cultures</td>
<td>N= 39</td>
<td>N=24 P value</td>
</tr>
<tr>
<td>Ophthalmological examination</td>
<td>35(100%)</td>
<td>16(76.2%)</td>
</tr>
<tr>
<td>Performance of Transthoracic Echocardiogram</td>
<td>32(97%)</td>
<td>7(38.9%)</td>
</tr>
<tr>
<td>Performance of Transoesophageic Echocardiogram</td>
<td>9(100%)</td>
<td>2(66.7%)</td>
</tr>
<tr>
<td>Directed imaging study</td>
<td>12(50%)</td>
<td>6(27.3%)</td>
</tr>
<tr>
<td>Removal of existing catheter within 24 h of diagnosis</td>
<td>24(92.3%)</td>
<td>16(100%)</td>
</tr>
<tr>
<td>Appropriate empiric selection and dosing of Antifungal therapy</td>
<td>38(97.4%)</td>
<td>20(90.9%)</td>
</tr>
<tr>
<td>Appropriate directed antifungal treatment</td>
<td>38(97.4%)</td>
<td>9(40.1%)</td>
</tr>
</tbody>
</table>

The 90-days mortality related to candidiaemia in the AST-ID management group was 10.3 %, while in the AST-ID recommendation group it was 20.8 % (p = 0.28).

Conclusions: The comprehensive management of patients with candidaemia by an AST-ID improves adherence to the diagnostic measures included in the candidaemia bundle, which prolongs the average stay. The directed treatments are correct to a greater extent and as a consequence related mortality decrease. We suggest that episodes of candidaemia should be managed by AST-ID in the centers where it is available, in order to provide patients the best standard of care. Future guidelines will probably address this issue.

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Abstract 8514

Direct detection of intact Klebsiella pneumoniae carbapenemase (KPC) enzymes from bacterial isolates using liquid chromatography coupled with high-resolution Orbitrap mass spectrometry

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Background: Carbapenem resistance in bacteria is an urgent concern. Infections by these organisms have limited therapeutic options, increased mortality rates, and can spread quickly through a hospital environment. Rapid detection of these resistance mechanisms is essential to improve patient management and prevent hospital transmission. Klebsiella pneumoniae carbapenemases [KPCs] are endemic in the United States and are found globally. Herein, we present a method for direct from colony detection of intact KPC using mass spectrometry.

Materials/methods: Clinical isolates were evaluated for the presence or absence of KPC genes using either whole genome sequencing or polymerase chain reaction (PCR). Intact cells from clinical isolates were mechanically lysed and centrifuged. The protein-containing supernatant was extracted and transferred to a short solid phase extraction (SPE) column, from which proteins are eluted, ionized via electrospray ionization (ESI), and introduced to the mass spectrometer (MS). KPC variants were detected via dissociation of intact protein ions via tandem mass spectrometry (MS/MS), forming diagnostic fragment ions representative of the presence of the target enzymes.

Results: Protein fragment ions produced from KPC variants possess specific characteristics, such as mass-to-charge ratios (m/z) and correct charge states, thereby providing the opportunity to correctly identify the intact proteins. These fragments are individually informative, but collectively produce sequence information corresponding specifically to KPC variants. Additionally, MS alone is not always capable of detecting specific proteins in a complex mixture, yet MS/MS performs this task well. To date, more than 30 species of Enterobacteriales as well as Pseudomonas aeruginosa have been evaluated to detect KPC-2, KPC-3, KPC-4 and KPC-5. Our evaluations have shown zero false positives with near 100% sensitivity of KPC detection.

Conclusions: These data describe a method for direct and rapid detection of KPC enzymes using liquid chromatography, electrospray ionization, and tandem mass spectrometry. It does not require time-consuming protein digestion or lysate purification steps, yet provides accurate results and could be extended to detection of other carbapenemases to improve turnaround time of resistance detection.

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Using point prevalence methodology to evaluate antimicrobial prescribing in the UK’s largest renal dialysis centre
Aneeka Chavda*, Anan Ghazy1, Laura Whitney1, Mark Gilchrist1, Alison H. Holmes1,2
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Background: The outpatient haemodialysis population are amongst the most vulnerable to infections and have a higher risk of colonisation with multi-drug resistant organisms (MDRO)1. A rise in antibiotic use and increased hospital contact within this group are key factors for accelerating the acquisition of MDRO. Antibiotic prescribing and stewardship practices in this setting are under-researched in comparison to in-patient prescribing. Here we present point prevalence antibiotic prescribing data from the largest single haemodialysis service in the UK serving 1400 patients.

Materials/methods: This is a prospective observational study across eight satellite hospital outpatient haemodialysis units which are affiliated with a large tertiary academic institution. Data were collected over 3 months from October to December 2019 by a member of the Infectious Diseases Pharmacy team. All adult patients receiving intermittent haemodialysis the day prior to data collection were included. Baseline demographic and antibiotic prescribing data were collected for by review of prescription charts and medical records. Each antibiotic regimen prescribed was reviewed independently by a Consultant microbiologist and an Infectious Diseases Pharmacist to determine appropriateness of the prescription.

Results: At the time of this abstract 405 patients had been reviewed from 6 of the 8 haemodialysis centres. 4% of patients were identified as being on antibiotics at the time of data collection. 25% of patients had a documented antibiotic allergy of which 66% did not specify the nature of the allergy. 45% of the antibiotic prescriptions had a documented indication and 72% had a review date specified on the medication chart. The most commonly prescribed antibiotics were vancomycin and meropenem. The appropriateness of antibiotics prescribed will be reported once independent review is complete.

Conclusions: Interim results show that despite low prevalence of antibiotic prescribing there is significant exposure to broad spectrum antibiotics within this cohort. Of concern is poor documentation of indication and antibiotic allergies. Gaining an understanding of antimicrobial prescribing patterns in this setting will inform the development of an outpatient haemodialysis antibiotic stewardship framework, focusing on interventions to minimise unnecessary exposure to antimicrobials, curtailing the risk of MDRO acquisition and improving patient outcomes.


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Multidisciplinary interventions to reduce nosocomial transmission of influenza

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Background: Seasonal influenza is an under-recognised cause of nosocomial infection. During the 2016-17 winter, 112/315 (36%) adult inpatients with confirmed influenza at Cambridge University Hospitals (CUH) acquired their infection in hospital. Subsequent genomic and epidemiological investigations confirmed extensive patient-to-patient transmission. However, the impact of clinical and infection control practices in reducing influenza transmission are poorly understood. The aim of this study is to describe a range of interventions over three winters and their impact on clinical practice, hospital-acquired infection and mortality.

Materials/methods: CUH is a 1100-bed teaching hospital with high staff uptake of influenza vaccination. Data were derived from electronic records for all patients with PCR-confirmed influenza attending CUH from August 2016-April 2017 (n=348) and compared to cohorts from August 2017-May 2018 (n=763) and August 2018-April 2019 (n=823). Four key interventions were introduced prior to the 2017/18 winter: 1) improved isolation procedures, with dedicated side room capacity for suspected respiratory virus cases; 2) increased frequency of laboratory testing; 3) changes in antiviral prescribing and wider oseltamivir availability; 4) comprehensive staff education for emergency and acute medicine specialties. Additionally, point-of-care influenza testing (Cepheid GeneXpert) was available in the Emergency Department during the 2018/19 winter.

Results: Isolation of adult patients on admission rose from 48% of influenza cases in 2016-17 to 93% in 2018-19. Over the same period, the median time from admission to swabbing fell from 9 hours to 2 hours, while the delay from admission to first antiviral dose fell from 45 hours to 7 hours. The proportion of influenza infections acquired in hospital fell from 36% in 2016-17 to 17% in 2018-19. Adult inpatient mortality fell from 9.7% to 3.6%.

Conclusions: Influenza is an important cause of morbidity and mortality in secondary care. Better use of existing resources and the utilisation of rapid diagnostics have led to considerable improvement in patient management and are associated with a reduction in hospital-acquired infection and inpatient mortality. Although focused on a single centre, these findings are likely applicable in many secondary care settings. Responding to this challenge requires interdisciplinary engagement, utilising a range of approaches to better understand, manage and prevent transmission.

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Half of prescribed antibiotics are not needed: a pharmacist-led antimicrobial stewardship intervention and clinical outcomes in a referral hospital in Ethiopia

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Background: Intense antibiotic consumption in Low- and Middle-Income Countries (LMICs) is fueled by critical gaps in laboratory infrastructure and entrenched syndromic management of infectious syndromes. Few data inform the achievability and impact of antimicrobial stewardship interventions, particularly in Sub-Saharan Africa. Our goal was to demonstrate the feasibility of a pharmacist-led laboratory-supported intervention at Tikur Anbessa Specialized Hospital in Addis Ababa, Ethiopia, and report on antimicrobial use and clinical outcomes

Materials/methods: This was a single-center prospective quasi-experimental study conducted in two phases: (i) intervention phase (November 2017 to August 2018), during which we implemented weekly audit and immediate feedback sessions on antibiotic prescriptions of hospitalized patients, and (ii) post-intervention (September 2018 to January 2019) during which we audited prescriptions but provided no feedback to treating teams. The AMS team consisted of 4 clinical pharmacists and one ID specialist. Our primary outcome was antimicrobial utilization (measured as days of therapy (DOT) per 1000 patient-days and duration of antibiotic treatment courses); secondary outcomes were length of hospital stay and in-hospital all-cause mortality

Results: We collected data on 1,111 individual patients (707 during the intervention and 404 in the post-intervention periods). Ceftriaxone, vancomycin, cefepime and meropenem were the most commonly prescribed antibiotics; 96% of the recommendations made by the AMS team were accepted. The AMS team recommended to discontinue antibiotic therapy in 54% of cases during the intervention period. Once the intervention ceased, total antimicrobial use increased by 51.6% and mean duration of treatment by 4.1 days/patient. Mean LOS stay and crude mortality also increased significantly post-intervention (LOS: 19.8 vs 24.1 days in hospital death 6.9% vs 14.7%). These differences remained significant after adjusting for potential confounders.

Conclusions: An AMS intervention focused on duration of antibiotic treatment was feasible and had good acceptability in our setting. Cessation of audit-feedback activities was associated with immediate and sustained increases in antibiotic consumption reflecting a rapid return to baseline prescribing practices, and worse clinical outcomes (increased length of stay and in-hospital mortality). Pharmacist-led audit-feedback activities can effectively reduce antimicrobial consumption and result in better-quality care, but require organizational leadership for sustainable benefits.

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Detection of respiratory Mycoplasmataceae during prolonged mechanical ventilation

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¹University of Pennsylvania, Philadelphia, United States

Abstract third-party references: Centers for Disease Control and Prevention (CDC), National Institute for Allergy and Infectious Diseases

Background: Mycoplasma pneumoniae is a common cause of community-acquired lower respiratory tract infection (LRTI), but the role of Mycoplasmataceae in ventilator-associated LRTI is not well understood. Recent investigations of the lung microbiome during critical illness and mechanical ventilation have identified the persistence of bacteria of the family Mycoplasmataceae, including Mycoplasma and Ureaplasma species, in the lower respiratory tract. We sought to characterize the prevalence and persistence of Mycoplasmataceae in the lower respiratory tract, as well as host and respiratory microbiome features associated with Mycoplasmataceae detection, in patients dependent on mechanical ventilatory support.

Materials/methods: We enrolled 83 subjects at the time of admission to an academic long-term acute care hospital (LTACH) for ventilator weaning, performed longitudinal sampling of endotracheal aspirates, followed by 16S rRNA gene sequencing (Illumina HiSeq), and bacterial community profiling (QIIME2). Statistical analysis was performed with R and Stan; mixed effects models were fit to relate the abundance of respiratory Mycoplasmataceae to host and other respiratory microbiome features.

Results: Of the 83 subjects enrolled, 66 had Mycoplasma species detected in the lower respiratory tract on consecutive days, and 9 had Ureaplasma species detected in the lower respiratory tract on consecutive days. Overall both Mycoplasma and Ureaplasma were observed with high proportional abundance but low absolute read counts; no significant differences were observed between genera. However, individual subjects demonstrated high absolute abundance, confirmed by quantitative 16S qPCR. The abundance of lower respiratory Mycoplasmataceae was significantly associated with younger age and lower serum white blood cell count; an association was observed with the diagnosis of hematologic malignancy, but this did not reach statistical significance.

Conclusions: We identified a high prevalence of lower respiratory Mycoplasmataceae during mechanical ventilation and long-term acute care. In general, Mycoplasma and Ureaplasma species were detected with high relative but low absolute abundance, but in some cases high absolute abundance was observed.

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Abstract 8521

Nation-wide audit with feedback of antibiotic stewardship in Norwegian hospitals: a low cost initiative with many opportunities

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Background: In January 2016, The Norwegian Ministry of Health and Care Services launched their Action Plan against Antimicrobial Resistance. For hospitals, antibiotic stewardship programs (ASP) became mandatory, and an explicit target of 30% reduction in the combined use of five groups of broad-spectrum antibiotics by the end of 2020 was set. KAS’ mandate is to support rational use of antibiotics, and we decided to offer voluntary audits to all hospital trusts. We also wanted to find out whether audit with feedback is a useful method to assess ASP in hospitals.

Materials/methods: KAS developed an interview guide with 40 questions, covering seven focus areas closely linked to the ASP as described in the action plan. We conducted the audits as single-day visits, relevant documents were collected beforehand. In each hospital, we interviewed the medical director individually and conducted group interviews with other hospital leaders, the ASP-team, junior and senior doctors and nurses, respectively. Findings and points of advice were summed up in a final report.

Results: All 22 hospital trusts and private hospitals in Norway were audited from October 2017 to April 2019. The four northernmost hospital trusts were audited (mandatorily) by the Northern Regional Health Authority (NRHA) by a comparable method, the remaining 18 by KAS. The total estimated workload for two auditors combined was 7 days (6-10) for each visit. Final reports were sent to the hospital management and published on KAS’ website 33 days (median) after the visit. Main findings were: a) lack of specific targets at clinic and unit level, b) recognized stewardship measures such as audits of antibiotic use and mandatory reevaluation within 48-72 hours were only sporadically implemented, and c) nurses were only to a limited extent involved in antibiotic stewardship. NRHA’s findings were similar: lack of leadership accountability and quality improvement methodology in clinical units, potentially leading to risk of unnecessarily broad-spectrum treatment.

Conclusions: A complete, nationwide audit provide unique and comprehensive insight in antibiotic stewardship in hospitals and is feasible with a reasonable use of resources. The feedback with analyses identifies targets for further improvement of antibiotic use in hospitals.

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Abstract 8523

Clonality and molecular resistance to tetracyclines of *Neisseria gonorrhoeae* among men who have sex with men using post-exposure prophylaxis with doxycycline

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**Background:** High incidence of sexually transmitted infections has been reported among MSM using PrEP for HIV prevention. PEP with doxycycline has shown to reduce the incidence of syphilis and chlamydia infections among MSM in the ANRS IPERGAY trial, but not of GC [Molina et al, Lancet ID, 2018]. Few strains of GC were available for the assessment of phenotypic resistance. We wished to assess the clonality and impact of doxycycline PEP on tetracycline resistance among GC strains using molecular tests.

**Materials/methods:** Within the ANRS IPERGAY PrEP trial, MSM were enrolled in a prospective randomized (1:1) open-label sub-study of PEP with doxycycline [200 mg within 24h after sex] or no PEP. All subjects were tested for STIs at baseline, and every two months including real-time PCR assays for GC detection at 3 sites (urine, throat and anus). GC-positives samples by NAATs were analyzed for the molecular detection of tetracycline resistance mediated by acquisition of the *tet* (*M*) determinant or/and mutations in S10 protein. Clonality targeting the two alleles *porB* and *tbpB* (NG-MAST) was investigated by nested PCR

**Results:** From July 2015 to June 2016, 232 subjects were enrolled in the study. Among them, 42 patients had 70 GC-positive samples [2 urines, 32 anus and 36 throats] available for further testing. The overall rate of GC resistance to tetracyclines was 82.9% [64.3% at low level and 18.6% at high level]. Five GC infections were diagnosed at baseline, 4 were resistant to tetracyclines. Thirty-eight patients acquired a GC infection during the study. Tetracycline resistance was observed in 17/19 patients (89.5%) in the PEP arm and 14/19 patients (73.7%) in the no PEP arm (p=0.41). Fifteen NG-MAST profiles were characterized; the most frequent were ST 5624 (21%), ST 5441 (12.5%) and ST 5793 (12.5%). By comparison, these STs were found in 3.1%, 9.7% and 2.6%, respectively, in France over the same period.

**Conclusions:** Tetracycline resistance among GC strains in MSM was high, with or without doxycycline PEP. Additional studies with a larger sample size are needed to confirm these findings and assess the clonality of gonococcal strains circulating within this population.

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Chlorhexidine resistance of bacterial flora of HCWs’ hands: is there any impact related to the routine use for hand hygiene?

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Background: Although guidelines recommend the use of chlorhexidine gluconate (CHG) for hand hygiene (HH), the impact of the routine use on antimicrobial resistance is not clear. We aimed to analyze the impact on the CHG susceptibility among isolates obtained from hands of healthcare workers (HCW) during its routine use for HH.

Materials/methods: Crossover study at a tertiary care hospital in São Paulo, Brazil from April 2016 to April 2018. In two units (intervention) we established routine use of CHG for HH and at other two units (control) regular soap was provided. At intervals varying from 4 to 10 months we swapped the units. Before each swap, we put HCW’s hands inside a sterile bag containing a solution of phosphate-buffered saline, Tween 80 and sodium thiosulfate and inoculated on Brain Heart Infusion. Next, it was plated on MacConkey and Mannitol agar. MALDI TOF was used for identification. Agar dilution was performed for Staphylococcus spp. and Gram-negative bacilli (GNB). All Staphylococcus spp. with MIC ≥ 8 and GNB with MIC ≥64 were tested for inhibition of efflux pump. If a decrease of two dilutions occurred, we searched the genes qacA/B and cepA among Staphylococcus spp. and GNB respectively, by polymerase chain reaction.

Results: We obtained 262 samples from HCW’s hands yielding 428 isolates, Acinetobacter spp. (8%), Enterobacter spp. (8%), Klebsiella spp. (4%), Pseudomonas spp. (3%), Stenotrophomonas spp. (5%), Staphylococcus spp. (58%) and others (14%). Staphylococcus spp. were less frequent in the intervention (43% X 61%, OR 0.61, CI 0.48-0.81, p=0.029). Among Staphylococcus spp. and GNB, the proportion of chlorhexidine resistance (RCHG) was 12% and 14%, respectively. All resistant isolates recovered susceptibility with pump-efflux inhibitor. For Staphylococcus spp. pump inhibited, 53% had gene qacA/B. Four Klebsiella spp. had cepA amplified. There was a non-significant increase in Staphylococcus spp. RCHG in the intervention group (4% to 6%, p=0.9).

Conclusions: We did not find significant difference in RCHG during routine use of CHG for HH, although we observed a trend in resistance increase. Although genes qacA/B and cepA may play a role, further investigation is needed to clarify other reasons of increased MIC to CHG.

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Abstract 8526

Screening of risk groups detects only a minority of patients with carbapenemase-producing Gram-negative bacilli
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Background: Patients admitted to Dutch hospitals with certain risk factors [e.g. stay at foreign hospital] are isolated and screened for resistant micro-organisms. In our tertiary care hospital, risk factor surveys are used which should be completed at or within one month before hospital admission. We investigated the yield of carbapenemase producing Gram negative bacilli [GNB] identified in admitted patients by this targeted screening.

Materials/methods: We retrospectively analysed carbapenemase producing GNB from our laboratory information management system [GLIMS] from January 2014 to July 2019. After excluding 10 Acinetobacter baumanii isolates associated with an outbreak, 65 isolates were included for analysis, including only the first isolate per species per patient. Electronic patient files [if available] were checked for risk factors recorded in the survey.

Results: Sixty-five carbapenemase producing GNB isolates from 53 individual patients were detected, mostly Klebsiella pneumoniae [n=28], Escherichia coli [n=12] and Pseudomonas aeruginosa [n=10]. A minority of isolates were detected in screening cultures of patients with risk factors for colonization [n=20] or in cultures performed for contact tracing [n=3]. Six isolates were found in patients suspected of colonization with another species of carbapenemase producing GNB, either in follow-up cultures for known colonization [n=4] or during large-scale outbreak screening for A. baumanii [n=2]. Most isolates however seemed entirely unexpected: 23 were first identified in clinical cultures and 13 were found in routine weekly screening cultures on the ICU and haematology wards. Twenty-seven of these unpredicted isolates were collected after introduction of an electronic patient file, enabling analysis of the screening survey. While screening questionnaires were not completed in 14 cases, 11 of the remaining 13 isolates were cultured from patients who had negative answers on all screening questions in the survey.

Conclusions: Most patients with carbapenemase producing GNB isolated in our hospital were missed with our current screening policy. Imperfect adherence to completing risk screening surveys plays a role, although many unexpected isolates were cultured from patients with none of the specific risk factors. A more targeted screening policy is needed to avoid admission of colonized patients without proper infection prevention measures.

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Can HLA type I and II alleles presence be associated with the clinical spectrum of chikungunya virus infection
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Background: Virulence factors, as well as host immune response, play an important role in disease susceptibility via the Human Leukocyte Antigen (HLA). There are no known studies associating the presence of HLA class I and II alleles with the chikungunya virus (CHIKV) infection in Latin America. We aim to identify which HLA alleles are present in patients with the CHIKV infection when compared to healthy controls, as well as their association with the clinical spectrum of the disease.

Materials/methods: We carried out a cross-sectional analysis nested in a community cohort based on the COPCORD study related on our population. We included patients 18 years and older with serological confirmation of CHIKV infection. We performed HLA typing of HLA-A, HLA-B and HLA-DRB1 alleles. We used two-by-two tables to establish associations between allele presence and clinical characteristics.

Results: Data from 65 patients with confirmed CHIKV infection were analysed for HLA typing. Most patients were mestizo females. CHIKV infection was associated with the presence of HLA-A*68 (p=0.005; OR: 8.90, CI: 1.88-42.13), HLA-B*35 (p=0.03; OR: 2.02, CI: 1.06–3.86), HLA-DRB*01 (p=0.001; OR: 5.70, CI: 1.95–16.59), HLA-DRB1*04 (p=<0.001; OR: 7.37, CI: 3.33-16.30) and HLA-DRB1*13 (p=0.004; OR: 3.75, CI: 1.50-9.39) compared to healthy subjects. A statistically significant relationship was found between the presence of rash in the face or the abdomen and the presence of HLA-B*35 and HLA-DRB1*04.

Conclusions: Our study demonstrated that in our cohort, HLA type I and type II alleles are associated with CHIKV infection, and specifically an HLA type II allele with dermatological symptoms. The results suggest, that further research and of set a path for future investigation on genes outside the HLA system to help elucidate the pathophysiology of the CHIKV infection as well as its interaction with its host.

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Emergence of plasmid-mediated AmpC genes in Enterobacter cloacae complex strains from a sepsis outbreak in a neonatal intensive care unit

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Abstract third-party references: Institut of Integrative Biology of the cell CNRS, CEA, Paris-Saclay University, Gif-sur-Yvette, France, AP-HP-Université Paris-Saclay, Service de Bacteriologie-Hygiène, Hôpital Antoine-Béclère, Clamart, France

Background: The dissemination of plasmid-mediated ampC genes [pAmpC] conferring resistance to third-generation cephalosporins has been widely reported around the world making this a public health problem. pAmpC enzymes are most often found in nosocomial Escherichia coli and Klebsiella pneumoniae strains and there are few published reports regarding occurrence of these enzymes in other genera. In this study we described the prevalence of pAmpC encoding genes in Enterobacter cloacae complex (ECC) isolates collected from a sepsis outbreak in a neonatal intensive care unit (NICU).

Materials/methods: Among 60 non-related ECC strains, 25 cefotaxime resistant isolates were obtained from the outbreak in NICU. The isolates were identified by MALDI-TOF and antimicrobial susceptibility was performed by disk diffusion according to Antibiogram Committee of the Microbiology French Society (CA-SFM, 2018). PCR and sequencing were employed to detect pAmpC genes (ACT, MIR and CMH) and whole genome sequences (WGS). The clonal relatedness of pAmpC-positive isolates was evaluated by enterobacterial repetitive intergenic consensus (ERIC)-PCR method.

Results: In total 25 Isolates of ECC were positive for presence of pAmpC genes among those $\text{bla}_{\text{ACT-like}}$ (19/25) was the most prevalent gene followed by $\text{bla}_{\text{MIR-like}}$ (5/25) and $\text{bla}_{\text{CMH-like}}$ (1/25). All strains were susceptible to carbapenems. (ERIC)-PCR analysis showed clonal relationship between $\text{bla}_{\text{ACT-like}}$ isolates and non-clonal relationship between $\text{bla}_{\text{MIR-like}}$ isolates. Two new alleles $\text{bla}_{\text{MIR-like}}$ and $\text{bla}_{\text{CMH-like}}$ were identified by WGS. The amino acid sequences showed 89% identity between $\text{bla}_{\text{MIR-like}}$ and $\text{bla}_{\text{MIR-14}}$ with 14 amino acid changes. $\text{bla}_{\text{CMH-like}}$ show 2 amino acid changes with the other 5 alleles reported in GenBank.

Conclusions: Plasmid-mediated $\text{bla}_{\text{ACT-like}}$ ampC genes was highly prevalent in this study. A two novel alleles plasmid-mediated AmpC [MIR/CMH] in E. cloacae complex were identified. The highly prevalence found in this work is worrisome due to their possible plasmidial location that could be disseminated and favored the selection of multiresistant strains.

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First national survey on colistin resistance among \textit{Escherichia coli} in Belgium

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**Background:** Since the emergence of carbapenemase-producing \textit{Enterobacteriaceae}, colistin is considered as a antibiotic of last resort. We conducted a national survey to determine: 1) the presence of \textit{Escherichia coli} colistin-resistant (COL-R) mediated by the transferable resistant determinants MCR; 2) the characteristics of patients infected or colonized by \textit{mcr}\textsuperscript{-positive} \textit{E. coli}.

**Materials/methods:** All hospital-based and community-serving laboratories were invited to refer non duplicate colistin-resistant \textit{E. coli} collected from clinical specimens (fecal specimens excluded) to the National Reference Center (NRC) between May and October 2019. Colistin susceptibility was tested by automated system or by broth microdilution available in local laboratories. Putative COL-R isolates were sent to the NRC with a case structured report with clinical data. At the NRC, colistin susceptibility was verified using broth microdilution method and confirmed COL-R strains were further tested by multiplex PCR targeting plasmid-mediated colistin-resistance genes \textit{mcr-1}\textsuperscript{1} to \textit{mcr-5}\textsuperscript{1} and by disk diffusion method for their susceptibility profile to other antimicrobials. Reference strains \textit{E. coli} ATCC25922 and \textit{E. coli} NCTC 13846 were included in each run for susceptibility testing and PCR as quality control.

**Results:** Of the 107 isolates (1 to 14 isolates per laboratory) from 25 hospital-based and 3 community-serving laboratories collected by the NRC during the 6-month study period, 86 \textit{E. coli} isolates (80%) were confirmed COL-R by broth microdilution. Among COL-R isolates, 32 (37%) strains isolated from 17 laboratories (including 3 community-serving) were tested positive for \textit{mcr-1} by PCR. All \textit{mcr}\textsuperscript{-positive} strains were susceptible to carbapenems and six were resistant to third-generation cephalosporins conferred by an ESBL phenotype. All but two isolates were isolated from urines mainly from hospitalized patients (n=18). Twelve isolates were isolated from outpatients and twenty-five strains were considered as clinically significant.

**Conclusions:** Our survey data confirm the common circulation of \textit{mcr}-positive \textit{E. coli} causing mainly urinary tract infections both in hospitalized and ambulant patients, although most of the strains remain susceptible to the majority of antimicrobials. The high proportion (20%) of false COL-R isolates also highlights the difficulty to achieve correct determination of colistin resistance by Belgian routine laboratories.

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Abstract 8535

**An outbreak of hypervirulent and multidrug-resistant clone (ST2096) *Klebsiella pneumoniae* silently transmitting in a Saudi Arabia western region hospital: a clinical and molecular surveillance study**

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**Background:** The global nosocomial dissemination of high-risk multi-drug resistant (MDR) *Klebsiella pneumoniae* strains has been a growing threat in health-care facilities. Epidemiological studies are infrequently combined with pathogen genomics and clinical observations of an outbreak to suggest changes in policy and procedures of infection control. In this study, we employed Whole-genome sequencing (WGS) phylodynamic data, the influence of clinical practice, and infection control methods to understand the infection course, transmission map, and the clinical gaps aiding the successful transmission of a potentially lethal MDR and hypervirulent clone ST2096.

**Materials/methods:** We collected 235 MDR *Klebsiella pneumoniae* isolates from 220 patients of King Abdulaziz medical city within the Ministry of National Guard - health affairs (MNGHA) hospital (Jeddah, Saudi Arabia) between 2014-2018. All the isolates were sequenced at high genome-coverage using the Illumina technology. The clinical metadata of the identified outbreak cases were collected, and the isolates were tested for antibiotic resistance phenotypic using broth microdilution (BMD). We analyzed the sequencing data to identify the antibiotic resistance profile, virulence factors, the clonal relationships between *K. pneumoniae* isolates, and transmission patterns.

**Results:** We identified an ongoing clonal transmission of 99 hypervirulent MDR ST2096 *K. pneumoniae* strain of the cc14, followed by the global high-risk clone ST14 of the same clonal group. ST2096 silently transmitted within the hospital and was found to be associated with high mortality (58.6%). The transmission of ST2096 predominated over other sequence types until the end of our collection period in March 2018. We identified the outbreak index case arriving at the hospital in December 2016. The index case carried a hypervirulent and highly resistant *K. pneumoniae* ST2096 isolate, which had been transferred between several wards for treatments and clinical-related tests.

**Conclusions:** The benefits of combined deep and active WGS surveillance, transmission model, and applications of infection control are needed to avoid clinical outbreaks and the dissemination of fatal infections. This study identified *K. pneumoniae* ST2096 strain as an emerging MDR and extensively-drug resistant (XDR), hypervirulent, and vastly communicable clone that constitute a considerable danger to patients.
"Beanbag" tree of indirect transmission events

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Pharmacokinetic, efficacy and safety of micafungin administered at high doses to neonates suffering from invasive candidiasis: results from a phase II study

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Background: The few available studies on pharmacokinetic and on the appropriate dosage in neonates limit the possibility of recommending micafungin as drug of first choice in the therapy of neonatal invasive candidiasis. We aimed to study the pharmacokinetic profile of micafungin administered at high dose to neonates suffering from invasive candidiasis and to evaluate the proportion of success, of failure and the safety of this therapy.

Materials/methods: During a Phase 2 Study plasma, CSF levels, efficacy and safety of micafungin, administered at a dose of 8 mg/kg/day for a mean of 16.7 days, at a concentration of 2 mg/ml, to 53 neonates suffering from systemic candidiasis and candida meningitis were studied. Micafungin plasma and CSF levels were measured by HPLC on blood and CSF capillary samples, picked up by microtube with EDTA.

Results: Fifty-three patients were enrolled in study, 37 with a proven candidiasis. Three patients had Candida meningitis. In 31/37 (83.8%) patients with proven candidiasis we observed the mycological eradication. The AUC₂₄ was higher than 166 h * mg /L in 46/52 (88.5%) patients, compared with the 75h * mg /L -139 h * mg /L range, effective in adults exposed to 100 mg /day. CSF concentrations were between 1.3 and 1.80 mg /L. Five/53 (9.4%) patients died without relation with the use of micafungin. The most frequent side effect was the transient increase in gamma glutamyl transferases (11/53, 2.8%).

Conclusions: Micafungin at high doses is effective and safe in the treatment of neonatal candidiasis.

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Abstract 8539

**How does blood volume cultured in Europe comply with guidelines? Results of a 125-centre ESGBIES/CTCB survey**

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**Background:** Poor volume of blood cultured affects the performance of the microbial diagnosis of sepsis. This ESGBIES survey assessed the real-life total volume of blood cultured at the European level, identified factors for poor volume and quantified gap to guidelines.

**Materials/methods:** European volunteer participants extracted from routine the data related to 50 successive clinical episodes for which blood cultures (BC) were collected from adult patients. Data included the number of samplings over a 24-h period, the number of bottles per sampling, the volume of blood per bottle (estimated from the difference between mean empty bottle weight and post sampling bottle weight, taking account of blood density, 1.055), laboratory characteristics, method characteristics. For each center, key-performance indicators for ordering, sampling and clinical impact were determined, which corresponded to rates of: i) episodes with ≥4 bottles, ii) bottles with volume of blood >5 ml, iii) episodes with minimal or compliant volume of blood during a 24 h sampling period [20-80 ml], respectively. Student t-test and \( \chi^2 \) were used for comparison between groups as appropriate.

**Results:** 125 laboratories from 16 countries participated, totaling 5,313 episodes and 20,323 bottles. Compliance with guidelines was poor: 0.9% of the centres had >80% of the bottles with >5 ml of blood; 42.6% and 5.2% of the centres had >80% episodes with >4 bottles collected and >20 ml of blood cultured, respectively. Total blood volume <30 ml per 24 h was more frequent in: Southern than Northern and Eastern countries \( (p<10^{-4}) \), hospitals than clinics \( (p<10^{-4}) \), centres without protocolized preanalytics \( (p<10^{-4}) \) or specific training \( (p<0.03) \), emergency room than other wards \( (p<10^{-4}) \), or when only one BC set was drawn \( (p<10^{-4}) \). Interestingly, centres with advanced BC instrument that monitors blood volume performed better \( 49.1\% \) and 59.1% series >20 ml with bactec-FX® and Virtuo® instruments vs 41.2% and 42.4% with Bactec and BactAlert 3D systems, respectively, \( p<10^{-4} \). Neither elderly \( (p=0.43) \) nor ISO15189 accreditation \( (p=0.68) \) impacted blood volume >30 ml, although laboratory accreditation positively influenced volume in the subgroup France \( (p=0.03) \).

**Conclusions:** This study provides for the first time an overview and determinants of bloodstream infection diagnosis quality in Europe. Regular external quality assessment should improve diagnostic quality.

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Changing profile of invasive disease-causing Staphylococcus aureus in Australia

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Background: Staphylococcus aureus is a significant human pathogen. However, the population responsible for invasive disease is not panmictic but rather composed of mixtures of genetically distinct lineages that undergo temporal fluctuations in prevalence. These populations often display different clinically relevant characteristics, subsequently shifts in lineage prevalence can drastically alter the phenotypic/genotypic profile of the population, with downstream implications for disease management and prevention. Here we present work exploring an invasive S. aureus population, using combined genomic and phenotypic data, modelling the impact that changes in population composition have had on clinically relevant bacterial features, including antimicrobial resistance, virulence, and geographic movement.

Materials/methods: Collection included S. aureus bacteraemia (SAB) isolates from two large multicentre cohort studies; a subset of the Australian and New Zealand Cooperative in Staphylococcal Sepsis study (n=526, 2007-2008) and the Vancomycin Efficacy in Staphylococcal Sepsis in Australasia study (n=221, 2011-2012), supplemented with the sequence data for MRSA identified in the 2015 Australian Staphylococcal Sepsis Outcome Program (n=387). This collection was subjected to phenotypic and genomic profiling of antimicrobial resistance and virulence characteristics, and detailed phylogeographic modelling.

Results: The S. aureus population responsible for invasive disease in Australia demonstrated extensive genetic diversity. However, the proportion of different lineages has markedly changed over the time-frame sampled, reflecting a complex clonal replacement event denoted by the rapid decrease of the predominant MRSA lineage (ST239) and replacement by multiple MRSA (ST22, ST45, ST93) and MSSA (ST30, ST8) lineages. This has coincided with a population-level decrease in carriage of resistance genes, increase in phenotypic antimicrobial susceptibility (including vancomycin), and increased carriage of virulence genes; characteristics which align with the lineages most altered in prevalence. Phylogeographic modelling identified that the replacing lineages demonstrated a higher frequency of interstate movement, suggesting that the new population may have potentially enhanced geographic mobility.

Conclusions: This works highlights that invasive S. aureus populations are diverse and fluid, and regular surveillance is required to capture changes in population composition. However, this needs to be complemented with detailed profiling of the lineages involved to understand the implications of these changes on the management and prevention of invasive staphylococcal disease.

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Abstract 8545

**Epidemiology, complications, and outcomes of vertebral diskitis/osteomyelitis among patients with *Staphylococcus aureus* bacteraemia**

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**Background:** *Staphylococcus aureus* bacteremia (SAB) is associated with significant morbidity, mortality, and a high risk of hematogenous seeding at distant sites. The aim of the current investigation is to evaluate the epidemiology of vertebral osteomyelitis among patients with SAB, and to describe management, interventions and associated outcomes.

**Materials/methods:** We retrospectively reviewed all adults admitted to Mayo Clinic in Rochester MN with SAB between July 2006 and December 2017. Cases of SAB were identified using Advanced Cohort Explorer (ACE) based on diagnostic codes and microbiology data that included positive culture results. Vertebral osteomyelitis cases were defined based on diagnostic imaging criteria. Modified Duke criteria were used to define infective endocarditis (IE) cases. We reviewed the index hospitalization and assessed outcomes at 3-month follow up.

**Results:** During the study period, 1324 patients were hospitalized at our institution with SAB. Median age was 62 years. Of them, 104 (8%) had vertebral diskitis/osteomyelitis. Most patients presented with fever, back pain and malaise. An epidural abscess was identified on imaging in 15%. Seventeen (16.3%) patients had concomitant IE. The median duration of bacteremia was 5 days and 36% of isolates were methicillin resistant (MRSA). Eighty-three patients underwent surgical intervention. For methicillin susceptible (MSSA) isolated, the primary antibiotic therapy was either cefazolin in 62% and semisynthetic penicillin in 21.6%. For MRSA cases, the most commonly administered antibiotic was vancomycin in 83.2%; daptomycin was used in 12%. Overall, the median duration of antibiotic regimen was 42 days. Twenty-one patients died due to SAB-related complications. Post-discharge follow up data were available in 102 of the patients. During the 3-month follow up period, 4 (3.8%) patients suffered SAB relapse.

**Conclusions:** Vertebral diskitis/osteomyelitis was diagnosed in only 8% of our SAB cohort. Despite prolonged, parenteral antibiotic therapy and a large majority of patients undergoing surgical intervention for attempted cure, 21% of them died secondary to SAB-related complications. Vertebral diskitis/osteomyelitis remains a formidable complication of SAB and evaluation of potential interventions to improve outcomes is warranted.

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**Abstract 8548**

**Epidemiology of bloody diarrhoea in Georgia and haemolytic-uraemic syndrome associated with it**

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**Background:** According to WHO there are about 1.7 Billion cases of diarrhea annually, 760000 children under 5 years die from complications or irrelevant treatment. One of the feared conditions is a bloody diarrhea, caused by different pathogens like Salmonella, Shigella and others including Shiga toxin-producing *Escherichia coli* (STEC), which also causes Hemolytic Uremic Syndrome (HUS). HUS is characterized by symptom triad: thrombotic microangiopathy, thrombocytopenia, and acute kidney injury. In USA HUS is found in 6% of diarrheas caused by STEC 0157:H7. But other strains have their role too. Lethal outcome is registered in about 5% of cases.

**Materials/methods:** Study report: We present you the results of a study made by Georgian doctors, based on 760 clinical cases of bloody diarrhea between years 2005 and 2016. The goals were the following: 1) Studying epidemiological features of bloody diarrhea and HUS in Georgia and revealing possible disease outbreaks. 2) Raising awareness among individuals under risk and evaluate level of knowledge among medical personnel 3) Provide practical recommendations for avoiding this disease and unwanted complications. The research was conducted in two steps: I. Retrospective study; II. Prospective study. The Data collected from recordings of different Georgian hospitals were registered in electronic data base. Incidence, prevalence, relative risk confidence interval and p-value were calculated. Analysis of identified pathogens were held.

**Results:** 760 registered cases. 14.7% (112 cases) complicated with HUS. 51% of cases (387 cases) in women. First registered outbreak was in 2009 – 25 patients complicated with HUS (12 children; 2 deaths). *E. coli* 0104:H4 was identified during this outbreak, same strain that caused epidemic of Hus-complicated bacterial infections in Europe 2011. Pathogenic strains of *E. coli* 0126, 0104:H4, 0119, 0128, 033 and 045 were found.

**Conclusions:** Incidence rises in warm months of the year. Most cases of HUS are in children between 1-4 and almost none found in children under 1 year. High mortality is registered during outbreaks, especially in cases complicated with HUS. Chances are high after consuming non-cleaned vegetables, certain types of ice-cream and animal contacts. Studies must be held for identifying outbreak sources.

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**Abstract 8551**

**Evaluation of the new BL-RED electrochemical test for the detection of 3GC-resistant Enterobacteriaceae directly from positive blood cultures**

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**Background:** Bloodstream infections (BI) are expensive healthcare and the mortality rate is high. The rapid identification of the pathogen as well as the rapid antimicrobial susceptibility testing (AST) is decisive to clinical management and to avoid an excessive exposure to broad-spectrum treatment.

The aim of the present study was to evaluate the performance of a new electrochemical test, BL-RED™ (β-lactamase rapid electrochemical detection, AirDiag), in the rapid detection of third generation cephalosporin-resistant (3GC-R) Enterobacteriaceae from positive blood cultures (PBC).

**Materials/methods:** One hundred and fifty isolates with various β-lactamase content previously characterized was selected. This panel consisted of isolates: 3GC-susceptible (n = 50), Extended Spectrum β-Lactamase (ESBL) producers (n = 41), chromosomal- (n = 31) or plasmid-mediated (n = 10) AmpC producers, extended-spectrum OXY (n = 3) and carbapenemase (n = 30, including 12 ESBL and 3 AmpC) producers.

Approximately 100 CFU of each isolate were inoculated into sterile blood culture bottles and incubated in a BACTEC™ FX (BD) automated system. The BL-RED™ test was performed as soon as the bottle was positive, according to the manufacturer’s recommendations. The results were compared with those obtained by conventional technique (AST by disc diffusion method following EUCAST recommendations).

**Results:** The sensitivity and specificity of the BL-RED™ assay in the detection of class A (ESBL, KPC, OXY) β-lactamase-producing Enterobacteriaceae were respectively 87.5% (5 CTX-M and 1 SHV producers not detected) and 100%.

The overall sensitivity and specificity of BL-RED™ in the detection of 3GC-resistance were 46.7% and 100% (VPN 54.2%, VPP 100%). The assay failed to detect AmpC-overproducing isolates (sensitivity 2.4%) or metalloenzymes-producing isolates (0%).

**Conclusions:** The BL-RED™ assay was easy to use and efficient for the early detection of most ESBL-producing Enterobacteriaceae, one hour after the positivity of the blood culture, allowing rapid adequacy of antimicrobial therapy and improved prognosis. However, the test did not reliably detect all 3GC-R isolates and a high level of vigilance is required with overproduced AmpC Enterobacteriaceae.

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Abstracts 2020

Abstract 8555

**Inflammatory response of murine macrophages and alveolar epithelial cells following exposure to Aspergillus fumigatus spores**

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**Background:** Exposure to *Aspergillus* spores is associated with symptoms of airway tract inflammation in people living in damp dwellings or in exposed professionals, that can lead to severe diseases such as allergic bronchopulmonary aspergillosis or chronic pulmonary aspergillosis. To better understand the setting of inflammation processes, our aim was to study the pulmonary inflammation induced by the exposure to *Aspergillus fumigatus* spores in cell culture systems using murine alveolar epithelial cells and macrophages.

**Materials/methods:** RAW 264.7 mouse macrophages and MLE-15 mouse alveolar epithelial cells were cultured in DMEM and RPMI 1640 media, respectively, supplemented with fetal calf serum and 1% penicillin-streptomycin, at 37°C and 5% CO₂. Cells were seeded in 12-well culture plates. Confluent wells were treated with *Aspergillus fumigatus* spores at a multiplicity of infection of 3 and incubated for 4 h. A lactate dehydrogenase cytotoxicity test was performed on both cell lines. RNA extraction was performed with the All-in-One DNA/RNA/Protein Miniprep kit (BioBasic). Reverse transcription was performed with the Superscript IV Reverse Transcriptase kit (Invitrogen). Gene expression of defined cytokines was quantified with TaqMan Gene Expression Assays (ThermoFisher). Real-time reverse transcription PCR results were expressed using the $2^{-\Delta\Delta C_t}$ method. The TATAbox Binding Protein gene was used as endogenous control.

**Results:** Lactate dehydrogenase test showed no cytotoxicity for the 4-h exposure to *A. fumigatus* spores of both cell lines. After 4-h exposure of RAW 264.7 cells to *A. fumigatus* spores, significant inductions of IL-1β [P<0.0001], TNF-α [P=0.015], CCL-2 [P=0.0027] and CXCL-2 [P<0.0001] gene expression were observed, with 57, 5, 8 and 68-fold inductions, respectively. After a 4-h exposure of MLE-15 cells to *A. fumigatus* spores, gene expression of GM-CSF, CXCL-1 and CXCL-2 was markedly low compared to that of RAW cells (4, 3 and 4-fold inductions, respectively).

**Conclusions:** Unlike MLE-15 alveolar epithelial cells, RAW 264.7 macrophages exhibited a strong induction of defined proinflammatory cytokine gene expression following the exposure to *A. fumigatus* spores. The strongest inductions concerned the gene expression of IL-1β and CXCL-2, key cytokines in inflammatory processes involved in leukocyte recruitment and activation.

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Evaluation of obesity as a risk factor for drug-resistant Enterobacteriaceae among hospitalised adults

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Background: Gram-negative (GN) antibiotic resistance is a global concern that requires a better understanding of contributing risk factors. These concerns are heightened in patients with obesity as antibiotics may be inadequately dosed, leading to suboptimal systemic exposure, antibiotic failure, and potential emergence of antibiotic resistance. The objective of our study was to determine if obesity is associated with presence of multidrug-resistant organisms (MDRO) among Enterobacteriaceae.

Materials/methods: We conducted a multicenter, retrospective cohort study of adult hospitalized patients with at least one specimen sampled for bacterial culture yielding an Enterobacteriaceae from November 2016 to May 2017. Study groups were stratified by obesity status based on body mass index (BMI): BMI<30 kg/m² (non-obese) and ≥30 kg/m² (obese). Analysis of covariates included basic demographics, history of prior antibiotic therapy, presence of immunosuppression, transfer from healthcare facility, sampling specimen from a critical care unit, and comorbidities. The primary outcome was the presence of GN MDRO on culture defined as presumptive extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae [ceftriaxone resistance] or carbapenem-resistant Enterobacteriaceae [CRE]. A multivariable logistic regression model was fit to estimate the adjusted odds ratio while controlling for potential confounders.

Results: The final analytic sample consisted of 366 patient patients, 238 non-obese and 128 obese patients. There were no significant differences between study groups expect for higher median creatinine clearance (71.9 versus 48.2 mL/minute, p<0.001) and higher proportion of history of cancer (18 versus 9.7%, p=0.022) in obese patients. The most common GN species identified was E. coli (64.2%). There was a higher proportion of GN MDRO in obese versus non-obese patients (18.8 versus 11.3%, p=0.051). In the multivariable logistic regression analysis, obesity was independently associated with GN MDRO after controlling for confounders (adjusted odds ratio, 1.92; 95% CI 1.03-3.60).

Conclusions: Among adult hospitalized patients, obesity was independently associated with GN MDRO (presumptive ESBL or CRE). Obesity may be a significant risk factor for antibiotic resistance. We hypothesize this may be partly mediated due to inadequate antibiotic dosing and systemic exposure. Further studies are needed to investigate the causal pathway to elucidate effective interventions to reduce the emergence of drug resistance.

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Abstract 8559

Characterising outer membrane permeability for β-lactam antibiotics in Acinetobacter baumannii strain HUMC1

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Background: The outer-membrane (OM) poses unique challenges for antibiotic penetration. While Acinetobacter baumannii (AB) is believed to be poorly penetrable, there is a dearth of OM permeability data on clinically relevant β-lactam antibiotics. This study characterized the OM permeability of six clinically-relevant β-lactams in multidrug-resistant MDR-AB via LC-MS/MS.

Materials/methods: Clinical AB isolate HUMC1 was grown to 10^7 CFU/mL in broth and washed four times in PBS (containing 1.14 mM Mg^{2+} and Ca^{2+}). Half of these bacteria were lysed to evaluate the periplasmic β-lactamase activity; the other half was concentrated by 10-fold and served as intact bacteria to characterize OM permeability. One separate intact bacteria suspension was incubated in PBS for 120 min. During that incubation, bacteria-free supernatant samples were obtained at 3, 15, 30, 60 and 120 min to assess the time-dependent β-lactamase activity in extracellular space. The time-course of extracellular β-lactam concentrations was determined over up to 120 min in control, lysed and intact bacteria via LC-MS/MS (LLOQ: 0.03 mg/L for each β-lactam).

Results: For lysed bacteria, β-lactams were freely exposed to β-lactamases. Therefore, the hydrolysis was rapid for all drugs. For imipenem, meropenem, sulbactam, carumonam and cefepime, extracellular β-lactamase activity caused minimal hydrolysis. When the OM remained intact, drugs had to penetrate the OM before being hydrolyzed in periplasm. Therefore, the slope of concentration decline (intact bacteria profile) indicated the rate of OM permeability (Figure). Extracellular β-lactamase significantly hydrolyzed ceftazidime; this caused the extracellular concentrations in the cell-free PBS control to decline. We simulated the concentration decline of ceftazidime in this control, and the profiles overlapped with the observed profiles in intact bacteria indicating very slow penetration of ceftazidime.

Conclusions: OM permeability was rapid (>200 nm/s) for imipenem, intermediate for meropenem, sulbactam and cefepime (approximately 20 nm/s), slow for carumonam (3 nm/s), and very slow for ceftazidime (<1 nm/s). Our assay successfully accounted for the extracellular β-lactamase activity. This novel assay therefore extended the scope of strains for OM permeability studies. Future studies in a large collection of strains with different OM porin patterns are warranted.

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Performances of a new random access system for hepatitis B and C viral load quantification

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Background: Viral load (VL) monitoring for hepatitis B and C is essential to evaluate disease progression and treatment response. Automated, random-access and rapid systems are becoming standard to provide reliable VL to clinicians. The aim of this study was to evaluate the performances of the recently launched NeuMoDx for HBV-DNA and HCV-RNA quantification.

Materials/methods: 373 HBV-VL and 373 HCV-VL routinely quantified on the Beckman-Veris Dx system were either retrospectively (frozen samples; n=178 HBV, n=249 HCV), or in parallel (fresh primary tubes; n=103 HBV, n=124 HCV) tested using NeuMoDx specific reagents. Linearity range of these assays was assessed on serial dilution of high tittered plasmas containing different HBV genotypes (A-E, n=10) and HCV genotypes (1a, 1b, 2-5, n=12).

Results: Overall test failure, corresponding mostly to internal control amplification failure was 2.3% and was not influenced by the matrix type, frozen plasma or plasma from primary tube. For HBV-VL, the overall Kappa qualitative agreement was 74%, with 27 (12.6%) discrepancies [Veris Positive/NeuMoDx negative]; discrepant sample VL ranged from 1.1 to 2.6 log IU/mL. Correlation between both HBV assays on 72 quantified samples by both methods was excellent (r=0.963) with a mean bias [NeuMoDx-Veris] of 0.21 log IU/mL. For HCV-VL, the overall qualitative agreement reached 94%, with 9 (2.8%) discrepancies. Among those, 8 HCV-VL were detected positive [HCV-VL from 17 to 71 IU/mL] on NeuMoDx while negative on Veris. The r-correlation factor between both HCV assays on 106 samples was 0.960 with a mean bias [-0.14 log IU/mL] [NeuMoDx-Veris]. Serial dilutions confirmed the claimed linear ranges for HBV and HCV whatever the tested genotypes. On NeuMoDx, the mean turnaround time was 72' [55-101] for HBV and 96' [78-133] for HCV and depended on the number of loaded samples on the system.

Conclusions: These first results obtained on the NeuMoDx confirmed the overall good functionality of this system based on microfluidic with short turnaround time, simple training, full traceability and easy handling. Preliminary results on HBV- and HCV-VL look promising and should be challenged with further comparisons with other systems.

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Is periodic screening of donor faeces with temporary quarantine storage effective in preventing transmission of multidrug-resistant organism during faecal microbiota transplantation?

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Abstract third-party references: On behalf of the Netherlands Donor Feces Bank (NDFB) study-group

Background: The FDA recently issued a warning after transfer of faeces containing an extended-spectrum beta-lactamase (ESBL)-producing Escherichia coli by faecal microbiota transplantation (FMT), which led to bacteraemia in two immunocompromised patients. This prompted our national donor feces bank to re-evaluate the donor screening protocol, which includes periodic multi-drug resistant organisms (MDRO) screening of donors with additional screening after foreign visits. Faecal suspensions are stored in quarantine during a three months period, until re-screening results are available.

Materials/methods: A retrospective cohort study was performed. Data from January 2016 until October 2019 of (potential) NDFB faeces donors on previously performed tests for MDRO were analysed. Furthermore, the presence of MDRO was assessed in faecal suspensions that were approved for patient treatment between January 2017 and April 2019 using a selective broth enrichment media with subsequent subculturing on selective solid media. All MDRO isolates that had been detected in donor faeces were subjected to Whole Genome Sequencing using the Illumina NovaSeq6000 platform with subsequent core-genome MultiLocus Sequence Typing (cgMLST).

Results: Six out of 16 active donors (38%) were MDRO-positive at some point during their donor activities, with a median duration of donor activity of 268 days. This included 10 MDRO-positive samples among 96 tested faeces samples (10.4%). Seventy-one percent of the detected MDROs was an ESBL-producing E. coli. Among results of all initial screenings, 7 of 66 potential donors (11%) were MDRO-positive. Importantly, no MDRO were detected in 170 faecal suspensions that were approved for patient treatment with the current screening protocol. Furthermore, cgMLST of all detected MDRO isolates revealed that two donors carried an identical MDRO isolate in their faeces.

Conclusions: Healthy donors have a relatively high risk to become colonised with a MDRO at some point during their donor activities. This study shows that our current screening protocol is effective in preventing the presence of MDRO in approved faecal suspensions.

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Hospital outbreak of carbapenem-resistant Enterobacteriaceae associated with an OXA-48 plasmid hosted mainly by Escherichia coli ST399

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Background: A hospital ward outbreak of carbapenem-resistant Enterobacteriaceae was detected by routine surveillance. Despite robust infection prevention and control interventions, the outbreak continued for 18 months.

Materials/methods: A ward outbreak epidemic alert was triggered when carbapenem-resistant Enterobacteriaceae samples were recurrently found upon screening in a hospital ward. Bacterial isolation and whole genome sequencing were performed to ascertain all known resistance genes carried, MLST type and strain background, plasmid backbone and type of plasmid/plasmids carried and associated virulence factors present. Fifty-five isolates were cultured from 48 patients during ten consecutive months from May 2016 to February 2017. All clinical isolates showing carbapenem-resistant were archived and investigated.

Results: Whole genome sequencing and subsequent analysis revealed a conserved promiscuous OXA-48 carrying plasmid as the defining factor within this outbreak. Four different species of Enterobacteriaceae were involved in the outbreak. E. coli ST399 accounted for more than half of the isolates. Comparative genomics of publicly available E. coli ST399 sequence data showed that outbreak isolates formed a specific clade. The OXA-48 plasmid identified in the outbreak differed from other known plasmids by a few homologous recombination events. We estimate an upper bound to the plasmid conjugation rate to be rconj0.13 conjugation events per lineage per year.

Conclusions: Our analysis suggests co-adaptation between the plasmid and its main bacterial host to be a main driver of the outbreak. This supports roles for both plasmid conjugation and clonal expansion in the evolution of the outbreak. A specific E. coli ST has not previously been reported as the majority host in a plasmid-borne outbreak of carbapenem resistance.

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Polyclonal antibody anti-CR3-RP Ab inhibits biofilm of *Candida albicans* and decreases an expression of the genes related to biofilm-formation and cell surface hydrophobicity

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**Background:** Treatment of biofilm formed by *Candida* sp. is very often problematic due to increasing resistance to antifungals (ATF). Thus, it is of importance to focus a research on alternative ways of treatment. One of the alternative approaches in anti-fungal therapy could be through using surface antigens or antibodies directed against them. Presented research was aimed at an impact of polyclonal antibody (Ab) anti-CR3-RP to biofilm of *C. albicans* resistant to common ATF and possible role of this Ab in regulation of biofilm-associated genes and cell surface hydrophobicity.

**Materials/methods:** The XTT reduction assay was used to measure viability of biofilm in the presence of fluconazole (FLC) and anti-CR3-RP Ab [added at the adherence phase and the 24-h pre-formed biofilm]. Quantitative real-time PCR was used to determine changes in the *ALS1, ALS3, ALS9, BCR1*, and *CSH1* gene expression in biofilms formed w/wo Ab. Changes in hydrophobic properties of biofilm was estimated by N-octane assay and calculated in percentage of hydrophobic cells after treatment w/wo Ab.

**Results:** The anti CR3-RP Ab was able to inhibit biofilm of *C. albicans* SC5314 and the FLC-resistant *C. albicans* CCY29-3-164 strain when added to the adherence phase [decrease of metabolic activity of SC5314 and CCY29-3-164 in 70% and 35%, respectively]. Moreover, Ab also demonstrated activity against the 24-h pre-formed biofilms [decrease of metabolic activity in 30% for both strains], which compared favorably to levels of inhibition achieved by treatment with FLC. Real-time PCR showed a decrease of relative expression of the biofilm-associated genes [2x for *ALS1*, 4x for *ALS9*, 3x for *BCR1*, and 2x for *CSH1*] in both biofilms of *C. albicans* formed in the presence of Ab. In addition, changes in the cell surface hydrophobicity of yeasts was observed after 1h-treatment with Ab. N-octane assay proved a decrease of hydrophobicity in 40% for SC5314 and 15% for CCY29-3-164.

**Conclusions:** Our results point to a high potential of anti-CR3-RP Ab in eradication of resistant *Candida* biofilms and its role in regulation of genes associated with biofilm development.

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Tolerance of prolonged oral tedizolid (TDZ) antibiotic therapy for peri-prosthetic joint infections (PJIs): results of a pilot multi-centre French study

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Background: Linezolid (LZD) has proven efficacy in patients treated for PJIs but prolonged therapy is limited notably by bone marrow and neuro-toxicity. TDZ is an oxazolidinone close to LZD which exhibits a higher intrinsic antibacterial activity and a better toxicity profile than LZD. Data on the clinical and biological tolerance of oral TZD prolonged therapy in patients treated for PJIs are lacking.

Materials/methods: We conducted a prospective pilot study in 3 national referent centres for bone and joint infections in France (Lille-Tourcoing, Paris and Lyon) from August 2018 to August 2019. All patients were operated and the decision to use TZD was taken in the setting of multidisciplinary meetings and given the off-label use of TDZ, and informed written consent was obtained in every patient. The planned duration of TZD treatment had to be at least 6 but not more than 12 weeks.

Results: Thirty-four patients (18/16 M/F) of mean age 73.5 ± 10.1 years were included. ASA score was 2 in 18 (53%) cases and a previous revision for infection was noted in 11 patients (32%). Surgical interventions consisted in retention of the infected implants and one/two stage-replacements in 12 (35%) and 18/4 (53/12%) patients, respectively. Microbiology was dominated by Staphylococcus spp. (n=22, including 10 S. aureus) and Enterococcus spp. (n=8). The mean duration of TZD therapy in 30 patients (88%) who completed the planned therapy was 61±19 days [42-88]. TZD was associated to another antibiotic in 19 patients (56%), including rifampicin in 17 cases (50%). At least one adverse event likely related to TZD was recorded in 15 patients (44%). Four patients (12%) had to prematurely stop TZD therapy for failure (n=3) and anaemia (n=1 related to haemorrhagic erosive gastritis). Haemoglobin at baseline and at the end of TZD therapy was 10.5±1.6 and 11.5±1.7 g/dL, respectively. No cases of thrombocytopenia, leucopenia, neurotoxicity or drug-drug interaction were recorded during TZD therapy.

Conclusions: The results of the present pilot study show a favorable toxicity profile of TZD, allowing prolonged treatment in patients treated for PJIs. Larger size clinical studies are warranted to confirm these preliminary results.

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Investigating the effect of wastewater treatment systems on antimicrobial resistance and virulence factors
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Background: Water pollution by antibiotics may contribute to the spread of antimicrobial resistances (AMRs) worldwide and hence poses a serious threat to global public health. Sewage often collects strongly contaminated water with potentially resistant bacteria, and must hence be managed adequately to remove chemicals and favour the growth of non-pathogenic bacteria. Engineered chemical and physical treatments impact the structure of microbial communities in water treatment plants, hence affecting the pool of antimicrobial resistance genes (ARGs) and virulence factors (VF). The present study aimed at investigating the effect of secondary and tertiary treatments on the microbial communities and their resistance and mobility genes in waste water treatment plants (WWTP).

Materials/methods: Twenty-six water samples were collected along the industrial processes of WWTP, including biological secondary and tertiary treatment, in France, Spain, and in The Netherlands. The V3-V4 region of the 16S rRNA was sequenced with 300 bp-read using a MiSeq for microbiota profiling. Taxonomical assignment of reads was performed with an in-house bioinformatic pipeline using QIIME (Caporaso, 2010) and EzBioCloud database (Yoon, 2017). Shotgun metagenomics was performed on a subset of 13 samples. Assembled metagenomics and raw reads were used to identify ARGs, VF genes and MGEs, using homology searches with proteins of the CARD database (Jia, 2017), VF databases and plasmid databases, respectively.

Results: The biological treatments changed the composition of microbial communities that are dominated by well-known faecal bacteria belonging to Proteobacteria, Firmicutes, and Bacteroidetes in raw waste water. In the four WWTP sampled, sewage secondary treatment successfully decreased ARGs from all classes, including the most prevalent multidrug efflux pumps. However, the three different tertiary treatments implemented in the industrial processes showed divergent effect on the resistome. VFs exhibiting the biggest decrease in relative abundance after treatment were biofilm regulators such as bfmR, motility proteins and catalases.

Conclusions: Understanding the occurrence of AMR in waste water systems and defining the performances of treatment strategies is key to introduce effective intervention measures to reduce the selection for AMR and virulence in the environment.

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Comparing ethanol lock therapy versus vancomycin lock on a salvation strategy for totally implantable vascular access device infections due to coagulase-negative staphylococci (the ETHALOCK study): a prospective randomised clinical trial

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Background: effectiveness of ethanol lock therapy (ELT) in central line associated bloodstream infections (CLABSI) has been previously suggested on retrospective studies. A recent prospective study found that ELT did not prevent treatment failure. However data are small and none of these studies focus on totally implantable venous access device (TIVAD). Thus far the 2009 IDSA guidelines on managing intravascular catheter related infections have not positioned this strategy.

Materials/methods: a 2-arms, randomized, double-blinded, multicentre trial was set to compare the efficacy of ELT versus vancomycin lock in TIVAD infections due to coagulase negative staphylococci (CoNS), either or not associated with bacteremia. Patients were randomly assigned (1:1) to receive either ELT (ethanol 40% + enoxaparin) or vancomycin lock, for 10 days in both arms. Lock therapy was renewed every day, dwelling in the lumen for 24 hours. A systemic antibiotic course was given in case of bacteremia. The primary outcome, assessed after a 12 weeks follow up, was treatment success defined as clinical and biological cure, or non-attributable death or catheter removal. Secondary outcome was ELT tolerance and complications. All-cause mortality at 14 weeks and the TIVAD removal rate and its cause were also assessed. This trial is registered with Clinicaltrials.gov, number NCT02411331.

Results: 62 patients with TIVAD infection have been included between 2015 and 2019. 19 of them were complicated with bacteremia. Cure rate was 54.84% (17/31) in vancomycin lock group and 61.29% (19/31) in ELT group (p=0.61). There was no difference between infections complicated with bacteremia (cure rate was 50% in vancomycin group [5/10] and 77.78% in ELT group [7/9], p=0.35) and infections without bacteremia (cure rate was 57.14% in vancomycin group [12/21] and 54.55% in ELT group [12/22], p=0.86). Adverse effects happened equally in both group.

Conclusions: ELT is not an efficient solution to treat TIVAD infections due to CoNS, complicated or not with bacteremia. Catheter salvage strategy should be considered only in patients with poor health condition or precious catheter.

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Abstract 8577

Chorioamnionitis: time for changes in management?
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Background: Chorioamnionitis is one of the most important risk factors associated with early-onset neonatal sepsis (EOS). However, the exposed infants with confirmed EOS is low and empirical therapy represents the first cause of antibiotic use in newborns.

Since September 2018, a new protocol was established in the neonatology unit in our hospital, whereby children > 35 weeks don’t receive antibiotic treatment while they remained asymptomatic and without alterations on the analytic parameters.

Our purpose was the description of the microbiological diagnosis of chorioamnionitis and the therapeutic management of neonates, after this protocol was established.

Materials/methods: Between October 2017 - September 2019, 204 placental samples from women with clinical suspected chorioamnionitis (>35 weeks of gestation) were collected, plated in thioglycolate broth, blood agar, MacConkey agar, chocolate agar, and selective media for S. agalactiae, Neisseria gonorrhoeae, Gardnerella vaginalis and Candida spp. and incubated at 37°C 24 or 48 hours for anaerobios.

Since December 2018, Anyplex™ II STI-7 Detection (Seegene) was performed to molecular detection of sexual microorganisms transmission.

Women and children data were collected.

Results: In 76 samples some microorganism was found (17 polymicrobial). Gram negative bacilli (n=38), Enterococcus (n=16), S. agalactiae (n=12) were the most common microorganisms found in cultures.

Ureaplasma spp was the most frequently detected by PCR method (n=24).

Before protocol establishment, all infants exposed to suspected clinical maternal chorioamnionitis (n=149) received antibiotics, following the current recommendations of the American Academy of Pediatrics (AAP) and the CDC; however, in 64% of the placental samples no microorganisms were isolated. Only 3.3% (n=5) of the infants developed some symptom and one positive blood culture (Enterococcus faecalis) was detected.

Following new protocol, only 27% (n=43) of children were treated (presence of symptoms or abnormal laboratory results) and no cases of positive blood culture occurred. The antibiotic use decreased in 73% ([149/149 (100%) vs 43/158 (27%)].

Conclusions: Clinical maternal chorioamnionitis diagnosis, based in non specific criteria lead to unnecessary treatment in newborns.

According to these data, the combination of microbiological, analitical and clinical criteria with and expectant attitude results in a decrease in costs and toxic effects of antibiotic therapy, without an increase of EOS.

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Abstract 8578

**Directly detecting imipenemase (IMP) carbapenemase with high-resolution Orbitrap mass spectrometry**

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**Background:** Carbapenemase-producing organisms (CPOs) are becoming a serious global public health threat as a consequence not only of rapid propagation of successful clones, but also of horizontal gene transfer of resistance genes. Additionally, CPOs are frequently associated with high morbidity and mortality rates.

Imipenem-type metallo-β-lactamase (IMP) producing organisms contain carbapenemase enzymes that confer antibiotic resistance to almost all antibiotics with the exception of a select few of last-resort. These precious antibiotics are intentionally seldom-administered with the intent of preventing microbe exposure leading to developed novel resistances to our last line of defense. Imipenem, a noted last-resort antibiotic due to its unusually high potency and effectiveness against a broad spectrum of microbes, is catalytically metabolized by what are typically difficult-to-treat IMP-producing bacteria.

Herein, we present an approach for directly detecting IMP from cultures using short LC gradient methods that leverage tandem mass spectrometry (MS/MS).

**Materials/methods:** Single bacterial colonies on agar were harvested, mechanically lysed, centrifuged, and lysates were extracted. The proteins in the lysate were bound to RP-4H monolithic solid phase extraction columns and chromatographically eluted with subsequent ionization and transfer to a mass spectrometer for analysis. Using MS/MS, ions with mass-to-charge ratios \(m/z\) corresponding to intact IMP were dissociated such that diagnostic fragment ions were detected and used to confirm the presence of the protein.

**Results:** To date, multiple species of both Enterobacteriales and *Pseudomonas aeruginosa* that had been previously determined to harbor IMP genes using whole genome sequencing were evaluated. MS/MS of IMP isolates resulted in production of informative fragments, having specific \(m/z\) and charge states. The combination of these fragments provided sufficient information to determine the presence of IMP in 10 of 10 isolates. Furthermore, non-carbapenemase-producing isolates showed negative results from the assay.

**Conclusions:** Directly detecting IMP on short gradients facilitates clinical adoption. This approach involves the direct measurement of the active carbapenemase, making it extremely selective due to the sequence-specific molecular weight of the proteins. Although this shows great promise for the strains we have evaluated, IMP often has low expression levels and the limit of detection has yet to be systematically evaluated in clinical samples.

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Abstract 8580

**Ultimate survival of Serratia marcescens in chlorhexidine**

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**Background:** Chlorhexidine is an antiseptic widely used. In December 2014 there was an outbreak of *Serratia marcescens* (*Sm*) associated with 2% aqueous solution of Chlorhexidine (asC, Bohmclor ®) in Spain. In our hospital we isolate the strain in three presentations of 2% asC i36 and i37 batches and in 0, 5% asC i35 batch, that were prepared in October 2014. We have studied the survival of these strains until September 2018, and also of different strains of clinical isolates.

**Materials/methods:** Colony counts of Sm outbreak strain of the contaminated stock bottles were performed at monthly intervals. Experimental inoculation of 10 ml of chlorhexidine with different concentrations of isolates of other bacteria from clinical sources, (gram positives, gram negatives and yeasts). Colony counts were done at the time of inoculation and 7 days later. We also inoculated 1-10 ml of SmOS 0,5 McFarland solution in bottle stock solution of 250 ml with colony counts performed at monthly intervals.

**Results:** Sm was isolated in three presentations of asC i36 during 6 months but in the i37 batch it remained viable until july 2018 (44 months); in 0, 5% asC i35 batch was negative in the first month. We found no growth in experimental inoculation of 10 ml of chlorhexidine with different concentrations of all isolates from clinical sources at the time of inoculation up to 7 days. The experimental contamination of the stock bottles of 250 ml of chlorhexidine obtained positive cultures with high colony counts. Surprisingly the 5 ml and 10 ml inoculations only survived for 3 months and the inoculation of only 1 ml remained viable 12 months.

**Conclusions:** Sm may survive in 2% asC for prolonged periods. We describe a survival of 44 months what has never been described to date. We have more questions than answers to explain what are the factors on this extreme survival depends. *Serratia marcescens* may survive in 2% asC for prolonged periods. We describe a survival of 44 months what has never been described to date. We have more questions than answers to explain what are the factors on this extreme survival depends

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Abstract 8587

**Rickettsiosis in southern Tunisia: serodiagnosis, epidemiology and severe cases**

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**Background:** Rickettsioses are emerging infectious diseases caused by obligate intracellular bacteria belonging to the genus *Rickettsia* and are transmitted by arthropods. Although classified as neglected diseases, they continue to cause severe illnesses and death worldwide. Our aim was to determine the seroprevalence of *Rickettsia* in our region and describe epidemiological and clinical characteristics of patients.

**Materials/methods:** All *Rickettsia* serodiagnosis carried out in the laboratory of Microbiology, Habib Bourguiba University-Hospital, Sfax (Tunisia) between January 2016 and August 2019 were included. Serum samples were tested for the presence of antibodies against *R. Typhi* and *R. conorii* by micro immunofluorescence assay. The positivity criteria were: IgG ≥ 1:128 and IgM ≥ 1:64, seroconversion or significant elevation of IgG (x4) between two sera.

**Results:** During the study period, 2424 serology were performed. Forty-Eight rickettsial infection cases were retained. Rickettsial diseases occurred in patients 4 to 86 years of age. A recrudescence of rickettsioses was observed during the autumn season (52%). 58% of the patients had IgG titer ≥ 1:128 and IgM titer ≥ 1:64. Seroconversion was observed in 17% of cases and a significant elevation of IgG between two sera was noted in 25%. Tests were positive for spotted fever group in 70.8%, typhus group in 12.5% and a cross reaction between the two groups was noted in 16.7%. Clinically, fever was noted in 71% of cases; fever was associated to cutaneous rash in 58.4%. Pneumonia was observed in 8.3% of cases. Other clinical symptoms have been observed such as uveitis and Confusion. Two cases of severe rickettsiosis have required ICU admission of two young adults. Biological abnormalities such as cytolysis, renal failure and thrombocytopenia have been noted. One of the patients had convulsions and myocarditis, but he improved with doxycycline. The other patient had fatal outcome due to an aggravation of a dilated cardiomyopathy.

**Conclusions:** In Tunisia, Mediterranean Spotted Fever caused by *Rickettsia conorii* is the most common rickettsiosis. Rickettsial diseases can be presented with variable but serious clinical forms. Serology is of great benefit especially in the presence of a clinical polymorphism.

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Abstract 8588

Diagnostic impact of molecular detection of enteropathogenic bacteria compared to stool culture

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Background: Gastroenteritis is a common disorder usually caused by infection and characterized by the acute onset of diarrhea. Molecular diagnosis using syndromic panels allows the detection of multiple pathogens that cause this process. Our goal is to evaluate the diagnostic performance of a commercial molecular method compared to conventional techniques in the detection of bacterial pathogens.

Materials/methods: Seven-hundred and thirty-nine stool samples with a Bristol score equal to or greater than 5 were processed, 352 samples (47.6%) from community health centers and 387 (52.4%) from hospital, both emergencies and hospitalization. Samples were transferred to Cary-Blair medium and processed using usual culture media for the detection of enteropathogenic bacteria. DNA extraction was performed from the liquid transport medium (Microlab Starlet, Hamilton). A syndromic panel of bacteria was used for real-time PCR amplification (Allplex GI Bacteria I / II Assay, Seegene) following the manufacturer’s instructions.

Results: The molecular method allowed to detect enteropathogens in 234 samples (31.7%), while conventional culture could only recover 59 (8.0%). In 38 samples, more than one pathogen was detected by the syndromic panel. The pathogens detected, in order of frequency, were 69 Aeromonas spp. (9.3%), 62 Campylobacter spp. (8.4%), 54 Escherichia coli with enteropathogenic potential (EPEC, EAEC, EIEC, ETEC, STEC and O157) (7.3%), 47 Clostridiodes difficile toxin B (6.4%), 10 Salmonella spp. (1.4%), 7 Yersinia enterocolitica (0.9%), and 4 Vibrio spp. (0.5%).

Conclusions: The highest diagnostic performance of the molecular method compared to the culture occurred in the detection of E. coli (54 vs 0). The detection in Campylobacter was almost doubled (62 vs 36), however the range and median of the Ct in the samples with positive culture (23.0-38.6 and 27.5) was lower than the samples with negative Campylobacter culture (26.4-43.8 and 35.4), which shows the highest sensitivity of the molecular method. The molecular detection performance of Aeromonas spp. with respect to culture is also very relevant (69 vs 16), although it should be noted that the median Ct of the positive samples is high (42.3) and of uncertain clinical significance.

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Hospital physicians’ perspective on antibiotic prescribing and antimicrobial resistance: a qualitative study

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Background: Antimicrobial resistance (AMR) is a growing threat to global health. To develop targeted antibiotic stewardship interventions, it is crucial to understand health care workers’ and, in particular, prescribing physicians’ behaviour. To our knowledge, there have been few studies exploring physicians’ attitudes and beliefs towards AMR from countries with low antibiotic resistance rates. This qualitative study aimed to investigate physicians’ views on AMR as well as factors affecting their prescribing behaviour.

Materials/methods: After giving their informed consent, 14 physicians with varied clinical experience and affiliation and a high antibiotic prescribing activity were recruited at the Østfold Hospital Trust, a 380-bed secondary care centre in Norway. Aided by an interview guide, semi-structured interviews were held and audio-taped, then transcribed verbatim and analyzed using thematic analysis. Interviewing was continued until no new themes were identified.

Results: Regarding AMR, three main themes emerged; «A knife at the throat», «Fear of losing control» and «Ethical responsibility». AMR was unanimously perceived as a real threat. Although the situation in Norway was felt to be under control, many found the subject of AMR generally to be under-debated. Most respondents feared not only for the safety of future patients but also drew lines to their own personal life. Increased ethical dilemmas were anticipated from a frequent wish to «do everything» for the patient versus an escalating AMR.

Regarding antibiotic prescription practices, three themes emerged: «Cover one’s back», «In the clinical squeeze» and «Supporting tools». There was a willingness among physicians to fight AMR and prescribe restrictively, and infectious disease consultants were used for support. However, barriers to rational prescribing was a «just in case» prescribing attitude, high patient turn-over versus lack of resources, fear of colleague or patient disapproval, and a partly suboptimal microbiology sampling.

Conclusions: The study identified factors of importance to further develop targeted interventions against AMR. In particular, some structural barriers were identified which may prove modifiable. A great foundation for improvement was found in our hospital physicians’ awareness of AMR and a readiness to optimize their prescription habits.

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An intervention bundle to improve compliance with clinical guidelines for \textit{Clostridioides difficile} infection: a quasi-experimental study

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\textbf{Background:} Although \textit{Clostridioides difficile} is a common cause of health care–associated infection, the compliance with clinical practice guidelines is poor.

\textbf{Materials/methods:} The aim of our interventional study was to evaluate the impact of a bundle of measures for patients with a first episode of \textit{C. difficile} infection (CDI): provision of talks and workshops, antimicrobial stewardship and optimization of treatment. Patients diagnosed with a first episode of CDI at our institution from February to December 2017 \{“intervention group”\} were prospectively included and compared with a retrospective cohort of patients diagnosed during a previous 12-month period \{2015\} in which no systematic intervention had been implemented \{“non-intervention group”\}. Specific anti-CDI treatment was considered appropriate if it adhered to current clinical practice guidelines, and was used at optimal doses and duration, without duplication or combination with unnecessary drugs.

\textbf{Results:} Overall, 172 and 231 first episodes of CDI were included in the intervention and non-intervention group, respectively. Anti-CDI treatment was appropriate in more episodes within the intervention group \{75.6\% [130/172] vs. 64.5\% [149/231]; \textit{P}-value=0.023\}. The improvement in compliance with guidelines was mainly at the expense of reducing overuse for non-severe episodes \{8.0\% [10/125] vs. 23.4\% [40/172]; \textit{P}-value<0.001\} and reducing underuse for severe episodes \{27.7\% [10/36] vs. 36.6\% [15/41]; \textit{P}-value = 0.5\}. The intervention led to an increase in the use of oral vancomycin \{50.6\% [87/172] vs. 34.5\% [79/231]; \textit{P}-value<0.001\} and fidaxomicin \{3.5\% [6/172] vs. 0\% [0/231]; \textit{P}-value<0.001\} and a decrease in the use of oral metronidazole \{36\% [62/172] vs. 54.5\% [126/231]; \textit{P}-value=0.0014\} and intravenous metronidazole \{7.6\% [13/172] vs. 23.8\% [55/231]; \textit{P}-value=0.005\}. The number of patients who received systemic antibiotics concomitantly with the anti-CDI treatment was reduced in the intervention group \{19.2\% [33/172] vs. 26.8\% [62/231]; \textit{P}-value=0.08\}. The rate of recurrent CDI episodes was numerically lower in the intervention group, without statistical significance \{12.2\% [21/172] vs. 14.7\% [34/231]; \textit{P}-value=0.56\}, with a lower proportion of patients experiencing more than one relapse \{5 vs. 11 patients; \textit{P}-value=0.55\}.

\textbf{Conclusions:} A bundle of evidence-based measures for patients diagnosed with a first episode of CDI provided a better compliance with clinical practice guidelines and might reduce the rate of relapses.

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Performance and comparison of the rapid Vivalytic STI multiplex assay for the detection of sexually-transmitted infections (STI) in specimens from male patients attending an STI dermatologist practice

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Background: Point of care Multiplex STI assays enable timely results for immediate patient treatment and prevent spreading of sexually transmitted infections. The Vivalytic STI Multiplex assay from Bosch is a fully automated cartridge-based-system that processes specimens from nucleic acid extraction to results analysis. It detects 10 pathogens simultaneously, including Neisseria gonorrhoeae (NG), Mycoplasma genitalium (MG), Ureaplasma urealyticum (UU), Chlamydia trachomatis (CT), Trichomonas vaginalis (TV), Haemophilus ducreyi (HD), Mycoplasma hominis (MH), Treponema pallidum (TP), Herpes simplex virus I (HSV1) and Herpes simplex virus II (HSV2).

The objectives of this non-interventional study are to: 1) Analyse the performance of Vivalytic STI Multiplex assay from specimens collected with dry FL00Swabs®. 2) Detect the yield of different collection sites. 3) Compare Vivalytic STI Multiplex assay to Cepheid Xpert(R) CT/NG assay for CT and NG detection.

Materials/methods: This study contains clinical specimens: urethral (US), anal (AS) and pharyngeal swabs (PS) collected from primarily MSM patients attending an STI dermatologist practice. US collection with FL00Swabs® 551C, AS and PS collection with FL00Swabs® 552C, elution in 1 ml tube of eNAT™ medium code 606C (COPAN) and addition of 300µl of eNAT™ specimens to each cartridge. Duplicate specimens are collected from same patients and tested with both, the Vivalytic STI Multiplex and the Xpert(R) CT/NG according to manufacturer’s methods.

Results: In the 112 clinical specimens, 78 negatives and 34 positives were detected with the Vivalytic assay. A single pathogen was detected in 22 specimens (1CT, 2MH, 9UU, 2MG, 2NG, and 2TP), 2 pathogens in 7 specimens (1UU+NG, 1UU+MH, 2UU+MG, 1TP+HSV2, 1UU+HSV2, and 1CT+UU) 3 pathogens in 5 specimens (1CT+MH+UU, 1MH+UU+TP, 1MH+UU+MG, 1CT+MG+UU, and 1MH+UU+MG). Eighty-seven samples were tested with both, the Vivalytic STI Multiplex and the Xpert(R) CT/NG with generally matching results.

Conclusions: The generated data demonstrates that the Vivalytic assay detected a substantial number of mixed infections. A rapid point-of-care multiplex test may support on-site diagnosis resulting in immediate patient treatment and antibiotic stewardship. Vivalytic STI Multiplex performed well compared to Cepheid Xpert(R) CT/NG assay for CT and NG detection.

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Abstracts 2020

Abstract 8593

What constitutes a healthy faecal microbiome?
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Background: Disruption of gastrointestinal microbiota by antimicrobials leads to dysbiosis, resulting in opportunistic colonisation by potential pathogens such as Clostridium difficile and multi-drug resistant organisms (MDRO). Understanding the relative risk of antibiotic predisposition to such colonisation to facilitate the optimal development of novel therapeutic strategies (including microbiota disruption preventatives and restoratives) is of major importance. We have previously established a successful, clinically reflective in vitro gut model of CDI, which can be used to investigate the relative risk of pathogen colonisation following antimicrobial challenge.

Materials/methods: Two gut models (fed with faecal slurry, n=4 healthy donors) were run simultaneously; one model was supplemented with standard gut model media, the other with mucin and extra bile acids. The microbial populations reached 'steady-state', and were monitored for a further 5 weeks. Models were challenged with both low [week 6] and high dose [week 7] Clostridium difficile spores and carbapenem-resistant Enterobacteriaceae to assess the efficacy of colonisation resistance provided by the microbiota.

Sequential faecal samples from the same healthy donors (n=4) on 5 occasions were compared with gut model samples using bacterial taxonomic analysis and metagenomic profiling. Multiple tools/databases were used to quality control and annotate 16S (Cutadapt, QIIME, SILVA) and shotgun sequencing (DIAMOND, NCBI-nr) data. MEGAN and R were used for annotation and graphics.

Results: Longitudinal sampling demonstrated limited intra-donor bacterial variation, in contrast to inter-donor variation [Figure]. Microbial populations within our gut models were stable throughout; these contributed to colonisation resistance upon exposure of pathogens [i.e. prevention of growth/expansion]. The most dominant families (Ruminococcaceae, Lachnospiraceae and Bacteroidaceae) were similar between the two models. We identified a core set of bacteria at the genera and family level, associated with colonisation resistance upon pathogen exposure. There were 24 detected families common among donors and models and 4-5 different families unique to each set.

Conclusions: Longitudinal microbiome characterisation has enabled identification of a 'core microbiota' common to the different sample types. We found close microbial similarities between gut models and healthy faecal samples, and demonstrated robustness of model microbiota populations over time. This will provide important baseline data when defining microbial alterations during dysbiosis.

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Abstract 8602

**Vertical transmission of the gene blaKPC-3 in clinical isolates of carbapenemase resistant *Klebsiella pneumoniae***

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**Background:** Carbapenem-resistant *Klebsiella pneumoniae* are major threats in healthcare facilities. The propagation of carbapenem resistance determinants can occur through vertical transmission, with the genetic elements being transmitted during host cell division, or by horizontal transmission, with the same genetic element being transferred among distinct bacterial hosts. This work aimed to track carbapenem resistance transmission by *K. pneumoniae* isolates obtained from hospitalized patients.

**Materials/methods:** A set of 40 clinical isolates of *K. pneumoniae* isolates recovered over a period of two years were screened for carbapenem resistance. This procedure resulted in the identification of five isolates from two patients, which were characterized based on conjugation assays, resistance phenotype and genotype, capacity to form biofilm, whole genome sequencing, and plasmid characterization by pulsed field gel electrophoresis and optical DNA mapping.

**Results:** The five isolates harboured the blaKPC-3 gene, were multidrug-resistant and belonged to multilocus sequence type ST147. The blaKPC-3 gene was integrated in conjugative plasmids with 140 kbp, in three isolates, or 55 kbp, in two isolates, belonging to the replicon types FIA/FIIk or N/FIIk, respectively. Although the five isolates belonged to ST147, they could be divided into two groups harbouring a distinct blaKPC-3 plasmid suggesting the blaKPC-3 gene was being spread via bacterial transmission. All isolates harboured the virulence determinants, type 3 fimbriae encoding *mrk* operon (*mrk*ABCDFHIJ), which can be involved in mucous adherence, tissue colonization and biofilm formation, and the *wzi* gene involved in capsule attachment to the host cell surface. The *mrk* operon could be responsible for the classification of the isolates as weak to moderate biofilm producers. In addition, only isolates with 55 kbp plasmid harboured the virulence genes: *fyu*A, a gene involved in ferric *yersiniabactin* uptake, *irp2* and the cluster *gbr*AEPQSTUX both involved in production of *yersiniabactin*, which is essential for disease establishment.

**Conclusions:** Although all isolates harboured the same gene variant and belonged to the same MLST group, carbapenem resistance in this healthcare facility was transmitted vertically and not through horizontal gene transfer.

Determining the mode of transmission of antibiotic resistance in healthcare facilities is essential to promote its control and using polyphasic approaches may be essential.

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**Abstract 8603**

**Bloodstream infections caused by Enterococcus spp.: incidence, clinical features, and outcomes**

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**Background:** Enterococcus faecalis and faecium have become increasingly important pathogens, especially in Healthcare-associated infections. We aimed to evaluate the clinical features, outcomes and the risk factors for mortality in Enterococcal Bloodstream infections (E-BSI).

**Materials/methods:** All subjects with a positive blood culture for *E. faecalis* or *E. faecium* between 2015-2016 were enrolled. E-BSI were defined as community acquired (CA-BSI), healthcare-associated (HCA-BSI) or hospital acquired (HA-BSI). Antibiotic therapy for Enterococcus spp. was defined as appropriate if the following criteria were met: first administration of an active antibiotic, second the administration of combination therapy (at least two drugs, with the exception of Daptomycin), third ≥15 days of treatment. The 21”and 28” day mortality was investigated.

**Results:** We reported 201 episodes of E-BSI. Infection rate was 2.4/1000 days of hospital admission. E. faecalis represented 52.1% of E-BSI: *E. faecalis* (and *E. faecium*) had resulted resistant to ampicillin in 3.1% (*E. faecium*, 22.2%), to gentamicin in 16.2% (47.3%) and to vancomycin in 2.2% (23.3%). Most were HA-BSI (78,1%). Patients' characteristics were reported in Table 1. Only 52 patients (25.8%) received an appropriate therapy. No differences with statistical significance, between the appropriate vs not-appropriate therapy group, except for infectious endocarditis which was more frequent in the first group (p= 0.003); although only 59% of patients underwent echocardiography. At the univariate analysis mortality is associated with resistance to Vancomycin (p=0.042), Sepsis (p=0.003) and Septic shock (p=0.007), confirmed by the multivariate analysis. During the hospitalization death rate was 26%. Median survival time was 65 days from blood positivity. 75.3% survived for 21 days and the survivability curve at day 28th of follow up, showed no difference between appropriate vs not-appropriate therapy.

**Conclusions:** Enterococcus confirms to be an HA and HCA infection. The advanced age, prevalent comorbidities, high invasiveness and medicalization suggest that the infection occurs in frail patients. A quarter of subjects received an appropriate therapy: reasons were premature stopping, monotherapies, or inactive drug on Enterococcus spp. Nevertheless, the antibiotic therapy was not associated with lower mortality, probably because of this frail population it tended for a poor outcome even though an appropriate treatment. Furthermore, E-BSI intracardiac sources were not ever well deepened.

<table>
<thead>
<tr>
<th></th>
<th>Appropriate Treatment (N=149)</th>
<th>Not Appropriate Treatment (N=52)</th>
<th>Total (N=201)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (Female)</td>
<td>89 (59.73%)</td>
<td>35 (67.31%)</td>
<td>124 (61.69%)</td>
<td>0.333</td>
</tr>
<tr>
<td>Age – average (sd)</td>
<td>69.95 (12.65)</td>
<td>68.65 (13.90)</td>
<td>68.02 (12.96)</td>
<td>0.537</td>
</tr>
<tr>
<td>Comorbidities (at least 1)</td>
<td>171 (99.30%)</td>
<td>57 (96.61%)</td>
<td>198 (98.51%)</td>
<td>0.153</td>
</tr>
<tr>
<td>Comorbidities (2 most frequent)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>45 (30.2)</td>
<td>22 (42.31)</td>
<td>67 (33.33%)</td>
<td>0.111</td>
</tr>
<tr>
<td>COPD</td>
<td>38 (25.5)</td>
<td>13 (25)</td>
<td>51 (25.37)</td>
<td>0.943</td>
</tr>
<tr>
<td>Charlson index – median (interquartile-range)</td>
<td>5 (4-5)</td>
<td>6 (5-6)</td>
<td>5 (4-6)</td>
<td>0.111</td>
</tr>
</tbody>
</table>

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Abstract 8607

Weekly surveillance of bacterial, viral and parasitic infections involving private and public medical analysis laboratories through 317833 diagnostic tests in the Provence-Alpes-Côte-d’Azur region, 2014-2019

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Background: Infection surveillance is essential to optimize their clinical and diagnostic management and to better understand their epidemiology. A network (PACASurvE) for weekly surveillance of infections and analyzes of laboratories of medical biology (LBM) was created in 2013 in Provence-Alpes-Côte-d’Azur (PACA). In particular, it analyzes data from CERBA, a specialized LBM. We present here the analysis of the data of this laboratory for the period 2014-2019.

Materials/methods: The study covers the period 11/2014-07/2019 (57 months). The weekly data consisting in the numbers of tests and positive diagnoses (pos.) were collected from the CERBA LBM, which carries out specialized medical biology analyzes transmitted by private and public LBMs of PACA region. The data was analyzed using Excel and R softwares.

Results: 110 different diagnostic tests for bacterial [n= 50], viral [58] or parasitic [2] infections were monitored, corresponding to respiratory infections [n= 39 tests] or neurological infections [24], gastrointestinal infections [9], hepatitis [7], tropical [6] or sexually transmitted [14] infections, or rash [7]. Of the 317833 tests performed, 29,362 (9.2%) were found to be pos. (on average: 1301 tests and 120 positive tests involving 196,888 patients [mean age= 42±21 years, 64% female]. A diagnosis was found for 22694 patients from 386 LBM located majoritarily in Bouches-du-Rhône (9,899 [44%]) and Var (23%). The most frequent tests targeted Chlamydia trachomatis [n = 3946], HPV [1647], hepatitis B [HBsAg] [1243] and C [1016], anti-HEV IgM [917], detection of Clostridium difficile [533], or Bordetella pertussis [475] by PCR. Changes were observed, for example between 2016 and 2017 and between 2017 and 2018 for the number of anti-HEV IgM tested (+17% and +18%, respectively) and of pos. (+7% and +27%, respectively), and between 2015 and 2017 for the proportion of C. difficile tests found pos. (+212%).

Conclusions: Collection within the PACASurvE network of tests and diagnoses of bacterial, viral and parasitic infections constitutes a unique database for monitoring and studying the epidemiology of infections at the regional level.

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Abstract 8608

Rise in Campylobacter jejuni antimicrobial resistance in Split-Dalmatia County, Croatia: 2013 - 2018

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Abstract third-party references: University Clinical Hospital Centre Split, EFWISG, Public Health Institute of Split and Dalmatia County, University of Split School of Medicine

Background: Tracking changes in antibiotic resistance among human Campylobacter jejuni isolates through ongoing surveillance data could provide valuable clinical and public health information.

Here, we aimed to compare the resistance rates of C. jejuni to antibiotics in the largest Croatian county of Split - Dalmatia (SDC) between 2013 and 2018.

Materials/methods: In a population-based laboratory surveillance program for campylobacteriosis in SDC from the 1st January to the 31st December 2018, C. jejuni were collected from stool samples of all the patients hospitalized with gastroenteritis (n = 55) and symptomatic outpatients (n = 289). Antimicrobial susceptibility testing of all 331 C. jejuni isolates was done by disc diffusion method according to EUCAST guidelines. Resistance rates detected in SDC in 2018 were compared with the results obtained in SDC in 2013.

Results: Approximately 79% (260) of the C. jejuni isolates were resistant to ciprofloxacin (CipR), whereas 36% (119) of isolates were resistant to tetracycline (TcR); of the latter, 117 C. jejuni isolates were also co-resistant to ciprofloxacin (TcR/CipR) - in a total 35%. Although two MDR resistant C. jejuni were also detected, resistance to erythromycin and gentamicin was infrequent (≤ 0.6%). However, the prevalence of ciprofloxacin resistant C. jejuni (p < 0,001) and TcR/CipR co-resistant C. jejuni (p < 0,01) increased sharply after 2013.

Conclusions: A high prevalence of CipR resistant and TcR/CipR co-resistant C. jejuni strains were detected in patients in SDC, Croatia, in 2018, as well as significant increases of resistance and co-resistance during the five-year period 2013 - 2018. These results suggest that therapeutic options in campylobacteriosis are very limited and warrant further studies of campylobacter resistance mechanisms and epidemiology.

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Abstract 8610

High-throughput bacterial phenotyping to characterise antimicrobial resistance mechanisms

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Background: Current approaches to studying antimicrobial resistance (AMR) are constrained by limitations in traditional bacterial phenotyping methods. Recent advances in high-content imaging (HCI) enable detailed morphological studies of individual bacteria that cannot be captured using existing approaches. Using the Opera Phenix (PerkinElmer) we have developed a HCI platform to study thousands of bacteria growing under specific conditions in 96-well plates. We illustrate the potential of this approach using Klebsiella pneumoniae, a major reservoir of AMR, as an exemplar.

Materials/methods: Bacterial cultures were incubated for 2 hours before staining with fluorescent dyes and imaging using the Opera Phenix. Image analysis was performed in Harmony. Over 60 morphological features were measured per bacterium. This platform was used to study how antimicrobials affect the morphology of Klebsiella pneumoniae, Escherichia coli, Salmonella Typhimurium and Staphylococcus aureus. A collection of 150 Klebsiella pneumoniae isolates, representing species diversity, was assessed in the presence of ciprofloxacin at the minimum inhibitory concentration of each isolate. RNAseq was conducted on five K. pneumoniae isolates in the presence of antimicrobials in parallel with HCI.

Results: Distinct, quantifiable phenotypic changes were observed in the presence of each antimicrobial class (Figure 1). These changes were similar among the Gram-negative isolates. Comparable phenotypic changes were observed across the K. pneumoniae species in response to ciprofloxacin. Each antimicrobial class induced distinct patterns of differential gene expression. Despite extensive morphological changes, there was minimal effect on transcription in response to cefuroxime, meropenem and colistin. Ciprofloxacin induced extensive changes, up-regulating genes that likely contribute to AMR: efflux pumps; plasmid-mediated resistance (qnr, bla, cat); polymerases that induce mutagenesis (umuC/D); and genes associated with plasmid replication.

Conclusions: HCI is a powerful tool to study phenotypic changes at the level of individual bacteria. This enables rapid assessment of large microbial collections in standardised conditions and has a range of potential applications, including accurate phenotyping of resistance and evaluation of novel agents. We have identified multiple pathways that are upregulated under antimicrobial pressure which may promote AMR. Further work is required to determine whether these morphological and transcriptomic changes are reproducible across the diversity of K. pneumoniae and other species.

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Abstract 8616

**Comparison of six simple methods for ribosomal DNA extraction directly from nail sample suspected to onychomycosis for PCR-based assay**

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**Background:** Since extraction DNA directly from the nail sample suspected to onychomycosis reduces diagnosis time and is a primary and crucial step which has a principal effect on PCR results, in the current study six simple methods for extraction DNA directly from nail were applied and compared by evaluating the presence, appearance and intensity of PCR products visualized on agarose gels and amplified from DNA extracted by each of the methods.

**Materials/methods:** After preparing pooled sample from nails with onychomycosis, total DNA was extracted using six different methods, including mechanical grinding, boiling, glass bead, conical bullet, potassium hydroxide and the use of a commercial kit. In order to DNA purification except for the commercial kit method, a conventional phenol chloroform DNA purification protocol was used. To evaluate the efficacy of each method, the internal transcribed spacer (ITS) region gene was chosen as representative markers for ribosomal DNA.

**Results:** Among the six DNA extraction methods, the boiling method was the most cost effective, followed by the glass bead and conical bullet. All three methods produced high intensity bands on agarose gels and were characterized by no or minimal smear formation; however, boiling was less expensive.

**Conclusions:** Boiling was the most suitable methods regarding its amplicon quality, easiness, quickness and cost effectiveness.

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IgM antibody to pneumococcal serotype 3 polysaccharide activates the classical pathway

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Abstract third-party references: funded in part by an investigator initiated grant from Pfizer, inc.

**Background:** Serotype 3 Streptococcus pneumoniae (SP3) is a virulent pathogen across the age spectrum. In US, SP3 now accounts for ~65% of vaccine type invasive pneumococcal disease (IPD) in individuals 65 years of age and older. Characteristically, SP3 uses multiple strategies to evade host defense including displaying a mucoid capsule that enable resistance to phagocytosis and binding Factor H to limit surface C3 binding.

**Materials/methods:** We evaluated complement deposition to the surface of SP3 by flow cytometry. Strains were isolated from Massachusetts' children from nasopharynx, blood, and lung. We compared surface binding of normal human complement in the absence and presence of anti-type 3 polysaccharide immune rabbit sera (provided by Dr. Rick Malley, Boston Childrens Hospital) and anti-type 3 polysaccharide IgM monoclonal antibody (provided by Dr. Moon Nahm, WHO Pneumococcal Reference Lab, UAB). Once flow analysis of our 80 isolates is completed (40 invasive and 40 nasopharyngeal colonizers) we will compare complement binding on serotype 3 strains grouped by site of disease versus colonization and by phenotypic appearance (mucoid vs. non-mucoid).

**Results:** Preliminary results demonstrate that IgM monoclonal antibody activates complement binding through the classical pathway as demonstrated by an increase in C4 deposition on the surface of serotype 3 strains for all 20 strains tested to date. Deposition of C4 occurs in a dose related manner.

**Conclusions:** Our data suggest IgM to capsular polysaccharide may play an important role in host defense against serotype 3. Epidemiologic data suggests the introduction of PCV13 into NIP schedule has had limited, if any, impact on colonization and invasive disease due to serotype 3 pneumococci. Understanding the role of IgM and IgG anti-capsular antibody for serotype 3 is necessary to develop new strategies for prevention of SP3 disease.

**Fig 1.** IgM binding to SP3.
Red: in presence of 0.1% IgM
Blue: in presence of 3% IgM;
Orange: in presence of 5% IgM

**Fig 2.** C4 binding to same SP3 in figure 1, detected with anti C4 PE.
Red: in presence of 0.1% IgM
Blue: in presence of 3% IgM;
Orange: in presence of 5% IgM

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Characterisation of the unique contributions of bedaquiline and rifabutin against actively-growing and nutrient-starved populations of *Mycobacterium abscessus*

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**Background:** Bedaquiline and rifabutin have each shown promise for use in the treatment of *Mycobacterium abscessus* lung disease. Previous studies in our lab suggested that bedaquiline and rifabutin exert *in vitro* bactericidal activity against nutrient-starved and actively-growing populations of *M. abscessus*, respectively, and we hypothesized that combining these drugs would result in enhanced bactericidal activity across culture conditions. The objective of this study was to evaluate the specific activity of bedaquiline and rifabutin alone and in combination against actively-growing, nutrient-starved, and intracellular *M. abscessus* populations.

**Materials/methods:** Time-activity curves of bedaquiline and rifabutin against *M. abscessus* subsp.* abscessus* strain ATCC 19977 were determined in the following culture conditions: actively-growing [cation-adjusted Mueller-Hinton or Middlebrook 7H9 broth]; nutrient-starved in phosphate-buffered saline for 7 or 14 days; and intracellular infection in THP-1 cells. All activity was measured by determining bacterial colony forming units before and after drug exposures. Minimum bactericidal activity (MBC) was defined as the lowest concentration that killed 99% of the bacteria.

**Results:** For bedaquiline, limited to no bactericidal activity was observed against actively growing *M. abscessus*, while potent killing was observed against nutrient-starved bacteria. The addition of rifabutin at 1, 2, or 4 µg/mL did not increase bedaquiline killing against actively growing cultures but did increase the killing against nutrient-starved bacteria by 4-, 16, and 32-fold, respectively. For rifabutin, concentration-dependent bactericidal activity was observed against actively-growing bacteria, but activity decreased with increased time of nutrient starvation such that the MBC was ≥64 µg/mL after 14 days of nutrient starvation. The addition of bedaquiline did not impact rifabutin activity against actively-growing bacteria, but did increase the killing against nutrient-starved *M. abscessus*; the MBC against bacteria nutrient-starved for 14 days decreased to 1 and 0.25 µg/mL in the presence of 0.03 or 0.125 µg/mL bedaquiline, respectively. Bedaquiline added bactericidal activity to rifabutin against intracellular *M. abscessus* only after the fifth day of drug exposure.

**Conclusions:** Exposure of nutrient-starved bacteria to both drugs significantly decreased the MBC of each drug, suggesting synergistic killing against non-replicating bacteria. These data support the *in vivo* evaluation of bedaquiline-rifabutin combinations against *M. abscessus* infection.

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Abstract 8620

**Clostridioides difficile infection incidence and consumption of selected antibiotics: EU/EEA countries 2008—2018**

Pete Kinross*1, Liselotte Diaz Högberg1, Sarah Tschudin-Sutter2, Klaus Weist3, Carl Suetens4

1European Centre for Disease Prevention and Control, [ECDC], Solna, Sweden, 2University Hospital Basel, University Basel, Basel, Switzerland

Abstract third-party references: on behalf of ECDC HAI-Net C. difficile infection and ESAC-Net participants

**Background:** In the 2011-2012 and 2016-2017 European Centre for Disease Prevention and Control (ECDC) point prevalence surveys in European Union/European Economic Area (EU/EEA) acute care hospitals (ACHs), the proportion of healthcare-associated infections that were *Clostridioides* (*Clostridium*) difficile infection (CDI) was 3.6% and 4.9%, respectively. In the 2018 ESCMID guidance to prevent CDI in ACHs, the recommendation with the strongest quality of evidence is ‘restriction of antibiotic agents/classes’. This study describes current CDI incidence in EU/EEA ACHs and EU/EEA trends in consumption of selected antibiotics relevant to CDI.

**Materials/methods:** Since January 2016, ECDC coordinates CDI incidence surveillance in ACHs in EU/EEA countries. The ECDC CDI protocol minimum data requirement includes collection, by ACH staff, of the number of hospitalised patients who match the current ESCMID CDI case definition and aggregate denominators.

National-level antimicrobial consumption data in EU/EEA countries are available from the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) as WHO Defined Daily Doses (DDDs)/1,000 inhabitants/day. Joinpoint regression (v4.7.0.0) assessed annual changes in EU/EEA-level population-weighted means.

**Results:** As of 20 November 2019, 23 EU/EEA countries had reported CDI data from 2016-2018, with >47,000 CDI cases for >150 million patient-days from 1,806 ACHs. In 2016-2018, the mean hospital-level incidence was higher in tertiary hospitals [3.87 cases/10,000 patient-days] than in secondary or primary hospitals [3.49 and 2.41 cases/10,000 patient-days, respectively]. In 2016-2017, the crude annual national-level CDI incidence ranged from 2.4 to 7.5 cases/10,000 patient-days.

Twenty-eight EU/EEA countries reported antimicrobial consumption data for 2008—2018. Annual consumption and multi-year trends differed between countries for both total and hospital sector consumption of fluoroquinolones [Anatomical Therapeutic Chemical code J01MA], clindamycin [J01FF01], third-generation cephalosporins [J01DD] and amoxicillin-clavulanic acid [J01CR02]. For example, whilst during 2008-2018, EU/EEA-level hospital sector fluoroquinolone consumption decreased by 3.6% (95%CI: 1.6%-5.5%), in 2018, the range of national-level consumption rates was 0.04-0.36 DDDs/1,000 inhabitants/day.

**Conclusions:** CDI is common in all types of ACHs in EU/EEA countries. The range of national consumption of the selected antibiotics suggests that further reductions are achievable. All ACHs should consider integrated surveillance of CDI and consumption of key antimicrobials, to enable locally-targeted CDI prevention.

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Implementation of model-based therapeutic drug monitoring of vancomycin

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Abstract 8622

Background: Vancomycin therapeutic drug monitoring (TDM) based on the area-under the concentration-time curve (AUC) and pharmacokinetic (PK) modelling may improve attainment of target exposure and safety (Neely et al. Antimicrob. Agents Chemother 2018;62). The objective of this study was to report our experience with model-based TDM of vancomycin.

Materials/methods: This was a retrospective analysis of data collected in our center from 2015 to 2019 in patients who underwent routine vancomycin TDM on at least two occasions. Bayesian analysis was performed using BestDose™ software to estimate pharmacokinetic parameters and AUC based on measured concentrations in each patient. We compared the proportion of patients achieving concentration and AUC targets before and after TDM by using the Fisher exact test for paired data.

Results: Data from 82 patients (35 women and 47 men) were available. Initial values (mean ± SD) of age, body weight and creatinine clearance were as follows: 79 ± 13 years, 67 ± 16 kg and 61 ml/min ± 29 ml/min. Vancomycin was administered by intermittent infusion in 64 patients and by continuous IV in 18 patients. The median (min-max) number of TDM occasions was 3 (2-17). Vancomycin dosage was modified in 76% and 63% of patients on the first and second TDM occasion, respectively. Vancomycin model-based TDM results are shown in Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Before TDM (N=82)</th>
<th>After first TDM (N=82)</th>
<th>After second TDM (N=52)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose mg/24h</td>
<td>1800 (400-5500)</td>
<td>1325 (0-4500)</td>
<td>1225 (0-4500)</td>
</tr>
<tr>
<td>Css/Cmin &lt; 15 mg/L</td>
<td>34.2%</td>
<td>11.0%**</td>
<td>13.4%**</td>
</tr>
<tr>
<td>15 ≤ Css/Cmin ≤ 20 mg/L</td>
<td>14.6%</td>
<td>28.0%</td>
<td>46.2%**</td>
</tr>
<tr>
<td>Css/Cmin &gt; 20 mg/L</td>
<td>51.2%</td>
<td>61.0%</td>
<td>40.4%</td>
</tr>
<tr>
<td>AUC24 &lt; 400 mg.h/L</td>
<td>25.6%</td>
<td>12.2%</td>
<td>9.6%</td>
</tr>
<tr>
<td>400 &lt; AUC24 &lt; 700mg.h/L</td>
<td>50.0%</td>
<td>71.9%**</td>
<td>77.0%**</td>
</tr>
<tr>
<td>AUC24 &gt; 700mg.h/L</td>
<td>24.4%</td>
<td>15.8%</td>
<td>13.4%</td>
</tr>
</tbody>
</table>

Comparison versus first TDM *p<0.05; **p<0.01

Conclusions: AUC and model-based TDM of vancomycin is feasible in routine practice. While a controlled study is necessary to confirm our findings, they show that this intervention was associated with frequent dose adjustment, a lower proportion of underexposure and a higher proportion of therapeutic exposure to vancomycin over therapy.

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Evaluation of the performance of a commercial rapid diagnostic test for cystic echinococcosis in a clinical setting

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Background: Cystic echinococcosis (CE) is a cosmopolitan zoonosis caused by the tapeworm Echinococcus granulosus. It causes the formation of cysts prevalently in the abdomen of humans. Abdominal CE is usually diagnosed by ultrasound (US) with serology playing a complementary role. In recent years, Rapid Diagnostic Tests (RDTs) have become part of the routine serological diagnosis in many laboratories. We present our retrospective evaluation of the performance of a commercially available RDT.

Materials/methods: We retrospectively enrolled samples from patients seen at a single tertiary care center for CE. Patients were referred as having a suspect CE lesion or were known CE patients seen from September 2017 to July 2019. All patients were tested with two tests: VIRAPID HYDATIDOSIS RDT (Vircell, Spain) and ELISA RIDASCREEN ECHINOCOCCUS IgG (R-Biopharm, Germany). We collected data relating to the final diagnosis (CE vs non-CE) and CE stage according to the WHO-Informal Working Group classification. Sensitivity and specificity were then calculated for all tests. Differences in test performances were assessed using the Wilcoxon Rank test.

Results: We included 246 samples in our evaluation. Of these, 174 (70.7%) belonged to patients with CE cysts or to residual lesions from surgical treatment. Fifty-one patients (29.3%) had active or transitional cysts (CE1-CE3). Seventy-two sera (29.3%) came from patients who had non-parasitic lesions. The overall sensitivity and specificity were 47% and 89.6% for the ELISA, 65.2% and 81.8% for the RDT. If only active lesions were considered, sensitivity increased to 84% and 78% respectively. The RDT proved more sensitive in detecting active cysts (p=0.017). Combining the two tests gave a sensitivity of 45% and 48% (including or excluding active cases).

Conclusions: Our evaluation of the diagnostic performance of the tests showed lower sensitivity and specificity values compared to findings from other research groups. This could be explained by differences in cohort composition, as well as by the inclusion of sera specimens from all anatomic locations, something which is known to influence serological results. The overall performance of the tests confirms that serology still plays a complementary role in the diagnosis of CE.

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Abstract 8627

A rapid method for direct detection of intact OXA-48-like carbapenemases using liquid chromatography and high-resolution Orbitrap mass spectrometry

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Background: Carbapenem resistance in Gram negative bacteria is a continuously growing global threat. Although significant efforts have been made to mitigate the spread of carbapenemase-producing organisms (CPoS), there is a dire need to maximize detection of these bacteria. Among other carbapenemases produced in Enterobacterales, the OXA-48-like family of carbapenemases present challenges for some routine susceptibility testing due to low-level carbapenemase activity. In an effort to increase detection fidelity, we have shifted from phenotypic and molecular techniques to develop a method that focuses specifically on the intact proteins. Herein we present a method combining liquid chromatography (LC) and mass spectrometry (MS) for direct and rapid detection of intact OXA-48-like carbapenemases.

Materials/methods: Clinical isolates of Enterobacteriales have been evaluated for the presence of OXA-48-like carbapenemases using combinations of whole genome sequencing (WGS) or polymerase chain reaction (PCR), phenotypic susceptibility testing, and a novel mass spectrometric assay. In an automated sample preparation, bacterial cells are mechanically lysed, centrifuged, and protein-containing supernatant is transferred to a solid phase extraction (SPE) column. Proteins are eluted from the column, ionized via electrospray ionization (ESI), and introduced to the MS. Clinically-relevant variants within the OXA-48-like family are evaluated. Carbapenemase-non-producing isolates are evaluated for comparison.

Results: Tandem mass spectrometry (MS/MS) is used to dissociate intact OXA-48-like carbapenemases, which allows protein-specific fragment ions to be identified for the utmost confidence in identification. Several species of Enterobacteriales have been evaluated. Combining LC with MS/MS has been found to have a dramatic impact on overall sensitivity. To date, over 20 OXA-48-like-producing isolates, most of which having low-MICs to ertapenem, have had carbapenemases detected, including OXA-48, OXA-162, OXA-181, OXA-232 and OXA-244, while carbapenemase-non-producing isolates have all produced negative results.

Conclusions: The use of LC-MS is an effective method for identifying the intact mass of carbapenemases; however, with the added implementation of MS/MS fragmentation, we are able to enhance our sensitivity with extremely high confidence for identification. As phenotypic evaluations of this carbapenemase go so easily undetected, it is critical to establish a sensitive method of direct detection of OXA-48-like carbapenemases.

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Abstract 8628

The impact of Zika virus epidemic on maternal mental health in Brazil
Tamila Araujo1, Tania De Araujo1, Darci Neves2, Silvia Ferrite2, Leticia Marques2, Iracema Lua1, Guilherme Werneck*3

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Abstract third-party references: Supported by CNPq and FAPESB

Background: The Zika virus epidemic in Brazil started in 2015, with one of the main consequences being the Zika virus congenital syndrome, which not only compromises the child’s development but may also have an impact on family life, especially maternal mental health. This study aimed to estimate the prevalence of depression among mothers of babies born during the Zika virus epidemic in Salvador, Bahia, Brazil.

Materials/methods: A cross-sectional study with baseline data from the cohort study “Effects of Zika virus-associated congenital neurological manifestations on child development: a prospective cohort study in the context of Primary Care in Salvador-BA-Brazil.” The sample consisted of women living in Salvador whose children were born during the Zika virus epidemic in Brazil, 2015-2016 (N=264: 154 mothers of children with the syndrome and 110 mothers of typical children). Depression was assessed by the PHQ-9 scale.

Results: Mothers of children with congenital Zika virus syndrome were predominantly young (<28 years, 53.9%), black race (90.7%), with partner (59.7%), high school (48.7%), income lower than one minimum wage (55.2%), and without paid work (83.8%). Among mothers of children not affected, predominated those older than 28 years (51.8%), black race (90.6%), with a partner (61.8%), high school (57.3%), and income higher than the minimum wage (52.7%). The proportion of mothers without paid activity was lower than among affected mothers but still high (70.9%). The depression prevalence among mothers of babies with the syndrome was 39.0% versus 25.0% among mothers of babies without the syndrome [53% higher in affected mothers, prevalence ratio: 1.53; 95%CI:1.05-2.23].

Conclusions: The study revealed more vulnerable characteristics for the mothers of children with the Zika syndrome: they were younger and with lower income. They also had a higher percentage of exclusion from the labor market [13% higher]. The depression prevalence was high in both groups but increased substantially among mothers of children with the syndrome. The study highlights the need to broaden the focus of epidemic attention to groups whose impacts of the epidemic are less visible, such as the mental health of affected mothers. Strategies related to health promotion in this group are needed.

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**Lactobacillus iners in vaginal microbial community**

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**Background:** The role of *Lactobacillus iners* in maintaining a healthy vagina environment is unclear weather it is detected in normal conditions, as well as in vaginal dysbiosis and bacterial vaginosis (BV).

**Materials/methods:** The vaginal swabs of 93 females in reproductive age were examined by classical microbiological protocols and by molecular methods of 16S rRNA DNA sequence analysis for identification of different *Lactobacillus* spp., as well as *Gardnerella vaginalis*, *Ureaplasma urealiticum* and *Mycoplasma hominis*. Three groups were analysed according the Nugent score: negative for BV (0-3) (n=51); intermediate for BV (4-6) (n=23) and indicative for BV (7-10) (n=19).

**Results:** A total of 22 different lactobacilli were identified, predominantly *Lactobacillus iners* (as a single strain in 39 of total 93 females and once in combination with other lactobacilli), *L. crispatus* and *L. casei* (in combination together and with other lactobacilli, in 26, 33 and 30 cases, respectively). No statistically significant association was observed between *L. iners* and BV as well as intermediate BV (Pearson Chi-square: 2.500, p = 0.11 3846). *L. iners* was the most frequent in subjects with vaginal pH>4.5 as a single strain, as well as together with other bacteria (*G. vaginalis*, *U. urealiticum*, *M. hominis*). *L. crispatus*, *L. casei* and other 19 lactobacilli were almost always in combination of 2, 3, 4, 5 and 7 lactobacilli and less frequent in vaginal pH>4.5 and other bacteria.

**Lactobacillus iners** in females with other detected or isolated bacteria

<table>
<thead>
<tr>
<th>Other bacteria / other results</th>
<th>Females (No)</th>
<th>No L. iners (%)</th>
<th>No L. crispatus / L. casei (%)</th>
<th>Other 19 lactobacilli</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>G. vaginalis</em></td>
<td>38</td>
<td>18 (42.4)</td>
<td>7 / 6 (18.4 / 15.8)</td>
<td>24 (63.2)</td>
</tr>
<tr>
<td><em>U. urealiticum</em></td>
<td>40</td>
<td>19 (47.5)</td>
<td>13 / 13 (32.5 / 32.5)</td>
<td>23 (57.5)</td>
</tr>
<tr>
<td><em>M. hominis</em></td>
<td>14</td>
<td>7 (50.0)</td>
<td>1 / 1 (71 / 71)</td>
<td>4 (28.6)</td>
</tr>
<tr>
<td>vaginal pH&gt;4.5</td>
<td>36</td>
<td>17 (42.2)</td>
<td>7 / 6 (19.4 / 16.7)</td>
<td>18 (50.0)</td>
</tr>
</tbody>
</table>

**Conclusions:** Further studies of the pathogenicity factors, lactic acids and H₂O₂ production are needed to explain the role of *L. iners* as the most frequently detected lactobacillus in healthy and disturbed vaginal niche as well as its interaction with other bacteria.

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Abstract 8630

**Evaluation of an immunochromatographic assay for rapid identification of PBP2a-positive *Staphylococcus aureus***

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**Background:** Methicillin-resistant *Staphylococcus aureus* (MRSA) is a significant pathogen causing both health-care-associated and community-acquired infection. Rapid and accurate detection of this pathogen is crucial for the use of appropriate antimicrobial therapy and the control of nosocomial spread. The molecular tests have been proposed, providing results in less than two hours; however, cost, equipment requirements and the need for specific technical expertise and training have limited widespread routine use.

**Objective:** Evaluate the PBP2a Culture Colony Test™ (Alere®) a rapid immunochromatographic qualitative assay for the detection of penicillin binding protein 2a (PBP2a) direct from *S. aureus* culture.

**Materials/methods:** A total of 107 *S. aureus* strains were assayed for methicillin resistance: Vitek2® (bioMérieux), CHROMagar® MRSA II (BD Becton Dickinson), disk diffusion in agar for cefoxitin 30 μg and immunochromatography PBP2a SA Culture Colony Test (AlereTM). The results of conventional tests were compared with the “gold standard” real time PCR SmartCycler (Cepheid®) with RealCycler SAMAPV kit.

**Results:** A total of 107 *S. aureus* strains were isolated from clinical samples: blood 72,82% (78), abscess 3,73% (4), biopsy 0,93% (1), respiratory 3,73% (4), wound exudates 5,60% (6) and nasal swab 1 3,08% (1 4). 57 (53,27%) were MRSA and 50 (46,73%) MSSA. Panton-Valentine leukocidin (PVL) gene is detected in 2,80% of MRSA strains (2 abscess, 1 biopsy). The concordance between the results obtained using immunochromatographic tests and using molecular techniques was 100%, with a Cohen’s kappa coefficient of 1 (p<0.001).

<table>
<thead>
<tr>
<th>Test</th>
<th>Specificity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxacillin agar dilution</td>
<td>57/57</td>
<td>50/50</td>
</tr>
<tr>
<td></td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Vitek2</td>
<td>57/57</td>
<td>50/50</td>
</tr>
<tr>
<td></td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>CHROMagar MRSA II</td>
<td>57/57</td>
<td>48/50</td>
</tr>
<tr>
<td></td>
<td>100%</td>
<td>96%</td>
</tr>
<tr>
<td>ICPBP2a</td>
<td>56/57</td>
<td>50/50</td>
</tr>
<tr>
<td></td>
<td>98,25%</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Conclusions:** An assay for quickly differentiating between MRSA and MSSA was highly sensitive, highly specific, and inexpensive in actual hospital use and led to rapid prescription of appropriate antistaphylococcal therapy 24–48 hours after culture specimens were collected.

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**Abstract 8631**

**Antimicrobial resistance of Escherichia coli strains isolated from frugivorous (Eidolon hervum) and insectivorous (Nycteris hispidia) bats in Southeast Nigeria, with detection of CTX-M-15-producing isolates**

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**Background:** Antimicrobial resistance (AMR) is one of the greatest global public health challenges, and extended-spectrum beta-lactamases (ESBL) is one of the most relevant mechanisms. The role of food-producing and companion animals as reservoirs of AMR is well documented. However, the role of wildlife in the ecology of antimicrobial resistant and pathogenic bacteria is poorly understood. Analysis of the antimicrobial resistance genes (ARGs) together with molecular typing of *E. coli* strains from bats will contribute with useful data to predict potential risks associated with *E. coli* strains in these animals. This study was conducted to determine the antimicrobial resistance pheno/genotypes and to carry out the molecular typing of *E. coli* isolates from frugivorous (*Eidolon hervum*) and insectivorous (*Nycteris hispidia*) bats in Nigeria.

**Materials/methods:** Thirty-five lactose fermenting bacterial isolates obtained from liver (n=16), intestine (n=11) and spleen (n=8) of frugivorous (n=15) and insectivorous (n=20) apparently health bats in two locations in Southeast Nigeria were identified as *E. coli* isolates by Maldi-TOF. Susceptibility of the *E. coli* isolates to antimicrobial agents was tested by the disk diffusion method (EUCAST). PCR assays were performed to detect the presence of ARGs and phylogenetic-groups. Multiplex PCR/sequencing as well as multilocus sequence typing were performed on cefotaxime (CTX)-resistant strains to identify the ESBL gene type and sequence type (ST), respectively.

**Results:** Resistance to at least one of the antimicrobial agents tested was observed in 25 isolates (71.4%). Eight (22.9%) of the strains showed multidrug resistant (MDR) phenotype [resistant to three or more classes of antimicrobials]. Two strains were resistant to CTX which harbored the *bla*\(_{CTX-M-15}\) gene type and belonged to lineages ST10184 and ST2178. TetA was detected in all tetracycline-resistant strains (100%) while *intI* (n=8) and *bla\(_{TEM}\) (n=7) were also found in some of the strains. The *E. coli* strains were ascribed to four phylogenetic groups: A=4, B1=21, B2=8 and D=2.

**Conclusions:** Bats in Nigeria can be considered as environmental reservoirs and possible sources of MDR, including ESBL-producing *E. coli* strains belonging to virulence-associated phylogenetic groups. Therefore, due consideration should be given to wildlife in AMR risk assessment framework in Nigeria.

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Abstract 8634

Fast and reliable detection of group B Streptococcus during antepartum screening: evaluation of the PCR-based Simplexa GBS Direct assay in comparison to routine culture after Lim Broth enrichment and from ESwabs without enrichment.

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Background: Group B Streptococcus (GBS) remains the most common cause of neonatal sepsis and meningitis in many countries, mainly due to its vertical transmission from mothers to newborns at the time of delivery. Antepartum testing of vaginal/rectal colonization by GBS at week 35-37 of gestation from broth-enriched culture represents a valuable tool for the clinical management of pregnant women screening candidates for intrapartum antibiotic prophylaxis (IAP). The aim of this study is to evaluate the performance of a fast PCR-based assay compared to culture (gold standard), as an efficient alternative for GBS colonization antepartum screening, after Lim Broth enrichment (validated samples) as well as directly from ESwabs without enrichment (non-validated samples).

Materials/methods: Sixty-nine vaginal/rectal specimens collected antepartum with ESwabs (Copan) were enriched overnight in Lim Broth (bioMérieux), followed by a 48h incubation on chromogenic medium (bioMérieux). All of the enriched samples were tested in parallel with the Simplexa GBS Direct assay (DiaSorin Molecular). The same samples were also tested with the Simplexa system but from the primary ESwabs. Discordant samples were resolved with the Xpert GBS Assay (Cepheid) with a modified off label protocol from the Lim enriched specimens [1]. Sensitivity/specificity were defined after discrepancy resolution.

Results: Sixteen out of 69 (23.2%) samples were positive with Simplexa after enrichment, with a concordance to culture of 94.2%. Four of those were positive with Simplexa but negative by culture, of which two were confirmed positive by Xpert GBS (Ct-values: 34.6-41.5). Sensitivity/specificity of Simplexa were 100% / 96.2%, respectively. When the same 69 ESwabs were tested without enrichment, Simplexa showed a 95.7% concordance with culture, and a sensitivity/specificity of 85.7% / 98.2%, respectively.

Conclusions: This study shows excellent performance of the Simplexa assay after Lim Broth enrichment, and promising results directly from ESwabs. This fast and sensitive approach may represent a significant advantage for improving patient management by reducing the turnaround time by 24-48h. Moreover, its ease of use and simplified workflow would provide another valuable advantage, especially for 24/7 laboratories.


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Abstract 8635

Characterisation of a newborn species: Klebsiella spallanzanii

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Background: During the European project SpARK, which aims to characterize and study the transmission of Klebsiella in humans, animals and environment, we isolated and sequenced 37 Klebsiella strains collected in the province of Pavia (Italy) from Jul-2017 to Sept-2018. We found 4 strains belonging to Ko3 phylogroup of K. oxytoca complex. One strain of Ko3, strain SG271, was previously isolated.

This work aimed to describe Ko3 phylogroup and to compare it to the Klebsiella oxytoca complex through a genomic comparative analysis.

Materials/methods: Phylogenetic analyses were performed based on 3814 genes of the core genome, gyrA gene, rpoB gene, 16s rRNA and bla-OXY gene. Two genome similarity indexes were evaluated: Average Nucleotide Identity (ANI), and in silico DNA-DNA Hybridization (isDDH). Biochemical-metabolic characteristics of the Ko3 were analysed with API20E and Biolog. The peptide mass fingerprinting was obtained through MALDI-TOF. One genome was also sequenced with Oxford Nanopore. Genome annotation was performed by Prokka. Plasmids, resistance and virulence factors were searched through the tool ABRicate. Clusters of Orthologous Groups of proteins (COGs) were identified by COGnitor.

Results: The phylogenomic analysis of core genome shows that the Ko3 isolates formed a well-defined cluster with SG271. The well-defined clustering of Ko3 strains was supported also by phylogenetic analysis of the gyrA, rpoB and blaOXY loci. The ANI nucleotide identity between Ko3 and the type strains of other K. oxytoca phylogroups was below 96%. The isDDH relatedness ranged 36.3–44.1%. Ko3 phylogroup shared the metabolic profile with Ko8, but they differed by Ko8 unique ability to utilize 3-O-methyl-glucose. Protein fingerprinting of Ko3 obtained with MALDI-TOF displayed two characteristic peaks. All these analyses guarantee a new species that we named K. spallanzanii.

Conclusions: The size of K. spallanzanii genome sequenced with a hybrid approach based on Illumina and Oxford Nanopore was 6280958 bp, thus large for a member of the Klebsiella genus. This genome had a GC content of 53.4%, low compared to its close relatives, with 6035 putative protein predicted. No known resistance and virulence factors were found. Plasmid analysis and COG analysis are currently ongoing.

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Abstract 8636

**Efficacy of a screening and prophylaxis protocol to prevent infections in patients treated with anti-CD20/CD52 for multiple sclerosis**

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**Background:** Monoclonal antibodies (MAbs) have changed the efficacy of multiple sclerosis (MS) treatments. Infective complications have been observed in patients on MAbs targeting lymphoid cells surface antigens, namely anti-CD52 (alemtuzumab, ALM) and anti-CD20 agents (ocrelizumab [OCR] and rituximab [RTX]). Despite these emerging data, there is no standardized consensus regarding pre-treatment testing, vaccinations, patient education before and during therapy or infection monitoring strategies.

**Materials/methods:** We conducted a retrospective/prospective real-life study to evaluate the efficacy of a program of screening and prophylaxis for infective adverse events (IAE) in patients affected by MS-related disorders treated with MAbs directed against CD20/52 antigens.

All patients referring to the Centre of Neurodegenerative Diseases of Naples, University of Naples "Federico II", who started ALM (Lemtrada®), OCR (Octrevus®) or RTX (Mabthera®, off-label use) from 1 November 2015 to 30 June 2019 were recruited. From the 1st of February 2018 all patients were evaluated by an infectious disease specialist (IDs) before infusion to rule out active infection and underwent a complete serological screening for viral infections. Moreover, they started a prolonged anti-HSV prophylaxis and add to the recommended schedule an anti-Listeria/JJP prophylaxis with Cotrimoxazole. Therefore, we retrospectively evaluated IAE incidence before the introduction of the above-mentioned protocol and then prospectively to evaluate the effect on IAE incidence of this intervention.

**Results:** We enrolled 256 patients, 101 retrospectively (pre-intervention group, PREG) and 155 prospectively (post-intervention group, POST).

No statistically significative differences emerged between the two groups in terms of age, sex and clinical characteristics of the neurological disease. Conversely, in PREG group most of the patients were treated with alemtuzumab (57.4% vs 20.6%, p<0.001) and the follow-up period was longer than in POST group (732 vs 215 days, p<0.001). In PREG 34 patients experienced one or more infective adverse events (IAE) while in POST 20 patients received diagnosis of infection. Our screening and prophylaxis protocol resulted associated with a reduction in IAE incidence at univariate (p<0.001) and multivariate analysis (p=0.003) (Figure 1).

**Conclusions:** In patients affected by MS treated with anti CD20/CD52, a standardized protocol of screening and prophylaxis for IAE resulted effective and safe in reducing such events.

**Figure 1:** Risk factors for infective events

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
<td>95CI</td>
</tr>
<tr>
<td>Pre intervention group</td>
<td>1.231</td>
<td>1.833-6.401</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.676</td>
<td>1.019-3.796</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.141</td>
<td>0.036-4.344</td>
</tr>
<tr>
<td>Monoclonal experienced patient</td>
<td>0.710</td>
<td>1.065-3.886</td>
</tr>
<tr>
<td>Alemtuzumab</td>
<td>0.694</td>
<td>1.087-3.687</td>
</tr>
<tr>
<td>Rituximab</td>
<td>0.503</td>
<td>0.876-3.121</td>
</tr>
<tr>
<td>Ocrelizumab</td>
<td>1.430</td>
<td>1.875-9.307</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>0.024</td>
<td>0.259-4.060</td>
</tr>
<tr>
<td>Hypogammaglobulinemia</td>
<td>0.300</td>
<td>0.354-5.147</td>
</tr>
</tbody>
</table>

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**Abstract 8638**

**Childhood brucellosis: characteristics and outcomes in a sample from an endemic country**

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**Background:** Brucellosis is a zoonotic infectious disease caused by *Brucella* spp. that affects multiple body systems and may lead to several complications. Saudi Arabia is one of the countries where brucellosis is endemic. Studies on childhood brucellosis are limited. Therefore, the objective of this study was to describe characteristics and outcomes of pediatric patients infected with brucellosis in an endemic country.

**Materials/methods:** This was a retrospective descriptive study in a Saudi tertiary academic medical center. Pediatric patients aged < 18 years with confirmed brucellosis (via culture, serology, or both) who received antibiotic therapy were included. Descriptive statistics including mean ± standard deviation and percentages were used. Outcomes of different antibiotic treatment regimens were described in terms of clinical cure, mortality, and hospital length of stay of admitted patients.

**Results:** A total of 16 pediatric patients met the inclusion criteria. Mean age of patients was 9.1 years, they were mostly males (62.5%), and about half were hospitalized (56.3%). Only five patients (31.3%) had their parents reporting the consumption of a dairy product as a potential risk factor for brucellosis. Serologically, both baseline median antibody titer for *Brucella melitensis* and *B. abortus* were 1 280. Only half (50%) complained of arthralgia and were febrile at presentation. All but two cases were uncomplicated brucellosis. The two complicated brucellosis were a case of neurobrucellosis and brucella orchitis. While white blood cells elevation was not significant (mean=6.7 cells/mm$^3$), both C-reactive protein and erythrocyte sedimentation rate were elevated at baseline (28.1 and 28.8, respectively). Regimens administered varied considerably, but about half of the patients received at least three antibiotics (Table); however, all but one patient (93.8%) experienced clinical cure and none died.

**Conclusions:** Brucellosis is an endemic zoonotic disease that can infect both adults and children. This study describes the characteristics of brucellosis reported in children infected in an endemic country and provides an evidence of the positive prognosis associated with appropriate antibiotic therapy active against *Brucella* spp.

Table. Antibiotic regimens used for childhood brucellosis

<table>
<thead>
<tr>
<th>Regimen</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminoglycoside+trimethoprim/sulfamethoxazole+rifampin</td>
<td>4</td>
</tr>
<tr>
<td>Trimethoprim/sulfamethoxazole+rifampin</td>
<td>3</td>
</tr>
<tr>
<td>Aminoglycoside+trimethoprim/sulfamethoxazole</td>
<td>2</td>
</tr>
<tr>
<td>Doxycycline+rifampin</td>
<td>2</td>
</tr>
<tr>
<td>Aminoglycoside+doxycycline+docfibraxone</td>
<td>1</td>
</tr>
<tr>
<td>Doxycycline+trimethoprim/sulfamethoxazole+docfibraxone</td>
<td>1</td>
</tr>
<tr>
<td>Aminoglycoside+trimethoprim/sulfamethoxazole+docfibraxone</td>
<td>1</td>
</tr>
<tr>
<td>Doxycycline+rifampin+ceproflaxin</td>
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</tr>
</tbody>
</table>

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Abstract 8642

Development of a methodology for reverse transcription and amplification of small RNA amounts in serum for whole genome sequencing of hepatitis A virus

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Background: Whole genome sequencing has become a very useful tool that complements classical techniques in molecular studies. However, the main obstacle to further molecular analyzes is the small number of molecules after nucleic acids extraction, especially when microorganism load in the host is low. New techniques allow to extract and / or to work with amounts of nucleic acids of the order of picograms, undetectable by most routine quantification techniques. This fact calls into question many of the negative results obtained by previous techniques and opens up new ways of applying molecular biology to epidemiological studies. Objective: To develop a methodology capable of detecting viral sequences in low quantity, for subsequent sequencing and molecular characterization.

Materials/methods: RNA was extracted from 10 serum samples of positive HAV patients using Speedtools RNA Virus Extraction Kit (Biotools B&M Labs S.A.). The RNA obtained could not be quantified by spectrophotometric, fluorometric or electrophoretic methods for subsequent sequencing. cDNA was synthesized by reverse transcription of RNA with SMARTER-Seq Stranded Kit (Takara Bio). For this purpose, 7 µl of extraction product were taken with a contribution of between 10pg and 10ng of total starting RNA, regardless of the quality or RIN (RNA integrity number) obtained in the Bioanalyzer. In order to transcript both rRNA and ncRNA, “random” approach was used. The kit is also capable of eliminating cDNA of human origin, derived from the rRNA that could be synthetized by capture with selective probes. Subsequently, cDNA libraries were loaded into a mid-output NextSeq 550 (Illumina) run.

Results: Following this methodology, we were able to detect the small amount of RNA present in the studied samples. Sequencing generated between 8 and 26 million readings per sample, with a length of 2x150bp. These readings were filtered and analyzed by comparison in database for molecular characterization.

Conclusions: The new tools, such as SMARTER-Seq Stranded Kit (TakaraBio), are capable of working with quantities of undetectable nucleic acids by conventional methods. This kit allows the integrated elimination of cDNA derived from rRNA, abundantly present after cDNA synthesis, from total RNA entries. This provides an extremely sensitive workflow and highly reproducible data.

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Abstract 8643

**Descriptive study of Lyme disease suspected patients with discordant serological tests: negative enzyme immunoassay and positive immunoblot**

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**Background:** Diagnosis of disseminated Lyme borreliosis is based on clinical and serological criteria. The guidelines recommend a two-step approach for serological tests: first enzyme immunoassay (EIA) and in case of positivity, confirmation by immunoblot. This approach is very controversial, especially about the EIA sensitivity.

As part of a reference center for Lyme borreliosis, we are led to see patients whose diagnosis is difficult to establish. In some cases, with serological discordance, we are led to control serological test in our reference center and sometimes request an immunoblot test regardless of the result of the EIA.

**Materials/methods:** We performed a retrospective observational study by analyzing the medical records of patients with negative EIA and positive immunoblot. The objective is to evaluate in this specific population if the diagnosis of Lyme borreliosis would have been missed in front of a negative EIA.

**Results:** Between 2013 and 2017, 3102 patients had EIA test. Among them, 1233 had a positive or doubtful test and 1869 a negative test. Among the patients with negative test, 216 had an immunoblot performed at the request of the clinician, of whom 38 had a positive or doubtful result. Of these patients, 37 were subjected to descriptive analysis. The M/W sex ratio was 1.05 and the mean age 48 years. Six patients had a history of confirmed erythema migrans and 9 patients of possible erythema migrans. Articular symptoms were present for 27 patients [including 2 patients with mono/oligo arthritis of large joints compatible with the diagnostic criteria, the others presenting with polyarticular damage without objective inflammatory signs], neurological symptoms for 22 patients [headache, root pain]. No cardiac conduction disorders and no atrophic acrodermatitis have been reported. None of the patients had a lumbar or joint puncture. In total, no patient met the confirmed borreliosis criteria, and 12 patients met the possible borreliosis criteria defined by French guidelines.

**Conclusions:** The proportion of patients with negative EIA and positive immunoblot is low and none of these patients presented a clinical picture suggestive of Lyme borreliosis. These results confirm the achievement of serology in two steps proposed in the majority of guidelines.

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Abstract 8644

Prominent role of oprD mutations in carbapenem-resistant Pseudomonas aeruginosa strains in a previous context of VIM-1 outbreaks

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Background: Pseudomonas aeruginosa is a common opportunistic pathogen and a major cause of infection in hospitalized patients. P. aeruginosa had an extraordinary capacity for developing resistance by the selection of mutations in its chromosomal genes. The aim of this study was to characterize 53 P. aeruginosa strains isolated from purulent specimen to identify the molecular mechanisms responsible for their resistance to carbapenems and epidemiology changes in a clinical context with history of VIM-1 discovery and outbreaks.

Materials/methods: Antimicrobial susceptibility was tested by broth micro-dilution. Molecular characterization of the most frequent carbapenemase genes (blaKPC, blaIMP, blaVIM, blaNDM, and blaGES) and oprD gene presence/absence was investigated by PCR and sequencing. Efflux pumps involvement was investigated by phenotypic test using antimicrobial susceptibilities test in presence of CCCP.

Results: The molecular characterization revealed that only 4 of 53 strains harbor carbapenemases: 3 strains with blaVIM-1 and one strain with blaGES-5.

Efflux pumps involvement in the carbapenems resistance by phenotypic test was very low (3 strains).

We have characterized all our strains for oprD gene. 30% of strains have no amplification of oprD gene, suggesting a deletion of this. Sequences of oprD amplicons of the other strains reveal the presence of different mutations other than IS insertion or deletion that can be responsible of carbapenem resistance.

Sequence analysis revealed the presence of different mutations inside the oprD gene and all of them result in a reading shift that bring a premature stop codon.

Conclusions: Molecular analysis revealed that OprD mutations or deletion plays a very important role in carbapenem resistance of P. aeruginosa isolated in our hospitals.

The number of oprD mutations registered let us to think to be in presence of hyper mutable strains.

Carbapenemase producing strains is a minority in the strains isolated now days: just 3 VIM-1 and one GES-5. Also efflux seems not plays a prominent role (3 strains).

The mechanism of carbapenem resistance in P. aeruginosa clinical isolates in our clinical context is completely changed.

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Abstract 8645

**Characteristics and management of skin and soft tissue infections caused by Panton-Valentine leukocidin-producing Staphylococcus aureus (PVL-SA): a retrospective study of 99 cases**

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**Background:** Staphylococcus aureus (SA) is a major human pathogen with multiple virulence factors such as the Panton-Valentine leukocidin (PVL). PVL-SA cause recurrent skin and soft tissue infections (SSTI) and necrotizing pneumonia, in healthy young people with a high risk of human-to-human transmission. The study aims were to describe the clinical characteristics, evaluate the diagnosis delay and optimize the care pathway of patients with PVL-SA SSTI.

**Materials/methods:** Descriptive analysis of a retrospective study of patients with a PVL-SA SSTI followed by the Infectious Diseases Department between March 2009 and March 2019. Patients over 15 years and 3 months with a bacteriological specimen of a PVL-SA positive skin lesion were included. In our center, the search for PVL is performed systematically in case of SSTI positive to Staphylococcus aureus. Patients with PVL were reported to the Department of Infectious Diseases for specific consultation.

**Results:** 99 patients were included, 52% were men and the median age was 29. 88% had no comorbidity, 16% practiced a profession at risk of PVL-SA and 20% practiced a risky hobby, 32% traveled outside Europe in the year, a contagion was found in 16%. 43% had a previous history of SSTI. The median of diagnostic delay was 6 days, the median of consultation delay was 9 days. PVL-SA resistant to meticillin was present in 28%. 77% of patients had a single skin abscess. 45% of the cutaneous lesions were on the lower limbs, 29% on the trunk and 21% at the axillary level. 91% received surgical treatment. Postoperative antibiotic therapy was amoxicillin/clavulanic acid in 57%, 3% just received an antitoxicnic antibiotic. During the consultation, 56% had active infection. Linezolid was prescribed for 55% of patients. 93% had cutaneous decontamination, 60% of patients were recovered, 20% were lost to follow-up and 20% recidivated.

**Conclusions:** PVL-SA cause recurrent SSTI in healthy young people, a collaboration between surgeon, bacteriologist and infectious disease specialist is necessary for a quick diagnosis and to set up specific therapeutics in order to avoid relapse.

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In vivo and in vitro synergistic activity of colistin combining with meropenem and sulbactam against multidrug-resistant and pandrug-resistant Acinetobacter baumannii clinical isolates

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Background: Multidrug-resistance (MDR) and pandrug-resistance (PDR) in Acinetobacter infections is an increasing health concern. Colistin has been reported to be frequently used clinically in these infections, single or combined with other antimicrobials. There is no report regarding the potential synergistic effects of colistin combining with meropenem or sulbactam. In this study, we investigated the synergistic activity of colistin combining with meropenem and sulbactam against MDR and PDR Acinetobacter baumannii clinical isolates both by in vitro and in vivo methods.

Materials/methods: The antibacterial activity of colistin, meropenem and sulbactam against sensitive (n=3), MDR (n=3) and PDR A. baumannii clinical isolates (n=3) was investigated. The A. baumannii ATCC 19606 was also included. Minimum inhibitory concentrations (MICs) of antimicrobial agents were determined by reference broth microdilution method. The synergistic activity of colistin with meropenem and sulbactam was evaluated by checkerboard method. Interactions between the selected antibiotics were determined by calculating the fractional inhibitory concentration (ΣFIC) index. Galleria mellonella was used as an experimental model for in vivo activity testing. The larvae were infected with 10^8 CFU / ml bacteria, the antimicrobials were injected and incubated at 37 °C and observed for 120 hours for death.

Results: Both combinations, colistin meropenem and colistin sulbactam had additive effect on PDR isolates (with ΣFIC = 0.51–1.48) while additive effect or synergism on MDR isolates (with ΣFIC = 0.04–0.53). No interactions by both combinations were reported on sensitive isolates and reference strain. The larvae infected by PDR isolates and treated with colistin, meropenem or sulbactam alone or colistin meropenem combination were all dead; while 80% were dead in the colistin sulbactam combination group. In the larvae group infected by MDR isolates, death rates were as follows; treated with colistin 50%, with meropenem 90%, with sulbactam 90% and with colistin+meropenem combination 30%.

Conclusions: Our results indicate that colistin with combination to both sulbactam and meropenem has enhanced activity and may be promising for life threatening MDR and PDR Acinetobacter infections. This study is also remarkable to be the first for evaluating colistin combinations on clinical isolates by both in vitro and in vivo methods.

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Abstract 8654

**Comparison of the performances of three commercial real-time PCR kits with an in-house real-time PCR assay for the diagnosis of invasive aspergillosis**

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**Background:** Early diagnosis of invasive aspergillosis is crucial for better prognosis. Yet, conventional mycological techniques have low sensitivity and galactomannan antigen detection is subjected to false negative and false positive reactions. Real-time PCR assays are required not to yield cross reaction with other fungi genus such as *Penicillium* and to reach low limits of detection of *Aspergillus* DNA to be of clinical utility. Our aim was to assess the performances of three commercial real-time PCR kits compared with the performances of an in-house real-time PCR assay.

**Materials/methods:** The MycoGENIE® Aspergillus fumigatus (MycoGENIEAf) and Aspergillus spp. (MycoGENIEAspp) Real-Time PCR Kits and the Fungiplex Aspergillus PCR Kit were compared to an in-house real-time PCR assay targeting *Aspergillus fumigatus* 28S rRNA gene (28SqPCR). A standard curve was generated for the four assays with serial dilutions of *A. fumigatus* DNA. The four assays were also tested on 4 pg/µl DNA from 10 species of *Aspergillus* and *Penicillium*.

**Results:** The lower limit of detection of all four assays was 10 spores/ml of *A. fumigatus*. The serial dilutions of *A. fumigatus* DNA yielded mean threshold cycles (Ct) 0.14, 1.79 and 3.35 higher for MycoGENIEAspp, MycoGENIEAf and Fungiplex, respectively, than for 28SqPCR. 28SqPCR and MycoGENIEAf detected only *A. fumigatus* DNA. MycoGENIEAspp detected 4 pg/µl DNA of all species of *Aspergillus*, but with Ct values ranging from 21.11 for *A. terreus* to 40.76 for *A. nidulans* and 43.49 for *A. ustus*; meanwhile Ct values were 29.68 for *P. purpurogenum* and 24.34 for *P. chrysogenum*. Fungiplex detected 4 pg/µl DNA of all species of *Aspergillus* with Ct values ranging from 25.64 for *A. niger* to 30.15 for *A. ustus*; *P. purpurogenum* was not detected and Ct value was 38.49 for *P. chrysogenum*.

**Conclusions:** Although the lower limit of detection of all four assays was 10 spores/ml, MycoGENIEAf and Fungiplex yielded higher mean Ct values than 28SqPCR. MycoGENIEAspp yielded Ct values quite as low as those obtained with 28SqPCR. However, the weak detection of some *Aspergillus* species combined with the sensitive detection of non-clinically relevant *Penicillium* species makes its results difficult to interpret.

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Abstract 8656

Diagnostic accuracy of synovial cell count at reimplantation in periprosthetic knee infection undergoing two stage procedure

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Background: Time to reimplantation in patients with prosthetic joint infection (PJI) undergoing 2-stage exchange can be difficult to establish. Clinical signs disappearance, negative microbiology at reimplantation, and serum biomarkers (ESR, CRP) normalization do not identify accurately patients at risk of recurrence. Despite synovial fluid analysis (WBC count and neutrophils percentage) represents an effective tool to diagnose PJI, only cut-off value adopted at the time of PJI diagnosis has been standardised. Aim of this study was to evaluate the accuracy of synovial WBC and neutrophil percentage before definitive reimplantation in patients with periprosthetic knee infections undergoing 2-stage exchange.

Materials/methods: Seventy-two synovial fluid aspirates from patients undergoing the second step of 2-stage procedure after clinical findings disappearance, negative microbiology at reimplantation, and serum biomarkers (ESR, CRP) normalization were evaluate in a case-control study (1:3 ratio). Synovial WBC count and relative neutrophil percentage from patients who developed PJI recurrence (18 cases, Group A) were matched with those obtained from a comparable group of patients reporting definitive cure (54 cases, Group B). The diagnostic performance of these tests was assessed by receiver operating characteristic (ROC) curve analysis. The sensitivity and specificity (and 95% CIs) were calculated for each of the cut-off values and the area under the curve (AUC) was calculated.

Results: Median synovial fluid leukocyte and neutrophil percentage were significantly higher in patients with recurrence of periprosthetic infection than in those reporting infection eradication [WBC (cells/µL), 2001 (804-2776); Vs. 400 (80-1200), p<0.001; % Neutrophil count, 64% (22-90) Vs. 39% (11-78), p<0.001]. In predicting PJI recurrence, synovial WBC count >1068/µL had 94% sensitivity and 97.3% specificity, instead, Neutrophils percentage >50% had 78% sensitivity and 81% specificity. Diagnostic accuracy was higher for WBC (AUC 0.99, 95% CI 0.96-1.0) than for PMN percentage (AUC 0.76, 95% CI: 0.60-0.91).

Conclusions: On the basis of our investigations, a cut-off value at reimplantation of synovial WBC count >1068/mL was useful to predict recurrence of infection in patients with periprosthetic knee infections undergoing 2-stage exchange procedure. Adopting these cut-off values, synovial fluid cell count is a diagnostic test useful to establish the optimal timing for reimplantation with elevated diagnostic accuracy.

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Identification of a clinically relevant anal HPV infection in HIV-positive men having sex with men: data from Czech anal cancer screening programme

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Background: The prevalence of anal high-risk HPV (hrHPV) infection is very high in HIV positive men having sex with men (HIV+MSM). A long-term anal HPV infection together with impaired immunity in this population increases the risk for the development of an HPV-induced anal carcinoma (AC), with its incidence up to 131/100000. Therefore, screening for curable (pre) malignant anal lesions is justified in HIV+MSM to reduce morbidity and mortality connected to the invasive stadium of AC. Because of an analogy of AC and cervical cancer, the same screening approach, based on the detection of clinically relevant hrHPV infection might be useful. The aim of our study is to identify a clinically relevant HPV infection in anal samples using HPV genotyping, mRNA hrHPV detection, and methylation analysis of cellular genes while correlated to the anal cytology results.

Materials/methods: HPV genotyping, hrHPV mRNA expression, and methylation analysis were performed in anal smears taken from 171 Czech HIV+MSM. Results were correlated to the anal cytology findings.

Results: 117 anal smears (68 %) tested positive for at least one hrHPV type, 44 (26 %) tested negative, and 10 samples were not analyzable. There was no significant difference in the ratio of normal/abnormal cytology findings between hrHPV positive and negative groups. Transcriptional activity of hrHPV was proven in 48 %, and methylation in 31 % of hrHPV DNA positive smears. The most significant difference in the prevalence of abnormal cytology was between the group of transcriptionally active hrHPV positive smears with methylation (85 %) and a group of hrHPV positive patients without detected transcriptional activity and without methylation (24 %), p = 0.0002.

Conclusions: HPV genotyping seems not to be a sufficient tool in defining clinically relevant hrHPV infection in anal cancer screening HIV+MSM cohort. Both follow-up procedures, that is a detection of transcriptional activity and methylation analysis are better for distinguishing patients with abnormal cellular changes related to the viral oncological process.

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Are carbapenems a choice in OXA-163 carbapenemase-producing Enterobacterales infections? Clinical outcomes of 29 OXA-163 infections in a general hospital in Argentina

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Background: The emergence of carbapenemase-producing Enterobacterales represents a global health problem. OXA-163 is a variant of OXA-48 betalactamase, with limited in-vitro hydrolytic effect on carbapenems (CBP). Clinical data about patients with infections due to OXA-163-producing Enterobacterales is limited to a few case reports in Argentina and Egypt.

Materials/methods: Retrospective descriptive study of infections due to OXA-163-producing Enterobacterales between 2012-2018 in a single center in Argentina. Epidemiological, clinical and microbiological data was recalled. Pathogen identification and antimicrobial susceptibility testing were performed using conventional and automated methods (PHOENIX BD®, MALDI-TOF-MS®). The presence of OXA-163 was confirmed by immunochromatographic lateral flow assay (K-SeT RESIST-3 O.O.K, Britania) and PCR/DNA sequencing.

Results: 29 patients OXA-163-producing Enterobacterales were identified, 6 were excluded from the clinical analysis due to lack of data. Of the remaining 23 patients, 70% were adult men, median age 63 (IQR 46-67) and 1.1% were male neonates. Ninety-one % had previous antibiotic use, 70% were admitted to the ICU and 65% had a surgery within 90 days prior to the OXA-163 infection. Median hospital stay before infection was 15 days [RIC9-38]. Distribution of infections was: 43% urinary, 17% intra-abdominal and 18% primary bacteremia. The most frequent isolate was K. pneumoniae (66%). Figure 1 shows the antibiotic susceptibility profile. ESBL coproduction was detected in 45% strains, KPC-type carbapenemase in 2.5% and NDM-type carbapenemase in 2.5%. Only 44% of the initial empirical therapy was considered appropriate. Definitive treatment included CBP in 78% with monotherapy administered in 67% of the infections. Median duration of adjusted treatment was 11 days (IQR 7-19) and clinical resolution at day 7 occurred in 83% of the cases. The 30 day overall mortality was 17%.

Conclusions: Infections due to OXA-163-producing Enterobacterales are associated with high mortality. Although OXA-163 is classified as a carbapenemase, in this study we found that CBP susceptibility is usually preserved in OXA-163-producing Enterobacterales and CBP monotherapy may be considered as an effective treatment option.

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Antibiotic resistance in anaerobic infections in a hospital in Tenerife
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Background: During last decade the importance of anaerobic bacteria infections has increased; especially due to the high number of patients with several comorbidities. Moreover, antimicrobial resistance has also experiment an increment and empiric antibiotic therapy is becoming a challenge.

Our objective was to determinate the incidence and antibiotic susceptibility of anaerobic bacteria.

Materials/methods: Between January 2014-September 2019, 284 isolates (1 for patient) were collected from: blood (18.66%), abscesses (15.84%), peritoneal fluids (35.91%), other sterile fluids (5.63%), skin and soft tissues (10.21%) and others (13.75%); plated on BD Schaedler-KV, SNVS, BEE and incubated 48h at 37ºC in anaerobic atmosphere. Antimicrobial susceptibility was tested by broth microdilution method, with the ATB tm ANA (bioMérieux).

Results: Bacteroides spp was the most frequent anaerobic bacteria detected, in 84.15% of the cases (48.53% B.fragilis); Prevotella in 7.39%, Fusobacterium in 4.57% and 3.89% for gram positive cocci.

Fusobacterium susceptibility to amoxicillin-clavulanate was 84.71%, 23.07% to penicillin, 92.30% to metronidazole and cefoxitin, 91% to clindamycin and 92.30% to penicillin. No resistant isolates to imipenem were detected.

Prevotella showed 90.47% susceptibility to amoxicillin-clavulanate, 90.47% to imipenem and cefoxitin, 28.57% to penicillin, 95.35% to clindamycin and 95.35% for piperacillin-tazobactam.

All gram positive-cocci isolates were susceptible to cefoxitin, 77.77% to amoxicillin-clavulanate, 88.98% to imipenem, 55.55% to penicillin and metronidazole; and 88.88% for clindamycin and piperacillin-tazobactam.

The following table describes susceptibility distribution in Bacteroides

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<tbody>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>91.66%</td>
<td>70.37%</td>
<td>88%</td>
<td>85.71%</td>
<td>68.42%</td>
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<td>Imipenem</td>
<td>95.83%</td>
<td>91.22%</td>
<td>92%</td>
<td>87.75%</td>
<td>84.21%</td>
<td>81.88%</td>
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<tr>
<td>Penicillin</td>
<td>37.5%</td>
<td>33.33%</td>
<td>16%</td>
<td>28.57%</td>
<td>21.05%</td>
<td>13.63%</td>
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<tr>
<td>Cefoxitin</td>
<td>86.66%</td>
<td>89.47%</td>
<td>90%</td>
<td>93.77%</td>
<td>86.42%</td>
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<tr>
<td>Clindamicyn</td>
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<td>94.73%</td>
<td>66%</td>
<td>59.18%</td>
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<tr>
<td>Metronidazol</td>
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<td>94%</td>
<td>79.59%</td>
<td>89.47%</td>
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<tr>
<td>Pipertazobactam</td>
<td>50%</td>
<td>75.43%</td>
<td>86%</td>
<td>86.67%</td>
<td>78.94%</td>
<td>86.36%</td>
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Conclusions: Antimicrobial susceptibility to anaerobic bacteria has persistently decreased among last years, especially in Bacteroides group, with remarkable changes in susceptibility patterns.

According to our data, although metronidazol and imipenem could still be considered as the elected drugs in anaerobic infections, gradually increases in resistance have been observed in Bacteroides.

These statistics should indicate that individualized susceptibility of each isolate for a correct treatment choice is becoming essential nowadays.

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Delayed diagnosis and increase mortality in native vs prosthetic/device-related coagulase-negative staphylococci infective endocarditis

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Background: Coagulase-negative staphylococci (CoNS) are able to produce biofilm and to affect to prosthetic valve and cardiac devices. To the contrary native valve CoNS infective endocarditis (IE) is seldom described. The increase in the last decade of invasive intravascular techniques in elderly and frail patients may have increased CoNS infections. The aim of this study was to compare native CoNS IE with prosthetic/device-related IE.

Materials/methods: Prospective observational study of patients diagnosed with IE from January 2003 - January 2019 was performed in a tertiary reference center in Badalona (Barcelona), Spain. 475 IE, 177 (37.3%) staphylococcal infections, and 79 (44.6%) by CoNS were registered in the study period. Patients were classified into 2 groups: Group 1: native IE, Group 2: prosthetic/device-related IE.

Results: Among the 79 CoNS IE, group 1 included 22 patients (27.8%), and group 2, 57 patients (72.2%). Group 2 included 25 (73.5%) patients with biological prosthetic valve, 8 (23.5%) patients with mechanical prosthetic valve and 1 (2.9%) patient with mitral valve repair. No significant differences were found in according to age, gender, nosocomial acquisition, hemodialysis, liver cirrhosis and reinfection. However patients from group 1 had significantly a higher Charlson Index (4.5 vs 2.9, p 0.005), a longer diagnosis delay (8.9 vs 3.8 days, p 0.039), more renal chronic failure (7 (37.8%) vs 6 (10.5%), p 0.022), higher aortic IE (15 (68.2%) vs 19 (33.9%), p 0.006), more valvaral insufficiency at the diagnosis or evolution (19 (86.4%) vs 27 (51.9%), p <0.01), more complications (20 (90.9%) vs 35 (61.4%), p 0.013), cardiac failure (19 (91.8%) vs 15 (31.2%), p<0.01), greater surgical indication (19 (86.4%) vs 33 (60%), p 0.032) and a higher mortality (15 (68.2%) vs 25 (43.9%), p 0.053).

Conclusions: CoNS native valve endocarditis is not an infrequent infectious complication that affects comorbid and frail patients. The clinical suspicion is poor and that may lead the high rate of complications seen in the study.

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**IntFinder: a freely-available user-friendly web tool for detection of class 1 integrons in next-generation sequencing data using k-mer alignment**

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**Abstract third-party references:** UNIETAR, SENECYT, DTU Food

**Background:** Class 1 integrons are the most frequent genetic platforms capable to capture and express antibiotic resistance genes embedded within gene cassettes. These genetic elements are involved in the acquisition shuffling and dissemination of multi-resistance among clinically important bacteria. Despite its importance, few bioinformatics tools for integron detection have been developed to aid the understanding of antimicrobial resistance dynamics, but they are intended for users with effective programming knowledge. Filling a gap, we aimed at creating an open-access bioinformatics tool to enable detection of class 1 integrons in NGS data by users without any programming skills.

**Materials/methods:** From the whole list of integrons with attributed integron (In) numbers available in INTEGRALL (http://integrall.bio.ua.pt/), we curated 1,356 accessions to create a Class 1 integron database. We used Nucleotide BLAST 2.8.1+ to detect genes that defined the integron conserved regions 5’ (intI1) and 3’ (qacEΔ1, sul1, and orf5). We wrote a script using k-mer alignment (KMA) to match an input sequence with a database entry according to a user-defined similarity threshold. We tested IntFinder by analyzing 2,097 plasmids from NCBI refseq, and we compared the results with those obtained by existing tools such as Integron Finder and Integron Visualization and Identification Pipeline (I-VIP) run using default parameters.

**Results:** IntFinder integrates a python script and a database of 1,331 integrons in fasta format. At 90%, 95%, and 100% similarity, IntFinder detected integrons in 390, 359, and 243 plasmids encompassing 134, 129, and 97 different In numbers, respectively. Integron Finder and I-VIP detected integrons not detected by IntFinder in 139 and 72 plasmids, respectively. This was due to strict inclusion criteria for IntFinder database which encompasses exclusively class 1 integrons with an assigned In number. The three tools categorized integrons differently and only IntFinder follows the standard In nomenclature.

**Conclusions:** IntFinder is a bioinformatics tool to enhance capacity to detect class 1 integrons with assigned In numbers in NGS data in settings with limited bioinformatics expertise. IntFinder is freely available at https://cge.cbs.dtu.dk/services/IntFinder-1.0/, and it can be used online by non-bioinformaticians or it can be downloaded to be used in the command line.

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Genotypic investigation of Leishmania spp. in dog population of northern Greece

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Background: The incidence of leishmaniasis in Greece has been increasing in recent years and Leishmania infantum seems to be the main cause of the cutaneous (CL) and visceral (VL) form of the disease, although sporadic cases of CL due to L. tropica have also been reported. In addition, it is well known that a large proportion of endemic dogs are infected even if they remain asymptomatic or seronegative. Serological techniques detect most of the symptomatic and a proportion (up to 50%) of asymptomatic dogs. In view of the above and the fact of the close relationship between canine morbidity and the increasing human incidence of the disease in endemic areas, genotypic investigation of leishmaniasis in dogs is crucial.

Materials/methods: Sixty-two whole blood and serum samples collected from dogs (32 male and 30 female, 8 months to 11 years old) were subjected in the study. The vast majority of the dog population exhibited mild to very severe clinical form of VL (n=46) while 16 dogs were asymptomatic. PCR for the internal-transcribed-spacer-1 (ITS1) region of rRNA gene was applied to all extracted DNA samples. RFLP (with HaeIII) and Sequencing analysis was performed to all positive amplicons for Leishmania species identification and confirmation. The sequences obtained were compared for their homology to known sequences in the GenBank database (http://www.ncbi.nlm.nih.gov/BLAST). Serological detection of IgG Leishmania antibodies was performed by an indirect Elisa kit.

Results: Among 62 tested samples, 20 (32.2%) were PCR positive and confirmed at the genus level by comparison with the deposited Genebank sequences with the BLAST tool. PCR, RFLP analysis, revealed the L. infantum electrophoretic pattern for all positive samples. Seventeen PCR-positive samples were symptomatic while 3 were non-symptomatic. IgG antibodies were not detected in 4 of the PCR positive samples, which points to cases of recent early-stage infection.

Conclusions: Our findings confirm the prevalence of L. infantum in our country. However, low rates of Leishmania DNA detection in blood are probably correlated with the duration of parasitemia. Furthermore, the genotypic investigation of Leishmania at the species level with additional genetic loci (eg kDNA) appears to be essential for conducting safer conclusions.

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Abstract 8667

**Performances of a new random access system for human immunodeficiency virus RNA quantification**

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**Background:** Human immunodeficiency virus (HIV) RNA quantification is a key marker at diagnosis and to monitor treatment of this infection. Automated, standardized and rapid systems are essential tools to provide fast and reliable viral load (VL) quantification to clinicians. The aim of this study was to evaluate the performances of the recently launched NeuMoDx for HIV-RNA quantification with a peculiar focus on HIV diversity.

**Materials/methods:** 103 HIV positive frozen plasmas previously quantified for HIV-VL using Veris Dx (Beckman) were selected to represent a wide range of VL (from 1.55 to 6.74 log copies/mL) and genetic strain diversity (B subtype n=34 (33%), non B n=69 (67%): CRF02_AG n=21, non-typable n=8, A-like n=5, C n=4 and 31 other rare subtypes). Twenty-seven fresh blood samples tested with Veris were analyzed in parallel on NeuMoDx.

**Results:** Overall, only one (0.8%) test failure occurred on a frozen plasma sample and corresponded to internal control amplification failure. One sample was not properly processed due to insufficient volume. Quantification was obtained on NeuMoDx for 98 samples and 3 low VL samples (1.64, 1.66, 2.62 log cop./mL) of different subtypes (CRF02_AG, non-B not typable and B, respectively), were not detected. VL obtained on both system were well correlated (r=0.92) with a mean bias of -0.35 log cop./mL (NeuMoDx-Veris). Quantification differences were more important toward the lower linearity range. Seven samples presented more than 1 log copies/mL differences between the two techniques and all but one belonged to subtype B. Among the 27 fresh analyzed samples on primary tubes, 12 had low HIV-VL below Veris quantification level (35 cop./mL) and 5 (42%) were quantified with NeuMoDx with VL ranging from 0.48 to 2 log cop./mL. Among the 15 remaining negative samples as classified with Veris, one was quantified at 1.2 log cop./mL with NeuMoDx.

**Conclusions:** These first results obtained on the NeuMoDx confirmed the overall good functionality of the system based on microfluidic with short turnaround time, simple training, full traceability and easy handling. These preliminary data did not highlight any major issue on this double target challenging assay. Further evaluations are ongoing to confirm this pilot study.

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Background: Gastric cancer has been associated with Epstein-Barr Virus (EBVaGC) in 10% of all gastric cancers and is characterized by a distinct molecular profile. Recently it has been shown that in EBVaGC there are no TP53 mutations, nevertheless it may be observed accumulation of wildtype p53 in these tumors. In this study we aimed to analyze the potential role of mdm2 protein, the major p53 negative regulator, as the explanation for the p53 dysregulation in EBVaGC.

Materials/methods: We used tumor samples collected from formalin-fixed paraffin-embedded (FFPE) tissue blocks collected from IPO-Porto patients with EBV-positive (EBVaGC, n=12) and EBV-negative (EBVnGC, n=28) gastric cancers. MDM2 mRNA expression levels was assessed by two-step real-time PCR and protein expression was analyzed in tissues by immunohistochemistry (IHC).

Results: IHC demonstrated that mdm2 is present in 5/12 EBVaGC and 10/27 EBVnGC, with 80% of EBVaGC showing expression in the majority of cells, compared with 20% in EBVnGC (p=0.089). A significative difference was found when compared high mdm2 expression in EBVaGC and EBVnGC diffuse histological subtype (p=0.048). Regarding the MDM2 mRNA levels, a significative increased expression was observed in EBVaGC, when compared with EBVnGC intestinal type (p=0.034) and a trend when compared to EBVnGC indeterminate type (p=0.057).

Conclusions: Our study shows that mdm2 may be an important marker for EBVaGC, which is reflected in the higher accumulation in tissue. Furthermore, this is probably explained by the increased transcriptional activity, enhanced by some viral protein or miRNA which may contribute for the dysregulation in the p53-mdm2 balance in these cancers.

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Neurologic complications in Chagas disease: results from a systematic review of published literature

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Background: Chagas Disease (CD) is a parasitic infection caused by Trypanosoma cruzi, endemic in Latin America with an increasing impact on public health also in non-endemic countries. Although the cardiac and gastrointestinal involvement have been widely explored, little knowledge on neurologic manifestations of CD has been achieved. Here we present the first results of our systematic review on the neurologic involvement of CD.

Materials/methods: We conducted a systematic review of the literature from January 1, 2000 to October 4, 2019 using the PubMed and Embase databases. Relevant studies were investigating using the following string of MeSH terms: ((Chagas disease OR American trypanosomiasis) AND (neurolog* OR transplant OR brain OR complications OR central nervous system OR meningoencephalitis OR neuro chagas OR chagoma OR stroke OR HIV OR AIDS OR immunosuppression OR reactivation)). Only articles in English, Spanish and Portuguese were included in the analysis elaborated by four reviewers. Both human and animal studies were included. Studies on the peripheral nervous system were excluded.

Results: A total number of 3844 papers (2581 from PubMed, 1263 from Embase) were reviewed; 341 records were included and subsequently divided into category as showed in Figure 1. The analysis of the scientific production over the years showed a growing linear trend (+13.53%). Overall, studies on the central nervous involvement represented the dominant part (271/341, 79.5%) and included studies on ischemic stroke (91/271, 33.6%) and on typical neurologic findings in CD, meningoencephalitis, animal studies and studies on pathogenesis of cerebral involvement of CD (180/271, 66.4%). The most frequent topics of included studies were related to infectious and tropical diseases/internal medicine 172/341 (50.4%), neurology 105/341 (30.8%), cardiology 43/341 (12.6%).

Conclusions: The increasing body literature on the neurologic involvement of CD demonstrates the need of the scientific community to better define this multiform clinical entity. Although less common than the gastrointestinal and cardiac involvements, it can represent an emergency, especially in the context of acute CD or during CD reactivation in immunosuppression. The interest in this topic of different medical disciplines underlines the need for a multidisciplinary management of CD patients.

Figure 1. Flow chart of study selection process

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**Abstract 8675**

**High-frequency of Specific Polysaccharide Antibody Deficiency (SPAD) in adults with unexplained recurrent and/or severe bacterial infections: the SPIDAC French Study**


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**Background:** Antibody deficiencies are the most frequent primary immunodeficiencies (PIDs) in adults and are mainly revealed by recurrent and/or severe bacterial infections. The objective of this study is to evaluate a systematic research strategy of PIDs in adults with unexplained bacterial infections.

**Materials/methods:** A prospective study was conducting in 15 centers in North of France (NCT02972281). Main inclusion criteria were recurrent benign upper and lower respiratory tract infections [group 1], severe upper and lower respiratory tract infections requiring hospitalization [group 2], and/or invasive infections documented with encapsulated bacteria [group 3]. Main exclusion criteria were all local [including tobacco use] and general associated conditions which could explain infections. If no PID diagnosis was made, response to polysaccharide antigens was assessed after PPV23, as previously published.

**Results:** From March 2015 to September 2019, 106 patients were included [34 males, mean age 42 years], and full data were available in 88 at the time of the present analysis. Thirty-four PIDs were diagnosed, giving an estimated frequency between 31.1% [n=34/106] to 37.5% [n=34/88]. Specific Polysaccharide Antibody Deficiency (SPAD) was the most frequent diagnosis by far [n=30/34, 88%], and was made in 13, 7 and 8 patients from groups 1 to 3, respectively. According to infectious history, SPAD patients were on surveillance [N=25] or treated with preventive antibiotics [N=4] or with immunoglobulins replacement therapy[N=6], the latter being dramatically efficient in all cases.

**Conclusions:** This study highlight the high prevalence of SPAD among adults with unexplained recurrent and/or severe bacterial infections. SPAD should be screened in those patients.

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Allergic bronchopulmonary aspergillosis (ABPA) complicating chronic obstructive pulmonary disease (COPD) without asthma: responses to antifungal therapy
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Background: Allergic bronchopulmonary aspergillosis (ABPA) is traditionally associated with asthma and cystic fibrosis. Aspergillus hypersensitivity and ABPA is present in 8-18% and 1-3% (respectively) with chronic obstructive pulmonary disease (COPD); however little is known about the significance of ABPA complicating COPD (ABPA-COPD). Case studies have demonstrated good responses to oral corticosteroids; however, it is not known whether antifungal therapy is beneficial in ABPA-COPD.

Materials/methods: We extracted clinical data from patients with a COPD and ABPA diagnosis at the National Aspergillosis Centre, Manchester University NHS foundation trust, UK. ABPA was diagnosed as having: ABPA symptoms, Total IgE (TlGE) >1,000kU/L, raised Aspergillus specific-IgE, and radiology consistent with ABPA. Exclusion criteria: asthma or cystic fibrosis history, other forms of pulmonary aspergillosis, lung function not consistent with COPD, age <40 years, no COPD predisposing factor.

Relevant medical history, symptoms, sputum culture, Aspergillus serology, radiology and response to antifungal therapy was extracted.

Results: Fifteen patients were included. Five were male. Median age 70 (56-81). Average MRC dyspnea scale and % predicted FEV1 was 2.93 and 66.4% respectively. Average TlGE was 4,562kU/L (1,193 - 32,615).

Eight of 15 patients were treated with Itraconazole. Two stopped within 1 month because of adverse events (AEs). Four stopped at 1-7 months because of AEs. 75% reported no improvement in symptoms. One of 8 patients reported a significant improvement (MRC dyspnoea scale increased from 4 to 2).

Patients who received >1 month of Itraconazole had an average TlGE of 2,375kU/L. In 80%, TlGE dropped to <1,000kU/L within 1 year. Two patients had TlGE available within 3 months of Itraconazole commencement, all had a TlGE decline >25% within 3 months.

4 of 15 patients received Amphotericin B nebulisers (AmpB), all stopped within three weeks because of AEs, one patient reported symptom improvement.

Conclusions: This is the first study to describe ABPA-COPD treatment with antifungal therapy. Oral Itraconazole gives a good serological response. However Itraconazole and AmpB may not be practical because the majority report no symptomatic improvement and experience AEs. Improvements reported could be explained by concomitant corticosteroids. High AEs could be explained by patient factors associated with COPD [elderly, co-morbidities].

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**Abstract 8680**

**Activity of ceftolozane-tazobactam and combinatorial regimens against a contemporary collection of carbapenem-resistant Pseudomonas aeruginosa**

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**Background:** Pseudomonas aeruginosa remains an important cause of hospital-acquired infections, globally. P. aeruginosa strains have become multidrug resistant (MDR) through multiple mechanisms and are increasingly resistant to carbapenems and other beta-lactams. The purpose of this study was to evaluate the in vitro activity of newer agents such as ceftolozane-tazobactam (CT), meropenem–vaborbactam (MV) and other relevant comparators and combinations against a contemporary collection of carbapenem-resistant *P. aeruginosa* clinical isolates.

**Materials/methods:** Antimicrobial susceptibilities were determined for 46 carbapenem-resistant *P. aeruginosa* strains from unique patients within 2 medical centers (University of Kentucky, Lexington KY and Methodist Healthcare System, San Antonio, TX). Minimal inhibitory concentrations (MICs) were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) breakpoints. Isolates testing non-susceptible to at least one agent in ≥ 3 antimicrobial classes were defined as MDR and isolates testing non-susceptible to at least one agent in ≥ 5 antimicrobial classes were defined as extensively drug resistant (XDR). Synergy testing was performed on 10 meropenem-resistant XDR isolates. Combinatorial effects of meropenem+tobramycin and MV+tobramycin were evaluated using synergy tests and interpreted based on calculations of the fractional inhibitory concentration index (FICI).

**Results:** Of the 46 meropenem-resistant strains, 89% were classified as MDR and 39% were classified as XDR. All (100%) isolates were resistant to piperacillin-tazobactam, 80% to ciprofloxacin, 70% to amikacin, 80% to tobramycin, and 20% to cefepime. CT demonstrated 100% in vitro activity against both MDR and XDR isolates while all isolates were resistant to MV. Of the isolates evaluated for synergy testing, one demonstrated synergy between meropenem+tobramycin (FICI<0.5); however, all remained non-susceptible. None of the isolates demonstrated synergy with MV+tobramycin; however, additivity resulted in MV susceptibility (MIC < 8 ug/mL) in 25% of isolates.

**Conclusions:** CT demonstrated *in vitro* effectiveness against both MDR and XDR carbapenem-resistant *P. aeruginosa* strains, while MV had poor activity as both monotherapy and in combination with tobramycin against these isolates. These data provide insight into the potential value and pitfalls of these therapies as either empiric or targeted treatment of MDR *P. aeruginosa* infections.

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Keep the attention high on Putative Invasive Pulmonary Aspergillosis (PIPA) in medical wards and intensive care units: a four-year retrospective analysis

Keep the attention high on Putative Invasive Pulmonary Aspergillosis (PIPA) in medical wards and intensive care units: a four-year retrospective analysis

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Background: Invasive pulmonary aspergillosis (IPA) outside the haematological ward, bears a troublesome diagnosis. We aimed to describe features of aspergillosis, through the criteria of “Putative Invasive Pulmonary Aspergillosis” (PIPA), introduced by Blot and colleagues in the Intensive Care Unit (ICU) and extending them into Medical Wards (MW)

Materials/methods: All patients with an Aspergillus spp. positive culture on low airways samples (BAL or BA) from 2012 to 2016 were retrospectively included in the study. Subjects with previous history of haematological diseases or IPA were excluded. The study population was divided into three groups (e.g. Proven diagnosis, Diagnosis of PIPA and Aspergillus spp. respiratory tract colonization).

Results: 78/80.9570 (0.09%) of admitted, fulfilled entry criteria. Overall Aspergillus spp. positivity on respiratory samples was 0.97/ every 1000 hospital admissions (4.94/1000/HA in the ICUs and 0.28/1000/HA in MWs, Figure 1). 52/78 (66,6%) had a diagnosis of PIPA: 69.2% of them in the ICU. The remaining (33.4%) were defined as colonized. Antifungal therapy was appropriate in 88.5% of subjects with PIPA and 37.5% of colonized (p<0.0001), confirmed comparing deads vs alives (p=0.001). In the univariate analysis patients with PIPA in the ICUs had more frequently COPD (p=0.018), sepsis or septic shock (p<0.0001), acute kidney injury (AKI, p=0.010), needed more surgery (p<0.0001), mechanic ventilation (MV, p<0.0001), vasopressors (p<0.0001), hemodialysis (p<0.0001), blood (p<0.0001) or platelets (p=0.043) transfusions. PIPA in MW had more often a history of smoke (p=0.0025), interstitial lung disease (p=0.035) and inhaled steroid therapy (p=0.008). Overall mortality within 21 days was 50%; 54.2% in ICU, 36.8% in MW (p=0.622). Factors associated to death in univariate analysis were: length of hospitalization (p=0.006), influenza (p=0.048), radiological pneumonia (p=0.042), liver transplant (p=0.048), AKI (p<0.0001), ARDS (p=0.019), sepsis and septic shock (p<0.0001).

Conclusions: We reported a lower incidence of PIPA in MWs compared to previous published data by Russo et al and Falcone et al. Furthermore, putative aspergillosis in ICUs had higher disease severity and needed more organ support than MWs cases: cases of PIPA in ICU and MW are emerging, despite that, trends are difficult to demonstrate given the problematic diagnosis.

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Salivary microbiota profiling for discrimination between individuals in forensic science
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Background: Many applications of forensic sciences require distinguishing individuals. Standard Short Tandem Repeat (STR) profiling can fail due to mixture or degradation of host-DNA, or in presence of monozygotic twins that are indistinguishable. Salivary microbiota represents an interesting alternative since bacterial DNA is protected by its circular conformation and robust cellular walls. Microbiota profiles could be used as a fingerprint for personal identification since it varies between individuals and remains stable over time. 16S rRNA metagenomics is affordable, actionable on low-DNA templates and compatible with legislation preventing sequencing of suspects’ DNA. In this longitudinal prospective study, we evaluate the ability of 16S rRNA metagenomics to discriminate individuals, including monozygotic twins, from salivary samples.

Materials/methods: Thirty pairs of healthy twins, confirmed monozygotic by STR profiling, are included with visits at recruitment and after 1, 12 and 13 months. A health questionnaire is submitted at each visit. Spit saliva is collected in 50ml tubes and DNA is extracted with the Nucleospin Soil kit [Macherey-Nagel]. Samples are attributed randomly to sequencing runs to prevent systematic batch effects. 16S rRNA libraries are prepared according to the V3V4 Illumina protocol and sequenced on MiSeq. Positive controls (ATCC-2002) and negative controls (extraction and PCR reagents) are included for each batch. Reads are processed into Amplicon Sequence Variants (ASVs) with DADA2 and classified by RDP against the EzBioCloud database.

Results: Inclusion and one-month follow-up samples were obtained from 30 pairs of volunteers, for which library preparation and sequencing are ongoing (21/120 sequenced, one pair from the same individual due to randomization). Read processing into ASVs increases the distance between unrelated samples compared to conventional Operational Taxonomic Units (OTUs) clustering (Figure). Once sampling and sequencing completed, we will compare intra versus inter-individual microbiota variation. A statistical model will be developed to express the support for the hypothesis that two samples belong to the same individual. A sub-study on a subset of samples will assess that these observations remain valid when sampling dry saliva on surfaces, a targeted case scenario for forensic applications.

Conclusions: Preliminary results on a limited number of samples confirm the “idiosyncrasy” of the saliva microbiota.

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Abstract 8685

**Enterobacter spp. infections: epidemiology and risk factors for resistance to third generation cephalosporins**

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**Background:** Third generation cephalosporin-resistant (TGC-R) *Enterobacteriacea* constitute WHO level 1 priority due to alarming increase in incidence. Suboptimal treatment translates to high mortality and costs. Epidemiological data from Central America is scarce.

**Materials/methods:** Observational, retrospective cohort study of patients with *Enterobacter* spp. infection in a tertiary care teaching hospital in San Jose, Costa Rica from 2014-2017. Only one episode per patient was recorded. Phenotypic analysis of the antibiogram (VITEK® 2, BioMérieux) was used to detect resistance to TGC. Clinical data collected and analyzed using T-test and Chi2 or Fisher’s when appropriate. ORs were calculated by multivariate logistic regression for binary outcomes; HRs for death using Cox regression.

**Results:** 1,842 samples were analyzed, with increasing incidence over time. *E. cloacae* represented 73% of samples. Isolates corresponded to respiratory samples (n=608, 33%), urine (n=497, 27%), surgical wound (n=387, 21%), peritoneal fluid (n=166, 9%), bloodstream (n=129, 7%), perianal abscess (n=18, 1%), CSF (n=13, 0.7%), bone (n=13, 0.7%) and pleural fluid (n=11, 0.6%). Male sex (60%) predominated. *Enterobacter* spp. infections were mainly of nosocomial origin (79%) with a strong positive correlation between hospital days and time to a positive culture. (rs=0.623, p<0.00001). Resistance to TGC increased from 25% in 2014 to 33.5% in 2017. Coinfection was noted in 38% of samples, most frequent *P. aeruginosa* (21%), *E. coli* (19%) and *K. pneumoniae* 18%. Patients diagnosed with respiratory (OR 2.6, CI 1.60-4.28, p=0.0001) and intraabdominal infections (OR 3.9, CI 2.63-5.76, p=0.0001) were more likely to develop resistance. Overall mortality was 32%, highest in males (69%) (p=0.0001) and the elderly. Hospital-acquired strains carry double mortality (OR 2.1, p=0.00001, CI 1.46-3.14). Resistant isolates denote higher risk of death (45%) than susceptible counterparts (27%) (OR 2.24, p=0.004, 1.70-2.95) HR for death were malignancy (HR 2, p=0.0001, 1.43-2.89) and renal disease (3.2, p=0.0001, 2.5-6.7).

**Conclusions:** *Enterobacter* spp. infections are predominantly nosocomial with mortality being highest in elderly men. Admission for intraabdominal and respiratory tract infections confer a higher risk for resistant strains. Renal disease triplicates the risk of death and solid malignancy doubles it. Antimicrobial stewardship, infection control and limiting indwelling catheters are critical measures to improve outcomes.

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Abstract 8686

Osteomyelitis in sickle cell adults: descriptive study in a high-income country
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Background: Sickle cell disease (SCD) mainly affects populations from sub-Saharan Africa and the Indian sub-continent. Osteomyelitis (OM) is one of the main infectious complications in SCD patients, with an estimated prevalence of between 12 and 18% in low-income countries, adults and children combined. There are few data on OM in SCD adults in high-income countries.

Materials/methods: This monocentric observational study included all patients followed in a reference centre who had at least one OM with microbiological documentation in adulthood. The objective was to characterize the clinical and microbiological profile of this complication.

Results: Seventeen patients were included (15/17 (88%) SS genotype, median age at diagnosis of OM 23 years, 7/17 (41%) women, 15/17 (88%) sub-Saharan origin), corresponding to a prevalence in our centre of 1.2% (17/1464). In 16/17 (94%) of the cases, the infection had started while the patients were in a high-income country. The most frequent locations were the lower limbs (9/17, 54%) with multifocal forms in 8/17 (40%) of cases. Microbiological documentation was obtained by bone sampling (5/17, 29%) or blood cultures (7/17, 42%). The most common germs found were non-typhi Salmonella (6/17, 35%) and Staphylococcus spp. (5/17, 29% including methicillin-sensitive Staphylococcus aureus (4/5) and Staphylococcus epidermidis (1/5)). Other rarer pathogens were also detected (Clostridium difficile, Pantoea agglomerans or Propionebacterium acnes).

Antibiotic therapy was systematic, with a median duration of 90 days, and 9/17 (75%) of patients required surgical debridement (sequestrectomy or drainage of Brodie’s abscess). At the last follow-up visit, 3 patients had relapsed or had persistent OM despite appropriate medical and surgical treatment.

Conclusions: The epidemiology of OM in SCD differs between low- and high-income countries: non-typhi Salmonella in Europe and the USA and Staphylococcus aureus in sub-Saharan Africa and the Middle East. Susceptibility factors in SCD patients include immunosuppression and bone or periosteal infarctions that are the bedrock of infection. Our study finds a lower prevalence and over-representation of Salmonella compared to low-income countries. The supposed entry point is digestive translocation, via parietal micro-infections. The evolution is generally favourable without relapse, even in the absence of surgical management.

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Abstract 8687

X-ray induced changes in substrate specificity of OXA-48

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Background: X-ray irradiation is widely used in diagnostic and therapeutic. To our knowledge, the effect of X-ray exposure was never evaluated on carbapenemase-producing Enterobacteriaceae (CPE). OXA-48, one of the most prevalent carbapenemase hydrolyzes penicillins and carbapenems, but not expanded-spectrum cephalosporins (ESC). Here we evaluated the effect of X-ray exposure on OXA-48 producing Enterobacteriaceae, in respect to ESC resistance selection.

Materials/methods: K. pneumoniae 14003, E. coli 109B1 and S. marcescens Sm1 were used in the study. The three isolates harbored a plasmidic blaOXA-48 gene. The bacteria were exposed to different doses of X-ray and plated on ceftazidime (4 X MICs) containing plates and on TSA plates in order to count the surviving bacteria. All the analyses were done in duplicate. Disc diffusion antibiograms and MIC determinations were used to assess phenotypical changes. Whole genome sequencing (WGS) was performed using an Illumina Miseq platform. Mutated blaOXA-48 genes were cloned and expressed in E. coli TOP10. OXA-48 mutants were purified and their kinetic parameters determined and compared with those of OXA-48. Structural analysis was also performed.

Results: In the three species the phenotypical changes were the same, an increase in the susceptibility for all the β-lactams except for ceftazidime, which showed a reduction in the susceptibility. The sequence analysis revealed mutations in OXA-48. In K. pneumoniae 14003 study 11 mutants were recovered, 10 of them with the mutation W157L and one with W157R. In E. coli 109B1 8 mutations were observed, W157R, L158P, W157R-L158F, G160C, G160D, G160S, P68S and L139R-A141V. While in S. marcescens Sm1 two mutations were observed F156S and W157R. Interestingly, almost all the mutations were located in the Ω loop of OXA-48. All the pTOPO(blaOXA-48-mutated) E. coli TOP10 presented increased MIC values for ceftazidime and reduced for imipenem. The kinetic parameters confirmed these results.

Conclusions: X-ray irradiation produced ceftazidime resistant mutants with decreased susceptibility for all the other β-lactams. W157, that is frequently mutated in OXA-48, correspond to an amino-acid that stabilizes the KCX motif that is important for the activity of the enzyme.

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Human transcriptomic response to vaccination with recombinant VSV expressing Ebola virus glycoprotein

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Background: rVSV-ZEBOV is a live-attenuated recombinant vesicular stomatitis virus vaccine expressing Zaire Ebolavirus glycoprotein G and is the first vaccine licensed against Ebolavirus disease. Here we studied the blood transcriptomic response upon administration of a single dose of vaccine.

Materials/methods: Whole blood RNA from 64 healthy volunteers, 51 vaccinated either with $10^7$ or $5 \times 10^7$ PFU of rVSV-ZEBOV and 13 injected with placebo, collected at different time points after vaccination, was analysed by targeted transcriptome sequencing. At each time point, differentially expressed genes (DEGs) were identified with edgeR, ranked by FDR, and used to find biological signatures assessing the activation of 346 blood transcription modules.

Results: Between baseline and day 1 after vaccination, 5,469 DEGs were detected. This number decreased over time: at day 28 no DEGs were detected. Functional analysis identified 145 different modules affected by vaccination. Innate immunity pathways were activated from day 1 to day 14. At days 2 and 3, neutrophil modules were downregulated and complement-related modules upregulated. T-cell and cell-cycle associated modules were upregulated at days 7 and 14, while at day 28 no modules remained activated. Correlation analysis of module activation with ZEBOV glycoprotein-specific antibody titres identified seven significant directly correlated modules at day 14 after vaccination, including two related to B cell activation.

Conclusions: Vaccination with rVSV-ZEBOV produced a significant modulation of gene expression over time. This live viral vector induced a strong and durable modulation of genes associated with innate response, with upregulation of T cell- and cell-cycle-associated genes at days 7 and 14. The activation of seven blood transcription modules at day 14 after vaccination could be correlated with the magnitude of antibody response against Ebola glycoprotein at day 28.

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Trimethoprim-sulfamethoxazole as de-escalation agent in bloodstream infections due to Enterobacter spp, Serratia marcescens and Citrobacter freundii

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Background: Enterobacter spp. Serratia marcescens and Citrobacter freundii (ESC group) are associated with higher antibiotic resistance rates because they are able to produce high levels of AmpC betalactamases in the presence of beta-lactams and select resistant mutants. Trimethoprim-sulfamethoxazole (TMP-SMZ) could be a useful option to de-escalate the empirical antibiotic treatment but there is little evidence of its efficacy and safety in the treatment of infections by this type of microorganisms. The aim of our study was to analyse the efficacy and safety profile of TMP-SMZ as de-escalation agent in bloodstream infections due to ESC-group microorganisms.

Materials/methods: this study included all patients over 18 years of age with ESC-group bacteraemia, collected and evaluated prospectively and consecutively in the University Hospital of Vigo between January 1, 2015 and December 31, 2017. They were classified in two groups: TMP-SMZ de-escalation group and no-switch group. We excluded patients with inadequate empirical treatment. De-escalation was defined as change empirical treatment to TMP-SMZ within 96 hours after index blood cultures were performed. Propensity score was calculated using a multivariable logistic regression model in which the dependent variable was a binary indicator of de-escalation strategy. The primary and secondary outcomes was 30-day all-cause mortality and 90-day recurrence of infection.

Results: During the study period we included 63 patients who met eligibility criteria (37 in TMP-SMZ group and 26 in no-switch group. Characteristics of both groups patients are shown in Table 1. Overexpression of AmpC betalactamase was present in 20 (32%) of ESC group isolates. Most frequent source of infection was urinary (39%), followed by intraabdominal (27%) and respiratory (16%). Betalactam+betalactam inhibitor was the first choice as empirical treatment (34%), followed by carbapenem (25%) and 3rd G cephalosporin (23%). In multivariate analysis adjusted by propensity score only septic shock (OR 4.22 [95% CI 1.55-23.35]) and urinary source (OR 0.36 [95% CI 0.18-0.74]) were associated with 30-day mortality.

Conclusions: TMP-SMZ could be a safe and effective option to de-escalate empirical antibiotic treatment in patients with ESC-group bloodstream infections.

<table>
<thead>
<tr>
<th></th>
<th>TMP-SMZ group (n=37)</th>
<th>No-switch group (n=26)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years [range]</td>
<td>65 [32-83]</td>
<td>61 [18-88]</td>
<td>0.23</td>
</tr>
<tr>
<td>Sex male, n (%)</td>
<td>19 (51)</td>
<td>16 (60)</td>
<td>0.55</td>
</tr>
<tr>
<td>Charlson Index&gt;2, n (%)</td>
<td>11 (30)</td>
<td>11 (42)</td>
<td>0.04</td>
</tr>
<tr>
<td>Urinary source, n (%)</td>
<td>33 (52)</td>
<td>159 (71)</td>
<td>0.002</td>
</tr>
<tr>
<td>Median hospital stay, days [range]</td>
<td>15 [11-77]</td>
<td>18 [5-44]</td>
<td>0.21</td>
</tr>
<tr>
<td>Septic shock, n (%)</td>
<td>5 (13)</td>
<td>8 (31)</td>
<td>0.03</td>
</tr>
<tr>
<td>30-day mortality, n (%)</td>
<td>3 (8)</td>
<td>5 (19)</td>
<td>0.04</td>
</tr>
<tr>
<td>90-day recurrence, n (%)</td>
<td>2 (5)</td>
<td>2 (8)</td>
<td>0.64</td>
</tr>
</tbody>
</table>

Table 1. Demographic, clinical and outcome characteristics of patients in TMP/SMZ vs no-switch group.

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Abstract 8694

Performance of EUCAST’s rapid antibiotic susceptibility testing on sterile body fluids in blood culture bottles
Stefan Zimmermann*1, Jasmin Kaur Jasuja1, Irene Burckhardt1

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Background: A shortened time to report is crucial for patients with symptoms of septicemia, but also patients with severe infections, e.g. joint infections or peritonitis, might benefit from RAST results. It was proven that inoculation of sterile body fluid in blood culture bottle (BC) is beneficial. EUCAST’S RAST has been evaluated for positive BCs and was further evaluated for its applicability on sterile body fluids in BCs to reduce time to report when using total lab automation (TLA). The objective of this study was to test the applicability of RAST on blood cultures and sterile body fluids in blood culture bottles and to evaluate its performance.

Materials/methods: Positive blood culture bottles (BACTEC™ Aerobic, BACTEC™ Anaerobic, BACTEC™ PED) inoculated with sterile body fluid from patients (e.g. joint fluid, ascites, etc.) were sub-cultured on standard agars and Mueller-Hinton agar. On latter, six antibiotic discs were added (cefoxitin, ampicillin, vancomycin, piperacillin/tazobactam, meropenem, ciprofloxacin). Subculture and streaking were done on a TLA. Subcultures were imaged after 6h and 23h. RAST plates were imaged and MALDI-TOF MS was performed after 6h and inhibition zones were measured using the TLA software and interpreted due to EUCAST RAST. MIC values were determined using VITEK2 panels for all isolates.

Results: In the time period of November 2018 to August 2019 Staphylococcus aureus (n=143), Enterococcus spp (n=72) and Escherichia coli (n=33) were the most frequent detected pathogens. Comparison of RAST and MIC results showed 5.6% of major errors for Enterococcus spp. in Ampicillin and 3.9% in Vancomycin. 7.7% of minor errors were found for E. coli. Very major errors were not found for any pathogen. 3 and 18 samples were found within area of technical uncertainty (ATU) in gram-positive cocci and E. coli, respectively. Category agreement between MIC values and RAST was 94.6%.

Conclusions: Applicability and performance of RAST from positive blood cultures became a routine method in our lab, but also use of sterile body fluid in blood culture bottle is promising and patients may benefit from the more rapid AST results. Further investigation of ATU is necessary and more EUCAST breakpoint, e.g. for koagulase-negative staphylococci are needed.

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Abstract 8697

Treatment outcome and clinical characteristics of patients with community-acquired pneumonia treated in an infectious disease intensive care unit

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Background: Patients admitted to an intensive care unit with a primary diagnosis of community-acquired pneumonia (CAP) have a high in-hospital mortality rate and often demand complex treatment. This study aimed to evaluate the clinical and epidemiological characteristics of patients with severe CAP, as well as to compare treatment outcomes in an infectious disease intensive care unit (IDICU) with the literature data on the outcome of patients with severe CAP in non-IDICUs.

Materials/methods: This research is a retrospective analysis of data collected on 305 patients treated in an IDICU with a primary diagnosis of CAP in the period between January 2016 and December 2018 in an 18 bed IDICU of University Hospital for Infectious Diseases in Zagreb, Croatia.

Results: The research included 305 patients (67% male) with CAP, with a median age of 63 years (IQR 50-71), median Charlson Comorbidity Index of 3 (IQR 2-5) and a median APACHE II score of 16 (IQR 13-22). The average length of hospital stay was 14 days. The most frequent infectious agents were the influenza virus and Streptococcus pneumoniae. CAP was complicated with sepsis in 15% of the cases. Almost 50% of the patients developed multiple organ failure (MOF). Around two thirds of the treated CAP patients required some method of intensive medicine life support, most commonly mechanical ventilation (67%), hemodialysis (34%) and VV ECMO (18%). The most common complications were ARDS, pleural effusion and pneumothorax. At discharge only 14% of the patients were completely independent, 30% had reduced functional ability and 27% of the discharged patients were completely dependent and immobile. The specific in-hospital mortality rate for CAP was 28%.

Conclusions: Patients treated for CAP in an IDICU have numerous comorbidities and severe forms of this disease regularly requiring ICU life support. The in-hospital mortality of CAP in IDICU was lower than the CAP mortality of patients with similar APACHE II score in non-IDICUs (32-55%) as stated in the literature. This could indicate that treatment outcome could depend on patient characteristics but also on the type of ICU.

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Abstracts 2020

Abstract 8697

Treatment outcome and clinical characteristics of patients with community-acquired pneumonia treated in an infectious disease intensive care unit

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Background: The use of polymyxins such as colistin has increased in Colombia due to the KPC dissemination in the country. Consequently, resistance to colistin is increasingly reported among KPC-producers. Resistance to polymyxin has been attributed to mobile colistin resistance (mcr) genes and chromosomal mutations. Among these mutations, the inactivation of the mgrB gene by the integration of an insertion sequence (IS) or its complete deletion is the most common mechanisms of polymyxin resistance in clinical isolates of Klebsiella pneumoniae (Kpn). Herein, we describe the mechanism of resistance to polymyxins in clinical isolates of carbapenem-resistant Kpn (CR-Kpn) from Colombia.

Materials/methods: Twenty-four CR-Kpn isolates resistant to polymyxin B (PMB) recovered in clinical institutions from six Colombian cities between 2009 and 2019 were analyzed. The minimum inhibitory concentration (MIC) for PMB was confirmed by broth macrodilution, and the presence of carbapenemases by qPCR. Illumina whole-genome sequencing (WGS) was performed to identify changes in the genes encoding for PhoP/PhoQ, PrmA/PrmB and MgrB associated with resistance to polymyxins.

Results: According to both EUCAST and CLSI 2019 breakpoints for colistin (resistance at MIC >2 mg/L, and ≥4 mg/L, respectively), polymyxin resistance was found among all studied isolates, with PMB MIC ranging from 4 to ≥16 mg/L. Most isolates (18/24) carried blaKPC-3 and belonged to ST258 (17/24); 6 isolates were KPC-2 producers and 1 carried blaNDM-1. Most of isolates carried a truncated mgrB gene, the common mutation was insertion at nucleotide position 74, explaining the PMB resistance; amino acid substitutions in the PmrA/PmrB system were found in 6/24 isolates; additional substitutions in PhoP/PhoQ or mcr genes were not identified. Table 1 summarizes the results obtained by WGS.

Conclusions: We found a clonal dissemination of polymyxin and carbapenem-resistant Kpn ST258 harboring blaKPC-3 in the last 10 years in Colombia. The main resistance mechanism identified was the insertional inactivation of the mgrB gene. Active surveillance is warranted to contain the dissemination of Kpn isolates with dual polymyxin and carbapenem resistance associated with very few therapeutic options left for treatment.

Table 1. Molecular characterization of polymyxins and carbapenem-resistant Kpn isolates.

<table>
<thead>
<tr>
<th>CITY</th>
<th>YEAR</th>
<th>ST</th>
<th>β-LACTAMASES</th>
<th>POLYMYXIN RESISTANCE MECHANISM</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 BOGOTA</td>
<td>2010, 2011, 2019</td>
<td>258</td>
<td>KPC-3, SHV-12, SHV-182, TEM-1, OXA-2</td>
<td>Truncated MgrB (5)</td>
</tr>
<tr>
<td>2 IBAGUE</td>
<td>2016, 2017</td>
<td>129</td>
<td>NDM-1, OXA-1, CTX-M-15</td>
<td>Truncated MgrB (2)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>258 (4)</td>
<td>KPC-2, SHV-161, SHV-182, TEM-1</td>
<td>Truncated MgrB, N105K, A246T, G256R (4)</td>
</tr>
<tr>
<td>1 NEIVA</td>
<td>2017</td>
<td>219</td>
<td>KPC-2, CTX-M-15, SHV-145, TEM-1</td>
<td>Truncated MgrB (1)</td>
</tr>
<tr>
<td>2 PASTO</td>
<td>2015, 2017</td>
<td>258</td>
<td>KPC-2, OXA-2, SHV-145, TEM-1/KPC-3</td>
<td>Truncated MgrB (2)</td>
</tr>
</tbody>
</table>

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Abstract 8701

Molecular epidemiology of carbapenem-resistant *Klebsiella pneumoniae* isolates in France 2018

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**Background:** *Klebsiella pneumoniae* is an important pathogen responsible of nosocomial infections. Carbapenem resistance in *K. pneumoniae* is mainly associated with acquired carbapenem-hydrolyzing β-lactamases. These β-lactamases can be serine-β-lactamases like Ambler class A enzymes (KPC) and class D oxacillinases (OXA-48) or class B Metallo-β-lactamases (NDM, IMP, and VIM). According to the latest results of the French National Reference Center in last years, the most prevalent carbapenemase was OXA-48. The aim of our study is to obtain epidemiological data on carbapenem-resistant *K. pneumoniae* clinical isolates recovered in France in 2018.

**Materials/methods:** We performed genetic characterization of carbapenem-resistant *K. pneumoniae* strains by analysing WGS of 689 clinical isolates collected from different regions of France. Isolates were processed via Illumina (Next500, 2X150-bp) and Illumina reads de novo assemblies were performed using CLC Genomics Workbench v12. Antibiotic resistance gene determination, Multi-locus sequence typing, plasmid analysis and phylogenetic studies were done using software available at the Center for genomic epidemiology. Plasmids were extracted using Kieser method for the most prevalent STs.

**Results:** The most prevalent carbapenemase was OXA-48 (58% of presence in the isolates) follow by NDM-1 (16% of presence in the isolates) and OXA-48 like (9% of presence in the isolates). 150 different STs were observed with the ST 307 being the most prevalent one (106 isolates), followed by ST 147 (64 isolates), ST 11 (56 isolates) and ST 405 (40 isolates) and ST 101 (26 isolates). All the isolates belonging to the ST 405 were OXA-48 producers, and all possessed the prototypical IncL plasmid. These isolates came from all over the country, suggesting the dissemination of a high risk clone. For the other STs, the prevalence of the different carbapenemases was variable. For ST307, 69% produced OXA-48-like and 23% NDM-like, ST147 expressed mostly NDM (61%).

**Conclusions:** In our study the most prevalent carbapenemase was OXA-48. The isolates belonging to the ST 405 were all OXA-48 producers, what indicate a strong relation between the ST 405 and the presence of blaOXA-48 gene. On the other hand, the carbapenem-resistant *K. pneumoniae* belonging to ST 147 harbored in most case a NDM-like gene.

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Abstract 8702

Aspergillosis complicating severe influenza in intensive care unit patients: a retrospective case-control study

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Background: Invasive pulmonary aspergillosis (IPA) has been recognized as a complication of influenza infection even in immunocompetent patients. We aimed to understand the incidence of IPA among critically ill patients with influenza infection over multiple seasons.

Materials/methods: A retrospective case-control study was conducted in a single center in Chicago. Data was collected over 9 seasons (March 2009-March 2018) from adult patients admitted to the ICU at a large urban tertiary care center with influenza. Patients were included if they had a positive influenza PCR test, were ≥ 18 years, were admitted to the ICU, and developed IPA. IPA was defined per both the EORTC/MSG criteria as well as the revised AspICU criteria. A random cohort of 114 influenza positive patients admitted to the ICU who did not develop IPA were also identified for comparison. Descriptive statistics were calculated. In univariable analysis, we compared categorical variables by Fisher’s exact test and Chi-square test and continuous variables by Student’s t-test where appropriate.

Results: A total of 345 patients with influenza were admitted to the ICU over the study period. The overall rate of IPA in the study population was low at 1.7% (6/345). Factors associated with development of IPA in those with severe influenza pneumonia were hematological malignancy (p=0.03), history of hematopoietic stem cell transplant (p=0.00), non-transplant related immunosuppression (p=0.00), and history of solid organ malignancy (p=0.01). There was no significant difference in outcomes such as overall length of stay, need for mechanical ventilation or renal replacement therapy, and death. Other coinfections were common with incidences of 46.7% [bacterial], 11.7% [viral], and 13.3% [non-aspergillosis fungi].

Conclusions: The incidence of IPA was significantly lower (1.7%) in our study over 9 influenza seasons than has been reported in similar studies. Malignancy and immunosuppression were risk factors strongly associated with the development of IPA. IPA did not significantly predict morbidity and mortality among critically ill influenza patients.

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Abstract 8703

The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS): results of antimicrobial prescribing at Ghana’s National Referral Centre

Mariyam Mirfenderesky¹**, Joyce Mahungu², Asiwome Aggor³, Ann Versporten⁴, Ines Pauwels⁴, Herman Goossens⁴, Daniel Ankrah³

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Abstract third-party references: Common Wealth Association for Antimicrobial Stewardship, Tropical Health Education Trust, Commonwealth Pharmacy Association, biomerieux

Background: The Korle Bu Teaching Hospital is a 2000 bedded tertiary hospital in Accra, and Ghana’s national referral centre. In February 2019 a health partnership was formed with a UK institution in order to build professional capacity, and develop antimicrobial stewardship and infection prevention and control programmes. The first comprehensive surveillance of antimicrobial use at the institution was undertaken to establish a baseline, and identify required stewardship interventions.

Materials/methods: A standardized method for surveillance of antimicrobial use in hospitals [www.global-pps.com] was conducted over three days by 15 pharmacy professionals in June 2019. The survey included all inpatients receiving an antimicrobial at 8am on the day of the PPS. Data included details on antimicrobial agents, reasons and indications for treatment and a set of quality indicators.

Results: 988 patients were admitted to 69 wards. Antimicrobial prevalence was 53%, which varied between ward type [46% in adult medical, 57% in adult surgical, 69% in paediatric medical, 50% in paediatric surgical and 48% in neonatal units]. Out of all antimicrobials prescribed, 41.2% were for community acquired infections and 14.9% for health-care associated infections. The main indications for prescribing were prophylaxis for obstetric and gynaecological reasons [20.2%], sepsis [9.5%] and pneumonia [9.2%].

Systemic antibiotics accounted for 83.5%, of which amoxicillin with beta-lactam inhibitor [17.5%], metronidazole [11.8%] and ceftriaxone [11.5%] were most often prescribed. Surgical prophylaxis accounted for 33.0% of all antimicrobial use of which amoxicillin with beta-lactam inhibitor [33.3%], cefuroxime [19.9%] and metronidazole [18.0%] were most often prescribed; and overall 78% were prescribed >1 day. Guidelines were missing in 25% of antibiotic prescriptions. Guideline compliance was 89%. Stop/review dates were completed in 33.4% with a documented reason recorded in 53% of prescriptions.

Conclusions: The Global-PPS is an important tool used to establish baseline prescribing, and identify areas for improvement. Moving forward, interventions to decrease the duration of surgical prophylaxis, with a focus on obstetrics and gynaecology, guideline revision and development, and tools to improve quality indicators are identified as initial targets to improve antimicrobial prescribing at this institution.

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Changing seroprevalence of viral diseases among young adults in a tertiary care educational university hospital? Experience with 1993 cases

Meltem Isikgöz Tasbakan¹, Deniz Akyol*¹, Aysin Zeytinoglu¹, Husnu Pullukcu¹

¹Ege University Medical Faculty Hospital, Izmir, Turkey

Background: The risk of vaccine-preventable and other transmissible infections for health-care workers and also for medical students is high due to direct contact with patients. Thus, screening and immunization policies of medical students should be performed regularly in order to assess their immunity and serostatus against relevant viral diseases. Herein, we aimed to evaluate the serologic test results of medical students retrospectively in a tertiary-care educational university hospital.

Materials/methods: The study included students who were attending medical school between 2008-2019. Serologic test results concerning hepatitis (A, B and C), measles, mumps, rubella, varicella-zoster and HIV were reviewed retrospectively from medical records of students including all preclinical and clinical semesters. Anti-HAV IgG, HBsAg, anti-HBcIgG, anti-HBs, anti-HCV, measles IgG, mumps IgG, rubella IgG, varicella-zoster IgG and anti-HIV were studied by ELISA method.

Results: There were a total of 1993 students (mean age 22.20 ± 2.43 years and 51.48% female). Virus-specific immunity rates were: rubella 96.15% in 1223 students, varicella-zoster 90.42% in 595 students, mumps 82% in 750 students, measles 72.95% in 880 students, anti-HBs 92.32% (vaccinated) in 1654 students, anti-HCV 0.20% in 1480 students, hepatitis A 30.8% in 1662 students and anti-HIV 0.09% in 1024 students.

Conclusions: Our results indicate that approximately two-third of the medical students were seronegative for hepatitis A and seropositivity rates for mumps and measles were not satisfactory especially for Turkey considering endemicity. Therefore, medical students in a health care set up should undergo vaccination against hepatitis A, B, mumps and measles after prevaccination immunity screening.

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Detection of hepatitis B virus reactivation and near complete sequencing of the viral genome by high-throughput sequencing in a kidney transplant

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Abstract 8712

**Background:** Hepatitis B virus (HBV) serology indicating past resolved infection is often associated with HBV DNA persistence as covalently closed circular DNA in hepatocyte nuclei. This allows viral reactivation in case of severe immunosuppression. Renal transplant recipients constitute a group at high risk of such HBV reactivation. Next-generation sequencing is gradually emerging in routine clinical diagnosis. Here, we describe the obtention of a near complete HBV genome using this technology directly from the plasma of a renal transplant presenting HBV reactivation.

**Materials/methods:** HBV serology was performed with Abbott Architect assays, Abbott Diagnostics, Chicago, IL, USA. HBV viral load was performed with the Veris DxN Beckman-Coulter Diagnostics assay, Brea, CA, USA. Next-generation sequencing used Illumina technology on MiSeq with the paired-end protocol (Nextera XT protocol, Illumina Inc, San Diego, CA, USA).

**Results:** HBV reactivation was diagnosed in a 73-year-old male patient from Madagascar, in France since 1975. He received a kidney transplant in August 2016 and was subsequently treated with azathioprine/prednisone/ciclosporin A/thymoglobulin. Pre-transplant serology showed HBsAg-negativity/anti-HBs-negativity/anti-HBc-positivity, indicating past resolved infection. In February 2019, during routine post-transplant follow-up, HBV serology showed HBsAg-positivity/anti-HBs-negativity/anti-HBc-positivity. Viral load was 42480000 IU/mL. The patient was clinically asymptomatic, without liver cytolysis. Quasi-complete genome sequencing was performed directly from the plasma DNA extract by next-generation sequencing. The genome obtained has a size of 3182 nucleotides and mean coverage (± standard deviation) is 753±269 reads/nucleotide position (min-max: 155-1200). Mean nucleotide diversity is 0.4±2.1% (0.0-45.8). Viral genotype is D2. HBsAg amino acid substitutions P120Q/L (10% of the quasispecies), P142L (40%), R122K (59%), and G145R (100%) described as altering HBsAg antigenicity and associated with immune escape, and a drug resistance-associated substitution in reverse transcriptase (I169L) were observed. The patient was treated with Entecavir 0.15 mg/day.

**Conclusions:** This case demonstrates the importance of systematic monitoring of HBV reactivation in renal transplant patients with a serologic profile indicating past resolved hepatitis B, and the value of next-generation sequencing in routine diagnosis to characterize more comprehensively the viruses involved in these reactivations.

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Perioperative administration of cefepime-daptomycin combination during prosthetic joint replacement is associated with high bone and synovial concentrations

Eric Senneville1, Olivier Robineau2, Benoit Brunschweiler3, Yves Herpe4, Beltrand Eric5, Antoine Grillon6, Cédric Joseph3, Blondiaux Nicolas6, François Jehl7

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Background: It is recommended to start the administration of broad-spectrum antibiotics during prosthesis replacement for periprosthetic joint infection (PJI) peroperatively and to continue the treatment until the samples culture results are available. However, data demonstrating that antibiotics are present in the surgical site at concentrations exceeding the MICs of usual bacteria at the moment the new prosthesis is inserted are lacking.

Materials/methods: We conducted a prospective pilot study in two national referent centres for bone and joint infections in France (Lille-Tourcoing and Amiens) between January and August 2017. Patients with PJI operated with one or two-stage replacement during which cefepime-daptomycin combination (2d q8h and 10mg/kg, respectively) administered intravenously as peroperative empirical antibiotic treatment were included, provided they had given an informed written consent. Bone and synovial biopsies were taken just before the insertion of the new prosthesis and were frozen before grouped shipment to a central laboratory for determination of the tissue concentrations of each antibiotic. Serum concentrations of each antibiotic were also assessed at the same time.

Results: Eighteen patients of mean age 67.83 ±12.4 years with PJIs (7 total hip and 11 total knee prosthesis) were included. Surgical interventions consisted in one/two-stage-replacement in 11/7 cases. Microbiology was dominated by Staphylococcus spp. (n=9, including 8 coagulase negative staphylococci) and Gram negative rods (n=6, including 2 E. coli and 2 E. aerogenes). Cultures were sterile in 4 cases. The mean delay between the end of the intravenous administration of cefepime and daptomycin and intraoperative sampling was, respectively 37.7±16.6 and 34.5±16.9 mn. Blood and synovial/bone concentration values were respectively, 39.6±25.9 mg/L and 14.4±15.5, 13.7±18.5 mcg/g of tissue for cefepime and 96.2±33.5 mg/L and 15.5±6.5, 12.5±16.5 mcg/g for daptomycin. Median MIC of cefepime for Gram negative rods was 1mg/L and that of daptomycin for Gram positive cocci was 0.38mg/L.

Conclusions: The present study suggests that cefepime-daptomycin combination administered peroperatively during one or two-stage replacement in patients with PJIs is associated with surgical site, including bone, concentrations well above the MICs of usual pathogens.

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Antimicrobial susceptibility testing by MALDI-TOF MS of lipids determines true MICs in six hours
Matthew Sorensen1, Erik Nilsson1, Francesca Gardner1, Salma Ramadan1, David Goodlett2, Robert Ernst*2
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Background: Accelerating antimicrobial susceptibility testing [AST] is recognized as needed for improved infectious disease outcomes. Regardless, any AST test's results must be useful to clinicians. In particular, there is no good substitute for minimum inhibitory concentration (MIC), which is often critical to infectious disease diagnosis and treatment.

We have developed a rapid AST test that determines true MICs via MALDI-TOF MS of deuterium-labeled membrane lipids. This highly sensitive measurement of growth allows accelerated determination of MICs.

Materials/methods: Broth dilution AST was performed on Gram-negative and -positive bacterial species, including ESKAPE pathogens, using both custom and standard [Sensititre, ThermoFisher] microdilution plates, with growth media containing up to 10% deuterium oxide (D2O). After six hours, incorporation of deuterium to membrane lipids was measured by MALDI-TOF MS in negative ion mode using norharmane matrix.

Results: Lipids from the initial inoculum have hydrogen with the natural isotopic distribution. However, bacteria growing in D2O-containing media produce lipids enriched in deuterium, which exhibit a mass shift detected by MALDI-TOF MS, allowing growth to be sensitively determined.

As shown in Figure 1, Escherichia coli YD626 was transfected with the mcr-1 plasmid, conferring colistin resistance. Transfected and WT YD626 isolates were grown in microdilution plates, and MALDI spectra collected, as described above. For each concentration, growth was estimated as the ratio of deuterium-labeled to -unlabeled peaks. As expected, mcr-1 conferred colistin resistance to YD626: growth was detected at 2.0 µg/ml with mcr-1, four times higher than without mcr-1. Additional bacterial species have been successfully evaluated against various antimicrobials covering most of the major antimicrobial classes.

Conclusions: We have demonstrated a new, rapid AST that can use existing AST microtiter plates and media. Our novel method thus accelerates AST testing, while retaining proven methods and materials. AST by MALDI-TOF MS detection of deuterium incorporation into lipids during growth therefore promises fast, practical, and credible AST.

Figure 1: Deuterium incorporated into lipids during growth shows that colistin-resistant E. coli has an MIC four time higher than colistin-susceptible E. coli.

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Abstract 8721

Computerised registry as a potential tool for surveillance and management of complex bone and joint infections in France

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Abstract third-party references: Scientific Council for Complex Bone and Joint Infections Referral Centers

Background: The French registry for complex bone and joint infections (BJI) was created in 2012 in order to facilitate a homogeneous management of patients presented for multidisciplinary advice in referral centers for BJI, to monitor their activity and to produce epidemiological data. We aimed here to present the genesis and characteristics of this national registry and provide the analysis of its data quality.

Materials/methods: A centralized online secured database gathering the electronic case report forms (eCRF) was filled for every patient presented in multidisciplinary meetings (MM) among the 24 French referral centers. Metrics of this registry were described from 2012 to 2016. Data quality was assessed by comparing essential items from the registry with a controlled dataset extracted from medical charts of a random sample of patients from each center. Internal completeness and consistency were calculated.

Results: From 2012 to 2016, 30,607 presentations in MM were recorded corresponding to 17,748 individual patients, [mean age: 62.1 years, 61.8 % males]. BJI was considered as complex for 63% of cases, and 44% had prosthetic joint infections. The controlled dataset, available for 19 centers, included 283 patients. Global consistency and completeness were estimated at 88.2% and 88.9% respectively considering missing items in the eCRFs as negative results.

Conclusions: This national registry is one of the largest prospective databases on BJI and its acceptable data quality parameters allow further use for epidemiological purposes.

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Abstract 8722

**Cabotegravir and bictegravir placental transfers in ex vivo human cotyledon perfusion**

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**Background:** Data on placental transfer is lacking for the most recent HIV integrase inhibitors (INI), bictegravir and cabotegravir. They will inevitably be used in the coming years by pregnant women on antiretroviral therapy, thereby potentially exposing fetuses in utero, without safety data. Our objective was to determine the placental transfer of bictegravir and cabotegravir in the ex vivo human cotyledon perfusion model.

**Materials/methods:** Maternal-to-fetal transfer across the term human placenta was investigated using the open-circuit ex-vivo dually perfused cotyledon model. Cabotegravir or bictegravir was added to a maternal perfusate containing 2 g/liter of human albumin and antipyrine, a marker to validate the cotyledon’s viability. INI tested concentrations were chosen close to post-dose plasma C24h. INI maternal and fetal concentrations were determined using UPLC-MS/MS (LOQ < 5 ng/mL). Median (IQR25-75%) of values are presented.

**Results:** 5 experiments were validated for cabotegravir and 6 for bictegravir. Results are presented in the Table. After 90 min of perfusion, the maternal-to-fetal ratio was 5% (interquartile range, IQR : 5-16) for cabotegravir and 7% (IQR : 6-9.5) for bictegravir. The median cotyledon accumulation index was 4% (IQR : 3-5) for cabotegravir and 4% (IQR : 3-5) for bictegravir.

**Conclusions:** Placental transfer of both cabotegravir and bictegravir was similar and low. This may limit the potential for fetal toxicities, but also be a limit to their usefulness at the time of labor and delivery to reduce the risk of vertical HIV transmission. The safety and efficacy of these new INI in pregnancy require more investigation.

Table. Maternal-to-fetal transfer of cabotegravir and bictegravir in the open-circuit ex-vivo dually perfused human cotyledon model after 90 min of perfusion

<table>
<thead>
<tr>
<th></th>
<th>N experiments</th>
<th>Maternal Concentration (ng/ml)*</th>
<th>Fetal Concentration (ng/ml)*</th>
<th>Fetal-to-maternal ratio (%)*</th>
<th>Clearance Index*</th>
<th>Cotyledon Accumulation index %*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cabotegravir</strong></td>
<td>5</td>
<td>550 (344-788)</td>
<td>48 (37-54)</td>
<td>5% (5%-16%)</td>
<td>22% (19%-20%)</td>
<td>10% (2% -21%)</td>
</tr>
<tr>
<td><strong>Bictegravir</strong></td>
<td>6</td>
<td>1850 (1455-1960)</td>
<td>128 (112-142)</td>
<td>7% (6%-9.5%)</td>
<td>21% (17%-29%)</td>
<td>4% (3%-5%)</td>
</tr>
</tbody>
</table>

*Median (IQR25-75%)

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Abstract 8726

**Clostridioides difficile infection in haematological patients: a 14-year experience**

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**Background:** The hematological population is particularly susceptible to Clostridioides difficile infection (CDI), however little is known about specific risk factors and markers of recurrence and poor evolution. Our objective was precisely to assess the epidemiological, clinical characteristics, and outcome of CDI in hematological patients during a 14 year period in a large teaching hospital.

**Materials/methods:** From January 2006 to September 2019 (ongoing study), all episodes of CDI patients aged > 2 years with hematological disease were prospectively collected in a database (cases). For clinical assessment, all cases were reviewed and 140 controls (hematological patients with C. difficile-negative diarrhea) were randomly selected. Epidemiological and clinical data were collected by reviewing hospital medical records.

**Results:** During the study period, the number of CDI episodes in hematological patients was 162. Patients' median age was 56.0 and 53.7% were male. The most common hematological disease was acute myeloid leukemia (30.9%), followed by Non-Hodgkin lymphoma (25.9%) and acute lymphoid leukemia (9.3%). When compared to controls, independent risk factors for CDI were previous antibiotics (94.4% vs 69.9%; p<0.001) and proton pump inhibitors (PPIs) (60.7% vs 39.3%; p=0.007). Cases had a higher comorbidity index (3.0 (IQR 2-6) vs 2.0 (IQR 2-2); p<0.001), more days of diarrhea (3 [IQR 0.5-7] vs 2 [IQR 1-4]), more abdominal pain (39.1% vs 21.6% p=0.004) and more abdominal distension (11.8% vs 0.0%; p<0.001). Severe CDI accounted for 10.5% and severe complicated CDI for 13.6% of the episodes. Recurrence rate was 14.2% and treatment failure 4.0%. Independent risk factors for R-CDI were female sex (p=0.019) and chemotherapy (p=0.020). Overall 30-day mortality was 5.5% and mortality attributable to CDI was 1.2%.

**Conclusions:** Despite the high susceptibility of hematological patients, the majority of CDI episodes were non severe and mortality due to CDI was low. Independent risk factors for CDI in this population were antibiotics and PPIs and risk factors for R-CDI were female sex and chemotherapy. Diarrhea due to CDI lasted longer, caused more pain and abdominal distension than diarrhea due to other causes in the hematologic population. Mortality rates were similar to those of the hematological population without CDI.

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Abstract 8729

Differences in clinical characteristics and prognosis of patients with AmpC-producing Enterobacteriaceae versus Escherichia coli bloodstream infection

Adrian Sousa*, María Teresa Pérez-Rodríguez, Milagros Suárez, Patricia Diéguez, Olalla Lima, Andrea Cabaleiro, Anton Ótero, Francisco Vasallo Vidal, Rebeca Longueira, Ana López-Domínguez, Andrés Nodar, Manuel Crespo

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Background: Enterobacter spp, Serratia marcescens and Citrobacter freundii (ESC group) present common characteristics that differentiate them from other Enterobacteriaceae: they are able to produce high levels of AmpC betalactamases in the presence of beta-lactams, trend to select resistant mutants, difficulties in antibiotic treatment and greater morbidity and mortality. The aim of our study was to analyze and compare the clinical, epidemiological and prognostic characteristics of bacteremias produced by ESC group vs. those produced by Escherichia coli.

Materials/methods: This study included all patients over 18 years of age with GNB bacteremia, collected and evaluated prospectively and consecutively in the University Hospital of Vigo between January 1, 2015 and December 31, 2017. They were classified in two groups: Escherichia coli vs ESC bloodstream infections group. The primary outcome was 30-day all-cause mortality.

Results: During the study period we included 287 patients who met eligibility criteria (224 in E.coli group and 63 in ESC group: 37 Enterobacter spp, 16 Serratia marcescens and 10 Citrobacter freundii). Characteristics of both groups patients are shown in Table 1. Overexpression of AmpC betalactamase was present in 20 (32%) of ESC group isolates. Most frequent source of infection was urinary (49%), followed by intraabdominal (25%) and respiratory (10%). Betalactam+betalactam inhibitor was the first choice as empirical treatment (34%), followed by carbapenem (25%) and 3rd G cephalosporin (23%). Inadequate empirical treatment was higher in ESC group [44% vs 22%; p=0.03]. All-cause 30-day mortality was significantly higher in ESC group. In multivariate analysis only septic shock [OR 6.02 [95% CI 1.55-23.35]], Charlson Index>2 [OR 2.50 [95% CI 1.31-4.79]] and urinary source [OR 0.36 [95% CI 0.18-0.74]] were associated with 30-day mortality.

Conclusions: Bloodstream infections due to ESC group affected patients with more comorbidities, cause longer hospital stays, more inadequate empirical treatments and are associated with greater mortality. The only 30-day mortality associated factors were septic shock, higher Charlson Index and a urinary source of infection.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ESC group (n=63)</th>
<th>E. coli group (n=224)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years [range]</td>
<td>72 [38-85]</td>
<td>61 [18-88]</td>
<td>0.03</td>
</tr>
<tr>
<td>Sex male, n (%)</td>
<td>35 (55)</td>
<td>135 (60)</td>
<td>0.55</td>
</tr>
<tr>
<td>Charlson index&gt;2, n (%)</td>
<td>35 (56)</td>
<td>99 (44)</td>
<td>0.02</td>
</tr>
<tr>
<td>Nosocomial acquisition, n (%)</td>
<td>46 (73)</td>
<td>80 (36)</td>
<td>0.001</td>
</tr>
<tr>
<td>Urinary source, n (%)</td>
<td>33 (52)</td>
<td>159 (71)</td>
<td>0.002</td>
</tr>
<tr>
<td>Median hospital stay, days [range]</td>
<td>28 [11-77]</td>
<td>14 [5-44]</td>
<td>0.001</td>
</tr>
<tr>
<td>Previous ICU stay, n (%)</td>
<td>25 (40)</td>
<td>58 (26)</td>
<td>0.002</td>
</tr>
<tr>
<td>Previous antibiotic treatment, n (%)</td>
<td>29 (46)</td>
<td>56 (25)</td>
<td>0.001</td>
</tr>
<tr>
<td>Septic shock, n (%)</td>
<td>21 (34)</td>
<td>44 (20)</td>
<td>0.03</td>
</tr>
<tr>
<td>30-day mortality, n (%)</td>
<td>16 (25)</td>
<td>29 (13)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Table 1. Demographic, clinical and outcome characteristics of patients in ESC vs E.coli group.

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Epidemic *Clostridioides difficile* isolates are significantly more lethal and persist at higher rates than non-epidemic isolates in hamsters following vancomycin treatment

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**Background:** Previous reports have suggested that epidemic *Clostridioides difficile* ribotypes are hypervirulent and that their characteristics can dramatically impact clinical disease. Some evidence has shown that epidemic ribotypes have a higher rate of sporulation than non-epidemic isolates, which is thought play a role in the persistence of *C. difficile* in recurrent infections. Support for this association has largely been investigated *in vitro*, but not *in vivo*. Therefore, studies were conducted in a hamster model of *C. difficile* infection to evaluate the virulence of 13 epidemic and non-epidemic isolates as well as their abilities to persist following vancomycin treatment in the model.

**Materials/methods:** Median lethal dose (LD$_{50}$) studies involved orally infecting male Golden Syrian hamsters with 6 epidemic or 7 non-epidemic isolates in a titer range of 800 to 30,000 spores per isolate, and persistent infection studies involved orally infecting hamsters with ~4.7 log$_{10}$ spores of 2 vancomycin-sensitive epidemic or non-epidemic isolates. Clindamycin (10 mg/kg) was SC administered 24 hours after infection, and for persistent infection studies, vancomycin (20 mg/kg) was orally administered once daily for 5 days starting 18 hours after dosing clindamycin. Feces were daily collected from sterile cages to determine CFU/spore and toxin titers, and survival census was recorded up to 11 days post-infection.

**Results:** Mean LD$_{50}$ values in the hamster CDI model were 3.56 and 3.97 log$_{10}$ spores for epidemic and non-epidemic isolates, respectively, and these values were determined to be significantly different by the extra sum-of-squares F test ($p \leq 0.05$). Mean toxin titers associated with feces collected from epidemic infected hamsters had up to 2-4 times more Toxin A and B within 4 days of infection as compared to hamsters infected with non-epidemic isolates. Epidemic isolates also had increased persistence in hamsters with 3 times more spores remaining in their feces at the end of vancomycin treatment as compared to non-epidemic infected hamsters.

**Conclusions:** These results suggest that epidemic *C. difficile* isolates can persist in the gastrointestinal tract at a higher rate than non-epidemic isolates following treatment, which can lead to higher rates of severe recurrent infections in at risk patients.

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Abstract 8731

**Genetic antimicrobial resistance determinants found in Escherichia coli and other environmental microorganisms isolated from raw vegetables expended in Ibarra, Ecuador**

Alejandra Plasencia1, Alejandra Pinto1, Santiago Salazar1, Valeria Olmedo1, Pedro Barba*1

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**Background:** Antimicrobial resistance has a great concern worldwide. The dynamic of arise and spread of resistance genes must be identified in environmental bacteria to understand its possible implication in clinic.

**Materials/methods:** Six vegetables products were sampled by triplicate in three popular markets in Ibarra – Ecuador (tomato, coriander, parsley, lettuce, celery and pepper). All samples were filtered and cultivated on 3 μg/mL ceftriaxone supplemented MacConkey agar. *Escherichia coli* type- and nontype-colonies were picked out. ESBL doble disc synergy test were performed in all recovered isolates. Specie identity was achieved by MALDI-TOF. *bla_CTX,* *bla_SHV,* *bla_TEM,* *bla_KPC,* *bla_NDM* and *mcr-1* resistance genes variants were identified by PCR and sanger sequencing.

**Results:** 54 vegetables samples were included in the study, 9 of each class. Third generation cephalosporin (3GC) resistant bacteria were observed in 36/54 samples (67%). 54 isolates were recovered. *Acinetobacter calcoaceticus* and *E. coli* were the mayor species identified (23/54 and 20/54 isolates, respectively). *Achromobacter spanius, Rahnella aquatilis* and various species of *Pseudomonas* genera also were found. ESBL phenotypic production was identified in 29 isolates (14/29 isolates were *E. coli*). 6/29 and 4/29 ESBL isolates were *Rahnella aquatilis* and *Achromobacter spanius*, respectively. Ten isolates show the presence of ESBL genes [seven *E. coli* isolates]. The mayor ESBL variant found was *bla_CTX-M-55* [four isolates], following of *bla_CTX-M-65* [two isolates] and *bla_CTX-M-8* [two isolates]. Two isolates showed co-presence of *bla_CTX-M-55* and *bla_CTX-M-65*. Three *Achromobacter spanius* isolates and two *Rahnella aquatilis* showed *bla_KPC*. Two non-*E. coli* isolates also presented *bla_NDM* and *bla_MCR* variants. Two *E. coli* isolates showed the presence of *mcr-1.1*. This variant was also found in *Acinetobacter calcoaceticus* (4 isolates) and *Achromobacter spanius* (3 isolates), and *mcr-1.3* variant was found in *Rahnella aquatilis* (two isolates).

**Conclusions:** This study prove the presence of 3GC resistant microorganism in vegetables spending in Ibarra. *bla_CTX-M-55* and *bla_CTX-M-65* was the mayor ESBL genes found proving the success of this variants in the environment. The presence of *bla_CTX-M-55* and *mcr-1* resistance genes in environmental species alerts us to the importance of environmental resistome study to best antimicrobial resistant dynamics understanding and its implication in the clinic.

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Abstract 8739

**Bacteriological profile of urinary tract infection in a rural area in Uganda**

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**Background:** Urinary tract infections (UTIs) are a frequent cause of infection that are usually managed with broad-spectrum empirical treatments favoring the emergence of antimicrobial resistance. This problem is accentuated in rural areas in developing countries with low accessibility to medicines and lack of a microbiological diagnosis. The aim of this study was to investigate the etiology and antimicrobial susceptibility in UTIs in a rural hospital in northern Uganda.

**Materials/methods:** Prospective study conducted at the Saint Joseph Kitgum hospital (Uganda) between April-June 2019, which includes 139 patients with suspected UTI and who presented leukocyturia. Urine samples were cultured quantitatively according to accepted laboratory procedures. All microorganisms isolated in Uganda were subsequently identified in Spain by MALDI-TOF mass spectrometry. In the field, antibiotic susceptibility was determined for all isolates using the Kirby–Bauer disk diffusion method, according to EUCAST guidelines, and these results were confirmed in Spain using the Becton Dickinson Phoenix M50 device.

**Results:** A total of 102 microorganisms were isolated, of which 94 showed more than $1 \times 10^5$ colony forming units/ml. Two organisms were isolated in three patients. The microorganisms identified were: *Staphilococcus* spp (n=34), *Escherichia coli* (n=28), *Klebsiella pneumoniae* (n=2), *Enterobacter cloacae* (n=2), *Enterococcus* spp (n=21) [ *E. faecalis* (16), *E. faecium* (4), *E. hirae* (1)], *Streptococcus* spp (n=6), *Pseudoglutamicibacter cumminsi* (n=2), *Acinetobacter baumanii* (n=2), *A. junii* (n=1), *Corynebacterium amycolatum* (n=1), *C. coyleae* (n=2) and *Pseudomonas putida* (n=1). High resistance to amoxicillin (66.2%) and ciprofloxacin (44.6%) was found. Nitrofurantoin (9.6%) and Imipenem (2.2%) were the antibiotics with lowest resistance. In 19 of the gram-negative bacteria, high resistance to third generation cephalosporins was found. The resistances obtained in Uganda and Spain have similar values (deviation between 2 and 6%) except in the case of ciprofloxacin (30%).

**Conclusions:** Because of the increased development of resistance, new strategies are needed for the treatment of UTI in rural areas of developing countries. Bacteriological cultures make antibiotic treatment for UTI more specifically and thus more effectively. We found significant levels of antibiotic resistance for the First line of treatment of Uganda (amoxicillin and ciprofloxacin). It is recommended to start using antibiotics such as nitrofurantoin.

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Leptospirosis in hospitalised patients in Ambatondrazaka, Madagascar: incident cases and exposure factors

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Abstract third-party references: Institut Pasteur de Madagascar, Direction Internationale de l’Institut Pasteur, INTERREG FEDER TROI, Fondation Pierre Ledoux Jeunesse Internationale, DP One Health Indian Ocean

Background: Leptospirosis is considered a major public health problem in the Indian Ocean Islands. However, in Madagascar, human seroprevalence studies are contradictory and only 3 confirmed human cases have been reported in the literature.

Materials/methods: The main objective of the study was to identify incident cases of leptospirosis among febrile patients over 5 years old hospitalized in the Centre Hospitalier Régional de Référence d’Ambatondrazaka, in Madagascar. Polymerase chain reaction (PCR) on blood and urine were performed at inclusion time as well as IgM- and IgG ELISA, which was repeated 7 to 14 days later. The secondary objective was to identify exposition factors through a matched nested case-control study. Exposition factors were collected through a detailed paper questionnaire.

Results: Between the 25.01.2018 and the 15.03.2019, 323 patients were enrolled in the study. Among them 26 were confirmed cases (based on PCR) and 53 were probable cases (presence of IgM antibodies). Cases (confirmed and probable) presented more consciousness disorders (38% / 25%, p = 0.01) but less fatigue (91% / 98%, p = 0.01) and less clinical signs of hepatic impairment (13% / 23%, p = 0.048). Overall 46% had had prior antibiotherapy and 7% of them died during the study. Rainy season (OR = 1.8; 95% CI = [1.05-3.01]) and farming (OR = 1.99; 95% CI = [1.33-1.48]) were positively associated with leptospirosis, whereas exposition to cattle (OR = 0.4; IC 95% = [0.24-0.69]) and a higher level of education (OR = 0.58; 95% CI = [0.36-0.96]) were negatively associated with it.

Conclusions: We show for the first time the heavy burden of leptospirosis in Madagascar. The awaited results on circulating strains (currently being identified) should help improve knowledge on animal reservoirs and will enable, if necessary, to reassess performances of diagnostic tests used in Madagascar in order to develop better control strategies for the disease.

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**Abstract 8742**

**Rapid MALDI-TOF MS-based method for vancomycin-resistant *Enterococcus faecium* detection**

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**Abstract third-party references**: European Union’s Horizon 2020 research and innovation programme under grant agreement No 868365

**Background**: *Enterococcus faecium* is increasingly becoming a nosocomial threat due to its ability to rapidly spread and cause outbreaks in hospital settings. Recently, q vancomycin resistance on *E. faecium* has been on the rise and that is the reason why *E. faecium* is included in the ESKAPE group for highly resistant microorganisms. The main objective of this study was to develop a MALDI-TOF MS based method of analysis of *E. faecium* clinical strains that could differentiate vancomycin-resistant (VRE) from vancomycin-susceptible (VSE) Enterococci.

**Materials/methods**: A total of 140 strains were included in this study (82 susceptible, 27 vanA strains and 31 vanB strains, all confirmed by molecular methods) and cultured overnight in Columbia agar.

In order to assay the reproducibility of the MALDI-TOF-based method, each isolate was analyzed in duplicates and each spot was read twice. This approach was performed during 3 consecutive days, yielding a total of 12 spectra in the range of 3.000 to 10.000 Da.

Protein spectra were analyzed by Clover Bacterial Analysis software (Clover Biosoft, Spain). All spectra were preprocessed by a pipeline of a) baseline subtraction using Top-Hat filter, b) smoothing via Savitzky-Golay filter, c) peak alignment and d) TIC normalization. Finally, 30 PLS-DA (Partial Least Squares Discriminant Analysis) was applied to discriminate the different groups of isolates.

**Results**: The implementation of PLS-DA to protein spectra allowed the correct classification of 75/82 susceptible and 27/31 vanB *E. faecium* isolates. The total accuracy of the assay was 91.15% (Figure 1). Besides, *E. faecium* vanA isolates could be correctly differentiated from *E. faecium* vanB isolates in 93.1% of the cases.

**Conclusions**: The developed method has shown its ability to correctly differentiate above 90% of the *E. faecium* vanB isolates from the VSE analyzed. A PLS-DA-based algorithm for the discrimination of *E. faecium* vanB vs. VRE isolates is proposed as a first step, followed by vanA vs vanB discrimination. Although further studies are needed in order to demonstrate its usefulness in a clinical setting, MALDI-TOF could be a promising way for rapid detection of VRE in laboratory routine detection of resistance mechanisms.

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A case of cystic hydatid disease acquired in Ireland
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Background: Cystic hydatid disease is caused by the cestode Echinococcus granulosus. Humans are infected by ingesting eggs released in the faeces of infected dogs. The liver or lungs are most frequently affected. Treatment depends on the WHO stage as determined on ultrasonography. A ‘watch and wait’ approach is recommended for late-stage, calcified cysts. Hydatid disease is not thought to be endemic in Ireland.

Case Report: In January 2019, an 86 year old female presented to Galway University Hospital with a three-day history of right upper quadrant pain and vomiting. She was a sheep farmer and had never travelled outside Ireland.

Two years previously, a CT scan had identified an 11.6x9.2x11.4cm cystic lesion in the right lobe of the liver with a calcified rim consistent with a hydatid cyst. Given the patient’s frailty, and following the WHO guidelines, a ‘watch and wait’ management approach had been adopted.

On admission she was stable and apyretic. Laboratory investigations revealed a neutrophilia, normal eosinophil count and elevated C-reactive protein. A CT scan demonstrated a ruptured hydatid cyst and right sided pleural effusion.

The patient was reviewed by the Infectious Diseases team. Albendazole 400mg, orally, twice daily was commenced initially and then Praziquantel added. She was deemed unfit for surgical intervention. Over the following weeks the pleural effusion increased in size and the patient clinically deteriorated. The input of Palliative Care was sought and the patient died 6 weeks following admission. Hydatid serology sent early in the admission was negative.

Conclusions: We describe the first reported case of cystic hydatid disease acquired in Ireland. The two previously reported Irish cases had travelled to areas of high prevalence. The late disease stage suggests a previously unrecognised endemicity of E. granulosus, rather than recent spread to the island.

Hydatid serology was negative, despite characteristic radiological findings. However, hydatid serology is known to be poorly sensitive, especially in late disease.

At diagnosis, in light of her WHO stage, surgical management was not pursued. Our patient then presented with a ruptured cyst - a described complication. More research is necessary to determine the limits of the ‘watch and wait’ approach.

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Risk factor for nosocomial and surgical site infection after cardiac surgery

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Background: Infection in patients after cardiac surgery is one of the most severe complications. In 2005 Fowler et al elaborated a score to identify patients with higher risk for major infections. In the last years, bilateral internal mammary artery (BIMA) has been associated with enhanced overall long-term outcome, compared with single internal mammary artery. However, BIMA has also related to a higher risk of surgical site infection. The aim of the study was analyzed the impact of BIMA in the outcome of infection after cardiac surgery.

Materials/methods: Adult patients undergoing cardiac surgery between February 1st and December 31st 2018 were prospectively included. Clinical characteristics of patients, hospital stay before surgery, type of intervention (urgent/elective, revascularization/valve surgery), time on-pump were gathered. The incidence of any kind of infection was collected. Differences between patients with and without infection were analyzed.

Results: Ninety-three patients were identified, 14 (15%) suffered a nosocomial infection: 7 respiratory infection, 6 surgical site infection and 1 urinary tract infection.

Fowler index >= 14 was associated in multivariable analysis with nosocomial infection (OR = 6.8, 95% IC 2.0-23.5, p = 0.002). After studying the different variables included in Fowler index, we found that only arteriopathy (OR = 7.3, 95% CI 1.6-32.4, p = 0.009) and chronic lung diseases (OR = 4.1, 95% IC 1.2-14.8, p = 0.028) were related to a higher risk of infection.

For surgical site infection, Fowler index >= 14 was not associated with higher risk of infection, not in univariable analysis, neither in multivariable analysis. The only factor related to surgical site infection was BIMA (OR = 11.7, 95% IC 1.3-105.4, p = 0.028)

Conclusions: Risk factors for surgical site infection after cardiac surgery were different from those associated with nosocomial infection. BIMA was the most important risk factor for sternal wound infection. In these patients, all preventive infection measures should be implemented in order to reduce the incidence of infection.

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**Infectious complications after chimeric antigen receptor modified T cells in adolescent and young adult relapse/refractory B cell precursor acute lymphoblastic leukaemia: report of the French experience**

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**Background:** Chimeric antigen receptor T cells (CAR-T) is a promising therapy for patients with relapse/refractory (R/R) B cell precursor acute lymphoblastic leukemia (BCP-ALL). However, this population is at high risk of infectious complications (IC) due to preexisting immunosuppression and CAR-T therapy itself (cytokine released syndrome (CRS), prolonged hypogammaglobulinemia).

**Materials/methods:** Patients treated with Tisagenlecleucel for R/R BCP-ALL in the Adolescent Young Adult Unit (AYA) of Saint-Louis Hospital from July 2018 to July 2019 were included. Data on IC were retrospectively collected. The aim was to describe IC in this population.

**Results:** 21 patients were included (7 women (33.3%), 14 men (66.7%)). Median age was 22 y.o. (18-29). 20 patients received CAR-T for BCP-ALL relapse (median 2nd relapse (1-6)) and one patient for primary refractory disease. 13 patients had a previous history of bone marrow transplantation (61.9%).

6 (28.6%) patients were bridged with immunotherapy. All patients received anti-pneumocystis, antiviral and antifungal prophylaxis. Lymphocytes count was <200/mm3 at D0 for all. 14 patients (66.7%) received G-CSF. Median time until aplasia recovery was 13 days (0; NR). 13 patients (61.9%) developed fever. Median grade of CRS was 2 (1-5). 8 patients (38%) had to be transferred to intensive care unit. 4 patients underwent neurotoxicity (median grade 3 (2-4)). 6 patients received tocilizumab and steroids, 3 of them received siltuximab. Median follow up was 6.2 months.

29 IC were documented. 16 early IC (D0-D30) in 9 patients: 9 bacterial (including 2 clostridium difficile colitis), 1 fungal (aspergillosis), 6 viral (3 CMV reactivation, 1 rotavirus, 1 HHV-6-B and 1 parainfluenzae). 13 late IC (>D30) were diagnosed in 10 patients: 8 bacterial (including bacteriemia to providencia stuartii, pseudomonas aeruginosa, serratia marcescens, enterobacter cloacae, E.Coli), 2 fungal (alternaria, mucor) and 3 viral.

95.2% patients were alive at D30 (1 toxic death); 6 patients died after D30 but not from IC alone (28.6%).

**Conclusions:** BCP-ALL patients receiving CAR-T cells are at high risk of IC. They developed viral reactivation, bacteriemia and invasive fungal infections. Prospective record of these IC is necessary to better understand their incidence and the correlation between CRS and infection.

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Abstract 8754

Epidemiology and risk factors for *Clostridioides difficile* at a referral cancer centre in Mexico: a case-control study

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Abstract third-party references: Instituto Nacional de Cancerologia

Background: *Clostridioides difficile* infection (CDI) is the most common cause of nosocomial diarrhea. Community onset healthcare facility-associated (CO-HCFA) and community-associated (CA) CDI has increased. Patients with cancer have a higher risk of CDI. We investigated clinical characteristics, and outcomes in patients with CDI at a cancer referral center in Mexico.

Materials/methods: We included patients with cancer and diarrhea between January 2015 and December 2018. Medical records were retrospectively reviewed. Demographics, clinical characteristics, laboratory, outcomes, and 30 day-mortality were recorded. Cancer diagnosis-matched participants were randomly selected as controls. Logistic regression analysis was conducted.

Results: One-hundred and forty-eight CDI cases were reported: 72 (49%), 68 (46%) and 8 (5%) for healthcare facility-onset (HO), CO-HCFA, and CA-CDI, respectively. Seventy-seven (52%) were women; median age 49 years (QR 31.25-61.0). Seventy (47%) patients had a solid neoplasm and 78 (53%) a hematologic malignancy (OR, 0.95; 95% CI, 0.6-1.5; p=0.82). The most frequent symptoms at diagnosis were: abdominal pain 93 (63%), fever 72 (49%), and ≥ 4 diarrheal evacuations (40%). Relapse was observed in 12 patients (8%). Incidence rate of CDI was 0.49 X 1000 patient-days. During the study period an increase on CO-HCFA and CA-CDI was observed (Figure 1). Overall 30-day mortality was 16%; 8 patients with CDI and NAP027 died (4.05%). Risk factors associated with CDI were: the use of previous antibiotics (OR, 3.42; 95% CI, 1.95-6.02; p=<0.001), and proton pump inhibitors (PPI) (OR, 2.16; 95% CI, 1.27-3.70; p=0.005), abdominal pain (OR 2.19; 95% CI, 1.30-3.68; p=0.003), and ≥ 4 episodes of diarrhea/24 h (OR 2.17; 95% CI, 1.27-3.68; p=0.004). According to antibiotic type, quinolones (OR, 2.62; 95% CI, 1.14-6.02; p=0.023) and cephalosporins (OR, 2.19; 95% CI, 1.13-4.28; p=0.21) were related to CDI.

Conclusions: In this cohort the rate of CDI was lower compared to other series. Risk factors were similar to those previously reported in non-cancer patients. The number of CDI increased by almost three times, from 2015 to 2018. The associated mortality was similar to that reported in non-cancer patients.

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**Clostridioides difficile** infection cases at Instituto Nacional de cancerologia (2015-2018)

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Abstract 8756

Zika, dengue and chikungunya viruses seroprevalence among adolescents in Brazil
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Background: The recent emergence of Zika (ZIKV) and chikungunya (CHIKV) viruses in highly endemic dengue virus (DENV) contexts has posed major challenges for surveillance services in Brazil, particularly due to the overlap of symptoms associated with limited laboratory support. The objective was to describe the serological profile of dengue, Zika and chikungunya infections among adolescents and the association with previous history of dengue infection and yellow fever vaccination.

Materials/methods: Cross-sectional study conducted among adolescents from the Study of Cardiovascular Risk Factors in Adolescents (ERICA), recruited in 2014 and reassessed in 2018. Serum samples were tested for anti-DENV IgG, anti-DENV IgM, anti-ZIKV IgG and anti-CHIKV IgG using a commercial ELISA kit (Euroimmun, Germany).

Results: Seroprevalence in 2018 was 83.4% for dengue, 49.3% for Zika and 15.2% for chikungunya, not varying with age and race. Dengue and Zika seropositivity were more frequently found among young females, while chikungunya seropositivity were more frequent among males. The most frequent serological profiles were adolescents who tested positive for dengue and Zika simultaneously and negative for chikungunya [35.5%], as well as adolescents who tested positive only for dengue [34.1%]. Additionally, 11.5% tested negative and 10.6% tested positive for the three arboviruses. When combined with previous diagnostic reports by these arboviruses, the tests indicated an asymptomatic or oligosymptomatic frequency of 83.1% for dengue, 13.1% for chikungunya, and 45.1% for Zika. Among those who reported anti-yellow fever vaccination, 49% tested positive for Zika, while in the group that reported not being vaccinated, 58% tested positive for this same arbovirus (p=0.351). Dengue seroprevalence in 2014 was 75.7% [IgG], no IgM seropositivity was detected. Previous seropositivity for Dengue [2014] was associated with Zika seroprevalence in 2018 (p=0.011) but not with Chikungunya (p=0.677).

Conclusions: The findings suggest a wide and “silent” circulation of dengue, Zika and Chikungunya viruses, evidenced by the expressive frequency of participants with positive serology without previous diagnosis of acute disease. Associations between previous dengue fever infection and present Zika might indicate cross-reactivity between serological tests. There is a need for studies that seek to better characterize the infection profile of these arboviruses through more accurate diagnostic tests.

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Dysbiosis in a triplet with an autism spectrum disorder: a case study

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Background: We present a case of triplets, one diagnosed with an Autism Spectrum Disorder (ASD). While patients with ASD are characterized by deficits in language and social interaction, these are often accompanied by gastrointestinal (GI) symptoms. Approximately half of children with ASD have GI problems as well, and there appears to be a positive correlation in severity of GI symptoms and autistic severity. Trials of vancomycin and fecal microbiota transplant (FMT) have shown that altering the microbiome of the gut has success in improving both GI and ASD symptoms. The purpose of this study was to compare the microbiome of an autistic child with that of the child’s biological siblings and mother, in the hopes of elucidating perturbations possibly associated with ASD.

Materials/methods: Next-generation sequencing was performed on fecal samples from a mother and her 3 siblings, two healthy and one with ASD (Sibling #3). Following stool collection, DNA was then extracted, quantitated, and normalized for downstream library fabrication utilizing shotgun methodology. Prepared and indexed libraries were subsequently pooled and sequenced on the Illumina NextSeq 550 System. Metagenomic readout data was analyzed for relative abundances of defined bacteria and overall microbiome diversity as measured by Shannon index.

Results: The ASD patient (Sibling #3) was found to possess lower Bifidobacteria and Prevotella to the patient’s healthy mother, and overall lower biodiversity as measured by the Shannon Index. Additionally, healthy Sibling #1 was found to have greater bacterial diversity than the mother, more Prevotella and Bifidobacter than Sibling #2.

Conclusions: Our findings demonstrate the role of dysbiosis in ASD, and the utility of microbiome sequencing in order to draw conclusions regarding etiology and potential treatment modalities. Sequencing of the microbiome also presents potential insights in determining the optimal donor for a patient. As highlighted in Figure 1, Sibling #1 has greater microbial diversity and more Bifidobacterium than the mother, and more Prevotella than Sibling #2 and Sibling #3.

Figure 1. Comparative diversity of the gut microbiome of a patient with ASD (Sibling #3) and the patient’s biological siblings and mother.

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Correlation between vaginal microbiota diversity and human papilloma virus induced cervical carcinogenesis in population of Santander, Colombia

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Background: Specific composition of vaginal microbiota could predispose of coinfection with Human Papillomavirus (HPV) showing higher risk to progress to dysplasia, therefore require closer follow-up protocols and/or early intervention treatment. Objective: To determine the differences of the vaginal microbiota diversity among women with normal cytology HPV +/-, cervical dysplasia, and cervical cancer.

Materials/methods: Six groups of patients were evaluated according to HPV status and dysplasia degree, the groups were Normal cytology and negative HPV (n = 6), Normal cytology and positive HPV (n = 4), CIN I (n = 6), CIN II (n = 4), CIN III (n = 5), and cervical cancer (n = 3). DNA extraction was performed on samples obtained by cervical brushing. DNA library preparations from V3 and V4 regions of 16S rRNA gene, were performed by using the Nextera XT index kit following ILLUMINA protocols, sequencing of amplicons were carried out in a MiSeq sequencer. The data analysis was fulfil using the MG-RAST on-line server. For taxonomic, phylogenetic and statistical analysis the MEGAN Community, STATA and R software were used.

Results: Three Community State Type (CST) were identified within the samples as follows: normal cytology and negative HPV samples were dominated by CST I composed mainly of *Lactobacillus crispatus* (4/6; 66.6%), normal cytology and positive HPV samples (3/4; 75%), CIN I (3/6; 50%), CIN II (4/4; 100%) and CIN III (3/5; 60%) presented a predominance of CST IV which was characterized by having an abundance of anaerobic microorganisms such as *Prevotella*, *Gardnerella*, *Megasphaera* and others, but only *Megasphaera* presented statistically significant differences (p <0.01) with respect to samples without HPV infection. The CST III depicted an abundance of *Lactobacillus iners*, showed dominance in Cancer samples (2/3; 66.6%) and to a lesser extent in CIN III (2/5; 40%).

Conclusions: HPV infection is related with an increase of microbial richness and diversity present in the vagina. The composition of the vaginal microbiota could play a principal role in the persistent of HPV infection and development of premalignant cervical lesions and cancer progression.

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Human milk oligosaccharides exhibit biofilm inhibition and eradication activity against biofilms formed by yeast isolated from cystic fibrosis patients

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Abstract third-party references: I submit the abstract on behalf of Sylwia Jarzynka.

Background: Recent years statistically significant increase in the incidence of infections and colonizations caused by Candida species are observed from cystic fibrosis patients. Yeast produce virulence factors, which enable to infect host organism. Ability to form biofilm structure is one of them. Biofilm production is associated with decrease of treatment effectiveness and enhance of antifungal resistance. Research are currently performed to find compounds, which may affect directly on inhibition and eradication of fungal biofilm. Compounds which may become effective are human milk oligosaccharides (HMOs). The aim of this study was evaluation of potential anti-biofilm properties of oligosaccharides isolated from human milk.

Materials/methods: Human milk was obtained from five healthy donors. Milk samples were pooled, next in the skimming milk proteins were precipitated. The oligosaccharides fraction had been cleaned and lyophilized. 25 Candida strains (C. albicans, C. glabrata) were isolated from sputum culture of adult patients suffered from cystic fibrosis. Spectrophotometric method and quantitative method based on multiple dilution were performed for biofilm formation and determine influence of oligosaccharides on biofilm. Measurement of optical density was carried out after staining by crystal violet using microtiter plate. Quantitative method indicated decrease of colony forming unit per mL in dose dependent manner of oligosaccharides.

Results: Differential level of biofilm production was observed in Candida species (p<0.0001). Partial capacity to inhibition was demonstrated by using oligosaccharides isolated from human milk at optimal concentration 20 mg/mL, which was determined as minimal biofilm inhibitory concentration – MBIC (p<0.05). Static influence of oligosaccharides was observed on eradication biofilm produced by Candida strains (p<0.005). The lack of effect of lactose contained in breast milk on the antimicrobial activity of oligosaccharides tested in the experiment was determined.

Conclusions: Human milk oligosaccharides may be natural, easily absorbed potential compounds that inhibit fungal biofilm, enhance the effect of antifungal drugs, or be used in the prophylaxis of fungal infections as oral or inhaled preparations.

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Abstract 8764

Genomic characterisation and pathogenicity determination of the classical, hypermucoviscous and hypervirulent Klebsiella pneumoniae isolates in Mexico

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Abstract third-party references: Instituto Nacional de Salud Publica

Background: K. pneumoniae is one of the main pathogens causing hospital-(HAI) and community-(CAI) acquired infections. It is highly resistant to antibiotics and its pathogenicity has increased, which is classified as classical (cKpn) and hypervirulent (hvKpn) K. pneumoniae.

Materials/methods: The species was identified by VITEK and by PCR-multiplex. The hypermucovisosity was determined by string test, virulence factors by PCR, production of extended spectrum ß-lactamases (ESBL) by Kirby-Bauer, carbapenemases by CarbaNP, resistance to colistin by Polymixin-NP. Its pathogenicity was determined in murine model, serum resistance and neutrophil phagocytosis. The genomes were sequenced by Illumina, and phylogenetic analyses were performed and virulome and resistome were determined.

Results: A total of 91.5% of the isolates corresponded to K. pneumoniae, 4.3% to K. quasipneumoniae and 4% to K. variicola. According to the string test and virulence factors it was determined that 91.8% are cKpn, 6.1% [24/392] were classified as hypermucoviscous [hmwKpn] [not hvKpn] and 2% hvKpn. The 3.0% were identified in cKpn with resistant to colistin, which 100% were producers of ESBL, of which 54.5% were also producers of NDM-1 and KPC-2. Both cKpn and hvKpn were sensitive to pathogenicity tests. However, the K. pneumoniae isolates were K1 [1] and K2 [6] and K. quasipneumoniae K1 [1] also showed the hypermucoviscous phenotype and showed resistance to pathogenicity tests. The genomes of the cKpn and hvKpn strains contain a larger number of genes of resistance to antibiotics [resistome] and a smaller number of virulence factors [viruloma]. The virulome of hvKpn is greater and with a smaller resistome, however, 50% of the isolates were producers of ESBL, observing an increase in their resistome. The hvKpn with serotype K1, corresponded to colibactin-producer K. pneumoniae ST23, which genotoxin has been associated with cancer of colon.

Conclusions: The colistin-resistant cKpn are producers of ESBL and / or carbapenemases, being pathogens difficult to treat in HAI. An increase in antibiotic resistance was observed in hvKpn strains, isolated from CAI, however, it was also identified in IAAS. The hvKpn K1 [ST23] is a public health problem in Asian countries and this study describes this clone for the first time in Mexico.

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Impact of imipenem MIC in the outcome of patients with OXA-48 carbapenem-resistant Klebsiella pneumoniae bacteraemia

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Background: Carbapenem-resistant Enterobacteriaceae are a concerning emerging pathogen around the world. Combination of carbapenem and other active drug is one of the main options in the treatment. Most of the studies are carried out with meropenem, and information about the useful of imipenem is scarce. The objective of the study was analyzed the impact of imipenem MIC in outcome of patients with OXA-48-positive carbapenem-resistant Klebsiella pneumoniae bacteraemia.

Materials/methods: Retrospective study of adult patients with bacteremia due to OXA-48-positive carbapenem-resistant Klebsiella pneumoniae between December 2015 and January 2018. Epidemiologic characteristics, comorbidities, source and severity of infection and clinical outcome were collected. Due to meropenem-MIC was ≥8 µg/ml in all the strains, 1g/6 h in extended perfusion of imipenem was the carbapenem used in treatment. We classified the patients among those which strains has an imipenem-MIC ≤4µg/ml and those with >4µg/ml; comparator were patients treated with ceftazidime-avibactam.

Results: A total of 91 patients with OXA-48-positive carbapenem-resistant K. pneumoniae were identified, 72 were treated with imipenem or ceftazidime-avibactam (28 patients received imipenem ≤4µg/ml, 21 imipenem >4µg/ml and 21 ceftazidime-avibactam). Comorbidity index was high and was similar among the three groups (Charlson index >3; imipenem ≤4µg/ml, 61% vs. imipenem >4µg/ml, 57% vs. ceftazidime-avibactam, 48%, p=0.655), however those on ceftazidime-avibactam and imipenem >4µg/ml groups had less frequently dementia (dementia; imipenem ≤4µg/ml, 29% vs. imipenem >4µg/ml, 4% vs. ceftazidime-avibactam, 5%, p=0.016).

Among patients treated with imipenem ≤4µg/ml, urinary source was the most common (imipenem ≤4µg/ml, 61% vs. imipenem >4µg/ml, 30% vs. ceftazidime-avibactam, 19%, p=0.008). Catheter was the most common source on imipenem >4µg/ml and ceftazidime groups (imipenem ≤4µg/ml, 21% vs. imipenem >4µg/ml, 35% vs. ceftazidime-avibactam, 43%, p=0.265). Combination therapy was used only in patients who received imipenem treatment (imipenem ≤4µg/ml, 82% vs. imipenem >4µg/ml, 91% vs. ceftazidime-avibactam, 0%, p <0.001).

Clinical cure was lower in patients with imipenem-MIC >4µg/ml (imipenem ≤4µg/ml, 75% vs. imipenem >4µg/ml, 61% vs. ceftazidime-avibactam, 95%, p=0.027) and 14-day mortality was lower in patients that received ceftazidime-avibactam (imipenem ≤4µg/ml, 25% vs. imipenem >4µg/ml, 35% vs. ceftazidime-avibactam, 5%, p=0.052)

Conclusions: Imipenem-MIC >4µg/ml was related with a lower clinical cure in patients with OXA-48 carbapenem-resistant bloodstream infection. However, mortality was lower among patients treated with ceftazidime-avibactam regardless of imipenem-MIC of the strains.

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Abstract 8767

Outcome of a screening programme for the prevention of neonatal invasive early-onset Group B Streptococcus infection in a maternity unit of the University Hospital “Dr Dragisa Misovic” (Belgrade, Serbia)

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Background: Group B Streptococcus (GBS) emerged as the leading cause of newborn infection worldwide. In order to reduce burden of GBS disease of a newborn, during 2017 Serbia developed the First National Guideline for the Prevention of perinatal GBS disease. Recommendations from this Guideline suggest antenatal screening for GBS colonization and intrapartum antimicrobial prophylaxis (IAP) to colonized women or applying IAP to all women with certain obstetric risk factors during labor. The aim of this study was to investigate impact of a screening test for GBS in all pregnant women from 35 - 38 gestational weeks, its influence on reducing GBS EOS (early-onset sepsis) among newborns and to compare results before and after bringing recommendations from Guideline into clinical work.

Materials/methods: We conducted an observational, analytic, single-center study at Obstetrics Department of University Hospital “Dr Dragisa Misovic” (Belgrade, Serbia). The screening test for GBS was vaginal rectal swab.

Results: During the period of 2017-2018 in this study were retrospectively included more than 4200 mothers and newborns. Among 2200 newborns, before the implementation of screening test, 4 (2 ‰,) had GBS EOS and 13 (6 ‰) had suspected GBS EOS due to elevated CRP. However, after the GBS screening implementation, no confirmed neonatal GBS EOS was found (0/2157) and 3‰ (7/2157) infants had suspected GBS EOS. Vaginal GBS colonization was found at the 9th month of pregnancy in 22.15% mothers so IAP was administered to all of those women. The antibiotic of choice was Penicillin G (5 million IU + 3 million/4h, iv). Alternative antibiotic was Clindamycin (900 mg/8h, iv). Before the implementation of Guideline all neonates at risk required complete blood count and blood culture followed by a 48-hour period of observation with a standardized physical examination. However, after implementation of Guideline only standardized physical examination was performed.

Conclusions: Identifying high-risk neonates susceptible for development of an early-onset sepsis is a challenge. The ambiguity of clinical presentation can easily be overlooked and result in delayed treatment. In Serbia, universal systematic antibiotic therapy is recommended in all GBS positive mothers which significantly decrease the incidence of an early neonatal GBS infection.

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Abstract 8769

The impact of rapid identification of blood culture pathogens by MALDI-TOF MS and their direct antibiotic susceptibilities on antimicrobial stewardship at a large district general hospital, United Kingdom

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Background: Matrix Assisted Laser Depolarisation/Ionisation and Time of Flight (MALDI-TOF) identification coupled with direct sensitivities of Blood culture (BC) isolates have revolutionised the management of sepsis.

The aim of this study is to evaluate the usefulness of MALDI-TOF identification and direct susceptibilities on positive blood culture isolates and whether it improves antimicrobial stewardship

Materials/methods: All positive BC were prospectively reviewed on a daily basis over a period of six weeks. Demographics, clinical data and turnaround times of identification of BC pathogens and their sensitivities were collected. The impact of the rapid identification and availability of direct antibiotic susceptibility on antibiotic stewardship and clinical management of these patients were analysed.

Discrepancies between direct and final susceptibilities by phoenix and the impact on patient management were also analysed.

We excluded blood cultures that were not thought to be clinically significant. We also excluded those patients who died before their BC flagged positive, or those that had more than one blood culture for the same infection episode

Results: We included a total of 100 significant blood cultures. Gram negative organisms were isolated in 54%. Urosepsis was identified as the source of infection in 33%, followed by intra-abdominal sepsis in 16%.

Same day MALDI-TOF identification was available in only 5 cases, and the next day for 56 cases. 34/56 could potentially have been identified on the same day and in 50% of these cases this would have impacted on patient management. This could either be due to failure of the organism to grow or delayed subculture.

Direct sensitivities, when available in timely manner, impacted on the advice given in 70% of the cases. Antibiotic susceptibility by phoenix was compared with the direct sensitivity and showed discrepancy in 22% and resulted in change of antibiotic management in 53%.

Conclusions: Rapid identification of BC pathogens has substantial impact on patient management. Further evaluation is needed to ensure processing of positive BC is streamlined to allow earlier identification of isolates. Microbiologists need to be aware of the possibility of discrepancy in susceptibilities while advising on antibiotic management

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**Abstract 8770**

**Developing a molecular toolbox for *Staphylococcus haemolyticus*: mimicry-by-methylation**
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**Background:** *Staphylococcus haemolyticus* is common among normal skin flora, yet it is also increasingly common as the cause of nosocomial infections. Knowledge of the causative links between virulent phenotypes and the responsible genes of *S. haemolyticus* in the hospital environment is lacking, as are the molecular tools required to characterize suspected virulence genes. Active restriction modification (RM) systems makes genetic modification challenging in staphylococci. RM systems recognise specific DNA methylation patterns which allow them to detect and destroy incoming foreign DNA.

**Materials/methods:** We are developing a set of molecular tools which circumvent these systems in *S. haemolyticus*. Ten *S. haemolyticus* isolates were selected for Single Molecule Real-Time (SMRT) genome sequencing and methylome analysis. We identified the recognition sequences which undergo methylation in these genomes, as well as the genes responsible for the RM systems associated with these methylation patterns.

**Results:** One of the recognition sequences (GAGG) and its associated methylase gene, a fusion m5C-m6A methylase, was found in 4 of the 10 genomes sequenced. A BLAST search revealed that this methylase gene is also present in 25% of the *S. haemolyticus* genomes in our collection.

**Conclusions:** Expressing this fusion methylase in *E.coli* has allowed us to develop a mimicry-by-methylation tool which increases transformation efficiency in *S. haemolyticus* strains bearing this RM system.

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Optimising antimicrobial stewardship: an evaluation of temocillin in the treatment of Gram-negative bacteraemia

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Background: The spread of multi-drug resistant Gram-negative bacteria continues to be an emerging threat to public health worldwide. Gram-negative septicaemia remains an important therapeutic challenge, associated with significant morbidity and mortality. In Scotland alone, a total of 4,738 cases of E.coli bacteraemia were reported for 2018 (rate of 87.3 per 100,000 population). Over the last decade there has been a growing awareness that improvements to stewardship and robust surveillance is needed. Empirical management guidelines should always be interpreted alongside individual patient findings and be guided by local epidemiology and resistance rates.

Temocillin (6-α-methoxy-ticarcillin) is an attractive carbapenem ‘sparing’ agent for the treatment of Enterobacterales bloodstream infections (BSI), being resistant to most extended-spectrum β-lactamases and AmpC enzymes. The aim of this study was to evaluate the utility of temocillin in the treatment of BSI and assess clinical outcome.

Materials/methods: A retrospective analysis was performed over 6 months (September to February 2019). Data was analysed from five large university teaching hospitals within Greater Glasgow and Clyde, the largest NHS organisation in the UK serving a population of 1.2 million. Only cases were the patient had been actively treated were included for analysis. The source of infection and management was reviewed for each case. The 30-day, 90-day and all-cause mortality rate were determined for the study population.

Results: A total of 468 patients were identified, of these 42% received temocillin as primary targeted treatment (first month; September 2018 n=86). In 56% of cases the patient had a urinary tract source. 34% of cases were related to an intra-abdominal infection. E.coli was the most common pathogen isolated (56%). Less than 3% of all isolates tested temocillin resistant; 8% tested piperacillin-tazobactam (tazocin) resistant and 10% tested gentamicin resistant in vitro (either on disc diffusion testing or Vitek AST testing). When comparing 30-day mortality, no statistically significant difference in mortality was found using Chi-Square calculation when comparing temocillin as primary therapy.

Conclusions: Our study provides a valuable evaluation of the utility of temocillin in the management of BSI and supports the importance of effective surveillance to promote stewardship and the judicious use of antimicrobial agents.

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Abstract 8772

Genomic epidemiology of paediatric invasive Group A Streptococcus infections in British Columbia, Canada
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Background: Group A Streptococcus can cause invasive infections (iGAS) with significant morbidity and mortality. In recent years there has been a rise of iGAS incidence in Canada overall, as well as in the province of British Columbia (BC). iGAS of emm1 type was overrepresented in BC children, notably rising between 2015 and 2017. iGAS cases of emm1 type were more likely to have a severe presentation than other emm types. Whole genome sequencing (WGS) was used to evaluate the relatedness and potential transmission dynamics of pediatric emm1 iGAS isolates, with a focus on cases admitted to the BC Children’s Hospital.

Materials/methods: All iGAS isolates in BC are sent to the National Microbiology Laboratory (NML) for typing. A subset of pediatric emm1 cases diagnosed between 2010 and 2017 was identified for WGS (n=23), along with a selection of contemporaneous adult emm1 iGAS cases for “background” comparison (n=29). All isolates were sequenced using MiSeq Illumina technology. Sequences were analyzed for phylogenetic relatedness using SNVPhyl pipeline with the oldest strain in the dataset as a reference strain. A total of 70 sites were used to construct the phylogeny, using 86.2% of the core genome. Strains were analyzed for the presence of antimicrobial resistance (AMR) genes using an AMR detection pipeline (RGI and StarAMR tools), with results compared to those of phenotypic AMR testing.

Results: BC iGAS emm1 isolates were a heterogeneous population. No significant clustering of pediatric emm1 iGAS isolates was observed. Several small clusters (2-4 isolates) of 0 to 3 single nucleotide variants (SNVs) apart were seen. Some of these clustered in space and time and in one case represented a known epidemiologically linked pair. Others, despite close phylogenetic relatedness, were isolated in different BC regions, months to years apart. Only 3 strains carried AMR genes (ermB and tetM). There was phenotypic confirmation of erythromycin resistance but phenotypic tetracycline resistance testing was not done.

Conclusions: Despite over-representation of emm1 type among pediatric iGAS cases in BC there was no evidence of a unique emergent pediatric strain in circulation. WGS could be used to confirm strain relatedness of epidemiologically linked cases.

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Abstract 8773

Implementation of a full-length HIV-1 NGS assay into clinical diagnostics

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Background: New anti-retroviral treatment regimens targeting previously un-sequenced regions of HIV-1 have necessitated the development of whole genome next generation sequencing (NGS) strategies. These allow in-depth analysis of HIV-1 viral genomes and quasispecies in a rapid, yet cost effective manner. While Sanger sequencing remains the gold standard for HIV-1 drug resistance testing for treatment-naïve patients and for monitoring drug resistance mutations following anti-retroviral treatment (ART), it is limited by the non-detection of resistance-associated mutations (RAMs) with prevalence below 20%. The high coverage and depth of sequencing achievable with NGS allows for the detection of minor variants (MVs) at very low level. However, larger datasets are required to evaluate the use of MVs as a predictor for virological failure.

Materials/methods: Almost full-length HIV-1 amplification was achieved using a four RT-PCR method spanning ~600 – ~9000 nucleotides of the viral genome (HXB2). For NGS, 10µl of pooled amplicon was utilized with the Nextera® FLEX library preparation kit and sequencing performed on a MiSeq using the V2 reagent kit with 500 cycles. Analysis was with an in-house de novo assembly pipeline using an Iterative VirusAssembler (IVA). Drug resistance and virus tropism predictions (20% and 5% frequency) were made using the Stanford database (https://hivdb.stanford.edu/) and Geno2Pheno web service (http://coreceptor.geno2pheno.org/) respectively and compared with the Sanger sequencing data.

Results: At 20% frequency, almost complete concordance was observed between Sanger and NGS RAM predictions of both clinical samples (100) and multiple external quality assurance (EQA) schemes. Good coverage of all HIV-1 major subtypes was observed with a median read depth of ~1000 at viral loads as low as 1000 copies/ml. As expected, additional RAMs were predicted at 5% minor variant threshold.

Conclusions: It is now becoming cost effective and practical to introduce HIV-1 NGS into clinical service. Further, new and emerging ART treatments target regions of the viral genome often not included with current targeted sequencing approaches, highlighting the advantage of incorporating NGS in diagnostic practice. However, the critical question remains: “what is the clinical significance of additional read depth achieved with HIV-1 NGS and can the results generated predict treatment outcomes and guide patient management?”

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**Should we change our diagnostic strategy for the detection of verotoxigenic *Escherichia coli* infection?**

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**Background:** Shiga toxin-producing *Escherichia coli* (STEC) have emerged within foodborne pathogens in developed countries. STEC can cause bloody diarrhoea and the life-threatening haemolytic-uremic syndrome. In Spain, STEC infection is a notifiable disease since 2015, but the notification rate seems to be still very low. Since 2013 we have included in our Microbiology Service a new protocol to analyze specifically for STEC in suspected cases. The aims of this study are: (i) to determine the role of STEC as etiological agents of bacterial gastroenteritis in two cross-sectional sampling in 2016, and (ii) to assess if our internal protocol established since 2013 can detect STEC cases that are not specifically requested.

**Materials/methods:** (i) To know role of STEC as etiological agents of gastroenteritis, 223 faecal cultures from July and December 2016 were analyzed by streak culture in MacConkey agar and subsequent molecular detection of the *stx1* and *stx2* genes. (ii) Between 2013 and October 2019, 394 faecal cultures on MacConkey agar originating from suspected cases or specific requests for STEC were sent to the National Center for Microbiology for the detection of the main diarrhoeagenic pathotypes of *E. coli* by molecular testing of their respective virulence genes.

**Results:** The relative importance of STEC infection was low (1/223; 0.4%), since only one sample was *stx*-positive (*stx1*). From suspected cases, 14% (52/394) were positive for any diarrhoeagenic pathotype, with STEC being present in 21% of positives (Figure 1). Half of the isolates belonged to the enterohaemorrhagic serotype O157:H7. Only 9% of positive cases for STEC had been expressly requested by the clinicians.

**Conclusions:** STEC is not a common cause of gastroenteritis in our area. From suspected samples, other pathotypes have been detected more frequently than STEC. Since 2013, almost 90% of the positive cases have been detected due to our protocol, thus increasing the total number of STEC that should be notified.

**Figure 1.** Diarrhoeagenic pathotypes of *E. coli* detected among STEC suspected cases of gastroenteritis [aEPEC: atypical enteropathogenic *E. coli*, EAEC: enteraggregative *E. coli*, EIEC: enteroinvasive *E. coli*, Others include mixed infections such as aEPEC with EAEC or enterotoxigenic *E. coli*].

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Abstract 8783

Contribution of vaginal culture to predict early-onset neonatal infection in case of preterm premature rupture of membrane before 34 weeks’ gestation

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Background: Preterm Premature Rupture of Membrane (PPROM) is a major cause of morbidity and mortality for the mother and neonate. The vaginal microbial profile in PPROM is poorly known, particularly regarding the risk of early-onset neonatal infection (EONI), which is of importance for antibiotic prophylaxis. Our objective was to determine clinical and microbiological risk factors for EONI in case of PPROM before 34 weeks’ gestation (WG).

Materials/methods: A single center, retrospective cohort study. Patients with PPROM before 34 WG from 2008 to 2016 were categorized according to outcome in 2 groups, with or without EONI. The primary outcome was to determine if a positive endocervical culture was associated with EONI. Secondary outcomes were the association between EONI and vaginal dysbiosis (lack of lactobacilli), between EONI and histopathological chorioamnionitis and the correlation between pathogens including Group B Streptococci (GBS) and E. Coli in maternal vaginal swabs and in neonates with EONI.

Results: 268 patients were included, 39 in the EONI group and 229 in the non-EONI. The prevalence of EONI in our population of PPROM before 34 WG was 14.5 %. The endocervical culture was positive for 16.9% at admission and 24.8% at delivery, with no difference between the groups. The presence of lactobacilli was higher in the non-EONI than in the EONI group at time of rupture (74.4% vs 52.94; p=0.01) and at time of delivery (41.57% vs 10.71%; p<0.001), whereas clinical chorioamnionitis was more frequent in the EONI than in the non-EONI group (94.7% vs 38.8%, p<0.001). After adjustment, a vaginal flora rich in lactobacilli before delivery tended to be protective against EONI (OR=0.21, 95% CI 0.04, 1.02, p=0.03), while clinical chorioamnionitis was significantly higher in EONI (OR=5.22, 95% CI 1.5, 18.19, p<0.01). We found no statistically significant concordance between the maternal microbiological samples and the neonatal samples.

Conclusions: The presence of lactobacilli in the vagina was protective for neonatal infection in PPROM, but the presence of pathogenic bacteria at admission and at delivery was not predictive of EONI in this study. Clinical evidence of intra-uterine infection had the strongest association with EONI.

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A Monte Carlo simulation modelling meropenem bolus to prolonged infusion dosing and expected suppression of resistance in *Pseudomonas aeruginosa*

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**Background:** Previous in vitro data indicates a meropenem trough concentration of 6.2 times the minimum inhibitory concentration (x MIC) could suppress resistance development in *Pseudomonas aeruginosa*. The same effect was seen at a trough 1.7 x MIC when meropenem was used in combination with tobramycin.

**Materials/methods:** This Monte Carlo simulation in 5000 patients utilized pharmacokinetic profiles from 49 patients, studied in 3 cohorts: non-obese patients (<120 kg), obese non-critically ill patients (≥120 kg) and obese critically ill patients (≥120 kg). Bolus doses ranged from 250-1000 mg paired with infusion doses ranging from 500-1500 mg. Boluses were modeled over 5, 15 and 30 minutes and bolus plus infusion time totaled 3 hours. All doses were modeled on 8-hour intervals. Outcomes included probability of target attainment (PTA) trough concentrations 6.2 x MIC and 1.7 x MIC at both first dose (FD) and steady state (SS).

**Results:** In the three cohorts, all doses in achieved >90% PTA trough 1.7x MIC at both FD and SS for MICs of 0.25 mg/L or lower. In the <120 kg and ≥120 kg non-critically ill groups, >90% PTA trough 6.2 x MIC was achieved at both FD and SS at an MIC 0.25 mg/L for all doses with the exception of 500mg/500mg. In the ≥120kg critically-ill group, >90% PTA trough 6.2 x MIC was achieved at 0.125 mg/L consistently with only certain doses achieving the same target for higher MICs. PTA 6.2 x MIC=2mg/L was consistently <90% in all three cohorts, but PTA >90% was achievable for 1.7 x MIC=2mg/L in the non-obese and obese non-critically ill patients with a 500/1500 mg dose at SS.

**Conclusions:** Given global concerns over multi-drug resistant *P. aeruginosa*, exploring strategies that may suppress resistance development could prove useful. Additional data is needed to determine if meropenem BPI is a safe and effective treatment modality.

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Abstract 8786

**Linezolid resistance in coagulase-negative Staphylococcus spp. in six private hospitals in Sao Paulo, Brazil**

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**Background:** Linezolid is an oxazolidinones antibiotic, indicated for treatment of infections caused by multidrug-resistant gram-positive organisms. Resistance to linezolid is unusual, but it is being observed an increase in the number of cases of linezolid-resistant Staphylococcus spp. worldwide. The most common linezolid resistance mechanism is consequence of a single mutation G2576T in 23S ribosomal ribonucleic acid (rRNA).

**Materials/methods:** Between March-May/2019, linezolid-resistant coagulase-negative Staphylococcus spp. (CoNS) isolated from blood cultures in a microbiology lab that perform 8,000 blood cultures/month from 33 private hospitals, in Sao Paulo, Brazil, were selected. The species were identified by mass spectrometry using Vitek MS (Biomerieux, France) and resistance to linezolid, based on minimal inhibitory concentration (MIC), was detected by Vitek2 (Biomerieux, France) and confirmed by diffusion-gradient method E-test (Biomerieux, France), using European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria. All isolates were submitted to Pulsed Field Gel Electrophoresis (PFGE) for clonality analysis and polymerase chain reaction (PCR) for 23S rRNA to detect G2576T mutation were performed. PFGE’s clonal pattern was defined as >=95.0% of similarity.

**Results:** Ten *Staphylococcus epidermidis* and seven *Staphylococcus capitis* linezolid-resistant isolates were identified on blood cultures from patients of six hospitals (linezolid MIC range: 1 2-64mg/L *S. epidermidis* and 1 2-48mg/L *S. capitis*). Among *S. epidermidis*, G2576T mutation was detected by PCR in six isolates (60.0%), whereas it was detected in all *S. capitis* isolates (Figure). One clone was found among *S. epidermidis*, involving seven isolates from a same hospital (clone A), as well as three *S. capitis* isolates from the same hospital and one from another hospital that belonged to the same clone named clone B (Figure).

**Conclusions:** Despite its low frequency, resistance to linezolid is being observed in CoNS isolates. We have observed that most *S. epidermidis* had G2576T mutation not detected by PCR, suggesting that other mechanisms might be the reason for linezolid resistance. The clonal pattern detected by PFGE involving *S. epidermidis* and *S. capitis* isolates from the same hospital suggest a common source of infection and the possibility of a resistance mechanism transmission between species.

**Figure.** PFGE clonality analysis and characteristics of samples. Up: *Staphylococcus epidermidis*. Down: *Staphylococcus capitis*.

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Rapid detection of *Mycobacterium abscessus* complex and associated antibiotic resistance directly in cystic fibrosis samples

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**Background:** *Mycobacterium abscessus*, a bacterium closely related to the causative agent of tuberculosis, is of growing clinical concern. While *M. abscessus* can be found in the environment, it can cause life-threatening infections in certain susceptible populations. For example, chronic respiratory *M. abscessus* infections in people with Cystic Fibrosis (CF) are associated with more severe respiratory symptoms and accelerated declines in lung function.

Despite disappointing success rates due to extreme antimicrobial resistance (AMR), current best therapy involves intensive and long courses of multiple antimicrobials. A key laboratory process is to generate macrolide and amikacin AMR profiles, as treatment guidelines differ for *M. abscessus* infections that demonstrate acquired AMR against these antibiotics. Current methods for detection of *M. abscessus* and AMR are dependent on culture, which have limitations including long turnaround times, a tendency to be overgrown by other bacteria, and a limited capacity to detect infections with mixed resistance. As these limitations can impede effective and timely treatment, rapid culture-independent methods for *M. abscessus* detection and AMR characterisation are needed.

**Materials/methods:** We developed PCR-based methods for *M. abscessus* detection and characterisation of key macrolide and amikacin acquired resistance mechanisms. These PCR methods were applied to clinical respiratory samples (over 900 CF samples to date). PCR results were compared to gold-standard bacterial culture methods.

**Results:** Compared to culture, the *M. abscessus* detection assay’s sensitivity was 83.8% and specificity was 97.8%. Direct AMR characterisation results were concordant for most samples where both culture and PCR results were available. Discordant results were due to samples where PCR detected a mix of resistant and susceptible strains, whereas the cultured organism was susceptible-only. PCR results were generated the day after sample receipt, compared to the 2-3 weeks generally required for culture.

**Conclusions:** Molecular methods can detect most *M. abscessus* infections in CF and characterise associated AMR, and have the potential as an adjunct to culture to rapidly inform treatment. Notably, >80% of positive patients could have clinically-informative macrolide and amikacin AMR information within hours by PCR compared to weeks by culture. Potential implications of the mixed AMR samples remain to be explored, and investigations are ongoing.

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Abstracts 2020

Abstract 8794

Prevalence and outcome of Clostridioides difficile infection in a multi-centre study in Southern Brazil
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Abstract third-party references: Fundação Araucária-PR / SESA-PR / CNPq / MS-Decit

Background: Clostridioides difficile is the main cause of antimicrobial associate diarrhea and a frequent health-care associate infection. C. difficile infection (CDI) is related to high mortality, severe cases and recurrent infection. In Brazil few data are available about epidemiology and recurrence of CDI. The aims of this study were to identify the prevalence, clinical characteristics and outcomes of CDI in eight Brazilian Hospitals.

Materials/methods: This was a multicenter prospective cohort which included inpatients presenting diarrhea, older than 18 years, that had used antimicrobials in the last 90 days. The stools samples and clinical baseline dates were obtained by assistance staff. The follow-up clinical data (60 days) and outcome were obtained from medical records. Stools samples was tested using enzymatic immunoassay (EIA) to glutamate dehydrogenase antigen (GDH) and A/B toxins. Positive GDH samples were also evaluated by real time polymerase chain reaction (qPCR) for the presence of genes coding for toxin B (tcdB), binary toxin (cdt), and C. difficile hypervirulent strain marker (tcdC deletion). A case of CDI was defined with a positive test for toxin-producing C. difficile in stool by EIA or qPCR.

Results: During the study, were included 351 patients. Among of them, 62 (17.7%) were defined as CDI. The EIA was GDH and toxin negative for 266 patients, GDH and toxin positives tests for 26 and discordant (GDH positive and toxin negative) for 59 patients. The gene tcdB (toxin B) was detected in 26 samples with toxin positive results and in 36 samples with toxin negative result in EIA. PCR have also detected cdt (binary toxin) genes in ten samples and tcdC deletion (hipervirulent strain trial) in two samples. All patients with CDI have received antimicrobial therapy. Among of them, 52 have presented primary cure and 10 have died with diarrhea symptoms. The outcome was not evaluated in four patients. Among of others, 38 have had general cure and 10 have recurrence of CDI.

Conclusions: C. difficile infection is prevalent in Brazilians hospitals and related to high mortality and recurrence of infection. Detection of tcdC gene deletion warns to risk of hypertoxigenic strains circulation.

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Abstract 8796

**Genetic diversity of invasive, non-invasive and colonising Group B Streptococcus isolates in Southern Brazil**

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**Background:** Group B Streptococcus (GBS) remains an important cause of invasive infectious disease. It has increasing among nonpregnant patients, such as young adults with underlying medical conditions, and elderly individuals, due to their ability to persist in different host site. We characterize capsular typing, resistance profile, and genetic relatedness of GBS isolated from outpatient and inpatient in a Brazilian academic care hospital (HU-UFSC).

**Materials/methods:** Three-hundred forty-seven GBS strains were collected between 2015 and 2017. AST was performed using disk-diffusion. PCR was used to detect MLSB resistance genes, capsular types, and hypervirulent GBS adhesion (HvgA). MLVA was carried out to discriminate strains. Isolates with similarity of 60% were considered to belong to the same cluster.

**Results:** GBS isolates were classified as invasive (I), noninvasive (NI), or colonizing (C) strains recovered from neonates, nonpregnant, and pregnant patients. Resistance to erythromycin and clindamycin was 23% and 15.6%, respectively. The *erm*(TR) and *mef*(A/E) genes were widely detected in our GBS isolates (n = 45 and n = 44). The *erm*(B) gene was also detected in some isolates (n = 18). The *erm*(TR) and *mef*(A/E) further *erm*(B) and *mef*(A/B) co-production genes were found. These isolates with MLSB coding genes showed a great diversity of MLSB phenotypic profiles among them: iMLSB, cMLSB and susceptible isolates. We found serotypes Ia (42.4%), V (23.9%), II (12.9%), III (7.5%), Ib (4%), IV (2.3%), and IX (1.4%). HvgA gene was detected only in 16 isolates. Forty-two MLVA types (MTs) were identified considering all the isolates and this result yielded Gaston and Hunter’s diversity indices of 0.879. The most frequent MTs was MT12 (25.4%), MT18 (14.4%), MT4 (12.4%), MT26 (11.8%), MT6 (6.6%), and MT40 (3.2%). The other 36 MLVA types represented 26.2% of the isolates.

**Conclusions:** Isolates sharing the same MT were groups into different serotypes and MLSB resistance determinants. This could be related to the occurrence of capsular and resistance genes switching by genome rearrangement or horizontal transfer genes. These findings revealed a substantial genetic diversity among I, NI, and C GBS strains.

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Abstract 8797


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**Background:** Surgical site infection (SSI) after median sternotomy is an uncommon complication of cardiovascular surgery. Although infrequent PSM is one of the most serious and feared with a high mortality rate (14-47%) and cost of treatment. Most cases appear after 2nd week following surgery, but a small group can occur in the first 7 days, representing a diagnostic challenge.

**Materials/methods:** To describe PSM´s clinical characteristics, microbiology, medical and surgical management and outcome in a single reference cardiovascular center, an observational, descriptive study was carried out between 6/1988 and 12/2018. All consecutive cases of PSM were prospectively collected in a database and were evaluated and treated by the same surgical and infectious diseases team.

**Results:** A total of 191 PSM cases were registered out of 11,533 surgeries performed (incidence rate: 1.65%); 41/191 (21.46%) were in the first week (early-onset). Mean age: 68 (SD + 16.5); 31 men (75.6%). BMI: 27.35 (SD: + 4.96). DBT 16 (39%), chronic renal failure 5 (12.2%). Previous cardiac surgery 6 (14.64%). Type of surgery: CABG: 19 (46.34%), valve replacement 8 (19.5%), combined 10 (24.4%), heart transplant 2 (4.3%). Clinical presentation: fever: 148 (78%); wound discharge: 25 (61%), erythema 6 (14.6%), sternal instability 9 (21%) and sepsis: 18 (44%). Microbiology: GPC 18 (44%; S. aureus 55.5%), GNB 18 (44%). Blood cultures: 27 positive (65.8%); subxiphoid samples: 33/35 (94.28%). Surgery: 33 underwent open debridement and primary closure. In-hospital mortality: 8 (19.5%).

**Conclusions:** Early onset PSM is an unusual but complex and frequently subtle disease that requires a high index of suspicion to be identified. The clinical manifestations are nonspecific and difficult to interpret because of the proximity of cardiac surgery. Fever being the most frequent symptom, many times is interpreted as of non-infectious origin. It demands combined medical and surgical approach in order to decrease the mortality. Wound [subxiphoid] aspiration is an extremely easy way to perform rapid diagnosis, yielding high microbiology performance. Immediate debridement, drainage and primary closure could be an interesting approach offering short time of hospitalization and a similar mortality to that observed with other strategies.

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Abstract 8803

**The emerging non-conventional invasive aspergillosis: 5-year experience**

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**Background:** Invasive aspergillosis (IA) is a recognized cause of morbi-mortality in patients with "classic" immunosuppression (IS) (onco-hematologic or SOT). However, recently, attention has shifted towards new populations at risk. Objective: to describe our large IA series and their main underlying conditions.

**Materials/methods:** Prospective registry of IA cases validated by a multidisciplinary collaboration group (COMIC) in a tertiary centre, according to local and international guidelines. Study period: Oct-2014 and July-2019. A pre-established protocol was fulfilled including demographics, clinical, radiological and microbiological characteristics, antifungal therapy and outcome.

**Results:** During the study period, IA was diagnosed in 93 patients, 81.7% male (7 proven/75 probable/11 possible) in the following wards: medical 52.7%, Haematology 30.1%, ICU 10.8% and surgical 6.5%. Regarding underlying conditions, 41.9% had classic IS – CIS – 32/39 haematological and 7/39 SOT) and 53.8% had non-classic IS – NCIS – (solid organ cancer 18/50, advanced liver disease 16/50, COPD 8/50, advanced HIV 4/50, autoimmune diseases 1/50 and other IS 3/50). 4 patients (4.3%) had no recognized IS.

Differences between NCIS and CIS were: use of corticosteroids (63% vs. 25.6%; p<0.001), neutropenia (3.7% vs. 64.1%; p<0.001), acute liver failure (25.9% vs. 0%; p=0.001), influenza virus infection (18.5% vs. 2.6%; p=0.019), antifungal prophylaxis (1.9% vs. 48.7%; p<0.001) and Charlson comorbidity index [4 (IQR 3-7) vs. 2 (IQR 2-3); p<0.001]. There was no difference in age – 64 (IQR 53-71) vs. 64.5 (IQR 53.5-78) p=0.28. Regarding IA clinical presentation, NCIS had presented with less fever than CIS (51.9% vs. 82.1%; p=0.001) and more Aspergillus fumigatus infection (74.1% vs. 43.6%; p=0.001). The differences between NCIS and CIS in sensitivity of serum galactomannan (GM) were 59.5% vs. 52.2% (p=0.15) in GM-BAL. No significant differences were found in needed ICU admission or septic-shock. Regarding the outcome, no differences in overall mortality (51.9% vs. 53.8%; p=0.85) or IA-related mortality (40.7% vs. 28.2%; p=0.21) were observed.

**Conclusions:** Non-classic immunosuppression is responsible for more than half of IA cases in a recent large series. The prompt recognition of new risk factors is essential for improving the outcome of this severe condition.

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Abstract 8804

**Exposure to maternal antiretroviral therapy in utero frequently differs between twins**

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**Background:** Placental passage of drugs in twins is poorly understood, and unknown regarding antiretroviral (ARV) therapy. In the event of large differences in the exposure of 2 twins to the same maternal treatment, this could have a clinical impact in terms of prevention of perinatal transmission or adverse effects. Our objective was to describe the frequency of transplacental passage differences between antiretrovirals between twins.

**Materials/methods:** We conducted a retrospective, multicenter study. Samples were taken simultaneously for the 2 fetuses by venipuncture of the umbilical cords after delivery. We considered that a difference in concentrations of more than 50% between twins was a substantial difference (ratios below 0.67 or above 1.50).

**Results:** We analyzed 29 pairs of twins for which the concentration of at least one ARV was available for a twin pair. There were 27 dichorionic and 2 monochorionic diamniotic pregnancies. Cord blood concentrations differed by more than 50% for at least one ARV between the 2 twins in 9 twin pairs, 8 dichorionic and 1 monochorionic diamniotic. Discordant concentrations were observed for several nucleoside reverse transcriptase inhibitors (tenofovir, emtricitabine, lamivudine, zidovudine) and protease inhibitors (atazanavir, lopinavir, saquinavir); within individual twin pairs placental transfer was discordant for one or more ARVs, but identical for others.

**Conclusions:** Concentrations differed in nearly one third of twin pairs. This may be due to both interindividual genetic variability of placental transporters between dizygotic twins and to physiological differences between twins.

**Table. Twin cord blood concentration ratios**

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<td>Proportion of twins with discordant drug concentrations</td>
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Linking the resistome to the microbiome: a culture-free method links plasmid, virus, and antimicrobial resistance genes to their hosts in complex microbial populations

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Background: The rapid spread of antibiotic resistance is a global health threat. A range of environments have been identified as reservoirs of the antibiotic resistance genes (ARGs) found in pathogens, but we lack understanding of the origins of these ARGs and their spread from environment to clinic. This is partly due to an inability to identify the bacterial hosts of ARGs and the mobile genetic elements that mediate horizontal gene transfer due to the loss of intra-cellular contiguity upon DNA extraction.

Materials/methods: In two recent studies we describe the application of proximity-ligation (Hi-C) methods for the determination of the in situ host range of numerous ARGs, viruses, plasmids, and integrons within complex microbiome samples. This method forms physical junctions between sequences present within the same cell prior to DNA extraction. Subsequent sequencing generates a dataset that robustly connects mobile elements to their hosts and can accurately assemble de novo genomes directly from mixed communities without culturing.

Results: Our application of this technology to highly complex wastewater and rumen samples yielded hundreds of novel ARG-, virus-, and plasmid-host interactions, as well as over a thousand new microbial genomes. In the case of wastewater sample analysis, we assembled >1000 genome clusters and identified >300 ARG-host affiliations from a single sample. In a study analyzing a rumen sample, we used SMRT long read technology as well as Hi-C to detect 188 novel viruses and their host associations. We will also describe other published and upcoming projects applying this technology.

Conclusions: These studies highlight the power of the proximity-ligation approach to deconvolving microbiome samples and foreshadow the development of rapid culture-free strategies for tracking and managing the spread of antimicrobial resistance.

References:
1. Linking the Resistome and Plasmidome to the Microbiome; Thibault Stalder et al., 2019, ISME J
2. Assignment of virus and antimicrobial resistance genes to microbial hosts in a complex microbial community by combined long-read assembly and proximity ligation; Derek Bickhart et. al., 2019, Genome Biology

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Accuracy of chikungunya case definition in patients with arbovirus illness seeking care in an urban emergency department in Rio de Janeiro, Brazil

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Abstract third-party references: Supported by Faperj.

Background: Chikungunya (CHIKV), dengue and zika share similar clinical features, which makes a clinical diagnosis complex in regions where the three arboviruses co-circulate. We evaluated the accuracy of the World Health Organization’s (WHO) CHIKV case definition against the gold standard of laboratory diagnosis, in individuals with suspicion of arboviral illness seeking care in an urban emergency department (ED) in Rio de Janeiro, Brazil, from January to June 2018.

Materials/methods: A cross-sectional study was conducted enrolling consecutive patients with arbovirus illness without an evident focus of infection. CHIKV RT-PCR and CHIKV IgM serology were performed. Odds ratio (OR) was used as the association measure to identify the clinical features related to CHIKV against the laboratory diagnosis of CHIKV [i.e., defined as either a positive RT-PCR or IgM]. Stepwise logistic regression was done with forwarding selection to identify the best CHIKV prediction model, with a significance level of 5%. The diagnostic accuracy of the WHO CHIKV case definition was evaluated.

Results: A total of 172 subjects were included. The prevalence of CHIKV infection was 110/172 (64%) and 62/172 (36%) had other febrile illnesses. Participants had a mean age of 39 ±15.5 years, females predominated (52.3%), and 65% presented within three days after onset of illness. Among CHIKV-infected patients, 92/172 (53.5%) were positive by RT-PCR and 10.5% only by IgM. CHIKV patients presented much earlier after onset of symptoms (2 vs. 3.5, p= 0.007) and reported most frequently arthritis (61.8% vs. 33.9%, p <0.0001), arthralgia (96.4% vs. 79%, p <0.0001), and conjunctivitis (35.5% vs. 16.1%, p = 0.007) compared to CHIKV-negative subjects, respectively. After adjustments for other clinical predictors, arthritis/arthralgia [aOR: 6 (95%CI 1.8-19.7)] and the presence of conjunctivitis [aOR: 2.3 (95%CI 1.5-2.5)] were positively associated with CHIKV. The sensitivity, specificity, and accuracy of the CHIKV case definition was 85.45% (95% CI 77.46% to 91.45%), 38.71% (95% CI, 26.60% to 51.93%) and 68.6% (61.10% to 75.45%) respectively.

Conclusions: Arthritis/arthralgia and conjunctivitis were positively associated with CHIKV. The current definition for CHIKV had a lower accuracy, in our setting, where other arboviruses co-circulate

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Abstract 8813

Antimicrobial susceptibility testing directly from positive blood culture with the Reveal Rapid AST System: clinical results for Gram-negative pathogens

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Background: Obtaining phenotypic antimicrobial susceptibility test (AST) results directly from positive blood culture is of increasing importance with the evolution and spread of drug-resistant blood stream infection. Here we report the first clinical results of the Specific Diagnostics Reveal Rapid AST system on Gram negative patient samples.

Materials/methods: Remnant material from positive clinical monomicrobial Gram negative blood cultures was diluted 1:1000 in Pluronic water and inoculated into MicroScan (Beckman Coulter) dried antibiotic plates, sealed with Specific’s sensor sheet, and placed in the Reveal instrument where it was rocked and incubated at 37°C. Sensor changes above each well were optically monitored to detect the volatile emissions that are a sign of population growth, thereby ascertaining which antimicrobial-containing wells were growing and thus MIC. MIC was compared to that of VITEK2® (bioMérieux) performed after isolate growth. Essential Agreement (EA) was defined as the Reveal and VITEK2 MIC being within one two-fold dilution, while Categorical Agreement was defined as exact agreement in results interpreted according to CLSI clinical breakpoints. The assay determined MIC for all 25 Gram negative antimicrobial agents present on the MicroScan Gram negative plate. The few disagreements between Reveal and VITEK2 will be adjudicated by broth microdilution (BMD) at the end of the study. Experiments were performed in duplicate, with QC strains used to verify Reveal system performance.

Results: Clinical samples with 28 distinct strains tested in duplicate were assayed directly from positive blood cultures, with a total of 74S bug-drug combinations tested, with 16.4% of the assays resistant as assessed by VITEK2 results interpreted with CLSI breakpoints. Using VITEK2 as the reference, Reveal results yielded EA of 97.36% and CA of 95.03%, with no very major errors (VME) for this sample set. discords with VITEK2 will be adjudicated by BMD at the end of the study. Average time to result was 5.7 hours across this highly resistant set of clinical Gram-negative samples.

Conclusions: In this first study with clinical samples, the Reveal Rapid AST system showed excellent agreement in MIC determination compared to VITEK2, providing a preliminary indication of same-shift AST utility in a clinical setting.

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**Abstract 8814**

**Evaluation of a urinalysis predictive model and the performance of direct-from-urine susceptibility testing**

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**Background:** Antimicrobial susceptibility testing (AST) for urinary tract infection (UTI) has an approximately 48 hour turnaround time and as a result, often plays little role in guiding therapeutic decision making. In this study, we investigate an AST method which inoculates disk diffusion (DD) testing directly from urine specimens. Only 30% of urinalysis-positive specimens yield significant growth, thus, performing Direct-AST (D-AST) for all urinalysis positive specimens is a waste of resources for ~70% of specimens. To better predict which patients would benefit from D-AST, we developed a predictive urinalysis model designed to optimize urinalysis specificity.

**Materials/methods:** Specimen inclusion criteria were the following: urinalysis positive and clean catch specimens collected in the Emergency Department. D-AST of cefazolin (CZ), nitrofurantoin (FUR), trimethoprim-sulfamethoxazole (SXT), and ciprofloxacin (CIP) were inoculated to Mueller Hinton (MH) and a MacConkey (MAC) agar on the day of collection. Results were compared to standard of care (SOC) DD. In total, there were 69 evaluable specimens for CZ and NITRO, 39 for CIP, and 42 for SXT.

**Results:** CZ testing yielded an overall categorical agreement (CA) of 95.7% and 98.6% on MH and MAC agars, respectively. FUR testing yielded an overall CA of 95.6% and 92.8% on MH and MAC agars, respectively. SXT testing yielded an overall CA of 95.2% for both MH and MAC agars. CIP testing yielded an overall CA of 97.4% for both MH and MAC agars.

Using this approach, we determined that 78.6% of nitrate positive patients had UTI. Of the nitrate negative patients, 70.0% with >50 WBC’s and numerous bacteria visualized, had UTI. Thus D-AST will only be applied to specimens meeting these criteria.

**Conclusions:** Overall categorical agreement for all antibiotics and all media was >90%. Direct AST yielded VME’s for CZ and FUR. However, in the CZ VME event, zone sizes for the D-AST and the SOC differed by 2 mm (16 mm vs. 14 mm, respectively). Thus, adopting a zone size cutoff of 16 mm would have eliminated the CZ VME. The FUR VMEs both occurred on MAC and thus, adopting the MH agar for direct AST would have eliminated all VMEs.

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**Abstract 8818**

**Improved specie identification of *Staphylococcus argenteus* with MALDI-TOF MS using an extended MSP library**

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**Background:** *Staphylococcus argenteus* was up to recently known as a divergent *Staphylococcus aureus* clonal lineage. It was recognized as a novel species in 2015 and is a member of the *S. aureus* complex. Of importance is that methicillin-resistance strains are described for both species. As *S. aureus* and *S. argenteus* are closely related and share many characteristics, it is difficult to distinguish the two species with routine diagnostics.

Specie identification of bacteria with Matrix Assisted Laser Desorption/Ionisation Time of Flight (MALDI-TOF) mass spectrometry (MS), is a common method in routine diagnostics. However, current MALDI-TOF MS system (Bruker MALDI Biotyper with the MBT 8468 MSP library 2019) cannot accurately differentiate the two species.

The aim of this study was to evaluate if it is possible to improve the MALDI-TOF MS method for the identification of *S. argenteus* by creating a new MALDI-TOF mass spectral profile (MSP) library from local strains of *S. argenteus* and *S. aureus*.

**Materials/methods:** Clinical strains were selected and determined to species level by *nuc* gene sequencing (Sanger methodology) as either *S. argenteus* or *S. aureus*. Then the strains were analyzed with MALDI-TOF MS and new Mass Spectra Profiles (MSP) were created. All of the strains were divided into two groups. One group of strains was used to create a new MSP library and the second group of strains was used to test and validate the new library.

**Results:** Using *nuc* sequencing 16 *S. argenteus* strains and 20 *S. aureus* strains were determined to the specie level and were included in the study. When the *S. argenteus* strains were analysed with the MALDI Biotyper and the MBT 8468 MSP library then 43% of the *S. argenteus* strains could not be identified accurately. When the new MSP library were added all *S. argenteus* strains could be identified correctly with MALDI Biotyper. Specie specific mass spectra differences could also be identified.

**Conclusions:** By expanding the existing MALDI Biotyper library with a custom made library of MSPs from local strains, we were able to improve the identification accuracy and the ability to distinguish *Staphylococcus argenteus* from *Staphylococcus aureus*.

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Abstract 8820

**Fc-mediated Fcγ receptor engagement of CD377, a novel antiviral Fc-conjugate, translates into potent antibody-dependent cellular phagocytosis and antibody-dependent cellular cytotoxicity activity**

Simon Döhrmann*, Rajvir Grewal†, Elizabeth Abelovski†, Tom Brady†, Wanlong Jiang†, Zhi-Yong Chen†, Allen Borchardt†, Jason N. Cole†, Leslie W. Tari†

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**Background:** Cidara's AVCs (antiviral Fc-conjugates) are novel, immunotherapeutic conjugates of potent, antiviral agents with the Fc domain of human IgG1. CD377 is an AVC development candidate for the prevention and treatment of seasonal and pandemic influenza that has demonstrated potent, broad-spectrum activity and efficacy in multiple influenza challenge mouse models. Herein, we characterize Fc-mediated interaction of CD377 with Fcγ receptors and the function of CD377 in antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis (ADCP) against influenza.

**Materials/methods:** CD377 interaction with multiple Fcγ receptors (human and murine) was determined by ELISA. For ADCC and ADCP experiments, MDCK cells were infected with varying multiplicity of infection (MOI) for 18-24 h and treated with CD377 ranging from 0.1 – 1000 nM. ADCC and ADCP was determined according to manufacturer’s instructions.

**Results:** CD377 binding affinity to human Fcγ receptors (I, IIa, IIIa) was comparable to unconjugated Fc (hIgG1 Fc), demonstrating that the conjugation chemistry did not interfere with Fc-mediated effector functions of the antiviral Fc-conjugate, CD377. Additionally, the Fcγ receptor binding profiles of CD377 are comparable to those observed for a full-length human IgG1 antibody.

Immune cells, such as NK cells and macrophages, are crucial mediators of host defense against influenza infection. A hallmark of macrophage function in immunity is phagocytosis of antibody-opsonized infected cells. CD377 mediated MOI- and dose-dependent ADCP via FcγRIIa engagement (Figure). NK cells have been demonstrated to be important in immune defense against influenza infection by inducing apoptosis of infected cells through the release of perforin/granzymes. CD377 induced robust ADC via FcγRIIIa engagement with MOI- and dose-dependency against multiple seasonal and pandemic influenza A/H1N1, influenza A/H3N2, and influenza B strains.

**Conclusions:** CD377 triggers potent, broad-spectrum induction of ADCP and ADCC, thereby contributing to immune defense against multiple seasonal and pandemic influenza A and B strains. This potent induction of Fc-mediated effector function of CD377 in combination with potent efficacy in lethal mouse models of influenza infection support further development of CD377 for the prevention and treatment of influenza infection.

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CD377, a novel antiviral Fc-conjugate, demonstrates potent broad-spectrum activity in multiple in vitro assays against influenza A and B

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Background: AVCs (antiviral Fc-conjugates) are novel, long-acting immunotherapeutic conjugates of potent antivirals and the Fc domain of human IgG1.

CD377 is an AVC development candidate for the prevention and treatment of seasonal and pandemic influenza, comprising a novel neuraminidase inhibitor (NI) conjugated to IgG1 Fc, designed to provide broad-spectrum coverage of influenza A and B, including drug-resistant strains. CD377 has demonstrated efficacy in multiple lethal influenza mouse models. Herein, we characterize the activity of CD377 in multiple in vitro assays against influenza A and B strains including clinically relevant baloxavir- and NI-resistant mutants.

Materials/methods: CD377 was tested alongside oseltamivir, zanamivir, or baloxavir at concentrations ranging from 0.01 nM to 10,000 nM. Neuraminidase inhibition (NAI) activity was determined using a commercial NA-Fluor kit. Cytopathic effect (CPE) was determined against influenza A after 3 days and B strains after 5 days in MDCK SIAT1 cells. Activity in plaque reduction assay (PRA) was determined in MDCK cells after 48–72 h depending on virus strain tested.

Results: CD377 demonstrated potent NAI activity in a low nM range (IC50 0.01 – 23.55 nM) against influenza A/H1N1, influenza A/H3N2, and influenza B strains. The activity of CD377 did not shift against variants that confer resistance/reduced susceptibility to oseltamivir (H275Y, E119V), to oseltamivir and zanamivir (R292K), or to baloxavir (I38T/L/M) in NAI.

In the cell-based assays, CD377 demonstrated up to 100-fold increased potency than oseltamivir or zanamivir against influenza A and B wild-type strains. Notably, CD377 activity did not shift against H1N1 H275Y or H3N2 R292K mutants. The activity of CD377 in PRA or CPE was on par with or greater than that of baloxavir.

Conclusions: CD377 demonstrated potent, broad-spectrum antiviral activity in vitro against multiple seasonal and pandemic H1N1 and H3N2, and B strains. While CD377 shares a mechanism with approved NIs, its potency in cell-based assays was superior to oseltamivir or zanamivir, and comparable to or greater than baloxavir. This potent antiviral activity of CD377 in multiple in vitro assays, combined with efficacy in lethal mouse models of influenza infection support further development of CD377 for prevention and treatment of influenza infection.

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Abstract 8833

**Optimising the microbiological diagnosis of prosthetic joint infection: a 5-year evaluation**
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**Background:** Arthroplasty is an effective surgical intervention that improves quality of life. In Scotland over the last decade the number of primary knee and hip arthroplasties have almost doubled, with 15,091 cases being performed in 2018. Periprosthetic infection albeit rare, remains a major complication that continues to pose a diagnostic and therapeutic challenge.

The aim was to evaluate the impact of our interventions (restructuring of workflow, microbiological processing and integration into our electronic management order comm system) over the last 5 years and assess if through effective diagnostic stewardship in a routine laboratory an improvement in the microbiological diagnosis of PJI could be achieved and sustained.

**Materials/methods:** A retrospective analysis was performed over 5 years; 4-month time periods May-August, 2015 [pre-intervention] to 2019. Data was analysed from two large university teaching hospitals within Greater Glasgow & Clyde, the largest NHS organisation in the UK. Only cases where a PJI diagnosis [knee or hip arthroplasty] had been confirmed according to either the clinical practice guidelines by the Infectious Diseases Society of America or on clinical judgement were included for analysis. The number of intra-operative samples, the culture positive rate and time to positivity [growth of a significant organism] and the causative organism[s] isolated were assessed for each case.

**Results:** A total of 177 patients were identified over the post-intervention study period [2016 to 2019]. Following interventions the mean number of intra-operative specimens sent per case increased and was found to be sustained at 6 [2017-2019] compared to 4 in 2015. A statistical significant increase in the positive culture rate [significant pathogen being cultured] was also demonstrated [Chi-square test: P value < 0.0001].

**Conclusions:** PJI remains an important complication of arthroplasty. Through effective diagnostic stewardship and development of an integrated standardised laboratory strategy for processing orthopaedic specimens, a significant and sustained improvement in the microbiological diagnosis and management of PJI was achieved.

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Abstract 8839

**CD377, a novel antiviral Fc-conjugate, demonstrates superior reduction of viral burden and cytokine levels compared to oseltamivir in a lethal mouse model of influenza A(H1N1) infection**

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**Background:** AVCs (antiviral Fc-conjugates) are novel, long-acting immunotherapeutic conjugates of potent antivirals and the Fc domain of human IgG1. CD377, an AVC development candidate for the prevention and treatment of influenza A and B, comprises a novel neuraminidase inhibitor conjugated to IgG1 Fc. CD377 has demonstrated potent, broad-spectrum activity against influenza at levels greater than current influenza antivirals and efficacy in multiple influenza challenge models. Herein we characterize the activity of CD377 on viral lung burden and host immune responses in a lethal mouse model of influenza infection.

**Materials/methods:** BALB/c mice were challenged intranasally with $3 \times 10^2$ PFU (3 x LD95) of mouse-adapted influenza A/ Puerto Rico/8/1934 (H1N1). Treatment was started 2 h post-challenge with either CD377 as a single subcutaneous dose (0.1 – 3 mg/kg) or oral oseltamivir (5 or 50 mg/kg BID x 4 days). At day 4 post-infection, lungs were harvested; cytokine levels were determined via ELISA and viral burden was determined by plaque assay.

**Results:** CD377 demonstrated a dose-dependent reduction in viral lung burden resulting in 1.06 log at 0.1 mg/kg, 2.12 log at 0.3 mg/kg, 3.17 log at 1 mg/kg, and 3.63 log at 3 mg/kg compared with PBS control titers of $5.1 \times 10^7$ PFU/g (Figure). Oseltamivir demonstrated minimal effects on reduction of viral lung burden with 0.8 and 0.78 log reductions at the humanized dose (5 mg/kg) and 50 mg/kg, respectively. Minimal difference in lung burden was observed between negative controls, PBS and hIgG1 Fc of 0.47 log. The dose-dependent reduction of viral burden by CD377 correlated with a dose-dependent reduction of multiple cytokines TNF-α, IL-6, MCP-1, MIP-1α, and KC, which at the 3 mg/kg dose approached levels observed in uninfected control mice (Figure). Oseltamivir showed a lesser effect on cytokine reduction compared to CD377.

**Conclusions:** CD377 demonstrated a superior profile compared to oseltamivir in controlling infection and inflammation in a lethal H1N1 influenza model. CD377 mediated protection via multi-log reduction in viral lung burden correlating with reduction in pro-inflammatory cytokines. These results underscore the novel mechanism of action of AVCs and support further development of CD377 for prevention and treatment of influenza infection.

**Figure:** CD377 reduces viral burden and cytokine MCP-1 with dose-dependency. CD377 efficacy in a lethal mouse model of influenza A/PR/8/1934 (H1N1) reduces (A) viral burden and (B) MCP-1 levels in the lung in dose-dependency on day 4 post-infection.

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Abstract 8845

Analysis of early outcomes in the STRIVE Trial of rezafungin once-weekly treatment of candidaemia and invasive candidiasis

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Background: Front-loading of antimicrobials (ie, achieving and maintaining high drug exposure early in therapy) has been shown to be a pharmacometric determinant of efficacy. Rezafungin is a novel echinocandin that demonstrates a long half-life and front-loaded plasma exposures. The Phase 2 STRIVE trial [NCT02234862] evaluated the safety and efficacy of rezafungin once weekly (QWk) compared with once daily (QD) caspofungin in the treatment of candidaemia and/or IC. Secondary efficacy endpoints were evaluated to assess treatment response throughout the course of therapy, including at Day 5, by which point patients had either received one dose of QWk rezafungin or 5 doses of QD caspofungin.

Materials/methods: Adults (≥18 y) with systemic signs and mycological confirmation of candidemia and/or IC were randomized to receive rezafungin 400 mg QWk, rezafungin 400 mg on Week 1 followed by 200 mg (400 mg/200 mg) QWk, or caspofungin 70 mg on Day 1 followed by 50 mg OD for ≥14 days. Overall response (resolution of clinical signs of infection + mycological eradication) at Day 5 and time to negative blood culture were determined for rezafungin (pooled), as both groups received 400 mg in Week 1 versus caspofungin.

Results: At Day 5, the rate of overall success was 62.3% (76/122) for rezafungin and 55.7% (34/61) for caspofungin [Table]. Rates of mycological cure at Day 5 were 69.7% and 62.3%, respectively. Rezafungin-treated patients demonstrated a shorter time to negative blood culture (median: 19.5 hours versus 22.8 hours for caspofungin, log-rank p=0.02) [Figure]. While small differences favoring rezafungin were noted initially, the probability of a negative blood culture reached its maximum difference about 24 hours after the first dose.

Conclusions: Early efficacy of rezafungin was demonstrated based on outcomes of overall success, mycological success and time to negative blood culture. These findings support front-loaded plasma exposure as a pharmacometric determinant of efficacy and the development of rezafungin for treatment of candidaemia and IC.

<table>
<thead>
<tr>
<th>Outcome at Day 5</th>
<th>Rezafungin 400 mg/400 mg QWk N= 76</th>
<th>Rezafungin 400 mg/200 mg QWk N= 46</th>
<th>Rezafungin QWk Pooled N=122</th>
<th>Caspofungin 70 mg/50 mg QD N= 61</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall success</td>
<td>42 (55.3)</td>
<td>34 (73.9)</td>
<td>76 (62.3)</td>
<td>34 (55.7)</td>
</tr>
<tr>
<td>Mycological Cure</td>
<td>50 (65.8)</td>
<td>35 (76.1)</td>
<td>85 (69.7)</td>
<td>38 (62.3)</td>
</tr>
</tbody>
</table>

Figure. Time to Negative Blood Culture following Treatment with Rezafungin vs Caspofungin

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Abstract 8857

Epidemiological profile, mortality and causes of death in the first year of newly HIV-diagnosed patients of a national referral centre in Costa Rica from January 2015 to December 2017

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Background: The HIV epidemic continues to be a serious health threat despite the efforts made by the healthcare providers. In Costa Rica, there are still large HIV-related epidemiological gaps and also lacks representative and quality local data to support strategic interventions.

Materials/methods: A retrospective, observational and descriptive study was conducted. Late presentation, follow-up after diagnosis and survival curves were also analyzed.

Results: The population of newly diagnosed HIV patients was mostly male [9 to 1 male: female ratio], young adults, under 29 years of age, Costa Rican, single, residing in the province of San José and with incomplete schooling. In the majority of patients, 87.6% ART was started (461) and the mostly used combination was TDF, xTC and EFV for 61.7% (325). 26.7% of the patients had advanced disease at presentation and 44.0% with late diagnosis. Mortality in the first year after the diagnosis was 7.5%. The main identifiable cause of death was CNS toxoplasmosis opposite of what is reported worldwide literature which describes tuberculosis. Regarding mortality, several protective factors were identified: < 40 years (RR 0.25 IC95% 0.15-0.42), viral load < 100 000 copies / ml (RR 0.2, IC95% 0.1-0.4) and ART (RR 0.2 IC95% 0.1-0.3). And as for its risk factors: incomplete high school or lesser educational status (RR 2.7 IC95%: 1.5 - 4.7), late diagnosis (RR 5.6 IC95% 2.8-11.4) and advanced disease (RR 5, 1 IC95% 2.9-9.0). The patients were not linked to proper healthcare, and important delay in each point of the process that goes from the diagnosis to the beginning of the ART was detected.

Conclusions: There are important differences in survival among newly diagnosed patients. In this national referral center in Costa Rica, 26.7 % of new HIV patients were diagnosed with advanced disease and 44 % with late presentation. Mortality in the first year after HIV diagnosis was 7.5 %, and it was significantly influenced by age, schooling, presence of ART, viral load and CD4 count. The main cause of death identified was CNS toxoplasmosis.

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**Abstract 8858**

**Macrolide-resistant *Mycoplasma pneumoniae* detection**

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**Background:** Mycoplasma pneumoniae is a major cause of community-acquired pneumonia, especially in infants and children. Macrolides have been recommended for the treatment of Mycoplasma pneumoniae infections because of their low MIC and high safety profile. However, macrolide-resistant *M. pneumoniae* (MRMP) has become increasingly prevalent worldwide, especially in Asia. MRMP infections have been associated with alternative therapy and higher chance of complications. The increasing trend of the resistant strain highlights the need for a timely diagnosis of MRMP for the clinical management and infection control of patients.

**Materials/methods:** The aim of the study was to determine the prevalence of MRMP in Hong Kong. Nasopharyngeal swabs (flocculated swabs from Copan, Italy) were collected in viral medium. Sputum and bronchial lavage samples with a standard collection procedure were obtained from patients for the period of February, 2019 to October, 2019 from Hong Kong Adventist Hospitals. In total, 7,160 patient samples were received during this period for PCR testing using Filmarray respiratory panel. Wherein, there were 428 (6.0%) positive cases of *M. pneumoniae*. These positive cases were tested for macrolide resistant genotype at 23S rRNA position A2063G by simple-probe real-time PCR coupled to melting curve analysis in Rotorgene Q platform.

**Results:** The macrolide resistance genotyping was successfully carried out on all 428 positive *M. pneumoniae* samples. Simple-probe real-time PCR coupled to melting curve analysis identified 18 cases (4.2%) as having the MRMP genotype by detecting the A2063G transition.

**Conclusions:** Mycoplasma pneumoniae is a common cause of respiratory tract infection in Hong Kong. Targeted antibiotic therapy is required for the patients with serious symptoms. Macrolides, fluoroquinolones and tetracyclines are treatment options for *M. pneumoniae* patients, but only macrolides have been approved for use in young children. In our study, patients with the A2063G mutation, detected by conventional PCR coupled to melting curve analysis, are more likely required a change of therapy from macrolides to fluoroquinolones or tetracyclines. This was consistent with our records which showed that these patients had changed their antibiotic regimen. In conclusion, a rapid diagnosis of *M. pneumoniae* and macrolide resistant strain would definitely help the clinicians for antibiotic selection.

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Abstract 8862

Depicting the pathogenicity and genomics traits of hypermucoviscous Enterobacteriaceae clinical isolates

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Background: Hypervirulent K. pneumoniae displays a distinctive phenotype named hypermucoviscosity. Two plasmid-borne regulators rmpA and rmpA2 are involved in the HMV phenotype acting in the cps locus. An increasing population of K. pneumoniae, K. variicola and K. quasipneumoniae isolates displaying the hypermucoviscous phenotype without rmpA and rmpA2 genes associated have been reported worldwide. Some forms of immunodeficiency such as diabetes represents a greater risk for infections with classical and hypervirulent K. pneumoniae strains.

Materials/methods: In this project were included a collection of K. variicola (1), K. pneumoniae (5), K. quasipneumoniae (1), K. oxytoca (1) and E. coli (1) with hypermucoviscous phenotype; without rmpA and rmpA2 genes associated. We performed antimicrobial susceptibility test, plasmid profile, chemical plasmid curing, serum resistant killing assay and resistance to phagocytosis. Male Balb/c mice healthy and diabetic mice of 7 weeks old were inoculated with 10^7 to 10^8 CFU. Survival curve and LD50 were determined. The complete genomes were determined and Roary, Artemis and ACT were used for comparative genomics.

Results: K. variicola 8917 was successfully curated; we observed that the hypermucoviscous phenotype is lost when the plasmid is segregated. K. variicola 8917 inoculated in the healthy mice was able to induce 100% mortality at higher doses (10^8) in contrast with its cured variant Δ8917 showed a decrease in virulence and mortality. We did not observe changes when diabetic mice were inoculated with K. variicola 8917; however, diabetic mice die faster (18h) at higher doses (10^9). K. pneumoniae 3478 showed resistance to serum and E. coli 10270 was resistant to phagocytosis. The pan genome of hypermucoviscous strains was composed for 17,667 genes, a core-genome of 344 genes and the variable genome of 5100 genes. These strains possessed classical virulence factors and 50% of the strains were multidrug resistant.

Conclusions: In general, the pathogenicity was heterogeneous among the hypermucoviscous isolates. K. variicola decreases its pathogenicity when the phenotype is absent in cured strain. The diabetic mice showed greater susceptibility during the infection caused by hypermucoviscous isolates. The hypermucoviscous phenotype has expanded to various bacterial genus.

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Abstract 8863

Rapid, non-invasive detection of Legionella and resolution of species diversity in clinical infections using the Karius test, a microbial cell-free DNA sequencing test for pathogen detection

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Background: Legionella species can cause lower respiratory tract infection or a systemic febrile illness (“Pontiac fever”). Infections can occur sporadically or in the context of outbreaks associated with environmental sources. Legionella is difficult to culture and urine antigen testing only detects Legionella pneumophila serogroup 1 which is thought to cause most clinical infections. However, many additional Legionella species can cause disease and are undetected by urine antigen testing.

Materials/methods: Karius Test (Redwood City, CA) results from the prior two years were reviewed for detections of Legionella. The Karius Test is a CLIA-certified/CAP-accredited next generation sequencing (NGS) plasma test that detects microbial cell free DNA (mcfDNA). After mcfDNA is extracted and NGS performed, human sequences are removed and remaining sequences are aligned to a curated pathogen database of >1000 organisms. Organisms present above a statistical threshold are reported. The time to result reporting is 24 hours (on average) from sample receipt.

Results: The Karius Test detected Legionella in 29 patient samples including 25 adults (86%) and four children. Twenty-one patients (72%) were immunocompromised; 23 patients (79%) had a pulmonary focus with a presumptive lower respiratory tract infection. Thirteen samples were positive for Legionella pneumophila (45%), four samples were positive for Legionella bozemaniae (14%), two samples each were positive for Legionella anisa (7%), Legionella cincinnatiensis (7%), Legionella micdadei (7%), Legionella sainthelensi (7%), and one sample each was positive for Legionella feeleii (3.5%) and Legionella brunensis (3.5%). To our knowledge this is the first reported detection of Legionella brunensis as a cause of human infection. The majority (75%) of infections in immunocompetent individuals were caused by Legionella pneumophila whereas Legionella identified in immunocompromised individuals were more commonly non-pneumophila species (67%).

Conclusions: The Karius Test detected a broad diversity of Legionella species causing infections, most of which were non-pneumophila species undetectable by the urine antigen test. Plasma mcfDNA NGS offers a rapid, non-invasive means of detecting a broad diversity of known and potentially novel Legionella species. Accurate species-level identification of Legionella also has important public health implications given the pathogen’s association with environmental outbreaks.

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Abstract 8864

**Species distribution and antifungal susceptibility of Candida spp. causing candidaemia in China: an update from the CHIF-NET study**

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**Background:** Candidemia is the most common, serious fungal infection, and antifungal resistance has become a notable challenge. Here we report the most recent surveillance results (1 August, 2014 to 31 July, 2017) of candidemia from the China Hospital Invasive Fungal Surveillance Net (CHIF-NET) study.

**Materials/methods:** The study encompassed 77 hospitals across China over three years. Species identification of causative Candida spp. was by mass spectrometry supplemented by DNA sequencing. Antifungal susceptibility was determined using the Clinical and Laboratory Standards Institute broth microdilution method.

**Results:** A total of 4,010 isolates were collected from candidemia patients. Although C. albicans remained the most common species, non-albicans Candida species accounted for over two-thirds of isolates – predominated by C. parapsilosis complex (27.1%), C. tropicalis (18.7%) and C. glabrata complex (12.0%). Most C. albicans and C. parapsilosis complex isolates were susceptible to all antifungal agents (resistance rate <5%). However, there was a consistent decrease in voriconazole susceptibility to C. glabrata sensu stricto over the three years (the non-wild-type phenotype rose from <20% to ~50%). In addition, the fluconazole resistance rate in C. tropicalis tripled from <10% in 2009-2010 to >30% in 2016-2017. Moreover, amongst less common Candida species, over one-third of C. pelliculosa isolates were co-resistant to fluconazole and 5-flucytocine, and >56% of C. haemulonii isolates were multidrug resistance.

**Conclusions:** Non-albicans Candida species has become predominant cause of candidemia in China, and azole resistance is notable amongst C. tropicalis and C. glabrata. In addition, co-resistance and multi-drug resistance has emerged in less common Candida species.

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Abstract 8865

**Patient risk factors associated with development of acute kidney injury after combination antibiotic therapy for methicillin-resistant Staphylococcus aureus (MRSA) bacteremia**

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**Background:** The CAMERA2 trial compared the combination of a β-lactam with standard antibiotic therapy vs standard therapy alone for MRSA bacteremia. Acute kidney injury (AKI) occurred more commonly in the combination (23%) compared to the standard therapy (6%) group. This study aims to identify patient and treatment factors associated with the development of AKI in the CAMERA2 cohort.

**Materials/methods:** Two definitions of AKI were used: 1) modified RIFLE (1.5-fold increase in the serum creatinine days 1-7 or new renal replacement from days 1-90; as specified in the trial protocol), and, 2) modified KDIGO (modified RIFLE OR ≥26.5µmol/L increase from baseline creatinine to day 2). Patients were excluded if they were randomized in error; were on dialysis at randomization; or had no baseline or follow-up creatinine or 90-day follow-up. Variables associated with AKI on univariate analysis (P<0.10) or clinically relevant to the development of AKI (age, sex, baseline creatinine) were included in multivariable models.

**Results:** Of the 356 patients enrolled, 87 were excluded from the analysis [54 chronic dialysis, 22 insufficient creatinine measurements, four randomized in error, seven loss to follow-up]. Overall, AKI occurred in 43/269 [16.0%] or 65/269 [24.0%] patients using the modified RIFLE or modified KDIGO criteria respectively.

On univariate analysis, development of modified RIFLE AKI was associated with lower age [mean age difference -7.4 years [-1.5, -13.4] for AKI] and lower baseline creatinine [difference -35.1 [-14.0, -56.3] for AKI]. Development of modified KDIGO AKI was associated with lower age [-5.2 years [-0.1, -10.3]].

On multivariate analysis, allocation to combination therapy was the only predictor of AKI for modified RIFLE [aOR 4.4, 95% CI 2.0-9.7] and modified KDIGO [aOR 2.4 [1.4-4.2]] criteria. Within the combination group, the receipt of flu(cloxacillin) only [n=106] verses cefazolin only [n=25] was not statistically significantly associated with AKI [modified RIFLE [aOR 6.4 [0.73, 55.5]] or modified KDIGO [aOR 2.1 [0.58, 7.3]]].

**Conclusions:** Combination therapy with a β-lactam was independently associated with AKI using RIFLE and more recent KDIGO definitions. A direct comparison between flu(cloxacillin) and cefazolin was limited by the small sample size but point estimates suggest AKI is more likely with flu(cloxacillin).

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Abstract 8871

Prevalence of latent tuberculosis in the adult population of the National Institute of Respiratory Diseases in the period 2016-2019 through an interferon-gamma release assays

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Background: Tuberculosis (TB) is one of the most relevant causes of disease and mortality around the world, mainly in Africa and Asia. TB is currently the ninth cause of death worldwide, and the main cause by an infectious disease, outgrowing mortality by HIV related infections. By 2008, it was estimated that 30% of the world population has a latent (LTBI) or active (ATBI) infection. The treatment of LTBI infection is one of the best strategic elements towards eradicating TB. In Mexico, studies on LTBI prevalence have reported estimations that range from 35 to 76% positivity with IGRAs, but with no nation-wide representativeness, so the magnitude of the national problem remains unknown. It’s important to perform a study to assess the magnitude of the problem. The objective was to determine the prevalence of latent tuberculosis infection in the adult population with an IGRAs.

Materials/methods: A retrospective study including adult patients attended at the INER and had an IGRAs. The results were obtained using descriptive statistics; percentages, means ± SD. It was used chi2, to compare characteristics the patients with IGRAs positive, negative and indeterminate. The prevalence of TB was obtained from the ratio of the total tests conducted against the total of positive tests.

Results: 507 patients were included. The average age was 51 years ± 16.45. The prevalence of latent tuberculosis was 23% (116/461). The prevalence increased in patients with more than 60 years. We observed a higher prevalence in women, contact with tuberculosis and health workers, 34% and 32% respectively. We found a low prevalence in patients with HIV, 15% similar to what’s found in patients with DM2. 46 patients had an undetermined IGRA result. The factors associated with an indeterminate result were immunosuppressants, HIV infection and hypoalbuminemia.

Conclusions: The prevalence of tuberculosis in population treated at the INER was similar to the estimated by the WHO.

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Abstract 8872

**Airborne antibiotic-resistant *Staphylococcus epidermidis* in inpatient wards linked to deep surgical site infections**

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**Background:** Hospital-associated multiple antibiotic resistant *Staphylococcus epidermidis* (MRSE) strains remain important causes of healthcare-associated infections (HAI) despite significant improvement in infection prevention and control measures to stop contact transmission. Here, we investigate the prevalence of MRSE and other microorganisms in the air in a hospital, and compare MRSE in air with MRSE causing deep surgical site infections (SSI) or blood stream infections (BSI).

**Materials/methods:** The setting was a tertiary care University hospital in Northern Sweden serving 900 000 inhabitants. From April 3 to May 9 2017, microorganism in the air were sampled by 14 cm settle blood agar plates in the acute orthopedics ward, the cardiothoracic critical care unit, the general ICU, the neonatal ICU, and in three operation theatre suites. Eight agar plates were placed for 8 h twice a week at each site. Microbiological work included incubation, colony forming unit (cfu) counts, MALDI-TOF, and antimicrobial susceptibility tests. Airborne MRSE resistant to cefoxitin + ≥3 more antimicrobials, and MRSE judged with high clinical certainty as causes of BSI or deep SSI associated with surgical implants 2015-2017 were genome sequenced using illumina technology.

**Results:** Coagulase-negative staphylococci and *Micrococcus* spp. were commonly airborne at all seven sampling sites. Median total microbial surface deposition ranged 534-2790 cfu/m²/h. Additional microorganisms identified included multiple species of fungi, *Bacillus* spp. *Enterococcus* spp., and *Streptomyces* spp. One *Staphylococcus aureus* cfu was identified at the neonatal ICU, but not at other sampling sites. Air loads of MRSE were highly variable among sites and sampling dates (0-9.2 cfu/m²/h), suggesting that airborne skin scales from certain individuals carrying MRSE contributed to variation. There were no airborne MRSE in the operation theater suits or in the neonatal ICU. Whole-genome analyses of relationships among MRSE from air (n=133) and MRSE from BSI or deep SSI (n=27) illustrated very close relationships (Figure 1).

**Conclusions:** These data suggest that airborne MRSE with potential to cause HAI are present in inpatient wards, but not in operation theatre suits. Future work should investigate the potential role of a transmission route from airborne skin scales to the nasal epithelium by inhalation.

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Activity of imipenem-relebactam against a genetically diverse collection of carbapenemase-producing and non-producing carbapenem-resistant Enterobacteriaceae

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Background: Carbapenem-resistant Enterobacteriaceae (CRE) poses a significant global public health threat. Resistance among CRE is particularly complex, owing to numerous possible resistance mechanisms, including the production of carbapenemases, porin mutations, efflux pumps, and extended-spectrum beta-lactamases (ESBLs). Imipenem-relebactam (IMI-REL) is a novel β-lactam/β-lactamase inhibitor combination for the treatment of Gram-negative infections. In this study we evaluated the in vitro activity of IMI-REL against a contemporary collection of CRE isolates that have been genotypically characterized.

Materials/methods: We compared the in vitro activities of 20 antimicrobial agents by broth microdilution, including IMI-REL, against 97 CRE clinical isolates that were recovered from unique patients at 2 medical centers in South Texas. MICs were interpreted based on Clinical and Laboratory Standards Institute breakpoints; interpretive criteria for imipenem (IMI) were applied to IMI-REL. Molecular characteristics and resistance mechanisms were analyzed using whole-genome sequences.

Results: CRE isolates represented 9 unique species: Klebsiella pneumoniae (n=50), Enterobacter cloacae (n=29), Klebsiella aerogenes (n=5), Escherichia coli (n=3), Morganella morgani (n=2), Serratia marcescens (n=3), Citrobacter freundii (n=3), Klebsiella oxytoca (n=1), and Hafnia alvei (n=1). Interestingly, only 64% of isolates harbored carbapenemases [KPC-2 (41), KPC-3 (14), and OXA-48 like enzymes (7)]. Among K. pneumoniae, isolates belonged to ST258, ST307, ST678, ST25, ST1500, and ST273. The addition of relebactam restored in vitro IMI susceptibility to 98% of CRE isolates harboring KPC and/or ESBL/CMY as well as 40% of those harboring OXA-48 like enzymes. Notably, IMI-REL had 100% activity against 3 polymyxin-resistant KPC-producing Klebsiella isolates that harbored the plasmid-mediated mcr-1 gene. Among K. pneumoniae isolates, 58% [all ST258 strains] contained mutations in ompK35 and/or 44% in ompK36. The in vitro activity of IMI-REL was not impacted by ST, KPC type, nor whether they harbored mutations in ompK35 and/or ompK36. IMI-REL had no activity against all 3 S. marcescens isolates that contained SME-3 with 1 co-harboring KPC-2.

Conclusions: This study highlights the diversity of resistance mechanisms underlying CRE in South Texas with almost 40% not harboring a carbapenemase. IMI-REL was highly effective against CRE including isolates producing carbapenemases with porin mutations, as well as all those that were also polymyxin-resistant.

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Background: Community-acquired pneumonia (CAP) is among the most common causes of mortality in patients admitted in intensive care unit (ICU). *Streptococcus pneumoniae* remains one of the most common causative pathogens in severe CAP. However, multidrug-resistant bacteria, respiratory viruses and polymicrobial infections are frequently underestimated. We aimed to provide new trends in microbial etiology of severe CAP in ICU.

Materials/methods: Adults admitted for severe CAP to the ICU of the Nîmes University Hospital (France) were studied retrospectively during a 12-month period. Microbiological testing methods included conventional cultures from different respiratory samples (e.g. sputum, protected distal bronchial samples and bronchoalveolar lavage); urinary antigen testing for detection of *S. pneumoniae* and *Legionella pneumophila*; multiplex real-time polymerase chain reaction (PCR) (Seegene Allplex™ Respiratory panel, Eurobio-Ingen, France) performed on all respiratory samples for detection of 21 pathogens, including 16 viruses and 5 atypical bacteria; and multiplex real-time PCR (R-DiaLeg™, Diagenode, Belgium) targeting all *Legionella* species performed on respiratory samples.

Results: A total of 128 patients (median age: 67 years; 62.2% male) were enrolled. Microbial etiology was determined in 74 patients (57.8%). Respiratory viruses were the most frequently isolated pathogen group (37 of 74 patients; 50%), of which Influenza A virus in 13 patients (17.6%), Rhinovirus (RhV) in 10 (13.5%) and Influenza B virus in 5 (6.8%). The most commonly identified bacterial pathogens were: *S. pneumoniae* in 12 patients (16.2%), the so-called PES (*Pseudomonas aeruginosa*, extended-spectrum ß-lactamase Enterobacteriaceae, and methicillin-resistant *Staphylococcus aureus*) pathogens in 11 patients (12.9%), *Legionella* species in 6 (8.1%) including *L. pneumophila* in 4 (5.4%) and non *L. pneumophila* in 2 (2.7%), *Haemophilus influenzae* in 3 (4.1%) and *Moraxella catarrhalis* in 3 (4.1%). Two or more pathogens were present in 14 patients (18.9%) (most commonly RhV together with a bacteria).

Conclusions: Respiratory viruses have become the most frequent organisms isolated in ICU patients admitted for severe CAP, with Influenza viruses as leading pathogens, exceeding *S. pneumoniae*. Viral infections are prone to severe bacterial super-infections. Among severe bacterial CAP, PES pathogens occur in many cases. These new trends should be considered for the management of severe CAP in ICU.

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Abstract 8880

Clinical practice variation in the management of Staphylococcus aureus bacteraemia among infectious disease specialists in Latin America: an international study

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1Facultad de Medicina Clínica Alemana, Universidad del Desarrollo, Santiago, Chile, 2Instituto de Ciencias e Innovación en Medicina, Santiago, Chile, 3Millennium Initiative for Collaborative Research On Bacterial Resistance (MICROB-R), Iniciativa Científica Milenio, Santiago, Chile, 4Hospital Clínico Magallanes, Punta Arenas, Chile, 5Hospital Clínico Barros Luco Trudeau, Santiago, Chile, 6Facultad de Ciencias Médicas, Universidad Nacional de Rosario, Rosario, Argentina, 7Instituto de Inmunología Clínica y Experimental de Rosario (IDICER), Rosario, Argentina, 8Grupo de Resistencia Antimicrobiana y Epidemiología Hospitalaria, Universidad El Bosque, Bogotá, Colombia, 9Unidad de Medicina Interna Clínica Good Hope, Lima, Peru, 10Escuela de Medicina, Universidad Peruana Unión, Lima, Peru, 11Facultad de Medicina Alberto Hurtado, Universidad Peruana Cayetana Heredia, Lima, Peru, 12Servicio de Infectología, Hospital Nacional Arzobispo Loayza, Lima, Peru, 13Instituto de Medicina Tropical Alexander von Humboldt, Lima, Peru, 14Universidade Federal de São Paulo - UNIFESP, Department of Internal Medicine, Division of Infectious Diseases, São Paulo, Brazil

Background: SAB carries severe complications. Evidence shows that consultation with infectious diseases specialists (IDs) is associated with better outcomes. However, divergent practices among IDs may obscure these benefits. We evaluated the consistency of practice in the management of SAB among IDs across 5 LA countries.

Materials/methods: We applied an anonymous on-line survey to IDs from Chile, Peru, Brazil, Colombia, and Argentina. The survey consisted of 14 questions related to diagnosis (n=4), management (n=5) and demographic information (n=5), and was distributed by e-mail and text messages between 06/20/19 to 11/20/19.

Results: We collected 741 responses (Argentina=267, Chile=124, Colombia=70, Brazil=200, and Peru=80), 86% and 14% corresponded to adult and pediatric IDs, respectively; 29% of respondents worked at teaching institutions. Working in a non-teaching hospital and having >10 years of practice were significantly associated with higher probability of drawing follow-up blood cultures solely when patients remained febrile/unstable (OR, [95%CI] = 1.7 [1.07-2.67]; 2.1 [1.44-3.09], respectively). Seventy-nine percent of the sample reported to perform an echocardiogram always/almost always. Pediatrics IDs choose to perform a transthoracic echocardiogram more frequently than adult IDs (65% vs 10%, P<0.01). Conversely, transesophageal echocardiogram was more frequently preferred by adult IDs (28% vs. 9%, P<0.01)

Cefazolin/cephalothin and oxacillin/cloxacillin were the first-line therapy for methicillin-susceptible SAB in 51% and 47% of cases, respectively. Daptomycin (monotherapy or combination) was the preferred option to treat persistent methicillin-resistant SAB (62%). Most IDs (72%) treat uncomplicated SAB for a minimum of 14 days; subjects with >10 years of practice were more likely to prescribe shorter (7 days) courses of therapy (OR =3.25, [2.01-5.26]). Thirty-one percent of IDs would consider 1/2 positive blood cultures with S. aureus a contamination and would not prescribe treatment, with significant differences by country [Argentina 21%, Chile 22%, Colombia 36% Brazil 37%, Peru 61%; P<0.01]. Years of experience and type of hospital were not associated with the preference of not treating at all.

Conclusions: We found great variation in the management of SAB among IDs in LA, with notable differences between countries, type of specialists, practice type, and years of experience. Adherence to guidelines should be reinforced to improve SAB outcomes.

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Abstracts 2020

Abstract 8882

**Resistance and virulence determinants of faecal Salmonella spp. isolated from slaughter animals in Benin**

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**Background:** *Salmonella* spp. are one of the leading foodborne pathogens worldwide naturally found in the intestines of many animals. People that are in direct contact with the infected animals or their cages may become ill. The aim of this study was to determine the prevalence, antibiogram and virulence genes associated with *Salmonella* serovars from fecal samples of animals intended for consumption in Southern Benin.

**Materials/methods:** The collection of animal faeces, namely poultry, sheep and pigs for the search for Salmonella was conducted in the cities of Allada, Abomey-Calavi, Cotonou, Porto- Novo, Adjara and Cocotomey characterized by the strong presence of breeders and large markets. The bacteriological analysis was conducted according to the current AFNOR standard (NF U: 47–100). Kirby Bauer techniques were used to perform the susceptibility testing. The isolates were tested for different virulent genes using PCR with five sets of specific primer pairs. The genes of virulence that were targeted for amplification by PCR were invA, spvR, spvC, fimA and stn.

**Results:** Out of a total of 406 samples, 2.46% were positive. The isolates identified were multidrug-resistant *Salmonella* spp. to penicillins, first generation cephalosporins and some aminoglycosides. All *Salmonella* isolates produced invA gene of 284 bp, fimA of 85 bp and stn of 260 bp. The spvC gene (571 bp) was present in 10% of the isolates whereas the spvR gene (310 bp) was found in 20% of the isolates. The control strain possessed all the tested genes. The invA gene implies that strains are able to invade epithelial cells. The fimA and stn genes present in all isolates show that they are capable of causing gastrointestinal illness in humans. The presence of spvC and spvR genes suggests the possibility of these strains to produce toxins.

**Conclusions:** The presence of multidrug resistant *Salmonella* spp. in the faeces of animals is of major concern and the presence of virulence genes confirms the possible pathogenicity of these strains. The present study is therefore of paramount importance in the surveillance of salmonellosis.

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Abstract 8884

**A new approach of antibiotic stewardship in geriatric facilities**

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**Background:** Antibiotics are frequently prescribed and often inappropriately used in geriatric facilities; antimicrobial resistance is a real challenge. We evaluate the impact and acceptability of an antimicrobial stewardship with on-site visits in a geriatric hospital.

**Materials/methods:** In a 200 beds Parisian geriatric hospital grouping acute medicine, long-term, psychogeriatrics and palliative cares, collaboration has been set up with clinical infectious and infection control experts since 2016. Bi-monthly on-site visits, in addition to phone calls (available every day), were implemented. Clinical, biological and microbiological data was collected for every infectious medical advice. A satisfaction questionnaire was administered to geriatricians.

**Results:** From December 2016 to November 2019, 291 advices including 213 initial advices (IAs) and 78 follow-ups were collected. Among the IAs, 12% had known multidrug-resistant bacteria (MDRB) colonization. IAs concerned pulmonary infections (33%), urinary tract infections (26%) bacteremia (17%), and abdominal infections (7%). For 63 patients, antibiotic wasn’t initially prescribed (lack of bacterial infection arguments, need of more explorations) but was introduced for 9 (14%) patients after IA. In contrary, a total of 11 treatments (7%) have been stopped. During the 3 years IAs numbers decreased but proportion of antibiotic modification increased from 38% in 2017 (34/90), 40% in 2018 (23/57) to 51% in 2019 (26/51). Modifications mainly concerned the drug change (68% in 2017, 61% in 2018, 58% in 2019). Dose or length modifications were less frequent (5% in 2017, 15% in 2018, 12% in 2019). Drug changes concerned replacement of third-generation cephalosporins by amoxicillin (10%), “new drug” prescription (as dalbavancin) or other different modifications. Among the 3 initial prescriptions of carbapenem, 2 have been secondarily changed by antibiostewardship. Site visits seemed more personalized than phone calls for 26 (87%) of 30 geriatricians and 24 (80%) were very satisfied with this organization. The intervention of the stewardship team was mainly requested for therapeutic opinions and complex situations.

**Conclusions:** This new strategy of antibiotic counseling with on-site visits by infection control experts enabled to reduce antibiotic prescription and to perform antibiotic escalation. Antibiotic stewardship in geriatric hospital could reduce pressure of MDRB selection and inappopriate prescriptions and is well accepted by geriatricians.

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Inter- and intraspecies spread of mcr-1 between twenty-nine distinct Enterobacteriaceae isolates from one patient

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**Background:** Colistin is one of the most critically important last-resort antibiotics that used to treat infections caused by multidrug-resistant bacteria. Colistin resistance is a growing global threat in the field of antimicrobial resistance. After the initial report in 2015, the transmissible colistin resistance gene, mcr-1, was first discovered in China then spread worldwide. Significantly, mcr-1 has been found in different plasmid types, such as IncI2, IncHI2, and IncX4, which also containing other antimicrobial resistance determinants such as extended-spectrum β-lactamases simultaneously. These transferable plasmids likely facilitate the inter- and intraspecies spread of mcr-1 gene among Enterobacteriaceae.

**Materials/methods:** Here, we describe a unique case of sequential isolation from one patient with three species of MCR-1-producing producers, and characterize the inter- and intraspecies dissemination of mcr-1 gene via Illumina and PacBio sequencing, and plasmid analysis.

**Results:** Here we report the unexpected isolation of 29 distinct MCR-1 producing Enterobacteriaceae isolates from a single patient over 30 months. The phylogenetic tree analysis revealed within-host evolution of 19 Escherichia coli and 9 Klebsiella aerogenes isolates, respectively. Plasmid analysis demonstrated that mcr-1 gene was carried by transferrable 66 kb IncI2 plasmids and 94 kb pO111 plasmids. We present evidence that inter- and intraspecies spread of mcr-1 gene among Enterobacteriaceae isolates from the same patient.

**Conclusions:** So far, reports on inter- and intraspecies spread of antimicrobial resistance genes in a single patient are rare. Isolation of various MCR-1-producers from the same patient has never been described thus far. In this study, we report the first known sequential isolation of twenty-nine distinct MCR-1-producing Enterobacteriaceae isolates from multiple specimens obtained from the same patient. The MCR-1-producing isolates in this patient may due to exposure to other colonized/infection patients, since MCR-1-producers was identified from isolates in this hospital early in 2014. The fact that 29 isolates possessed mcr-1 in one patient is of particular concern as it indicates that MCR-1-producers can colonizations or infections within a single patient over several years. Importantly, this case reinforces the idea of inter- and intraspecies dissemination of the mcr-1 gene in clinical Enterobacteriaceae isolates through horizontal gene transfer during human infection.

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Abstract 8889

Probiotics for recurrent *Clostridioides difficile* infection: a systematic review and meta-analysis
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**Background:** Around a quarter of patients initially treated for *Clostridium difficile* infection (CDI) will develop a recurrence of CDI – contributing to increased healthcare costs, prolonged use of antibiotics [and associated risks], and an increase in morbidity and mortality. The disturbance of the gastrointestinal microbiota due to antibiotic treatment of recurrent CDI, has garnered attention around the role of probiotics as a potential treatment option in an attempt to restore microbial balance. The objective of this study is to assess the efficacy of the use of probiotics in conjunction with standard of care, in the prevention of CDI recurrence through a systematic literature review.

**Materials/methods:** The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, grey-literature sources, references of included studies from systematic reviews on similar topics, consultation with field experts and trial registries were searched from inception to September 2019, with no limit on language or publication date. Selection criteria involved both randomized control trials (RCT) and non-randomised observational studies reporting recurrent CDI incidence, and including patients who were receiving probiotics of any strain, dose or method of ingestion, with at least one CDI occurrence. Two authors independently screened articles, extracted data and assessed risk of bias. GRADE guidelines were used to rate confidence in effect estimates per outcome.

**Results:** 8 studies including 696 participants met the eligibility criteria. 5 RCTs were pooled in the meta-analysis, resulting in probiotics reducing the incidence of recurrent CDI by 43% (pooled relative risk, 0.57 [95% CI, 0.35 – 0.93]) in comparison to placebo. Moreover, lactobacilli strains reduced recurrent CDI by 60% (pooled relative risk, 0.40[95% CI, 0.10 – 1.51]) in comparison to *Saccharomyces boulardii* strain which only reduced CDI recurrence by 35% (pooled relative risk, 0.65 [95%CI, 0.41-1.05]) among randomised studies. There were no significant findings in regards to adverse events between groups. According to the findings reported in the observational studies analyzed, probiotics may confer beneficial results in CDI recurrence prevention.

**Conclusions:** Moderate quality of evidence suggests probiotics may result in a small reduction in recurrent CDI patients with at least one CDI occurrence.

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Evaluating the performance of a host-protein signature for distinguishing between bacterial and viral disease in adults with Lower Respiratory Tract Infection (LRTI): results from the OBSERVER clinical study

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Background: Failure to distinguish between bacterial and viral infection in LRTI patients is a major healthcare problem contributing to antibiotic misuse and antimicrobial resistance. A novel assay that integrates blood levels of three immune-proteins TRAIL/IP-10/CRP was developed to assist in differentiating bacterial from viral disease. The assay exhibited high performance in previous blinded pediatric validation studies. We evaluated the assay’s diagnostic performance and potential clinical utility in adult patients, focusing on patients suspected for LRTI.

Materials/methods: OBSERVER (NCT03011515) is an EU Horizon 2020 funded study (grant No. 684589), the first to validate the signature in adult LRTI patients. For every participant recruited at the emergency departments of three hospitals in Israel, we collected medical history, physical examination, routine lab, imaging and respiratory multiplex PCR data. The assay outcomes are bacterial, viral or equivocal. Reference standard outcome of bacterial, viral, indeterminate or non-infectious, was assigned by expert panel majority adjudication. Indeterminates were excluded from the analysis.

Results: We included 492 in this analysis. Age ranged from 18 to 98 years (mean 54.6). Clinical syndromes included: 29% pneumonia, 27% URTI, 17% acute bronchitis, 6% asthma or COPD exacerbation and 13% unspecified LRTI or viral infection.

The assay demonstrated high diagnostic performance for distinguishing bacterial from viral disease (Figure 1).

In this cohort, antibiotics were prescribed to 105/195 patients with viral reference outcomes, indicating an overuse rate of 54%. Of these, 78 yielded viral index test outcomes, supporting the potential of the assay to reduce overuse by 74%.

Conclusions: The TRAIL/IP-10/CRP assay demonstrated high diagnostic performance and potential utility for differentiating between bacterial and viral disease in adult patients presenting to the emergency department with suspicion of LRTI. Use of this new assay can help to close the gap between guidelines antibiotic prescription recommendations and reported prescribing rates and improve adherence to the guidelines.

<table>
<thead>
<tr>
<th>Assay Performance (with 95%CI)</th>
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<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
</tr>
<tr>
<td><strong>Test equivocal rate:</strong></td>
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</tbody>
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<tr>
<th>Performance of common biomarkers (with 95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biomarkers (cutoff value)</strong></td>
</tr>
<tr>
<td>WBC (15K)</td>
</tr>
<tr>
<td>ANC (10K)</td>
</tr>
<tr>
<td>CRP (40mg/l)</td>
</tr>
<tr>
<td>PCT (0.25ng/ml)</td>
</tr>
</tbody>
</table>

Figure 1: assay diagnostic performance for distinguishing bacterial from viral infection in patients presenting to the emergency department with suspected lower respiratory tract infection.

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Abstract 8892

Octenidine: new insights in the detailed killing mechanism on Gram-negative bacteria at a cellular and molecular level

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Background: Octenidine (OCT) is a well-tolerated antiseptic molecule, which is widely used for wound management, skin- & mucous membrane antisepsis and infection control. Its antimicrobial spectrum covers (multi-drug resistant) bacteria, fungi and enveloped viruses. However, the detailed molecular mechanism has not been elucidated so far. The objective of our study was to investigate the mode of action of OCT’s potent effect on Gram-negative bacteria by using Escherichia coli as model organism as well as corresponding membrane model systems.

Materials/methods: Effects of OCT on cellular morphology were observed by electron microscopy, changes affecting membrane integrity [surface charge, fluidity, permeabilization and depolarization] by zeta potential, fluorescence microscopy and spectroscopy, while specific interactions of OCT with membrane phospholipids were addressed using differential scanning calorimetry, X-ray scattering and fluorescence techniques.

Results: OCT neutralizes the surface charge of E. coli leading to disruption of the outer membrane and dramatic loss of cell wall at higher concentrations. In turn OCT penetrates through the periplasmic space reaching the inner membrane. Membrane model systems composed of bacterial inner membrane phospholipids showed that OCT inserts into the hydrophobic fatty acyl chain region of the bilayer inducing complete lipid disorder. The loss of membrane integrity is also reflected in in vitro experiments as demonstrated by membrane depolarization and changes in membrane fluidity of E. coli and eventual disruption as shown by electron microscopy.

Conclusions: Insertion of OCT into the outer and inner membrane of E. coli results in a chaotic lipid arrangement that leads to rapid disruption of the cell envelope. Note that this kind of action demands a defined number of OCT molecules per cell to induce cell death. Thus, when used in very low concentrations, not all bacteria will be covered with sufficient numbers of OCT molecules, which can be misinterpreted as tolerance or adaption. We propose that this very rapid and unspecific mode of action based on purely physical interactions is on one hand the basis of the very broad antimicrobial profile and on the other hand makes it unlikely that resistance towards this molecule will occur.

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Abstracts 2020

Abstract 8893

**Risk factors for amputation in diabetic foot infections**

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**Background:** Lower extremity amputation is an important cause of morbidity and mortality in patients with diabetic foot infection (DFI). We aimed to determine the risk factors for lower extremity amputation in DFI.

**Materials/methods:** Data of patients who were hospitalized for DFI between 2010 and 2019 were recorded retrospectively from the hospital records. The clinical data of patients who did and who did not undergo amputation were statistically analyzed.

**Results:** Data were collected for 401 patients including 280 (69.8%) men. The mean age was 59.6±11.1 (29-81) years. Thirteen (3.2%) of the patients were type 1 diabetes and mean duration of diabetes was 14.1±9.2 years. The causes of the DFI were as follows; ischemic ulcer (33.7%), trauma (13.5%), neuropathic ulcer (11.5%), venous ulcer (10.5%) burn injury (2.7%) and idiopathic (25.4%). Of these patients, 47.4% had right foot wound, 43.6% had left foot wound and 9% had bilateral foot wounds. Treatment modalities included medical treatment (146, 36.4%), debridement/drainage (88, 21.9%), minor amputation (71, 17.7%) and major amputation (96, 23.9%).

Male sex (p=0.047), ischemic wound (p=0.024), forefoot wound (p<0.001), osteomyelitis (p=0.005), peripheral arterial disease (p=0.001), low hemoglobin levels (p=0.002), high leukocyte levels (p<0.001), high platelet levels (p=0.021), high glucose levels (p=0.016), high erythrocyte sedimentation rate levels (p=0.005), high C-reactive protein levels (p<0.001) and high procalcitonin levels (p=0.039) were found to be significant factors in amputated patients. Among these factors, forefoot infections (OR:3.347, 95% CI:1.408-7.956; p=0.006) and peripheral arterial disease (OR:4.99, 95% CI: 1.225-20.324; p=0.025) were independent risk factors in predicting amputation in DFI (Figure).

Mean duration of follow-up was 23.7±22.9 months; 146 (46.8%) patients completely recovered, 63 (%20.2) patients developed a chronic foot ulcer and 103 (%33) patients required re-operation. The overall mortality rate was found 3%.

**Conclusions:** Early recognition of need for amputation is also crucial in terms of limiting amputation level and decreasing mortality. We conclude that these clinical parameters are simple, broadly available and cost-effective promising parameters in predicting amputation in DFI.
## Abstracts 2020

### Figure: Risk factors for amputation in patients with diabetic foot infection

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>All patients (n=210, 100%)</th>
<th>Amputation (Major Amputation) (n=35, 100%)</th>
<th>p</th>
<th>Odds Ratios</th>
<th>95% Confidence Intervals</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean ± SD</td>
<td>62.6±11.1</td>
<td>66.6±11</td>
<td>0.777</td>
<td>0.547</td>
<td>0.353-0.852</td>
<td>0.575</td>
</tr>
<tr>
<td>Married (%)</td>
<td>385 (46.5%)</td>
<td>120 (75.7%)</td>
<td>0.034</td>
<td>3.123</td>
<td>0.487-19.5</td>
<td>0.023</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>34 (6.5%)</td>
<td>17 (10.2%)</td>
<td>0.714</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2D years</td>
<td>70 (19.4%)</td>
<td>33 (19.2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment of diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>255 (93.3%)</td>
<td>106 (63.9%)</td>
<td>0.009</td>
<td>10.989</td>
<td>4.575-25.9</td>
<td>0.000</td>
</tr>
<tr>
<td>Oral antidiabetic drug</td>
<td>60 (18.5%)</td>
<td>27 (16.2%)</td>
<td>0.763</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No treatment</td>
<td>31 (17.1%)</td>
<td>18 (9.4%)</td>
<td>0.871</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of observation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic observation</td>
<td>199 (40.3%)</td>
<td>77 (41.8%)</td>
<td>0.461</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic observation (≤1 year)</td>
<td>23 (3.7%)</td>
<td>11 (5.5%)</td>
<td>0.075</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of/prediabetes procedures</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of diabetes</td>
<td>44 (11.4%)</td>
<td>14 (9.4%)</td>
<td>0.125</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History of amputation</td>
<td>63 (15.7%)</td>
<td>25 (15.5%)</td>
<td>0.752</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cause of wound</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Traumatic</td>
<td>136 (32.7%)</td>
<td>67 (40.1%)</td>
<td>0.028</td>
<td>0.367</td>
<td>0.225-1.542</td>
<td>0.196</td>
</tr>
<tr>
<td>Nonsurgical</td>
<td>55 (12.9%)</td>
<td>17 (10.2%)</td>
<td>0.159</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Various causes</td>
<td>45 (10.5%)</td>
<td>23 (13.2%)</td>
<td>0.269</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burn</td>
<td>42 (10.5%)</td>
<td>12 (7.1%)</td>
<td>0.955</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Location of the wounds</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right foot</td>
<td>196 (46.9%)</td>
<td>65 (40.4%)</td>
<td>0.205</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left foot</td>
<td>178 (42.8%)</td>
<td>71 (41.2%)</td>
<td>0.488</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilateral foot</td>
<td>55 (13.2%)</td>
<td>11 (6.4%)</td>
<td>0.314</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection</td>
<td>154 (36.4%)</td>
<td>54 (32.1%)</td>
<td>0.366</td>
<td>3.447</td>
<td>1.437-9.356</td>
<td>0.006</td>
</tr>
<tr>
<td>Middle foot</td>
<td>102 (24.3%)</td>
<td>41 (24.4%)</td>
<td>0.354</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hind foot</td>
<td>65 (15.7%)</td>
<td>25 (15.5%)</td>
<td>0.780</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of infection</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulcer</td>
<td>83 (23.8%)</td>
<td>31 (18.9%)</td>
<td>0.800</td>
<td>1.191</td>
<td>0.645-2.176</td>
<td>0.530</td>
</tr>
<tr>
<td>Clinical parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemoglobin</td>
<td>14.3±3.0</td>
<td>10.2±1.8</td>
<td>0.022</td>
<td>0.754</td>
<td>0.451-1.296</td>
<td>0.004</td>
</tr>
<tr>
<td>Leucocytes</td>
<td>113.3±37.0</td>
<td>101.1±27.5</td>
<td>0.001</td>
<td>1.000</td>
<td>1.000-1.000</td>
<td>0.358</td>
</tr>
<tr>
<td>Platelet</td>
<td>250±145.0</td>
<td>258±146.0</td>
<td>0.248</td>
<td>1.000</td>
<td>1.000-1.000</td>
<td>0.991</td>
</tr>
<tr>
<td>Glucose</td>
<td>241±77.2</td>
<td>257±42.9</td>
<td>0.245</td>
<td>1.000</td>
<td>0.997-1.000</td>
<td>0.542</td>
</tr>
<tr>
<td>Lactate</td>
<td>6.1±3.1</td>
<td>5.9±3.4</td>
<td>0.085</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESR</td>
<td>62±23.7</td>
<td>76±29.3</td>
<td>0.095</td>
<td>0.908</td>
<td>0.908-1.352</td>
<td>0.700</td>
</tr>
<tr>
<td>Crea</td>
<td>13.5±19.5</td>
<td>18.7±14.1</td>
<td>0.464</td>
<td>1.044</td>
<td>0.924-1.166</td>
<td>0.519</td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>1±0.6</td>
<td>1±0.6</td>
<td>0.039</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Microbiological analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation of Gram positive bacteria</td>
<td>70 (17.1%)</td>
<td>22 (12.2%)</td>
<td>0.170</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation of Gram-negative bacteria</td>
<td>143 (34.3%)</td>
<td>66 (39.5%)</td>
<td>0.143</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isolation of multiple bacteria</td>
<td>39 (9.7%)</td>
<td>14 (8.4%)</td>
<td>0.320</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical course</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healing of ulcer</td>
<td>145 (35.6%)</td>
<td>73 (43.7%)</td>
<td>0.061</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic wound formation</td>
<td>83 (19.5%)</td>
<td>9 (5.6%)</td>
<td>0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection site of resection</td>
<td>103 (25.0%)</td>
<td>41 (25.3%)</td>
<td>0.979</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Only the values found to be significant in univariate logistic regression analysis were evaluated in multivariate logistic regression analysis. Significant p values are indicated by bold characters in the table. SD: Standard deviation, ESR: Erythrocyte sedimentation rate, Crea: Creatinine.

Presenter email address: tunademirdal@hotmail.com
Abstract 8895

**Diversity of colistin resistance mechanisms in carbapenemase-producing Klebsiella pneumoniae isolated in Bulgaria from 2013 to 2018**

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Abstract third-party references: Partially supported by The Bulgarian National Science Fund under Grant No KП-06-М23/6

**Background:** Colistin-based antimicrobial regimes have been used successfully for the treatment of carbapenemase-producing *Klebsiella pneumoniae* (CPKP) infections, but mutational and plasmid-mediated colistin resistance (CR) has been reported, compromising even the combinatorial therapeutic regimes. We report molecular mechanisms in colistin-resistant clinical isolates detected among CPKP referred to the National Reference Laboratory for AMR in Bulgaria between 2013 and 2018.

**Materials/methods:** A collection of 322 non-duplicate CPKP with PCR-confirmed carbapenemases was screened for CR by the BMD method according to EUCAST. Carbapenemase genes, ESBL, pAmpC, plasmid aminoglycoside and quinolone resistance determinants were studied by PCR and sequencing. Genotyping by MLVA8, MLST and PBRT was conducted. PCR detection of mcr genes 1 to 8, sequencing of the entire mgrB, phoPQ, pmrAB and crrB and qRT-PCR for the expression levels of pmrCDH, phoP and crrC were performed for studying mechanisms of colistin resistance.

**Results:** Forty colistin resistant CPKP strains were confirmed. Of these, 23 (57%) were XDR, 9 (22%) were PDR and 8 were MDR. The *bla*NDM-1 was detected in 33 strains (from eight hospitals) associated with incA/C plasmids and *bla*CTX-M-15 all belonging to ST11, whereas seven strains were KPC-2 producers distributed in ST15 and ST258. ArmA contributing to the PDR phenotype was detected in eleven ST11 strains from four hospitals, all co-producing *bla*NDM-1 and *bla*CTX-M-3/15. The qnrB2 and *aac(6’)Ib-cr* genes were found in 15 and 9 strains respectively. While *mcr* genes were absent, various alterations or complete lack of *mgrB* were responsible for CR in 80% of the isolates. Most of the novel missense substitutions found in *mgrB*, *pmrB* and *phoP* as well as an indel in *mgrB* were predictably deleterious. A common expression pattern was observed, consistent with a significant upregulation of the L-Ara4-N operon apparently through increased *phoPQ* and *pmrAB* activation and mediated by *pmrD*.

**Conclusions:** Colistin was registered in Bulgaria in 2014 but its use in hospitals was effectively initiated in 2015. This study shows that CR-CPKP has been introduced prior to colistin use. Noteworthy, CR has been associated mostly with MDR/XDR CPKP and the PDR strains seem to emerge in 2017 following the apparent acquisition of the *armA* gene.

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Abstract 8897

Fosfomycin susceptibility testing by different methods in multidrug-resistant urinary Klebsiella pneumoniae isolates

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Background: The emergence of multidrug-resistant (MDR) gram negative bacilli creates a challenge in the treatment of urinary tract infections. Fosfomycin has regained attention because of its in vitro activity against extended-spectrum beta lactamase (ESBL) positive Klebsiella pneumoniae isolates. Rapid and accurate antibiotic susceptibility testing (AST) for fosfomycin is necessary for clinical microbiology laboratories. For this reason, we aimed to determine the susceptibility of fosfomycin by using gradient test, disk diffusion and VITEK2 AST system (BioMerieux, France) and compare with the results of agar dilution as reference method.

Materials/methods: A total of 251 ESBL-positive Klebsiella pneumoniae strains isolated from urine specimens were collected from May 2018 to 2019 in Marmara University Hospital Clinical Microbiology Laboratory, Istanbul. Minimum inhibitory concentrations (MICs) of fosfomycin were determined by the agar dilution method in accordance with EUCAST guidelines. The MIC of fosfomycin was determined by supplementation with 25 mg/L glucose-6 phosphate and fosfomycin in a concentration of 0.25-1024 µg/mL. AST were performed using VITEK2 system, by Gradient test (Liofilchem, Italy) and disk diffusion. Results were evaluated in comparison with agar dilution method according to EUCAST criteria.

Results: Of these ESBL positive K. pneumoniae isolates (n:251), 20 (8%) were also carbapenemase (CP) positive. Fosfomycin susceptibility was 81.8% in ESBL positive and 70% in carbapenemase positive isolates. MIC90 was determined as 8/256 µg/mL. The categorical agreement was 90%, 88.4% and 83.5% in gradient test, disk diffusion and VITEK2 system respectively when compared with agar dilution (Table 1).

<table>
<thead>
<tr>
<th>Method</th>
<th>MICs</th>
<th>Very MICs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Categorical</td>
<td>Total</td>
</tr>
<tr>
<td></td>
<td>Agreement (%)</td>
<td>(n=)</td>
</tr>
<tr>
<td>Gradient test</td>
<td>21/223 79.7%</td>
<td>223/251 (68.9%)</td>
</tr>
<tr>
<td>Disk diffusion</td>
<td>20/223 90.0%</td>
<td>223/251 (68.9%)</td>
</tr>
<tr>
<td>Automated AST (VITEK2)</td>
<td>19/223 86.1%</td>
<td>223/251 (68.9%)</td>
</tr>
</tbody>
</table>

Conclusions: Fosfomycin has a high activity (>80%) against ESBL positive K. pneumoniae. Therefore determination of fosfomycin susceptibility is important for the laboratories to lead the treatment options particularly for the MDR isolates. Rapid and automated method (VITEK2 AST) results for fosfomycin is relatively low whereas gradient test results were acceptable with high in categorical agreement. Agar dilution still seems to be the gold standard as suggested by the guidelines.

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Abstract 8909

**Amikacin resistance mechanisms in Mycobacterium abscessus**

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**Background:** Mycobacterium abscessus (mAB) is a multidrug-resistant nontuberculous mycobacteria (NTM) causing chronic respiratory and iatrogenic health-acquired infections. Clarithromycin and amikacin (AMK) are the drugs of choice although inducible clarithromycin resistance is present in strains of the subspecies *bolleti* and in most strains of *subsp. abscessus* (*erm41* sequevar t28). Contrarily, *subsp. massiliense* and *subsp. abscessus* *erm41* sequevar c28 are intrinsically clarithromycin susceptible. Therefore, AMK became the first therapeutic choice for all mAB whatever the subspecies. Recently, liposomal AMK was approved for NTM treatment. Since AMK resistance emerged due to its increased usage, we investigated mAB clinical isolates for AMK mechanisms of resistance. Several genetic mutations have been observed in *in vitro* mutants but only one mutation (*rrs* a1 408g) have been observed in clinical isolates so far.

**Materials/methods:** From all mAB clinical isolates received in our reference laboratory from November 2012 until June 2018, isolates yielding AMK MIC≥64 mg/L by Sensititre RAPMYCO (ThermoFisher) were considered resistant. PCR sequencing of *hsp65, erm41, rrl* and *rrs* was performed together with the GenoType® NTM-DR for subspecies assignment and clarithromycin and AMK genotypic resistance. All resistant isolates were re-tested for AMK MIC by broth microdilution CLSI reference method.

**Results:** 42 AMK resistant isolates were investigated from 29 patients (17 men, 12 women, median age 24 years, range 7-77). The isolates distributed as five *subsp. massiliense*, six *subsp. bolletii*, four *subsp. abscessus* *erm41* sequevar c28 and 27 *subsp. abscessus* t28. Morphotypes were primarily rough (26, 62%). The *rrs* mutation a1 408g was found in 26 strains, all showing MIC≥8,192 mg/L, but four strains with MIC>8,192 µg/mL did not show this mutation. Seven strains had MICs ranging from 64 to 512 mg/L, which could indicate enzymatic mechanism. Finally, five strains had MIC<64 mg/L and no *rrs* mutation, indicating they were probably wild type. The 17 strains with no *rrs* mutations are undergoing whole genome sequence analysis.

**Conclusions:** mAB isolates with a1408g *rrs* mutation are AMK resistant at a high level precluding their use, whereas isolates without this mutation should be studied further in order to know if high AMK concentrations achieved locally can overcome resistance.

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Abstract 8915

Bacterial iron-uptake pathways: gates for the transport of antibiotics
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Background: Vectorization of bactericide compounds by siderophores (iron chelators produced by bacteria) is a promising Trojan horse strategy able to considerably increase the efficacy of drugs by overcoming the impermeability of the bacterial wall, especially that of Gram-negative bacteria. In such a Trojan horse strategy, the idea is that each time a bacterium internalizes a ferric ion, a molecule of drug is transported as well.

Iron is a cofactor of many redox-dependent enzymes and thus essential for growth and virulence. During infection, an important aspect of the innate immune system is to limit iron availability to invading microbes, a strategy called nutritional immunity. To overcome this problem of iron accessibility, bacteria had to develop diverse and efficient iron uptake processes. Pseudomonas aeruginosa is able to express in order to get access to iron several strategies: a ferrous iron uptake pathway, two haem uptake pathways and several iron acquisition pathways involving siderophores.

Materials/methods: Using proteomic and molecular biology approaches, we have investigated how P. aeruginosa adapts the expression of its iron acquisition pathways depending on its environment and in the absence or presence of siderophore-antibiotic conjugates and catechol compounds present in the host like (L-DOPA, dopamine and norepinephrine, siderophore often having catechol groups to chelate iron).

Results: We have shown that the catechol type siderophore-antibiotic conjugates were clearly more efficient in inducing the expression of their corresponding transporters than other siderophore-antibiotic conjugates because of their very high affinity for iron. In parallel, a significant repression of the expression of the other iron uptake pathways were as well observed, indicating clearly that bacteria opt for the use of the catechol siderophores to get access to iron when such compounds are present in their environment.

Conclusions: The data also point out that catechol siderophores are the most promising siderophores for antibiotic vectorization. This study indicated as well that catecholamines (L-DOPA, dopamine and norepinephrine) are able to transport iron into bacteria and may affect bacterial growth during infection.

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Different expression of CD26 and CD66 receptors on PBMCs from MERS Coronavirus infected patients

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Abstract third-party references: King Abdulaziz City for Science and Technology

Background: Middle East respiratory syndrome-coronavirus (MERS-CoV) is a novel emerged virus which often cause severe lower respiratory infection leading to pneumonia, renal failure and death especially in patients with co-morbidity. Recent in-vitro reports demonstrated that the MERS-CoV utilizes CD26 (dipeptidyl peptidase-4) and/or CD66 (carcinoembryonic antigen-related cell adhesion molecule 5) receptors for cell infection and blocking these receptors with specific antibodies could prevent the infection. Considering the role of peripheral blood mononuclear cells (PBMCs) in clearing pathogens, we aimed in this study to assess the susceptibility of these cells to MERS-CoV infection by measuring the expression levels of CD26 and CD66 receptors on cell surface.

Materials/methods: In this study we evaluated the expression level of CD26 and CD66 receptors on peripheral blood mononuclear cells (PBMCs) including CD4+T cells, CD8+T cells, and on monocytes from MERS-CoV patients (n=20) and healthy controls (n=20) using flow cytometry.

Results: We found that there was a significant increase in the expression level of CD66 receptor on CD4+T cells (mean MFI= 404.9 ± 34, P< 0.03), CD8+T cells (mean MFI= 534.6 ± 52.6, P< 0.03), and on monocytes (mean MFI= 346 ± 18.9, P< 0.004) from MERS-CoV patients compared with those of healthy controls (CD4+T cells; mean MFI= 325 ± 19.7, CD8+T cells; mean MFI= 392.4 ± 37.7, monocytes; mean MFI= 266.8 ± 20.6). There was a significant increase in the expression level of CD26 receptor on monocytes from MERS-CoV patients [mean MFI= 862.8 ± 116.4, P< 0.04] compared with those of healthy controls [mean MFI= 610.2 ± 67.6]. There were no statistical significant difference between the expression level of CD26 on CD4+ T cells [mean MFI= 896 ± 122], and CD8+ T cells [mean MFI= 1134 ± 122.6] from MERS-CoV patients and those of the healthy controls [CD4+T cells; mean MFI= 819.4 ± 106, CD8+T cells; mean MFI= 902 ± 144.4].

Conclusions: The increased expression levels of CD66 receptor on PBMCs and CD26 receptor on monocytes from MERS-CoV patients highlights the importance of investigating the role of these receptors during the course of MERS-CoV infection.

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Impact of selective digestive and oropharyngeal decontamination on the gut microbiome and resistome in intensive care patients

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Background: Selective decontamination of the digestive tract (SDD) and of the oropharynx (SOD) are prophylactic interventions to reduce mortality and infectious complications in intensive care unit (ICU) patients. These involve daily administration of topical antibiotics (amphotericin B, tobramycin and colistin) during their ICU stay. Here we aimed to compare the gut resistome and microbiome of patients receiving SDD, SOD or standard care.

Materials/methods: A cluster randomised controlled study was conducted in the ICU of the University Hospital Antwerp [UZA], Belgium from 2014–2016. In total, 200 rectal swabs were collected from patients (P) (n=75) receiving standard care (n=58; P=20), SOD (n=86; P=32) and SDD (n=56; P=23). Metagenomic DNA was isolated (FastDNA, MP Biomedicals), libraries were generated (Nextera XT), followed by shotgun-sequencing (2 x 100 bp, HiSeq2500, Illumina) targeting ≈80 million reads/sample. Non-human reads were mapped against the NCBI-nr database. MEGAN Ultimate 6 was used for taxonomic classification to compare normalised samples. Relative abundances of antibiotic resistance genes were calculated by mapping reads against the CARD database using DIAMOND in blastx mode with 97% identity.

Results: Of the 200 samples, 171 (P=74) passed the sequence quality cutoff and underwent further analysis [Figure 1A]. Microbial diversity [Shannon-Weaver diversity index: SID] in patients receiving SDD [2.0 ± 1.05; 7 genera] was reduced compared to those receiving standard care [2.2 ± 0.63; 9 genera] (p=0.42). In contrast, the SID in patients receiving SOD was very similar to those receiving standard care [2.4 ± 0.82; 11 genera] (p=0.38). Dominant microbial genera after treatment were Bacteroides and Alistipes (standard care), Clostridium (SDD), and Bacteroides and Enterococcus (SOD). Enterobacteriaceae were reduced during both SDD and SOD. Relative abundance of beta-lactamases was lower during SDD and SOD, while aminoglycoside and macroline resistance genes (aph(2’)-Ia, ermB and ermC) were more abundant during SDD. No significant changes were observed in the relative abundance of tetracycline resistance genes [tet] across all three treatment groups [Figure 1B].

Conclusions: Our data indicate that, among the three treatments studied, SDD led to a higher decrease in microbial diversity and to an increased relative abundance of both aminoglycoside- and macroline-resistance genes.

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Abstract 8931

**Actinomycosis: a case series of 10 patients from an infectious diseases department**

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**Background:** Actinomycosis is a rare chronic disease caused by *Actinomyces* species. These are anaerobic Gram-positive commensal bacteria of the human mouth, digestive and genital tracts, with low virulence, making it difficult to distinguish between colonization and infection. We reviewed the cases of actinomycosis treated in our Infectious Diseases Department.

**Materials/methods:** Retrospective study of actinomycosis cases treated in an Infectious Diseases Department of a Portuguese tertiary care hospital in the last 5 years. Data were collected from individual medical records. *Actinomyces* were identified using MALDI-TOF technology, PCR techniques or histopathological examinations.

**Results:** Ten cases were identified: 4 cervicofacial, 2 pulmonary, 2 cutaneous and single cases of gastrointestinal and genitourinary actinomycosis. Five of them were women and age ranged between 19-70 years. Median time of follow-up was 9 months (IQR 6). Except in one case, several risk factors for active disease were identified (the most common: poor oral hygiene in 4 cases, active cancer in 3 and chronic pulmonary disease in 2). Diagnosis was made combining clinical data (presence of symptoms and/or active inflammation in biopsies) with identification of *Actinomyces* by histopathological examinations (in 5 cases, 3 of them complemented by PCR techniques) or culture of samples (5 cases). *Actinomyces* species identification was made in 7 cases: *A. radingae* and *A. naeslundii* accounted for 2 cases each and *A. odontolyticus*, *A. europaeus* and *A. neuii* for one case each. Most of them underwent an initial regimen of intravenous penicillin or ampicillin followed by chronic oral therapy (mainly amoxicillin; due to gastrointestinal intolerance one patient underwent maintenance therapy with clindamycin and doxycycline). Median time of completed oral treatment was 9 months (IQR 8). Source control was performed in 6 cases. Five patients were considered cured (given symptoms resolution and/or imaging improvement), one patient died of pharynx cancer, one was lost on follow-up and three are still on treatment but significantly improved.

**Conclusions:** Our case series describes the diagnostic and treatment approach of a rare disease. In fact, there are few cases reported and a lack of clinical trials regarding treatment options. Physicians must be acquainted with typical actinomycosis presentations to overcome this problem.

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Vaginal carriage of *Enterobacter cloacae* and *Klebsiella pneumoniae* among pregnant women in Bukavu, Democratic Republic of Congo: prevalence, risk factors and adverse pregnancy outcomes

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**Background:** In sub-Saharan Africa, three percent of newborns die within the first month of life. Neonatal sepsis (NS) causes one fourth of these deaths and is caused by maternal vaginal bacteria that are transmitted to the fetus/newborn just before/during birth. In Bukavu, DRC, we previously showed that the major pathogens causing NS are *Enterobacter cloacae* (EC) and *Klebsiella pneumoniae* (KP). In the current study, we aimed to assess the prevalence of vaginal carriage of EC and KP, and to identify associated risk factors and adverse pregnancy outcomes.

**Materials/methods:** We followed 553 women from Bukavu, DRC during pregnancy and delivery and quantified EC and KP in a subset of 330 cervicovaginal lavages (CVLs) (taken in first trimester) using newly developed and validated in-house quantitative PCR assays. All women and newborns were subjected to an extended clinical examination, all women to a gynecological examination. Vaginal infections including bacterial vaginosis were diagnosed by Gram-stain and wet mount of vaginal smears. Questionnaires were used to ask about sociodemographics, reproductive health history, sexual behavior, vaginal hygiene practices, vaginal signs and symptoms. Different multivariate logistic regression models were built for both EC and KP to identify risk factors and adverse pregnancy outcomes.

**Results:** The prevalence of EC and KP carriage was 42.4% [95% CI, 37.2 - 47.8%] and 12.1% [95% CI, 9.0 - 17.8%], respectively. The concentration of EC was low for all EC-positive women (< 2.5log^3 EC/ml CVL), while KP concentrations ranged from 3.63log^2 to 6.25log^6 KP/ml CVL. Carriage of EC was significantly and independently associated with a previous premature delivery [aOR 13.43], previous dysuria [aOR 6.26], and borderline with anal intercourse [aOR 6.85, p=0.054]. KP carriage was independently and significantly associated with a disturbed vaginal microbiome [aOR 3.01], maternal tachycardia [aOR 4.14], previous abortion [aOR 2.04], C-section [aOR 3.43] and polypnea/apnea of the newborn [aOR 8.49].

**Conclusions:** We found EC carriage to be highly prevalent, but at low concentrations; KP carriage was relatively low, at moderate concentrations. Both EC and KP were independently associated with [a history of] adverse pregnancy outcomes.

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Home-based care of low-risk febrile neutropenia in children: an implementation study in a tertiary paediatric hospital

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Background: Home-based management of low-risk febrile neutropenia (FN) is safe, improves quality of life and reduces healthcare expenditure. A formal low-risk paediatric program has not been implemented in Australia. We aimed to describe the implementation process and evaluate the clinical impact on length of stay (LOS) and patient safety.

Materials/methods: This prospective study incorporated three phases: implementation, intervention and evaluation. A low-risk FN implementation toolkit was developed and included a care-pathway, patient information, home-based assessment and educational resources. The program had executive-level endorsement, a multidisciplinary steering committee, and a dedicated nurse specialist. All children with cancer and low-risk FN were eligible to be transferred to home-based after an overnight period of observation for intravenous antibiotics with a nurse visiting daily. Low-risk patients were identified using a locally-validated decision rule and suitability for home-based care using disease-, chemotherapy and patient-level criteria. Plan-Do-Study-Act methodology was used to evaluate clinical impact and safety pre- and post-implementation and key barriers were identified.

Results: Over 18 months, 336 children with FN were screened: 130 (39%) were low-risk, of which 63 were transferred to home-based care. Compared to pre-implementation there was a significant reduction in in-hospital median LOS (4.6 to 1.5 days, p<0.001) and 291 in-hospital bed days were saved. Eight (13%) patients needed readmission and there were no adverse outcomes. A key barrier was timely screening of all patients, and program improvements, including utilising the electronic medical record for patient identification, have been implemented.

Conclusions: This program significantly reduces in-hospital LOS for children with low-risk FN. Ongoing evaluation, including formal economic and quality of life impact assessments, will inform sustainability and identify areas for improvement. The paediatric low-risk FN toolkit is available online (www.cancerandinfections.org) and, together with these outcomes, will support national scale up.

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Abstract 8939

Risk factors for mortality in bloodstream infections in cancer patients
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Background: Blood stream infections (BSI) are related to increased morbidity and mortality in cancer patients. Our aim is to determine the risk factors of mortality in cancer patients,

Materials/methods: Single center retrospective cohort study was performed in Haematology and Oncology Units in Çukurova University Medical School Hospital from January 2015 to December 2017. Patients with first episode of bacteremia were enrolled to the study. Patients of whom multiple microorganisms yielded in the blood culture were excluded. BSI diagnosis was performed according to CDC criteria. Demographic characteristics, infection data and risk factors were recorded prospectively by infection control committee. Multidrug resistance (MDR) was defined for gram positive and negative bacteria according to an international expert proposal for interim standard definitions for acquired resistance by Magiorakos AP, et. al.

Results: 220 bacteremia patients were enrolled to the study according to inclusion and exclusion criteria. Of the patients 122 were male (55.5%), mean age was 48.4 16.3 years. 53.6% of the patients was primary bacteremia (20.9%, n=46, catheter related vs. 32.7%, n=72, non catheter related). Most common secondary bacteremia source was pneumonia (37.3%, n=82). In hospital mortality rate was 51.8% (n=114). Most common pathogen was Acinetobacter baumannii. Of the isolated 202 bacteria 62.7% (n=138) was MDR. Significant risk factors for mortality were peripheral venous catheter (p=0.006, OR=0.192; CI:0.054-0.684), urinary catheter (p<0.001, OR=3.021; CI:1.724-5.292), haematologic cancer (p=0.004, OR=0.424; CI:0.237-0.760), MDR (p=0.002, OR=2.690; CI:1.456-4.970), diagnosis (p=0.001), isolated microorganism (p<0.001), length of stay (p=0.002) in univariate analysis. MDR (2.26; CI:1.375-3.714), secondary bacteremia (1.975;CI:1.321-2.952) and length of stay (0.975;CI:0.964-0.987) was significant risk factors in cox regression model. MDR was also associated with decreased survival (log rank: 0.006, figure 1).

Conclusions: Longer stay in the hospital, secondary bacteremia and MDR was found as risk factors of mortality. MDR was also also associated with decreased survival. Besides increased infection control practices, broader spectrum antibiotics can be thought for empirical treatment of cancer patients with bacteremia symptoms.

![Survival Functions](image.png)
Abstract 8941

**Evaluation of HIV-1 and hepatitis B and C viruses quantification by a new molecular system in comparison to established routine methods**

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Abstract third-party references: Abbott Molecular

**Background:** Nowadays, HIV-1, HBV and HCV viral load testing is the backbone for monitoring antiviral treatments. The objective of the current study was to evaluate the analytical performance for the molecular quantification of HIV-1, HBV, and HCV using the new Abbott Alinity m system and to determine the correlation with the molecular methods used routinely in our laboratory.

**Materials/methods:** A total of 153 HIV-1, 195 HBV, and 190 HCV leftover plasma and serum samples with known viral loads were re-analyzed with the Alinity m system. Previous clinical routine testing had been performed with Siemens kPCR (HIV-1) and Roche cobas 6800 (HCV, HBV). Samples were collected between July 2017 and April 2019 and selected according to their viral loads in order to represent the entire quantification ranges of the assays. In case of insufficient sample volume, a dilution protocol following the manufacturer’s instructions was applied.

**Results:** Alinity m assays showed a high linear correlation when compared to the respective routine methods: R² was 0.93 for HIV (kPCR compared to Alinity m), 0.96 for HBV and 0.92 for HCV (both: cobas 6800 compared to Alinity m). Slope and intercept point were 0.94/0.29 (HIV-1), 0.93/0.45 (HBV), and 0.87/0.64 (HCV). The mean biases between Alinity m and the routine methods were low: Alinity m minus routine method was 0.10 log cp/ml (HIV-1), 0.17 log IU/ml (HBV), and -0.01 log IU/ml (HCV). Sixteen out of 153 HIV-1 samples (10.4%), fifteen out of 195 HBV samples (7.7%) and twenty-one out of 190 HCV samples (11.1%) showed a difference >0.5 log.<1.0 log and one out of 153 HIV-1 samples (0.7%), five out of 195 HBV samples (2.6%) and nine out of 190 HCV samples (4.7%) showed a difference >1.0 log. Alinity m yielded higher viral load values in 59%, 80% and 60% of the cases, respectively. No differences in HBV and HCV quantification were observed between serum and plasma samples.

**Conclusions:** The Alinity m system showed a high concordance in HIV-1, HBV and HCV molecular quantification compared to the routine methods used in our laboratory and in many other laboratories.

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Abstract 8944

Antibiotic resistance patterns of *Staphylococcus aureus* isolated in blood cultures in primary care

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**Background:** Patient care methods have significantly changed over time, due to decreased length of stay in hospital so the epidemiology of bacterial infections has evolved. The *Staphylococcus aureus* (*S.aureus*) resistance to antibiotics was especially monitored in hospitals whereas that has few been documented in the community. The objective of this study was to evaluate MRSA rate isolated in blood cultures in primary cares and describe the different resistant patterns of these *S.aureus* strains.

**Materials/methods:** From 1st January 2015 to 31st December 2018, antibiograms of *S. aureus* isolated from blood culture were collected in a large network of laboratories across France. Administrative and microbiological data were downloaded by laboratories on an e-platform dedicated to the surveillance. Strains isolated from patients living at home or nursing home residents were included in the analysis. Hospitalised patients and screening samples were excluded. Statistical analyses were performed using Student test or variance analysis as appropriate.

**Results:** The total number of 504 *S.aureus* antibiograms included varied from 90 in 2015 (147 laboratories) to 171 in 2018 (742 laboratories across 11 French regions). The proportion of MRSA strains was 11% (n=90) in 2015, 16% (n=86) in 2016, 11% (n=157) in 2017 and 10% (n=171) in 2018 (non significative, NS). MRSA strains was isolated from patients living at home in 88% of cases every year. Among this MSSA strains, 4% were resistant to fluoroquinolones in 2015 to 3% in 2018 (NS). The proportion of MSSA resistant to erythromycin varied from 12% in 2015 to 18% in 2018. Among this MRSA isolates, 90% were resistant to fluoroquinolones in 2015 to 65% in 2018 (NS). The proportion of MRSA resistant to erythromycin varied from 30% in 2015 to 11% in 2018 (NS).

**Conclusions:** *Staphylococcus aureus* bacteraemia is an important cause of morbidity and mortality. Suboptimal treatments are associated with poor patient outcomes. In order to optimize the treatment, the resistance patterns of the circulating *S.aureus* in the community must be studied. This study suggests that MRSA strains isolated from blood culture were more susceptible to fluoroquinolones and erythromycin over time.

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Abstract 8947

National reporting of severe *Clostridioides difficile* infections in Germany between 2014 and 2018
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Background: *Clostridioides difficile* infection (CDI) is responsible for 15–25% cases of antibiotic-associated diarrhoea and accounts for 10% of all healthcare-associated infections in Germany. Since the early 2000s, there has been a marked increase in the incidence and severity of CDI and several major outbreaks. In response, Germany introduced mandatory reporting of severe CDI (sCDI) in 2007. We analysed the criteria that triggered reporting sCDI and the trend in sCDI reporting over a five-year period.

Materials/methods: sCDIs are defined according to the four-criteria definition from the European Centre for Disease Prevention and Control’s surveillance protocol. We analysed data that were continuously reported for all regions from 2014 to 2018, thus focusing solely on this three reporting criteria: i) Admission to an intensive care unit for treatment of CDI or its complications (ICU), ii) Surgery (colectomy) for toxic megacolon, perforation or refractory colitis (Surgery), iii) Death within 30 days after diagnosis if CDI is either a primary or contributing cause (Death). Each sCDI case could be reported due to one or more criteria. We counted sCDI criterion separately and calculated the percentage of each criterion among the sum of all three sCDI criteria together.

Results: The reported sum of the three sCDI criteria was 1,239 in 2014 and was consistent at 1,811, 1,803 and 1,757 between 2015, 2016 and 2017 respectively, and decreased to 1,507 in 2018. Reported “ICU” data were relatively stable between 35% and 39% during 2014 and 2018, and similarly for “Surgery”, which remained fairly stable at around 7%. Reported “Death” data ranged between 53% and 59% during the observed period.

Conclusions: Reporting of the three sCDI criteria (“ICU”, “Surgery” and “Death”) in Germany increased initially and then reached a plateau. A decrease was then observed from 2017 to 2018 and a possible further decrease suggested from preliminary data until October 2019. This may be in line with data from the US and Europe, which suggest the incidence of CDI may have peaked in recent years and is leveling off or slightly declining.

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Abstract 8950

The Global Point Prevalence Survey of Antimicrobial Consumption and Resistance (Global-PPS): an opportunity to lead global stewardship actions in Belgian hospitals?

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Background: The 'Grand Hôpital de Charleroi' with 1154 beds capacity had set new antibiotic stewardship priorities in 2008, but several structural challenges hampered major improvements in appropriate antimicrobial prescribing. Using the standardized Global-PPS [www.global-pps.com], we aimed to improve the quality of antimicrobial prescribing guided by quality indicators and goals to be reached by 2019, as defined by the Belgian Antibiotic Coordination Committee (BAPCOC) (table).

Materials/methods: Based on the first hospital-wide Global-PPS, conducted in March 2015, we initiated stewardship interventions, consisting of dedicated education of surgeons and anesthetists to antibiotic prophylaxis, systematic review of antibiotics during systematic infectious diseases physician and clinical pharmacist rounds, point analyses and feedback, and standardization of antibiotic delivery rules. The impact of these interventions was assessed by a follow-up PPS conducted in October-November 2017.

Results: Out of 862 and 763 admitted patients, 29.6% and 26.3% were on antibiotics in 2015 and 2017 respectively [see table for details by activity medicine, surgery and intensive care units (ICU)]. Most quality indicators improved in 2017 as compared to 2015 (in green, table) but the BAPCOC target “indication antibiotic therapy noted in the patient chart in >90% of cases” was reached only for ICU.

Conclusions: This PPS gave us an opportunity to lead a global action which reinforced global awareness amongst physicians and staff. Results highlighted indicators not provided by other databases such as reason in notes and guideline compliance. It helped us to measure results of actions and to show favourable trends. As the BAPCOC goals have not yet been reached, a third follow-up Global-PPS is ongoing to further measure results of ongoing actions.

Table. Quality indicators for antibiotic prescribing following two Global-PPS

<table>
<thead>
<tr>
<th>Baseline and BAPCOC antibiotic indicators with target</th>
<th>2015 Global-PPS</th>
<th>2017 Global-PPS</th>
</tr>
</thead>
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<tr>
<td></td>
<td>Medical</td>
<td>Surgical</td>
</tr>
<tr>
<td>N admitted patients</td>
<td>596</td>
<td>196</td>
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<tr>
<td>N antibiotics (ATC J01)</td>
<td>176</td>
<td>76</td>
</tr>
<tr>
<td>Antimicrobial Prevalence (%)</td>
<td>26.5</td>
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<td>Indication noted in patient chart &gt;90%</td>
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<td>30.7</td>
<td>47.4</td>
</tr>
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</table>

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Re-evaluating and refining predictors of bacterial infection in children with cancer and febrile neutropenia

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Background: Seventeen paediatric febrile neutropenia (FN) clinical decision rules (CDRs) that risk stratify children with cancer and FN for infection have been derived. Collectively they include 29 different variables with 15 common across >1 CDR. Validation studies show reduced performance in external settings. Our objectives were to evaluate the association between variables common across FN CDRs to predict bacterial infection and refine existing CDRs using these data.

Materials/methods: Prospectively collected data from the multisite (n=8) Australian-PICNIC study which enrolled 858 FN episodes in children with cancer were used. Variables common across >1 CDR were analysed. Disease/chemotherapy were excluded given treatment changes over time. For recalibration, rules not including chemotherapy or disease factors and with variables common across >1 CDR were considered. Recalibration included re-evaluation of beta-coefficients (logistic model) or recursive-partition analysis (tree-based models).

Results: Ten variables were able to be analysed. On univariate analysis, location, temperature, hypotension, rigors, severely unwell and decreasing platelets, white cell count (WCC), absolute neutrophil count (ANC) and absolute monocyte count (AMC) were significantly associated with bacterial infection. The multivariable model included temperature, platelets and severely unwell, with an AUC 0.67, sensitivity of 93% and specificity of 23% (threshold 15%).

Five rules were recalibrated: three use monocyte count and temperature (Klaassen, Baorto, Rackoff) one used haemoglobin, platelets, rigors and requirement for in-patient care (SPOG-bacteraemia) and one used chemotherapy intensity, haemoglobin, platelets and WCC (SPOG-AE). The optimal AMC cut-off was 0.015 cells/mm3 (originally 0.1 or 0.15) and temperature 39.5°C. The SPOG-bacteraemia and SPOG-AE recalibration set three factors at ‘1’ and dropped haemoglobin as uninformative. Across all rules, recalibration increased the low-risk yield but reduced sensitivity (least in SPOG-AE rule).

Conclusions: Degree of marrow suppression (low platelets), features of inflammation (height of temperature) and clinical judgement (severely unwell) have been consistently shown to predict infection in children with FN. Exclusion of disease factors and recalibration of existing CDRs is a novel way to improve diagnostic performance and maintain relevance over time.

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Which dosage of amoxicillin in infective endocarditis? Development of a simple predictive medicine tool for adaptation

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Abstract third-party references: On behalf of the NAMAP study group

Background: Amoxicillin is recommended by European guidelines as first-line treatment in streptococci or enterococci infective endocarditis (IE) (45% of monomicrobial IE). Regimen is linearly adapted to the weight but other potentially interesting co-variates such as renal function are neglected. Objectives were to identify which co-variates influenced pharmacokinetics (PK) of amoxicillin in IE treatment in order to develop a simple tool based on identified co-variates for individual adaptation.

Materials/methods: Patients treated with amoxicillin administered by continuous infusion for an IE at Nantes University Hospital between January 2013 and May 2019 were included retrospectively via the Nantes endocarditis cohort. Dialyzed patients were excluded from the study. The population PK analysis was performed using Pmetrics package for R (NPAG algorithm). Influence of weight, ideal weight, height, body mass index, body surface area, glomerular filtration rate adapted to the body surface area and calculated by the CKD-EPI method (GFR in mL/min) and serum protein level on amoxicillin PK were tested. A nomogram was then developed to determine the daily dosage to achieve a steady-state concentration between 20 mg/L (free fraction above 4CMI, 100 % of time for an MIC ≤ 4 mg/L) and 80 mg/L.

Results: One hundred and sixty patients were included. Seventy-nine percent were male and the median age was 72. Streptococci were identified in 124 cases and Enterococcus faecalis in 36 cases. The initial median dosage of amoxicillin was 12 g/day (from 2 g to 20 g/day). Median GFR was 78.77mL/min (from 12.68 to 136.07 mL/min). Population pharmacokinetic analysis was performed on 540 amoxicillin plasma concentrations. A two-compartment model best described amoxicillin PK and the GFR covariate significantly improved the model when included to the elimination constant Ke. To achieve a steady state concentration between 20 mg/L and 80 mg/L with a probability of 0.9, the daily dose should be from 0.0001 x GFR^2 + 0.06 1.3 x GFR + 1.157 (g/day) to -0.0004 x GFR^2 + 0.2073 x GFR + 0.6325 (g/day), respectively.

Conclusions: This work allowed the development of personalized medicine tool which can help to increase achievement of the PK-PD targets in IE treated by amoxicillin.

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Background: Several commercial multiplex PCR systems for respiratory pathogens have become available. They demonstrate high accuracy but data on clinical significance of test results is scarce. Especially significance of multiplex respiratory bacterial pathogen PCR is unclear.

Materials/methods: We analyzed burden of detected respiratory pathogens estimated with the length of parental work absenteeism in a prospective study with pediatric ED patients during one epidemiological year in Oulu, Finland. We obtained nasal swabs of 737 children for the detection of 16 viral and seven bacterial pathogens. The parents filled out symptom diaries throughout the study. Follow up data and viral PCR results were available for total of 505 children, bacterial data was available for 244 children.

Results: The most common detected viruses were Rhinovirus (n=156, 31 %), followed by Adenovirus (n=48, 9.5 %), Metapneumovirus (n=47, 9.3 %) and RSV (n=38, 7.5 %). Streptococcus pneumoniae PCR was positive for 118 children (48 % of the tested), Haemophilus influenzae was positive for 51 (23 %) and Mycoplasma pneumoniae for 2 (0.8 %) children. We did not find any cases of Legionella pneumophila, Chlamydia pneumoniae, Bordetella pertussis or Bordetella parapertussis. Mean length of parental work absenteeism was 4.7 days (SD 14.2). We did not find significant differences between the viruses nor between negative and any positive virus PCR results. Positive Streptococcus pneumoniae PCR was associated with longer absenteeism (2.3 days for PCR negative vs. 4.1 days for PCR positive children, 95 % CI for difference -3.1 - -0.46, p = 0.009). Positive pneumococcal PCR was also associated with longer absenteeism when present at the same time with rhinovirus (1.9 days vs. 3.5 days, 95 % CI -3.1 - -0.31, p = 0.046), adenovirus (1.6 days vs. 4.5 days, 95 % CI -4.9 - -0.98, p = 0.007) and RSV (0.28 days vs. 4.0 days, 95 % CI -6.8 - -0.65, p = 0.023). We did not find significant changes associated to Haemophilus influenzae PCR.

Conclusions: Positive Streptococcus pneumoniae PCR is associated with longer parental work absenteeism independently of simultaneous viral PCR findings in children. PCR testing could have clinical significance when predicting burden of the disease.

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Dynamics and distribution of attributable and non-attributable mortality in Staphylococcus aureus bacteraemia

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Background: Mortality from S. aureus bacteraemia remains high. However, the dynamics and risk factors leading either directly or indirectly to death are largely unknown.

Materials/methods: From January 2013 until April 2015, we performed a prospective observational cohort study of consecutive hospitalised adult patients with S. aureus bacteraemia at 17 European centres (United Kingdom, Spain, Germany) and assessed predictors of mortality. The treating physicians categorised mortality as either directly S. aureus-attributable or not directly attributable.

Results: Median age of 985 included patients was 65 years (IQR 51-75) and 63.2% (623) were male. Death at 30 days and 90 days occurred in 17.3% (170) and 28.4% (270), respectively. S. aureus-attributable mortality accounted for 50% (85) of deaths at 30 days and for 36% (99) at 90 days. The focus-stratified ratio between attributable and non-attributable mortality ranged from 3.5 (15.4% vs. 4.4%) and 1.3 (19.1% vs. 14.6%) for endocarditis to 0 (0% vs. 8.6%) and 0 (0% vs. 22.9%) for surgical wound infections [see Figure]. Higher age and SOFA-Score were independently associated with both attributable and non-attributable 30-day and 90-day mortality in multivariable analysis. Only the attributable mortality was increased in female patients [adjusted hazard ratio (aHR) 1.68, 95% confidence interval (CI) 1.09-2.60, for 30-day- and aHR 1.51, 95% CI 1.01-2.28, for 90-day mortality] and in patients with persistent bacteraemia [aHR 2.81, 95% CI 1.82-4.33, for 30-day- and aHR 2.55, 95% CI 1.71-3.8, for 90-day mortality] but not the non-attributable mortality. Attributable mortality decreased after focus removal [aHR 0.41, 95% CI 0.21-0.81, for 30-day and aHR 0.44, 95% CI 0.25-0.79, for 90-day mortality] but not the non-attributable mortality. In contrast, higher Charlson score was associated with non-attributable mortality [aHR 1.13, 95% CI 1.06-1.21, for 30-day and aHR 1.12, 95% CI 1.05-1.19, for 90-day mortality] but not with attributable mortality.

Conclusions: Death after S. aureus bacteraemia is often perceived as not directly attributed to S. aureus. Future interventions to improve outcome should not only focus on direct but also indirect and late effects of S. aureus bacteraemia.
Abstracts 2020

**Figure:** Differentiation between *S. aureus* attributable and non-attributable mortality from a cumulative incidence analysis of competing events; stratified according main infectious focus

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Late spot evaluation reveals enhanced phage lytic activity

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Background: The wide use of antimicrobials has resulted in an increase of antimicrobial resistance. Accordingly, this public health concern makes it imperative to find novel therapeutic agents. Lytic bacteriophages specifically infect and kill bacterial hosts, even drug-resistant strains, thus allowing to consider phages as medical products. For this purpose, it is crucial to examine lytic activity of bacteriophage cocktails and their antimicrobial effect over various conditions. To assess phage cocktail efficacy, spot test should be applied.

Materials/methods: 49 Staphylococcus aureus strains acquired from peritoneal dialysis and hemodialysis patients, one S.aureus reference strain ATCC 4336 and seven commercial bacteriophage cocktails containing S.aureus phages – six produced by Eliava BioPreparations, Ltd. [Staphylococcal, Pyo, Ses, Fersisi, Enko, Intesti] and one by Microgen, Ltd. [Pyobacteriophage] were used. To detect phage titer plaque assay was performed. A spot test was implemented to detect the lytic ability of phages. The results of spot tests were evaluated following overnight incubation for 18h and 144h. A positive lytic effect was characterized as confluent, partial lysis or individual plaques, while a negative effect as no lysis.

Results: All seven commercial bacteriophage cocktails displayed steady improvement in lytic activity over time. Increase of confluent lysis at 144h vs 18h for Staphylococcal, Pyo, Fersisi, Enko and Pyobacteriophage cocktails was observed, respectively for more than 2 \(n=2 \rightarrow 4\), 3.3 \(n=3 \rightarrow 10\), 3 \(n=1 \rightarrow 3\), 1.8 \(n=5 \rightarrow 9\) and 2 \(n=3 \rightarrow 6\) times. Result of Intesti phage cocktail after 18h showed no confluent lysis in any of the strains, conversely after 144h 4 strains displayed confluent lysis.

Conclusions: The obtained data indicate that later reading of spot test results shows improved interaction between bacteriophage cocktails and S.aureus strains, i.e. lytic activity. Thus, our study suggests that bacteriophages might need more time than 18h to lyse the bacterial host and to overcome bacterial resistance. Variations of optimal lysis time could be explained by bacteriophage viral nature. Furthermore, difference among phage cocktail lytic activity could be clarified because of each cocktail different content of various S.aureus viral phagotypes and their titer differences.

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Impact of time to central venous catheter removal on the mortality of adults with non-severe catheter-related candidaemia

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Background: Catheter-related candidemia (CRC) comprises a significant part of Candida spp. bloodstream infections. Management requires adequate antifungal treatment and effective source control. Central venous catheter (CVC) removal is often delayed due to the severity of candidemia, with prompt source control being usually performed in patients with an already lower risk of death. Thus, the impact of time to CVC-removal on survival of candidemic patients remains controversial. We sought to analyze the effect of early CVC-removal on the mortality rates of adults with non-severe CRC.

Materials/methods: Retrospective cohort including all cases of CRC in adults diagnosed from 2010-2018 in a tertiary university hospital. CRC was confirmed if semi-quantitative roll-plate culture of the CVC tip yielded $\geq 15$ CFU of the same Candida species in bloodstream. Non-severe cases were defined as those with a Pitt-score $\leq 1$. Early CVC-removal occurred within 48 hours from index candidemia. Primary outcome was mortality at 14 and 30 days. Secondary outcomes included complications (ocular candidiasis, thrombophlebitis, endocarditis, and dissemination), and hospital length of stay (HLOS).

Results: Overall, 154 patients with confirmed CRC were included and 99/154 (64.3%) presented a Pitt-score $\leq 1$. Early CVC-removal was performed in 54/99 (54.5%) and late removal in 45/99 (45.6%). Baseline characteristics are described in Table 1. Median time to CVC-removal in each group was 1 (0-2) vs. 4 (3-32) days, $p<0.001$. Patients whose CVC was removed earlier had lower mortality rates at 14 days [1 (1.9%) vs. 8 (17.8%), $p=0.01$] and at 30 days [8 (14.8%) vs. 15 (33.3%), $p=0.03$]. There were more complications among patients with late CVC-removal [11 (24.4%) vs. 8 (14.8%), $p=0.31$]. No difference in the median HLOS was observed between groups among survivors [27.5 (6-164) vs. 23 (7-130) days, $p=0.36$]. In the multivariate analysis, early CVC-removal was an independent protective factor from 30-day mortality [OR 0.3, CI95% (0.107-0.856), $p=0.024$], whereas age [OR 1.02, CI95% (0.986-1.068), $p=0.2$] and solid tumor [OR 1.18, CI95% (0.433-3.263), $p=0.738$] were not predictors.

Conclusions: Early CVC removal is associated with a better prognosis among adults with non-severe CVC-related candidemia. Thus, clinically eligible patients with presumed CRC should have the CVC ideally removed within 48 hours.

Table 1. Baseline characteristics of adult patients with CVC-related candidaemia according to the timing of CVC removal.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Early CVC-removal* (n=54)</th>
<th>Late CVC-removal** (n=49)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years), median (IQR)</td>
<td>65.5 (36-83)</td>
<td>72 (23-91)</td>
<td>0.02</td>
</tr>
<tr>
<td>Comorbidities</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solid tumor, n (%)</td>
<td>25 (46.3)</td>
<td>30 (66.7)</td>
<td>0.04</td>
</tr>
<tr>
<td>Charlson Comorbidity Index, median (IQR)</td>
<td>6 (1-14)</td>
<td>7 (1-11)</td>
<td>0.19</td>
</tr>
<tr>
<td>Therapeutic management</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Echinocandin as initial antifungal, n (%)</td>
<td>13 (24.1)</td>
<td>13 (28.9)</td>
<td>0.65</td>
</tr>
<tr>
<td>Time to CVC-removal (days), median (IQR)</td>
<td>1 (0-2)</td>
<td>4 (3-32)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Outcomes, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complications</td>
<td>8 (14.8)</td>
<td>11 (24.4)</td>
<td>0.31</td>
</tr>
<tr>
<td>14-day mortality</td>
<td>1 (1.9)</td>
<td>8 (17.8)</td>
<td>0.01</td>
</tr>
<tr>
<td>30-day mortality</td>
<td>8 (14.8)</td>
<td>15 (33.3)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

*CVC: central venous catheter; *Early CVC-removal: within 48 hours from index candidaemia; **Late CVC-removal occurred anytime after 48 hours, during the same episode of candidaemia

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Abstract 8966

Drug-resistant Neisseria gonorrhoeae and Mycoplasma genitalium identified in the private healthcare sector in South Africa

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Background: Neisseria gonorrhoeae and Mycoplasma genitalium are two of the causative pathogens of the male urethritis and vaginal discharge syndromes. Diagnostics tests are not routinely performed as these syndromes are managed using a syndromic approach, which means limited data are available in South Africa on these pathogens. Most available data are linked to the public healthcare sector [serving >80% of the population]. This study was designed to determine the antimicrobial resistance (AMR) of N. gonorrhoeae isolates and M. genitalium strains in the private healthcare sector.

Materials/methods: Neisseria gonorrhoeae isolates and positive M. genitalium DNA samples were collected from a private sector diagnostic laboratory from August 2018 to June 2019. The AMR profiles of the N. gonorrhoeae isolates were determined following EUCAST guidelines. Macrolide resistance of M. genitalium was screened for using a validated real-time PCR assay coupled with melting curve analysis targeting the 23S rRNA gene, and confirmed using Sanger sequencing. The quinolone resistance determining regions (QRDR) of gyrA and topoisomerase of macrolide resistant strains were determined by Sanger sequencing.

Results: Twenty-one N. gonorrhoeae isolates were collected and all were found to be susceptible to azithromycin, cephalosporins and spectinomycin. High rates of resistance to tetracycline (19/21; 90%), penicillin (18/21; 86%) and ciprofloxacin (13/21; 62%) were observed. Twenty-seven M. genitalium positive DNA samples were collected. The screening PCR assay detected five mutations (5/27), which was confirmed by the sequence data as follows: three strains (3/27) harboured an A-to-G transition at position 2071 and in two strains (2/27) an A-to-G transition at position 2072 (M. genitalium numbering). Two macrolide resistant strains harboured mutations in the QRDR, which included a mutation linked to moxifloxacin and sidafloxacin treatment failure.

Conclusions: The prescribing behaviour of doctors as well as the availability of antibiotics in the private healthcare sector differ significantly from that in the public healthcare sector where resistance patterns are different. This study highlights the importance of the introduction of STI diagnostics and enhanced surveillance systems to monitor and track the emergence of drug resistant N. gonorrhoeae and M. genitalium strains in the private healthcare sector.

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Antibiotic resistance profile of ESKAPE pathogens in Limpopo, South Africa: A two-year retrospective analysis

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Background: The acronym ESKAPE encompasses two Gram positive and four Gram negative pathogens ([Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter species] which are the leading cause of nosocomial infections worldwide. These pathogens are amongst the twelve multidrug resistant organisms listed by World Health Organization (WHO) for which new antibiotics are urgently needed. This study describes the antibiotic resistance analysis of the ESKAPE pathogens in Limpopo province, South Africa.

Materials/methods: Retrospective data containing routine antimicrobial susceptibility test (AST) results for the ESKAPE pathogens isolated between January 2017 and December 2018 were sourced from the National Health Laboratory Services data warehouse (CDW) and the local laboratory information system (LIS). TrakCare. Vitek 2 machine was used for identification of these pathogens and susceptibility results were ascertained from minimum inhibitory concentrations and interpreted using Clinical and Laboratory Standards Institute guidelines. The analysis aimed at also detecting the district with most of these pathogens.

Results: 23,397 ESKAPE pathogens were eligible for analysis. Klebsiella pneumoniae was most frequently isolated (n = 7,547, 32%), followed by Staphylococcus aureus (n = 6,352, 27%), the least was Enterococcus faecium (n = 999, 4.2%). A reduction in rates of extended spectrum beta-lactamase (ESBL) production in K. pneumoniae was observed (49% in 2017 and 44% in 2018) however the carbapenem resistance among K. pneumoniae and Enterobacter spp. was <1%. High rates of multi-drug resistance were observed in A. baumannii (n = 1,943, 8.3%) with 52% resistance to carbapenems and <1% resistance to colistin. Capricon district had most of these ESKAPE pathogens (n = 14,305, 61%).

Conclusions: This study describes the magnitude of antimicrobial resistance in the rural Limpopo province of South Africa. These findings attest to the global spread of multidrug resistant ESKAPE pathogens and the risk of outbreaks even in the most rural hospitals. This also signal the need for enhancement of antimicrobial stewardship and infection control measures this two provincial tertiary hospital.

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Abstract 8971

**Multi-centre study performance results of ETEST delafloxacin for antimicrobial susceptibility testing against Gram-positive organisms and Pseudomonas aeruginosa**

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**Background:** Delafloxacin (DFX), BAXDELA brand name, is a fluoroquinolone antibacterial indicated for the treatment of adults with the following infections caused by designated susceptible bacteria: Acute Bacterial Skin and Skin Structure Infections (ABSSSI) and Community-Acquired Bacterial Pneumonia (CABP). This study evaluated the performance of ETEST® DFX, a new gradient diffusion strip (FDA cleared but not yet CE marked) for determining antimicrobial susceptibility of Gram-positive organisms and *Pseudomonas aeruginosa* as compared to CLSI M07 broth microdilution reference method (BMD).

**Materials/methods:** A population of 625 isolates including 287 *Staphylococcus aureus* (methicillin-resistant and methicillin-susceptible isolates), 46 *Staphylococcus haemolyticus*, 32 *Staphylococcus lugdunensis*, 127 *Enterococcus faecalis* and 133 *Pseudomonas aeruginosa* were tested at 4 clinical trial sites, including one internal laboratory using ETEST® DFX and BMD. Results were analyzed in terms of essential (EA), category (CA) agreements, minor (mE), major (ME) and very major (VME) error rates using FDA breakpoints in Table 1.

### Table 1:

<table>
<thead>
<tr>
<th>Organism</th>
<th>Interpretive criteria for Delafloxacin (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Susceptible</td>
</tr>
<tr>
<td><strong>ABSSSI indication</strong></td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em> (MRSA and MSSA isolates)</td>
<td>≤ 0.25</td>
</tr>
<tr>
<td><em>Staphylococcus haemolyticus</em></td>
<td>≤ 0.25</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>≤ 0.12</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>≤ 0.5</td>
</tr>
<tr>
<td><strong>CABP indication</strong></td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em> (MSSA isolates only)</td>
<td>≤ 0.12</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>≤ 0.5</td>
</tr>
</tbody>
</table>

**Results:** Results are summarized in Table 2. ETEST® DFX performance for each organism met FDA acceptance criteria for EA (≥90%), CA (≥90%), ME (≤3%) and VME (≤2%).

### Table 2:

<table>
<thead>
<tr>
<th>Organism</th>
<th>EA (%)</th>
<th>CA (%)</th>
<th>ME (%)</th>
<th>VME (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ABSSSI indication</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em> (MRSA and MSSA isolates)</td>
<td>96.5</td>
<td>93.0</td>
<td>7.8</td>
<td>0.0</td>
</tr>
<tr>
<td><em>Staphylococcus haemolyticus</em></td>
<td>100.0</td>
<td>93.5</td>
<td>6.5</td>
<td>0.0</td>
</tr>
<tr>
<td><em>Staphylococcus lugdunensis</em></td>
<td>100.0</td>
<td>Not Applicable</td>
<td>Not Applicable</td>
<td>Not Applicable</td>
</tr>
<tr>
<td><em>Enterococcus faecalis</em></td>
<td>100.0</td>
<td>96.1</td>
<td>3.9</td>
<td>0.0</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>98.5</td>
<td>95.5</td>
<td>4.5</td>
<td>0.0</td>
</tr>
<tr>
<td><strong>CABP indication</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em> (MSSA isolates only)</td>
<td>97.3</td>
<td>91.8</td>
<td>8.2</td>
<td>0.0</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em></td>
<td>98.5</td>
<td>95.5</td>
<td>4.5</td>
<td>0.0</td>
</tr>
</tbody>
</table>

**Conclusions:** ETEST® DFX shows very good clinical performance characteristics for determining Delafloxacin MIC of *S. aureus*, *S. haemolyticus*, *S. lugdunensis*, *E. faecalis* and *P. aeruginosa*.

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Abstract 8975

**Role of epitopes of four immunogenic Group B streptococci (GBS) proteins and their derivatives in differentiation between pregnant GBS carriers and non-carriers**

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**Abstract third-party references:** Supported by the National Centre for Research and Development [grant no. TANGO2/340018/NCBR/2017]

**Background:** Group B Streptococci (GBS) are opportunistic pathogens, which can cause life-threatening infections in newborns. Currently, screening of pregnant women for GBS carriage is based on time-consuming culture methods. Therefore, the aim of this study was to determine the ability of chosen core epitopes of the immunoreactive GBS proteins and their derivatives to detect GBS carriers in immunoenzyme assay using antibodies present in pregnant women’s blood.

**Materials/methods:** The epitopes (n=12) of four immunoreactive GBS proteins: enolase, elongation factor Tu, inosine 5’-monophosphate dehydrogenase and molecular chaperone GroEL were detected by PEPSCAN, synthesized and conjugated with BSA protein. Phenotypic diagnosis of GBS carriage was conducted according to CDC guidelines. Patients (n=50) were monitored over the three trimesters of gestation. Serum samples were examined by ELISA assay in 96-well plates coated with the single epitopes conjugated with BSA protein and representative for four immunoreactive GBS proteins. Core epitopes and their derivatives were examined both individually and in combinations. Both IgG and IgM class antibodies were studied. This study was supported by the National Centre for Research and Development [grant no. TANGO2/340018/NCBR/2017].

**Results:** Among the 50 patients examined, 10 were colonized with GBS in the vagina or rectum. High immunoreactivity of the investigated epitopes in the presence of GBS-positive serum (mean absorbance value=1.6 nm) was discovered, whereas weak immunoreactivity (mean absorbance value=0.13) was observed in the presence of samples from non-carriers. Absorbance for IgM antibodies was noticeably higher for serum samples originating from patients with fresh carriage. Moreover, seroconversion for IgG was observed. The derivatives of epitopes demonstrated reactivity at least as high as core epitopes. These results allowed determining the cut-off point of absorbance equal to 0.2 nm, according to which patients could be qualified as GBS-carriers or GBS-non carriers.

**Conclusions:** In our study, we showed that epitopes of enolase, elongation factor Tu, inosine 5’-monophosphate dehydrogenase and molecular chaperone GroEL of GBS demonstrated high immunoreactivity and specificity; therefore, they can be considered as good markers in immunodiagnostic assay for detection of GBS carriage in pregnant women.

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**Abstract 8976**

**Dipstick urinalysis: an alternative screening test for urine cultures to rule out negatives?**

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**Background:** Urine samples account an important part of the clinical microbiology laboratories. However the culture process is time consuming and a large proportion is reported as negative. To reduce unnecessary culture process, easy and rapid resulting screen tests are needed.. The aim of the research is to assess the validity of dipstick test as screening method in comparison with urine culture and flow cytometry.

**Materials/methods:** The urine specimens submitted to Marmara University Hospital Clinical Microbiology Laboratory were simultaneously screened with flow cytometry (Sysmex UF 1000i, Japan), and dipstick test (Mediatape UC-9A). In addition to these methods urine cultures were performed. Dipstick nitrite (NT) and leukocyte esterase (LE) tests results were compared with urine culture and flow cytometry. The collected data were analyzed in SPSS 20.0.

**Results:** A total of 555 urine specimens were enrolled in our study. Of these 49.5% were from children and 50.5% from adult patients. Urine cultures were reported as negative in 49% (n=272), mixed growth in 38.7% (n=215), and positive in 12.8% (n=68). Dipstick leukocyte esterase test resulted negative in 95.6% of these culture negatives and in 94.2% of UF1000i negatives. Nitrite test was determined negative of culture negatives and of UF1000i negatives as 98.2% 98.9% respectively. Of 98.3% urine culture negatives both dipstick nitrite+leukocyte esterase were analyzed as negative. When leukocyte esterase+nitrite test were evaluated together, the negative predictive value was 98.3% and positive predictive value 47%. The specificity of dipstick leukocyte esterase, nitrite and leukocyte esterase + nitrite were determined as 98.2%, 85.6%, 98.3% respectively.

**Conclusions:** Dipstick leukocyte esterase+nitrite test with >98% negative predictive value (NPV) can be an acceptable alternative test to detect negative cultures rapidly for clinical microbiology laboratories. However it should be noted that microbiology laboratories should be aware of samples from neutropenic and pediatric patients as screening systems can give false-negative results.

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Abstract 8979

Lichtheimia corymbifera cutaneous infection

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Background: Mucorales is the most studied order of zygomycete fungi. They are ubiquitous, fast-growing molds (soil, water, food, surgical material) and play a major role in carbon cycle. Rhizopus is the most common genera associated to infection in humans and the 80% of mucormycosis cases are related to 4 genera of this order (Rhizopus, Rhizomucor, Mucor or Lichteimia, also called Absidia). Although rare, the incidence of infection caused by these filamentous fungi is increasing. It is the third cause of invasive fungal infection, after candidiasis and aspergillosis and most cases are reported in immunocompromised hosts with hematological malignancies, diabetes mellitus, transplantation. Trauma, burn, bite are the main risk for local infection in immunocompetent patients.

Materials/methods: Retrospective study of microbiological isolates of mucorales from January 2010 to October 2019 from Hospital La Fe, Valencia, Spain. We used mass spectrometry (MALDI-TOF) or microscopical analysis to identify molds, after 4-5 days of incubation on Sabouraud plates at 30 ºC.

Results: A total of 45 isolates from skin samples (34 skin exudates and 11 biopsies, 3 from the soft palate) were reported, 30 (66.6 %) male and 15 (33.3%) female with a median age of 47 years. The samples grew of Rhizopus (13), Mucor (22), Syncephalastrum racemosum (2) and Lichteimia corymbifera. Lichteimia corymbifera was isolated in 8 samples. Five of eight isolates had clinical relevance, 6 patients were older than 50 years (6 males, 3 females) and all of them presented risk factors such as burns (3), trauma (2), diabetes mellitus (1), chronic kidney disease (1) and leukemia (1). Surgical treatment was needed in 5 of 8 patients together with bi-antifungal therapy. Thirty-day survival rate was 5/8, similar to 1-year survival rate.

Conclusions: Local cutaneous infection is the main reported mucoral infection in our hospital, although rhinocerebral and pulmonary zygomycosis by Lichteimia corymbifera seems to be more frequently described in literature.

In our hospital, Lichteimia corymbifera in an opportunistic pathogen secondary to local injury and no systemic disease was reported. Therefore, it should be borne in mind when dealing with burn and immunocompromised patients.

Radical surgery combined with antifungal therapy, according to in vitro susceptibility, should be initiated soon for improving the survival prognosis.

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Abstract 8981

**A genomic snapshot of antimicrobial resistance in Campylobacter fetus**

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**Background:** The increase in antimicrobial resistance (AMR) in *Campylobacter* is a worldwide public-health concern. *Campylobacter fetus* is primarily associated with fertility problems in sheep and cattle but can also cause severe infections in humans and requires antimicrobial treatment. It is unknown how AMR in *C. fetus* is developing. By using whole genome analysis, we determined the resistance gene content of different *C. fetus* lineages, the location of resistance genes (on the chromosome or mobile elements), and the presence of resistance genes over time in *C. fetus* isolates from different hosts. The aim is to investigate the emergence of resistance in *C. fetus* from the pre-antimicrobial era until now.

**Materials/methods:** *C. fetus* isolates obtained between 1942 - 2019 from animals (n=102) and humans (n=31) were Illumina sequenced and assembled using SPAdes. *C. fetus* genomes from public databases (n=161) were included and plasmid contigs of all genomes were predicted using RFPlasmid (github.com/aldertzomer/RFPlasmid). The Harvest suite was used for reconstruction of single-nucleotide polymorphism (SNP) based phylogeny, and BEAST for time-resolved evolutionary tracking of the genomes. Resistance genes were identified using ResFinder, and *gyrA* genes were aligned to reference resistance genes in *Campylobacter*.

**Results:** The SNP phylogeny divided 294 *C. fetus* isolates in 11 MLST lineages, of which ST20 and ST6 were overrepresented with human isolates. Forty human and 33 animal isolates carried resistance genes, of which 19% were associated with plasmids carrying tetracycline (*tetO*) and aminoglycoside resistance genes (*ant(6)-Ib, aph(3’)-III*), first detected in 1999. *GyrA* mutations were present in 55 isolates, first detected in 1962. If all these mutations confer resistance to fluoroquinolones, and the mechanism of the intrinsic resistance to nalidixic acid with absence of resistance to ciprofloxacin in wild-type *C. fetus* is currently being studied.

**Conclusions:** The overall SNP diversity in *C. fetus* after 70 years was extremely low. Chromosomal mutations in *gyrA* appeared in the 60ths in ovine isolates. Two lineages were associated with humans, carrying most of the plasmid associated tetracycline and aminoglycoside resistance genes that most likely, given their gene homology, are shared with other *Campylobacter* species.

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Abstract 8984

**Early-onset prosthetic valve endocarditis: features in a contemporary cohort**

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**Abstract third-party references:** Supported by Faperj, Rio de Janeiro, Brazil.

**Background:** Early onset prosthetic valve endocarditis (EO-PVE) is an infrequent complication with incidence ranging from 1 to 6%. It occurs up to 12 months after valve implantation and is a healthcare-associated infection due to contamination of the prosthesis during surgery or in the early postoperative period. Mortality ranges from 15 to 80%.

**Materials/methods:** This is an analysis of a prospectively implemented cohort of adult patients with definite IE from January 2006 to September 2019. Comparison between IE affecting valve prosthesis inserted for less than 1 year (EOPVE) and the remaining cohort was done using Jamovi 1.0.7 software. The ICE CRFs were used to collect data.

**Results:** EOPVE accounted for 25/359 (7%) of IE; males were less often affected compared to the cohort (48.0% vs 65.2%, p=0.09), but there was no difference in age. Episodes were more often acute (84.0% vs 50.9%, p=0.006). Patients with EOPVE more often had COPD (16.0% vs 4.9%, p=0.028), coronary artery disease (24.0% vs 8.5%, p=0.014), atrial fibrillation (30.4% vs 12.7%, p=0.021), heart failure, HF (56% vs 34.8%, p=0.037) and CABG in the past (12.5% vs 2.7%, p=0.046). In EOPVE significantly less often there was aortic or mitral regurgitation (20.7% vs 42.7% and 28.0% vs 49.3%, respectively), but more often paravalvular abscess (27.5% vs 18.9%, p=0.033) and conduction disturbances (18.2% vs 6.8%, p=0.082). No differences were seen regarding clinical features or frequency of blood culture positivity, but acute renal failure was more often seen in EOPVE (47.8% vs 26.1%, p=0.028). EOPVE was less frequently associated with *S. aureus* (0 vs 12.3%, p NS) and to viridans group streptococci (8% vs 27.8%, p=0.031) but more frequently with coagulase-negative staphylococci, CNS (24% vs 6.2%, p=0.002), and to non-HACEK Gram negatives, GN (16% vs 4.4%, p=0.038). Surgery was less often indicated for EOPVE (72 vs 89.9%, p=0.009). In-hospital mortality was similar (28% vs 25.7%).

**Conclusions:** Patients with EOPVE had hospital associated etiology (GN and CNS), less often had surgery indicated, possibly due to technical difficulties, or refusal, and despite its severity, had similar mortality compared to the other cases of IE.

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Antimicrobial susceptibility of Streptococcus dysgalactiae subspecies equisimilis isolates recovered from invasive infections in Portugal

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Abstract third-party references: On behalf of the Portuguese Group for the Study of Streptococcal Infections

Background: Invasive infections by beta-hemolytic Streptococcus dysgalactiae subspecies equisimilis (SDE) are increasingly reported worldwide together with significant antimicrobial resistance. We determined the genomic background and antimicrobial susceptibility of SDE isolates recovered from invasive infections in Portugal to evaluate the genetic traits responsible for resistance and to identify the associated lineages.

Materials/methods: A total of 316 SDE isolates were recovered from invasive infections in Portuguese hospitals from 2011 to 2017. Antimicrobial susceptibility to 12 antimicrobial agents was evaluated by disk diffusion according to CLSI guidelines. Genomic sequences (Illumina) were obtained for all isolates. Antimicrobial resistance genes and multilocus sequence typing (MLST) information were extracted and clonal complexes (CCs) were defined by goeBURST at the single-locus-variant level.

Results: Resistance was found to erythromycin (30%, n=95), tetracycline (16%, n=51), clindamycin (8%, n=26), levofloxacin (4%, n=12), streptomycin (3%, n=9) and gentamicin (0.3%, n=1). Overall, 133 (42%) of SDE isolates were resistant to at least one antimicrobial agent and 17 (5%) to three or more. Erythromycin resistance was associated with CC17 (p<0.001), the most frequent CC identified (32% of all isolates). CC17 included 56% (n=53) of erythromycin resistant isolates, mostly expressing an inducible MLSₐ resistance phenotype conferred by ermA (n=50) or ermB (n=3) genes. Resistance to tetracycline decreased from 39% to 7% (p=0.01) over the study period and was associated with CC15 (p<0.001), which included 43% (n=22) of all tetracycline resistant isolates carrying either tetM alone or in combination with tetL (n=2). Different amino acid substitutions were present in levofloxacin resistant isolates, the most common being S81F in GyrA and S79F in ParC, mostly among CC17 isolates (n=8/12). The genes ant6-la, aph(3’)-III and satA4 were detected in combination in 6/9 of streptomycin resistant isolates, while the single gentamycin resistant isolate carried the aac(6’)-le-aph(2’)-la gene. Resistance to aminoglycosides had a polyclonal background.

Conclusions: A high resistance to multiple antimicrobials was observed among invasive SDE from Portugal. Resistance was found among multiple lineages indicating it emerged in various successful lineages, despite the high prevalence of some clones. Further analysis of the genomic information will allow the identification of the MGEs associated with resistance.

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Abstract 8987

**Plant-based biomolecules against antibiotic-resistant microbes in skin infections and diseases**


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**Background:** Staphylococcus aureus is the most common cause of surgical site infections which are among the most common hospital acquired infections. Treatment of *S. aureus* is challenging due to the emergence of multi-drug resistant strains such as methicillin-resistant *S. aureus* (MRSA). New antistaphylococcal compounds provide a promising therapeutic strategy. We have evaluated the antimicrobial activity of different polyphenolic compounds extracted from three different nordic berries on development of biofilm and as treatment of mature biofilm caused by three different strains of MRSA.

**Materials/methods:** Three MRSA strains were used: SAP 231 (a clone from USA 400), MRSA 1 (a wild type strain extracted from a wound exudate), and MRSA 2 (a wild type strain extracted from a paronychia). Biofilm development was induced in 96-well plates for 24h using $10^6$-colony-forming-units inoculums in tryptic-soy broth (TSB) supplemented with 0.5% glucose with or without berry extracts. In second test bacterial biofilm of each strain was grown in the same setting 24h and thereafter the anti-biofilm effect of the berry extracts was tested by treating the mature biofilm with TSB supplemented with 0.5% glucose with or without berry extracts for 24h. Effect of the berry extract on both the biofilm development and the mature biofilm was evaluated by adding TSB with 10% of alamarBlue® and by measuring the fluorescence at 560/590 nm (ex/em). The statistical data were analyzed by the nonparametric Wilcoxon test with a level of statistical significance of $p<0.05$.

**Results:** The results obtained are shown in Figure 1:
Figure 1. Results of biofilm viability in the prevention and treatment of MRSA biofilm using different berry extracts. CSSE1: cloudberry side stream extract 1. CSSE2: cloudberry side stream extract 2. RBHE: raspberry press cake, hydrothermal extract. BCCE1: Bilberry cell culture extract 1. CSSE3: cloudberry side stream extract 3. BCCE2: Bilberry cell culture extract 2.*: p-value<0.05, **: p-value<0.01, ***: p-value<0.001 for Wilcoxon test.

Conclusions: Berry extracts showed an inhibitory effect both on the biofilm development and on mature biofilm of three different strains of MRSA. Major advantages in local treatment are high level of antimicrobial compound in infection focus and limited systemic side effects.

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**Abstract 8989**

**Virulence factor prediction: comparison of databases and their use for *Staphylococcus aureus* genomes analysis**

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**Background:** Virulence can be defined as the ability of a microbe to induce disease. Variations of bacterial virulence are attributed to i) the presence/absence of virulence factors (VFs) encoded on mobile genetic elements (MGE) or the chromosome, but also ii) mutations in VFs modifying the protein activity, as well as iii) changes in the expression of these VFs. Reference databases can be used to identify and annotate known VFs in bacterial genomes. This work aimed at investigating and comparing the content of existing public databases for the annotation of bacterial VFs.

**Materials/methods:** Amino acid sequences and annotations of VFs were retrieved from five different sources: 1) the Pathosystems Resource Integration Center (PATRIC), 2) Victors, 3) Swiss-Prot, 4) the Virulence Factor Database (VFDB) and 5) the pathogen-host interaction database (PHI-base). Comparisons were made by clustering VFs at 90% sequence identity. The conservation of VFs was investigated for complete genomes of *Staphylococcus aureus*.

**Results:** Comparative analyses revealed that VFs from the five databases are highly heterogeneous. Out of over 1,200 non-redundant VFs, only 74 were found in all 5 databases and 240 in 4 out of 5 databases. Out of 252 *S. aureus* VFs, only 2 are listed in all five databases (the alpha-hemolysin and the staphylococcal protein A), and more than 75% are conserved in most *S. aureus* genomes. The annotation of most VFs is supported by a single reference to scientific literature in Victors (98%), PATRIC (94%) and PHI-base (92%), whereas more than 50% of Swissprot entries have more than one reference.

**Conclusions:** These results highlight the lack of consistency in VF databases and limited support for the annotation of many virulence factors. It reflects the difficulty of databases curation in the context of a loose definition of virulence. This limits the predictive value of VF identification in terms of disease outcome and clinical usefulness for patient management. The construction of a database containing curated clinically-relevant VFs, comparative data and a defined ontology is essential to overcome current limitations and allow target VF analysis in the routine of diagnostic laboratories.

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Abstract 8990

Severe community-acquired pneumonia in the Czech Republic
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Background: The aim of the study is to describe patients with severe community-acquired pneumonia (CAP) in the Czech Republic and to test the reliability of the scoring systems on the same group. A similar study has not been published in the Czech Republic yet.

Materials/methods: The prospective observational study launched on 1.9.2017 includes adults with severe CAP treated in three Czech ICU.

Results: By 31.5.2019, 74 patients, 21 women and 53 men, aged 20-87 with median age of 62.5 years were enrolled. The underlying chronic disease was present in 53 (71.6%) patients, most frequently chronic lung disease in 26 (35.1%) and diabetes in 20 (27%) persons, smokers were 36 (48.6%). The main symptoms were cough and dyspnea in 64 (86.5%) persons and pathological auscultation findings in 64 (86.5%). Eight (10.8%) patients had initial hypotension and 51 (68.9%) patients had low oxygen saturation. The most common pathogens were Streptococcus pneumoniae in 22 (29.7%) and influenza viruses in 16 (21.6%) patients, in 23 (31.1%) the etiology was not proved. Third-generation cephalosporins in 37 (50%) and aminopenicillins in 20 (27%) patients was the most commonly used empiric treatment. This treatment was evaluated as effective in 60 (80%) patients. Mechanical ventilation was necessary in 46 (62.2%) patients, vasopressors in 40 (54.1%) and renal replacement therapy in 10 (13.5%) patients. Forty-seven (63.5%) patients were discharged, 17 (23%) were transferred to long-term care facilities and 10 (13.5%) patients died. Seven established and three newly created pneumonia scoring systems were evaluated at admission. SMART-COP (AUC 0.707) and CURB-65 (AUC 0.700) showed the best predictive value of the need for intensive care (mechanical ventilation or vasopressors).

Conclusions: The results of the study confirmed that patients with severe CAP often have underlying chronic disease and S. pneumoniae and influenza viruses are the main pathogens. Although the initial antibiotic treatment was effective in most patients and all methods of intensive care were provided, the outcome was unsatisfactory in more than a third of patients. The established scoring systems SMART-COP and CURB-65 demonstrated the best sensitivity and specificity in intensive care needs predictions.

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Abstract 8992

Unexpected detection of clinical isolates of Proteus mirabilis producing OXA-48 but susceptible to carbapenems and piperacillin-tazobactam

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Background: Detecting enterobacteria producing OXA-48 is challenging as they can be carbapenem-susceptible or even present carbapenem MICs below the EUCAST screening-cutoff for carbapenemase detection. During routine work in our laboratory, we occasionally found Proteus mirabilis (Pm) isolates susceptible to ertapenem/meropenem and producing OXA-48. We have retrospectively and prospectively studied a set of Pm clinical isolates to evaluate how frequently these organisms are detected.

Materials/methods: All Pm from blood cultures or with an ESBL-phenotype from any other clinical sample obtained from May-2017 to May-2019, and all Pm from any clinical sample from May-2019 to July-2019 were considered (one isolate per patient). Pm were identified by MALDI-Tof (Bruker). The following tests were performed in all isolates: modified carbapenem inhibition method (mCIM), beta-carba (Beta-C; BioRad) and immunochromatography (IC; both OXA K-Set and NG-Test CARBA; NG Bio-tech). When any of the test was positive, a PCR with specific primers for OXA-48 and amplicon sequencing was done, and susceptibility testing was performed by broth microdilution (Sensititre DKMGN panels, Thermo Fisher) and a temocillin disc (30 mcg).

Results: One hundred and seven Pm (diagnostic samples: 91, rectal swabs: 16) were collected. Thirty (28%) isolates were positive with the two IC tests (diagnostic samples: 23, rectal swabs: 7); in all of them, the presence of blaOXA-48 was confirmed. Among these 30 isolates, two (6.7%) were negative with mCIM, and another two (6.7%) different isolates were negative with Beta-C. None of the isolates negative by IC were positive by either mCIM or Beta-C. In 26/30 (86.7%) isolates with OXA-48, MICs (mg/L) of ertapenem, meropenem and piperacillin-tazobactam were <=0.125, <=0.125 and <=1/4, respectively, and the inhibition-zone of the temocillin disc was >11 mm. For the remaining 4 isolates, ertapenem, meropenem and piperacillin-tazobactam MICs and inhibition-zones of temocillin were <=0.125-1, <=0.25-0.25, and <=1/4-8/4 mg/L and 6-25 mm, respectively.

Conclusions: A relevant unexpected proportion of Pm isolates from both diagnostic and surveillance clinical samples in our center harbored blaOXA-48 gene, but are highly susceptible to ertapenem, meropenem, piperacillin-tazobactam and temocillin. Additional strategies are needed to identify these organisms to avoid a hidden reservoir of OXA-48.

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Abstract 8993

Carbapenem resistance mechanisms uncovered by nanopore sequencing in wastewater canalisations from Ghana
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Background: Wastewater plays a critical role in antimicrobial resistance dissemination, especially in developing countries where health control measures are scarce. Carbapenems are last resort antibiotics, which are used in hospitals to treat infections caused by multi-drug resistant bacteria. The main goal of this study was to determine the mechanisms responsible of carbapenem-resistant bacteria from wastewater canalisations around three hospitals and one wastewater treatment plant (WWTP) located in the region of Tamale (Ghana).

Materials/methods: In 2017, samples were obtained from the canalisations before and after the centers and from their main drains. Isolates resistant to carbapenems were selected in MacConkey agar plates supplemented with imipenem. Bacterial species were identified by MALDI-TOF. Minimum Inhibitory Concentrations MICs to the most clinically relevant carbapenems were accomplished according to the EUCAST guidelines. Eight selected isolates belonging to different bacterial species were sequenced by Nanopore WGS, and the subsequent analysis were performed by Porechop, Unicycler, Bandage and Abricate.

Results: A total of 18 isolates showed high MIC values to carbapenems. Most of the isolates (n=15) belonged to different species of the genus Pseudomonas and were generally recovered from all canalisations around the hospitals, whereas the other isolates (n=3) were identified as one Escherichia coli and 2 Citrobacter freundii. All Pseudomonas isolates harbored the carbapenemase gene bla_VIM-5 and a novel variant of the beta-lactamase bla_CAR in the case of P stutzeri, integrated in the chromosome and flanked by mobilizable structures. P. guariconensis isolates shared an unidentified plasmid encoding the carbapenemase gene bla_DIM-1. Enterobacteriaceae isolates presented several carbapenemase genes distributed in different plasmids, including bla_NDM-1, blaCTX-M-15 and blaOXA-48. Further analysis will uncover the total structure of these resistance genes and the mobile elements involved in their dissemination.

Conclusions: This study revealed the high presence of diverse beta-lactam and carbapenem resistance genes, some of them described for the first time, which were broadly disseminated in different Pseudomonas species. Furthermore, some Enterobacteriaceae isolates carried an alarming plethora of carbapenem resistance genes. However, the dissemination of these Enterobacteriaceae and their resistance determinants was remarkably lower compared to the Pseudomonas isolates, which were circulating in all wastewater canalisations of Tamale.

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Modelling pathogen transmission in intensive care units by integrating screening and antibiogram data

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Abstract third-party references: COMBACTE-MAGNET Consortium

Background: Hospital-acquired infections remain a major cause of morbidity and mortality worldwide, particularly in immunocompromised patients. Understanding the transmission dynamics of multi-drug resistant bacteria in intensive-care units (ICUs) is essential for designing and tailoring successful infection control strategies. Previous approaches have concentrated on infectious disease outbreaks. Far less has been done for endemic hospital frameworks. The challenge remains in distinguishing frequently imported cases from outside and acquisitions within the ward. Our aim is to tackle this problem by integrating only data routinely collected in ICUs, such as screening and antimicrobial susceptibility testing and to investigate the added value of antibiograms for recovering the transmission trees in nosocomial non-outbreak settings.

Materials/methods: We use stochastic SI models where ICU patients from an open study population either belong to the susceptible or colonized compartment. A susceptible patient may become colonized at a certain transmission rate. Two acquisition routes are considered. The endogenous route is independent of other patients and may be due to e.g. an overgrowth of the pathogen caused by antibiotic selection pressure. Cross-transmission is usually due to temporarily contaminated hands of health-care workers. We aim to extend a Bayesian data-augmented Markov Chain Monte Carlo method allowing for unobserved cases, as well as including information on antibiograms. By comparing the antibiograms involved in potential transmission pairs, we can confirm or rule out person-to-person transmissions. We conduct both simulation studies and use data on Pseudomonas aeruginosa from two ICUs of the University hospital of Besançon (UHB, France). The parameters and relative contributions of the transmission routes will be determined and compared to the results of the model without information on antibiograms.

Results: Endogenous route and cross-transmission account for a similar proportion of transmissions of Pseudomonas aeruginosa in the two ICUs of UHB, i.e. 55 (crI: 41-69%) and 45% (crI: 28-58%) respectively. Adding antibiogram data is expected to significantly reduce the uncertainty in the estimates.

Conclusions: Integrating antibiograms with routine surveillance data represents a promising approach to improve the understanding of transmission dynamics of pathogens in ICUs. The developed methods pave the way to further integrate genetic sequences with epidemiological data in nosocomial settings.

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Abstract 9001

Micro-elimination of hepatitis C in HIV co-infected persons in Slovenia: analysis of HCV infection in a national HIV cohort

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Background: Globally, the prevalence of hepatitis C virus (HCV) infection in HIV-positive persons has been estimated at 6.3%, with approximately 2.3 million being co-infected. In Slovenia, the management of all HIV-infected persons has been organized systematically for over three decades and centralised at one medical centre, which has performed regular HCV screening since the mid-1990s. With the advent of direct acting antivirals (DAAs), a national “test-and-treat” strategy for HCV elimination in this sub-population was prepared. The aim of this study was to evaluate the strategy at the national level.

Materials/methods: All HIV-infected persons in Slovenia who tested anti-HCV positive were identified in the national HIV cohort, managed at the Clinic for Infectious Diseases, University Medical Centre Ljubljana, and included in the study retrospectively. Active infection was defined with HCV RNA positivity. Demographic, virological, and clinical data on HCV infection were extracted from patients’ medical records.

Results: Of all 668 HIV-infected persons, 45 (6.7%) were HCV co-infected and 84% of them were male. The average age at HIV and HCV diagnosis was 33.64 ± 8.7 and 36.18 ± 9.69, respectively. 20/43 (46%) were men who have sex with men, and 9/43 (21%) were injecting drug users. At first presentation, 34/45 (76%) were asymptomatic, 7/45 (16%) had AIDS, and 4/45 (9%) had acute HIV syndrome. 24/45 (53%) acquired HCV infection after being HIV diagnosed, 16/45 (36%) were found to be HIV/HCV co-infected at first presentation, and 5/45 (11%) were managed for HCV before being diagnosed HIV-positive. 15/45 (33%) presented acute HCV infection. HCV genotype 1 was predominant (22/44; 50%), followed by genotypes 4 (11/44; 25%), 3 (8/44, 18%), 2 (1/44; 2%) and 1+4 (1/44, 2%), respectively. 4/45 (9%) spontaneously cleared HCV, one died before HCV treatment, and 35/35 of treated (100%) were cured; 4 of them (11%) got reinfected. 6/45 are currently scheduled to receive DAAs, 3 with re-infection.

Conclusions: This study demonstrated that in Slovenia, the micro-elimination of HCV in HIV patients was achieved. Regular HCV screening needs to continue at high risk of infection or re-infection.

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Efficacy of teicoplanin-loaded targeted nanoparticles in a Staphylococcus aureus thigh infection model

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Background: Targeted therapy may be one of the most important developments in medical sciences in near future. Also, if antibiotics can be targeted, that may be the best way of preventing side effects, slowing down the antimicrobial resistance by lowering the unnecessary exposure in long-term. We used short oligonucleotide chains called aptamers that have ability to specifically attach to different molecules and/or cells including Staphylococcus aureus. The aim of our study was to determine in-vivo efficacy of teicoplanin-loaded aptamer-targeted nanoparticles on mice thigh infection model.

Materials/methods: For the purpose of targeting, teicoplanin was loaded in mesoporous silica nanoparticles and the pores were blocked using specific aptamers in order to prevent the release of teicoplanin in the absence of S. aureus. To analyze the efficacy of these nanoparticles, mice thigh infection model was used. 16 female immuno-competent BALB/c mice were divided into 4 groups as non-infected/PBS treated, infected/teicoplanin treated (40 mg/kg), infected/targeted-teicoplanin treated (40 mg/kg teicoplanin), infected/PBS treated. Thigh infection induced by injecting 3x10^5 CFU S. aureus ATCC 29213 on both thighs. Single dose intraperitoneal treatment was administered 2 hours after the initial infection and mice were sacrificed at the end of 24 hours and thigh muscles were removed for bacteriologic and histopathologic analysis (H&E).

Results: Teicoplanin and targeted-teicoplanin was able to reduce the number of bacteria on thigh muscles for 79% and %44 respectively. Inflammation scores were also found correlated with bacteriologic response in histopathological examination of the muscle tissue. These results indicated that the targeting antibiotics using nanoparticles may be an effective way on the treatment of infectious diseases.

Conclusions: Targeted treatment of infectious diseases may be a great hope to win the battle against bacterial infections and one of the most important healthcare problems of today, antimicrobial resistance, in long-term. Our results showed that teicoplanin is active when capsulated inside nanoparticles in a way that will never be released in the absence of a specific pathogen. We believe that this approach may be translated into clinic with more detailed investigations of the efficacy of different loading doses, specificity and toxicity.

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Evaluation of potential implication of the wastewater microbiome in fungal pathogens spreading using next-generation sequencing technology

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Background: Fungi are considered to be among the main causes of infectious diseases, especially, for immunocompromised patients. Pathogenic fungal species are ubiquitous in the environment with important diversity within wastewater treatment plants (WWTPs). They may constitute a serious threat to human health, since it is showed that fungi are not completely removed by conventional WWTPs processes. In addition, antifungal resistance and emergence of life-threatening fungal species, not previously well identified, characterized or not yet cultivated, make patients treatment very complex. Therefore, it is important to manage and control the source of pathogens contamination, to reduce fungal infections incidence.

Materials/methods: Twenty-three wastewater sludge samples were collected from the Seine-Morée WWTP, started de novo without external sludge inoculation, for 236 consecutive days. Metagenomic DNA was extracted according to Nucleo spin soil DNA kit. The eukaryotic diversity was investigated by PCR amplification of the V9 region of the 18S rRNA gene. The resulting PCR fragments were sequenced on Illumina MiSeq platform at Genoscope. Sequence reads affiliation was performed by blast using SILVA 132 18S database. BIOM files (abundance + taxonomy) were constructed and imported in R (version 3.5.2) for statistical analysis.

Results: A total of 74,432 high-quality sequence reads [345 OTUs] were obtained for the twenty-three samples. These sequences are affiliated with nine different fungal phyla among which a not yet cultivated Cryptomycota phylum was the most predominant making up to 76 % of the total fungal population. Among the potential human fungal genera-containing pathogen species, we counted 45, totaling 8035 reads. Candida and Pichia were the two most important genera reported for Ascomycota phylum, while Lichtheimia and Rhizopus were observed for Mucoromycota phylum. These genera represent the most persistent potential fungal pathogens within the WWTP microbiome, over the 236-sampling days.

Conclusions: The overall results of this study highlight that treated wastewater and sludge represent a potential source of pathogenic fungi. Hence, it is important to consider human fungal pathogens during safety evaluation for any agricultural or recreational water use.

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Background: Extra-pulmonary tuberculosis (EPTB) infection is an increasing problem in the Philippine setting. Local programs have been formulated to tackle this entity, however, there is limited domestic literature as to the profile and characteristics of these patients. The aim of this study is to determine the prevalence, distribution and pattern of EPTB according to their demographical data and collect data that may later be used in the treatment and observation of such cases.

Materials/methods: The medical records of patients diagnosed to have EPTB in Makati Medical Center from January 2016 to December 2018 were reviewed. Demographics, clinical profile, site of EPTB, comorbidities, drug susceptibility and testing data were collected.

Results: Pulmonary Tuberculosis had 4,361 (93.6%) cases while 296 (6.3%) were extra-pulmonary. Male to female ratio was 1.3 (p=0.512). Mean age of genders was 36.5 for male and 32.9 for female with difference of 1.4 (p=0.8395). Most common sites seen in the lymphatics (35%), GI (19%), bones and joints (12.35%). Most common presenting sign or symptom was a palpable mass (42%), then pain (21%), fever and respiratory symptoms (11%). HIV infection (21%), Hypertension (12%) and previous tuberculosis treatment (9.4%) were frequent findings in the history.

Conclusions: The proportion of EPTB was 6.3% compared to 1% in the last surveillance report in 2013. No significant correlation was found as to differences in gender, age groups and comorbidities. Most common sites of EPTB were found in the lymphatics followed by GI and pleural forms presenting as palpable masses, diarrhea, vomiting, cough and shortness of breath.

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Abstract 9007

**Title:** Anti-biofilm activity of bacteriophage $\phi$WL-3 conjuncted with ciprofloxacin, fosfomycin, gentamicin, meropenem or ceftriaxone against a ciprofloxacin-ceftriaxone-resistant *Escherichia coli* clinical isolate

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**Background:** *Escherichia coli* is among the most common cause of Gram-negative prosthetic joint infections (PJIs) and ciprofloxacin is the first-line recommended antibiotic for anti-biofilm therapy. Due to emergence of fluoroquinolone resistance, the management of *E. coli* PJIs becomes more challenging with an increased rate of treatment failure. Here, we investigated the efficacy of a newly isolated bacteriophage $\phi$WL-3 as a therapeutic agent in combination with ciprofloxacin, fosfomycin, gentamicin, meropenem or ceftriaxone against the biofilm of a ciprofloxacin/ceftriaxone resistant *E. coli* strain.

**Materials/methods:** Bacteriophage $\phi$WL-3 was isolated from hospital sewage targeting a ciprofloxacin/ceftriaxone resistant *E. coli* clinical strain obtained from a patient diagnosed with PJI. Twenty-four-hour old biofilm formed on porous glass beads were exposed to antibiotics alone or combined with bacteriophage $\phi$WL-3 [10^8 PFU/mL] simultaneously for 24h or in a staggered manner (first bacteriophage for 4h followed by antibiotic for 24h). Recovering bacteria after treatment were detected by measuring growth-related heat production at 37°C for 48h by isothermal microcalorimetry. The minimum biofilm bactericidal concentration (MBBC) was defined as the lowest concentration of antibiotic that strongly reduced biofilm cells viability and led to the absence of heat flow production.

**Results:** All tested antibiotics presented high MBBC values (ranging from 32 to $>1024$ µg/mL) when tested alone against biofilm [Table 1]. A simultaneous administration of $\phi$WL-3 and antibiotics showed an improved antibiofilm activity for fosfomycin, gentamicin or meropenem, but not for ciprofloxacin and ceftriaxone. However, the highest antibiofilm efficacy was observed after staggered exposure, where the MBBC of ciprofloxacin could also be decreased from $>1024$ to 4 µg/mL. In contrast, ceftriaxone showed no improved activity in either case.

**Conclusions:** The co-administration of bacteriophage with antibiotics improved considerable the antibiotic efficacy against biofilm, especially after staggered exposure. Our data suggest the use of bacteriophages could restore the susceptibility of biofilms to antibiotics, as seen in our case with ciprofloxacin. These results have implications for optimal combined treatment approaches.

**Table 1. Summary of minimum biofilm bactericidal concentrations**

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>MBBC$_{antibiotic}$ [µg/mL]</th>
<th>MBBC$_{antibiotic/\phi}$ [µg/mL]</th>
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<tbody>
<tr>
<td></td>
<td>Simultaneous</td>
<td>Staggered</td>
</tr>
<tr>
<td>ciprofloxacin</td>
<td>$&gt;1024$</td>
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<td>fosfomycin</td>
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<tr>
<td>gentamicin</td>
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<td>8</td>
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<tr>
<td>meropenem</td>
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<td>4</td>
</tr>
<tr>
<td>ceftriaxone</td>
<td>$&gt;1024$</td>
<td>$&gt;1024$</td>
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</table>

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Continuous infusion versus intermittent antipseudomonal β-lactam antibiotics for acute pulmonary exacerbations of cystic fibrosis: effect on the respiratory microbiome

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Background: Acute pulmonary exacerbations (PEx) of cystic fibrosis (CF) in patients infected with Pseudomonas aeruginosa are treated with intravenous anti-pseudomonal β-lactam and aminoglycoside therapy. In vitro and modelling data suggest that administration of β-lactams by a continuous infusion (CI) can increase bacterial killing when compared to standard intermittent (SI) administration but the impact on the respiratory microbiome in CF has not previously been described. Whether this differs between different antipseudomonal β-lactams is also unknown.

Materials/methods: We performed a prospective, randomized, cross-over study comparing SI versus CI intravenous antipseudomonal β-lactam therapy (cefepime, ceftazidime, piperacillin-tazobactam, ticarcillin-clavulanate or meropenem) in combination with tobramycin for treatment of PEx in adult patients with P. aeruginosa. Spontaneously expectorated sputa at Day 0, 3 and 7 (CI: n = 22, SI: n = 18) had quantitative bacterial load (Real time PCR 16S rRNA gene), quantitative pseudomonal load (Real time PCR oprL gene) and microbiome (V1 to V3 hypervariable region 16S rRNA gene metagenomic sequencing) analysis performed.

Results: There were no significant differences in either total bacterial (P = 0.697) or pseudomonal load (P = 0.989) between the SI and CI groups at day 7. The microbiota composition also did not differ significantly between the groups (PERMANOVA P = 0.178, square root ECV= 4.22, 9922 permutations). However, significant reduction in mean total bacterial (P = 0.004) and pseudomonal (P = 0.03) loads were observed for the CI ceftazidime group but there was no significant difference in the SI ceftazidime group. For meropenem, no significant differences were observed in either group. There were significant differences in the microbiome composition at Day 7 between ceftazidime and meropenem for both SI (t 2.17, P = 0.002, 1813 permutations) and CI (t 1.63, P = 0.06, 6642 permutations) groups. At day 7, those treated with ceftazidime, had more Streptococcus and Prevotella in their sputa than those treated with meropenem. In contrast, those treated with meropenem, had more Pseudomonas.

Conclusions: CI intravenous anti-pseudomonal β-lactam therapy has similar clinical efficacy and impact on the microbiome when compared to SI treatment but there were differences within antibiotic subgroups.

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Abstract 9009

**Community-Acquired Bacteraemia (CAB) in senior adults: risk factors, outcomes and correlation with frailty**
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**Background:** Increasing life expectancy has led to an increase in the very-elderly (≥85 years) population. The characteristics of community-acquired bacteraemia (CAB) in this population are not well studied. Our objectives were to describe the characteristics of CAB in the very-elderly population and to determine which risk factors are associated with poor outcomes.

**Materials/methods:** A prospective, observation single-centre case-control study was carried out in a tertiary university hospital in Leeds, United Kingdom. Cases were patients aged ≥85 years presenting with signs and symptoms of infection and a bacteraemia within 48 hours of admission to hospital. A control group of patients aged between 65-84 were matched on a 1:1 basis by gender. Informed consent was obtained from all patients or (where the patient lacked capacity) a nominated consultee. Data on clinical characteristics including assessment of frailty, microbiological characteristics and outcomes were collected.

**Results:** Seventy-four patients were recruited between Nov 2018-July 2019, 37 patients were in the case group (aged ≥85) and 37 in the control group (aged 65-84). Fever was reported in 10.8% and 13.5% patients in the control and case groups respectively. At presentation, 37.8% of cases presented with an altered mental state compared to 29.7% of controls. In the case group 48.6% had CAB due to a UTI compared to 24.3% in the control group. Median CRP was 77 (IQR 44-202) and 142 (IQR 59-251) respectively. Median Rockwood frailty score was 6 (IQR 4-6) in cases versus 3 (IQR 3-5) in controls. Median qSOF score was 2 in both groups (IQR 1-2). Mortality at 28 days was 0% in the control group and the case group and 10.8%. At 90 days, mortality was 5.4% & 21.6% respectively (p 0.041).

Several challenges were encountered during the study. These included difficulties in gaining informed consent and the inability to recruit patients who died soon after admission to hospital.

**Conclusions:** Very-elderly patients were more likely to have bacteraemia due to UTIs, were frailer and had a higher mortality at 90 days. We also found that recruitment of this group is challenging and this needs to be considered during the study design stage.

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Abstract 9015

Biofilm killing activity of bacteriophage $\phi$WL-3 against antibiotic-resistant Escherichia coli clinical isolate

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**Background:** The treatment of implant-associated infections caused by *Escherichia coli* has become more challenging due to the increase of antibiotic resistance. The use of bacteriophages as bactericidal agents has been revalued as a promising alternative approach in the treatment of bacterial infections. The implementation of therapies using bacteriophages requires not only optimal dosage but also an optimal time of antimicrobial exposure. In our study, the time-killing kinetic of bacteriophage $\phi$WL-3 was investigated on *E. coli* biofilms.

**Materials/methods:** $\phi$WL-3 was isolated from hospital sewage targeting a ciprofloxacin/ceftriaxone-resistant *E. coli* clinical strain. The antimicrobial activity against *E. coli* ATCC-25922 and the clinical strain was investigated by microcalorimetry. Twenty-four-hour old biofilms were formed on porous glass beads and exposed to $\phi$WL3 at $10^8$ PFU/mL for 24h. Samples were collected at times 0h, 4h, 8h, 12h and 24h of incubation for determination of bacterial concentration. Addition of ciprofloxacin [4 µg/mL] at 4h of bacteriophage pre-treatment was also analyzed. Viable bacteria on the beads were detected by colony-counting after plating of sonication fluids. Bactericidal effect was defined as a $\geq$3-log$_{10}$ CFU/mL reduction (99.9% kill) compared to concentration at time zero.

**Results:** Microcalorimetry analysis showed that $10^6$ PFU/mL $\phi$WL3 completely lysed $10^7$ CFU/mL of *E. coli* clinical isolate, whereas a higher titer ($10^8$ CFU/mL) was necessary to completely lyse *E. coli* ATCC-25922. Time-killing kinetic of $\phi$WL3 revealed a rapid decrease of bacteria cell viability within the first 4h of incubation at 37 °C against the clinical strain, with an approximately 2-log$_{10}$ CFU/mL reduction. No cell reduction was observed for *E. coli* ATCC-25922 within 24h. The addition of ciprofloxacin after 4h pre-treated with bacteriophages lead to a complete biofilm eradication (Figure 1).

**Conclusions:** Our results suggest a notable dependency between the bacteriophage and the bacterial strain involved on its isolation in terms of treatment efficacy. The possible impact of host specificity for the therapeutic use of bacteriophages should be further investigated. Nevertheless, bacteriophage/antibiotic combinatorial treatment seems to provide a more broad therapeutic potential, including antibiotic-resistant strains.

**Figure 1.** Effect of bacteriophage $\phi$WL3 and/or ciprofloxacin on viability of *E. coli* ATCC-25922 and clinical strain biofilms at different time points.

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Abstract 9016

**Urinary tract infection and fungaemia due to Saprochaete capitata in a patient with acute myeloid leukaemia**

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**Background:** *Saprochaete capitata* is a non-fermentative, non-capsular, urease-negative yeast-like fungi. It is found in the skin, respiratory tract and gastrointestinal tract microflora of healthy people as well as animal and vegetal all environmental sources. *S.capitata* infection is rarely seen and often reported from immunocompromised patients. *S.capitata* is considered to be intrinsically resistant to echinocandins; combination of voriconazole and amphotericin B is recommended for treatment.

**Materials/methods:** In this study, a case of urinary tract infection and fungemia associated with *S. capitata* in a 58-year-old female patient who developed acute myeloid leukemia during the treatment of metastatic ovarian carcinoma is presented. Antibiotic treatment and prophylactic posaconazole was initiated to the patient due to the presence of fever. Caspofungin was added to the treatment of the patient due to the continuation of fever. Urine and blood samples from patient were sent to the microbiology laboratory. Yeast growth was detected in the patient’s urine and blood cultures. Dry and cream-colored yeast colonies were growth on SDA agar medium after 24 hours. In the gram stained preparations, *S. capitata*’s artrospores and annelloconidis were seen. The Vitek MS (Biomerieux / France) was used to identify the isolate. Antifungal susceptibility of the isolate was studied by microdilution method (SensititreYeastOne, ThermoScientific, UK)

**Results:** The fungi was identified as *S. capitata* by Vitek MS. MIC values for amphotericin B, fluconazole, voriconazole, caspofungin, fluconosine, posaconazole and itraconazole were determined as 0.5µg/ml, 4µg/ml, 0.06µg/ml, 8µg/ml, ≤0.06µg/ml, 0.25 µg/ml, 0.12µg/ml, respectively.

**Conclusions:** In our case, fungemia and urinary tract infections developed under the treatment of caspofungin and the MIC value was determined as 8 µg / ml. This has shown us that echinocandins are not an effective treatment for *S.capitata* infections as they are in other studies. In neutropenic patients, it should be considered that the causative agent is *S.capitata*, especially if continuing fever despite echinocandin treatment.

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Abstract 9017

**Impact of hand hygiene intervention on hand washing ability of school-aged children**

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**Background:** To assess the current knowledge related to hand washing and efficiency of intervention on hand washing techniques amongst school children.

**Materials/methods:** A randomized control trial was conducted amongst class II students of a private school in Korangi, Karachi. Pre-intervention assessment including baseline knowledge and observed practices of hand washing in comparison with World Health Organization (WHO) standard hand washing techniques was done. This was followed by education and demonstration of proper hand washing steps by principal investigator utilizing visual aids. Participants were then randomized into two group: Group A (education only group) and Group B (education along with glow gel application group). First post-intervention assessment was conducted on same day where both groups were observed for the hand washing steps and scored for hand washing technique. In addition, participants of group B were shown germs under Ultraviolet (UV) light. School was revisited after 1 week later and participants were reassessed for their hand washing technique along with cleanliness grade after applying glow gel and observing under UV light. Data was entered and analyzed using SPSS version 21.0.

**Results:** No significant differences were found in median hand washing scores pre-intervention between both the groups (Group A vs B: 4 vs 5, p-value=0.659), while significant improvement in median hand washing scores was seen post intervention in group B as compared to group A (7 vs 6, p-value=0.011). However, no significant differences were seen in median hand washing scores at follow-up between both the groups (Group A vs B: 9 vs 8.5, p-value=0.715) but a significant improvement was observed in both the groups in the hand washing practices from baseline (p-value=0.000). On the contrary, no significant differences were found in median cleanliness grade between both the groups (Median for both the groups was 5, p-value=0.695).

**Conclusions:** Hand washing education utilizing various aids is an effective method to improve children’s hand washing capability. This short term intervention was effective even in absence of glow gel, but no cleanliness of hands was observed in both the groups.

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Abstract 9020

The impact of antimicrobial stewardship for outpatient parenteral antimicrobial therapy

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Background: The outpatient parenteral antimicrobial treatment (OPAT) provides patients the opportunity to complete treatment safely and effectively, while avoiding complications due to prolonged hospitalization. Despite the benefits, risks with drug-related and central venous catheter (CVC)-related complications exist. For these reasons, advising antimicrobial stewardship is a crucial factor in optimizing clinical outcomes and combatting antimicrobial resistance. The Infectious Diseases Society of America recommends that all patients should have Infectious disease (ID) expert review prior to initiation of OPAT.

Materials/methods: Our objective was to evaluate whether a consultation of infectious diseases (ID) physician prior to discharge for OPAT improves the adequacy of the prescription of antibiotics in the OPAT.

It was a prospective analysis of the patients visited by ID physician prior to the discharge to the OPAT. The study was performed from May 2016 to June 2017 at Germans Trias i Pujol Hospital, a 600-bed teaching hospital.

Results: Of 341 patients included during the study period, 141 patients (41.3%) maintained the same antimicrobial treatment as in Hospital, 100 patients (29.3%) changed choice of IV antimicrobial (optimization or de-escalation) and 90 patients were discharged with either oral treatment (84 patients, 24.6%) or without antibiotic treatment in 6 cases (1.8%).

Among the 90 patients without OPAT criteria, there was no related return due to therapeutic failure. The median age of this group was 70.1 years (SE 15.9 years) and 68.9 % were man. The mean Charlson Index was 2.5 (SE 1.8). The most common diagnosis was urinary infection (45.7%), followed by respiratory infection (33.3%) and intra-abdominal infection (9 %). Among them 6.7% of the infection agents were mutirresistant.

Conclusions: In our study, ID physician enabled the optimization or de-escalation (29%) of antimicrobial therapy, the early implementation of sequential oral therapy, and helped to reduce treatment duration.

90 patients (26%) of potential OPAT’s cases were avoided through ID intervention, probably reducing the risk of healthcare-associated complications.

Avoiding OPAT when there are other treatment alternatives reduce OPAT overuse, is cost saving and improve the quality and safety of the OPAT service.

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Abstract 9021

**Acinetobacter baumannii-complex related osteomyelitis**

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**Background:** *Acinetobacter baumannii* complex (ABC) is an increasingly important cause of osteomyelitis, particularly in cases related to traumatic etiology.

**Materials/methods:** Observational retrospective study of cases of microbiologically confirmed ABC osteomyelitis between 2007 and 2015. Susceptibility profile of isolates was assessed, as well as the following: sex; age; length of hospital stay; Charlson’s index; physical status classification according to American Society of Anaesthesiologists (ASA) score; presence of comorbidities or immunosuppression; history of illicit drug use, active smoking or alcohol abuse; osteomyelitis classification; need for soft tissue repair and use of negative pressure therapy. Antimicrobial drugs for treatment and their duration were observed, as well as report of adverse events. Outcomes were evaluated after 12 months follow up.

**Results:** A total of 171 patients with ABC osteomyelitis were treated. Mean age was 43.2 years (7-88), most of them were male (78.4%). Charlson’s index was between 0 and 2 in 92.4% of patients and comorbidities were identified in 33.9%. Immunosuppressive conditions were identified in 18.7%. Active smoking and alcohol abuse was present in 6.4% and 5.8%. ASA Score was II in 51.5%. Most cases were diagnosed as post-traumatic osteomyelitis (64.9%) and inferior limbs were responsible for 62% of affected topography. Soft tissue repair was required in 32.5% and use of negative pressure in 25.1%. Acute osteomyelitis was identified in 52.6% of cases. Co-infection occurred in 72.5%, being *S. aureus* (19.4%) and *P. aeruginosa* (17.7%) the most frequent agents. Overall susceptibility was 61.4% to amikacin, 58.5% to gentamicin, 43.3% to ampicillin-sulbactam, 15.8% to cefepime, 14.6% to ciprofloxacin and 33.3% to meropenem. Colistin (19.9%), ampicillin-sulbactam (18.7%) and tygecil (18.1%) were the most frequently used drugs, mean treatment length was 72.6 days. Average hospitalization time was 77.9 days. Adverse events occurred in 21.6% of patients and change of antimicrobial drug due to them was required in 3.5% of cases. After 12 months of the end of treatment, remission was achieved in 53.8%.

**Conclusions:** Most cases of ABC osteomyelitis were post-traumatic and affected lower limbs. Co-infection was present in most patients and susceptibility rate was below 60% for most antimicrobials, including carbapenems.

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Abstract 9028

Medical software approach for French ILI sentinel surveillance
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Background: Electronic medical record (EMR) have been widely adopted by primary care physicians. This huge data source could be used for providing data to sentinel surveillance system. In 2014, an experimental project has been settled with a medical software editor and the French sentinel network for epidemiologic surveillance based on GPs reporting, to develop an exchange plug-in enabling to detect patient who potentially met the criteria of cases definition, and to export automatically some information. Aims were to evaluate the impact of this system on GP's participation and on the quality of data collected comparing with traditional ways of reporting, and to validate it through the influenza-like illness (ILI) surveillance.

Materials/methods: Case identification was based on 4 different medical coding classifications. We collected numbers and data of GP’s reports associated to a count of different cases and a number of monitored days during the ILI season. We calculated activity defined as the monitored period covered by a report. Data quality was evaluated by the completeness of ILI cases (age, sex, vaccine, treatment or hospitalization). Finally, we studied incidence of ILI. We compared three groups of GPs: 2 traditional surveillance processes (website, desktop software) and the exchange plug-in.

Results: We investigated, between 01/10/2018 and 14/04/2019, 379 GPs aged 51 on average, with 19 years of seniority in medical practice and enrolled in the surveillance network from 11 years on average. At overall, 14,653 reports were done, and 9,624 ILI cases reported by 215 GPs using exchange plug-in, 175 GPs using the desktop software and 183 using the website. Reports were more frequent (every 2.9 days vs 4.4 and 5.1), activity (24.8 weeks vs 21.0 and 15.8) and average reported cases (76.0 vs 73.4 and 53.5) were higher with the exchange plug-in. Completeness was higher for exchange plug-in users only for age and sex. Incidence characteristics were the same between the 3 groups.

Conclusions: GPs using the exchange plug-in reported more cases and more frequently than traditional surveillance process. This new approach provided a validated and efficient framework within the traditional ILI surveillance.

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Abstract 9029

The impact of war on cutaneous leishmaniasis disease transmission and its control in Syria

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Background: Cutaneous leishmaniasis (CL) - “Aleppo Boil” - is transmitted by sandflies and has devastating, and sometimes fatal, outcomes. CL is synonymous with northern Syria, where, since the outbreak of war in 2011, there has been a dramatic evolution of CL transmission. This has paralleled the destruction of cities, towns and health services, mass population displacement, and emergency disease control efforts.

Materials/methods: Data on the scale and timing of urban destruction, population displacement and emergency prevention and case management control efforts across northern Syria, were compared against newly published data (12th Dec 2019) on number of CL cases for the period 2011-end 2018, extracted, cleaned and merged from three different surveillance systems: the Ministry of Health (MoH) routine surveillance system, the MoH/WHO sentinel-syndromic Early Warning Alert and Response System (EWARS), and surveillance data collected by the international NGO The Mentor Initiative. The impacts of war and control efforts on the evolution of disease were analyzed, and seasonality of transmission, access, reporting completeness, and other factors were accounted for.

Results: The analysis of the different data sets indicates that rapid rise in CL cases correlated closely with timing and scales of urban destruction and population displacement, and scale of sandfly prevention and case management activities. Cases peaked in 2015, decreased in 2016, remained stable in 2017, and increased overall again in 2018 and 2019, whilst targeted control efforts showed significant reductions in accessible areas. The data also indicates that mass population displacement from historically identified epidemiological hot spots of disease, such as Aleppo, were responsible for the spread of CL in some governorates, which previously did not experience CL at notable levels, prior to the war.

Conclusions: War in Syria has created the perfect conditions for the exponential increase of sandfly populations and their epidemic transmission of CL. In addition, mass population displacement from affected areas has caused a significant and rapid geographic expansion of CL, threatening populations inside Syria, and some countries hosting Syrian refugee populations. However, large scale control efforts have proven effective at reducing and controlling transmission, where security allows access.

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Abstract 9034

Association of carbapenemase-producers in hospital effluents with carbapenemase-producer’s infection incidence and sewages heavy metals concentrations: results from the Canalis project

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Background: Hospitals effluents could play a role in the generation and spread of carbapenemases-producing Gramnegatives (CPB). In these effluents, the presence of CPB from patients is combined with the selective pressure of spilled antibiotics and heavy metals. Carbapenemase genes have been found along with metals efflux pumps. Our study investigates the prevalence of CPB from hospitals effluents regarding to CPB incidence rate, antibiotics consumption and heavy metals discharge.

Materials/methods: Sewage were monthly collected from 4 hospitals [HA, HB, HC and HD] in the South of Spain during a 12-month period. Unconcentrated wastewaters were quantitatively inoculated on chromogenic selective media and analyzed to detect heavy metals [Zn, Cu, Hg, Pb, Co, Cr and Al] by inductively coupled plasma mass spectrometry. Counting, identification by Maldi TOF and detection of carbapenemase by lateral immunochromatography and PCR of each different colony was performed. CPB bacterial counts were related (Spearman correlation) with CPB infection incidence density/1000 occupied bed, antibiotics [ertapenem, meropenem, piperacillin/tazobactam, ciprofloxacin and levofloxacin] as DDD per 1000 patient day, and heavy metals concentrations.

Results: CPB mean was 3,15 log CFU/ml in the period of study [maximum mean at HB 4,5 log CFU/ml, p<0,05]. KPC producers were more frequently detected in 3 hospitals [HA, HB and HD] and VIM producers were more frequent in HC during the study period. CPB count was found negatively correlated with consumption of ciprofloxacin (r=-0,45, p=0,002), levofloxacin (r=-0,47, p=0,001) piperacillin/tazobactam (r=-0,61, p<0,001) and meropenem (r=-0,512, p<0,001) and HB had the lowest DDD for these antibiotics (p<0,001). On the contrary, CPB discharge was found moderately correlated with Cu (r=0,381, p=0,014), Hg (r=0,373, p=0,016), Co (r=0,474, p=0,002) and Al (r=0,302, p=0,058) sewages concentrations, showing HB the highest Hg (p=0,026) and Al (p<0,001) values. Likewise, the correlation was positive with the CPB incidence density (r=0,330, p=0,027), with a mean of 0,138 and HB had the highest (p<0,001).

Conclusions: 1) Different CPB count were found in the 4 hospital effluents studied; 2) in our area, higher CPB count in these effluents are directly related with heavy metal contents of sewages along with incidence of infected cases, but inversely related with antibiotic consumption.

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Worldwide diversity of tegumentary leishmaniasis and the risk of mucosal lesions: a clinical report in 459 European travellers

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Background: Tegumentary leishmaniasis (TL), a frequent and heterogeneous dermatological infection in travellers, can spread from the skin to oral mucosa. Clinical presentation impacts therapeutic management.

Materials/methods: From 2006 through 2019, the LeishMan consortium collected precise demographic and clinical data on 464 episodes of TL in 459 patients.

Results: Episodes were acquired in 47 countries. Compared to lesions acquired in the Old World (279 episodes), lesions acquired in the New World (185 episodes) were more frequently ulcerative (75% v 47%), less frequently papulonodular (5% v 25%), larger (3 v 2 cm), more frequently on the limbs (61% v 47%) and less frequently on the face (17% v 38%). Mucosal involvement was unexpectedly less frequent in New World than in Old World infections (2.7% v 5%). Compared to patients with only skin lesions, patients with mucosal lesions were older (58 v 30 years), more frequently immunosuppressed (37% v 3.5%), with skin lesions more frequently on the head (64% v 29%), but with similar rates of lymphangitis (15.5% v 15%). Identification of infecting Leishmania species in 122 patients delineated 3 typical forms. Children infected with L. major in Africa had rapidly evolving multiple lesions of the limbs; 40-70 year-old tourists infected with L. infantum in Southern Europe had a slowly evolving facial lesion and mucosal involvement in 22% of cases; young adults infected in Latin America with the L. braziliensis complex had a rapidly evolving ulcer of the lower limbs with lymphangitis and mucosal involvement in 35% and 6% of cases, respectively.

Conclusions: Analysis of TL acquired in 4 continents delineates well-demarcated clinical forms. Infections with L. infantum acquired in Europe display higher rates of mucosal involvement than infections with L. braziliensis acquired in Latin America, especially in immunosuppressed patients. The relatively low rate of mucosal involvement supports the use of local therapy in most patients regardless of the continent of infection. Based on the topography and numbers of lesions, most patients can be treated locally.

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Abstract 9036

**Cost analysis of a Point-of-Care diagnostic test for detecting influenza A/B and respiratory syncytial virus in the ER setting in Norway**

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**Background:** New point-of-care (POC) tests for influenza A/B and RSV are available with a turnaround time (TAT) of approximately 20 minutes and excellent accuracy, enabling physicians at the emergency room (ER) to quickly identify the need for isolating patients. As a POC test has additional costs, the objective was to evaluate the difference in costs of care associated with using a POC test analysed directly at the ER (POC ER) versus a PCR lab batch test.

**Materials/methods:** A previously developed health economic model was adapted to the Norwegian ER setting, comparing the isolation and test costs of using a POC ER versus a lab batch test over a time horizon of one year from the healthcare perspective. Patients were ≥18 years presenting with unspecified lower respiratory symptoms. The main outcome of the analysis was the total isolation and test costs per patient tested. For patients tested with a POC ER test the result was available before admission to the ward allowing basing the decision on isolation on the test’s result, leading to no unnecessary isolation and to late isolation of 1.7% (influenza A), 4.8% (influenza B), and 3.0% (RSV) of patients. Results of the lab batch test were available with an average delay of 1.5 days, leaving the decision on isolation to the physician’s opinion upon admission to the ward. Of the patients isolated, 50% was isolated unnecessarily and 15% of the patients with influenza A/B or RSV were missed and isolated late.

**Results:** For influenza A/B the average isolation and test costs per patient tested were expected to be €1,597 for the POC ER and €3,289 for the lab batch test, leading to incremental costs of -€1,692, indicating cost-savings of 51.4%. For RSV the average isolation and test costs per patient tested were expected to be €601 for the POC ER and €1,219 for the lab batch test, leading to incremental costs of -€618, indicating cost-savings of 50.7%.

**Conclusions:** Using a POC ER test is expected to result in considerable cost-savings from a healthcare perspective by preventing unnecessary and late isolation, which outweigh the additional test costs by far.

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Abstract 9039

Evaluation of hepatitis B vaccine efficacy and factors affecting its response in patients receiving anti-tumour necrosis factors

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Background: Anti-TNF agents are widely used in chronic inflammatory diseases (CIDs) and have potent immunosuppressive effects. However, the response rate of patients to hepatitis B virus (HBV) vaccination receiving anti-TNF agents is quite low. We aimed to assess the efficiency of HBV vaccination in CID patients receiving anti-TNF agents as well as in healthy controls. We also evaluated the impact of different factors on the efficacy of HBV vaccination.

Materials/methods: Patients with CIDs (inflammatory bowel disease [IBD], rheumatological diseases, and psoriasis) receiving anti-TNF agents and healthy controls vaccinated for HBV were included in the study. An adequate immune response and an effective immune response to HBV were defined as >10 and > 100 mIU/mL, respectively. Binary logistic regression analysis was performed to investigate the risk factors affecting non-response rate of vaccine.

Results: Among 274 participants, 187 were CID patients and 87 were healthy controls. The mean age of the patients with CID (43.9 ± 11.7 years) was significantly higher than that of the healthy controls [31.4±7 years] (P=0.000). Percentage of male participants (59.9%) in patients with CID was significantly higher than that of the healthy controls (42.5%) (P=0.007). Adequate immune response was 60.8% and 94.3% in patients with CID and healthy controls (P=0.000), respectively, whereas effective immune response was 38.2% and 75.9 (P=0.000), respectively. In logistic regression analysis, male gender (OR, 0.408; 95% CI, 0.201-0.830; P=0.013), use of infliximab (OR, 2.694; 95% CI, 1.203-6.035; P=0.016) and sertoluzimab (OR, 3.307; 95% CI, 1.287-8.498; P=0.013), vaccination after anti-TNF treatment (OR, 0.224; 95% CI, 0.083-0.602; P=0.003) were identified as risk factors of non-response to HBV vaccine.

Conclusions: Non-response rate to HBV vaccine is significantly higher in CID patients compared to that in healthy controls. In CID patients, the rates of adequate and effective immune response as well as median level of anti-HB titers were significantly lower than those in healthy controls. Non-response rates were higher in IBD group than those in psoriasis and rheumatological diseases. Infliximab and sertoluzimab usage, male gender, and vaccination after anti-TNF treatment were risk factors of non-response. Therefore, HBV vaccination should be given to CID patients before initiation of anti-TNF treatment and awareness should be spread on this subject.

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Abstract 9040

**Comparison of diagnostic performance of two Aspergillus antigen ELISAs**

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**Background:** Aspergillus spp. are ubiquitous and opportunistic pathogenic fungi. Inhalation of their spores can cause life-threatening invasive aspergillosis (IA) in immunocompromised patients. Current diagnostic guidelines recommend serial screening for Aspergillus antigen in serum or bronchoalveolar lavage fluid samples from patients at risk of IA. Only few enzyme-linked immunosorbent assays (ELISAs) based on monoclonal antibodies with high specificity for Aspergillus antigens are commercially available. We assessed the serodiagnostic performance of the novel Aspergillus-specific galactomannoprotein (GP) ELISA (EUROIMMUN) by comparing it to the Platelia Aspergillus galactomannan (GM) ELISA (Bio-Rad).

**Materials/methods:** Diagnostic performance of the two ELISAs was assessed by analysing serum samples from 43 patients with IA and 77 without IA. The agreement between manual versus automated processing of the GP ELISA using the EUROIMMUN Analyzer I was evaluated in sera from 16 patients with IA and eight fungus-spiked pooled sera.

**Results:** The GM ELISA identified 24 true positive and 77 true negative samples, whereas the GP ELISA identified 27 true positive and 74 true negative samples. The two assays had a positive and negative agreement of 90% and 88%, respectively. The overall agreement between the ELISAs was substantial (Cohen’s $\kappa = 0.65$). Nine IA patients were correctly identified with the GP ELISA but missed by the GM ELISA. The GP ELISA classified two IA patients as negative for Aspergillus antigen, which were identified by the GM ELISA. Manual and automated processing of GP ELISAs agreed almost perfectly (Cohen’s $\kappa = 0.91$, one discrepant sample was close to cut-off).

**Conclusions:** The GM ELISA correctly identified more patients without IA, whereas the GP ELISA correctly identified more patients with IA. Although each test identified cases that were not detected by the competitor, their performance in the serodiagnosis of IA was comparable. Overall, the assays are similarly suitable for screening of patients at risk for IA. However, serial testing and use of further diagnostic tools are recommended by standard guidelines. Furthermore, our results demonstrated that the GP ELISA can be reliably processed on fully automated systems, thus providing high-throughput analysis for monitoring patients at risk of IA.

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Abstract 9045

**Unusual mechanisms of resistance to ceftazidime-avibactam in Klebsiella pneumoniae**

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**Background:** The emergence of carbapenem resistant Enterobacteriales (CRE) has urged the development of new drugs. Cef-tazidime-avibactam (caz-avi) is used for its treatment but resistance has surfaced. The most prevalent resistant mechanism is the mutation of blaKPC-3 gene. The aim of this study is describe the mechanisms of resistance of Klebsiella pneumoniae (KP) to caz-avi in patients not previously exposed to the drug.

**Materials/methods:** Twenty seven multi-drug resistant KP collected at the University of São Paulo Bacteriology Laboratory from 2013 to 2016 corresponding to colonization or health-care associated infection patients were analyzed. One isolate per patient was included.

Susceptibility was performed by Broth microdilution (BMIC), efflux pump performance was evaluated with Carbonyl Cyanide 3-Chlorophenylhydrazone (CCCP). Typing, resistome and comparative genomic was assessed by Whole genome sequencing (WGS).

**Results:** The isolates belong to eleven different lineages; the most frequent ST was 11 (n=9). All isolates were susceptible to caz-avi but one. None of the twenty-seven isolates harbored KPC-3, seventy percent of the isolates harbored KPC-2 but none had mutations.

The resistant isolate was obtained from a corporal fluid, its BMIC was evaluated and corroborated by different persons. Additionally, its MIC was not altered when CCCP was added, other efflux pump inhibitors should also be tested. When analyzed by WGS no previously described resistance mechanisms were found. However, unknown mutations in efflux pumps [acrR and ramR, CRP, emrB, emrR, marR, marA, msbA, patA ] and membrane porines [ompK36 and ompK37] genes were identified. A comparative genomic analysis was performed with a clonal susceptible KP aiming to find genes involved in the resistance mechanism. Thirteen genes including two involved in response to antibiotic were present only in the resistant isolate (Figure 1). This KP is been analyzed to clarify the resistance mechanism.

**Conclusions:** This work highlights the importance of caz-avi emerging resistance even without previous exposure to the drug. Therefore, caution in prescription of the new antibiotics for CRE is strongly recommended. Other mechanisms as efflux pumps and porine modification should be profoundly evaluated in order to elucidate ceftazidime-avibactam resistance.

Figure 1. Comparative Genomic Analysis of two Klebsiella pneumoniae isolates (resistant and susceptible)

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Abstract 9046

**Using whole genome sequencing to assess *M. leprae* transmission in French overseas Territories**

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**Background:** Our National reference center for mycobacteria diagnosed 154 cases of leprosy (multibacillary forms) from 2001 to 2019 in French Overseas territories. Most of them were diagnosed in New-Caledonia (NC) and Mayotte (MY), two islands in the Pacific and Indian Ocean, respectively. Importantly, over the last 10 years, new cases of pediatrics leprosy were diagnosed showing the persistence of leprosy transmission. Here we applied whole genome sequencing (WGS), in order to investigate *Mycobacterium leprae* transmission dynamic.

**Materials/methods:** Since *M. leprae* does not grow in vitro, *M. leprae* DNA was extracted directly from positive skin biopsies using DNA Microbiome kit (QIAamp, Qiagen) in order to eliminate DNA from human cells and skin microbiota. WGS data were produced by Illumina sequencing technology. Sequencing data were solved using Bionumerics (Applied Maths) and mapped on the reference genome *M. leprae* TN (NCBI Reference Sequence: NC_002677.1). Datasets were composed by 8 genomes from NC, 6 genomes from Mayotte and 2 laboratory strains (Thai53 and Hairaku).

**Results:** The mean coverage of sequenced genomes was 116X. The comparison of the 16 genomes to the reference genomic sequence of *M. leprae* TN generated 412 single nucleotides polymorphisms (SNP). Genome analysis of NC *M. leprae* strains showed a cluster of 6 strains from the 3K subtype, with only 10 SNP differences. The other NC genomes belonged to subtypes 1C and 4N. Interestingly, all the genomes from MY, belonged to subtype 1D but differed by 15 to 50 SNP.

**Conclusions:** WGS is an interesting tool to differentiate *M. leprae* strains can be used for molecular epidemiology analysis of cases occurring in isolated islands. In the two studied islands, transmission seemed to have occurred differently, strains being nearly identical in NC whereas showing more diversity in MY.

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In vivo virulence of different clones of OXA-48-producing Klebsiella pneumoniae in Galleria mellonella infection model

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Background: Infections by carbapenemase-producing Klebsiella pneumoniae represent an increasing threat to human health. Despite its significance, only a few studies have evaluated the “in vivo” virulence of these bacteria. Recently, “in vivo” non-mammalian animal models of infection have been developed for virulence studies. The Galleria mellonella larvae model has been tested with different bacterial and fungal pathogens, showing a good correlation with models in mammals. The objective of this study was to compare the virulence of different clones of OXA-48-producing K. pneumoniae in the G. mellonella model.

Materials/methods: Five isolates of OXA-48-producing K. pneumoniae previously characterized at the molecular level and belonging to different clones (ST15, ST104, ST147, ST326 and ST405) were evaluated. Two solutions of each of the clones were prepared in PBS at 10⁷ colony forming units (CFU)/mL and 10⁵ CFU/mL. 10 µL of each solution were injected in the hemocoele of larvae (40 larvae per strain; 10⁵ CFU and 10³ CFU per larvae). Then, they were incubated at 37ºC for ten days and survival data were recorded daily. A non-manipulated control group (temperature control), another one inoculated with PBS and a third one with heat-killed bacteria were also evaluated. Tests were performed in duplicate and independently. Survival data were interpreted with the GraphPad Prism 6 program using Kaplan-Meyer curves and performing statistical analysis by the Log-rank test (Mantel-Cox) with a significance level p<0.05.

Results: Kaplan-Meyer curves are shown in Figure 1. Virulence of OXA-48-producing K. pneumoniae strains was low to moderate. As expected, virulence was significant higher for the 10⁵ CFU/larvae inoculum, being also the virulence differences between analyzed strains more marked. Virulence of ST405 was statistically significant higher with respect to the other clones (p=0.045), while virulence of ST147 and ST104 was statistically significant lower (p=0.0016 and p=0.049, respectively).

Conclusions: Statistically significant differences were found in the virulence of representative strains of five high-risk international clones of K. pneumoniae involved in carbapenemase spread. Further studies are required to validate these experiments and to analyze the correlation between the virulence found, the virulence gene content of the strains and the clinical outcomes of patients infected by them.
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Figure 1. (A) Mortality curves of different clones of Klebsiella pneumoniae, generating by inoculating $10^5$ UFC/larvae (●), $10^6$ UFC/larvae (▲) and PBS (■). (B) Comparison of virulence between the different clones using the $10^5$ UFC/larvae inoculum.

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Trends in antimicrobial resistance in Gram-negative pathogens among haematological patients: results of multi-centre study

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Background: The goal was to evaluate the trends in antimicrobial resistance among gram-negative pathogens from blood culture in haematological patients during various periods.

Materials/methods: Gram-negative rods isolated from blood culture in 11 hospitals from 9 cities in Russia in 2002-2018 were studied. Susceptibility was determined by the broth microdilution method [CLSI 2018, EUCAST 2018 for colistin]. Extended-spectrum beta-lactamases (ESBL) production was confirmed by phenotypic tests. PCRs were performed for detection of blaCTX-M genes, groups of blaCTX-M, blaNDM-1, blaOXA-48, blaVIM, blaIM, blaOXA-23, blaOXA-24/40, blaOXA-58.

Results: A total of 2338 gram-negative isolates were evaluated, of those 1180 were isolated in 2003-2010 and 1158 in 2011-2018. There were no differences in distribution of pathogens in these periods. The rate of Escherichia coli was 35% vs 34.5%, Klebsiella pneumoniae 17.1% vs 25.2%, Pseudomonas aeruginosa 15.9% vs 16%, Enterobacter cloacae complex 7.2% vs 6.2%, Stenotrophomonas maltophilia 4.7% vs 3.5%, Acinetobacter baumannii 4.6% vs 4.3%, Aeromonas spp. 0.4% vs 0.3%, other Enterobacteriales 6.5% vs 5.8%, other non-fermentative gram-negative rods 8.6% vs 4.5%, accordingly. Differences were revealed in antimicrobial resistance for K.pneumoniae and A.baumannii [Table]. In K.pneumoniae the rate of carbapenemase producing strains rose from 2% to 27.1% (p<0.001), carbapenem and colistin non-susceptible isolates from 5.9% to 21.9%, 1.5% to 12.3%, accordingly (p<0.001). The prevalent carbapenemase genes in K.pneumoniae were blaOXA-48. There was increase in detection of carbapenemase genes in A.baumannii from 37% to 94% (p<0.001), carbapenem non-susceptible strains from 66.7% to 94% (p<0.001). A. baumannii harboring blaOXA-23 and blaOXA-48 rose from 18.5% to 42% (p<0.01), from 11.1% to 48% (p<0.001). Susceptibility to colistin in A. baumannii was stable during the study. The rate of carbapenem non-susceptibility and carbapenemase-producers in P.aeruginosa was not change. The predominant carbapenemase genes in P.aeruginosa were blaOXA-48 (97% vs 100%). The level of trimethoprim-sulfamethoxazole resistance in S.maltophilia slightly increased from 8.9% (2003-2010) to 12.5% (2011-2018).

Conclusions: The distribution of gram-negative pathogens causing blood stream infections in haematological patients did not change in contrast to determinants of resistance which increased in K.pneumoniae and A.baumannii.

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Prevalence of human papilloma virus 16, 18 and other high-risk genotypes in Baku, Azerbaijan

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Background: Cervical cancer is one of the most common female malignancies. Human papillomavirus (HPV) is thought to be the primary cause of cervical intraepithelial neoplasia and cervical cancer. The aim of this study was to determine HPV type distribution in women with and without cervical neoplasia from Azerbaijan and to estimate the potential future impact of an HPV 16/18 and other high risk genotypes.

Materials/methods: A total 172 cervical swab samples were included in the study. All samples sent to Clinical Microbiology Laboratory of Thalassemia Center, Baku, Azerbaijan between October 2018 - November 2019. In our study, HPV types 16, 18 and other high-risk genotypes (31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68) were differentiated. HPV genotype determination was performed by multiplex real-time PCR method (Rotor-Gene Q, Qiagen, California, USA) using HPV Genotypes 1 4 Real-TM Quant (Sacace, Como, Italy) kit.

Results: HPV positivity was detected in 57 (33.1%) of 172 cervical specimens. Single HPV genotypes were detected in 16 (28%), two different HPV genotypes in 16 (28%) and multiple HPV genotypes in 5 (8.9%) specimens. HPV type 16 was found in 11 (19.6%), HPV type 18 was found in 14 (25%) and high risk groups were found in 38 (67.8%) of HPV positive samples.

Conclusions: The prevalence of HPV type 18 in our region was higher than HPV type 16. The detection of HPV types in the diagnosis of genital HPV infections is important for epidemiological studies. The 33.1% positivity rate for our region suggests that screening programs in our country should be expanded especially for the early diagnosis of oncogenic HPV types. Cytology results of our patients will be discussed in poster presentation.

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Impact assessment of the results of BIOFIRE FILMARRAY pneumonia panel plus for the detection of pathogenic bacteria and individualised therapeutic targeting

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Background: The etiological diagnosis of bacterial pneumonia is based on the identification of causal pathogens by cultures, which require prolonged incubation periods and have limited sensitivity. The BIOFIRE® Filmarray® Pneumonia Panel plus enables rapid and accurate automated testing for 27 bacteria and viruses that cause pneumonia directly from patient samples and can improve diagnostic accuracy to guide antibiotic treatments. In this study, we hypothesise that improved detection of pathogens by BIOFIRE® Filmarray® can improve culture-based diagnosis and cause changes for therapeutic management.

Materials/methods: From April 2019 - Nov 2019 we enrolled 20 adult patients admitted to the Medical ICU with acute respiratory failure within 24 h of intubation for mechanical ventilation. We performed BIOFIRE® Filmarray® Pneumonia Panel plus to determine pathogen identification in lower respiratory tract samples, and assessed individualized antimicrobial stewardship.

Results: 20/22 patients could perform culture. 14/20 patients (60%) presented significant bacterial counts cultures. BIOFIRE® Filmarray® Pneumonia Panel plus detected a pathogen in 20% of the culture-negative patients, and most of them had been exposed to broad-spectrum empiric therapy. When Filmarray reported > 10^7 copies / ml, concordance with a significant count (>10^6) was 85%. Filmarray® had an overall 59% impact on the antibiotic adequation. For patients without treatment or with incorrect treatment, Filmarray® result always guided a change in therapy. For FILMARRAY® negative samples, change/deescalation in antimicrobial treatment were made only in 49% of the cases. On the other hand, in patients with adequate broad-spectrum empirical treatment, the filmarray results were followed only in 43% of cases.

Conclusions: FILMARRAY® Pneumonia Panel plus allows a faster and enhanced detection of pathogenic bacteria; FILMARRAY® offers a substantial opportunity for individualized therapeutic targeting and antimicrobial stewardship in ICU patients with mechanical ventilation pneumonia.

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Abstract 9061

**The rational of antibiotic failure in Helicobacter pylori**

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**Background:** Antibiotic failures in *Helicobacter pylori* and the novel mechanism of bacterial resistance against antibiotic lead us to investigate the causes of antibiotic failure in patients with *H. pylori* in Ilam, Iran.

**Materials/methods:** 120 *H. pylori* isolates were collected from Mostafa Khomeini Hospital, Ilam, Iran and Rasoul-e-Akram Hospital, Tehran, Iran. Afterward, *H. pylori* were identified by phenotyping methods and *urea* gene was subjected to confirm isolates as *H. pylori*. Initially, antibiotic susceptibility testing was performed by disc diffusion for metronidazole and clarithromycin. *rdxA* gene also evaluated to confirm the resistance strains. Bacteria were cultured in stationary phase and mixed 1 milliliter from 24 hours incubated suspension bacteria and lyse solution. Then, they were vortex for 10 seconds and kept on 10 minutes in room temperature. Then, 200 macro liter of Lysis enzyme solution added and incubated in 37 °C with 200 rpm. Finally, solutions were cultured in Luria-Bertani media and grown colonies were considered as persister cells. For confirmation of persistence those susceptible isolates were subjected for MIC with both metronidazole and clarithromycin and 5 folds greater than MIC were cultured and evaluated their growth. If bacteria were positive in culture it was considered as peresistant. After DNA extraction PCR was performed with specific primers.

**Results:** Our results demonstrated that among 120 *H. pylori* isolates, 35 % (n=42) were sensitive, 16.6 % (n=20) were intermediate and finally 48.4% (n=58) of isolates showed resistance to metronidazole. Clarithromycin resistance was observed in 21.6 % (n=26) isolates. Overall, 35% (n=42) of isolates showed susceptibility to both metronidazole and clarithromycin [figure 1]. This 42 isolates were chosen to evaluate as persister cells.

The persister assay analysis demonstrated that 38.1% (n=16) that were antibiotic susceptible *H. pylori* were persister cells. The confirmation was performed by MIC for both antibiotics.

**Conclusions:** This study demonstrates that, there were Metronidazole and clarithromycin resistant isolates among 120 mentioned collection, which can be one of the most important reasons to fail of treatment. In addition, among Metronidazole and Clarithromycin sensitive isolates the persister cells were observed that can be the novel cause of failure to treatment and recurrent of infectious.

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Abstract 9062

National survey of Neisseria gonorrhoeae isolates by whole genome sequencing in France in 2018

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Background: According to WHO estimates, there are 106 million new cases of gonorrhea each year. Epidemiological surveillance of Neisseria gonorrhoeae (NG) has become a major issue, due to both the increasing number of cases and the emergence of multidrug-resistant clinical isolates. This study reports a national survey by using combination of clinical data and whole genome sequencing for investigating GC isolates infections in France.

Materials/methods: From 1 September to 31 December 2018, 127 laboratories in metropolitan France and French overseas islands were asked to collect strains obtained in NG culture associated with anonymous clinical data. Isolates of NG were sent to the Associated Laboratory of the National Reference Center for bacterial STI and 7 antibiotics MICs were determined by Etests (Biomerieux). Molecular determinants of resistance and genotyping were obtained by Whole Genome Sequencing (WGS), Illumina technology (Nextseq, Illumina, San Diego, CA). Data analysis was performed by the in silico genome study (NG-MAST, NG-MLST and NG-STAR).

Results: Clinical information from 223 NG-infected patients reported a predominance of men (161; 72.2%). The age ranged from 15 to 75 years old (mean: 30 years), 5.8% were HIV-infected, 18.4% were coinfected by Chlamydia trachomatis or Treponema pallidum. From the 158 cultivated NG isolates, 110 (69.6%) were isolated from genital sites and 44 (27.8%) from extragenital sites: anus (43; 97.7%) and throat (1; 2.3%). NG isolates were resistant to tetracycline, ciprofloxacin, azithromycin in 62.2%, 61.4%, and 7.6% of cases, respectively and all were susceptible to ceftriaxone and cefixime. Only 3 NG isolates had a ceftriaxone or cefixime MIC >0.032 mg/L. The NG isolates were largely distributed into 42 different MLST Sequence Types with minor clusterisations, ST1583 (n=20; 12.7%) and ST9263 (n=18; 11.4%) being more prevalent.

Conclusions: This survey showed no resistance to the first-line antimicrobial treatment. The combination of clinical data with phenotypic study and high throughput WGS of strains provides important data for monitoring circulating strains on a national scale. Observation of a larger collection of strains would be of interest for our 2019 survey.

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Abstract 9063

In vitro evaluation of single or combined bacteriophages targeting different Staphylococcus aureus clinical isolates

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Background: The decreasing effectiveness of classic antibiotic therapies due to an increased diffusion of multidrug-resistant bacterial strains and to the occurrence of biofilm-associated infections requires investigations with alternative therapies. Among such therapies, the use of bacteriophages is a promising treatment strategy. In this work, we analyzed the performance of three bacteriophages as monotherapeutic agents or as a phage cocktail against different Staphylococcus aureus (SA) isolates.

Materials/methods: Three SA-targeting bacteriophages (ϕM, ϕE and ϕT) isolated from human saliva, MRSA ATCC-43300 and two clinical isolates, SA1 and SA2, were used for this study. The susceptibility of each bacterial strain to the bacteriophages was determined by broth-microdilution assay. Moreover, the ability of each bacteriophage or a combination of all three as a cocktail to prevent biofilm formation on glass porous beads and to eradicate pre-established 24h-old biofilms was investigated by isothermal microcalorimetry.

Results: MRSA ATCC-43300 was susceptible to all three bacteriophages with MIC values of $10^5$ PFU/mL for ϕM and $10^6$ PFU/ml for ϕE and ϕT, whereas SA1 was susceptible to ϕM and ϕE (MIC $10^7$ PFU/ml) and SA2 to ϕE (MIC $10^7$ PFU/ml). The phage cocktail showed the highest activity in preventing biofilm formation against MRSA ATCC-43300 and SA1, but had an analogous activity than ϕE alone against SA2. Biofilm treatment revealed high efficacy of ϕM against MRSA ATCC-43300 with more than 90% reduction of the heat-flow production compared to the growth control. Overall, our results presented a variable antibiofilm efficacy of bacteriophages depending on the strain tested (Figure 1).

Conclusions: The cocktail was found to be superior to the individual phages in preventing biofilm formation against those bacterial strains susceptible to at least two of the three bacteriophages within the cocktail. However, compared to individual phages, the cocktail did not always have an improved antibiofilm activity against tested strains. Further studies including more clinical strains and phages with broader host range should be investigated to design phage cocktails with optimized antibiofilm activity.

Figure 1. Microcalorimetry analysis of the antibiofilm activity of bacteriophages ϕM, ϕE, ϕT and the cocktail ϕM/E/T against MRSA ATCC-43300 and two S. aureus clinical isolates. GC, growth control.

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Abstract 9066

Evaluation of PrimeStore molecular transport medium for long-term preservation of mycobacterial RNA at ambient temperature and subsequent detection of Mycobacterium tuberculosis Ag85B

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Background: In this study, we have investigated the potential of PrimeStore Molecular Transport Medium (PS-MTM) to release and preserve Mycobacterium tuberculosis RNA from raw sputum without requiring cold chain steps. The hypothesis is that the procedure would have utility in clinical trials of anti-TB drugs or in patient treatment monitoring as a surrogate marker of antibiotic effect. Working with RNA is challenging, however. It is highly labile and prone to rapid decay. After isolation, RNA must immediately be stored at -80°C, or must be converted into cDNA for longer storage. We show in this study that raw sputum samples transferred into PrimeStore Molecular Transport Medium (PS-MTM) resulted in the release and preservation of mRNA from cells without the need for freezing at ultra-low temperature.

Materials/methods: Forty auramine smear-positive sputum specimens (scanty, 1+, 2+ and 3+) were collected in PS-MTM and kept for up to 90 days at ambient temperature. RNA extractions were performed using an miRNeasy Mini Kit (QIAGEN®). The resultant RNA was quantified using a NanoDrop Spectrophotometer (Thermo Fisher Scientific). The ratio of absorbance at 260 and 280 nm (i.e. the A260/A280 ratio) was used to determine purity of RNA. Optimisation of the real-time PCR assay was achieved by using Mycobacterium tuberculosis Ag85B primers and TaqMan probes on the QuantStudio 5 real-time PCR system.

Results: Extracted RNA (host and mycobacterial) was detected in all samples in our study, with an average ratio of 1.67 recorded for A260/A280 despite long-term storage at ambient temperature. Real time PCR was positive for the viable M. tuberculosis in the patient sputum consistent with diagnosis of active disease during laboratory diagnosis of the patients. The PCR assay was able to detect both the mycobacterial DNA (IS6110) and the mycobacterial mRNA (Ag85B).

Conclusions: PS-MTM was able to preserve RNA, including the smaller mycobacterial mRNAs, for longer than three months when stored at room temperature without the use of a cold chain protocol.

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Antimicrobial resistant and enteropathogenic bacteria in 'filth flies': a cross-sectional study from Nigeria
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Background: ‘Filth flies’ breed in garbage, animal and human faeces and can be colonized with numerous bacterial species. The aim of this work was to study the intestinal colonization of ‘filth flies’ with Extended-spectrum beta-lactamase producing Enterobacterales (ESBL-E), Staphylococcus aureus, Campylobacter sp., Salmonella sp., Shigella sp. and Yersinia enterocolitica in Nigeria.

Materials/methods: Flies (n=2000) were sampled from 109 urban, semi-urban and rural sites in Southern Nigeria. Sequencing of the cytochrome oxidase gene was used for species identification of flies. After enrichment in BHI-broth, homogenized flies were screened for the targeted pathogens. Bacterial species identification was done using MALD-TOF and antibiotic susceptibility testing was done with Vitek 2 automated system. Isolates were screened for resistance genes and enterotoxins. Genotyping included E. coli phylogrouping, spa-typing multilocus sequence typing (MLST) and whole genome sequencing.

Results: Of a randomly selected subset of flies, Musca domestica (44.8%, 179/400) was predominant followed by Chrysomya putoria (21.6%, 85/400) and Musca sorbens (18.8%, 75/400). Flies were colonized with S. aureus (13.8%, 275/2000) and ESBL-E (0.8%, 16/2000). No other enteropathogenic bacteria were detected. S. aureus were positive for chp (100%, 275/275) and scn (97%, 267/275) but negative for sak. All S. aureus belonged to MLST sequence type ST15 and spa types t674, t1980, t5305 and t6313. The staphylococcal enterotoxin SEI was most common (26%, 70/275), followed by the SEA (12%, n=32/275). Other enterotoxins were not detected (SEB, SEC, SED, SEE, SEF, SEG and SEH). Four S. aureus were methicillin resistant (mecA positive). The ESBL E. coli (n=15) belonged to phylogroup D (n=2), B2 (n=1), ST10 (n=5), ST617 (n=2), and singular occurrences of other STs.

Conclusions: ‘Filth flies’ can carry antimicrobial resistant bacteria in Nigeria while enteric bacteria were rarely detected. Enterotoxin-positive S. aureus might be the main reason for food poisoning by ‘filth flies’ in the study area.

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Direct sequencing from clinical samples in the diagnostic microbiology laboratory without capital expenditure or specialised bioinformatic training is possible using nanopore technology

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Abstract third-party references: Barts and the London Charity

Background: The use of ‘next generation sequencing’ for the direct detection of microbes in clinical specimens has been advocated for several years. Its implementation in diagnostic laboratories has been hampered by high capital cost and the need for bioinformatic expertise to interpret results. Nanopore sequencing requires no capital cost, and is suitable for low volume use without the need for batching. The introduction of dedicated software has made reliable results much easier to achieve without formal training. We assessed the feasibility of nanopore sequencing using the MinION (Oxford Nanopore) to sequence clinical samples from which no results of clinical significance had been obtained after routine analysis but where infection still suspected.

Materials/methods: Samples were referred by infection specialists from patients with diagnosis or management uncertainty following standard culture and molecular testing (16S PCR). After initial depletion of human DNA with saponin/nuclease method, DNA was extracted, and libraries prepared using the Rapid PCR Barcoding Kit. After two hours of sequencing, the results were analysed using WIMP, software provided by ONT. Infection specialists were informed, and action taken based on the result recorded.

Results: Ten specimens were tested. The turnaround time was 10 hours and all organisms detected with routine diagnostic tests were detected by MinION. Additional organisms were detected in all samples tested. A plausible cause of infection was found in 6 clinical samples which had not been detected by standard methods were culture and 16S negative, and the result impacted patient management (see table).

Conclusions: MinION sequencing detected clinically plausible microorganisms not detected by routine methods in a variety of samples and results helped inform clinical management. MinION sequencing is suitable for use as a routine method for supporting diagnosis of infection where the results of conventional methods are considered inadequate or incomplete.

Table. Results obtained from a variety of clinical specimens

<table>
<thead>
<tr>
<th>Patient condition/Sample tested</th>
<th>Culture</th>
<th>16S PCR</th>
<th>MinION results</th>
<th>Clinical Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected meningitis/CSF</td>
<td>Negative</td>
<td>Negative</td>
<td>S. pneumoniae</td>
<td>- Antibiotics rationalised</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>- Immunological investigations undertaken</td>
</tr>
<tr>
<td>Suspected infection/Breast Abscess</td>
<td>E. cloacae</td>
<td>Not applicable</td>
<td>S. pyogenes</td>
<td>Antibiotics rationalised</td>
</tr>
<tr>
<td></td>
<td>A. lwoffii</td>
<td></td>
<td>E. cloacae</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Coagulase negative</td>
<td></td>
<td>A. lwoffii</td>
<td></td>
</tr>
<tr>
<td></td>
<td>S. pyogenes</td>
<td></td>
<td>S. warneri</td>
<td></td>
</tr>
<tr>
<td></td>
<td>E. cloacae</td>
<td></td>
<td>S. simulans</td>
<td></td>
</tr>
<tr>
<td></td>
<td>A. baumannii</td>
<td></td>
<td>S. haemolyticus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mixed anaerobes</td>
<td></td>
<td>A. baumannii</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>A. mediterraneis</td>
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<td></td>
<td></td>
<td></td>
<td>P. interferia</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>E. massiliensis</td>
<td></td>
</tr>
<tr>
<td>Suspected infection/Arytenoid abscess</td>
<td>Negative</td>
<td>Not applicable</td>
<td>H. influenzae</td>
<td>Antibiotics rationalised</td>
</tr>
<tr>
<td>Suspected Endocarditis/ Epidural abscess</td>
<td>Coagulase negative</td>
<td></td>
<td>S. aureus</td>
<td>Antibiotics rationalised</td>
</tr>
<tr>
<td></td>
<td>Staphylococcus</td>
<td></td>
<td>S. capitis</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>S. epidemics</td>
<td></td>
</tr>
<tr>
<td>Suspected infection/ Prosthetic hip joint tissue</td>
<td>Negative</td>
<td></td>
<td>S. aureus</td>
<td>Antibiotics rationalised</td>
</tr>
<tr>
<td></td>
<td>E. cloacae</td>
<td></td>
<td>E. cloacae</td>
<td></td>
</tr>
<tr>
<td>Suspected Endocarditis/Whole blood</td>
<td>Negative</td>
<td>Not applicable</td>
<td>S. aureus</td>
<td>Antibiotics rationalised</td>
</tr>
</tbody>
</table>

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Background: Metallo-\(\beta\)-lactamase-producing \textit{Pseudomonas} spp. are important agents of healthcare-related infections in Brazil. The presence of carbapenemases makes treatment with beta-lactams unfeasible and is often an indicator of multiresistance. The most common metallo-\(\beta\)-lactamase (MBL) in \textit{Pseudomonas} spp. in Brazil is SPM, however we observed an increase in the detection of MBL VIM in the last years.

Materials/methods: During the period from January 1, 2015, to January 30, 2019, as part of the Bacterial Resistance monitoring Network of ANVISA-Brazil, the Laboratório de Pesquisa em Infecção Hospitalar (LAPIH/IOC) received 35 MBL-producing \textit{P. aeruginosa} \(n=33\) and \textit{P. putida} \(n=2\), positive for \textit{bla}\textsubscript{VIM-like} gene by PCR. The \textit{bla}\textsubscript{VIM} was sequenced using the ABI Prism 3700 DNA Sequencer. The evaluation of carbapenemase activity was performed by CARBA NP, Blue Carba and mCIM/eCIM. The antimicrobial susceptibility was evaluated by disk diffusion method and broth microdilution test according the BrCAST. Molecular typing was performed using PFGE and MLST.

Results: The allelic variant found among the isolates were \textit{bla}\textsubscript{VIM-2} \(n=34\) and \textit{bla}\textsubscript{VIM-24} \(n=1\). All of them presented activity of MBL by CARBA NP, 94.2\% by mCIM/eCIM, but the Blue Carba identified them as serino-carbapenemase. All isolates were considered multiresistant. The most common resistance was to imipenem and meropenem \(100\\%\), followed doripenem \(93.3\%\), amikacin \(93.3\%\), cefepime \(86.6\%\), ciprofloxacin \(86.6\%\), levofloxacin \(86.6\%\), ceftazidime \(80\%\), gentamycin \(73.3\%\), piperacillin/tazobactam \(66.6\%\), and Aztreonam \(33.3\%\). The lowest non-susceptibility rate was for Aztreonam \(33.3\%\). All VIM producers showed susceptibility to polymyxin \(MICs 0.25\text{-}1\ mg/L\) and resistant to ceftolozane-tazobactam \(256\ mg/L\), 85.7\% resistant to cefazidime-avibactam \(1.5\text{-}256\ mg/L\). PFGE analyses of \textit{P. aeruginosa} revealed 15 different pulsotypes with the predominance of a clone \(n=16\) corresponding to ST2559. Other ST found including ST1015, ST111, ST233 and ST381. Both of VIM-2-producing \textit{P. putida} isolates belonging to the same clone.

Conclusions: The results suggest the dissemination of \textit{bla}\textsubscript{VIM-2} and the first description of \textit{bla}\textsubscript{VIM-24} in Brazil. Blue Carba did not show good results for VIM detection. Although SPM is most common MBL in Brazil, our study indicate an increase in the detection of \textit{bla}\textsubscript{VIM-2} in \textit{Pseudomonas} spp. suggesting a change in the epidemiological profile in Brazil.

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**Who should we test for arboviral infection? Rational diagnostic testing in an era of increased global prevalence**

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**Background:** Approximately 3000 returning travellers attend the Hospital for Tropical Diseases (HTD) emergency walk-in clinic each year. In our practice as elsewhere, there is substantial overlap in clinical presentation of arboviral infections, defined here as dengue, Zika and chikungunya. We reviewed our investigation of suspected arboviral infection, focusing on clinical and laboratory predictors of a positive diagnosis.

**Materials/methods:** Data for patients presenting between September 2015 and March 2019 were extracted from a prospective clinical database, combined with laboratory data and analysed in R. A 'positive' arboviral result was defined as a positive PCR or documented seroconversion to dengue, Zika or chikungunya. A negative result was defined as PCR and all serological tests negative. An indeterminate result was defined as a single positive serological result without demonstrated seroconversion. Clinical features and laboratory parameters associated with positive and negative tests were compared where clinical data were available.

**Results:** 10,595 patients attended the HTD walk-in clinic between September 2015 and March 2019. Of these, 2318 patients were investigated for arboviral infection. 168 tested positive (116 dengue, 40 Zika, 2 chikungunya), 1548 were negative, and 602 were indeterminate, so excluded from further analysis. Presenting symptoms were documented for 136 arboviral positive and 1382 negative patients.

Reports of fever, headache, rash and arthralgia/myalgia were all significantly higher in those with a positive result (chi-squared comparisons p < 0.05). Presence of a rash had the largest discordance [64% vs. 29%, p < 0.0001] and was the strongest individual positive and negative predictor of a positive arboviral test [PPV 0.18 [95% CI 0.14-0.21], NPV 0.95 [95% CI 0.94-0.96]]. Rash plus headache had a positive predictive value of 0.23 [95% CI 0.18-0.29].

**Conclusions:** It is difficult to clinically distinguish arboviral infections from other common presentations, and only a small proportion of tests yielded a positive result. Diagnostic testing should focus on patient groups with a higher prior probability of infection.

The limitations of a retrospective dataset are being addressed by collection of a contemporary prospective dataset. An in-depth analysis of these data and a diagnostic algorithm to optimise arbovirus testing of returning travellers will be presented.

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Implementing a scalable bioinformatics infrastructure to enable national clinical pathogen genomics services

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Background: In 2017 the Welsh Government launched the Genomics for Precision Medicine Strategy, including over £8M of investment to date to develop new clinical genomics services to enable better, more personalised and more precise medical care. A key component of this strategy has been the development of clinical Pathogen Genomics services, all of which are underpinned by microbial bioinformatics. This presentation will introduce the bioinformatics infrastructure which over the last 18 months has underpinned the development of clinical genomics services focused on HIV, Influenza, Clostridioides difficile and Mycobacteria tuberculosis and non-tuberculosis Mycobacteria.

Materials/methods: We have used a combination of software containers and the nextflow workflow engine running on top of virtualized cloud computing resources in order to build our systems. Combining bioinformatics software and enterprise IT, our bioinformatics infrastructure provides a single software framework operating on top of an integrated, redundant, computational infrastructure that enables the processing of genomic sequence samples from a range of pathogens, sequenced using both Illumina and Nanopore sequencing technologies.

Results: The provision of a core, modular, automated infrastructure has enabled the processing of over 150,000 individual jobs from over 8,000 patient samples in the last 18 months. This infrastructure has underpinned the development of four clinical services, including two that have achieved ISO 15189 accreditation. By moving to genomics approaches, and combining this with automated, easily managed bioinformatics/software systems, we have been able to decrease assay costs, improve turnaround times, and increase test resolution – supported with only a small bioinformatics team.

Conclusions: In order to implement services based upon next generation sequencing, the bioinformatics elements are critical. Here we introduce the service that we have built in Wales, which now underpins a set of national services across multiple pathogen types. This work provides a template for others who are also seeking to develop services based on next generation sequencing in their own clinical laboratory.

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Random forest and multilevel multivariable analyses to assess risks for colonisation with multidrug-resistant Gram-negatives in 27 long-term care facilities in high endemic settings

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Background: Residency in long-term care facilities (LTCFs) increases the likelihood of colonization with multidrug-resistant Gram-negative bacteria (GNB). Knowledge of individual level risk factors is mainly limited to small cohort or prevalence studies applying conventional statistical analysis. We prospectively assessed the prevalence rate and risk factors for colonization by extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-Ent) and carbapenemase-producing gram-negative bacteria (CP-GNB) in a large cohort of LTCFs in high endemic setting.

Materials/methods: A point prevalence survey (PPS) with rectal screening (RS) was conducted in 27 LTCFs in north Italy in high endemic setting for ESBL-Ent in a 12-month period. Epidemiological and clinical variables including presence of medical devices and percutaneous endoscopic gastrostomy (PEG) on the PPS day, history of hospitalization and surgery within one year of study inclusion, and antibiotics within three months were collected. The presence of ESBL-Ent and CP-GNB was assessed using a selective culture on chromogenic medium and PCR. Risk analysis was performed using Random Forest (RF) and multilevel multivariate logistic regression model with a random component at local unit was used to account for the underlying structure of the sampling procedure. Association with colonization was considered for a p value < 0.05.

Results: In the study period 1933 RSs in 2890 residents were performed. The prevalence rates were: 51% (95CI: 49%-53%) for ESBL-Ent and 3.5% (95CI: 3%-4.5%) for CP-GNB. Carbapenemase-producing Enterobacteriaceae were 8% of total isolated Enterobacteriaceae. KPC was the most frequent carbapenemase (80% - CI95: 69%-88%) detected followed by MBL (19%; 95CI:11%-30%) and OXA-48 (6%; 95CI:2%-14.5%). Previous hospitalization (OR1.4), the presence of urinary cather (OR1.8), PEG (OR7.2), bedsores (OR1.5), and peripheral venous cather (OR1.6) were independently associated (p<0.05) with ESBL colonization at multivariate analysis and RF. At the analysis of feature fluoroquinolones usage ranked high in predicting colonization.

Conclusions: The prevalence rate of colonization by ESBL- and CP-GNB among LTCF residents in high setting for antimicrobial resistance reflects the rate in local hospitals. Intervention to reduce the colonization rates in these settings must be linked to referred hospitals and include antibiotic stewardship targeting quinolones and infection control measures for the management of devices.

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Metabolomic comparison of biofilm matrix of six species of Candida

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Abstract 9091

**Background:** Nowadays there is an enormous effort to develop new diagnostic and therapeutic strategies to identified and eliminate biofilms. Candida spp. is the most relevant forming-biofilm. The metabolomic studies are important to understand the growth process and the components immersed in their development of resistance to antibiotics.

**Materials/methods:** Eleven Candida isolates were selected from clinical samples: 2 Candida albicans (blood culture), 1 Candida auris (blood culture), 2 Candida glabrata (blood culture and pleural fluid), 2 Candida krusei (ascitic liquid and intrabdominal catheter), 2 Candida parapsilosis (Intraabdominal catheter) and 2 Candida tropicalis (blood culture and gallbladder catheter). Furthermore 7 reference strains were studied: C. albicans ATCC® 90028, C. parapsilosis ATCC® 22019, C. krusei ATCC 6258®, C. tropicalis ATCC® 750, C. glabrata ATCC® 90030, C. auris VPCI 479/P13 and C. auris KCTC® 1 7809 were used as control strain. Biofilms were processed using Matrix-Assisted Laser Desorption/Ionization-Time of Flight mass spectrometry (MALDI-ToF MS) and Gas Chromatography quadrupole Time of Flight mass spectrometry (GC-QToF) obtaining metabolomic information. Data was analyzed using NTSYSpc version 2.0 and veni's diagram using the Venny free software tool, (CNB-CSIC).

**Results:** A total of 353 molecules were identified using (MALDI-ToF MS) and (GC-QToF): 70.8% (257) proteins, 8.21% (29) peptides and amino acids; 5.66% (20) carbohydrates, 3.68% (13) lipids and 9.62 (34) other molecules. Metabolomic analysis of the 3 C. albicans strains, share 6 proteins with metabolic functions, not found in other species. C. krusei had only 2 distinctive molecules one protein and one nucleotide. C. glabrata presented 1 protein, 1 organic acid and 1 fatty acid. A different result was obtained with C. tropicalis, which had 20 different proteins present exclusively in their biofilm matrix, many of these proteins have metabolic and structural function. C. parapsilosis and C. auris share molecules with the other species, but no distinctive molecules were found.

**Conclusions:** Matrix biofilm of each Candida species tested had distinctive metabolomic profiles. Proteomic profiles are species-specific and could be useful to elaborate immunoassay as a diagnostic test and new treatment strategies.

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Abstract 9093

Characterisation of a new class 1 integron carrying \textit{blaVIM-1} and \textit{blaGES-7} in extensively and pandrug-resistant \textit{Pseudomonas aeruginosa} ST155 isolates from patients with ventilator-associated pneumonia

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**Background:** \textit{Pseudomonas aeruginosa} is one of the major pathogens isolated in ventilator-associated pneumonia (VAP). The aim of this study was to characterise seven \textit{P. aeruginosa} isolates co-producing \textit{VIM-1} and \textit{GES-7} recovered from patients suffering from VAP in an intensive care unit (ICU) at a Spanish hospital.

**Materials/methods:** Seven carbapenem-resistant \textit{P. aeruginosa} isolates recovered from respiratory-tract samples of seven patients who developed a VAP while hospitalized in an ICU were analysed in this study. Isolates were identified by Vitek-2 system and species confirmation was performed by MALDI-TOF (Vitek-MS). Antimicrobial susceptibility test (AST) was performed by broth microdilution using the following antibiotics: aztreonam, piperacillin-tazobactam, ticarcillin-clavulanate, ceftazidime, cefepime, imipenem, meropenem, gentamicin, tobramycin, amikacin, netilmicin, ciprofloxacin, levofloxacin, colistin, polymixin B and fosfomycin. EUCAST breakpoints were applied. The strains were subjected to whole-genome sequencing (WGS) on an Illumina MiSeq platform in order to analyse their resistome and virulome.

**Results:** AST results demonstrated that 2 isolates were extensively drug-resistant (only susceptible to colistin, MICs between 1-2 mg/L) and 5 isolates were pandrug-resistant (non-susceptible to all agents in all antimicrobial classes) according to Magiorakos el al. criteria [2012]. WGS analysis revealed a pangenome of 6764 genes, comprising 6252 core and 512 accessory genes. Between 69 and 376 SNPs differences were found among the isolates. All isolates belonged to the “high-risk” international clone ST155 and harboured 52 antibiotic resistance (AR) genes, including the metallo-\(\beta\)-lactamase gene \textit{bla}_{\text{VIM-1}}, two copies of \textit{bla}_{\text{GES-7}}, \textit{aac(3)-I}, \textit{aac(6')-Ib4}, \textit{aph(3’)-XV}, \textit{ant(3’’)-Ia}, \textit{catB3} and \textit{su1}, which were located in a new class 1 integron (Figure). Other AR determinants such as the beta-lactamase gene \textit{bla}_{\text{OX A-396}} and the \textit{catB7}, \textit{crpP} and \textit{fosA} genes, conferring resistance to chloramphenicol, ciprofloxacin and fosfomycin, respectively, were also identified. Two-hundred and nineteen virulence genes were identified by using VFDB (>97% identity, >60% coverage). All strains contained \textit{exoS} gene, suggesting an invasive phenotype. No plasmid replicons were documented.

**Conclusions:** It is alarming the occurrence of extensively-and pandrug-resistant \textit{P. aeruginosa} of the “high-risk” international clone ST155 co-producing VIM-2 and GES-7 among VAP patients in our hospital, which drastically reduces the antimicrobial therapy options to treat common infections in ICUs such as VAP.

**Diagram:**

- \texttt{ind1}
- \texttt{catB3}
- \texttt{bla\_GES-7}
- \texttt{aac(3’)-I}
- \texttt{bla\_GES-7}
- \texttt{bla\_VIR-1}
- \texttt{aph(3’)-XV}
- \texttt{ant(3’’)-Ia}
- \texttt{su1}
- \texttt{orf5}
- \texttt{IS6100\_tnpA}

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Streptococcus agalactiae in adults in England and Wales 2014-2015, large scale recombination and capsular shifting

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Background: Recombination is a key contributor to bacterial clonal diversity and can lead to capsule switching in Streptococcus agalactiae (GBS). This impacts vaccine development through shifting virulence determinant association to altered capsular loci outside vaccine coverage.

Materials/methods: Genomic analysis of 183 invasive and 11 non-invasive isolates determined capsular type, MLST, presence of virulence factors, antimicrobial resistance genes, phylogeny and genetic recombination. Phylogenetic relationships between the most prevalent clonal clades were also compared to presence of antimicrobial resistance genes and age/gender groups.

Results: GBS serotypes III (26.8%), Ia (26.2%) and V (14.9%) were most common in adults, but differed in gender/age distributions. Most isolates (n=185) grouped to 5 clonal complexes: CC1, CC8, CC17, CC19 and CC23 with common associations between specific serotypes and virulence genes. Serotype V/αlP3, serotype II and III/bca+cbo and serotype Ia/bibA predominantly clustered in CC1, CC8 and CC23, respectively, whereas serotype III/rib clustered in CC17 and CC19. All isolates carried at least one pilus island; mostly PI-1+PI-2a, but PI-1+PI-2b exclusively co-located to CC17 isolates. Large recombination events mediating capsular switching from CC1-serotype V to serotype Ib (n=2), II (n=2) and VI (n=2) were found, and CC19-serotype III to serotype V (n=8), CC23-serotype Ia to serotype V (n=2) and a hypervirulent CC17 (hvgA positive) serotype III to serotype IV (n=1).

Conclusions: This is the first extensive genomic investigation of GBS isolates from adults in England and Wales. The main serotype isolates from adults were split between serotypes III, Ia and V. A significant number of mismatches between expected clonal clades corresponding to capsular serotype were found [17/195 isolates]. This is particularly concerning with the emergence of the rare case of hypervirulent hvgA virulence factor present in a strain with serotype IV capsular determinants. This highlights the need for improved and continuing surveillance to inform vaccine development as escape mutations emerge.

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Abstract 9098

**In vitro anti-biofilm and immunomodulatory effects of functionalised magnetite nanoparticles**

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**Background:** Nanoparticles are currently investigated to increase the specificity and efficiency of antimicrobials by allowing the use of lower amounts of drugs, the stabilization of volatile or less stable compounds and modulation of microbial behaviours. This study aimed to obtain, characterize and investigate the antibiofilm effect of magnetite nanoparticles (NPs) functionalized with various essential oils (EOs) (i.e. obtained from Eugenia caryophyllata, Cinnamomum verum) and antibiotics (i.e. ceftriaxone, cefuroxime, cefotaxime) and to evaluate their ability to interfere with the production of cytokines in vitro.

**Materials/methods:** Functional NPs were obtained by co-precipitation and physico-chemically characterized by TEM, SEM, IR and XRD. Gram positive, Staphylococcus aureus and Gram negative, Pseudomonas aeruginosa clinical and laboratory strains were utilized in this study. The antimicrobial effect was analyzed by qualitative (agar diffusion method) and quantitative (minimum inhibitory concentration, MIC) assays. Biofilm formation and attachment were analyzed by microdilution crystal violet method, while the production of inflammatory interleukins was evaluated by enzyme linked immunosorbent assay (ELISA), using HeLa cells.

**Results:** The study revealed that the functionalized magnetite NPs present different minimum inhibitory concentrations (MICs) ranging from 0.01 mg/mL (S. aureus) to 0.5 mg/mL (P. aeruginosa) in planktonic cultures while biofilm formation is inhibited by concentration higher than 0.05 mg/mL in all strains. Subinhibitory concentrations of the obtained aqueous NPs dispersions significantly inhibited microbial attachment and biofilm formation in vitro, including clinical antimicrobial resistant strains, the effect being maintained for at least 3 days. ELISA results demonstrated that the EOs functionalized nanoparticles have the ability to promote the production of proinflammatory cytokines, especially interferon gamma (IFNγ) and interleukin 1 (IL1) in stimulated cells, suggesting they could be useful in immunomodulation.

**Conclusions:** The obtained magnetite NPs proved a great ability to stabilize and potentate the antimicrobial effects of EOs and antibiotics. These materials showed an enhanced efficiency in biofilm inhibition and also stimulated the release of inflammatory cytokines, which could significantly impact on the progression of the infectious process.

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Abstract 9104

Secretion of TNFα by human macrophages is dependent of the sequence type of clinical Legionella pneumophila isolates

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Background: Legionnaires' Disease (LD) is mainly caused by Legionella pneumophila serogroup 1 (Lp1), an environmental bacterium that could infect alveolar macrophages in human lungs. The clinical frequencies of the different sequence type (ST) from Lp1 are not correlated to the environmental representation, suggesting that some strains are more able to induce a lung infection. Several risk factors for LD have been identified, including anti-TNFα therapy. TNFα is a major cytokine that regulates the inflammatory process. In this study, we have evaluated the ability of various clinical isolates to modulate TNFα secretion from macrophage to better understand the impact of strain variability in LD inflammatory response.

Materials/methods: We challenged the human macrophage-like cell line U937 with a cohort of 108 Lp1 clinical strains belonging to 40 STs for TNFα secretion and intracellular multiplication capability. Lactate dehydrogenase (LDH) and caspase-3 assays were used to evaluate necrosis and apoptosis, respectively. We have established a double-staining technique to detect simultaneously L. pneumophila and TNFα on the single-cell level by flow cytometry.

Results: Lp1 isolates induce differential TNFα secretion from macrophages. The number of colony-forming units indicated that this differential TNFα secretion is not associated with a differential growth of Lp1 isolates in macrophages. Interestingly, we observed that ST1 isolates induced significantly more TNFα secretion than the others STs meaningfully involved in LD, such as ST20, ST23, ST40, ST47 and ST146. Since it has been recently suggested that TNFα was mainly produced by uninfected cells rather than by infected macrophages, we evaluated these populations by flow cytometry. Surprisingly, we observed that both infected and uninfected macrophages produce TNFα during infection with all Lp1 isolates. Finally, we showed that macrophages infected by ST1 strains display a significant increase of LDH release and caspase-3 activation compared to macrophages infected by other strains whereas treatment of macrophages with antibody against TNFα reversed these effects.

Conclusions: TNFα secretion by human macrophages is dependent of the ST of Legionella isolates. The observation that ST1 strains induce a more efficient host immune response could explain the high prevalence of these strains for immunocompromised patients.

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Abstract 9106

Characterisation of mcr-5 action suggests a unified mechanism for polymyxin resistance
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Background: A growing number of mobile colistin resistance (MCR) proteins is threatening the renewed interest of colistin as a “last-resort” defense against carbapenem-resistant pathogens.

Materials/methods: Whole-genome sequencing was used to elucidate a mcr-5-harboring plasmid, phylogenetic tree was applied to give its evolutionary place, and integrated biochemical assays were conducted to address its enzymatic action.

Results: Here, the comparative genomics of a large plasmid harboring mcr-5 from Aeromonas hydrophila and the structural/functional perspectives of MCR-5 action are reported. Whole genome sequencing has identified the loss of certain parts of the Tn3-type transposon typically associated with mcr-5, providing a clue toward its mobilization. Phylogeny of MCR-5 suggests that it is distinct from the MCR-1/2 sub-lineage, but might share a common ancestor of MCR-3/4. Domain-swapping analysis of MCR-5 elucidates that its two structural motifs (transmembrane domain and catalytic domain) are incompatible with its counterparts in MCR-1/2. Like the rest of the MCR family, MCR-5 exhibits a series of conservative features, including zinc-dependent active sites, phosphatidylethanolamine-binding cavity, and the mechanism of enzymatic action. In vitro and in vivo evidence that MCR-5 catalyzes the addition of phospho-ethanolamine to the suggestive 4′-phosphate of lipid A moieties is integrated, and results in the consequent polymyxin resistance. In addition, MCR-5 alleviates the colistin-induced formation of reactive oxygen species in E. coli.

Conclusions: Taken together, the finding suggests that a growing body of MCR family resistance enzymes are functionally unified.

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Abstract 9107


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Background: Carbapenemase-producing Enterobacterales (CPE) have been listed as a critical priority problem by the WHO. The Spanish study CARBA-ES-19 aims to provide data on the current situation of the most important CPE (Klebsiella pneumoniae and Escherichia coli) in Spain.

Materials/methods: From February 2019 to May 2019, 72 hospitals representing all 50 Spanish provinces collected the first ten non-duplicate K. pneumoniae or E. coli using the screening cutoff for CPE recommended by EUCAST. Carbapenemase characterization was performed by phenotypic methods and confirmed by PCR. Participating hospitals also registered the number of infections caused by K. pneumoniae and E. coli and the number of admissions/patients-day to calculate the prevalence and incidence rates of CPE.

Results: 408 CPE (382 K. pneumoniae and 26 E. coli) were collected. The carbapenemases detected in K. pneumoniae were OXA-48-like (268; 70.2%), KPC (76; 19.9%), VIM (29; 76.9%), NDM (14; 37%), and IMP (1; 0.3%). In E. coli were OXA-48-like (20; 76.9%), VIM (4; 15.4%), KPC (2; 7.7%) and NDM (1; 3.9%). Six K. pneumoniae and one E. coli isolates produced two types of carbapenemases. The overall prevalences of carbapenemase-producing K. pneumoniae and E. coli were 2.6% (range, 0 to 19.2%) and 0.05% (range, 0 to 0.4%), respectively. The overall incidence rate and incidence density rate of CPE were 0.04% (range, 0 to 0.7%) and 0.08% (range, 0 to 1.02%), respectively. At least one case of CPE was identified at 63 (87.5%) hospitals, which were located in 46 of the 50 (92%) Spanish provinces. OXA-48 was the most widely distributed carbapenemase in 41 provinces, followed by VIM in 18, KPC in 14, NDM in 7 and IMP in one. Of the 408 CPE, 220 (53.9%) were collected from urine and 53 (13%) from blood samples. Prevalences of carbapenemase-producing K. pneumoniae and E. coli from urine were 1.4% and 0.02%, respectively; and from blood were 5.9% and 0.02%, respectively.

Conclusions: We found a wide geographic distribution of CPE with > 90% of the Spanish provinces affected, but also a great geographic variability in the incidence of CPE and in the carbapenemases types.

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Abstract 9109

Conservation in p24 capsid protein regions in HIV-1 groups M, O, P and N
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Background: HIV p24 capsid protein has an essential structural and functional role in the viral cycle. This highly conserved protein is considered genetically fragile, as changes in its sequence reduce viral fitness. P24 is an interesting target for the design of vaccines, diagnostic tests and new antiretroviral drugs against HIV. This study analyzes, for the first time, the conservation of each p24 secondary structure regions in HIV-1 M, O, P and N groups.

Materials/methods: All p24 sequences ascribed to the 4 HIV-1 groups were downloaded from the US Los Alamos-HIV-Sequence-Database, including subtypes, sub-subtypes and CRF from group M with >3 available sequences. Using a bioinformatics tool developed in our laboratory, we inferred consensus sequences for each group and a consensus consensus for HIV-1 at amino acid level. Then, we analyzed residue conservation in each region of the N-terminal (ß strand, Cyp-A loop and α-helixes 1-7) and C-terminal Domains (Inter-Domain Region [IDR] and α-helixes 8-11 including the Major Homology Region [MHR]), as described in RCSB Protein Data Bank.

Results: We downloaded all 38,827 available p24 sequences of 99 variants of group M (8 subtypes, 7 sub-subtypes and 84 CRF), 104 of group O, 4 of P and 11 of N. Although the overall structure of p24 was highly conserved, conservation of certain regions differed within groups and type of structure. Figure 1 describes the different level of conservation of p24 regions in each group (A) and median conservation for each region (B) within HIV-1. The most conserved regions were α-helixes 1, 2 and 5, followed by α-helixes 11, 7, 8 and MHR and α-helixes 4, 3, 9, 10 and the IDR. The less conserved were ß strand, α-helix 6 and Cyp-A loop (90-93%). Previous studies based in group M stated that α-helixes were the most fragile regions; we observed intermediate or low conservation of some helixes when considering all variants. Discrepancies were reduced when analyzing only group M sequences.

Conclusions: Since p24 genetic variability can impact on new diagnostic and therapeutic methods based on this protein, conservation studies must always consider all circulating HIV-1 variants worldwide for correct analysis.
Abstracts 2020

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Abstract 9112

Presence of carbapenem- and colistin-resistant Gram-negative bacteria in illegally imported foods to Europe
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Background: The emergence of antimicrobial resistant (AMR) bacteria in food-producing animals has provoked a great concern in the presence of AMR bacteria in associated foodstuff. Likewise, enforced mobility of people has become a major issue in the recent years. A strong intra-European transmigration has become a matter for mobility systems due to million of employees living or working outside their home countries. However, little information is available on the rate of AMR bacteria importation via contaminated illegal food, consequently, defining a neglected route of transmission.

Materials/methods: A total of 170 animal-originated foods (meat and dairy samples) recalled from travellers’ luggage at the International Bilbao airport (Spain) were taken and analysed for the presence of carbapenem- and colistin- enterobacteriaceae. Samples of 25 g were 1:10 diluted in buffered peptone water and incubated at 37°C for 24 hours, and streaked on selective agar media for testing carbapenem (Brilliance CRE, Oxoid) and colistin (CHROMID Colistin R, bioMerieux) resistance. Colonies grown in the respective media were identified using MALDI TOF Biotyper (Bruker Daltonics) and an antimicrobial sensitivity test was performed using MICROSCAN (Beckman Coulter). Further confirmation of the nature of the resistance mechanisms was performed using specific PCRs, and a set of the isolates were submitted to Whole Genome Sequencing.

Results: Fourteen (8.2%), eight (4.7%) and four (2.4%) food samples contained isolates tested resistant to colistin, carbapenems and resistance to the two families of antibiotics, respectively. In addition, 2 extra food samples possessed isolates with intermediate resistance two carbapenems which were also resistant to colistin. Most of the isolates belong to the order Enterobacterales, mainly to the families Enterobacteriaceae, Hafniaceae, Yersiniaceae and Morganellaceae, and to the order Xanthomonadales.

Conclusions: This study shows the presence of enterotoxigenic carbapenem- and colistin- resistant Gram negative in foods illegally entering the EU, and highlights illegal importation of food as route of AMR spread. Several of the bacterial species with resistant to one or both antibiotic families are known nosocomial agents [eg. Stenotrophomonas maltophilia, Hafnia or Serratia]. Consequently Uncontrolled entry of food stuffs into the EU can be a relevant neglected route of AMR dissemination.

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Abstract 9114

**Therapeutic response of meropenem and azithromycin in the treatment of extensively drug-resistant (XDR) typhoid fever in a lower-middle income country**

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**Background:** *Salmonella Typhi* is one of the leading causes of bacterial illnesses in Pakistan. With the emergence of extensively drug resistant (XDR) *Salmonella Typhi*, treatment options are limited. Here we report the clinical manifestations and the response to treatment with meropenem and azithromycin either alone or in combination for the treatment of patients with XDR Typhoid during an outbreak setting in Pakistan.

**Materials/methods:** We reviewed the records of culture confirmed XDR typhoid patients – both inpatient and outpatient - who visited Aga Khan University Hospital (AKUH), Karachi and Aga Khan Secondary Care Hospital, Hyderabad during April 2017 to June 2018. Frequency of clinical symptoms at presentation, relapse of disease, unplanned treatment extension and complications developed while on antimicrobials was recorded. Means with standard deviation were calculated for duration of treatment, time to defervescence, and cost of treatment.

**Results:** Records of 60 culture confirmed XDR typhoid patients admitted at the AKU hospitals were reviewed. Most, (n=33; 55%) were male. Mean age of the cases was 9.63 ± 1.22 years. About three quarter (n=45) of the patients were treated as inpatient. Fever and vomiting were the most common (n=47; 78% each) symptoms at the time of presentation. Oral azithromycin alone (n=20; 33%), intravenous meropenem alone (n=10; 17%), or a combination of azithromycin and meropenem (n=30; 50%) were the options used for treatment. Average [95% confidence interval] time to defervescence was 7.5(5.7-9.3), 5.3(2.6-8.0), and 7.0(5.6-8.4) days for each treatment option respectively whereas there were 2, 1 and 2 treatment failures in each treatment option respectively. There was no significant difference in time to defervescence (p=0.330) across the groups. Cost of treatment per day for azithromycin was US$0.14 whereas it was US$42.95 for meropenem.

**Conclusions:** Azithromycin, meropenem alone or in combination are the only treatment options for XDR Typhoid. Time to defervescence and treatment failure were similar across groups. Clinical trials are needed for more robust evidence.

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Levonadifloxacin (WCK 771), a recently approved benzoquinolizine fluoroquinolone exhibits potent in vitro activity against methicillin- and quinolone-resistant Staphylococcus aureus: a report from Indian tertiary care hospital

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Background: Staphylococcus aureus is a clinically challenging pathogen due to its virulence and multiplicity of antibiotic resistance mechanisms. Levonadifloxacin (WCK 771) is a broad-spectrum benzoquinolizine fluoroquinolone with well-differentiated mechanism of action (primary target - DNA gyrase) driven potent activity against methicillin resistant/quinolone-resistant S. aureus (MRSA/QRSA). Levonadifloxacin and its prodrug alalevonadifloxacin (WCK 2349) have recently received regulatory approval in India for the indication of acute bacterial skin and skin structure infections (ABSSSIs) with concurrent bacteremia and diabetic foot infections. As levonadifloxacin would be available soon for clinical use in India, the present study was undertaken to evaluate the in-vitro activity of levonadifloxacin against recent S. aureus isolates collected from a large tertiary care hospital located in South India.

Materials/methods: Recent (2018-2019) non duplicate S. aureus (n= 662) cultures were isolated from the pus, respiratory specimens and blood collected from various units of Christian Medical College and Hospital, Vellore. Species identification and MRSA characterization were undertaken employing MALDI-TOF and cefoxitin disks, respectively. The minimum inhibitory concentrations [MIC] of levonadifloxacin and comparator drugs viz., levofloxacin, vancomycin, teicoplanin, linezolid, erythromycin, clindamycin and co-trimazole were determined using CLSI recommended broth micro-dilution method (BMD). Mutations in the quinolone resistance determining region (QRDR) were identified using whole genome sequencing.

Results: Among 662 isolates, methicillin susceptible (MSSA) and MRSA were 49% (n= 325) and 51% (n=337), respectively. Levonadifloxacin inhibited 96.4% and 99.4% of all tested isolates at 0.5 mg/L and 1 mg/L, respectively. Levonadifloxacin retained potent activity against QRSA and MRSA isolates (MIC90 of 0.5 mg/L) with 16 times lower MICs than levofloxacin. The genomic analysis of QRDR regions in 17 QRSA (levonadifloxacin MIC: 0.25 - 2 mg/L) revealed double mutations, gyrA S84L, parC S80F (n = 8); and gyrA S84L, parC S80Y (n = 9). All the isolates were susceptible to vancomycin and linezolid.

Conclusions: In conjunction with several clinically relevant favourable features such as bactericidal action, class-leading lung concentrations, freedom from monitoring safety parameters and oral option, the potent activity against contemporary MDR S. aureus isolates revealed in this study supports levonadifloxacin’s clinical use for serious MRSA infections as potentially a new standard of care.

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Abstract 9116

Four-year experience of carbapenem-resistant Acinetobacter baumannii in a Spanish tertiary hospital: the threat still exists?

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Background: In the era of the difficult-to-treat Enterobacterales infections, other multidrug-resistant bacteria, such as Acinetobacter baumannii, seem to have disappeared; but A. baumannii is a pathogen with high morbidity and mortality in some settings, especially in the intensive care unit (ICU). The aim of the study is to describe the epidemiological, demographic and molecular characteristics of carbapenem resistant A. baumannii clinical (CRAB) isolates in a 500-bed Spanish tertiary hospital in the last 4 years.

Materials/methods: We performed a retrospective study of all clinical samples with an isolate of A. baumannii between January 2016 and October 2019. The microorganisms were identified by MALDI-TOF mass spectrometry (Bruker®) and the antimicrobial sensitivity was obtained by MicroScan WalkAway (Beckman Coulter®). The characterization of carbapenemases was evaluated in 53 CRAB isolates by using the Eazyplex® SuperBug Complete A (Amplex) according to manufacturer’s instructions, which detects KPC, NDM, OXA-48, VIM, OXA-23, OXA-40 and OXA-58.

Results: 492 (83%) out of 595 A. baumannii isolates from 228 patients (67% men – 33% women) were CRAB, with a median age of 69 years old (15-98). 20% of the total were found in 2016, 34% in 2017, 39% in 2018 and 7% in 2019. The more frequent CRAB isolates were from respiratory tract infections (37%), urinary infections (23.4%) and bacteremia (18.6%). There were also 2 CRAB isolates in the cerebrospinal fluid. Half (52%) of the infected patients were previously colonized. The distribution by type of carbapenemase was: 15.2% OXA-23, 68.6% OXA-40 and 16.2% co-production OXA-23 and OXA-40. By hospitalization wards, the number of CRAB isolates was significantly higher in the intensive care unit (43.3%) followed by internal medicine and the emergency ward with 11.5% and 11%, respectively.

Conclusions: 1) CRAB isolates in our setting still be a problem, mostly affecting men aged >65 years; however in 2019 there is a decrease. 2) CRAB in ICU is significantly higher than other hospital wards, probably associated with the use of invasive devices and prolonged stays. 3) The most frequent CRAB isolates corresponded to respiratory tract infections. 4) Interestingly, a high percentage of carbapenemase OXA-40 is observed in CRAB isolates and no NDM carrier has been found.

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Cotrimoxazole in bone and joint infections is the “old” antibiotic still relevant
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Background: Cotrimoxazole (trimethoprim-sulfamethoxazole) has shown an effectiveness in the management of staphylococcal infections of osteosynthesis devices and joint prostheses. In recent years, an increase in resistance of Gram-negative bacteria has been reported worldwide. Furthermore, bone and joint infections may be often polymicrobial. In this study, we studied the effectiveness of high oral doses of cotrimoxazole on a broad spectrum of microorganisms.

Materials/methods: We included in a single-center, a retrospective study of 129 patients who started curative treatment during hospitalization with a high-dose cotrimoxazole orally alone or combined with another anti-infective agent from January 1, 2013 and who stopped treatment before the December 31, 2017 for any documented osteoarticular infection with or without equipment of the limbs or spine. We evaluated the efficacy defined as the absence of relapse at one year after discontinuation of antibiotic therapy. We also assessed tolerability and treatment-related adverse events.

Results: Of these 129 patients, 31.8% (41) had an adverse effect on treatment requiring early or late cessation and 21.7% (28) were lost before the end of one year of follow-up. Sixty cases were fully treated and the overall efficacy of treatment was 60.0% (36 of 60 patients). The polymicrobial infection rate was 61.7% (37/60). 55.6% of patients were cured (15 of 27 patients) in Staphylococcus aureus infections, 58.8% (10/17) in coagulase-negative staphylococcus infections and 60.5% (26/43) in enterobacteria infections.

Conclusions: The results of the present study confirm that oral high-dose cotrimoxazole can be an interesting alternative for the oral treatment of osteoarticular infections. Its effectiveness is now proven not only for multi-resistant staphylococcal infections but also for GNB and polymicrobial infections. We suggest that cotrimoxazole can be used in complex polymicrobial or multiresistant Gram-negative infections with devices and may have an interest in the management of open fractures. “Old” cotrimoxazole remains an interesting weapon, not only for staphylococcus, but also for gram-negative bacteria and polymicrobial bone and joint infections. Nevertheless, treatment with cotrimoxazole is frequently complicated by adverse effects and needs to be carefully monitored.

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Screening and characterisation of multidrug-resistant Enterobacteriaceae in healthy companion animals in close contact with humans

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Background: The role of companion animals as potential sources and reservoirs of antimicrobial resistant bacteria represent growing concerns worldwide. The aim of this study was to evaluate the presence of extended-spectrum β-lactamases (ESBL) and Carbapenemase-producing Enterobacteriaceae or Acinetobacter spp. as well as Methicillin-Resistant Staphylococcus aureus (MRSA) bacteria faecal carriage in healthy companion animals (CAs) in close contact with humans.

Materials/methods: Between January 2016 and October 2019, 79 healthy companion animals (54 dogs and 25 cats) living in close contact with humans in 54 households, were enrolled in this study. The pet owners were informed of the procedures and conducted the fecal sample collection from their companion animals with sterile gloves, containers and plastic bags. Informed consent was obtained. Fecal samples were inoculated on MacConkey agar plates containing 1.5µg/mL cefotaxime, 1.0 µg/mL meropenem, CHROMagar Acinetobacter, CHROMID® OXA-48 plates and Oxoid™ Brilliance™ MRSA (Thermo Fisher Scientific). Beta-lactam genes were screened by PCR and sequencing. The species identification was performed PCR. Susceptibility tests were performed by microdilution with MicroScan® Neg MIC Panel Type 44 (Siemens, Sacramento, CA, US), and results interpreted according to EUCAST.

Results: Third-generation cephalosporin-resistant Enterobacteriaceae were detected in 9.3% of the dogs (n=5/54) and in 4% of the cats (n=1/25). In dogs, among these 3CG-resistant Enterobacteriaceae: i) one Escherichia coli was positive for the blaCTX-M-15 gene, with resistance to fluoroquinolones, sulfamethoxazole/trimethoprim, penicillins and aminoglycosides; ii) other carried a blaCMY-2 gene, with the corresponding phenotype of resistance; iii) other multidrug-resistant E. coli harbored the blaCTX-M-79 + blaCMY-2 genes; iv) an E. coli harbored the blaCMY-2 + blaTEM-32 genes; v) one multidrug-resistant Klebsiella pneumoniae was simultaneously positive for the blaCTX-M-15 + blaTEM-1 + blaSHV-110 genes. Among cats, only one 3CG-resistant Enterobacteriaceae harbored the blaCTX-M-15 + blaCMY-2 genes. In both groups of CAs neither carbapenemase-resistant Enterobacteriaceae/Acinetobacter spp. nor MRSA were detected.

Conclusions: The isolation of multidrug-resistant Enterobacteriaceae in healthy companion animals is an emerging problem and dissemination of resistant bacteria through fecal contamination of the environment should not be neglected and is a concern towards animal and human health.

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Abstract 9123

Impact of non-use of levofloxacin prophylaxis during neutropaenia on reduction of resistance among Gram-negatives causing bloodstream infection in haematopoietic stem cell transplantation patients: very successful preliminary data

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Background: Universal prophylaxis with quinolones is a strategy used by several centers to reduce the febrile episodes and bloodstream infections (BSI) during the period of neutropenia in hematopoietic stem cell transplantation (HSCT) patients. This strategy can lead to selection of resistant bacteria and it has been associated with increase of resistance among gram-negative bacilli (GNB) all over the world. So we evaluate the impact of non-use of universal levofloxacin prophylaxis during neutropenia on the reduction of antibiotic-resistance in GNB causing BSI in HSCT patients.

Materials/methods: Quasi-experimental study of before (2016-2018) and after (2019) to assess the density of incidence (DI) of BSI using two denominators: patients-day and neutropenia-day; the profile and susceptibility of microorganisms causing BSI in HSCT patients at HC-FMUSP, Brazil. We compared DI of BSI related to central venous catheter (CVC-BSI) from January 2016 to June of 2019 as well as mucosal barrier injury (MBL-BSI) from 2018 to 2019. In December 2018, we stopped the levofloxacin prophylaxis during the neutropenia period in our Bone Marrow Transplantation Unit. Statistical analysis was performed using Epi-Info version 7 from CDC.

Results: A total of 297 HSCT were performed during the study-period. The CVC-BSI DI in 2016, 2017, 2018 and 2019, were respectively: 4.6; 1.4; 0.6 and 6.3 BSI/1000 patients-day. In 2018 and 2019, MBL-BSI DI was 13.8 and 26.4 BSI/1000 neutropenia-day. The profile of microorganisms causing BSI in 2017-2018 and 2019 were respectively 11/22 (50%) and 20/35 (57.1%) of GNB, being 6/11 (54.5%) and 0/20 carbapenem-resistant (p=0.005). In 2019, only 2/20 (10%) GNB causing BSI was ESBL-producing and all others were susceptible to third generation cephalosporin. Regarding mortality, only one death occurred due to MBL-BSI caused by K. pneumoniae ESBL producer.

Conclusions: Although, the suspension of the use of quinolones as prophylaxis lead to an increase of MBL-BSI as expected, our data showed a significant reduction of resistance among GNB causing BSI with only one death. Nowadays we are able to handle fast progressing BSI using third generation cephalosporin. Thus, non-use of levofloxacin prophylaxis during neutropenia had important impact on reducing resistance among GNB and appears to be a safe strategy.

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Abstract 9125

**Nosocomial influenza**

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**Background:** Nosocomial influenza is associated with substantial morbidity and a mortality of 9-16% in partly historic reports. Hospital outbreaks are not uncommon but are likely substantially under-reported. The proportion of nosocomial infections among patients hospitalized for influenza in a few studies has varied from 4-20%. This may be explained by regional differences in transmission rate but may also depend upon diverse properties of dominating influenza strains during different seasons. We performed a retrospective study of hospitalized influenza patients during five seasons to determine mortality in patients with nosocomial infections, and also to investigate if influenza subtypes correlated with the proportion of nosocomial infections and hospital outbreaks.

**Materials/methods:** Influenza-PCR positive adult patients (>18 years), hospitalized in Skåne County, Sweden, during 2013-2018, were evaluated retrospectively. Medical records were examined to identify nosocomial infections, 30-day mortality, and influenza subtypes. Nosocomial infection was defined as an influenza-PCR positive hospitalized patient who had developed symptoms indicative of influenza ≥ 3 days after hospital admission, and who had no prior signs of infectious respiratory disease and/or unexplained fever. Influenza subtypes were available from the Medical Microbiology Department, Skane University Hospital.

**Results:** Out of 3466 hospitalized influenza patients, 358 (10%) were nosocomial infections. The proportion of nosocomial infections varied between seasons (3-22%). In total, 236 (15%) of H3N2, 34 (5%) of H1N1, and 87 (7%) of influenza B infections were nosocomial (p < 0.0001). A total of 60 clusters were identified. Clustered cases were more common for H3N2 (72%) than for H1N1 (38%) and influenza B (36%). Mortality in nosocomial influenza was 8%, did not differ between subtypes, and was similar to hospitalized non-nosocomial influenza cases. Mortality in H3N2 nosocomial infection was associated with higher age (87 years) as compared to influenza B (76 years) and H1N1 (67 years).

**Conclusions:** In our evaluation over 5 influenza seasons, influenza H3N2 cases were responsible for a majority of nosocomial infections, often as a part of clustering. Elderly hospitalized patients may be specifically vulnerable to nosocomial influenza H3N2 infection. Mortality in nosocomial influenza was lower than previously reported and similar to non-nosocomial influenza.

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A home humidifier responsible for Legionnaires’ disease: input of WGS for genomic investigation in a ST1 case

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Background: The L. pneumophila ST1 clone has been shown to colonize hospital water networks worldwide and to be often implicated in nosocomial Legionnaires’ disease (LD) cases. Here, we evaluated the contribution of Whole Genome Sequencing (WGS) for resolving investigation of a 60-year-old woman ST1 LD case after a 14-day hospitalization for a pulmonary pre-transplant evaluation.

Materials/methods: To investigate this case, sputum was cultured and the potential sources of exposure, i.e. hot water from shower and washbasin of the 2 rooms attended by the patient, were cultured according to NF T90-431 standard. The history revealed the use of a home humidifier filled with tap water from her home, which she had kept over her hospitalization period; the patient claimed that she had not used hospital tap water in this humidifier while hospitalized. The tank water that had not been thrown at the time of LD diagnosis was cultured.

Results: The sputum grew L. pneumophila serogroup 1 (Lp1). The 4 hospital water samples tested negative for L. pneumophila (< 10 CFU/L), as all samples that had been tested coincidentally at the time of the onset of symptoms and for 2 years on the building water network (hot water outlet and return, and points of use). The water of the humidifier tank grew Lp1 (300 CFU/L). The clinical and environmental strains were analysed by Sequence-Based Typing; both were ST1 strains. We could not formally conclude on the source of infection as ST1 strains are widespread and account for 10% of LD cases. The strains analysis was thus complemented by WGS, the mapping of sequence reads and phylogenetic analyses being performed as described by David et al. (CID, 2017). They showed a same common ancestor, with no SNP.

Conclusions: We report a health-care associated ST1 LD case related to use of a domestic humidifier filled with patient’s home water before hospitalization. Such sources have been rarely described so far (n=4), and the increasing use of aerosolizing devices would require special attention when investigating LD cases. Combined with medical history and epidemiological data, WGS was determinant to resolve the investigation.

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Abstracts 2020

Abstract 9131

Carbapenemase-producing *Klebsiella pneumoniae* belonging to sequence type 23 is a predictor of poor outcome in haematological patients

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**Background:** The aim of this study was to compare bloodstream infections (BSI) caused by carbapenemase-producing *K. pneumoniae* belonging to sequence types [ST] 23 and ST395 in haematological patients.

**Materials/methods:** Prospective study (2014-2019) included haematological patients with BSIs caused by carbapenemase-producing *K. pneumoniae*. Carbapenemase genes (*bla*OXA-48*,* *bla*KPC*, *bla*VIM*, *bla*NDM and *bla*IMP) and virulence genes (*iucA*, *rm-pA*, *rmpA2*) were tested by PCR. Multiplex PCR was performed to detect K1,K2,K5,K20,K54 and K57 serotype-specific alleles. Multilocus sequence typing (MLST) was performed according to the protocol described in Institut Pasteur MLST on a website ([http://bigsdb.pasteur.fr/klebsiella/primers_used.html](http://bigsdb.pasteur.fr/klebsiella/primers_used.html)).

**Results:** During the study period 39 patients had BSI caused by carbapenemase-producing *K. pneumoniae*, of them 14 (36%) of isolates belonged to ST23 (*K. pneumoniae*-ST23), 13 (33%)–to ST395 (*K. pneumoniae*-ST395), 4 (10%)–to ST377, 3 (8%)–to ST512 and each one to ST13, ST11, ST874. The majority of isolates harbored *bla*OXA-48* (90%), followed by *bla*OXA-48+, *bla*NDM and *bla*KPC (5% each). Outcome of infections caused by *K. pneumoniae* belonging to the predominant STs such as ST23 (n=14) and ST395 (n=13) was evaluated, all isolates (n=27) harbored *bla*OXA-48. There were no differences in age (48 vs 56 years), underlying disease and phase of therapy, neutropenia and its duration. Infections caused by *K. pneumoniae*-ST23 and *K. pneumoniae*-ST395 were presented as BSI (57% vs 77%), BSI+pneumonia (29% vs 23%), BSI+pneumonia+meningitis (1.4% vs 0%). Capsular type K57 was detected in all *K. pneumoniae*-ST23 compared to *K. pneumoniae*-ST395 (100% vs 0%, p<0.0001), whereas capsular type K2 was associated with *K. pneumoniae*-ST395 (38% vs 0%, p<0.01). Virulence genes were detected more often among *K. pneumoniae*-ST23 (93% vs 46%, p=0.01). Septic shock, vasopressor administration and higher Pitt bacteremia score were statistically significantly associated with BSIs caused by carbapenemase-producing *K. pneumoniae*-ST23 (p<0.05). Overall 30-day survival was lower (p=0.04) among patients with infections caused by *K. pneumoniae*-ST23 compared to *K. pneumoniae*-ST395 (61.5% vs 21%), especially in presence of virulence genes (67% vs 15%) (figure a,b).

**Conclusions:** *K. pneumoniae*-ST23 was associated with capsular type K57 and virulence genes. Septic shock, vasopressor administration and higher Pitt bacteremia score were significantly associated with BSIs caused by *K. pneumoniae*-ST23. The main predictor of poor outcome in patients with BSI caused by carbapenemase-producing *K. pneumoniae* was affiliation to ST23.

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Abstracts 2020

Abstract 9132

Aminoglycoside resistance mechanisms in invasive Klebsiella pneumoniae and Escherichia coli: a threat of rmtC mediated resistance

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Background: Aminoglycosides (Ags) are often used in combination with other antibiotics and provide a valuable therapeutic option for treating multidrug resistant bacterial infections. Aminoglycoside resistance (AgR) due to 16S ribosomal methyltransferases (RMTs) seems to emerge as real threat that limit the use of these antibiotics for salvage therapy. In this study, we aimed to investigate genetic determinants of RMTs together with aminoglycoside modification enzymes (AgMEs) in invasive Klebsiella pneumoniae and Escherichia coli.

Materials/methods: Fifty K. pneumoniae and 49 E. coli, isolated throughout the year 2016 and exhibited resistance to at least amikacin or gentamicin in routine susceptibility testing (VITEK® 2 Compact, BioMérieux, France) were included in the study. Amikacin, gentamicin, tobramycin, and netilmicin MICs of the isolates were determined by standard broth microdilution method (BMD) in the study isolates. Genetic determinants of RMTs [armA, rmtA, rmtB, rmtC, rmtD, rmtE, rmtF, rmtG, npmA] and AgMEs [aac(3)-II, aac(3)-I, aac(6’)-Ib, ant(2’’)-I] were investigated by PCR.

Results: Twelve of 50 (24%) K. pneumoniae isolates exhibited high level resistance (>256 mg/L) to all Ags tested in BMD. High level aminoglycoside resistance was not detected in any of the E. coli isolates. rmtC was the most common (13/50) RMT gene followed by armA (2/50) in K. pneumoniae (Table 1). aac(3)-II was found together with aac(6’)-Ib in 64% of K. pneumoniae and 32.7% of E. coli isolates.

Conclusions: rmtC encoded high level aminoglycoside resistance seems to be a threat in K. pneumoniae in our hospital, especially considering high risk of multidrug resistance in such isolates.

Table 1. Distribution of aminoglycoside resistance genes in Klebsiella pneumoniae and Escherichia coli isolates exhibiting resistance to amikacin and/or gentamicin

<table>
<thead>
<tr>
<th>AgR genes</th>
<th>K. pneumoniae</th>
<th>E. coli</th>
</tr>
</thead>
<tbody>
<tr>
<td>aac(3)-II</td>
<td>9 (18)</td>
<td>23 (46.9)</td>
</tr>
<tr>
<td>aac(3)-II + rmtC</td>
<td>1 (2)</td>
<td>0</td>
</tr>
<tr>
<td>aac(6’)-Ib</td>
<td>4 (8)</td>
<td>9 (18.4)</td>
</tr>
<tr>
<td>aac(6’)-Ib + rmtC</td>
<td>3 (6)</td>
<td>0</td>
</tr>
<tr>
<td>aac(3)-II + aac(6’)-Ib</td>
<td>20 (40)</td>
<td>15 (30.6)</td>
</tr>
<tr>
<td>aac(3)-II + aac(6’)-Ib + rmtC</td>
<td>9 (18)</td>
<td>0</td>
</tr>
<tr>
<td>aac(3)-II + aac(6’)-Ib + armA</td>
<td>2 (4)</td>
<td>0</td>
</tr>
<tr>
<td>aac(3)-II + ant(2’’)-I</td>
<td>1 (2)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>aac(3)-II + aac(6’)-Ib + ant(2’’)-I</td>
<td>1 (2)</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

*AgR, aminoglycoside resistance

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Abstract 9133

**Risk factors for epilepsy and cysticercosis in Abidjan, Ivory Coast: a case-control study**

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**Background:** Cysticercosis is due to the larva of the *Taenia solium* human tape worm. Seizures are the main clinical symptoms of the disease, and WHO considers this disease as one of the main causes of epilepsy in tropical countries. The aim of this study was to analyze the association between cysticercosis and epilepsy in Abidjan.

**Materials/methods:** A case control study was conducted including patients suffering from epilepsy and attending the neurology clinic of the three main hospitals of the town, and age-matched patients attending dispensaries of the same area, without neurological symptoms. Data related to socio-cultural and nutritional habits were collected as well information on the household and its environmental context. All the patients were blood sampled and cysticercosis specific serology was done using Tsang et al methods. Variable comparisons were conducted using Mac Nemar, Student or Wilcoxon matched tests when relevant. Conditional logistic regression model was built.

**Results:** Overall, 226 epileptics and 226 age-matched non-epileptic patients were included. Epileptics were more often males (69% vs. 55%; p=0.001), without professional occupation (21% vs. 9%; p=0.005). Presence of pigs in the surrounding was more frequent for epileptics (5% vs. 1%; p=0.019), as well as a poorer environmental setting of the household with open air defecation (5% vs. 0%, p=0.001) and no facilities for waste water elimination (39% vs. 28%, p=0.020). However, no significant difference was found between the two groups for cysticercosis positive serology (8.41% vs. 4.42%, p=0.13). Multicomponent analysis confirmed that factors related to epilepsy were the gender, the family status, the professional employment and the area of residence.

**Conclusions:** This study didn't support association of epilepsy and cysticercosis in the urban setting of Abidjan. The main factors associated with the disease in comparison with the control group are related to the way of life of the epileptic which could be either related to risk factors for other infectious diseases (toxoplasmosis, schistosomiasis etc) or to a social exclusion of these patients.

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Abstract 9134

Laboratory diagnosis and circulation of respiratory syncytial virus (A and B subgroups) and influenza virus A (H1 and H3 subtypes) and B in a three-winter season (2016-17 to 2018-19) hospital-based survey in northern Italy

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Background: Respiratory syncytial virus (RSV), Influenza A (IAV) and B (IBV) virus are among the leading causes of viral upper and lower respiratory infections and a significant cause of hospitalization and even death in ‘at-risk’ individuals, such as children and older adults.

We analysed a three-winter seasonal circulation of RSV (A and B subgroups), IAV (H1 and H3 subtypes) and IBV in the population with influenza-like illness (ILI) attending to the University Hospital of Parma, Italy.

Materials/methods: Respiratory samples (n=2066), collected in three winter seasons (December 2016-March 2019) from 1875 patients with ILI, were analyzed by conventional and molecular methods for viral detection and subtyping at the Virology Unit of the University Hospital of Parma, Italy.

Results: Among the 810 RSV and/or IV positive samples, 22.8% were RSV A, 34.9% RSV B, 34.8% IAV and 7.4% IBV. As to RSV subgroups, RSV A prevailed in 2016/2017, and was reversed by RSV B in the last two seasons. RSV was identified in children ranged from 1 month to 1 year and in elderly (>50 years). Concerning IV, all the epidemic seasons were characterized by the prevalence of IAV; IAV-H3 dominated in 2016/17, while all samples resulted positive for IAV-H1 in 2017/2018; finally, both subtypes co-circulated in the 2018/19. As regards IBV circulation, a significant increase of IBV was detected only in the 2017/2018, vs a negligible number of cases in the 2016/2017 and no cases in the 2018/2019 winter seasons. Both IAV and IBV infections were most prevalent among children ranged from 1 to 6 years and ≥ 50 year-old adults.

Conclusions: This study represents a useful tool for the surveillance of viral infectious agent circulation and variability, as the considered population is mostly represented by hospitalized pediatric and elderly patients who more often can develop adverse events upon RSV or IV infection.

Remarkably, RSV A responsible for the most severe clinical pictures in infants was reversed by RSV B in the two last winter seasons, possibly related to new genetic variants.

Also of interest, IBV peaked only in 2017/18, according to the European Centre for Disease Prevention and Control data.

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Modulation of toll-like receptors and interferons signalling pathways by sub lethal dose of scopolamine gives protection from Japanese encephalitis virus infection in embryonated chick model

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Background: Japanese encephalitis (JE) has become a global health concern due to specific antiviral therapy and thus demands new potential strategies to combat the disease. Toll like receptors and Interferon mediated intracellular signalling plays a pivotal role in the initiation of innate immune response via induction of interferons (IFNs) controlling the viral replication and subsequent severity of the infection. The study was conducted to evaluate the effect of Scopolamine, an active component of *Atropa Belladonna* plant in controlling JE virus infection in chick embryo, which is already an established model for study of host pathogen interactions and screening of antiviral agents.

Materials/methods: In our study twelve day old embryos were pre-treated with Scopolamine to investigate whether it can give protection from JE virus infection and subsequent pathogenicity. Total RNA from Chorioallantoic membrane (CAM), Brain and Amniotic fluid were extracted and the viral load was determined. Semi quantitative RT-PCR for gene expression analysis was carried out. Histological analysis of Brain and CAM tissues were performed to determine the extent of pathogenicity and morphological changes. All the experiments were replicated thrice and data's were represented as mean ±SD. One way and Two way analysis of variance, t-test were applied for the analysis of differences among different test groups. For correlation study Pearson’s correlation was used.

Results: There was significant decrease in the viral loads in the Brain, CAM and Amniotic fluid of the embryo in Scopolamine pre-treated groups compared to the infection groups. There were significant changes for IFNs and IRFs both in CAM and brain tissue among the four groups. Nevertheless, Scopolamine pre-treated group also showed significant up-regulation of IFN-α and TLR3, TLR7, TLR8 mRNA. The histological changes showed significant reduction of necrosis, inflammation and other co-morbid pathology in the Scopolamine pre-treated groups.

Conclusions: Scopolamine exerts the antiviral effect by influencing the TLR signalling pathway which is one of the contributing factors in the immune-pathogenicity of JE virus infection. The present study may pave the way in the development of targeted immunotherapy through targeting specific molecules of TLR, IFN and other signaling pathways in future against JE by altering the innate immune signalling.

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**Abstract 9140**

**The profile of virulence gene exoS, exoT, exoU and exoY from gene encoding effector protein type III secretion system of *Pseudomonas aeruginosa* in clinical isolates in Sanglah Hospital Bali**

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**Background:** *Pseudomonas aeruginosa* is one of the Gram-negative rods bacteria that causes opportunistic and nosocomial infections. Type III secretion system (TTSS) is main virulence factor of *P. aeruginosa*. There are four effector proteins TTSS *P. aeruginosa* they are ExoS and ExoT possessed GAP and ADPRT activities, ExoU as potent cytotoxin exhibits phospholipase A, activity and ExoY is a adenylil cyclase that elevates cAMP eukaryote cells. This study was aimed to know the distribution and proportion virulence genes exoS, exoT, exoU dan exoY of gene encoding effector protein TTSS *P. aeruginosa* from clinical isolates in Sanglah general hospital 2015.

**Materials/methods:** *Pseudomonas aeruginosa* isolates were obtained from clinical specimens were then grouped into blood, sputum, urine and pus specimens which had been identified phenotypically by Vitek2 Compact system (bioMérieux, Inc., Marcy-l’Etoile - France), and then continued by genotipic detection by PCR method. The characterization of genes encoding effector proteins TTSS *P. aeruginosa* were performed by dupleks PCR (dPCR) method that separated into two dPCR consisted of dPCR to genes exoS paired with exoT and dPCR to genes exoU paired with exoY.

**Results:** In total 124 *P. aeruginosa* isolates from blood, sputum, urine and pus specimens known the proportion of each genes exoS, exoT, exoU and exoY were 92,7%, 97,5%, 58,1% and 92,7%, respectively. The isolates genotypically exoS+/exoT+/exoU+/exoY+ accounted for 55,65% dan 57,26%, respectively.

**Conclusions:** The distribution and proportion virulence genes exoS, exoT, exoU and exoY of gene encoding effector protein TTSS *P. aeruginosa* were independent to various kind of specimens (blood, sputum, urine and pus). There were no significant differences between distribution and proportion of each virulence genes to each kind of specimens.

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The probability of infection caused by carbapenemase-producing Enterobacterales (CPE) in haematological patients with rectal carriage of CPE

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Abstract 9141

**Background:** The aim of this study was to evaluate the probability of CPE-infection in haematological patients colonized by CPE.

**Materials/methods:** Prospective study (2015-2018) included haematological patients with colonization of gut by CPE. Genes of carbapenemases \( \text{bla}_{\text{OXA-48}}, \text{bla}_{\text{KPC}}, \text{bla}_{\text{VIM}}, \text{bla}_{\text{NDM}} \) and \( \text{bla}_{\text{IMP}} \) were detected by real-time PCR.

**Results:** During the study period 76 patients were included (39 male, 37 female; median age 42 years). The majority of patients had acute leukemia 34 (45%) and non-Hodgkin lymphoma 23 (30%). 52 (68%) received chemotherapy, 15 (20%) underwent hematopoietic stem cell transplantation [12 – allogeneic, 3 – autologous]. 46 (60%) patients were transferred from another hospital, median time from admission to our center till the first isolation of CPE from gut was 40 days, excluding 17 (22%) patients who were colonized by CPE at admission. Overall 81 CPE were isolated from gut in 76 patients: \( \text{K.pneumoniae} \) – 68 (84%), \( \text{E.coli} \) – 5 (6%), \( \text{E.cloacae} \) – 4 (5%), \( \text{C.freundii} \) – 2 (2%), \( \text{S.marcescens} \) – 1 (1%), \( \text{M.morganii} \) – 1 (1%). Isolates harboring \( \text{bla}_{\text{OXA-48}} \) predominated – 64 (79%), followed by \( \text{bla}_{\text{NDM}} \) – 10 (12%), \( \text{bla}_{\text{OXA-48}+\text{bla}_{\text{NDM}}} \) – 6 (7%), \( \text{bla}_{\text{KPC}} \) – 1 (1%). The probability of CPE-infection was 56% (figure a). Risk factors for CPE-infection were as follows (\( p<0.05 \)): presence of central line, admission to intensive care unit (ICU), appearance of CPE-colonization in ICU, CPE-colonization of more than 1 site, parenteral nutrition.

**Conclusions:** The probability of CPE-infection among CPE-rectal carriers was 56%. The most common pathogen was \( \text{K.pneumoniae} \) harboring \( \text{bla}_{\text{OXA-48}} \). The probability of CPE-infection was significantly higher in patients who had more than 1 site of CPE-colonization and among ICU-patients.

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Abstracts 2020

Abstract 9145

**Impact of influenza Point-of-Care testing in the emergency department on clinical care of adult patients at three hospitals in Lanarkshire, Scotland: an observational study**

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**Background:** Rapid influenza molecular tests with similar sensitivities to laboratory-based polymerase chain reaction (PCR) are gradually being introduced at the front door of UK hospitals. We examined the impact of influenza point-of-care testing (POCT) on patient journey and management during the influenza season across three adult acute hospitals in Lanarkshire, Scotland.

**Materials/methods:** Cobas Liat influenza A/B POCTs were instituted in the emergency department (ED) at University Hospitals Hairmyres, Monklands and Wishaw between December 2018 and March 2019. Patients tested for influenza on presentation during this period were compared to those tested by real-time reverse transcriptase PCR between December 2017 and March 2018 (pre-POCT). Outcomes of interest included patient time in the acute assessment areas (including ED, medical assessment unit and ambulatory care unit), hospitalisation rate, antiviral and antibiotic utilisation, time to antivirals, and length of stay.

**Results:** In total, 733 and 1202 patients were included in the 2017/18 (pre-POCT) and 2018/19 (POCT) seasons, respectively. A higher proportion of the pre-POCT cohort were influenza PCR positive (38.9 vs. 34.2%, p=0.04). The POCT group had a lower rate of hospital admission (76.3 vs 90.9%, p<0.001) and spent less time in the acute assessment areas (3.7 vs. 5.3 hours, p=0.001).

POCT was associated with significantly shorter time to influenza result (median turnaround time 3.0 vs. 24.6 hours, p<0.001). Similar proportions of influenza PCR positive patients were prescribed antivirals among the pre-POCT and POCT groups (80.6 vs. 80.1%), but substantially fewer influenza-negative patients in the POCT cohort received antivirals (1.3% vs. 35.2%, p<0.001). Median time to the first dose of antivirals was shorter in the POCT group (5.2 vs. 15.3 hours, p<0.001). A lower proportion of patients in the POCT cohort received antibiotics (68.5 vs. 86.3%, p<0.001). Furthermore, the median length of hospital stay was shorter in the POCT group (5 vs. 6 days, p<0.001).

**Conclusions:** Notwithstanding the limitations of a before-and-after study, influenza POCT was associated with shorter time in acute assessment areas, timelier influenza diagnosis, more rapid and prudent antiviral prescribing, in addition to lower rates of hospitalisation, antibiotic use, and shorter length of stay.

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Bacteriophage therapy in orthopaedic and cardiovascular surgery: first clinical experience with difficult-to-treat infections

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Abstract third-party references: Suppported by: PRO - IMPLANT Foundation

Background: Antibiotics have limited activity in the treatment of multidrug-resistant or chronic biofilm-associated infections, in particular when implants cannot be removed. Lytic bacteriophages can rapidly and selectively kill bacteria, and can be combined with antibiotics. However, clinical experience in patients with surgical infections is limited. We investigated the outcome and safety of local application of bacteriophages in addition to antimicrobial therapy.

Materials/methods: Patients with complex orthopedic and cardiovascular infections were included, in whom standard surgical treatment was not feasible or impossible. Before inclusion, patient informed consent was obtained and the treatment was performed in agreement with the Article 37 of the Declaration of Helsinki. Bacteriophages were provided by ELIAVA Institute in Tbilisi, Georgia, after performing susceptibility testing of the isolated pathogen. Bacteriophages were applied during surgery in the surgical site and continued through percutaneous drains placed during surgery three times per day for the following 5-14 days. Patients were followed-up on regular clinical visits at 3, 6 and 12 months.

Results: We included 6 patients (2 female and 4 male). Median age was 57 years, range 36-80 years. 3 patients had left ventricular assist device (LVAD) infection, 1 cardiovascular implantable electronic device (CIED) infection, 1 periprosthetic joint infection (PJ) and 1 chronic posttraumatic osteomyelitis. The infection was polymicrobial in 3 patients (including gram-negative rods and staphylococci), Pseudomonas aeruginosa was isolated in 2 cases and Staphylococcus aureus in 1 patient. 5 patients underwent surgical revision with retention of the implant (if present), one patient with LVAD infection was treated conservatively. At follow-up of 12 month, 5 patients were without signs or symptoms of infection, whereas in one patient with LVAD infection, a relapse was observed with emergence of phage-resistant Pseudomonas aeruginosa. In this patient, no surgical revision was performed.

Conclusions: Bacteriophage therapy may represent a valid additional approach, when standard antimicrobial and surgical treatment is not possible or feasible, including in difficult-to-treat infections. In our case series, 5 of 6 patients were infection free after 1 year. Further studies need to address the optimal bacteriophage administration route, concentration, duration of treatment and combination with antimicrobials.

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Abstract 9159

**Surveillance for control of antifungal resistance in Candida bloodstream infections fails to inform antifungal stewardship in European countries**

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**Background:** Resistance monitoring among *Candida* isolates represents a new challenge for epidemiological surveillance due to the increasing resistance trends, especially among non-*albicans* strains. COMBACTE-Magnet EPI-Net’s surveillance network rose to this challenge by performing the first systematic assessment of resistance rates in *Candida* blood-isolates in Europe, in order to provide barrier-free access to existing data.

**Materials/methods:** The protocol was developed following the guidance already in place for antimicrobial resistance surveillance among bacteria (SUSPIRE-protocol). Surveillance systems and studies reporting data on *Candida* blood-isolates were searched through Google engine and Pub-Med from January-2005 to August-2019. Data reported from 28 EU and 4 EFTA countries with no language restriction were considered. To increase representativeness, only multicentre studies with at least 12-months consecutive surveillance were included. Final assessment of existing surveillance included: surveillance systems’ characteristics, reporting modalities and study quality.

**Results:** Out of 53 retrieved national surveillance, 14 reported on *Candida* isolates but only Austria, Italy, Norway, Spain and UK included resistance data. Azole resistance in *C.albicans*, was the most frequently reported, while data on *C. glabrata, C.parapsilosis*, echinocandin and amphotericin B-resistance was reported in 4 surveillance only. The average isolates tested per-year varied between 19 and 454.

Among 318 publications, 26 studies from 13 countries were included. More than a half was supported by private companies. The most tested antifungal agents were fluconazole (96%), voriconazole (77%), amphotericin B (73%), and caspofungin (50%). The most reported *Candida* species were *C.albicans* (96%), *C.parapsilosis* (98%), and *C.glabrata* (85%). Multi-drug-resistant *Candida* was reported in 3 studies only. No data on *Candida auris* resistance were reported. Broth microdilution, S.YeastOne and E-test were used in 10, 5 and 2 studies, respectively. CLSI reference was used in 16 studies (62%).

Detailed description of microbiological methods was not available for 83% of surveillance systems and 35% of the included publications.

**Conclusions:** Anti-fungal resistance surveillance among *Candida* blood-isolates is fragmented and heterogeneous. Scarce reporting of microbiological methods and inclusion of low number of samples hinder the validity and representativeness of the data, delaying the application of a translational approach to the threat of antifungal resistance and the identification of relevant target for antifungal stewardship.

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Assessment of de-escalation of empirical antimicrobial therapy in medical wards with high rates of multidrug-resistant bacteria: a multi-centre prospective cohort study

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Background: De-escalation of empirical antimicrobial treatment has been considered a key component of antimicrobial stewardship programs. However, this strategy has not been adequately evaluated in settings with increased prevalence of multidrug-resistant (MDR) bacteria. The aim of this study was to identify frequency, associated factors and safety of de-escalation in Greek medical wards (MW), with recognized MDR prevalence.

Materials/methods: Prospective observational study conducted in six centers during a 6-month period in 2017-2018, analyzing the first septic episode of patients with microbiologically documented infections including sepsis or septic shock. Patient characteristics including admission diagnosis, illness severity, empirical antibiotic regimen, culture results, length of hospital stay (LOS), and 28-day mortality were recorded. Antibiotic de-escalation was defined as change to narrower spectrum antibiotics or discontinuation of part of the initial antibiotic regimen on the basis of culture results.

Results: A total of 142 patients were enrolled, male 78 (54.9%); Charlson comorbidity index (CCI) mean 4.97 (SD 2.48); SOFA score mean 2.88 (SD 2.26). Escherichia coli was the most frequent pathogen (49.2%), followed by Klebsiella pneumoniae (17.6%), Pseudomonas aeruginosa (7%) and Proteus mirabilis (4.9%). Urinary tract, abdominal sources and the lung were the most frequent sites of infection (66.9%, 5.6% and 6.3% respectively); primary bacteraemia was 6.3%. Overall 46.4% of infections were bacteraemic, 56.3% of patients had sepsis and 12.6% septic shock. De-escalation (DE) was applied in 72/142 patients (50.7%) and 9/29 (31%) in difficult to treat pathogens (p=0.08). Carbapenem de-escalation was achieved in 11/20 patients (55.5%). 28-day crude mortality was 23.9% for the whole cohort and 8.3% for de-escalated patients (p=0.01). There was no significant difference in age, diagnosis, admission CCI and SOFA scores and total antibiotic duration between DE and non-DE.

Conclusions: Antimicrobial de-escalation was applied in 50.7% of patients with sepsis or septic shock in medical wards with prevalence of MDR pathogens, including those with difficult to treat bacteria and was associated with favorable clinical outcomes. Although no causality can be demonstrated, careful clinical selection of patients can result in reduction of unnecessary antibiotic use without compromising safety.

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The bacterial gut microbiota during controlled human infection with Necator americanus larvae

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Background: Hookworms are soil-transmitted helminths which use immune-evasive strategies to persist in the human duodenum where they are responsible for anemia and protein loss. Despite mass drug administration, hookworm is still responsible for a high burden of disease globally, underscoring the need for an effective vaccine. A controlled human hookworm infection (CHHI) model was developed to aid vaccine development. Apart from their pathogenic role, hookworms are increasingly investigated for attenuating autoimmune disease, as they induce immunoregulation. Currently, little is known about the bacterial-helminth relationship during helminth infection. The current study explored temporal changes in the gut microbiota in response to human infection with Necator americanus in a CHHI model with healthy volunteers.

Materials/methods: Twenty-four healthy volunteers were included in a randomized CHHI, of which 20 completed the study. Volunteers were exposed to cumulative doses of 50, 100 and 150 larvae. The 150 larvae group received first infection at trial week 0, the 100 group at trial week 2 and the 50 larvae group at trial week 4. Fecal samples were collected for bacterial microbiota profiling at weeks 0 (baseline), 4, 8, 14 and 20 of the trial.

Results: All volunteers developed patent infection. Heavy gastrointestinal (GI) complaints were observed in 11 volunteers and were not associated with the larval dose. No differences in microbiota richness, diversity and stability were observed between the three study groups, nor were significant differences in abundance of individual bacterial taxa found. Overall, bacterial richness increased from week 8 to week 20 (p=0.017) of the trial. Volunteers with heavy GI had transient instability of the microbiota during the first eight weeks (p=0.047) and a rapid recovery at week 20 (p=0.004). Additionally, eosinophil count significantly correlated with microbiota stability (Jaccard, r=-0.26, p=0.02). Barnesiella, amongst other taxa, was found to be more abundant in the heavy complaints group throughout the study (p<0.05).

Conclusions: We found a remarkable stability of the gut microbiota in response to N. americanus infection over the twenty-week study period, although transient instability was observed in individuals with heavy GI complaints. This instability correlated with eosinophil counts, suggesting a relationship between microbiota and eosinophilic enteritis.

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Background: Influenza vaccination is recommended for all patients aged >6 months, and hospitalization provides an opportunity for vaccination in patients with limited access to care. We sought to assess the cascade of care in administering influenza vaccinations.

Materials/methods: In a 500-bed US hospital, nurses complete a screening tool for influenza vaccination embedded in the electronic medical record as part of the admissions process for adults. The tool assesses 1) if patients are eligible for vaccine (have not received influenza vaccination during the current season), 2) if any medical contraindication or egg/latex allergy exist, and 3) if the patient refuses the vaccination. If the patient does not refuse, influenza vaccine is automatically ordered with the next morning's medications. Between 10/1/2018 and 3/30/2019, we calculated frequency of tool completion, the responses to each step in the tool, frequency of vaccine administration and the pooled influenza vaccination rate/100 eligible encounters. Differences in vaccination rate were calculated by each nursing unit, by 3 nursing unit types [intensive care unit (ICU), ward, mother/baby] and by individual nurse completing the tool. Only the first completed tool per encounter was included.

Results: Among 13,437 unique patient admissions by 779 nurses, 12,936 (96%) had the tool completed. Most (55%) patients did not have prior influenza vaccination, and few patients had allergies (latex: 1.2%, eggs: 1.2%) or medical contraindications (0.7%). Of the 6,597 eligible patients without allergy/contraindication, 4,654 (71%) declined the vaccine. Only 1,943 (14%) of screened encounters had an order for influenza vaccine, but only 1,169 (61%) of those with orders had an influenza vaccine administered (Figure 1). The highest rates of vaccination/100 eligible patients were in the ICU (20), followed by wards (17) and mother/baby units (12). By individual nursing unit, the median vaccination rate/100 eligible encounters was 9.3 [range: 2.1-25.5]. Nurses varied in vaccination rate/100 eligible encounters varied widely [median: 5.4; range: 0-100].

Conclusions: During the 2018-2019 influenza season, nearly half of adult patients were not vaccinated before hospitalization, and <10% of those eligible for influenza vaccination received the vaccine. Scripting nursing interactions or other standardization efforts may improve influenza vaccination rates among inpatients.

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Background: In countries with high endemicity for carbapenem-resistant Enterobacteriaceae (CRE) colonization of long-term care facilities (LTCFs) residents play an essential role in the spread between community and healthcare facilities. Rapid identification of colonized patients are therefore essential for a prompt start of infection control measures. Aim of the study was to compare specificity and sensitivity rapid molecular tests in detecting CRE on rectal swab in LTCFs residents in a high endemic country.

Materials/methods: A point prevalence survey (PPS) with rectal screening (RS) was conducted in 27 LTCFs in north Italy in high endemic setting for ESBL-Ent in a 12-month period. Rectal swabs were inoculated onto ChromID ESBL agar (bioMerieux, Marcy l’Etoile, France) with an Ertrapenem disk (10ug) and on McKonkey agar with a Meropenem disk (10ug). Resistance to carbapenems were confirmed with immunocromatographic Lateral flow assay Carba5 (NG Biotech). Rapid molecular test were done using the CRE ELITe MGB kits (Elitech Group, Italy) with the ELITe InGenius RT (Real Time PCR) which detect KPC, NDM, VIM, IMP, and OXA-48 like families, performing a complete run of 12 samples in 2h and 30 min. Sensitivity, specificity and negative and positive predictive value were calculated according to standard methods.

Results: Overall, we screened 1947 residents. CRE were identified in (70/1947) 3.5% of cultures and in (124/1947) 6.37% of molecular tests with a concordance of 96%. CRE ELITe MGB identified 50 positive residents not identified from conventional cultures (50/124, 40%). The carbapenem resistant genes were classified with the real time PCR as KPC in 55% of the positive samples; the remaining were NDM/VIM/IMP. Sensitivity and specificity of the molecular test were 94% and 97% respectively, with a NPV of 99.7%.

Conclusions: Molecular tests identify 40% more CRKP colonized residents in LTCFs than conventional cultures. Moreover, molecular methods could give a rapid evidence of the type of carbapenemas produced. Cost-effectiveness studies are needed to define the role of rapid tests linked to infection control measures in containing the spread of CR-KPC outside the hospital in high endemic countries.

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Abstract 9182

**Surveillance of Mycobacterium leprae in Analamanga region of Madagascar**

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**Background:** Leprosy still remains a major problem of public health in Madagascar with over 1500 reported new cases per year in these last years. The Centre d’Infectiologie Charles Mérieux (CICM), named by the Ministry of the Public Health as the National Reference Laboratory for the surveillance of resistance to anti-leprosy therapy, ensures the diagnosis and study of resistance of leprosy cases reported by the Programme National de Lutte contre la Lèpre (PNLL) from the region of Analamanga, Bongolava and Itsy. The lack of reliable diagnostic tools especially for the early stage and differential of the disease is of major concern. We report here the first results stemmed from PCR RLEP, recently added to the diagnosis algorithm.

**Materials/methods:** Patients have been recruited by dermatologists from the University Hospital of Befelatanana and during scheduled mass consultations in other parts of the island. Skin biopsies have been sampled as well as some earwax. Microscopic diagnosis after Ziehl-Neelsen staining and PCR targeting the repeated sequences of M. leprae genome were performed.

**Results:** Since August 2012, 124 skin biopsy and earwax have been analyzed by microscopy and PCR RLEP. One hundred and fourteen (92%) patients were clinically classified as multibacillary (MB), and 10 (8%) were classified paucibacillary (PB). From skin biopsies, 103 specimen were positive with either smear microscopy or PCR RLEP. Among MB, 64 (56%) were smear microscopy positive versus 98 (86%) were PCR RLEP positive. Among the 10 PB patients, three were PCR positive but none were smear positive. Twenty-one (17%) specimen remain negative for both methods: 14 among MB patients and 7 among PB ones.

**Conclusions:** The PCR RLEP correlates with clinical presentations and allows confirming more cases than smear microscopy. As bacteriology drives the polychemotherapy regimen of leprosy patients, these results questions the role of PCR RLEP in patient classification. More data on clinical outcome will give evidence about.

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Abstract 9183

Travel-related meningitis: results from a thirteen-year retrospective study
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Background: Meningitis is a rare but potentially severe cause of morbidity in travelers. Few data are available on microbiological data in this setting. The aim was to describe the etiologies of meningitis in travelers and compare them to meningitis in non-travelers.

Materials/methods: This monocentric observational study included all consecutive patients hospitalized for meningitis between January 1, 2002 and December 31, 2015. Meningitis was classified as bacterial (culture or PCR positive in the cerebrospinal fluid (CSF)), viral (PCR positive in CSF), or probably viral (favourable outcome without antibiotic therapy within 7 days of diagnosis) or without etiology. A patient was considered as a traveler if he had left metropolitan France within a month before the onset of symptoms.

Results: Two hundred and ninety-six patients were included, including 47 travelers [median age 31 years [26-37], 23 (48.9%) women]. The main destinations were sub-Saharan Africa [n=11, 23.4%], Maghreb [n=10, 21.3%] and Europe [n=6, 12.8%]. For 7 patients [14.9%], symptoms had started during the stay but none had been repatriated. Thirty-five [74.5%] had viral meningitis [22 documented and 13 probable], 11 [23.4%] had meningitis of undetermined etiology and 1 [2.1%] had bacterial meningitis. Microbiology showed a clear predominance of Enterovirus [n=15, 31.9%] and Herpesviridae [HSV 2, 3 cases and VZV, 2 cases]. One [2.1%] patient had meningitis due to mumps virus. The only bacterial meningitis was due to Mycoplasma pneumoniae in a young man returning from Ivory Coast. Only 2 [4.3%] meningitis were due to a non-cosmopolitan etiology: dengue fever in a patient returning from Malaysia and Toscana virus after a stay in Italy.

When comparing with the non-travelers group, the two populations were no different in age and sex (p=0.69 and 0.57 respectively). The proportions of bacterial (p=0.14, OR 0.21 [0.04-1.18]), documented viral (p=0.59, OR=1.19 [0.64-2.2]), probably viral (p=0.59, OR=1.3 [0.65-2.6]) and undetermined (p=0.97, OR=0.95 [0.46-1.96]) meningitis were not different.

Conclusions: The diagnostic approach to meningitis in traveler should focus on cosmopolitan etiologies. Tropical causes must be mentioned in second intention, especially in case of an evocative epidemiological context.

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Abstract 9185

**Etiology of viral and bacterial gastroenteritis in a third-level hospital in Spain in relation to age**

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**Background:** Acute gastroenteritis (AGE) is one of the most common infectious diseases. Viral pathogens cause most of these cases. However, bacteria, parasites, and fungus can also cause AGE. The aim of this study was to establish the prevalence of different enteropathogens in our hospital in relation to age.

**Materials/methods:** This study was conducted from January 2018 to August 2019. We studied stool samples received from patients with suspected gastroenteritis. The identification of bacterial species was carried by mass spectrometry MALDI-TOF (Bruker Daltonics®) and the study of Rotavirus and Adenovirus by detection of antigens by immunochromatographic methods (MonlabTest®), as well as for Norovirus (CerTest Biotec®) in all those samples in which it was requested. In addition, the study of parasites was carried out by the concentration technique (VircellMiniSystem - Total-Fix®). Only one sample per patient was considered.

**Results:** 6274 samples were processed as coproculture, of which 356 (5.67%) were positive. The study of viral antigens of Adenovirus and Rotavirus was carried out in 1549 samples, while that of Norovirus was carried out in 388. Finally, the study of parasites was carried out on 4447 samples and the one most frequently observed was *Giardia lamblia* on 41 occasions (0.92%). The results are observed in the next table.

<table>
<thead>
<tr>
<th>Age</th>
<th>Positive coprocultures</th>
<th>Aeromonas spp.</th>
<th>Campylobacter spp.</th>
<th>Salmonella spp.</th>
<th>Adenovirus</th>
<th>Rotavirus</th>
<th>Norovirus</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;5</td>
<td>187</td>
<td>23</td>
<td>126</td>
<td>47</td>
<td>25</td>
<td>110</td>
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<tr>
<td>6-12</td>
<td>58</td>
<td>-</td>
<td>50</td>
<td>8</td>
<td>2</td>
<td>15</td>
<td>1</td>
</tr>
<tr>
<td>13-18</td>
<td>23</td>
<td>-</td>
<td>16</td>
<td>6</td>
<td>-</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>19-65</td>
<td>54</td>
<td>3</td>
<td>39</td>
<td>12</td>
<td>3</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>&gt;65</td>
<td>24</td>
<td>3</td>
<td>12</td>
<td>9</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>356</td>
<td>29 (8.15%)</td>
<td>242 (67.98%)</td>
<td>82 (23.03%)</td>
<td>31 (2%)</td>
<td>131 (3.6%)</td>
<td>38 (9.75%)</td>
</tr>
</tbody>
</table>

**Conclusions:** The age group with the highest number of positives was the one formed by 5-years-old children. The most frequently isolated bacterial enteropathogen was *Campylobacter* spp. followed by *Salmonella* spp. Rotavirus was the main viral etiologic agent, but regarding the samples in which the virus study was requested, Norovirus was the most prevalent. It is likely that the presence of Norovirus and the other gastrointestinal viruses is underdiagnosed because their studies are not usually included in the diagnosis.

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Abstract 9194

Validation of a semi-automated surveillance of surgical site infections: improving exhaustiveness, representativeness and efficiency

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Background: Traditionally, Surgical Site Infections (SSIs) surveillance implies manually review of patient charts, which is labour intensive, time-consuming and prone to error. Its representativeness is frequently unknown, though local data is used in the Healthcare-Associated Infections Surveillance Network (HAI-Net). We aimed to assess the exhaustiveness of SSIs surveillance in a tertiary care teaching hospital in Porto, Portugal, and to address whether a semi-automated model, using electronic health records’ data to select patients with high-risk of SSI for subsequent manual review, was valid and could improve efficiency.

Materials/methods: Colorectal surgeries performed between January 2016, and December 2018, were selected. For each hospitalization, post-surgical antibiotic use, positive cultures, C-reactive protein (CRP>50; CRP>100mg/dL), leukocyte counts (>11.000/mm³), body temperature (>38°C), surgical re-intervention, post-discharge visit to the emergency room and hospital readmission were retrieved. Representativeness was evaluated by comparing characteristics of the procedures registered in the HAI-Net with the non-included ones. Within HAI-Net procedures, the validity of each variable (or combination of variables) was tested using as the gold-standard the presence of a SSI registered in the current surveillance system. The proportion of medical records flagged by each criterion for manual review was estimated, as a measure of efficiency.

Results: Out of 1330 colorectal procedures, 743 (56%) were registered in HAI-Net (SSI risk: 10.6%). Non-included procedures were more likely to be emergent interventions and presented higher proportions of antibiotic use and other proxies of infection. CRP presented the highest sensitivity (92%; 95%CI 84%-97%) followed by antibiotic use (89%; 95%CI 79%-95%). However, the latter showed a higher positive predictive value (22%, or 23% if considering antibiotic use or positive culture). Antibiotic use flagged fewer procedures for manual review (47.7%) than any other criteria.

Conclusions: Current surveillance is neither exhaustive nor representative: it systematically misses procedures with high risk of infection. Thus, reported incidence is likely underestimated. Antibiotic use seems to be a good criterion to select procedures for manual review. Rather than just saving time, by demanding merely half of procedures to be manually reviewed, it may also improve the exhaustiveness and representativeness of surveillance. Nevertheless, all criteria need to be validated prospectively before their application.

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Abstract 9200

Risk factors for carbapenem-resistant Enterobacteriaceae infections among rectal carriers in carbapenemase co-circulation setting: data from SPACE-CP study

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Background: Scoring systems to predict carbapenem-resistant Enterobacteriaceae (CRE) infections are useful to select adequate therapy. Those models were created in CRE-bla_KPC environments. Thus, designing strategies to evaluate other classes of CRE (e.g. CRE-bla_NDM) is crucial because their treatment varies. Our aim was to detect risk factors for CRE infections among CRE-bla_KPC or CRE-bla_NDM rectal carriers. Secondary outcome was to assess exclusive factors for each CRE.

Materials/methods: Retrospective study among CRE-bla_KPC and CRE-bla_NDM rectal carriers from a tertiary hospital of Buenos Aires Province (Argentina) from July 2016 to July 2019. We compared patient with and without CRE infections to identify general and specific risk factors for developing them. Extra-rectal sites were studied according to physicians’ criteria. Rectal swabs cultures were performed in transferred patients from other center, admitted to critic areas or shared room with CRE-colonized. Molecular techniques were used to detect CRE genes. Possible associated factors in univariate analysis were included in the logistic regression model. Statistics measurements were executed by R-Studio 3.0.

Results: 320 carriers (48.6% CRE-bla_KPC, 28.6% CRE-bla_NDM and 21.6% both) were included. 58.7% were male, the median age was 66 years (IQR 21). 11.2% developed a CRE infection (7% bacteremic, 4.2% non-bacteremic). Adjusted model showed that at least one extra-rectal colonized site (aOR 3.0 [IC95% 1.1-7.9] p=0.03) was the only linked factor to any kind of CRE infection. Surprisingly, surveillance swab cultures did not predict episodes by the same resistance mechanism: CRE-bla_KPC (OR 1 [0.44-2.37] p=0.9) and CRE-bla_NDM (OR 2.1 [95% CI 0.6-6.8] p=0.2). Also, this tendency was observed taking into account at least one extra-rectal colonized site for CRE-bla_KPC (OR 1.9 [0.5-6.9] p=0.4) and CRE-bla_NDM (OR 4.5 [0.9-22.8] p=0.1) infections. Finally, no distinctive factors were evident concerning sex, age, previous antibiotic use, surgical procedures, length of stay and prior comorbidities.

Conclusions: Extra-rectal colonization was a marked risk factor for any CRE infection in our colonized population. Conversely, no specific factors for predicting each class of event were detected. These findings highlight the ubiquitous conditions for the acquisition of both CRE and the inability to predict each one in context of co-circulation.

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Travel patterns and knowledge of risk of infections during international travels in solid organ transplantation

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Abstract third-party references: The work was supported by Plan Nacional de I+D+i 2013-2016 and Instituto de Salud Carlos III, Subdirección General de Redes y Centros de Investigación Cooperativa, Ministerio de Ciencia, Innovación y Universidades, Spanish Network for Research in Infectious Diseases (REIPI RD16) - co-financed by European Development Regional Fund “A way to achieve Europe”, Operative program Intelligent Growth 2014-2020

Background: International travel (IT) after SOT may pose a risk of medical complications and infection acquisition that could be prevented with adequate information and advice prior to the trip as well as updating vaccinations if necessary.

Materials/methods: Prospective, multicenter survey performed in 3 Spanish hospitals during Nov.18 to Nov.19. Survey was anonymous and voluntary for SOT recipients. Questionnaire has two parts: 1ª) for all SOT recipients with questions aimed at assessing the level of knowledge of vaccination status, ways of transmission and prevention measures for transmissible travel-related infection. In addition, patterns of pre-SOT travels were explored (destinations and frequency). 2º) For those who had travel after SOT, questions regarding destinations, frequency, medical encounter, adherence to recommendations and complications during the trip were considered. Changes in travel patterns before and after SOT were analyzed.

Results: 258 SOT recipients participated in the survey (163 kidney, 35 cardiac, 48 liver, 12 combined organs). Median time from tx to survey: 10 m (1 - 520). 193 (74.8%) were transplanted > 6 months. Age (median): 57 yrs-o (19-84). 29 (11.2%) were foreign-born (82.7% from high-risk countries).

| Unknown vaccination status (infection; %) | HAV 35.3%; HBV 25.6%; measles [29%], chicken-pox [26%], meningococcal (40.7) |
| % recipients known way of transmission (T) and prevention measures (P) | HIV (T 91%, P 88%), syphilis (T 81%, P 75%), HAV (T 46%, P 40%), HBV (T 57%, P 53%), malaria (T 46.9%, P 35%), TB (T 38.7%, P 34.8%) |
| Pre-SOT IT | IT 50% (129 pts). 38% to high-risk areas. |
| Main destination: Europe [42%] |
| Post-SOT IT (SOT > 6 months) | IT 15% (39 pts). Reasons IT: 68.9% tourism, 14.9% business, 12.6% VFR, 3.4% others. |
| Main destination: Europe [67%] |
| 60% medical advice (<50% follow) |
| Travel-complications: 7.7% (2 bacterial infections, 1 cardiac) |

Conclusions: Low level of knowledge about vaccination status and prevention measures of travel-transmissible infections has been detected in SOT patients. Medical education should be implement. Patients continue travelling after SOT. Frequency and destinations of IT are modified, avoiding countries at risk of infection or with difficult access to health. Complications were infrequent. Medical advice by ID/Travel medicine specialists is recommended, especially for high-risk trips.

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Relevance of intra-hospital patient movements for the spread of healthcare-associated infections: a mathematical modelling study

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Abstract third-party references: This work is funded by the Netherlands ZonMw grant number 547001005 within the 3rd JPI ARM framework, co-fund grant no 681055 for the consortium EMerGE-Net.

Background: The impact of patient movements inside the hospital on pathogen spread is not well studied. The aim of this study is to analyze patient movement patterns between hospital wards to assess if movement patterns differ between patients at high or low risk of colonization. Next, we aim to quantify the impact of intra-hospital patient movement patterns on pathogen spread using agent-based simulations.

Materials/methods: We analyzed patient electronic medical record data from five hospitals and stratified patients into low-risk and high-risk groups based on specific ICD-10 codes. Movement patterns were extracted and visualized as networks, and network centrality measures were calculated. Next, we simulated the spread of a pathogen inside one hospital, using an agent-based model – where agents represent patients and inter-ward patient movements were modelled.

Results: Risk stratification of patients according to ICD-10 codes revealed that length of stay, patient age, and mean number of movements per admission were higher in the group we defined as high-risk. Movement networks in all hospitals displayed a high variability among wards concerning their network centrality and connectedness with a few highly connected wards and many weakly connected peripheral wards. Simulating the spread of a pathogen in such a network of wards showed positive correlation between ward prevalence and network centrality measures.

Conclusions: This study highlights the importance of inter-ward patient movements and their possible impact on pathogen spread. Targeting interventions to wards of higher (weighted) degree during an outbreak may help to control the spread of pathogens. Moreover, when colonization status of patients coming from different wards is unknown, a ranking system based on ward centralities may be used as a potential intervention to mitigate pathogen spread.

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Early experience with percutaneous vegetation suction (Penumbra) versus valve replacement surgery for right-sided infective endocarditis in people who inject drugs

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Background: Infective endocarditis (IE) carries significant morbidity and mortality. IE valve replacement surgery can be life-saving, but remains controversial in people who inject drugs (PWID) due to perceived risks of re-infection due to recidivism. Percutaneous vacuum suction (PVS) can effectively remove valve vegetations without valve replacement, but data surrounding this technique are limited. The objective of this study was to describe early experience with PVS (Penumbra) in PWID compared to valve replacement surgery in right-sided IE.

Materials/methods: Retrospective cohort study performed at two medical centers in the southeast United States and included hospitalized PWID with definitive right-sided IE who received PVS or valve replacement from 1/14-8/19. Patient characteristics and outcomes were described and compared.

Results: 58 patients were included: 38 PVS, 20 valve replacement surgery. Baseline patient demographics were similar between groups; 44 (76%) of patients were women, and the median (IQR) age was 31 (27-40) years. Twenty-six (45%) patients presented with septic shock on admission, and 53 (91%) had noted septic pulmonary emboli. Fifty-one (88%) patients had a previous history of IE in which they received long-term antibiotic therapy prior to intervention. Sixty organisms were identified from 57 patients; the most common organisms were 26 (43%) methicillin-resistant Staphylococcus aureus, 18 (30%) methicillin-sensitive Staphylococcus aureus, 5 (8%) Pseudomonas aeruginosa, 3 (5%) Serratia marcescens, and 8 (13%) other organisms. Patients who received PVS had a shorter median (IQR) duration of therapy (13 [6-30] days vs. 18 [13-35] days, P=0.04), and 4 (7%) patients died in the hospital compared to none who received valve replacement surgery (P=0.3). There were no differences between PVS and valve replacement surgery regarding 30-day readmission (13% vs. 15%, P=1.0), 12-month readmission (47% vs. 55%, P=0.8), 30-day mortality (15% vs. 0%, P=0.08), and 12-month mortality (24% vs. 15%, P=0.5). PVS patients less commonly had repeat embolic events in the preceding year when compared to valve replacement surgery (11% vs. 40%, P=0.02). Among patients who received PVS, 19 (31%) required blood transfusions post-procedure.

Conclusions: PVS was associated with similar outcomes as valve replacement surgery. Additional data are needed to support PVS in improving outcomes for PWID.

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**Abstract 9208**

**Improved taxon identification from similarity searches using Taxonomic Vote**

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**Background:** Despite its limitations, the most popular method to identify the source taxon of a nucleotide sequence relies on obtaining the best hit in a BLAST search. Usually, this corresponds to the source organism or its closest relative present in the database. However, in certain situations the first hit can be misleading, even an artifact, because BLAST does not identify orthologous sequences nor close evolutionary relatives but only sequences sharing segments of high similarity that may arise through additional processes to shared inheritance or phylogenetic history. We propose an alternative method, denoted Taxonomic Vote (TV), to gain insight about the overall taxonomy of a sample and that of the sequences obtained from it.

**Materials/methods:** TV is based on the results obtained by BLAST+ or any similarity search program yielding scored results against predefined databases. At first, a BLAST+ search is made for each query sequence/contig/read. The first 500 hits for each query are considered but only those with a score not lower than 90% of the best-hit score are included in subsequent analyses. With these, the TV algorithm performs a vote (counting the number of occurrences of each taxon) in each taxonomic level and estimates at what level a robust taxonomic identification has been produced. This results in different TV classes dependent on how well a gene is identified at each taxon level.

**Results:** TV allows obtaining the most probable taxonomy for each query and evaluating how many queries in a sample are well identified. Also, it gives information about the taxonomy of the sample for each taxonomic level, contributing to create a very approximate idea of the closest relative organism to that in the sample of interest. We have applied this method to characterize unknown cultures and to ascertain contaminant sequences in HTS data.

**Conclusions:** Although TV was developed to evaluate the taxonomic content of a sample, it can be applied to many other situations, such as the identification of contamination in high-throughput sequencing studies, characterizing horizontal gene transfer events, or identifying the taxonomic contents of metagenomic samples. The method will be available in a publicly accessible repository.

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Abstract 9209

The emergence of new STs of blaNDM-positive hypervirulent Klebsiella pneumoniae isolates in an oncology hospital, Russia

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Abstract third-party references: The Russian Science Foundation (grant number 18-75-10117) supported this work.

Background: The confluence between two Klebsiella pneumonia (Kp) pathotypes - "hypervirulent" (hvKp) and carbapenem-resistant (CR) classical (cKp), due to acquisition of virulence genes by cKp is a huge healthcare worldwide concern. Most outbreaks of hvKp and CR infections are reported from Asia and caused by K1 capsular type belonging to clonal complex 23. The simplest, although not very reliable, method for screening for hypervirulence is hypermucoviscosity detection by the string test. Highly sensitive and specific hvKp biomarkers were proposed by Russo in 2018. In the current study we report emergence hypermucoviscous (hm) CRKp isolates in an oncology hospital in St. Petersburg, Russia.

Materials/methods: Sixteen string-test positive CRKp isolates recovered in an oncology hospital from 2017 to 2018 were subjected to whole-genome sequencing on the Illumina platform and assembled de novo by SPAdes (BioProject PRJNA522420). Genomes were screened with Kleborate. The virulence of selected isolates was assessed in a mouse lethality assay. LD_{50} values were determined using the Reed and Muench method. The uniqueness of results observed for hvKp ST395 K2 bla_{NDM} was confirmed with Standalone BLAST based on analysis of 7245 Kp genomes from the ftp NCBI server.

Results: HmCRKp isolates belonged to two STs: ST395 \( (n=9) \) and ST147 \( (n=7) \). Four groups of HmCRKp isolates were distinguished based on the presence of hvKp biomarkers and LD_{50} values (Table). Highly virulent representative isolate ST395/K2 harboring bla_{NDM} was recovered from a deceased patient. According to our knowledge, this is the first report about hvKp ST395/K2.

Conclusions: In this study we observed two new clones long-term circulating in St. Petersburg oncology hospital – ST147/K20 and ST395/K2 harboring bla_{NDM} and hvKp biomarkers, simultaneously. ST395/K2 bla_{NDM} – positive Kp isolates belongs to dangerous highly virulent previously unregistered clone.

<table>
<thead>
<tr>
<th>Number of Isolates</th>
<th>ST</th>
<th>K-type</th>
<th>Biomarkers of cKp and hvKp differentiation</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td>blaq_{AmpA} blaq_{AmpB} blaq_{TemA}</td>
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</table>

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Pharmacodynamics of common antibiotics against uropathogenic *Escherichia coli* revealed significant antibiotic tolerance and persistence of intracellular bacteria

Ivana Kerkez*1, Marta Putrins1, Paul Tulkens3, Tanel Tenson2, Françoise Van Bambeke1

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**Abstract third-party references:** University of Tartu, Institute of Technology

**Background:** Urinary tract infections (UTIs) are a severe public health problem with high rate of recurrent infections. The major causative agent of UTIs is uropathogenic *Escherichia coli* (UPEC). Many studies revealed ability of UPEC to invade bladder epithelial cells as well as macrophages. Internalization leads to increased formation of persisters and better protection of pathogen from immune system and antibiotics. The aims of this study were to establish an in vitro model of infection of macrophages with UPEC and to compare pharmacodynamic properties of commonly-prescribed antibiotics against intra- and extracellular bacteria. Fluorescent marker protein Timer was used to gain better insight into physiological heterogeneity of bacteria surviving the antibiotic treatment.

**Materials/methods:** Mouse macrophage cell-line J774 was infected with opsonized and fluorescently labelled CFT073 strain. Non-phagocyted bacteria were eliminated by short incubation with gentamicin. Infected cells were exposed to a range of clinically relevant concentrations of antibiotics for 24h and analysed by CFU plating, flow cytometry and/or confocal microscopy. For measuring extracellular activity, the bacteria were exposed to the same concentrations of antibiotics in medium.

**Results:** A MOI of 50 was used to infect permissive J774 cells. An extracellular concentration of gentamicin equivalent to 3x its MIC was needed to prevent extracellular growth and macrophage killing within 24hours. Flow-cytometry and microscopy analysis of intracellular bacteria revealed that while cell division is restricted bacteria remain metabolically active. Extracellular and intracellular E<sub>max</sub> for used antibiotics are shown in the Figure Panel A. Extracellularly Sulfamethoxazole and Trimethoprim had bacteriostatic effect, while all other antibiotics were bactericidal. Intracellularly, the activity of all tested antibiotics was reduced in comparison with their activity in broth. Our fluorescent reporter-protein showed that a subpopulation of intracellular bacteria was metabolically active even in the presence of high level of host-cell permeable antibiotics [Figure Panel B].

**Conclusions:** All antibiotics failed to eradicate intracellular UPEC completely, even when bactericidal in broth. Among the drugs tested, fluoroquinolones are the most effective, killing almost 99.9% of intracellular bacteria.

Panel A – E<sub>max</sub> for used antibiotics against extra- and intracellular bacteria. Panel B – fluorescence microscopy image of infected macrophages after 24h ciprofloxacin 100xMIC treatment

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Abstract 9219

Outcomes of people who inject drugs with infectious endocarditis and valve replacement surgery

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Background: Infective endocarditis (IE) is a common disease state observed in people who inject drugs (PWID). Valve replacement surgery (VRS) is often necessary for disease management and improved patient outcomes; however, active injection drug use may deter surgical intervention due to risk of reinfection. The objective of this study was to compare the outcomes of PWID who received VRS to those who did not receive VRS.

Materials/methods: Retrospective cohort performed at a large academic medical center in the southeast United States that included hospitalized PWID with definitive IE who received VRS and those who did not receive VRS (no-VRS) from 1/14-10/18. The primary outcome of interest was all-cause 12-month mortality; secondary outcomes included short-term mortality and readmission. Patient characteristics and outcomes were described and compared.

Results: 178 patients were included: 41 (23%) VRS, 137 (77%) no VRS. Patient demographics were similar between groups, except patients who received VRS were more likely to present in septic shock (73% vs. 35%, \(P<0.001\)); 103 (58%) patients were women and the median (IQR) age was 33 (27-45) years. Native-valve IE was most common in VRS and no-VRS groups (91% vs. 93%, \(P=1.0\)), and the most frequent IE types were left-sided (54% vs. 24%, \(P=0.001\)), right-sided (32% vs. 64%, \(P=0.001\)), both left and right-sided (15% vs. 6%, \(P=0.1\)), and unknown (0% vs. 5%, \(P=0.4\)). 216 organisms were identified from 176 patients; the most commonly identified organisms were 37% methicillin-resistant Staphylococcus aureus, 25% methicillin-sensitive S. aureus, 9% streptococci, 9% enterococci, 5% P. aeruginosa, 1% Candida spp., 23% other organisms. Patients who received VRS had no significant differences in in-hospital (0% vs. 8%, \(P=0.07\)) and all-cause 12-month mortality (15% vs. 12%, \(P=0.6\)), as well as all-cause 12-month readmission (54% vs. 53%, \(P=1.0\)) when compared to no-VRS patients, respectively. However, patients who received VRS were less likely to have an infection-related readmission within 90 days compared to no-VRS patients (26% vs. 72%, \(P<0.001\)). In multivariable regression, left-side IE was the only variable associated with all-cause 12-month mortality (Table 1).

Conclusions: VRS did not have a mortality benefit in PWID, but was associated with fewer short-term infection-related readmissions.

**Table 1: Variables associated with all-cause, 12-month mortality**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total Population</th>
<th>UnadjOR (95% CI)</th>
<th>AdjOR (95% CI)</th>
</tr>
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<tr>
<td>Valve replacement surgery</td>
<td>41 (23%)</td>
<td>1.3 (0.5-3.6)</td>
<td>Not tested</td>
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<tr>
<td>Left-sided IE</td>
<td>55 (31%)</td>
<td>6.2 (2.4-16.3)</td>
<td>6.1 (2.2-17.1)</td>
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<td>Cardiovascular disease</td>
<td>11 (6%)</td>
<td>3.2 (0.8-13.0)</td>
<td>Not tested</td>
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<tr>
<td>Previous history of IE</td>
<td>36 (20%)</td>
<td>2.3 (0.8-6.2)</td>
<td>2.8 (0.9-8.3)</td>
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<tr>
<td>Septic shock on admission</td>
<td>65 (37%)</td>
<td>2.2 (0.9-5.4)</td>
<td>1.7 (0.6-4.7)</td>
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<tr>
<td>MRSA IE</td>
<td>80 (45%)</td>
<td>1.5 (0.6-3.8)</td>
<td>Not tested</td>
</tr>
<tr>
<td>Other concurrent infections</td>
<td>76 (43%)</td>
<td>0.5 (0.2-1.4)</td>
<td>Not tested</td>
</tr>
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</table>

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Abstract 9221

An audit of cadaveric liver and kidney organ transport fluid microbiology cultures in a tertiary referral centre

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Background: UK national guidance mandates routine microbiological testing of solid organ transport fluid (OTF) at recipient abdominal transplant centres despite limited evidence in the literature of the impact of this practice. Infections are a source of morbidity and mortality in transplant patients and transport fluid represents a potential vector for the transmission of infection.

This retrospective audit aims to establish adherence to routine culturing of all liver and kidney graft OTFs in a tertiary referral centre, an epidemiological surveillance of positive results and 12-month follow-up of these patients.

Materials/methods: Recipients receiving liver and kidney grafts from deceased donors between 1st September 2017 and 1st September 2018 were identified. Transport fluid samples were processed in standard laboratory manner. The hospital’s electronic clinical records were used to track outcomes at 12 months post-transplantation.

Results: Of 368 transplants carried out, 351 OTF samples were received and 62 (18%) were culture-positive. Of these, coagulase-negative Staphylococci accounted for 21 isolates, Enterobacteriaceae accounted for 19 isolates each, Staphylococcus aureus for 7 (1 of which was Panton-Valentine Leukocidin-producing MRSA), Pseudomonas spp. for 3, Lactobacillus spp. for 3 and Enterococcus spp. for 2 (1 of which was vancomycin-resistant) with varying other micro-organisms in the rest.

There were 9 (15%) cases of fungal growth in OTFs – all Candida spp.; out of these, 4 received targeted antifungal therapy. In 13 cases (31% of OTFs) culture-positive isolates were specifically treated (9 bacterial).

Overall 12-month mortality was 6.8%; 10% of culture-positive OTFs died within 12 months compared with 6.5% of culture-negative OTFs. 24% of deaths at 12 months occurred in culture-positive OTFs despite making up 18% of OTFs received.

Conclusions: In our centre, rates of culture-positive OTF samples were lower compared to rates reported by other transplant centres. The spectrum of microorganisms isolated predominantly represents those of gastrointestinal or skin flora. Their presence may indicate that sterility was compromised during the harvesting procedure. Candida spp. were isolated in a significant proportion of culture-positive OTFs; in these cases recipients typically would require targeted treatment. UK-based OTF contamination data is scarce and further research is needed to elucidate the relationship with nosocomial infection.

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Tackling resistance to carbapenem and colistin in clinical isolates of *Acinetobacter baumannii*

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Abstract third-party references: Supported partially by Trinity College Dublin and the Master program in Infection Control Management.

**Background:** Resistance to antibiotics is a serious threat in the 21st century. The healthcare sector is being severely affected by the presence of resistant bacteria and their associated nosocomial infections. *Acinetobacter baumannii* has been classified as a critical pathogen by the WHO and rightly so due to its notorious presence in the hospital and health centres. *A. baumannii* resistance to even last resort antibiotics, such as carbapenems and colistin establishes the need for new treatment strategies.

**Materials/methods:** In this study, we analysed a collection of 29 *A. baumannii* clinical isolates from different countries (Ireland, Germany and Portugal). The antibiotic resistance profile of these isolates was determined against 24 different antibiotics and isolates resistant to doripenem or colistin selected. Synergistic combinations of antibiotics with efflux pump inhibitors were performed. The efflux pump inhibitors comprised the phenothiazines: Thioridazine, Chlorpromazine, Promazine, Trifluoperazine, and the proton motive force disrupters: 1-{1-Napthylmethyl}piperazine and Carbonyl cyanide m-chlorophenyl hydrazine (CCCP). These tests were conducted by checkerboard assays and synergies assessed with fractional inhibitory concentration index analysis. The ability of the isolates to produce biofilms was evaluated by the crystal violet method. Isolates showing strong biofilm forming capabilities were selected for treatment with the most active synergistic combinations.

**Results:** All clinical isolates tested were MDR with 11 showing resistance to carbapenems (meropenem, imipenem and doripenem) and 3 to colistin. Thioridazine and trifluoperazine had a higher antibacterial activity (MIC from 50 to 400 mg/L). When synergistic combinations of doripenem and the efflux inhibitors were tested against resistant isolates these not affected. We speculate that this could be due to the presence of other factors that contribute to resistance, namely the presence of carbapenemase enzymes. However, thioridazine and CCCP proved very effective against colistin-resistant isolates of *A. baumannii* (FIC 0.206 – 0.46), demonstrating the important role that efflux has in colistin resistance. In colistin-resistant isolates, synergistic combinations of colistin and thioridazine or CCCP showed good biofilm disruption capabilities (biofilm reduction of 2-3 log).

**Conclusions:** The use of combination therapy could provide new ways to treat multidrug resistant *Acinetobacter baumannii*, namely in isolates that present resistance to colistin.

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Abstract 9224

Genomic surveillance at the regional scale: antimicrobial-resistant Klebsiella pneumoniae ST11 isolates in the Valencian community, Spain

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Abstract third-party references: Red de Vigilancia de Resistencias a Antimicrobianos de la Comunitat Valenciana

Background: Antimicrobial resistance (AMR) is a major threat to public health and a serious concern worldwide. Klebsiella pneumoniae is one of the main agents causing nosocomial infections, especially in intensive care and neonatal units. In the Valencian Community (Spain, population 5.5 million), similarly to other regions around the world, there has been an emergence of multidrug-resistant (MDR) strains of K. pneumoniae, mainly due to clonal complexes ST11 and ST307. In order to study the molecular epidemiology and the evolution of these clones in the Valencian Community (VC), we have collected more than 800 ESBL producing K. pneumoniae isolates from 8 different hospitals across the VC from 2014 until 2019.

Materials/methods: Next-generation sequencing was performed with Illumina NextSeq (2x150 paired-ends) using Nextera libraries. The resulting reads were analysed using ARIBA and SRST2 to obtain the ST of each sample and we used ST11 isolates for further analyses. Cleaned reads were mapped using Bowtie2. Variant calling and consensus alignment were made with samtools and vcftools. A maximum likelihood tree was constructed using IQTREE. Dated phylogenies and short-term phyldynamics and evolutionary parameters were estimated with BEAST.

Results: We have obtained complete genome sequences of 136 K. pneumoniae ST11 isolates. Most isolates fall into 4 well-supported clades with strong but not perfect association to a single hospital in 3 of them. Genetic diversity was very low within clades, indicating a recent common ancestry (colonization from a single clone). We inferred the time of the common ancestor for two clades [May-2012 and January-2008, for clades A and D, respectively]. Clade A corresponds to a community outbreak with many cases associated to hospitalization, whereas clade D is associated to a possible transmission of pOXA-48. Transmissions between hospitals of ST11 were frequent but our results also point to at least two independent introductions of this ST in the CV.

Conclusions: These analyses reinforce the idea that genomic surveillance studies are necessary to control and eliminate the transmission of resistance to antibiotics within and between hospitals since they provide essential information about the within and between hospitals dynamics of the most serious variants of this and other microorganisms.

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Abstracts 2020

Abstract 9225

Comparison of a new MALDI-TOF MS platform, Autof MS1000, with Bruker Biotyper for mucoid bacterial strains identification
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Background: Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) is widely used in clinical microbiology species identification for its fast speed and high accuracy. However, some mucoid bacterial strains often got unsatisfied identification due to the rich of mucous strands. The Autof ms1000 system (Auto Experimental Instrument Co. Ltd., China) was recently developed for microbial identification. We aimed to compare its performance on clinical mucoid bacterial strains with that of Bruker Biotyper (Bruker Daltonics GmbH, Germany).

Materials/methods: A total of 76 mucoid bacterial strains (including 52 Klebsiella pneumoniae and 24 Pseudomonas aeruginosa strains) were collected from a tertiary hospital in China from June to October 2019. The specimens were inoculated in 5% sheep blood agar, and then incubated for 18–24 hours at 35°C. For both Autof ms1000 and Bruker Biotyper, a single bacterial colony from the agar was smeared onto the target plate directly, and some other single colonies were washed with deionized water and then smeared onto the target plate. The matrix solution was α-cyano-4-hydroxycinnamic acid, and the peptide profile was acquired and analyzed by using their software respectively. All the strains were confirmed by 16S rDNA sequencing.

Results: For the method without pretreatment, the accuracy of Autof ms1000 at both the species and genus levels were higher than Bruker Biotyper (90.8% vs. 56.6%, P<0.05 for species level, and 92.1% vs. 67.1%, P<0.05 for genus level, respectively). For the method with deionized water, Autof ms1000 and Bruker Biotyper presented excellent performance (98.7% vs. 92.1%, P>0.05 for species level, and 100.0% vs. 96.1%, P>0.05 for genus level, respectively).

Conclusions: Autof ms1000 presented a higher accuracy in identification of clinical mucoid bacterial strains than Bruker Biotyper, and washing strains with deionized water was suggested in MALDI-TOF MS identification.

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Do we re-admit after outpatient artemether-lumefantrine? Evaluating the safety and efficacy of an ambulatory guideline for the treatment of uncomplicated Plasmodium falciparum malaria in a busy district general hospital in east London, UK

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Background: In 2018 there were 1683 imported cases of malaria to the United Kingdom, 82% were Plasmodium falciparum. Current UK Malaria treatment guidelines (2016) advocate admission for all patients with P. falciparum. Evidence on the safety of ambulating patients with uncomplicated P. falciparum in non-endemic countries since the widespread introduction of artesunate combination therapy (ACT) is lacking. 50-60 patients present to Homerton University Hospital (HUH), London, with P. falciparum annually. Approximately 80% are uncomplicated and ACT is first line treatment. We designed and implemented an ambulatory pathway for the management of adult patients with P. falciparum, with post-implementation monitoring of safety and efficacy.

Materials/methods: In September 2017 Infectious diseases, ambulatory and emergency care specialists retrospectively reviewed 52 cases of malaria presenting to HUH in the previous year. An ambulatory guideline with strict inclusion and exclusion criteria was developed and introduced in November 2018. Monthly data was collected prospectively on all adult patients (>16 years) who presented to HUH with P. falciparum: including demographics, parasitaemia, guideline compliance, and follow up data. Preliminary analysis for 1st December 2018 – 31 October 2019 given here.

Results: 32 adult patients were treated for P. falciparum at HUH during the study period. All patients acquired P. falciparum in Sub-Saharan Africa, 63% in Nigeria. Average age was 45 years. Median parasitaemia at presentation was 1.1% (IQR 0.2 – 2.2%). 24/32 cases had initial parasitaemias of <2%. 21 patients were admitted, 11 patients were ambulated (35%). Day 2 parasitaemia results were available for 23/32 patients – 22/23 patients’ parasitaemia decreased; 1 admitted patient’s parasitaemia increased (1.1% to 2.2%) but this was after a delay in administering ACT. No ambulated patients clinically deteriorated on treatment or required subsequent admission. All ambulated patients attended for follow up blood films, clinical review and completed treatment. No patients were lost to follow up. Following the introduction of the ambulatory malaria pathway there was a significant reduction in number of bed days for malaria patients from 121 (2016/17) to 46 (p=0.04).

Conclusions: Ambulatory treatment of uncomplicated P. falciparum malaria with ACT is safe, effective and cost-saving in our patient population, but requires adherence to a clear management pathway.

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Abstract 9231

Sharing of MLVA clusters of Listeria monocytogenes among bovine and human invasive clinical isolates

Ilena Drigo*,1, Elena Mazzolini1, Cosetta Bacchini1, Antonio Barberio1, Lisa Barco1, Monia Cocchi1, Laura D’este1, Michela Favretti1, Tolinda Gallo1, Antolla Gattuso3, Antonia Anna Lettini1, Eliana Schiavon1, Alexander Tavella1, Fabrizio Agnoletti1

1Istituto Zooprofilattico Sperimentale delle Venezie, Legnaro, Italy, 2Asui Ud Dipartimento di Prevenzione - Ambulatorio Malattie Sessualmente Trasmissibili (MST), Udine, Italy, 3Istituto Superiore di Sanità, Roma, Italy

Background: The scope of this work is to explore whether domestic bovines host Listeria monocytogenes (Lm) of pathogenic potential for humans.

Materials/methods: Sampling of bovine milk and faeces was carried out from 2018 and 2019 in Triveneto region. Lm strains collected in the same study area from 2015 and belonging to the IZSVe collection were also included. All strains were characterized by MLVA and serotyping; carriage of hlyA, actA, inlA, prfA and plcA genes was investigated by PCR. MIC of 13 antimicrobials (Table 1) was determined by broth microdilution. Results were compared with ones obtained from humans Lm (HLm).

Results: From 612 farms 11 Lm were isolated (9 from faeces/gut and 2 from milk samples). Overall, 53 HLm and 11 bovine Lm (BLm) were characterized. 58.5% of HLm were serotype 1/2a, 24.5% 4b, 13.2% 1/2b and 3.8% 1/2c. 63.6% of BLm were serotype 4b, 18.2% serotype 1/2a and 0.9% 1/2b.

Minimum spanning tree analysis showed 2/36 MLVA profiles shared between humans and bovines. All strains resulted positive for the studied virulence genes. MIC distribution is reported in table 1.

Conclusions: The role of bovine as possible reservoir of Lm affecting human needs to be assessed. In this study we observed a low percentage of bovines colonized by Lm, however, most of BLm are strictly correlated to HLm by MLVA. HLm and BLm showed comparable MIC distribution for all antimicrobials with the exception of sulfamethoxazole-trimethoprim. Differently from the HLm, all BLm showed sulfamethoxazole-trimethoprim MICs >ECOFF.

Table 1. MIC distribution of HLm and BLm. Vertical bars indicate the epidemiological cut-off of the antibiotic

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<th>Antimicrobial concentration mg/L</th>
<th>0.004</th>
<th>0.008</th>
<th>0.016</th>
<th>0.032</th>
<th>0.064</th>
<th>0.125</th>
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<th>1</th>
<th>2</th>
<th>4</th>
<th>8</th>
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Abstract 9232

Imported dengue fever in French travellers: a multi-centre retrospective study
Conan Pierre-Louis*1, Cécile Ficko1, Alice Perignon2, Christophe Rapp1, Eric Caumes2

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Background: Dengue fever is the most extensively spread arthropod-borne viral disease in the world. Viremic travelers play a key role in the globalization of infection in disease-naive countries that house Aedes.

Materials/methods: Multicenter retrospective descriptive study from 2008 to 2015 of all laboratory-proven cases of dengue fever in 2 university-affiliated hospitals.

Results: Two hundred and seventy-four patients were included (median age 34 years [IQR 24-47] - 141 males). The majority were white Europeans (220, 80.3%) who stayed in Southeast Asia (117, 42.7%), Latin America and the Caribbean (94, 34.3%). Mean reason for travel was tourism (203, 74.1%). DF trends in Paris mirrored the global activity of dengue fever with two peaks in 2010 and 2013. New or atypical areas of transmission were highlighted (Madeira and sub-Saharan Africa). Digestive signs accounted for 49.4 % of patients. Two patients (0.73%) had a severe dengue fever without lethal cases. NS1 antigen testing showed a 80.2 % sensitivity in our series and allowed a quick diagnosis. 70.1 % of patients were viremic during the activity period of Aedes and likely to cause autochthonous secondary cases.

Conclusions: Travelers are epidemiological sentinels. Analysis of imported cases provides information about viral circulation in endemic areas. Practitioners must consider dengue fever in travelers with suggestive signs and must be aware of mosquito bite prevention measures for viremic patients.

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Graphene oxide sheets affect expression of biofilm formation key genes in Escherichia coli
Claudia Vuotto*, Lucia Pappalardo1, Gianfranco Donelli1, Iolanda Francolini2
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Background: Graphene-based nanomaterials are constituted by single layers of carbon atoms with unique mechanical properties, large surface area, chemical stability, and superior electric and thermal conductivities. Among them, graphene oxide (GO) has the greatest potential for application in the biomedical field. GO is under investigation for infection control even if its antimicrobial and mostly anti-biofilm activity is still under debate, and very little is known.

Materials/methods: GO sheets, thoroughly characterized by Fourier transform infrared spectroscopy, X-ray Photoelectron Spectroscopy, Raman Spectroscopy, and Atomic Force Microscopy, were used at different concentrations (from 0.01 to 1 mg/mL) to evaluate their ability to inhibit planktonic and biofilm growth of Escherichia coli CFT073 by cell count, biofilm production assay, field emission scanning electron microscopy and RT-qPCR. The expression level of 9 genes involved in fimbriae production (fimA, fimH, csgA), oxidative stress (soxR, oxyR, dps) and iron homeostasis (tonB, iscR) was evaluated.

Results: Different concentrations of low-defects, 2-3 layers GO sheets, with specific physico-chemical properties, were put in contact with E. coli cells in planktonic and biofilm mode of growth. GO sheets did not cause substantial inhibition and damage of planktonic cells at 0.01 and 0.1 mg/mL of GO while 1 mg/mL significantly reduced cell viability after 3 h (p<0.01). On the contrary, a significantly reduction of adhesiveness of E. coli onto glass after 20h incubation time, as well as an almost total disappearance of adhesive fibers, were detected at 0.1 and 1 mg/mL of GO. RT-PCR revealed, after GO exposure, that the most significant reduction in genes expression concerned those involved in curli expression (csgA), and in iron availability (tonB, iscR), while an increase in the expression of dps, an alternative iron-storage protein important for the defense against hydrogen peroxide, was detected.

Conclusions: We hypothesize that the analysed GO, due to its definite physico-chemical properties, negatively interferes, in a concentration-dependent manner, on the biofilm-forming abilities by affecting curli production and pathways related to iron metabolism.

Our findings provide new insight on the possible mechanism behind GO anti-biofilm activity against E. coli and could contribute to the development of novel anti-biofilm compounds or surface coatings.

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A study to determine the frequency of QT interval prolongation in people treated with bedaquiline for drug-resistant tuberculosis

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Background: Bedaquiline (BDQ) is a recent addition to the drug-resistant tuberculosis (DR-TB) armamentarium. In the licensing trials, excess mortality was observed in the BDQ treatment arm, which whilst not clearly related to QTc prolongation, resulted in a black-box warning of the risk of arrhythmias and sudden death associated with BDQ therapy. The aim of this study was to determine the incidence of QTc prolongation and cardiac events in patients receiving BDQ DR-TB therapy under routine conditions.

Materials/methods: This was a retrospective cohort study of routinely collected data at a DR-TB hospital in KwaZulu Natal, South Africa, from September 2017 to February 2019. Medical records, including ECG data, were transcribed using a digital collection tool. The QT interval was corrected for heart rate using the Fridericia formula (QTcF). The primary outcome, a prolonged QTcF, was defined as QTcF >500ms, QTcF change >60ms from baseline, or both.

Results: A consecutive sample of 419 medical records was reviewed. Patients had a median age of 36 years (29-44), 278/419 (66.4%) were male and 311/419 (74.2%) were HIV positive. 418/419 patients (99.8%) were receiving concomitant levofloxacin and clofazamine. The observed retention rate was 84.0% over 26 weeks of BDQ therapy. The mean QTcF was 406.0ms at baseline increasing to 433.3ms by week 12 and 437.5ms at week 24. 19/419 patients (4.5%) had a QTcF >500ms and 62/419 patients (14.8%) had a QTcF change >60ms. There were no arrhythmias or deaths attributable to arrhythmias. QTcF >500ms was more common in older patients [OR 3.61, 95%CI [0.81-18.0] for age>50 vs. age<=30] and females compared to males [OR 2.36, 95%CI [0.84-6.72]]. The QTcF declined after prolongation without clinical sequelae, whether drugs were interrupted (QTcF change -45.4ms, n=11) or not (QTcF change -26.8ms, n=10).

Conclusions: BDQ prolonged the QTcF but no arrhythmias or related deaths were observed. Management of QTcF prolongation with or without an interruption to BDQ therapy did not affect the outcome in patients, although the small sample and inconsistent ECG frequency limit these inferences.

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Clinical characteristics and treatment of 255 patients hospitalised with bacterial cellulitis
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Background: Acute bacterial cellulitis (BC) is one of the most common skin and soft tissue infections. It places a substantial burden on the hospital system. This study assessed the clinical characteristics and treatment of BC in one healthcare center.

Materials/methods: We retrospectively analyzed data of 255 patients with BC hospitalized at one university hospital center in Zagreb in 2018. The diagnosis of BC was based on clinical and laboratory features.

Results: In 2018, 4.6% of all hospitalizations in our center were due to BC. The mortality rate was 2.7% (7 patients). More than half of the patients were female (54.9%) and the majority (74.1%) were older than 65 (median 65.5 years, IQR 20.0). At admission, the majority of patients (83.1%) were febrile (median 38.4°C, IQR 1.2) while 29.8% appeared unwell. The most common localization was the lower extremity (83.9%). Nearly all patients (93.3%) had at least one risk factor. This was the first documented episode of BC for 52.2% of the patients. Chronic ulcers were the most common entry site of infection (35.3%), while 11.8% of patients had no determinable entry site. Blood cultures were obtained in all patients at admission, with 4.7% being positive. At admission, C-reactive protein was elevated in 98.8% patients (mean 141.7 mg/L, IQR 132.6). Leukocytosis was present in 70.2% patients (mean 13.5x10^9 cells x mm³, IQR 6.0). The mean duration of fever after initiation of parenteral antibiotic was 3.1 days. In 35.3% of patients antibiotic therapy was changed. Complications arose in 23.1% of patients. Cefazolin was the most common antibiotic initiated at admission (45.1%), while 27.1% patients received combination antimicrobial therapy. The mean duration of parenteral treatment was 10.4 days (IQR 4.0). Cefazolin was associated with the shortest hospital stay (mean 9.6 days, IQR 4.0).

Conclusions: We observed a discrepancy between the relatively short time to defervescence and the relatively long duration of parenteral therapy and hospitalization. There is a potential space for shortening the length of parenteral therapy. However, the relatively high complication rate and comorbidities should be taken into mind.

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Cat scratch disease in children and adults: what a difference?
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Background: Cat-scratch disease (CSD) is a zoonotic infection caused by Bartonella henselae. The typical manifestations of CSD include regional lymphadenitis and fever. However, CSD can have a wide variety of clinical manifestations that can lead to incorrect diagnoses and prolonged hospital stays. Is the presentation of the disease different in children and adults?

Materials/methods: This retrospective monocentric study was performed between January 1, 2010 and December 31, 2018. Patients (children and adults) with positive PCR for Bartonella henselae were included. For each patient, epidemiological context, clinical picture, histological analyses and treatment were investigated.

Results: 78 patients with catch-scratch disease (CSD) were diagnosed by PCR at the CHRU de TOURS in 2010-2018, the group consisted of 43 children and 35 adults, median age 20.37 years (9.62 in children group and 34.83 in adults). 72 (92.3%) had an isolated localization. Axillary and inguinal lymph nodes were affected the most often, in respectively 30 and 21 patients. Fever is present in 36 patients (54%), whereas sweats and an impairment of the general state were found only in 7 and 9 patients respectively. The mean time from symptom onset was 22.3 days. Inflammatory syndrome with moderate level of CRP was found in 24 (48%) patients. 55 of 57 patients had contact with cats when the question was asked. From 36 cases with histological examination, 19 (52.8%) had classical CSD features of suppurative granulomatous lymphadenitis. Surgical drainage occurred in 32 patients and 51 received antibiotics. 11 patients had complications with hepatosplenic localization, meningoencephalitis, endocarditis and glomerulonephritis. Two differences in course of disease in children and adults were found: a larger inflammatory syndrome (p 0.05) and more complications in adults (p 0.01).

Conclusions: Bartonella henselae is a common pathogen in children but also in adults in whom serious complications may occur more frequently.

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Hepatitis C reflex testing in Spain in 2019: a story of success

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Background: In 2017 we conducted a survey across hospital diagnostic laboratories, finding that only 31% of them were providing reflex testing (HCV antibodies and HCV RNA on the same sample). As a consequence, Spanish Societies of ID & Clin Microbiology [GEHEP-SEIMC], Hepatology [AEEH, SEPD] and the Viral Hepatitis Elimination Alliance (AEHVE) signed a position document with recommendations on reflex testing. Training and dissemination activities to promote reflex testing implementation in Spanish hospitals were also developed. In 2019, we have evaluated reflex testing implementation in Spain.

Materials/methods: Cross-sectional study with data collection through a survey addressed to hospitals of the Hospitals National Catalogue with the following inclusion criteria: 1) general hospital (monographic, e.g., psychiatric hospitals are excluded), 2) with at least 200 beds, and 3) public, or teaching hospital if private. A questionnaire with the variables of interest, designed by a scientific committee composed of hepatologists and microbiologists, was sent to the selected hospitals. The fieldwork was carried out in September and October 2019.

Results: In 2019, 161 hospitals were surveyed, and 129 (80,1%) responded, vs 90/160 (56,3%) who responded in 2017 (p<0,001). Reflex testing is now implemented in 89% of Spanish hospitals (115/129), in 2017 only 31% (28/90; p<0,001) performed reflex testing. The number of hospitals that implemented alert systems to communicate HCV active chronic infection rose from 68,9% (2017) to 86,0% (2019) (p=0,002). Access to dried blood spot (DBS) and/or point of care testing in 2019 in Spain was: 10,9% for antibody testing from DBS; 15,5% for RNA testing from DBS; 36,4% for point of care (POC) RNA testing; 0,85% for antibody POC testing. Overall, 43,4% of Spanish hospitals has access to at least one of DBS/POC testing strategies.

Conclusions: In Spain, the proportion of hospitals that perform reflex testing for chronic HCV infection has significantly increased to 89% in 2019. Recommendations, training and dissemination measures performed since 2017 may be responsible for this increase. However, in 2019 new screening strategies such as DBS and POC testing are poorly implemented in Spanish hospitals.

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**Easy technique for ultra-fast identification of positive blood cultures with MALDI-TOF MS**

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**Background:** Bacteremia is associated with high rates of morbidity and mortality. International guidelines recommend instauration of empirical broad-spectrum antibiotics to be tailored upon availability of microbiological results from positive blood cultures (BC). Multiple MALDI-TOF MS methods directly performed on positive BC have been developed aiming at a time reduction to identification yet some are laborious, require various reagents and are costly. In this study we evaluate an ultra-fast (UF) identification approach requiring limited hands-on time, no specific reagents and based on a 1-hour broth incubation of positive BC followed by MALDI-TOF MS identification.

**Materials/methods:** This study was performed at the microbiology laboratory of the Cliniques universitaires Saint-Luc over a 1-month period on all routine positive BC. Briefly 5 drops of each positive bottle (Bactec culture vials, Becton Dickinson®) were inoculated in a 1ml Tryptic Soja Broth (TSB) followed by a 1-hour incubation at 35°C. Subsequently, TSB was centrifuged (2 minutes, 13000RPM) and the pellet was spotted twice on a target with 1µl formic acid and 1µl matrix for MALDI-TOF MS identification. Results were compared with routine identification based on subculture MALDI-TOF MS. Testing was performed once a day.

**Results:** 206 positive BC comprising 91 aerobic, 79 anaerobic and 36 pediatric bottles were tested. 198 positive BC were monomicrobial and 8 were polymicrobial. Routine MALDI-TOF MS identified 119 Gram-positive cocci, 83 Gram-negative bacilli, 4 Gram-negative cocci, 3 Gram-positive bacilli and 5 Yeast. Considering monomicrobial bottles, UF MALDI-TOF MS led to 125/198 (63.1%) concordant results and 31/198 (15.6%) discordant results compared to routine identification as well as 42/198 (21.2%) no results. Sub-analysis of all UF MALDI-TOF MS results with a minimum score of 1.7 (112/198) improved concordance to 93.8% (105/112). 7 identifications remained discordant with routine testing and consisted in *Staphylococcus* coagulase-negative identifications suggesting contamination during testing. Among the 8 polymicrobial BC, UF MALDI-TOF MS identified 1 of the 2 strains in 6 bottles and no strains in 2 bottles.

**Conclusions:** The UF MALDI-TOF MS identification approach shows good performances with a cut-off score ≥1.7 and could replace costly and hands-on time requiring approaches for direct MALDI-TOF MS identification.

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Abstract 9245

Designing a feasible, locally-appropriate socioeconomic intervention for TB-affected households in Nepal: a mixed-methods study

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Abstract third-party references: Wellcome Trust, UK, Academy of Medical Sciences, UK

Background: Tuberculosis (TB), the leading single infectious diseases killer globally, is driven by poverty. Having TB worsens impoverishment due to lost income and out-of-pocket costs which frequently become “catastrophic”, leading patients to abandon treatment or even die. WHO’s 2015 End TB Strategy recommends eliminating catastrophic costs through provision of socioeconomic support for TB-affected people. We conducted a mixed-methods study to identify the socioeconomic barriers and facilitators to accessing TB diagnosis and care, and inform design and implementation of a socioeconomic support intervention for TB-affected households in Nepal.

Materials/methods: The study consisted of two integrated, complementary projects. Project 1 was a quantitative, prospective case-control study of 221 people on TB treatment and 112 randomly-selected TB-unaffected controls; and Project 2 consisted of qualitative focus group discussions with 56 key stakeholders including people with TB, community representatives, and National TB Program staff and volunteers. Existing and potential socioeconomic interventions in Nepal and the findings from Projects 1 and 2 were then discussed with the key stakeholders at a two-day national, multi-sectoral workshop in Kathmandu, which culminated with the participants selecting the most promising intervention design for further trial evaluation.

Results: The workshop elicited that Nepal has existing social protection coverage but this is limited to free basic health care and cash-transfers or allowances for chronic diseases, disability, old- or young-age, or the extremely poor. The existing socioeconomic support for TB-affected households is restricted to counseling for treatment adherence and insufficient cash-transfers for food and nutritional support for people with drug-resistant-TB (DS-TB) only. Participants shortlisted two potential socioeconomic interventions [Table 1]. In a subsequent vote on these interventions, the majority of participants chose an intervention that included community-based psychosocial counselling during household visits and an integrated, enhanced cash transfer program, which provided additional payments to high-risk patients (e.g. extremely poor, HIV-TB coinfection, MDR-TB, Table 1).

Conclusions: This mixed methods research was the first of its kind in Nepal to evaluate barriers to TB care and involve local stakeholders to design a locally-appropriate socioeconomic intervention package to address these barriers. The chosen intervention is now being refined for trial evaluation.

Table 1: Design of and votes for psychosocial and economic elements of potential integrated socioeconomic support package for people with TB.

<table>
<thead>
<tr>
<th>Psychosocial element</th>
<th>Votes</th>
<th>Economic element</th>
<th>Votes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CB-DOTS provider / CHV assess stigma level at household visit</td>
<td>21% (3/15)</td>
<td>Monthly basic cash transfer for all patients, DR-TB NR 5000 (24 USD), DS-TB NR 1000 (9 USD)</td>
<td>12% (4/34)</td>
</tr>
<tr>
<td>CB-DOTS provider / CHV links whole household to TB support</td>
<td>21% (3/15)</td>
<td>Packet money for people with DR-TB in public NR 1600 (12 USD)</td>
<td></td>
</tr>
<tr>
<td>CB-DOTS provider / CHV assess stigma level at household visit</td>
<td>21% (3/15)</td>
<td>Conditional cash transfer for multidrug-resistant-TB patients, DR-TB NR 5000 (24 USD), DS-TB NR 1000 (9 USD)</td>
<td></td>
</tr>
<tr>
<td>CB-DOTS provider / CHV assess stigma level at household visit</td>
<td>79% (38/49)</td>
<td>Monthly basic cash transfer for all patients, DR-TB NR 5000 (24 USD), DS-TB NR 1000 (9 USD)</td>
<td>88% (35/40)</td>
</tr>
<tr>
<td>CB-DOTS provider / CHV assess stigma level at household visit</td>
<td>79% (38/49)</td>
<td>Packet money for people with DR-TB in public NR 1600 (12 USD)</td>
<td></td>
</tr>
<tr>
<td>CB-DOTS provider / CHV assess stigma level at household visit</td>
<td>79% (38/49)</td>
<td>Additional cash transfer for socially vulnerable people with TB, NR 2000 (17 USD)</td>
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</tr>
</tbody>
</table>

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Abstract 9246

Detection of linezolid-resistant enterococci carrying optrA and/or poxtA in raw-frozen dog foods commercialised in the EU: trend or threat?

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Abstract third-party references: The work was supported by UID/MULTI/04378/2019 with funding from FCT/MCTES through national funds.

Background: Raw-food-based diets have grown popularity recently as a healthier choice. Increasing controversy regarding their safety is installed, with limited scientific evidences showing their role as vehicles for transmission of antibiotic-resistant bacteria. Dogs have been described as reservoirs of clinically-relevant ampicillin-resistant (AmpR) Enterococcus faecium (Efm), but strains origin remains unknown. We aimed to characterize enterococci obtained from processed [dry/wet] and non-processed [raw-frozen] foods of main brands commercialized in Portugal.

Materials/methods: Forty-six samples [wet-n=22/dry-n=15/raw-frozen-n=9 foods; 24-international brands] from supermarkets/stores-n=8 and veterinary clinics-n=1 were included (September-November 2019). Raw-frozen samples were mainly constituted of salmon, chicken, turkey, calf, deer or duck, being a mixture of different meat types (muscle/viscera), fruits and vegetables. Samples [25g] were pre-enriched (37ºC/16-18h) in Buffered-Pettone-Water (ISO6887-2), enriched without/with different antibiotics (BHI-broth+Amp-16µg/mL or vancomycin-6µg/mL or chloramphenicol-16µg/mL) and plated in Slanetz-Bartley-agar without/with the same antibiotics. Different morphotypes/plate were saved and antibiotic susceptibility studied [13 antibiotics-disk-diffusion; linezolid-microdilution; Amp-Etest; EUCAST/CLSI]. Identification of species (sodA), search of optrA/poxtA (linezolid-resistance) and ptsD (clinically-relevant Efm marker) genes was done by PCR. MLST (pubmlst.org) was done in representatives and WGS is ongoing.

Results: Enterococcus (n=163) were identified in 19/46 (41%) (8/15-dry, 2/22-wet, 9/9-raw) of samples and identified as Efm (n=91), E. faecalis (Efs, n=59) or other species (n=13). Eighty-four were deeply studied. All 9 raw-frozen meat samples [Efm+Efs; n=30 each] carried Multi-Drug-Resistant (MDR) enterococci [n=20-Efm+22-Efs] including to ampicillin/ciprofloxacin/erythromycin/tetracycline/streptomycin/chloramphenicol-100% each, linezolid-78%, and gentamicin/quinupristin-dalfopristin-67% each. Linezolid-resistance (MIC=8-16mg/L) was detected in MDR enterococci carrying optrA+poxtA [5-Efs+3-Efm], only optrA [3-Efs, one ST40; 1-Efm] or only poxtA [2-Efm], corresponding to 78% of raw-frozen and 15% of all samples. MDR-AmpR-Efm (MIC=8->256 mg/L; n=18, one ST80) were identified in all raw-frozen samples and some carried optrA-n=1, poxtA-n=2 and/or ptsD-n=9. AmpR-linezolid-resistant-Efm were limited to one raw-frozen brand. In contrast, only one MDR-Efm (erythromycin/tetracycline/gentamicin) was detected in a wet sample.

Conclusions: Our study demonstrates that raw-frozen-foods for dogs carry MDR enterococci including to last-resource molecules for the treatment of human infections (linezolid). The close contact of pets with humans and the commercialization of the studied brands in different EU countries pose an international Public Health risk if transmission of such strains occurs between dogs and humans.

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Evidence for diminishing returns in supplementary immunisation activities: a spatio-temporal analysis of oral polio vaccination

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Background: The dramatic reduction in poliovirus incidence over the past decade has been driven by both routine immunisation (RI) and supplemental immunisation activities (SIAs). Whilst SIAs have been proven beneficial, the actual effectiveness of activities remains largely unknown and non-polio-endemic countries with under-immunised children remain at risk of circulating vaccine derived poliovirus outbreaks (cVDPVs).

Materials/methods: Multiple data sources are integrated within a Bayesian spatial-temporal analysis and implemented in the BUGS language in R: (1) Demographic and Health Surveys (DHS), (2) Multiple Indicator Cluster Surveys (MICS), and (3) Polio Information System (POLIS) data. Spatiotemporal analyses identify the spatially varying probability of being protected from poliomyelitis and using modelling, we aim to test hypotheses that SIA effectiveness depends on: time, SIA activities, RI, and remoteness.

Results: Combining vaccination history from DHS and MICS with POLIS data shows that substantial subnational spatial variation of immunity exists within countries and OPV dose-histories vary by data source. Our per-dose SIA mechanistic model highlights that in some contexts, SIAs alone can be as effective as RI, but often diminishing returns are exhibited, such that the effectiveness of the first SIA is high, but this effectiveness plateaus with subsequent activities. Furthermore, SIA effectiveness can be used to estimate SIA coverage.

Conclusions: Combining data from DHS, MICS and POLIS gives our analysis more power than previous approaches and shows that substantial spatial variation of immunity exists within countries. This is the first time, to our knowledge, that polio SIA effectiveness has been estimated from multiple data sources. This research will be used to improve polio programming within the Global Polio Eradication Initiative.

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**Abstract 9249**

**Rickettsioses: a series of 80 cases**

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**Background:** Rickettsioses are zoonotic diseases. They are common in Tunisia. Their main presentation is spotted fever. The diagnosis is based on a cluster of epidemiological and serological arguments. The aim of this study is to determine the epidemiological, clinical, biological, therapeutic, and evolutionary characteristics of rickettsioses in Mahdia’s region.

**Materials/methods:** This is a descriptive retrospective study of patients hospitalized at Taher Sfar Mahdia Hospital (2010-2016) for febrile syndrome due to rickettsioses which was diagnosed in the presence of epidemiological, clinical and/or serological arguments.

**Results:** Our study includes eighty patients with an average age of 31 years (19 days to 80 years) and with a sex ratio = 0.9. The physical examination showed fever, rash, and black spot in 97.5%, 51.3%, and 8.7% of cases respectively. Retinitis was objectively in the fundus in two cases. The biological abnormalities were: thrombocytopenia (42.5%), leukocytosis (16.3%), leukopenia (12.5%) and hepatic cytolysis (60%). The serology of rickettsioses detected anti-*Rickettsia conorii* antibodies (68.6%) and anti-*Rickettsia typhi* antibodies (31.3%). An antimicrobial therapy was prescribed in 75% of cases: doxycycline (55%), clarithromycin (23%) and fluoroquinolone (21.7%). The average duration of antimicrobial therapy was 9.7 days (2 to 21 days). The evolution was favorable for all our patients.

**Conclusions:** Our study shows that rickettsioses are a common cause of hospitalization either in children and adults. They are often underestimated because of the lack of specificity of the clinical presentation and the rapid means of diagnosis.

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Population-level antimicrobial consumption is associated with cultural factors in 37 high-income countries: a global ecological analysis

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Background: Previous studies evaluating the cultural and structural factors underpinning the large variations in the consumption of antibiotics between high-income countries have reached different conclusions as to whether corruption and cultural factors such as the degree of uncertainty avoidance (UA) and performance-orientation versus cooperation-orientation (POCO) play a role. These studies have been limited to Europe and we therefore aimed to expand this analysis to all high-income countries with available data.

Materials/methods: Using antimicrobial consumption data from the IQVIA MIDAS database, linear regression models were constructed with country-level cephalosporin, fluoroquinolone and macrolide consumption (standard doses/1000 population/year) as the outcome variables and country-specific scores of UA and POCO (obtained from the Hofstede Index), GDP/capita, world region and markers of effective governance (Control of Corruption and Regulatory Quality extracted from World Bank data) as the explanatory variables. All data, excluding the Hofstede Indices, used country-level averages for the years 2013 to 2015.

Results: Complete data was available for 37 countries from 4 world regions. Consumption of cephalosporins, macrolides and fluoroquinolones were all associated with POCO and UA but not the markers of effective governance (Table 1). In the case of macrolide consumption, the association with UA narrowly missed statistical significance. Repeat analyses limited to Europe - the region with the greatest number of countries in the dataset - as well as analyses excluding the world region dummy variables revealed very similar findings.

Conclusions: Previous studies have found that doctors in uncertainty-tolerant countries are more likely send their patients away with a comforting talk, without any prescription. When advocating not to prescribe antibiotics, one of the arguments used, is that this will reduce the emergence of antimicrobial resistance which is would be good for the whole population. Populations that are more orientated towards cooperation tend to show more concern for other members of society and may thus be more receptive to this message than performance-oriented societies. More thought should be given to construct stewardship campaigns that are tailored to the local extent of UA and POCO.

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Long-read sequencing for the diagnosis and characterisation of pathogens in severe pneumonia: the role of simulation and standards in clinical metagenomics pipeline development

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Background: Clinical use of metagenomics for severe pneumonia is now feasible due to improved enrichment methods and the real-time analysis potential of nanopore sequencing. Analysis remains challenging due to low biomass samples, similarity between pathogens and commensals, and clinical importance of relative abundance in interpretation. In preparation for a clinical study, we developed and validated a respiratory microbiome DNA standard and clinical pipeline for diagnosis and characterisation of respiratory pathogens.

Materials/methods: To test demultiplexers (n=4), we combined reads from samples sequenced on single-sample flowcells. We developed a quantified DNA standard containing respiratory pathogens and commensals, including species identified as closely related by MASH distance, and sequenced this repeatedly (SQK-RPB004, R9.4 flowcells, Oxford Nanopore Technologies). Data were used to train a nanopore-specific read simulator, generating labelled reads from each genome in the standard. These were combined and downsampled, and subjected to different long-read correctors (n=3), classifiers incorporating in-house post-processing (n=4), and metagenomic and species-specific assemblers (n=4). We used the results to develop an optimised pipeline for real-time species identification during sequencing and a more stringent, deferred pipeline for pathogen characterisation.

Results: Optimised demultiplexing assigned 94.6% of reads correctly. Remaining reads were unassigned with only 0.01% misassigned. The pipeline preserves relative abundance with a mean difference from true relative abundance of 0.59% per species (range 0.09-1.8%). Metagenomic assembly had more mismatches than species-specific assembly, and had misassemblies between highly related species (e.g. Neisseria), but was sufficient for classification of contigs to confirm species. Assembly using species-binned reads was of high quality (99.93% of the genome, LG50 = 1.67, 1.55 mismatches and 2.92 indels per 100 kbp on average across 6 species). Comparison of simulation and sequencing data shows species-specific assemblies following classification are comparable at equivalent quantities, but reveals biases due to wet-laboratory processes.

Conclusions: Nanopore-based sequencing has potential for clinical diagnosis and characterisation of respiratory pathogens. Simulation reveals substantial biases introduced during wet-laboratory and analysis processes. Both simulation and a site-specific microbiome standard were needed to develop a high-fidelity pipeline and are recommended as part of validation of future clinical metagenomic pipelines.

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Failure to complete treatment for latent tuberculosis infection in Portugal, 2013-2017: geographic, socio-demographic and medical associated factors

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Background: There is conflicting evidence about factors associated with failure to complete treatment (FCT) for latent tuberculosis infection (LTBI). We aim to identify the geographic, socio-demographic and medical factors associated with FCT in Portugal, highlighting the two main metropolitan areas of Porto and Lisbon.

Materials/methods: We performed a retrospective cohort study including LTBI patients that started treatment in Portugal between 2013 and 2017. We calculated adjusted odds-ratios (aOR) and 95% confidence intervals (95%CI) using multivariable logistic regression to identify geographic, socio-demographic and medical factors associated with FCT.

Results: Data on completion of treatment were available for 15,478 of 17,144 patients (90.3%). Of those, 2,132 (13.8%) failed to complete treatment. Factors associated with FCT were being older than 15 years (aOR: 1.65 [95%CI=1.34-2.05] for those aged 16 to 29), being born abroad (aOR: 2.04 [95%CI=1.19-3.50] for Asia, aOR: 1.57 [95%CI=1.24-1.98] for Africa), having a chronic disease (aOR: 1.29 [95%CI=1.04-1.60]), alcohol abuse (aOR: 2.24 [95%CI=1.73-2.90]), and being intravenous drug user (aOR: 1.68 [95%CI=1.05-2.68]). Three-month course treatment with isoniazid plus rifampicin was associated with decreased FCT when compared to 6- or 9-month courses of isoniazid-only (aOR: 0.59 [95%CI=0.45-0.77]). In Lisbon metropolitan area, being born in Africa, and in Porto metropolitan area, alcohol abusing and being intravenous drug user were distinctive factors associated with FCT.

Conclusions: Socio-demographic and medical factors associated with FCT may vary by geographical area and should be taken into account when planning interventions to improve LTBI treatment outcomes. This study reinforces that shorter course treatment for LTBI might reduce FCT.

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Improving country-level antimicrobial prescribing with the implementation of a uniform and standardised surveillance method: the Global-PPS Chilean experience, year 2015 and 2017

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Background: A standardized method for surveillance of antimicrobial use (AMU) [www.global-pps.com] was performed in Chile in 2015 and 2017. We aimed to compare antimicrobial prescribing indicators from both audits, and analyzed their contribution for improving AMU.

Materials/methods: The Global-PPS included 12 and 27 chilean hospitals respectively. Hospitals were guided by a central local team, which provided continuous assistance for conducting the survey. The survey included all inpatients receiving an antimicrobial at 8am on the day it was conducted. Data included antimicrobial agents used, source of infections treated, and quality indicators of AMU. Local data was reported to each participating center through local meetings and written documents including guidance to improve their AMU.

Results: PPS included 3043 patients (2504 adults) in 2015 and 6809 patients (5540 adults) in 2017. Overall antimicrobial prevalence was 35.6% and 42.2%, respectively. Increase in antimicrobial prevalence was significantly explained by an increased AMU in hemato-oncology wards, both in adults (17.5 to 49.6%) and pediatrics (20.8 to 27.1%). Top 3 sources of infection, both in 2015 and 2017, were pneumonia, skin and soft tissue infections and intrabdominal infections. Missing guidelines decreased, from 2015 to 2017, in medical wards (34.1% to 25.5%), surgical wards (30.0 to 26.3%), and intensive care wards (21.8% to 20.5%). For both periods, top three most prescribed systemic antibiotics were ceftriaxone (mean 18.3%), metronidazole (mean 10.9%) and cefazolin mainly prescribed for surgical prophylaxis (mean 8.7%). Guidelines compliant prescriptions increased, from 2015 to 2017, in medical wards (62.2 to 77.9%), surgical wards (52.1 to 64.8%), and intensive care wards (54.3 to 67.6%). Prolonged surgical prophylaxis decreased from 63% to 44%. However, reason and stop/review date written in notes did not improve (84.0% versus 84.2%) and (38.5% versus 36.7%) in 2015 and 2017, respectively

Conclusions: Global PPS contributed to further develop collaborative networks with voluntary participation, which have obtained significant information regarding AMU, in a local and national perspective. An improvement of antimicrobial prescribing was observed, which we attributed to the provided guidance to each hospital, pointing out potential useful local interventions. Continued efforts are needed to further improve the quality of prescribing.

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Abstract 9260

The dissemination and reservoirs of ESBL-producing Escherichia coli in intensive care unit
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Background: ESBL-EC is an important pathogen for blood infection. For tracking the dissemination and reservoirs of ESBL-producing Escherichia coli (ESBL-EC) in hospital, it need an understanding of the epidemiology of ESBL-EC in hospital-related environments and patient carriage.

Materials/methods: We collected samples from patients and surroundings once a week in an ICU for three months in 2019. Except for gathering rectal swabs and oral swabs from inpatients, the environmental samples were collected as follows. Sterilized swabs were dipped by fresh TSB and wiped the surface of bed units. After incubating the swabs in a tube with TSB at 37 degree for 24 hours, the culture were inoculated on Chromagar plates for screening ESBL-producing Escherichia coli. The positive culture and the original information of strains were recorded.

Results: A total of 122 ESBL-producing Escherichia coli isolates were collected in 12 weeks. About a half were carried by patients, of which most were isolated from rectal swabs. Even though some patients undergone powerful antibiotic treatment, gut-colonized ESBL-EC of these patients could co-colonized with CRKP or CRAB rather than being erased. Patients acted as reservoirs as well as "comfortable medium" for the dissemination of carbapenem-resistance genes. Another half of isolates were from surroundings of bed units. About 70% ESBL-EC were isolated from water sinks. There was a patient who carried ESBL-EC at the second week and lost it for 9 weeks. But we isolated ESBL-EC for 2 months from water sinks and bed curtains of this patient's bed unit. At 11th week, ESBL-EC reappeared in this patient rectal swabs. Further STs of these ESBL-EC needed to be detected for exploring the dissemination routes.

Conclusions: Patient carriage and water sinks are two major reservoirs for ESBL-EC in ICU. A better view of ESBL-EC colonization in ICU could help us take measures to control the related infection. Under rough antibiotic stresses, ESBL-EC could maintained in guts and might evolve into carbapenem-resistance bacteria.

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**Abstract 9263**

**Interferon gamma release assay and tuberculin skin test agreement in latent tuberculosis infection diagnosis among healthcare workers at a tertiary Hospital in western Saudi Arabia**

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**Background:** Diagnosis and treatment for Latent TBI is an essential component of TB elimination. Two tests are available, TST and IGRA. Data on diagnostic performance and agreement between these tests are limited. This study aimed to assess the agreement of IGRA test with the traditional TST in diagnosing latent TBI among Health Care Workers.

**Materials/methods:** Retrospective review of medical records of HCWs was conducted at King Abdulaziz Medical City, Jeddah, Saudi Arabia from June 2018 to September 2019. Records were included when both IGRA-TB and TST were performed simultaneously or within a month for purpose of preemployment or periodic screening. The cut-off for TST was 10mm.

**Results:** A total of 746 healthcare workers had simultaneous IGRA-TB and TST results. Most of them were females (68.7%). Saudi represented 46.3%, followed by Filipinos (25.9%) then Malaysians (13.9%). Half of the HCWs were non-clinical staff (50.2%). Nurses, physicians and allied health professionals represented 22.5%, 21.4% and 5.9%, respectively. Dual positive results were identified in 24.9%, positive IGRA-TB in 31.6% and positive TST in 36.3%. Among females, 26.9% had dual positive results compared to 21.1% among males (p=0.09). Dual positive results were the highest among Filipinos (48.2%), Malaysians (40.8%), then Saudi (5.4%) (p=0.001). Based on job categories, high prevalence of dual positive results was observed among non-clinical staff (39.2%) and nurses (36.8%) compared to allied health (12.9%), and physicians (6.3%) (p=0.001). Mean ±SD age of HCWs with dual positive test was higher (38.5 ±8.9) than those with either test positive (34.4 ±9.1) or dual negative result (29.4 ±6.0) (p=0.001). There was good overall agreement between IGRA-TB and TST (82.6%, kappa 0.61, p=0.001). Lower agreement was observed in the low incidence groups [Saudi, physicians/allied health and young age], kappa= 0.32, 0.43, 0.43, respectively.

**Conclusions:** This study revealed relatively high burden of latent TB infection among healthcare workers in King Abdulaziz Medical City, Saudi Arabia. Most of the cases were from southeast Asia. Choice of a screening test depends on TB burden, test cost and population to be tested. Longitudinal study is required to determine diagnostic performance of dual positive compared to either test positive.

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Abstract 9269

**Infectious disease specialist intervention in the neonatal intensive care unit: a safe approach to reduce antibiotic exposure in neonates**

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**Background:** Neonatal sepsis is a major cause of neonatal mortality and morbidity. Prompt initiation of antibiotics in newborns with clinical suspicion of sepsis improves outcome but leads to an overuse of antibiotics in a population vulnerable for long term adverse effects of these medications.

Studies on adults have shown that including infectious disease specialist (IDS) in the care of patients improves the appropriateness of antibiotic prescription, decreases antibiotic consumption and improves outcome in patients with severe infection. However, for patients on neonatal intensive care units this data is missing so far. In 2018 we established a weekly proactive audit of antibiotic use on our 12-bed neonatal intensive care unit as joint interdisciplinary rounds between an IDS and the neonatologist taking care of the patients.

**Materials/methods:** Patient-related therapy adjustments were systematically documented; antibiotic use before and after audit as well as ABS strategies (de-escalation, duration of treatment, dose and administration optimization) were analyzed as well as antibiotic use in infants weighing less than 1500g [Data from the German Neonatal Infection Surveillance Network (NeoKISS; "Krankenhaus-Infektions-Surveillance-System) and outcome data (mortality, BPD- and IVH-rate) in the 12 months prior/post the establishment of the interdisciplinary rounds.

**Results:** Weekly interdisciplinary rounds were established in March 2018. In the following 12 months joint rounds were performed on 404 patients. 86 (21%) of those patients were diagnosed with an infection and 90 (22%) received antibiotics at the time of the interdisciplinary rounds. 79 interventions regarding antibiotic use were made. This led to a reduction in antibiotic use in infants weighing <1500g by 26% with a particular high reduction in the use of broad-spectrum antibiotics (3rd Generation Cephalosporines by 60%, Carbapenems by 40% and Glycopeptides by 50%). There was no significant change in mortality, BPD- or IVH rate prior/post intervention.

**Conclusions:** Infectious disease specialist intervention can safely improve the appropriateness of antibiotic prescription and decreases antibiotic consumption in the neonatal period and can therefore help to reduce long term adverse effects of antibiotic overuse in this age group.

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Turn around time and performances of blood cultures with regard to hospital organisation

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Background: Bloodstream infections (BSI) are associated with a high mortality, particularly if first-line antimicrobial therapy is inadequate. Blood culture (BC) efficiency is critical for BSI diagnosis but the results are usually available long after the treatment has started because of delayed BC positivity.

Materials/methods: Our hospital is a 850-bed university hospital with about 1,000 patients yearly hospitalized with BSI. We measured the positivity rate, the time to incubation and to positivity, and the number of BSI episodes diagnosed during two periods with different organization for BC incubation. During the first period [2015-2016], the organization was classical with the BC bottles incubated in BACT/Alert incubators in the bacteriology lab but this lab being closed during nights (from 18.30 pm to 7:30 am). During the second period [2017-2018], the incubators were replaced by Bact/ALERT VIRTUO enabling to implement one incubator in the emergency lab opened 24/7 since it does not require specialized technicians to introduce the BC bottles. A second incubator was still present in the lab for the bottles incubated during the day.

Results: Whereas the number of BC processed during the period 2 was similar to those of period 1 (30,974 and 30,821, respectively), the number of positive BC was higher during period 2 (3,293 vs. 2,757) as well as the positive BSI episodes (1,192 and 1,003). The increase was especially significant for patients from the emergency rooms (100,000 visits per year) for which 333 BSI episodes vs. 229 were diagnosed. The median time to incubation was significantly shorter during period 2 (1.52 h vs. 6.88h). These changes were observed whatever the bottle [aerobic or anaerobic] and for BC sampled during night or day. For BSI due to Gram-negative bacilli, we observed a median decrease in time to positivity of 6 hours leading to a total of 13 hours between sampling and positivity.

Conclusions: Operational changes like incubating 24/7 in an easy of use and efficient BC automate can reduce not only the time to positivity but lead also to an increase in BC positivity and of the number of the sepsis episodes microbiologically diagnosed as BSI.

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Abstract 9280

Chitosan-coated magnetite nanoparticles as a biocompatible nystatin carrier: physicochemical characterisation and in vitro fungicidal determination

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Background: Nystatin (Nyst) is a tetraene diene polyene antibiotic with low solubility in water, which is broadly used in antifungal treatments. In this study, super-paramagnetic iron oxide nanoparticles (SPIONs) were synthesized via a chemical co-precipitation procedure and its antifungal activities against pathogenic yeasts were determined.

Materials/methods: The nanoparticles were coated with chitosan (CS) as a biocompatible and stabilizing agent. Then, Fe3O4/CS/Nyst nanocomposite was prepared by immobilizing Nyst on CS based on chemical interactions. Fe3O4/CS/Nyst nanocomposite was characterized by X-ray diffractometry (XRD), Fourier-transform infrared spectrophotometry (FT-IR), vibrating sample magnetometry (VSM), transmission electron microscopy (TEM), field emission scanning electron microscopy (FESEM), and energy-dispersive X-ray spectroscopy (EDX). Antifungal activity of the nanostructure was tested against yeast microorganisms including Candida species by broth microdilution method according to the Clinical Laboratory Standard Institute (CLSI). The cytotoxicity of Fe3O4/CS/Nyst on human cell lines was determined by MTT assay.

Results: The FTIR analysis revealed the binding of CS on the surface of Fe3O4 NPs and also the loading of Nyst on the nanostructure. The nystatin drug loading was measured by Uv-Vis showing a 22% loading capacity on the nanostructure. TEM revealed Fe304/CS/Nyst nanocomposites in monodispersed spherical shape with a mean diameter of ~10-20 nm. Synthesized nanostructures exhibited good activity against representative microorganisms of public concern.

Conclusions: The formulated nystatin-loaded modified chitosan-magnetic nanoparticles showed a good encapsulation and loading efficiency coupled with magnetic responsivity. This Fe304/CS might be used in targeted therapy of mucosal infections such as esophageal candidiasis by using an external magnetic field.

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Abstract 9281

**Increase of carbapenemase-producing Enterobacteriaceae in a Portuguese hospital from 2016 to 2019**

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**Background:** Carbapenemase-producing Enterobacteriaceae (CPE), specially *K. pneumoniae* (CP-Kp), is an increasing health threat globally. The aim of this study was to perform a molecular and epidemiological survey of CPE isolates and their susceptibility to colistin in a Portuguese Hospital.

**Materials/methods:** CP-Kp isolates (n = 118) were collected from biological samples from patients admitted to Hospital Centre of Médio Tejo, Portugal, between January 2016 and September 2019. Antimicrobial susceptibilities were determined by automatic Vitek2-BioMérieux and colistin MICs confirmed by broth microdilution. Both GeneXpert (Cepheid) and NG-Test CARBA 5 immunochromatographic assay (NG Biotech, Guipry, France) were used to screen for CPE.

**Results:** Of the patients 55% were male; 35.8% with age between 81-90 years. Clinically significant CPE isolates were most frequently cultured from urine (69.2 %), blood cultures (13.3%), respiratory tract (4.2%). Total number of CPE in this study were 120 strains. The annual number of CPE strains increased from one (0.8%) in 2016 to 53 (44.2%) in 2019. The most frequent carbapenemases were KPC [n = 113; 94.2%] followed by OXA-48-like [n = 7; 5.8%]. One strain of *A. baumannii* and other of *E. aerogenes* also produced KPC-carbapenemase during the time analysed. All CPE strains were resistant to quinolones, aminoglycosides and beta-lactams tested. There was an increase of nitrofurantoin efficacy in CPE strains [n = 83] [0% in 2016 to 18.9% [n = 40; yr 2019]] from urine. Susceptibility to fosfomycin in urine CPE strains [n = 83] oscillated from 51.7% [n = 29; yr 2016] to 77.5% [n = 40; yr 2019]. Colistin resistance increased from 0% in 2016 to 13.2% in 2019.

**Conclusions:** CP-Kp are still rare in this region, however results showed a gradually increasing over time, and appearance in other Enterobacteria. Also, a decrease of susceptibility to colistin is relevant, one of the last resort antimicrobial agent. Most frequent clinically significant isolations are from urine. Distressingly, some patients are colonized by CP-Kp, which is known to survive for long periods in the hospital environment and nursing homes. Real-time surveillance using screening methods, rapid response and coordinated outbreak investigation are crucial in controlling the spread of CP-Kp.

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Multi-omics approaches to understand the regulation of biofilm formation in high biofilm-forming clinical isolate of Candida parapsilosis

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Background: Biofilm formation of Candida parapsilosis on central venous catheters puts patients at increased risk to develop bloodstream infection with C. parapsilosis. An important, if not the major, virulence factor of C. parapsilosis is its ability to form biofilms. Interestingly, the major biofilm regulator BCR1 does not affect biofilm formation of high, spider-like, biofilm forming clinical strains indicating a novel regulatory mode. This study was set up to investigate regulation of biofilm formation of high, spider like, biofilm forming strains.

Materials/methods: The genomes of 5 C. parapsilosis clinical isolates with high (3 isolates) and no (2 isolates) biofilm forming abilities from bloodstream infection were whole-genome sequenced using PacBio technology. In liquid phase, high biofilm forming strains show yeast cell aggregation, which we consider an early biofilm forming stage. Total RNA isolated from early biofilm cultures was subjected to RNA sequencing performed by Illumina HiSeq 2500 with 2 x 125 reads. Protein isolated was subjected to whole proteomic analysis performed by LC-MS. Construction of deletion mutants and complementation was performed by using the SAT1 flipping strategy. Crystal violet staining was used to assess biofilm formation on a polystyrene surface. The cell morphology was assessed by light microscopy, confocal laser scanning microscopy, TEM and SEM.

Results: We have previously categorized clinical strains of C. parapsilosis from bloodstream infection into no, low, and high biofilm formers. Here, we performed whole genome-, RNA- sequencing and proteomic analysis of 5 selected isolates with no- and high biofilm forming ability to understand the regulation of biofilm formation in clinical isolates of C. parapsilosis. Transcriptome comparison between high and no biofilm formers revealed altered expression of 94 genes with expression of selected genes to be confirmed by qRT-PCR. Integration of proteomic data with transcriptomic data resulted in 36 differently regulated genes. Deletion of candidate genes affecting biofilm formation in high biofilm forming strains is in progress.

Conclusions: This study demonstrates that a multi-omics approach between no and high biofilm forming strains is a successful strategy to identify candidate genes involved in regulation of biofilm formation in the clonal species C. parapsilosis.

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Abstracts 2020

Abstract 9287

Integrating genome-wide association study with bulk and single-cell RNA sequencing reveals a role for LY86 in the anti-Candida host response

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Background: Candida bloodstream infection, i.e. candidemia, is the most frequently encountered life-threatening fungal infection worldwide, with mortality rates up to almost 50%. In the majority of candidemia cases, Candida albicans is responsible. Worryingly, a global increase in the number of patients who are susceptible to infection (e.g. immunocompromised patients), has led to a rise in the incidence of candidemia in the last few decades. Therefore, a better understanding of the anti-Candida host response is essential to overcome this poor prognosis and to lower disease incidence. However, small patient group sizes have limited our ability to gain such understanding.

Materials/methods: Here, we conducted a systems genetic study using candidemia genome-wide association data, bulk and single-cell transcriptomic analyses of immune cells stimulated with Candida albicans. We performed differential expression analysis upon Candida stimulation in single-cell expression data to reveal the important cell types involved in the host response against Candida. We performed the integration of candidemia genome-wide SNP data from a large patient cohort with Candida-response expression QTLs identified in peripheral blood mononuclear cells from 150 samples. We carried out gene knockdown experiments and migration assays in monocytes to reveal the function of candidemia risk genes.

Results: Gene expression analysis in single-cell data upon stimulation confirmed the known major role of monocytes, but more interestingly, also uncovered an unprecedented role for NK cells. Moreover, combining the power of bulk RNA-seq with the high resolution of single-cell RNA-seq data led to the identification of 27 Candida-response QTLs and revealed the cell types potentially involved herein. Integration of these response QTLs with a GWAS on candidemia susceptibility prioritized LY86 as a risk gene for candidemia. By performing knockdown experiments of LY86 and cell migration assays we describe a novel mechanism through which this gene affects the immune response against Candida infection.

Conclusions: Altogether, our integrative systems genetics approach identifies previously unknown mechanisms underlying the immune response to Candida infection. We expect that such an approach can be generalized to other infectious diseases for which small patient group sizes have restricted our ability to unravel the disease mechanism in more detail.

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Abstract 9288

Descriptive analysis of patients with influenza virus admitted to intensive care unit from 2010 to 2019

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Background: Influenza is a major public health concern, especially in critically ill patients. This work aims to describe the characteristics of patients with influenza virus admitted to ICU.

Materials/methods: Retrospective descriptive study includes patients diagnosed with influenza between 2010 and 2019 admitted to ICU in a reference hospital for a population of 450000 inhabitants. The diagnosis was obtained by nasopharyngeal smear, sputum or bronchotracheal aspirate. Epidemiological variables, risk factors, severity at admission, treatments administered, life support measures and mortality were collected.

Results: A total of 89 patients were included (mean 9.8/year). Average age 60.5 years old (16-86), 63% male. Mean APACHE-II score was 19.1, and SOFA 6.3. 28 patients (31.4%) had received vaccine. It was identified influenza A H1N1 in 49 patients (55%), seasonal influenza A in 28 (31.4%), B in 11 (12.3%) and in 1 it was not typified. Comorbidities were present in many of them: COPD 33 (37%), hematological diseases 11 (12.3%), obesity 13 (14.6%), pregnancy 5 (5.6%), chronic renal failure 6 (6.7%), immunosuppression 10 (11.2%), asthma 6 (6.7%), diabetes 15 (16.8%), HIV 1 (1.1%), and 20 patients (22.4%) had no comorbidities. In 62 cases (69.6%) the radiology was positive. 43 patients (48.3%) needed vasoactive drug infusion, and 9 (10%) continuous renal replacement. 84 patients (94.4%) needed mechanical ventilation (MV), from which 66 (74.2%) received non-invasive MV (NIMV), 29 (32.6%) invasive, and 32 (35.9%) both. In 33 (37%) there was a failure of NIMV support, needing orotracheal intubation. 8 patients (9%) needed prone position. 77 (86.5%) were treated with oseltamivir, during an average of 6.5 days [mean 5.5 days between symptoms started and first dose]. 76 patients (85.4%) received empiric antibiotherapy, coexisting respiratory bacterial infection in 28 (31.5%). The length of stay in ICU was 11.26 days. 22 patients (24.7%) died, 20 of them (91%) in ICU. For them, the median APACHE-II was 24 points, SOFA 8.25, and the time between symptoms started and treatment was 5.9 days.

Conclusions: Most patients presented influenza A H1N1 and MV. The subgroup of patients who died had a higher incidence of immunosuppression, severity and more time between symptoms and treatment.

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Abstract 9290

Delayed treatment response in healthcare-associated infections by OXA-48 carbapenemase-producing Enterobacteriaceae

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Background: Carbapenem-resistant Enterobacteriaceae (CRE) are important causes of health-care associated infections and present a great challenge to clinicians. We set out to investigate the impact of carbapenemase-producing Enterobacteriaceae infections on the response to treatment in pediatric cancer patients receiving chemotherapy at National Cancer Institute, Cairo University.

Materials/methods: During a six month period extending from June to December 2017, 151 febrile episodes among 129 neutropenic pediatric cancer patients were included in the study; their clinical characteristics and the response to treatment were investigated. Blood cultures from febrile patients were performed; isolates were identified and their antibiotic susceptibility profile determined by Vitek-2. Enterobacteriaceae isolates were further tested by multiplex PCR for the presence of carbapenem-resistance genes: bla\textsubscript{OXA-48}, bla\textsubscript{KPC}, bla\textsubscript{NDM} and bla\textsubscript{VIM}.

Results: Eighty-five Enterobacteriaceae, carbapenem-resistance, isolates were recovered from blood cultures and they included: Escherichia coli (n=45/85, 53%) and Klebsiella pneumoniae (n=40/85, 47%). Carbapenem-resistance genes were detected in 41.2% (n=35/85) of the tested isolates, as follows: bla\textsubscript{OXA-48} (n=33/85, 38.8%), bla\textsubscript{KPC} (n=4/85, 4.7%) and bla\textsubscript{NDM} (n=3/85, 3.5%); the concomitant presence of bla\textsubscript{OXA-48} with either bla\textsubscript{KPC} or bla\textsubscript{NDM} was detected in (n=4/85, 4.7%) and (n=1/85, 1.17%), respectively; bla\textsubscript{VIM} was not detected in any of the tested isolates. A percentage of 85.7% (n=30/35) of PCR positive patients and 30% (n=15/50) of PCR negative patients had fever till day 10 of the episode; a significant difference was observed in the response to antimicrobial therapy in febrile patients harboring carbapenem-resistance genes and those missing them, (p=0.009). Colistin was added in the treatment of 34% of the febrile episodes (n=51/151); it was significantly more used in bla\textsubscript{OXA-48} PCR positive patients (n=23/35, 65.7%) compared to PCR negative patients (n=6/50, 12%), p <0.001.

Conclusions: The presence of bla\textsubscript{OXA-48} was associated with delayed response to antimicrobial therapy and the need for colistin addition in high risk patients.

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Abstracts 2020

Abstract 9291

**Antibiotic stewardship: assessment of education and awareness tools for improving citizen involvement**

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**Background:** The development of bacterial resistance to antibiotics could become one of the leading causes of death in the world by 2050 if nothing changed. The consumption of antibiotics in France is high and stable over 10 years despite the continuous awareness of prescribers. The objective was to evaluate information materials to aware users to the issue of bacterial resistance and the correct use of antibiotics by focusing messages around the main role of the gut microbiota.

**Materials/methods:** Quantitative, cross-sectional, descriptive study conducted in France from February 2018 to February 2019, involving users by paper questionnaire, email or social network. Creation of fact sheets explaining the bacterial resistance and its consequences, the pivotal role of the gut microbiota, the concept of “One Health”, and the principles for better use of antibiotics. We included users over the age of 15, speaking French and answering the questionnaire before and after reading fact sheets. Comparison of knowledge using a score obtained before and after information.

**Results:** Five hundred and sixty-nine users were included between November 2018 and February 2019, 83% of whom were female and 32% of the participants consumed an antibiotic at least once a year. Overall success rate before information was 65.0%, up to 93% for gut microbiota questions. The overall median score increased from 15/22 [IQR [12-17]] before information to 18/22 [16-19] after information (p <0.001). The average percentage of correct responses for bacterial resistance increased from 56.9% before information to 65.9% after information (p <0.001). The major gain in knowledge was about 30% for questions about antibiotic indications.

**Conclusions:** Information on the bacterial resistance and the good use of antibiotics makes it possible to aware the users. Users’ knowledge of the microbiota can help raise awareness of the ecological impact of antibiotics and participate largely to improve antibiotics use especially in the community.

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Abstract 9292

Microbiome changes among patients who transitioned from *Clostridioides difficile* negative to *C. difficile* positive using systematic screening tests

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**Background:** Colonization with toxigenic *Clostridioides difficile* (*Cdiff*) is necessary for *Cdiff* infection to occur. Here we aimed to understand the microbiome disruptions associated with transitioning from *Cdiff-* to *Cdiff+* [N2P] in patients who underwent systematic *Cdiff* screening tests.

**Materials/methods:** Five high-incidence *Cdiff* inpatient units in Milwaukee, WI performed screening upon admission and weekly thereafter using nucleic-acid-amplification tests (NAAT; Xpert*®* *C. difficile*, Cepheid, CA). Available stool samples underwent 16S rDNA sequencing. Non-metric multidimensional scaling (NDMS) plots were constructed based on non-parametric comparison testing analysis (ADONIS) of Bray-Curtis distance matrices. Twenty-four samples also underwent shotgun metagenomics sequencing. Reads were filtered for quality, assembled, and individual samples were mapped back to contigs. Taxonomic and protein identity were assigned with Kaiju and COGs, PFAM, and InterproScan, respectively. Anvi’o was used for visualization and downstream analyses. Linear mixed models were used to investigate the association between groups and relative abundance of individual species over time. Data was fitted using arcsine square-root or logit transformation.

**Results:** A total of 606 stool samples from 120 patients underwent 16S rDNA sequencing [N2P n=44; Negative-control [always *C. difficile* (-)] n=47; Positive-control [always *C. difficile* (+)] n=19]. N2P patients were on average 60 years old, 50% male, 91% had hematology-oncology diagnoses, 31% had bone marrow transplants, and 64% were exposed to antibiotics. These demographics and exposure variables were not statistically different when compared to Negative-controls or Positive-controls. Diversity indexes and the number of OTUs were no different between *Cdiff-* and *Cdiff*+ samples belonging to N2P or between *Cdiff-* samples within N2P and Negative-controls. NDMS showed similar distribution of *Cdiff-* and *Cdiff*+ samples belonging to N2P patients (Fig1A); however, overtime abundance of *Clostridioides*, *Lachnoclostridium*, and *Coprococcus* increased while *Blautia* abundance decreased. Negative-controls and Positive-controls showed differences in two NDMS quadrants (Fig1B); Positive-controls in the right-lower quadrant had lower *Bacteroides* and higher *Clostridioides* than Negative-controls. Analysis of metagenomic data (Fig1C) showed that N2P compared to Negative-controls had increasing levels of *Coprobacter* and *Desulfovibrio* and decreasing levels of *Ruminococcus*, *Coprococcus*, *Blautia*, and *Bacteroides*.

**Conclusions:** N2P patients had similar demographics, drug-exposures, underlying comorbidities, diversity indexes, and number of OTUs compared to controls. However, compared to controls, abundance differences in specific taxa were observed.

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Morphogenesis and pathogenesis regulation of *Candida albicans* by probiotic bacterium: *Pediococcus acidilactici*

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**Background:** Oral candidiasis is a frequent form of candidiasis, caused by *Candida* species in particular, *Candida albicans*, which normally reside on mucosal surfaces. The transition of *C. albicans*, from yeast to hyphae allows the attachment to oral epithelial cells, followed by biofilm formation, invasion and tissue damage. Hence, the effect of *Pediococcus acidilactici* on growth, biofilm and germ tube formation of *C. albicans* were investigated in vitro as well as in vivo.

**Materials/methods:** Inhibitory activity of *P. acidilactici* on *Candida* species growth was determined by the broth microdilution method and inhibition of *C. albicans* biofilm formation was measured using XTT assay. Also, expression of seven genes as Agglutinin-like protein 1 (ALS1,3), hyphal cell-wall protein (HWP1), secreted aspartyl proteinase (SAP4,6), Enhanced filamentous growth 1 (EFG1) and Enhanced activated protein 1 (EAP1) were analyzed by RT-PCR with different concentrations of *P. acidilactici*. The experimental activity of the probiotic bacterium was assessed in an animal model by culture and histopathological methods in three groups of mice including those treated with probiotics, fluconazole and distilled water as the control.

**Results:** *P. acidilactici* inhibited the growth of Candida species at concentrations of 8-512 µg/mL. This probiotic bacterium inhibited the biofilm and germ tube formation in a dose-dependent manner. RT-PCR analysis showed a reduction in gene expression following the treatment with this bacterium. The *P. acidilactici* significantly reduced the CFUs in mice receiving this probiotic treatment compared to the control group. Histopathological analyses showed that Candida colonization was diminished in mice following the administration of probiotic.

**Conclusions:** Our data provide new insight into the biotherapeutic effects of *P. acidilactici* by inhibition of *Candida* species growth, germination, and biofilm formation. Also, the obtained data suggest that this bacterium can reduce Candida colonization and fungal burden on mucosal surfaces and relieve signs and symptoms of oral candidiasis. Further studies are still needed to clarifying the effects of the secreted biosurfactant and byproducts of this bacterium on adhesion, morphogenesis and pathogenesis of *Candida* yeasts.

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Evaluation of the EasyScreen ESBL/CPO kit for the detection of β-lactam resistance genes

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Background: Antibiotic resistance has become a major international concern for public health, especially with the spread of the carbapenemases producing Enterobacteriaceae (CPE). Thus development of efficient and reliable detection tests is essential to prevent spread of these deadly bacteria in hospital settings and to assist clinicians with appropriate antibiotic therapies. Here we have evaluated the performance of the novel molecular diagnostic test, the EasyScreen™ ESBL/CPO for β-lactam resistance genes detection.

Materials/methods: EasyScreen™ ESBL/CPO [Genetic Signatures] is a rapid in vitro nucleic acid amplification assay for the qualitative detection of 15 β-lactamase (including carbapenemase) genes and the colistin encoding mcr-1 gene. The assay is based on real time PCR technology, fluorescent probes, and 3base™ technology. More than 300 bacterial isolates [Enterobacterales, Pseudomonas aeruginosa, Acinetobacter baumannii] were isolated from agar culture. One colony was suspended in extraction buffer, which lyses and converts the nucleic acids into a 3base DNA form [all cytosine bases are converted as thymine bases]. The bacterial DNA is then added to the 6 PCR tubes, with primers for three targets plus one internal control. The targeted genes are blaKPC, blaVIM, blaIMP, blaNDM, blaIMI, blaSme, blaOXA-48, blaGES, blaSHV, blaTEM, blaCTX, blaDHA, blaCMY, blaOXA-23, blaOXA-51, and mcr-1.

Results: EasyScreen™ ESBL/CPO is able to detect the major carbapenemases [NDM, VIM, IMP, KPC, OXA-48, IMI, Sme] and their variants in Enterobacteriaceae and in Pseudomonas aeruginosa with nearly a sensitivity of 100% but also some plasmid-encoded cephalosporinases and their variants [CMY, DHA]. However, the detection of the chromosomally-encoded CMY and DHA, where less efficiently detected and some OXA-23 and OXA-51 variants were not detected. Finally, EasyScreen™ ESBL/CPO was not able to distinguish between penicillinase and ESBL variants of TEM and SHV, and similarly between GES-ESBLs and GES carbapenemases.

Conclusions: Our data showed that EasyScreen™ ESBL/CPO is an efficient and rapid (<3h from colony to result) detection test for the most frequently encountered penicillinases [including ESBLs], carbapenemases, cephalosporinases and mcr-1 in Enterobacteriaceae, P. aeruginosa, and A. baumannii. EasyScreen™ detection Kit is compatible with most existing automated nucleic acid extraction and real-time PCR instruments and can be fully automated.

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The polymorphism rs2305619 of Pentraxin 3 is associated with susceptibility of non-HIV-related cryptococcosis in a Chinese Han population

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Background: To conduct association analysis between the polymorphism rs2305619 of Pentraxin 3 (PTX3) and the susceptibility to non-HIV-related cryptococcosis, which may provide molecular evidence for early risk prediction of disease, individualized treatment, and prognosis monitoring.

Materials/methods: Using SNaPshot SNP typing technique, PTX3 rs2305619 was typed on 97 non-HIV-related cryptococcosis patients and 120 healthy controls. The results were analyzed by SHEsis software.

Results: PTX3 rs2305619 polymorphism was associated with the risk of cryptococcal infection. Compared with the healthy controls, the proportion of rs2305619 A/A homozygotes increased in the non-HIV-related cryptococcosis patients (OR 2.076, 95% CI: 1.026–4.203, P=0.040). In the non-HIV-related cryptococcosis without immunocompromised underlying diseases group, this increase was more obvious (OR 2.708, 95% CI: 1.217–6.027, P=0.015). While, the proportion of G/G homozygotes in non-HIV-related cryptococcosis patients reduced (OR 0.539, 95% CI: 0.311–0.936, P=0.028). In the non-HIV-related cryptococcosis without immunocompromised underlying diseases group, this reduction was more obvious (OR 0.331, 95% CI: 0.160–0.683, P=0.003).

Conclusions: The rs2305619 polymorphism of PTX3 was associated with susceptibility to non-HIV-associated cryptococcosis. The rs2305619 A/A genotype increased the risk of cryptococcal infection, while the G/G genotype reduced the risk of cryptococcal infection.

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Abstract 9311

Genomic characterisation of clinical Enterococcus faecium from Tunisia: remarkable identity with ampicillin-resistant strains obtained from animals/meat in the same area

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Abstract third-party references: The work was supported by UID/MULTI/04378/2019 with funding from FCT/MCTES through national funds.

Background: MDR-Enterococcus faecium (Efm) infections continue to increase worldwide, including in Tunisia where genetic characterisation of clinical enterococci remains scarce. We aimed to characterize Efm causing human infections in healthcare institutions from Tunisia and to position them within the worldwide Efm epidemiology by genome comparison with those available in public and personal databases.

Materials/methods: Efm isolates (n=29; August-2011 -March-2016) from two private clinics (Tunis-north) and one regional hospital (Gafsa-southwest) were analysed. Species were identified by PCR. Antibiotic susceptibility testing (disk-diffusion: 13-antibiotics; E-test:ampicillin) was performed [EUCAST, 2019] and transfer of vancomycin-vanA and ampicillin-pbp5 resistance done by conjugation (1:1-donor:recipient-EfmGE1). Clonality was established by SmaI-PFGE. WGS-Illumina was done for representative Efm (n=10) that were analysed through CGE [MLST/ResFinder/PlasmidFinder/CSIphylogeny] and in house databases of virulence factors (n=41 VF). They were compared with strains from non-clinical sources in Tunisia [our collection/PMID:31243458] as well as other regions [GenBank public genomes].

Results: Clinical Efm (48% MDR) were resistant to erythromycin-55%, ciprofloxacin-48%, high-level-aminoglycosides-45%, ampicillin-41% (AmpR); quinupristin-dalfopristin-38%; tetracycline-28%; glycopeptides-14%. Three ICU-patients from one of the clinics (2016) were infected with the same bloodstream vancomycin-resistant-vanA-MDR (glycopeptides/ampicillin/ciprofloxacin/erythromycin/tetracycline/gentamicin/streptomycin) ST80 clone, which was enriched in relevant virulence markers (ptsD/orf1481/IS16/complete-acm/scm/espA/4-pili-gene-clusters). vanA-Tn1546 was located on a conjugative pRUM-like plasmid. These Efm were compared with GenBank ST80-Efm available genomes and infection-derived Efm from Australia/2012 and Malaysia/2011 (vanA) were the closest (262-271 -SNPs) ones. Among Tunisian AmpR-Efm (n=12), two clinical strains were closely related to a non-clinical AmpR-Efm from bovine-meat (ST18/3-SNPs) and two cow-milk/bovine-meat (ST17/0-29-SNPs) from Tunisia, all with similar MICAmp (128->256 mg/L) and VF (ptsD/orf1481/IS16/complete-acm/scm/espA/4-pili-gene-clusters; hyl in ST17). The pbp5 gene was transferred by the VanA-AmpR-ST80-Efm and AmpR-ST17-Efm. Clinical/bovine-meat ST18-AmpR-Efm and ST203-AmpR-Efm [2014-2016] from Tunisia differed in 15-20 SNPs and 86-SNPs from French [2000-2009] and U.S.-AmpR-VRE-linezolid-resistant [2014] clinical strains, respectively.

Conclusions: Clinical-MDR-Efm clones causing human infection in Tunisia can be closely related to clinical-Efm of other continents. Identical AmpR-MDR-Efm strains carrying markers associated with an increased risk of human infection (high-level-AmpR + relevant-VF) were found in clinical and animal sources from Tunisia or other countries, emphasizing the global/continuous transmission of relevant Efm across different hosts/settings and the urgent need of One Health measures to contain their spread.

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Abstract 9313

**Echinocandin resistance in emerging multidrug-resistant yeast *Candida auris* and investigation into the mechanism of resistance**

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**Background:** *Candida auris* is a rapidly emerging multidrug resistant yeast of worldwide importance. Resistance to echinocandins, the drug of choice for treatment of *Candida* infection is of concern. The present study was conducted to determine the burden and mechanism of echinocandin resistance in *C. auris* isolates.

**Materials/methods:** Antifungal susceptibility testing of *C. auris* (n=144) were performed by CLSI broth microdilution technique against echinocandins (caspofungin, anidulafungin and micafungin). Sequencing of the FKS gene was carried out for isolates with high echinocandin minimum inhibitory concentration (MIC). Expression levels of putative chitin synthase genes (*CHS1* and *CHS2*) and β-1,3-glucan synthase (*BGS*) were determined after sub optimal drug treatment. The results were correlated with quantity of cell wall chitin content using flowcytometry. Growth kinetics of resistant mutants and wild type (WT) isolates and impact of chitin binding dye, calcofluor white (CFW) on their growth was also analysed.

**Results:** Seven (4.86%) isolates had MIC above the tentative clinical breakpoint of ≥2 mg/L for caspofungin. Four isolates had intermediate MIC of 1 mg/L for capofungin. FKS sequence of two isolates carried a novel mutation, F635Y. Three isolates carried previously reported mutation S639F, while two isolates demonstrated no target site mutation. *CHS1* transcript levels were not different in resistant isolates with WT FKS gene (6.52±2.04) and in those with intermediate MIC (7.93±1.18), but significantly different from resistant isolates with a mutation in FKS gene (2.90±0.97). There was no significant difference in *BGS* expression levels in resistant isolates with and without mutation (1.49± 0.31 and 2.74±0.37 respectively). However, increased expression of *BGS* in isolates with intermediate caspofungin MICs (8.34±2.20) was noticed. Flowcytometric analysis showed significant difference in the chitin content of mutant and WT resistant isolates. Growth of resistant isolates with mutation in FKS gene was more strongly inhibited by higher concentrations of CFW compared to wild type isolates. Growth kinetic behaviour was similar for all isolates.

**Conclusions:** Although, mutations in FKS1 gene is most commonly reported mechanism of echinocandin resistance, other yet unknown mechanisms could account for resistance. Resistant mutants were more susceptible to CFW and growth kinetics suggests no fitness cost associated with echinocandin resistance-conferring mutations.

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Abstract 9314

**Successful reduction of urinary catheter days and inadequate catheterisation after introduction of a prevention bundle**

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**Background:** Catheter-associated urinary infections (CAUTIs) are frequent and one of the most preventable nosocomial infections. We assessed the effectiveness of an intervention bundle to reduce urinary catheter-days and to prevent catheter-related infectious and non-infectious complications.

**Materials/methods:** This before-after study was carried out in a regional 62-bed hospital in Switzerland with a prevention bundle consisting of three evidence-based measures: training session emphasizing adequate indications for catheterization and appropriate antibiotic therapy, catheter insertion only according to defined criteria with daily re-evaluation, and training of personnel for safe insertion and handling of bladder catheters. We prospectively included all patients with preexisting or newly placed urinary catheters (in place for ≥24 hours). Catheter episodes per number of discharged patients, catheter-days per bed days, catheter dwell time, indications for catheterization, as well as infectious (CAUTIs) and non-infectious complications were compared between the 2-month period before and the 4-month period after a 5-week implementation phase.

**Results:** A total of 193 catheter episodes were included: 101 among 510 discharged patients before and 92 among 894 discharges after intervention (p<0.001). Overall, there was a significant reduction of catheter days during the post-intervention period (1898/10,000 hospital bed days vs. 1269/10,000 hospital bed days, p<0.001). Catheter dwell time increased from 5.8 to 7.4 days (p=0.16). Among placed catheters, there was a trend towards reduction of incorrect indications before and after intervention (11/101 vs. 5/92, p=0.17). Incorrect indications were catheterization for incontinence (5% vs. 0%, p=0.03) and for urinary tract infection (3% vs. 3%, p=0.9). The most frequent correct indications for catheterization were urinary retention (41% vs. 46%, p=0.6), followed by urine-monitoring (35% vs. 39%, p=0.7) and surgery (15% vs. 18%, p=0.6). The overall rate of CAUTIs was low both before (3/101, 3%) and after intervention (2/92, 2%) (p=0.9). Most of them (4/5) were related to preexisting urinary catheters. Only one patient in the post-intervention period experienced a non-infectious complication (bleeding).

**Conclusions:** This intervention bundle brought a significant reduction of catheter days, probably due to a reduction of insertions due to incorrect indications. The low baseline-infection rate prevented us from showing a reduction in CAUTI-incidence.

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Abstract 9317

**AST for fastidious bacteria: a reliable automation to standardise the EUCAST disk diffusion test**

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**Background:** Fastidious bacteria antimicrobial resistance (AMR) is a growing threat to public health. EUCAST implemented a disk diffusion based antimicrobial susceptibility test (AST) using Mueller Hinton + 5% mechanically defibrinated horse blood + 20 mg/L β-NAD (MH-F) agar plates.

Copan established and validated an automated workflow starting from MH-F streaking, antibiotic disks dispensing, CO₂ incubation and AST plates digitalization to facilitate results analysis on the screen.

The aim of this study was to compare the automated workflow, from sample preparation to digital measurement of the inhibition zone diameters (IZD) on the Copan WASP® and WASPLab®, to the reference manual preparation method.

**Materials/methods:** In this study an assessment of the automated system reproducibility was performed. Quality control strains (QCs), proposed by EUCAST, of *S.pneumoniae* ATCC 49619, *H.influenzae* ATCC 49766 and *C.jejuni* ATCC 33560, processed in triplicate for 5 days, were tested with both the automated and manual methods against most of the antimicrobials specified in the EUCAST protocol. In addition, 14 clinical strains, representative of species requiring MH-F for disk diffusion, were analysed in triplicate by both methods. All the disks IZD were read by two operators with both manual calliper and the digital measuring tool.

**Results:** In the QC strains tested, a total of 8700 IZD were measured: for all the strain/drug combinations, the mean diameter of the inhibition zone was within the EUCAST QC range for both workflows. During the 5 days testing, the average difference between IZD obtained with the manual and the automated workflows for each combination strain/drug, showed to be less than 1 mm. In the clinical strains tested, a total of 5280 inhibition zones were measured and a 97.9% categorical agreement was obtained with 0.4% of Very Major Error, 1.5% of Major Error and 0.2% of Minor Errors.

**Conclusions:** Together with previously validated protocols for aerobic bacteria, the present study demonstrates that WASP® and WASPLab® automation are offering a reliable strategy to properly perform, manage and standardize disk diffusion test for fastidious organisms.

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Abstract 9320

**Screening the antifungal activities of monoterpenes and their isomers against Candida species**

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**Background:** Increasing occurrence of non-albicans Candida species with intrinsic or acquired resistance to antifungals as well as the emergence of multidrug Candida species coupled with the limited antifungal agents challenges the treatment of candidiasis. Consequently, a class of secondary metabolites of plants exhibiting decent antifungal activity. Therefore, this study aimed to evaluate the antifungal potential of various monoterpenes including Carvone, Limonene, Pinene, Menthone, Menthol, Camphor, Thujone, Citronellol, and Piperitone against standard and clinical isolates of Candida.

**Materials/methods:** Minimum inhibitory concentration (MIC) of compounds were determined, using broth Microdilution method based on M27-A3 protocol documented by clinical laboratory standard institute (CLSI).

**Results:** Amongst the tested monoterpenes, oxygenated terpenoids showed strong antifungal activity. Specifically, alcoholic terpenoids such as (±)-Citronellol possess more efficacy than the corresponding ketonic ones with MIC, ranging from 0.03 to 2.00 µl/ml. Among the examined yeasts, C. tropicalis was the most susceptible species to (±)-Citronellol. Moreover, the examined monoterpenes successfully inhibited the growth of fluconazole-resistant Candida species. Moreover, statistical analysis showed no statistically significant difference between the (+) and (−) isomers, except for (±) α-Pinenene and (±) Menthone (P value < 0.05).

**Conclusions:** Considering the significant antifungal activity of the examined monoterpenes, they could be used in controlling or treating candidiasis. Pleasant taste and odor of these monoterpenes in addition to their safety and GRAS grades makes them appropriate additive or preservative compounds in food and cosmetics products. Furthermore, these data might help researchers to predict EOs antifungal activities, after determining its constituents.

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Abstract 9321

Exploring barriers to penicillin allergy de-labelling in a UK teaching hospital

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Background: Penicillin allergy is commonly reported by patients but the prevalence of type 1 hypersensitivity is low. An inappropriate penicillin allergy label is associated with adverse outcomes. This survey aimed to explore the barriers to penicillin allergy de-labelling.

Materials/methods: During World Antibiotic Awareness Week 2019, healthcare workers at an English teaching hospital were invited to participate in an anonymous electronic survey. Respondents were asked knowledge-based questions about the prevalence of penicillin allergy and its association with adverse outcomes. Respondents were asked to identify barriers to penicillin allergy de-labelling experienced within their practice.

Results: In total there were 105 respondents: 55 (52.4%) doctors, 20 (19.1%) pharmacists, 18 (17.1%) nurses, and 12 (11.4%) other healthcare workers. Duration of professional experience was evenly distributed – 0-2 years (21; 20%), 2-5 years (17; 16.2%), 5-10 years (35; 33.3%), and >10 years (32; 30.5%). Overall, 47 (44.8%) correctly identified the prevalence of reported penicillin allergy and 65 (61.9%) identified the prevalence of true IgE-mediated (type 1) allergy to penicillin. Pharmacists and respondents with >5 years’ experience were more likely to give a correct answer. Only 20 (19.1%) correctly identified all the complications associated with penicillin allergy. The majority of respondents (78.4%) felt that avoiding penicillin is harmful in patients with a history of intolerance (not allergy) to penicillin. The most commonly reported barriers to removing an inappropriate penicillin allergy label were unreliable history, fear of harm, and uncertainty in assessing risk (both clinician and patient uncertainty). Doctors and pharmacists were more likely to report barriers related to acquiring an allergy history, risk assessment, and time constraints. Nurses were more likely to report lack of training, knowledge, and experience.

Conclusions: The low prevalence of type 1 allergy to penicillin was well recognised. Although the majority felt that avoiding penicillin is harmful in patients with a history of intolerance to penicillin, understanding of the complications related to penicillin allergy was poor. Future initiatives to remove an inappropriate penicillin allergy label should be supported by educational activities for both healthcare staff and patients. A concerted system-wide approach to penicillin allergy de-labelling across primary and secondary care is required.

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Abstract 9323

Impact of out-of-hours results and infection specialist intervention on the time to the first appropriate antimicrobial therapy in patients with Gram-negative bacteraemia: the South London CLAHRC cohort experience

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Abstract third-party references: NIHR South London CLAHRC

Background: It is urgent to identify interventions in the bacteraemia pathway to reduce the time to the first appropriate antimicrobial treatment (TFAAT). In the UK, the infection specialist (IS) manages patients with Gram-negative bacteraemia (GNB), prompted by positive blood culture (BC) results during working hours (DWH). Out-of-hours (OOH) results are acted on the following day. IS intervention (ISI) improves outcome of infections. We evaluated the impact of OOH results and ISI on the TFAAT of patients with GNB.

Materials/methods: Ambispective cohort of GNB episodes from three hospitals (October 2014-December 2015). Data: clinical-microbiological-epidemiological information; date-time for laboratory results (Gram/identification/susceptibility testing), ISI and treatments. TFAAT: time (hours) from BC sampling to first appropriate antimicrobial therapy (according to in vitro susceptibility). BC positivity time (BCPT): time in the day when BC bottles flagged positive [DWH [08:01-18:00], OOH [18:01-08:00]]. TFISI: time (hours) to first ISI from first result. Methods: Cox regression: best predictive model for TFAAT (event) that included IS intervention/OOH. Episodes in adults off appropriate antimicrobial at the BCPT were included. Quantitative variables are expressed as median (p25, p75), regression outputs as HR [95% CI].

Results: 366 of 800 episodes recorded [181/366 [49%] DWH] had available clinical-microbiological-outcome data; 278 had treatment data. Among 73/278 [26%] episodes off appropriate antimicrobial treatment at BCPT, the DWH group compared to the OOH had shorter TFAAT [42 [24,45] vs 57 [35,97]], p=0.019) and TFISI [3 [1,18] vs 11 [7,17], p<0.01]; there was strong correlation between TFAAT and the time from BC sampling to Gram stain [DWH r=0.7 vs OOH r=0.559]; there was no correlation between TFAAT and ISI/TFISI. In the final model [adjusted by TFISI, comorbidity and severity] both antimicrobial resistance [28 [2,390], p=0.013] and a non-urinary source [24 [1,441], p=0.033] significantly increased the TFAAT; the association with TFISI was not significant.

Conclusions: Antimicrobial resistance and a non-urinary source were associated with TFAAT delays in GNB. There may be subgroups of patients where the OOH results delayed the TFAAT although this association was not identified in the final overall model. This information will help to optimise workflows and resources to improve the management of patients with GNB.

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Complete genome sequencing and identification of *Mycobacterium chimaera* by MALDI-TOF MS: a modified approach to discriminate *Mycobacterium chimaera* and *Mycobacterium intracellulare*

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**Background:** *Mycobacterium chimaera* is an opportunistic biofilm-forming pathogen intrinsically resistant to numerous classes of antibiotics. Since 2004, several outbreaks were observed worldwide due to the contamination of water tanks of heater-cooler units (HCUs) used during open-heart surgery. The invasive infections caused by *M. chimaera* are characterized by a mortality rate of about 50%. Until now, only 18 cases of invasive *M. chimaera* infections have been reported in Italy with 7 deaths and 55 contaminated HCUs (http://www.trovanorme.salute.gov.it/norme/renderNormsanPdf?anno=2019&cod-Leg=67585&parte=1%20&serie=null).

**Materials/methods:** From January 2016 to July 2019, all water samples collected from the HCUs were processed according to ECDC guidelines (https://www.ecdc.europa.eu/en/publications-data/eu-protocol-case-detection-laboratory-diagnosis-and-environmental-testing). Five *M. chimaera* strains isolated from clinical samples and collected in the period 2015-2019 were included in the study. Identification was performed using DNA probes (GenoType NTM-DR). Whole Genome Sequencing (WGS) was performed using Illumina NextSeq platform. Identification of *M. chimaera* strains was also using MALDI-TOF MS with standard protocols. A modified algorithm (Panada AB et al., JMM 2017; 66:670-7) based on the analysis of specific peaks was used in order to discriminate *M. chimaera* from *M. intracellulare*. Twenty *M. intracellulare* strains were used as control for the algorithm evaluation using at least 8 replicates.

**Results:** Twenty-eight out of 40 (70.0%) water samples were positive for *M. chimaera* and in 20 of them, WGS was performed. Of note, 12/20 (60.0%) *M. chimaera* strains belonged to subgroup 1.1 (with <10 single nucleotide polymorphism), which also includes 1 of 5 clinical sample identified in 2015. Logarithmic ratio (log(IQ)) between the sum of the intensity of selected peaks for *M. chimaera* (n=3) and *M. intracellulare* (n=3) spectra were used for discrimination analysis. The median log(IQ) observed was 0.37 (range 0.28-0.51). Among intra-samples variability, the mean of coefficient of variation was 20.4% (SD 9.9%) evaluated in 8 replicates for each sample.

**Conclusions:** Most of the strains isolated from HCUs belonged to subgroup 1.1 also reported as the same clone responsible for outbreaks globally occurred. Moreover, the logarithmic approach applied to MALDI-TOF MS demonstrate a valid and powerful tool to discriminate *M. chimaera* and *M. intracellulare*.

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Abstract 9329

**Accuracy of sepsityper methodology for identifying microorganisms directly from positive blood culture bottles using MALDI-TOF MS**

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**Background:** Processing of positive blood cultures traditionally involves subculture and agar growth to obtain organism identification. Sepsityper, a sample preparation method, enables MALDI identification directly from a positive blood culture bottle. Although our laboratory has utilized the direct Sepsityper method for some time, it has been considered a provisional identification tool and MALDI of agar growth has always been performed to provide definitive identification. This analysis evaluated accuracy of direct Sepsityper identification compared with growth MALDI identification, with a view to increasing clinical confidence in the Sepsityper ID and reducing unnecessary repeat MALDI processing.

**Materials/methods:** Results from 1263 positive blood culture bottles which had undergone both direct Sepsityper and growth MALDI methods were analyzed.

**Results:**

112/1263 (8.87%) gave no peaks / no ID with Sepsityper.

205/1263 (16.2%) yielded mixed growth on agar. Sepsityper correctly identified at least one of the organisms present in 195/205 (95.1%), but it only detected all organisms present in 2/205 bottles.

946/1263 (74.9%) gave an ID with Sepsityper and yielded a pure growth of a single organism.

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Direct Sepsityper ID versus growth MALDI ID for cultures which grew a single organism</th>
</tr>
</thead>
<tbody>
<tr>
<td>929/946</td>
<td>Complete match</td>
</tr>
<tr>
<td>12/946</td>
<td>Sepsityper ID accurate to genus level</td>
</tr>
<tr>
<td>5/946</td>
<td>Sepsityper ID erroneous</td>
</tr>
</tbody>
</table>

For most commons organisms, the ID given by direct Sepsityper was unchanged on growth MALDI ID. This included all E coli, Enterococcus faecalis, Klebsiella spp, Micrococcus spp, Proteus mirabilis, Pseudomonas aeruginosa, Staphylococcus aureus, Staphylococcus epidermidis.

The 5 erroneous Sepsityper IDs were unusual organisms to found in blood cultures: Pantoea, Peptoniphilus, Prevotella, Weissella, Cutibacterium.

Sepsityper IDs accurate to genus level included 9 very closely-related organisms.

**Conclusions:** Sepsityper accurately identified 98.2% of positive blood cultures containing a single organism. Any bottle with a common organism ID on Sepsityper and yielding pure agar growth did not require repeat MALDI ID from agar growth. In this analysis, this accounted for at least 560/1263 (44.34%) positive cultures analyzed.

All Sepsityper results giving an uncommon organism ID, genus level ID or no ID, plus any mixed growth on subculture required confirmatory growth MALDI.

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Abstract 9330

Clinical class 1 integron patterns and relative antibiotic resistance gene carriage in urban compartments
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Background: The presence and versatility of gene transfer mechanisms in bacteria have shown antibiotic resistance genes (ARGs) do not respect phylogenetic, geographical or ecological borders, causing the use of antibiotics on one place, such as households, to impact the wider resistome, such as medical systems and the wider environment. Therefore, studying bacterial traits behind acquisition, expression, and spread of ARGs may be more important than studying ARGs themselves.

Materials/methods: Here we combined targeted sequencing of the clinical class 1 integron gene-cassette (clintI1) and qPCR to determine the i) relative abundance, ii) dynamics and iii) ARG-cassette diversity across a urban network in Spain, which includes two main hospitals [HP], community wastewater sources [only] [CM], and the wastewater treatment plant [WWTP] influent [INF], WWTP effluent [EFF], and recycled activated sludge [RAS] as well as water column and sediments upstream [RU and SRU] and downstream [RD and SRD] of the WWTP discharge point (Figure 1).

Results: Results show that clintI1 was much more abundant than other integrons in all urban wastewater compartments despite wide variations in their normalized abundances. Subsequent clintI1 gene-cassette sequencing showed much higher ARG diversity in hospital waste cassettes and much lower diversity in RAS and downstream river sediment cassettes [Figure 1]. clintI1 gene-cassettes were dominated by ARGs coding from aminoglycoside, β-lactam, and carbapenem inactivating enzymes, especially from hospital wastewaters samples [Figure 1]. These show that clintI1 may be an important evolutionary factor in increasing antimicrobial resistance in wastewater bacteria. However, the carriage of clintI1 varies widely across wastewater network compartments; greatest in hospital wastewaters and a lowest in RAS.

Conclusions: Overall, the higher abundance of clintI1 in hospital wastewater confirm that may be useful for assessing "risk" in wastewater releases, suggesting our data that the carriage of ARGs in the clintI1 correlates with antibiotic use. Furthermore, clintI1 has been identified as a key driver in the dissemination of emerging clinical ARGs from hospital wastes into the environment.

Figure 1: Clinical class 1 integron patterns across a wastewater network: i) Relative abundance [clintI1 per 1000 bacteria], ii) dynamics [relative abundance of empty-clintI1], and iii) ARG-cassette diversity (richness).

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**Abstract 9331**

**Bacterial growth in antiseptics, disinfectants and soaps in a tertiary care hospital, Ouagadougou, Burkina Faso**

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**Background:** To assess the hospital environment as a reservoir of antimicrobial resistance (AMR), we sampled in-use soaps, disinfectants and antiseptics in a tertiary care hospital in Burkina Faso.

**Materials/methods:** In August-September 2019, liquid samples (6ml) were collected from in-use disinfectants and antiseptics in different hospital wards. Dispensers and bar soaps were swabbed with NRSII Transwabs (MedicalWire). 100 µl of each sample was inoculated in triplicate on Tryptic Soy Agar (TSA)+0.7%Lecithin (Difco) and MacConkey agar (Oxoid). Quantitative count was done from the TSA after 24 hours of incubation. Identification was done from Gram-negative colonies with Phoenix M50 equipment (Becton Dickinson).

**Results:** Out of 171 samples collected, 68 showed growth with Gram-negative bacteria (39.8%). Nine samples included growth of Enterobacteriaceae (including *Klebsiella pneumoniae* (n = 2) and *Enterobacter cloacae* (n = 5), of which all except one (460 CFU/ml), showed confluent growth, indicating heavy contamination. From most of the grown samples, two or more different bacterial species were isolated (40/68, 58.8%). Among a total of 133 isolates, the key organisms were *Shewanella putrefaciens* (n = 22, 16.5%), *Pseudomonas aeruginosa* (n = 14, 10.5%) and *Sphingomonas paucimobilis* (n = 13, 9.8%). Soaps were most frequently contaminated (45/75, 60%), followed by disinfectants (7/23, 30.4%), as shown in the table below. EB = Enterobacteriaceae, NF = Non-fermentative organism, Other species = *Moraxella* (n = 2), *Chromobacterium violaceum* (n = 2), *Pasteurella multocida* (n = 1), *Suttonella indologenes* (n = 1), *Aeromonas* sp. (n = 1).

<table>
<thead>
<tr>
<th>Sample type</th>
<th>Total collected</th>
<th>EB</th>
<th>EB + NF</th>
<th>NF</th>
<th>NF + Other</th>
<th>EB + NF + Other</th>
<th>Other</th>
<th>Total growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiseptic</td>
<td>73</td>
<td>1</td>
<td>1</td>
<td>13</td>
<td>1</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disinfectant</td>
<td>23</td>
<td>2</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soap</td>
<td>75</td>
<td>3</td>
<td>5</td>
<td>53</td>
<td>4</td>
<td>2</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>171</td>
<td>3</td>
<td>5</td>
<td>53</td>
<td>4</td>
<td>2</td>
<td>68</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions:** Assessment of in-use antiseptics, disinfectants and soaps in different hospital wards in a tertiary care hospital in Burkina Faso showed high contamination rates, including the presence of possible pathogens. Further research will include AMR testing and molecular typing to compare these environmental with clinical isolates.

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Abstract 9334

The first blood-stage controlled human malaria infection model in Europe for Plasmodium vivax vaccine efficacy testing

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Background: Plasmodium vivax has been viewed for many decades as a "benign" parasite. However, current estimates suggest it accounts for 7.5 million malaria cases each year, among 2.5 billion people living at risk of infection, with a significant burden of morbidity and mortality. Unfortunately, efforts to control the parasite lag far behind those for its cousin, P. falciparum, largely because of critical bottlenecks in vaccine development. A key problem is limited access to P. vivax parasite inocula for use in a controlled human malaria infection (CHMI) model to provide an early indication of vaccine efficacy. To date, only groups in the Americas have performed sporozoite challenges in human volunteers and the only blood-stage challenges have been performed in Australia.

Materials/methods: In 2018/19, we undertook the first proof-of-concept studies in Europe of P. vivax CHMI (ClinicalTrials.gov Identifiers: NCT03377296 and NCT03797989), demonstrating we could safely infect two healthy UK adult volunteers with P. vivax by the bite of infected mosquitoes produced and transported from southern Thailand. We obtained 250mL of blood from the volunteers at threshold parasitaemia/clinical criteria, and generated a viable, sterile GMP-like bank of cryopreserved P. vivax-infected erythrocytes. We then tested the safety and feasibility of blood-stage infection at three dilutions of the inoculum in six malaria-naïve UK volunteers. This blood bank has since been utilised in a pilot safety and efficacy trial of the high priority blood-stage vaccine candidate P. vivax Duffy Binding Protein [ChAd63-MVA PvDBP_RII], in Oxford, September 2019 (N=5; NCT04009096).

Results: Infectivity of the blood bank was robust, with even the lowest 1:20 dilution resulting in blood-stage infection. All volunteers were diagnosed within 1-2-16 days of infection. Symptoms were mainly mild-moderate, compatible with clinical malaria, and all volunteers were safely managed as outpatients, completing a course of antimalarials. The pilot efficacy trial was successfully completed and data will be presented.

Conclusions: This human challenge model provides a key platform for progression of P. vivax malaria vaccine candidates to Phase Ila efficacy testing. The model has since been taken forward to a head-to-head comparison of two leading blood-stage P. vivax vaccine candidates, with challenge planned for April 2020.

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Abstract 9337

Surgical site infections in orthopaedic surgery: a retrospective analysis of the risks associated with multi-drug resistant bacteria isolation

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Background: Surgical Site Infections (SSI) are a frequent complication of orthopaedic surgeries, that negatively impact on both morbidity and mortality of patients, causing prolonged hospitalizations and an increase of healthcare-associated costs.

Materials/methods: We conducted a retrospective monocentric study at Tor Vergata Hospital, Rome, between 2016 and 2018. Patients admitted to the Orthopaedic ward for at least 48 hours who underwent surgery were enrolled if they presented clinical signs of SSI and had at least one microbiological isolate collected intra-operatively or from the surgical wound. Clinical and microbiological data were analysed, together with data on duration of hospitalizations and infection impact on functional outcome up to 6 months after the diagnosis. Statistical analysis was performed using Pearson’s chi-square test for categorial variables and univariate and multivariate logistic regression.

Results: Among 2269 patients who underwent orthopaedic surgery, 83 (3.6%) developed a SSI: 40/83 (48%) patients developed osteomyelitis or prosthetic joint infection (PJI), 43/83 (52%) had a superficial or deep infection, without bone and joint involvement. Compared with the latter, PJI and osteomyelitis were more frequently associated with methicillin-resistant Staphylococcus aureus (MRSA) [7% (3/43) Vs 32.5% (13/40); p=0.003] and there was an increased trend of multidrug resistant (MDR) Gram-negative bacteria (GNB) isolation [18.5%(8/43) Vs 35%(14/40); p=0.09]. At univariate analysis, increased age [OR 1.04 (CI95% 1 - 1.07); p=0.013], cardiovascular comorbidities [OR 5.34 (CI 95%1.39-20.5); p=0.015], long-term care facility stay [OR 4.9 (CI95% 1.54-15.5); p=0.007] and longer hospital stay [OR 1.01 (CI95% 1-1.02); p=0.017] were associated with MRSA isolation, while at multivariate analysis only longer hospitalization showed a significant association [OR 1.01 (CI95% 1-1.02); p=0.039]. MDR-GNB isolation was associated with longer hospitalization, urinary and intravascular catheters use at univariate analysis, and only with longer hospitalization at multivariate analysis [OR 1.78 (CI95% 1.22-2.5); p=0.002]. More often patients with PJI and osteomyelitis had worse functional outcome compared to patients without bone involvements [16/40 (40%) Vs 4/43 (9%); p=0.001].

Conclusions: In our population MRSA and MDR-GNB often were associated with the development of PJIs and osteomyelitis. Screening measures and prevention strategies might be implemented accounting for patient specific risk factors, improving both short and long-term outcomes in orthopaedic patients.

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Abstract 9339

**VIM-producing Pseudomonas aeruginosa isolated in Southern Tunisia, 2012-2018**  
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**Background:** *Pseudomonas aeruginosa* (*P. aeruginosa*) is one of the major opportunistic pathogens implicated in serious nosocomial infections. The emergence of multidrug-resistant strains of *P. aeruginosa* is of global concern. A high number of carbapenemases were reported in *P. aeruginosa* isolates, they include mainly class B enzymes (metallo-β-lactamases).

The aim of this study was to determine the spread of VIM-producing *P. aeruginosa* in a Tunisian hospital between 2012-2018.

**Materials/methods:** Clinical isolates of ceftazidim and imipenem resistant *P. aeruginosa* obtained from patients hospitalized at a University Hospital in Sfax-Tunisia between 2012 and 2018 were included. Specific primers were used in PCR based assays to amplify metallo-β-lactamases encoding genes: *bla*VIM. O-serotyping was determined by slide agglutination test using O-specific anti-sera.

**Results:** During the study period, 504 non-repetitive strains of CAZ/IPM-R *P. aeruginosa* were isolated. 49% of these isolates were from patients hospitalized in Intensive Care Unit. CAZ/IPM-R *P. aeruginosa* was isolated mainly from respiratory samples (31%), pus (24%) and blood cultures (15.3%). The study focused on 352 strains that were conserved. PCR showed that 27.3% of isolates (96/352) harbored *bla*VIM gene. The frequency of acquiring this metallo-β-lactamases had increased since 2016 but this result is not statistically significant. PCR sequencing of the amplified fragments obtained from representative isolates revealed *bla*VIM-2. The serotype 012 (56.3%) and the serotype 011 (34.4%) were the most frequently identified in the VIM-producing isolates.

**Conclusions:** During the last years, *bla*VIM-2 became the most often reported acquired MBL genes in *P. aeruginosa* worldwide. In our hospital, the spread of VIM-2-producing *P. aeruginosa* clinical isolates is alarming and poses challenges for the treatment of hospital infections due to this species. Antimicrobial selection pressure could allow silent spread of these genes. A continued surveillance and a study of the epidemiological link between these strains should be adopted to limit their further dissemination.

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It takes two to tango: antimicrobial resistance and virulence contribute to the success of particular *Acinetobacter baumannii* clones

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**Background:** In our country, carbapenem-resistant *Ab* was associated with ST98, ST103, ST208 and, more recently ST218 (Oxford-scheme), with a dominant clone being usually associated with a particular period. These clonal shifts were primarily explained by an increased antimicrobial resistance (AMR) profile. In this study we aimed to explore genomic and biochemical differences among these clones that could further explain the *Ab* diversity and evolution that occurred in our hospitals in the last two decades.

**Materials/methods:** A total of 112 carbapenemase-producing-Ab isolates [ST98/OXA-40, ST103/OXA-58, ST208/OXA-23, ST218/OXA-23] were included. Isolates were initially characterized using FT-IR-ATR/PCA analysis. Representatives of different FTIR-ATR/MLST-clusters were randomly selected for WGS (n=12). WGS was performed with Illumina HiSeq (2x150bp), assembly with SPAdes 3.9.0, and annotation with Geneious R10. AMR genes and SNP analysis were determined by ResFinder and CSIPhylogeny tools-Center for Genomic and Epidemiology. SNP tree was visualized using iTOL. Virulence genes were identified with VFanalyzer tool-Virulence Factors Database.

**Results:** *Ab* clones evolution-ST103 (2001-2004), ST98 (2002-2006), ST208 (2006-2010) and ST218 (2010-2015) was consistently accompanied by an increase in AMR genes content: of note, transition to carbapenemases conferring higher carbapenem MICs, increasing number of aminoglycoside resistance genes (ST218-armA). Virulence factors enrichment was also observed: siderophores, adhesins, biofilm-associated factors, quorum-sensing and cytotoxic enzymes. Visual inspection of the phylogenetic tree was congruent with MLST. Overall, analyzed isolates presented 2-19300 SNPs. Within clusters, a smaller variation was observed within ST208 (2-5-SNPs), and larger within ST218 (9-131-SNPs). Among clones, a larger difference was observed between ST103 and ST218 (819300 SNPs), being lower between ST208 and ST218 (F1600 SNPs). FTIR-ATR clustering was congruent with MLST but, contrarily to SNP analysis, a higher relatedness was observed between ST98 and ST103, explained by the surface sugar composition extracted by WGS, associating both ST98 and ST103 capsules with fucosamine, ST208-capsule with pseudaminic acid and ST218-capsule with legionaminic acid that better resembles the siaic-acid from mammalian cells.

**Conclusions:** In this study, WGS together with FTIR-ATR-biochemical information allowed to describe the carbapenem-resistant *Ab* dynamics that occurred in our country, and also worldwide. This evolution was essentially promoted by consecutive virulence and AMR gene pool enlargement, together with pathogen-host adaptation.

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Abstract 9342

**Sepsis diagnosis: have we solved the riddle yet?**

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**Background:** Sepsis is a complex condition that has severely impacted mortality rates of patients in many countries. Diagnosis is equally complex and dependent on many factors for each test, especially in culture negative cases. We present data from an observational study of blood cultures received from 1139 patients suspected with sepsis over one year for factors which impact sepsis diagnosis such as volume of blood, contamination rates, site of draw, and biomarkers. The impact of these factors on positivity, relation with mortality and length of hospital stay was also studied.

**Materials/methods:** The Department of Microbiology received 2158 blood cultures from 1139 patients in 2018. Data such as time to positivity, volume of blood, site of draw, rate of contamination, immune markers like procalcitonin (PCT), WBC (white blood cell) count, polymorphonuclear leukocyte count, C reactive protein, lactate dehydrogenase, length of stay and mortality was collected from all 1139 patients. All data was analysed by programming language R.

**Results:** Of the 2158 cultures analysed, the blood cultures were positive in 383 bottles (17.8%). Gram-negative organisms were most commonly isolated in 61.7% cases and Gram-positive organisms in 33.1% (P < 0.01). We found a trend of association (P = 0.193) between adequate volume and higher rate of culture positivity (19.6% cases) compared to inadequate volume (16.5% cases).

We found a trend of association between positivity of the culture and the sites of blood drawn (P = 0.078). Samples were positive when cultures were drawn from the neck line in 50.8% cases, peripheral-arm in 23.6% cases and leg in 18.2% cases, 7.4% site not mentioned.

Culture positivity significantly correlated with increase in PCT (P=0.03). Similar results were seen with other biomarkers as well, albeit with less significance. Interestingly, in majority of the culture negative cases (ranged from 75% to 87%) we observed the higher levels of different biomarkers, particularly CRP and lactate dehydrogenase (Figure 1).

**Conclusions:** Our observational study in a large sepsis cohort highlights the importance of adequate blood volume and combination of biomarkers such as PCT, CRP, lactate dehydrogenase and polymorphonuclear leukocyte counts in improving the diagnosis of sepsis.

*Fig.1: Relation of biomarkers to blood culture results (no growth)*

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Abstract 9345

**What does the space-time dynamics of arboviral diseases epidemic in Curaçao tell us? Unravelling potential factors of disease persistence and spread**

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**Background:** In the last 5 years, the Americas and Curaçao have witnessed major arbovirus epidemics. Dengue, chikungunya and Zika viruses are all transmitted by *Aedes aegypti* and currently co-circulate in Curacao island. To understand the behavior of these diseases and design tailored interventions for prevention and outbreak response, we characterized the spatiotemporal dynamics of the three arboviruses between 2014-2016 in Curacao. Additionally, we unraveled potential associated factors of disease dynamics through spatial analysis and fitting generalized linear models (GLM).

**Materials/methods:** Laboratory confirmed cases of dengue, chikungunya, and Zika obtained from the Ministry of Health in Curaçao were used for analysis. The spatial and temporal patterns of dengue occurrence were examined at Geozone level over a period of 3 years. Clusters of dengue, chikungunya and Zika cases and incidence in space and time were detected using Anselin’s Local Moran I. We quantified the persistence of these viruses as the maximum number of consecutive weeks reporting cases per Geozone. Finally, a GLM was applied to evaluate if the case spatial distribution depends on socio-demographic and climatic factors.

**Results:** From 2014 to 2016, nearly 5000 cases of dengue, chikungunya and Zika were reported. Significant space and space-time clusters (P<0.05) were primarily concentrated in urban areas and in smaller but densely populated areas, all situated around the central-east part of the island. Dengue, chikungunya and Zika persistence was greater in the same hotspot areas. Preliminary results show that number of households per Geozone, unemployment rate and non-active economic status were good predictors for arboviral diseases occurrence (AIC: 1026.1; P<0.001). Further analysis will be conducted using climatic data extracted from remote sensed data.

**Conclusions:** Our findings contribute to a better understanding of the spatial dynamics of arboviral diseases in Curaçao high-lighting the role of densely populated urban centers and crowded conditions in maintaining persistent dengue transmission and as sources of disease spread. An integrated approach of dengue prevention and control can inform targeted control measures maximizing the allocation of resources to high risk areas.

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**Abstract 9346**

**Evolutionary insights of multidrug-resistant hypervirulent ST23 *Klebsiella pneumoniae* predominantly driven by ICEKp**

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**Background:** The emergence and global expansion of multidrug resistant (MDR) hypervirulent *Klebsiella pneumoniae* (hvKp) has been a cause of serious concern. Recently there are reports of MDR clones acquiring virulence plasmid and hvKp acquiring resistance. Despite this, the prevalence and evolution of hvKp at the national level is poorly understood in India. In this study we investigate the events that led to the evolution of two ST23 hypervirulent MDR Kp isolated from bacteremic patients by comparative genomics.

**Materials/methods:** Two MDR hypervirulent Kp isolates were subjected to whole genome sequencing and hybrid genome assembly using Ion Torrent and MinIon platforms. Genomes were analysed to determine the resistance and virulence genes and plasmids. The timed evolution of ST23 *K. pneumoniae* from India was estimated using Bayesian phylogenetic method BEAST v.1.10 with *K. pneumoniae* NTUH-K2044 as reference.

**Results:** The hybrid genome of both the isolates belonged to ST23 with K1 capsule type and O1v2 O antigen type. Both study isolates harboured seven putative distinct plasmids replicons in common namely IncA/C, IncFIB (pQil), IncFIB, IncX, ColRNAI, Col440II along with the virulence plasmid. Virulence plasmids of isolates were characterised by the presence of chloramphenicol resistance gene (*catA1*), possibly inserted through IS110 transposase. Both the study isolates were found to carry yersiniabactin locus ybt9 located in ICEKp3. Multiple MDR plasmids harbouring resistance genes encoding for β-lactamases, aminoglycoside modifying enzymes, fluoroquinolone resistance, sulfonamide resistance, trimethoprim resistance, and rifampicin resistance were present. Phylogenetic analysis based on Core genome SNPs showed the Indian MDR hvKp isolates formed a monophyletic cluster with reference strain. Two clades were formed and Indian isolates grouped with two oldest strains M109, NCTC9494; and NTUH-K2044. These were estimated to be evolved around 1872. Two MDR hvKp isolates along with another susceptible Indian isolate dated back 1959. Both genomes were submitted to NCBI with accession numbers CP035905-CP035912 and CP036190-CP036198.

**Conclusions:** Carbapenem resistant ST23 *K. pneumoniae* incidence is extremely challenging for infection control. Presence of *catA1* on virulence plasmid indicates the potential of other resistance genes being carried by virulence plasmid. Phylogenetic analysis shows that Indian MDR hvKp have evolved from susceptible global hvKp isolates.

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**Fig. 1a:** Circular representation of chromosome of *K. pneumoniae* isolates BA4656 and BA35918 genome displayed using CG View server with reference genomes SGH10 and NTUH-2044. KV154505 is the reference used for ICEKp3. SGH10 and NTUH-2044 have ICEKp10 and ICEKp1 respectively. **Fig. 1b:** Comparison of virulence plasmid of hv K. pneumoniae isolates BA4656 and BA35918 with virulence plasmids from *K. pneumoniae* strains SGH10, NTUH-K2044, AP6555 and E225. The plasmid carried virulence genes including *mpa*, *mpal*, *pvi* and *psc* gene clusters along with heavy metal resistance encoding *lce* and *pco* gene clusters. *catA1*, coding for chloramphenicol resistance with IS110 was inserted in plasmids of BA4656 and BA35918.
Abstract 9350

A prolonged measles outbreak in a vaccine refusing community, Austria, 2019
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Background: In Austria, the population measles immunity is estimated to be below 95%. By 21 January 2019, Public Health authorities of two neighboring provinces reported 10 confirmed measles cases, which exceeded the expected number. The AGES conducted an investigation to identify further cases, assess vaccination status and recommend prevention measures.

Materials/methods: Probable cases were residents of province A or B, with clinical presentation of measles after 1 January 2019, and linked to a confirmed case with positive RNA virus detection. Descriptive epidemiology was performed. We collected data on age, rash onset, certificate-based vaccination status and reason for being unvaccinated by telephone interview. Contact history was used to identify chains of transmission.

Results: By 11 March 2019, we identified 47 cases (41 confirmed), 40 (85.1%) were unvaccinated. We identified transmission chains in two provinces, affecting communities with different attitudes towards vaccination. In province A, 35 cases with a median age of 7 years (IQR: 1-11) occurred between 09 January-20 February, belonging to one transmission chain with four case generations. In province B, between 10 January-01 March, we identified 12 cases belonging to five further, unlinked chains of transmission, each of which subsided after two generation (5 primary, 7 second generation cases, median age: 22 years, IQR: 11-35). Of the 31 vaccine-eligible cases of province A, 25 were unvaccinated, of which 13 were vaccine refusers. Of the 12 province B cases, none of the 11 unvaccinated had a vaccination-refusing attitude. Ring vaccination was hardly accepted in province A, where a prolonged measles outbreak occurred, in comparison to province B, where short-lived transmission chains were identified.

Conclusions: A prolonged measles outbreak in a vaccination-refusing community, compared to five short-lived transmission chains, concurrently occurring in the neighboring province, illustrates how vaccine refusal hampers control of transmission. We recommend information campaigns by the national health authority to increase knowledge and vaccine confidence in the Austrian vaccine-hesitant population-groups.

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Abstract 9351

BCR1-independent biofilm formation of outbreak related Candida parapsilosis isolates from nosocomial bloodstream infections

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Background: Candida parapsilosis is notable for its ability to form biofilms on medical devices and to be frequently associated with nosocomial outbreaks. A nosocomial outbreak of C. parapsilosis was reported from a hospital in Southern Sweden in 2006. Four patients admitted to the haematological ward had acquired bloodstream infections, associated with intravascular catheters, with the same strain of C. parapsilosis within a month.

Materials/methods: Crystal violet staining and the metabolic XTT assay were used to assess biofilm formation. The cell morphology was assessed by light and confocal laser scanning microscopy. The genome of a C. parapsilosis outbreak isolate, SMI828 [high spider like biofilm former] and in independent bloodstream isolate SMI416, which did not form biofilms, were whole-genome sequenced using PacBio technology. In the liquid phase, the high biofilm forming strain showed yeast cell aggregation, which we consider an early biofilm forming stage. RNA isolated was subjected to RNA sequencing performed by Illumina HiSeq 2500 with 2 x 125 reads. Construction of deletion mutants and complementation was performed by using the SAT1 flipping strategy.

Results: Robust high levels of biofilm formation with a complex biofilm structure consisting of macrocolonies with spider-like appearance composed of aggregated yeast cells and pseudohyphae was characteristic for all eight C. parapsilosis isolates from the outbreak on three different surfaces: silicone, thermanox and polystyrene. Taking SMI828 as an example, biofilm formation was independent of the biofilm regulator Bcr1. Whole genome sequencing of outbreak isolates indicated the presence of a chromosomal translocation compared to the reference strain CDC317. Transcriptome comparison of the outbreak isolate with no biofilm formers revealed altered expression of multiple genes and expression of selected genes was confirmed by qRT-PCR.

Conclusions: Our results indicate that BCR1 independent high biofilm formation is a characteristic feature of the isolates involved in a nosocomial outbreak of catheter related bloodstream infection with a biofilm-specific gene expression pattern. This finding has implications for the development of treatment strategies targeting attachment and biofilm formation.

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Abstract 9353

Rapid identification of *Candida auris* from direct blood culture positive samples by MALDI-TOF MS from patients with *candidaemia* in a tertiary care hospital

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**Background:** *Candida auris* is a recently described agent of fungemia that poses a serious global health threat. *C. auris* is known to cause outbreaks in healthcare settings and notable for its antifungal resistance; often multidrug-resistant. *C. auris* is difficult to identify; polymerase chain reaction, DNA sequencing and MALDI-TOF MS can correctly identify it. Therefore, it is important to rapidly identify *C. auris* in a hospitalized patient and the healthcare facilities can take special precautions to prevent its spread. The study used of MALDI-TOF-MS as a rapid method of identification of *Candida auris* directly from positive blood cultures and analysed the associated risk factors.

**Materials/methods:** To identify the *Candida auris* from direct positive blood cultures by MALDI-TOF MS. A prospective study was conducted from February 2017 to June 2019 by taking 8 ml of positive blood cultures. After multiple washings and treating with triton X -100, it was directly subjected to the MALDI-TOF MS assay. The clinical data of candidemia cases due to *C. auris* infection were determined for significant associated risk factors.

**Results:** Of the 167 candidemia cases reported during the study, 31 (18.85%) were due to *C. auris*; being the 3rd most common species after *C. tropicalis* and *C. parapsilosis*. The age ranged from 4-day old neonate to 80 years old and there was female preponderance (*n* =18). MALDI-TOF MS was able to rapidly identify all *Candida auris* species on the same day when the blood culture was flagged positive thereby shortening the time for species identification by MALDI-TOF MS from culture. The underlying risk factors significantly associated with *C. auris* candidemia were diabetes mellitus, underlying respiratory illness, gastrointestinal surgery, prior antifungal exposure. Mortality was seen in 51.61%. All isolates were resistant to fluconazole (MIC ≥ 64µ/ml).

**Conclusions:** MALDI-TOF MS is a useful tool for rapid identification of *Candida auris* directly from positive blood culture. Identification of *C. auris* in a hospitalized patients can help the healthcare facilities in infection control measures and precautions to prevent its spread in the healthcare center.

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Abstract 9355

**Adaptation and validation of a quantitative vanA/vanB PCR on a high-throughput PCR system**

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**Abstract third-party references:** Consumables were provided by Roche Diagnostics

**Background:** Vancomycin resistant enterococci (VRE) are one of the leading causes of intensive care-related blood stream infections in Europe, with high mortality rates (20-50%). It is of paramount importance to determine risk factors for transmission and infection in VRE carriers. The bacterial load in enteral colonization may be associated with a higher probability of transmission and might play a role in facilitating infection. We established a quantitative vanA/vanB real time PCR assay on the open mode of the automated PCR system Cobas6800 (VRE-LDT) for screening and quantification directly from rectal swabs.

**Materials/methods:** We used a published vanA/vanB real time PCR assay (Fang et al. 2008), introduced 5’ acetylation to primer ends and optimized concentrations for the cobas PCR master. Limits of detection (LOD), (2 fold dilutions of strains ATCC 51299 (vanB) and SX6010 (vanA), n=20 repetitions per dilution) of the assay were determined using spiked modified Amies-Media. Inclusivity of the assay was tested on 50 vanB-positive strains and 27 vanA-positive strains (5x10^6 CFU/mL). Linear range was determined by dilution series (1:10). For clinical validation, we tested 176 rectal swabs (eSwab, Copan), which were positive with VRE by culture after broth enrichment.

**Results:** All isolates (n=77) from inclusivity testing were detected. LOD was 102 CFU/mL for vanA and 141 CFU/mL for vanB, while linear range determined in Amies-media went down to 650 CFU/mL for vanA (R²=0.998) and to 1100 CFU/mL for vanB (R²=0.998). Clinical validation: 153/176 enrichment culture positive samples (1 vanA, 171 vanB, 4 vanA/vanB) were detected by the VRE-LDT (22 invalid due to insufficient volume in swab, one false negative). Quantification in rectal swabs revealed a median VRE load of 4.6x10⁵ CFU/mL (range: 5x10⁷–<1.41 CFU/mL) in clinical specimens.

**Conclusions:** The newly validated quantitative VRE-LDT is a useful and sensitive tool for the detection and quantification of the vanA/vanB resistance determinant directly from rectal swabs. Sample volume requirements may be a concern in routine practice.

The new assay could be employed in investigating the role of VRE burden in transmission and infection establishment.

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Abstract 9360

**Sepsis caused by Salmonella Paratyphi B variant producing a blaOXA-48 in a traveller patient**

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**Background:** Whole genome sequencing is taking an increasingly important place in clinical microbiology. We describe here the case of a blaOXA-48 producing *Salmonella enterica* serovar paratyphi B variant Java sepsis in a traveler that was identified through sequencing. The patient, 27 year-old with no medical history consults for prolonged hyperthermia after visiting Australia, Hong Kong, Singapore, Uruguay, and United States. Blood culture turned positive for a *Salmonella enterica* OMA+ Vi+ producing an OXA-48. We used WGS to precisely identify the variant of this atypical isolate and to describe the environment of this blaOXA-48 gene.

**Materials/methods:** We performed a WGS using both MiSeq and MinION technologies. Assembly and annotation were performed using Spades and Arg-annot respectively. Identification of the species was done by rMLST ([https://pubmlst.org/rmlst/](https://pubmlst.org/rmlst/)) and DNA/DNA hybridization. The presence of the blaOXA-48 gene was confirmed using Abricate and we described in genomic environment.

**Results:** The genome of this isolate was assembled into a unique chromosome of 4.77 Mb length and 52.3 GC%. Interestingly the strain was identified as a *Salmonella enterica* serovar paratyphi B variant Java, corresponding to a ST86. Whereas the Vi agglutination test was positive, we did not find this toxin in the genome of this species that is not known to carry it in literature. We are currently confirming the test to better understand this discrepancy. The strain carried 3 plasmids, including a small Col156 plasmid of 7,999 bp carrying a blaOXA-48 gene. It also carries resistance a qnrB19 gene conferring resistance to fluoroquinolones but remain susceptible to ceftriaxone. We are currently comparing our genome with the other *S. paratyphi* B to try to identify the origin of the isolate and to know if this carbapenemase have already been found in a genome.

**Conclusions:** We describe the case of a sepsis caused by a *Salmonella* paratyphi B variant Java producing an OXA-48 carbapenemase. After a treatment by ceftriaxone IV during 10 days, the patient cured. This variant is known in literature to be multi-drug resistant but to our knowledge, this is the first description of a major Salmonella producing OXA-48.

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Abstracts 2020

Abstract 9361

**Sub-standard and falsified antibiotics: a systematic review**

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**Background:** Antimicrobial Resistance (AMR) is one of the greatest threats faced by humanity. Substandard and Falsified (SF) antibiotics are hypothesized to be a neglected contributing factor in the spread of AMR. Previous studies have estimated the global prevalence of SF medicines between 10 and 28%. The World Health Organization (WHO) reported an estimated modelled case fatality rate in the treatment of childhood pneumonia of 8,000 to 18,000 per 1% prevalence of SF antibiotics. The aim of this study is to review the global prevalence and distribution of SF antibiotics and the quality of the available evidence.

**Materials/methods:** We searched PubMed, Embase, Google and Google Scholar for publications studying antibiotic quality. Results were entered into the Infectious Diseases Data Observatory online medicines database. Publications reporting on the prevalence of SF antibiotics were considered for quantitative analysis. Those which had prevalence as a primary endpoint were assessed using the 26 items from the Medicines Quality Assessment Reporting Guidelines (MEDQUARG).

**Results:** From the 6,955 screened entries, 560 were relevant to antibiotic quality. Ninety-one (16.2%) were prevalence surveys that qualified for quantitative analysis. Publication years ranged from 1992 to 2019. The total number of antibiotic samples was 11,767. The median number of samples per survey was 46 (18-133). The median prevalence of poor-quality antibiotics was 20% (7.4-39%) but with important caveats for generalizability. Amoxicillin, ampicillin, tetracycline and ciprofloxacin were the most commonly surveyed antibiotics. No data were found for carbapenems, piperacillin, vancomycin and other antibiotics in the WHO “Reserve” group. MEDQUARG scores were assigned to 71 (78%) qualifying prevalence surveys. The median score was 11 (7-14) out of 26.

**Conclusions:** Our review raises concerns that SF antibiotics are widely spread with an alarming prevalence in Low-and-Middle-Income Countries (LMIC). The quality of the evidence is poor, and most studies are of small size, making aggregation of data and interpretation difficult. Urgent research is needed to assess the epidemiology and impact of SF antibiotics on human health and AMR.

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Study of brain-derived neurotrophic factor gene expression in brain tissue of rat infected to acute and chronic toxoplasmosis: a study in animal model

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Background: Brain-derived neurotrophic factor is a protein encoded by a gene called BDNF. This protein promotes the development of the peripheral and central nervous system. Many evidence suggests that BDNF plays important roles in memory, learning, behavioral disorder, energy intake and energy metabolism. In some studies, infection with Toxoplasma has been shown to alter the level of BDNF in the brain.

The aim of this study was to determine the effect of acute and chronic infections of the dominant strain of Toxoplasma in Iran on the expression of BDNF gene expression in rat brain tissue.

Materials/methods: Sixty adult male Wistar albino rats (230-300 g) were allocated in to the six groups. Three groups inoculated by 200000 tachyzoite of T. gondii RH strain and three groups were controls without inoculation. After two, five and ten weeks, groups 1, 2 and 3 and their controls' brain removed.

In brief, total RNA from the brain was extracted using RNAX_Plus Cinnagen kit according to the manufacturer's instructions and then synthesized by cDNA synthesis kits (Fermentas Co). In the next step, primers designed for BDNF gene, as well as beta-actin gene, were used as a housekeeping gene for control and comparison in real time PCR reaction with cyber green fluorescence color

Results: Acute T. gondii infection can reduce the expression of T. gondii genes by 7.54 fold compared to the control group, which is significant statistically. There was no significant difference in the expression of the gene in the five week and ten week chronic infection groups compared to the control group.

Conclusions: The results of this study showed that acute infection with RH T. gondii can reduce the amount of BDNF expression in the rat brain, while chronic toxoplasmosis infection has no significant effect on BDNF gene expression. By performing microscopic examination and injection of brain suspension into mice, it was determined that the T. gondii RH strain was not able to produce cysts.

Key words: BDNF, gene expression, acute toxoplasmosis, chronic toxoplasmosis

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Abstract 9364

Patient perceptions of antimicrobial resistance: are we getting the right messages across?
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Background: Patient perceptions of antimicrobial resistance (AMR) and its potential physical and psychological consequenc- es are extremely important in an era of increasing resistance. Patients colonised/infected with resistant Gram-negative organ- isms (rGNO) are at increased risk of death and prolonged hospital stay, require isolation in side rooms (SR), among others. There are no guidelines about how the issues around AMR should be discussed with patients. We aimed to assess the un- derstanding of inpatients about AMR, explore the quality of information given by the healthcare professionals (HCP) and the emotional impact associated with colonisation/infection by rGNO.

Materials/methods: Patients. Consecutive adult inpatients with colonisation/infection by rGNO (October 2017 - January 2018), identified using routine surveillance systems. For each case, a control of similar age on the same ward was selected.

Methods Semi-structured interview: combination of closed and open questions in five categories (knowledge of AMR, quality of information received from healthcare professionals (HCP), psychological impact, information preferences, open comments-feedback). The infection control advice had already been given routinely as per national and local recommendations, that did not change during the study period. Analysis: Descriptive analyses.

Results: 11 patients with rGNO and 15 controls were interviewed. The rGNO group were more likely to answer they had knowl- edge about AMR (83% vs 57%); only 6% showed a ‘good’ level of understanding. In the rGNO group, 58% of interviewees report- ed not been informed by HCP about AMR/rGNO; 58 % said they did not know they had rGNO; 27% recalled being told they needed to be in a SR but no-one recalled being told details about the isolation characteristics or expected duration. 56% of interviewees reported they would react negatively if told they were colonised with a resistant bacteria. Diagnostic disclosure preferences were: by a doctor (80%), in a private room (58%), be accompanied by relatives/friends (46%), be offered the choice to disclose to family/friends (23%).

Conclusions: An important proportion of patients with rGNO had sub-optimal understanding of antimicrobial resistance and its consequences, were not aware of their status and disclosed negative associated emotions. Communication to patients with rGNO can be improved.

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"Tell me and I forget, involve me and I learn": citizen science for mosquito management in a Dutch Caribbean island

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Background: Mosquito-borne diseases (MBD) such as dengue, chikungunya and Zika are expanding worldwide, becoming an increasing threat to public health. The three responsible viruses have been transmitted by yellow fever mosquito *Aedes aegypti* in Curaçao. There is need to improve the methods for surveillance and control of both mosquito and MBD. Monitoring of adult mosquitoes has proven more accurate to determine high-risk transmission areas than larva/pupa. Engaging citizens in surveillance and control efforts of MBD has been effective in the past, since scientific information is collected while MBD education and prevention objectives are achieved. Therefore, we aimed to determine the effectiveness of an economic do-it-yourself Sticky Gravid Ovitrap (SGO) as a new surveillance method for adult mosquitoes within a citizen science framework.

Materials/methods: A total of 104 households were recruited and two kind of ovitraps were deployed per household, for comparison purposes, a commercial ovitrap (BG-GAT) was paired to the SGO. Each household was visited once weekly to collect trapped mosquitoes for analysis. Additionally, a mosquito breeding site assessment was carried out. and vector immatures indices were calculated. Lastly, we applied a KAP questionnaire regarding mosquito and MBD prevention.

Results: The SGO trap index (number of traps positive for mosquitoes) varied between 4% to 20%, compared to 56-72% for BG-GAT traps. BG-GAT traps were 5.25 times more likely to trap mosquitoes than the SGO traps. However, to be able to quantify mosquito relative density, the deployment of 3 traps per house would be necessary. No significant association was found between *Aedes* immature stages indices and *Aedes* adult mosquito data (W=0.110, p>0.05). The majority of individuals interviewed were willing to participate on mosquito surveillance (86%), 90% of them reported that having a trap at home was not a nuisance while 70% would make use of an app for surveillance of mosquito and suitable breeding sites.

Conclusions: This potential adult mosquito surveillance method continues to be evaluated. Classic immature indices seem not to be related to adult mosquito population and therefore only loosely to disease risk. Citizen engagement could be a critical step to perform the integrated management of *Aedes aegypti* in Curacao.

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Hybrid genome based approach for investigation of molecular basis of international high risk clone ST357

Pseudomonas aeruginosa circulating in India

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Background: Pseudomonas aeruginosa is a common nosocomial pathogen causing opportunistic infections. Carbapenem resistant P. aeruginosa have been frequently isolated from several hospitals worldwide and are denominated as high-risk clones (HRC). In India, international HRC ST357 seemed endemic, however there is a lack of whole genome-based studies. We performed whole genome sequencing (WGS) and hybrid genome assembly approach for improved genomic analysis.

Materials/methods: A total of 9 carbapenem resistant P. aeruginosa belonging to ST357 isolated from blood and respiratory tract infections were chosen. WGS was done by both short read (Ion-Torrent) and long read (Oxford Nanopore Technology-Minion) technologies. An in house developed de-novo hybrid assembly based approach was employed to combine short and long reads to achieve more accurate genomic information. The genomes have been deposited in the GenBank under the accession no’s: CP032569, CP033432, CP034368, CP034434-36, CP034409, CP034369, CP033439. Genomes were analyzed for antimicrobial resistance, virulence/pathogenicity, mobile genetic elements and phylogenetic evolution.

Results: De novo hybrid assembly of P. aeruginosa genomes using short and long read has yielded a complete circular chromosome of all the study isolates. Extra chromosomal elements such as plasmids were not observed. In the molecular phylogeny, ST357 being the only HRC belonging to Group 2 cluster, whereas the previously well-characterized international HRCs ST244, ST111, ST664, ST125, ST233 and ST235 were found within the large Group 1 cluster (Figure-1). Isolates harbored AMR genes against 10 classes of anti-pseudomonalas with >15 AMR genes present in each genomes. blaNDM was present in five of the isolates (2 blood and 3 respiratory), with three of the respiratory isolates harboring two copies of blaNDM-1 and one with blaNDM-1+blaNDM-11. Seven different extra chromosomal regions integrated into the genomes were observed in seven isolates. Presence of novel MDR-transposon Tn6649 and five novel integrons In1615-16, and In1622-24 carrying AMR genes have also been found.

Conclusions: Hybrid genome assembly based approach provides a complete and closed chromosomal genome sequence for a GC-rich challenging organism like P. aeruginosa. HRC ST357 harbors multiple drug resistant markers, favoring its survival in the hospital environment, thereby causing nosocomial spread. This approach can be employed for future genomic analysis of P. aeruginosa.

Figure 1: Maximum likelihood phylogenetic tree of 700 P. aeruginosa genomes derived using SNIPPY. Bolded branches (Red) indicates this study isolates

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Multidrug-resistant *Klebsiella pneumoniae* ST231: the new endemic super bug of India?

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**Background:** Among the carbapenem resistant *K. pneumoniae* (Kp), ST258 is the KPC epidemic clone prevalent in Europe and America while in India, endemic to NDM and OXA48-like carbapenemases, there is lack of data on prevailing genotypes. Previous study from our centre showed that Kp belonging to ST231 was the predominant genotype among susceptible, carbapenem resistant and colistin resistant isolates from various centres across India. Hence in the present study, two ST231 Kp were characterised by whole genome sequencing (WGS).

**Materials/methods:** A total of 37 ST231 isolates were obtained from six Indian centres. Two representative isolates were subjected to WGS using Ion Torrent and MinIon platforms and hybrid assemblies were generated. Antimicrobial resistance genes, virulence characters and plasmids were studied. Phylogenetic tree was constructed using core genome SNPs along with global ST231 Kp isolates.

**Results:** Both the isolates were extensively drug resistant (XDR); one being susceptible to colistin while the other being resistant. Colistin resistance was chromosomally mediated. Both hybrid genomes belonged to K51 and O1v2. Yersiniabactin locus ybt14 was carried on chromosomal ICEKp5. None of the ST231 Kp studied was hypervirulent. Interestingly, IncL/M plasmid known to carry *bla*OXA-48 like was absent. Chromosomal integration of two copies of *bla*CTX-M-15 in both isolates was associated with ISEc9 transposase. Chromosomal virulence genes encoding for iron uptake and biofilm formation were also present.

**Table 1:** Results of hybrid genomes of two ST231 *K. pneumoniae*

<table>
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<tr>
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<td>aadA2, emrB, sul1, dirA12</td>
<td>absent</td>
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**Conclusions:** ST231 is the predominant genotype circulating among carbapenem and colistin resistant *K. pneumoniae* in India. They are predominantly-blaoxa-232 carriers harboured on ColKP3 plasmid and are responsible for increase in OXA48-like carbapenemases in India. This genotype has the potential of thriving in hospital environments and poses the threat of acquiring virulence plasmid. Containment of this genotype is of utmost importance in order to prevent it from emerging as hypervirulent XDR *K. pneumoniae*.

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Abstract: Current multiple sclerosis (MS) treatments consist of immunomodulatory agents, immunosuppressants or selective immunosuppressants and could impact on immune system. These disease-modifying therapies (DMTs) may result in high risk of opportunistic infections including TB, mainly related to the reactivation of latent TB infection (LTBI). Approximately two billion people worldwide are infected with Mycobacterium tuberculosis and about one in 10 will develop tuberculosis (TB) at some point of their lives.

Materials/methods: At the Neuroinfectious Unit of Policlinico Umberto I (Rome), a TB screening by QuantiFERON®-TB Gold In-Tube (QFT-GIT) for MS patients candidate for DMTs was carried out. Following screening, LTBI diagnosis was based on medical history, physical examination, and exclusion of active TB disease by chest X-ray (if necessary, sputum smear microscopy, sputum culture and Mycobacterium tuberculosis PCR testing). Before started DMTs, each patient diagnosed with LTBI was undergone to TB prophylaxis with isoniazid plus rifampin for three months.

Results: One hundred and nine MS patients (56 females, 53 males) with a median age [interquartile range (IQR)] of 48.5 (39.7-55.2), median years of disease (IQR) of 9 (3-17.7) and median Expanded Disability Status Scale (IQR) of 4 (2-6), were enrolled. The 5.5% (6/109) of the patients enrolled was from Romania, the 0.9% (1/109) from Argentina, the 0.9% from Asia (1/109) and the 92.6% (101/109) from Italy. At baseline, the 7.3% (8/109, two from Romania and six from Italy) of MS patients showed QFT-GIT positivity. Active TB was excluded and DMTs was started at least one month after TB prophylaxis. To date, four patients are at six months of ocrelizumab (anti-CD20 monoclonal antibody) treatment, two patients at seven months of teriflunomide (oral DMT immunomodulator) treatment, one patient at five months of dimethyl fumarate (oral DMT immunomodulator) treatment. No TB reactivation was observed.

Conclusions: The TB screening in MS patients candidate to DMTs must be considered standard care as part of disease management. The use of two active molecules on TB allowed an earlier starting of DMTs avoiding a possible TB reactivation. Furthermore, LTBI management in MS patients could contribute to reduce the transmission, morbidity, and mortality of active disease in global population.

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Abstract 9377

Discontinuation of antimicrobial therapy during fever of unknown origin in adult neutropenic patients according to ECIL-4 criteria: RELAPS, a descriptive cohort study

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Background: In neutropenic patients with fever of unknown origin [FUO], discontinuation of antibiotics recommended according to ECIL-4 criteria, 2011. However, data concerning the risk of febrile recurrence are limited. The objective of our study was to analyse risk factors and morbidity-mortality of febrile recurrences after antibiotics discontinuation in this population.

Materials/methods: We prospectively enrolled all neutropenic patients with FUO admitted to a French teaching hospital between February 2018 and September 2019 for which a discontinuation of antibiotics, according to ECIL-4 criteria, has been achieved. Medical records were reviewed retrospectively: underlying disease, duration of aplasia, recurrence rate, bacterial documentation, severity to assess risk factors for febrile recurrence. Risk factors of recurrence were compared using Cox regression analysis.

Results: A total of 86 patients corresponded to 92 cases were enrolled. Underlying diseases were mainly acute leukemias (58%; 50/86) and lymphomas (8%; 7/86). Neutropenia was due to allograft (47%; 44/92), autograft (9%; 8/92) and induction (35%; 32/92). Recurrence fever was observed in 57% of cases (52/92) and a bacterial documentation was obtained for 52% (27/52) of them. 67% (n=18/27) of documented recurrence fever were not covered by first line empirical antibiotic therapy (9 Enterococcus spp, 4 Staphylococcus spp, 3 anaerobes, 2 BLSE and one candidemia). On average 7 [0;25] days of antibiotics were spared for each neutropenic episode. No sepsis shock or sepsis-related mortality was reported due to antibiotic discontinuation. Median time of aplasia was significantly lower in the no recurrence subgroup compared to the recurrence subgroup (16 days vs 21 days respectively, p<0.001). On multivariable analysis, risk factors identified for fever recurrence were the presence of colitis [hazard ratio [HR] 3.1; 95 IC [1.3-7.6]; p=0.015], mucositis [HR 3.2; 95 IC 1.7-6.2; p<0.001] and lymphoma as underlying disease [HR 3.7 [1.6-9.0]; p<0.01]. The initial duration of antibiotic therapy did not influence the risk of recurrence [HR 1.0 [0.9-1.1]; p=0.5].

Conclusions: Discontinuation of antibiotic therapy during neutropenia did not appear to induce a higher morbidity-mortality rate. Febrile recurrences were correlated with a longer duration of neutropenia, the presence of colitis, or mucositis and lymphoma.

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Incidence, risk factors and outcome determinants of healthcare-associated blood stream infection at a neonatal intensive care unit in North India

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Background: Bloodstream infection (BSI) is one of the most common causes of nosocomial infection in neonatal intensive care units (NICU). In low-middle income countries, laboratory confirmed BSI (LCBI) rates are two to three times higher than those of high-income countries, which makes HA surveillance in the intensive care unit (ICU) essential for infection control. Aim of the present was to.

Materials/methods: Active surveillance to determine the incidence, risk factors, outcome determinants and antibiotic pre-scription practices of LCBI s (as per CDC) in a level 2 NICU was carried out over a period of 4 years from 2016-2019. A pre-designed questionnaire containing risk factors associated with LCBI s was filled under supervision of nursing staff involved in multifaceted infection prevention plan.

Results: Over the study period 65 episodes of LCBI were identified. Cumulative incidence of LCBI was 2.71 neonates per 1000 patient days with incidence density of 3.4, 3.17, 1.21 and 3.05 for the year 2016, 2017, 2018 and 2019 respectively. Incidence of LCBI in neonates with weight less than 750 gm was 24.02 per 1000 patient days. Independent risk factors for LCBI were: preterm neonates, extremely low birth weight neonates (p<0.01), duration of NICU stay more than 14 days, premature rupture of membrane in mothers, neonate born through meconium-stained amniotic fluid, endotracheal intubation, prior hospitalization and surgical intervention after the birth. Major pathogens causing LCBI were Candida species (43.1%), Acinetobacter baumannii (29.2%), Klebsiella pneumoniae (21.5%) and Escherichia coli (6.2%). LCBI was associated with a mortality rate of 21.54% (14 out of 65). LCBI due to MDR GNB resulted in dose dispensed of 200 per 1000 patient days for Colistin and 450 per 1000 patient days for Meropenem.

Conclusions: The results of our study can be used to identify high-risk neonates for LCBI in resource-constrained settings and highlights the need for strengthening risk-targeted surveillance for LCBI in neonatal ICUs. The results of the present study can be used to design and implement an antibiotic stewardship policy and introduce interventions to reduce LCBI.

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Background: Identification and antibiotic susceptibility testing of microorganisms isolated from blood cultures (BC) are crucial for early and effective treatment of patients with blood stream infections (BSI). Karolinska University Laboratory (KUL) handles more than 100,000 referrals for blood culturing every year. Approximately 98% originate from four of the largest tertiary care hospitals in the region: Karolinska University Hospital in Solna and Huddinge, Danderyd Hospital, and South Hospital. Previously we reported negative effects of long transport time on time to detection of microorganisms from BC, emphasizing the need to place BC systems units closer to patients.

Materials/methods: During 2017 a collaboration between Clinical Microbiology, Laboratories for community care and pre-analyses and Clinical Chemistry-KUL 24/7 was initiated, aiming at shortening turn-around-times (TAT). We hypothesized that by placing a semi-automated blood culture system (Bact/ALERT VirtuO/Myla, BioMérieux) at hospital laboratories with 24-h service, time from sampling to incubation would significantly shorten. Positive BC bottles are transported to Clinical Microbiology for further analyses, and we hypothesized shorter TAT from sampling to preliminary microscopy-based results.

Results: In 2018 relocation of BC systems were initiated, with deployment in each of the four hospitals in intervals. In September 2019 a total of 10 units had been deployed at 24/7 laboratories. Statistical analyses based on a total of 49,096 BC bottles show, as expected, an improvement with on average 90% (from 5.7 h to 0.6 h median time) in TAT for sampling to incubation, compared to 50,031 BC bottles from the same time period a year prior to relocation. Analyses of 5,976 positive bottles within the cohort show an improvement of 8.7 h (27%) in median time to preliminary results (compared to 5,996 the year before). Further, we observed a positive effect in distribution of positive bottles over a 24-h period, with a larger portion of positive bottles determined positive during regular opening hours for Clinical Microbiology.

Conclusions: The relocation of blood culture units to laboratories with 24/7 service have significantly improved TAT for blood cultures in Clinical Microbiology, without any adjustment in laboratory opening hours. Further improvements could be possible with further optimization of transports and work-flows.

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Abstract 9384

Development of attenuated bovine herpesvirus 4 as a safe, inexpensive, single-dose vaccine to control Streptococcus suis infection in domestic pigs

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Background: Streptococcus suis is a worldwide pathogen of pigs, causing meningitis and septicaemia. S. suis represents a major problem for the swine industry. There are currently no commercial vaccines that are protective against all 35 S. suis serotypes. Consequently, antibiotic usage is extremely high in pig farming, which has contributed to antimicrobial resistance (AMR) in both pig and human isolates. S. suis is also a rapidly emerging zoonotic pathogen.

A vaccine against S. suis would significantly reduce antibiotic use in the swine industry, thereby helping control AMR. Bovine herpesvirus 4 (BoHV-4) is a new vaccine vector platform capable of inducing high levels of immunity in livestock species, potentially representing an effective and inexpensive means of control.

Materials/methods: Previously identified protective antigens from S. suis, Sly and 38kDa, were cloned into the BovH-4 vector followed by genetic characterization. Restriction enzyme digestion followed by electrophoresis showed maintenance of genome integrity. PCR using primers flanking the site of insertion of the S. suis genes within the BoHV-4 genome combined with Sanger sequencing showed preservation of S. suis gene sequence.

Results: Following this extensive in vitro characterization, vaccine vectors were reconstituted in bovine cells and vectors were shown to express Sly and 38kDa antigens by western blot. Virus stocks have been prepared and will shortly be tested for immunogenicity and efficacy in rodents and pigs. Additional novel S. suis antigens have been identified using the Reverse Vaccinology pipeline Vaxign. Novel B cell epitopes in both known and novel immunogenic antigens were identified using BepiPred, ABCPred and BCEPred. Conservation of epitopes across species was identified using MEGAX software. These novel second generation epitopes will be inserted into the BoHV-4 for immunological and efficacy testing.

Conclusions: BoHV-4 is a new vector platform suitable for targeting important bacterial pathogens such as S. suis in livestock. Identification of immunogenic peptides by reverse vaccinology approaches is a potentially promising approach to identify additional antigens from these bacteria that may be targeted to interrupt AMR acquisition in livestock species.

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CRISPR typing of *Salmonella enterica* serovar Typhimurium from clinical and non-clinical sources reveals the possible transmission from environment to humans

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**Background:** *Salmonella Typhimurium* is one of the most common serotypes identified among Non-Typhoidal *Salmonella* (NTS). Traditional serotyping based on the phenotypic variation of O- and H-antigen is the gold-standard for the identification and classification of *Salmonella* isolates. Global evolution of distinct genotypes of *S. Typhimurium* led to frequent discrepancies when identified by conventional methods. High resolution molecular techniques such as Multi Locus Sequence Typing (MLST) & Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) typing can be alternative for classical methods. This study is an attempt to characterize *S. Typhimurium* clinical isolates using MLST and CRISPR typing and compare with non-clinical isolates to identify the potential transmission from environment to humans.

**Materials/methods:** *S. Typhimurium* clinical isolates (*n=50*) were identified and classified based on conventional serotyping (Kauffmann–White scheme) and biochemical tests. MLST and CRISPR typing were performed to accurately identify the NTS serovars and to identify the genetic relationships among clinical and non-clinical *S. Typhimurium* in India. Serotypes and subtypes were assigned based on MLST and CRISPR typing and compared with the phenotypic results. The phylogenetic relationship between isolates from different sources was demonstrated in MLST based Maximum Likelihood (ML) phylogenetic tree.

**Results:** Among *S. Typhimurium* ST36 (50%) found to be the predominant sequence type followed by ST19 (42%) and ST31 3 (8%). CRISPR types of all the clinical isolates were distributed according to the STs and no clonal distribution was observed within STs. Although CRISPR types on non-clinical isolates revealed subtypes within ST19 and ST36, similar clones were present in both study sources. MLST based phylogenetic tree revealed the relationships among strains from different sources and potential transmission from environmental to humans.

**Conclusions:** Mismatches occurred in serovar designation between MLST/CRISPR database and serotyping due to the misinterpretation of the antigenic structures. Presence of similar CRISPR types in clinical and non-clinical sources revealed potential transmission from environmental to humans. CRISPR Subtyping is a powerful tool to track the *Salmonella* transmission between humans, animals and plants (One Health Concept).

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Abstracts 2020

Abstract 9389

An optimised strategy for linkage to care of patients newly diagnosed of active hepatitis C infection

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Background: Spain is on-track for hepatitis C elimination and is expected to reach WHO elimination goals by 2024. However, special efforts must be made to avoid diagnostic burn-out and to find all patients that may be diagnosed, treated and cured. We have been actively working on reflex testing (HCV antibody and, when positive, viremia detection on the same sample) in the last years. We have also found from previous evaluations that in addition to reflex testing, active communication strategies for effective linkage to care are also necessary. Here we present a novel communication strategy that has increased the number of patients that have access to treatment and cure.

Materials/methods: we have performed a pilot, prospective study in which all patients diagnosed in our laboratory of chronic hepatitis C active infection, were candidates for a direct medical appointment at our hospital for treatment evaluation. We have analyzed: a) number of patients that have attended the medical appointment, b) time since diagnosis to medical appointment, c) number of patients that have started treatment, and d) time since diagnosis to treatment initiation.

Results: during the study period (January-September 2019), 33 patients have been diagnosed of chronic active infection in our laboratory. Mean age was 59, and 67% were male. Mean core antigen levels were 3184 fmol/L [1112.04-6154.41], and genotype distribution was as follows: 21.2% 1a, 42.4% 1b, 9.1% 2, 6.1% 3, and 9.1% 3a (12.1% without assigned genotype). Mean fibrosis score was 8.3 kpa. As of the end of September, 94% of the patients have attended their medical appointment. After treatment evaluation, three patients were not eligible (over 95 years of age, multiple comorbidities). Time since diagnosis to medical appointment was 13 days [7.5-19] for the pre-summer period, and 25.5 days for the summer period [20.5-37.25]. All patients that started treatment were on the first appointment. Treatment was started with Sofosbuvir/Velpatasvir 12 weeks [n=6], or Glecaprevir/Pibrentasvir B/12 weeks [n=15].

Conclusions: direct medical appointment strategies have shown a great success on linkage to care and hepatitis C treatment initiation. In addition, a reduction on time since diagnosis to treatment has also been achieved.

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Abstract 9390

**Update on Candida auris in Russia**

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**Background:** Candida auris is currently considered one of the top threats in public health as it is capable to cause outbreaks in hospitals and tends to survive for a long time in hospital environment. The aim of the present study was surveillance of C. auris infections in Russia and evaluation of the pathogenicity of strains with different morphology of colonies.

**Materials/methods:** C. auris was isolated from patients samples with Sabouraud dextrose agar (Oxoid, UK) and chromogenic agar (Liofilchem, Italy). The identification was performed with MALDI-TOF mass spectrometry (Bruker Daltonics, USA). Study of isolates included sequencing of ITS and D1-D2 regions as well as ERG11 gene (ABI 3130, USA). Susceptibility to antifungal preparations was assayed with Sensititre panels (Thermo Fisher Scientific, USA). Pathogenicity of C. auris strains, isolated from patients, was studied in a murine model without previous immunosuppression.

**Results:** 97 strains of C. auris were isolated in 3 regions of Russia. All studied strains clustered with isolates of Indo-Pakistan origin, demonstrated K143R mutation in ERG11 gene, typical to South Asian clade, and had high level resistance to fluconazole. Susceptibility to amphotericin B and other azoles was variable. Most isolates were susceptible to echinocandins.

Experimental studies of 2 types of C. auris strains that differed in the size of colonies in murine model showed low pathogenicity of both. During 5-weeks of observation all mice demonstrated no signs of systemic infection. The fungus was isolated from blood vessel and renal tissue in 2 (12.5%) mice at the end of follow up period.

**Conclusions:**

1. C. auris strains, belonging to South Asian clade, are being isolated from patients in different regions of Russia.
2. C. auris strains demonstrate high level resistance to fluconazole and variable resistance to amphotericin B and other azoles. Most strains are susceptible to echinocandins.
3. C. auris showed low pathogenicity in murine model without immunosuppression, though was able to persist in blood vessel and renal tissue of few mice.

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The concordances of genotypic and phenotypic drug susceptibility testing of Mycobacterium tuberculosis isolates from MDR TB patients

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Background: Antimicrobial resistance is one of the most important threats of global tuberculosis control. Rapid and accurate detection of resistance to either Rifampicin or Isoniazid is crucial for selection of treatment regimens. Genotypic drug susceptibility testing (gDST) and phenotypic drug susceptibility testing (pDST) results must be considered collectively to reach a final interpretation of drug resistance.

Aim: to evaluate the concordances of the pattern of mutations of gDST and the level of drug resistance for RMP and INH of the isolates from MDRTB patients for rapid and reliable correction of treatment schemes.

Materials/methods: In study were included 6952 patients with new and previously treated pulmonary TB, examined during 2014-2018 years. From these 57.1% were positive by microscopy, 66.2% by GeneXpert and 69.98% by culture method. The pDST results of 4865 M.tb strains of MGIT960 method, were correlated with the gDST results of MTBDRplusv.2. The mutation types in the rpoB gene, and the presence of inhA mutation in the same M.tb isolates was correlated correspondingly with the different level of MIC for Rifampicin and Isoniazid of individual strains, assessed by MGIT 960.

Results: From 157 M.tb isolates with presence of inhA mutations only (INH low resistance), in 31% of cases these strains were susceptible on higher MIC demonstrated by pDST. From 114 M.tb isolates with genotypic RIF resistance without S531 and H526 mutations, and/or without wild genes, the pDST demonstrated that 28.8% of these strains were susceptible on higher MIC.

Discussion: The patients with low-level genotypic resistance should have additionally information about the level of phenotypic resistance. For reliable DST results, phenotypic and genotypic methods should be used in parallel, to be phased in without loss of existing solid culture and DST capacity.

Conclusions: pDST is still required, for corrective of rapid gDST results, in special from smear-negative specimens for detect XDR-TB. Different levels of phenotypic resistance could take into account in the procedures used by pDST of M.tuberculosis.

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Abstract 9395

Global spread of poultry-associated *Campylobacter jejuni* genotypes to the Peruvian Amazon

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**Background:** *Campylobacter* is the leading bacterial cause of gastroenteritis worldwide and incidence is high in low- to middle-income countries. Disease epidemiology is different to that of the developed world, where infection is mostly associated with consumption of contaminated meat products. Infection is endemic among young children and asymptomatic carriage is thought to be common. Widespread malnutrition encourages asymptomatic colonization and is associated with deficits in early childhood growth, leading to poor cognitive and physical development.

**Materials/methods:** In this study, we sequence and characterize an archived collection of *Campylobacter jejuni* isolates (n=62) from children enrolled in the Peruvian cohort of the MAL-ED study.

**Results:** In combination with disease severity scores determined from detailed symptom records, we identify the genotypes involved in disease. Epidemiological differences in disease presentation were reflected in the genomes, specifically by the absence of common global disease lineages, including the host generalist ST21 and ST45 clonal complexes. Despite this, our Peruvian collection was more diverse than a representative global collection of genomes and many local disease cases were attributed to rare STs, not commonly isolated from other countries or reservoir sources. Phylogenetic analysis could not discriminate symptomatic and asymptomatic isolates, suggesting that asymptomatic carriage is not restricted to specific ecological groups or clonal complexes. Using probabilistic source attribution methods, we identify chicken as the primary source of infection in 78.4% of the isolates, which is significantly higher than previous attribution studies in developed countries.

**Conclusions:** A better understanding of the genotypes underlying differences in disease epidemiology will support work to improve infant health globally and guide intervention strategies.

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Burden of influenza C in a paediatric population with severe respiratory disease
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Background: Compared to other respiratory viruses, there are fewer studies on influenza C (FluC) even though it causes a similar spectrum of disease. FluC is more prevalent in children than adults and has high rates of co-infection with other respiratory viruses. Our goal was to determine the burden of FluC and its co-infection rate in hospitalized pediatric patients tested in the Canadian province of Alberta (pop: 4.4 million, <10 year old pop: 0.55 million).

Materials/methods: We included hospitalized patients ≤10 years old tested with the Luminex NxTAG Respiratory Pathogen Panel (RPP) from July 2, 2018-April 22, 2019. Specimens from the same patient received within 30 days of the first were excluded. We included specimens collected from the lower respiratory tract (auger suction, bronchoalveolar lavages, bronchial washes, and endotracheal tube aspirates) and all specimens from intensive care patients. We screened all available specimens for FluC using an in-house RT-PCR (Pabbaraju et al. 2013 doi:101111/irv.12099) and lineages were determined by sequencing the hemagglutinin esterase gene.

Results: Of 598 specimens (from 334 males and 264 females), 1.5% (n=9) were positive for FluC from either Kanagawa or Sao Paulo lineages. Peak incidence was in January (n=3) and March (n=3). Of the 9 cases, 5 patients (55.6%) had a co-infection including RSV A/B (n=2), RSV B and enterovirus/rhinovirus (n=1), parainfluenza-3 (n=1), and human metapneumovirus (n=1). In our cohort, the incidence of FluC was higher than the following RPP targets: influenza B (n=0), parainfluenza-1 (n=3), coronavirus 229E (n=2), coronavirus NL63 (n=5), coronavirus HKU1 (n=1), M. pneumoniae (n=4) and C. pneumoniae (n=0).

Conclusions: The burden of FluC in a pediatric population with lower respiratory disease and/or admitted to the intensive care unit is greater than some other commonly tested pathogens. This study suggests that the role of FluC, both as a single or co-infecting agent, is under-appreciated and contributes to the burden of pediatric respiratory infections in hospitalized cases. For this reason, inclusion of FluC should be considered in the design of future multiplex assays.

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**KpnBR: Brazilian genomic database for monitoring resistance and virulence of *Klebsiella pneumoniae***

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**Abstract third-party references:** CNPq, Bill and Melinda Gates

**Background:** The emergence and dissemination of critical-priority multidrug-resistant (MDR) *Klebsiella pneumoniae* (*Kp*) is a One Health issue worldwide. On the other hand, convergence of virulence and resistance, and identification of highly virulent or hypervirulent *K. pneumoniae* (*hvKp*) lineages is a worrying topic of public health interest. In Brazil, KPC-2-producing *K. pneumoniae* has acquired an endemic status, whereas highly virulent and hvKp strains have emerged. In this context, this work aims to create a cured and integrated genomic database, named *Klebsiella pneumoniae* Brazilian Resistance and Virulence Database (KpnBR), for surveillance and monitoring dynamic of critical-priority *K. pneumoniae*, with identification of high-risk resistant and/or virulent clones, mapping outbreaks and hotspots.

**Materials/methods:** KpnBR web database contains a metadata file, based on reports from an automated bioinformatic pipeline called PIPA, which includes all genomic background of *K. pneumoniae* strains (i.e., resistome, virulome, MLST, etc). Currently, KpnBR hosts genomic data from 113 *Kp* genomes obtained from this study, and 80 further *Kp* genomes obtained from the freely and publicly available NCBI database.

**Results:** KpnBR database (http://app.kpnbr.com.br) shows a worrying landscape of *K. pneumoniae* in Brazil, where, in the last 15 years, dissemination of KPC-2 producers has been associated with the pandemic CC258, identified in environmental and clinical settings. CTX-M-15-positive *Kp* ST340 is now found in human, food-producing and companion animals, highlighting a One Health problem. In addition, polymyxin-resistant strains are increasing. Finally, convergence of resistance and virulence has enhanced, whereas highly virulent (ST307, ST340, ST11) and hvKP (ST23/K1) *Kp* lineages have begun to be identified at the human-animal interface.

**Conclusions:** The KpnBR can contribute to the development of strategies for prevention, genomic surveillance, diagnosis and treatment of *K. pneumoniae* infections in Brazil with high endemicity of carbapenem-resistant.

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Longitudinal microbiome analysis defines expected and aberrant antibiotic effects on the human respiratory microbiome

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Abstract third-party references: National Institute for Allergy and Infectious Diseases, Centers for Disease Control and Prevention

Background: Antibiotics are defined by their spectra of activity. But the observed impact of an antibiotic on a complex microbial community depends not only on microbial killing, but also on community membership at time of antibiotic initiation, inter-taxa interactions, and neighboring environmental communities that may contribute to microbial succession. We sought to define expected and aberrant effects of commonly used antibiotics on the human respiratory tract microbiome by longitudinal sampling of patients admitted to a long-term acute-care hospital (LTACH) with ventilator-dependent respiratory failure.

Materials/methods: From 83 subjects enrolled at the time of their admission to an academic LTACH, we obtained 1691 endotracheal aspirate specimens. We performed 16S rRNA sequencing (Illumina HiSeq), sequence error correction and binning (QIIME2 and DADA2), and applied a phylogenetic transform to account for compositionality. Statistical analysis was performed with R and Stan; mixed effects models were fit to evaluate aggregate and subject-level antibiotic effects.

Results: We observed 10834 amplicon sequence variants, with 8586 associated phylogenetic balances, across all specimens. We evaluated the variance of phylogenetic balance, which captures the degree to which clades co-vary, to identify exclusionary dynamics associated with antibiotic exposure. Antibiotic exposure significantly reduced balance variance; the greatest balance variances were observed in the pre-antibiotic and post-antibiotic periods. Significant differences in exclusionary dynamics were observed across antibiotics (cefepime, meropenem, piperacillin-tazobactam, and intravenous vancomycin) and subjects.

Conclusions: Longitudinal microbiome analysis reveals features that discriminate differential antibiotic impacts on the respiratory tract microbiome, as well as subject-level differences in post-antibiotic succession.

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How partnership network and HPV type interaction shape the distribution of HPV infection before and after vaccine introduction

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Background: Human papillomaviruses (HPV) are common sexually transmitted infections, characterized by a large diversity of genotypes. HPV prevalence usually peaks at ages 20-24 years, a characteristic that most compartmental mathematical models fail at reproducing. Current vaccination protecting against a subgroup of genotypes, it is key to better understand whether and how genotypes interact to anticipate the impact of vaccination. Here we use a novel realistic agent–based-model of HPV transmission over a heterosexual partnership network in France and assess the impact of assumptions regarding HPV vaccine (V) and non-vaccine (NV) genotypes interaction on HPV epidemiology after vaccination.

Materials/methods: Gender-specific data regarding sexual behaviour in France were used to model a dynamic partnership network with heterogeneous and age-specific sexual activity. Transmission rates and natural immunity parameters were calibrated to match HPV genotype prevalence by age. Ecological interactions between genotypes (competitive, neutral, or synergistic), mechanisms (altering the infection duration or the acquisition probability) and context of interaction (between groups of genotypes or between genotypes) were tested in a series on hypothetical scenarios to investigate their effect on the dynamics post vaccine introduction.

Results: Please copy and paste the corresponding text here In our simulations, infection had reached >70% of the population by the age of 29 years. An important part of infected people (61%) were co-infected by at least two types, a phenomenon observed in individuals with both high and low sexual activity. In all investigated scenarios, vaccine introduction modified NV genotypes prevalence, except for two cases: (i) no interaction and (ii) interactions independent from vaccine inclusion. The pre/post vaccine prevalence ratios of NV ranged 0.92–0.82 in synergistic interactions scenarios and ranged 1.08–1.14 in competitive scenarios. Interestingly, predicted post-vaccination variations of V and NV were stronger for individuals with fewer partners () compared with others.

Conclusions: The proposed agent-based model reproduces realistic patterns of HPV infection and age-distributions. Our simulations results suggest that better knowledge of genotype interactions is key to anticipate accurately the impact of existing and future anti-HPV vaccines targeting a subgroup of genotypes.

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**Abstract 9409**

**Molecular surveillance of mcr gene in gut microbiome of healthy individuals, acute diarrhoea and inflammatory bowel diseases patients from India**

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**Background:** The aim of this study was to assess the prevalence of mcr (Mobilized Colistin Resistance) gene in gut microbiota of healthy and diseased individuals from different parts of India. The limitation of detecting colistin resistance in unculturable and fastidious microbes in the human gut microbiota can be overcome by culture-independent approach wherein the metagenomic DNA representing the DNA of culturable and nonculturable microbes can be targeted by PCR screening followed by confirmation.

**Materials/methods:** Faecal samples from healthy and diseased subjects (n=484) and hen’s eggs ready for human consumption (n=104) from different parts of India were subjected to screening by mcr 1-5 multiplex PCR. Samples screened positive were further confirmed by nested PCR, restriction enzyme digestion and sequencing. Whole genome sequencing of colistin resistance bacterial isolates (Klebsiella pneumoniae, Vibrio cholerae, Pseudomonas aeruginosa, Campylobacter jejuni) were conducted to explore the resistance genes and mobile genetic elements that carry the resistance genes.

**Results:** A total of 24 out of 484 (4.9 %) faecal samples were positive for mcr-1, which included 2% samples of inflammatory bowel disease patients (1 out of 48), 4.3% acute diarrhoea patients (15 out of 350) and 21% healthy subjects (8 out of 38) living in Leh, the northernmost union territory of India amidst The Himalayas. The present finding of a high prevalence of mcr-1 in healthy subjects from Leh, who have no history of prescribed colistin intake is quite perplexing. Among the 104 screened hen’s eggs meant for human consumption, 15 were culture positive for bacteria and 1 carried the mcr-1 mobile genetic. This study depicts the current scenario of the presence of mobile colistin resistance gene mcr-1 in Indian population, highlighting the potential risk of emergence of polymyxin resistance.

**Conclusions:** Till now, to the best of our knowledge this is the first study in India relating the prevalence of mcr-1 gene in the gut metagenome of healthy and diseased individuals with due consideration of dietary habits and other environmental factors, which may potentially contribute to the emergence and spread of mcr-1 harbouring human associated microbiota.

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ABSTRACT BOOK – 30th ECCMID 2020

Abstract 9412

A critical appraisal of the new antibiotic prescription chart using HAPPI [Hospital Antibiotic Prudent Prescribing Indicators] in a large UK district hospital

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Background: A point prevalence audit was conducted respectively in October 2018 and January 2019 at a large UK district hospital to assess the appropriateness of antibiotic use according to the requirements of Public Health England and NHS Improvement 2018/19.

Materials/methods: Ten antibiotic prescriptions were reviewed per ward according to the following three care elements:

1. Appropriate choice of antibiotic[s]
2. Antibiotic review within 24 - 72 hours?
3. Length of course of antibiotic documented on the prescription chart?

Results: A total of 654 antibiotic prescriptions were reviewed in the study and the breakdown is shown below.

<table>
<thead>
<tr>
<th>Month/Year</th>
<th>Oct-18 (N=328)</th>
<th>Jan-19 (N=326)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appropriate antibiotic choice</td>
<td>90%</td>
<td>90%</td>
</tr>
<tr>
<td>Antibiotic review within 72 hours (%)</td>
<td>43%</td>
<td>39% ↓</td>
</tr>
<tr>
<td>Stopped date specified on the antibiotic prescription chart</td>
<td>17%</td>
<td>28% ↑</td>
</tr>
</tbody>
</table>

Both audits found 90% of compliance with appropriate antibiotic choice which demonstrated that clinicians were aware of the hospital antimicrobial guidelines. There was an improvement in the length of antibiotic course being specified in the 2nd audit after a strong advocate of prudent use of antibiotic among hospital staff through the social media in November 2018. However, hesitation has been illuminated in the antibiotic review within 72 hours by the clinicians; which may indicate that a rapid diagnostic test analysis and a simplified procedure for microbiologist consultation are necessary.

Conclusions: Antibiotic review is a crucial part of antimicrobial stewardship to combat bacterial resistance and hospital acquired infections. It requires multi-disciplinary approach from an operational level to clinical directorate level to achieve success. Lack of antibiotic review could be due to operational system failure [design of the prescription chart], lack of motivation/engagement by senior clinicians and microbiologists, and insufficient training/advocate of antimicrobial stewardship among junior doctors, pharmacy and nursing staff. Suggestion includes constant surveillance of antibiotic prescriptions, a set-up of an “e-referral” procedure for easier access of microbiologist’s advice, regular feedback of the antibiotic usage to the relevant stakeholders/directorates to enhance their engagement in antimicrobial stewardship, and a widespread message of the harm of antibiotic abuse and bacterial resistance to patients and the community.

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Abstracts 2020

Abstract 9413

**Adequate exposure time of cold atmospheric pressure plasma on *Staphylococcus aureus* biofilms**

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**Background:** *Staphylococcus aureus* biofilms play a significant part in pathogenicity and result in persistent infections in tissue, external and indwelling devices. Considering escalation in Antibiotic Resistance, one of the influential technologies is the Cold atmospheric plasma (CAP). It had found a diverse advantage in the food industry and the health care system. Consequently, exploration of the effects of bacterial biofilms affected by CAP is essential for the annihilation of pathogenic biofilms.

**Materials/methods:** The two-day-old biofilms of *Staphylococcus aureus* (ATCC 6538) were established in (96-well plate) in tetrad using the TSBG medium. They were exposed to the (Helium) CAP exposure for 0 to 360 s. Following CAP treatment the plates were sonicated to resuspend biofilms in the aquatic estate for further analysis. Features of the CAP affected biofilms including the overall structure and viability of bacteria were investigated. Biomass of the biofilms estimated by Crystal violet (CV) staining and the comprehensive construction of biofilms were measured by Optical Density (OD). Number of culturable colonies and cell viability of CAP treated biofilms evaluated by Colony-forming-unit (CFU) and MTT assay respectively.

**Results:** In the first 60 s the OD increasing showed that the CAP treated biofilms became stiffer compared with the non-treated control wells. Between 30 s to 60 s of CAP exposure, the CFU and MTT records increased, subsequently with more exposure up to 360 s all three CV, CFU and MTT amounts decreased.

**Conclusions:** We have indicated that the short CAP exposure (≥60s) could increase the firmness of biofilm thus shelters interior bacteria from antibacterial factors. The mentioned rigidity results in pseudo-CFU count. This is an unexpected effect of CAP in preserving the biofilm structure. The CFU and MTT increase until 60 s, though by lasting the CAP exposure time, the biofilm structure breaks down. Afterward, More CAP exposure to the biofilms reduces the CFU, MTT, and the OD of solubilized CV. For that reason, adequate CAP exposure time must be considered for absolute destroying the biofilms beside kill entirely its containing bacteria, moreover prevention of wrong results.

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Abstract 9415

Prevalence of genes encoding 16S rRNA methyltransferase in carbapenemase-producing Serratia spp. in south Brazil

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Background: Serratia spp. are members of Enterobacterales Order and have been emerged as an opportunistic pathogen associated mainly with nosocomial infections. These species are intrinsically resistant to many antibiotics and the treatment of infections caused by Serratia spp is a challenge, mainly in carbapenemase producers. Since aminoglycosides are an option to these strains, the aim of this study is to evaluate the distribution of genes encoding 16S rRNA methyltransferases in carbapenemase-producing Serratia spp. with high-level aminoglycoside resistance from various clinical specimens in South of Brazil.

Materials/methods: One hundred and fifteen carbapenemase-producing Serratia spp., being 114 blaKPC and 1 blaNDM, isolated on 94 patients from clinical specimens (colonization or infection) during January 2014 and December 2017 were evaluated for aminoglycoside high-level resistance according to Rapid Aminoglycoside NP Test. Serratia spp. were identified by the MAL-DI-TOF method and all samples positive on Rapid Aminoglycoside NP Test were investigated for the presence of 10 different 16S rRNA methyltransferases by two multiplex PCR and confirmed by single PCR.

Results: Serratia marcescens was the only species identified in 115 isolates and 15 samples were positive on Rapid Aminoglycoside NP Test, indicating high-level aminoglycoside resistance. Of them, five (4.3%) samples were positive on multiplex PCR for genes encoding 16S rRNA methyltransferases and confirmed by single PCR, being 3 rmtD and 2 rmtB, all in Serratia marcescens KPC-producers. This seems to be the first report of co-production blaKPC and rmtD in Serratia marcescens.

Conclusions: This study showed a prevalence of 4.3% of genes encoding 16S rRNA methyltransferases in Serratia marcescens. These results emphasize the need to survey aminoglycosides high-level resistance when this bacteria is found in clinical specimens. Therefore, plazomicin, a novel broad-spectrum aminoglycoside inactive by methylases but active against aminoglycoside-modifying enzymes, could be an option for carbapenemase-producing Serratia spp in 95.7% of the cases.

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Factors contributing to the duration of hospitalisation of patients with bacterial cellulitis
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Background: Bacterial cellulitis (BC) presents a therapeutic challenge. The optimal choice of antimicrobial agent and duration of treatment for BC continue to be heavily debated. Our aim was to analyze risk factors and treatment regimens associated with a prolonged hospital stay.

Materials/methods: We conducted a retrospective analysis of data from our cohort of 255 patients admitted to our university hospital from January 1st 2018 to December 31st 2018 with BC as the primary diagnosis. Statistical evaluation was done using Student’s t-test and ANOVA where applicable.

Results: The mean duration of hospital stay for all patients was 11.2 days. The factors we found to be associated with a prolonged hospital stay were acute kidney injury at admission; cardiac decompensation at admission; the clinical observation that the patient appears unwell at admission; a history of cardiovascular disease; as well as chronic venous insufficiency. Age >65 years was also associated with a significantly longer hospital stay, as was identification of pathogens in a skin swab. Patients with no determinable gateway for infection had a significantly shorter hospital stay. We observed no significant difference in the duration of hospitalization for patients with other comorbidities; neither was there any relation of CRP levels at admission or highest documented axillary temperature to length of hospital stay.

Cefazolin was the most commonly used antibiotic in our sample (45.1% patients) and was associated with the shortest hospital stay, significantly shorter than cloxacillin or clindamycin (the second and third most commonly used monotherapy agents). Patients treated with monotherapy had a significantly shorter hospital stay than those initially treated with multiple antibiotics.

Conclusions: The most significantly prolonged hospital stay was observed in patients with a toxic appearance and end organ damage at admission. Based on our data, cefazolin was the antibiotic associated with the shortest hospital stay. Patients receiving combined antimicrobial therapy were observed to have a prolonged clinical course, but this can likely be attributed to these patients having a more complex presentation.

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Abstract 9420

Evaluation of salivary protein rTiSP14.6 as a marker of exposure to the bite of the insect Triatoma infestans, vector of Trypanosoma cruzi

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Abstract third-party references: Supported by Fundación Mundo Sano and Instituto de Salud Carlos III

Background: The Triatoma infestans insect is the main vector that transmits the Trypanosoma cruzi protozoan, the causative agent of Chagas disease (CD). In Latin America, this vector has been controlled thanks to insecticides, but its monitoring is essential to identify new infestations. As the population at-risk of exposure can develop an immune response against the salivary gland proteins of this insect, it is postulated that the detection of antibodies against these proteins could be an epidemiological marker of infestation and exposure. Therefore, in this work we have evaluated the potential of the highly immunogenic recombinant protein rTiSP14.6, a 14.6 kDa salivary protein of T. infestans, as an epidemiological marker of exposure to the vector bite.

Materials/methods: 1191 samples of sera were analyzed. 1081 out of them were from the Latin American population, 29 were from individuals born in Spain, children of Latin American or non-Latin American mothers who had made a stay in endemic area for T. cruzi, and 81 samples were from to individuals without risk of exposure to T. infestans. All samples were previously characterized by serological detection of anti-T. cruzi antibodies using ELISAs (conventional and recombinant) and indirect immunofluorescence assays. Of these, 178 were from individuals with a positive diagnosis for CD. The detection of antibodies against the rTiSP14.6 protein was performed using the ELISA technique.

Results: Out of the 178 positive samples for T. cruzi infection, 9 showed antibodies against the recombinant salivary protein of T. infestans. On the other hand, 81 samples from the population with a negative diagnosis for CD presented high levels of antibodies against the rTiSP14.6 protein, 79 out of them had lived in endemic areas. It was mostly detected in the Bolivian population (p=0,032).

Conclusions: Although no correlation was observed between the detection of anti-salivary protein rTiSP14.6 and T. cruzi infection, its detection in a non-infected population from endemic area corroborates its potential utility as an epidemiological marker of exposure.

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Abstract 9421

First use of Fourier-transform infrared spectroscopy in Romania for investigating Klebsiella pneumoniae strains isolated from a possible cluster

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Background: Strain typing is commonly used in infection control for epidemiological investigation. Gold standard methods are DNA-based techniques, as PFGE and WGS. New Fourier-transform infrared (FTIR) spectroscopy method relies on carbohydrate composition of bacteria and has been used in last years in veterinary and food microbiology; lately there have been studies on its usefulness in clinical microbiology for rapid analysis of outbreaks.

Materials/methods: There were analyzed 19 isolates of Klebsiella pneumoniae with similar antibiotype (OXA-48-type producers) isolated in a 6 months period for identifying a possible epidemiological link between strains. These were isolated from 10 patients admitted in the same hospital ward (n=17) and from environmental samples (n=2). The strains were identified by MALDI TOF Biotyper (Bruker Daltonik GmbH) and analyzed using PFGE at the National Reference Laboratory. IR Biotyper (Bruker Daltonik GmbH) was used to identify the clusters and to compare with PFGE results. Analyzing all 19 strains three times on different days assessed the reproducibility of the technique.

Results: Cluster analysis was used to determine clonal similarities between strains. Our results show that FTIR spectroscopy adequately clustered 14 isolates as possible cluster, while three isolates were misclassified probably based on their biological variations. All 17 isolates showed the same pulsotype. Furthermore, 5 isolates were ruled out from the main cluster according to FTIR spectroscopy as it was by PFGE showing high discriminatory power. Results are visualized as dendrogram.

Conclusions: FTIR spectroscopy proves to be a fast and reliable tool in assessing a possible outbreak. Besides its sensibility to bacterial growth and environmental conditions, this technique could be easy implemented in clinical microbiology laboratory to help monitor infection control measures.

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Molecular and epidemiological characterisation of an outbreak of Candida auris in a Spanish hospital

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Background: Candida auris is an emerging multi-drug resistant yeast. Currently, it is considered a global threat due to its high-level environmental resistance and transmissibility. C. auris outbreak in La Fe Hospital (Valencia, Spain) began in 2016 and till now, it has become the largest one worldwide.

Materials/methods: A total of 111 C. auris strains 100 Spain, and other countries (2 Colombia, 1 Korea, 2 Brazil, 2 Oman, 2 Japan and 2 from Venezuela) and 8 reference strains: Candida albicans CS5314, Candida haemulonii ATCC® CBS123?1, Candida psedohaemulonii ATCC® CBS12370, Candida doubushaemulonii ATCC® CBS7798, Candida tropicalis BIOC10, Candida lipolytica ATCC® 340, Candida parapsilosis ATCC® 22019 and Candida krusei ATCC® 564 were analyzed.

RAPD (Random Amplified Polymorphic DNA): PCR-RAPD reactions were made using a Ready-To-Go RAPD Analysis Beads® (Amersham Biosciences Corporation, Piscataway, NJ, EE. UU.) kit. Oligonucleotides selected for assay were M2 (5'-CTTGATTGCC-3') and P4 (5'-AAGAGCCCGT-3'). Nuclease free water was used as a negative control. All reactions were done in duplicate and different days. PCR products were analyzed using electrophoresis on agarose gel 2. RAPD profiles were analyzed with Bionumerics® v. 7.6 (Applied Maths®) constructing an UPGMA dendrogram.

Results: All Spanish isolates were clustered in 4 clades (A to D). 40 Isolates included in clade A with 75% of similarity. Clade B grouped 8 isolates with 80% of similarity. Clades C included 24 isolates and cluster D 8, both with 80 and 85% of similarity, respectively.

Conclusions: C. auris isolates from the Spanish outbreak are clonal. Nevertheless, there seems to be a relationship with the isolates from Oman.

The RAPD technique allows preliminary characterization of isolates in epidemic situation; however, these results must be confirmed with a robust tools such as PFGE or WSG.

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Multi-resistant *Escherichia coli* in long-distance migratory birds: how graylag geese (*Anser anser*) and pink-footed geese (*Anser brachyrhynchus*) can act as vectors for antimicrobial resistance

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Abstract third-party references: Norwegian University of Life Sciences (NMBU)

**Background:** Migratory birds carries resistant *E. coli* strains over large distances. The continuous increase in geese populations poses a threat concerning global antimicrobial resistance. Recent studies show antimicrobial resistance patterns in wildlife, carrying resistance genes against drugs listed on the "WHO's List of Essential Medicines". Close contact interactions between wildlife and human populations pose a threat for the global health situation, where wildlife habitat are exposed to spillage from wastewater runoff with antibiotic residues and resistant coliform bacteria.

**Materials/methods:** During autumn 2015 and 2019, 201 cloaca samples were collected from Graylag- and Pink-footed geese landing close to farm areas in the middle of Norway. These samples were screened and isolated for resistant *E. coli*. All isolates were tested using disc diffusion and minimum inhibitory concentration methods (EUCAST). DNA was extracted and analyzed using whole genome sequencing.

**Results:** 39 of the samples from 2015 (35%) showed a prevalence for antimicrobial resistance for one or more drugs, whereas 26 of the samples from 2019 (29%) showed more or less the same patterns. In total, there were multiple isolates resistant against colistin, tetracycline, nalidixic acid, ampicillin, ciprofloxacin, trimethoprim and sulfamethoxazole. Several of these isolates had multi-resistant patterns. ST-469 was the predominant sequence type (23%), and ST-1126 come second place (17%) where all ST-1126 strains were carrying the tet(A) gene. Most interesting is the ST-744 clonal complex (11%), all carrying the gyrA and parC mutations, along with several resistance genes. This sequence type is closely related to human clonal complexes. Finally, one complex (3%), ST-2165, carried the qnrS1 gene for quinolone resistance.

**Conclusions:** Around one third of the *E. coli* samples were resistant against one or more antibiotic drugs, indicating that migrating birds can act as vectors for resistant bacteria. Genomic analysis indicates both horizontal and vertical transmission of resistance genes closely related to human isolates. To figure out the zoonotic capability of *E. coli* found in migratory birds, further testing of human and livestock populations living closely to wildlife should be performed.

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Study on Bartonella related to small mammals in the Canary Islands, Spain

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Abstract third-party references: Funded by ProID2017010092 Project (Comunidad Autónoma de Canarias, FEDER 2014-2020), Funded by Fundación CajaCanarias 2015BIO20

Background: Bartonella genus is comprised of several species of zoonotic relevance, some of them considered emerging nowadays. Rodents are reservoirs for some of these Bartonella species, and their associated vectors contribute to the maintenance and dissemination of the pathogen. The aim of the present study was to analyze Bartonella species along the Canary Islands (Spain) in rodent and their ectoparasites, and its possible repercussion to public health.

Materials/methods: A total of 304 small mammals, including black rats (Rattus rattus) and mice (Mus musculus domesticus) were captured in Tenerife, La Palma, El Hierro and Lanzarote (Canary Islands, Spain) in both urban and rural areas, as well as 264 fleas collected from them. Molecular analyses were carried out based on the gltA gene, to detect and identify Bartonella species.

Results: The overall prevalence of Bartonella organisms in rodents was 13.5%, whereas the prevalence in fleas was 17.4%. Zoonotic Bartonella elizabethae, Bartonella tribocorum and Bartonella rochalimae were identified in rodents and fleas in all the islands analyzed. About 16.5% of Bartonella-positive rodents were captured in intradomiciliary or peridomesticary settings of urban areas, which supposes a potential risk of acquiring Bartonella for the population. Besides, at least three flea species were identified as carriers of Bartonella in our study.

Conclusions: Our results indicate that rodents species and fleas act as reservoirs and vectors, respectively, in this archipelago, and the prevalence and distribution of the pathogen along the islands including urban areas, show the need to establish a routine procedure of diagnosis of bartonellosis in public healthcare, as Bartonella species may be the causative agents of human infections of unknown origin in the Canary Islands (Funded by Fundación CajaCanarias 2015BIO20 and ProID2017010092 Project [Comunidad Autónoma de Canarias, FEDER 2014-2020]).

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Diagnostics and treatment of invasive aspergillosis in B-cell lymphoma patients after cytostatic chemotherapy and autologous stem cell transplantation

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**Background:** Invasive aspergillosis (IA) in B-cell lymphoma patients after cytostatic chemotherapy (CCT) and autologous stem cell transplantation (ASCT) is not studied enough today.

**Materials/methods:** The prospective study included 813 B-cell lymphoma patients: Hodgkin lymphoma (HL) – 363, 16-65 years (median – 33), and non-Hodgkin lymphoma (NHL) – 450, 19-74 years (median – 50). For the IA diagnosis criteria EO-RTS/MSG 2008 were used.

**Results:** Frequency of IA in patients with B-cell lymphoma was 4.98% (HL – 5.6%, NHL – 4.5%, p=0.49), in patients with relapse of NHL - 10.25%, after ASCT – 2.85% (HL – 2.35%, NHL – 3.33%, p≥0.05). The main etiology agents were Aspergillus fumigatus (41%), A.niger (39%), and A.flavus (14%). Risk factors for IA were: relapse of lymphoma (p=0.005), B-symptoms (p=0.035) and radiation therapy in anamnesis (p=0.041), profound neutropenia (p=0.000), concurrent lung (p=0.007) and renal pathology (p=0.03). Clinical symptoms of IA were nonspecific: fever 68%, cough 48%, dyspnea 32.5%. Chest CT scan sings of IA were: focal changes 63.5%, infiltrates 58.7% and “ground-glass opacity” 23%. Galactomannan test was positive in BAL fluid and serum in 83.6% cases. The presence of septate mycelium in BAL was observed at microscopy in 15.5% patients. Aspergillus spp. culture was obtained in 34.7% of patients with B-cell lymphoma (HL – 20.4%, NHL – 46.3%, p=0.004). “Probable” IA was diagnosed in 92.9%, “proven” – in 7.1% of cases. The main antifungal drug was voriconazole – 79%. In patients with IA the 12-weeks overall survival (OS) was 84.9% (HL – 88.1%, NHL – 82.1%). The use of bronchoscopy and voriconazole improved 12-weeks OS (88.1% vs 64.7%, p=0.011; 92.6% vs 71.1%, p=0.004, accordingly). IA did not influence on 2- and 4-year OS, 1-,2-,3- year progressive-free survival (PFS) and 1-,2-,5- year relapse-free survival (RFS) in patients with induction chemotherapy. IA did not influence on 2-year OS, 1-,2-year PFS and 1-,2-year RFS in patients with relapsed or refractory B-cell lymphoma (p>0.05).

**Conclusions:** Frequency of IA in patients with B-cell lymphoma was 4.98%. Early diagnosis with bronchoscopy and adequate therapy with voriconazole of IA allowed to conduct cytostatic chemotherapy. IA did not influence on OS, PFS and RFS in B-cell lymphoma patients with induction and anti-relapse chemotherapy.

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Abstract 9428

Meningitis due to Toscana virus: analysis of clinical and laboratory features of the cases observed in the period 2008-2018 at the Careggi University Hospital, Florence, Italy

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Background: Toscana virus (TOSV) is an emerging arbovirus which is estimated to cause more than half cases of aseptic meningitis during the summer season in Central Italy. Moreover, increasing number of cases have been reported in other Mediterranean countries. However, the current knowledge of clinical and laboratory features of TOSV relies on few available data from limited cases series.

Materials/methods: We retrospectively collected data from medical records of all patients diagnosed with TOSV meningitis (TOSVm), admitted at the Infectious and Tropical Diseases Unit, Careggi Hospital, Florence, Italy, during the lapse 2008-2018. As control group, we collected data of patients diagnosed with aseptic meningitis in the same period, wherein TOSVm was excluded by serological and/or molecular testing. Cases of meningitis due to bacterial (Listeria monocytogenes, M. tuberculosis) and herpetic etiologies were excluded from further analysis.

Results: A total of 104 and 222 cases of aseptic meningitis were included in TOSVm and control group, respectively. Sex distribution, median age and Charlson comorbidity index were comparable between the two groups. As for clinical presentation, presence of nausea/vomiting (67/104, 64% vs 95/222, 43%, p<0.001) and stiff neck (48/104, 46% vs 73/222, 33%, p=0.021) were significantly more frequent in TOSVm group at univariate analysis. Moreover, TOSVm patients had slightly lower white blood cells (7140 vs 7970 /μL, p=0.014) and platelets count (179000 vs 220000 /μL, p=0.001), and higher values of cerebrospinal fluid (CSF) mean leukocyte (511 vs 155 cells/μL, p<0.001), protein (1.22 vs 0.81 mg/dL, p<0.001) and lactate (32 vs 22 mg/dL), with a lower CSF/blood glucose ratio (49% vs 58%, p<0.001). Multivariate analysis by stepwise-forward regression produced a model which includes CSF lactate concentration, plasmatic platelets count and presence of nausea/vomiting, with highest correlation for TOSVm diagnosis.

Conclusions: To the best of our knowledge, we reported data of the largest TOSVm cohort available to date. The study evidenced some clinical and laboratory peculiarities observed in TOSVm patients, with respect to a control group of aseptic meningitis. Our findings may contribute to better define the clinical picture of TOSVm, in order to drive the diagnostic work-up of aseptic meningitis.

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Abstract 9429

Diabetic foot osteomyelitis: an epidemiological retrospective analysis in a Portuguese university hospital

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Background: Osteomyelitis is one of the expressions of diabetic foot infection, often requiring hospitalization and amputation. We aimed to evaluate the microbiological profile and clinical characteristics of patients admitted with Diabetic foot osteomyelitis in our hospital, and to analyze the antimicrobial therapy strategy to establish future local guidelines for empirical treatment.

Materials/methods: Retrospective analysis of adult patients admitted in our center, with Diabetic foot osteomyelitis, from 2015 to 2016. Microbiology results, antibiotic susceptibility profiles and medical records were reviewed.

Results: Of the 103 processes analyzed, 61 patients were admitted with clinical and radiologic criteria of osteomyelitis, and 45 (73.8%) fulfilled the diagnosis of Diabetic foot osteomyelitis. 73.3% were male, with a median age of 64 years. In 82.2% of the infections forefoot was affected. Osteomyelitis was present in 46.7% of neuropathic foot and in 53.3% of neuroischaemic foot. At the diagnosis, 8.9% patients had fever and 57.8% had received previously antibiotic.

Concerning to microbiology, bone biopsy was performed in 37.8%, and soft tissue biopsy in 24.4%. Infections had microbiologically identification in 77.6%. 51.1% were polymicrobial, Staphylococcus aureus (47.2%) was the most identified microorganism (58.8% were MSSA), followed by Enterobacteriaceae (51.4%), Enterococcus spp. (25%) and Pseudomonas aeruginosa (14.3%). There were no fungal or anaerobes isolated. Carbapenem and piperacillin-tazobactam were used as part of empirical therapy in 39%, Teicoplanin in 32%, and Vancomycin in 9.8%. Oral antibiotics covered isolated agents in 71.4% of the cases. Besides antibiotic therapy, 55.6% needed minor amputation.

Conclusions: This study, allowed us to determine the local epidemiology of diabetic foot osteomyelitis. Most of the infections were polymicrobial, becoming a treatment challenge. Although most of patients admitted had neuroischaemical foot infections, and a smaller number neuropathic, was not possible to evaluate if there were pathogens differences between them. Since, 71.4% of microorganisms were covered by oral antibiotics, we hypothesize that an early diagnosis and a previous antimicrobial management optimization could diminish hospital admissions and amputations. We highlight the importance of a multidisciplinary management of this pathology and concluded that further studies are needed to establish local empirical treatment guidelines.

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Abstract 9430

**Blocking mycobacterial efflux pumps might potentiate efficacy of antimycobacterial drugs in vitro**

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**Background:** *Mycobacteria,* especially *Mycobacterium avium* complex (MAC), are highly drug-resistant and cause difficult-to-treat infections. Efflux pumps of varying specificity and mechanism contribute greatly to their drug-resistance. Inhibition of efflux pumps to potentiate antimycobacterial drugs is an emerging field of interest. Here, we investigate the effect of thioridazine as a non-specific efflux pump inhibitor alone and together with antimycobacterial drugs, as well as drug outflow over time under influence of thioridazine.

**Materials/methods:** Minimum inhibitory concentration (MIC) of thioridazine was determined per CLSI guidelines for *M. avium* ATCC700898. Synergism between thioridazine and drugs recommended in the treatment of MAC was determined by checkerboard titration using the fractional inhibitory concentration index (FICI). Time-kill assays (TKs) were performed with thioridazine alone and in combination with drugs showing low FICIs. Here, we incubated the bacteria in bottles and quantified colony forming units at pre-determined time points. For single-drug assays, we used a two-fold serial dilution range starting at 32x MIC and ending at 0.25x MIC. For multi-drug assays, we screened concentrations from 2x MIC to 0.5x MIC for the partner drugs alone and in combination. The effect of thioridazine on *M. avium*-infected human macrophages was assessed by incubating *M. avium*-infected macrophages together with thioridazine for a maximum of 6 days, quantifying *M. avium* bacterial load on day 0 and 6 as well as assessing macrophage viability based on morphology. An efflux assay was performed with MAC pre-incubated with ethidium bromide, with and without thioridazine, assessing outflux using increasing fluorescence over one hour in a LightCycler 480.

**Results:** The MIC of thioridazine against *M. avium* was 16 µg/mL. We found lowest FICIs between thioridazine and rifampicin or clarithromycin (FICI = 0.5). In TKs, thioridazine achieved >2 log kill at concentrations > 2x MIC (figure a). Synergy in TKs was observed together with clarithromycin, but not rifampicin (figure b, c). In human macrophages, thioridazine alone could lower the bacterial burden and was synergistic with clarithromycin (figure d). Thioridazine inhibited the efflux of ethidium bromide (figure e).

**Conclusions:** Efflux pump inhibition is a potent tool for increasing antimycobacterial efficacy, but thioridazine shows little efficacy against *M. avium* within macrophages.

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Abstract 9433

Superior discriminatory capacity of qSOFA over SIRS criteria for predicting mortality and extensiveness of organ failure in sepsis

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Background: The new sepsis definition (Sepsis-3) raised the debate about usefulness, sensitivity and specificity of newly introduced quick Sequential Organ Failure Score (qSOFA) and previously used Systemic Inflammatory Response Syndrome (SIRS) score. We aimed to compare discriminatory capacity of the qSOFA vs SIRS criteria measured on admission for predicting lethal outcome and extensiveness of organ failure in patients with sepsis (defined by Sepsis-3 definition).

Materials/methods: 407 consecutive septic patients were included. qSOFA and SIRS scores on admission were available. For predicting in-hospital mortality, the area under the receiver operating curve (AUC ROC) was constructed. Organ failure was measured by SOFA score. Spearman’s correlation was used for correlation of qSOFA and SIRS scores with extensiveness of organ failure.

Results: For predicting in-hospital mortality, AUC for qSOFA (0.681, 95%CI 0.633-0.726, p<0.001) was greater than SIRS (0.542, 95%CI 0.492-0.591, p=0.167), which was not predictive. In-hospital mortality of patients with qSOFA 0, 1, 2 and 3 points was: 7.6%, 28.9%, 41.2% and 57.9% (p<0.001). Mortality of patients with SIRS 0, 1, 2, 3 and 4 points was: 28.0%, 24.3%, 30.0%, 28.9% and 45.0% (p=0.400). Sensitivity and specificity for different thresholds for qSOFA and SIRS are given in Table 1. Finally, qSOFA correlated better with organ failure (SOFA score) extensiveness (p<0.001, r=0.352) than SIRS score (p=0.011, r=0.126).

Table 1. Sensitivity and specificity for predicting mortality for different thresholds for qSOFA and SIRS

<table>
<thead>
<tr>
<th>Points</th>
<th>Sensitivity</th>
<th>95% CI</th>
<th>Specificity</th>
<th>95% CI</th>
<th>+LR</th>
<th>95% CI</th>
<th>-LR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>qSOFA</td>
<td>≥1</td>
<td>93.10</td>
<td>86.9-97.0</td>
<td>31.96</td>
<td>26.6-37.7</td>
<td>1.37</td>
<td>1.2-1.5</td>
<td>0.22</td>
</tr>
<tr>
<td></td>
<td>≥2</td>
<td>50.00</td>
<td>40.6-59.4</td>
<td>74.23</td>
<td>68.8-79.2</td>
<td>1.94</td>
<td>1.5-2.5</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>=3</td>
<td>9.48</td>
<td>4.8-16.3</td>
<td>92.25</td>
<td>94.7-98.8</td>
<td>3.45</td>
<td>1.4-8.4</td>
<td>0.93</td>
</tr>
<tr>
<td>SIRS</td>
<td>≥1</td>
<td>93.97</td>
<td>88.0-97.5</td>
<td>6.19</td>
<td>3.7-9.6</td>
<td>1.00</td>
<td>0.9-1.1</td>
<td>0.98</td>
</tr>
<tr>
<td></td>
<td>≥2</td>
<td>65.52</td>
<td>56.1-74.1</td>
<td>41.58</td>
<td>35.9-47.5</td>
<td>1.12</td>
<td>1.0-1.3</td>
<td>0.83</td>
</tr>
<tr>
<td></td>
<td>≥3</td>
<td>26.72</td>
<td>18.9-35.7</td>
<td>77.66</td>
<td>72.4-82.3</td>
<td>1.20</td>
<td>0.8-1.7</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>≥4</td>
<td>7.76</td>
<td>3.6-14.2</td>
<td>96.22</td>
<td>93.3-98.1</td>
<td>2.05</td>
<td>0.9-4.8</td>
<td>0.96</td>
</tr>
</tbody>
</table>

Conclusions: In patients with sepsis, qSOFA score on admission had greater accuracy for predicting lethal outcome than SIRS, and correlated better with organ dysfunction (SOFA) score. Still, concerns about the low sensitivity of qSOFA≥2 criterion, as well as low specificity of SIRS≥2, seem to be grounded.

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Abstract 9434

Retrospective analysis of antibacterial resistance among uropathogen *Escherichia coli* in a veterinary teaching hospital (Italy, 2014-2019)

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**Background:** Urinary tract infections (UTIs) often require long follow-up periods and repeated antimicrobial therapies that can lead to the onset of antimicrobial-resistance. *Escherichia coli* is the most frequent bacterium involved in uncomplicated UTIs in pet animals in which treatment is sometimes threatened by the steady increase in the number of strains bearing concurrent resistance to various antimicrobial agents. The study aimed to report the variation of antibacterial resistance of urinary pathogen *E. coli* (UPEC) isolated from pets in a veterinary teaching hospital, North Italy (Turin) during a 5-and-a-half-year period (2014-2019).

**Materials/methods:** This retrospective study was carried out on *E. coli* strains (n= 219) collected from dogs (n=139) and cats (n=80) with UTI. Each strain was tested to 18 antibiotics belonging to 8 categories: aminoglycosides, carbapenems, folate pathway inhibitors, not-extended spectrum cephalosporins: 1st and 2nd generation, extended spectrum cephalosporins: 3rd and 4th generation, penicillins, penicillins + β-lactamase inhibitors, quinolones, following Kirby-Bauer method and interpreted according to the EUCAST guidelines. Isolates were classified as MDR (multidrug-resistant), XDR (MDR susceptible to only one or two antibiotic categories) and PDR (resistant to all agents tested). Data were analyzed using χ2 test, Pearson’s correlation among years and variance-weighted least-square regression models with STATA 15.1, choosing a significance level of α=0.05.

**Results:** Out of 219 UPEC, 114 (52.05%) of them were MDR, of which 37 were XDR and 1 was PDR. Increasing resistance among years was seen for 4 out of 8 classes of antimicrobial agents. An overall increase in MDR proportion (coeff. = 0.074; 95CI 0.038-0.110), and in the number of concurrent resistances (coeff. = 0.297; 95CI 0.126-0.467) were assessed. A significative difference in the baseline level of resistances and the rising of them was observed between dogs and cats.

**Conclusions:** Approximately half of isolated strains were MDR (52.05%), but they came all from clinically ill patients, which might suggest that the prevalence in the general pet population is lower. Nevertheless the upward trend of antimicrobial resistance of UPEC to various antibiotics, the rise in the amount of concurrent resistances and the presence of XDRs and a PDR strain, poses serious public health issues.

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Detection of pathogenic Vibrio species in estuary water samples in southwest Spain

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Background: Vibrio spp are aquatic bacteria that are ubiquitous in warm estuarine and coastal waters with low to moderate salinity. Several species of Vibrio are pathogens that can cause potentially serious infections such as septicemia, gastroenteritis, wound infections and otitis. In Europe Vibrio infections are not reportable (with cholera exception) and, consequently, accurate estimates of Vibrio spp are not available. The sea surface temperature of estuaries has increased as a result of climate change and Vibrio is considered the most reliable biomarker of climate change. Our objective has been to measure the presence of Vibrio with pathogenic potential in an area with high risk, due to low salinity and high temperature suitable for the appearance of infectious outbreaks.

Materials/methods: Water samples were collected in 6 estuarine points (Guadalquivir river outfall, SW Spain) with a biweekly frequency between July and September 2019. Parameters, such as temperature, pH and salinity were measured, and 500 ml of water was filtered (10 μm, 2.0 µm and 0.45 µm membrane filters (Millipore). Filters were inoculated in alkaline peptone water 2% NaCl and plated to TCBS agar (Becton Dickinson) and ChromID Vibrio agar (BioMerieux). Identification were done by MALDI-TOF MS (Bruker Daltonics). V. parahaemolyticus were screened for the presence of tdh and trh virulence genes by PCR.

Results: Ten species were isolated. V. alginolyticus was the most predominant (14) followed by V. harveyi (9), V. parahaemolyticus (8), V. fluvialis (7), V. natriegens (7), V. navarrensis (3), V. albensis (2), V. vulnificus (1), V. diazotrophicus (1) and V. furnissii (1). Detection of tdh and trh genes was negative for all V. parahaemolyticus isolates. The species with the highest pathogenic potential were related to the points of lowest salinity and highest temperature. Median water temperature was 26.3 ºC (range = 25.3-29.1º C).

Conclusions: Several species of Vibrio with high human pathogenic potential have been isolated in coastal waters but is important to highlight the isolation of V. vulnificus, V. parahaemolyticus and V. navarrensis strains. Although the pathogenic potential of V. alginolyticus is low, its high presence in seawater samples justifies the increasingly frequent isolation in clinical samples.

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Comparison of different nucleic acid extraction methods for viral metagenomic analysis

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Background: In recent years, the development of viral metagenomics next-generation sequencing (mNGS) approaches have contributed to improve the characterization of the human virome. However, differences in mNGS protocols may impact virome characterization. In particular, the impact of viral nucleic extraction techniques on downstream analyses remains unknown. The objective of this study was to compare the performances of 3 different methods of extraction for respiratory virome characterization.

Materials/methods: Two respiratory samples from hospitalized patients with respiratory infections were selected: 1 nasopharyngeal aspirate positive for RSV, 1 bronchoalveolar lavage positive for HSV. One mock sample comprising 5 viral strains combined in equimolar ratio was also used. Nucleic acids were extracted in triplicate using one of the following methods: the manual QIAamp Viral RNA Mini Kit extraction (Qiagen) and two automated extraction platforms (MagNA Pure, Roche and EMag, Biomérieux). A single mNGS workflow was used for characterization of DNA and RNA respiratory viruses. Performances of the methods were compared in term of sensitivity, cross-sample contamination and reagents contamination (kitome).

Results: MagNA Pure and EMag yielded higher viral reads (0.22% to 0.23% viral reads) than QIAamp (0.04% viral reads). Higher relative abundance of RNA viruses was observed in the mock sample using QIAamp, compared to the other methods. Cross-sample contamination, evaluated using negative template controls (NTC) between each sample, were higher using MagNA Pure representing up to 37% of the reads in the NTC. Finally, QIAamp was associated with higher reads mapping to bacteriophages, including Siphoviridae/Microviridae/Podoviridae/Myoviridae families that likely belong to the kitome.

Conclusions: Although the potential of mNGS technology is very promising, several factors such as cross-sample contamination and kitome contamination can lead to misinterpretation. Our results highlighted the importance of nucleic acid extraction, which has an impact on number of viral reads, cross-sample contamination and kitome contamination by NGS analysis. Here, the automated platform EMag seems to be the best extraction platform for the respiratory virome characterization.

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Abstract 9441

Phased-primer library preparation improves 16S rRNA metagenomics sequencing quality with limited impact on output
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Background: Widely used for amplicon-based metagenomics, Illumina sequencing quality is affected by sequence conservation of the 16S rRNA. The strong bias towards sequencing the same nucleotide in all clusters at each cycle reduces the contrast from signals emitted by colored fluorescent dideoxynucleotides. Thus, Illumina recommends spiking libraries with up to 30% of PhiX to increase sequence diversity, at the expense of reducing the exploitable throughput. Alternatively, Qiagen recently released QIAseq “phased-primers” kits introduce 0-11 nucleotides between adapters and primers to randomly shift sequences. In the present study, we compared standard Illumina library preparation with QIAseq for V3V4 16S rRNA metagenomics.

Materials/methods: Two negative extraction controls, three ATCC-2002 mock-community, 15 respiratory, and 12 fecal samples were prepared with both QIAseq and Illumina V3V4 protocols. Libraries were sequenced on Illumina Miseq. Reads were processed into Amplicon Sequence Variants (ASVs) by a pipeline based on DADA2 [Callahan 2016]. Sequences were rarefied at 20,000 for alpha and beta-diversity analyses. Moreover, V3V4 amplicons extracted from reference genomes of the ATCC-2002 bacteria by in silico PCR were compared to raw sequences and ASV with Qiime2 q2-quality-control plugin [Bolyen 2019].

Results: The average phred sequencing quality score was significantly better with QIAseq (35.4 vs 32.9, p<0.001), allowing more reads to pass filters in DADA2 pipeline (79.9% vs 67.8%, p<0.001). Despite these differences, Shannon alpha-diversity remained highly correlated (Pearson R = 0.98, p<0.001) and Bray-Curtis beta-diversity distance low between pairs of samples (mean = 0.15, sd = 0.21). Surprisingly, more sequences without mismatch, but also more sequences with more than 3 mismatches were found in ATCC-2002 raw reads prepared with Illumina compared to QIAseq (Figure). Noteworthy, similar error profiles were found for both preparations after read error correction by DADA2.

Conclusions: Phased-primers significantly improved sequencing quality and reduced sequencing errors for amplicon-based metagenomics. However, the effect on generated ASVs is minimal thanks to the effective error-correction provided by DADA2. Cost-efficiency analysis must consider the higher proportion of reads passing filters that would allow to sequence more samples in the same run.

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Tuberculosis (TB) and cancer: why a previous TB infection may not alert us in a near future

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Background: it is believed that chronic inflammation during TBC may lead to cancer development. Although its pathogenesis is imperfectly known, several reports implicate TBC as a risk factor for cancer, especially in lung disease.

Co-existence of tuberculosis and cancer has been stated, particularly pulmonary tuberculosis being a risk factor for developing lung cancer. Fibrotic scars frequently found next to lung cancer development would explain this finding.

However, the nature of the relationship between pulmonary or non-pulmonary scarring and cancer remains uncertain and results are inconsistent.

Materials/methods: we conducted a computed retrospective review from microbiologically documented tuberculosis infections occurred over the past 13 years in Ávila, Spain (2006-2018). Our objective was to describe their localization and cancer relationship over time.

Results: 162 tuberculosis patients were finally included. Tuberculous lymphadenitis was found in 12 cases (12/162, 7.4%). We also found 6 miliary cases (3.7%), 5 tuberculous peritonitis (3.1%), 3 osteoarticular TBC (1.8%), 4 genitourinary TBC (2.5%), 2 cerebral forms (1.2%) and 1 case of hepatic and neonate TBC (0.6% each).

29 patients (29/162, 17.9%) had cancer; of them, 10 patients were diagnosed with cancer before TBC (34.5%), and 19 were newly diagnosed with cancer after TBC diagnosis (65.5%). The latter (all men but a woman with non-Hodgkin lymphoma) were divided into different categories according to organ involvement: 6 hematological (6/19, 31.6%), 5 colorectal (26.3%), 3 pulmonary (15.8%), and 1 cerebral, choanalcarcinoma, gastric, tongue and bladder cases (5.3% each).

TBC involvement for those who developed cancer after TBC diagnosis was variable: 8 pulmonary, 4 miliar, 3 genitourinary, 2 peritoneal, 1 lymphadenitis and 1 osteoarticular.

Finally, from the 10 previous-to-TBC cancer diagnosed patients, 7 developed pulmonary tuberculosis (70%), and 1 genitourinary, cerebral or lymphadenitis (10% each). Tumors site was principally digestive, prostatic, endometrial (2/10 each, 20%), and skin, lung, testicles and bladder (10% each).

Conclusions: our data do not show any apparent increase in cancer development amongst patients previously diagnosed with TBC. Moreover, there is no evidence that any tumor predisposes to suffering from TBC.

The link between tuberculous scarring and promotion of cancer needs to be deeply studied.

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Abstract 9444

Investigation of colistin resistance mechanisms in Klebsiella pneumoniae strains
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Background: Increasing rate of infections caused by multiple drug resistant Gram-negatives has led to resuscitation of colistin. As a result, colistin resistance, mainly among Klebsiella pneumoniae strains has also been increased. The aim of this study was to investigate molecular mechanisms behind colistin resistance.

Materials/methods: Colistin-resistant 9 K. pneumoniae strains isolated from clinical samples of different patients were involved in this study. To identify the mechanisms of resistance, expression levels of pmrA, pmrB, pmrD, and pmrK genes were measured with or without pre-exposure to colistin. Also, presence of mcr-1 gene was investigated by real-time PCR as well as rapid cassette test.

Results: As a result of the study, significantly increased expression levels of the pmrD and pmrK genes were observed in the experiments with or without previous colistin exposure both. Statistically significant increase in expression level of pmrB gene could only be detected in previous colistin exposure group which also showed increased the expressions of pmrD and pmrK genes compared with unexposed group. However, after colistin exposure, we have also detected an unexpected reversal of increased expression of pmrA gene. Relative median increase rates were found 3.4-fold for pmrA (p<0.05), 1.3-fold for pmrB (p=0.89), 5.8-fold for pmrD (p<0.01), and 17.6-fold for pmrK (p<0.01) without previous colistin exposure. When we have exposed bacteria to sub-inhibitory doses of colistin previously, we observed that the up regulation of pmrB, pmrD and pmrK genes were increased to 1.6-fold (p<0.05), 15.9-fold (p<0.01), and 70-fold (p<0.01) respectively. Unexpectedly, median expression levels of pmrA gene were found decreased with the previous colistin exposure. None of the 9 tested strains were positive for mcr-1 gene by both methods used.

Figure 1. Mean 2-ΔΔCq values for pmrA, pmrB, pmrD, and pmrK genes.

Conclusions: Colistin resistance is a growing problem in the treatment of infections caused by multiple drug resistant bacteria. We believe that more detailed data related to colistin resistance mechanisms and how the resistance spread among bacteria is crucial to prevent these infections as well as to control overuse of colistin.

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**Abstract 9445**

**Culture-dependent analysis of the bacterial profile of breast milk samples from women with diagnosis of subacute lactational mastitis**

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**Background:** Lactational mastitis is a common and under-diagnosed condition that affects approximately one third of breastfeeding women. Subacute forms due to their nonspecific clinical manifestations are difficult to diagnose. In mastitis, techniques culture-independent have revealed a loss of bacterial diversity and predominance of some genera in milk samples. If an infectious etiology is suspected, bacterial culture of breast milk may be indicated. The aim was to describe, by culture, potential pathogens in breast milk samples from diagnosed women with subacute lactational mastitis and its antimicrobial susceptibility.

**Materials/methods:** Retrospective, descriptive study including 1493 cultures of maternal milk [663 patients], from 43 Primary Care Centers of the city of Barcelona, during June 2014-June 2018.

Quantitative cultures (10µL) were carried out. Based on some related articles and guidelines a bacterial count \(>10^3\)CFU/mL was considered. According to growth characteristics, cultures were classified into three categories: probably related to infectious process \(>10^3\)CFU/mL and \(\leq 3\) morphotypes), microbiota without clinical significance \(<10^3\)CFU/ml -except for *Staphylococcus aureus*-, or \(>10^3\)CFU/mL and \(>3\) morphotypes), and those with growth of microorganisms considered as contaminants. Identification and antimicrobial testing was only carried out on the first culture category isolations.

**Results:** Bacterial growth was observed in 90% (1346) of total cultures. 57.9% (774) were in the first culture category and 32.4% (222) and 9.7% (67) in the two remaining, respectively. Out of 1047 microorganisms identified, the most prevalent were coagulasa-negative staphylococci (CoNS) (49.2%, 515), followed by *S.aureus* (14.9%, 156), *Streptococcus* spp. (16.2%, 170) and *Cutibacterium* spp. (9.2%, 96). Antimicrobial resistance extract in *Staphylococcus* spp. is shown in the table:

<table>
<thead>
<tr>
<th>Microorganisms</th>
<th>Meticilline (%)</th>
<th>Clindamycin (%)</th>
<th>Quinolones (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CoNS</td>
<td>43.1</td>
<td>44.9</td>
<td>28.1</td>
</tr>
<tr>
<td>S.aureus</td>
<td>5.4</td>
<td>9.2</td>
<td>12.1</td>
</tr>
</tbody>
</table>

**Conclusions:** *Staphylococcus* spp. and *Streptococcus* spp. were the most frequently isolated. There is an upward trend in the resistance of first line antibiotics used in primary care. Coincidence of the breast milk bacterioma core with the genera commonly involved in subacute mastitis added to the lack of rigorous cut-off point, makes difficult the culture interpretation. Clinical-microbiological correlation studies are necessary to support the indication and interpretation of maternal milk cultures.

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Abstract 9448

Inappropriate use of interferon gamma release assays in a UK teaching hospital

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Background: It is estimated that between a quarter and a third of the world’s population has latent tuberculosis (LTBI). Interferon gamma release assays (IGRA) can be used to help diagnose LTBI. The UK National Institute for Health and Care Excellence (NICE) have published guidelines for the use of IGRAs during LTBI screening.

We had concerns that IGRAs were being used inappropriately in our institution, particularly during the assessment of patients for active TB, a practice which is not recommended by NICE or WHO. Inappropriate use of IGRAs has the potential to lead to unnecessary investigations and anti-tuberculosis therapy. Our aim was to determine the appropriateness of IGRA testing against the NICE Guidelines.

Materials/methods: Data were collected for all patients who had an IGRA between January and April 2018 at Manchester University NHS Foundation Trust and compared to the NICE guidelines.

Results: In total 202 patients had an IGRA, with a mean age of 48. IGRAs were sent outside of guideline recommendations in 90 cases (45%). Of these, 59 were done for immunosuppressive medication for which there is negligible or no increased risk of active TB. These included rituximab, azathioprine, ciclosporin, methotrexate, hydroxychloroquine and sulfasalazine. A further 28 were sent inappropriately during the work up of possible active TB.

112 tests were deemed appropriate, including 97 for immunosuppressive medication which increase the risk of active TB, 8 for close TB contact, 4 for conditions causing immunosuppression, 2 for NHS employees from high incident settings and 1 for a research case.

IGRAs were positive in 12 cases (5.9%), 5 of which were sent inappropriately. Of these 5, 1 attended TB clinic and completed LTBI treatment, 2 had alternative diagnoses, sarcoid and active TB. It was noted that 2 positives who were tested appropriately were previously treated for LTBI.

Conclusions: Nearly half of IGRAs were deemed inappropriate. Incorrect use of IGRAs on this scale, especially in areas with higher background rates of LTBI, could have significant cost implications with regard to test cost, unnecessary clinic appointments and anti-tuberculosis therapy. Further education on the indications for IGRAs is required to reduce inappropriate testing.

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Incidence, risk factors and clinical impact of invasive pulmonary aspergillosis in patients hospitalised with influenza infection

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Background: Invasive Pulmonary Aspergillosis (IPA) typically occurs in immunocompromised subject. Recently, cases of IPA in immunocompetent patients have been reported associated with severe influenza virus infection.

Materials/methods: We performed a retrospective observational study in a large italian hospital during the past flu season (January–April 2019) to evaluate incidence, risk factors and clinical impact of IPA in patients with a diagnosis of influenza. We included patients with influenza confirmed by PCR on respiratory samples. For the diagnosis of IPA, we adopted the modified AspICU algorithm. We also developed a risk predictive model for IPA through machine learning techniques (decision trees), to try to identify IPA high risk patients who would benefit from antifungal prophylaxis.

Results: We enrolled 77 patients with flu, 5 of them have developed IPA. Associated risk factors were: smoking (p=0.011), COPD (p<0.001), lymphocytopenia (p<0.001) and corticosteroids (p<0.001). Clinical course of patients with IPA was more severe in terms of needs of hemodialysis (p=0.003), ECMO support (p=0.012), orotracheal intubation (p<0.001), ICU admission (p<0.001). The mortality rate was higher in IPA group (100%) compared to patients without Aspergillus coinfection (8%) (p<0.001). The predictive model has highlighted two variables as decisive in risk assessment: lymphocytes<340/µl and methylprednisolone>0.65 mg/kg/day.

Conclusions: IPA represents a frequent complication in hospitalized patients with influenza infection. Our data revealed smoking, COPD, steroid treatment and lymphocytopenia at the diagnosis of influenza as risk factors for development of IPA in patients hospitalized with influenza virus infection. Due to extremely severe prognosis, antifungal prophylaxis in IPA high risk patients should be considered and its effectiveness should be studied on larger population. Furthermore, in our study, the methodology for the prediction of IPA risk using machine learning techniques, seemed to provide interesting insights about relevant IPA associated factors. Nonetheless these findings needed to be confirmed and validated on larger cohorts.

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**Abstract 9451**

**Dengue fever in returning travellers: a retrospective study in London, UK**

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**Background:** Dengue fever is common worldwide, however clinicians in Europe may rarely manage it. We present a case series of acute dengue from Ealing Hospital in West London, which serves an ethnically diverse population with a large proportion of migrants from the Indian sub-continent.

**Materials/methods:** Patients were identified from the laboratory information management system (Winpath®) and clinical data obtained from electronic patient records from 01/05/2014-25/11/2019.

Cases of acute dengue fever were defined as: virus IgM immunoassay positive, or viral RNA detected using polymerase chain reaction (PCR).

**Results:** Over the study period, 126 blood samples were sent. 23 patients had acute dengue: 4 (17%) PCR positive, 10 (43%) IgM positive, and 9 (39%) both PCR and IgM positive.

Most (17) patients presented in winter and autumn months, reflecting an increase in cases associated with the rainy season in Asia. The median age was 32 (IQR 28-44). Most had travelled to South Asia (11, 47%), particularly India, followed by South-East Asia (8, 35%).

All patients presented with fever. Other common symptoms were arthralgia/myalgia (8, 35%), headache/retro-orbital pain (5, 22%), and rash (4, 17%).

At presentation, thrombocytopenia (15, 65%), leucopenia (22, 96%) and transaminitis (5, 22%) were often already present, but they tended to develop further during the course of the illness. During admission 21 (95%) developed thrombocytopenia, 21 (95%) developed leucopenia, and 13 (59%) developed transaminitis. One 18-year-old patient had severe dengue with liver involvement and plasma leakage and died of haemophagocytic lymphohistocytosis.

**Conclusions:** Most patients in our analysis had travelled to India, reflecting the local epidemiology of our population who were visiting friends and relatives. This highlights the need to improve pre-travel bite avoidance advice to this group.

The classical biochemical picture of thrombocytopenia, leukenopaenia and transaminitis may not be seen at presentation. Therefore, clinicians must have a high index of suspicion and recognise the need for close monitoring. Most returning travellers have a mild clinical course but a small proportion develop severe complications that necessitates intensive care support.

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Abstract 9452

KPC-producing and colistin-resistant Klebsiella pneumoniae ST258 persistence during wastewater treatment plant processes

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Background: Carbapenem resistance (CR) in wastewaters and surface waters represents an important issue, as resistance strains could disseminate via agriculture to humans and animals and ultimately cause difficult-to-treat infections. Here we investigated the CR and ESBL producing strains within and near a wastewater treatment plant (WWTP) from South Romania.

Materials/methods: Wastewater samples were collected in April 2019 from influent, residual sludge, effluent, as well as upstream and downstream of the WWTP, filtered through 0.45 µm pore filters, inoculated on selective chromogenic agar plates (ChromID ESBL, CARBA). CR and ESBL counts were estimated from several volumes and/or dilutions. Six colonies were randomly selected from each phenotype/sample identified by MALDI-TOF-Ms and analyzed for antibiotic susceptibility patterns. Strains with similar antibiotic resistance (AR) profiles from each sampling point were subjected to whole genome sequencing (WGS).

Results: Quantification of target colonies from chromogenic media is summarized in table 1

<table>
<thead>
<tr>
<th>Sample</th>
<th>ESBL KESC</th>
<th>CARBA KESC</th>
<th>WGS selected strains (ST)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upstream WWTP</td>
<td>7.50E+00</td>
<td>Absent/Below detection limit</td>
<td>3 ESBL (ST219)</td>
</tr>
<tr>
<td>Influent</td>
<td>3.50E+04</td>
<td>1.74E+03</td>
<td>4 CR (ST258)</td>
</tr>
<tr>
<td>Residual sludge</td>
<td>7.73E+02</td>
<td>8.00E+01</td>
<td>1 CR (ST258)</td>
</tr>
<tr>
<td>Effluent</td>
<td>1.00E+03</td>
<td>6.75E+01</td>
<td>4 CR (ST258)</td>
</tr>
<tr>
<td>Downstream WWTP</td>
<td>9.07E+02</td>
<td>7.25E+01</td>
<td>3 CR (ST258)</td>
</tr>
</tbody>
</table>

45 Klebsiella pneumoniae (21 ESBL and 24 CR) were selected from each sampling point, all expressing multidrug resistance profile, with 12 CR strains being resistant also to colistin. WGS data revealed that all selected CR strains are ST258 KPC-2 producing K. pneumoniae and have an IS26Kpn insertion in mgrB gene. AR genes to several other classes of antibiotics are present. Core genome comparison analyses (Ridom SeqSphere) suggests they represent the same clone. ESBL strains belonged to different STs (table 1) and mainly harbored blaCTX-M-15 and various blaSHV alleles.

Conclusions: Here we report the presence of a K. pneumoniae ST258 KPC-producing and colistin resistant clone in all sampling points (including downstream of the WWTP) but upstream point, highlighting that this successful clone could survive in the WWTP and evade in surface waters.

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Abstract 9455

**Consumption of antibiotics effective against multi-resistant Gram-positive pathogens: data of German hospitals from 2015-2018**

Birgitta Schweickert*, Marcel Feig1, Marc Schneider1, Karin Gruenschn1, Willrich Niklas1, Michael Behnke5, Luis Alberto Pena Diaz2, Petra Gastmeier1, Doreen Richter1, Hans-Peter Blank1, Hartwig Wehrmeyer1, Tim Eckmanns1, Muna Abu Sin1

1Robert Koch-Institut, Department for nosocomial infections and surveillance of antimicrobial resistance and antimicrobial consumption, Berlin, Germany, 2Charité University Medicine Berlin Campus Benjamin Franklin, Institute for Hygiene and environmental medicine, Berlin, Germany

**Background:** In the light of constantly decreasing rates of methicillin-resistant *Staphylococcus aureus* and a steep increase of vancomycin-resistant *Enterococcus faecium* in blood culture isolates over the last years, the consumption of antibiotics used for the treatment of multiresistant grampositive pathogens should be assessed. Hospital consumption data from 2015-2018 derived from the German Antibiotic Consumption Surveillance (AVS)-system have been analyzed.

**Materials/methods:** The calculation of antibiotic consumption values is based on the ATC (Anatomical Therapeutic Chemical) /DDD (Defined Daily Dose) method of WHO (ATC/DDD-version 2019). Target value is the antibiotic consumption density (CD) expressed in DDD per 100 patient days (PD). The CDs of vancomycin, linezolid, daptomycin, tigecycline, ceftobiprole mediocaril and ceftaroline fosamil are presented as medians with interquartile range. The analysis relies on data submissions of general acute care hospitals from 2015 to 2018 and is confined to hospitals, which consistently provided data for the whole time period (n=90). Data have been analyzed for the whole hospital and differentiated according to hospital size (≤800/>800 beds).

**Results:** The data reveal that the median CDs of total antibiotic consumption and of the selected antibiotic substances are higher in hospitals >800 beds than in hospitals ≤800 beds and partly show an opposite course over time for both size categories (Table 1). This also applies for the proportional use in relation to total consumption. The median CDs of vancomycin slightly increased from 2015 to 2018 in hospitals >800 but showed a decline in hospitals ≤800 beds. The use of linezolid increased in hospitals of both size categories with a more pronounced rise in hospitals ≤800 beds. Daptomycin is used in less than 50% of the hospitals ≤800 beds in 2015/16 but the median CDs reveal a rise over time for hospitals of both size categories. The consumption of tigecycline shows a relatively constant course. Fifth generation cephalosporins were only used sporadically in <10 hospitals.

**Conclusions:** Descriptive analysis of routine surveillance data shows an increase of the consumption of linezolid and daptomycin, albeit at a low level. The analysis of an association with the changing epidemiology of MRSA and VRE requires further investigation.

**Table 1. Consumption densities (DDD/100 patient days (PD), median (IQR)) of total consumption and selected antibiotics from 2015 to 2018**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>2015 Median (IQR)</th>
<th>2016 Median (IQR)</th>
<th>2017 Median (IQR)</th>
<th>2018 Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>0.65 (0.4-4.1)</td>
<td>0.77 (0.6-6.4)</td>
<td>0.58 (0.4-4.1)</td>
<td>1.3 (0.55-4.3)</td>
</tr>
<tr>
<td>Linezolid</td>
<td>0.24 (0.1-2.2)</td>
<td>0.25 (0.1-2.3)</td>
<td>0.33 (0.2-2.6)</td>
<td>0.34 (0.2-2.7)</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>0 (0-0.4)</td>
<td>0.2 (0-0.2)</td>
<td>0.1 (0-0.4)</td>
<td>0.1 (0-0.3)</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>0.62 (0.6-0.6)</td>
<td>0.62 (0-0.4)</td>
<td>0.3 (0-0.4)</td>
<td>0.3 (0-0.4)</td>
</tr>
<tr>
<td>Ceftobiprole mediocaril</td>
<td>0 (0-0.01)</td>
<td>0 (0-0.01)</td>
<td>0 (0-0.01)</td>
<td>0 (0-0.01)</td>
</tr>
<tr>
<td>Ceftaroline fosamil</td>
<td>0 (0-0.01)</td>
<td>0 (0-0.01)</td>
<td>0 (0-0.01)</td>
<td>0 (0-0.01)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>2015 Median (IQR)</th>
<th>2016 Median (IQR)</th>
<th>2017 Median (IQR)</th>
<th>2018 Median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>43.4 (47.6-61.1)</td>
<td>52.1 (42.5-59.4)</td>
<td>53.1 (48.1-61.7)</td>
<td>100 (49.7-58.3)</td>
</tr>
<tr>
<td>Total ≤800 beds</td>
<td>63.5 (56.6-71.5)</td>
<td>66.6 (56.6-71.7)</td>
<td>66.6 (55.5-76.9)</td>
<td>66.6 (52.6-73.7)</td>
</tr>
</tbody>
</table>

*Total: ATC/DD (antibiotics), 201: AMOXICILLIN, POLIAXOS
*Portion (%): proportion of total consumption

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Application of a user-friendly, end-to-end metagenomics platform for rapid pathogen identification in children with osteoarticular infections

Rita Stinnett1, Nanda Ramchandar2,3, Heng Xie1, Steven Flygare1, Toni Schwarz1, Kate Broadbent1, Amy Davis1, Lauge Farnaes2,3, Robert Schlaberg*1,4

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Background: Osteoarticular infections may cause substantial morbidity in children. Rapid, accurate and comprehensive pathogen detection is critical in directing antimicrobial therapy and prevention of long-term sequelae. In adults, metagenomic sequencing has been demonstrated to increase the diagnostic yield compared to standard care testing, and there is growing interest in implementing metagenomic testing in the routine diagnostic workup. However, complexities of metagenomic data analysis pose barriers for adoption. We present a metagenomic shotgun RNA and DNA assay built on a user-friendly software platform that supports all steps from sample to report. We used this assay for rapid pathogen identification in hospitalized children with osteoarticular infections.

Materials/Methods: Children hospitalized with a diagnosis of osteomyelitis and/or septic arthritis were enrolled in an IRB-approved study. Operative samples (swabs and synovial fluid) were analyzed by shotgun metagenomic RNA and DNA sequencing with the Explify platform. This platform provides easy-to-use metagenomic analysis including quality control (QC) and quality filtering of sequencing data, identification of a customizable set of pathogens using curated databases, reproducible result interpretation, result review, and report generation.

Results: A total of 31 samples from 21 children were analyzed by metagenomic sequencing (2 samples were available for 10 patients). For use in this study, interpretive criteria were defined for >700 relevant bacteria and fungi that have been implicated in the pathogenesis of osteoarticular infections based on published data. Metagenomic sequencing detected a putative pathogen in 14 of 21 (67%) patients. Putative pathogens detected included Staphylococcus aureus, Kingella kingae, and Enterobacter cloacae. Predominant detections in this study were consistent with the known etiology of pediatric osteoarticular infections and were corroborated by standard of care testing.

Conclusions: Analysis of metagenomic sequencing data with the Explify platform provided rapid pathogen identification (<1 hour from data availability to result). The use of evidence-based interpretive criteria maximized the diagnostic yield while limiting detection of non-pathogenic microorganisms that often complicate interpretation of metagenomic sequencing results. The Explify platform provides user-friendly access to comprehensive application-specific QC, pathogen detection, and identification of antimicrobial resistance markers.

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Abstract 9459

In vitro activity of novel β-lactam and β-lactam enhancer combination, cefepime-zidebactam (WCK5222) against Gram-negative clinical isolates with high-level carbapenem resistance rate: report from a large tertiary care centre in India

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Background: Antimicrobial agents currently available for clinical use show limited activity against multi-drug resistant (MDR) Enterobacterales and Pseudomonas aeruginosa, emphasizing the urgent need for MDR Gram-negatives active novel agents. WCK5222 (FEP-ZID) is a combination of cefepime and a PBP2 binding β-lactam enhancer antibiotic, zidebactam. FEP-ZID is being developed for the treatment of infections caused by MDR/XDR Gram negatives including Enterobacterales and P. aeruginosa. In this study, we evaluated the in-vitro activity of cefepime-zidebactam against contemporary clinical isolates of E. coli, K. Pneumoniae and P. aeruginosa collected from a large tertiary care center in India.

Materials/methods: A total of 528 nosocomial clinical isolates comprised of E. coli (n=155), K. pneumoniae (n=232) and P. aeruginosa (n=141), collected from January 2017 to August 2019 at Christian Medical College, Vellore, India were included in this study. The isolates included those expressing class A ESBLs, AmpC, Class B and D carbapenemases. Susceptibility testing was performed against cefepime-zidebactam (1:1) and comparator antibiotics by CLSI recommended broth microdilution method.

Results: Meropenem non-susceptibility was observed in 52% of Enterobacterales (E.coli & K.pneumoniae) and 63% P. aeruginosa isolates. FEP-ZID demonstrated potent activity against E.coli with MIC50/90 of 0.12/0.25 mg/L and K. pneumoniae MIC50/90 with 0.25/2.0 mg/L. All tested P. aeruginosa isolates were inhibited at FEP-ZID MIC of ≤16 mg/L. Ceftazidime-avibactam, imipenem-relebactam, ceftolozane-tazobactam showed limited activity with MIC90 of >16 mg/L against all three pathogens group.

Conclusions: While β-lactam and β-lactamase inhibitors, ceftazidime-avibactam, imipenem-relebactam and ceftolozane-tazobactam suffer from important spectrum gaps, β-lactam and β-lactam enhancer, FEP-ZID exhibits potent and comprehensive activity against MDR Gram negatives irrespective of the associated resistance mechanisms. The present in-vitro study findings further support the clinical development of cefepime-zidebactam for the treatment of MDR Gram-negative infections.

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Direct detection of *Escherichia coli* in clinical samples by an ultrasensitive fluorescent copper nanoparticles-aptasensor

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**Background:** *Escherichia coli* (*E. coli*) is a particularly significant pathogen and has always been a serious threat to human health. Conventional culture-based detection methods are quite time-consuming and other quick detection methods are usually based on complex pre-treatments. Therefore, the development of a convenient, rapid and cheap strategy will be very desirable and practical for the direct detection of *E. coli* in clinical samples.

**Materials/methods:** We designed a capture probe complex that contained specific *E. coli*-aptamer and partly hybridized signal trigger sequence, which had the ability of binding to viable *E. coli* directly. The trigger sequences would be liberated when the capture probe complexes bound to *E. coli*, and reacted with three hairpins successively to initiate the triple strand migration reaction, producing numerous hairpin-A-B-C complexes with scaffolds of copper nanoparticles ([CuNPs]), thus providing significantly enhanced fluorescent signals (shown in Fig. 1). Sensitivity, specificity, reproducibility and linear correlation of the nanoparticles-aptasensor were tested and verified. In order to evaluate the clinical application of this strategy, *E. coli* at the concentrations from 10 to 10⁵ CFU/mL in various clinical samples including blood, urine, cerebrospinal fluid, pleural effusion, and ascites were detected.

**Results:** The strategy achieved an ultrasensitive detection limit of live *E. coli* down to 10 CFU/mL with a linear range from 10 to 10⁵ CFU/mL, and no significant fluorescence intensity increase was observed upon the addition of other clinical pathogenic bacteria except for *E. coli*. The linear range between the fluorescence intensity and viable *E. coli* concentration was from 10 to 10⁴ CFU/mL in different clinical samples.

**Conclusions:** In this study, we provide a novel DNA extraction-free, label-free and enzyme-free strategy for direct detection of viable *E. coli* in clinical samples by an ultrasensitive fluorescent copper nanoparticles-aptasensor, which shows an ultrasensitive detection limit and a high specificity, as well as a low cost.

![Fig. 1 Schematic illustration of the DNA extraction-free, label-free and enzyme-free direct detection of viable *E. coli* based on a novel ultrasensitive fluorescent copper nanoparticles-aptasensor.](image)

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Abstract 9463

Evaluation of on-site polymerase chain reaction technology for cerebrospinal fluid samples at Cork University Hospital versus referral to reference laboratories in suspected cases of meningitis or encephalitis

Rachel Barry¹, Catherine Dempsey¹, Louise Barry¹, Carmel Hooton¹, Claire Reynolds¹, Molly Cremin¹, Susanna Felsenstein¹, Dan Corcoran¹

¹Cork University Hospital, Cork, Ireland

Background: Currently, cerebrospinal fluid (CSF) samples from Cork University Hospital, that require molecular diagnostics for viral/bacterial pathogens, are sent to the National Virus Reference Laboratory and the Irish Meningitis and Sepsis Reference Laboratory. This introduces a significant delay for a critical result (turn-around time [TAT] 72hrs - 7 days). Temporary funding from The Strategy for the Control of Antimicrobial Resistance Ireland (SARI), a health service initiative, was sought to facilitate on-site testing using FilmArray® polymerase chain reaction technology, with a predicted TAT of 2 hours for a result.

Materials/methods: Our aims were to perform in-house validation of FilmArray® technology for CSF samples, versus referral to reference laboratories (n=100); secondly, to perform a clinical audit evaluating differences in length of stay and antimicrobial prescribing, based on rapid acquisition of a result; and finally, to provide a cost analysis of our findings.

Any CSF with abnormally high white cell count was tested on the FilmArray®. Samples were simultaneously sent to reference laboratories to correlate results and allow comparison of TAT. Clinical audit was facilitated through communication with the attending clinical team, data collection sheets, and medical chart reviews.

Results: Preliminary results (n=44/100) have shown a TAT of 8 hours (FilmArray®) versus 6 days (reference laboratories). In cases of enterovirus meningitis, length of stay was reduced by 2.4 days. Unnecessary antimicrobials were stopped in 48% of cases. In 2 cases an unexpected pathogen was isolated and essential antimicrobials were started. Total savings, including cost of bed days and early cessation of antimicrobials, amounted to €71,387 (deducting €150/cost of test).

Conclusions: On-site rapid molecular testing for CSF is cost-effective, reduces length of stay, and improves antimicrobial stewardship practices.

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Abstract 9467

**Carbapenem-resistant Enterobacteriaceae infections: more could be worst?**

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**Background:** Carbapenem-resistant Enterobacteriaceae (CRE) infections have worldwide spread during the last years. CRE dissemination was attributed to clonal spread (bla\_KPC gene) and less commonly by horizontal gene transference. The last one could be responsible for isolation several CRE in the same sample. Our aim was to compare infected patients with polymicrobial isolates by several CRE (CRE-S) and patients with polymicrobial isolates being only one of them CRE (CRE-M).

**Materials/methods:** A retrospective, case-control descriptive study was conducted at a teaching Hospital. Period: 2010-2017.

Adult inpatients with CRE infections were included and divided in two groups.

We compared epidemiological, demographic, clinical and microbiological characteristics of patients in Group A: polymicrobial isolates with CRE-S and Group B: polymicrobial isolates with CRE-M.

Identification was done by MALDI-TOF MS Bruker Daltonics, Germany, Biotyper 3.1 and susceptibility test by Phoenix100 system BD.

The presence of KPC-carbapenemase was confirmed phenotypically and genotypically

**Results:** Group A: 16 patients/17 episodes and Group B: 41 patients/episodes.

No differences statistically significant were found between age, sex, co-morbidities, Charlson Score, length of stay (days), antibiotics previously and mortality.

Surgical site infections episodes of CRE-S were the only statistically significant variable

\(p: 0,005\) OR 1,8 IC 1,26-2,5

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A(n:17)</th>
<th>Group B(n:41)</th>
<th>p=</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic previously</td>
<td></td>
<td></td>
<td>0,34</td>
</tr>
<tr>
<td>Surgical site (SS)</td>
<td>15 (88%)</td>
<td>20 (49%)</td>
<td>0,005 (OR 1,8 IC 1,26-2,5)</td>
</tr>
<tr>
<td>Bacteremia without focus</td>
<td>1</td>
<td>3</td>
<td>0,7</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>0</td>
<td>4</td>
<td>0,23</td>
</tr>
<tr>
<td>Secondary peritonitis</td>
<td>0</td>
<td>2</td>
<td>0,49</td>
</tr>
<tr>
<td>Others</td>
<td>1</td>
<td>12</td>
<td>NS</td>
</tr>
<tr>
<td>Mortality at 30 days</td>
<td>8/17 (47%)</td>
<td>17/41 (41%)</td>
<td>0,45 (OR 0,7 IC 0,2-2,4)</td>
</tr>
<tr>
<td>Mortality at 60 days</td>
<td>10/17 (59%)</td>
<td>19/41 (46%)</td>
<td>0,28 (OR 0,6 IC 0,11,89)</td>
</tr>
</tbody>
</table>

**Conclusions:** In our study infections by CRE-S had similar outcome compared with infections by CRE-M. CRE-S isolation predominated in surgical site infections.

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Abstract 9469

Integrons & antibiotic resistance: do integrons provide 'adaptation on demand'?  
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Background: Mobile integrons are widespread and clinically relevant drivers of antibiotic resistance, present in some settings in up to 60% of Gram-negative clinical isolates. Acting as genetic platforms, they allow bacteria to capture, express and re-order mobile antibiotic resistance gene cassettes, whose expression levels depend on their distance from the promoter, located at the start of the integron. Cassettes can be integrated and excised by the integrase enzyme, produced by the bacteria in time of stress. It has been hypothesized that integrons allow bacteria to adapt quickly to changing antibiotic pressures by reshuffling the cassette order, and therefore their resistance levels, such that integrons provide ‘adaptation on demand’.

Materials/methods: To test this ‘adaptation on demand’ hypothesis we used experimental evolution to test the impact of the integron integrase on evolvability. Specifically, we constructed a mobile integron carrying three resistance cassettes and either a functional or dysfunctional integrase. Using Pseudomonas aeruginosa, we tested the impact of the integrase on the bacteria ability to adapt to increasing doses of antibiotics when the relevant resistance cassette is located at the end of the array and can be brought forward by integrase activity, in the case of two different cassettes and their corresponding antibiotics (gentamicin and piperacillin). In the end starting and evolved populations were sequenced by Next Generation Sequencing to identify any integron rearrangements.

Results: When compared against the non-functional integrase control population, we saw an increase in evolvability against gentamicin but a decrease in survival against piperacillin. We identified extensive cassettes rearrangements as well as cassette duplications in nearly all the surviving populations with a functional integrase in the gentamicin experiment. While the frequency of rearrangements was much lower in the piperacillin populations, we observed unexpected integron-mediated inversions in the plasmid backbone.

Conclusions: These results highlight the key impact of antibiotics and cassette characteristics on the potential integrase benefits and provide novel insights in the mechanisms controlling cassettes and integrase prevalence. We showed integrase activity is not limited to cassette shuffling or cassette acquisition, but may also promote cassette duplication and off-target recombinations, with far-reaching effects on plasmid maintenance and evolution.

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De novo hybrid genome assembly and genome analysis of polymyxin- and carbapenem-resistant clinical isolate *Klebsiella pneumoniae*

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**Background:** *Klebsiella pneumoniae* is the bacteria with special clinical and epidemiological significance due to the ability to form acquired multiple resistance. Polymyxins are currently the last resort for the treatment of infections caused by gram-negative multidrug-resistant *K. pneumoniae*, especially carbapenem resistant.

**Materials/methods:** Carbapenem- and polymyxin (32 mg/ml) resistant *K. pneumoniae* 20467 was analyzed by whole genome sequencing. Library preparation and sequencing were performed by BioSpark Limited Liability Company (Moscow, Troitsk). The DNA sequencing was performed using an Illumina NovaSeq 6000 platform (USA) and an Oxford Nanopore MinION sequencer (UK) according to manufacturer’s instructions. The Unicycler pipeline v0.4.8 was used for the hybrid assembly *de novo* of the Nanopore and the Illumina reads. The quality of genome assembly was estimated by using Quast server. The sequence annotation and additional gene prediction was performed by the RASTtk server. The Comprehensive Antibiotic Resistance Database and RASTtk server were used for identification of antibiotic-resistance genes. The sequences of the allelic variants of the resistant genes were taken from the Pasteur Institute database (https://bigsdb.pasteur.fr/).

**Results:** The *de novo* assembled genome of *K. pneumoniae* 20467 consists of a circular chromosome of length 5,365,937 bp with the average GC content of 56,6%, and of four circular plasmids of sizes 127,792 bp, 63,589 bp, 8,351 bp and 4,897 bp, and approximate multiplicities of 1.76x, 1.86x, 5.5x and 3.57x, respectively. The chromosome contained 108 RNA-genes (23 rRNA genes, 85 tRNA genes). A total of 5,304 predicted protein-coding genes were identified. Genes, involved in multidrug resistance, were found: 4 fluoroquinolone resistance genes (*gyrA_20, gyrB_1, parC_10 and parE_1*), 4 genes resistant to beta-lactamase [carbapenems] (*blaSHV_110, blaCTX_M_CTX-M-15, blaOXA_OXA-1, blaOXA_OXA-48*); 2 genes of resistance to aminoglycoside (*aac3 Ia c2 and aac6P lb b-cr*); one gene for resistance to fosfomycin (*fosA*). In the polymyxin resistance genes *phoP, pmrA, pmrB, arnA, arnB, arnC, arnD, eptA, arnF, arnT* no mutations were found. In polymyxin resistance gene *phoQ* P75T mutation was found [conservative in all 140 allelic variants of the *phoQ* P75 gene]. The mutation C39Y in the gene *mgrB* founded earlier by PCR was confirmed.

**Conclusions:** It is known that a functional defect in *mgrB* leads to resistance to polymyxins.

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**Abstract 9477**

**Do we need to screen the colibactin genomic island (CGI) for diagnosis of colorectal cancer? Paradigm of Klebsiella pneumoniae**

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**Background:** Colibactin is a bacterial genotoxin encoding by polyketide synthase (pks) genomic island in Enterobacteriaceae. This bacterial toxin induces cell cycle arrest, DNA double-strand breaks, senescence and DNA interstrand cross-links in infected eukaryotic cells and thus, as reported colibactin-producing Escherichia coli was associated with colorectal cancer in human. This bacterium has been reported as the main colibactin-producer despite that colibactin has been identified in other bacterial species. However, prevalence, origin, and structural genetic organization of the colibactin genomic island (CGI) among Enterobacteriaceae are unknown.

**Materials/methods:** Here, we aim to analyze 29’934 genomes of different bacterial genera with clinical interest including Klebsiella (n= 6’412), Escherichia (n= 18’000), Citrobacter (n= 287), Shigella (n= 2’000), Enterobacter (n= 800), Salmonella (n= 9’000), Proteus (n= 190), Serratia (n= 600), Yersinia (n= 700), and Morganella (n= 65) to investigate CGI in these genomes.

**Results:** As preliminary results, among the 6’412 analyzed genomes of K. pneumoniae, CGI was detected 187 genomes (2.92%). This latter with 55’140-bp of size exhibited highly conserved structure in this bacterial species. Interestingly, annotation of this CGI reveals the presence of transposable elements in both sides of the CGI, suggesting therefore a possible transfer to other bacteria. Analysis of available metadata of CGI-positive K. pneumoniae genomes (n=107 isolates), reveals that all were exclusively isolated from human and from different clinical samples including broncho-alveolar lavages, blood, liver abscess, respiratory tract secretion, sputum, wound, and urine. 36% of these KP isolates were reported in USA and 25% reported in China and Thailand. Thanks to our preliminary results, the prevalence of CGI (2.92%) in sequenced K. pneumoniae genomes appears not negligible and highlights therefore the importance to explore the presence of this CGI in genomes of Enterobacteriaceae with clinical interest. Since the CGI is located on transposable element, genome analysis of Enterobacteriaceae species will bring new insights on the potential transmission mechanism of the CGI in bacteria associated with colorectal cancer.

**Conclusions:** Expected findings of this study will highlight the needness to set up molecular diagnostic tools, such as specific CGI-qPCR that could be applied directly from rectal swab samples to diagnosis colorectal cancer.

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Co-aggregation of uropathogenic Klebsiella oxytoca with Klebsiella pneumoniae and probiotic Escherichia coli on the cell line

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Background: Polymicrobial infections account for up to 25% bacterial infections, especially in urological department. However, there is not enough data of interbacterial communication among uropathogenic bacteria. Oral bacteria form mixed bacterial aggregates that involve lectin-like adhesins and polysaccharide-containing receptors. Besides sugars, arginine prevents interbacterial coaggregation. During this study mixed adhesion of uropathogenic bacteria was performed.

Materials/methods: For infection GFP-labeled urine isolate Klebsiella oxytoca and td-Tomato-expressing K. pneumoniae, Enterobacter cloacae, Escherichia coli and probiotic E. coli Nissle (EcN) as a negative control were used. E. coli strains were grown for 48 h at 37 °C without shaking, while the rest strains were grown with shaking at 37 °C until OD600 0.5. Bacteria were treated with lactose (0.1 M), mannose (0.1 M) and arginine (0.05 M) for 30 min. Then 5 x 10^6 of each bacteria/well were added to bladder carcinoma cells 5637 in different combinations and plates were incubated for 2 h. Cell nuclei were stained with DAPI. Plates were analyzed with multicolor fluorescence detection system VideoScan (Aklides®). The measurement results were evaluated in software MaxiSlider and MaxiSliderAddon.

Results: During infection K. oxytoca formed coaggregates with K. pneumoniae and EcN, while coaggregation with the other bacteria was not significant. While mixed with K. pneumoniae, adhesion rate of K. oxytoca is increased compared to single K. oxytoca infection [2050±820 versus 513±123 bac/mm²]; presence of EcN caused more relevant increase of adhesion of K. oxytoca [6639±1790]. Mannose decreased EcN adherence to 46 % and in mixed infection decreased adhesion of K. oxytoca [3024±1802], but had no effect on the adherence of single Klebsiella. Lactose and arginine did not prevent the formation of coaggregates. In mixed infection 40-63 % of overall adhered K. oxytoca were coaggregated with K. pneumoniae, while the ratio of EcN-associated K. oxytoca was 56-88 %.

Conclusions: Adhesion rate of K. oxytoca is increased in model polymicrobial infection. This may indicate bacterial synergy in host colonization and their reinforcement of virulent properties of each other during infection.

Klebsiella oxytoca (green) in coaggregation with K. pneumoniae (red, A) and probiotic Escherichia coli Nissle (red, B) on the urothelial cells 5637.

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Longitudinal assessment of liver fibrosis rates using non-invasive APRI and Fib-4 scores in HIV, HBV and HIV-HBV co-infected patients

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Background: Liver disease is a major cause of mortality in patients infected with human immunodeficiency virus (HIV) and/or hepatitis B viral infection (HBV). Given the large Romanian cohort of HIV and HIV-HBV patients infected in early infancy, the current study analysed the progression and risk factors for liver fibrosis in HIV, HIV-HBV and HBV infected patients under long-term antiviral treatment.

Materials/methods: We performed a 6-year retrospective observational study at “Prof. dr. Matei Bals” National Institute of Infectious Diseases on 310 treated patients (113 HIV, 103 HBV and 104 HIV-HBV coinfected patients) with median ages of 49, 42 and 37 years (69% of HIV and HIV-HBV patients treated>10 years at enrolment). The rate of liver fibrosis was estimated at 4 time-points (at 6, 2-, 1- year prior and current data) using APRI and Fib-4 non-invasive scores. APRI scores <0.5 and Fib-4 values <1.45 were used to rule out fibrosis and APRI ≥1.5 and Fib-4 ≥3.25 indicated advanced fibrosis. Data was analysed using generalized estimating equations, nonparametrical Kruskal-Wallis and Pearson correlations.

Results: Over time most patients displayed normal transaminases (≥88% for each group) and advanced liver fibrosis was detected in coinfected patients only (0.05%, 5/104).

APRI and Fib-4 scores were discordant between groups, with consistently higher APRI scores in HIV-HBV-infected patients versus higher Fib-4 scores in HBV mono-infected patients as confirmed using non-parametrical Kruskal Wallis tests.

In all models Fib-4 and APRI scores were associated with plasma HIV RNA (B=1.056, p<0.001 and B=3.716, p<0.001 respectively) and HIV-HBV co-infection (B=-0.416, p<0.001 and B=-0.699, P=0.012).

Interestingly, at the last assessment cholesterol was significantly associated with both APRI and Fib-4 scores (p=0.002 and 0.001 respectively), in addition to HIV RNA, HBV DNA and treatment adherence.

Conclusions: We observed a low rate of liver fibrosis across groups over a 6-year period. Nevertheless, few HIV-HBV co-infected patients progressed to advanced liver fibrosis despite treatment.

It is probable that over time dyslipidemia plays an important role in the progression of liver disease in HIV and HIV-HBV co-infected patients, yet further data are still needed to confirm this effect.

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Knowing local cumulative antibiogram: does it matter?

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Abstracts 2020

Background: Antimicrobial resistance is a serious and growing threat to global health, with consequences in patient’s outcomes and with broad social and economic impact. Responsible use of antibiotics is a crucial instrument to tackle this threat.Cumulative antibiograms are tools that aim to improve knowledge about local antimicrobial resistance epidemiology and by doing so improve antibiotics use. Our aim was to evaluate the impact in antimicrobial appropriateness of a consistent use of cumulative antibiogram in antimicrobial prescription moments. As a secondary objective we assessed the impact in antibiotic therapy spectrum.

Materials/methods: The study was conducted in a public teaching hospital in 2019, with physicians working in Internal Medicine, Intensive Medicine, Infectious Diseases and General Surgery departments that agreed to participate and respond to the survey. Four case vignettes were assigned to each doctor, with selected amounts of information. The vignettes were constructed by two infectious diseases physicians using real patient data and numbered as Cases 1 to 4. There were two moments in the study: first, the physicians answered the vignettes; second, they were given the cumulative antibiogram and the same vignettes, and were asked to rethink their answers. Appropriateness was evaluated by comparing the answers with the actual susceptibility test. Statistical analysis was performed with IBM® SPSS® statistics, 25th.

Results: Seventy-one surveys were answered. Thirty eight percent of physicians commonly used the cumulative antibiogram to help their decision. Without consulting the cumulative antibiogram, appropriateness was low, ranging from 32.4% to 38.6%, with exception of vignette 3 with 72.9% appropriate therapies. After antibiogram use appropriateness rose to 47.1% - 71.8% (figure 1). Improvement in antimicrobial appropriateness was observed in all professional groups but it was only statistically significant in residents. There were excessive and unnecessary switches in antibiotic spectrum in Cases 1 to 3, 26.3%, 11.5% and 22.4% respectively.

Conclusions: An improvement in appropriateness with the use of cumulative antibiogram was seen. However, a risk of unnecessary broader-spectrum exists and warrants caution when introducing new tools, with careful evaluation of potential impact in antimicrobial use.

Figure 1. Impact of cumulative antibiogram use in appropriateness

Figure 2. Impact of cumulative antibiogram use

% of appropriateness

Before

After

Case 1 Case 2 Case 3 Case 4

*** p<0.001

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Characterisation of the host lipidome in Enterovirus-infected cells: implications on pathogenesis and potential antiviral strategies

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Background: Enterovirus A71 (EV-A71) and coxsackievirus A16 (CV-A16) are the most common causes of hand, foot, and mouth disease. Severe EV-A71 and CV-A16 infections may be associated with life-threatening complications. However, the pathogenic mechanisms underlying these severe clinical and pathological features remain incompletely understood. Lipids are known to play critical roles in multiple stages of the virus replication cycle. The specific lipid profile induced upon virus infection is required for optimal virus replication. The perturbations in the host cell lipidomic profiles upon enterovirus infection have not been fully characterized.

Materials/methods: Clinical isolates of EV-A71 and CV-A16 obtained from patients with hand, foot, and mouth disease were used in this study. Ultra-high performance liquid chromatography–electrospray ionization–quadrupole–time of flight-mass spectrometry (UPLC-ESI-Q-TOF-MS)-based lipidomics was performed to characterize the change in host lipidome upon EV-A71 and CV-A16 infections in human rhabdomyosarcoma (RD) cells (ATCC, CCL-136). MetaboAnalyst 3.0 (http://www.metaboanalyst.ca) and SIMCA-P V12.0 (Umetrics, Umeå, Sweden) were used for univariate and multivariate analysis, respectively. The host lipidomes were characterized and the in vitro antiviral effects of selected lipids which were significantly perturbed in EV-A71 and CV-A16 infection were evaluated. All experiments involving live EV-A71 and CV-A16 followed the approved standard operating procedures of the biosafety level 2 facility at the Department of Microbiology, The University of Hong Kong.

Results: A total of 47 lipids within 11 lipid classes in the categories of phospholipids, glycerolipids, fatty acyls, and sphingolipids were significantly perturbed after EV-A71 and CV-A16 infection. Among them, 4 polyunsaturated fatty acids (PUFAs), namely, arachidonic acid (AA), docosahexaenoic acid (DHA), docosapentaenoic acid (DPA), and eicosapentaenoic acid (EPA), were consistently upregulated (P<0.05) upon EV-A71 and CV-A16 infection. Importantly, exogenously supplying three of these four PUFAs, including AA, DHA, and EPA, in cell cultures significantly (P<0.001 to <0.05) reduced EV-A71 and CV-A16 replication.

Conclusions: Taken together, our results suggested that enteroviruses might specifically modulate the host lipid pathways for optimal virus replication. Excessive exogenous addition of lipids that disrupted this delicate homeostatic state could prevent efficient viral replication. Precise manipulation of the host lipid profile might be a potential host-targeting antiviral strategy for enterovirus infection.

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Abstract 9503

Application of a comprehensive, user-friendly metagenomic sequencing platform for rapid pathogen identification in a paediatric population with meningitis and encephalitis

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Background: Central nervous system (CNS) infections often present with nonspecific symptoms, resulting in a broad differential diagnosis including infectious and non-infectious etiologies. Rapid and accurate diagnosis is essential. In adults, metagenomic sequencing has been demonstrated to provide increased diagnostic yield compared to standard of care testing. There is growing interest in implementing metagenomic testing in routine diagnostic workup. However, complexities of metagenomic data analysis pose barriers for adoption. We present a metagenomic shotgun RNA and DNA assay built on a user-friendly software platform that supports all steps from sample to report. We used this assay for rapid pathogen identification in children hospitalized with a putative CNS infection.

Materials/methods: Children hospitalized with suspected meningitis or encephalitis were enrolled under an IRB-approved multi-center clinical study. Residual cerebrospinal fluid (CSF) was analyzed by shotgun metagenomic RNA and DNA sequencing and the Explify platform. The Explify platform provides easy-to-use metagenomic analysis, including quality control (QC), sequence quality filtering, identification of a customizable pathogen set using curated databases, reproducible result interpretation, result review, and report generation. Results were compared to standard laboratory testing.

Results: At the time of this analysis, a total of 51 samples from 51 enrolled children were analyzed by metagenomic sequencing. For use in this study, interpretive criteria were defined for >1800 relevant bacteria, viruses, parasites and fungi that are implicated in the pathogenesis of CNS infection based on published data. Metagenomic sequencing detected a putative pathogen in CSF samples from 12 of 51 (24%) patients. Putative pathogens detected included Streptococcus pneumoniae, Streptococcus agalactiae, Neisseria meningitidis, Haemophilus influenzae, herpes simplex virus and enteroviruses (Coxsackievirus B, Echovirus). Predominant detections in this study were consistent with known etiology of pediatric CNS infections and were corroborated by standard of care testing.

Conclusions: Analysis of metagenomic sequencing data with the Explify platform provided rapid (<72 hours from sample processing to result) and accurate pathogen identification. The use of evidence-based reporting criteria maximized diagnostic yield and expedited result interpretation. The Explify platform provides user-friendly access to comprehensive application-specific QC and pathogen detection, and identification of antimicrobial resistance markers.

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Abstract 9504

**Epidemiology of previous antibiotic treatment in a community setting infectious diseases consultation office**

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**Background:** Bacterial resistance is nowadays a growing problem of public health in hospitals and community. Antibiotic dispensation is over the counter in most of the developing countries. This study aims to evaluate the antibiotic treatment in the 3 months period before an Infectious Diseases consult in a community setting in a developing country.

**Materials/methods:** This is a prospective cohort study that took place in the community setting of the IDs consultation offices in a developing country from October 1st 2017 until January 1st 2018. Every consultation with previous antibiotic treatment for the same reason of the consult is included with the following features: age, gender, molecule, dose, duration of therapy, presence of fever, indication of treatment, bacteriologic result of cultures if done and the identity of the prescriptor. The data were collected on excel and served for statistics.

**Results:** 70 patients were evaluated with 68 eligible included in the study accounting 95 courses of antibiotics. The sex ratio F/M is 5/2 with a mean age of 43.7 years (18 – 82). The used molecules are cephalosporins in 17 episodes, macrolides [4], amoxicillin [5], amoxicillin-clavulanate [20], quinolones [34] and 11 miscellaneous. Fever is present in only 19 / 95 cases counting 4 / 19 true indications, 5 uncertain and 10 without indication for antibiotic treatment.

Nevertheless, antibiotics were prescribed even though the patients were non febrile in 76 cases (80%) including 7 / 76 true indications only. Besides, 35 courses of treatment were either with a wrong dosage or duration of therapy and were taken OTC by the patients themselves in 11 cases or prescribed by the pharmacist in one case or the physician in 23 cases. Cultures were performed in only 9 cases and were positive in 5.

Finally, the prescriptors were physicians in 49/95 episodes, pharmacists in 16/95 episodes and the patients themselves in 30/95 of the cases.

**Conclusions:** We clearly need more public health awareness for the misuses of the antibiotics, a proper and urgent education for physicians along with a law regulating the dispensation of antibiotics by the pharmacists.

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Background: Neonatal sepsis refers to an infection involving bloodstream in newborn infants less than 28 days old. It continues to remain a leading cause of morbidity and mortality among infants, especially in middle and lower-income countries. Signs and symptoms of neonatal sepsis can range from nonspecific or vague symptoms to hemodynamic collapse, i.e. septic shock.

Materials/methods: The retrospective study included 133 medical charts of Neonatal ICU during Dec/2016 to Jun/2017 period. We chose some symptoms, which are important for diagnosing neonatal sepsis and separated them in 3 groups: commonly-associated (≥50% cases), frequently-associated (25 to 50%) and occasionally-associated (<50%) with sepsis. Hyperthermia (>38.5°C), respiratory distress and tachycardia are in the first group; lethargy, poor feeding, bradycardia, jaundice and hepatomegaly are part of the second group; and, finally, the third group is consisted of hypothermia, seizures, abdominal distension and diarrhea.

Results: Five patients of 133 had sepsis and two of them had septic shock. The number of patients who had high temperature (>38.5°C) was six and there was no data about hypothermia cases. Of 133 neonates 105 (78.9%) had respiratory distress. CBC showed that 78 of newborns (58.6%) had high levels of WBC (>12,000) and 15 (11.3%) of them had left shift of leukocytes. Overall, 105 neonates were poor fed. Hepatomegaly and jaundice were found in 59 (44.4%) and 12 (9%) newborns, respectively. Abdominal distension was also among common symptoms [51.9%, n=69], with one (0.7%) case of diarrhea. Symptoms such as lethargy (6%, n=8), seizures (8.3%, n=11) and bradycardia (0.7%, n=1) were rarely reported.

Conclusions: In contrast to adult patients, the diagnostic criteria for neonatal sepsis are not perspicuous, therefore we assume that evaluation of these symptoms can be beneficial for early detection and prophylaxis of complications. Combined laboratory and clinical examinations can provide reduction of misdiagnosis.

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Abstract 9506

CSF diffusion of cefotaxime following high-dose administration in central nervous system infections: a multicentre retrospective study (DIFCEFO study)

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Abstract third-party references: On behalf of the DIFCEFO study group

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Background: Cefotaxime (CTX) is widely recommended to treat central nervous system (CNS) bacterial infections, especially bacterial meningitis. The recommended dosage varies depending on the guidelines. To date, limited data exist about cerebrospinal fluid (CSF) diffusion of cefotaxime in adults treated for CNS infections. The aim of the study was to describe the CSF diffusion of cefotaxime in patients treated for CNS infection with high-dose cefotaxime as recommended by French guidelines.

Materials/methods: We report pharmacological data from the DIFCEFO study (CSF diffusion of high-dose cefotaxime in CNS infections), a multicenter, observational, retrospective study. Adult patients who received high-dose cefotaxime as recommended by French Guidelines (defined as 200–300 mg/kg/day without upper limit, whether or not dexamethasone is coadministered) for CNS infections between January 2012 and October 2019 for whom cefotaxime was measured in CSF were included. Concomitant plasma dosages were also collected. Medical charts were retrospectively reviewed.

Results: Seventy four patients were included in the study, 54 with meningitis, 17 with brain abscess and 3 undocumented. Median age was 60 years (range: 24-88) and median glomerular filtration rate measured by CKD-EPI was 106 mL/min/1.73 m 2 (range: 8-189 mL/min/1.73 m 2). Forty six percent of patients received dexamethasone. Most isolated pathogens were Streptococcus pneumoniae (n=29), Escherichia coli (n=10) and Staphylococci (n=7). The median daily dosage of cefotaxime was 14 g (Q1:12; Q3:18) corresponding to a median of 204 mg/kg [Q1:164; Q3:247], 60% in continuous infusion. One hundred and twenty three CSF concentrations were measured (43 lumbar punctures and 75 external ventricular derivations and 5 undocumented). Median CSF cefotaxime concentration was 6.4 mg/L [Q1:3.3 mg/L; Q3:12.5 mg/L] and median CSF/plasma ratio was 23% [Q1:8.7%; Q3:32%]. In the subgroup of pneumococcal meningitis, median CSF cefotaxime concentration was 10.25 mg/L [Q1:5 mg/L; Q3:19.5 mg/L] and 100% of concentrations (n=42) were above the upper bound of the EUCAST MIC breakpoint for CTX-susceptible Streptococcus pneumoniae [MIC 0.5 mg/L].

Conclusions: Pharmacological data presented here demonstrate the good diffusion of cefotaxime in adults treated for CNS infection as recommended by French guidelines. Otherwise, concentrations measured in patients with pneumococcal meningitis were all above the targeted EUCAST MIC breakpoint.

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Parenteral colistin therapy induces rapid selection of colistin-resistant bacteria in human gut: first report from India

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Abstract third-party references: Center for Human Microbial Ecology, THSTI, Faridabad, Haryana

Background: Unregulated use of broad-spectrum antimicrobials owing to lack of stewardship and regulations, over-the-counter availability of antibiotics including colistin pediatric syrup and indiscriminate usage of polymyxins in animal husbandry and poultry farming, set the stage for selection of colistin resistant bacteria in India.

Materials/methods: A case-control study of fecal carriage of colistin resistant Enterobacteriaceae (colRE), and its genetic characterization was conducted. Patients in medical ICU and wards receiving parenteral colistin for at least five days were recruited as cases and an equal number of their healthy consenting adult family members, without any history of antibiotic intake in last 3 months served as controls. Stool samples were subjected to molecular screening and culture. Colistin resistance was confirmed by microbroth dilution. Metagenomic DNA extracted from stool samples and bacterial DNA extracted from colRE isolates were subjected to screening by mcr 1-5 multiplex PCR and confirmed by nested PCR, restriction digestion and sequencing.

Results: Seventeen out of 34 cases were culture positive for colRE in their stool, compared to 4 out of 34 controls (p<0.001). Half of the patients (8 out of 17) developed colRE carriage within first week of parenteral colistin therapy. None of the colRE isolates were positive for mcr gene. Out of 68 stool metagenomic DNA screened, 6 samples from the controls were positive for mcr1 gene, confirmed by nested PCR and sequencing. However, no colRE were isolated from the stool of those 6 subjects. Nonvegetarian dietary habit, particularly, consumption of chicken was found to be predominant (5 out of 6) among those detected positive for mcr1 gene, but this was statistically insignificant considering the entire study population (p= 0.101). One representative colistin resistant Klebsiella pneumoniae isolate was subjected to whole genome sequencing to analyse possible mechanism(s). mcr gene was not detected. Mutations were detected in arrT and AraC transcription-regulator proximal to the phoP and phoQ genes.

Conclusions: Our study showed rapid selection of colRE in the gut of unsuspecting patients receiving parenteral colistin. Though molecular presence of mcr gene in the gut of healthy Indian adults was detected, yet the colRE culture isolates were all negative for mcr.

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Abstract 9509

Clinical predictors of peripheral vascular graft infection by *Staphylococcus aureus*

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**Background:** Peripheral vascular graft infection (PVGI) is a predominantly staphylococcal disease. However, data in the literature about these types of infections are scarce. The objective of the study was to describe the clinical characteristics of PVGI by *Staphylococcus aureus* (SA-PVGI).

**Materials/methods:** An observational study of a prospective hospital-based cohort of adult patients with VGI. All patients admitted to hospital between 2009 and 2019 were included if they had a confirmed infrainguinal infection. The SA-PVGI cases were compared with all others (0-PVGI).

**Results:** Eighty-four cases of PVGI were included, of which 34 (40.5%) were SA-PVGI (17 methicillin-resistant isolates). In the 0-PVGI group, a microbiological diagnosis was reached in 42 cases and the most frequently isolated microorganisms were: *Enterobacteriaceae* (19), coagulase-negative staphylococci (15), *Enterococcus* sp. (8), *Pseudomonas* sp. (8), *Streptococcus* sp. (5), *Bacteroides* sp. (5) and *Propionibacterium* sp. (5). The infection was polymicrobial in 42.9% of 0-PVGI and 38.2% of SA-PVGI. *Enterobacteriaceae* were the most frequent microorganisms in polymicrobial SA-PVGI (8 of 13 cases). There were no significant differences between groups regarding the age, the comorbidity and the type of graft. No disparities in the infection management or in the in-hospital mortality rate were observed. The main differences in clinical features and outcomes are shown in Table 1. In addition, a statistically significant association was observed between graft thrombosis and the isolation of coagulase-negative staphylococci (p 0.019) and *Propionibacterium* sp. (p 0.045).

<table>
<thead>
<tr>
<th></th>
<th>SA-PVGI (n=34)</th>
<th>0-PVGI (n=50)</th>
<th>p</th>
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<tbody>
<tr>
<td>Fever</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>15</td>
<td>45.5</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>Severe sepsis/ septic shock</td>
<td>6</td>
<td>17.6</td>
<td>2</td>
</tr>
<tr>
<td>Positive blood culture</td>
<td>12/24</td>
<td>50</td>
<td>2/24</td>
</tr>
<tr>
<td>Graft thrombosis at presentation</td>
<td>8</td>
<td>23.5</td>
<td>23</td>
</tr>
<tr>
<td>In-hospital major amputation</td>
<td>6</td>
<td>18.8</td>
<td>19</td>
</tr>
</tbody>
</table>

**Conclusions:** SA-PVGI were significantly associated with systemic symptoms, sepsis and bacteremia. 0-PVGI were associated with graft thrombosis, mainly in infections by indolent microorganisms such as coagulase-negative staphylococci and *Propionibacterium* sp.

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Abstracts 2020

Abstract 9511

Adenovirus types associated with severe respiratory diseases in intensive care unit-admitted patients during the 2017-2019 period

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Background: Acute lower respiratory tract infections are caused by different viruses, including human adenoviruses (HAdVs). However, life threatening adenovirus infections, e.g. viral pneumonia and ARDS were reported and associated with a few adenovirus types, but appear to be rare. Aims of present study were to: i) determine the frequency of respiratory infections HAdV-associated in ICU-patients and ii) elucidate the impact of different HAdV genotype as cause of severe respiratory infections.

Materials/methods: Respiratory samples collected from ICU patients and tested for the presence of HAdV using a quantitative real-time PCR at the Molecular Virology Unit, Microbiology and Virology Department, of Fondazione IRCCS Policlinico San Matteo in Pavia (Italy) between 1st January 2017 and 30th October 2019 were included in this study.

Results: HAdV DNA was detected in respiratory samples from 9 (3.5%) of 260 patients hospitalized in ICU. The median age of positive patients was 55 years [24-78 years] with a median time of ICU stay of 22.5 days [range 5-80 days]. In almost all [8/9] patients HAdV was detected in bronchoalveolar lavages with viral load ranging from 2.7x10^2 to 6.7x10^7 DNA copies/ml. According to the phylogenetic analysis of the hexon gene sequences, the most prevalent HAdV types detected in patients with viral pneumonia were E4 (n=3), D37 (n=2), D56 (n=2), B3 (n=1) and B55 (n=1). Co-infections were observed in only 2/9 (22.2%), one with influenza A/H3N2 and one with H. influenzae. Almost all patients had a comorbidities and two out of 9 patients had ARDS at the ICU admission. The median value of PaO2/FiO2 ratio was 166 mmHg [range 61-310] and one patient required extracorporeal membrane oxygenation for 32 days.

Conclusions: Adenovirus respiratory infection may cause severe disease requiring ICU admission and mechanical ventilation, mostly in patients with underlying conditions. Unexpected HAdV types were observed in patients with severe infections. Monitoring respiratory viruses involved in severe infections, will improves the orientation of therapeutic and preventive measures, avoids unnecessary use of antibiotics, and helps control hospital infection.

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Clonality and genetic determinants of resistance in paired isolates of Klebsiella pneumoniae with divergent polymyxin B phenotypes

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Background: Infections caused by carbapenem and polymyxin B (PolB) resistant Klebsiella are a priority in terms of infection control worldwide. In this study we aimed at characterizing the molecular determinants of polymyxin resistance and clonal relationship in K. pneumoniae with divergent susceptibility phenotypes recovered from the same patients.

Materials/methods: A total of 25 pairs of isolates obtained from clinical samples collected at different dates (January 2015 to May 2017) from patients treated at Santa Casa de Misericórdia Central Hospital of São Paulo - Brazil were analyzed. Species identification was achieved by MALDI-ToF-MS and multiplex PCR as described by Fonseca et al. Presence of mcr-1 and integrity of mgrB were evaluated as described respectively by Liu et al. and Cannatelli et al. Mutations in pmrA, pmrB, phoP and phoQ were evaluated by full gene sequencing. PFGE was performed as described by Ribot et al., using XbaI. Polymyxin B (PolB) susceptibility was determined by broth microdilution as recommended by EUCAST using the interpretative criteria recommended for colistin.

Results: All isolates were positive for blaSHV-1 and were identified as K. pneumoniae. None of them were positive for mcr-1. Truncation of mgrB was observed in 5/21 PolB resistant isolates. No mutations were observed in the pmrA or phoQ. The R256G substitution in PmrB was observed in 5/21 PolB resistant isolates. This finding contrasts with a previous publication by Yi-Hsiang et al. The T157X and F204L substitutions were detected in isolates with a PolB MIC of 32 mg/L but were not present in isolates from the same clone with an MIC ≤ 0.5 mg/L; consequently these substitutions may be implicated in PolB resistance. Concerning PhoP, all sequenced isolates, both susceptible and resistant ones, had the L26Q substitution. This finding contrasts with a previous publication by Yi-Hsiang et al. Concerning clonality, 10 patients were infected by two different clones when evaluating isolates detected one week to 11 months apart.

Conclusions: Mutations R256G in PmrB and L26Q in PhoP do not confer PolB resistance. T157X and F204L substitutions in PmrB are implicated with PolB resistance.

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Abstract 9514

**Diversity and antimicrobial susceptibility of Gram-negative bacteria from Sparus aurata from aquaculture**

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**Background:** In aquaculture, a higher density of fish in a specific area is usually related with an increase in stress conditions, which leads to a greater tendency for infectious diseases and a higher antibiotic consumption. This study aimed to characterize antibiotic resistance (AR) in bacteria and understand bacterial diversity in *Sparus aurata* (sea bream) collected from aquaculture.

**Materials/methods:** During the years of 2018 and 2019 we collected samples of *Sparus aurata* (n=12) from fish farms and market. All samples were homogenized and further diluted (each dilution plated in selective media). Colonies with different morphology were selected and DNA extracted. Strains were identified by MALDI-TOF and amplification of the 16S rRNA gene. Antimicrobial susceptibility was assessed by disc diffusion and MIC methods for 20 antibiotics from 9 classes. The investigation of clinically important AR-encoding genes was performed by PCR-amplification. The whole-genome-sequencing from an *Enterobacter cloacae* strain was also performed.

**Results:** A total of 157 Gram negative strains from *Sparus aurata* were isolated. *Aeromonadaceae, Enterobacteriaceae, Hafniaceae, Shewanellaceae, Comomonadaceae, Erwiniaaceae, Erysipelotrichaceae, Moraxellaceae, Pseudomonadaceae* and *Yersiniaceae* families were identified. Decreased susceptibilities to β-lactam, phenicols, tetracyclines, quinolones, and trimethoprim/sulfamethoxazole antibiotics were found. The qnrB-19 gene, associated to diminished susceptibility to quinolones, was detected in two *Enterobacteriaceae*, one *Escherichia coli* (with disc diffusion of ciprofloxacin=21mm and flumequine MIC=16mg/L) and one *Leclercia adecarboxylata* (with disc diffusion of ciprofloxacin=24mm and flumequine MIC=4mg/L). Genomic analysis of Enterobacter cloacae from ST190 lineage, allowed to identify β-lactam (*blaACT-7*) and phosphomycin (*fosA*) resistance genes, integrase genes, iroN virulence factor, plasmids (col, IncFIB, IncFII) and phages.

**Conclusions:** We highlight the diversity of Gram-negative bacterial species from aquaculture samples. Some of these species and AR genes identified have already been detected in the human reservoirs. Thus, bacteria found in aquaculture might have the ability to acquire several AR-encoding genes and act as a reservoir of AR, which need to be monitored.

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Direct detection of Mycobacterium tuberculosis complex in clinical specimens from patients in Norway by two different polymerase chain reaction tests

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Background: Mycobacterium tuberculosis (Mt) is the causative agent of tuberculosis (TB). Our aim was to compare the use of two different assays for DNA amplification with the polymerase chain reaction (PCR) for detection of the Mt complex directly in human clinical specimens in Norway.

Materials/methods: Five hundred and fifteen clinical samples, including 370 airway samples and 145 extrapulmonary samples, were processed by culture (BACTEC MGIT, BD), direct microscopy and PCR. The PCR assays employed for qualitative detection of DNA from Mt complex cells in clinical specimens were the Roche COBAS® TaqMan® MTB real-time PCR test targeting the 16S rRNA gene and the Cepheid Xpert® MTB / RIF Ultra test targeting the gene encoding RNA polymerase B (rpoB).

Results: Among the 515 specimens, 71 were culture positive for Mt and 21 were culture positive for non-typable mycobacteria (NTM). Compared to culture, the COBAS® TaqMan® MTB test had a sensitivity of only 76% in Mt positive specimens, while the sensitivity of the Xpert® MTB / RIF Ultra test for Mt positivity was 100% in both airway specimens and extrapulmonary samples. No false positive reactions were detected with either test. However, COBAS® TaqMan® MTB was inconclusive (yielded “Invalid” result) in 9 out of the 21 cases that were NTM culture positive (42.8%), while Xpert® MTB / RIF Ultra yielded a negative result in all the 21 NTM positive samples. The COBAS® TaqMan® MTB test detected only 10 out of the 15 cases with multidrug-resistant (MDR) TB. In all the 15 MDR-TB cases, Xpert® MTB / RIF Ultra detected Mt positivity and the mutations encoding rifampicin resistance.

Conclusions: The Xpert® MTB / RIF Ultra test demonstrated much higher sensitivity and specificity in detecting Mt compared to culture than the COBAS® TaqMan® MTB test. The data imply that 24% of patients with TB will not be detected by COBAS® TaqMan® MTB, while many patients who do not have TB will appear to potentially be Mt positive by this test. The rapid procedure, more automation, semi-quantitation and concomitant detection of rifampicin resistance makes the Xpert® MTB / RIF Ultra test a valuable tool in mycobacterial diagnostics.

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Rapid identification of bacteria directly from positive blood cultures by a modified method using a Serum Separator Tube (SST) and MALDI-TOF MS

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Background: To evaluate a modified and simplified method, based on serum separator tube (SST), in the identification of bacteria directly from positive blood cultures (BC).

Materials/methods: Positives BC with no more than one hour since the positive signal were included. MALDI-TOF after 24 hours of incubation was considered the Gold Standard. The modified method is based on the use of 8 mL SST Gel. Briefly, 4 mL of blood are transferred to SST; centrifuged at 3000 rpm/10 minutes and discarded the supernatant. 1 μL inoculation loop is impregnated in the pellet and inoculated into the MALDI-TOF plate. 1 μL of 100% formic acid and 0.5 μL of matrix were added. To estimate the bacterial load, the microorganisms were counted in three fields of GRAM stain. Samples were assigned to 3 groups. 1: less than 50 microorganisms/field (MOF), 2: 51-100 MOF and 3: more than 100 MOF.

Results: We analyzed 253 positive BC of 195 patients. 156 (61.7%) Gram + and 97 (38.3%) Gram –. 68.8% (174/253) were correctly identified at the species level and 79.1% (200/253) at the genus level. Of the 174 BC identified at the species level, 66.1% (115/174) were with a score ≥1.70, 25.8% (45/174) with 1.31-1.69 and 8.1% (14/174) with 1.00-1.30. Total mean: 1.81±0.32. In Gram –, 92 (94.9%) were correctly identified both at the species and genus level. 88% (81/92) with a score ≥1.70, 10.9% (10/92) with 1.31-1.69 and 1.1% (1/92) with 1.00-1.30. Total mean: 1.95 ± 0.234. In Gram +, 82 (52.6%) and 108 (69.2%) were correctly identified at the species and genus level respectively. Of those, 41.5% (34/82) were with a score ≥1.70, 42.7% (35/82) with 1.31-1.69 and 15.9% (13/82) with 1.00-1.30. Total mean: 1.66 ± 0.342. The relation between bacterial loads, correct identification and mean score is represented in table 1.

Conclusions: This method allows us to obtain the etiological agent of bacteremia in less than half hour from a positive BC with a simple technical process.

<table>
<thead>
<tr>
<th>Species correct (%)</th>
<th>p</th>
<th>Mean score±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>GROUP 1 (≤50)</td>
<td>50/94 (53.2)</td>
<td>0.123</td>
</tr>
<tr>
<td>GROUP 2 (5-00)</td>
<td>44/66 (66.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GROUP 3 (&gt;100)</td>
<td>79/93 (84.9)</td>
<td>0.012</td>
</tr>
</tbody>
</table>

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Characteristics of vascular graft infection: a prospective single-centre cohort study

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**Background:** The optimal management of vascular graft infections (VGI) is unknown. We evaluated the clinical, microbiological, radiological and treatment characteristics of VGI.

**Materials/methods:** Consecutive patients with VGI treated at our institution between 01/2017 and 10/2019 were prospectively included. VGI was defined by presence of ≥1 criterion: sinus tract or exposed graft; purulence at surgical site; positive culture of intraoperative tissue/sonication fluid; positive blood culture without other infectious focus; inflammation in perigraft histopathology; perigraft abscess seen at preoperative CT/MRI or PET-CT.

**Results:** 33 patients were included, median age 67 (34-87) years. Reasons for primary graft implantation were aneurism (n=15), aortic dissection (n=10), aortic isthmus stenosis (n=5) and other (n=3). Median time from primary graft implantation to diagnosis of VGI was 6 (0-316) months; 31 were aortic and 2 were peripheral grafts. Importantly, 13 patients (39%) had simultaneously other intravascular devices such as prosthetic heart valves, pacemaker, cardiac resynchronization therapy (CRT) or implantable cardioverter defibrillator (ICD). Clinical manifestations included fever in 17 (51%) and surgical site infection signs in 4 patients (16%). MRI or PET/CT showed perigraft abscesses in 13 patients (39%), perigraft fluid in 2 patient (6%) and nonspecific signs in 9 (27%). 3 patients had simultaneous endocarditis/endoplastitis. VGIs were monomicrobial in 18 patients (54%), polymicrobial in 9 (27%) and culture negative in 6 (18%). Most frequent pathogens were Candida species (n=8), gram-negative bacilli (n=8), coagulase-negative staphylococci (n=7) and S. aureus (n=5). The pathogen was isolated from blood in 24 (72%) and from intraoperative samples in 14 patients (42%). Graft exchange was performed in 15, debridement & graft retention in 10 and no surgery in 7 patients. The median duration of antimicrobial therapy was 11.7 weeks. 20 patients (60%) received biofilm-active antibiotics, 11 long-term suppression. The most frequent postoperative complication was mediastinitis (8 patients), one patient died during hospital stay.

**Conclusions:** VGI was mostly diagnosed by positive blood cultures (72%) and MRI or PET/CT imaging (48%). Staphylococci, Candida and gram-negative bacilli were the predominant pathogens. The infected vascular graft was retained in about one third of patients and about every fourth VGI was complicated by mediastinitis.

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Abstract 9525

**Early diagnosis in sepsis: T2 bacteria magnetic resonance assay versus blood culture**

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**Background:** Sepsis is an entity with high morbidity and mortality in which response time is absolutely decisive. The application of the new molecular techniques in the microbiological diagnosis implies a faster identification of the pathogens. The goal of this study is to describe the performance of the magnetic resonance-based T2Bacteria Panel assay (T2BPA) for rapid detection of pathogens in whole blood samples of patients with diagnosis of sepsis in an every-day clinical setting.

**Materials/methods:** We performed a prospective observational study from May to November 2019. Patients admitted to the adult Emergency Department with an initial diagnosis of sepsis (SOFA ≥ 2) were included if a blood culture (BC) and T2BPA had been performed. First we analyzed the agreement between both tests, including the whole population and again after excluding subjects with infections from pathogens not included in T2BPA. Then we evaluated the diagnostic properties of the tests using an ad-hoc microbiological-clinical combined criteria as gold standard. These criteria include microbiological results from other samples yielding the same pathogen to assess true infection, along with clinical decision to treat when other samples were negative.

**Results:** Forty-five patients were included (mean age = 68.5 years). T2BPA and BC were positive in 37.7% and 40% of the cases, respectively. In 33.3% of cases, BC detected bacteria not included in the T2BPA. *E. coli* was the most frequent isolated bacteria (24.4%) by T2BPA, followed by *K. pneumoniae* (11.1%). The percentage agreement between both tests was 73.3%, with a Cohen’s kappa = 0.53 (moderate agreement) considering the whole population. After excluding subjects with infections from pathogens not detected from T2BPA, the percentage agreement increased to 84.6% with a good kappa agreement (0.71). The accuracy of the tests in the whole sample was 96% and 87% for T2BPA and BC, respectively (Table).

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>PPN</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2BPA</td>
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<td>0.93</td>
<td>0.88</td>
<td>1</td>
<td>0.96</td>
</tr>
<tr>
<td>BC</td>
<td>0.8</td>
<td>0.92</td>
<td>0.89</td>
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</tr>
</tbody>
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**Conclusions:** The T2BPA has shown a moderate-to-good agreement with current standard (BC) for pathogen detection in a real-world sepsis scenario. Furthermore, this faster technique yielded a higher diagnostic accuracy using a clinical-microbiological criteria as gold standard.

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Abstract 9527

Microbiota modifications in travellers to tropical and subtropical areas

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**Background:** Microbiota may be modified due to changes in diet, environmental factors and the use of antibiotics. These alterations can lead to colonization by multi-resistant enterobacteria (MRE), meticillin-resistant Staphylococcus aureus (MRSA) and/or enteroparasites, and this fact besides may pose a risk of transmission between health workers and patients.

The objective of this study was to determine an eventual colonization by MRE, MRSA and intestinal protozoa in previously uninfected travellers to tropical or subtropical areas. In addition, the burden of colonization by these microorganisms in health-workers and inpatients was measured.

**Materials/methods:** A prospective study in the Regional Hospital of Loreto (Iquitos, Peru) and the Notre Dame de la Santé Hospital (Dschang, Cameroon) was performed. Different chromogenic agars for the detection of carbapenemases-producing enterobacteria (CPE), Extended-spectrum beta-lactamases (ESBL) and MRSA were used. A stool sample and a nasal exudate were taken in every patient; in the case of travellers, the sample collection was carried out before and after travelling.

Pathogenic protists were also detected by qPCR (Giardia duodenalis, Entamoeba histolytica/dispar), ssu-PCR (Cryptosporidium, Blastocystis) and ITS-PCR (Enterocytozoon bieneusi).

**Results:** Four travellers (27%) acquired ESBL, two CPE (13%) and one SAMR (11%). One of the cooperant aid workers acquired Entamoeba histolytica in Peru; and another one acquired Giardia duodenalis in Cameroon. Additionally, two aid workers travelled to Cameroon with Blastocystis spp or Entamoeba dispar.

Considering local population, in Cameroon 9p had ESBL (60%), 2p CPE (13%), 7p MRSA (26%), 2p Giardia duodenalis, 4p Blastocystis spp, 1p Entamoeba dispar. In Peru 2p were colonized by ESBL (22%), 3p CPE (33%) and 16p MRSA (26%). No enteroparasite DNA was detected in any subject in Peru.

Matching inpatient information with travelling aid workers, Cameroon was found to have a higher proportion of ESBL acquisition (61%) compared to Peru (25%) (p=0.027), as well as a higher ratio of gastrointestinal parasites (36%) compared to Peru (5%) (p=0.017).

**Conclusions:** Subtropical populations show a high prevalence of EMR colonization. Travelling to these areas increases the risk for EMR and enteroparasites acquisition, with a possible subsequent dissemination in the country of origin.

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Abstract 9529

Identification of methicillin resistance in Staphylococcus spp. of dogs with pyoderma

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Abstract third-party references: Bill & Melinda Gates Foundation, CNPq, FAPERJ, CAPES

Background: Staphylococcus sp. is a comensal bacteria from skin and other sites microbiome of asymptomatic animals. They can also be associated with skin infections (pyodermitis and otitis). S. pseudintermedius and S. schleiferi are among the main causes of skin and otitis bacterial infections. The potential of zoonotic transmission of canine bacteria has been demonstrated elsewhere. Since there is an increasing number of infections caused by multidrug-resistant bacteria in dogs, chief among them Methicillin resistant S. pseudintermedius, there is a great need for studies new studies. Thus, the present study aimed to determine tehddiversity of Staphylococcus sp. isolated from dogs with topical bacterial infections and the presence of methicillin resistance among them.

Materials/methods: Samples of 100 animals with dermatopathies (pyoderma and otitis) were collected with sterile swabs. Species identification was performed by mass spectrophotometry (MALDI-TOF) and methicillin resistance was evaluated with the detection of meca gene. In order to assess possible risk factors a questionnaire with epidemiological information was performed with the dog’s owners.

Results: A total of 270 colony forming units were obtained, being 57% S. pseudintermedius; 26% S. schleiferi; 4% S. haemolyticus; 2% S. intermedius; 2% S. sciuri; 2% S. epidermidis; 2% S. hominis; 2% S. simulans; 1% S. aureus; 1% S. sropheyticus; 1% S. warneri and 1% S. delphini. Among the samples 35% were methicillin resistance, where the highest percents were 40% Staphylococcus pseudintermedius and 15% to Staphylococcus schleiferi. Importantly, among these animals 52% of them sleep in their guardians’ beds and 90% have chronic pyoderma processes.

Conclusions: The present study shows high rates to methicillin resistance, showing the importance of antimicrobial susceptibility testing to diagnosis and treatment. Avoiding empirical choises and reinforce zoonotic and anthropozoonotic potencial of those samples.

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Deciphering resistome and virulome of Gram-negative bacteria isolated from farmed fish and molluscs
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Background: The use of antibiotics in aquaculture has resulted in the emergence of reservoirs of antibiotic resistant bacteria in farmed fish and other animals, as well as in the aquatic environment. The aim of this study was to analyse the whole genome sequence (WGS) and resistome of a selection of isolates collected from different bacterial and animal species combination that reported non-susceptibility to at least one of the tested antibiotics, including 20 antimicrobial agents from 9 classes (β-lactams, aminoglycosides, folate pathway antagonists, fusidic acid, glycopeptides, mupirocin acid, phenicols, quinolones, and tetracyclines).

Materials/methods: In this study, 50 Gram negative isolates [including 21 Enterobacteriaceae, 11 Hafniaceae, 8 Aeromonadaceae, 3 Vibriaceae, 2 Shewanellaceae, 2 Pseudomonadaceae, 1 Morganellaceae, 1 Yersiniaceae, and 1 Rhodospirillaceae] were analysed. These strains were collected among samples of Sparus aurata (from an aquaculture tank and from a market), and Mytilus galloprovincialis (from a market). WGS was performed on a MiSeq Illumina platform. INNUca was used for quality control of reads, de novo assembly and contigs quality assessment. Prokka and ABRicate were used for genome annotation and screening for antibiotic resistance and/or virulence factors-encoding genes, respectively. Freeware web-based resources [e.g., PathogenFinder, ResFinder, CARD, VirulenceFinder, PlasmidFinder, PHAST].

Results: Results obtained allowed the identification of not only antibiotic resistance genes, but also virulence factors, efflux pumps and phages. We highlight the presence of the qnrB19 gene, which confers resistance to quinolones, in a Leclercia adecarboxylata strain [from a skin sample of S.aurata, from an aquaculture tank] and in an Escherichia coli [from an intestine sample, from S.aurata obtained in a market]. Furthermore, we detected a mcr-9 gene in an Enterobacter cloacae [from a muscle sample of S.aurata, from an aquaculture tank], co-producing β-lactam (blaACT-1 2-type) and phosphomycin [fosA2-type] resistance genes. MCR-9-encoding gene was firstly described in USA, in a clinical Salmonella Typhimurium isolate, which demonstrates the high transmission potential of this colistin resistance determinant.

Conclusions: In conclusion, this work highlights the resistance mechanisms that are being promoted in aquaculture environments, thereby allowing antibiotic resistance to develop and spread via food fish and the environment, resulting in significant human health threats.

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**Abstract 9533**

**Endocarditis management and OPAT in the POET era**

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**Background:** The use of at least six weeks of intravenous antimicrobial therapy in the treatment of infective endocarditis (IE) has been challenged by the POET study, which reported non-inferiority of completing courses with oral therapy, following at least 10 days intravenous therapy (IVT). Outpatient Parenteral Antimicrobial Therapy (OPAT) services, including our own, already facilitate the discharge of IE patients. Adopting partial oral antimicrobial therapy for endocarditis could improve patient experience, reduce IVT-related morbidity and be cost-effective. We considered whether the POET study is applicable to patients referred to our OPAT service and if adopting its protocols could significantly reduce costs.

**Materials/methods:** Records of all patients managed by our OPAT service between January 2015 and March 2019 were reviewed. We established: (1) The number of OPAT patients fulfilling the POET study eligibility criteria (modified to accept echocardiogram confirmation performed outside of the 48 hours prior to randomisation/inclusion). (2) The number of days of OPAT which could have been replaced with monitored oral therapy (taking the first possible time for an oral switch to be hospital discharge) and (3) The comparative costs of providing OPAT care vs monitored oral therapy. Costs considered included medications, therapeutic drug monitoring, supporting IVT administration and review appointments.

**Results:** Our OPAT cohort consisted of 25 patients treated for 26 separate episodes of IE. 5/26 (19%) of episodes fulfilled POET study inclusion criteria. Switching to monitored oral antibiotics would have replaced 141 days of OPAT, median of 31 days per patient (range 18-33) and saved £1,500 per episode.

**Conclusions:** In our OPAT cohort, the POET study would have been directly applicable to a sizable minority (19%) of patients. The predicted cost savings per patient are derived from a reduction in the costs of supporting IVT administration. The stringency of inclusion criteria of the POET study led to the exclusion of a number of patients who were clinically very likely to have endocarditis, were stable and able to tolerate oral medications. Exploring whether an oral switch could safely be made in this group would be an interesting area for future study.

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Ability of antibiotic-loaded bone cement to prevent bacterial adhesion, biofilm formation and selection of resistance

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Background: Antibiotic-loaded bone cement (ALBC) has a number of different uses in primary and revision total joint arthroplasty. Despite the release of antibiotics from ALBC, over time bacteria may adhere to the surface, grow in biofilms, and develop infections.

Materials/methods: In this study, we evaluated a commercially available calcium-sulphate/hydroxyapatite ALBC loaded with gentamicin, vancomycin or without antibiotics to evaluate the ability of clinically relevant strains of S. aureus, S. epidermidis and P. aeruginosa to adhere and form biofilm. Furthermore, the capability of the tested antibiotics to select for antibiotic resistance was also evaluated to confirm the safe use of the product. In order to standardize the experimental conditions, loaded or unloaded ALBC discs were produced. Microbial adhesion ability was evaluated in the first hours of contact with the discs surface and measured by colony counting, while biofilm formation was assessed after 48 hours of incubation and analyzed by confocal laser microscopy. The ability to select for microbial resistance was evaluated by serial cultures on agar plates containing gentamicin- or vancomycin-enriched discs.

Results: Vancomycin loaded cement totally impaired Staphylococcal adhesion even of those isolates showing reduced susceptibility to glycopeptides, while gentamicin resistant strain still displayed a residual adherence on gentimicin-loaded cement. In contrast, gentamicin resistant P. aeruginosa was unable to attach to gentamicin-loaded cement. Similarly, biofilm formation by all staphylococci was drastically impaired on ALBC with significantly higher mortality rates on the residual sessile cells of all the isolates, made exception for the gentamicin resistant. In none of the clinical strains was observed any stable or transient adaptation to the two antibiotics.

Conclusions: Though biofilm formation or microbial adhesion were not totally prevented for some of the clinical strains, our in vitro results indicate that the tested calcium-sulphate/hydroxyapatite bone cement is a reliable strategy for the prevention or the treatment of orthopedic infections.

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Abstract 9537

Spinal implant-associated infections: results from a four-year prospective cohort study
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Background: Spinal implant-associated infections (SIAI) are severe complications after spine instrumentation. We evaluated the clinical, laboratory, microbiological and radiological characteristics and treatment approaches in patients with SIAI.

Materials/methods: Consecutive patients with SIAI treated between 2015 and 2019 were prospectively included. SIAI was defined by: (i) significant microbial growth from intraoperative tissue or sonication fluid, (ii) intraoperative purulence, secondary wound dehiscence or implant on view, (iii) radiographic evidence of infection and fever, increasing back pain or neurologic impairment, (iv) peri-implant inflammation in histopathology.

Results: A total of 252 patients were included, 154 patients had early-onset infection and 98 patients had late-onset infection. The median age was 67 [8-90] years, 133 [53%] were females. The most common reason for spinal stabilization was degeneration in 144 patients [57%] followed by tumor metastasis in 43 [17%]. 96 patients [38%] had one or more previous spine surgeries. The site of spinal instrumentation was lumbar/sacral in 115 [46%], thoracic in 86 [34%] and cervical in 51 patients [20%]. The median number of fused segments was 3 [1–16]. Clinical manifestations included wound healing disturbance in 143 patients [57%], increasing back pain in 93 [37%], implant on view in 14 [5%], neurologic impairment in 59 patients [23%] and fever in 38 [15%]. Serum CRP was elevated in 193 patients [76%]. Most infections were postsurgical [n=247], 3 were hematogenous and 2 contiguous. Imaging showed epidural, intraspinal, paravertebral or subcutaneous abscess in 63 patients [25%], implant loosening in 38 cases [15%] and implant failure in 16 [6%]. 41/63 abscesses were present in early-onset infections and 30/38 implant loosening were observed in late-onset infections. Monomicrobial infection was observed in 148 [59%], polymicrobial in 69 [27%] and culture-negative in 33 patients [13%]. Predominant pathogens were coagulase-negative staphylococci [n=94], S. aureus [n=52] and gram-negative rods [n=45]. Surgery included debridement and implant retention in 157 patients [62%], partial implant exchange in 38 [15%] and complete exchange in 44 [17%].

Conclusions: Wound healing disturbance was the most common manifestation in early-onset SIAI whereas late-onset SIAI manifested with increasing back pain. Abscesses were found in 25 % of SIAI. The predominant pathogens were staphylococci.

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Abstract 9538

**Genetic diversity of the Plasmodium vivax circumsporozoite protein in isolates from Brazilian Amazon rainforest and Rio de Janeiro Atlantic Forest**

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**Abstract third-party references:** Supported by FAPERJ, CNPq, CAPES, DECIT and SVS/MS

**Background:** *Plasmodium vivax* is the most widespread human malaria parasite outside Africa and is the predominant parasite in the Americas. Increasing reports of *P. vivax* severity disease together with the emergence of drug-resistant strains, underscore the urgency of the development of vaccines against vivax malaria. Circumsporozoite protein is a major preerythrocyte vaccine target in *Plasmodium* species. The knowledge about their genetic diversity and population structure could help to predict the vaccine efficacy and the origin and spread of novel parasite variants.

**Materials/methods:** We investigated *pvcsp* polymorphisms in 210 isolates from endemic Brazilian Amazon (BA) and non-endemic Rio de Janeiro Atlantic Forest (AF), where the *pvcsp* diversity remains unknown, as well in imported cases from 9 non-Brazilian countries. The region flanking *pvcsp* was amplified by PCR and sequenced. The polymorphisms were analysed using NovoSNP and BioEdit software and the DnaSP and MEGA4 programs.

**Results:** The *pvcsp* sequences revealed 48 polymorphic sites: 46 affecting the central region (CR) and two affecting the C-terminal region of the encoded protein. All isolates corresponded to VK210 variant, but 25 VK210 sub-types generating 13 allotypes in repeat motif, associated with length polymorphism in nonapeptides repeats units, were disclosure. The nonapeptides allotypes ([GDRADGQPA / type 1] and [GDRAGQPA / type 2] consisting of 7 to 19 and 1 to 14 repeats, respectively, were presented in all samples. Type 10 was found in 71% of samples and type 3 in 17%. The other nine allotypes were unique from this study and appeared in low frequency and all but one of them (type 13) were detected in more than one locality. The window analysis showed a quite similar pattern of nucleotide diversity between BA and AF (x=0.052).

**Conclusions:** Our data suggest that CR was, in part, under purifying selection due to the high number of synonymous polymorphisms contributing by the fixation of the VK210. On the other hand, the CR repeat units 19 and 20 has been accumulating non-synonymous SNPs probably by an immune-modulated balance selection.

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Monitoring mosquito populations and detection of West Nile virus and Usutu virus in mosquito pools collected in Attica regional units, Greece, 2017-2018

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Background: WNV is an emerging vector-borne pathogen in Europe. WNV human cases in Greece are transmitted by Culex pipiens mosquitoes. In this study we present data on mosquito surveillance activities and detection of WNV and Usutu viruses in three Regional Units (R.U.) of the Region of Attica (East Attika, South Sector and West Sector of Athens), for the period of June 2017 to December 2018.

Materials/methods: Collection of adult mosquitoes was performed by BG-Sentinel traps (CO2, Lure), in 8 fixed sampling sites, in urban and rural locations on a weekly basis. Mosquitoes were morphologically identified to species level and only female Culex pipiens were pooled (2-200 adults). RNA extraction was performed by an automated extraction system and samples were analyzed by Real-Time PCR protocols specific for WNV and Usutu. Positive samples were subjected to conventional PCR for verification.

Results: A total of 56,654 adult mosquitoes were collected, with larger variety and number of species in the East Attica R.U. (n = 37,810), followed by West Athens R.U. (n = 9,928) and South Athens R.U. (n = 8,916). In total, 384 mosquito pools were analyzed and 46 positive samples were recorded (11.9%). 30/267 positive mosquito pools for WNV were isolated from the East Attica R.U., 8/47 in West Athens R.U. and 8/99 in South Athens R.U. All samples but one was negative for Usutu virus, however with a high Cycle threshold/(Ct) and low viral load. Conventional PCR for both pathogens verified our findings.

Conclusions: Results of this study highlight WNV circulation among mosquitoes in the Attica region in the absence of human cases during 2017 and in WNV re-emergence during 2018 and the risk for Usutu virus introduction in the country. Mosquito surveillance actions are of major importance in order to design and apply Integrated vector management programs and public health interventions.

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Abstract 9542

Outcome of infections caused by carbapenemase-producing Enterobacterales in patients with haematological disorders

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Background: The aim of this study was to evaluate outcome according to the type of infection and regimen of antimicrobial therapy in haematological patients with infections caused by carbapenemase-producing Enterobacterales (CPE).

Materials/methods: Prospective study (2014–2019) included haematological patients with CPE-infection. Genes of carbapenemases bla_{OXA-48}, bla_{KPC}, bla_{VIM}, bla_{NDM}, and bla_{IMP} were detected by real-time PCR. The outcome was evaluated at 30 days from the first episode of infection caused by CPE.

Results: A total of 58 patients with CPE-infections were included in the study (32 male, 26 female; median age 46.5 years). The prevalent underlying disease was acute leukemia (48%) and non-Hodgkin lymphoma (28%); 35 (60%) patients received chemotherapy; 14 (24%) of patients underwent hematopoietic stem cell transplantation (HSCT), 12/14 (86%) had allogeneic HSCT.

CPE-infections were attributable to blood stream infection (BSI) (n = 24; 41%), BSI + pneumonia (n = 16; 28%), pneumonia (n = 12; 20%), urinary tract infection (n = 5; 9%), cellulitis (n = 1; 2%). The majority of CPE-infections were caused by K. pneumoniae (96%), followed by S.marcescens (2%) and E.coli (2%). The majority of clinical isolates harbored bla_{OXA-48} (88%), followed by bla_{NDM} (5%), bla_{OXA-48+NDM} (3%), bla_{IMP} (3%). Overall 30-day survival was 53% (Figure a). Patients with BSI+pneumonia caused by CPE had statistically significantly lower survival compared to patients with pneumonia only (25% vs 83%, p=0.004) (Figure b).

Outcome according to the regimen of antimicrobial therapy was evaluated. Overall 30-day survival in patients treated with ceftazidime/avibactam-containing regimen was higher in comparison to patients treated with other antibiotics (67% vs 50%, p>0.05) (figure c).

Conclusions: In patients with CPE-infection most common type of infection was BSI (n = 40; 69%) caused by K.pneumoniae (96%) harboring bla_{OXA-48} gene (88%). Survival rate was 53%. Patients with BSI+pneumonia caused by CPE had significantly worse outcome in comparison to patients with pneumonia. Patients treated with ceftazidime/avibactam-containing regimen had slightly higher rates of survival.

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Abstract 9543


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Abstract third-party references: Hospitals participating in "WHOnet Greece AMR Surveillance Network"

Background: Longitudinal studies on the evolving antimicrobial resistance patterns of bloodstream isolates is crucial for assessing the progression and magnitude of the problem and evaluating the implemented interventions for its management. The aim of our study was to evaluate and compare trends in carbapenem non-susceptibility of three key Gram-negative bloodstream pathogens; Klebsiella pneumoniae, Acinetobacter baumannii and Pseudomonas aeruginosa between two 8-year periods; 2002-2009 and 2010-2017, before and during the gradual implementation of a national action plan to combat infections from these carbapenem resistant organisms.

Materials/methods: Routine susceptibility data of bloodstream isolates from 27 tertiary Greek hospitals participating in the WHONET-Greece AMR surveillance network from 2002 to 2017 was used. Dummy-variable regression was used to compare the trends of the two periods.

Results: During the first period, a significant \((p<0.01)\) increasing temporal trend was observed in the non-susceptibility of K. pneumoniae and A. baumannii bloodstream isolates to carbapenems, ranging from 0.7% to 32.6% and 16.3% to 59.3% in wards, and from 33.6% to 70.2% and 31.5% to 85.3% in ICUs respectively.

A significant \((p<0.01)\) increasing temporal trend was also observed in the second period in carbapenem non-susceptibility of K. pneumoniae and A. baumannii, which ranged from 45% to 55% and 79.7% to 94.4% in wards and from 80.8% to 86.9% and 95.3% to 98.1% in ICUs respectively. During both periods, P. aeruginosa nonsusceptibility to meropenem remained stable in wards \([2002-2009: 28.7%-28.6%; 2010-2017: 38.7%-39.7%]\), with a decreasing trend observed in ICUs \([2002-2009: 64.5%-59%; 2010-2017: 61%-50%]\). By comparing the trend slopes between the two periods, we found that for K. pneumoniae isolates, the slope decreased by 71.7% in wards \((p<0.001)\) and 79.7% in ICUs \((p=0.003)\), while for A. baumannii isolates the slope decreased by 77.8% and 94.1% in wards and in ICUs respectively \((p<0.001)\).

Conclusions: Non susceptibility of bloodstream K. pneumoniae and A. baumannii isolates to carbapenems was found to display an intertemporal increasing trend. However, the observed decrease in its slope as well as the decreasing trend in carbapenem resistance of P. aeruginosa might be regarded as consistent with the launch of the national campaign for AMR focusing both to infection control and antibiotic stewardship practices.

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Non-human primate injuries in returning travellers: implications for pre- and post-travel management

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Abstract 9548

Non-human primate injuries in returning travellers: implications for pre- and post-travel management

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Background: Non-human primates (NHPs) carry a range of zoonotic pathogens that pose risks to humans. Whilst significant human infections following NHP bites, or other injuries are rare, the consequences can be very high, especially for rabies and simian Herpes B virus infections.

The literature around NHP injury is limited. We aim to characterise the frequency and nature of NHP injury in a central London clinic for returning travellers, and identify areas to improve standards of care.

Materials/methods: We conducted a database search of records from September 2015 to March 2019 using selected keywords to identify attendances to the Hospital for Tropical Diseases (HTD) walk in service, where NHP injury was a component of the presenting complaint. NHP injury was confirmed by case note review, and data collected on country, type and anatomical site of injury, pre- and post-exposure management.

Results: 128 cases of confirmed NHP injury were identified in 11001 attending returned travellers episodes. The most common countries of injury were Indonesia (44/128, 35%), Thailand (37/128, 29%), India (10/128, 8%) other South Asian countries (14/128, 11%) (Figure 1). Bites were the most commonly reported injury (88/128, 69%), followed by scratch (38/128, 30%).

Rabies vaccine status at presentation was more reliably documented than tetanus (50% vs 24%), as was post-exposure rabies management (84% vs 24%). Of those with documentation, 16/60 were fully vaccinated. The remaining 44/60 reported partial, or no vaccination. In-country rabies management was documented in 101 patients. 77/101 (76%) patients received some form of post-exposure prophylaxis (PEP), including 12 receiving rabies immunoglobulin prior to HTD presentation. In HTD clinic, rabies PEP was administered to 90/120 patients. Consideration of Herpes B prophylaxis was rarely documented, and administered to 4 patients.

Conclusions: This data represents one of the largest returning traveller NHP injury datasets. Emphasis on prevention and management of potential NHP injuries in the pre-travel consultation is paramount, particularly for travellers to select regions, including South and South East Asia. Inconsistencies in documentation and management plans present opportunities to further protocolise the management of NHP injuries using clinical proformas and local guidelines.

Strategies for the above will be presented.

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Adaptation to host of a *Staphylococcus schleiferii* responsible of an elbow prosthetic infection

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**Background:** Prosthetic joint infections represent a devastating complication in orthopaedic surgery with heavy cost for patients in terms of life quality and for the health system because of prolonged hospitalization. These infections are considered as the typical biofilm-related infections. Coagulase negative staphylococci are the most frequently pathogens. *Staphylococcus schleiferii* was described in 1988 as a zoontic agent but in the last years it has been associated to severe infections such as endocarditis or, less frequently, prosthetic joint infections. In this study we investigated the ability of an *S. schleiferii* isolated from elbow prosthetic infection to modulate biofilm production during antibiotic treatment.

**Materials/methods:** The strain was isolated from periprosthetic tissues collected before (isolate 1) and after (isolate 2) a 5 months period of antibiotic treatment of a 66 years old male with a chronic HCV related liver disease, rheumatoid arthritis and diabetes. Biochemical identification and susceptibility testing were performed on a Vitek2 Compact (bioMerieux). MIC were further confirmed by broth microdilution test according to EUCAST procedure. To confirm strain identity, the whole genomes of the 2 isolates were compared by means of nanopore sequencing approach. Moreover, biofilm production and interference on biofilm formation by gentamicin, oxacillin, rifampicin and vancomycin at from ½ X to 8 X MIC concentrations were also evaluated.

**Results:** Both isolates were susceptible to gentamicin, oxacillin, rifampicin and vancomycin, without significant changes in MIC values. Sequencing confirmed that the 2 isolates belonged to the same strain. Significant differences were observed in biofilm production, with isolate 2 producing higher amount of biomass than isolate 1. When biofilm was put in contact with increasing gentamicin and vancomycin concentrations, isolate 2 showed a greater biomass than isolate 1.

**Conclusions:** Results of this study evidence the capability of an *S. schleiferii* strain responsible of a prosthetic joint infection to adapt to antibiotic therapy, by increasing biofilm production. The tested antibiotics exhibited a different ability to modulate biofilm production in the 2 isolates. It may be hypothesized that the ability to adapt to changed environmental conditions might be related to infection persistence.

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Abstract 9558

**Comparative effectiveness of stewardship interventions in reducing *Clostridioides difficile* infection incidence**

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**Background:** Antibiotic utilization in nursing homes is highly variable across jurisdictions in North America and Europe. The objective of this study was to quantify the comparative benefit of antibiotic stewardship strategies targeting prescribing dimensions of antibiotic initiation, duration, or selection, using real-world data on antibiotic prescribing and *C. difficile* infection risk.

**Materials/methods:** We conducted a cohort study of residents of over 600 Ontario nursing homes in the 2014 to 2017 period. We simulated antibiotic course exposures for the population corresponding to each of 4 intervention targets: (1) reducing a percentage of antibiotic initiations, (2) changing a percentage of long antibiotic courses (8-14 days) to short courses (5 days), (3) substituting a percentage of high-risk antibiotic courses for medium or low risk courses often used for the same indication, and (4) the combination of all three of these interventions. We previously developed a Poisson regression model of antibiotic-associated *C. difficile* infection risk, which estimated nursing home resident specific risk as a function of antimicrobial agent and duration of exposure. This model was used to project *C. difficile* infection incidence across Ontario as a function of intervention coverage.

**Results:** The baseline population included almost all nursing home residents in Ontario between 2012 and 2017 corresponding to 212,314 unique patients. The prevalence of antibiotic use in the prior 90 days was 27.0% in the baseline cohort. We identified 2,432 cases of *C. difficile* infection, for an incidence of 1.68 per 100,000 resident-days. Interventions targeting initiation were the most effective [incidence rate ratio (IRR)=0.973 per 10% increase in coverage, 95%CI: 0.962-0.986], followed by interventions targeting high risk antibiotic prescribing [IRR=0.986 per 10% increase in coverage, 95%CI: 0.975-0.998]; interventions targeting reductions in duration were the least effective [IRR=0.997 per 10% increase in coverage, 95%CI: 0.985-1.009]. The combined intervention that decreased all 3 target prescribing behaviors led to a 4.2% reduction in *C. difficile* infection incidence (IRR=0.958 per 10% increase in coverage, 95%CI: 0.946-0.970).

**Conclusions:** Strategies targeting reductions in antibiotic initiation have substantially larger impacts than strategies targeting antibiotic substitution or duration when it comes to *C. difficile* infection risk in nursing homes.

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Abstract 9563

**Antimicrobial stewardship and perioperative antimicrobial prophylaxis: results of an educational intervention**

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**Background:** Worldwide, perioperative antimicrobial prophylaxis (PAP) represents a major indication of antibiotic consumption. Aim of this study is to investigate inappropriateness in PAP prescription and assessing the role of an Antimicrobial Stewardship (AS) intervention in a University Hospital performing more than 40,000 surgical procedures per year.

**Materials/methods:** PAP inappropriateness was defined according to the ASHP guidelines2 and divided in four main categories: indication, duration, timing and prescribed molecule (type). In the procedures lasting longer than 4 hours, we underlined whether an adjunctive dose of antibiotic was administered or not (repeat). Between 2013 and 2019 we conducted a continuous AS intervention over 11 departments of specialised and general surgery, based on active participation of the prescribers (both surgeons and anaesthesiologists) in drafting and reviewing the local PAP guidelines. Here, we report the results of the PAP appropriateness before (baseline, April 2013) and at the end (April 2019) of the AS educational intervention.

**Results:** We collected a total of 708 PAP prescribed to 698 patients (mean age 55.6±17.7 y). The overall prevalence of PAP inappropriateness dropped, from 62.9% (n=258/410) at baseline to 32.2% (n=96/298) at post-intervention (figure 1). A significant improvement (p<0.001) between pre- and post-intervention was also detected for each category: indication (from 41.2% to 4.0%), type (from 41.2% to 16.1%), timing (from 7.6 to 2.0%), duration (from 29.5% to 15.1%). In 2019, three departments have been identified as the main drivers of the remaining SP inappropriateness.

**Conclusions:** Though results cannot be generalized to all hospital populations, participative AS interventions may be highly effective in improving PAP appropriateness rates. Once identified the main causes of PAP inappropriateness, tailored AS interventions for each department may be beneficial. Further studies are needed to evaluate specific outcomes as incidence of surgical site infections and antimicrobial resistance.

Table 1: the table reports the total number of inappropriate PAP cases observed for each category.

**Figure 1:** the table reports the total number of inappropriate PAP cases observed for each category.

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Abstracts 2020

Abstract 9564

**Economic evaluations of malaria interventions: a systematic review**

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**Background:** Although malaria is declining in parts of the world, it still claimed around 500,000 lives in 2016 and in some areas the burden of malaria has even increased. At the same time, there is a huge gap in funding of malaria interventions. Decisions on investment of scarce resources need to be based on evidence of relative costs and consequences of interventions.

**Aim:** The aim of this review is to assess the cost-effectiveness of different interventions to diagnose, treat and control malaria and to identify the interventions that provide good value for money in different settings.

**Materials/methods:** A systematic review of economic evaluations of malaria interventions that were published between 2011 and 2017 was conducted. Within a narrative synthesis the costs and effectiveness or benefit estimates were compared across different interventions, regions and types of analyses. All reported outcome measures were inflated to 2016 US$ for standardization and selected results were presented adjusted for purchasing power parity.

**Results:** 62 studies were included in this review. Rapid diagnostic testing, artemisinin combination therapies, seasonal malaria chemoprophylaxis, intermittent preventive treatment in pregnancy, insecticide-treated nets and larviciding were found to be cost-effective. Treatment with artemisinin-naphthoquine, intermittent screening and treatment in pregnancy and mass screening and treatment were not cost-effective. Indoor residual spraying and vaccination could be valuable interventions in specific settings. Lack of standardization in methodology and reporting of economic evaluations limited comparability and usefulness of included studies.

**Conclusions:** Many cost-effective interventions exist to diagnose, treat and prevent malaria. It is important to tailor malaria control policies to the local context, depending on malaria endemicity, resistance against drugs and insecticides, accessibility and coverage levels of implemented interventions.

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Abstract 9565

Severe respiratory diphtheria caused by *Corynebacterium ulcerans*: lessons learned from a rare emerging infection

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Background: *Corynebacterium ulcerans* is a zoonotic, aerobic, Gram positive bacillus which can produce diphtheria toxin and cause diphtheria. We present a case of severe respiratory diphtheria caused by a toxigenic strain of *C. ulcerans*, highlighting learning points from the case.

Materials/methods: A 76 year-old lady was admitted to hospital with difficulty breathing and swallowing following one week of sore throat and cough. She developed rapidly progressive stridor and required emergency intubation with fiberoptic laryngoscopy, which showed upper airway oedema and copious mucopurulent secretions in the nasal cavity. She was transferred to the intensive care unit (ICU), and treated with empirical broad spectrum antimicrobials for sepsis of unknown source. On day 3 of admission, *C. ulcerans* was isolated from oropharyngeal tissue collected during intubation. Following advice from Public Health England (PHE) the patient was treated with diphtheria antitoxin and the antimicrobial treatment was changed to benzylpenicillin and clarithromycin; the pharyngeal and laryngeal oedema improved. Toxigenicity of the *C. ulcerans* strain was confirmed by the PHE reference laboratory. On day 11 she developed a ventilator-associated pneumonia. She was treated for this and extubated after three weeks' admission. Contact tracing for community and healthcare contacts identified no community contacts and 39 healthcare worker contacts who had failed to wear appropriate personal protective equipment (PPE) during intubation and while the patient was ventilated on ICU. Two microbiology laboratory staff who had manipulated the *C. ulcerans* were also identified as potential contacts. All healthcare worker contacts were screened for *C. ulcerans* carriage and given prophylactic antimicrobials. They were excluded from work pending the screening results in line with PHE guidance. No healthcare worker carriers were identified. The patient had a companion dog, which was found to be negative for *C. ulcerans*.

Results: n/a

Conclusions: This case adds to the current knowledge of *C. ulcerans* as an emerging pathogen with public health implications. Learning points include: the need for improved compliance with routine infection prevention and control procedures for respiratory protection; logistics of supply and administration of diphtheria antitoxin in the UK; poor awareness of *C. ulcerans* as a cause of diphtheria among laboratory staff.

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Abstract 9566

**Cytomegalovirus reactivation in allogeneic stem cell transplant recipients: frequency, time to reactivation and dynamic of viraemia in different types of donors and in repeated episodes**

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**Background:** Cytomegalovirus (CMV) remains leading to high morbidity and mortality in allogeneic stem cell transplant (Allo-SCT). High immunosuppression increases the risk of reactivation and allows repeated reactivation episodes. However, immunosuppression varies in accordance to donor types. In this study, we compared CMV reactivation in different Allo-SCT: Related (RD), unrelated (URD), and haploidentical (Haplo) donor SCT and analyzed the dynamic of repeated CMV episodes.

**Materials/methods:** Prospective cohorts of Allo SCT (from 2013 to 2019). Patients were screened by CMV quantitative PCR (Taqman Sistem – artus CMV Qiagen) in plasma. The screening started on the first week after SCT, repeated once a week until D+100, and after D+100 if immunosuppression was maintained. Repeated episode was defined if at least two negative CMV CRP results were obtained after the first episode. The following variables were analyzed: time after SCT to reactivation, initial viral load, highest viral load within the event, duration of viremia, and response to treatment.

**Results:** There were 123 Allo-SCT performed. Median age was 47 years (ranging 1 to 70), and acute leukemia represented 63%. RD, URD, and Haplo were 72 (58%), 30 (24%), and 21 (17%), respectively. The median duration of follow-up was 251 days. CMV reactivation was documented in 84 (68%), with a median number of 2 (1 – 9) episodes per patient. RD, URD, and Haplo had similar frequencies of reactivation (64%, 70%, and 81%; p=0.33). URD-SCT had earlier reactivation than others (median D+6, versus D+37 and D+ 21 in RD and Haplo, p<0.001). A total of 192 CMV reactivation episodes were analyzed: 100 in RD, 55 in URD, and 37 in Haplo. Haplo-SCT reached the highest viral loads (median of 1070 copies/mL vs., 373 and 163 copies/mL in RD and URD-SCT; p=0.036). First CMV reactivation episode reached higher viral load (median 1897 vs. 143 copies/mL; p<0.001) and longer viremia (median 28 vs. 14 day; <0.001), compared with repeated ones.

**Conclusions:** Reactivation of CMV occurred with different dynamics by SCT donor type and in the first or repeated episode. Treatment and preventive strategies should be adapted, considering these different scenarios.

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Abstract 9571

**Trichomonadine association with Pneumocystis jirovecii: a retrospective study**

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**Background:** Pneumocystis pneumonia (PCP) is a serious condition caused by *Pneumocystis jirovecii* in immunocompromised patients. Human trichomonesis, caused by trichomonadines, is mainly represented by sexually transmitted infections, caused by *Trichomonas vaginalis*. However, the presence of trichomonadine has been described several times at the pleuropulmonary level and an association with PCP has recently been demonstrated. We thus studied the prevalence of detection and the diversity of trichomonadine species as well as the risk factors favoring the unusual presence of the parasite at the pulmonary level from the respiratory samples of patients with detection of PCR-positive *Pneumocystis jirovecii* DNA.

**Materials/methods:** Our retrospective study, over a period of 12 years in Reims, northern France included 349 patients with positive *Pneumocystis jirovecii* real-time PCR. The presence of trichomonadines on respiratory samples was screened using primers targeting rRNA. Positive samples were sequenced to allow species identification.

**Results:** At first, it allowed us to describe the local epidemiology of PCP. Our local analysis verifies the data from the literature. In a second step, the trichomonadine research by PCR has shown that the detection of the parasite at the pulmonary level is not anecdotal (12%) and that it is more frequently present in patients with HIV (p < 0.0001) and hypoxemic (p < 0.026). The species identified are not limited to *Trichomonas tenax*, commensal of the oral cavity, since we found in particular a new species associated with empyemas: *Tetratrichomonas empyemagena*. Our results also demonstrate a correlation between trichomonadins and the presence of numerous *Pneumocystis jirovecii* cysts on direct examination (p = 0.0008).

**Conclusions:** The pathogenic potential of trichomonadines, however, remains unclear and further studies are needed.

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Abstract 9575

**Clinical and financial impact of an empiric antibiotic prescribing policy: single department experience**

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**Background:** The development of local suited protocols is a useful tool to help improving the judicious use of antibiotics, which is primordial to face the challenge of antibiotic resistance. This study aims to evaluate the clinical outcomes of mortality, clinical and microbiologic failure of a single department Empiric Antibiotic Prescribing Policy (EAPP) and to assess the financial impact resulting from its application.

**Materials/methods:** An EAPP was developed for the most prevalent infections considering clinical practice guidelines and local microbiology data. Clinical data of 159 consecutive empiric antibiotics prescriptions after the application of the EAPP, from March 1st to July 31st 2019 was collected and analyzed prospectively. A control group constituted by 234 empiric antibiotic therapy prescriptions in patients admitted in the same department, over the same period of time in 2018 was analyzed retrospectively.

**Results:** Compliance with the EAPP reached 86.2%. The use of broad-spectrum antibiotics as Piperacillin/Tazobactam and Carbapenems was reduced from 25.2% in the control group to 4.4% after the EAPP (p<0.001). No significant change in mortality occurred between the two groups. The median length of antibiotic use was reduced from 7 (±2.8) to 5 (±1.5) days (p<0.001) and the duration of hospitalization from a median of 8 [IQR 5-18] to 7 [IQR 4-10] days (p<0.001). Oral therapy was increased to 52.2% from 21.4% in the control group (p<0.001). Although EAPP advocated the use of narrower spectrum schemes, clinical failure was reduced from 19.7% to 10.1% (p=0.013). There was a reduction in the percentage of multiresistant bacteria isolated (34.3% vs 26.4%), although this was statistically non-significant. The total expense with antibiotics of the department decreased from €11917 (€53.90 per patient) to €6543 (€27.50 per patient).

**Conclusions:** The antibiotic schemes from the EAPP and duration of therapy proposed for each condition proved to be effective and safe. The authors believe that the clear definition of failure criteria helped reducing the wide spectrum antibiotic prescriptions by preventing early escalation in cases which proved to evolve favorably with the EAPP recommended option. We believe the EAPP is a valuable tool to curb inadequate antibiotic use and therefore reduce induction of resistance.

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Abstract 9588

Carbapenemase-producing *Pseudomonas aeruginosa* in south Brazil
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**Background:** Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) is an important pathogen of hospital infection associated with increased morbidity and mortality rates. The resistance in *P. aeruginosa* to carbapenems is up to 70% in some Brazilian hospitals. Different mechanisms may contribute to carbapenem resistance in *P. aeruginosa*. Although, the carbapenemases production, mainly the metallo-β-lactamases (MBLs), is the most important because its hydrolyzes almost all clinically-available β-lactams antibiotics and are often carried on transferable structures as plasmids. This study aims to report the prevalence of carbapenemases types in CRPA collected in different hospitals in the South of Brazil.

**Materials/methods:** The study included 557 clinical unique strains of CRPA from inpatients by different hospitals on Paraná (225) and Santa Catarina (332) states located in the South of Brazil, collected between January 2011 and October 2017. The *blaSPM*, *blaIMP*, *blaVIM*, *blaGIM*, *blaNDM*, and *blaKPC* carbapenemases genes were assessed by multiplex real-time PCR (qPCR) following previously reported conditions.

**Results:** The strains were isolated from bronchoalveolar lavage (50), tracheal aspirate (130), blood (90), sputum (20), cerebrospinal fluid (7), ascitic fluid (1), pleural fluid (1), peritoneal fluid (5), synovial fluid (1) and urine (252). A hundred ninety (32.9%) out of the 557 CRPA isolates recovered from clinical specimens were carbapenemase producers. The *blaSPM* gene was found in 131 (22.7%) isolates, followed by *blaKPC* in 33 (5.7%), *blaIMP* in 15 (2.6%) and *blaVIM* in 11 (1.9%).

**Conclusions:** In Brazil, SPM remains the predominant carbapenemase in *Pseudomonas aeruginosa*. However, other carbapenemases have emerged including KPC which has exceeded the IMP and VIM types in this study.

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Listeriosis in Ávila, Spain: a real warn amongst immunocompromised hosts

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Background: Listeriosis is an uncommon but potentially serious foodborne infection caused by Listeria monocytogenes. It generally affects elderly people, pregnant women and immunosuppressed hosts, and is an increasingly life-threatening disease, crossing the intestinal barrier, the placenta and the blood-brain barrier producing gastroenteritis, maternal-fetal infections and meningoencephalitis. It is most commonly diagnosed from a positive culture of a sterile site. The treatment of choice includes the use of intravenous ampicillin alone or in combination with gentamicin.

Materials/methods: a marked increase in reported cases of listeriosis during 2019 in Spain motivated a retrospective survey in our Institution (Hospital Nuestra Señora de Sonsoles, Ávila, Spain). We retrospectively describe the epidemiological patterns and trends of this serious infection among patients diagnosed in our province, Ávila, Spain, from 2002 through 2019.

Results: overall, 31 cases were identified; the majority of them were admitted to the Internal Medicine Department (15/31, 48.4%) and were from rural settings (18/31, 58.1%).

Blood stream infection was found in 26/31 patients – 83.9%.

The most common clinical syndromes in these patients were primary bacteremia (13/31, 42%) and meningitis or meningoencephalitis (9/31, 29%); the latter, all with signs of romboencephalitis, mononeuritis or cranial nerve palsy. Surprisingly, we did not find any perinatal, nor neonatal cases in our records. Other clinical presentations were as follows: bacteremic pneumonia (3/31, 9.7%), bacterial peritonitis (2/31, 6.5%), and 1 case of complicated diverticulitis, spondylodiscitis, arthritis and abdominal abscess (1/31, 3.3% each).

In general, 17 patients deceased (54.8%), and listeriosis related mortality accounted for a 38.7% of the patients (12/31), the rest being related to concomitant illnesses (5 patients, 16.1%, all with different kinds of cancer).

Most of the 31 cases involved immunocompromised patients (27/31, 87%), mostly due to malignancies (18/31, 58.1%), and overlapping in some cases with chronic liver disease (5/31,16.13%), chronic renal failure (7/31, 22.6%), or diabetes mellitus (9/31, 29%).

Only 1 patient was not treated. He deceased from non-Hodgkin lymphoma complications. All the rest received specific antibiotics.

Conclusions: our study shows a higher trend regarding the epidemiology of listerial infections. Immunosuppressed patients are at the highest risk of developing listerial serious infections and death, especially those with malignancies.

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Abstract 9593

Genomic epidemiology of NDM-producing Enterobacteriaceae in Portuguese hospitals

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Abstract third-party references: National NDM-study group

Background: New Delhi metallo-β-lactamase (NDM)-producing Enterobacteriaceae were rarely identified in Portugal, with the first case reported during an NDM-1-producing Providencia stuartii outbreak, in 2014/2015. The aim of this study was to analyze the whole genome sequence (WGS) and resistome of NDM-producing Enterobacteriaceae strains referred to the Laboratory of Antibiotic Resistances and Healthcare Associated Infections, at National Institute of Health Dr Ricardo Jorge from 2016 onwards.

Materials/methods: WGS was performed on a MiSeq Illumina platform. INNUca was used for quality control of reads, de novo assembly and contigs quality assessment. Prokka and ABRicate were used for genome annotation and screening for antimicrobial resistance and/or virulence genes, respectively. Phylogenetic inference was performed with chewBBACA pipeline, using the core genome MultiLocus Sequence Typing (cgMLST) schema. The evolutionary relationship was accessed by Minimum spanning trees (MST) using the PHYLOViZ.

Results: During the study period, 28 Enterobacteriaceae isolates (11 Klebsiella pneumonia, 6 Providencia stuartii, 6 Escherichia coli, 3 Enterobacter cloacae, 1 Klebsiella oxytoca and 1 Proteus mirabilis) collected in eleven different Portuguese hospitals, were included in the study. From those, 23 were NDM-1 producers while 5 were NDM-5-producing E. coli. The results obtained demonstrated the diversity of genetic structures associated with blaNDM-type gene, including: (i) host bacterial specie; (ii) plasmid types and associated mobile genetic elements; and (iii) blaNDM variants.

Conclusions: In conclusion, the emergence and spread of NDM-producing Enterobacteriaceae in Portugal has been driven by multiple mechanisms. Indeed, genomic and epidemiological data can yield a useful map of an outbreak and facilitate the control of nosocomial transmission.

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Abstract 9594

First description of GES-20-producing Pseudomonas aeruginosa in Brazil
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Abstract third-party references: Fundação de Amparo à Pesquisa do Estado de São Paulo, Fleury Medicine and Health

Background: Pseudomonas aeruginosa is a major agent of healthcare-related infections worldwide. Empirical treatment of serious infections caused by this species usually includes carbapenems. Carbapenemase production is the most efficient resistance mechanism and molecular detection can aid in faster antimicrobial therapy adjustment. Consequently it is important to know the local molecular epidemiology.

Materials/methods: Eleven carbapenem-resistant nosocomial P. aeruginosa isolates able to hydrolyze imipenem in spectrophotometric assay but negative for known carbapenemase genes had the full genome sequence determined. Isolates were collected from private hospitals located at the city of São Paulo, Brazil. Genomic DNA extraction was performed using the Illustra Bacteria Genomic Prep Mini Spin Kit before libraries were prepared using the Nextera XT DNA Library Preparation kit. DNA sequencing was performed using the MiSeq reagent kit v3 150 cycles. De novo assembling was performed using the Geneious software. Resistance genes were detected using CARD/RGI. MLST type was determined analyzing the contigs at the PubMLST homepage. Imipenem and meropenem MICs were determined according to the EUCAST guidelines.

Results: Four isolates belonged to ST277, three belonged to ST1560 and one of each belonged to ST224, ST309 and ST313. A single isolate had a new MLST pattern designated ST3187. The isolate pertaining to ST309, had the GES-20 carbapenemase and the GES-19 ESBL. All other isolates were negative for known carbapenemase genes, but had three different types of OXA-50 variants with similarities varying 98.85 to 99.62%. These isolates had imipenem MICs ranging from 8 to 32 mg/L. The isolate expressing GES-20 was recovered from the urinary tract of a patient with nephrolithiasis in July 2013. The blaGES-20 gene was found to be located in a class 1 integron flanked upstream by the blaGES-19 ESBL and downstream by the aacA4 aminoglycoside resistance gene [Figure]. The integron is identical to the In724 described in Mexico, except that qacH gene is absent. The isolate expressing GES-20 had imipenem MIC > 32 mg/L and meropenem MIC > 128 mg/L.

Conclusion: This is the first description of GES-20 from Brazil. Our preliminary findings concerning OXA-50 variants indicate that these variants may be implicated in imipenem resistance in P. aeruginosa.

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Abstract 9595

**Evolution of awareness and knowledge of congenital cytomegalovirus infection among healthcare providers in France between 2011 and 2018**

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**Background:** Cytomegalovirus (CMV) is the first cause of congenital viral infection, concerning 1% of newborns, of whom 10% have major symptoms. Antenatal and postnatal treatments, although promising, are still under evaluation. The importance of hygiene counselling to prevent CMV infection is established and should be systematic. Our objective was to evaluate health care providers’ awareness of CMV maternal and congenital infection in France.

**Materials/methods:** A questionnaire was sent in 2018 by e-mail to obstetricians, pediatricians, midwives and laboratory physicians, members of medical or midwives’ associations. We evaluated their knowledge concerning CMV epidemiology, transmission, symptoms in adults, newborns and long-term effects. Scoring was based on 30 points. We then compared the results to a previous study of our group published in 2012.

**Results:** The questionnaire was completed by 597 respondents. Most of them (91%) were unaware of the precise transmission route of CMV. One third (33%) was wrongly convinced that in utero therapy for congenital CMV infection was standard of care in France at the time of the study. Recommendations of HAS (Haute Autorité de Santé) and CNGOF (Collège National des Gynécologues et Obstétriciens Français) were known by less than half of the respondents. However the majority of the respondents correctly answered more than one half of the questions. The better their knowledge of CMV, the better was the hygiene advice given to patients. Between 2011 and 2018 we note an improvement in knowledge for the doctors and the midwives concerning the routes of transmission, symptoms in adults and the long-term effects of CMV infection.

**Conclusions:** This study shows an improvement in knowledge among healthcare providers, but there are still gaps. To bridge these gaps, health care providers should improve their knowledge about congenital CMV by various means: medical reviews, continuing medical education, meetings, conferences, the internet. Moreover, better knowledge will allow for better information for pregnant women as recommended by HCSP and CNGOF in France.

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Abstract 9596

**eHealth-based antimicrobial stewardship programme focused on individual prescriptions assessment: sustainability at 4 years**

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**Background:** Assessment of individual antibiotic prescriptions are a pillar of Antimicrobial Stewardship Programs as 30 to 50% of all worldwide antibiotic prescriptions are inappropriate and are the main drive for antibiotic resistance, a Public Health problem. eHealth is a major tool for ASP activities. Authors present the results of the first four years of an eHealth-based innovative solution that includes new order forms, automated pop-ups and emails, whenever antibiotics are conditioned or are in disagreement with local recommendations, allowing analysis and interventions directed to the physicians in charge of the patients. In this way, both back-to-end [audit and feedback] and front-to-end [conditioning] strategies are adopted, being complemented by education, awareness and feedback information about consumption.

**Materials/methods:** For the purpose of this work, evaluation of ASP activities are based on antibiotic consumption of relevant antibiotics as defined by ECDC/EFSA and EMA, expressed as Defined Daily Doses (DDD), obtained from the Pharmacy and administrative software. No other information, such as patient outcome, length of stay, bacterial resistance pattern or economic evaluation, is considered.

**Results:** Since full implementation of ASP activities (January 2015), relevant variations are as follows: Ertapenem -66%; Ceftriaxone -55%; Ciprofloxacin -57%; Meropenem -52%; Levofloxacin -49%; Colistin +250%. Reductions were most accentuated in the first year of interventions, were in the desired direction and have been maintained throughout the time. Some observed variations are the result of local bacteria incidence or the implementation of new therapeutic strategies.

**Conclusions:** Implementation of an eHealth-based ASP for assessment of individual prescriptions had a huge impact on the profile of antibiotic prescription, which is maintained after 4 years of full activity. Long-term sustainability of ASP is a challenge requiring combination of factors where a combination of eHealth, real-time continuous conditioning and audit and feedback of individual prescriptions, as well awareness and education are essential.

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Abstract 9599

**The burden of chronic pulmonary aspergillosis on the respiratory service at a district general hospital**

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**Background:** Wigan is a town located 17 miles North West of The City of Manchester with a population just over 325,000. It was known as major mill town and coal mining district and is covered by Wigan Infirmary, a district general hospital (DGH) with 513 beds.

A recent report from the National Aspergillosis Centre (NAC) based in Manchester, UK; highlighted Wigan as the home of the highest number of referrals with Chronic Pulmonary Aspergillosis (CPA) with 63 patients of 522 (12%) under active follow up. This was a significantly higher case burden than expected for a DGH that warranted further investigation.

**Materials/methods:** A retrospective analysis of electronic case-notes of all patients admitted to Wigan Infirmary with a diagnosis of CPA or invasive pulmonary aspergillosis (IPA) within a six-year period from January 2013 to December 2018. We also reviewed the case-notes of all the outpatients diagnosed with CPA and referred to the NAC during this period.

**Results:** Patients were diagnosed with CPA and classified according to the ESCMID guidelines. 41 patients were admitted during this period, 37 with CPA and 4 with IPA. 78 were diagnosed with CPA as outpatients and received treatment at the NAC.

Overall, 63% had COPD, 85% had a smoking history of >10 pack years. 68% of patients had been treated with inhaled steroids. 87% of patients lived in postcodes in the most deprived 50% of areas for health and disability according to the 2015 English Indices of Deprivation, with 24% of patients living in the most deprived areas.

Mortality was high, 21% of inpatients died before they could be referred to the NAC. 43% of outpatients with CPA died by the time of the analysis.

**Conclusions:** The burden of pulmonary aspergillosis is higher than expected in the Wigan area with an estimated prevalence of 35/100,000 population, compared with the estimated national burden of 5.7/100,000. The reasons for the raised burden are unclear, but probably health deprivation, a high prevalence of chronic lung disease and smoking related morbidity and mortality are factors. Further comparative studies from similar populations are required to understand the burden of CPA further.

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Abstract 9600

A systematic evaluation of the anti-plasmodial activity of low molecular weight heparin against human malaria parasite Plasmodium falciparum

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Background: Despite the global effort to decrease mortality and morbidity, malaria still causes 435,000 deaths and more than 200 million infection cases according to World Health Organization report 2018. Plasmodium falciparum is the most lethal malaria parasite among other malaria spp, and account the majority of malaria death cases. Antimalarial drug resistance has emerged in many affected areas, representing the hallmark malaria treatment delay and failure. Pfalciparum drug resistance has been reported to all known antimalarial therapies. There is high demand to develop a new approach to face antimalarial drug challenge. Heparin has shown anti-plasmodial activity by inhibiting Pfalciparum growth via blocking merozoite invasion into erythrocyte. This activity seems to be mediated by interfering with major merozoite surface (MSPs), resulting in merozoite failure to invade the erythrocyte and establish a new life cycle. Heparin has been used clinically to treat patients with malaria infection, but due to its highly anticoagulation activity, heparin has been halted to be used as an adjunct therapy. Whilst heparin and other heparin mimetics their growth inhibition activity has been evaluated, a systematic exploration of this activity of range of Low Molecular Weight Heparins (LMWHs) has not. In this study, a systematic side by side comparison of the in vitro growth inhibition of commercial LMWHs are explored. In addition, exploration of using LMWHs as adjunct therapy has been evaluated.

Materials/methods: Growth inhibition and invasion blocking activity of LMWHs are determined using standard growth inhibition assay by Flow cytometry using two distinct parasite clones. The invasion blocking activity of LMWHs is determined by light microscopy. All experiments were done as technical triplicate in three biological repeats (n=9). All anti-plasmodial activity of LMWHs has been compared with unfractionated heparin.

Results: LMWHs showing anti-plasmodial activity by blocking merozoite invasion to the erythrocyte in two Pfalciparum clones. This activity is correlated with the molecular weight and chain length of LMWHs

<table>
<thead>
<tr>
<th>Compound</th>
<th>Mean EC_{50} (µg/ml)</th>
<th>Mean MW kDa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heparin</td>
<td>5.6-9.1</td>
<td>&lt;15</td>
</tr>
<tr>
<td>Dextran sulphate</td>
<td>12.3-22.3</td>
<td>&lt;15</td>
</tr>
<tr>
<td>Sevuparin</td>
<td>5.2</td>
<td>8</td>
</tr>
<tr>
<td>Tinzaparin</td>
<td>39.8-55.5</td>
<td>6.8</td>
</tr>
<tr>
<td>Dalteparin</td>
<td>39.5-47.5</td>
<td>6</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>64.1-83.3</td>
<td>4.2</td>
</tr>
<tr>
<td>Reviparin</td>
<td>80.9-87.5</td>
<td>3.9</td>
</tr>
</tbody>
</table>

Conclusions: LMWHs offer base for development LMWHs with high growth inhibition and low coagulation activity to support the effort in malaria eradication and elimination

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Abstract 9601

Unexpected low antibiotic resistance of *Klebsiella* spp. isolated from children’s faeces, water samples, soil and animals from Andean rural homes in Cajamarca, Peru

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**Background:** The dissemination of multidrug-resistant strains (MDR) with a potential to express resistance to multiple drugs represents a threat of dissemination in the community. Reports of MDR strains in livestock populations, the environment and the community demonstrate that the transmission and persistence of these bacteria also occur outside the clinical setting. This study aimed to identify *Klebsiella* spp in feces of children under six years and samples of water, soil and animals from wells, and establish their level of antimicrobial resistance.

**Materials/methods:** The study was located in the provinces of San Marcos and Cajabamba in Cajamarca, with altitudes between 2,200 and 3,900 m above sea level. Samples of children's feces (stored in Cary Blair), water, soil and animals (rectal swabs) were collected from households (n=40) in rural areas. The water samples were analyzed for thermotolerant (fecal) coliforms using the membrane-filtration method and the soil samples were enriched with LB Broth. *Klebsiella* spp isolates were obtained after seeding water samples positive for enterobacteria and identified using chromogenic and conventional media following standard methods. The antibiotic resistance pattern of *Klebsiella* was determined against 14 antibiotics by disk-diffusion method according to the guidelines of the Clinical and Laboratory Standards Institute.

**Results:** Of 200 samples, 253 coliforms were isolated and 11% (28/253) were identified as *Klebsiella* spp, 67.86% (n=19) *K. pneumoniae* and 32.14% (n=9) *K. oxytoca*. The isolates only displaying unexpected lower levels of resistance high levels of resistance to all tested antibiotics. Only 5 (17.86%) were no susceptible to ciprofloxacin [3 resistant and 2 intermediate], of these only 2 isolates showed intermediate resistance levels to nalidixic acid, while suggests the presence of transferable mechanisms of quinolone resistance unable to confer resistance to nalidixic acid. Finally 3 isolates in, addition to ampicillin resistance, displaying at time resistance to cotrimoxazol and tetracycline, and other 2 showed resistance to cefoxitin and amoxicillin plus clavulanic acid. No isolate showed resistance to the remaining tested antibiotics.

**Conclusions:** There is evidence of low antibiotic resistance of *Klebsiella* spp isolated from children, water, soil and animals in Cajamarca, Peru.

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Big data analysis of all bacterial genomes establishes a triple whammy of carbapenemases, ICEs and multiple clinically-relevant bacteria

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Background: Carbapenemases inactivate most β-lactam antibiotics, including carbapenems, and have been frequently reported among Enterobacteriaceae, Acinetobacter spp. and Pseudomonas spp. Traditionally, the horizontal gene transfer of carbapenemase-encoding genes (CEGs) has been linked to plasmids. However, given that integrative and conjugative elements (ICEs) are possibly the most abundant conjugative elements among prokaryotes, we conducted an in-silico analysis to ascertain the likely role of ICEs in the spread of CEGs among all available bacterial genomes.

Materials/methods: All RefSeq bacterial genomes available in NCBI were downloaded (n=107,887) and blasted against a local database of 688 carbapenemases using diamond v0.9.25. The CEG-bearing genomes were annotated with prokka v1.14.0, and the GenBank files were used as input to mine ICEs on the standalone version of ICEfinder. Hits corresponding to putative plasmids were excluded from the following analyses. The translated coding sequences of extracted ICEs were analyzed on the standalone CONJscan module of MacSyFinder v1.0.5 to predict MPF families. To identify the multi-locus sequence type of each CEG-bearing ICE, we used mlst v2.16.1. Associated mobile genetic elements were annotated using GalileoTM AMR. Among the ICEs, we also search for antibiotic resistance genes [amrfinder v3.2.3], bacteriocins, ribosomally synthesized and posttranslationaly modified peptides [Bagel4], restriction-modification systems [REBASE], and CRISPR arrays as well as their associated [Cas] proteins [CRISPRCasFinder].

Results: We detected 7457 CEGs, of which 118 were located within putative ICEs among several clinically-relevant bacterial species [including Klebsiella pneumoniae, Escherichia coli, Citrobacter freundii, Enterobacter hormaechei and Pseudomonas aeruginosa]. We also identified a Bacillus subtilis strain with an NDM-1-encoding ICE. Most CEGs detected within ICEs belong to the KPC, IMP, and NDM families and different mechanisms were likely responsible for the acquisition of these genes. The majority of CEG-bearing ICEs belong to the MPF2, MPF6, and MPF6 classes and often encode additional adaptive traits such as resistance to other antibiotics [e.g., aminoglycosides and fluoroquinolones], restriction-modification systems and bacteriocin production.

Conclusions: This study provides a snapshot of the different CEGs associated with ICEs among all bacterial genomes and sheds light on the underappreciated contribution of ICEs to the spread of carbapenem resistance globally.

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Oral empiric antibiotic treatment given in an ambulatory setting for febrile neutropenic patients with a solid tumour, predicted at low-risk for serious complication

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Background: Evaluation of the safety and feasibility to discharge patients with febrile neutropenia assessed by MASCC score, as low risk patients, after a preliminary evaluation in the emergency room.

Materials/methods: Prospective study in a single oncology hospital, in all adults with febrile neutropenia (FN) induced by chemotherapy and/or molecularly targeted therapy for solid tumors. Patients assessed as low risk, eligible for oral antibiotic, such as moxifloxacin, were discharged from the emergency room, after a clinical exam, consideration of psycho-social environmental criteria, initial laboratory and microbiological tests, chest X-ray and a first dose of antibiotics. A follow up at consultation, reassessed the patients in order to readjust the treatment, if needed. The primary objective was the resolution of febrile neutropenia without serious complications.

Results: Out of 160 episodes of febrile neutropenia at low risk for complications [Intention To Treat:ITT] presented in the emergency room, between October 2008 and July 2014, 118 were included [modified Intention To Treat: mITT] in the study. They did not have any severe complications, but 5.08% needed admission. The rate of successful response to the empirical treatment was 87.29%, while the risk to develop adverse events was 7.6% and further infections was 6.78%.

Conclusions: The study shows that the immediate discharge and the oral empiric antibiotics in an outpatient treatment, in febrile neutropenic episodes, was feasible and safe for carefully selected patients.

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Abstract 9614

Prevalence and susceptibility profile of Corynebacterium glucuronolyticum in semen cultures

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Background: Corynebacterium glucuronolyticum (CG) is a rare species isolated from male patients with genitourinary tract infections, probably being part of the normal male genitourinary microbiota that is only recently being acknowledged as a potential pathogen, most often implicated in cases of urethritis and prostatitis in men. Thus, different research groups have contributed by highlighting its important role in non-gonococcal urethritis in men, in chronic bacterial prostatitis (CBP); in the pathogenesis of persistent cystitis in males without predisposing factors and its adverse influence on various laboratory parameters of semen. The aim of this study is to analyze the prevalence and antimicrobial susceptibility of CG in semen cultures in Alava, (North of Spain, Basque Country) over the last 2 years.

Materials/methods: Between 2017 and 2018 semen specimens were inoculated on Columbia Blood Agar supplemented with colistin and nalidixic acid and PVX chocolate agar (bioMerieux®, France) and incubated at 37 °C aerobically under 5% CO₂ atmosphere. A significant growth (>1 × 10⁴ CFU/mL), as a pure culture, on blood-containing media of an organism producing, tiny, white-yellow, non-hemolytic colonies of about 1.5 mm of diameter-sized, that grew better after 48 h. The colonies were catalase positive, identified as CG by MALDI-TOF® (Bruker Daltonics, Germany). Agar disk diffusion test performed according to the EUCAST guidelines.

Results: 40 of total of 1177 screened semen specimens, a total of 3.39% patients aged between 20 to 73 (mean age 45.1) had CG as a single isolate in significant quantities. 57.14% showed resistance to ciprofloxacin, 15.38% tetracycline, 10.53% gentamicin, 72% erythromycin, and 82.35% to clindamycin but all isolates were susceptible to penicillin, vancomycin, linezolid and rifampicin. Individuals with CG isolates, 25% have a diagnosis of infertility, 7.5% hematospermia, 15% prostatitis and different diagnosis 57.5%.

Conclusions: All C. glucuronolyticum strains are susceptible to penicillin, vancomycin, linezolid and rifampicin but quinolones, tetracycline, macrolides and lincosamides must be tested because of trend towards resistance. Although C. glucuronolyticum is not frequently isolated in clinical genitourinary samples, its potential pathogenicity has been demonstrated; we suggest therefore to consider the organism in the differential diagnostics of bacterial diseases of the urinary tract.

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Abstract 9621

**Evaluation of the antifungal stewardship programme at St George's Hospital, London 2018-19**

Angela Natalee Rusdiah1, Ting Yee Yau2, Clare Logan1,2, Tihana Bicanic1,2

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**Background:** Antifungal stewardship (AFS) has risen to prominence with outbreaks of multi-drug resistant Candida auris and national incentives in England. St George’s introduced AFS in 2010, demonstrating reduction of inappropriate prescribing without compromising clinical outcomes and resistance rates in a published evaluation from 2010-16.

**Materials/methods:** From October 2018-November 2019, adult inpatients receiving treatment with Amphotericin B, echinocandins or azoles [except oral prophylaxis] were reviewed in a weekly ward round by an Infectious diseases consultant and Antimicrobial Pharmacist. Patient demographics, antifungal drug and duration, invasive fungal infection (IFI) risk factors and final EORTC diagnostic classification, use of biomarkers, stewardship advice, length of hospital stay and inpatient mortality were prospectively recorded.

**Results:** 109 patients (55%M) median age 58 had a total of 179 antifungal courses reviewed. Common IFI risk factors were broad-spectrum antibiotic exposure (78%), central line (38%), haemato-oncological disease (28%), critical care (19%), abdominal surgery (16%) TPN (16%).

Prescriptions reviewed were echinocandins in 26%, Ambisome® and IV fluconazole IV (19% each). Rationale for prescribing was targeted in 35%, empiric in 25%, pre-emptive in 10% and prophylaxis in 29% of episodes. 160 recommendations were made, commonly further investigations (30%), antifungal switch or de-escalation (27%) and duration of therapy (14%).

Of those receiving targeted antifungals, 73% ultimately had proven/probable/possible IFI. Implementation of on-site weekly beta-D-glucan testing in May 2019, midway through this evaluation, reduced median laboratory turnaround-time to 9d (overall for 2018-19) compared to 12d for 2010-16. Inappropriate antifungal prescribing decreased: the proportion of patients receiving empiric or pre-emptive antifungal therapy who ultimately had no IFI on EORTC criteria was 52% for 2018-19: significantly reduced compared to two periods 2010-16 and 2016-18 when 75% of patients had no IFI (p=0.038, chi square test).

Median[IQR] length of stay was longer for patients with proven/probable/possible IFI: 37(25-53) v 27 (15-48) days in those with no IFI (p=0.4). Overall in-hospital mortality was 22%, compared to 28% in 2010-16 (further subgroup analyses and statistical comparisons of LOS, mortality and antifungal treatment duration by prescribing indication will be presented).

**Conclusions:** Recent implementation of in-house BDG biomarker testing has resulted in further reductions in inappropriate antifungal prescribing without compromising on clinical outcomes.

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Neutrophilia is associated with lung tissue damage in pulmonary tuberculosis

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Background: Tuberculosis remains a major cause of morbimortality in low-middle income countries such as Brazil. Regardless of anti-tuberculous treatment (ATT), in some patients the infection is countered at the expense of great tissue destruction and pulmonary sequelae. Despite its chronic evolution, the role of neutrophils is crucial in the immune response against Mycobacterium tuberculosis. These cells become strong producers of proteinases, reactive oxygen species and extracellular traps (NETs), which are related to tissue damage and bacteria growth in different infections. This study aimed at understanding the possible mechanisms of tissue damage in TB and underlying biomarkers of poor prognosis during ATT.

Materials/methods: The study enrolled a cohort of 325 presumed pulmonary TB cases in Rio de Janeiro, Brasil. Chest radiographs (CXR), blood count, results of inflammatory markers (C-reactive protein - CRP, erythrocyte sedimentation rate - ESR, ferritin and albumin), smear microscopy (AFB) and sputum culture were obtained before (T0) and after 60 (T60) and 180 (T180) days of treatment. Subjects were classified as TB or RS (respiratory symptomatic) based of AFB or sputum culture. The groups were compared using univariate analysis performed in GraphPad Prism v6.0.

Results: TB patients showed higher counts of neutrophils (figure 1-A) and platelets, and lower lymphocytes when compared with RS patients (p ≤ 0.001). CRP, ESR and ferritin levels were higher in TB patients, while albumin was lower, when compared to RS. TB patients with neutrophilia had higher mycobacteria load and number of cavitations (figure 1-B), and bilateral disease (figure 1-C). Additionally, TB patients with neutrophilia showed more persistence of positive culture after 60 and 180 days of ATT (figure 1-D). 69.8% of TB patients with neutrophilia on T0 did not show improvement on radiological images after 180 days of treatment.

Conclusions: Our results suggest that a neutrophil-mediated hyperinflammatory response aggravate lung tissue damage and may contribute to poor prognosis and treatment failure. The identification of this inflammatory profile may enable early intervention with adjuvant therapies aimed at controlling tissue damage.

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Abstract 9626

**Structural study of new KatG mutations selected on isoniazid-resistant strains of *Mycobacterium tuberculosis* in vivo**

Andra-Cristina Bostanaru*1, Mihai Mares2

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**Background:** In the course of this study, we identified new mutations in the KatG, the role of which has never been characterized before. For these mutations, structural and biochemical studies have been undertaken to establish their contribution in resistance to isoniazid (INH).

**Materials/methods:** katG genes coding for the wild-type protein and six new mutants A162E, D189G, H270R, Q461P, G494D and F658V have been included in this study. Expression and purification of KatG in *Escherichia coli* was carried out by cloning the katG genes in the pET30 expression vector. The crystal structure of the *M. tuberculosis* KatG protein (Zhao X., code-PDB 2CCA) was used to model the position and the consequences of the new mutations in the KatG.

**Results:** The KatG protein contains a covalently bound heme surrounded by a proximal and a distal pocket. Of all the mutations studied, H270R, which was identified in a clinical strain of high level of INH resistance (INH-R), appears to be of great interest since H270 is part of the proximal pocket and is covalently linked to the heme. Thus, H270R causes loss of the covalent bond linking the heme and, consequently, of the catalytic activity of KatG. The mutation A162E, linked to a high level of INH-R, is located in a alpha-helix situated close to the distal pocket and creates steric hindrance in this region. Two others mutations (F658, Q461P), found in strains showing a low level of INH-R, are located in alpha-helices positioned far from the heme. F658V leads to steric hindrance, while Q461P likely contributes to the destabilization of the alpha-helix secondary structure. Finally, D189G and G494D, conferring low and high-level of INH-R, respectively, modify the pattern of ionic interactions in regions located far from the heme pocket, and their role in the KatG protein is less obvious.

**Conclusions:** These results shed light on the importance of KatG mutations other than S315T in resistance to INH and will be integrated in a global strategy involving molecular modeling and biochemical studies to increase our ability to predict resistance to INH, a goal particularly important to improve the treatment of tuberculosis patients.

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Abstract 9627

**Clinical profile and associated comorbidities to predict outcomes in patients with scrub typhus with acute kidney injury: a study from Central India**

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**Background:** Scrub typhus is an acute febrile illness caused by Orientia tsutsugamushi. Scrub typhus is a challenging clinical problem which contributes to the burden of acquired Acute Kidney Injury (AKI).

**Materials/methods:** The medical records of last four years (2016-19) were analysed for the key clinical, laboratory and in hospital stay parameters. Scrub typhus infection was diagnosed by ELISA technique.

**Results:** 39 patients were analysed (male 22, female 17). The distribution of the was as follow, in year 2019 (n=14), 2018 (n=6), 2017 (n=7), 2016 (n=12). 28 patients were referred from outside a radius of 30 km and nine were from the close vicinity. 12 cases presented with both overlapping paroxysm of fever and shaking chills with sweating. Four patients were both hypertensive and diabetic. The mean age was 51 years, no of days of admission was 9.1 days, no of days of ICU stay was 4.4, the mean platelet values were 91,000/mcl, with all the patients having thrombocytopenia. The mean TLC count was 11159/mcl. 14 patients were 60 years and above. The mean serum urea was 97 (mg/dl) and mean serum creatinine was 2.5 (mg/dl). The details are described in the table. There was one mortality due to multi-organ dysfunction, severe thrombocytopenia, stress cardiomyopathy and respiratory failure. 33 (85%) patients responded to doxycycline 200 mg/day in two divided dose.

**Conclusions:** Our study highlights the association of scrub typhus with AKI as the complication. The early addressal of thrombocytopenia and multi-organ failure is important to improve the outcomes with associated AKI. The timely diagnosis of scrub typhus with varied clinical manifestations is important to have minimal clinical impact of the AKI.

**Table: Clinical and Biochemical Parameters**

<table>
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<tr>
<th>Parameters (n=39)</th>
<th>Mean (SD)</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Range</th>
<th>95% CI</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
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<td>79</td>
<td>90</td>
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<td>52</td>
<td>51</td>
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<td>No of days of ICU Stay</td>
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<tr>
<td>No. of days of fever before admission</td>
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<td>2</td>
<td>30</td>
<td>28</td>
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<td>TLC (mcl)</td>
<td>11159 (6809)</td>
<td>1100</td>
<td>23100</td>
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<tr>
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<td>15</td>
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<td>Platelet (000)</td>
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<tr>
<td>Fever (F)</td>
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<td>97 (59)</td>
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<td>237</td>
<td>78 to 116</td>
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<td>Serum Creatinine (mg/dl)</td>
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<td>SGOT (AST) (Units/l)</td>
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<td>713</td>
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<td>134 to 215</td>
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<td>Sodium levels (mmol/L)</td>
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<td>Potassium levels (mmol/L)</td>
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<td>2.8</td>
<td>7</td>
<td>4.2</td>
<td>3.8 to 4.3</td>
</tr>
</tbody>
</table>

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Abstracts 2020

Abstract 9629

A point prevalence study of carbapenemase-producing Enterobacteriaceae colonisation of drains in a tertiary care hospital

Sara Woods*, Nuala O Connell†, Lorraine Power‡

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Background: Carbapenemase Producing Enterobacterales (CPE) are an increasing problem worldwide. There is mounting evidence for the role of the environment as a source of potential cross transmission in the hospital setting. In our centre there has been an outbreak of CPE, predominantly Klebsiella pneumonia carbapenemase (KPC), with an increase in numbers in recent years. In this study we sought to quantify the number of clinical wash-hand basins (WHB) colonised with CPE.

Materials/methods: Over a fourteen month period environmental testing of the drains of WHB and showers was carried out in a tertiary referral hospital. Superficial and/or deep swabs were taken from the drains, inoculated on to selective chromogenic agar(s) and incubated aerobically at 37°C overnight. Isolates were identified by MALDI-TOF. Enterobacterales were then tested for CPE enzymes/encoding genes by molecular analysis (Cepheid Xpert’s Carba-R assay). A number of CPE detected isolates were sent for confirmation to the National CPE Reference Laboratory, Galway.

Results: In fourteen months (March 2018-April 2019), 214 swabs were taken from 94 hospital drains in 13 wards. Twenty-one percent (20/94) of drains had CPE detected. Eight out of twenty-nine (28%) CPE positive drains remained positive on repeat testing. All these isolates had KPC, one had KPC and Verona integron-encoded metallo-β-lactamases (VIM) and another KPC and IMP-type CPE.

Conclusions: We demonstrated that there is a reservoir of CPE in the hospital drains. This represents a possible source of ongoing cross transmission within these wards. In April 2019, we consulted with a UK based consultant microbiologist, chair of the healthcare infection society working party on water, to advise on solutions which are currently being implemented.

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**Abstract 9630**

**Comparison of the Panther Fusion MRSA assay with conventional culture for patient swabs in Amies transport medium with charcoal**

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**Background:** Screening and pre-emptive isolation of patients at increased risk for infection with methicillin-resistant Staphylococcus aureus (MRSA) are important elements of the Dutch search and destroy policy to prevent MRSA transmission in the healthcare setting. Since MRSA screening with conventional culture can take up to 3 days, molecular tests with a shorter turnaround time (TAT) are often used to lift ‘unnecessary’ barrier precautions for MRSA-negative patients.

**Materials/Methods:** Nasal, pharyngeal and rectal swabs were collected in charcoal containing Amies transport medium (ATM). MRSA screening was performed using (i) direct conventional culture on ChromID MRSA agar (18-24 hours at 35-37°C), (ii) conventional culture on ChromID MRSA agar after overnight enrichment using a desferal® containing Columbia broth, (iii) Panther Fusion® MRSA PCR assay on direct patient material, and (iv) Panther Fusion® MRSA PCR assay after overnight enrichment in a desferal® containing Columbia broth.

**Results:** MRSA PCR screening results were available for 1107 patient materials before and after enrichment. In total, we identified 68 true MRSA+ patient materials from 34 different patients using conventional culture with enrichment as the gold standard. After enrichment, discrepant MRSA screening results were observed in 24/1107 (2.2%) patient materials (16 were PCR+/Culture-; 8 were PCR-/Culture+), resulting in a sensitivity of 88.2% and specificity of 98.4% of the MRSA PCR. Without enrichment, the yield of the MRSA PCR dropped almost 3-fold to a sensitivity of 35.2% with a specificity of 99.7%. None of the true MRSA+ patient materials initially missed by PCR (hence before enrichment) were detected by direct conventional culture. Charcoal containing ATM did not result in invalid MRSA PCR test results (<0.5%).

**Conclusions:** In our low-prevalence MRSA setting, the Panther Fusion® MRSA assay, if applied after enrichment, has a very high predictive negative value even when charcoal containing ATM is used, and therefore could be applied to shorten pre-emptive isolation of patients at high-risk for MRSA infection. With further reduction of the TAT using direct PCR without enrichment, the yield of the MRSA PCR significantly dropped compared to conventional culture with enrichment but not compared to direct conventional culture.

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Abstract 9632

Measuring and mapping the burden of antimicrobial resistance in enteric infections

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Background: Antimicrobial resistance (AMR) is a threat to global health. The GRAM project aims to synthesize global AMR data, produce maps of the distribution of AMR and incorporate the burden attributable to AMR into the Global Burden of Disease (GBD) study estimates.

Salmonella Typhi and Paratyphi cause an estimated 14 million cases of enteric (typhoid) fever and 135,000 deaths; whilst Shigella infections cause an estimated 220,000 deaths and 264 million episodes of shigellosis per year. Both diseases are transmitted faeco-orally.

Materials/methods: We performed two systematic reviews of worldwide studies published between 1990 and 2018, reporting the prevalence of AMR in a) Salmonella Typhi and Paratyphi A (blood culture) and b) Shigella (stool culture). MDR (resistance against ampicillin, chloramphenicol and co-trimoxazole) and fluoroquinolone non-susceptibility (FQNS) were assessed. We performed random effects meta-analyses, stratified by GBD region and 5-year time period. Heterogeneity was assessed using the I² statistics. A descriptive analysis of ceftriaxone and azithromycin resistance was conducted.

We evaluated global antibiotic sales data (IQVIA, WHO) and data on antibiotic use from household surveys to produce estimates on global antibiotic consumption as covariate for the geospatial model to predict resistance.

Results: We extracted data from 384 articles, comprising 94,616 S. Typhi and 29,731 S. Paratyphi A isolates. With the exception of MDR S. Typhi in South Asia, which declined between 1990 and 2018, resistance trends worsened for all regions. For Shigella, we extracted data from 521 studies, comprising 123,202 isolates. High prevalence of FQNS Shigella was identified in North Africa and the Middle East and Southern Sub-Saharan Africa.

Data gaps were notable throughout our study. These not only pertained to AMR surveillance data [especially in Africa and the Middle East], but also antibiotics sale data. Incomplete reporting of antimicrobial susceptibility testing and lack of quality control were identified.

Conclusions: We aim to use geospatial modelling techniques to produce granular maps of the prevalence of AMR S. Typhi and Paratyphi and AMR Shigella. It is essential that targeted public health interventions, which include improvements in water quality and sanitation, the deployment of vaccination and an informed choice of treatment are implemented.

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The potential impact of molecular rapid identification of pneumonia by The BIOFIRE FILMARRAY pneumonia panel on antimicrobial stewardship and patient management at a large district general hospital, United Kingdom

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Background: Pneumonia remains a worldwide health problem with a high rate of morbidity and mortality. Microbiological diagnosis of pneumonia is fundamental to ensure appropriate antibiotic therapy, which is a big challenge for conventional microbiological methods. The development of molecular diagnostics for pneumonia has been a major advance in the microbiological diagnosis of respiratory pathogens in recent years. The aim of this study is to explore the potential impact BioFire® FilmArray® Pneumonia Panel (PnP) with or without procalcitonin on antimicrobial stewardship.

Materials/methods: Total of 55 Respiratory samples collected from critically ill patients admitted to intensive care unit (ICU) at West Hertfordshire hospitals NHS trust, with radiologically confirmed new onset, pneumonia were taken for standard culture and sensitivity and molecular diagnosis using the PnP. Serum procalcitonin levels were measured. A microbiologist and intensivist reviewed antimicrobial prescriptions, inflammatory markers, procalcitonin results and daily SOFA data to determine: 1) Changes in antimicrobial prescription 2) Missed opportunities to change antimicrobial prescriptions. Further 60 patients from ICU, respiratory wards and outpatient clinics were also included in this study and data are under review.

Results: Data on 30 patients were included, 21 men, age range 26 to 86 (mean 60.9), APACHE score range 7 to 38 (mean 17). PnP resulted in the additional detection of 13 bacteria not cultured using standard technique. Antibiotics were stopped or de-escalated in eight and missed in seven patients. Earlier detection of resistance in two occasions by PnP. Serum procalcitonin levels were measured. A microbiologist and intensivist reviewed antimicrobial prescriptions, inflammatory markers, procalcitonin results and daily SOFA data to determine: 1) Changes in antimicrobial prescription 2) Missed opportunities to change antimicrobial prescriptions. Further 60 patients from ICU, respiratory wards and outpatient clinics were also included in this study and data are under review.

Conclusions: The results of this exploratory project suggest that pneumonia panel and appropriate procalcitonin results provide valuable information, with potential for better antimicrobial stewardship, specifically shorter courses.

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Abstract 9634

14-year evolution of antimicrobial consumption in a Belgian tertiary hospital based on the BeH-SAC surveillance
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Background: Surveillance of antimicrobial consumption is one of the key elements of an antimicrobial stewardship program. All Belgian hospitals have access to an interactive platform where the “Belgian Hospitals – Surveillance of Antimicrobial Consumption” (BeH-SAC) can be consulted. This tool consists of both numerator (consumed units per drug in defined daily doses [DDDs]) and denominator data (patient days and admissions). Feedback reports per hospital are provided with benchmarking and stratification.

In this study we describe and evaluate the 14-year evolution of antimicrobial consumption in the Ghent University Hospital based on BeH-SAC.

Materials/methods: Data from 2003 until 2017 were extracted for the Ghent University Hospital including a benchmark of all Belgian tertiary hospitals (=7) expressed in DDD/1000 patient days. Units with psychiatric beds and day clinics were excluded.

Results: The antibiotic (J01) consumption in 2017 was 646.8 DDDs/1,000 patient days, which is an increase of 3.6% compared to 2003 (624.3 DDDs/1,000 patient days). Also the median antibiotic (J01) consumption for the 7 tertiary hospitals increased with 11.6% (560.2 DDDs/1,000 patient days in 2003 versus 625.6 DDDs/1,000 patient days in 2017).

In 2017 amoxicillin in combination with a beta-lactamase inhibitor [J01CR02], flucloxacillin [J01CF05] and cefazoline [J01DB04] were the most frequently used products. For these three products the consumption increased comparing 2003 with 2017 for amoxicillin in combination with a beta-lactamase inhibitor with 67.9%, for flucloxacillin with 66.2% and for cefazolin with 51.8%.

The benchmark with the 7 university hospitals shows a moderate consumption in the Ghent University hospital of piperacillin-tazobactam [J01CR05] (41.5 DDDs/1,000 patient days in the Ghent University hospital versus median consumption of 51.3 DDDs/1,000 patient days) and meropenem [J01DH02] (23.4 DDDs/1,000 patient days in the Ghent University hospital versus median consumption of 34.3 DDDs/1,000 patient days).

Conclusions: Although BeH-SAC provides data which can be used for benchmarking and for assessing interventions further improvement is necessary with focus on detailed data per diagnose and a shorter delay. Furthermore data should be provided on the level of medical discipline and not aggregated for surgical or medical wards.

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**Abstract 9635**

**Characterisation of extended-spectrum β-lactamases by mass spectrometric analysis**

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**Background:** According to the recent report of WHO (World Health Organization), the emergence and infection of antibiotic resistant or antibiotic multidrug-resistant bacteria causes serious problems worldwide. In order to solve these problems, the development of new antibiotics is inevitable, but the emergence of antibiotic resistant bacteria is so fast that it is incomparable with the development of new antibiotics. Therefore, it is necessary to develop a rapid and accurate diagnosis of antibiotic resistant bacteria. Recently, mass spectrometry has enabled rapid and accurate identification of microorganisms. Mass spectrometric studies of antibiotic resistant proteins must be accompanied by a more accurate and reliable diagnosis of antibiotic resistant microorganisms. Here, we characterized the ESBL proteins that are directly involved in antibiotic resistance through mass spectrometry.

**Materials/methods:** We constructed standard bacterial cells harboring β-lactamase genes such as CTX-M. A target protein from the standard strains was purified and well-characterized by the high resolution mass spectrometry (e.g. Thermo Q Exactive HF-X). A peptide mapping and top-down mass analysis was performed by nanoflow LC-MS/MS system. We also developed methods to detect the target protein from clinical strains on the different MS platforms (Bruker MALDI-TOF and Agilent 6545XT Q-TOF).

**Results:** We identified CTX-M proteins from standard strains transforming the CTX-M gene, one of the ESBL classes related to β-lactam antibiotic resistance. In addition, CTX-M protein was confirmed by mass spectrometry from clinical strains, previously identified as ESBL. CTX-M proteins were mapped with 143 peptides (90.38% coverage). Interestingly, the N-terminal region was not observed in all cases (standard and clinical strains). Sequence coverage of the truncated CTX-M proteoform was 100% when considering sequences without the N-terminal region. Accurate mass and identification upon the proteoform was confirmed by Top-down mass analysis (<10ppm & E = 2.36E-25).

**Conclusions:** We have developed methods for the detection of antibiotic resistance proteins using various methods of mass spectrometry. In this study, we demonstrated a truncated proteoform through mass spectrometry, which has β-lactamase activity and consistently expressed in clinical strains. We expect that direct detection of the proteoform is a good target for rapid monitoring of CTX-M series.

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Abstract 9638

**Misidentification of *Staphylococcus argenteus* by MALDI-TOF MS**

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**Background:** *Staphylococcus argenteus* belongs to *Staphylococcus aureus* clonal complex (CC) 75 lineage. Infections caused by *S. argenteus* are underestimated because *S. argenteus* is often misidentified as *S. aureus* using standard identification test.

*S. argenteus* usually have the same virulence factors and antibiotics resistance genes as *S. aureus*. However, *S. argenteus* lacks staphyloxanthin, a carotenoid pigments protect against oxidative stress and impair neutrophil killing. Although the majority of *S. argenteus* are negative for the genes encoding Panton-Valentine-Leucocidin (PVL), studies showed that some strains can acquire PVL.

Cultivation followed by species identification of 100 *S. aureus* isolates from unselected patients in Hong Kong Adventist Hospital in 2019 by Vitek MALDI-TOF MS (bioMerieux, Marcy l’Etoile, France) and Bruker Biotyper MALDI-TOF MS (Bruker Daltonics, Bremen, Germany) showed that 2% of isolates identified by Vitek MALDI-TOF MS with confidence value of 99.9% using IVD knowledgebase version 3.2 were actually *S. argenteus*.

**Materials/methods:** A total of 100 *S. aureus* isolates from unselected patients in Hong Kong Adventist Hospital obtained in 2019 were studied. The types of specimens from which the isolates obtained included abscesses, blood, body fluids, urine, high vaginal swab and pus. Analysis of the isolates was performed by two Matrix Assisted Light Desorption/Ionization Time of Flight Mass Spectrometry (MALDI-TOF MS) platforms (Bruker Daltonics, Bremen, Germany; bioMerieux, Marcy l’Etoile, France). *Escherichia coli* strains ATCC® 8739 and MB11464 were used as calibration standards in Vitek MALDI-TOF MS and Bruker Biotyper MALDI-TOF MS respectively.

**Results:** In this study, 2 out of 100 (2%) *S. aureus* isolates identified by Vitek MALDI-TOF MS (bioMerieux, Marcy l’Etoile, France) with confidence value of 99.9% using IVD knowledgebase version 3.2 were identified as *S. argenteus* by Bruker Biotyper MALDI-TOF MS (Bruker Daltonics, Bremen, Germany) with score values > 2.0. Species-level identification was confirmed by sequencing.

**Conclusions:** Vitek MALDI-TOF MS (bioMerieux, Marcy l’Etoile, France) cannot distinguish *S. argenteus* from *S. aureus* whereas Bruker Biotyper MALDI-TOF MS (Bruker Daltonics, Bremen, Germany) can accurately identify *S. argenteus* at species-level.

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Systematic blood culture testing identifies a large proportion of patients in whom antibiotics could be safely discontinued: hospital-associated infections in a tertiary care hospital in Ethiopia

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Background: Hospital Associated Infections (HAI) and Antimicrobial Resistance (AMR) have emerged as major threats for Low-Resource Settings (LRS). Interventions to decrease rates of HAI and AMR depend on diagnostic bacteriology capacity, which is lacking throughout Africa. We recently implemented a laboratory strengthening intervention in Ethiopia’s largest referral hospital, with systematic blood culture testing of patients with suspected HAI. Prior to this study, fewer than 1% of patients with suspected infection had microbiologic testing. Our goal was to characterize clinical outcomes and AMR patterns associated with HAI and blood stream infections (BSI), and assess antimicrobial usage.

Materials/methods: This was a single-center correlational study of patients hospitalized at Tikur Anbessa Specialized Hospital (TASH) October 2017 - October 2018. HAI suspects had blood culture testing using an automated platform. Results were reported to clinicians, without additional interventions. We collected clinical and antimicrobial usage data. Primary outcomes were proportion of patients with blood stream infections (BSI), resistance patterns, and 14-day status. We also assessed days of therapy (DOT) pre- and post-blood culture testing.

Results: We enrolled 978 patients; 777 had blood culture testing. Of these, 237 (30%) had a BSI. Enterobacteriaceae were isolated in 49% of the cases; 90% of these were broadly resistant to cephalosporins; 42% of Klebsiella sp and 12% of E. coli were also resistant to carbapenems. Mortality at 14-days was 31% and 21% in those with and without BSI, respectively. Other predictors of death were malignancy and exposure to >4 antibiotics prior to blood culture testing. Pre-testing, DOT was 10 days vs 2 days in those with and without BSI, respectively. After blood culture testing, DOT were comparable between the 2 groups (median 20 vs 18 days, respectively).

Conclusions: BSI are frequent and fatal among patients with suspected HAI in Ethiopia, despite heavy empiric antibiotic therapy. Pan-resistant blood isolates are alarmingly common. This study provides evidence that investing in systematic blood culture testing in LRS identifies a large proportion of patients in whom antibiotics could be safely discontinued - but also shows that adequate training and stewardship are necessary to achieve substantial reductions in antibiotic consumption and better outcomes.

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Clinical evolution of yellow fever patients in the 2017-2018 outbreaks in Minas Gerais, Brazil: preliminary analysis of risk factors for death

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Background: Yellow fever (YF) is a viral disease, caused by a flavivirus, which is transmitted to humans by arthropod bites. There are two cycles of the disease, wild and urban, with different vectors.

YF has a variable clinical spectrum that usually consists of a biphasic clinical condition, with a first phase of acute febrile illness, followed by evolution to spontaneous cure or to a second phase, characterized by jaundice and hemorrhagic symptoms, that correspond to severe forms.

Despite being an immune preventable disease, wild outbreaks of YF are frequent in Brazil, as occurred in 2017 and 2018 in the State of Minas Gerais, with 1,582 reported cases and 260 suspected deaths from the disease. Most cases were attended at a secondary hospital in Belo Horizonte city, reference for the care of patients with suspected AF.

This study aims to describe the evolution of these patients, with emphasis on their clinical and demographic aspects.

Materials/methods: Retrospective analysis of medical record data from 256 patients diagnosed with AF admitted in the Hospital from January 2018 to March 2019. Only patients over 18 years, with positive serology or viral isolation were included.

Results: To date, data from 94 patients have been reviewed. The median time between the onset of symptoms and the date of hospitalization was 4 days (4 in the deaths group x 3 among survivors, without statistical significance). The mortality rate was 22.3% [21/94], reaching 46.6% among patients requiring ICU hospitalization. INR correlated with death (median 2.57x1.02, p<0.01). Elevation of transaminases also increased the risk of death, with a median TGO at admission of 1,454UI/L [8,134x765, p<0.01], and a median TGP of 1,319UI/L [4,253x793; p<0.01]. The same association was observed for total bilirubin levels, with admission median of 6.8x0.9mg/dL (p<0.01). The clinical variables correlated with death were dialysis, bleeding and encephalopathy, all with p<0.01.

Conclusions: The findings of this study corroborate some risk factors for death already described in the literature, such as increased transaminases and INR. However, to date, no study has shown the association of death with increased bilirubin, which is considered a "benign" marker.

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Outbreak of mixed cases of gastrointestinal and cutaneous anthrax in the rural village of northern Luzon, Philippines, March 2017

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Background: On March 21, 2017, FETP team was sent to Cayapa Village, Abra due to increasing cases of foodborne illness. Epidemiologic investigation was conducted to verify the diagnosis, establish existence of outbreak, identify risk factors, and recommend control and prevention measures.

Materials/methods: We conducted a 1:3 case-control study for cutaneous and 1:2 case-control study for gastrointestinal anthrax. A suspect case was a previously well resident of Cayapa Village who developed the following from February 27 - March 14, 2017:

- Cutaneous anthrax: skin lesion (papular, vesicular or depressed black eschar)
- Gastrointestinal anthrax: abdominal pain or diarrhea and any of the following: vomiting, fever, difficulty swallowing, and lymphadenopathy.

Confirmed case was a suspect case positive for Bacillus anthracis on bacterial culture or rt-PCR test. A control was well resident negative for Bacillus anthracis. We collected serum specimens and soil samples for laboratory confirmation. We conducted environmental survey and key informant interview. We used Stata ver.13 to analyze data.

Results: Thirty-eight suspect cases were identified. Majority (21, 55%) were males. Age ranged from 6-85 years (Median: 26). For gastrointestinal anthrax, clinical manifestations were abdominal pain (26, 90%), fever (16, 55%), and diarrhea (14, 48%). One (3%) had lymphadenopathy. For cutaneous anthrax, aside from eschar, clinical manifestations were fever (57%), headache, body malaise, and abdominal pain (36% each). All had history of consuming and handling by-product of dead water buffalo. All 11 serum specimens and five soil samples were negative for Bacillus anthracis. After multivariate analysis, eating uncooked meat of dead animal (Adj.OR=6.95% CI: 1.7-18.4) was a risk factor for gastrointestinal anthrax while handling raw meat of dead animal (Adj.OR=7.4, 95% CI: 6.1-902.5) and eating uncooked meat of dead animal (Adj.OR=16, 95% CI: 1.3-185.2) were risk factors for cutaneous anthrax.

Conclusions: The epidemic curve indicates a point source outbreak. We found valid statistical and temporal association of eating and handling by-product of dead water buffalo and anthrax infection. The clinical manifestations were all consistent with Bacillus anthracis as evidence by presentation of eschar including lymphadenopathy observed from a case. Hence, we conducted massive information education campaign of properly handling and disposal of animal carcasses in the community.

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Abstracts 2020

Abstract 9681

Levels of evidence supporting European and American community-acquired pneumonia guidelines

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Background: Optimal clinical decisions should be supported by clinical practice guidelines (CPG) based on evidence generated from randomized clinical trials (RCT).

Materials/methods: We evaluated the class and level of evidence (LOE) supporting international community-acquired pneumonia (CAP) guidelines and their variation over time. 2019 Infectious Diseases Society America/American Thoracic Society (IDSA/ATS) and 2011 European Respiratory Society/European Society Clinical Microbiology Infectious Diseases (ERS/ESCMID) CPG and immediate predecessors (2007 and 2005) were evaluated. Number of recommendations and distribution as LOE A (supported by multiple RCT or a single, large RCT), B (supported by data from a single RCT or observational studies) and C (expert opinion, case studies or standard of care) were identified.

Results: Overall, recommendations for diagnosis, management and prevention were graded as strong in 51.4%, 62.9% and 23.5% in spite that they were supported by LOE A in 5.7%, 11.1% and 52.9%, respectively. In 2019 ATS/IDSA guidelines (39 recommendations), 7.7% (n=3) recommendations were classified as LOE A, 30.8% (n=12) as LOE B, and 61.5% (24%) as LOE C. Across 2011 ERS/ESCMID guidelines (68 recommendations), 21.2% (n=14) recommendations were classified as LOE A, 4.6% (n=3) as LOE B, and 74.2% (n=49) as LOE C. When comparing with prior versions, the proportion of recommendations that were LOE A did not significantly increase in ERS/ESCMID (21.2% vs 20%) and decreased in ATS/IDSA (7.7% vs 32.0%).

Conclusions: In conclusion, large randomized trials or network meta-analysis including comparison of regimens to identify high probability of best cure and mortality are an unmet clinical need.

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**Abstract 9700**

**The penicillin allergy delabelling program: a prospective multicentre interventional study**

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**Background:** Penicillin allergies are associated with inferior patient and antimicrobial stewardship outcomes. We implemented a whole-of-hospital program at two Australian centres to assess the efficacy and safety of inpatient delabelling for low-risk penicillin allergies.

**Materials/methods:** Patients ≥ 18 years reporting an antibiotic allergy were prospectively assessed and those with a low-risk penicillin allergy offered a single-dose oral penicillin provocation or direct label removal based on history (direct delabelling), as appropriate. The primary endpoint was the proportion of low-risk penicillin allergy patients delabelled. Key secondary endpoints were antibiotic utilization pre (index admission) and post-delabelling (index admission/90-days). Propensity score analysis using inverse probability of treatment weighting was used.

**Results:** Between 21 January and 31 August 2019 we prospectively assessed 1,791 patients reporting 2,315 antibiotic allergies; 1,225 patients reported ≥ 1 penicillin allergies – 29% (355/1,225) overall were delabelled. 64% (355/558) with a low-risk penicillin allergy were delabelled – 161 based on history and 194 via oral provocation. 97% (194/200) of patients were negative on oral penicillin provocation. In the delabelled patients (n=355), antibiotic usage pre and post-testing is demonstrated in Figure 1. In the delabelled patients (n=355) we observed an increase in narrow spectrum penicillin usage (aOR 10.51 [95% CI [5.39, 20.48]], improved appropriate antibiotic prescribing (aOR 2.13 [1.45, 3.13]) and a reduction in restricted antibiotic usage (aOR 0.30 [0.27, 0.54]). In the propensity score analysis there was an increase in narrow spectrum penicillins (OR 10.89 [5.09, 23.31]), beta-lactam/beta-lactamase inhibitors (OR 6.68 [3.94, 11.35]) and a reduction in restricted antibiotic use (OR 0.52 [0.36, 0.74]) and inappropriate prescriptions (RRR 0.43 [0.26, 0.72]) in the delabelled compared with the non-delabelled cohort. There was no difference in total antibiotic usage between the cohorts. There was no difference in mortality or length-of-stay.

**Conclusions:** This multicentre whole-of-hospital health services intervention resulted in significant impacts on both utilization of preferred antibiotics therapies and appropriate prescribing. Direct oral provocation in this large inpatient cohort, with multiple comorbidities, was safe and effective.

**Figure 1:** Antibiotic utilization in the delabelled cohort

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Paediatric meningoencephalitis due to entero- and human parechoviruses in Cork, Ireland - epidemiology and neurodevelopmental follow-up by parental report

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**Background:** Epidemiological data on paediatric infections caused by human Parechovirus (hPEV); and the impact of both entero- and parechoviral meningoencephalitis (EVME; hPEVME) on neurodevelopmental outcome remains subject to intensive research. hPEV in particular is emerging as a neurotropic pathogen, with the potential for neurological sequelae, especially prior to myelination being complete. Our goal was to 1) describe distribution of circulating picornaviruses causing paediatric morbidity at a large center in Ireland and 2) initiate prospective neurodevelopmental assessment of children who had experienced EVME or hPEVME in infancy.

**Materials/methods:** All samples submitted for virology work-up from children aged 0-16 years by University Hospital Cork between 01/2014 and 12/2018 were included for analysis of circulating picornaviruses (n=199). Where possible, serotyping was performed. In those with picornaviral meningoencephalitis, clinical presentations, laboratory findings and imaging were reviewed. Between October and December 2019, parents of children with infantile meningoencephalitis were asked to complete an age-matched ASQ3 questionnaire.

**Results:** CSF analysis identified 86 children with meningoencephalitis, n=63 EV\(^+\); n=23 hPEV\(^+\). 68 (80%) were aged ≤3 months at time of illness. hPEVME patients were significantly younger (P<0.05). 9/10 hPEV serotyped were type3. 38/86 (44%) submitted an ASQ3, 29/38 had been ≤3 months at the time of illness, 35/38 ≤2 years. Based on ASQ3 data, 2/10 hPEV\(^+\) and 6/27 EV\(^+\) children warranted observation, 1/10 and 3/27 developmental follow-up, respectively. Parental concern was expressed in 4/10 hPEV\(^+\) and 14/27 EV\(^+\) children. Neither age at diagnosis, WBC\(_{\text{max}}\) in CSF or virus identified were associated with ASQ3 score or parental concern.

**Conclusions:** In this cohort currently undergoing prospective assessment, available data indicates that approximately 10% of patients who experienced EVME or hPEVME in infancy require observation and/or physician-directed follow-up later in childhood. Clinical parameters available during the acute illness did not predict later expressed parental concerns. Parental concern exceeded level of concern identified by ASQ3 questionnaire. Detailed prospective patient assessment will identify if this is the result of parental perception, or if sensitivity of parental assessment outperforms ASQ3 in identifying subtle neurocognitive sequelae of viral meningoencephalitis in infancy.

**Figure 1. Cases of paediatric enteroviral (EV) and parechoviral (hPEV) meningoencephalitis over time**

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**Abstract 9703**

**BacteriaGame, a serious game to revise knowledge in medical Bacteriology**
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**Background:** For a long time, the educational game has been developed in order to encourage the motivation and interaction of students. In medical studies, few students attend the course of Bacteriology and we observe thereafter, real gaps in the knowledge of students in this discipline. We thus just created an educational game “BacteriaGame” born from the collaboration within our University Paris 13 between our laboratory of the medical school and the “Ludomaker”, a laboratory of educational games.

**Materials/methods:** The game lasts approximately 20 minutes and can be used by maximum 8 players. Briefly, it is an association game between 20 main bacteria and their characteristics (bacterial family, direct examination, commensal site, pathogenicity, type of community or nosocomial infection, type of diagnosis and antibiotic treatment). Players must associate these characteristics with the bacteria that they have drawn at the start of the game and whose identification they keep hidden. The other players have to guess these bacteria thanks to the characteristics which are visible on the table. Bonus questions add to the difficulty and the possibility of earning points.

**Results:** We tested this game during teaching in the 3rd year of medicine. The students formed 8 groups of 6 students and were able, after a brief explanation, to play it independently thanks to the rules available. The teacher was present and could intervene between the different game tables and an evaluation of the game was then carried out by the students [score between 1 and 4]. This evaluation was found to be very positive with 72% of the participants who gave scores 3 and 4.

**Conclusions:** We want to extend the use of this game which has shown great success with students and at national congresses to other levels of students [resident in medicine and pharmacy]. In this context we plan to study in the next weeks the impact of the use of this game on the learning outcomes of students at different levels by assessments before and after use.

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Efficacy and safety of oral Ibrexafungerp in 41 patients with refractory fungal diseases, interim analysis of a phase 3 open-label study (FURI)

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Abstract third-party references: Supported by SCYNEXIS, Inc.

Background: Candida infections resistant to currently available antifungals are an emerging global threat. Ibrexafungerp is an investigational broad-spectrum glucan synthase inhibitor antifungal with activity against Candida and Aspergillus species, including azole- and echinocandin-resistant strains. A Phase 3 open-label, single-arm study of oral ibrexafungerp (FURI) [Clinicaltrials.gov NCT03059992] is ongoing for the treatment of patients (≥18 years) with fungal diseases who are intolerant of or refractory to standard antifungal therapies.

Materials/methods: An independent Data Review Committee (DRC) provided an assessment of treatment response for 41 patients who completed therapy by October 2019. Patients were enrolled in 22 centers from 6 countries. Patients were eligible for enrollment if they had proven or probable, invasive or severe mucocutaneous candidiasis and documented evidence of failure of, intolerance to, or toxicity related to a currently approved standard-of-care antifungal treatment or could not receive approved oral antifungal options (e.g., susceptibility of the organism) and a continued IV antifungal therapy was undesirable or unfeasible.

Results: The 41 patients assessed had the following infection types: intra-abdominal abscesses, oropharyngeal candidiasis, esophageal candidiasis, candidemia, and others. The DRC adjudicated 23 patients (56%) as achieving complete or partial response, 11 patients (27%) maintaining stable disease, 6 patients (15%) with progression of disease and one case was considered indeterminate. The efficacy of oral ibrexafungerp by pathogen was as follows:

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Complete or Partial Response</th>
<th>Stable disease</th>
<th>Progression of Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. glabrata</td>
<td>9</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>C. albicans</td>
<td>5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>C. krusei</td>
<td>2</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>C. parapsilosis</td>
<td>3</td>
<td></td>
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</tr>
<tr>
<td>C. glabrata / C. albicans</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. krusei / C. albicans</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C. tropicalis / C. albicans</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>C. glabrata / C. dubliniensis</td>
<td></td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>

1 patient outcome indeterminate, 1 patient’s organism not identified

Ibrexafungerp was well-tolerated with the most common treatment-related adverse events being of gastrointestinal origin. No deaths due to progressive fungal disease were reported.

Conclusions: Preliminary analysis of these 41 cases indicate that oral ibrexafungerp provides a favorable therapeutic response in the majority of patients with difficult to treat Candida spp. infections, including those caused by non-albicans Candida species.

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Abstract 9730

Clinical effectiveness of individualized, c-reactive-protein-guided durations and fixed, seven-day durations of antibiotic therapy compared to 14-Day Durations for Gram-Negative Bacteremia: A Multicenter, Non-inferiority Point-of-Care-Randomized Clinical Trial

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Background: Gram-negative bacteremia is frequent and results in substantial antibiotic use. We compared individualized, C-reactive-protein-(CRP) guided antibiotic durations and fixed 7-day courses to fixed 14-day courses.

Materials/methods: This multicenter non-inferiority trial randomized adults 1:1:1 on day 5 (±1) of effective antibiotic therapy for fermenting, gram-negative bacteremia to a total duration that was (1) CRP-guided [antibiotic(s) discontinued when CRP decreased by ≥75% from peak, beginning on day 5], (2) 7 days, or (3) 14 days; patients were followed thereafter for 90 days. Patients who were febrile on day 5, severely immunosuppressed, or had recurrent or complicated infection (e.g., abscess) were not eligible for inclusion. Patients, investigators and ward physicians were blinded to allocation until antibiotic discontinuation. Non-investigators were additionally blinded to the CRP algorithm used for antibiotic discontinuation. The primary outcome was incidence of clinical failure by day 30, requiring either relapse (recent bacteremia), local suppurative complication, distal complication, restarting of gram-negative-directed antibiotic therapy due to clinical worsening suspected to be due to the initial organism, or death due to any cause through day 30; the non-inferiority margin was 10%. Secondary outcomes included incidence of Clostridioides difficile infection.

Results: Among 504 patients randomized (median age 79 years [IQR 68-86], female sex 306/503 [61%]), 493 (98%) day-30 follow-up. The urinary tract (348/503, 69%) and Escherichia coli (373/503, 74%) were the most common infection site and etiology, respectively. Median duration in the CRP arm was 7 days (IQR 6-10). Clinical failure occurred by day 30 in 4/164 (2.4%), 11/166 (6.6%), and 9/163 (5.5%) in the CRP, 7-day and 14-day arms, respectively (difference -3.1% [95%CI -7.3, 1.1], P=.126, for CRP- versus 14-day arm; and 1.1% [95%CI -4.1, 6.3], P=.426, for 7 versus 14-day arm). By day 90, failure occurred in 10/143 (7.0%), 16/151 (10.6%) and 16/153 (10.5%), respectively. Clostridioides difficile infection occurred in 0/49 (0%) of patients receiving <7 days of antibiotics, 5/245 (1%) receiving 7-10 days, and 8/201 (4%) receiving >10 days.

Conclusions: In adults with uncomplicated gram-negative bacteremia, individualized/CRP-guided and fixed 7-day durations were non-inferior to 14-day durations of antibiotic therapy. C-reactive-protein-guided durations are antibiotic sparing and safe.

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Abstract 9734

A randomised trial of two 2-dose influenza vaccination strategies for patients following autologous haematopoietic stem cell transplantation

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**Background:** Recommendations for dose, type and timing of seasonal influenza vaccination of patients following autologous haematopoietic stem cell transplantation (autoHSCT) are inconsistent in clinical guidelines. We sought to evaluate seroprotection and seroconversion rates associated with two 2-dose schedules.

**Materials/methods:** A randomised single-blind control trial of two influenza vaccination strategies was conducted at a quaternary cancer centre during the Southern Hemisphere 2019 influenza season (ACTRN12619000617167P). AutoHSCT patients in their first year post-transplant were randomised 1:1 to trivalent (TIV) high dose (HD) followed by quadrivalent standard dose (SD) vaccine 4 weeks later (HD-SD arm) or two SD vaccines 4 weeks apart (SD-SD arm). Haemagglutination inhibition (HI) assay for TIV strains was performed at baseline, 1 and 2 months post-first dose. Patients were prompted weekly to report influenza-like-illness (ILI), which also triggered testing. Evaluable outcomes were seroprotection (HI titre ≥40) and seroconversion (4-fold titre rise) rates, unadjusted geometric mean titres (GMT) and GMT ratios at 1 and 2 months following initial vaccination. Outcomes in each arm were compared utilising chi-square or Fisher’s exact test with \(p<0.05\) considered statistically significant.

**Results:** Sixty-eight patients were enrolled (34 per arm) with median age of 61.5 years, majority male (68%) and myeloma the most common transplant indication (68%). Median time from autoHSCT to first vaccine dose was 2.0 (95% CI 0.9-10.5) months in HD-SD arm compared to 4.3 months (95% CI 0.92-11.8) in the SD-SD arm (\(p=0.06\)). For HD-SD and SD-SD arms, percentage of patients achieving seroprotection was 78.8% and 79.4% for H1N1, 87.9% and 91.2% for H3N2 and 81.8% and 94.1% for influenza-B/Yamagata respectively (all \(p>0.05\)). Seroconversion rates, GMT and GMT ratios were not significantly different between arms across influenza strains or time periods except for a higher GMT ratio 1 month following HD compared to SD vaccination (5.96 vs. 3.61, \(p=0.047\)). There was no difference in the number of patient-reported episodes of ILI or laboratory proven influenza between arms.

**Conclusions:** High seroprotection rates against all influenza strains can be achieved early post-autoHSCT with two-dose vaccine schedules. Although post-vaccination GMTs were comparable, the HD-SD arm showed greater gains in titres as reflected by higher GMT ratio.

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Diabetic status and the risk of tuberculosis: a nationwide population-based study

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Background: Tuberculosis (TB) infections continue to be a concern worldwide and it remains deadly communicable disease. Diabetic mellitus (DM) appears to be a risk factor for lower respiratory infections including TB and to have a profound adverse impact on TB treatment outcome. To evaluate the association between DM duration and the incidence of TB in general population.

Materials/methods: We identified 6,312,283 subjects who are free of TB until one year after the day of their health examination (2009) and were followed up until December 31, 2018 using the database of the Korean National Health Insurance Service. Cox proportional hazard regression was used to assess adjusted hazard ratios (aHR) of DM status for TB with adjustment for potential confounders.

Results: A total of 30,917 individuals were diagnosed with TB during follow-up period. An increased risk of TB incidence was observed in DM subjects compared to non-DM subjects (aHR 1.49, 95% confidence interval [CI] 1.45-1.53). While subjects with impaired fasting glucose showed a decreased risk of TB incidence (aHR 0.96, 95% CI 0.93-0.98), the risk of TB incidence was increased with as the duration of DM increased (aHR 1.32, 95% CI 1.25-1.40 in the new-onset DM; aHR 1.46, 95% CI 1.39-1.53 in the DM with duration < 5 years; aHR 1.54, 95% CI 1.48-1.60 in the DM with duration ≥ 5 years). Among non-DM subjects, a U-shaped association was noted between fasting glucose concentrations and the risk of TB.

Conclusions: DM status was an independent predictor for developing TB with a dose-response relationship. In non-DM subjects, there was a U-shaped association between fasting glucose concentrations and TB risk, suggestive of protective role of BMI on TB in non-DM subjects.

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Abstract 9739

**Siderophores of environmental *Pseudomonas* for application against human opportunistic pathogens**

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**Background:** Alternative approaches targeting multi-drug resistant pathogens are urgently needed. For successful pathogenesis, bacteria rely on virulence factors to directly target the host or to exploit their nutrients. Iron-scavenging siderophores fulfil both tasks and are indispensable for bacterial proliferation, which makes them excellent antimicrobial targets. Once the siderophore has bound iron, bacteria require a specific receptor for ferric-siderophore uptake. Here, we exploit this strategy by screening for siderophores of non-pathogenic environmental bacteria that cannot be used by opportunistic pathogens and thereby induce iron starvation and growth arrest in the pathogens. We focussed on pyoverdines, produced by fluorescent *Pseudomonas* bacteria, which are a class of siderophores with strong affinity for iron.

**Materials/methods:** In a first step, we screened 340 supernatants of environmental pseudomonads, containing pyoverdine, for their activity against 12 human opportunistic pathogens. To rule out any non-pyoverdine related pathogen inhibition we repeated the assay in iron-replete conditions. For the top candidates, inhibiting the growth of all pathogens, we established the minimal inhibitory (MIC) and half maximal inhibitory concentrations (IC₅₀) for each pathogen. We then crudely purified the candidate pyoverdines and subjected them to liquid chromatography–high resolution mass spectrometry (LC-HRMS) to determine their mass, relative abundance in the supernatant, and to elucidate their chemical structure.

**Results:** We identified seven pyoverdine candidates that strongly inhibited the growth of all pathogens exclusively under iron-deplete conditions, suggesting that the pyoverdines are indeed responsible for the observed growth inhibition. We further show that the crudely purified pyoverdines act in a concentration-dependent manner against the different pathogens. Our chemical analyses reveal that five out of seven top-candidate pyoverdines differ in their chemical structure. Currently, we are about to validate the antibacterial activity of these pyoverdines in vivo in our host model system *Galleria mellonella* and to test for their level of cytotoxicity against mammalian cells.

**Conclusions:** We establish a novel approach, based on the induction of iron starvation, to combat bacterial opportunistic pathogens, including members of the ESKAPE pathogens that increasingly become resistant to antibiotics.

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Phage cocktails in the treatment of bacteriophage insensitive mutants
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Background: The rising prevalence of antibiotic resistance in bacteria is an important health obstacle, given that about 2.25 million people sickened each year by antibiotic-resistant infections. If it continues, the world is heading towards a post-antibiotic era, in which alternative therapeutics such as phage therapy should be considered. Though bacteriophages are effective antibacterial agents, there is a possibility that the bacteria could develop resistant mutants against the infecting lytic phage. This study aims to eliminate the bacteriophage insensitive mutants using phage cocktails.

Materials/methods: For this study, Enterotoxigenic E. coli (ETEC) were collected from the diagnostic centre in Chennai, Tamil Nadu. The water samples were collected from sewage treatment plants in Karur district. The bacteriophages were isolated using phage enrichment method. Spot test and double agar overlay method were used to test the phage activity. Bacteriophage insensitive mutants (BIMs) were isolated and selected using challenge tests. The bacteriophages were characterized; absorption time, latency period, burst size, morphological analysis, and genomic analysis. Phage cocktail was prepared using characterized phages to eliminate BIMs. In vivo studies were performed using Galleria mellonella and the larvae were infected with $10^6$ CFU/mL bacteria and treated with $10^4$ PFU/mL phages.

Results: A bacteriophage EP1 was isolated against E. coli ETEC311. The host-range analysis showed that the phage was infecting 4/8 ETEC tested. Out of 4 ETEC isolates [ETEC311/235/315/326], BIMs was observed in 3 ETEC [235/315/326] isolates. In this regard, another bacteriophage EP2 was isolated to infect BIMs. Importantly, 2/3 BIM isolates [235A/315A] were eliminated using the phage EP2 but one BIM isolate [326A] was still resistant. In vivo studies showed that when treated with EP1, ETEC311 (no BIMs) infected larvae obtained 100% larval survival within 48hrs but ETEC235/315 (BIMs) infected was not. When infected with ETEC235/315 (BIMs) and treated with phage cocktail [EP1 and EP2], 100% survival was observed within 72hrs. No significant survival was observed in untreated and ETEC326 infected groups.

Conclusions: This study can be used as a strategy in the preparation of phage cocktails to combat BIMs. In future, studies on evolution of phage resistance can be used to guide therapeutic phage preparations.

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Abstract 9756

**Routine molecular point-of-care testing for influenza in hospitalised adults improves patient management and outcomes: results of a multicentre, randomised controlled trial (FluPOC)**

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**Background:** Influenza infections often remain undiagnosed in patients admitted to hospital due to lack of routine testing. When tested for, the diagnosis of influenza is delayed due to the long turnaround times of laboratory PCR, leading to inappropriate and late antiviral and isolation facility use. Molecular point-of-care tests (mPOCT) for influenza can deliver results in under 1 hour but high quality evidence for impact on clinical management and outcome is lacking.

**Materials/methods:** In this pragmatic, multicentre, randomised controlled trial we enrolled adults admitted to hospital with acute respiratory illness (ARI) during influenza season. Patients were randomised (1:1) to receive mPOCT for influenza or routine clinical care. The primary outcome was the proportion of influenza-infected patients who received antivirals. Secondary outcomes included; detection of influenza, time to antivirals, isolation facility use and clinical outcome measures.

**Results:** Between December 2017 and May 2019, 613 patients were enrolled (307 assigned to mPOCT and 306 to routine care) and all were analysed. 100/307 (33%) patients in the mPOCT group and 102/306 (33%) patients in the control group were influenza-infected. The median (IQR) turnaround time for results was 1.2 (1.1 to 1.4) hours in the mPOCT group and 23 (16 to 29) hours in the control group (p<0.0001). 100/100 (100%) influenza-infected patients were diagnosed in the mPOCT group but only 60/102 (59%) were diagnosed in the control group, p<0.0001. 99/100 (99%) influenza-infected patients received antiviral treatment in the mPOCT group versus 63/102 (62%) in the control group, relative risk 1.6 (95%CI 1.4 to 1.9); p<0.0001. Median (IQR) time to antivirals was 1·0 (0 to 2.0) hour in the mPOCT group versus 6·0 (0 to 12.0) hours in the control group (p=0.0039). 70/100 (70%) of influenza-infected patients in the mPOCT group were correctly nursed in single room accommodation versus 39/102 (38%) in the control group, p<0.0001. In the mPOCT group there were fewer adverse events and median Hospital Recovery Scale score was lower versus the control group (p=0.045).

**Conclusions:** Routine mPOCT for influenza was associated with enhanced detection of influenza, improvements in appropriate and timely antiviral and isolation facility use and better clinical outcome.

**Funding:** NIHR

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**Figure 1** Time-to-event curve showing antiviral use over time in influenza-infected patients

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Decreased sensitivity of rapid influenza diagnostic test among vaccinated adults in influenza season 2018-19

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Abstract third-party references: Funding: Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 777363. DRIVE collaboration receives support from the European Union’s Horizon 2020 research and innovation programme and EFPIA.

Background: The sensitivity of rapid influenza diagnostic tests (RIDTs) detecting viral antigens has proved low to moderate compared to RT-PCR tests. Their accuracy depends on the type of respiratory specimen, factors related to sampling such as transport medium and swab, time from symptom onset to sampling and patient age. We wanted to investigate whether prior influenza vaccination affects their sensitivity.

Materials/methods: During influenza season 2018-19 a prospective test-negative design (TND) influenza vaccine effectiveness (IVE) study was conducted at HUS Jorvi Hospital as a part of international DRIVE collaboration. Adult inpatients fulfilling severe acute respiratory infection (SARI)-criteria were recruited and swabbed for influenza. According to local sampling strategy, respiratory samples were first tested by RIDT and negative results were tested by RT-PCR in HUSLAB clinical laboratory. Positive RIDT and RT-PCR results were confirmed and influenza subtype was determined by real-time RT-PCR at the Finnish Institute for Health and Welfare (THL). Those tested positive at THL were considered laboratory-confirmed influenza (LCI) cases.

Results: Of the 69 LCI SARI cases that were tested for influenza with both RIDT and RT-PCR, 21 (30.4%) tested positive, 46 (66.7%) negative and 2 (2.9%) unclear with RIDT. The overall sensitivity of the RIDTs in detecting influenza was only 31.3%. Prior influenza vaccination during the current influenza season seemed to be associated with decreased sensitivity of the antigen test (OR = 0.374, 95% CI 0.124, 1.068, P = 0.066). Among those vaccinated over 14 days before sampling, 28 (77.8%) had false-negative RIDT results compared to 17 (56.7%) of the non-vaccinated. Patient age, influenza A subtype or genetic clade did not have a significant effect on the sensitivity of the RIDT.

Conclusions: Our data suggests an association between prior influenza vaccination and decreased sensitivity of RIDT. False-negative RIDT results and consequent underdetection of influenza cases may lead to insufficient use of infection-control measures and antiviral treatments and unnecessary use of antibiotics. Additionally, IVE may be overestimated due to false-negative influenza test results among vaccinated population. Thus, caution is warranted when interpreting negative RIDT results especially in areas with high influenza vaccination coverage.

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**Impact of the introduction of EUCAST's concept of the "Area of Technical Uncertainty"**

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**Background:** On the first of January 2019 the European Committee on Antimicrobial Susceptibility Testing, EUCAST, introduced the concept of "area of technical uncertainty" (ATU). One year later, the impact of the implementation of this new approach in the laboratory of our 1062-beds tertiary care teaching hospital was studied. The aim was to report on the incidence of ATU test results in a selection of common bacterial species and the subsequent impact on antimicrobial resistance categorisation.

**Materials/methods:** A retrospective analysis of clinical samples collected from February 2019 till November 2019 was performed. Susceptibility to amoxicillin-clavulanic acid and piperacillin-tazobactam in Enterobacterales (Escherichia spp., Klebsiella spp., Proteus spp.), piperacillin-tazobactam in Pseudomonas spp. and amoxicillin-clavulanic acid and cefturoxime in Haemophilus influenzae was studied. Primary antibiotic susceptibility testing was performed using disk diffusion with paper disks [Bio-Rad, France] and the ADAGIO 93400 automated system [Bio-Rad, France] for reading and interpretation. In case of inhibition zone in the ATU, strains were retested using gradient minimal inhibitory concentration method [E-test, BioMérieux, France].

**Results:** Overall, 14168 isolate-antibiotic combinations were tested in 7924 isolates, resulting in 1206 (8.5%) disk zone diameters in the ATU region.

For amoxicillin-clavulanic acid we observed a category change from S to R in 12% of the ATUs in Escherichia spp., 2/58 in Klebsiella spp. and 2/37 in Proteus spp. For piperacillin-tazobactam a category change from I to R was found in 28% of Escherichia spp., 15% of Klebsiella spp. and 4/5 of Proteus spp.. A category change from S to R occurred in 36% of Pseudomonas spp.. In Haemophilus influenzae the category changes for both amoxicillin-clavulanic acid (S to R) and cefturoxime (S or I to R) were less than 5%.

**Conclusions:** Additional testing due to ATU led to clinically relevant antibiotic susceptibility changes, in particular for piperacillin-tazobactam: very major errors (S to R) were observed in >25% of Pseudomonas spp., Proteus spp. and Escherichia spp..

We conclude that ATU testing has a substantial impact on the interpretation of antimicrobial resistance.

<table>
<thead>
<tr>
<th>Species</th>
<th>Antimicrobial agent</th>
<th>No. susceptible results (disk diffusion)</th>
<th>No. resistant results (disk diffusion)</th>
<th>No. of results in ATU (disk diffusion)</th>
<th>Clinical impact of ATU definition and additional E-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Escherichia spp. (2302 isolates)</td>
<td>AMC</td>
<td>2300</td>
<td>704</td>
<td>436 - 62</td>
<td>Category change S to R: 62/498 (12.4%) Category change I to R: 62/151 (27.81%) Category change R to S: 29/151 (19.28%)</td>
</tr>
<tr>
<td></td>
<td>TSP</td>
<td>3101</td>
<td>256</td>
<td>29 - 80 - 42</td>
<td>23/58 (4.5%)</td>
</tr>
<tr>
<td>Klebsiella spp. (1334 isolates)</td>
<td>AMC</td>
<td>989</td>
<td>337</td>
<td>56 - 2</td>
<td>19/102 (15.08%)</td>
</tr>
<tr>
<td></td>
<td>TSP</td>
<td>1012</td>
<td>246</td>
<td>55 - 52 - 19</td>
<td>14/102 (43.65%)</td>
</tr>
<tr>
<td>Proteus spp. (765 isolates)</td>
<td>AMC</td>
<td>695</td>
<td>33</td>
<td>35 - 2</td>
<td>1/37 (5.41%)</td>
</tr>
<tr>
<td></td>
<td>TSP</td>
<td>757</td>
<td>3</td>
<td>1 - 4</td>
<td>43/90 (40%)</td>
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<tr>
<td>Pseudomonas spp. (1689 isolates)</td>
<td>TSP</td>
<td>1248</td>
<td>340</td>
<td>59 - 33</td>
<td>33/92 (33.87%)</td>
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<tr>
<td>Haemophilus influenzae (583 isolates)</td>
<td>AMC</td>
<td>381</td>
<td>87</td>
<td>117 - 8</td>
<td>12/125 (9.6%)</td>
</tr>
<tr>
<td></td>
<td>Cefuroxime IV</td>
<td>304</td>
<td>175</td>
<td>94 - 14 - 6</td>
<td>4/114 (3.51%)</td>
</tr>
<tr>
<td>Total of 1934 isolates</td>
<td></td>
<td>10787</td>
<td>2175</td>
<td>882 - 146 - 178</td>
<td>37/114 (17.3%)</td>
</tr>
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</table>

**Presenter email address:** eveline.vanhonacker@gmail.com
Abstract 9810

**Antibiotic resistance prediction by analysis of whole genome sequence data using ARESdb**

Ines Ferreira*1,2, Stephan Beisken1, Lukas Lueftinger1, Thomas Weinmaier1, Matthias Klein3, Johannes Bacher3, Robin Patel4, Arndt Von Haeseler2, Andreas Posch1

1 Ares Genetics GmbH, Wien, Austria, 2 Center for Integrative Bioinformatics Vienna, Max Perutz Laboratories, University of Vienna and Medical University of Vienna, Vienna, Austria, 3 Curetis GmbH, Holzgerlingen, Germany, 4 Mayo Clinic, Rochester, United States

**Abstract third-party references:** Ares Genetics GmbH

**Background:** Whole genome sequencing (WGS) is now routinely performed in clinical microbiology laboratories to assess isolate relatedness. With appropriately developed analytics, the same data can be used for prediction of antimicrobial susceptibility.

**Materials/methods:** We assessed WGS data for antibiotic susceptibility testing (AST) prediction using ARESdb compared to broth microdilution phenotypic susceptibility testing on clinical isolates from a multicenter clinical trial of the Unyvero LRT Application (Curetis). For the trial, more than 2,000 patient samples were collected from ICUs across nine hospitals and tested for LRT infection. The isolate subset used in this study included 566 clinical isolates originating from 455 LRTI culture-positive patient samples. Isolates were sequenced using the Illumina Nextera XT protocol and FASTQ-files with raw reads uploaded to the ARESdb cloud platform (ares-genetics.cloud, released for research use in 2020). The platform combines Ares Genetics’ proprietary database ARESdb, with state-of-the-art bioinformatics tools and curated public data. Binary AST classification models were trained using a k-mer-based approach on approximately 10,000 de novo genome assemblies per species-compound pair dependent on availability of AST data for 21 antibiotics. Intermediate and susceptible dose-dependent phenotypes were treated as susceptible.

**Results:** WGS-predicted susceptibility showed 89% categorical agreement with phenotypic susceptibility across a total of 129 species-compound pairs analyzed. Categorical agreement exceeded 90% in 78 and reached 100% in 32 species-compound pairs (Table).

**Conclusions:** Results of this study add to the growing body of literature showing that, with improvement of analytics, WGS data could be used to predict antimicrobial susceptibility. With continuous expansion and availability of sequenced isolates and reference AST data, together with an improved understanding of AMR, predictive AST could be incorporated into clinical practice.

<table>
<thead>
<tr>
<th>Species</th>
<th>Compounds</th>
<th>Isolates</th>
<th>Categorical Agreement (%)</th>
<th>Species-Compound Pairs with ≥90% CA</th>
<th>Species-Compound Pairs with 100% CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter baumannii</td>
<td>11</td>
<td>19</td>
<td>199/209 (95.2)</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>15</td>
<td>40</td>
<td>653/660 (94.6)</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>15</td>
<td>48</td>
<td>677/720 (14.0)</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>9</td>
<td>128</td>
<td>950/1038 (91.5)</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>10</td>
<td>135</td>
<td>1153/1350 (85.4)</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Enterobacter cloacae</td>
<td>10</td>
<td>37</td>
<td>313/370 (84.6)</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Other</td>
<td>15</td>
<td>153</td>
<td>1011/11/4 (98.1)</td>
<td>32</td>
<td>16</td>
</tr>
<tr>
<td><strong>Overall (all species)</strong></td>
<td><strong>21</strong></td>
<td><strong>566</strong></td>
<td><strong>89%</strong></td>
<td><strong>78</strong></td>
<td><strong>32</strong></td>
</tr>
</tbody>
</table>

Table: Categorical agreement (CA) per species for whole genome sequencing based susceptibility prediction in comparison with broth microdilution for analyzed ESKAPE pathogens as well as *E. coli*, sorted by categorical agreement in descending order as well as for the overall study.

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Abstract 9814

**Vancomycin loading doses in the emergency department: a Bayesian approach**

Karan Raja1*, Ashita Debnath2, Caroline Bezzubik2, Brandon Chen1, Mark Attalla1, Ruben Patel1, Soo Kang1, Mitesh Patel1, Mona Philips1

1Clara Maass Medical Center, Belleville, United States, 2Ernest Mario School of Pharmacy, Piscataway, United States

**Background:** Appropriate vancomycin dosing is imperative in the first 24 – 48 hours of critical illness to ensure adequate drug concentration and effectiveness while avoiding adverse events. Recent data confirm the ratio of area-under-the-curve to minimum inhibitory concentration (AUC/MIC) predicts efficacy. Vancomycin loading doses theoretically achieve earlier effective concentrations. Bayesian dosing programs utilize population kinetics to estimate patient-specific AUCs and dosing strategies. There is an opportunity to employ Bayesian dosing tools to identify optimal loading doses for critically ill patients. This study sought to compare current loading dosing practice with Bayesian dosing tool recommendations.

**Materials/methods:** The electronic medical record was queried to identify all adult patients given a single vancomycin dose for sepsis treatment in the ED during a one-month period. Patients with a BMI over 30 were excluded as these patients fell outside of the Bayesian dosing software limits. Patients with antibiotic indications not requiring a loading dose were also excluded. Bayesian dosing software was used to extrapolate troughs and AUC24 achieved with the actual dose administered and to calculate a population-based, single loading dose and its associated troughs and AUC24. The primary outcomes evaluated were the dose, anticipated AUC, and trough difference between actual and Bayesian calculated loading doses. Continuous data were analyzed using student’s t-test.

**Results:** Of 121 patients, 43 met inclusion criteria. A loading dose was not indicated in 38 patients and 40 patients had a BMI >30. The Bayesian-calculated loading dose was 119% greater than the actual dose given, with an associated 217% greater modeled AUC24. The AUCs achieved for actual and Bayesian-calculated loading doses were 204.6 mcg*h/mL and 424 mcg*h/mL, respectively \( p<0.05 \). The average actual dose administered was 15.5 mg/kg (1,006 mg) while the average recommended dose from the Bayesian model was 33.1 mg/kg (2,180 mg). The extrapolated troughs for actual and Bayesian-calculated loading doses were 4.3 mcg/mL and 9.1 mcg/mL, respectively \( p<0.05 \).

**Conclusions:** This study demonstrates current dosing strategies in our ED likely achieve sub-therapeutic vancomycin AUC24. The results support application of Bayesian dosing tools for calculating loading doses to increase the likelihood of achieving target AUCs rapidly and potentially decrease clinical failures.

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Increased enterococcal abundance and low microbial diversity are early predictive markers of a microbiota primed for development of Clostridioides difficile infection

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Background: Clostridioides difficile infection (CDI) is the most common form of infectious antibiotic-associated diarrhoea (AAD) causing considerable morbidity and mortality in acute-care facilities. Identification of early markers predictive of CDI in hospitalized patients could substantially contribute to decreasing the CDI burden.

Materials/methods: In this European, prospective, longitudinal cohort-study including 1,007 patients aged ≥50 years receiving broad-spectrum antibiotic treatment with penicillins + beta-lactamase inhibitors, other beta-lactam antibiotics, or fluoroquinolones during hospital stay, we characterized faecal samples using high-resolution, single-nucleotide 16S rRNA gene profiling before (D1, n = 945) and after antibiotic treatment (D6, n = 737). CDI was defined according to the ESCMID diagnostic guidelines.

Results: C. difficile carriage was observed in 51/945 (5.4%, D1) and 50/737 (6.8%, D6) patients. Among patients who developed diarrhoea within 90 days, those with CDI (n=14) exhibited significantly lower diversity (p≤0.016) and a distinctly different microbial composition at D1 compared to those with non-C. difficile AAD (n=64) and no diarrhoea (n=669, 198 lost to follow-up, Figure). At D1, the microbiota was enriched for Enterococcus spp. in patients who later developed CDI, for Clostridiales Incertae Sedis XI, Blautia and Ruminococcus spp. in patients developing non-C. difficile AAD, and for Blautia luti, Porphyromonas, Prevotella, and Bifidobacterium spp. in non-diarrheic patients. Antibiotic treatment reduced microbial diversity and induced class-specific dysbiosis; beta-lactam treatment specifically increased enterococcal abundance, and fluoroquinolone treatment depleted Prevotella spp.

Conclusions: Our findings of a distinct, low-diversity CDI-associated microbiota can be exploited for enriching high-risk patients in prospective clinical trials and for the development of predictive, microbiota-based diagnostics for clinical management of patients at high risk of CDI.

Figure. Characterization of microbial diversity in baseline (D1) samples. CDI patients [blue] display significantly lower alpha diversity in terms of Shannon (A) and Chao1 indices (B), compared to AAD [light blue], and ND patients [green] at D1. Cladogram demonstrating significantly higher abundances of Actinobacteria, Alphaproteobacteria and Enterococcus spp. in the gut microbiota of CDI patients at baseline (D1) compared to AAD and ND patients (C). AAD: patients with antibiotic-associated diarrhoea. CDI: patients with confirmed C. difficile infection. ND: non-diarrheic patients. *: p<0.05. **: p<0.01. ***:p<0.001.

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Phenotypic and genotypic characterisation of BLNAR and BLPACR strains of *Haemophilus influenzae*: a rare finding of presence of ESBLs and highly resistant ftsI mutations in Australian isolates.

Syeda Naqvi*,1; Hemalatha Varadhan1, Rodney Givney1

1 John Hunter Hospital, NSW Health Pathology, Hunter, Newcastle, Australia

**Background:** *Haemophilus influenzae* is responsible for respiratory tract and severe invasive infections such as meningitis and sepsis. The purpose of this study was to characterise the dual mechanism of β-lactam resistance among *H. influenzae* isolates from Australia.

**Materials/methods:** 100 *H. influenzae* isolates which were resistant to both ampicillin and amoxicillin-clavulanate on initial disk diffusion were collected from 2017 to 2019 and phenotypically classified as pBLNAR and pBLPACR based on nitrocefin hydrolysis. Disk diffusion results were verified with gold standard broth microdilution (BMD using EUCAST) and also by CLSI disk diffusion standards to look for concordance. Whole genome sequencing was performed on 44 of these isolates to study *ftsI* and *bla* genes using Illumina MiSeq platform. The Nullarbor pipeline v2.0.20180910 was used to perform de novo assembly using SKESA v2.2. Point mutations associated with resistance (in particular in the transpeptidase domain of penicillin-binding protein 3 encoded by *ftsI* gene) were investigated using the Resistance Gene identifier (RGI) implemented in The Comprehensive Antibiotic Resistance Database (CARD).

**Results:** Among the pBLNAR strains, 25.5% isolates had ampicillin MIC of 1mg/L at the borderline of susceptible range, and 4.6% had a low MIC of 0.5mg/L, making them Low BLNAR [L-BLNAR] strains. Conversely, 100% pBLPACR strains had a very high MIC (8mg/L). Both BLNAR and BLPACR, had a very similar pattern of amoxicillin-clavulanate MIC, higher if *ftsI* gene mutations were of Ubukata group III or Skaare nomenclature group III and III like (D350 N, S357N, S385T and L389F), which have not been previously reported in Australian isolates (Figure 1). Furthermore, we were able to detect three different types of ESBLs in our isolates, which are not previously reported in *H.influenzae*.

**Conclusions:** EUCAST standardized disk diffusion showed better correlation with genotype than CLSI methods. Detecting of *ftsI* mutations and ESBLs in *H.influenzae* may have critical management and infection control implications. WGS is a promising modality to understand β-lactam resistance mechanisms in depth in *H. influenzae*.

**Figure 1:** *ftsI* mutations in our study isolates based on Skaare et al. nomenclature.

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Abstract 9828

Intact EfrEF operons seem essential for chlorhexidine tolerance among Enterococcus faecalis from different hosts and genetic backgrounds

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Background: Chlorhexidine (CHX) is used in the hospital, community and food-animal production settings (hand-hygiene, skin-antisepsis, oral-care and patient-washing; 1200-40000mg/L). Its activity against Enterococcus faecalis-Efs, a major nosocomial pathogen, has been scarcely explored in strains from diverse epidemiological and genetic backgrounds. The EfrEF operon [coding for a heterodimeric ABC transporter] and its transcriptional regulator ChlR were demonstrated to have an important role in CHX tolerance in the Efs-V583 reference strain, by deletion and complementation experiments (doi:10.1128/AAC.00267-18). However, no studies exploring ChlR-EfrEF in diverse Efs strains are available. Here, we evaluated CHX activity and the occurrence and variability of the ChlR-EfrEF operon among Efs from different origins and clonal lineages.

Materials/methods: Efs isolates (n=55; 1999-2018; 4 countries; 46 STs; multidrug-resistant: 31%), recovered from humans [hospitalized-patients-infection, n=12; hospital/healthy-humans/long-term-care-patients surveillance, n=18], food [raw-poultry-carcass, n=7; ready-to-eat-salads, n=2], food-animal-production-settings [piggery, n=8; aquaculture, n=3; aviary, n=1], aquatic-environment [hospital-sewage, n=3; river-water, n=1] were included. CHX-Minimum-Inhibitory-Concentration (MIC\textsubscript{CHX}) was determined by broth-microdilution (range:1 -32mg/L; ISO20776-1:2006;37ºC/24h) in log-phase strains followed by CHX-Minimum-Bactericidal-Concentration (MBC\textsubscript{CHX}) (NCCLS:1999; 37ºC/48h). The ChlR-EfrEF operon was searched by PCR followed by sequencing, using the Efs-V583 (GenBank accession no:AE016830.1) as reference strain. Occurrence of truncated proteins within the ChlR-EfrEF operon was evaluated by the DNA translate tool of ExPASy SIB Bioinformatics Resource Portal (https://web.expasy.org/translate/).

Results: MIC\textsubscript{CHX} ranged between ≤1-8mg/L (modes of 4mg/L; 69% of Efs) and MBC\textsubscript{CHX} ≤1≥32mg/L (modes of 4mg/L/33% and 8mg/L/35% of Efs). Efs associated with infection (n=12) or other sources (n=43) showed the same MIC\textsubscript{CHX}=8mg/L but different MBC\textsubscript{CHX} (8 vs ≥32mg/L, respectively). Vancomycin-resistant Efs [3-clinical/ST2/ST6/ST159; 1-hospital-surveillance/ST6] showed similar MIC\textsubscript{CHX} and MBC\textsubscript{CHX} values (4-8mg/L). Differences among MIC\textsubscript{CHX}/MBC\textsubscript{CHX} were not detected among MDR/non-MDR strains (8≥32mg/L). The ChlR-EfrEF operon was present in all Efs studied, but those with MIC\textsubscript{CHX}≤1mg/L showed EfrE (n=2; aquaculture/healthy-human; both ST40) or EfrF (n=1; piggery-manure/St1200) truncated.

Conclusions: CHX presented good activity against MDR-Efs from different sources and clonal lineages. The variability of ChlR-EfrEF operons among diverse Efs strains was here demonstrated for the first time. In accordance with the studies performed with Efs-V583, our data also show the importance of an intact ChlR+EfrE+EfrF operon for chlorhexidine tolerance in different strains.

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Colistin resistance detection: an easy test for routine laboratories

Deniz Guneser*1, Kübra Özgüler2, Turgut Bozan1, Aysegul Karahasan1

1Marmara Üniversitesi Pendik Edf. Ve Arş. Hastanesi, Medical Microbiology Department, Istanbul, Turkey, 2Marmara University Faculty of Medicine, Medical Microbiology Department, Istanbul, Turkey

Background: Colistin, as an old antibiotic, became last crucial therapy option due to increasing rates of multidrug resistant (MDR) gram negative bacteria. Yet a rapid and user-friendly susceptibility testing remains to be needed for clinical microbiology laboratories.

Aim: In this study, we compared the accuracy of colistin disk broth elution test (CBDE) to that of broth microdilution (BMD) which is the gold standard, in clinical isolates.

Materials/methods: We included MDR Klebsiella pneumoniae [n: 33] and Acinetobacter baumannii [n: 46] strains in our study. Blood isolates consisted 40.5% of strains. BMD was performed as recommended by EUCAST [colistin sulfate powder, Sigma-Aldrich, USA; cation adjusted Mueller Hinton Broth, Becton Dickinson, USA; 96 well polystyrene plates, TPP, Switzerland]. CBDE was performed with cation-adjusted Mueller-Hinton broth [Sigma-Aldrich], 3 tubes per isolate; to which 1, and 2 colistin 10-µg disks (Oxoid, UK) were added, generating final concentrations in the glass tubes of 0 (growth control), 2, and 4 µg/ml, respectively (CLSI M100, 30th ed.; 2020). All experiments were accomplished in duplicates. We interpreted categorical agreement discrepancies as very major error (false susceptibility by CBDE) and major error (false resistance by CBDE). Other antimicrobials were studied by disk diffusion method and VITEK 2 system (bioMérieux, France), then interpreted as recommended by EUCAST.

Results: As seen in Table, very major error was detected in any of the isolates. However, in 9 A. baumannii and in 2 K. pneumoniae isolates major error was detected.

Conclusions: Colistin is one of the very limited drug options in patients infected with MDR bacteria. In a recent past there was no reliable laboratory test except BMD for colistin susceptibility. However, BMD is costly and time consuming. In January 2020, CLSI suggested to implement CBDE test for colistin testing. There are very limited number of publications regarding this issue. We may conclude that, CBDE is an easy to perform and cheap test, but if an isolate was found to be resistant by CBDE, the result should be confirmed by BMD.

<table>
<thead>
<tr>
<th></th>
<th>CBDE</th>
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<tr>
<td></td>
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<td>K. pneumoniae</td>
</tr>
<tr>
<td></td>
<td>S</td>
<td>R</td>
</tr>
<tr>
<td>BMD</td>
<td>S</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>R</td>
<td>0</td>
</tr>
<tr>
<td>TOTAL</td>
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<td>21</td>
</tr>
</tbody>
</table>

*Major error

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Declining antibiotic use in Infants and falling asthma Incidence in children: New findings from population and prospective cohort studies suggest a causal link mediated through the gut bacterial community.

David Patrick*1,2, Hind Sbihi, Darlene Dai1, Abdullah Al Mamun1, Drona Rasali1, Caren Rose1, Fawziah Marra2, Rozlyn Boutin2, Charisse Petersen1, Leah Stiensma4, Geoff Winsor2, Anita Kozysrykij1, Meghan Azad2, Allan Becker7, Piush Mandhane6, Theo Moraes5, Malcolm Sears9, Padmaja Subbarao8, Brett Finlay2, Stuart Turvey2

1British Columbia Centre for Disease Control, Vancouver, Canada, 2University of British Columbia, Vancouver, Canada, 3University of British Columbia, Vancouver, Canada, 4Pepperdine University, Malibu, United States, 5Simon Fraser University, Burnaby, Canada, 6University of Alberta, Edmonton, Canada, 7University of Manitoba, Winnipeg, Canada, 8University of Toronto, Toronto, Canada, 9McMaster University, Hamilton, Canada

Abstract third-party references: Major Funding: British Columbia Ministry of Health, Pharmaceutical Services Branch; Canadian Institutes of Health Research; Allergy, Genes and Environment (AllerGen) Network of Centres of Excellence; Genome Canada. On behalf of the CHILD Cohort Study Investigators

Background: Asthma incidence among children is falling in some countries. Observational studies have linked infant antibiotic use with asthma risk. We hypothesized that falling asthma incidence is linked to reduced antibiotic prescribing at population level, that the same association can be demonstrated in individual children followed over time, and that this is mediated through changes in the gut bacterial community.

Materials/methods: Using administrative data from British Columbia, Canada (population=4·7 Million) we determined the association between antibiotic prescribing (age<1yr) and asthma incidence (ages 1-4yr) at the population level and applied Poisson regression to assess how antibiotic use would predict asthma rates at fine geographic scale. The CHILD prospective birth cohort (n=2644) examined the association at the individual level, with adjustment for key covariates. A mechanistic investigation (n=917) within CHILD used 16S rRNA gene sequencing to assess gut microbiota. Structural equation modeling was applied to explore direct and indirect causal pathways.

Results: Between 2000-14, asthma incidence (ages 1-4y) fell from 27 to 20 per 1000 and was associated with declining antibiotic use in infancy from 1254 to 489 prescriptions per 1000 (Rho=0·88, p<0·0001). Across local health areas, asthma incidence increased 24% with each 10% increase in antibiotic prescribing (IRR=1·24; 95%CI: 1·2-1·3; p<0·0001). In the CHILD cohort, after excluding children who received antibiotics for respiratory symptoms and adjusting for other key covariates, asthma was associated with infant antibiotic use (aOR=2·15; 95%CI: 1·37-3·39; p=0·00093) with a significant dose-response (p=0·00082). Increasing α-diversity of the gut microbiota at age 1yr was associated with a lower risk of asthma at age 5yr (interquartile aOR=0·68; 95%CI: 0·46-0·99; p=0·046). Some taxa that exhibited significant differences in their relative abundance between antibiotic-treated and asthma-diagnosed children compared with controls have previously been demonstrated to have immunomodulatory activity. Structural equation modeling provided evidence that the gut microbiota was a probable mediator between antibiotics and asthma (p=0·027).

Conclusions: Our findings suggest that a significant reversal in the asthma epidemic may be an unexpected dividend of community antibiotic stewardship efforts acting through preservation of the infant gut microbial community.

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The approach to HCV treatment in patients with haematologic malignancies: an ESGVH-ESGICH cross-sectional survey

Laura Ambra Nicolini, Andrea Lombardi, Matteo Bassetti, Malgorzata Karolina Mikulska

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Abstract third-party references: ESCMID study group for viral hepatitis (ESGVH), ESCMID study group for infections in compromised hosts (ESGICH)

Background: Evidence on safety and efficacy of direct acting agents (DAAs) against hepatitis C virus (HCV) in patients with haematological malignancies (HM) is low. This study aims at evaluating the current prescribing practice of HCV treatment in this setting.

Materials/methods: DAAs prescribers were invited to participate in a cross-sectional survey endorsed by two ESCMID study groups and they provided answers on their prescription choices in 12 clinical situations featuring patients with HM, stem cell donors and recipients.

Results: Between November 2019-January 2020, 33 specialists from 16 countries responded to the survey. All but one were Infectious Diseases specialists, median age was 41 (IQR 33-57) years, 41% were females (n=14), 40% (n=13) have worked as specialist for more than 10 years. Most of them (n=29) report having treated <20 patients with HM in the last year. All but one colleagues have access to pan-genotypic DAAs. The regimens currently used in naïve hematological patients are: sofosbuvir/velpatasvir (84.6%, n=22), sofosbuvir/velpatasvir/voxilaprevir (15%, n=4), glecaprevir/pibrentasvir (53.9%, n=14), grazoprevir/elbasvir (23%, n=6), sofosbuvir/ledipasvir (11.5%, n=3). The 96% (n=26) usually administer DAAs as first-line option in case of indolent lymphoma, while 52% (n=14) and 58% (n=15), respectively, consider co-administration of DAAs and chemotherapy for aggressive lymphoma or chronic lymphocytic leukaemia/multiple myeloma requiring immediate chemotherapy. Main perceived risks for treatment during chemotherapy are drug-drug interactions (56%, n=10) and paucity of evidence in this setting (39%, n=7). All but two specialists do not exclude HCV-infected stem cell donors, but 31% (n=8) harvest stem cells from HCV donors only after sustained virological response, while 38% (n=10) and 12% (n=3) once HCV-RNA is undetectable or HCV treatment is ended, respectively. Regarding transplant candidates, the 35% (n=9) schedule HCV treatment following transplantation and 64% (n=17) start HCV treatment before transplant. For stem cells transplant recipients, main reasons to postpone DAAs are ongoing severe bacterial infection (35%, n=9), opportunistic infection (31%, n=8), relapse of HM (27%, n=7), graft-versus-host disease (27%, n=7).

Conclusions: DAAs prescribers consult few patients with HM, they agree on the need for DAAs treatment but the timing is widely variable. Data on optimal timing and safety of DAAs are urgently needed.

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Pharmacokinetics study of cefiderocol in intensive care unit patients
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Background: Cefiderocol is a novel parenteral siderophore cephalosporine that shows potent efficacy against various Gram negative bacteria, including carbapenem-resistant strains, in vitro and in preclinical models of infection. Pharmacokinetics parameters of cefiderocol in patients are currently limited in the literature. The aim of this study was to characterize the pharmacokinetics of cefiderocol after multiple administrations in patients hospitalized in intensive care unit (ICU).

Materials/methods: Patients hospitalized in ICU, and treated with 3-hour intravenous infusions of cefiderocol were included in the study. For each patient, nine successive blood samples were collected at steady state: one sample prior to the start of the infusion for a residual concentration (C0), four samples at 30min, 1h, 2h and 3h during infusion and four samples at 15min, 1h, 2h and 3h after the end of the infusion. Cefiderocol plasma concentration was measured using an ultra-performance liquid chromatography system coupled with mass tandem spectrometry (UPLC-MS/MS), developed and validated in our laboratory. The pharmacokinetic parameters were performed using WinNonLin software.

Results: Seven patients were included in the study. They were treated for P. aeruginosa, A. xylosidans, K. pneumoniae or A. baumannii infection only susceptible to cefiderocol. Ventilated associated pneumonia was the most frequent infectious site [n=6]. The median age was 53 years old [23-73], patients were mostly women [4/7]. Patients were treated with a 2g TID regimen. The mean C0, Cmax, AUC0-8h, t1/2 and Vd were 42.1 ± 20.1 mg/L [21.5-76.3], 77.1 ± 12.9 mg/L [55.8-95.5], 448 ± 155 h.mg/L [306-682], 13 ± 11.3 h [3.3-30.8], and 26.7 ± 9.4 L [18.1-42.3], respectively. The coefficient of variation of C0, Cmax and AUC0-8h were 47.7%, 16.8% and 34.6%, respectively. One patient with renal hyperfiltration was treated with 2g QID regimen. For the QID regimen C0, Cmax, AUC0-6h, t1/2 and Vd were 18.5 mg/L, 75.6 mg/L, 228 h.mg/L, 1.4 h and 15.6 L, respectively.

Conclusions: This is the first prospective pharmacokinetic study of cefiderocol in intensive care unit patients. Our results suggest that there is significant inter-individual pharmacokinetic variability in this patient population; this argue to consider cefiderocol a candidate for therapeutic drug monitoring.

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Abstract 9864

Dose and duration of antibiotic treatment in children with community-acquired pneumonia in UK/Ireland: results from the randomised, double-blinded, non-inferiority factorial CAP-IT trial

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Abstract third-party references: On behalf of CAP-IT and PERUKI

Background: Amoxicillin is recommended for oral treatment of childhood community-acquired pneumonia (CAP). CAP-IT (ISRCTN76888927) investigated the effect of amoxicillin dose and duration on efficacy, safety and antimicrobial resistance.

Materials/methods: Children clinically diagnosed with uncomplicated CAP and planned for discharge from hospital or emergency departments were concurrently randomized (1:1 ratio) to 35-50 mg/kg or 70-90 mg/kg total daily dose and shorter (3d active, then 4d placebo) or longer (7d active) durations. The primary endpoint was clinically-indicated systemic non-trial antibiotic treatment for respiratory tract infection (RTI) during four weeks of follow-up as adjudicated by a blinded review committee. Adverse events and severity/duration of parent-reported symptoms and pneumococcal resistance were secondary endpoints. We tested, using time-to-event methods, the non-inferiority of lower dose to higher dose and shorter to longer duration (8% non-inferiority margin) for re-treatment.

Results: 824 children from 29 hospitals were randomized (February 2017 - April 2019). Ten never started any trial medication and were excluded. Median (IQR) age was 2.5 years (1.6-3.7); 52% male; 591/814 (73%) were discharged from ED; 223 (27%) from ward; 242 (30%) were on beta-lactam antibiotics at enrolment (100% <48h; 76% <24h). At presentation, 441 (54%) were febrile, 578 (71%) had tachycardia, 528 (65%) tachypnea. 767 (94%) children completed trial treatment. The primary endpoint was ascertained for 789 (97%) children. It occurred in 51/410 (12.6%) children receiving lower dose versus 49/404 (12.2%) higher dose (difference 0.4% [90%CI -3.7, 4.0]) and 51/413 (12.5%) shorter duration versus 49/401 (12.5%) longer duration (difference 0.1% [90%CI -3.8, 3.9]), both meeting non-inferiority criteria. Time to resolution of symptoms differed by randomization arm only for cough (median 2 days more with shorter duration, p=0.040) and sleep disturbance (p=0.026). There was a higher prevalence (p=0.005) of rash at day 8 in the longer treatment arm (9.3%) than the shorter treatment arm (4.1%), but mainly of slight severity.

Conclusions: In children with CAP discharged from hospital, the effectiveness of 3-day amoxicillin treatment was similar to 7-day treatment; 35-50 mg/kg/d was also non-inferior to 70-90 mg/kg/d. Analyses of antimicrobial resistance data are ongoing.

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Abstract 9866

**Surprisingly low levels of measles immunity in persons with HIV: a seroprevalence survey in a United States HIV clinic**

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**Abstract third-party references:** Research Support Fund grant - Nebraska Medicine and the University of Nebraska Medical Center

**Background:** Measles outbreaks have become increasingly common due to deteriorating vaccination rates, fluctuating herd immunity, and varying antibody decline. Limited knowledge exists regarding prevalence and risk factors associated with measles seronegativity among persons with HIV (PWH).

**Materials/methods:** This was a cross-sectional study conducted at an academic HIV clinic in Omaha, Nebraska. All PWH presenting to the clinic from November 2019 through January 2020 were invited to enroll. Participants were screened for the presence of measles IgG antibody. Demographic and clinical information was obtained through electronic medical record review. T-tests, chi-square tests, and Fisher’s-exact tests were used to compare characteristics. Simple and multivariable logistic regressions were performed to identify risk factors for measles seronegativity.

**Results:** 351 participants were enrolled with a seronegativity rate of 29.7%. Mean age was 48 years (range 20 to 74), 77% were male and 53% Caucasian. Mean CD4 nadir was 334 cells/mm3 (range 1 to 1675). At the time of testing, 86% and 87% of the seronegative and seropositive participants had an HIV RNA <50 copies/mL, respectively. Younger age was significantly associated with measles seronegativity (p=0.003). Birth year before 1957 was associated with seropositivity (p=0.016), but 6% of seronegative participants were born before 1957. All other risk factors evaluated, including written documentation of adequate vaccination, were not associated with seronegativity.

**Conclusions:** Our study demonstrates a measles seronegativity rate that is remarkably higher than the rate reported in the general population (5%), and, more importantly, is significantly higher than the rate needed to maintain herd immunity (5-7%). With higher than expected seronegativity and absence of notable risk factors aside from age, our findings support expanded measles immunity screening and consideration of revaccination for PWH who are at risk of measles exposure.

**Characteristics Associated with Measles Seronegativity in PLWH**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Seronegative</th>
<th>Seropositive</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age (years)</td>
<td>N=104</td>
<td>N=247</td>
<td></td>
</tr>
<tr>
<td>Born before 1957</td>
<td>6 (6%)</td>
<td>37 (15%)</td>
<td>0.016</td>
</tr>
<tr>
<td>Sex: Male</td>
<td>83 (80%)</td>
<td>188 (76%)</td>
<td>0.45</td>
</tr>
<tr>
<td>Race: Non-Hispanic white</td>
<td>61 (59%)</td>
<td>124 (50%)</td>
<td>0.25</td>
</tr>
<tr>
<td>CD4 nadir ≤200</td>
<td>42 (40%)</td>
<td>83 (39%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Opportunistic Infection History</td>
<td>26 (25%)</td>
<td>48 (19%)</td>
<td>0.24</td>
</tr>
<tr>
<td>Written documentation of vaccination</td>
<td>19 (18%)</td>
<td>27 (11%)</td>
<td>0.063</td>
</tr>
</tbody>
</table>

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A hospital outbreak of linezolid-resistant and vancomycin-resistant ST80 Enterococcus faecium harbouring an optrA-encoding conjugative plasmid investigated using whole-genome sequencing

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Background: Ireland had the highest rates of vancomycin-resistant Enterococcus faecium (VREfm) bloodstream infections in Europe between 2006-2018. Linezolid-resistance (LR) following acquisition of the resistance genes optrA, poxtA and variants of the cfr gene have been reported with increasing frequency worldwide. Recently, Ireland was also found to have the highest prevalence (22.7%) of gene-encoded linezolid resistance in E. faecium and E. faecalis isolates from hospitalised patients reported to date. Resistance was predominantly encoded on conjugative plasmids in diverse enterococcal lineages.

Materials/methods: Between 22nd October and the 1st November 2019, 34 VREfm were recovered from patient screening swabs (n=14) and environmental sites (n=20) on two wards and radiology of an Irish hospital. All isolates were screened for LR genes by PCR and underwent Illumina MiSeq whole-genome sequencing. Isolate relatedness was assessed using E. faecium core-genome MLST (BioNumerics). MinION sequencing (Oxford Nanopore) and hybrid assembly were used to resolve an optrA-encoding plasmid (pM19/0995). Isolate MiSeq reads were mapped against pM19/0995 and the percentage depth and breadth of coverage was calculated using BedTools coverage.

Results: Thirty-two VREfm belonged to ST80, while two were single-locus variants of ST80. Seventeen LR-VREfm harboured optrA, whereas the remaining 17 linezolid-susceptible (LS) VREfm lacked LR genes. A closely related cluster of 23 isolates involving nine patients denoting an outbreak (17 LR-VREfm [6 patients] and six LS-VREfm [three patients]) was revealed with an average pairwise allelic difference of 2 [range 0-10]. A majority (16/17) of LR-VREfm harboured a 58,684 bp conjugative optrA-encoding plasmid (pM19/0995). Five of the 17 samples that yielded optrA-positive ST80 isolates also yielded optrA-negative isolates. In three cases, the optrA-negative isolates were genetically indistinguishable from optrA-positive samples from the same sample apart from the absence of pM19/0995. In the remaining two samples, the optrA-negative isolates had different genetic backgrounds from optrA-positive isolates from the same sample, indicating a mixed population. These findings indicated the spread of a single optrA-positive VREfm clone, following plasmid acquisition.

Conclusions: This demonstrates the transmissible nature of linezolid-resistance in VREfm. Acquisition of optrA by VREfm on a conjugative plasmid is of concern to public health as it reduces treatment options for infected patients.

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**Abstract**

**Efficacy and Safety of Posaconazole versus Voriconazole for the Treatment of Invasive Aspergillosis**

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Abstract third-party references: Funding for this research was provided by Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc., Kenilworth, NJ, USA

**Background:** Invasive aspergillosis (IA) is a life-threatening disease with limited treatment options and is associated with delays ineffective treatment and significant early mortality. Posaconazole has been recommended as primary treatment, but novel [intravenous and oral] formulations of the broad-spectrum azole posaconazole are now also available.

**Materials/methods:** A randomised, prospective, phase 3, double-blind, double-dummy study compared posaconazole (1:1 randomisation) given for ≤12 weeks in the primary treatment of IA. More than 90 study sites in 23 countries enrolled subjects from 2013 through 2019 (ClinicalTrials.gov, NCT01782131; EudraCT, 2011-003938-14). Enrolled subjects were ≥13 years, weighed >40 to ≤150 kg and met criteria for proven, probable or possible disease per modified 2008 EORTC/MSG criteria. Those with chronic, relapse/recurrent or refractory IA were excluded. At randomisation, subjects were stratified by underlying disease risk [high risk: allogeneic stem cell transplant, liver transplant, relapsed AML]. Fungal disease classification and response outcomes were assessed by an independent adjudication committee (AC). Safety was monitored by an independent data monitoring committee. The primary endpoint was all-cause mortality through day 42 in the intent-to-treat population (ITT), with a 10% noninferiority margin.

**Results:** 575 randomly assigned subjects received ≥1 dose of study drug (ITT). The mortality rate through day 42 was 15.3% (44/288) in the posaconazole arm and 20.6% (59/287) in the voriconazole arm (95% CI: –11.5, 1.0). Of the 575 ITT subjects, 331 were AC-classified as having proven or probable infection [full analysis set [FAS] cohort]. Global clinical response rates in the FAS were similar between treatment groups: 45.4% and 45.0% at week 6 and 42.9% and 45.6% at week 12 for posaconazole and voriconazole, respectively. All subjects (ITT) were evaluated for safety. Reported drug-related adverse event (DRAE) rates in ITT subjects were 29.9% for posaconazole and 40.0% for voriconazole (95% CI: –12.9, –2.4). No deaths from DRAE occurred in posaconazole subjects versus three deaths from DRAE in voriconazole subjects.

**Conclusions:** Posaconazole was noninferior to voriconazole for the primary treatment of IA. Posaconazole [IV/tablet] was well tolerated with fewer DRAE. These findings support the use of posaconazole as primary antifungal therapy for IA.

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**Abstract 9874**

Efficacy and Safety of Posaconazole versus Voriconazole for the Treatment of Invasive Aspergillosis
Fosfomycin vs meropenem or ceftriaxone for bacteremia urinary tract infections caused by multidrug-resistant Escherichia coli: a randomised trial (FOREST)


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Abstract third-party references: On behalf of REIPI/GEIRAS/FOREST group

Background: The objective of this study was to demonstrate the non-inferiority of fosfomycin in bacteremia urinary tract infections (BUTI) due to multi-drug resistant E. coli (MDREC).

Materials/methods: A multicenter, open, randomised controlled trial in patients with BUTI due to MDREC comparing (1:1) intravenous fosfomycin (4 g/6h) vs. meropenem (1 g/8h) or ceftriaxone 1 g/24h if susceptible as targeted treatment was performed. Switch to oral drugs was allowed after 5 days. Randomisation was stratified by appropriate empirical therapy and cephalosporin-resistance. Endpoints were: primary, clinical and microbiological cure (CMC) at test-of-cure (TOC) in the modified intention-to-treat (mITT) population; secondary, clinical cure (CC) and microbiological cure (MC) in the clinically and microbiologically evaluable populations (CEP, CMP), respectively, 30-day mortality, recurrences and adverse events (AE). The calculated sample size for a non-inferiority margin of 7% was 198 patients. The study was funded by Instituto de Salud Carlos III; Registration: NCT02142751.

Results: 161 patients from 16 sites could be randomized; 143 formed the mITT population; 70 received fosfomycin and 73 the comparator (42 meropenem, 31 ceftriaxone). Both groups were similar in baseline features: median age, 70 years; male, 49%; Charlson index ≥3, 31%; urinary catheter, 30%; community-acquired infection, 50%; sepsis/shock, 26%; inappropriate empirical treatment, 26%. The endpoints are shown in the Table. More patients in the fosfomycin group did not reach CMC for reasons other than failure (12 [17.1%] vs. 4 [5.4%]; p=0.01). Six patients treated with fosfomycin and 1 with comparator suffered a heart failure [probable or definitive]. Two patients treated with fosfomycin developed a skin rash.

Conclusions: Even if the calculated sample size would be achieved, it is improbable that fosfomycin could demonstrate to be non-inferior to carbapenem or ceftriaxone for CMC; however, more patients in the fosfomycin arm did not reach CMC for reasons other than clinical and microbiological failure. In fact, failure, clinical or microbiological cure rates were similar in both arms in the appropriate populations. Withdrawn of patients because of AE was more frequent with fosfomycin, which must be interpreted considering the open design, but caution is needed in patients at risk of heart failure. Recurrences were more frequent with fosfomycin.

<table>
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<th>Table: Endpoints</th>
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<tr>
<td>Fosfomycin</td>
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<tr>
<td>Clinical and microbiocure (mITT)</td>
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<tr>
<td>Ceftriaxone</td>
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<tr>
<td>Meropenem</td>
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<tr>
<td>Ceftriaxone &amp; Meropenem</td>
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<tr>
<td>Clinical cure (CEP)</td>
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<td>Meropenem</td>
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<tr>
<td>Cep-R isolates</td>
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<td>Microbiocure (MC)</td>
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<td>30-day mortality</td>
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<td>Positive cultures</td>
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<tr>
<td>Recurrence</td>
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</tbody>
</table>

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Abstract 9879

**Safety, tolerability and clinical outcomes of RSV infection challenge in older adult volunteers**

Pete Dayananda*1, Stephanie Ascough1, Zoe Gardener1, Emma Bergstrom1, Seng Kuong Ung1, Mohini Kalyan1, Veda Avadhan1, Satwik Kar1, Suzanna Paterson1, Malcolm Begg2, Edith Hessel2, Peter Openshaw3, Christopher Chiu1

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**Background:** Respiratory syncytial virus (RSV) causes bronchiolitis in infants and is increasingly recognised as a cause of severe disease in the elderly. Current understanding of human immunity against RSV infection is incomplete and neither specific treatments nor effective vaccines are yet available. Controlled human RSV infection studies of healthy adult volunteers enable detailed longitudinal analysis of immune responses but studies in higher-risk volunteers have not previously been performed. To extend the applicability of the model to those at higher risk, we now report the development, safety and clinical outcomes of a human infection challenge study in older adults.

**Materials/methods:** We contacted and screened 381 prospective participants using health and protocol-defined inclusion/exclusion criteria. Twelve healthy adult volunteers aged 60-75 were inoculated intranasally with 10^4 PFU RSV Memphis-37, quarantined for 10 days and followed up for 6 months. All volunteers completed self-reported symptom diaries; viral load was measured daily by qPCR of nasal lavage and antibodies were quantified in serum and respiratory secretions.

**Results:** Of 381 participants contacted, 251 replied and 155 were excluded following pre-screening questions. Ninety-six participants were eligible for full screening; 24 attended and 12 were excluded based on safety-screening results. Following inoculation, 9 of 12 participants developed PCR-confirmed RSV infection. Reported symptoms were mild/moderate with no clinical/self-reported systemic symptoms, hence no trial ‘pausing/stopping’ rules were met. None of the volunteers developed fever (≥38°C) or had a National Early Warning Score (NEWS) >3, which would trigger clinical review.

On average, symptoms started on Day 4 post-inoculation and peaked at Day 7. The symptoms were primarily upper respiratory tract in nature and resolved by Day 10 post-inoculation. Up to Day 28, no participants reported unexpected adverse events or symptom recurrence.

**Conclusions:** We show that experimental infection with RSV in selected older adults has an acceptable safety profile with good attack rate and symptom distribution. We anticipate that efficacy testing of new therapeutic and vaccine candidates in this more clinically relevant age group will decrease the lead time from discovery to clinical practice and enable better understanding of age-related immunological changes and protective immunity against RSV in healthy older adults.

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Different impact of modification of voriconazole therapy following therapeutic drug monitoring (TDM) on the prevention of hepatotoxicity and visual symptoms: Japanese multicenter study

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Background: The pooled risk for hepatotoxicity was 13.6% and that for visual symptoms was 15.7% in patients underwent voriconazole therapy. We retrospectively evaluated the impact of antifungal stewardship on the modification of voriconazole treatment based on TDM, and the occurrence of adverse effects.

Materials/methods: Patients were reviewed at 5 institutions. Target trough concentration (Cmin) was defined as 1–5 µg/mL. Hepatotoxicity was defined as AST/ALT above three times normal/baseline.

Results: 401 patients were included. Loading dose was performed in 46.9%. Median maintenance dose was 3.8 mg/kg twice daily [interquartile range (IQR) 3.2–4.1]. Median day of TDM was 6 [IQR 5–7]. Modification was conducted in 103 of 108 patients with high initial Cmin (discontinuation 32; dose reduction 71) and in 23 of 44 patients with low initial Cmin (discontinuation 4; dose increase 19). Subsequent Cmin achieved target range in 77.9% of patients with dose reduction and 88.0% of patients with dose increase. Hepatotoxicity and visual symptoms occurred in 6.0% and 9.5%, respectively. Median day of the occurrence of adverse effect was 10 days [IQR 8–19] in hepatotoxicity and 4 days [IQR 2–7] in visual symptoms. Although higher initial Cmin tended to cause visual symptoms [area under the curve (AUC) 0.603, p=0.050, odds ratio (OR) 3.59], there was no significant correlation between hepatotoxicity and initial Cmin (AUC 0.562, p=0.292, OR 1.67), which mean the effect of dose modification based on initial Cmin. In contrast, significant correlation with Cmin at the occurrence of adverse effect was demonstrated in hepatotoxicity [AUC 0.725, p<0.001, OR 5.20] and visual symptoms [AUC 0.684, p<0.001, OR 5.89]. Cut-off Cmin to discriminate the occurrence of adverse effects was 3.5 µg/mL in hepatotoxicity and 4.2 µg/mL in visual symptoms. In patients without immediate discontinuation, 14 of 15 patients with hepatotoxicity and 27 of 30 patients with visual symptoms completed voriconazole therapy.

Conclusions: Low incidence of hepatotoxicity was demonstrated with the modification of voriconazole therapy. Because of early occurrence, significant impact on the prevention of visual symptoms was not obtained. A lot of patients with hepatotoxicity and visual symptoms completed voriconazole therapy with antifungal stewardship.

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Abstract 9896

**Validation of an isothermal amplification platform for microbial identification and antimicrobial resistance detection in blood: a prospective study**

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**Background:** Blood stream infections (BSI) and the associated complications remain a leading cause of morbidity and mortality in the hospital Intensive care unit setup. Nucleic acid amplification technique (NAAT) based identification of pathogens in BSI has revolutionized molecular diagnostics in comparison to traditional clinical microbiology practice of blood culture for pathogen detection. Main aim of the study was to evaluate an in-house developed lyophilized OmiX RapID Pathogen test based on isothermal amplification technology for the detection of top six BSI causing bacteria along with two major antimicrobial resistance (AMR) markers of Carbapenem and compare with to traditional blood culture-based detection and to establish concordance between the tests.

**Materials/methods:** 143 subjects admitted to Medical Intensive Care Unit (MICU) at Mazumdar Shaw Medical Center, A unit of Narayana Hrudayalaya, Bangalore, with either suspected or proven BSI, of either gender, of age >=18 years were enrolled for the study. Pathogen DNA was extracted from 200 µl blood culture sample using OmiX pReP method and amplified at isothermal conditions of 65°C and analyzed at real time using OmiX READ software.

**Results:** Among the processed 143 samples, 54 were true negative, 83 were true positive, 3 were false negative and 2 were false positive as analyzed by OmiX READ software. 91.3% of Gram-negative bacteria and 75% of Gram-positive bacteria were detected in true positive cases. With specificity of 100% and sensitivity of 95.69%, the OmiX RapID Pathogen detection kit could identify correct pathogens, even polymicrobial infection, along with the AMR markers in 4 hours of time.

**Conclusions:** We successfully demonstrated that OmiX RapID Pathogen test detects pathogens with 96.5% concordance in comparison to traditional blood culture. Henceforth, OmiX RapID Pathogen test can be used for diagnostic purpose in bacterial BSI. The study would help further to develop the OmiX pathogen DNA extraction and detection in whole blood independent of traditional culture techniques.

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Therapeutic drug monitoring of antibiotics in intensive care patients treated with extracorporeal membrane oxygenation (ECMO): an observational single-center study

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**Background:** Effective antimicrobial treatment is key to reduce the high mortality of bacterial sepsis in patients on intensive care units (ICUs). Dose adjustments are often necessary to account for pathophysiological changes or renal replacement therapy. Extracorporeal membrane oxygenation (ECMO) is increasingly being used for the treatment of respiratory and/or cardiac failure. However, it remains unclear whether dose adjustments are necessary to avoid subtherapeutic drug levels in septic patients on ECMO support. To evaluate and comparatively assess the mean serum concentrations of continuously applied antibiotics in intensive care patients being treated with and without ECMO.

**Materials/methods:** Between November 2018 and December 2019, we prospectively enrolled patients on a pneumological intensive care unit in southwest Germany who received antibiotic treatment with piperacillin/tazobactam, ceftazidime, meropenem, or linezolid. All antibiotics were applied using continuous infusion, and therapeutic drug monitoring of serum concentrations (expressed as mg/L) was carried out using high-performance liquid chromatography. Target concentrations were defined as 4-fold above the minimal inhibitory concentration (MIC) of susceptible bacterial isolates, according to EUCAST breakpoints.

**Results:** The final cohort comprised 105 ICU patients, of whom 30 were treated with ECMO. ECMO patients were significantly younger (mean age: 47.73 vs. 61.15 years; p=0.001), required haemodialysis more frequently (53.3% vs. 32.0%; p=0.048) and had an elevated ICU mortality (60% vs. 22.7%; p=0.0005). In the ECMO group, mean antibiotic serum concentrations were significantly lower for piperacillin (42.2 vs. 72.5; p=0.004), high-dose meropenem (6g/d) (22.0 vs. 41.5; p=0.022) and linezolid (8.2 vs. 12.6; p=0.005). We found high rates of insufficient antibiotic serum concentrations among ECMO patients, which did not reach the pre-specified MIC target (piperacillin: 48.4% vs. 13.0% in non-ECMO; linezolid: 34.8% vs. 15.0% in non-ECMO; meropenem standard-dose (3g/d) 6.1% vs. 3.1% in non-ECMO), whereas no such difference was observed for ceftazidime and meropenem in high-dose.

**Conclusions:** ECMO treatment was associated with significantly reduced serum concentrations of piperacillin, linezolid and, to a lesser extent, meropenem. Future studies are needed to assess the pharmacokinetic characteristics of antibiotics in ICU patients on ECMO support.

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Abstract 9898

Prospetive validation in children with adenovirus detection of a TRAIL/IP-10/CRP host-proteinassay for guiding antibiotic treatment decisions

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Background: Adenovirus infection can trigger bacterial-like immune responses leading to misdiagnosis and unwarranted antibiotic prescription. Previous studies showed that a host-protein assay comprising TNF-related apoptosis induced ligand (TRAIL), interferon gamma induced protein-10 (IP-10) and C-reactive protein (CRP) accurately differentiates between bacterial and viral infections. Here we examine the potential of the signature to reduce antibiotic misuse among adenovirus positive children.

Materials/methods: Children aged > 90 days with fever without source or respiratory tract infection were recruited in a prospective study at pediatric emergency departments [ED] in Germany and Italy [AutoPilot-Dx; grant #701088; NCT03052088]. Infection etiology was adjudicated by unanimous decision of three independent experts based on clinical, laboratory, radiological and follow-up data. Viruses were detected using multiplex PCR on nasopharyngeal swabs. The host-protein assay [ImmunoXpert™, MeMed] gives three possible outcomes: viral, bacterial or equivocal; equivocal is a valid result that does not provide clear-cut etiology determination.

Results: 628 out of 732 children (mean age 3.5 years, 41.9% female) with unanimous adjudication were assigned viral etiology. Of these, 78 (12.4%) had PCR detection of adenovirus [Panel A], with predominantly upper respiratory tract clinical syndromes [Panel B]. Twenty-three out of 78 adenovirus positive children were given antibiotics, representing overuse of 29.5%. Adoption of the host-protein assay would lead potentially to only 8 out of 78 adenovirus positive children being given unwarranted antibiotics [Panel C]; hence, a 3-fold reduction in antibiotic overuse (p-value < 0.01).

Conclusions: This study shows the potential of timely host-protein assay results in aiding the determination of infection etiology and reducing unwarranted antibiotics among adenovirus positive children.

Panel A

Panel B

Panel C

Index Test Result
<table>
<thead>
<tr>
<th></th>
<th>Antibiotic decision observed in study</th>
<th>Number of children given antibiotics if host-protein assay adopted</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Abx N=56</td>
<td>Abx N=23</td>
</tr>
<tr>
<td></td>
<td>(1.8%)</td>
<td>(17.4%)</td>
</tr>
<tr>
<td>Bacterial</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Equivocal</td>
<td>12 (21.6%)</td>
<td>3 (13.0%)</td>
</tr>
<tr>
<td>Viral</td>
<td>42 (76.2%)</td>
<td>16 (69.6%)</td>
</tr>
</tbody>
</table>

*Physician decision about antibiotics would be unchanged when result is equivocal

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Effect of CMV replication on relapse and survival in pediatric AML
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Background: Several studies have indicated better survival after stem cell transplantation (SCT) for acute leukemias, especially acute myeloid leukemia (AML), in case of cytomegalovirus (CMV) reactivation. Here, we investigated if CMV reactivation had an impact on survival after SCT for AML or acute lymphoid leukemia (ALL) in children.

Materials/methods: 177 pediatric allogeneic stem cell transplant recipients from our institution who received myeloablative conditioning were included. Transplant indications included AML, T-ALL and B-precursor ALL. CMV reactivation was correlated with relapse, mortality as well as acute graft-versus-host disease (GVHD) and was analyzed by Fisher’s Exact test or Chi-Square test (if n>100).

Results: From 177 patients included, 42 were transplanted for AML (24 %), 22 for T-ALL (12 %), and 113 for B-precursor ALL (64 %). Mortality and relapse rates (27-37% and 18-26%, respectively), CMV reactivation rates (21-36%) as well as numbers of negative CMV serology status (19-32%) of donor and recipient were comparable between different acute leukemias. When patients were analyzed altogether, CMV reactivation had no effect on relapse rates or mortality. However, a tendency towards fewer relapses after CMV reactivation was observed in AML patients (no relapse (0%) with CMV reactivation vs. 11 relapse cases (33%) without CMV reactivation; p=0.083). In those 128 leukemia patients capable of reactivating CMV, CMV reactivation had a protective effect on relapse rates in AML (no relapse (0%) with CMV reactivation vs. 11 relapse cases (44%) without CMV reactivation; p=0.017). Different effects of CMV on relapse rates and mortality in AML versus B-precursor ALL were noticed in 79 patients who did not reactivate CMV or who did reactivate CMV post SCT. In 17 AML patients, there were no relapses (0%) and 2 deaths (12%) in contrast to 17 relapse cases (27%) and 24 deaths (39%) in 62 children with B-precursor ALL (p=0.017 and p=0.044, resp.).

Conclusions: Latently CMV infected AML patients without documented CMV reactivation after SCT have a significant worse prognosis compared with all other AML patients. The protective effect of CMV reactivation in AML does not appear to be GVH-related.

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Abstract 9907

**In vivo efficacy of NP339 against Invasive Pulmonary Aspergillosis (IPA)**

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**Background:** NP339 is a novel, cationic, synthetic antifungal peptide with anti-mould and anti-yeast activity demonstrated *in vitro*. NP339 is highly differentiated from existing antifungal drug classes with a membrane-targeting, rapidly fungicidal mechanism of action. NP339 is being developed for intravenous and also inhaled administration as an intervention for invasive pulmonary aspergillosis (IPA). Here we demonstrate the *in vivo* efficacy of nebulised NP339 in a murine model of IPA.

**Materials/methods:** Immunosuppressed, male CD1 mice were infected via intranasal administration of *A. fumigatus* conidia. NP339 was nebulised as a monotherapy (*n*=8 mice/treatment group). Lung burden of *A. fumigatus* was assessed by plating of homogenates at clinical end point. A second model investigated the combination of NP339 & AmB. Survival and serum Galactomannan index (GMI) was assessed for up to 96h. *In vitro* interactions of NP339 and AmB were determined in parallel by broth microdilution checkerboards vs. four *A. fumigatus* strains. Metabolic activity was assessed at 24h by way of resazurin and FICIs were determined and annotated (Burkhart *et al* 2006).

**Results:** Nebulised NP339 monotherapy elicited a reduction in lung burden relative to vehicle control in a murine model of IPA. In subsequent experiments, all untreated mice and those given single treatments (NP339 or AmB only) succumbed to infection and were euthanised before the end of the study. In contrast, 25% of animals survived to 96h in the groups given both nebulised NP339 & IV AmB. Serum GM levels and mouse weight at day 3 also tracked with these findings. *In vitro* combinations of NP339 and AmB were additive against *A. fumigatus* with no negative drug interactions observed.

**Conclusions:** This initial study demonstrates the *in vivo* efficacy of nebulised NP339. Combining NP339 with a parenterally administered antifungal led to survival of test subjects in a well-established murine model of IPA. This data supports the future development of NP339 as a component of a dual therapy for IPA. Although there is potential to apply nebulised NP339 (to directly address lung tissue burden) in combination with other antifungal agents (to target disseminated infection), NP339 will be developed for administration by both routes for optimal outcomes.

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Abstract 9911

**Global distribution of the known mobile colistin resistance: mcr genes across different microbiomes**

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**Background:** Colistin is one of the last-line antibiotics for treatment of carbapenem-resistant Enterobacteriales, and its increasing use has led to the emergence of resistance in these and other Gram-negative pathogens. The extensive discovery of mobilised colistin resistance (mcr-1 to mcr-9), across pathobionts and plasmid types, highlights their transmissibility, posing a potential threat to human and animal health. We screened metagenomes from different sources and continents to gauge the prevalence and distribution of known mcr genes.

**Materials/methods:** For this global surveillance 11522 publicly available metagenomic assembly data (2008-2019), from ENA and other public databases, covering 32 different types of microbiomes across six continents, were screened using tblastn [Fig. 1a]. The full-length protein sequences of all known mcr genes (mcr-1 to mcr-9), were queried on ≥ 98% identity and 100% coverage. Exact sequence hits were extracted along with associated metadata including geographic, temporal and other information. This geographic distribution of mcr genes represented by latitude and longitude (regions) was visualized using the R (v.3.6) package “ggplot”.

**Results:** In total, 113 mcr gene hits (mcr-1, mcr-3, mcr-4, mcr-8 and mcr-9) were from 51 samples across 7 different microbiomes, and distributed in 23 regions across six countries and four continents [Fig.1b]. Over 70 % (n=83) of the mcr genes were detected in human gut metagenomes. Mcr-9 was most prevalent overall (n=79), in terms of highest temporal prevalence in metagenomes from the human gut (n=73), bioreactors (n=2), food (n=2) and fermentation (n=1) [Fig. 1c]. Mcr-3 (n=18) as the second most prevalent gene was found only in wastewater and freshwater metagenomes. Mcr-1 was frequently present but only in human gut metagenomes (n=12). Mcr-9 distributed most widely in 8 regions across North America, Europe, Asia and Africa, and mcr-1 and mcr-3 distributed in 3 regions across Europe, Asia and North America [Fig. 1b]. Mcr-4 and mcr-8 were only detected in one region of North America and Asia, respectively.

**Conclusions:** Our results show that the recently discovered mcr-9 is the most widely distributed mcr variant geographically and temporally. Importantly, we identified human gut metagenomes as the primary reservoir of these easily transmissible colistin resistance genes.
Microbiomes screened in this study

- Biofilter: 7
- Mixed Culture: 17
- Fermentation: 25
- Plant: 33
- Food: 78
- Freshwater: 120
- Soil: 154
- Bioreactor: 295
- Animal gut: 325
- Wastewater: 163
- Human Oral: 404
- Marine: 286
- Unspecified: 1050
- Human Skin: 1051
- Human Gut: 11522

Number of unique sample

Global map of mcr (node sized by hits)

Network between microbiomes and collection years (line thickness by hits)

Fig. 1
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Abstracts 2020

Abstract 9916

**Legionella pneumophila urinary antigen testing during an outbreak: Read it or not**

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**Background:** Legionnaires’ disease (LD) is a severe form of pneumonia, mostly caused by *Legionella pneumophila* (L.pn) serogroup 1. A qualitative L.pn urinary antigen test (LUAT) based on lateral flow immuno-chromatography is commonly used in clinical laboratories for the rapid diagnosis of LD. The antigen test can be read visually, or in conjunction with an automatic reader. However, not much is known about the real life benefit of such a reader for objective LUAT interpretation. During May and June 2019 an outbreak of L.pn serogroup 1, eventually linked to a cooling tower, caused 32 cases of LD around an industrial zone in Ghent, Belgium. We demonstrate the diagnostic impact of the systematic use of an automatic LUAT reader during this outbreak.

**Materials/methods:** In our secondary care hospital lab, urine samples of possible LD cases are analyzed with LUAT (Abbott BinaxNOW™ Legionella Urinary Antigen Card used with DIGIVAL™ reader) and lower respiratory samples, when available, with real-time PCR (BioGX Mycoplasma pneumoniae, Legionella pneumophila and Chlamydia pneumoniae open system reagents for BD MAX™) following manufacturer instructions. Positive respiratory samples are sent to the national reference lab (NRC UZ Brussels) for confirmatory testing by culture and PCR for L.pn and Legionella spp.

**Results:** During the outbreak our lab performed a total of 319 LUAT and 81 PCR. Twenty out of 32 LD cases (62.5%) linked to this outbreak were diagnosed in our lab. All these cases were LUAT positive. Noteworthy, seven of them (35%) were visually negative, but positive with the reader. A lower respiratory sample was available for 13 cases (65%), of which 3 were only reader positive on the urine sample. All 13 samples were PCR positive and confirmed at the NRC. No false positive LUAT results were seen.

**Conclusions:** During a LD outbreak, the use of an automatic reader increased the diagnostic sensitivity of LUAT considerably without loss of specificity.

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DAV132 protects intestinal microbiota of patients treated with quinolones. A European phase II randomized controlled trial

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Background: Antibiotic treatments elicit intestinal microbiota dysbiosis with short and long-term deleterious effects. A colon-targeted adsorbent, DAV132, prevents dysbiosis in healthy volunteers and so may protect antibiotic-treated patients.

Materials/methods: An open label, randomized clinical trial targeted hospitalized patients treated with oral/iv fluoroquinolones (FQ) for lower respiratory or urinary infections or febrile neutropenia prophylaxis. Patients were randomised 1:1 to receive DAV132 (7.5g tid orally), or not, during FQ treatment. Central laboratories evaluated plasma concentrations of FQ after 4d by LC-MS/MS, free faecal FQ concentrations, αβ diversity of the intestinal microbiota (16S rRNA gene profiling) at D1, D4, D6, End-of-FQ, 10 days after End-of-FQ, and 30 days after End-of-FQ. Resistance to colonisation by C. difficile (Cd) was assessed ex-vivo [suppression of Cd proliferation]. The primary endpoint [proportion of adverse events (AE) related to DAV132 and/or FQ] was adjudicated by blinded independent experts.

Results: 260 hospitalized patients at 24 sites (median age 71, ≥1 chronic comorbidity: 96%) were treated for 7.5d on average (79% iv) with levofloxacin (43%), ciprofloxacin (40%) or moxifloxacin (17%). Compared with the No-DAV132 arm, faecal FQ levels in DAV132-treated patients were reduced by more than 98.8%, whilst plasma levels did not change significantly. During FQ treatment, significant differences in all metrics of intestinal microbiota diversity were observed between the two arms, such as changes from D1 of the Shannon index at End-of-FQ (Δmean ± SEM at End-of-FQ: 0.56 ±0.17, p.003). The proportion of patients with DAV132- and/or FQ-related AEs did not differ significantly between arms ([4.8 vs. 10.8%, difference of proportions: 4.0%; 95% CI [-4.7; 12.6]]. No Cd infection occurred. Ex-vivo resistance to colonisation by Cd was markedly reduced in stool samples of patients receiving FQ only, but was maintained in those co-administered DAV132 (p=0.0003). Faecal carriage of vancomycin-resistant enterococci (VRE) was reduced in DAV132 treated patients (p=0.01).

Conclusions: DAV132 was well tolerated in elderly hospitalized patients with comorbidities. It neither altered antibiotic plasma concentrations nor elicited changes in concomitant drugs regimens. Intestinal microbiota diversity was protected and resistance to colonization by Cd was preserved. DAV132 is a promising, novel product to prevent antibiotic-induced intestinal dysbiosis.

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Abstract 9920

Expanding SARS-CoV-2 detection to a regional laboratory network: Proof-of-concept on the Luminex ARIES platform

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Abstract third-party references: Wojciech Swidzinski, Senior Field Applications Specialist EMEA, Luminex Corporation

Background: Reliable, simple and fast detection of SARS-CoV-2 seems to be a key element in the worldwide public health and individual patient management of the ongoing global COVID-19 outbreak. New ubiquitous walk-away PCR platforms with an open channel for lab developed tests (LDT) could increase diagnostic capacity, especially if set up in close cooperation with (and quality controlled by) a national reference lab. As the ARIES platform (Luminex) was already implemented in 4 labs of the Bilulu vzw group across Flanders, Belgium, we investigated transferring the design of the reference lab method of the University Hospitals of Leuven to this efficient platform, targeting the SARS-CoV-2 E-gene and ORFab region.

Materials/methods: As an initial design, EvaGreen dye was used to test the two primer sets separately with a positive RNA extract from SARS-CoV-2 provided by the national reference lab, on the ARIES system. RNA extract or a negative control were added directly into the ARIES PCR tube, together with primer mix and EvaGreen dye while nuclease free water was added to the sample chamber. Additionally, a patient sample, positive for HCoV-HKU1 (NxTAG Respiratory Pathogen Panel, Magpix, Luminex), was tested for possible cross-reactivity. Luminex SYNCT software was used to interpret PCR results and melting curves.

Results: Both targets, E-gene (ct value 16) and ORFab region (ct value 19.9) were detected for the RNA extract from SARS-CoV-2.

Conclusions: A first proof of concept implementing a consensus molecular SARS-CoV-2 screening on the ARIES instrument was successful. With a hands-on-time of 10 minutes, a turn-around-time of 2 hours and 5 minutes at a cost less than 30 EUR, this assay can be a simple and feasible 24/7 solution for many labs. Inter-laboratory testing and close cooperation with a national reference lab could support a safe and high quality expansion of testing capacity.

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Abstract 9922

Unmasking Higher-than-Expected Prevalence of Mycobacterium tuberculosis DNA in Respiratory Samples from US-born Patients in a Safety Net Hospital in Boston.

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Background: The recent description of sequential inflammatory stages characterizing early tuberculosis (TB) disease and reports of disease caused by differentially culturable M. tuberculosis have significantly complicated the diagnostic landscape. These detection gaps threaten global TB elimination goals.

Materials/methods: During early development of a new ultrasensitive molecular TB assay, we tested consecutive anonymized respiratory samples submitted to the microbiology laboratory for routine non-TB testing from patients admitted to a safety net hospital in Boston, and consecutive anonymized control samples from a community hospital. We subsequently performed a longitudinal study to determine clinical associations and outcomes.

Results: 18/146 (12.6%) anonymized specimens tested positive for M. tuberculosis DNA (TB-DNA), compared to 1/50 (2%) controls (p=0.03). The prospective study included 101 patients [median age 59, 63% male, 70% US-born]; 16/101 (15.8%) tested TB-DNA positive, with a clear bimodal age distribution. Whereas older TB-DNA positive subjects [n=12, mean age 62] had various infectious and non-infectious clinical syndromes commonly encountered in hospitalized patients, 3/4 young TB-DNA positive patients [mean age 22] presented with acute chest syndrome [3/16 vs. 0/85; p=0.003]. TB-DNA positive individuals were more likely to have been tested for M. tuberculosis infection prior to study inclusion [p=0.03], to be TST or IGRA-negative [p<0.001], and to have anemia [p=0.002] a known laboratory marker of TB disease. During a median 1,819 days [interquartile range 1,658–1,842] of follow up, 6/16 (38%) TB-DNA positive patients died a median 390 days [5–694] after hospital discharge, compared to 21/85 (25%) of those TB-DNA negative that died after a median 26 days [14–102] after discharge (p=0.30). Most TB-DNA positive patients died from septicemia [67% vs 14%, p=0.02].

Conclusions: We unexpectedly detected M. tuberculosis DNA in a presumably low TB risk population. In addition to unmasking novel clinical associations, our findings suggest a paucibacillary and inflammatory form of TB disease that is currently clinically unsuspected and undetectable with existing tools. These results require further investigation given the potential implications for patient outcomes and public health.

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Abstract 9930

Seven versus 14 days of antibiotic treatment for male urinary tract infection (PROSTASHORT): a randomized study

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Background: Despite a paucity of data on the optimal antibiotic duration for male urinary tract infections (UTI), current guidelines recommend antimicrobials for at least 14 days. Shorter duration may expose patients to recurrence whereas longer duration may lead to more side effects, C. difficile infections and increased antimicrobial resistance.

Materials/methods: Multicenter, non-inferiority (10% margin), double blind, randomized placebo-controlled trial comparing a short (7 days) versus a standard (14 days) treatment duration for febrile adult male UTI. After a 3-day initial treatment consisting in ofloxacin (400 mg/d), cefotaxime (3g/d) or ceftriaxone (1g/d), patients were assigned to receive oral ofloxacin, 200 mg bid, for 4 days and placebo for 7 days (short treatment arm) or oral ofloxacin 200 mg bid for 11 days (standard treatment arm). Male adults with febrile UTI defined by fever, at least one sign of UTI and urinary culture yielding a single pathogen, susceptible to quinolones and 3rd generation cephalosporin and normal ultrasound findings were randomized at day 3 if fever had resolved (T<38°C). Randomization was stratified on center, age and urological history. Main non-inclusion criteria were: septic shock, nosocomially acquired UTI, UTI in the past year, current urinary catheter.

The primary endpoint was resolution of fever and sterile urine up to 4 weeks after the end of treatment. Secondary outcomes included the acquisition of intestinal carriage of resistant gram-negative bacilli, the incidence of drug related adverse events and the recurrence of UTI during 12 weeks.

Results: 240 patients were included between March, 2015 and April, 2019, 115 and 125 in the short and standard duration arms, respectively. Median age was 60.4 years; 72 (30%) patients had a history of urological abnormalities.

Final results of intention-to-treat and per protocol analyses will be presented at the ECCMID meeting.

Conclusions: The results of this first multicenter, double blinded randomized trial comparing 7 days versus 14 days for the treatment of febrile male UTI should allow to better define the optimal duration of antibiotic treatment in this population.

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Are healthcare workers more worried but less prepared for novel COVID-19 as compared to non-healthcare personnel? Online Questionnaire based comparison of knowledge, attitude and practices during the current outbreak

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Background: World Health Organization has declared the current Coronavirus outbreak a Public Health Emergency of International Concern. To date, epidemiological data on attitude, practices and mental health issues of health professionals and the general public of the current outbreak is not available. Dissemination of the right information is necessary to understand the risks and initiate containment interventions. This study aimed to quantify the present knowledge, prevalent attitude and planned practices to counter the current COVID-19 outbreak and study differences in these parameters between healthcare (HCP) and non-healthcare personnel (nHCP).

Materials/methods: An anonymous online questionnaire-based cross-sectional survey was conducted among a section of the adult population consisting of both HCPs and nHCP. The questionnaire included 11 questions to assess knowledge in MCQ format, 6 questions to assess attitude on a 5 point Likert scale and 9 questions to assess practices on a 3 point Likert scale. The survey was circulated among peer groups and on social media platforms.

Results: There were a total of 470 respondents between 2nd to 11th Feb 2020 (342 HCP, 128 nHCP). Average score of the knowledge section was 76.5% (HPC 78%, nHPC 72%). For assessment of attitude, 5-point Likert Scale responses were converted into a weighted score by assigning graded points for each response. As per this weighted score, 92% HCP & 91% nHCP would avoid overseas travel, 55% HCP & 53% nHCP preferred to avoid public transport, 81% HCP and 88% nHCP agreed covering their cough would decrease the risk of transmission of COVID-19. 34% HCP and 53% nHCP admitted having never worn masks in public spaces. 20% HCP and 33.6% nHCP had never avoided public transport during previous outbreaks. 77% HCP & 70.3% nHCP were distressed about the current outbreak but only 25% HCP and 15% nHCP thought they might get infected.

Conclusions: Our survey found a low level of knowledge among both HCP and nHCP with HCP performing slightly better than nHCP. The recommended attitude and best practice scores were similar among both groups. The stress levels about the epidemic are higher among HCP. Wider dissemination of correct information is urgently needed.

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Abstracts 2020

Abstract 9942

**A cluster of COVID-19 in France, January-February 2020**

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**Background:** COVID-19 epidemic originated in December 2019 in Wuhan, China; as of 16/02/2020, the virus spread in 25 countries, including France. The proportion of severe cases was high in the first reports; extremely few cases under the age of 18 have been reported. First works estimated the basic reproduction number to be 2.2-3.6.

On 7/2, a COVID-19 case was confirmed in the UK in a British male who had traveled in Singapore and had then stayed in a French ski resort while being symptomatic. We investigated to identify potential secondary cases and interrupt transmission.

**Materials/methods:** A case for this cluster was a patient either symptomatic or asymptomatic with a sample positive for SARS-CoV-2, and an epidemiological link with the index case or a confirmed case linked to the index case.

**Results:** From 25 to 28/01, the index case, while symptomatic, stayed in a chalet in the French Alps with 12 other British adults and 3 children. Of those, five tested positive for SARS-CoV-2 in France (4 adults and a 9-year-old child). Moreover, 6 additional close contacts who had left the chalet in the meantime tested positive for SARS-CoV-2 (5 in the UK, 1 in Spain). On 14/02, one additional case was diagnosed; he had stayed in the chalet after the index case had left, suggesting tertiary transmission. Five of the 6 positive patients diagnosed in France had transitory mild fever at the end of January; at the time of the diagnosis, they had no fever, and mild symptoms (cough and/or running nose); one case had no symptoms. All other close contacts of the secondary cases who developed symptoms tested negative (including those linked to the infected child, who attended three schools and one ski class while symptomatic). The first negative sample from the cases was obtained 5 to 7 days after the first positive sample.

**Conclusions:** Our investigations indicated that one single individual spread SARS-CoV-2 in 11 others. In contrast, the infected child, despite very close interactions with a large number of contacts, did not transmit the infection. Mild cases are probably more frequent than initially suspected.

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Abstract 9943

**Novel Formulations of Polymyxin B to Mitigate Polymyxin-Induced Nephrotoxicity in Rats**

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**Background:** Despite its crucial role in treating life-threatening gram-negative infections, the clinical utilization of polymyxin B is limited due to the risk of acute kidney injury (AKI). In this study, we assessed four novel formulations of polymyxin B (VRP034_F21-24) with regard to their ability to reduce polymyxin-induced nephrotoxicity.

**Materials/methods:** Healthy male SD rats were treated with either standard polymyxin B [control] or one of the four formulations [treatment] at a dose of 25 mg/kg/day [human equivalent dose: 4mg/kg/day] in 4 divided doses for 2 days via subcutaneous injection (n=6 for each group). Serum samples were collected at baseline and on day 3 for analysis of serum biomarkers - KIM-1 [kidney injury molecule], cystatin-C, creatinine and urea. Necropsy was done on day 3 for gross observation and kidney was collected for histopathological evaluation. Data were compared with basal values and statistical analysis was performed to evaluate nephrotoxicity associated with each formulation.

**Results:** In the control group, a significant increase in all four serum biomarkers was observed on day 3 as compared to basal values [urea: 311% (p<0.001); creatinine: 700% (p<0.001); KIM-1: 180% (p<0.001); cystatin-C: 66% (p<0.01)]. In addition, clinical manifestations like pallor of the ears and pads with redness, muscular incoordination and respiratory distress, eventually leading to complete flaccidity of skeletal muscle with dyspnea, were noted in the control group. As a result, 50% animals died after the 8th dose before scheduled necropsy. On the contrary, animals treated with novel formulations did not show any significant increase across all four serum biomarkers on day 3 (p>0.05), except for KIM-1 in formulation VRP034_F24 that increased by 19% (p<0.01). Also, none of the animals died in the treatment groups. Histopathology of the kidney (Fig-1) confirmed necrotic changes in tissues with congestion and vacuolization in the control group, whereas, only minor tubular damage was noted in two (VRP034_F21, F24) of the four formulations tested and no appreciable damage was detected in the other two groups (VRP034_F22-23).

**Conclusions:** Novel formulations of polymyxin B [VRP034 F22-23] significantly mitigated the risk of AKI and can provide a safer alternative in treating resistant gram-negative infections.

**Figure 1:** Representative histopathological images of kidneys from rats in control and treatment groups:
- (VRP034_F21) - Kidney showing normal organization of glomeruli, mild tubular damage with vacuolization.
- (VRP034_F22) - Showing normal glomerular and tubular histology. The tubules were largely intact without the presence of any mononuclear infiltrates in the interstitium and blood vessels were also unremarkable. (VRP034_F23) - Showing normal glomerular and tubular histology. The tubules were largely intact without the presence of any mononuclear infiltrates in the interstitium and blood vessels were also unremarkable. (VRP034_F24) - Showing normal organization of glomeruli, mild tubular damage with vacuolization. (Control) - Showing necrotic changes in kidney tissues with congestion and vacuolization.

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Comparison of in-house and commercial RT-PCR assays for the diagnosis of 2019-novel Coronavirus (SARS-CoV-2) infection

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**Background:** in December 2019 an outbreak of pneumonia of unknown cause spread from Wuhan (Hubei) to China: it rapidly became a global concern due to the risk of worldwide diffusion. The etiologic agent has been promptly identified as a novel coronavirus, recently named SARS-CoV-2, closely related to SARS-CoV (about 79% sequence identity). L. Sacco University Hospital in Milan is one of the two Italian reference centers for bioemergencies diagnosis and treatment.

**Materials/methods:** between February 10th and 14th 2020 a total of 10 nasopharyngeal swabs, collected from COVID-19 (2019 novel coronavirus disease) suspected patients, were assayed using different in-house and commercial kits, based on the market availability. Viral RNA was extracted by NucliSENS® easyMag® (bioMérieux) eluting 500 µL of sample in 50 µL. The following assays were used according to manufacturers’ instructions: Novel Coronavirus (2019-nCoV) Real Time Multiplex RT-PCR Kit (targets: E gene, N gene, RdRP gene), Liferiver; TaqMan™ 2019 nCoV Assay Kit v1 (targets: N gene, Orf-1ab gene, S gene), Applied Biosystem; Allplex™ 2019-nCoV Assay (targets: E gene, N gene, RdRP gene), Seegene Inc; in-house protocol from Hong Kong University [targets: N gene, Orf-1b gene], available at WHO website [01/23/2020]. The 7500 RT-PCR System (Applied Biosystem) was used for all but Seegene assay, running on CFX96 (BioRad). Viral RNA extracted from frozen cell-culture supernatant, obtained from a SARS-CoV diagnosed patient at L. Sacco University Hospital in 2003, was included as positive control due to the high sequence identity.

**Results:** All samples resulted negative for SARS-CoV-2 with any assays. Viral RNA from SARS-CoV showed a positive signal in RT-PCR for the following gene targets: two out of three genes for Liferiver assay (E and N); E gene for Seegene assay; both N and Orf1b genes with Hong Kong protocol, whereas none of the three targets was detected by Applied Biosystem assay.

**Conclusions:** in-house Hong Kong protocol was able to detect SARS-CoV RNA for both gene targets. All commercial assays provided a good specificity for SARS-CoV-2: SARS-CoV RNA showed amplification profile negative for RdRP gene, or a pattern of positive results for E and/or N genes classified as negative according to manufactures’ interpretation.

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Abstract 9961

Unprecedented rates of azole-resistant *Aspergillus fumigatus* identified in the environment of Mekong Delta of Vietnam, with marked variability by ecological niche.

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**Background:** Rising rates of azole-resistance in environmental *Aspergillus fumigatus*, driven by agricultural azole use, are a major public health threat. Since the leading risk factor for aspergillosis is prior TB infection, this threat is greatest in high-TB low-income settings, which lack the capacity to diagnoseazole-resistance or to provide alternative treatments.

Globally, environmental resistance rates of 10-15% have been reported, 33% in high-azole-use niches, though Southeast Asian data are lacking. Vietnam has high TB-incidence, intensive farming, unregulated agri-chemical use, and limited fungal diagnostic capacity; together making azole-resistance both likely and clinically important. Therefore, we conducted an environmental sampling study.

**Materials/methods:** We collected samples in a rural province of Vietnam, from 150 locations distributed across the principal environmental niches (see table). We measured *A. fumigatus* susceptibility with EUCAST methodology, and concentration of agricultural azoles at all sample sites. We investigated the relationship between niche, azole contamination, and *A. fumigatus* resistance rates using logistic regression.

**Results:** Of 529 *Aspergillus* spp. isolates, 192 were *A. fumigatus* complex and 61 *A. fumigatus sensu stricto*. Of the 116 *A. fumigatus* complex tested to date, 60% were resistant to itraconazole (ITZ-R) (71% posaconazole (PSZ-R), 44% voriconazole (VRZ-R)), varying by niche (see table). ITZ-R rate in *A. fumigatus sensu stricto* was 85%. We detected azoles in 26/142 sites (see table). Compared to National Park, odds ratios for ITZ-R *A. fumigatus* were 0.56 (p=0.46) for shrimp farm, 1.73 (p=0.37) for rice farm, 3.92 (p=0.02) for rural residential, and 10.32 (p=0.001) for urban residential. Our models did not show a significant relationship between azole contamination and resistance, but the lowest rate of resistance was in the National Park, where no azoles were detected.

<table>
<thead>
<tr>
<th>Niche</th>
<th>ITZ-R n/N (%)</th>
<th>PSZ-R n/N (%)</th>
<th>VRZ-R n/N (%)</th>
<th>Azole present n/N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urban residential</td>
<td>21/25 (84%)</td>
<td>22/25 (88%)</td>
<td>15/25 (60%)</td>
<td>1/18 (5.6%)</td>
</tr>
<tr>
<td>Rural residential</td>
<td>21/25 (84%)</td>
<td>22/25 (88%)</td>
<td>13/25 (52%)</td>
<td>1/43 (2.3%)</td>
</tr>
<tr>
<td>Rice farm</td>
<td>17/32 (53%)</td>
<td>25/32 (78%)</td>
<td>14/32 (44%)</td>
<td>10/30 (33.3%)</td>
</tr>
<tr>
<td>Shrimp farm</td>
<td>4/17 (24%)</td>
<td>6/17 (35%)</td>
<td>4/17 (24%)</td>
<td>1/21 (4.8%)</td>
</tr>
<tr>
<td>National park</td>
<td>3/11 (27%)</td>
<td>3/11 (27%)</td>
<td>2/11 (18%)</td>
<td>0/30 (0%)</td>
</tr>
</tbody>
</table>

**Conclusions:** We found unprecedented levels of azole resistance, and have shown that rates vary by ecological niche. These alarming rates of resistance undermine the local validity of existing empiric azole therapy guidelines.

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Abstract 9962

Metagenomic Next-Generation Sequencing to Evaluate Changes in the Gastrointestinal Microbiome and Resistome of Patients with Varying Carbapenem-Resistant Enterobacterales Colonization Status

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Background: The purpose of this study was to identify changes in the intestinal microbiome and resistome that promote a favorable environment for carbapenem-resistant Enterobacterales (CRE) colonization and/or progression to infection among high-risk patients (i.e., ICU, oncology, solid and bone marrow transplant recipients).

Materials/methods: We screened >4,000 patients for intestinal colonization at admission and weekly thereafter for CRE by culturing >10,000 rectal swabs. The following goups were included: (a) patients with longitudinal samples who never acquired CRE, (b) patients CRE positive at admission who remained positive, (c) patients initially CRE negative who became CRE positive and did not progress to infection, and (d) patients initially CRE negative who became CRE positive and progressed to CRE infection. Long-read metagenomic next-generation sequencing (mNGS) using the Oxford Nanopore sequencing platforms of sequential swabs was performed on 133 swabs from 55 patients to assess diversity in the microbiome and resistome of patients. The CosmosID bioinformatics pipeline was applied to analyze data and perform comparative analyses (alpha-diversity; Shannon diversity).

Results: We found that the bacterial taxa diversity among samples for most patients is already disrupted at admission for high-risk patients and predominated by pathobionts (e.g. Enterococcus spp, Enterobacterales) (Figure 1A-D). The diversity of the resistome is higher relative to the microbiome among these patients (F.1A&B). Both the microbiome and resistome can shift considerably within a patient. Using Patient 2 as an example, the diversity index varied from 0.9 to 3.9 among 9 swabs. Upon deeper investigation, the differences in diversity for this specific patient align temporally with three separate admissions. The observed changes in diversity are possibly associated with separate microbiome disruption events accompanying those admissions (1C). However, upon progression to infection, the CRE dominated the microbiota prior to infection (CRE K. pneumoniae on Admission 2; 1C).

Conclusions: The microbiota of high-risk patients are disrupted at admission reducing colonization resistance and leading to an increased likelihood of CRE acquisition. An inverse relationship between the intestinal microbiome diversity and the resistome was observed and CRE dominated the microbiota prior to progressing to infection. As a next step, we will link clinical metadata to the mNGS results.

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Abstract 9964

Phase IIa dose escalation treatment of *Clostridioides difficile*-associated diarrhea with MGB-BP-3, a novel first in class DNA minor groove binding antibiotic

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Background: MGB-BP-3 is a synthetic polyamide related to Distamycin A, which selectively binds to the minor groove of microbial DNA, is highly active against gram positive pathogens, has been found to be bactericidal vs *C. difficile* and associated with lower sporulation in-vitro as compared to vancomycin. In the Hamster model of *C. difficile* infection, MGB has been shown to protect against death and prolongs post-treatment survival.

Materials/methods: In this sequential ascending dose escalation study, subjects [n=10-12/ dose level] with primary or first recurrent EIA toxin positive CDAD are treated with 125 mg, 250 mg, and lastly 500 mg bid for 10 days to assess initial cure at day 12 (IC) and followed for recurrence of CDAD 4 and 8 weeks post-treatment. Primary endpoints are safety, tolerability, and IC. Secondary endpoints includes sustained cure (SC) at 4 weeks post-treatment, pharmacokinetics of MGB in plasma and stool on days 1, 5, 10, 12, 14 and 17. Changes in the fecal microbiome over time as measured by qPCR and 16S sequencing are exploratory endpoints. In a subset of half of subjects, quantitative counts of *C. difficile* burden before, during and after treatment to day 38 assesses MGB effect on *C. difficile* in-vivo.

Results: As of 15 Feb. 2020, 30 subjects have been enrolled, and follow up to 4 weeks post-treatment will be completed before April 15. Of the 2 completed cohorts, in the 125 mg dose group, 10/11 attained IC; one subject failed despite microbiologic suppression of Cd, and SC was attained in 8/9 evaluable subjects (one protocol violation). Quantitative Cd cultures showed suppression to LLOD log 2 at day 10 in 7/8 subjects. In the 250 mg dose group, 11/11 attained IC and 8/8 completing follow up attained SC (3 pending). Including all subjects to date, MGB-BP-3 appears well tolerated with one subject in the lowest dose reporting transient dizziness. Safety testing to date has shown no drug related AE. qPCR showed preservation of Bacteroidetes and moderate reduction in Cluster IV and XIVa microbes.

Conclusions: MGB-BP-3 appears to be well tolerated and appears to merit further study as a CDAD treatment candidate.

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Pharmacokinetics of a newly developed oral ceftriaxone formulation (VRT001-C) in mice and rabbits

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Background: Ceftriaxone is among the most widely prescribed antibiotics globally due to its broad-spectrum activity and favourable pharmacokinetic properties. However, the clinical use of ceftriaxone in outpatient settings is limited by its poor oral bioavailability (<1%). VRT001-C, a novel oral ceftriaxone formulation, is currently in development and has previously reported bioavailability of 55% after intraduodenal administration in mice [Poster number: P4265, ECCMID 2020]. This formulation has since been updated to target faster drug release in human plasma (pH≈7.4) and in this study, we present the pharmacokinetic data of the revised formulation of VRT001-C after oral administration in mice and rabbits.

Materials/methods: 16 healthy Swiss albino mice (25-30g, both sex) and 6 New Zealand White rabbits (1.5-2kg, both sex) were fasted overnight and were administered either VRT001-C (Oral) or ceftriaxone (IV). Mice were dosed at 200mg/kg while rabbits were dosed at 50mg/kg (human equivalent dose of 1g across both species). After a single dose of either drug, plasma samples were withdrawn at various time points up to 24hrs and drug concentration was analysed using a validated HPLC method. PK parameters were calculated using noncompartmental analysis.

Results: In mice, the mean bioavailability of VRT001-C was 340% as compared to the IV group [AUC\text{0-inf} of 1424.03 ± 68.61 mg/L·h vs. 419.25 ± 5.36 mg/L·h]. This is likely due to the lower drug clearance of VRT001-C [5.61 ml/h vs 19.08 ml/h] resulting in a prolonged half-life [3.19 hrs vs. 0.82 hrs]. In rabbits, mean bioavailability of VRT001-C was 57% as compared to the IV group [AUC\text{0-inf} of 532.35 ± 46.5 mg/L·h vs. 930.82 ± 77 mg/L·h]. Similar to mice, the half-life of VRT001-C in rabbits was longer than that observed in the IV group [10.10 hrs vs. 2.18 hrs], however, unlike mice, the concentration-time curve for VRT001-C in rabbits depicted a sustained release profile. This was evidenced by a much higher C_{\text{max,IV}}/C_{\text{max,Oral}} ratio in rabbits as compared to mice [23x vs. 1.2x].

Conclusions: The high bioavailability of VRT001-C across both animal species indicates high intestinal permeability and provides promising evidence to further the development of VRT001-C for clinical use.

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Legionellosis in solid organ transplantation: ten years of French experience

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Background: Legionellosis is a life-threatening bacterial infection that may affect solid organ transplant (SOT) recipients. Little data are available on this rare though severe opportunistic infection among SOT recipients. So, we aimed to describe clinical manifestations, treatment features and outcome of legionellosis in SOT recipients.

Materials/methods: This French multicentric retrospective study included all patients with SOT and definite Legionella infection diagnosed from 2009 to 2019. We examined the hospital discharge databases to identify patients corresponding to the following codes: legionellosis (A481) and liver (Z944) or kidney (Z940) or lung (Z942) or heart (Z941) transplantation. Legionellosis was diagnosed in case of positive culture from respiratory sample, and/or positive urinary antigen test (UAT) and/or positive serology.

Results: Twenty-eight patients were included from 8 transplantation centers: 17 (61%) kidney, 7 (25%) liver and 4 (14%) heart transplant recipients. At diagnosis, median age was 61.5 years [range 27-81]. Median duration between transplantation and Legionella infection was 5 years [range 14 days to 42 years], 25% were health-care associated infections [7/28]. At diagnosis, 19 were febrile [68%], 22 had pulmonary symptoms [79%], 13 [46%] diarrhea, and 5 [18%] neurological symptoms. Thoracic imaging showed 25 [93%] alveolar consolidation, 19 [70%] interstitial pneumonia [8/11], 9 [33%] pleural effusion, 7 [26%] pulmonary nodules, 3 of them being excavated [11%]. Median duration between onset of symptoms and legionellosis diagnosis was 6.5 days [range 1-30]. UAT was performed in every patient: 4 [14%] were initially negative. Sixty percents of bronchoalveolar lavage culture were positive [6/10]. At time of diagnosis, 11% [3/28] of patients were already receiving empirical therapy active on Legionella. After diagnosis confirmation, 8 [29%] patients received monotherapy of spiramycin, 11 [39%] monotherapy of fluoroquinolone, 9 [32%] fluoroquinolone and spiramycin.

Median duration of antibiotic therapy was 19 days [range 3-114]. Fifteen patients [54%] were hospitalized in intensive care unit (ICU), 10 [36%] required mechanical ventilation, and 8 [29%] received catecholamine. Day-30 mortality rate was 11% [3/28].

Conclusions: Legionellosis in SOT recipients is rare [28 cases in 10 years], atypical [26% of nodular pneumonia, 14% with negative UAT], and severe [54% hospitalized in ICU, 11% of death].

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Outcomes of the novel β-lactam/β-lactamase inhibitor combination of cefepime-enmetazobactam versus piperacillin-tazobactam in adult patients with complicated urinary tract infections – the ALLIUM phase 3 trial

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Background: Development of new agents to treat infections caused by 3rd generation cephalosporin (3GC)-resistant Enterobacteriales, specifically those producing extended spectrum β-lactamas (ESBL), is a critical priority. Enmetazobactam is a novel ESBL-inhibitor developed in combination with cefepime. We present the results of the ALLIUM phase 3 trial that evaluated the efficacy, safety, and tolerability of cefepime-enmetazobactam versus piperacillin-tazobactam in adult patients with complicated Urinary Tract Infections (cUTI) or Acute Pyelonephritis (AP).

Materials/methods: Patients randomized 1:1 in a double-blind multicenter trial received either 2 g cefepime/ 0.5 g enmetazobactam or 4 g piperacillin/ 0.5 g tazobactam q8h by 2h infusion for 7 to 14 days. The primary efficacy parameter was the proportion of patients in the microbiological modified ITT population (m-MITT) who achieved overall treatment success at test-of-cure, defined as the composite of clinical cure and microbiological eradication. Only patients with a Gram-negative isolate non-resistant to cefepime-enmetazobactam (MIC ≤8 mg/L) and piperacillin-tazobactam (MIC ≤64 mg/L) were included in the m-MITT population. Two-sided 95% CI were computed using the stratified Newcombe method. The prespecified noninferiority margin was -10% with superiority testing in the event of confirmed noninferiority.

Results: 516 randomized patients received at least one dose of cefepime-enmetazobactam, and 518 at least one dose of piperacillin-tazobactam. Overall success in the m-MITT population occurred in 273 of 345 (79.1%) patients treated with cefepime-enmetazobactam versus 196 of 333 (58.9%) treated with piperacillin-tazobactam (difference, 21.2% [95% CI, 14.3% to 27.9%]). Clinical cure rates were 92.5% and 88.9% for cefepime-enmetazobactam and piperacillin-tazobactam, respectively (difference, 3.5% [95% CI, -1% to 8%]). Overall success in the m-MITT subpopulation of ESBL co-producing-positive infections was 73.7% [56/76] and 51.6% [34/66] for cefepime-enmetazobactam and piperacillin-tazobactam, respectively (difference, 30.2% [95% CI, 13.4 to 45.1]). Treatment emergent adverse events were reported in 50.0% [258/516] of patients treated with cefepime-enmetazobactam and 44.0% [228/518] with piperacillin-tazobactam; most were mild to moderate in severity (89.9% and 88.6% with cefepime-enmetazobactam and piperacillin-tazobactam, respectively).

Conclusions: Treatment of cUTI/AP patients with cefepime-enmetazobactam exhibits superior treatment outcomes to piperacillin-tazobactam. Cefepime-enmetazobactam is intended as a new empiric carbapenem-sparing option in settings where 3GC resistance mediated by ESBL is prevalent.

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Detection of SARS-CoV-2 by the first (RUO) commercial rapid multiplex PCR respiratory panel

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Background: Since the first cases of severe acute respiratory infections associated with SARS-CoV-2 (former 2019-nCoV) in China, more than 60,000 cases have been reported. Rapid isolation, the cornerstone for containing the outbreak, must rely on rapid and performant PCR-testing. We evaluated the first rapid multiplex-PCR allowing detection of SARS-CoV-2, in about an hour and fully compatible with close-to-patient testing.

Materials/methods: QIAstat-Dx Respiratory 2019-nCoV Panel (QIA-RP-nCoV) is a research use only (RUO) qualitative multiplexed nucleic-acid-based in-vitro diagnostic test detecting a large panel of respiratory viruses including SARS-CoV-2. To assess its sensitivity, we used serial dilutions of a positive SARS-CoV-2 nasopharyngeal swab, obtained from one of the four COVID-19 patients hospitalized at Bichat Claude Bernard university hospital. They were tested with QIA-RP-nCoV and the WHO recommended SARS-CoV-2 PCR provided by the Charité hospital, Berlin, with E gene (Eg) and RdRp individual detection. A positive broncho-alveolar lavage (BAL), bronchial- and tracheal-aspirates were also tested. Cross-reaction with human-coronaviruses (OC43, NL63, HKU1, 229E) was assessed.

Results: QIA-RP-nCoV and Charité methods detected the positive sample at 21.1 and 21.5 Cycle threshold (Ct), respectively, and both detected 1/10 (n=1), 1/100 (n=1), 1/1000 (n=1) and 1/10,000 (n=3) dilutions. The 1/100,000 dilutions, corresponding to 100 copies/mL of transport media, were positive for 3/5, 5/5 and 0/5 replicates for QIA-RP-nCoV, Charité-Eg and Charité-RdRp, respectively. The 1/1,000,000 dilutions were positive for 1/5 replicates with QIA-RP-nCoV and Charité-Eg. The tested BAL, bronchial- and tracheal-aspirates provided similar results with QIA-RP-nCoV and Charité-Eg methods (27.9, 29.1 and 21.3 for QIA-RP-nCoV and 28.2, 29.0 and 22.7 for Charité-Eg, respectively). No cross reaction was identified with other human-coronaviruses.

Conclusions: The RUO-version of QIA-RP-nCoV assay allows sensitive, specific and rapid, about one hour on demand vs four hours for the WHO method, detection of SARS-CoV-2 coupled with detection of all clinically relevant respiratory viruses. Our results are in line with the limit of detection provided by the manufacturer at 300 copies/mL. The analyzer and cartridge design allow its use in any laboratory, even not PCR-trained, but also permit point-of-care testing by direct use of the nasopharyngeal swab without further manipulation.

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Abstract 9977

An optimised dosing regimen vs. a standard dosing regimen of vancomycin for the treatment of late onset sepsis due to Gram-positive microorganisms in infants less than 90 days: the NeoVanc trial

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Abstract third-party references: the NeoVanc Consortium

Background: Vancomycin remains one of the most widely prescribed antibiotics for Gram-positive neonatal late onset sepsis (LOS). Robust neonatal clinical outcome data comparing different vancomycin dosing regimens is lacking. NeoVanc (NCT02790996) is a European, multicentre, phase IIb, randomised controlled, non-inferiority trial comparing an optimised and standard vancomycin regimen in infants aged ≤90 days with known/suspected Gram-positive LOS.

Materials/methods: Infants with clinical sepsis (≥3 clinical/laboratory criteria) or confirmed sepsis (Gram-positive blood culture and ≥1 clinical/laboratory criterion) were included. Participants were randomised 1:1 to an optimised regimen (loading dose [25 mg/kg] followed by 5±1 days of 15 mg/kg q1 2h or q8h dependent on postmenstrual age [PMA] or a standard regimen [10±2 day course at 15 mg/kg q24h, q1 2h, or q8h dependent on PMA]). The primary endpoint was successful outcome at end of vancomycin therapy and no clinically/microbiologically significant relapse/new infection requiring treatment with anti-staphylococcal antibiotics within 10 days of stopping vancomycin.

Secondary endpoints included safety and pharmacokinetics. ‘Per protocol’ was all participants receiving/not receiving the loading dose as randomised and ≥48h of study vancomycin.

Results: 242 infants were randomised between March 2017 and July 2019 from 22 neonatal intensive care units in 5 European countries. Per-protocol population is presented (183 participants): 55% were male, with a median (IQR) postmenstrual age of 32(29–37) weeks and postnatal age at onset of LOS of 14(8–25) days. Mean weight was 1663g(924g SD) and central lines were present in 115/183(63%) participants at randomisation. 133/183(73%) received antibiotics in the 7 days before randomisation. 179/183(97%) had positive blood culture for Gram-positive organisms of interest at randomisation, and 141/183(77%) received vancomycin according to the randomised duration. There were 4 deaths and 4 withdrawals/loss to follow-up prior to TOC. There were 40 post-randomisation exclusions.

128/129(72%) had a successful primary outcome. 2/165(1%) of all randomised infants had abnormal renal function at short-term follow-up.

Conclusions: NeoVanc is the largest LOS vancomycin trial to provide clinical efficacy and safety outcome data associated with alternative dosing strategies. Preliminary results are included (some events not yet adjudicated): final results comparing randomised groups and outcomes will be presented.

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Safety and immunogenicity of a replication deficient simian adenoviral vectored Chikungunya vaccine: results of a phase I, first-in-human, dose escalation trial.

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Background: Chikungunya is a mosquito-borne alphavirus. The disease consists of an acute febrile illness with often incapacitating polyarthralgia and/or polyarthritis, which lasts weeks to months. Chikungunya disease lead to considerable economic losses and increased burden to already thinly stretched healthcare systems, especially in developing countries. There are currently no licensed vaccines against CHIKV. A handful of candidates have now entered clinical trials, but most of them require ≥2 doses to induce strong immune responses. ChAdOx1 Chik is a replication deficient simian adenoviral vectored vaccine expressing the structural polyprotein cassette of CHIKV. We report final safety and immunogenicity data from a first-in-human clinical trial where ChAdOx1 Chik was administered as a single un-adjuvanted intramuscular dose.

Materials/methods: 24 healthy adult participants aged 18-50 years received an intramuscular injection of ChAdOx1 Chik at 3 escalating doses in Oxford, UK. The primary endpoint was safety and tolerability, whilst assessment of humoral and cellular immunogenicity was the secondary endpoint. Antibodies were measured by ELISA against E2 and neutralising antibody titres by PRNT80. T-cell responses were measured by IFN-γ ELISpot and flow cytometry. Participants were followed for 6 months.

Results: ChAdOx1 Chik was well tolerated at doses up to 5 x 10¹⁰ vp with no serious adverse reactions. The vast majority of adverse events were mild or moderate [95%, CI 95%: 89-98] and all were self-limiting in nature [medium duration = 2 days]. T-cell responses peaked at day 14 and persisted significantly above baseline for 6 months, with greater cytokine production from CD4+ when compared to CD8+ T-cells. Up to 89% [CI 95%: 67-97] of participants in the intermediate and high dose groups seroconverted at day 28 on ELISA. PRNT80 data showed that a single dose of ChAdOx1 Chik elicits protective neutralising antibodies [titres ≥ 1:10] for a selection of Chik isolates and as early as 14 days after vaccination.

Conclusions: ChAdOx1 Chik was safe and well tolerated. A single dose induced robust T-cell and antibody responses, with protective neutralising titres for up to 6 months. These results support further clinical development of ChAdOx1 Chik.
Abstracts 2020

Abstract 9983

**Microbiological and patients’ characteristics of excluded suspicions of SARS-CoV-19 infection in Paris, France**

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**Background:** Since last December, more than 660,000 COVID-19 cases have been declared worldwide. To date, Bichat Claude Bernard university hospital in Paris, a reference center hosting emerging infectious diseases in France, hospitalized 4 SARS-CoV-2 confirmed infections and excluded the infection among 86 other possible cases. Here, we describe the main characteristics of those excluded cases.

**Materials/methods:** Clinical and epidemiological data of possible patients addressed to our hospital up to the 12th of February 2020 were prospectively collected. We evaluated their demographic and microbiological characteristics.

**Results:** 35/86 (41%) were male, the median age was 32 years [IQR: 20-41]. 45 were Chinese foreigners visiting France, 26 travelers coming back from China (n=24) or Taiwan/Japan (n=2) and 15 had contacts with confirmed cases. 55 presented at least one general symptoms (42 fever, 4 chills, 13 headache, 14 myalgia and 10 asthenia) and 83 at least one respiratory symptom (77 cough, 25 odynophagia, 19 rhinorrhea, 7 dyspnea, 2 thoracic pain, 1 expectoration). Median duration between first symptoms and consultation was 2.5 days [1-31]. 42 (55%) were positive by multiplex PCR including 6 viral codetections and 1 associated to M.pneumonia. Among identified viruses, 27 were influenza (17 A, 7 B and 3 untyped), 9 rhinoviruses, 5 coronaviruses (2 NL63, 2 OC43 and 1 229E), 4 metapneumoviruses, 3 RSV, 3 adenoviruses and 2 parainfluenza. Virus negative and positive patients clinical presentation did not statistically differ despite a tendency to more fever among viral-infection (62 vs 31%, p=0.09). Influenza clinical presentation were not statistically different from other viruses despite higher proportion of fever (85 vs 39%, p=0.12) and myalgia (30 vs 8%, p=0.16). To note, 4/5 (80%) and 1/5 (20%) of patients presenting human coronaviruses also presented fever and myalgia, respectively.

**Conclusions:** Among the 86 first excluded suspicions of SARS-CoV-2 infections in our hospital in Paris, seasonal respiratory viruses, half influenza, were the leading cause of infections. Their epidemiology is similar to respiratory viruses currently circulating in France and they presented similar clinical characteristics to those reported for SARS-CoV-2 infections. Larger influenza vaccination should be use and help to reduce the number of suspicion.

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Safety and immunogenicity of a replication deficient simian adenoviral vectored Zika vaccine: preliminary results of a phase I, first-in-human, dose escalation trial.

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**Background:** Zika belongs to the Flaviviridae family of arthropod-borne RNA viruses and is mainly transmitted by Aedes mosquitoes. However, vertical transmission during pregnancy can cause severe lifelong disability. Despite up to 80% of cases being asymptomatic, Zika is now known to be associated with an increased risk of serious and poor neurological outcomes. There are currently no licensed vaccines against ZIKV and several candidates have now entered clinical trials, but not all of them are suitable for vaccination of pregnant women and of childbearing potential (live attenuated or replication competent vectored vaccines). ChAdOx1 Zika is a replication deficient simian adenoviral vectored vaccine expressing structural proteins of ZIKV. We report preliminary safety and immunogenicity data from an ongoing first-in-human clinical trial where ChAdOx1 Zika is administered as a single un-adjuvanted intramuscular dose.

**Materials/methods:** The ChAdOx1 Zika antigenic cassette contains the ZIKV precursor of membrane (prM) and envelope protein with deletion of the 3' transmembrane domain, but does include the DIII domain which is associated with cellular receptor binding and contains epitopes for neutralising antibodies. Healthy adult participants aged 18-50 years will be recruited at 3 escalating doses in Oxford, UK. The primary endpoint is safety and tolerability of ChAdOx1 Zika. The secondary endpoint is to assess humoral and cellular immunogenicity examined by ELISA and IFN-γ ELISpot respectively, at different timepoints. Participants will be followed for 6 months.

**Results:** Preliminary safety data shows that ChAdOx1 Zika was well tolerated at low and intermediate doses with no severe or serious adverse events reported to date. Local and systemic AEs were mild or moderate and so far resolved within 4 days. ChAdOx1 Zika induced T-cell responses even at the low dose, with responses peaking at 14 days post vaccination. Recruitment and follow-up are still ongoing. Only 7 participants had been recruited by the time of this abstract submission.

**Conclusions:** Preliminary results of this first-in-human trial show that ChAdOx1 Zika was well tolerated at 5x10⁹ and 2.5x10¹⁰ vp doses. A single dose of ChAdOx1 Zika elicited T-cell responses. Further data on safety and immunogenicity will be presented at the conference as they become available.
Abstract 9989

Outbreak of listeriosis associated to deli meat in Andalusia, Spain: main clinical results highlighting large number of cases and very low mortality

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Background: Listeria monocytogenes is an uncommon etiology of foodborne illness, the mortality of the outbreak-related invasive infection ranges 5-41%. Elderly people, immunocompromised patients, pregnant women and newborns have a higher risk of invasive listeriosis. At the end of July 2019, an increase in the cases of listeriosis was detected in Andalusia, Spain. A brand of deli meat was identified as the source of the outbreak through the epidemiological surveys and isolation of L. monocytogenes in the meat. The outbreak was publicly declared the August 15th 2019 and all the lots of this brand of deli meat withdrawn of sale.

Objective: to describe the clinical features and outcome of the outbreak-related patients with invasive listeriosis.

Materials/methods: We considered as outbreak-related cases those with a laboratory-confirmed invasive infection whose isolate of L. monocytogenes was the same subtype identified in the deli meat or could not be typed [including cases diagnosed through nucleic acid tests] but exposed to the contaminated product. All cases were notified to the Epidemiological Surveillance System of Andalusia. Clonal relationship was studied through by whole genome sequencing [cgMLST]. Clinical features were obtained from the clinical records.

Results: We identified 198 cases with invasive listeriosis as outbreak-related [176 confirmed by cgMLST: CT-8466] from July 22nd to September 24th 2019 in Andalusia.

Table: Clinical characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age med(IQR)</td>
<td>45 [32-62]</td>
</tr>
<tr>
<td>Female sex</td>
<td>114 [57.6]</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>89 [44.9]</td>
</tr>
<tr>
<td>Chronic disease</td>
<td>68 [34.3]</td>
</tr>
<tr>
<td>Immunodepression</td>
<td>21 [10.6]</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>35 [17.7]</td>
</tr>
<tr>
<td>Gastroenteritis at presentation</td>
<td>106 [63.6]</td>
</tr>
<tr>
<td>Clinical category patients with known data/no. total [%]</td>
<td>193/198 [97.5]</td>
</tr>
<tr>
<td>Bacteraemia</td>
<td>153 [77.3]</td>
</tr>
<tr>
<td>Central nervous system infection</td>
<td>27 [13.6]</td>
</tr>
<tr>
<td>Chorioamnionitis</td>
<td>9 [4.3]</td>
</tr>
<tr>
<td>Neonatal sepsis</td>
<td>4 [2]</td>
</tr>
</tbody>
</table>
One hundred and twelve (56.6%) patients received ampicillin, in 40 (20.2%) cases combined with gentamicin; oral amoxicillin was used in 101 (51%) patients; in 41 (20.7%) cases as sequential therapy and in 60 (30.3%) as the only treatment. Four (2%) patients died, all of them were more than 70 years old. Four pregnant women (11.4%) suffered a foetal loss and 5 (14.3%) a pre-term birth.

**Conclusions:** This outbreak of listeriosis showed a low mortality, which could be partially explained by the proportion of young and previously healthy people. Invasive infection was common in patients with gastroenteritis.

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Abstract 9992

**Multisite viral evolution in a COVID-19 infected patient treated by lopinavir/ritonavir**


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**Background:** An outbreak of COVID-19 has spread worldwide from Wuhan, China, in January 2020. The first European imported case was reported in France on January 20th. The 6th COVID-19-infected patient was diagnosed and hospitalized in our isolation department on the 29/01/20, i.e., 6 days after exposure. He was a French physician who acquired the disease after examining two sick Chinese from Wuhan visiting Paris with their Taiwanese guide, who was secondarily confirmed COVID-19 infected. He had self-medicated with amoxicillin and oseltamivir since 28/01/2020, when he developed myalgia, sore throat and mild fever prior admission.

He was investigated in as many sites as possible for COVID-19 viral carriage during his hospitalization.

**Materials/methods:** From Day 2 after his first symptoms, viral semi-quantitative determination was regularly conducted from multisite swabs and body fluids. We used two real-time Polymerase Chaine Reactions (RT-PCRs), a first-line screening assay targeting E gene and a confirmatory assay targeting RdRp gene of COVID-19.

Chest X-Ray showed a mild pulmonary opacity in the right lung at day 7 even though the patient had no lower respiratory infection signs. Chest CT-scan confirmed small areas of ground-glass opacities in both lower lungs. Thus lopinavir/ritonavir 200/100mg was prescribed twice a day orally for 10 days and the patient was closely monitored during and after this treatment.

**Results:** Virological results presented in Table 1 showed the presence of COVID-19 DNA not only in the upper respiratory sites but also in the tears, saliva and plasma. However stools and urines tested were negative.

The all-sites indetectability by RT-PCR was observed only 14 days after the occurrence of symptoms and 7 days after the lopinavir/ritonavir start. The outcome was good: absence of evolution towards severe pneumonia, and only digestive side effects (unformed stools).

Blood and fluids specimens have been stored for lopinavir pharmacological levels measurements.

**Conclusions:** We describe CoViD-19 multisite and prolonged viral excretion in a paucisymptomatic patient. Lopinavir boosted with ritonavir, did not seem to have a rapid impact on viral load clearance in this single patient. However it’s efficacy in CoViD-19 infection should be better evaluated in a prospective controlled study.

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Abstract 9993

**Dissociation between sustained negative nasopharyngeal swab and positive endotracheal aspirate in a patient presenting with COVID-19 pneumonia**

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**Background:** Detection of SARS-CoV-2 in Coronavirus disease 2019 (COVID-19) patients relies on a reverse transcriptase polymerase chain reaction (RT-PCR) assay performed on oral or nasopharyngeal swab (NPS). We report a case of a patient included in the Haute Savoie cluster who was linked to a confirmed index case and who subsequently developed COVID-19 pneumonia diagnosed by positive endotracheal aspirate (ETA) despite persistent negative NPS.

**Materials/methods:** Patient’s clinical characteristics were monitored daily during the quarantine in a French tertiary hospital. SARS-CoV-2 diagnosis was based on a RT-PCR assay developed by the French National Reference Centre for respiratory viruses targeting RdRp-gene. Other pulmonary viruses were detected using FilmArray® RP2+ (BioFire Diagnostics, SLC, USA).

**Results:** A 53-year-old man with no major medical history was hospitalized for quarantine in strict isolation after having been in contact with confirmed COVID-19 cases. On admission, the patient was asymptomatic and NPS was negative for SARS-CoV-2 detection. On day 5, he presented isolated fever (38.1°C), with no sign of upper or lower respiratory tract infection. Chest radiography performed on day 6 showed mild bilateral basal interstitial lung infiltrates. Thoracic CT-scan on day 7 confirmed these findings with patchy peripheral ground glass images of the left lower and middle lobes. NPS remained negative for SARS-CoV-2 and other respiratory viruses. Biological findings only disclosed a mild inflammatory syndrome (C-reactive protein, 1.2 mg/L). While fever persisted 3 days, other clinical parameters – including SpO2 – remained normal, with no sign of lower or upper respiratory tract infection until day 9 when patient presented mild dry cough and rhinorrhea. An ETA performed on day 8 was positive for SARS-CoV-2 confirmed by an induced sputum (I.S) on day 9, whereas NPS remained negative. Clinical follow-up is currently ongoing.

**Conclusions:** This is the first description of dissociated results between negative NPS and positive ETA in a patient with COVID-19 pneumonia. This observation suggests that for patients at high risk of COVID-19, even mild symptoms (i.e., isolated moderated fever) should prompt clinicians to perform chest CT-Scan and lower respiratory tract sampling to detect infection.

[Figure 1. Temperature and results for SARS-CoV-2 testing during follow-up.]

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Abstract third-party references: French Covid-19 Study Group

Background: On December 31, 2019, China reported a cluster of cases of pneumonia in Wuhan. The responsible pathogen is a novel coronavirus (SARS-CoV-2). Since the identification of the first imported cases in France, we launched a national cohort of patients with COVID-19.

Materials/methods: The objectives of this cohort are to describe: 1) clinical features of illness; 2) treatment used and their outcome; 3) virus replication, excretion and evolution in multiple sites; 4) host responses including innate and acquired immune responses; 5) host genetic variants associated with disease progression/severity. Patients are diagnosed with SARS-CoV-2 by semi-quantitative reverse-transcriptase polymerase chain reaction (RT-PCR) on nasopharyngeal (NP) swabs. Patients are hospitalised and discharged when symptoms resolve and two negative nasopharyngeal swabs 48 hours apart obtained. The cohort is sponsored by INSERM and approved by the French Ethics Committee on 05/02/2020 (NCT04262921). We used the ISARIC Clinical Characterisation Protocol to standardize data collection at the international level.

Results: On February 16, 2020, twelve patients (8 males, 4 females) were infected by SARS-CoV-2 in France: six in January and six in February (the ‘Haute-Savoie cluster’). Three were imported cases, two travelled to France with the index case, seven had transmission in France. Eleven were adults (median age=48) and one a child (age=9). Through analysis of clinical features and close monitoring of viral shedding, we characterized 3 clinical patterns: 1) pauci-symptomatic patients (n=9), when diagnosed early with high nasopharyngeal shedding decreasing over time, 2) patients with a two-step progression of the disease, worsening after 7-10 days, with lower respiratory tract infection despite a decreasing viral load (n=2); 3) rapid evolution towards multi-organ failures with stable SARS-CoV-2 shedding in NP swabs, and detection in blood (n=1, a 80 years-old patient). In three severe patients the investigational drug remdesivir was initiated, and in one pauci-symptomatic patient lopinavir/ritonavir. On February 16, 2020, five patients were discharged from the hospital and one died.

Conclusions: Standardised data and comprehensive virology and immunology sample collection implemented in this cohort, in line and in connection with other international cohorts, will contribute to a better understanding of the disease natural history and its treatment.

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Description of patients hospitalized as possible cases of COVID-19 in a Parisian hospital

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Background: An outbreak of acute respiratory disease in China lead to the discovery of a new type of coronavirus on January 3rd, named COVID-19. Given the epidemic risk in France, the French health authorities asked infectious disease specialists from reference health establishments to classify the suspect cases. All patients classified as possible COVID-19 case (PCC) were hospitalized in isolation rooms. The objective of our study is to describe the patients admitted in our department as PCC.

Materials/methods: We included all patients admitted in our hospital as PCC between the 25th of January and the 13th of February. We collected epidemiological, clinical and microbiological data and performed a retrospective cohort study. Lower respiratory infections (LRI) were defined by the presence of cough and fever. Incubation period was defined as the time between exposure, if dated, and the onset of symptoms or as the time between the end of the at-risk trip and the onset of symptoms if the patient had traveled. All the PCC had 2 nose-throat swabs, one for COVID research (RT-PCR) and another one for differential diagnosis research (Multiplex RT-PCR).

Results: Seventy-one patients, 31 men and 40 women, aged from 11 to 69 years (median age 33), were included. Five patients were immunocompromised, 6 had pre-existing lung disease, and 2 were obese. Thirty-eight patients had traveled in China within 3 weeks, and 15 had traveled to another country. Nine patients were in contact with a confirmed case of COVID-19 and 14 with a symptomatic Chinese. The median incubation was 7 days. Most frequent symptoms were cough (54), fever (28), arthromyalgia (22), headaches (22), runny nose and/or sore throat symptoms (19) and diarrhea (5). Twenty-two patients had LRI. Five patients were asymptomatic. One patient was confirmed with COVID-19, other infections were found in 37 cases (11 rhinovirus or enterovirus, 8 influenza A, 6 influenza B, coronaviruses, 2 HRSV, 1 Mycoplasma pneumoniae).

Conclusions: Thirty-eight patient (54%) admitted as a PCC traveled to China, 66 patients had symptoms (93%) including 22 LRI. One case of COVID-19 was confirmed, other infections were found in 37 patients (52%).

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European survey of Helicobacter pylori primary resistance to antibiotics: Evolution over the last 20 years

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Background: Antibiotic resistance of H. pylori is the main cause of failure of most current eradication regimens. As antimicrobial susceptibility testing [AST] is not always performed, it is important to have surveys to infer the treatments which can be used. For this purpose, European surveys were performed in 1998, 2008 and we report here the results of 2018.

Materials/methods: Centres were recruited on a voluntary basis, one for each small country and several for larger countries. The protocol was to include 50 adult patients who had not received previous eradication treatment. Information collected included demographic, clinical, and endoscopic results as well as AST results (clarithromycin, levofloxacin, metronidazole, amoxicillin, tetracycline, rifampicin) performed by Etest or disk diffusion according to a standardised procedure. Control strains were provided. A 10% random sample was sent from each centre to the coordinating centre. The Amplidiag® H. pylori+ClariR kit (Mobidiag) was used for clarithromycin testing and AST for the other antibiotics. A univariate and multivariate analysis were also carried out to define the risk factors of antibiotic resistance.

Results: The crude data show 1,234 H. pylori positive patients included in 24 centres from 18 countries. H. pylori resistance was present in 21.3% for clarithromycin, 16.0% for levofloxacin, 39.1% for metronidazole, 0.4% for amoxicillin, 2% for rifampicin compounds and none for tetracycline. The random selection of 142 strains showed an excellent concordance of results (>95%). The main discrepancies were linked to the presence of double populations not detected by Etest. In the multivariate analysis, the risk factors for resistance were essentially linked to the region of birth: Southern Europe for clarithromycin (OR: 3.7, 95% CI [1.4-9.5]) and outside Europe for metronidazole (OR: 2.7, 95% CI [1.2-6.2]).

Conclusions: These results indicate a global and continuous rise in H. pylori primary resistance to clarithromycin but lower than in the previous decade (9.9% in 1998, 17.5% in 2008, and 21.3% in 2018), a slight increase to levofloxacin, and a more important increase for metronidazole (from 33.1 to 39.5% since 2008). The risk factors for resistance were similar to those found 10 years ago.

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Using evidence-based infographics to increase parents’ understanding about antibiotic use and antibiotic resistance: a proof-of-concept study

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Background: Public misconceptions about antibiotic use persist despite the efforts of antibiotic awareness campaigns. These campaigns have often followed a top-down approach and have not sought input from the public. Communities need to see antibiotic campaign messages as relevant, accessible and important in order to have an influence on health-seeking behaviour and antibiotic use. We aimed to develop a series of evidenced-based infographics (EBIs) on antibiotic use for common infections in children and to evaluate their effectiveness at increasing parents’ understanding of antibiotic use and antibiotic resistance.

Materials/methods: There were three phases to this research. In phase 1 we set out to identify and summarise scientific evidence for the use of antibiotics for three common infections in children (sore throat, acute cough and otitis media). Phase 2 focussed on co-design of a series of prototype EBIs for each infection in focus groups with parents of young children and graphic designers, to test the face- and content validity. Phase 3 is testing the feasibility of EBIs in increasing parents’ understanding about antibiotic use and the perceived relevance of antibiotic resistance in an online survey.

Results: Parents mostly found the evidence displayed in the infographics novel and relevant to their families. However, for some parents, the presented evidence was either too medically-focussed where the outcome was not relevant to parents or not of immediate concern to parents. The manner in which the information was displayed influenced their understanding e.g. difficulty interpreting graphs. Superfluous components of the infographic were often questioned. Parents preferred one health message per visual using accurate and consistent terminology to avoid misinterpretation.

Conclusions: We have co-developed a series of EBIs with parents and professional graphic designers and identified how parents interpret EBIs on antibiotic use and antibiotic resistance. Phase 3 will evaluate whether EBIs can increase parents’ understanding about antibiotic use. If shown to be beneficial, this will inform novel approaches to improving antibiotic stewardship initiatives in the community.

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